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Imine as a Linchpin Approach for Distal C(sp2)–H Functionalization

Sukdev Bag, Sadhan Jana, Sukumar Pradhan, Suman Bhowmick, Nupur Goswami, Soumya Kumar Sinha, Debabrata Maiti

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Despite the widespread applications of C–H functionalization, controlling site selectivity remains a significant challenge. Covalently attached directing group (DG) served as an ancillary ligand to ensure proximal ortho-, distal meta- and para-C-H functionalization over the last two decades. These covalently linked DGs necessitate two extra steps for a single C–H functionalization: introduction of DG prior to C–H activation and removal of DG post-functionalization. We introduce here a transient directing group for distal C(sp^2)-H functionalization via reversible imine formation. By overruling facile proximal C-H bond activation by imine-N atom, a suitably designed pyrimidine-based transient directing group (TDG) successfully delivered selective distal C-C bond formation. Application of this transient directing group strategy for streamlining the synthesis of complex organic molecules without any necessary pre-functionalization at the distal position has been explored.

File list (2)

Imine as a linchpin approach for distal C(sp^2)–H functionalization

Sukdev Bag[1,2], Sadhan Jana[1,2], Sukumar Pradhan[1,2], Suman Bhowmick[1], Nupur Goswami[1], Soumya Kumar Sinha[1] & Debabrata Maiti[1*]

Despite the widespread applications of C–H functionalization, controlling site selectivity remains a significant challenge. Covalently attached directing group (DG) served as an ancillary ligand to ensure proximal *ortho*-[1], distal *meta*-[2-8] and *para*-C–H functionalization[8-9] over the last two decades. These covalently linked DGs necessitate two extra steps for a single C–H functionalization: introduction of DG prior to C–H activation and removal of DG post-functionalization. We introduce here a transient directing group for distal C(sp^2)–H functionalization *via* reversible imine formation[10-12]. By overruling facile proximal C–H bond activation by imine-*N* atom, a suitably designed pyrimidine-based transient directing group (TDG) successfully delivered selective distal C–C bond formation. Application of this transient directing group strategy for streamlining the synthesis of complex organic molecules without any necessary pre-functionalization at the distal position has been explored.

Evident from several paradigms of chemical transformations observed in nature, selective and efficient reactions relied either on inherent electronic nature of a molecule or through direct interaction with a metal center[13-17]. Discovery of proximity-driven C–H functionalization reactions by omitting the requirement of prefunctionalization has drawn significant attention in recent years[18-19]. Innate and directing group (DG) assisted strategies have been developed for selective C–H functionalization and greatly applied in late-stage diversification of natural products and pharmaceuticals[20]. Template-directed approach successfully promoted *meta*- and *para*-C–H bond functionalization of arene substrates[2-9]. To achieve exclusive distal C–H bond functionalization, various well-designed template-based assembly has been discovered by adopting distance and geometry correlation (Fig. 1a). However, additional steps for installation and removal of covalently attached directing group indicate substantial limitation. In addition, a high molecular weight scaffold comprising of significant number of chemically equivalent C–H bonds is prone to deliver less selective functional group incorporation. Alternative approach by overruling the extra-steps associated with covalently linked template-based assembly is highly desirable. We envision development of a temporary DG, which can be designed to bind substrate reversibly and can also accommodate a metal center *via* strong coordination (Fig. 1b).

An interesting substrate-cum-template-design can evolve around reversible imine formation with aldehyde or amine substrates, which are ubiquitous and inexpensive reagent. While proximal C(sp^2)–H functionalization with the aid of transient directing group (**TDG**) approach has been well appreciated in the community (Fig. 1b), the remote C(sp^2)–H functionalization *via in situ* imine formation remains yet an undiscovered domain[21-25]. The reason behind this unsolved problem is the selectivity issue arising from imine-*N* atom, which is prone to deliver the undesired *ortho*-C–H functionalization *via* stable 5-membered *endo*- or *exo*-carbometallation (Fig. 1c)[26-27]. Undermining the thermodynamically stable intermediate and favoring large metallacycle transition state (TS), an important factor is the formation of a suitable template-assembly, which will disfavor the proximal carbometallation with imine-*N* atom (Fig. 1c).

Phenyl ring on both side of imine linchpin was anticipated to be the productive combination in terms of rigid geometry and sufficient stability in reaction medium to deliver the desired remote C–H functionalization. In this regard, adopting distance and geometry correlation, biphenyl aldehyde was

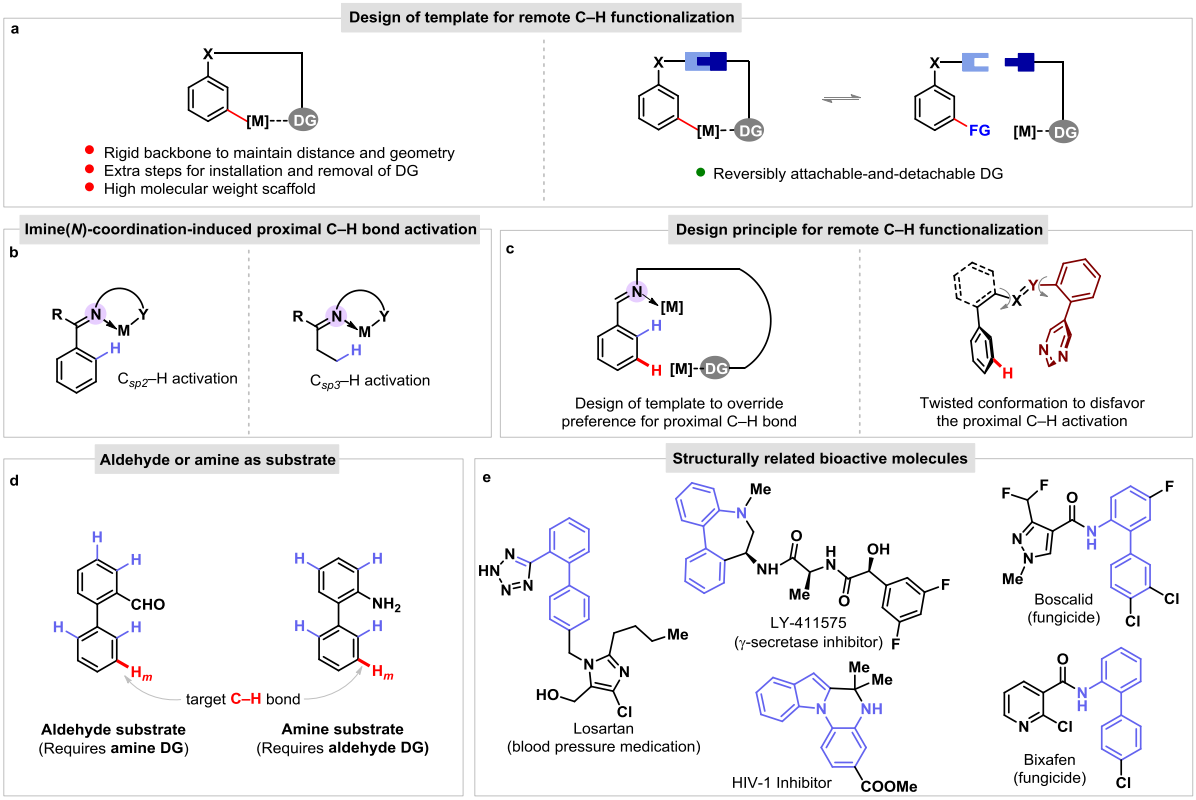

Figure 1 | **Transient directing group (TDG) assisted remote C–H functionalization. a**, Covalent template directed remote C–H functionalization *vs* TDG; X, Linker; M, Metal; DG, Directing Group; FG, Functional Group. **b**, TDG-assisted proximal C(sp^2)–H and C(sp^3)–H functionalization. **c**, Challenges associated with the TDG promoted distal C–H functionalization. **d**, Substrate design for remote C–H functionalization *via* imine formation. The red bonds in all figures highlight target C–H bond of interest.

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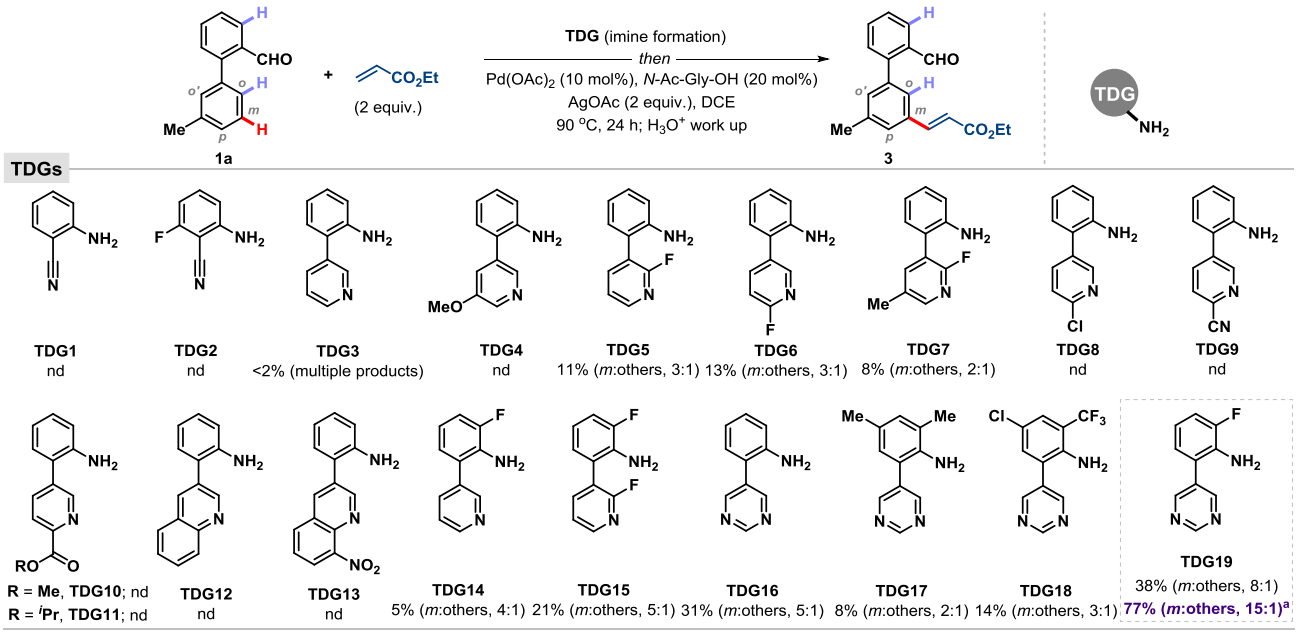

Figure 2 | **Template evaluation for distal C–H functionalization of biphenyl aldehyde**. Imine formation: 1a (0.2 mmol) and TDG (0.2 mmol) in ^{i}PrOH (2 mL) at 80 °C for 2 h; Olefination: $Pd(OAc)_2$ (10 mol%), *N*-Ac-Gly-OH (20 mol%), AgOAc (2 equiv.) and ethyl acrylate (2 equiv.) in 1,2-dichloroethane (DCE, 2 mL) at 90 °C for 24 h. [a]Imine formation: 1a (0.2 mmol) and TDG19 (0.19 mmol) in ^{i}PrOH (2 mL) at 80 °C for 2 h; Olefination: $Pd(OAc)_2$ (10 mol%), *N*-Form-Gly-OH (20 mol%), Ag_2CO_3 (25 mol%), $Cu(OAc)_2$ (3.5 equiv.) and ethyl acrylate (3 equiv.) in DCE (2 mL) at 90 °C for 24 h. Ratios of *meta*:others were shown in parenthesis and ratios were determined based on ^{1}H-NMR analysis of the crude reaction mixture; nd, not detected.

investigated as a substrate in substrate-cum-template-design cognition. We have investigated biphenyl aldehyde with 2-amino benzonitrile as the TDG (**TDG1** and **TDG2**) using palladium (II) acetate as catalyst and mono-protected amino acid (MPAA) *N*-Ac-Gly-OH as ligand (Fig. 2) (see Supplementary Information). These experiments resulted in either no product formation or trace amount of product with very poor selectivity perhaps due to the deactivation of palladium catalyst or formation of bidentate chelate with imine-*N* and π-bond of nitrile in 'side-on' fashion. In addition, competitive coordination from imine and nitrile can be detrimental as both have equivalent coordinating ability leading to the multiple product formation. To overcome these issues, we decided to synthesize heterocycle-based 2-(pyridin-3-yl)aniline transient directing groups. A macrocyclic TS with imine adduct having two biphenyls at two end of imine linchpin and palladium may promote a twisted conformation resulting in an unfavorable coordination mode with imine-*N* and can undermine the formation of *ortho*-selective products. Pyridine-based biphenyl templates (**TDG3** and **TDG4**) have either provided trace amount of olefination product or was found completely inactive. After further modification of TDGs, it was found that electron-deficient fluoro-substituted pyridine-based templates (**TDG5**-**TDG7**) could be significantly better than electron-rich pyridine-based ligand and delivered the desired olefination product at distal *meta*-position. Other variation of electron-deficient substitutions on pyridine ring such as chloro (**TDG8**) and nitrile (**TDG9**) did not provide any olefinated product. We anticipated that bidentate coordination with palladium may serve as an active catalyst pocket and free amine on another phenyl ring of biphenyl template (**TDG10** and **TDG11**) can act as a reversible binding site to deliver the desired product by confining the catalyst. However, none of the bidentate ligands provided expected olefination product probably due to the formation of unreactive palladium complex. Quinoline-based templates (**TDG12** and **TDG13**) were unsuccessful to deliver the desired product. Further fine-tuning of TDG showed that *ortho*-substitution with fluorine atom with respect to amine (**TDG14** and **TDG15**) can deliver the desired product in better yield and selectivity compared to the unsubstituted TDGs (**TDG3** and **TDG5**). Subsequently, we thought to focus on more electron-deficient monodentate ligand. Encouragingly, pyrimidine-based ligand (**TDG16**) provided promising yield in 5:1 *meta*-selectivity[28-30]. In contrast, *ortho*-methyl (**TDG17**) and trifluoromethyl substitution (**TDG18**) with respect to amine on pyrimidine-based templates resulted in poor yield (8% and 14%) and selectivity (*m*:others; 2:1 & 3:1). Such an observation suggests proper conformation of macrocyclic TS is the key factor for distal C–H functionalization that might be disturbed by steric hindrance arising from *ortho* substitutions. Finally, pyrimidine-based ligand with *ortho*- fluorine substitution (**TDG19**) provided promising result in terms of yield (38%) and selectivity (*m*:others; 8:1).

With the optimal directing group **TDG19**, we have tested several parameters to achieve synthetically useful yield and *meta*-selectivity. The use of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) as a solvent led to decomposition of imine and subsequently 1,2-dichloroethane (DCE) provided a superior result. Different proportionate mixture of DCE and HFIP failed to deliver the desired product. We tested several MPAA ancillary ligands and *N*-Form-Gly-OH is found to be most suitable (see Supplementary Information). Catalytic amount of silver(I) carbonate in conjunction with copper(II) acetate as an oxidant delivered 77% yield and 15:1 *meta*-selectivity.

Using the optimized conditions and **TDG19** as a transient directing group, we then tested C–C bond formation scope with differently substituted 2-phenylbenzaldehyde and alkenes (Fig. 3). Electron-neutral, electron-donating and electron-withdrawing substituents such as chloro, fluoro, carboxylate-containing substrates were all tolerated and provided the *meta*-selective products. Although biphenyl aldehyde with carboxylate unit (**11**) is prone to deliver multiple products, the current protocol provided *meta*-selective C–C bond formation. Sterically encumbered *para*-substituted methyl and chloro-containing arenes (**12**-**14**) delivered the desired product with excellent *meta*-selectivity. Interestingly, substrates bearing sterically demanding *di*-methyl substitutions (**16**-**20**) also provided *meta*-selective olefination by overriding the steric bias. Notably, electron-rich heterocycle-containing arenes (**21**-**24**) delivered mono-olefination in synthetically useful yield and *meta*-selectivity. Versatile biphenyl derivatives (**25**-**33**) were also found to be competent coupling partners with different alkenes. 1-Phenyl 2-naphthaldehyde (**34**) provided site selective olefination undermining any other possibilities. Notably, thiofuran (**35**-**37**) containing biphenyls were selectively alkenylated at C2 position.

After establishing a significant scope with biphenyl aldehydes and naphthaldehyde, we aimed to incorporate a variety of alkene coupling partners (Fig. 3). These included both short chain and long-chain olefins (**38**-**42**), β-substituted (**43** and **44**) and α,β-dicarboxylates (**45**), which consistently gave C–C bond formation products. Other important class of activated olefins such as vinyl ketone (**46** and **47**) and acrylonitrile (**48**) were utilized successfully in this reaction. Natural products and bioactive molecules appended acrylates that include testosterone (**49**), ergosterol (**50**), fenchyl alcohol (**51**) and oleyl alcohol (**52**) displayed useful coupling efficiencies under this protocol. Acrylate containing perfluoroalkene chain (**53**) were also coupled with 2-phenylbenzaldehyde exclusively at *meta* position. Notably, unactivated alkene such as allyl acetate (**54**) provided alkenylation product over facile formation of allylation product.

We next turned our attention to 2-phenylaniline substrates (Fig. 4) utilizing aldehyde group on pyrimidine-based TDG (**TDG20**). While electron-donating amine group is *ortho*- and *para*- directing, overruling the electronic bias and reaching to the *meta*-C–H bond of other phenyl ring is a significant challenge. Although, 2-phenylaniline gave distal olefination product under the present optimal reaction conditions, we experienced several difficulties such as formation of less selective olefinated product and mostly, generation of C–N coupled cyclized product (see Supplementary Information). After systematic investigations, it was found that copper (II) acetate was responsible for facile formation of C–N coupled side product. Accordingly, exclusion of copper (II) acetate and use of silver (I) carbonate provided

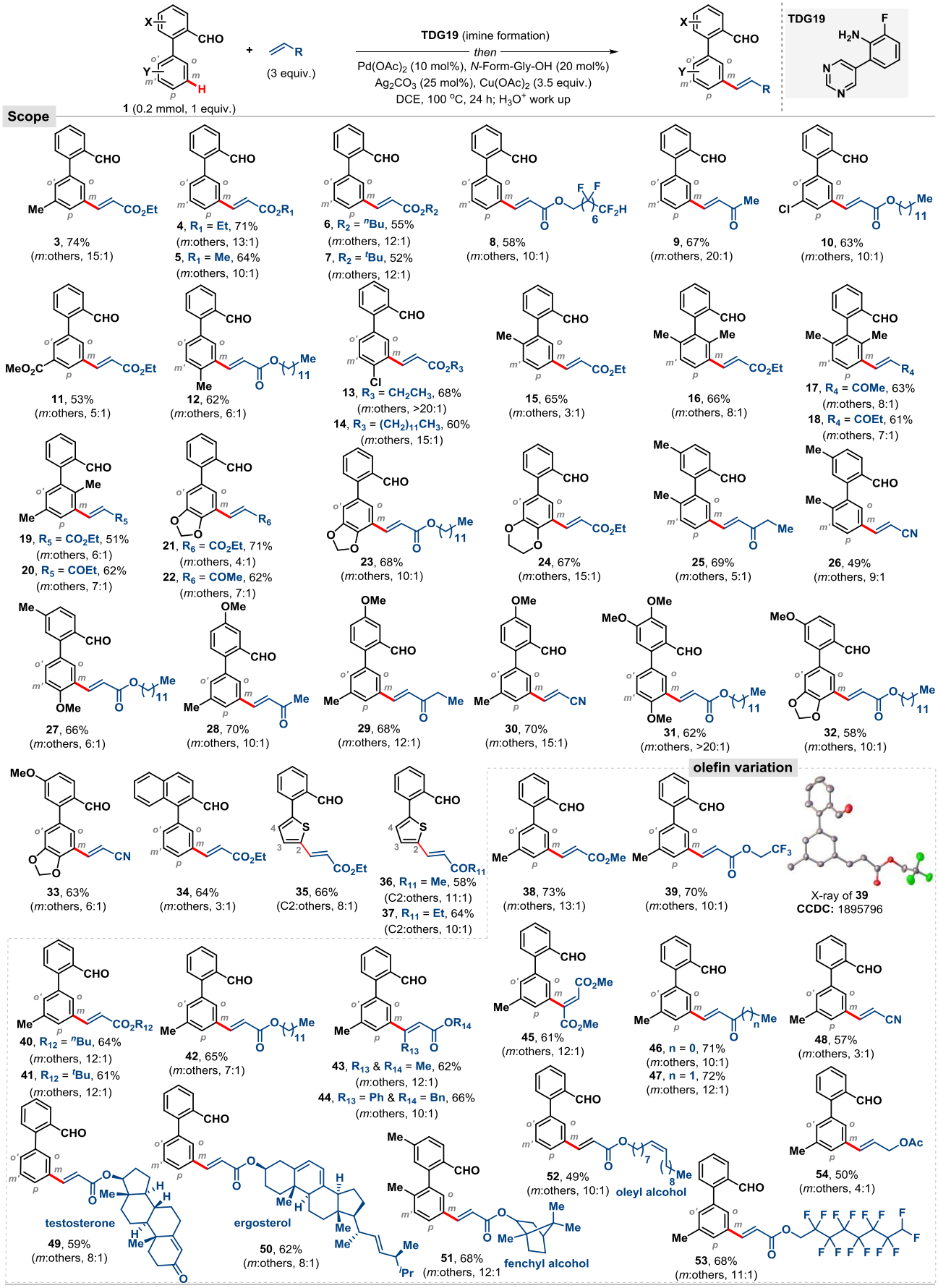

Figure 3 | Biphenyl aldehyde substrates for selective distal C–H functionalization. Scope with various alkenes are shown in dotted box. The isolated yields are reported and ratios of *meta*:others are shown in parenthesis.

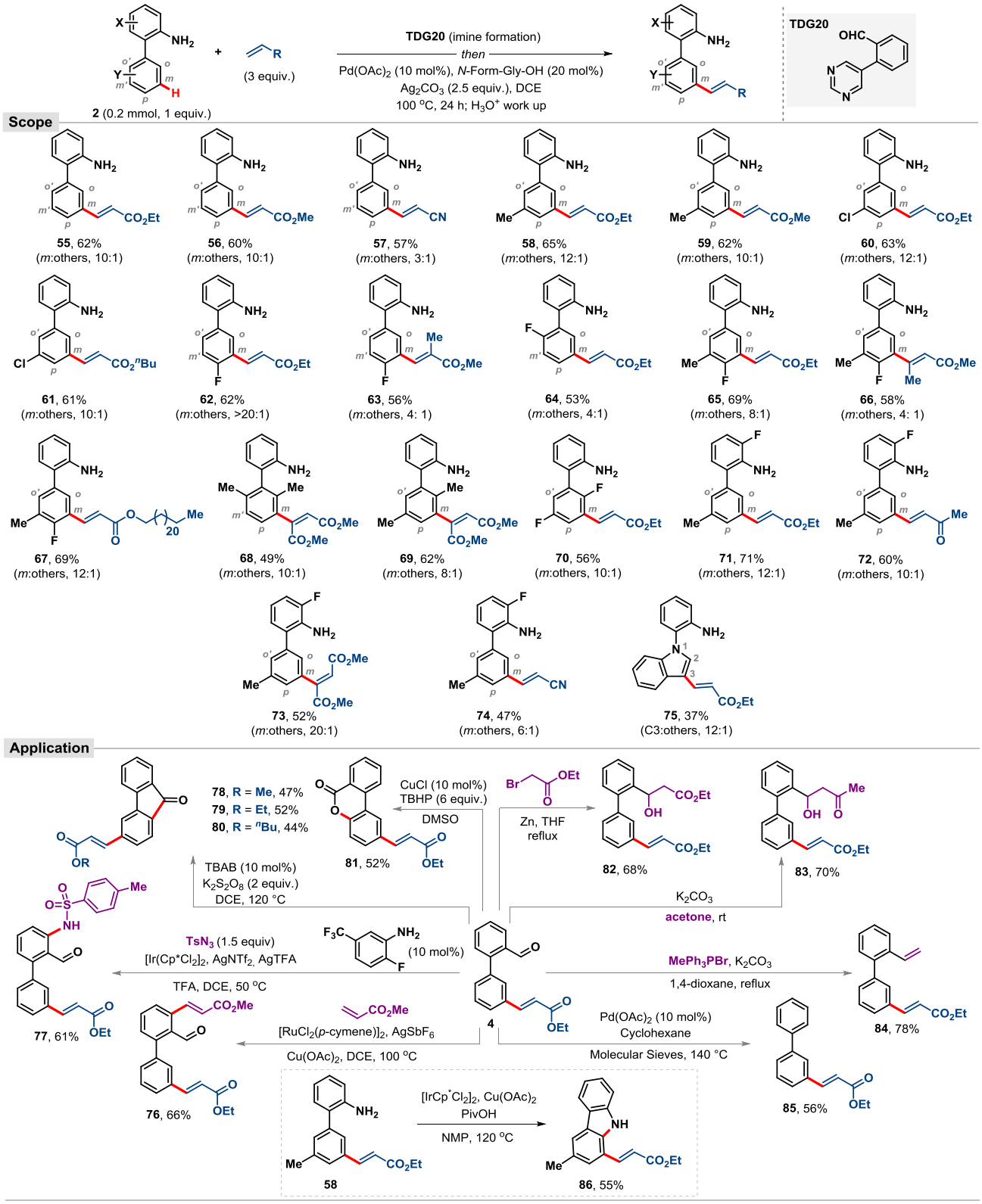

Figure 4 | Biphenyl amine substrates for selective distal C–H functionalization and post-synthetic applications of obtained *meta*-olefinated 2-phenylbenzaldehyde. Synthesis of carbazole from obtained *meta*-olefinated 2-phenylaniline is shown in dotted box. The yields are isolated and ratios of *meta*:others are shown in parenthesis.

excellent *meta*-selective olefination product (**55**; *m*:others, 10:1). With this modified reaction conditions, electron-rich and electron-deficient biphenylamine were evaluated and the desired olefination products were obtained with significant *meta*-selectivity. Interestingly, template geometry overrode the steric experience from di-substituted arene (**68**-**70**) and delivered preparatively useful yield of *meta*-selective olefination product. Both arene substituted biphenylamine was coupled with different alkene partners such as ethyl acrylate (**71**), methyl vinyl ketone (**72**), dimethyl fumarate (**73**) and acrylonitrile (**74**). Indole was functionalized selectively at C3 position with the aid of *N*-substituted 2-arylamine as a linchpin arene (**75**).

In addition to the distal C–H functionalization as the stepping stone for mono selective C–C bond formation, proximal transformation can also be promoted efficiently (**76** and **77,** see Supplementary Information). The *meta*-olefinated products of 2-phenyl benzaldehyde were expediently elaborated into corresponding fluorenone (**78**-**80**) and benzo[*c*]chromenone (**81**) *via*

oxidative cyclization. Furthermore, aldehyde group was converted to β-tertiary alcohols of ester (**82**) and carbonyl (**83**); and olefin (**90**). Decarbonylation can be promoted to obtain unsubstituted 3-phenyl cinnamate (**85**). *Meta*-olefinated 2-phenylaniline was successfully converted into cyclized carbazole moiety (**86**) present in numerous natural products.

In summary, we have developed a transient directing group approach to obtain selective distal C–H functionalization on synthetically important aldehyde and amine. Template design facilitated the formation of macrocyclic transition state to enable proximity-induced reactivity and selectivity. An array of substrate variation irrespective of electronic and steric demands on both aldehyde and amine were explored. The capability of this transformation to install complex molecules at the remote position and post-synthetic manipulation of prevalent aromatic aldehyde and amine groups render this strategy amenable towards practical applications.

Received (to be inserted automatically)

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METHODS SUMMARY

Transient directing group approach for *meta*-C–H olefination

An oven-dried screw capped reaction tube with a magnetic stir-bar was charged with 2-phenylbenzaldehyde (0.2 mmol) (viscous biphenyl aldehyde was weighed first), and **TDG19** (0.19 mmol, 36 mg) under air, followed by isopropyl alcohol (2 mL). The reaction mixture was stirred at 80 °C for 2 hours. Next, solvent was concentrated in vacuo and the residue was washed with pentane. The dry crude residue was subjected to $Pd(OAc)_2$ (10 mol%, 0.02 mmol, 4.5 mg), *N*-formyl glycine (*N*-Form-Gly-OH; 20 mol%, 8.3 mg), Ag_2CO_3 (25 mol%, 0.05 mmol, 14 mg) and $Cu(OAc)_2$ (3.5 equiv., 0.7 mmol, 127 mg) in the same reaction tube. Solvent 1,2-dichloroethane (DCE, 2 mL) was added in the reaction tube followed by addition of liquid alkene (3 equiv., 0.6 mmol) by micropipette under air (solid alkenes were weighed before adding solvent). The reaction tube was screwed by a cap fitted with a rubber septum and was vigorously stirred in a preheated oil bath at 100 °C. The reaction mixture was taken out after 24 h, diluted with 10 mL ethyl acetate and filtered through a celite pad. Next, the filtrate mixture was treated with 1 (M) HCl solution and stirred for ten minutes. Organic layer was separated and concentrated under vacuum. The crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

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Author contributions

S.B., S.J. and S. P. contributed equally to this work. S.B., S.J., S.P., N.G., S. Bhowmick, S.K.S. performed the reactions and analyzed the products. S.B. and D.M. conceived the concept. S.B. and D.M. designed the template and substrates. S.B., S.J. and D.M. wrote the manuscript.

Competing interests The authors declare the following competing financial interest(s): A patent application is filed based on the work described in this manuscript.

Additional information

Supplementary Information is linked to the online version of the paper at www.nature.com/nature

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Imine as a linchpin approach for distal C(sp^2)–H functionalizations

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Table of Contents

1. General considerations

Reagent information: Unless otherwise stated, all reactions were carried out under air atmosphere in screw cap reaction tubes. **TDG1** and **TDG2** are commercially available and purchased from Sigma Aldrich. Palladium (II) acetate was purchased from Alfa-Aesar. All the solvents were bought from Merck, TCI and Spectrochem insure sealed bottle and were used as received. Benzyldehydes, aniline derivatives, heterocycles, boronic acids, activated olefins and other reagents were bought from Sigma Aldrich, Alfa-Aesar, TCI and Spectrochem. For column chromatography, silica gel (100–200 mesh) from SRL Co. and neutral alumina from Merck was used. A gradient elution using petroleum-ether and ethyl acetate was performed, based on Merck aluminium TLC sheets (silica gel $60F_{254}$).

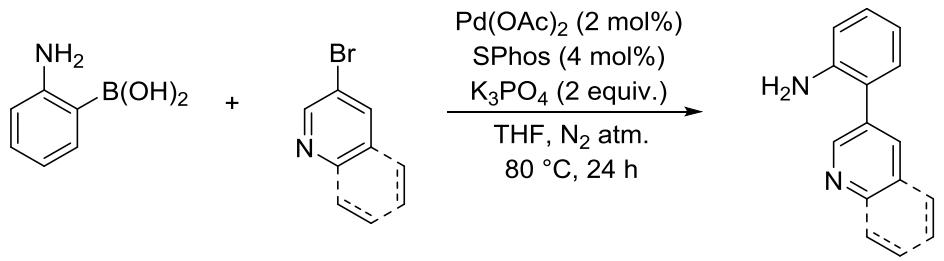
Analytical Information: All isolated compounds were characterized by ^{1}H NMR, ^{13}C NMR spectroscopy, gas chromatography (GC), high resolution mass spectrometry (HRMS), infrared spectroscopy (IR), etc. Copies of the ^{1}H NMR, ^{13}C NMR can be found in the Supporting Information. Unless otherwise stated, all Nuclear Magnetic Resonance spectra were recorded on a Bruker 400 MHz and 500 MHz instrument. Chemical shifts were quoted in parts per million (ppm) referenced to 0.0 ppm for TMS. All ^{1}H NMR experiments were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C NMR spectra were reported in ppm relative to deuterochloroform (77.23 ppm), unless otherwise stated, and all were obtained with ^{1}H decoupling. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, J, were reported in Hertz unit (Hz). NMR of the crude reaction mixtures were performed by using 1,3,5-trimethoxybenzene as the internal standard. All GCMS analysis was done by Agilent 7890A GC system connected with 5975C inert XL EI/CI MSD (with triple axis detector). High-resolution mass spectra (HRMS) were recorded on a Q-TOF micromass (YA-105) mass spectrometer and a Bruker Maxis Impact (282001.00081) in ESI mode. X-ray crystallography was recorded at Department of Chemistry, IIT Bombay.

Description of Reaction Tube:

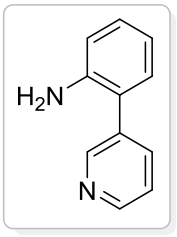
Pictorial description of reaction tube for *meta*-olefination: Fisherbrand Disposable Borosilicate Glass Tubes (16*125mm) with Threaded End (Fisher Scientific Order No. 1495935A) [left]; Kimble Black Phenolic Screw Thread Closures with Open Tops (Fisher Scientific Order No. 033407E);Thermo Scientific National PTFE/Silicone Septa for Sample Screw Thread Caps (Fisher Scientific Order No. 03394A).

2. Experimental section

2.1 General procedure A: Synthesis of amine-based transient directing groups (TDGs)

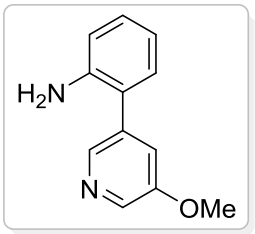


2-(pyridin-3-yl)aniline/2-(quinoline-3-yl)aniline/2-(pyrimidin-5-yl)aniline derivatives were prepared by the Suzuki cross-coupling reaction condition. A clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with 3-bromopyridine/3-bromoquinoline/5-bromopyrimidine (1 equiv., 4.0 mmol), 2-aminophenyl boronic acid (1.25 equiv., 5.0 mmol), palladium (II) acetate (2 mol%, 0.08 mmol, 18 mg), SPhos (4 mol%, 0.16 mmol, 66 mg) and K_3PO_4 (2 equiv., 8.0 mmol, 1700 mg). The cap was fitted with a rubber septum and the reaction tube was evacuated and back filled with nitrogen and this sequence was repeated three additional times. Under the positive flow of nitrogen 10 mL THF was added to the reaction mixture. The reaction mixture was vigorously stirred at 80 °C temperature for 24 h. Next, the reaction was allowed to cool at room temperature and dried using rotary evaporator. The reaction mixture was extracted thrice with ethyl acetate (3x20 mL) and brine solution (3x10 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude mixture was purified by column chromatography using silica gel and petroleum-ether/ethyl acetate as the eluent.

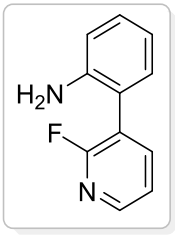


2-(pyridin-3-yl)aniline **:** Compound **TDG3** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (80/20, v/v).
Physical State: colorless oil.
Yield: 90% (613 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.66 (d, *J* = 2.2 Hz, 1H), 8.52 (dd, *J* = 4.8, 1.1 Hz, 1H), 7.75 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.30 (dd, *J* = 7.8, 4.9 Hz, 1H), 7.14 (td, *J* = 8.4, 1.2 Hz, 1H), 7.05 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.80 (t, *J* = 8.4 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 3.72 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 149.97, 148.28, 143.97, 136.61, 135.37, 130.56, 129.39, 123.60, 118.80, 115.91.
IR (thin film, cm^{-1}): 1028, 1127, 1158, 1191, 1257, 1299, 1339, 1362, 1411, 1450, 1497, 1577, 1618, 2854, 2927, 3029, 3060, 3206, 3330, 3446.

