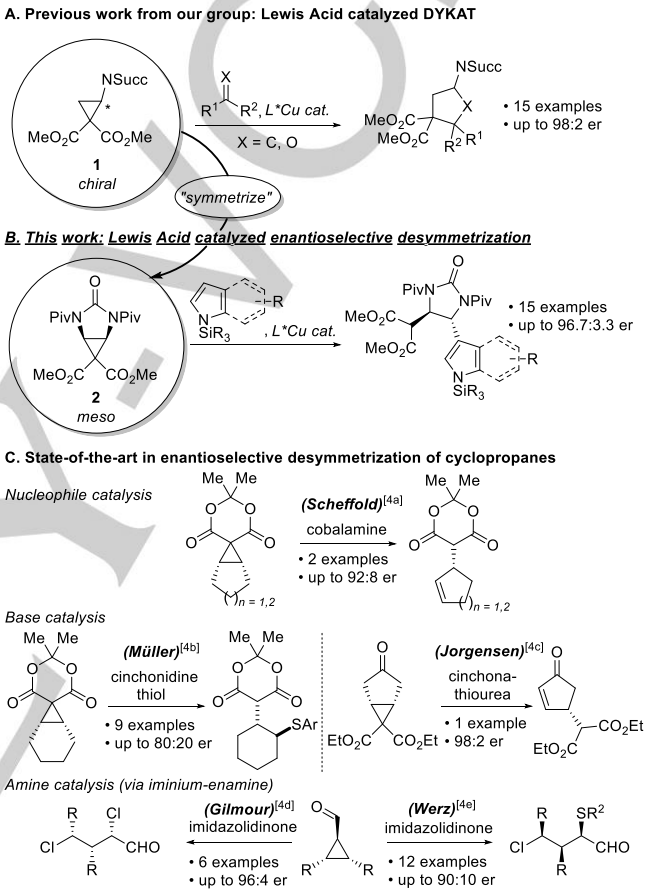
# Lewis Acid Catalyzed Enantioselective Desymmetrization of Donor-Acceptor *Meso*-Diaminocyclopropanes

Daniele Perrotta, Ming-Ming Wang and Jérôme Waser*[a]

**Abstract:** The first example of Lewis acid catalyzed enantioselective ring-opening desymmetrization of donor-acceptor *meso*-diaminocyclopropanes is reported herein. A copper(II)-catalyzed Friedel-Crafts alkylation of indoles and a pyrrole with an unprecedented *meso*-diaminocyclopropane delivered enantioenriched diastereomerically pure urea products, which are structurally related to natural and synthetic bioactive compounds. The development of a new ligand through the investigation of an underexplored subclass of BOX ligands was essential for obtaining high enantiomeric ratios.

Donor-acceptor cyclopropanes are versatile building blocks in organic synthesis.[1] Enantiomerically enriched derivatives can be obtained by performing asymmetric transformations. Donor-acceptor cyclopropanes are often themselves chiral, leading to two possible scenarios: kinetic resolution and DYKAT (dynamic kinetic asymmetric transformation).[2] Our group applied a DYKAT for the first time to donor-acceptor aminocyclopropanes (Scheme 1, **A**).[2i] However, a major drawback of DYKAT processes lies in their complex reaction mechanism, requiring both efficient facial selection and control over racemization. In contrast, the desymmetrization of achiral *meso* substrates leads often to a more straightforward development of enantioselective transformations.[3] We therefore designed a novel *meso*-diaminocyclopropane **2** (Scheme 1, **B**). Up to now, only nucleophile, base and amine (via iminium-enamine) catalysts have been reported for the desymmetrization of donor-acceptor *meso*- cyclopropanes (Scheme 1, **C**).[4]