HRMS (*m/z*): [M+H$^+$] calcd for $C_{11}H_{11}N_2$: 171.0917; found, 171.0918.
TLC: R_f = 0.6 (70:30 petroleum ether:EtOAc).

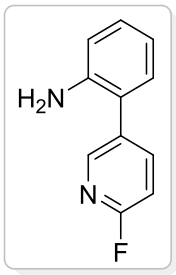


***2-(5-methoxypyridin-3-yl)aniline*:** Compound **TDG4** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (75/25, v/v).
Physical State: brown solid.
Yield: 89% (997 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.27 (d, *J* = 10.2 Hz, 1H), 7.31 (s, 1H), 7.21 – 7.14 (m, 1H), 7.10 (dd, *J* = 11.8, 7.6 Hz, 1H), 6.86 – 6.73 (m, 1H), 3.87 (dd, *J* = 11.6, 5.0 Hz, 2H), 3.77 – 3.61 (m, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 155.90, 144.04, 142.25, 136.41, 136.09, 130.68, 129.60, 123.59, 121.27, 118.98, 116.09, 55.82.
IR (thin film, cm^{-1}): 1110, 1398, 1484, 1552, 1578, 1734, 2855, 2924, 3347.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{12}H_{12}NaN_2O$: 223.0841; found, 223.0844.
TLC: R_f = 0.25 (70:30 petroleum ether:EtOAc).

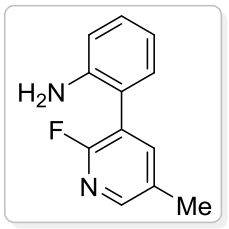


***2-(2-fluoropyridin-3-yl)aniline*:** Compound **TDG5** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (80/20, v/v).
Physical State: yellow oil.
Yield: 90% (677 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.24 (d, *J* = 4.5 Hz, 1H), 7.84 (t, *J* = 8.4 Hz, 1H), 7.29 (t, *J* = 6.1 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 6.86 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 3.66 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 147.21, 147.09, 144.27, 142.81, 142.77, 131.17, 130.05, 122.04, 122.00, 119.01, 116.36.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -74.21.
IR (thin film, cm^{-1}): 1002, 1045, 1116, 1159, 1202, 1244, 1308, 1374, 1422, 1457, 1500, 1567, 1599, 1622, 1732, 2928, 3234, 3368, 3462.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{11}H_{10}FN_2$: 189.0779; found: 189.0777.

TLC: R_f = 0.25 (70:30 petroleum ether:EtOAc).

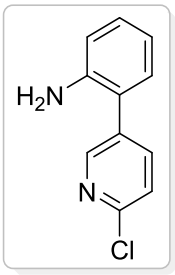


***2-(6-fluoropyridin-3-yl)aniline*:** Compound **TDG6** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (80:20, v/v).
Physical State: yellow oil.
Yield: 95% (715 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.31 (s, 1H), 7.91 (td, *J* = 8.1, 2.3 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.5 Hz, 1H), 7.02 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 3.68 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 148.04, 147.92, 143.96, 142.16, 142.10, 130.78, 129.75, 119.24, 116.17, 109.89, 109.59.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -68.45.
IR (thin film, cm^{-1}): 1000, 1040, 1110, 1155, 1200, 1237, 1301, 1364, 1412, 1442, 1527, 1568, 1570, 1601, 1711, 2920, 3219, 3328, 3451.
HRMS (ESI): [M+H$^+$] calcd for $C_{11}H_{10}FN_2$: 189.0779; found, 189.0778.
TLC: R_f = 0.4 (70:30petroleum ether:EtOAc).

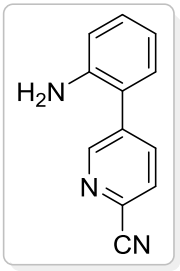


***2-(2-fluoro-5-methylpyridin-3-yl)aniline*:** Compound **TDG7** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (80/20, v/v).
Physical State: brown oil.
Yield: 79% (369 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.04 (s, 1H), 7.65 (dd, *J* = 9.1, 2.1 Hz, 1H), 7.26 – 7.21 (m, 1H), 7.11 (d, *J* = 7.4 Hz, 1H), 6.86 (t, *J* = 7.8, Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 3.71 (s, 2H), 2.38 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 159.12 (d, *J* = 237.0 Hz), 146.51 (d, *J* = 14.1 Hz), 144.11, 143.17 (d, *J* = 4.6 Hz), 131.39 (d, *J* = 4.8 Hz), 130.94, 129.74, 120.66 (d, *J* = 32.2 Hz), 119.72 (d, *J* = 4.1 Hz), 118.77, 116.13, 17.42.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -74.21.

IR (thin film, cm^{-1}): 1049, 1159, 1203, 1242, 1303, 1431, 1498, 1578, 1620, 2855, 2926, 3030, 3232, 3361, 3464.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{12}H_{11}FN_2$: 203.0976; found, 203.0979.
TLC: R_f = 0.7 (70:30 petroleum ether:EtOAc).

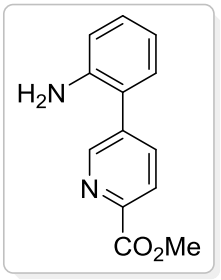


***2-(6-chloropyridin-3-yl)aniline*:** Compound **TDG8** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (80/20, v/v).
Physical State: Brown Solid.
Yield: 55% (450 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.50 (d, *J* = 2.3 Hz, 1H), 7.81 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.23 (td, *J* = 8.0, 1.4 Hz, 1H), 7.10 (dd, *J* = 7.6, 1.3 Hz, 1H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 3.73 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 150.17, 149.90, 143.75, 139.43, 134.20, 130.47, 129.74, 124.29, 122.33, 119.10, 116.09.
IR (thin film, cm^{-1}): 999, 1106, 1139, 1216, 1300, 1360, 1457, 1496, 1552, 1583, 1620, 2924, 3028, 3224, 3348, 3453.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{11}H_{10}ClN_2$: 207.0497; found, 207.0527.
TLC: R_f = 0.5 (70:30 petroleum ether:EtOAc).

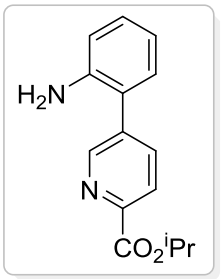


5-(2-aminophenyl)picolinonitrile: Compound **TDG9** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (70/30, v/v).
Physical State: brown solid.
Yield: 72% (562 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.87 (s, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.25 (m, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 3.88 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 151.49, 143.74, 139.20, 137.27, 131.92, 130.50, 130.45, 128.47, 121.76, 119.40, 117.32, 116.53.
IR (thin film, cm^{-1}): 1000, 1030, 1160, 1201, 1304, 1364, 1467, 1497, 1576, 1623, 2234, 2853, 2925, 3058, 3231, 3367, 3444.
HRMS (ESI): [M+H$^+$] calcd for $C_{12}H_{10}N_3$: 196.0796; found, 196.0808.
TLC: R_f = 0.3 (65:35 petroleum ether:EtOAc).

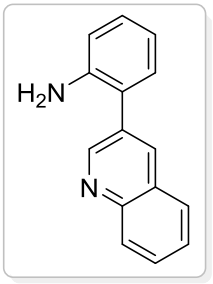


***Methyl-5-(2-aminophenyl)picolinate*:** Compound **TDG10** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (70/30, v/v).
Physical State: yellow solid.
Yield: 82% (749 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.87 (d, *J* = 1.5 Hz, 1H), 8.21 (d, *J* = 8.0 Hz, 1H), 7.99 (dd, *J* = 8.0, 2.1 Hz, 1H), 7.23 (td, *J* = 7.6 Hz, 1H), 7.13 (dd, *J* = 7.6, 1.2 Hz, 1H), 6.88 (t, *J* = 7.9 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 4.04 (s, 3H), 3.77 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 165.58, 150.11, 146.33, 143.75, 138.92, 137.35, 130.50, 130.04, 125.14, 122.51, 119.16, 116.21, 52.95.
IR (thin film, cm^{-1}): 1002, 1031, 1135, 1195, 1235, 1311, 1371, 1436, 1498, 1626, 1723, 2851, 2951, 3029, 3229, 3361, 3443.
HRMS (ESI): [M+H$^+$] calcd for $C_{13}H_{13}N_2O_2$: 229.0972; found, 229.0965.
TLC: R_f = 0.45 (60:40 petroleum ether:EtOAc).

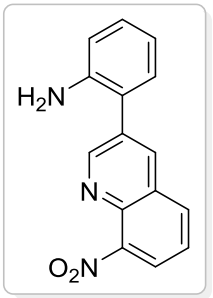


***Isopropyl 5-(2-aminophenyl)picolinate*:** Compound **TDG11** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (70/30, v/v).
Physical State: yellow oil.
Yield: 86% (882 mg isolated).

^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.87 (s, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.95 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 1H), 6.86 (t, *J* = 7.4 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 5.36 (dt, *J* = 12.5, 6.2 Hz, 1H), 3.75 (s, 2H), 1.43 (d, *J* = 6.3 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 164.80, 150.32, 147.22, 143.91, 138.73, 137.42, 130.66, 130.12, 125.23, 122.81, 119.29, 116.32, 69.77, 22.05.
IR (thin film, cm^{-1}): 1044, 1101, 1141, 1182, 1235, 1304, 1373, 1452, 1500, 1626, 1732, 2938, 2982, 3230, 3369, 3446.
HRMS (ESI): [M+H$^+$] calcd for $C_{15}H_{17}N_2O_2$: 257.1278; found, 257.1278.
TLC: R_f = 0.3 (70:30 petroleum ether:EtOAc).

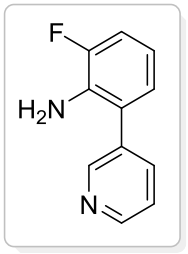


***2-(quinolin-3-yl)aniline*:** Compound **TDG12** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (75/25, v/v).
Physical State: brown solid.
Yield: 70% (616 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.05 (d, *J* = 2.1 Hz, 1H), 8.28 (d, *J* = 1.5 Hz, 1H), 8.17 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.76 (td, *J* = 8.5, 1.5 Hz, 1H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.28 – 7.21 (m, 2H), 6.92 (td, *J* = 7.5, 0.9 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 3.85 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm. 151.55, 147.16, 144.05, 135.47, 132.49, 130.87, 129.55, 129.46, 129.27, 127.96, 127.86, 127.03, 123.76, 119.09, 116.00.
IR (thin film, cm^{-1}): 1028, 1127, 1158, 1191, 1257, 1299, 1339, 1362, 1411, 1450, 1497, 1577, 1618, 2854, 2927, 3029, 3060, 3206, 3330, 3446.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{15}H_{13}N_2$: 221.1073; found, 221.1075
TLC: R_f = 0.5 (70:30 petroleum ether:EtOAc).

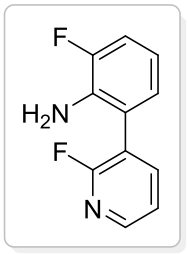


***2-(8-nitroquinolin-3-yl)aniline*:** Compound **TDG13** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (70/30, v/v).
Physical State: colorless oil.

Yield: 85% (902 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.20 (d, *J* = 2.1 Hz, 1H), 8.37 (d, *J* = 2.1 Hz, 1H), 8.06 (d, *J* = 7.7 Hz, 2H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.19 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.92 (td, *J* = 7.5, 1.0 Hz, 1H), 6.85 (dd, *J* = 8.1, 0.8 Hz, 1H), 3.73 (d, *J* = 41.7 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 154.14, 144.15, 138.54, 135.53, 134.77, 132.28, 131.00, 130.25, 129.14, 125.95, 123.94, 122.76, 121.58, 119.59, 116.52.
IR (thin film, cm^{-1}): 1028, 1127, 1158 1191, 1257, 1299, 1339, 1345, 1362, 1385, 1411, 1450, 1497, 1577, 1560, 1515, 1618, 2854, 2927, 3029, 3060, 3206, 3330, 3446.
HRMS (ESI): [M+H$^+$] calcd for $C_{15}H_{12}N_3O_2$: 266.0924; found, 266.0929.
TLC: R_f = 0.3 (70:30 petroleum ether:EtOAc).

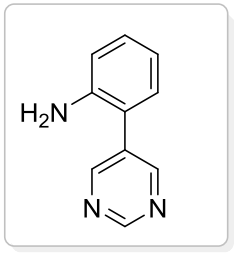


***2-fluoro-6-(pyridin-3-yl)aniline*:** Compound **TDG14** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (75:25, v/v).
Physical State: white solid.
Yield: 70% (527 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.59 (d, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.3 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.20 (ddd, *J* = 7.4, 3.5, 1.4 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 157.49, δ 142.95 (d, *J* = 31.8 Hz), 135.99 (d, *J* = 17.6 Hz), 132.43 (d, *J* = 3.6 Hz), 130.98 (d, *J* = 6.1 Hz), 128.85, 128.28, 126.23, 119.98 (d, *J* = 7.0 Hz), 103.15.
IR (thin film, cm^{-1}): 1002, 1036, 1110, 1172, 1247, 1471, 1589, 1735, 2851, 2925, 3050.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -75.19.
HRMS (**ESI**): [M+Na$^+$] calcd for $C_{11}H_9FN_2Na$: 211.0642; found, 211.0638.
TLC: R_f = 0.35 (70:30 petroleum ether:EtOAc).

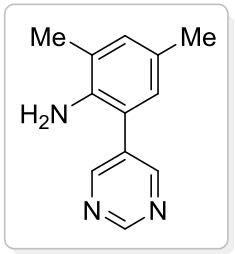


***2-fluoro-6-(2-fluoropyridin-3-yl)aniline*:** Compound **TDG15** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (75:25, v/v).
Physical State: white solid.

Yield: 75% (618 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.24 (dd, *J* = 3.2, 1.2 Hz, 1H), 7.83 (ddd, *J* = 9.4, 7.4, 2.0 Hz, 1H), 7.29 (ddd, *J* = 7.1, 4.9, 1.9 Hz, 1H), 7.05 (ddd, *J* = 10.8, 8.1, 1.3 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 1H), 6.79 – 6.72 (m, 1H), 3.77 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 160.51 (d, *J* = 239.6 Hz), 151.83 (d, *J* = 239.1 Hz), 147.34 (d, *J* = 14.4 Hz), 142.45 (d, *J* = 4.6 Hz), 133.06 (d, *J* = 13.3 Hz), 126.14 (d, *J* = 2.2 Hz), 121.89 (d, *J* = 4.4 Hz), 121.41, 120.55 (dd, *J* = 3.4 , 3.3 Hz), 117.98 (d, *J* = 7.8 Hz), 115.27 (d, *J* = 19.1 Hz).
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -68.37, -133.89.
IR (thin film, cm^{-1}): 1028, 1067, 1114, 1143, 1180, 1208, 1244, 1274, 1426, 1476, 1568, 1602, 1631, 2926, 3063, 3362.
HRMS (**ESI**): [M+H$^+$] calcd for $C_{11}H_9F_2N_2$: 207.0734; found, 207.0728.
TLC: R_f = 0.3 (70:30 petroleum ether:EtOAc).

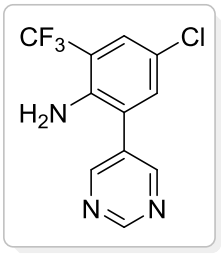


***2-(pyrimidin-5-yl)aniline*:** Compound **TDG16** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (70:30, v/v).
Physical State: yellow solid.
Yield: 85% (582 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.19 (s, 1H), 8.88 (s, 2H), 7.25 (t, *J* = 7.2 Hz, 1H), 7.09 (d, *J* =7.4 Hz, 1H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 3.79 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 190.63, 158.04, 156.71, 137.22, 134.19, 133.77, 132.28, 131.31, 130.57, 129.61.
IR (thin film, cm^{-1}): 1000, 1057, 1108, 1160, 1258, 1302, 1408, 1457, 1497, 1550, 1577, 1629, 1895, 2331, 2859, 2936, 3036, 3227, 3341, 3436.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{10}H_{10}N_3$: 172.0869; found, 172.0868
TLC: R_f = 0.3 (70:30 petroleum ether:EtOAc).

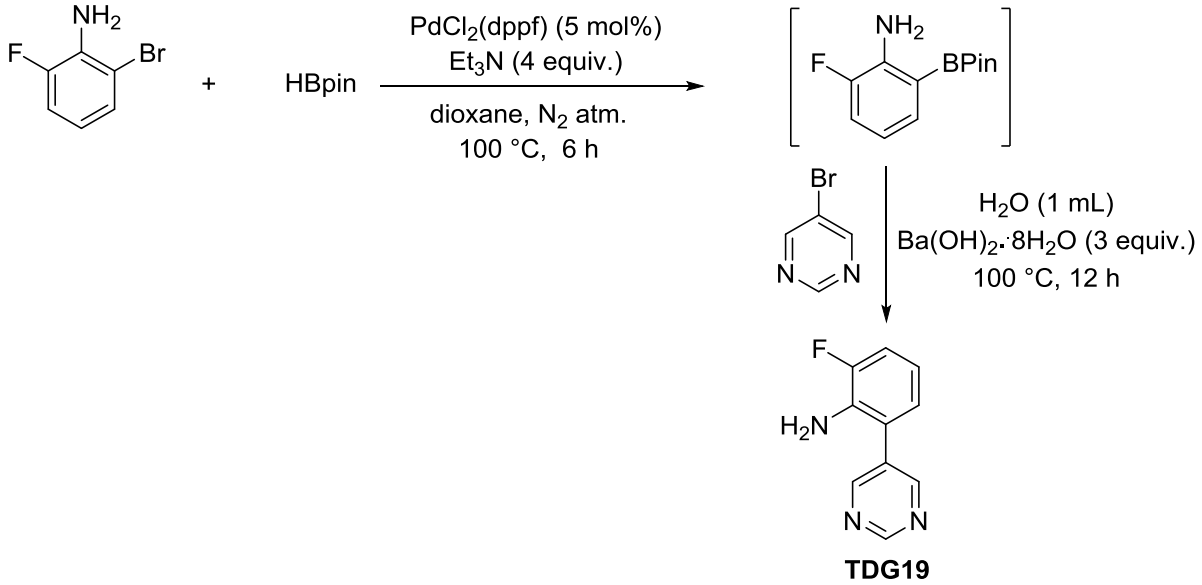


***2,4-dimethyl-6-(pyrimidin-5-yl)aniline*:** Compound **TDG17** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (70:30, v/v).

Physical State: yellow solid.
Yield: 76% (606 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.20 (s, 1H), 8.86 (s, 2H), 6.98 (d, *J* = 0.6 Hz, 1H), 6.78 (d, *J* = 1.3 Hz, 1H), 3.54 (s, 2H), 2.27 (s, 3H), 2.21 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 157.32, 157.12, 139.52, 133.90, 132.16, 128.71, 128.01, 123.30, 119.80, 20.31, 17.80.
IR (thin film, cm^{-1}): 1184.29, 1412.78, 1484.66, 1552.02, 1627.14, 1734.21, 2855.33, 2924.64, 3367.73.
HRMS (ESI): [M+H^+] calcd for $C_{12}H_{14}N_3$: 200.1182; found, 200.1178.
TLC: R_f = 0.26 (70:30 petroleum ether:EtOAc).

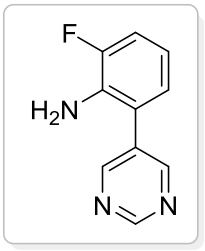


***4-chloro-2-(pyrimidin-5-yl)-6-(trifluoromethyl)aniline*:** Compound **TDG18** was prepared by general procedure A (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (75:25, v/v).
Physical State: colorless oil.
Yield: 70% (766 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.28 (s, 1H), 8.83 (s, 2H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 4.21 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 158.77, 157.37, 140.96, 134.02, 131.29, 127.69, 127.65, 125.14, 123.54, 122.98, 116.19 (q, *J* = 272 Hz, CF_3).
IR (thin film, cm^{-1}): 1019, 1132, 1213, 1242, 1345, 1430, 1499, 1578, 1620, 2877, 2825, 2930, 3131, 3261, 3474.
HRMS (*m/z*): [M+H^+] calcd for $C_{11}H_8ClF_3N_3$: 274.0353; found, 274.0359.
TLC: R_f = 0.2 (70:30 petroleum ether:EtOAc).



TDG19

Procedure for synthesis of TDG19: To a solution of 2-fluoro-6-(pyrimidin-5-yl)aniline (1.0 equiv., 2.5 mmol, 285 µL) in dioxane (10 mL) were added Et_3N (4.0 equiv., 10.0 mmol, 1.4 mL), $PdCl_2$(dppf) (5 mol%, 0.125 mmol, 92 mg), and pinacolborane (3.0 equiv., 1.0 mL, 7.5 mmol), dropwise. The mixture was stirrer at 100 °C for 6 h, then cool to room temperature, and water (1.0 mL), $Ba(OH)_2.8H_2O$, (3.0 equiv., 7.5 mmol, 2.37 g), and 5-bromopyrimidine (0.92 equiv., 2.3 mmol, 366 mg), were successively added. The mixture was stirrer at 100 °C for 12 h before addition of water (25 mL) at room temperature. The mixture was filtered through Celite. The eluent was extracted with ethyl acetate and the organic layer was purified by column chromatography using silica gel deactivated with 10 mol% Et_3N in hexane. 2-fluoro-6-(pyrimidin-5-yl)aniline was isolated as white solid.



***2-fluoro-6-(pyrimidin-5-yl)aniline*:** Compound **TDG19** was prepared by above procedure (2.5 mmol scale).

Eluent: petroleum ether/ethyl acetate (70/30, v/v).

Physical State: white solid.

Yield: 81% (383 mg isolated).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.17 (s, 1H), 8.85 (s, 2H), 7.06 (ddd, *J* = 10.7, 8.1, 1.4 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.79 (td, *J* = 7.9, 5.1 Hz, 1H), 3.86 (s, 2H).

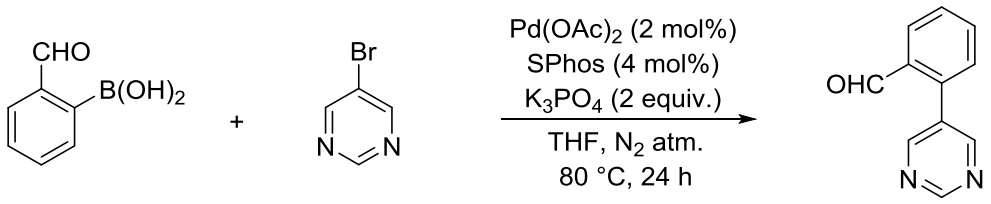
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 157.70, 156.79, 150.65 (s), 132.81 (d, *J* = 13.4 Hz), 132.39 (d, *J* = 3.2 Hz), 125.63 (d, *J* = 3.2 Hz), 121.89 (d, *J* = 3.5 Hz), 118.54 (d, *J* = 7.8 Hz), 115.74 (d, *J* = 19.2 Hz).

^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -133.51.

IR (thin film, cm^{-1}): 1062, 1182, 1215, 1246, 1277, 1299, 1344, 1412, 1488, 1555, 1580, 1652, 2855, 2925, 3219, 3339, 3433.

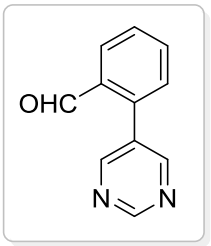
HRMS (ESI): [M+H$^+$] calcd for $C_{10}H_9FN_3$: 190.0771; found, 190.0775.
TLC: R_f = 0.4 (70/30 petroleum ether:EtOAc).

2.2 Procedure for synthesis of TDG20



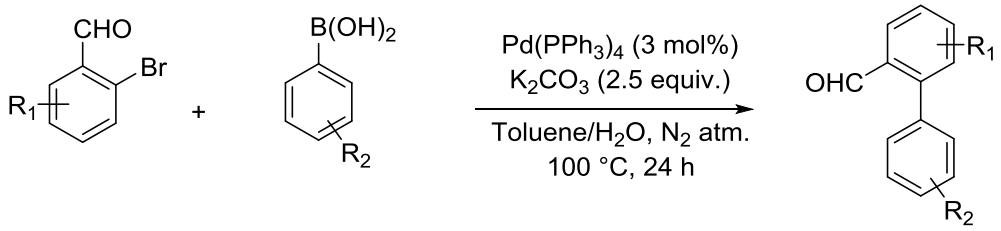
TDG20

2-(pyrimidin-5-yl)benzaldehyde was prepared by the Suzuki cross-coupling reaction condition. A clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with 5-bromopyrimidine (1 equiv., 4.0 mmol, 636 mg), (2-formylphenyl)boronic acid (1.25 equiv., 5.0 mmol, 750 mg), palladium (II) acetate (2 mol%, 0.08 mmol, 18 mg), SPhos (4 mol%, 0.16 mmol, 66 mg) and K_3PO_4 (2 equiv., 8.0 mmol, 1700 mg). The cap was fitted with a rubber septum and the reaction tube was evacua.ted and back filled with nitrogen and this sequence was repeated three additional times. Under the positive flow of nitrogen 15 mL THF was added to the reaction mixture. The reaction mixture was vigorously stirred at 80 °C temperature for 24 h. Next, the reaction was allowed to cool at room temperature and dried using rotary evaporator. The reaction mixture was extracted thrice with ethyl acetate (3x20 mL) and brine solution (3x10 mL). The organic layer was collected and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude mixture was purified by column chromatography using silica gel and petroleum-ether/ethyl acetate as the eluent.

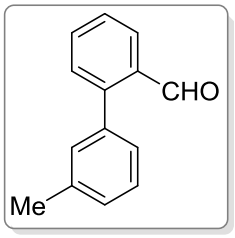


***2-(pyrimidin-5-yl)benzaldehyde*:** Compound **TDG20** was prepared by above procedure.
Eluent: petroleum ether/ethyl acetate (70/30, v/v).
Physical State: white solid.
Yield: 87% (641 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm).10.01 (s, 1H), 9.29 (s, 1H), 8.79 (s, 2H), 8.08 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.76 (td, *J* = 7.5, 1.3 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm). 190.63, 158.04, 156.71, 137.22, 134.19, 133.77, 132.28, 131.31, 130.57, 129.61.
IR (thin film, cm^{-1}): 1000, 1055, 1200, 1266, 1355, 1416, 1549, 1597, 1654, 1689, 2764, 2869, 2923, 3042.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{11}H_9N_2O$: 185.0709; found, 185.0710.
TLC: R_f = 0.3 (70:30 petroleum ether:EtOAc).

2.3 General procedure B: Synthesis of 2-phenylbenzyldehyde derivatives



Under an inert atmosphere, into a three-necked flask was charged with (1.0 equiv., 4.0 mmol, 740 mg) of 2-bromobenzaldehyde, (1.25 equiv., 5.0 mmol, 609 mg) of arylboronic acid, (2.0 equiv., 8.0 mmol, 1.7 g) of potassium carbonate, 8 mL of toluene and 8 mL of ion exchanged water to obtain a mixed solution, and argon was bubbled through this mixed solution for 20 minutes while stirring at room temperature. Subsequently, to this mixed solution was added 139 mg (3 mol%, 0.12 mmol) of tetrakis(triphenylphosphine)palladium, further, argon was bubbled through the solution for 10 minutes while stirring at room temperature. The mixed solution was heated up to 100 °C and reacted for 25 hours. After cooling to room temperature, the organic phase was evaporated under reduced pressure. The crude mixture was purified by column chromatography using silica gel and petroleum-ether/ethyl acetate (90/10, v/v) as the eluent.



***3'-methyl-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1a** was prepared by general procedure B (4.0 mmol scale).

Eluent: petroleum ether

Physical State: yellow oil.

Yield: 97% (761 mg isolated).

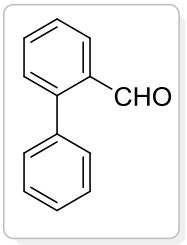
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.02 (s, 1H), 8.05 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.66 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 3.7 Hz, 1H), 7.24 – 7.20 (m, 2H), 2.45 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.65, 146.19, 138.18, 137.71, 133.75, 133.52, 130.85, 130.75, 128.87, 128.32, 127.67, 127.47, 127.28, 21.44.

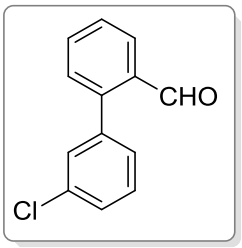
IR (thin film, cm^{-1}): 3032, 2922, 2847, 2751, 1692, 1648, 1597, 1471, 1392, 1257, 1197, 1160.76, 1103, 1035, 1000.

HRMS (m/z): [M+H+] calcd for $C_{14}H_{13}O$: 197.0960; found, 197.0963.

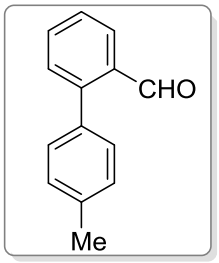
TLC: R_f = 0.7 (98:2 petroleum ether:EtOAc).



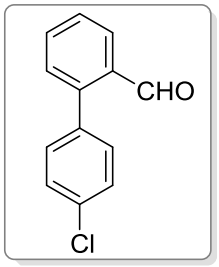
***[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1b** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether.
Physical State: yellow oil.
Yield: 95% (692 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.96 (s, 1H), 8.01 (d, *J* = 7.8 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.46 – 7.34 (m, 5H), 7.33 – 7.28 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.89, 145.65, 137.51, 133.49, 133.34, 130.59, 129.90, 128.24, 127.92, 127.56, 127.34.
IR (thin film, cm^{-1}): 3028, 2920, 2848, 2761, 1592, 1638, 1588, 1471, 1392, 1257, 1187, 1170, 1100, 1033, 1070.
HRMS (*m/z*): [M+H^+] calcd for $C_{13}H_{11}O$: 183.0804; found, 183.0805.
TLC: R_f = 0.7 (98:2 petroleum ether:EtOAc).



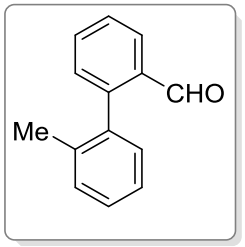
***3'-chloro-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1c** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether.
Physical State: colorless oil.
Yield: 87% (479 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.03 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.65 (td, *J* = 7.5, 1.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.43 – 7.39 (m, 4H), 7.25 (t, *J* = 1.8 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.01, 144.50, 139.84, 134.73, 133.91, 133.86, 130.86, 130.08, 129.82, 128.58, 128.54, 128.49, 128.07.
IR (thin film, cm^{-1}): 1023, 1080, 1104, 1161, 1195, 1253, 1393, 1464, 1560, 1593, 1691, 1947, 2753, 2849, 3063.
HRMS (*m/z*): [M+H^+] calcd for $C_{13}H_{10}ClO$: 217.0414; found, 217.0420.
TLC: R_f = 0.7 (98:2 petroleum ether:EtOAc).



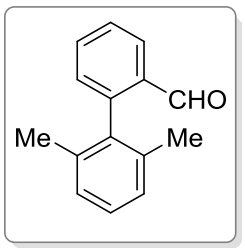
***4'-methyl-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1d** was prepared by general procedure B (0.4 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 95% (745 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.00 (s, 1H), 8.02 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.28 (s, 4H), 2.44 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.84, 146.21, 138.25, 134.99, 133.93, 133.73, 130.98, 130.22, 129.35, 127.74, 127.73, 21.38.
IR (thin film, cm^{-1}): 3026, 2848, 2922, 2751, 1910, 1690, 1596, 1475, 1392, 1448, 1516, 1160, 1113, 11043, 1005, 958.
HRMS (*m/z*): [M+Na^+] calcd for $C_{14}H_{12}NaO$: 219.0780; found, 219.0783.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).



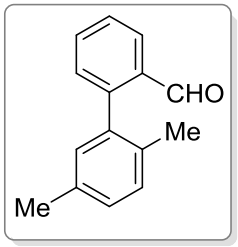
4'-chloro-[1,1'-biphenyl]-2-carbaldehyde: Compound **1e** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 85% (736 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.03 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.65 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.34 – 7.30 (m, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.13, 144.73, 136.45, 134.71, 133.90, 131.48, 130.89, 128.88, 128.35, 128.14.
IR (thin film, cm^{-1}): 1000, 1033, 1085, 1119, 1176, 1300, 1379, 1458, 1473, 1598, 1697, 2725, 2826, 3019, 3061.
HRMS (*m/z*): [M+H^+] calcd for $C_{13}H_{10}ClO$: 217.0414; found, 217.0420.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).



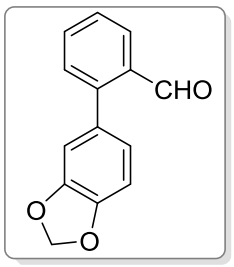
2'-methyl-[1,1'-biphenyl]-2-carbaldehyde **:** Compound **1f** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 87% (683 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.81 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.37 – 7.32 (m, 3H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.22 (d, *J* = 7.5 Hz, 1H), 2.14 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.18, 145.69, 137.55, 136.18, 133.89, 133.77, 130.82, 130.24, 130.15, 128.35, 127.88, 127.13, 125.75, 20.36.
IR (thin film, cm^{-1}): 3020, 3062, 2923, 2844, 2748, 1693, 1596, 1474, 1448, 1391, 1253, 1194, 1160, 1120, 1098, 1036, 1006.
HRMS (ESI): [M-H^+] calcd for $C_{14}H_{11}O$: 195.0810; found, 195.0786.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).



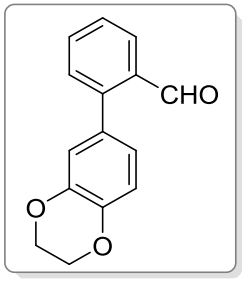
2',6'-dimethyl-[1,1'-biphenyl]-2-carbaldehyde **:** Compound **1g** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 96% (807 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.66 (s, 1H), 8.06 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.3 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.22 (dd, *J* = 7.4, 2.6 Hz,2H), 7.14 (d, *J* = 7.6 Hz, 2H), 1.98 (s, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.38, 145.26, 137.28, 136.46, 134.57, 133.77, 130.62, 128.17, 127.97, 127.61, 127.47, 21.06.
IR (thin film, cm^{-1}): 3022, 2923, 2841, 2745, 1734, 1693, 1651, 1597, 1462, 1390, 1256, 1195, 1159, 1107, 1045, 1004.
HRMS (ESI): [M+Na^+] calcd for $C_{15}H_{14}NaO$: 233.0937; found, 233.0934.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).



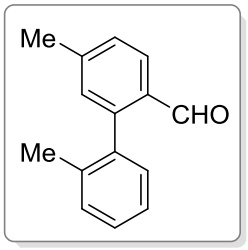
***4'-methoxy-2',5'-dimethyl-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1h** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 92% (774 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.79 (s, 1H), 8.04 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.63 (td, *J* = 7.5, 1.3 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.31 (dd, *J* = 7.6, 0.5 Hz, 1H), 7.19 (d, *J* = 7.8 Hz, 1H), 7.15 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.03 (s, 1H), 2.36 (s, 3H), 2.07 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.49, 146.02, 137.43, 135.26, 133.96, 133.78, 133.12, 131.01, 130.87, 130.10, 129.12, 127.82, 127.07, 20.99, 19.91.
IR (thin film, cm^{-1}): 3018, 2922, 2840, 2747, 1693, 1597, 1501, 1476, 1447, 1390, 1257, 1197, 1138.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{15}H_{14}NaO$: 233.0937; found, 233.0928.
TLC: R_f = 0.4 (95:5 petroleum ether:EtOAc).



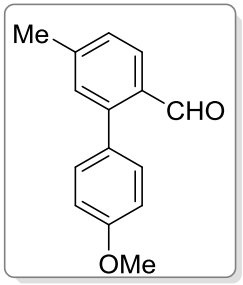
***2-(benzo[d][1,3]dioxol-5-yl)benzaldehyde*:** Compound **1i** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 97% (878 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 7.96 (dd, *J* = 7.8, 0.6 Hz, 1H), 7.60 – 7.52 (m, 1H), 7.42 (dt, *J* = 14.2, 3.6 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 1H), 6.90 – 6.81 (m, 2H), 6.81 – 6.72 (m, 1H), 5.99 (dd, *J* = 2.5, 1.5 Hz, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.39, 147.93, 147.83, 145.53, 133.90, 133.56, 131.58, 130.74, 127.65, 127.61, 124.15, 110.30, 108.25, 101.50.
IR (thin film, cm^{-1}): 3067, 2896, 2852, 2752, 1850, 1689, 1596, 1503, 1472, 1393, 1341, 1245, 1221, 1193, 1108, 1037.
HRMS (ESI): [M+H$^+$] calcd for $C_{14}H_{10}NaO_3$: 249.0522; found, 249.0516.
TLC: R_f = 0.5 (98:2 petroleum ether:EtOAc).



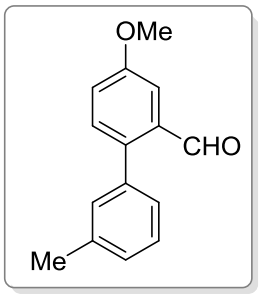
***2-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)benzaldehyde*:** Compound **1j** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 92% (884 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.00 (s, 1H), 7.97 (d, *J* = 7.7 Hz, 1H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 6.91 (t, *J* = 7.8 Hz 1H), 6.80 (dd, *J* = 8.2, 1.7 Hz, 1H), 4.28 (s, 4H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.59, 145.44, 143.81, 143.47, 133.72, 133.51, 130.98, 130.70, 127.50, 127.47, 123.46, 118.92, 117.25, 64.43, 64.37.
IR (thin film, cm^{-1}): 1068, 1100, 1127, 1195, 1224, 1245, 1281, 1311, 1391, 1416, 1450, 1475, 1509, 1583, 1652, 1690, 2750, 2926.
HRMS (*m/z*): [M+H^+] calcd for $C_{15}H_{13}O_3$: 241.0859; found, 241.0862.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



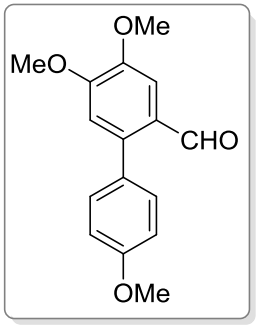
***2',5-dimethyl-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1k** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: brown oil.
Yield: 88% (740 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.94 (d, *J* = 0.6 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.30 – 7.26 (m, 5H), 7.24 (s, 1H), 2.46 (s, 3H), 2.43 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.32, 146.19, 144.50, 137.93, 134.98, 131.52, 131.40, 130.00, 129.11, 128.49, 127.71, 21.85, 21.21.
IR (thin film, cm^{-1}): 1038, 1121, 1182, 1208, 1256, 1394, 1450, 1488, 1514, 1602, 1682, 2752, 2847, 2921, 2954, 3026.
HRMS (*m/z*): [M+Na^+] calcd for $C_{15}H_{14}NaO$: 233.0936; found, 233.0939
TLC: R_f = 0.4 (95:5 petroleum ether:EtOAc).



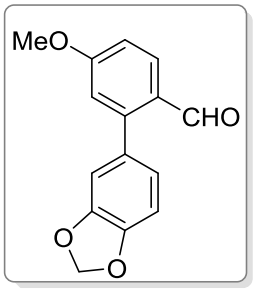
***4'-methoxy-5-methyl-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1l** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: brown oil.
Yield: 95% (1075 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.94 (s, 1H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 4.5 Hz, 1H), 7.22 (s, 1H), 6.99 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 3H), 2.45 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.55, 159.78, 145.99, 144.67, 131.66, 131.55, 131.41, 130.35, 128.50, 127.91, 114.02, 55.56, 22.01.
IR (thin film, cm^{-1}): 3354, 2957, 2934, 2839, 2752, 2544, 2297, 2052, 1893, 1682, 1603, 1514, 1462, 1394, 1295, 1266, 1244, 1209, 1120, 1028.
HRMS (*m/z*): [M+Na^+] calcd for $C_{15}H_{14}NaO_2$: 249.0886; found, 249.0889.
TLC: R_f = 0.6 (95:5 petroleum ether:EtOAc).



***3',4-dimethoxy-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1m** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: pale yellow oil.
Yield: 89% (805 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.95 (s, 1H), 7.51 (s, 1H), 7.35 (dd, *J* = 8.6, 2.0 Hz, 2H), 7.25 – 7.12 (m, 4H), 3.90 (s, 3H), 2.42 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.66, 159.26, 139.51, 138.28, 137.61, 134.68, 132.24, 131.16, 128.72, 128.44, 127.59, 121.57, 109.93, 55.78, 21.61.
IR (thin film, cm^{-1}): 3343, 2959, 2877, 2738, 2594, 2349, 2036, 1915, 1702, 1548, 1462, 1387, 1245, 1149, 1038.
HRMS (*m/z*): [M+H^+] calcd for $C_{15}H_{15}O_4$: 243.1015; found, 243.1020
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).

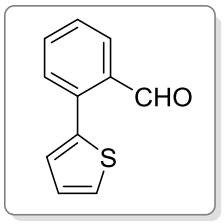


***4,4',5-trimethoxy-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **1n** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: yellow oil.
Yield: 93% (643 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.81 (s, 1H), 7.50 (s, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 6.82 (s, 1H), 3.96 (s, 6H), 3.85 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.44, 159.73, 153.56, 148.68, 141.40, 131.48, 129.99, 127.08, 113.97, 112.76, 108.74, 56.34, 56.25, 55.54.
IR (thin film, cm^{-1}): 1042, 1135, 1177, 1213, 1247, 1277, 1349, 1396, 1440, 1463, 1501, 1596, 1672, 1735, 2850, 2928, 3002, 3076.
.HRMS (*m/z*): [M+H$^+$] calcd for $C_{16}H_{17}O_4$: 273.1121; found, 273.1125.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).



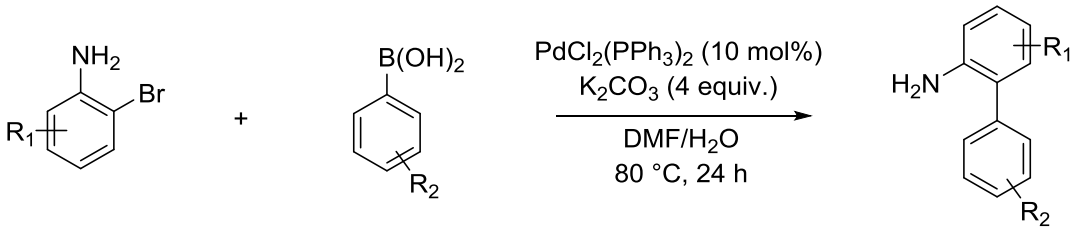
***2-(benzo[d][1,3]dioxol-5-yl)-4-methoxybenzaldehyde*:** Compound **1o** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 98% (1004 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.85 (s, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 6.96 (ddd, *J* = 8.7, 2.5, 0.6 Hz, 1H), 6.90 – 6.85 (m, 2H), 6.84 (d, *J* = 2.5 Hz, 1H), 6.80 (dd, *J* = 7.9, 1.8 Hz, 1H), 6.03 (s, 2H), 3.89 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.05, 163.50, 148.07, 147.78, 131.58, 130.04, 127.49, 123.87, 115.14, 113.81, 110.20, 108.17, 101.45, 55.62.
IR (thin film, cm^{-1}): 3072, 3008, 2900, 2844, 2760, 1678, 1593, 1483, 1448, 1397, 1338, 1298, 1232, 1178, 1099, 1036.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{15}H_{12}NaO_4$: 279.0627; found, 279.0629.

TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).

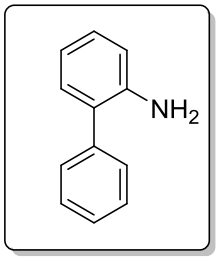


2-(thiophen-2-yl)benzaldehyde: Compound **1p** was prepared by general procedure B (4.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 73% (549 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.19 (s, 1H), 8.01 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.64 – 7.58 (m, 1H), 7.56 – 7.52 (m, *J* = 7.7, 1.3 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.46 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.14 (dd, *J* = 5.1, 3.5 Hz, 1H), 7.07 (dd, *J* = 3.5, 1.1 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.06, 138.78, 138.06, 134.22, 133.58, 131.36, 129.59, 128.24, 127.83, 127.76, 127.40.
IR (thin film, cm^{-1}): 3069, 2925, 2850, 2751, 1689, 1595, 1475, 1426, 1391, 1272, 1245, 1194, 1161, 1111, 699.
HRMS (*m/z*): [M+H^+] calcd for $C_{11}H_8NaSO$: 211.0188; found, 211.0194.
TLC: R_f = 0.7 (95:5 petroleum ether:EtOAc).

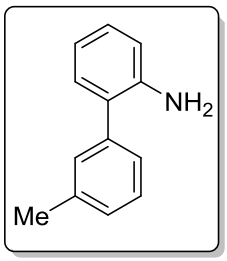
2.4 General procedure C: Synthesis of 2-phenylaniline derivatives



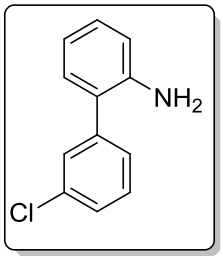
To a clean RB flask containing, arylboronic acid (4.35 mmol, 1.5 equiv.), K_2CO_3 (11.62 mmol, 4.0 equiv.) and $PdCl_2(PPh_3)_2$ (10 mol%) were added DMF/H_2O (13 mL/3 mL). To this resulting mixture 2- bromoanilines (2.9 mmol, 1.0 equiv.) was added and stirred at 80 °C for 24 h under nitrogen atmosphere. After completion of the reaction (monitor by TLC), water was added and extracted with ethyl acetate for 2-3 times. The combined organic layer was washed with saturated NaCl and dried over anhydrous Na_2SO_4. The organic layer was concentrated under vacuum, and the crude residue was purified by silica gel column chromatography (15%, petroleum ether/ethyl acetate) to afford the corresponding coupling product 2-aminobiaryls.



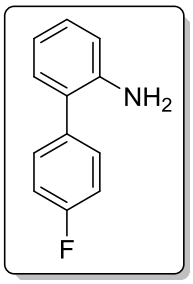
***[1,1'-biphenyl]-2-amine*:** Compound **2a** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: white solid.
Yield: 90% (447 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.54 – 7.49 (m, 4H), 7.43 – 7.39 (m, 1H), 7.22 (ddd, *J* = 15.5, 7.8, 1.5 Hz, 2H), 6.90 (td, *J* = 7.5, 1.1 Hz, 1H), 6.83 (dd, *J* = 7.9, 0.8 Hz, 1H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 143.56, 139.59, 130.51, 129.15, 128.87, 128.56, 127.69, 127.22, 118.70, 115.66.
IR (thin film, cm^{-1}): 1027, 1082, 1173, 1244, 1307, 1416, 1459, 1493, 1592, 1719, 1784, 1859, 1933, 2097, 2332, 2542, 2640, 2925, 3043, 3394.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{12}H_{12}N$: 170.0964; found, 170.0962.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



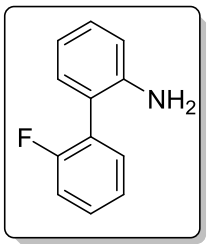
3'-methyl-[1,1'-biphenyl]-2-amine: Compound **2b** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 95% (505 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.35 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.0 Hz, 2H), 7.20 – 7.12 (m, 3H), 6.83 (td, *J* = 7.5, 1.1 Hz, 1H), 6.78 (dd, *J* = 7.9, 0.7 Hz, 1H), 3.75 (s, 2H), 2.41 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm). 143.51, 139.48, 138.48, 130.42, 129.83, 128.71, 128.41, 127.92, 127.81, 126.09, 118.62, 115.57, 21.50.
IR (thin film, cm^{-1}): 3468, 3378, 3021, 2922, 2856, 1792, 1692, 1614, 1478, 1448, 1295, 1250, 1215, 1157, 1094.
HRMS (ESI): [M+H^+] calcd for $C_{13}H_{14}N$: 184.1120; found, 184.1123.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).



3'-chloro-[1,1'-biphenyl]-2-amine: Compound **2c** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 92% (543 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.48 – 7.46 (m, *J* = 1.6 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.35 – 7.32 (m, 1H), 7.18 (td, *J* = 7.6, 1.5 Hz 1H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.84 (td, *J* = 7.5, 1.1 Hz, 1H), 6.77 (dd, *J* = 8.0, 0.9 Hz, 1H), 3.71 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 143.42, 141.41, 134.65, 130.34, 130.07, 129.23, 129.01, 127.32, 127.29, 126.12, 118.75, 115.77.
IR (thin film, cm^{-1}): 3470, 3376, 3211, 3061, 3026, 2926, 1785, 1693, 1615, 1560, 1469, 1497, 1406, 1295, 1258, 1158, 1098, 1079, 1050, 1018.
HRMS (*m/z*): [M+H^+] calcd for $C_{12}H_{11}ClN$: 204.0574; found, 204.0576.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

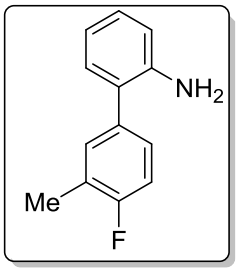


***4'-fluoro-[1,1'-biphenyl]-2-amine*:** Compound **2d** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 85% (461 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.46 – 7.41 (m, 2H), 7.20 – 7.17 (m, 1H), 7.17 – 7.13 (m, 2H), 7.13 – 7.10 (m, 1H), 6.84 (td, *J* = 7.4, 1.1 Hz, 1H), 6.78 (dd, *J* = 8.0, 1.0 Hz, 1H), 3.72 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 162.06 (d, *J* = 246.1 Hz), 143.54, 135.39 (d, *J* = 3.3 Hz), 130.77 (d, *J* = 7.9 Hz), 130.49, 128.67, 126.62, 118.74, 115.84, 115.65 (d, *J* = 5.2 Hz), 77.39, 77.07, 76.75.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -115.07.
IR (thin film, cm^{-1}): 3468, 3378, 3207, 2928, 2031, 1900, 1615, 1511, 1487, 1451, 1402, 1293, 1293, 1220, 1157, 1093, 1055, 1007.
HRMS (ESI): [M+H$^+$] calcd for$C_{12}H_{11}FN$: 188.0870; found, 188.0870.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

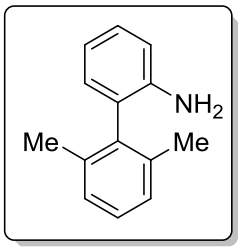


***2'-fluoro-[1,1'-biphenyl]-2-amine*:** Compound **2e** was prepared by general procedure D (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 85% (461 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.43 – 7.36 (m, 2H), 7.29 – 7.19 (m, 3H), 7.16 (d, *J* = 7.5 Hz, 1H), 6.88 (t, *J* = 7.5 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 3.64 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 143.63, 131.50 (d, *J* = 3.6 Hz), 130.53, 128.92 (d, *J* = 8.2 Hz), 128.69, 124.04, 121.04, 118.01, 115.64, 115.47, 115.25.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) **-**112.43.
IR (thin film, cm^{-1}): 3447, 3352, 3212, 2907, 2066, 1879, 1625, 1581, 1487, 1419, 1289, 1229, 1137, 1087, 946.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{12}H_{11}FN$: 188.0870; found, 188.0875.

TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).

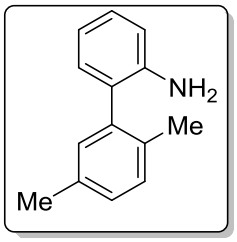


***4'-fluoro-3'-methyl-[1,1'-biphenyl]-2-amine*:** Compound **2f** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: yellow oil.
Yield: 87% (508 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.28 – 7.21 (m, 2H), 7.15 (td, *J* = 7.7, 1.0 Hz, 1H), 7.11 – 7.04 (m, 2H), 6.81 (td, *J* = 5.1, 2.6 Hz, 1H), 6.76 (dd, *J* = 8.0, 0.9 Hz, 1H), 3.70 (s, 2H), 2.32 (d, *J* = 1.8 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 160.62 (d, *J* = 245.0 Hz), 143.52, 132.21 (d, *J* = 5.2 Hz), 130.42, 128.50, 127.95 (d, *J* = 8.0 Hz), 126.86, 118.65, 115.29 (d, *J* = 22.3 Hz), 115.18, 14.6.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) **-**112.43.
IR (thin film, cm^{-1}): 3465, 3377, 3208, 3027, 2925, 1898, 1783, 1614, 1486, 1451, 1395, 1298, 1225, 1169, 1118, 1054, 1050, 988, 936.
HRMS (ESI): [M+H$^+$] calcd for $C_{13}H_{13}FN$: 202.1027; found, 202.1026.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).

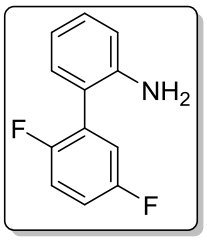


***2',6'-dimethyl-[1,1'-biphenyl]-2-amine*:** Compound **2g** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: greenish oil.
Yield: 96% (549 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.22 – 7.16 (m, 2H), 7.16 – 7.13 (m, 2H), 6.93 (dd, *J* = 7.5, 1.6 Hz, 1H), 6.83 (td, *J* = 7.4, 1.1 Hz, 1H), 6.79 (dd, *J* = 8.0, 1.1 Hz, 1H), 3.39 (s, 2H), 2.06 (s, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 143.55, 138.09, 137.36, 129.85, 128.34, 127.82, 127.69, 126.27, 118.68, 115.23, 20.39.
IR (thin film, cm^{-1}): 3468, 3378, 3061, 3019, 2855, 2736, 2609, 1930, 1785, 1612, 1449, 1496, 1377, 1100, 1041, 1002.

HRMS (*m/z*): [M+H$^+$] calcd for $C_{14}H_{16}N$: 198.1277; found, 198.1279.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).

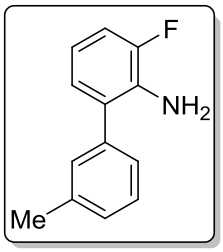


***2',5'-dimethyl-[1,1'-biphenyl]-2-amine*:** Compound **2h** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: brown oil.
Yield: 94% (538 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.27 – 7.21 (m, 2H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.13 – 7.06 (m, 2H), 6.88 (t, *J* = 7.4, 0.7 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 3.55 (s, 2H), 2.41 (s, 3H), 2.21 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 143.70, 138.52, 135.63, 133.77, 130.77, 130.24, 130.13, 128.46, 128.31, 127.69, 118.25, 115.07, 20.97, 19.23.
IR (thin film, cm^{-1}): 3442, 3312, 3092, 3001, 2863, 2749, 2621, 1910, 1775, 1633, 1458, 1401, 1377, 1138, 1045, 997.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{14}H_{16}N$: 198.1277; found, 198.1278.
TLC: R_f = 0.8 (90:10 petroleum ether:EtOAc).

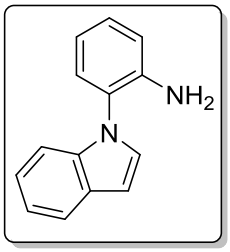


***2',5'-difluoro-[1,1'-biphenyl]-2-amine*:** Compound **2i** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: brown oil.
Yield: 85% (505 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.22 (td, *J* = 7.5, 2.1, 1H), 7.17 – 7.01 (m, 4H), 6.84 (td, *J* = 7.5, 1.1 Hz, 1H), 6.80 (dd, *J* = 7.8, 1.1 Hz, 1H 1H), 3.69 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 160.05 (dd, *J* = 243.3, 2.4 Hz), 144.00, 130.87 (d, *J* = 0.8 Hz), 129.62, 120.41, 118.60, 118.20 (dd, *J* = 23.6, 4.0 Hz), 117.65 (ddd, *J* = 34.4, 24.5, 6.4 Hz), 117.25, 116.87, 115.93, 115.55.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -118.59, -120.41.
IR (thin film, cm^{-1}): 3445, 3397, 3228, 3072, 2952, 1828, 1763, 1604, 1446, 1459, 1351, 1277, 1295, 1169, 1198, 1044, 916.

HRMS (ESI): [M+H$^+$] calcd for $C_{12}H_{10}F_2N$: 206.0776; found, 206.0773.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



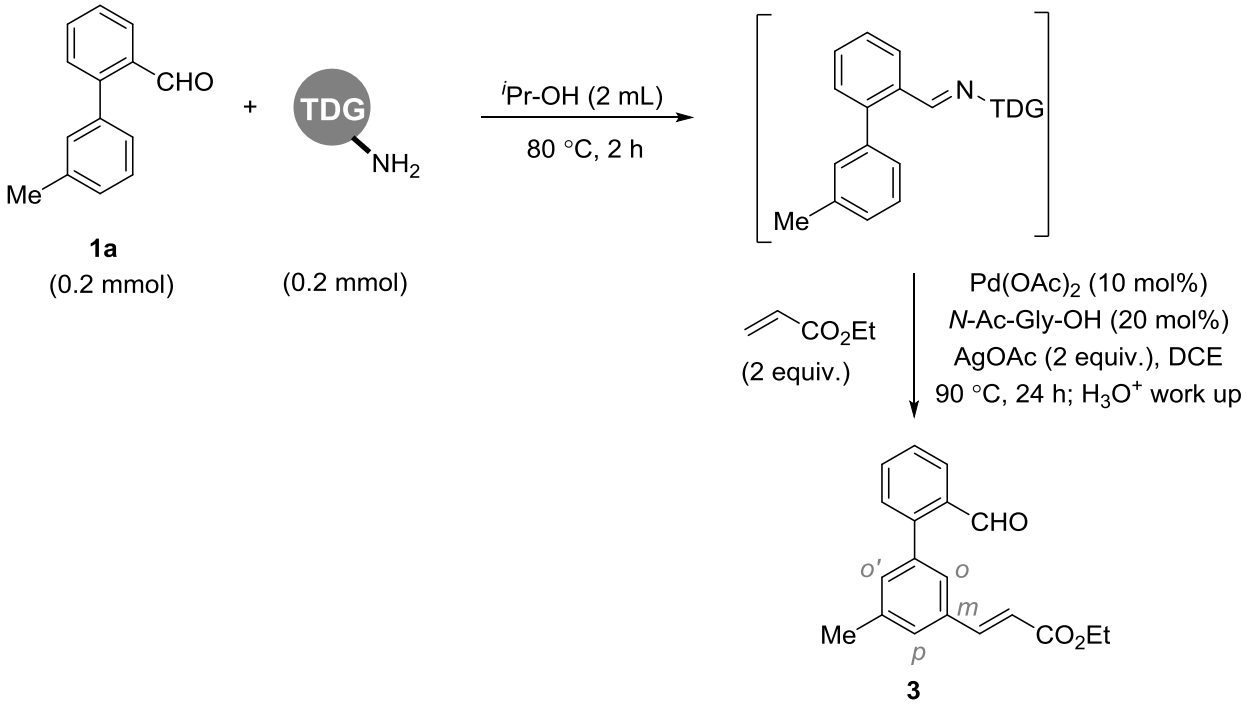
***3-fluoro-3'-methyl-[1,1'-biphenyl]-2-amine*:** Compound **2j** was prepared by general procedure C (2.9 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 75% (437 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.39 (t, *J* = 7.5 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.23 (d, *J* = 7.5 Hz, 1H), 7.06 – 7.00 (m, 1H), 6.96 (dd, *J* = 7.9, 5.3 Hz, 1H), 6.80 – 6.74 (m, 1H), 3.87 (s, 2H), 2.45 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 151.78 (d, *J* = 238.3 Hz), 138.65, 138.31 (d, *J* = 3.0 Hz), 132.20 (d, *J* = 12.5 Hz), 129.71, 129.70 (d, *J* = 3.3 Hz), 128.83, 128.32, 125.92, 125.51 (d, *J* = 2.9 Hz), 117.65 (d, *J* = 7.8 Hz), 113.96 (d, *J* = 19.0 Hz), 21.50.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -134.33.
IR (thin film, cm^{-1}): 3480, 3389, 3037, 3198, 2921, 1946, 1892, 1800, 1625, 1601, 1573, 1476, 1411, 1327, 1269, 1210, 1139, 1095, 1067.
HRMS (ESI): [M+H$^+$] calcd for $C_{13}H_{13}FN$: 202.1027; found, 202.1025.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).



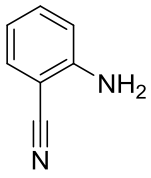
***2-(1H-indol-1-yl)aniline*:** Compound **2k** was prepared by modified literature procedure[1] (3.0 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: yellow oil.
Yield: 76% (713. mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.75 – 7.72 (m, 1H), 7.31 – 7.27 (m, 1H), 7.24 (q, *J* = 2.5 Hz, 2H), 7.21 (d, *J* = 1.8 Hz, 2H), 7.20 (s, 1H), 6.91 – 6.85 (m, 2H), 6.73 (dd, *J* = 3.2, 0.5 Hz, 1H), 3.59 (s, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 143.18, 136.41, 129.21, 128.67, 128.65, 128.60, 124.90, 122.26, 121.00, 120.20, 118.57, 116.29, 110.79, 103.25.

IR (thin film, cm^{-1}): 1010, 1063, 1136, 1229, 1260, 1311, 1331, 1453, 1512, 1618, 1699, 1781, 2918, 3052, 3204, 3372, 3468.
HRMS (*m/z*): [M+H^+] calcd for $C_{14}H_{13}N_2$: 209.1073; found, 209.1070.
TLC: R_f = 0.7 (80:20 petroleum ether:EtOAc).

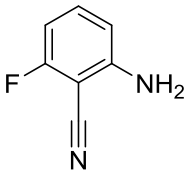
2.5 Transient Directing Group (TDG) variation for *meta*-C–H olefination



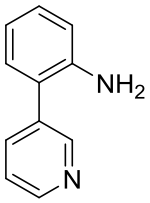
TDGs



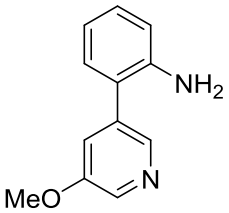
TDG1
nd



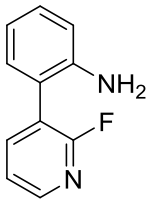
TDG2
nd



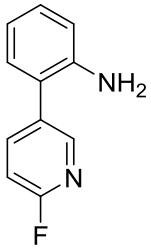
TDG3
<2% (multiple products)



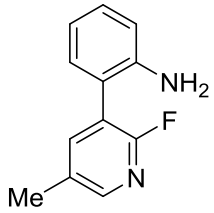
TDG4
nd



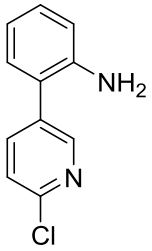
TDG5
11% (*m*:others, 3:1)



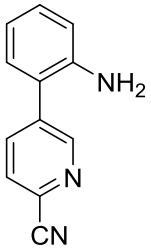
TDG6
13% (*m*:others, 3:1)



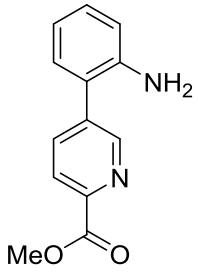
TDG7
8% (*m*:others, 2:1)



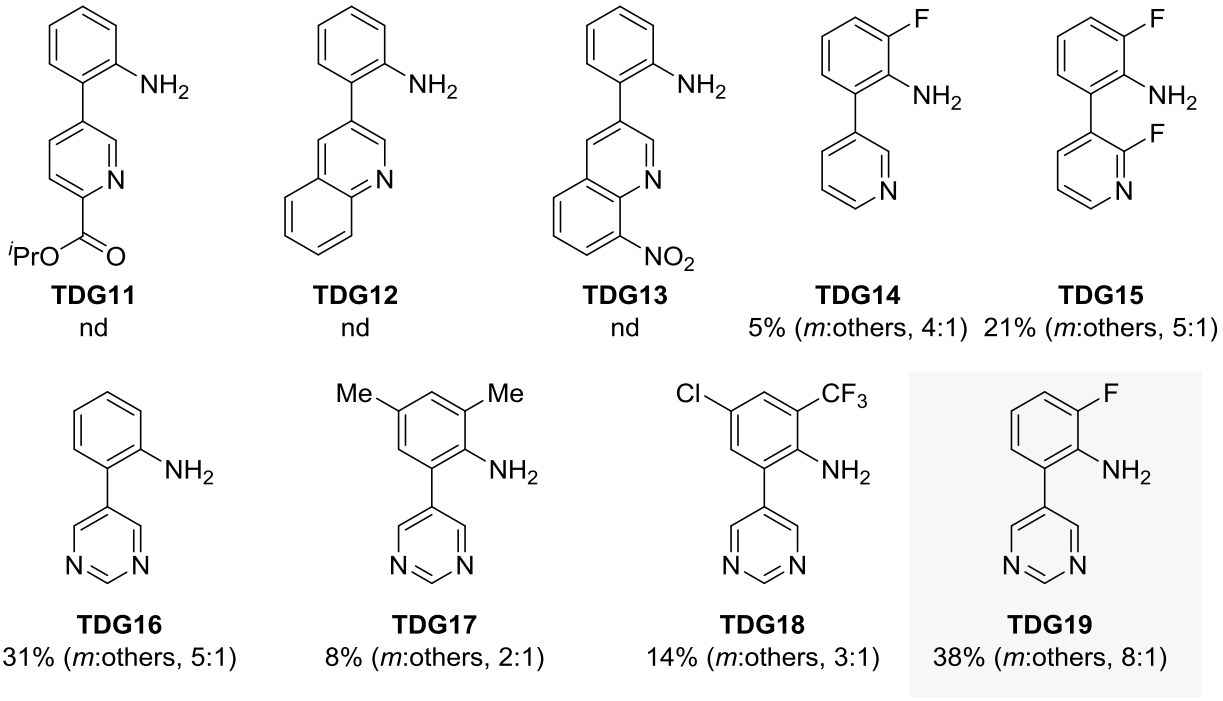
TDG8
nd



TDG9
nd



TDG10
nd



Reagents and reaction conditions: Step1: 1a (0.2 mmol), **TDG** (0.2 mmol) in ^{i}PrOH (2 mL) at 80 °C for 2h; concentrated under vacuum, the crude mixture was used for next step; **Step2:** $Pd(OAc)_2$ (10 mol%, 0.02 mmol), *N*-Ac-Gly-OH (20 mol%, 0.04 mmol), AgOAc (2 equiv., 0.4 mmol), ethyl acrylate (2 equiv., 0.4 mmol), DCE (2 mL) at 90 °C for 24 h.

Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

2.6 Optimization details for *meta*-C–H olefination of 2-phenylbenzyldehyde

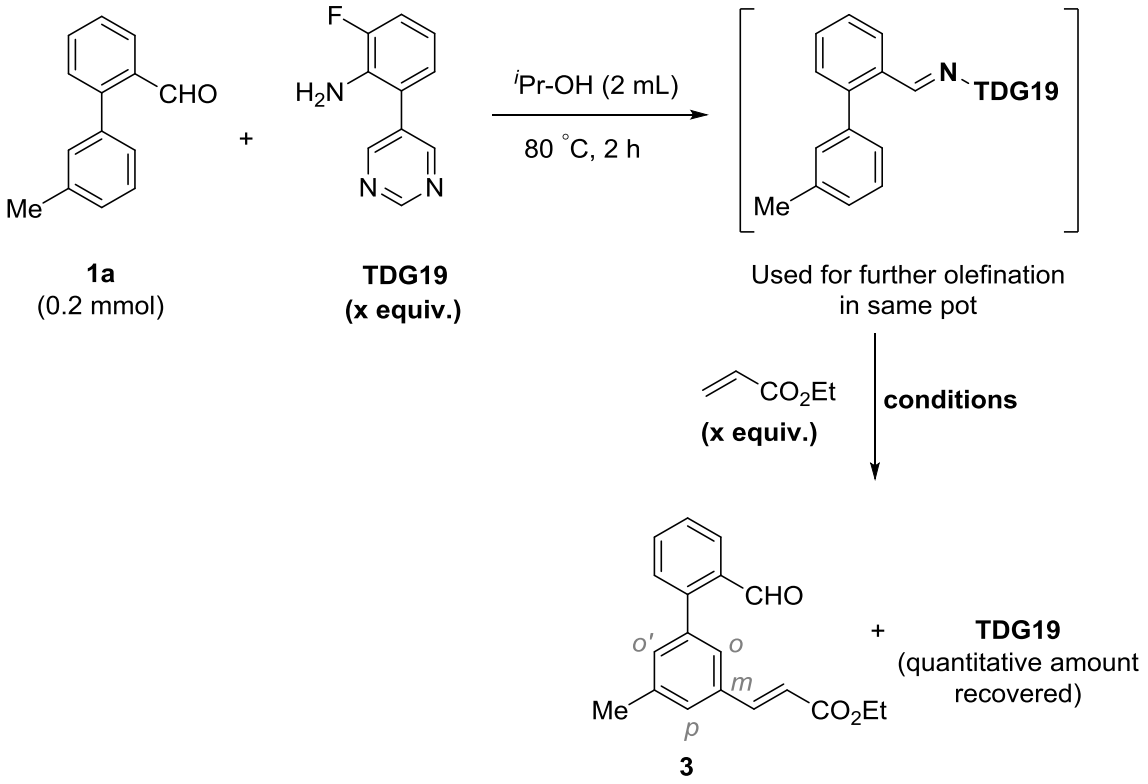
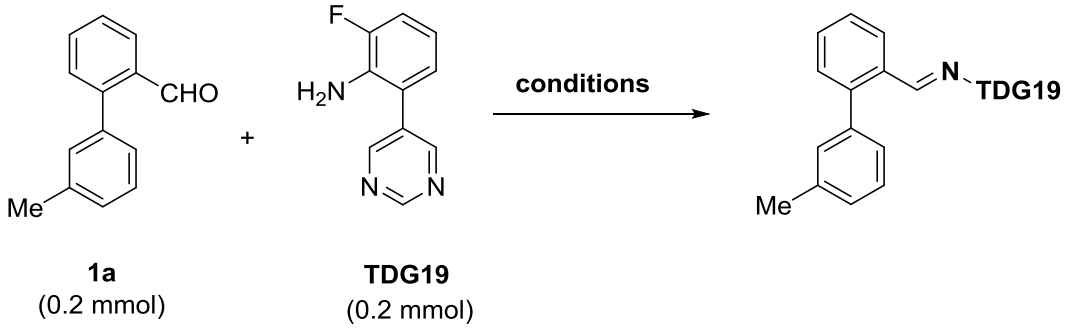


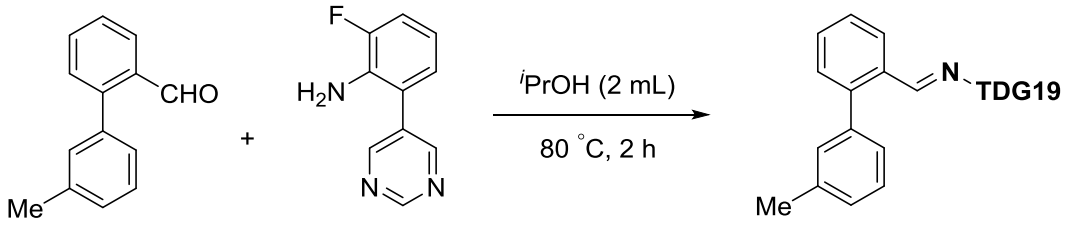
Table S1: Optimization of imine intermediate: Different conditions



Entry	Conditions	Yield[a]
1	MeCN, 80 °C	65%
2	DCM, rt	62%
3	DCM + 4 Å MS, rt	64%
4	Toluene, rt	40%
5	Toluene, 80 °C	45%
6	^{i}PrOH + cat. CH_3COOH, 70 °C	48%
7	MeOH + cat. *p*-TSA, 70 °C	nd
8	**^{i}PrOH, 80 °C, 2 h; dried, then decant with PE/diethyl ether**	**95%**

[a]Yield was measured by ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene.

Table S2: Optimization of TDG19 amount



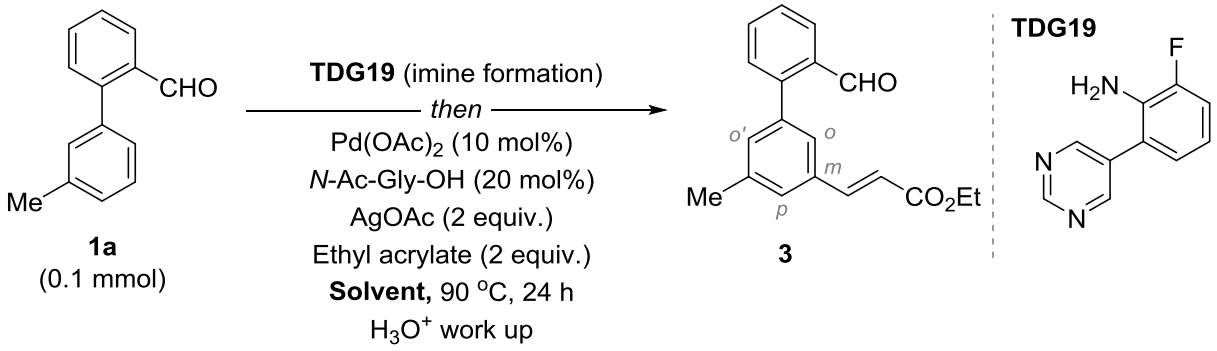
1a (0.2 mmol) **TDG19** **(x mmol)**

Entry	1a (mmol)	TDG19 (mmol)	Yield (%)
1	0.2	0.18	89
2	**0.2**	**0.19**	**95**[a]
3	0.2	0.2	95[b]
4	0.2	0.21	96[b]
5	0.2	0.22	96[b]

[a] **TDG19** was fully consumed. [b] Some amount of **TDG19** was left. *Note:* As free amine was detrimental for this reaction, we have selected **entry 2** for further use.

Optimization for *meta*-C–H olefination of 2-phenylbenzyldehyde:

Table S3: Solvent optimization

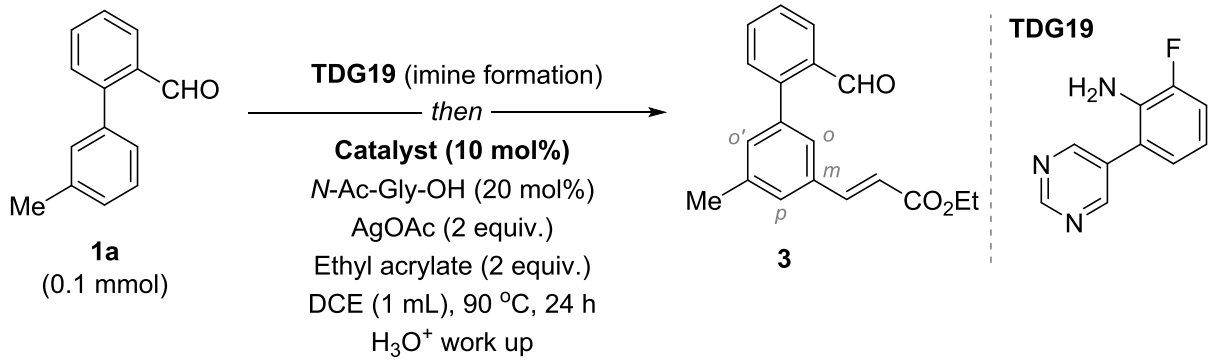


Entry	Solvent (1 mL)	Yield (*m*:others)[a]
1	HFIP	20% (5:1)
2	**DCE**	**38% (8:1)**
3	DCE (1 mL):HFIP (10 µL)	15% (5:1)
4	DCE (1 mL):HFIP (20 µL)	15% (5:1)
5	DCE (1 mL):HFIP (30 µL)	11% (5:1)
6	DCE (1 mL):HFIP (40 µL)	15% (5:1)
7	DCE (1 mL):HFIP (50 µL)	17% (5:1)

8	DCE (1 mL):HFIP (75 µL)	13% (5:1)
9	DCE (0.9 mL):HFIP (100 µL)	9% (4:1)
10	DCE (0.8 mL):HFIP (200 µL)	12% (5:1)
11	DCE (0.7 mL):HFIP (300 µL)	8% (4:1)
12	TFE	18% (3:1)
13	MeCN	11% (3:1)
14	1,4-Dioxane	5% (2:1)
15	TFT	3% (1:1)
16	^{i}PrOH	nd
17	DCM	8% (3:1)
18	THF	2% (1:1)
19	DMF	nd
20	$CHCl_3$	15% (4:1)
21	1,2-dibromoethane	13% (2:1)
22	2-Ethoxy ethanol	nd
23	EtOAc	6% (4:1)
24	1,2,3-TCP	20% (5:1)
25	Acetone	nd
26	Isoamyl alcohol	nd
27	CCl_4	nd
28	Cyclohexane	nd

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

Table S4: Catalyst optimization

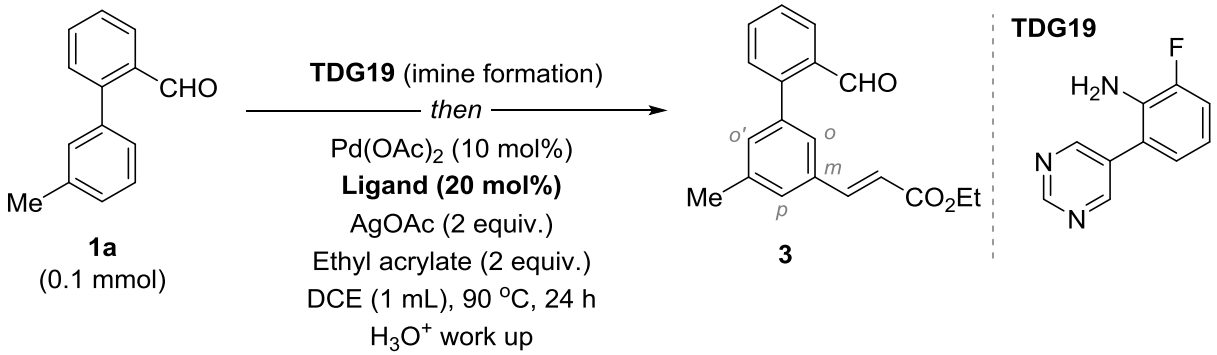


Entry	Catalyst	Yield (*m*:others)[a]
1	**$Pd(OAc)_2$**	**38% (8:1)**
2	$Pd(acac)_2$	18% (6:1)

3	$Pd(TFA)_2$	19% (3:1)
4	$Pd(OPiv)_2$	15% (5:1)
5	$Pd(CH_3CN)_2Cl_2$	8% (3:1)
6	$Pd(PPh_3)_4$	nd
7	$Pd_2(dba)_3$	nd
8	$PdCl_2(PPh_3)_2$	nd
9	$Pd(PhCN)_2Cl_2$	trace
10	$Pd(COD)Cl_2$	nd

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

Table S5: Ligand optimization

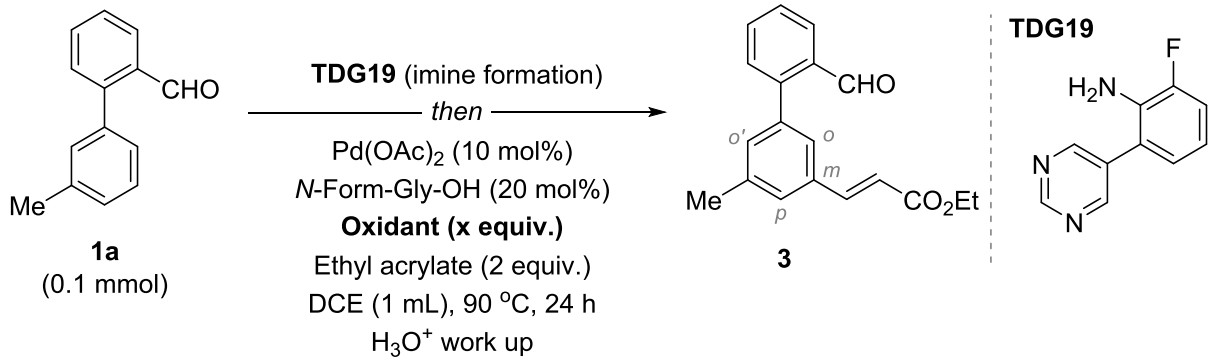


Entry	Ligand	Yield (*m*:others)[a]
1	*N*-Ac-Gly-OH	38% (8:1)
2	***N*-Form-Gly-OH**	**44% (12:1)**
3	2-Hydroxy-5-nitro pyridine	5% (2:1)
4	*N*-Ac-Nle-OH	18% (7:1)
5	*N*-Ac-Leu-OH	21% (8:1)
6	*N*-Ac-Val-OH	22% (5:1)
7	*N*-Ac-Ala-OH	18% (9:1)
8	*N*-Ac-Phg-OH	3% (2:1)
9	*N*-Ac-Trp-OH	2% (2:1)
10	Carbobenzoxy-Val-OH	nd
11	*N*-Boc-L-Alanine	10% (5:1)
12	*N*-Fmoc-L-Leucine	1%
13	*N*-Ac-L-Glutamic acid	3%
14	*N*-Boc-L-Phenylalanine	9% (4:1)
15	*N*-Ac-L-Histidine	1%
16	*N*-Boc-L-*tert*-Leucine	nd
17	*N*-Benzoyl-Leucine	2% (1:1)
18	*N*-Boc-L-Isoleucine	8% (2:1)
19	*N*-Benzoyl-Valine	2% (2:1)

20	*N*-Benzoyl-Phenylalanine	nd
21	2-hydroxypyridine	trace
22	2-Hydroxy-3-nitro pyridine	5% (2:1)
23	2-Hydroxy-6-methyl pyridine	nd
24	5-Chloro-2-hydroxy pyridine	trace
25	5-Chloro-2-hydroxy-3-nitro pyridine	nd
26	2-Hydroxy-4-methyl-5-nitro pyridine	trace
27	3-Methyl-2-hydroxy-5-nitro pyridine	trace
28	2-hydroxy-5-methyl-3-nitro pyridine	trace
29	2-hydroxy-5-trifluromethyl pyridine	16% (4:1)
30	2-hydroxy-4-methoxy-3-nitrile pyridine	8% (3:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

Table S6: Oxidant optimization

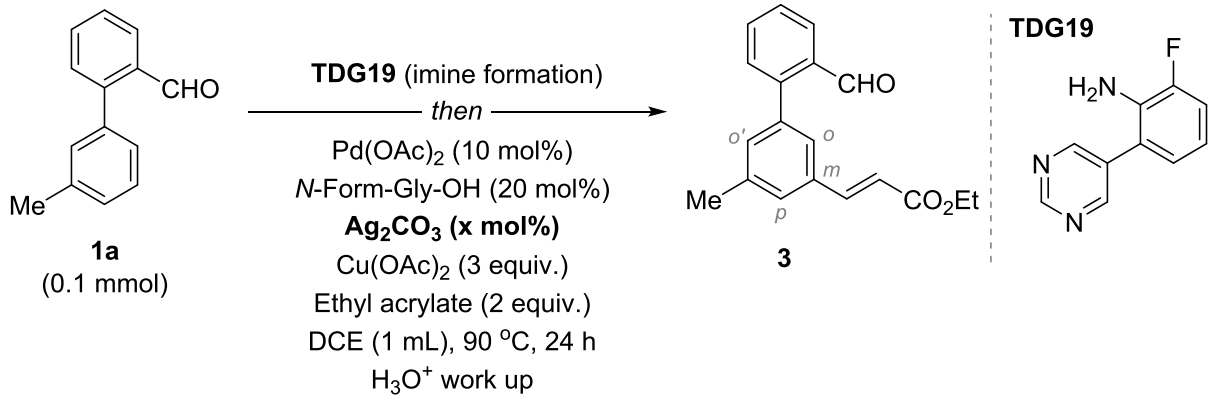


Entry	Oxidant (2 equiv.)	Yield (*m*:others)[a]
1	AgTFA	12% (1:1)
2	Ag_2CO_3	48% (12:1)
3	AgOAc	44% (12:1)
4	CuOTf	nd
5	Ag_2SO_4	22% (6:1)
7	$AgNO_3$	nd
8	$Cu(OAc)_2$	15% (6:1)
12	$Cu_2Cr_2O_5$	16% (2:1)
15	$CuCl_2$	nd
21	Ag_2CO_3:$Cu(OAc)_2$ (1:1)	43% (8:1)
22	Ag_2CO_3:$Cu(OAc)_2$ (1:2)	49% (8:1)
23	**Ag_2CO_3:$Cu(OAc)_2$ (1:3)**	**62% (12:1)**
24	Ag_2CO_3:$Cu(OAc)_2$ (2:1)	42% (7:1)
25	Ag_2CO_3:$Cu(OAc)_2$ (2:2)	44% (8:1)
26	Ag_2CO_3:$Cu(OAc)_2$ (2:3)	51% (10:1)

27	Ag_2CO_3:$Cu(OAc)_2$ (3:1)	46% (10:1)
28	Ag_2CO_3:$Cu(OAc)_2$ (3:2)	44% (5:1)
29	Ag_2CO_3:$Cu(OAc)_2$ (3:3)	38% (5:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

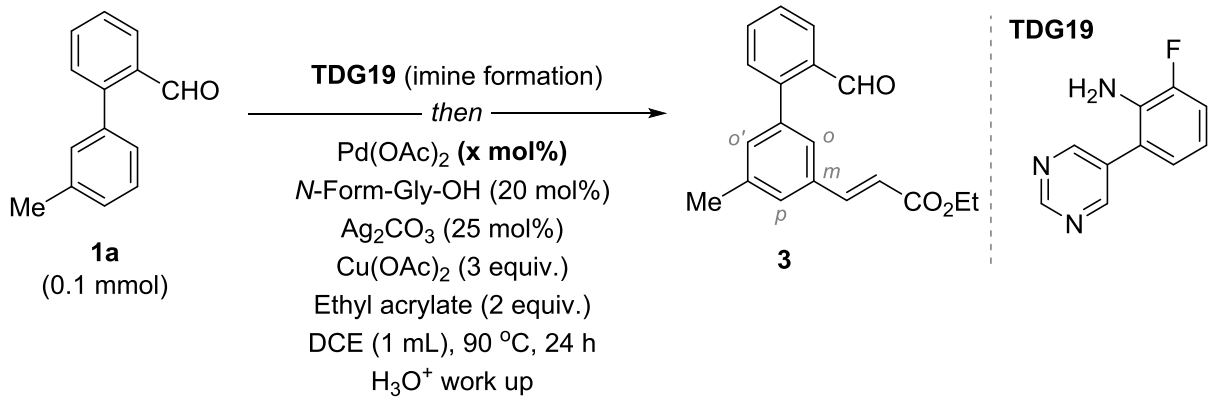
Table S7: Optimization of Ag_2CO_3 loading



Entry	Ag_2CO_3 (x mol%)	Yield (*m*:others)[a]
1	Without Ag_2CO_3	15% (6:1)
2	7 mol%	22% (10:1)
3	15 mol%	32% (13:1)
4	20 mol%	55% (14:1)
5	**25 mol%**	**65% (15:1)**
6	50 mol%	63% (15:1)
7	75 mol%	58% (14:1)
8	100 mol%	62% (12:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

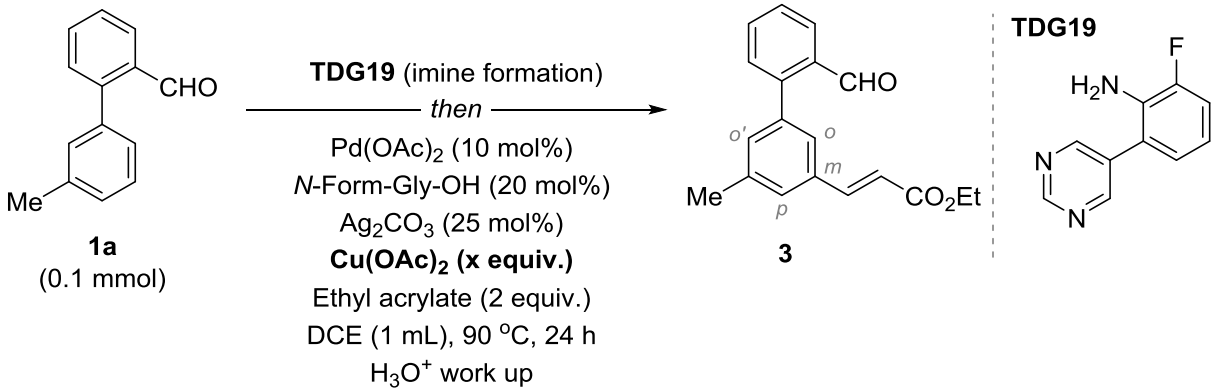
Table S8: Optimization of $Pd(OAc)_2$ loading



Entry	$Pd(OAc)_2$	Yield (*m*:others)[a]
1	1 mol%	5% (5:1)
2	2 mol%	8% (6:1)
3	3 mol%	16% (5:1)
4	4 mol%	19% (11:1)
5	5 mol%	26% (14:1)
6	6 mol%	38% (13:1)
7	7 mol%	53% (12:1)
8	8 mol%	62% (15:1)
9	9 mol%	63% (15:1)
10	**10 mol%**	**65% (15:1)**

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

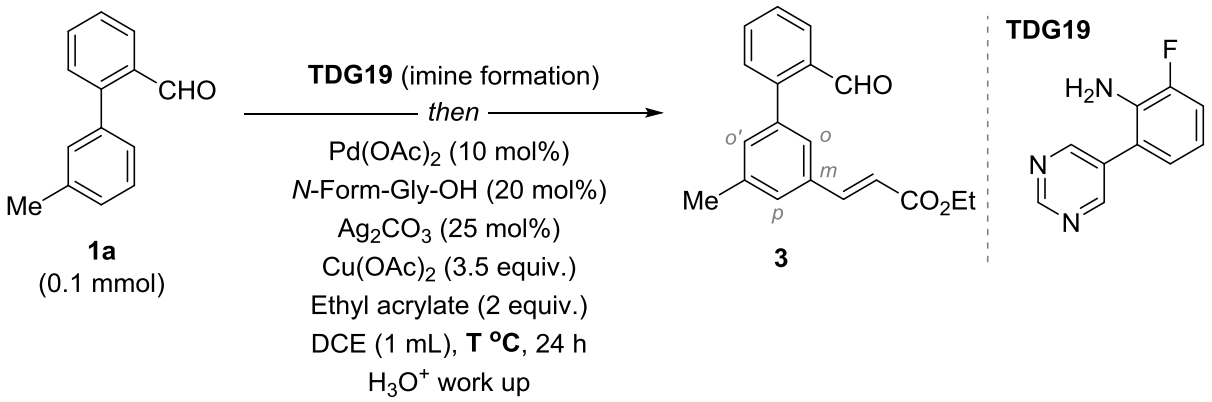
Table S9: Optimization of $Cu(OAc)_2$ loading



Entry	$Cu(OAc)_2$ (x equiv.)	Yield (*m*:others)[a]
1	0.5	43% (12:1)
2	1	48% (13:1)
3	1.5	50% (15:1)
4	2	55% (14:1)
5	2.5	62% (15:1)
6	3	65% (15:1)
7	**3.5**	**68% (15:1)**
8	4	66% (14:1)
9	5	59% (11:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

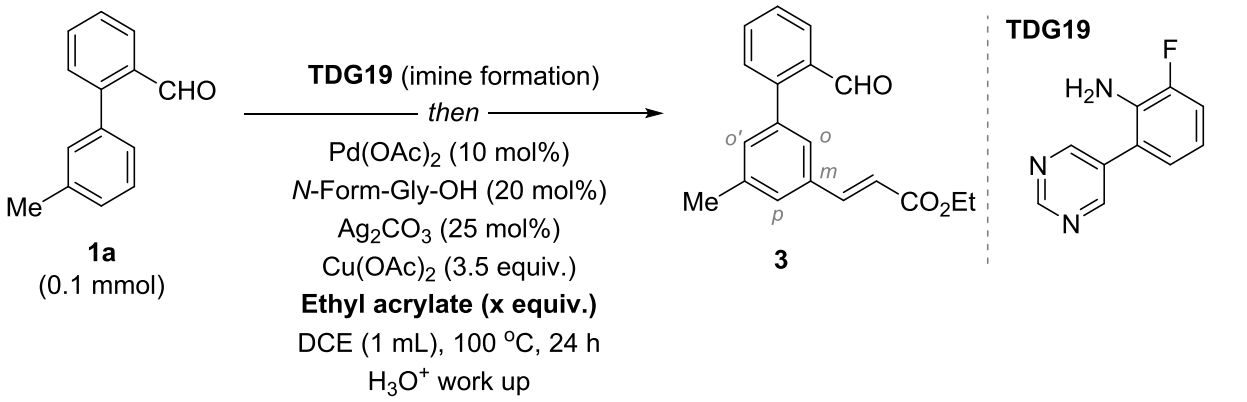
Table S10: Temperature optimization



Entry	Temperature (°C)	Yield (*m*:others)[a]
1	RT	nd
2	60	33% (15:1)
3	70	47% (15:1)
4	80	61% (15:1)
5	90	68% (15:1)
6	**100**	**72% (15:1)**
7	110	69% (11:1)
8	120	64% (9:1)
9	130	53% (8:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

Table S11: Optimization of olefin amount



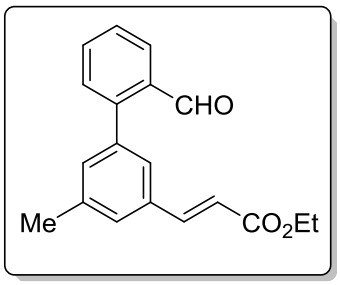
Entry	Ethyl acrylate (x equiv.)	Yield (*m*:others)[a]
1	1	43% (15:1)
2	1.5	58% (15:1)
3	2	72% (15:1)
4	2.5	74% (15:1)
5	**3**	**77% (15:1)**
6	3.5	76% (15:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. nd, not detected.

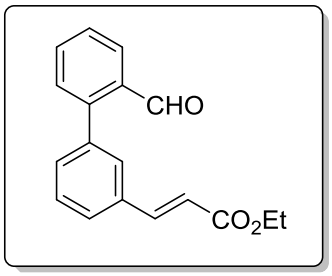
2.7 General procedure D: Procedure for *meta*-olefination of 2-phenylbenzaldehyde substrates:

An oven-dried screw capped reaction tube with a magnetic stir-bar was charged with 2-phenylbenzaldehyde (0.2 mmol) (viscous biphenyl aldehyde was weighed first), and **TDG19** (0.19 mmol, 36 mg) under air, followed by isopropyl alcohol (2 mL). The reaction mixture was stirred at 80 °C for 2 hours. The mixture was allowed to cool down and almost full conversion was observed in thin layer chromatography. Next, solvent was concentrated in vacuo and washed with pentane. The dry crude solid residue was subjected to $Pd(OAc)_2$ (10 mol%, 0.02 mmol, 4.5 mg), *N*-formyl glycine (*N*-Form-Gly-OH; 20 mol%, 8.3 mg), Ag_2CO_3 (25 mol%, 0.05 mmol, 14 mg) and $Cu(OAc)_2$ (3.5 equiv., 0.7 mmol, 127 mg) in the same reaction tube. Solvent 1,2-dichloroethane (DCE, 2 mL) was added in the reaction tube followed by addition of liquid alkene (3 equiv., 0.6 mmol) by micropipette under air (solid alkenes were weighed before adding solvent). The reaction tube was screwed by a cap fitted with a rubber septum and was vigorously stirred in a preheated oil bath at 100 °C. The reaction mixture was taken out after 24 h, diluted with 10 mL ethyl acetate and filtered through a celite pad. Next, the filtrate mixture was treated with 1 (M) HCl solution and stirred for ten minutes. Organic layer was separated and concentrated under vacuum. The crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

2.8 Characterization data for *meta*-olefination products of 2-phenylbenzaldehydes

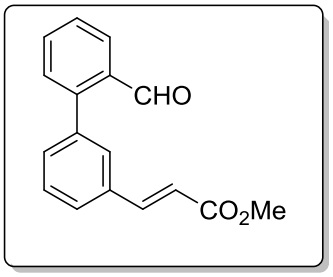


Ethyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **3** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 74% (43.6 mg isolated; *m*:others = 15:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.03 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.70 (d, *J* = 16.0 Hz, 1H), 7.65 (td, *J* = 7.5, 1.5 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.45 – 7.42 (m, 1H), 7.41 (s, 1H), 7.34 (s, 1H), 7.21 (s, 1H), 6.47 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.44 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.34, 167.01, 145.44, 144.14, 139.07, 138.71, 134.95, 133.96, 133.87, 132.82, 130.88, 128.58, 128.28, 127.94, 126.96, 119.41, 60.80, 21.54, 14.52.
IR (thin film, cm^{-1}): 1037, 1095, 1177, 1262, 1367, 1464, 1596, 1639, 1694.91, 2752, 2854, 2925.
HRMS (*m/z*): [M+Na^+] calcd for $C_{19}H_{18}NaO_3$: 317.1148; found, 317.1152.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).

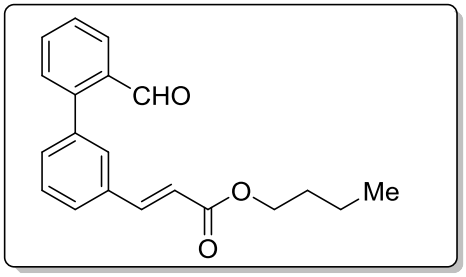


***Ethyl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **4** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 71% (39 mg isolated; *m*:others = 13:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 16.0 Hz, 1H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 6.6 Hz, 2H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.22, 166.96, 145.23, 143.97, 138.81, 135.05, 133.95, 133.93, 131.97, 130.93, 129.62, 129.21, 128.41, 128.09, 127.85, 119.65, 60.87, 14.51.
IR (thin film, cm^{-1}): 1036, 1100, 1179, 1262, 1367, 1467, 1597, 1639, 2856, 2926.

HRMS (ESI): [M+Na$^+$] calcd for $C_{18}H_{16}NaO_3$: 303.0997; found: 303.0993.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).

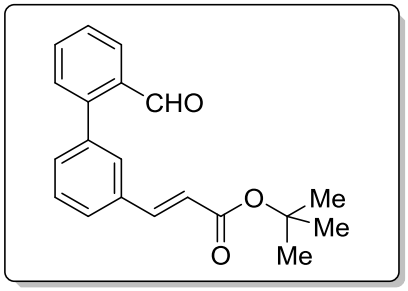


***Methyl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **5** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 64% (34 mg isolated; *m*:others = 10:1)
^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 9.98 (s, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 16.0 Hz, 1H), 7.67 (t, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 7.5 Hz, 1H), 7.55 – 7.48 (m, 3H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.40 (d, *J* = 7.5 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 3.82 (s, 3H).
^{13}C NMR (126 MHz, CDCl$_3$) δ (ppm) 192.18, 167.39, 145.19, 144.28, 138.84, 134.97, 133.94, 132.06, 130.93, 129.63, 129.22, 128.43, 128.11, 127.87, 119.16, 52.03
IR (thin film, cm^{-1}): 1034, 1103, 1170, 1195, 1274, 1322, 1394, 1435, 1596, 1639, 1692, 1718, 2752, 2852, 2951, 3062.
HRMS (ESI): [M+Na$^+$] calcd for $C_{17}H_{14}NaO_3$: 289.0835; found: 289.0833.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

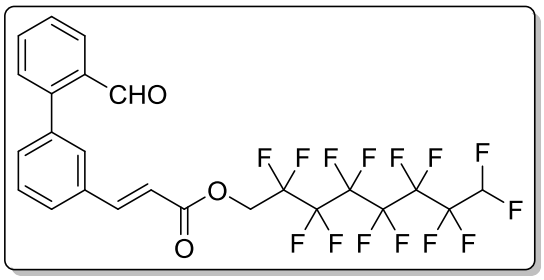


Butyl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **6** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 55% (34 mg isolated; *m*:others = 12:1)
^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 9.98 (s, 1H), 8.04 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.72 (d, *J* = 16.0 Hz, 1H), 7.66 (td, *J* = 7.5, 1.4 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.48 (m, 3H), 7.44 (d, *J* = 7.0 Hz, 1H), 7.39 (d, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 4.22 (t, *J* = 6.7 Hz, 2H), 1.73 – 1.65 (m, 3H), 1.47 – 1.41 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, CDCl$_3$) δ (ppm) 192.34, 166.46, 142.73, 136.66, 135.30, 130.65, 130.24, 129.33, 127.04, 126.46, 120.18, 60.73, 14.12.

IR (thin film, cm^{-1}): 1025, 1064, 1171, 1259, 1301, 1392, 1467, 1597, 1639, 1693, 2752, 2854, 2927, 2959, 3060.
HRMS (ESI): [M+H$^+$] calcd for for $C_{20}H_{21}O_3$: 309.1485, found 309.1489.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

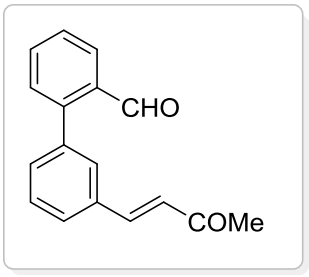


Butyl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **7** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 52% (32 mg isolated; *m*:others = 12:1)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.04 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 7.5 Hz, 1H), 6.42 (d, *J* = 16.0 Hz, 1H), 1.53 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.30, 166.26, 145.33, 142.90, 138.68, 135.21, 133.93, 131.70, 130.93, 129.51, 129.16, 128.36, 128.01, 127.81, 121.56, 80.97, 28.39.
IR (thin film, cm^{-1}): 696, 764, 801, 848, 980, 1030, 1103, 1150, 1196, 1257, 1298, 1323, 1368, 1392, 1473, 1597, 1638, 1695, 2851.
HRMS (ESI): [M+H$^+$] calcd for $C_{20}H_{21}O_3$: 309.1485, found 309.1490.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

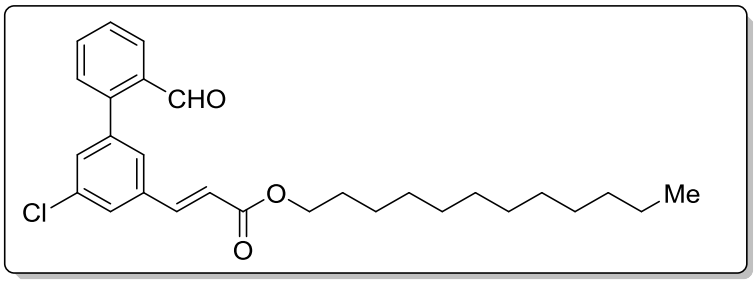


2,2,3,3,4,4,5,5,6,6,7,7,8,8-tetradecafluorooctyl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **8** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 58% (71 mg isolated; *m*:others = 10:1)
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.00 (s, 1H), 8.07 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.85 (d, *J* = 16.0 Hz, 1H), 7.69 (td, *J* = 7.5, 1.3 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.59 (d, *J* = 4.4 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 2H), 7.49 – 7.44 (m, 2H), 6.59 – 6.54 (m, 1H), 6.20 – 5.97 (m, 1H), 4.75 (t, *J* = 13.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 191.88, 164.94, 146.42, 144.76, 138.81, 134.18, 133.7 (d, *J* = 6.65 Hz, C-F), 132.42, 130.72, 129.62, 129.11, 128.31, 127.9 (d, *J* = 3.5 Hz, C-F), 116.96, 107. 5, 59.71 (t, *J* = 26.5 Hz, C-F).
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -119.39, -122.15, -123.33, -123.47, -129.39, -137.00.
IR (thin film, cm^{-1}): 1082, 1140, 1195, 1261, 1301, 1395, 1598, 1638, 1694, 1735, 2756, 2852.
HRMS (ESI): [M+Na^+] calcd for $C_{23}H_{14}F_{12}NaO_3$: 589.0644; found 589.0636.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

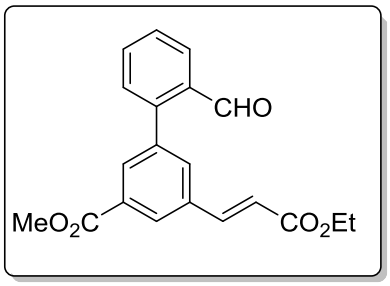


***(E)-3'-(3-oxobut-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **9** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: Colorless oil.
Yield: 67% (34 mg isolated; *m*:others = 20:1)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.04 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.67 (td, *J* = 7.5, 1.3 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 16.3 Hz, 1H), 7.54 (s, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 16.3 Hz, 1H), 2.39 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.17, 191.98, 144.91, 142.53, 138.69, 134.78, 133.77, 133.70, 132.00, 130.72, 129.67, 129.11, 128.26, 127.95, 127.93, 127.82, 27.74.
IR (thin film, cm^{-1}): 1104, 1197. 1258, 1359, 1394, 1414, 1473, 1597, 1690, 2751, 2849.
HRMS (ESI): [M+Na^+] calcd for $C_{17}H_{14}NaO_2$: 273.0886, found 273.0888.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

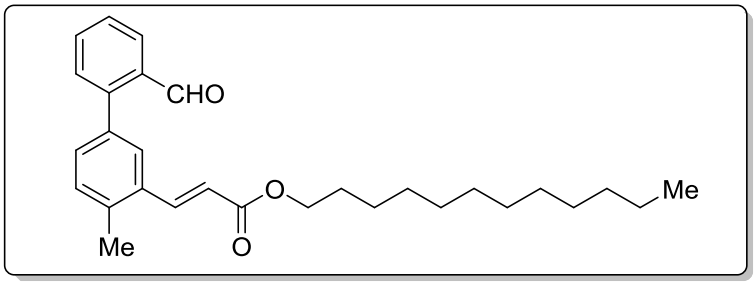


***Ethyl (E)-3-(5-chloro-2'-formyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **10** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: colorless oil.
Yield: 63% (57 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.05 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.67 (ddd, *J* = 7.5, 5.9, 1.4 Hz, 2H), 7.60 (d, *J* = 13.8 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.43 – 7.38 (m, 3H), 6.49 (d,

J = 16.0 Hz, 1H), 4.20 (t, *J* = 6.7 Hz, 2H), 1.73 – 1.66 (m, 2H), 1.42 – 1.34 (m, 2H), 1.27 – 1.24 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 191.62, 166.63, 143.66, 142.41, 140.51, 136.61, 135.34, 134.06, 133.86, 131.34, 130.83, 128.92, 128.45, 127.95, 127.51, 121.09, 65.26, 32.13, 29.86, 29.84, 29.80, 29.75, 29.56, 29.49, 28.89, 26.18, 22.90, 14.33.
IR (thin film, cm^{-1}): 3503, 2925, 2854, 2751, 1711, 1639, 1598, 1465, 1390, 1321, 1275, 1176, 981.
HRMS (ESI): [M+H$^+$] calcd for $C_{28}H_{36}ClO_3$: 454.2282; found 454.2285.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

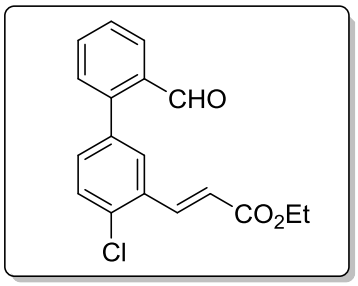


***Methyl (E)-5-(3-ethoxy-3-oxoprop-1-en-1-yl)-2'-formyl-[1,1'-biphenyl]-3-carboxylate*:** Compound **11** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: colorless oil.
Yield: 53% (36 mg isolated; *m*:others = 5:1)
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.96 (s, 1H), 8.28 (s, 1H), 8.10 – 8.05 (m, 2H), 7.75 (d, *J* = 16.1 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 6.57 (d, *J* = 16.1 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.96 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.64, 166.63, 166.27, 144.04, 142.83, 139.32, 135.44, 134.09, 133.88, 133.54, 132.32, 131.44, 131.02, 128.86, 128.64, 128.59, 120.89, 61.00, 52.78, 14.49.
IR (thin film, cm^{-1}): 1924, 1775, 1667, 1450, 1434, 1392, 1352, 1345, 1341, 1325, 1312, 1296, 1298, 1289, 1287, 1280, 1198.
HRMS (ESI): [M+H$^+$] calcd for $C_{20}H_{19}O_5$: 339.1227; found 339.1229.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

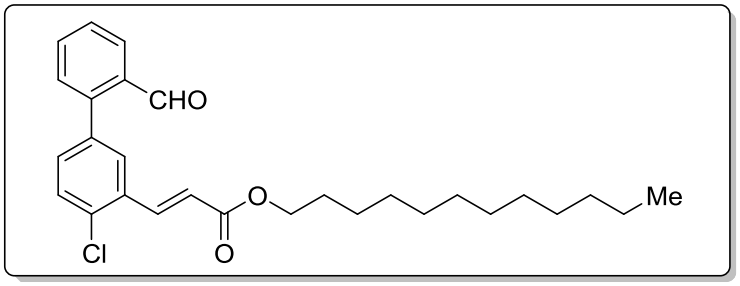


***Dodecyl (E)-3-(2'-formyl-4-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **12** was prepared by general procedure D (0.2 mmol scale).

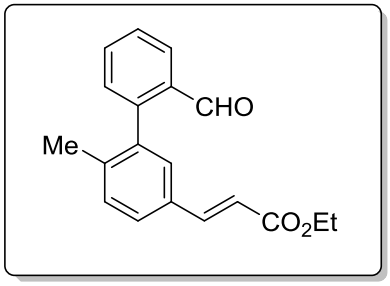
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: yellow oil.
Yield: 62% (54 mg isolated; *m*:others = 6:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.99 (s, 1H), 8.04 – 7.98 (m, 2H), 7.65 (td, *J* = 7.5, 1.4 Hz, 1H), 7.56 (s, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.9 Hz, 1H), 7.29 (dd, *J* = 6.5, 4.8 Hz, 2H), 6.39 (d, *J* = 15.9 Hz, 1H), 2.51 (s, 3H), 1.72 – 1.65 (m, 2H), 1.42 – 1.36 (m, 2H), 1.27 – 1.24 (m, 16H), 0.89 – 0.87 (m, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.40, 167.13, 163.09, 145.39, 141.79, 137.81, 136.17, 133.96, 133.89, 131.62, 131.13, 130.94, 130.25, 129.37, 128.17, 128.07, 127.76, 120.57, 65.07, 32.13, 29.86, 29.84, 29.80, 29.76, 29.56, 29.50, 28.93, 26.20, 22.90, 19.78, 14.33.
IR (thin film, cm^{-1}): 1045, 1174, 1215, 1251, 1376, 1467, 1597, 1637, 1697, 1716, 2855, 2926, 3022.
HRMS (ESI): [M+ Na^+] calcd for $C_{29}H_{38}NaO_3$: 457.2716; found, 457.2713.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



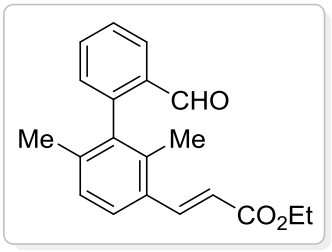
Ethyl (E)-3-(4-chloro-2'-formyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **13** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: yellow oil.
Yield: 68% (43 mg isolated; *m*:others > 20:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.75 (s, 1H), 8.12 (d, *J* = 16.0 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.32 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 191.83, 166.48, 144.02, 139.99, 137.27, 135.19, 134.08, 133.90, 133.23, 132.48, 130.90, 130.44, 129.13, 128.75, 128.52, 122.14, 61.06, 14.52.
IR (thin film, cm^{-1}): 2926, 2854, 2753, 1715, 1639, 1598, 1465, 1392, 1367, 1274, 1094, 1043, 980.
HRMS (ESI): [M+Na^+] calcd for $C_{18}H_{16}ClNaO_3$: 315.0782; found, 315.0781.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



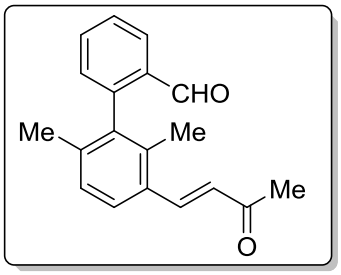
***(E)-4'-chloro-3'-(3-oxopentadec-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **14** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 60% (53 mg isolated; *m*:others =15:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.01 (s, 1H), 8.15 (d, *J* = 16.0 Hz, 1H), 8.07 (d, *J* = 7.7 Hz, 1H), 7.69 (td, *J* = 7.7, 2.0 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.61 – 7.53 (m, 2H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.35 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 4.24 (t, *J* = 6.7 Hz, 2H), 1.76 – 1.69 (m, 2H), 1.45 – 1.39 (m, 2H), 1.33 – 1.24 (m, 16H), 0.90 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 191.80, 166.55, 144.01, 139.94, 137.23, 135.17, 134.04, 133.87, 133.20, 132.44, 130.88, 130.40, 129.08, 128.72, 128.48, 122.11, 65.25, 32.12, 29.86, 29.84, 29.79, 29.75, 29.56, 29.49, 28.88, 26.17, 22.90, 14.33.
IR (thin film, cm^{-1}): 3503, 2925, 2854, 2751, 1711, 1639, 1598, 1465, 1390, 1321, 1275, 1176.
HRMS (ESI): [M+Na^+] calcd for $C_{28}H_{35}ClNaO_3$: 477.2166; found, 477.2168.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



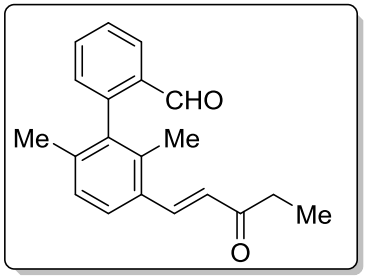
***Ethyl (E)-3-(2'-formyl-6-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **15** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: yellow oil.
Yield: 65% (38 mg isolated; *m*:others = 3:1)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.76 (s, 1H), 8.06 – 8.01 (m, 2H), 7.65 (t, *J* = 4.5 Hz, 2H), 7.51 (dd, *J* = 6.9, 5.0 Hz, 2H), 7.37 (d, *J* = 1.7 Hz, 1H), 7.34 – 7.30 (m, 2H), 6.42 (d, *J* = 16.0 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 2.11 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.86, 166.93, 144.61, 143.80, 142.38, 138.80, 138.31, 133.94, 130.72, 130.66, 129.64, 128.22, 127.80, 127.50, 120.80, 118.28, 60.51, 20.36, 14.31.
IR (thin film, cm^{-1}): 1036, 1096, 1174, 1265, 1318, 1366, 1392, 1448, 1597, 1637, 1711, 2750, 2843, 2936, 2984.
HRMS (*m/z*): [M+Na^+] calcd for $C_{19}H_{18}NaO_3$: 317.1148; found, 317.1148.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



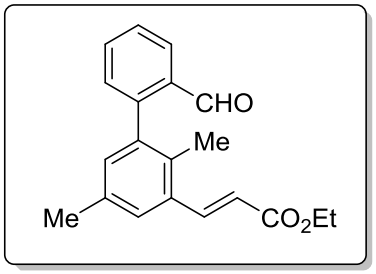
Ethyl (E)-3-(2'-formyl-2,6-dimethyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **16** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (93/7, v/v).
Physical State: Yellow oil.
Yield: 66% (43 mg isolated; *m*:others = 8:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.65 (s, 1H), 8.05 (dd, *J* = 7.8, 1.1 Hz, 1H), 8.00 (d, *J* = 15.8 Hz, 1H), 7.69 (td, *J* = 7.5, 1.4 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.18 (t, *J* = 7.8 Hz, 2H), 6.38 (d, *J* = 15.8 Hz, 1H), 4.27 (q, *J* = 7.1, Hz, 2H), 2.04 (s, 3H), 1.96 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.81, 167.03, 144.63, 142.50, 138.65, 138.17, 135.76, 134.54, 133.70, 131.83, 130.49, 128.08, 127.83, 127.72, 126.35, 119.63, 60.52, 21.36, 17.41, 14.35.
IR (thin film, cm^{-1}): 982, 1038, 1095, 1163, 1253, 1311, 1366, 1390, 1447, 1597, 1632, 1697, 2744, 2852, 2926, 2980.
HRMS (*m/z*): [M+Na^+] calcd for $C_{20}H_{20}NaO_3$: 331.1305; found, 331.1302.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



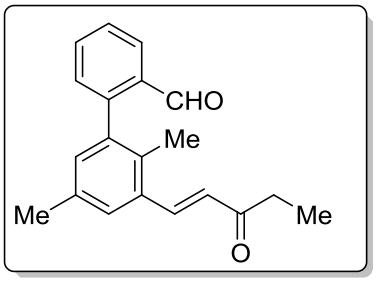
***(E)-2',6'-dimethyl-3'-(3-oxobut-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **17** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: colorless oil.
Yield: 63% (34 mg isolated; *m*:others = 8:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.65 (s, 1H), 8.06 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.85 (d, *J* = 16.0 Hz, 1H), 7.70 (td, *J* = 7.5, 1.4 Hz, 1H), 7.56 (d, *J* = 7.9 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.21 – 7.17 (m, 2H), 6.67 (d, *J* = 16.0 Hz, 1H), 2.40 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.34, 191.79, 144.50, 141.13, 139.01, 138.32, 135.99, 134.59, 133.68, 131.73, 130.48, 128.38, 128.15, 127.95, 127.84, 126.36, 27.86, 21.40, 17.38.
IR (thin film, cm^{-1}): 1043.32, 1113, 1195, 1253, 1360, 1448, 1597, 1695, 2746, 2923, 2987.
HRMS (ESI): [M+Na^+] calcd for $C_{19}H_{18}NaO_2$: 01.1199; found 301.1198.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



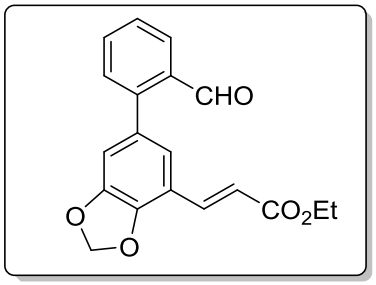
(E)-2',6'-dimethyl-3'-(3-oxopent-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde:
Compound **18** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 61% (36 mg isolated; *m*:others = 7:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.65 (s, 1H), 8.05 (d, *J* = 7.8 Hz, 1H), 7.89 (d, *J* = 15.9 Hz, 1H), 7.70 (td, *J* = 7.5, 1.3 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.19 (d, *J* = 4.7 Hz, 1H), 7.17 (d, *J* = 5.3 Hz, 1H), 6.69 (d, *J* = 15.9 Hz, 1H), 2.71 (q, *J* = 7.3 Hz, 2H), 2.05 (s, 3H), 1.97 (s, 3H), 1.18 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 201.03, 192.08, 145.40, 140.00, 138.66, 135.38, 134.37, 133.93, 133.85, 132.92, 132.80, 130.82, 128.03, 128.00, 127.32, 127.17, 34.46, 20.91, 16.61, 8.23.
IR (thin film, cm^{-1}): 1046, 1122, 1195, 1265, 1392, 1456, 1598, 1695, 2745, 2855, 2926.
HRMS (ESI): [M+Na$^+$] calcd for $C_{20}H_{20}NaO_2$: 315.1356; found 315.1354.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



***Ethyl (E)-3-(2'-formyl-2,5-dimethyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **19** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 51% (31 mg isolated; *m*:others = 6:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.79 (s, 1H), 8.09 – 7.98 (m, 2H), 7.67 (td, *J* = 7.5, 1.4 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.46 (s, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.06 (s, 1H), 6.44 (d, *J* = 15.8, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.37 (s, 3H), 2.12 (s, 3H), 1.38 (t, *J* = 7.1, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.05, 166.91, 145.41, 142.54, 138.58, 135.34, 134.26, 133.95, 133.80, 132.67, 130.82, 127.99, 127.28, 120.46, 60.58, 20.88, 16.60, 14.34.
IR (thin film, cm^{-1}): 1039, 1095, 1177, 1262, 1301, 1367, 1391, 1456, 1598, 1635, 1698, 2748, 2854, 2925.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{20}H_{20}NaO_3$: 331.1305; found, 331.1305.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

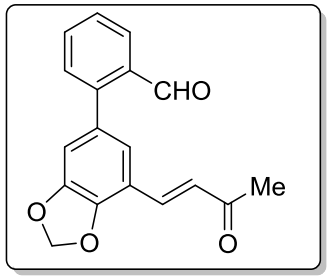


(E)-2',5'-dimethyl-3'-(3-oxopent-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde:
Compound **20** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 62% (36 mg isolated; *m*:others = 7:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.75 (s, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 15.6 Hz, H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.52 (t, *J* = 5.9 Hz, 1H), 7.45 (s, 1H), 7.28 (d, *J* = 9.1 Hz, 1H), 7.06 (s, 1H), 6.71 (d, *J* = 15.6 Hz, 1H), 2.72 (q, *J* = 7.3 Hz, 2H), 2.35 (s, 3H), 2.10 (s, 3H), 1.19 (t, *J* = 7.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 200.90, 191.83, 144.58, 140.00, 138.82, 138.27, 136.06, 134.58, 133.68, 131.93, 130.48, 128.12, 127.87, 127.79, 127.29, 126.28, 34.40, 21.39, 17.40, 8.26.
IR (thin film, cm^{-1}): 1036, 1121, 1194, 1258, 1356, 1449, 1608, 1667, 1695, 2745, 2853, 2938, 2977.
HRMS (ESI): [M+Na$^+$] calcd for $C_{20}H_{20}NaO_2$: 315.1356; found 315.1354.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

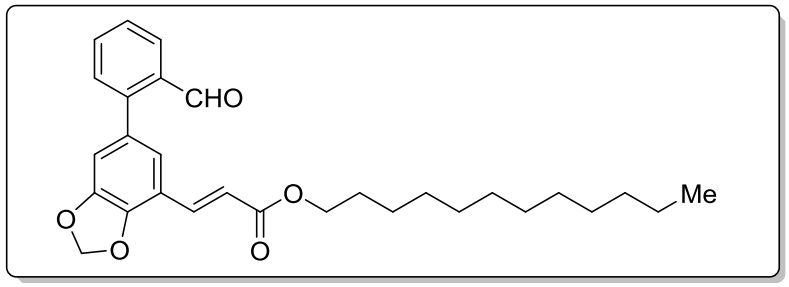


***Ethyl (E)-3-(6-(2-formylphenyl)benzo[d][1,3]dioxol-4-yl)acrylate*:** Compound **21** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (65/4, v/v).
Physical State: Yellow oil.
Yield: 71% (46 mg isolated; *m*:others = 4:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.03 (s, 1H), 8.03 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.67 – 7.65 (m, 1H), 7.64 – 7.62 (m, 1H), 7.52 (t, *J* = 7.1 Hz, 1H), 7.43 (d, *J* = 7.7 Hz, 1H), 6.92 (d, *J* = 1.6 Hz, 1H), 6.89 (d, *J* = 1.7 Hz, 1H), 6.71 (d, *J* = 16.1 Hz, 1H), 6.19 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.0, 166.9, 148.4, 146.6, 144.7, 138.3, 133.8, 133.6, 131.9, 130.6, 127.9, 127.8, 124.4, 122.0, 117.0, 111.2, 102.2, 60.6, 14.3.

IR (thin film, cm^{-1}): 1078, 1228, 1276, 1302, 1391, 1465, 1597, 1638, 1694, 2750, 2854, 2924, 3065.
HRMS (ESI): [M+Na$^+$] calcd for $C_{19}H_{16}NaO_5$: 347.0897; found, 347.0892.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

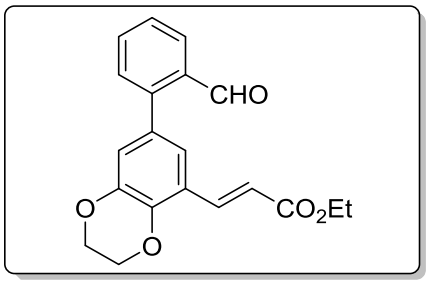


(E)-2-(7-(3-oxobut-1-en-1-yl)benzo[d][1,3]dioxol-5-yl)benzaldehyde:
Compound **22** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (956/4, v/v).
Physical State: Colorless oil.
Yield: 62% (36 mg isolated; *m*:others = 7:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.00 (s, 1H), 8.01 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.63 (td, *J* = 7.5, 1.4 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.46 (d, *J* = 16.4 Hz, 1H), 7.41 (dd, *J* = 7.7, 0.7 Hz, 1H), 6.96 – 6.88 (m, 3H), 6.17 (s, 2H), 2.38 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.43, 192.04, 148.46, 146.85, 144.65, 136.91, 133.85, 133.71, 132.06, 130.65, 130.14, 128.03, 127.94, 124.37, 116.97, 111.39, 102.25, 27.77.
IR (thin film, cm^{-1}): 1040, 1059, 1197, 1229, 1258, 1363, 1427, 1464, 1595, 1690, 2924, 3064.
HRMS (ESI): [M+Na$^+$] calcd for $C_{18}H_{14}NaO_4$: 317.0784; found 317.0789.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

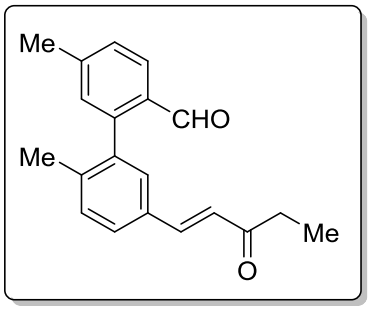


Dodecyl (E)-3-(6-(2-formylphenyl)benzo[d][1,3]dioxol-4-yl)acrylate: Compound **23** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: Yellow oil.
Yield: 68% (63 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.01 (s, 1H), 8.01 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.66 – 7.58 (m, 2H), 7.49 (dd, *J* = 9.7, 5.4 Hz, 1H), 7.40 (dd, *J* = 7.7, 0.8 Hz, 1H), 6.88 (dd, *J* = 12.9, 1.6 Hz, 2H), 6.68 (d, *J* = 16.1 Hz, 1H), 6.16 (s, 2H), 4.19 (t, *J* = 6.7 Hz, 2H), 1.74 – 1.61 (m, 2H), 1.43 – 1.36 (m, 2H), 1.28 – 1.24 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.24, 167.23, 148.62, 146.89, 144.95, 138.48, 134.07, 133.87, 132.13, 130.86, 128.17, 128.09, 124.66, 122.23, 117.26, 111.39, 102.41, 65.07, 32.12, 29.86, 29.84, 29.80, 29.74, 29.55, 29.50, 28.93, 26.18, 22.89, 14.32.
IR (thin film, cm^{-1}): 1078, 1168, 1228, 1276, 1302, 1361, 1391, 1426, 1465, 1597, 1638, 1694, 2750, 2854, 2924, 3064.
HRMS (ESI): [M+K$^+$] calcd for $C_{29}H_{36}KO_5$: 503.2192; found, 503.2194.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

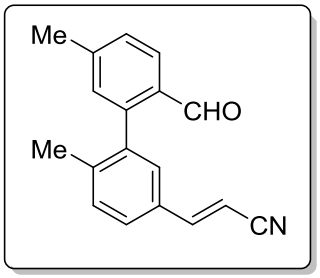


***Ethyl (E)-3-(7-(2-formylphenyl)-2,3-dihydrobenzo[b][1,4]dioxin-5-yl)acrylate*:** Compound **24** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: Colorless oil.
Yield: 67% (45 mg isolated; *m*:others = 15:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.04 (s, 1H), 8.03 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.94 (d, *J* = 16.2 Hz, 1H), 7.65 (td, *J* = 7.5, 1.4 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.54 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 6.96 (d, *J* = 2.1 Hz, 1H), 6.58 (d, *J* = 16.2 Hz, 1H), 4.46 – 4.42 (m, 2H), 4.37 – 4.35 (m, 2H), 4.28 (t, *J* = 7.1 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.26, 167.14, 144.76, 143.77, 142.87, 138.53, 133.73, 133.65, 130.63, 127.85, 127.74, 123.68, 122.67, 120.34, 64.59, 64.07, 60.53, 14.34.
IR (thin film, cm^{-1}): 1072, 1226, 1251, 1314, 1395, 1425, 1567, 1619, 1699, 2751, 2847, 2922, 3065.
HRMS (ESI): [M+H$^+$] calcd for $C_{20}H_{19}O_5$: 338.1159; found 338.1163.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

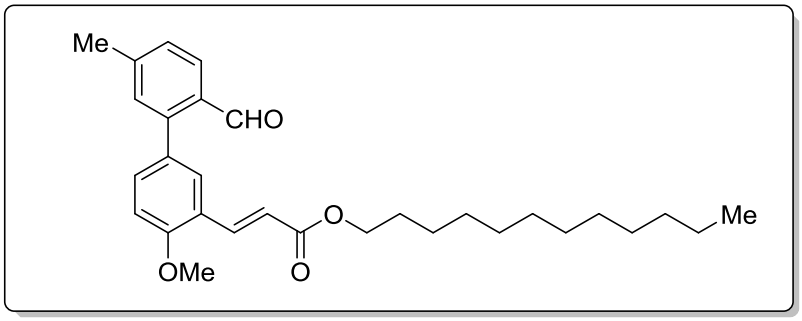


***(E)-2',5-dimethyl-5'-(3-oxopent-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **25** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: Colorless oil.

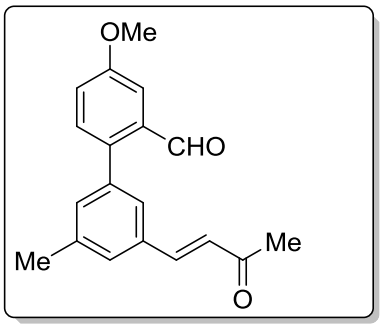
Yield: 69% (41 mg isolated; *m*:others = 5:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.96 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 15.9 Hz, 1H), 7.59 (s, 1H), 7.35 (d, *J* = 6.8 Hz, 1H), 7.32 (d, *J* = 4.7 Hz, 1H), 7.29 (d, *J* = 1.9 Hz, 1H), 7.26 (s, 1H), 6.72 (d, *J* = 16.0 Hz, 1H), 2.72 (q, *J* = 7.3 Hz, 2H), 2.53 (s, 3H), 2.50 (s, 3H), 1.20 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 200.70, 191.93, 145.31, 144.77, 139.01, 136.16, 133.76, 131.52, 131.32, 130.90, 129.98, 129.09, 128.90, 127.98, 127.66, 127.49, 34.76, 21.87, 19.59, 8.18.
IR (thin film, cm^{-1}): 1039, 1120, 1189, 1257, 1394, 1458, 1603, 1687, 2754, 2856, 2930, 2974, 3028.
HRMS (ESI): [M+Na$^+$] calcd for $C_{20}H_{20}NaO_2$: 315.1356; found 315.1354.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).



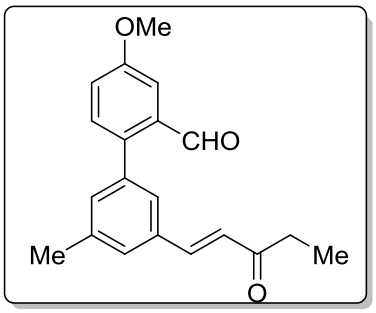
***(E)-3-(2'-formyl-5',6-dimethyl-[1,1'-biphenyl]-3-yl)acrylonitrile*:** Compound **26** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (96/4, v/v).
Physical State: Colorless oil.
Yield: 49% (26 mg isolated; *m*:others = 9:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.90 (s, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 16.6 Hz, 1H), 7.45 (s, 1H), 7.32 (d, *J* = 0.9 Hz, 2H), 7.27 (d, *J* = 0.7 Hz, 1H), 7.20 (s, 1H), 5.84 (d, *J* = 16.6 Hz, 1H), 2.48 (s, 3H), 2.47 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.70, 147.92, 144.83, 140.42, 137.06, 136.58, 132.72, 132.38, 131.45, 131.27, 131.07, 129.10, 128.26, 127.66, 126.81, 98.23, 21.72, 19.42.
IR (thin film, cm^{-1}): 1034, 1112, 1210, 1257, 1395, 1466, 1603, 1687, 2218, 2757, 2854, 2922.
HRMS (ESI): [M+Na$^+$] calcd for $C_{18}H_{15}NNaO$: 284.1045; found 284.1047.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).



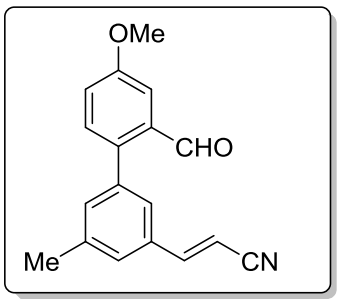
Dodecyl (E)-3-(2'-formyl-4-methoxy-5'-methyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **27** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: Colorless oil.
Yield: 66% (61 mg isolated; *m*:others = 6:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.94 (s, 1H), 8.01 (d, *J* = 16.2 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 2.2 Hz, 1H), 7.33 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.22 (s, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.56 (d, *J* = 16.2 Hz, 1H), 4.19 (t, *J* = 6.7 Hz, 2H), 3.96 (s, 3H), 2.46 (s, 3H), 1.73 – 1.65 (m, 2H), 1.43 – 1.36 (m, 2H), 1.28 – 1.24 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.14, 167.57, 158.39, 145.23, 144.89, 139.51, 133.13, 131.71, 131.55, 130.57, 130.31, 128.88, 128.21, 123.80, 119.95, 111.24, 64.92, 55.96, 32.12, 29.86, 29.83, 29.80, 29.75, 29.55, 29.51, 28.96, 26.19, 22.89, 22.04, 14.32.
IR (thin film, cm^{-1}): 1115, 1166, 1214, 1251, 1305, 1392, 1464, 1501, 1604, 1633, 1687, 2753, 2854, 2925, 3020.
HRMS (ESI): [M+Na$^+$] calcd for $C_{30}H_{40}NaO_4$: 487.2817; found, 487.2819.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).



(E)-4-methoxy-3'-methyl-5'-(3-oxobut-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde: Compound **28** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: Colorless oil.
Yield: 70% (41 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.93 (s, 1H), 7.53 (d, *J* = 16.3 Hz, 1H), 7.51 (d, *J* = 4.8 Hz, 1H), 7.41 (s, 1H), 7.36 (d, *J* = 8.7 Hz, 1H), 7.32 (s, 1H), 7.22 (d, *J* = 8.7 Hz, 1H), 7.19 (d, *J* = 8.7 Hz, 1H), 6.74 (d, *J* = 16.3 Hz, 1H), 3.91 (s, 3H), 2.44 (s, 3H), 2.39 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.27, 192.03, 159.40, 142.86, 138.92, 138.32, 138.23, 134.63, 134.55, 133.07, 131.98, 128.23, 127.70, 127.22, 121.49, 110.09, 55.67, 27.68.
IR (thin film, cm^{-1}): 1033, 1111, 1164, 1229, 1276, 1310, 1359, 1394 1438, 1465, 1498, 1605, 1686, 2756, 2853, 2928, 3007.
HRMS (ESI): [M+Na$^+$] calcd for $C_{19}H_{18}NaO_3$: 317.1148; found 317.1149.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

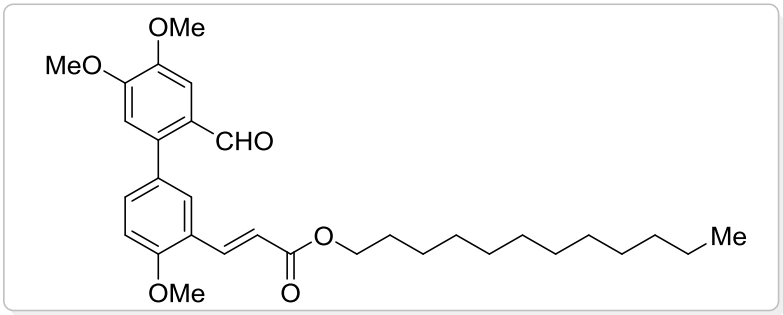


***(E)-4-methoxy-3'-methyl-5'-(3-oxopent-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde*:** Compound **29** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: Colorless oil.
Yield: 68% (42 mg isolated; *m*:others = 12:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.94 (s, 1H), 7.57 (d, *J* = 16.2 Hz, 1H), 7.52 (d, *J* = 2.8 Hz, 1H), 7.41 (s, 1H), 7.36 (d, *J* = 8.5 Hz, 1H), 7.32 (s, 1H), 7.21 (dd, *J* = 8.5, 2.8 Hz, 1H), 7.18 (s, 1H), 6.77 (d, *J* = 16.2 Hz, 1H), 3.91 (s, 3H), 2.70 (q, *J* = 7.3 Hz, 2H), 2.43 (s, 3H), 1.17 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 200.82, 192.08, 159.38, 141.65, 138.87, 138.33, 138.27, 134.80, 134.55, 132.94, 132.00, 128.30, 127.11, 126.58, 121.51, 110.04, 55.68, 34.27, 21.35, 8.20.
IR (thin film, cm^{-1}): 1035, 1119, 1164, 1189, 1229, 1276, 1308, 1393, 1462, 1499, 1607, 1688, 2853, 2936, 2972, 3570, 3855.
HRMS (ESI): [M+H$^+$] calcd for $C_{20}H_{21}O_3$: 309.1485; found 309.1483.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

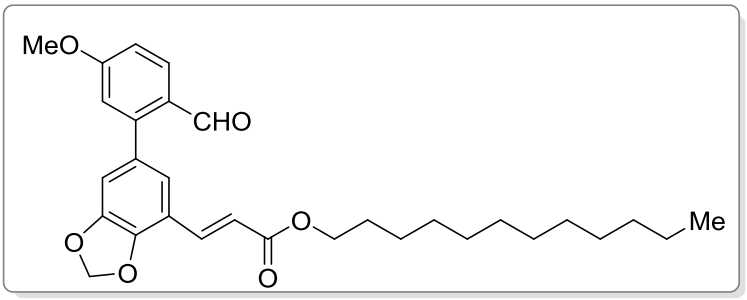


(E)-3-(2'-formyl-4'-methoxy-5-methyl-[1,1'-biphenyl]-3-yl)acrylonitrile:
Compound **30** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: Colorless oil.
Yield: 70% (39 mg isolated; *m*:others = 15:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.91 (s, 1H), 7.52 (d, *J* = 2.8 Hz, 1H), 7.41 (d, *J* = 16.7 Hz, 1H), 7.34 (d, *J* = 8.5 Hz, 1H), 7.31 (s, 1H), 7.22 (s, 3H), 5.92 (d, *J* = 16.6 Hz, 1H), 3.91 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.78, 159.53, 150.14, 139.17, 138.62, 137.76, 134.55, 133.75, 133.71, 131.95, 127.32, 126.18, 121.50, 117.98, 110.25, 97.14, 55.69, 21.32.

IR (thin film, cm^{-1}): 1033, 1075, 1163, 1230, 1278, 1310, 1395, 1464, 1499, 1604, 1686, 2218, 2761, 2851, 2927, 2954.
HRMS (ESI): [M+Na$^+$] calcd for $C_{18}H_{15}NNaO_2$: 300 0994; found 300.0995.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

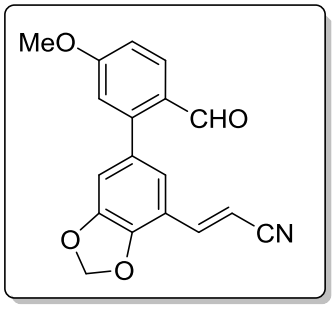


***Ethyl (E)-3-(2'-formyl-4,4',5'-trimethoxy-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **31** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State:Ccolorless oil.
Yield: 62% (63 mg isolated; *m*:others > 20:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.82 (s, 1H), 8.01 (d, *J* = 16.2 Hz, 1H), 7.52 (d, *J* = 2.2 Hz, 2H), 7.33 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.00 (d, *J* = 8.5 Hz, 1H), 6.82 (s, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 4.20 (t, *J* = 6.8 Hz, 2H), 3.98 (s, 6H), 3.96 (s, 3H), 1.73 – 1.67 (m, 2H), 1.43 – 1.35 (m, 2H), 1.27 – 1.22 (m, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 191.14, 167.57, 158.39, 153.74, 149.00, 140.68, 139.48, 133.26, 130.46, 130.22, 127.21, 123.78, 120.06, 112.72, 111.22, 108.95, 64.95, 56.49, 56.37, 55.99, 32.12, 29.86, 29.84, 29.80, 29.76, 29.55, 29.51, 28.96, 26.19, 22.89, 14.33.
IR (thin film, cm^{-1}): 1115, 1166, 1214, 1251, 1305, 1392, 1464, 1501 1604, 1633, 1687, 2753, 2854, 2925, 3020.
HRMS (ESI): [M+H$^+$] calcd for $C_{31}H_{43}O_6$: 511.3054; found 511.3054
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

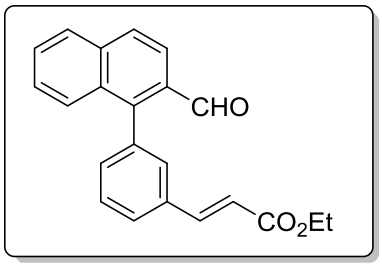


***Dodecyl (E)-3-(6-(2-formyl-5-methoxyphenyl)benzo[d][1,3]dioxol-4-yl)acrylate*:** Compound **32** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 58% (57 mg isolated; *m*:others = 10:1).

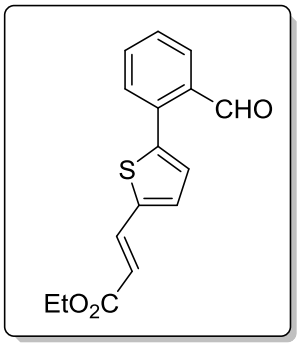
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.86 (s, 1H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 16.1 Hz, 1H), 7.00 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.91 (d, *J* = 1.4 Hz, 1H), 6.86 (d, *J* = 1.5 Hz, 1H), 6.83 (d, *J* = 2.5 Hz, 1H), 6.68 (d, *J* = 16.1 Hz, 1H), 6.16 (s, 2H), 4.20 (t, *J* = 6.7 Hz, 2H), 3.91 (s, 3H), 1.72 – 1.66 (m, 2H), 1.41 – 1.37 (m, 2H), 1.26 – 1.23 (m, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 190.84, 167.25, 163.82, 148.52, 147.47, 146.91, 138.49, 132.16, 130.56, 127.70, 124.40, 122.21, 117.21, 115.44, 114.25, 111.33, 102.40, 65.08, 55.87, 32.13, 29.86, 29.84, 29.81, 29.75, 29.56, 29.51, 28.94, 26.19, 22.90, 14.33.
IR (thin film, cm^{-1}): 1030, 1117, 1175, 1240, 1295, 1396, 1444, 1467, 1596, 1637, 1683, 1712, 2854, 2925.
HRMS (ESI): [M+Na^+] calcd for $C_{30}H_{38}NaO_6$: 517.2564; found, 517.2561.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).



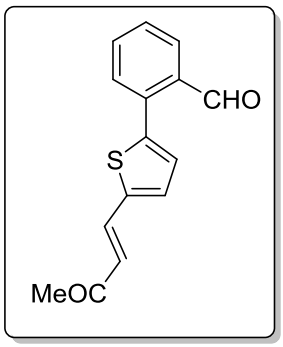
***(E)-3-(6-(2-formyl-5-methoxyphenyl)benzo[d][1,3]dioxol-4-yl)acrylonitrile*:** Compound **33** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 63% (39 mg isolated; *m*:others = 6:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.83 (s, 1H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.33 – 7.27 (m, 1H), 7.01 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.90 (t, *J* = 2.5 Hz, 1H), 6.83 – 6.79 (m, 2H), 6.21 (d, *J* = 16.7 Hz, 1H), 6.18 (s 1H), 3.91 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 190.41, 163.65, 148.46, 146.69, 146.61, 144.73, 132.37, 130.64, 127.41, 123.64, 118.08, 116.15, 115.41, 114.07, 111.97, 102.52, 100.29, 55.71.
IR (thin film, cm^{-1}): 1028, 1117, 1241, 1295, 1444, 1478, 1595, 1679, 2217, 2853, 2925.
HRMS (ESI): [M+H^+] calcd for $C_{18}H_{14}NO_4$: 308.0917; found 308.0921.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).



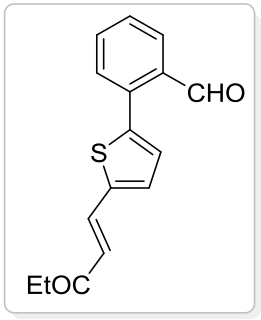
Ethyl (E)-3-(3-(2-formylnaphthalen-1-yl)phenyl)acrylate: Compound **34** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless oil.
Yield: 64% (42 mg isolated; *m*:others = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.89 (s, 1H), 8.08 (d, *J* = 8.66 Hz, 1H), 7.96 (t, *J* = 7.51, 2H), 7.75 (d, *J* = 16.0 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.61 (t, *J* = 4.1 Hz, 1H), 7.56 (d, *J* = 2.9 Hz, 1H), 7.50 – 7.47 (m, 1H), 7.45 (dd, *J* = 9.4, 4.2 Hz, 1H), 6.50 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.15 Hz, 2H), 0.88 (t, *J* = 6.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.38, 166.76, 145.48, 143.59, 136.13, 136.06, 134.72, 132.68, 132.26, 131.24, 130.38, 128.96, 128.72, 128.36, 127.94, 127.44, 127.13, 122.19, 119.60, 60.66, 14.25.
IR (thin film, cm^{-1}): 1036, 1100, 1179, 1262, 1367, 1467, 1597, 1639, 2856, 2926.
HRMS (ESI): [M+Na^+] calcd for $C_{22}H_{18}NaO_3$: 353.1148; found 353.1143.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).



***Ethyl (E)-3-(5-(2-formylphenyl)thiophen-3-yl)acrylate*:** Compound **35** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 66% (38 mg isolated; *m*:others = 8:1)
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.19 (s, 1H), 8.01 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.76 (d, *J* = 15.7 Hz, 1H), 7.63 (ddd, *J* = 7.7, 6.3, 1.3 Hz, 1H), 7.52 (dd, *J* = 14.1, 7.2 Hz, 2H), 7.27 (d, *J* = 3.7 Hz, 1H), 7.00 (d, *J* = 3.7 Hz, 1H), 6.27 (d, *J* = 15.7 Hz, 1H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 191.65, 166.79, 141.69, 141.56, 137.27, 136.68, 134.36, 133.91, 131.50, 131.29, 130.60, 129.06, 128.37, 118.04, 60.84, 14.51
IR (thin film, cm^{-1}): 1160, 1193, 1262, 1303, 1343, 1368, 1391, 1442, 1595, 1623, 1689, 2751, 2853, 2925, 3065.
HRMS (*m/z*): [M+Na^+] calcd for $C_{16}H_{14}NaO_3S$: 309.0556; found, 309.0556.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

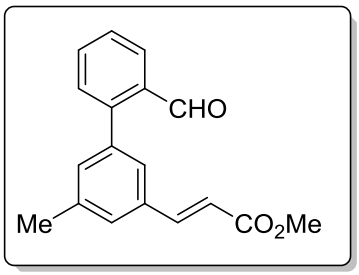


***(E)-2-(5-(3-oxobut-1-en-1-yl)thiophen-2-yl)benzaldehyde*:** Compound **36** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 58% (30 mg isolated; *m*:others = 11:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.18 (s, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.55 – 7.49 (m, 2H), 7.31 (d, *J* = 3.7 Hz, 1H), 7.02 (d, *J* = 3.76, 1H), 6.55 (d, *J* = 15.9 Hz, 1H), 2.35 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.57, 191.41, 142.08, 141.52, 136.97, 135.17, 134.18, 133.77, 132.03, 131.10, 130.57, 128.98, 128.25, 126.32, 27.85.
IR (thin film, cm^{-1}): 1002, 1055, 1099, 1193, 1252, 1359, 1392, 1438, 1481, 1528, 1592, 1664, 1687, 2752, 2852, 3015, 3067.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{15}H_{13}OS$: 256.0561; found, 256.0562.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

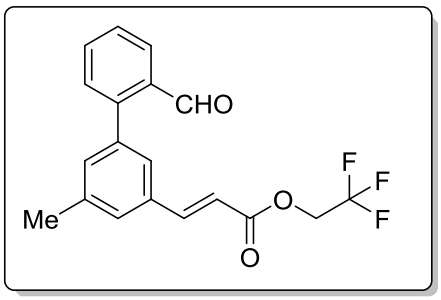


***(E)-2-(5-(3-oxopent-1-en-1-yl)thiophen-2-yl)benzaldehyde*:** Compound **37** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 64% (34 mg isolated; *m*:others = 10:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.23 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 1H), 7.69 (d, *J* = 15.8 Hz, 1H), 7.67 (td, *J* = 7.6, 2.1 Hz, 1H), 7.59 – 7.54 (m, 2H), 7.34 (d, *J* = 3.7 Hz, 1H), 7.05 (d, *J* = 3.7 Hz, 1H), 6.61 (d, *J* = 15.8 Hz, 1H), 2.69 (q, *J* = 7.3 Hz, 2H), 1.20 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 200.26, 191.52, 141.78, 141.72, 137.08, 134.19, 134.11, 133.78, 131.97, 131.11, 130.56, 128.95, 128.24, 125.27, 34.49, 8.23.

IR (thin film, cm^{-1}): 1035.69, 1117.68, 1194.53, 1259, 1357, 1392, 1596, 1663 1691, 2752, 2938, 2979.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{16}H_{14}NaO_2S$: 293.0607; found, 293.0601.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

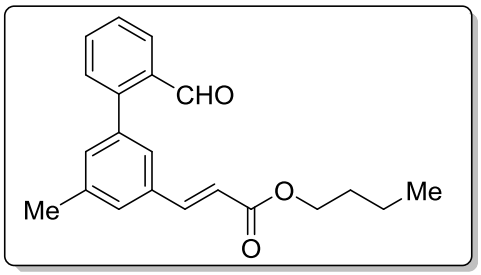


***Methyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **38** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 73% (41 mg isolated; *m*:others = 13:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.04 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.71 (d, *J* = 16.0 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.34 (s, 1H), 7.21 (s, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 3.81 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.32, 167.46, 145.40, 144.46, 139.09, 138.74, 134.86, 133.95, 133.88, 132.91, 130.88, 128.59, 128.30, 127.95, 126.96, 118.90, 51.99, 21.54.
IR (thin film, cm^{-1}): 1170, 1214, 1281, 1393, 1437, 1596, 1639, 1693, 2755, 2855, 2953, 3022.
HRMS (ESI): [M+Na$^+$] calcd for $C_{18}H_{16}NaO_3$: 303.0997; found, 303.0993.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

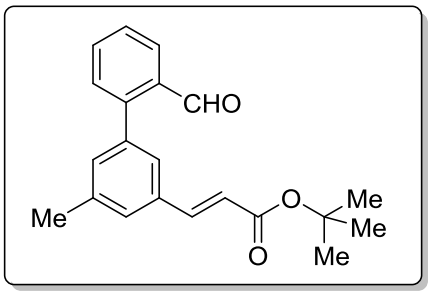


***2,2,2-trifluoroethyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **39** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: colorless solid.
Yield: 70% (49 mg isolated; *m*:others = 10:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.04 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.80 (d, *J* = 16.0 Hz, 1H), 7.66 (td, *J* = 7.5, 1.4 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.43 (dd, *J* = 9.6, 1.5 Hz, 2H), 7.37 (s, 1H), 7.25 (s, 1H), 6.53 (d, *J* = 16.0 Hz, 1H), 4.59 (q, *J* = 8.4 Hz, 2H), 2.45 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.24, 165.21, 146.75, 145.19, 139.25, 138.91, 134.33, 133.92, 133.47, 130.88, 128.83, 128.40, 128.05, 127.21, 123.3 (q, J = 270.6 Hz, CF_3), 117.00, 60.6 (q, J = 36.6 Hz, CF_3), 21.53.
IR (thin film, cm^{-1}): 1077, 1149, 1278, 1407, 1596, 1638, 1693, 1734, 2753, 2854, 2924.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -73.70.
HRMS (*m/z*): [M+Na^+] calcd for $C_{19}H_{15}F_3NaO_3$: 371.0865; found, 371.0864.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

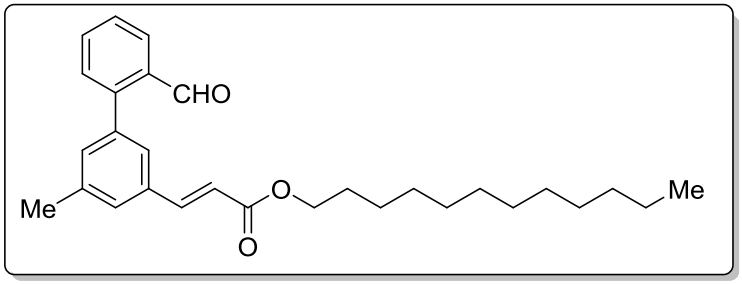


***Butyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **40** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 64% (41 mg isolated; *m*:others = 12:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.03 (dd, J = 7.8, 1.1 Hz, 1H), 7.69 (d, J = 16.0 Hz, 1H), 7.65 (td, J = 7.5, 1.3 Hz, 1H), 7.52 (t, J = 7.6 Hz, 1H), 7.45 – 7.41 (m, 2H), 7.34 (s, 1H), 7.20 (s, 1H), 6.48 (d, J = 16.0 Hz, 1H), 4.21 (t, J = 6.7 Hz, 2H), 2.44 (s, 3H), 1.71 – 1.66 (m, 2H), 1.46 – 1.41 (m, 2H), 0.96 (t, J = 7.4 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.32, 167.11, 145.46, 144.11, 139.07, 138.75, 135.00, 134.01, 133.86, 132.80, 130.89, 128.60, 128.29, 127.96, 126.96, 119.48, 64.73, 31.00, 21.53, 19.43, 13.94.
IR (thin film, cm^{-1}): 1175, 1215, 1262, 1392, 1459, 1596, 1640, 1696, 2854, 2926, 3021.
HRMS (ESI): [M+Na^+] calcd for $C_{21}H_{22}NaO_3$: 345.1461; found: 345.1461.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

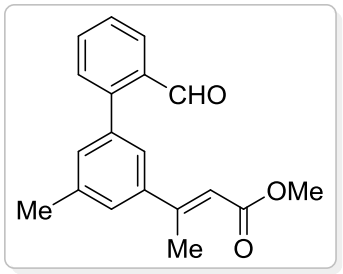


Tert-butyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **41** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/2, v/v).
Physical State: yellow oil.
Yield: 61% (39 mg isolated; *m*:others = 12:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.03 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.64 (td, *J* = 7.5, 1.4 Hz, 1H), 7.59 (d, *J* = 16.0 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.43 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.39 (s, 1H), 7.32 (s, 1H), 7.19 (s, 1H), 6.43 – 6.38 (m, 1H), 2.43 (s, 3H), 1.53 (s, 9H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.40, 166.32, 145.55, 143.07, 138.99, 138.62, 135.15, 133.96, 133.85, 132.56, 130.88, 128.53, 128.23, 127.89, 126.86, 121.35, 80.87, 28.41, 21.54.
IR (thin film, cm^{-1}): 1151, 1214, 1259, 1297, 1368, 1393, 1596, 1638, 1696, 2858, 2927, 2980, 3021.
HRMS (ESI): [M+Na^+] calcd for $C_{21}H_{22}NaO_3$: 345.1461; found, 345.1461.
TLC: R_f = 0.7 (90:10 petroleum ether:EtOAc).

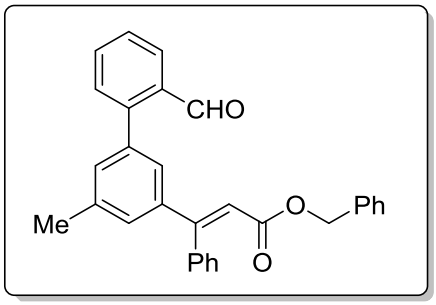


***Dodecyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **42** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 65% (56 mg isolated; *m*:others = 7:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.03 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.69 (d, *J* = 16.0 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.43 (dd, *J* = 9.5, 1.4 Hz, 2H), 7.34 (s, 1H), 7.20 (s, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 4.20 (t, *J* = 6.7 Hz, 2H), 2.44 (s, 3H), 1.72 – 1.67 (m, 2H), 1.45 – 1.36 (m, 2H), 1.25 (s, 16H), 0.87 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.17, 166.93, 145.25, 143.90, 138.85, 138.48, 134.75, 133.73, 133.67, 132.61, 130.67, 128.40, 128.08, 127.72, 126.73, 119.21, 64.84, 31.92, 29.66, 29.64, 29.60, 29.55, 29.35, 29.30, 28.72, 25.99, 22.70, 21.33, 14.13.
IR (thin film, cm^{-1}): 1168, 1262, 1295, 1393, 1466, 1596, 1641, 1696, 2854, 2925.
HRMS (ESI): [M+K^+] calcd for $C_{29}H_{38}KO_3$: 473.2455; found, 473.2453.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

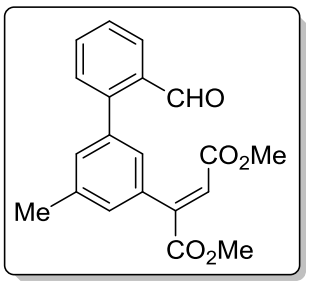


***Methyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)but-2-enoate*:** Compound **43** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).

Physical State: Yellow oil.
Yield: 62% (36 mg isolated; *m*:others = 12:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.03 (d, *J* = 7.7 Hz, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.35 (s, 1H), 7.27 (s, 1H), 7.19 (s, 1H), 6.17 (s, 1H), 3.76 (s, 3H), 2.60 (s, 3H), 2.45 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.47, 167.32, 155.51, 145.79, 142.74, 138.67, 138.32, 133.98, 133.84, 131.67, 130.95, 128.19, 127.88, 127.05, 125.40, 117.55, 51.40, 21.66, 18.34.
IR (thin film, cm^{-1}): 1168, 1214, 1437, 1596, 1629, 1696, 2855, 2926, 3021.
HRMS (ESI): [M+Na$^+$] calcd for $C_{19}H_{18}NaO_3$: 317.1150; found, 317.1148
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).

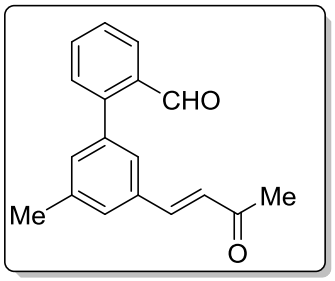


***Benzyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)-3-phenylacrylate*:** Compound **44** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 66% (57 mg isolated; *m*:others = 10:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.93 (s, 1H), 7.99 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.60 (td, *J* = 7.5, 1.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.39 – 7.36 (m, 5H), 7.32 – 7.29 (m, 3H), 7.23 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.20 – 7.18 (m, 4H), 7.08 (s, 1H), 6.43 (s, 1H), 5.05 (s, 2H), 2.38 (s, 3H)
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.30, 165.91, 156.72, 145.60, 141.39, 138.73, 138.57, 138.14, 136.00, 133.87, 133.80, 132.13, 130.90, 129.34, 129.11, 128.91, 128.64, 128.46, 128.30, 128.27, 128.16, 127.83, 127.39, 117.94, 66.30, 21.58.
IR (thin film, cm^{-1}): 697, 822, 864, 1004, 1155, 1197, 1269, 1377, 1455, 1496, 1594, 1693, 1721, 2750, 2856, 2924, 3032.
HRMS (ESI): [M+Na$^+$] calcd for $C_{30}H_{24}NaO_3$: 455.1624, found 455.1630.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

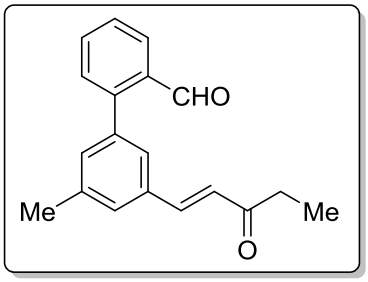


***Dimethyl 2-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)fumarate*:** Compound **45** was prepared by general procedure D (0.2 mmol scale).

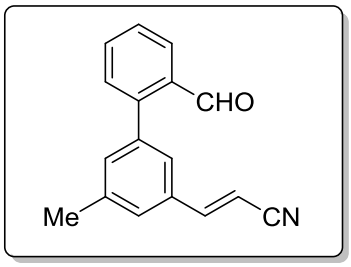
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: white semi-solid.
Yield: 61% (35 mg isolated; *m*:others = 12:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.95 (s, 1H), 8.03 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.65 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.41 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.35 (s, 1H), 7.29 (s, 1H), 7.25 (s, 1H), 6.35 (s, 1H), 3.95 (s, 3H), 3.79 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.16, 168.39, 165.50, 148.66, 145.08, 139.36, 138.94, 133.93, 133.90, 133.75, 133.26, 130.92, 128.43, 128.00, 127.35, 125.53, 118.14, 53.09, 52.35, 21.62.
IR (thin film, cm^{-1}): 1169, 1196, 1257, 1348, 1394, 1436, 1595, 1626, 1692, 1723, 2755, 2854, 2924, 2953.
HRMS (ESI): [M+Na$^+$] calcd for $C_{20}H_{18}NaO_5$: 361.1044; found, 361.1046.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



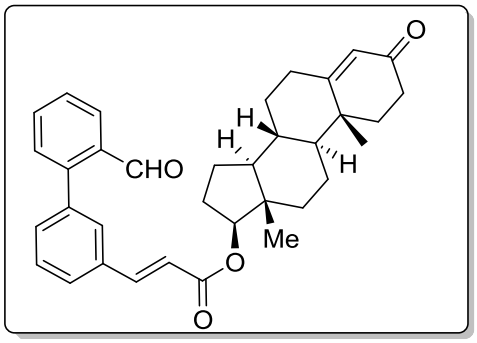
(E)-3'-methyl-5'-(3-oxobut-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde: Compound **46** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colourless oil.
Yield: 71% (37 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.04 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.66 (td, *J* = 7.5, 1.4 Hz, 1H), 7.55 – 7.51 (m, 2H), 7.44 (d, *J* = 6.5 Hz, 2H), 7.35 (s, 1H), 7.23 (s, 1H), 6.75 (d, *J* = 16.3 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 198.36, 192.32, 145.34, 142.93, 139.20, 138.83, 134.93, 133.91, 133.08, 130.88, 128.75, 128.34, 128.02, 128.01, 127.24, 127.22, 27.92, 21.56.
IR (thin film, cm^{-1}): 704, 765, 822, 871, 979, 1108, 1194, 1260, 1359, 1393, 1456, 1596, 1692, 2751, 2853, 2926.
HRMS (ESI): [M+Na$^+$] calcd for $C_{18}H_{16}NaO_2$: 287.1047, found 287.1052.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



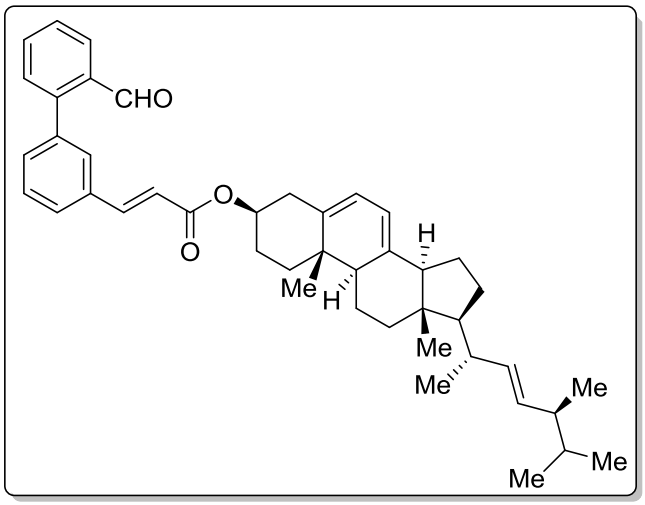
(E)-3'-methyl-5'-(3-oxopent-1-en-1-yl)-[1,1'-biphenyl]-2-carbaldehyde: Compound **47** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 72% (40 mg isolated; *m*:others = 12:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.99 (s, 1H), 8.04 (d, *J* = 6.7 Hz, 1H), 7.65 (td, *J* = 7.6, 1.3 Hz, 1H), 7.56 (d, *J* =16.2 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.36 (s, 1H), 7.22 (s, 1H), 6.78 (d, *J* = 16.2 Hz, 1H), 2.70 (q, *J* = 7.3 Hz, 2H), 2.45 (s, 3H), 1.17 (t, *J* = 7.3 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 200.80, 192.21, 145.22, 141.55, 138.94, 138.54, 134.85, 133.72, 132.75, 130.68, 128.61, 128.12, 127.75, 126.92, 126.64, 34.30, 21.36, 8.19.
IR (thin film, cm^{-1}): 1041, 1120, 1192, 1261, 1459, 1614, 1666, 1693, 2851, 2918.
HRMS (ESI): [M+Na$^+$] calcd for $C_{19}H_{18}NaO_2$: 301.1199; found 301.1198.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



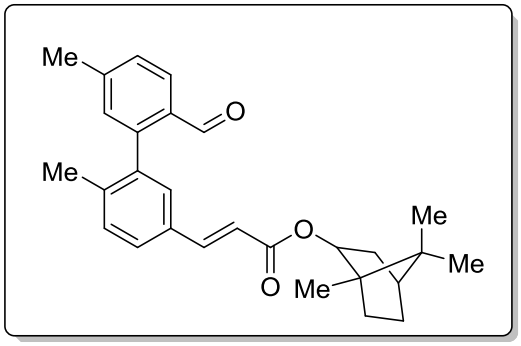
***(E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylonitrile*:** Compound **48** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 57% (28 mg isolated; *m*:others = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.95 (s, 1H), 8.04 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.66 (ddd, *J* = 7.5, 4.5, 1.4 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.45 – 7.40 (m, 2H), 7.34 (s, 1H), 7.26 (s, 1H), 5.93 (d, *J* = 16.6 Hz, 1H), 2.45 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.10, 150.26, 148.44, 144.88, 139.44, 139.11, 133.97, 133.75, 130.98, 130.84, 128.53, 128.17, 127.82, 126.19, 118.14, 97.45, 96.37, 21.52
IR (thin film, cm^{-1}): 701, 766, 821, 870, 967, 1041, 1108, 1194, 1261, 1394, 1453, 1595, 1620, 1691, 2217, 2752, 2854, 2925, 3065.
HRMS (ESI): [M+Na$^+$] calcd for $C_{17}H_{13}NaNO$: 270.0896, found 270.0892.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).



***(8R,9S,10R,13S,14S,17S)-10,13-dimethyl-3-oxo-2,3,6,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-17-yl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **49** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 59% (62 mg isolated; *m*:others = 8:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.94 (s, 1H), 8.00 (d, *J* = 7.7 Hz, 1H), 7.66 – 7.59 (m, 2H), 7.52 – 7.48 (m, 2H), 7.47 – 7.41 (m, 2H), 7.41 – 7.38 (m, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 6.49 – 6.43 (m, 1H), 6.13 – 5.96 (m, 1H), 3.96 – 3.81 (m, 1H), 2.50 – 2.09 (m, 2H), 2.06 – 1.79 (m, 4H), 1.75 – 1.49 (m, 6H), 1.45 – 1.25 (m, 4H), 1.29 – 0.98 (m, 7H), 1.01 – 0.78 (m, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.23, 192.06, 164.70, 145.25, 143.68, 139.70, 138.29, 135.34, 133.74, 133.67, 130.98, 130.72, 128.93, 128.08, 127.71, 127.63, 123.91, 122.45, 119.56, 82.72, 53.70, 50.29, 48.44, 42.74, 38.63, 35.41, 33.97, 33.13, 31.49, 27.61, 25.53, 24.87, 20.54, 17.40, 12.18.
IR (thin film, cm^{-1}): 1041, 1091, 1196, 1253, 1343, 1393, 1449, 1542, 1597, 1619, 1655, 1692, 1946, 2752, 2854, 2930, 3061, 3281.
HRMS (ESI): [M+Na^+] calcd for $C_{35}H_{38}NaO_4$: 545.2662; found 545.2666
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

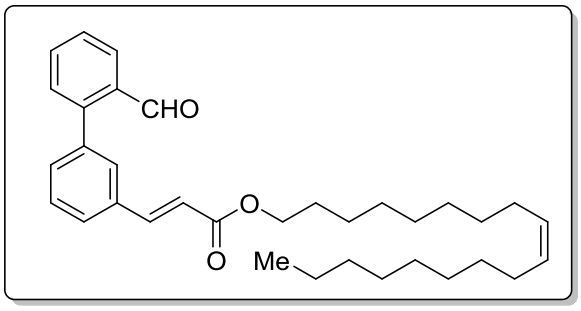


(3R,9R,10S,13S,14S,17S)-17-((2S,5S,E)-5,6-dimethylhept-3-en-2-yl)-10,13-dimethyl-2,3,4,9,10,11,12,13,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-yl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **50** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: colorless oil.
Yield: 62% (78 mg isolated; *m*:others = 8:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.04 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 16.0 Hz, 1H), 7.66 (td, *J* = 7. 6, 2.3 Hz, 2H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.53 (s, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 7.39 (d, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 5.60 (d, *J* = 3.5 Hz, 1H), 5.42 – 5.37 (m, 1H), 5.21 (t, *J* = 15.1, 2H), 4.85 (ddd, *J* = 15.8, 11.3, 4.5 Hz, 1H), 2.62 – 2.56 (m, 1H), 2.45 (t, *J* = 13.0 Hz, 1H), 2.07 – 1.98 (m, 4H), 1.96 – 1.82 (m, 4H), 1.73 – 1.60 (m, 6H), 1.50 – 1.43 (m, 2H), 1.41 – 1.29 (m, 4H), 1.04 (d, *J* = 6.6 Hz, 3H), 0.98 (s, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.82 (d, *J* = 6.1 Hz, 4H), 0.64 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.03, 166.33, 145.02, 143.69, 141.67, 138.51, 135.58, 134.84, 133.74, 131.98, 130.72, 129.44, 129.01, 128.20, 127.86, 127.65, 120.30, 119.77, 116.33, 73.10, 55.71, 54.54, 46.05, 42.82, 40.46, 39.04, 37.94, 37.13, 36.75, 33.10, 28.31, 28.22, 23.01, 21.13, 21.05, 19.98, 19.67, 17.62, 16.21, 12.08.
IR (thin film, cm^{-1}): 1012, 1170, 1255, 1371, 1457, 1597, 1638, 1692, 2870, 2957.
HRMS (ESI): [M+K$^+$] calcd for $C_{44}H_{54}KO_3$: 669.3705; found 669.3709.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

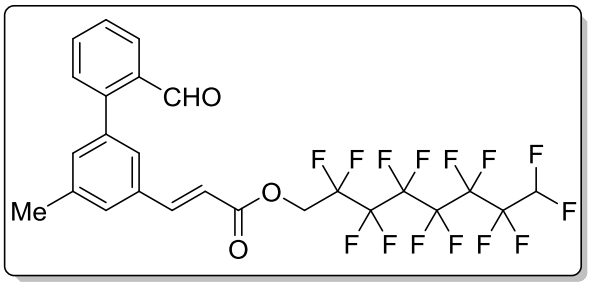


***(4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl (E)-3-(2'-formyl-5',6-dimethyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **51** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 68% (57 mg isolated; *m*:others = 12:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.92 (s, 1H), 7.98 (d, *J* = 15.9 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 1.3 Hz, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.28 (d, *J* = 3.4 Hz, 1H), 7.27 – 7.26 (m, 1H), 7.23 (s, 1H), 6.34 (d, *J* = 15.9 Hz, 1H), 4.80 (dd, *J* = 7.6, 4.0 Hz, 1H), 2.49 (s, 3H), 2.47 (s, 3H), 1.89 – 1.83 (m, 2H), 1.78 – 1.69 (m, 3H), 1.23 – 1.12 (m, 2H), 1.05 (s, 3H), 0.89 (s, 3H), 0.86 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.10, 166.54, 145.59, 144.93, 141.51, 137.62, 136.36, 133.85, 131.69, 131.59, 131.53, 131.00, 129.07, 128.14, 127.80, 120.84, 81.46, 49.12, 47.22, 45.30, 39.10, 33.97, 27.28, 22.05, 20.35, 20.22, 19.68, 11.74.

IR (thin film, cm^{-1}): 821, 980, 1017, 1054, 1109, 1174, 1260, 1304, 1391, 1457, 1604, 1636, 1710, 2751, 2928, 2955.
HRMS (ESI): [M+Na$^+$] calcd for $C_{28}H_{32}NaO_3$: 439.2297; found: 438.2293.
TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).

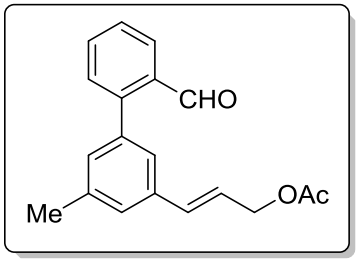


***(Z)-octadec-9-en-1-yl (E)-3-(2'-formyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **52** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 49% (48 mg isolated; *m*:others = 10:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 10.00 (s, 1H), 8.07 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.75 (d, *J* = 16.0 Hz, 1H), 7.68 (td, *J* = 7.5, 1.3 Hz, 1H), 7.63 (d, *J* = 7.8 Hz, 1H), 7.58 – 7.55 (m, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 5.37 (t, *J* = 7.5 Hz, 2H), 4.23 (t, *J* = 6.7 Hz, 2H), 2.10 – 1.97 (m, 4H), 1.72 (dd, *J* = 14.4, 6.8 Hz, 2H), 1.41 (d, *J* = 8.2 Hz, 2H), 1.38 – 1.28 (m, 20H), 0.90 (t, *J* = 6.9 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 191.97, 166.82, 145.01, 143.71, 138.58, 134.84, 133.73, 133.71, 131.74, 130.71, 129.99, 129.80, 129.39, 128.99, 128.19, 127.87, 127.66, 119.45, 64.86, 31.91, 29.77, 29.74, 29.53, 29.44, 29.32, 29.27, 29.23, 28.72, 27.22, 27.20, 25.98, 22.69, 14.12.
IR (thin film, cm^{-1}): 1103, 1166, 1258, 1300, 1392, 1466, 1597, 1639, 1694, 2750, 2853, 2924, 3004.
HRMS (ESI): [M+Na$^+$] calcd for $C_{34}H_{46}NaO_3$: 525.3339; found 525.3338.
TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).



***1,1,2,2,3,3,4,4,5,5,6,6,7,7-tetradecafluoroheptyl (E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **53** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).

Physical State: yellow oil.
Yield: 68% (84 mg isolated; *m*:others = 11:1)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.97 (s, 1H), 8.04 (d, *J* = 6.8 Hz, 1H), 7.79 (d, *J* = 16.0 Hz, 1H), 7.66 (td, *J* = 7.5, 1.3 Hz, 1H), 7.53 (t, *J* = 7.6 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.37 (s, 1H), 7.25 (s, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.06 (tt, *J* = 8.0, 5.1 Hz, 1H), 4.72 (t, *J* = 13.6 Hz, 2H), 2.45 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 192.24, 165.22, 146.84, 145.20, 139.25, 138.91, 134.31, 133.93, 133.50, 132.08, 130.88, 128.86, 128.40, 128.12, 128.03, 127.79, 127.20, 116.92, 107.78, 104.30, 60.11, 59.90, 59.68.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -119.37, -119.40, -119.43, -122.12, -123.34, -123.41, -123.42, -129.41, -136.95, -136.96, -137.07.
IR (thin film, cm^{-1}): 670, 695, 761, 797, 853, 982, 1018, 1139, 1194, 1260, 1396, 1452, 1597, 1638, 1693, 1735, 2856, 2925, 2964.
HRMS (ESI): [M+H^+] calcd for $C_{25}H_{17}F_{14}O_5$: 631.1044; found, 631.1046.
TLC: R_f = 0.6 (90:10 petroleum ether:EtOAc).



(E)-3-(2'-formyl-5-methyl-[1,1'-biphenyl]-3-yl)allyl acetate: Compound **54** was prepared by general procedure D (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 50% (29 mg isolated; *m*:others = 4:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.98 (s, 1H), 8.02 (d, *J* = 7.8 Hz, 1H), 7.64 (dd, *J* = 10.6, 4.3 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.28 (s, 1H), 7.20 (s, 1H), 7.09 (s, 1H), 6.66 (d, *J* = 15.9 Hz, 1H), 6.37 – 6.29 (m, 1H), 4.74 (d, *J* = 6.3 Hz, 2H), 2.41 (s, 3H), 2.10 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 192.70, 171.07, 146.04, 138.70, 138.32, 136.61, 133.94, 133.79, 133.67, 130.87, 130.77, 128.05, 127.72, 127.29, 125.74, 124.41, 65.12, 21.56, 21.20.
IR (thin film, cm^{-1}): 705, 767, 821, 868, 966, 1026, 1106, 1228, 1379, 1450, 1596, 1693, 1739, 2752, 2853, 2926.
HRMS (ESI): [M+Na^+] calcd for $C_{19}H_{18}NaO_3$: 317.1154, found 317.1159.
TLC: R_f = 0.3 (90:10 petroleum ether:EtOAc).

2.9 Optimization details of *meta*-C–H olefination of 2-phenylaniline

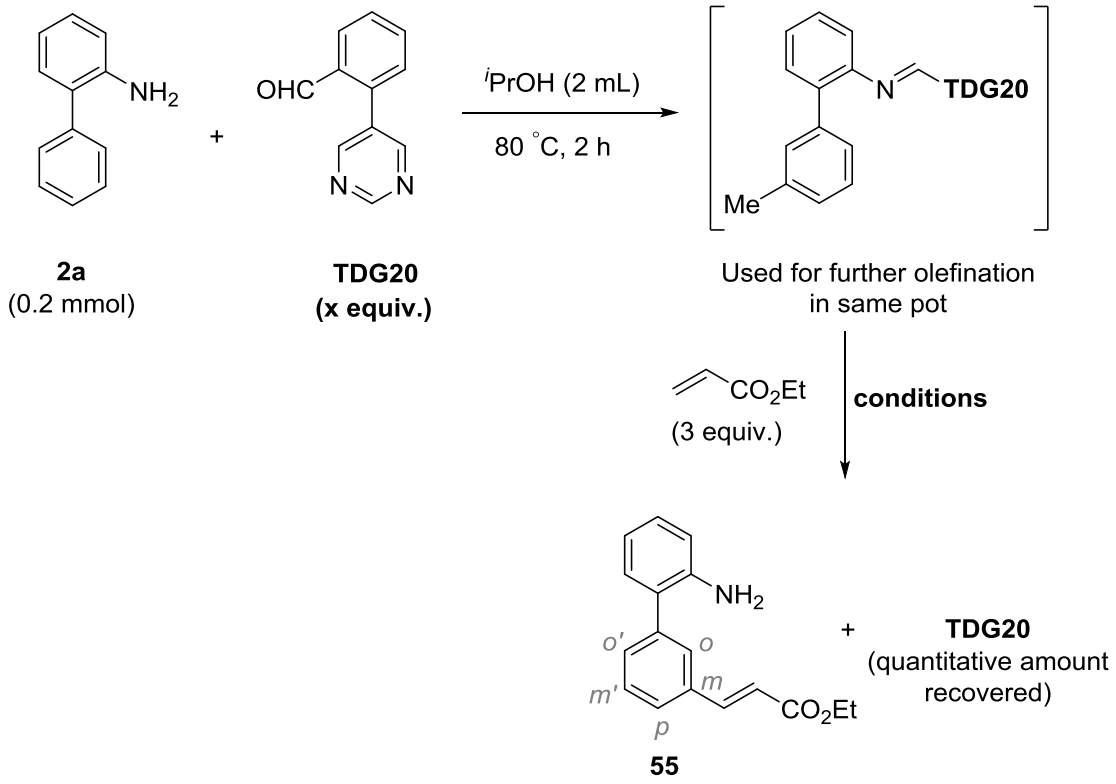
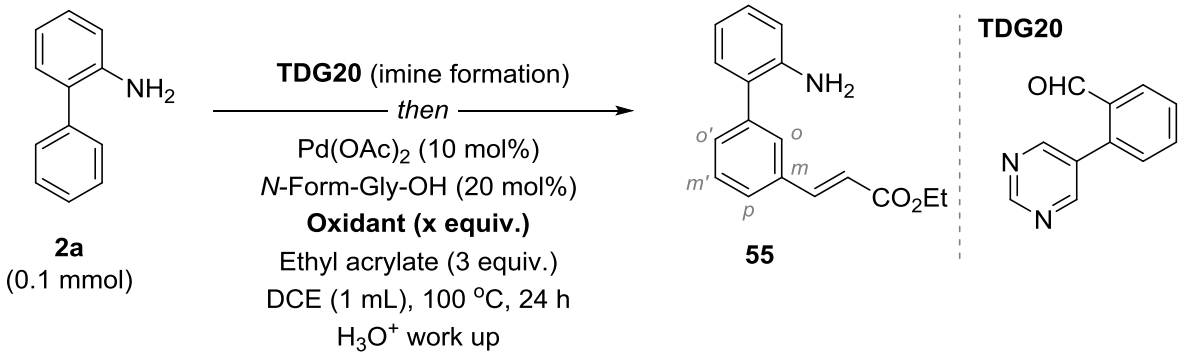


Table S12: Optimization of TDG20 amount

Entry	2a (mmol)	TDG20 (mmol)	Yield (%)
1	0.2	0.18	86
2	0.2	0.19	91
3	0.2	0.2	94
4	0.2	0.21	96
5	**0.2**	**0.22**	**97**

[a]Yield was measured by ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene.

Table S13: Optimization of *meta*-C–H olefination of 2-phenylaniline



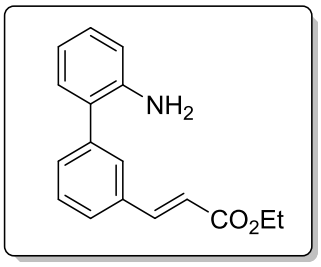
Entry	Oxidant	Yield (*m*:others)[a]
1	Ag_2CO_3 (25 mol%) + $Cu(OAc)_2$ (3.5 equiv.)	31% (5:1)[b]
2	Ag_2CO_3 (25 mol%) + CuOAc (3.5 equiv.)	7% (7:1)[c]
3	Ag_2CO_3 (25 mol%)	18% (7:1)
4	Ag_2CO_3 (50 mol%	32% (8:1)
5	Ag_2CO_3 (75 mol%)	45% (7:1)
6	Ag_2CO_3 (1 equiv.)	52% (10:1)
7	Ag_2CO_3 (1.5 equiv.)	57% (10:1)
8	Ag_2CO_3 (2 equiv.)	58% (10:1)
9	**Ag_2CO_3 (2.5 equiv.)**	**65% (10:1)**
10	AgOAc (3 equiv)	61% (10:1)
11	AgTFA (2.5 equiv.)	33% (4:1)
12	Ag_2CO_3 (1 equiv.) + AgOAc (1 equiv.)	35% (10:1)
13	Ag_2CO_3 (2.5 equiv.) + AgOAc (1 equiv.)	45% (10:1)
14	Ag_2CO_3 (2.5 equiv.) + AgOAc (2.5 equiv.)	37% (10:1)

[a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using 1,3,5-trimethoxybenzene (TMB) as internal standard. Doublet of olefin proton in ^{1}H NMR was used to measure the selectivity. Ratios of *meta*:others are shown in parenthesis. [b]27% C–N coupled carbazole product was observed. [c]21% C–N coupled carbazole product was observed. *Note:* C–N coupled carbazole product was observed when copper salt was used.

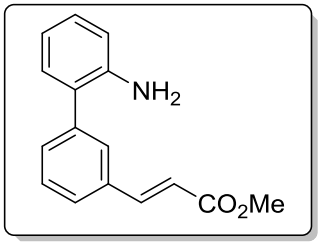
2.10 General procedure E: Procedure for *meta*-olefination of 2-phenylaniline substrates

An oven-dried screw capped reaction tube with a magnetic stir-bar was charged with 2-phenylaniline (0.2 mmol) (viscous 2-phenylaniline was weighed first) and **TDG20** (0.22 mmol, 40.5 mg) under air, followed by isopropyl alcohol (2 mL). The reaction mixture was stirred at 80 °C for 2 hours. The mixture was allowed to cool down. Next, solvent was concentrated in vacuo and washed with pentane. The dry crude residue was subjected to $Pd(OAc)_2$ (10 mol%, 0.02 mmol, 4.5 mg), *N*-formyl glycine (*N*-Form-Gly-OH; 20 mol%, 8.3 mg), Ag_2CO_3 (2.5 equiv, 0.5 mmol, 138 mg) in the same reaction tube. Solvent 1,2-dichloroethane (DCE, 2 mL) was added in the reaction tube followed by addition of liquid alkene (3 equiv., 0.6 mmol) by micropipette under air (solid alkenes were weighed before adding solvent). The reaction tube was screwed by a cap fitted with a rubber septum and was vigorously stirred in a preheated oil bath at 100 °C. The reaction mixture was taken out after 24 h, diluted with 10 mL ethyl acetate and filtered through a celite pad. Next, the filtrate mixture was treated with 1 (M) HCl solution and stirred for ten minutes. Organic layer was separated and concentrated under vacuum. The crude mixture was purified by column chromatography using silica gel (100-200 mesh size) and petroleum ether/ethyl acetate as the eluent.

2.11 Characterization data for *meta*-olefination products of 2-phenylanilines

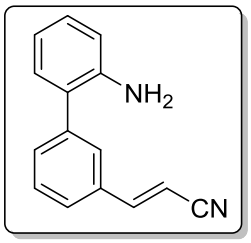


***Ethyl (E)-3-(2'-amino-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **55** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 62% (33 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 16.0 Hz, 1H), 7.63 (s, 1H), 7.52 – 7.44 (m, 3H), 7.18 (ddd, *J* = 7.9, 7.5, 1.6 Hz, 1H), 7.12 (dd, *J* = 7.6, 1.4 Hz, 1H), 6.84 (td, *J* = 7.5, 1.1 Hz, 1H), 6.78 (dd, *J* = 8.0, 0.9 Hz, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 167.16, 144.51, 143.66, 140.48, 135.28, 131.15, 130.57, 129.60, 129.07, 128.94, 127.03, 126.93, 119.00, 118.97, 115.95, 60.77, 14.53.
IR (thin film, cm^{-1}): 1036, 1094, 1179, 1270, 1314, 1367, 1415, 1455, 1478, 1638, 1708, 2928, 2981, 3373.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{17}H_{18}NO_2$: 268.1332; found, 268.1331.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

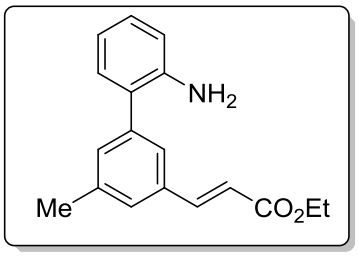


***Methyl (E)-3-(2'-amino-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **56** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: yellow semi-solid.
Yield: 60% (30 mg isolated; *m*:others = 10:1)
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.73 (d, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 16.0 Hz, 1H), 7.53 – 7.46 (m, 3H), 7.18 (td, *J* = 7.6, 2.1 Hz, 1H), 7.12 (dd, *J* = 7.5, 1.1 Hz, 1H), 6.84 (td, *J* = 7.5, 1.1 Hz, 1H), 6.78 (dd, *J* = 8.0, 0.9 Hz, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 3.81 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 167.40, 144.61, 143.45, 140.29, 134.98, 131.04, 130.36, 129.41, 128.89, 128.75, 126.88, 126.69, 118.80, 118.27, 115.75, 51.78.
IR (thin film, cm^{-1}): 1037, 1170, 1273, 1320, 1435, 1499, 1637, 1715, 2853, 2924, 3025, 3219, 3375, 3467.
HRMS (ESI): [M+H$^+$] calcd for $C_{16}H_{16}NO_2$: 254.1176; found, 254.1175.

TLC: R_f = 0.5 (85:15 petroleum ether:EtOAc).

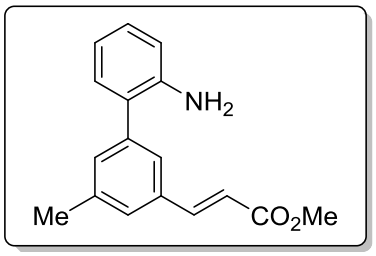


(E)-3-(2'-amino-[1,1'-biphenyl]-3-yl)acrylonitrile: Compound **57** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 57% (25 mg isolated; *m*:others = 3:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.57 – 7.54 (m, 2H), 7.51 (d, *J* = 16.7 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.44 – 7.41 (m, 1H), 7.20 (td, *J* = 7.6, 1.5 Hz, 1H), 7.10 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.85 (td, *J* = 7.6, 1.5 Hz, 1H), 6.79 (dd, *J* = 7.2, 2.0 Hz,1H), 5.92 (d, *J* = 16.7 Hz, 1H), 3.72 (s, 1H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 150.38, 148.78, 143.43, 140.62, 134.11, 131.96, 130.31, 129.65, 129.12, 128.05, 127.25, 126.20, 118.89, 118.12, 115.86, 96.81.
IR (thin film, cm^{-1}): 1158, 1190, 1298, 1413, 1452, 1481, 1498, 1525, 1579, 1618, 1699, 2217, 2921, 3058, 3210, 3370, 3461.
HRMS (ESI): [M+H$^+$] calcd for $C_{15}H_{13}N_2$: 221.1073; found 221.1078.
TLC: R_f = 0.4 (85:15 petroleum ether:EtOAc).

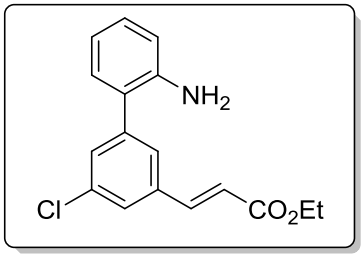


Ethyl (E)-3-(2'-amino-5-methyl-[1,1'-biphenyl]-3-yl)acrylate**:** Compound **58** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 65% (37 mg isolated; *m*:others = 12:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.67 (d, *J* = 16.0 Hz, 1H), 7.47 – 7.41 (m, 1H), 7.30 (t, *J* = 8.9 Hz, 2H), 7.17 (ddd, *J* = 7.9, 7.4, 1.6 Hz, 1H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.82 (tt, *J* = 8.9, 4.5 Hz, 1H), 6.77 (ddd, *J* = 8.4, 5.9, 2.1 Hz, 1H), 6.45 (t, *J* = 11.0 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 167.04, 144.49, 143.44, 140.17, 139.16, 134.98, 131.80, 130.31, 128.76, 127.57, 126.88, 125.93, 118.74, 118.51, 115.69, 60.53, 21.37, 14.33
IR (thin film, cm^{-1}): 1037, 1095, 1175, 1286, 1335, 1367, 1460, 1498, 1616, 1638, 1708, 1897, 2854, 2924, 2958, 3374, 3471.

HRMS (*m/z*): [M+H$^+$] calcd for $C_{18}H_{20}NO_2$: 282.1489; found, 282.1490.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

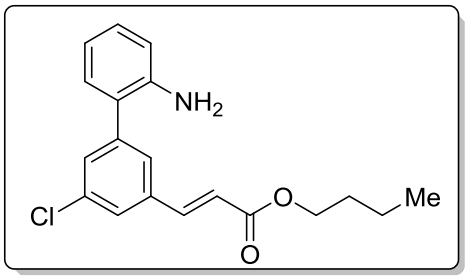


***Methyl (E)-3-(2'-amino-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **59** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: colorless oil.
Yield: 62% (33 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 16.0 Hz, 1H), 7.45 (s, 1H), 7.33 (d, *J* = 9.8 Hz, 2H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.13 (d, *J* = 6.4 Hz, 1H), 6.85 (t, *J* = 7.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 3.83 (s, 3H), 2.44 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 167.46, 144.78, 143.42, 140.20, 139.18, 134.92, 131.87, 130.30, 128.77, 127.60, 125.94, 118.75, 118.04, 115.70, 51.72, 21.35.
IR (thin film, cm^{-1}): 1035, 1152, 1264, 1390, 1412, 1547, 1601, 1720, 2867, 2945, 3017, 3264, 3382, 3442.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{17}H_{18}NO_2$: 268.1332; found, 268.1332.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

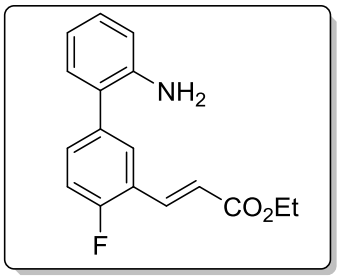


***Ethyl (E)-3-(2'-amino-5-chloro-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **60** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (91/9, v/v).
Physical State: colorless oil.
Yield: 63% (38 mg isolated; *m*:others = 12:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.66 (d, *J* = 7.6 Hz, 1H), 7.52 (d, *J* = 16.3 Hz, 3H), 7.22 (t, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 6.87 (t, *J* = 7.4 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H), 6.49 (d, *J* = 16.3 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.55, 143.35, 142.79, 141.96, 136.69, 135.29, 130.64, 130.24, 129.35, 127.02, 126.42, 125.32, 120.16, 118.90, 115.91, 60.76, 14.29.
IR (thin film, cm^{-1}): 1037, 1111, 1180, 1273, 1316, 1367, 1459, 1498, 1566, 1640, 1711, 2854, 2925, 3065, 3377, 3471.

HRMS (*m/z*): [M+H$^+$] calcd for $C_{17}H_{17}ClNO_2$: 302.0942; found, 302.0941.
TLC: R_f = 0.45 (85:15 petroleum ether:EtOAc).

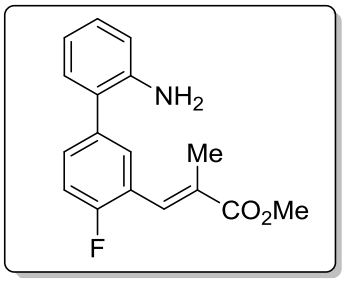


***Butyl (E)-3-(2'-amino-5-chloro-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **61** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (85/15, v/v).
Physical State: colorless oil.
Yield: 61% (40 mg isolated; *m*:others = 10:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.65 (d, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 16.8 Hz, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 6.90 (t, *J* = 7.4 Hz, 1H), 6.85 (d, *J* = 7.7 Hz, 1H), 6.49 (d, *J* = 16.8 Hz, 1H), 4.23 (t, *J* = 6.7 Hz, 2H), 1.72 – 1.69 (m, 2H), 1.48 – 1.44 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.65, 143.35, 142.75, 141.95, 136.70, 135.29, 130.63, 130.24, 129.34, 127.02, 126.43, 125.33, 120.50, 120.17, 118.90, 115.91, 64.67, 30.72, 19.19, 13.74.
IR (thin film, cm^{-1}): 1026, 1065, 1176, 1275, 1458, 1498, 1526, 1566, 1640, 1714, 2854, 2926, 2960, 3067, 3379, 3465.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{19}H_{21}ClNO_2$: 330.1255; found, 330.1255.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

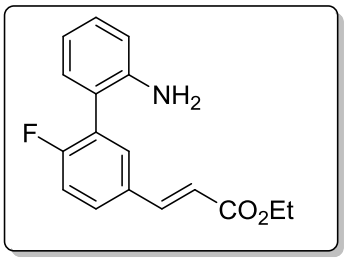


***Ethyl (E)-3-(2'-amino-4-fluoro-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **62** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 62% (35 mg isolated; *m*:others > 20:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.86 (d, *J* = 16.2 Hz, 1H), 7.66 (dd, *J* = 7.1, 2.2 Hz, 1H), 7.49 – 7.45 (m, 1H), 7.22 – 7.18 (m, 2H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.86 (td, *J* = 7.5, 1.2 Hz, 1H), 6.80 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.59 (d, *J* = 16.2 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.75, 160.50 (d, *J* = 254.5 Hz), 159.49, 143.46, 136.94, 132.37 (d, *J* = 8.7 Hz), 130.36, 129.70 (d, *J* = 3.1 Hz), 128.98, 125.84, 122.86 (d, *J* = 11.8 Hz), 121.29 (d, *J* = 6.5 Hz), 118.86, 116.62 (d, *J* = 22.1 Hz), 115.79, 60.68, 14.30.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -116.52.
IR (thin film, cm^{-1}): 982, 1032, 1105, 1177, 1226, 1257, 1278, 1367, 1397, 1484, 1637, 1708, 1898, 2853, 2927, 3373.
HRMS (ESI): [M+H^+] calcd for $C_{17}H_{17}FNO_2$: 286.1238; found, 286.1237.
TLC: R_f = 0.5 (85:15 petroleum ether:EtOAc).

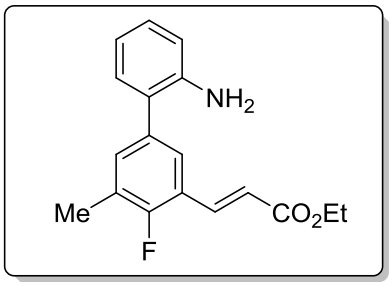


***Ethyl (E)-3-(2'-amino-4-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)but-2-enoate*:** Compound **63** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (98/8, v/v).
Physical State: colorless oil.
Yield: 56% (33 mg isolated; *m*:others = 4:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.34 – 7.32 (m, 1H), 7.18 – 7.14 (m, 2H), 7.11 (t, *J* = 7.6 Hz, 2H), 6.84 (t, *J* = 6.8 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 6.30 (s, 1H), 3.78 (s, 3H), 3.72 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 167.08, 160.36 (d, *J* = 231.1 Hz), 143.51, 139.27, 138.26, 135.36 (d, *J* = 3.8 Hz), 131.95 (d, *J* = 4.6 Hz), 130.43, 128.98 (d, *J* = 8.0 Hz), 128.59, 126.76, 126.07 (d, *J* = 16.0 Hz), 118.68, 115.75 (d, *J* = 20.2 Hz), 114.07, 52.04, 14.13.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -119.11.
IR (thin film, cm^{-1}): 1140, 1229, 1275, 1450, 1488, 1619, 1719, 2854, 2925, 3385, 3466.
HRMS (*m/z*): [M+Na^+] calcd for $C_{17}H_{16}FNNaO_2$: 308.1057; found, 308.1058.
TLC: R_f = 0.35 (85:15 petroleum ether:EtOAc).

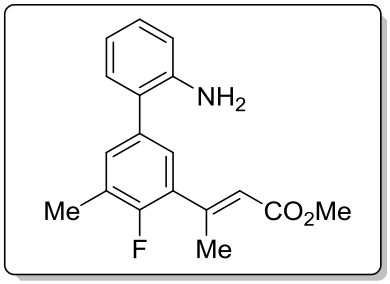


***Ethyl (E)-3-(2'-amino-6-fluoro-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **64** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (93/7, v/v).
Physical State: yellow oil.
Yield: 53% (30 mg isolated; *m*:others = 4:1).

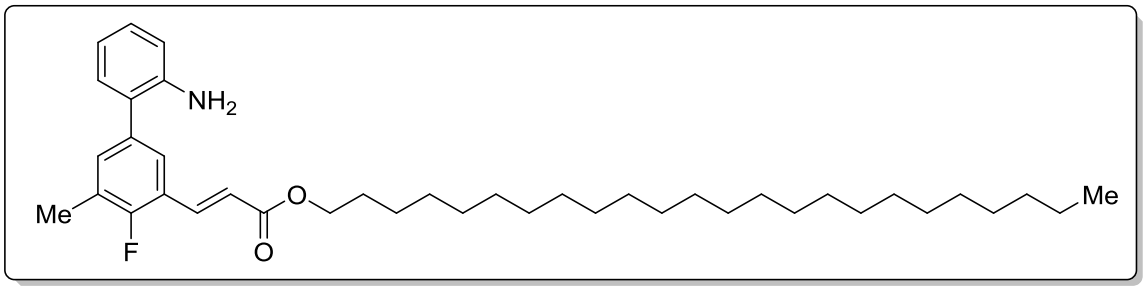
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.90 (d, *J* = 16.2 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.42 (td, *J* = 7.4, 1.7 Hz, 1H), 7.27 – 7.21 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.59 (d, *J* = 16.2 Hz, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 1.37 (t, *J* = 6.4 Hz, 3H).
^{13}C NMR (101 MHz, CDCl3) δ (ppm) 166.78, 159.50, 143.40 (d, *J* = 79.9 Hz), 137.13 (d, *J* = 3.6), 133.73 (d, *J* = 4.3 Hz), 130.94, 129.56, 129.45, 128.34 (d, *J* = 2.9 Hz), 124.73 (d, *J* = 4.3 Hz), 123.30 (d, *J* = 12.7 Hz),, 121.27 (d, *J* = 6.5 Hz), 121.00, 118.76, 116.02, 60.69, 14.31.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -116.17
IR (thin film, cm^{-1}): 1035, 1095, 1174, 1210, 1263, 1314, 1367, 1438, 1501, 1637, 1708, 2854, 2924, 2958, 3378, 3468.
HRMS (*m/z*): [M+H^+] calcd for $C_{17}H_{17}FNO_2$: 286.1238; found, 286.1237.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).



***Ethyl (E)-3-(2'-amino-4-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **65** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: yellow oil.
Yield: 69% (42 mg isolated; *m*:others = 8:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.87 (d, *J* = 16.2 Hz, 1H), 7.48 (dd, *J* = 6.4, 1.7 Hz, 1H), 7.32 (d, *J* = 5.8 Hz, 1H), 7.21 – 7.17 (m, 1H), 7.10 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.86, 160.12 (d, *J* = 5.4 Hz), 158.10, 143.40, 137.31 (d, *J* = 3.7, Hz), 135.33 (d, *J*= 4.3 Hz) 133.91 (d, *J* = 5.7 Hz), 130.32, 128.84, 126.95 (d, *J* = 2.7 Hz), 126.18 (d, *J* = 16.5 Hz), 122.52 (d, *J* = 12.7 Hz), 120.94 (d, *J* = 6.3 Hz), 118.82, 115.74, 60.62, 14.68 (d, *J* = 4.66 Hz), 14.31.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -120.75.
IR (thin film, cm^{-1}): 1040, 1095, 1180, 1273, 1298, 1367, 1475, 1638, 1710, 2854, 2925, 2958, 3373, 3469.
HRMS (ESI): [M+H^+] calcd for $C_{18}H_{19}FNO_2$: 300.1394; found, 300.1394.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

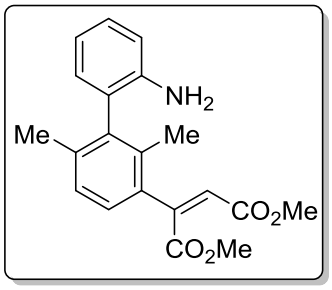


***Ethyl (E)-3-(2'-amino-4-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)but-2-enoate*:** Compound **66** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: colorless oil.
Yield: 58% (34 mg isolated; *m*:others = 4:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.21 – 7.18 (m, 2H), 7.11 (d, *J* = 6.7 Hz, 2H), 6.84 (t, *J* = 7.2 Hz, 1H), 6.78 (d, *J* = 6.7 Hz, 1H), 6.06 (s, 1H), 3.78 (s, 3H), 2.58 (s, 3H), 2.36 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.86, 160.12, 158.10, 143.40, 137.31, 135.33, 133.9 (d, *J* =25.4 Hz, C-F), 130.32, 128.84, 126.95, 126.41, 122.52, 120.98 (d, *J* =18.7 Hz, C-F), 118.82, 115.74, 60.62, 14.68, 14.65.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -119.56, -120.50.
IR (thin film, cm^{-1}): 1036, 1120, 1171, 1260, 1336, 1457, 1618, 1721, 2854, 2926.
HRMS (*m/z*): [M+H^+] calcd for $C_{18}H_{19}FNO_2$: 300.1394; found, 300.1398.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

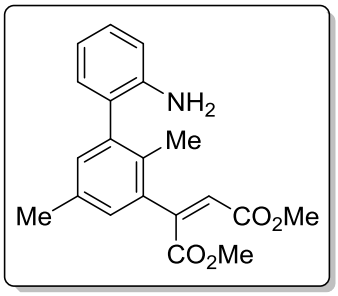


Tricosyl (E)-3-(2'-amino-4-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **67** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 69% (82 mg isolated; *m*:others = 12:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.87 (d, *J* = 16.2 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.19 (dd, *J* = 11.0, 4.4 Hz, 1H), 7.10 (dd, *J* = 7.5, 1.2 Hz, 1H), 6.85 (t, *J* = 7.3 Hz, 1H), 6.79 (d, *J* = 9.3 Hz, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 4.22 (t, *J* = 6.7 Hz, 2H), 2.36 (s, 3H), 1.77 – 1.67 (m, 4H), 1.45 – 1.37 (m, 4H),1.29 – 1.28 (m, 36H), 0.91 (t, *J* = 6.8 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.96, 157.21, 137.28, 135.41 (d, *J* = 25.4 Hz), 133.96, 133.88, 130.32, 128.84, 128.25, 128.11, 126.96 (d, *J* = 2.7 Hz), 126.18 (d, *J* = 18.2 Hz), 122.50 (d, *J* = 14.7 Hz), 122.50 (d, *J* = 14.7 Hz), 120.97 (d, *J* = 6.0 Hz), 118.87 (d, *J* = 6.8 Hz), 115.79, 115.75, 64.86, 31.94, 29.67, 29.60, 29.55, 29.37, 29.30, 28.71, 25.98, 14.65 (d, *J* = 4.2 Hz).
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -120.73.

IR (thin film, cm^{-1}): 1175, 1273, 1298, 1379, 1467, 1638, 1715, 2852, 2920, 3377.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{39}H_{61}FNO_3$: 594.4680; found, 594.4682.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

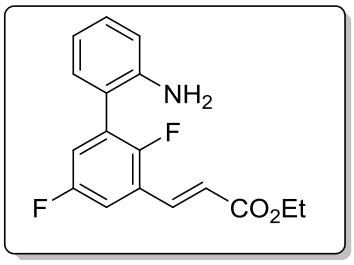


***Dimethyl 2-(2'-amino-4-fluoro-2,6-dimethyl-[1,1'-biphenyl]-3-yl)maleate*:** Compound **68** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: colorless oil.
Yield: 49% (33 mg isolated; *m*:others = 10:1)
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.27 – 7.24 (m, *J* = 7.9 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 2H), 6.92 (d, *J* = 6.2 Hz, 1H), 6.86 (t, *J* = 6.9 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.07 (s, 1H), 3.87 (s, 3H), 3.82 (s, 3H), 2.07 (s, 6H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 168.11, 165.48, 148.37, 138.83, 135.30, 133.22, 129.67, 128.51, 127.91, 127.76, 126.00, 123.47, 52.63, 52.07, 20.41, 17.66.
IR (thin film, cm^{-1}): 1168, 1198, 1226, 1256, 1343, 1435, 1497, 1616, 1727, 2854, 2924, 3382, 3473.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{20}H_{21}NNaO_4$: 362.1363; found, 362.1361.
TLC: R_f = 0.4 (80:20 petroleum ether:EtOAc).

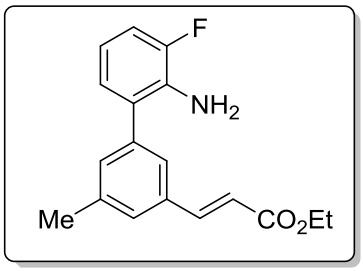


***Dimethyl 2-(2'-amino-2,5-dimethyl-[1,1'-biphenyl]-3-yl)maleate*:** Compound **69** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: colorless oil.
Yield: 62% (42 mg isolated; *m*:others = 8:1)
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.19 (d, *J* = 14.3 Hz, 2H), 7.15 (s, 1H), 7.09 (s, 1H), 7.01 (d, *J* = 7.0 Hz, 1H), 6.83 (t, *J* = 7.1 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.08 (s, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 2.36 (s, 3H), 2.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 167.96, 165.43, 148.41, 143.55, 139.81, 139.30, 135.83, 135.68, 131.98, 130.07, 128.72, 128.55, 123.67, 118.44, 115.16, 114.08, 52.66, 52.11, 20.78, 16.69.
IR (thin film, cm^{-1}): 1168.16, 1198.40, 1226.73, 1256.04, 1343.56, 1435.95, 1497.52, 1616.11, 1727.89, 2854.67, 2924.89, 3382.68, 3473.87.
HRMS (*m/z*): [M+Na$^+$] calcd for $C_{20}H_{21}NNaO_4$: 362.1363; found, 362.1363.
TLC: R_f = 0.4 (80:20 petroleum ether:EtOAc).

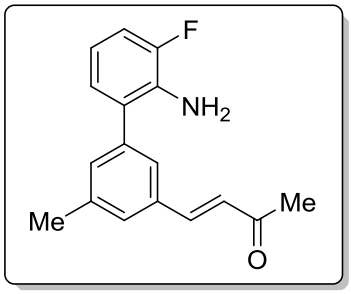


Ethyl (E)-3-(2'-amino-2,5-difluoro-[1,1'-biphenyl]-3-yl)acrylate: Compound **70** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 56% (34 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.82 (d, *J* = 16.2 Hz, 1H), 7.26 – 7.22 (m, 2H), 7.12 – 7.09 (m, 2H), 6.85 – 6.80 (m, 2H), 6.54 (d, *J* = 16.2 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 166.78, 159.50, 143.40 (d, *J* = 79.9 Hz), 137.13 (d, *J* = 3.6), 133.73 (d, *J* = 4.3 Hz), 130.94, 129.56, 129.45, 128.34 (d, *J* = 2.9 Hz), 124.73 (d, *J* = 4.3 Hz), 123.30, 121.27 (d, *J* = 6.5 Hz), 121.00, 118.76, 116.02, 60.69, 14.31.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) **-**117.50, -121.74.
IR (thin film, cm^{-1}): 1036, 1095, 1178, 1271, 1302, 1345, 1369, 1448, 1620, 1712, 2855, 2925, 2958, 3071, 3234, 3377, 3479.
HRMS (*m/z*): [M+H$^+$] calcd for $C_{17}H_{16}F_2NO_2$: 304.1144; found, 304.1143.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

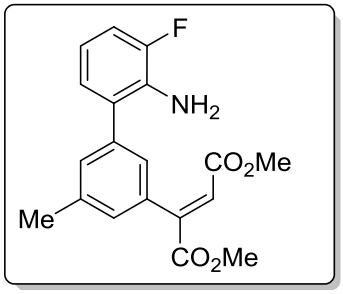


Ethyl (E)-3-(2'-amino-3'-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **71** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 71% (42 mg isolated; *m*:others = 12:1).

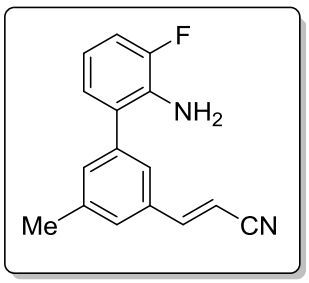
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 16.0 Hz, 1H), 7.45 (s, 1H), 7.37 (s, 1H), 7.32 (s, 1H), 7.03 (t, *J* = 7.2 1H), 6.93 (d, *J* = 7.1 Hz, 1H), 6.79 – 6.75 (m, 1H), 6.49 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 2H), 2.45 (s, 3H), 1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.95, 151.77 (d, *J* = 238.5 Hz), 144.27, 139.01 (d, *J* = 3.0 Hz), 135.14, 132.19 (d, *J* = 12.6 Hz), 131.53, 129.62, 128.80, 128.29, 127.91, 125.48 (d, *J* = 2.9 Hz), 118.74, 117.81 (d, *J* = 7.9 Hz), 114.29 (d, *J* = 19.0 Hz), 60.55, 21.36, 14.32.
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -134.18.
IR (thin film, cm^{-1}): 1038, 1096, 1172, 1215, 1272, 1367, 1477, 1597, 1629, 1710, 2856, 2927, 3383.
HRMS (ESI): [M+Na^+] calcd for $C_{18}H_{18}FNNaO_2$: 322.1214; found, 322.1215.
TLC: R_f = 0.4 (80:20 petroleum ether:EtOAc).



***(E)-4-(2'-amino-3'-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)but-3-en-2-one*:** Compound **72** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (91/9, v/v).
Physical State: colorless oil.
Yield: 60% (32 mg isolated; *m*:others = 10:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.52 (d, *J* = 16.3 Hz, 1H), 7.44 (s, 1H), 7.36 (s, 1H), 7.31 (s, 1H), 7.01 (ddd, *J* = 10.9, 8.1, 1.3 Hz, 1H), 6.91 (d, *J* = 7.7 Hz, 1H), 6.77 – 6.72 (m, 2H), 3.81 (s, 2H), 2.43 (s, 3H), 2.38 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.36, 151.77 (d, *J* = 238.85 Hz, C-F), 143.11, 139.45, 139.11 (d, *J* = 3.04 Hz, C-F), 135.09, 132.23 (d, *J* = 13.00 Hz, C-F), 131.85, 128.67 (d, *J* = 3.27 Hz, C-F), 128.08, 127.43, 126.00, 125.40 (d, *J* = 2.89, C-F), 117.86 (d, *J* = 7.58 Hz, C-F), 114.34 (d, *J* = 19.06 Hz), 27.69, 21.38.
^{9}F NMR (471 MHz, $CDCl_3$) δ (ppm) -134.33.
IR (thin film, cm^{-1}): 1064, 1172, 1215, 1254, 1360, 1433, 1477, 1625, 1668, 2856, 2924, 3020, 3371.
HRMS (ESI): [M+H^+] calcd for $C_{17}H_{17}FNO$: 270.1289; found 270.1284.
TLC: R_f = 0.4 (80:20 petroleum ether:EtOAc).

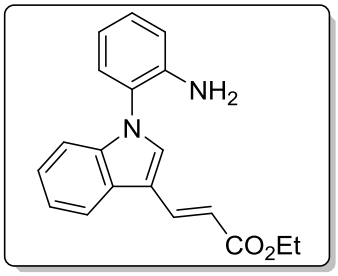


***Dmethyl 2-(2'-amino-3'-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)maleate*:** Compound **73** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (93/7, v/v).
Physical State: colorless solid.
Yield: 52% (30 mg isolated; *m*:others = 20:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.36 (d, *J* = 14.6 Hz, 2H), 7.27 (s, 1H), 7.00 (ddd, *J* = 10.8, 8.1, 1.3 Hz, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.76 – 6.71 (m, 1H), 6.35 (s, 1H), 3.96 (s, 3H), 3.79 (s, 3H), 2.42 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 168.11, 165.48, 148.37, 139. 18 (d, *J* = 34.3 Hz), 138.83, 135.30, 133.22, 129.67, 128.51, 127.91, 127.76, 126.00, 123.47, 120.64, 118.80, 115.33, 52.63, 52.07, 20.41
^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm).-134.18.
IR (thin film, cm^{-1}): 1021, 1048, 1168, 1197, 1269, 1348, 1436, 1478, 1597, 1626, 1722, 2854, 2925, 3383, 3473.
HRMS (ESI): [M+Na$^+$] calcd for $C_{19}H_{18}FNNaO_4$: 366.1112; found, 366.1112.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).



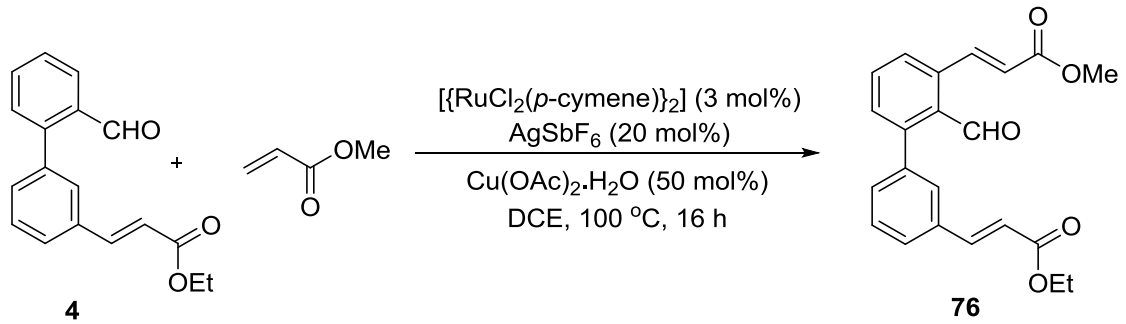
***(E)-3-(2'-amino-3'-fluoro-5-methyl-[1,1'-biphenyl]-3-yl)acrylonitrile*:** Compound **74** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (92/8, v/v).
Physical State: colorless oil.
Yield: 47% (24 mg isolated; *m*:others = 6:1).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.43 (d, *J* = 16.6 Hz, 2H), 7.37 (s, 1H), 7.37 (s, 1H), 7.29 (s, 1H), 7.06 – 7.02 (m, 2H), 6.91 (d, *J* = 7.6 Hz, 2H), 6.79 – 6.75 (m, 2H), 5.92 (d, *J* = 16.6 Hz, 2H), 3.77 (s, 2H), 2.46 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 150.32, 139.72, 134.13, 134.09, 132.61, 132.37, 128.79 (d, *J* = 114.96 Hz, C-F), 127.33, 125.50 (d, *J* = 3.76 Hz, C-F), 125.14, 118.13, 114.71, 114.56, 96.80, 21.35.

^{19}F NMR (471 MHz, $CDCl_3$) δ (ppm) -120.08.
IR (thin film, cm^{-1}): 1040, 1066, 1140, 1173, 1217, 1272, 1436, 1477, 1595, 1622, 2218, 2854, 2923, 3380, 3482
HRMS (ESI): [M+H^+] calcd for $C_{16}H_{14}FN_2$: 253.1136; found 253.1139
TLC: R_f = 0.4 (80:20 petroleum ether:EtOAc).

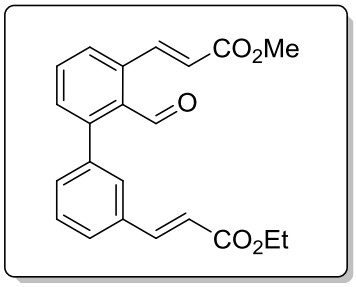


***Ethyl (E)-3-(1-(2-aminophenyl)-1H-indol-3-yl)acrylate*:** Compound **75** was prepared by general procedure E (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: colorless oil.
Yield: 37% (23 mg isolated; *m*:others = 12:1).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.99 (dd, *J* = 6.5, 2.0 Hz, 1H), 7.95 (d, *J* = 16.0 Hz, 1H), 7.51 (s, 1H), 7.33 – 7.30 (m, 1H), 7.28 (dd, *J* = 7.2, 2.0 Hz, 2H), 7.18 (td, *J* = 7.9, 1.5 Hz, 2H), 6.91 – 6.89 (m, 1H), 6.86 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.60 (s, 2H), 1.36 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 168.14, 142.88, 137.76, 137.62, 132.55, 129.87, 128.44, 126.03, 124.60, 123.68, 123.59, 121.92, 120.65, 118.73, 116.48, 114.02, 111.51, 60.17, 14.45.
IR (thin film, cm^{-1}): 1042, 1161, 1215, 1370, 1466, 1625, 1704, 2851, 2927.
HRMS (ESI): [M+H^+] calcd for $C_{19}H_{19}N_2O_2$: 307.1441; found 307.1443.
TLC: R_f = 0.5 (80:20 petroleum ether:EtOAc).

2.12 Post-synthetic applications of 4



Procedure: A modified procedure was followed from the literature report.[2] A 25 mL two-neck round bottom flask containing [{$RuCl_2$(*p*-cymene)}$_2$] (0.007 mmol, 4.4 mg), $AgSbF_6$ (0.071 mmol, 24.5 mg) and $Cu(OAc)_2$. (0.1785 mmol, 32.3 mg) was evacuated and purged with nitrogen gas three times. To the flask or tube were then added aldehyde (0.357 mmol), methyl acrylate (1.785 mmol, 170 µL) and 1,2-dichloroethane (7.0 mL) *via* syringes and allowed the reaction mixture to stir at room temperature for 5 min. Then, the reaction mixture was allowed to stir at 100 °C for 16 h under open atmosphere. After cooling to ambient temperature, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and silica gel, and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexanes and ethyl acetate as eluent to give desired product.



***Ethyl (E)-3-(3'-chloro-2'-formyl-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **76** was prepared by above procedure.

Eluent: petroleum ether/ethyl acetate (90/10, v/v).

Physical State: yellow oil.

Yield: 66% (85 mg isolated).

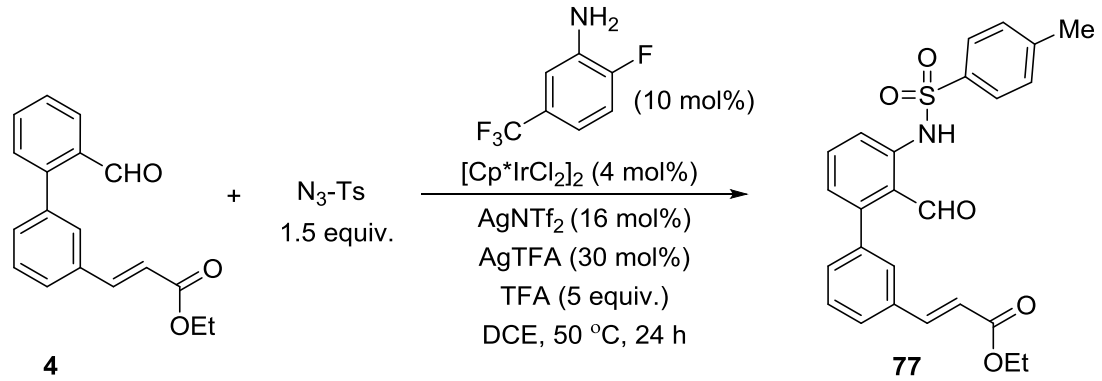
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 9.99 (s, 1H), 8.38 (d, *J* = 15.9 Hz, 1H), 7.71 (d, *J* = 16.0 Hz, 1H), 7.63 (d, *J* = 4.9 Hz, 2H), 7.61 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.49 (m, 2H), 7.47 (dd, *J* = 7.5, 3.3 Hz, 1H), 7.35 (d, *J* = 7.7 Hz, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 6.37 (d, *J* = 15.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 193.29, 167.07, 166.90, 146.22, 144.00, 143.77, 138.86, 136.42, 135.14, 133.00, 132.70, 132.14, 131.84, 129.48, 129.33, 128.06, 122.07, 119.82, 115.51, 60.89, 52.09, 14.50.

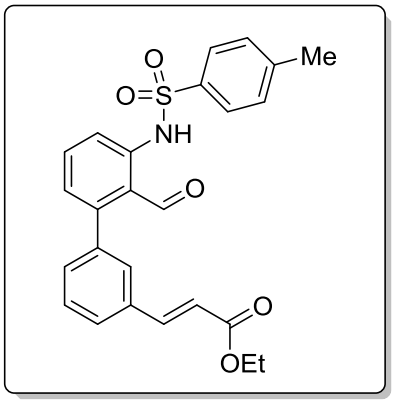
IR (thin film, cm^{-1}): 695, 755, 795, 864, 978, 1035, 1094, 1167, 1263, 1311, 1367, 1411, 1435, 1576, 1637, 1707, 2760, 2852, 2952, 2982.

HRMS (ESI): [M+Na$^+$] calcd. for $C_{22}H_{20}NaO_5$: 387.1203, found 387.1200.

TLC: R_f = 0.4 (85:15 petroleum ether:EtOAc).



Procedure: A modified procedure was followed from the literature report.[3] To a solution of compound **4** (0.2 mmol) and tosyl azide (0.3 mmol, 59.2 mg) in 1.0 mL of DCE were added $[Cp^*IrCl_2]_2$ (0.008 mmol, 6.4 mg), $AgNTf_2$ (0.032 mmol, 14 mg), AgTFA (0.06 mmol, 13.5 mg), 2-fluoro-5-(trifluoromethyl)aniline (0.002 mmol, 3.6 mg), and TFA (1.0 mmol, 77 μl). The mixture was stirred at 50 °C for 24 hours. Upon completion, the reaction mixture was cooled to room temperature and concentrated in vacuo. The crude residue was purified by column chromatography on silica gel using petroleum ether/EtOAc as eluent to afford the desired products.



Ethyl (E)-3-(2'-formyl-3'-((4-methylphenyl)sulfonamido)-[1,1'-biphenyl]-3-yl)acrylate: Compound **77** was prepared by above procedure.

Eluent: petroleum ether/ethyl acetate (70/30, v/v).

Physical State: yellow oil.

Yield: 61% (54 mg isolated).

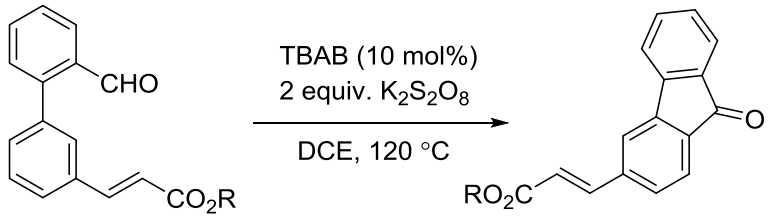
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 11.35 (s, 1H), 9.73 (s, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.72 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 16.0 Hz, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.41 (s, 1H), 7.27 (d, *J* = 9.4 Hz, 3H), 7.02 – 7.00 (m, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.39 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 195.09, 166.84, 148.20, 144.41, 143.63, 140.92, 138.39, 136.73, 135.49, 135.08, 131.85, 130.01, 129.54, 129.26, 129.15, 128.14, 127.59, 126.22, 125.18, 119.89, 119.42, 117.46, 60.91, 21.79, 14.50.

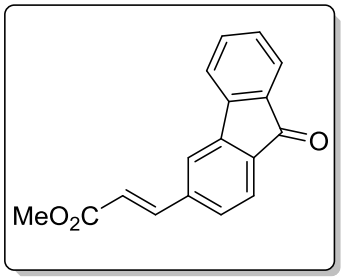
IR (thin film, cm^{-1}): 797, 896, 986, 1036, 1091, 1164, 1278, 1304, 1381, 1464, 1661, 1713, 2858, 2925.

HRMS (ESI): [M+Na$^+$] calcd for $C_{25}H_{23}NNaO_5S$: 472.1189, found 472.1188.

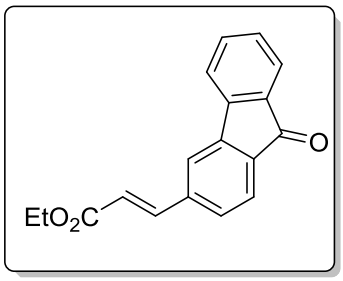
TLC: R_f = 0.4 (70:30 petroleum ether:EtOAc).



Procedure: A modified procedure was followed from the literature report.[4] To a 10 mL Schleck tube, Tetrabutyl ammonium bromide (TBAB, 10 mol%), $K_2S_2O_8$ (2.0 equiv.) and the tube was purged with argon for three times, followed by addition of aldehyde (0.2 mmol) and DCE (2.0 mL). The formed mixture was stirred at 120 ℃ under argon for 36 h. The solution was then cooled to room temperature, and DCE was removed under vacuum. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate) to afford the desired product.



***Methyl (E)-3-(9-oxo-9H-fluoren-1-yl)acrylate*:** Compound **78** was prepared by above procedure (0.2 mmol scale).
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 47% (25 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.82 (d, *J* = 16.3 Hz, 1H), 7.67 (d, *J* = 7.3 Hz, 1H), 7.54 – 7.50 (m, *J* = 7.9 Hz, 4H), 7.49 – 7.45 (m, 1H), 7.33 (t, *J* = 7.1 Hz, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 3.87 (s, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 193.99, 166.94, 145.09, 143.42, 139.02, 134.76, 134.35, 134.30, 134.02, 130.64, 129.44, 126.30, 124.32, 121.96, 121.33, 120.29, 51.93.
IR (thin film, cm^{-1}): 666, 756, 800, 872, 924, 1036, 1098, 1183, 1233, 1286, 1308, 1367, 1468, 1607, 1638, 1707, 2852, 2925.
HRMS (ESI): [M+Na$^+$] calcd. for $C_{17}H_{12}NaO_3$: 287.067; found 287.0680.
TLC: R_f = 0.4 (95:5 petroleum ether:EtOAc).



Ethyl (E)-3-(9-oxo-9H-fluoren-3-yl)acrylate: Compound **79** was prepared by the above procedure (0.2 mmol scale).

Eluent: petroleum ether/ethyl acetate (95/5, v/v).

Physical State: yellow oil.

Yield: 52% (52 mg isolated).

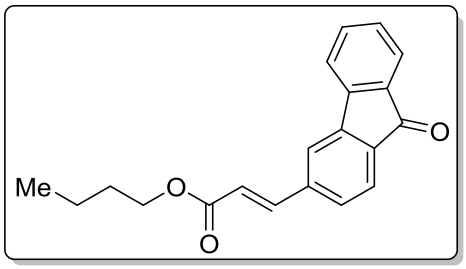
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.85 (t, *J* = 11.9 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 1H), 7.57 – 7.54 (m, 3H), 7.54 – 7.52 (m, 1H), 7.51 – 7.48 (m, 1H), 7.35 (td, *J* = 7.4, 2.3 Hz,1H), 6.58 (d, *J* = 16.2 Hz, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 194.05, 166.52, 145.12, 143.47, 138.78, 134.75, 134.50, 134.35, 134.08, 130.67, 129.45, 126.36, 124.34, 122.52, 121.25, 120.28, 60.76, 14.32.

IR (thin film, cm^{-1}): 666, 756, 800, 872, 924, 1036, 1098, 1183, 1233, 1286, 1308, 1367, 1468, 1607, 1638, 1707, 2852, 2925.

HRMS (ESI): [M+Na$^+$] calcd. for $C_{18}H_{14}NaO_3$: 301.0835, found 301.0831.

TLC: R_f = 0.4 (95:5 petroleum ether:EtOAc).



Butyl (E)-3-(9-oxo-9H-fluoren-3-yl)acrylate: Compound **80** was prepared by above procedure (0.2 mmol scale).

Eluent: petroleum ether/ethyl acetate (95/5, v/v).

Physical State: yellow oil.

Yield: 44% (27 mg isolated).

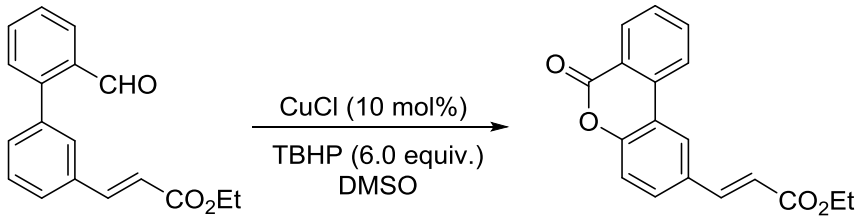
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 8.81 (d, *J* = 16.2 Hz, 1H), 7.66 (d, *J* = 7.4 Hz, 1H), 7.50 (ddd, *J* = 13.3, 10.9, 7.2 Hz, 5H), 7.32 (td, *J* = 7.2, 1.2 Hz, 1H), 6.56 (d, *J* = 16.2 Hz, 1H), 4.25 (t, *J* = 6.7 Hz, 2H), 1.76 – 1.69 (m, 2H), 1.47 (dd, *J* = 15.0, 7.5 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 194.21, 166.79, 145.31, 143.67, 138.96, 134.93, 134.72, 134.52, 134.29, 130.87, 129.64, 126.57, 124.54, 122.73, 121.43, 120.48, 64.86, 30.97, 19.42, 13.99.

IR (thin film, cm^{-1}): 667, 755, 800, 872, 923, 990, 1024, 1069, 1167, 1232, 1276, 1306, 1382, 1420, 1468, 1582, 1607, 1637, 1704, 2307, 2873, 2933, 2959, 3056.

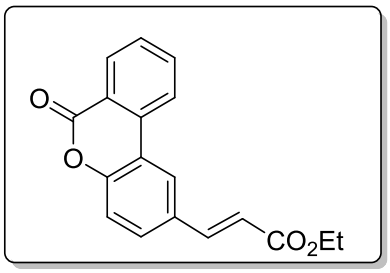
HRMS (ESI): [M+Na$^+$] calcd. for $C_{20}H_{18}NaO_3$: 329.1148, found 329.1146.

TLC: R_f = 0.25 (95:5 petroleum ether:EtOAc).



4 **81**

Procedure: A modified procedure was followed from the literature report.[5] The substrate **4** (0.25 mmol) and CuCl (5 mol%) were taken in a single neck round bottomed flask and then 2.0 mL DMSO was added. The reaction mixture was stirred and then TBHP (70% in water) (6.0 equiv.) was added drop wise. The stirring was continued at room temperature for 4h. After completion of the reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (3 x 20 mL). The combined organic layer was evaporated under reduced pressure and the crude product was purified by column chromatography using silica gel (60 -120 mesh) and hexane/ethyl acetate as eluent.



***Ethyl (E)-3-(6-oxo-6H-benzo[c]chromen-2-yl)acrylate*:** Compound **81** was prepared by above procedure.

Eluent: petroleum ether/ethyl acetate (95/5, v/v).

Physical State: yellow oil.

Yield: 52% (30 mg isolated).

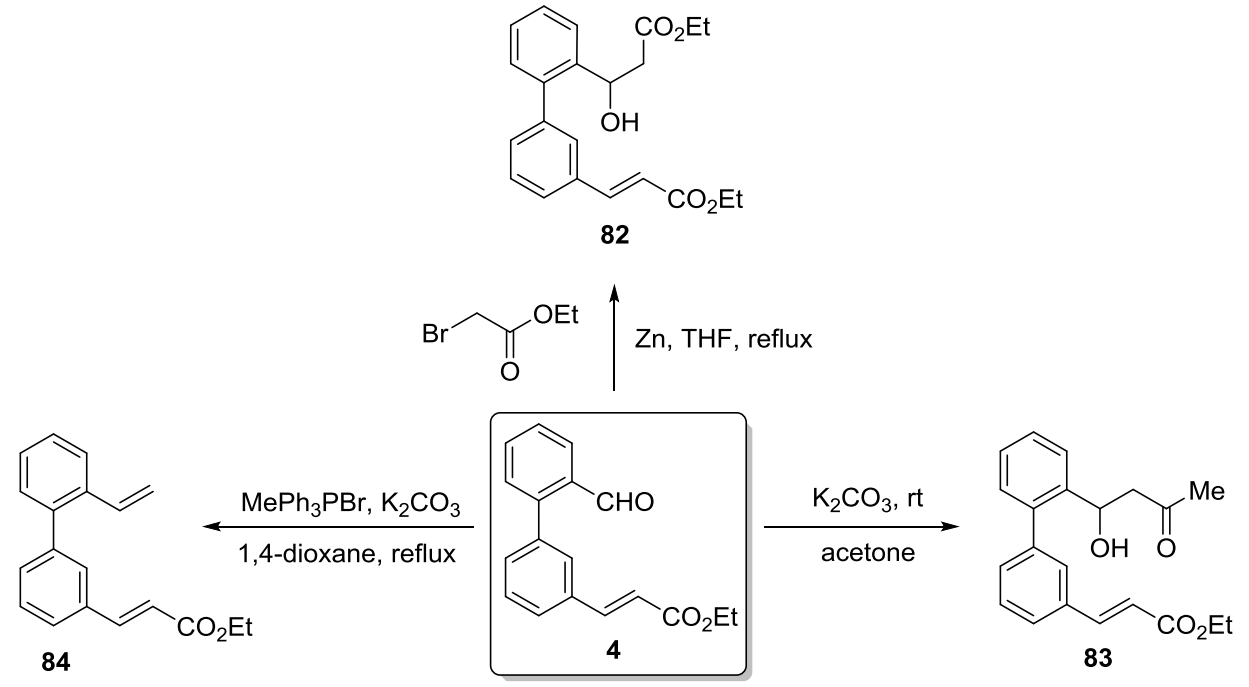
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.43 (d, *J* = 7.0 Hz, 1H), 8.20 (s, 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.88 (t, *J* = 7.7 Hz, 1H), 7.78 (d, *J* = 16.0 Hz, 1H), 7.68 (d, *J* = 8.7, 2.1 Hz, 1H), 7.63 (t, *J* = 7.9 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 6.51 (d, *J* = 16.0 Hz, 1H), 4.29 (q, *J* = 7.3 Hz, 2H), 1.36 (t, *J* = 6.6 Hz, 3H).

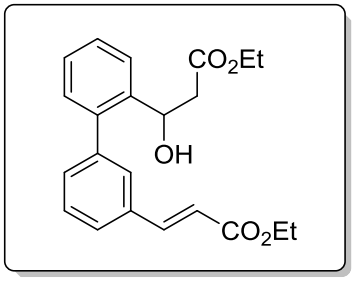
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.63, 166.27, 144.04, 142.83, 139.32, 135.44, 134.09, 133.88, 133.54, 132.32, 131.44, 131.02, 128.86, 128.64, 128.59, 120.89, 61.00, 52.78, 14.49

IR (thin film, cm^{-1}): 627, 747, 804, 869, 971, 1014, 1098, 1177, 1256, 1337, 1498, 1622, 1740, 2812, 2947.

HRMS (ESI): [M+H$^+$] calcd. for $C_{18}H_{15}O_4$: 295.0965; found: 295.0965.

TLC: R_f = 0.5 (90:10 petroleum ether:EtOAc).





***Ethyl (E)-3-(2'-(3-ethoxy-1-hydroxy-3-oxopropyl)-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **82** was prepared from the literature report (0.2 mmol scale).[6]

Eluent: petroleum ether/ethyl acetate (90/10, v/v).

Physical State: colorless oil.

Yield: 68% (50 mg isolated).

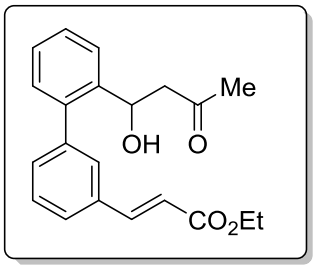
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.71 (d, *J* = 16.0 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.45 (dd, *J* = 16.2, 8.5 Hz, 3H), 7.35 (t, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 7.5 Hz, 1H), 6.47 (d, *J* = 16.0 Hz, 1H), 5.25 (d, *J* = 9.6 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.36 (s, 1H), 2.93 (dd, *J* = 17.6, 9.8 Hz, 1H), 2.77 (dd, *J* = 17.6, 2.4 Hz, 1H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.88, 166.69, 144.18, 141.28, 139.64, 139.44, 134.71, 130.95, 130.09, 128.93, 128.79, 128.36, 127.76, 126.96, 126.12, 118.95, 66.21, 61.56, 60.56, 50.65, 49.66, 14.31, 14.06.

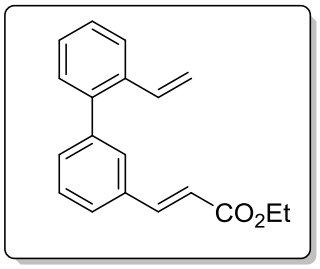
IR (thin film, cm^{-1}): 698, 760, 801, 864, 915, 983, 1034, 1095, 1178, 1263, 1317, 1367, 1414, 1474, 1638, 1709, 2932, 2980, 3503.

HRMS (ESI): [M+H$^+$] calcd. for $C_{22}H_{24}O_5$: 368.1624, found 368.1632.

TLC: R_f = 0.4 (85:15 petroleum ether:EtOAc).

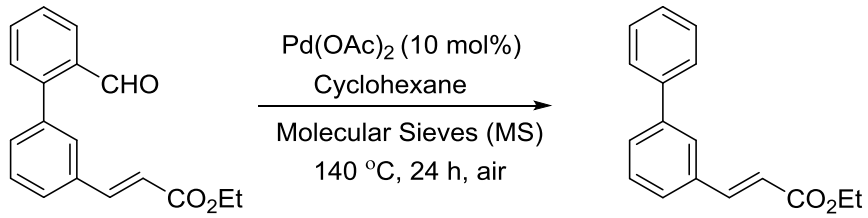


***Ethyl (E)-3-(2'-(1-hydroxy-3-oxobutyl)-[1,1'-biphenyl]-3-yl)acrylate*:** Compound **83** was prepared from the literature report (0.2 mmol scale).[6]
Eluent: petroleum ether/ethyl acetate (90/10, v/v).
Physical State: colorless oil.
Yield: 70% (51 mg isolated).
^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.71 (d, *J* = 16.0 Hz, 1H), 7.65 (d, *J* = 7.7 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.45 (dd, *J* = 14.5, 6.8 Hz, 3H), 7.37 – 7.32 (m, 2H), 7.20 (d, *J* = 7.3 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 5.24 – 5.19 (m, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.33 (s, 1H), 2.80 (dd, *J* = 17.7, 9.8 Hz, 1H), 2.63 (dd, *J* = 17.7, 2.3 Hz, 1H), 2.07 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 209.32, 167.11, 144.41, 141.63, 139.84, 139.79, 134.85, 131.17, 130.23, 129.13, 128.98, 128.54, 127.84, 127.13, 126.37, 119.12, 66.46, 60.80, 51.23, 30.74, 14.52.
IR (thin film, cm^{-1}): 698, 762, 802, 864, 982, 1036, 1094, 1177, 1270, 1317, 1366, 1415, 1474, 1637, 1707, 2930, 2980, 3488.
HRMS (ESI): [M+H$^+$] calcd. for $C_{21}H_{22}O_4$: 338.1519, found 338.1522.
TLC: R_f = 0.5 (85:15 petroleum ether:EtOAc).



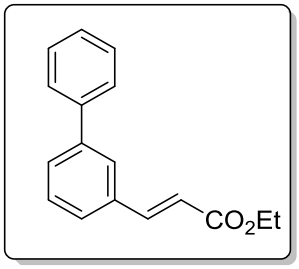
Ethyl (E)-3-(2'-vinyl-[1,1'-biphenyl]-3-yl)acrylate: Compound **84** was prepared from the literature report (0.2 mmol scale).[6]
Eluent: petroleum ether/ethyl acetate (97/3, v/v).
Physical State: colorless oil.
Yield: 78% (43 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.72 (d, *J* = 16.0 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.52 (d, *J* = 8.1 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.39 – 7.32 (m, 3H), 7.30 – 7.26 (m, 1H), 6.67 (dd, *J* = 17.5, 11.0 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 5.71 (dd, *J* = 17.5, 0.9 Hz, 1H), 5.21 (dd, *J* = 11.0, 1.0 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 167.21, 144.66, 141.78, 140.16, 136.00, 135.77, 134.53, 131.86, 130.17, 129.64, 128.84, 128.06, 127.99, 126.88, 126.08, 118.85, 115.41, 60.76, 14.53.
IR (thin film, cm^{-1}): 697, 762, 802, 865, 910, 985, 1039, 1094, 1178, 1264, 1318, 1367, 1471, 1639, 1712, 2981.
HRMS (ESI): [M+Na$^+$] calcd. for $C_{19}H_{18}NaO_2$: 301.0835, found 301.0831.
TLC: R_f = 0.5 (95:5 petroleum ether:EtOAc).



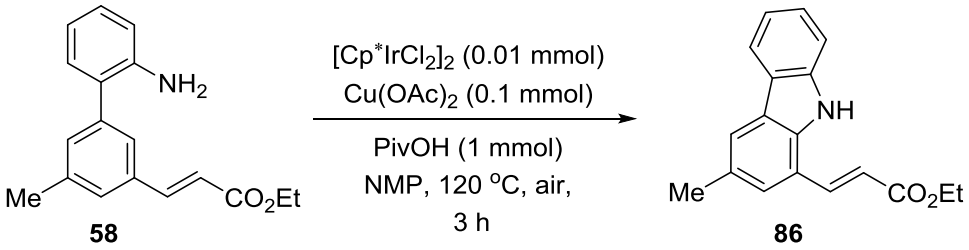
4 **85**

Procedure: A modified procedure was followed from the literature report.[7] A clean, oven-dried screw-cap reaction tube with a magnetic stir-bar was charged with molecular sieves (4 Å, 150 mg), aldehyde (0.2 mmol), and palladium acetate (10 mol%). Cyclohexane (1.5 mL) was added to this mixture with a syringe. The screw cap was closed tightly, and the tube was placed in a preheated oil bath at the required temperature. The reaction mixture was stirred vigorously at 140 °C for 24 h. After the completion of the reaction, the solvent was evaporated under vacuum and the residue was purified by column chromatography on silica gel using petroleum ether-ethyl acetate to obtain the desired product.

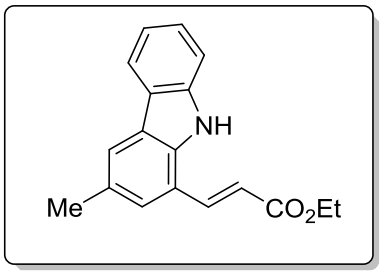


Ethyl (E)-3-([1,1'-biphenyl]-3-yl)acrylate: Compound **85** was prepared by above procedure.
Eluent: petroleum ether/ethyl acetate (95/5, v/v).
Physical State: yellow oil.
Yield: 56% (28 mg isolated).
^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.81 – 7.75 (m, *J* = 16.4, 3.6 Hz, 2H), 7.65 – 7.60 (m, 3H), 7.56 – 7.53 (m, 1H), 7.49 (t, *J* = 9.5, 5.7 Hz, 3H), 7.41 (t, 1H), 6.54 (d, *J* = 16.0 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm) 166.99, 144.53, 141.97, 140.45, 134.98, 129.33, 129.04, 128.90, 127.70, 127.15, 126.89, 126.82, 118.65, 60.57, 14.34.
IR (thin film, cm^{-1}): 1032, 1124, 1189, 1248, 1367, 1439, 1552, 2812, 2957.
HRMS (ESI): [M+Na$^+$] calcd. for $C_{17}H_{16}NaO_2$: 303.1043; found: 275.1038.
TLC: R_f = 0.4 (95:5 petroleum ether:EtOAc).

2.13 Post-synthetic applications of 58



Procedure: The procedure was followed from the modified literature report.[8] To a 20 mL two-necked flask with a reflux condenser and a rubber cup were added **58** (0.5 mmol), $[Cp^*IrCl_2]_2$ (0.01 mmol), $Cu(OAc)_2$ (0.1 mmol), PivOH (1.0 mmol) in NMP (3 mL). The resulting mixture was stirred under air at 120 °C for 3 hours. After cooling, the reaction mixture was extracted with ethyl acetate (100 mL), washed with aqueous $NaHCO_3$ (100 mL, three times), and dried over Na_2SO_4. Purification by column chromatography on silica gel using petroleum ether-ethyl acetate as eluent.



Ethyl (E)-3-(3-methyl-9H-carbazol-1-yl)acrylate: Compound **86** was prepared by above procedure (0.5 mmol scale).

Eluent: petroleum ether/ethyl acetate (80/20, v/v).

Physical State: pale yellow oil.

Yield: 55% (77 mg isolated).

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.47 (s, 1H), 7.69 (d, *J* = 16.0 Hz, 1H), 7.32 (s, 1H), 7.30 (s, 1H), 7.17 (ddd, *J* = 7.9, 7.4, 1.6 Hz, 1H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.83 (td, *J* = 7.5, 1.1 Hz, 1H), 6.77 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.46 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.41 (s, 3H), 1.33 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 167.04, 144.49, 143.44, 140.17, 139.16, 134.98, 131.80, 130.31, 128.76, 127.57, 126.88, 125.93, 118.74, 118.51, 115.69, 60.53, 21.37, 14.33.

IR (thin film, cm^{-1}): 1031, 1115, 1167, 1284, 1305, 1377, 1445, 1495, 1608, 1787, 1917, 2874, 2914, 3341.

HRMS (*m/z*): [M+H$^+$] calcd for $C_{18}H_{18}NO_2$: 280.1333; found, 280.1334.

TLC: R_f = 0.4 (90:10 petroleum ether:EtOAc).

2.14 References

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