Herein, we present the first example of enantioselective desymmetrization of nitrogen-substituted cyclopropanes for the Friedel-Crafts alkylation of indoles using a copper catalyst bearing an unprecedented BOX (bisoxazoline) ligand (Scheme 1, **B**). The methodology delivered enantioenriched urea derivatives as products, which are highly important core structures in natural and bioactive compounds such as Tulongicin A (**3**),[5a] Biotin (**4**)[5b] or (-)-Agelastatin A (**5**)[5c-d](Figure 1).[5]




**Scheme 1.** DYKAT of aminocyclopropanes (**A**). This work: enantioselective desymmetrization of donor-acceptor *meso*-diaminocyclopropanes (**B**). State-of-the-art in enantioselective desymmetrization of cyclopropanes (**C**). Succ = succinyl, Piv = pivaloyl.

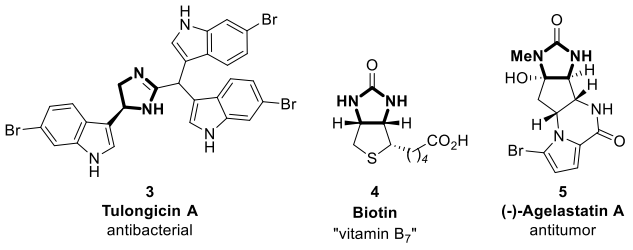



**Figure 1.** Occurrence of urea derivatives in synthetic and natural bioactive compounds.

The investigation of the proposed transformation required first an adequate donor-acceptor *meso*-diaminocyclopropane. Based

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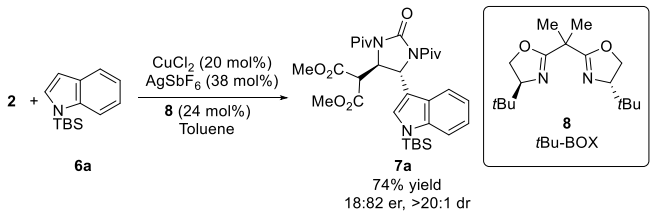
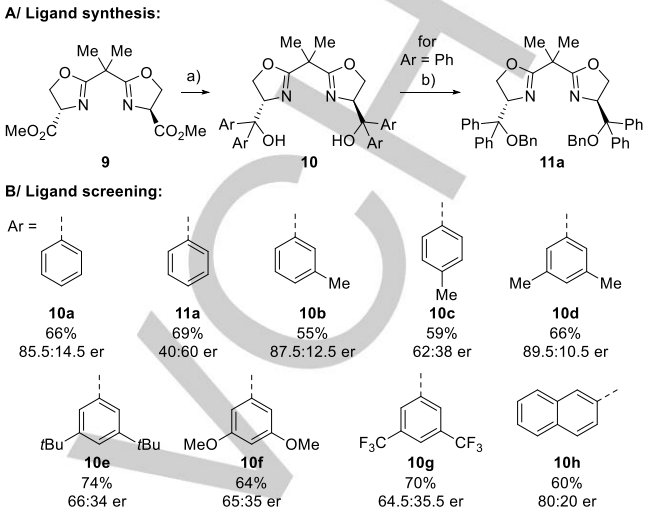
on our previous work,[2i] an imide urea functionality as the donor, and a bis-ester as the acceptor were chosen (cyclopropane **2**). The Friedel-Crafts alkylation with indoles was examined first.[2e,8] We focused our effort on copper-bisoxazoline (BOX) complexes as catalysts.[2i] Both the electron-withdrawing group on the urea and the *N*-substituent on the indole showed a strong effect on enantioselectivity (see *SI* for details). The best compromise between enantiomeric ratio (er) and solubility was achieved by using a pivaloyl group on urea **2** and *tert*-butyldimethysilyl (TBS) protected indole **6a** (Scheme 2). Copper(II) was identified as the best metal, hexafluoroantimonate(V) as the best counterion, and BOX ligands such as **8** as a promising class of ligands. In toluene as solvent, the desired product could be obtained in 74% yield and 18:82 er as a single diastereoisomer.



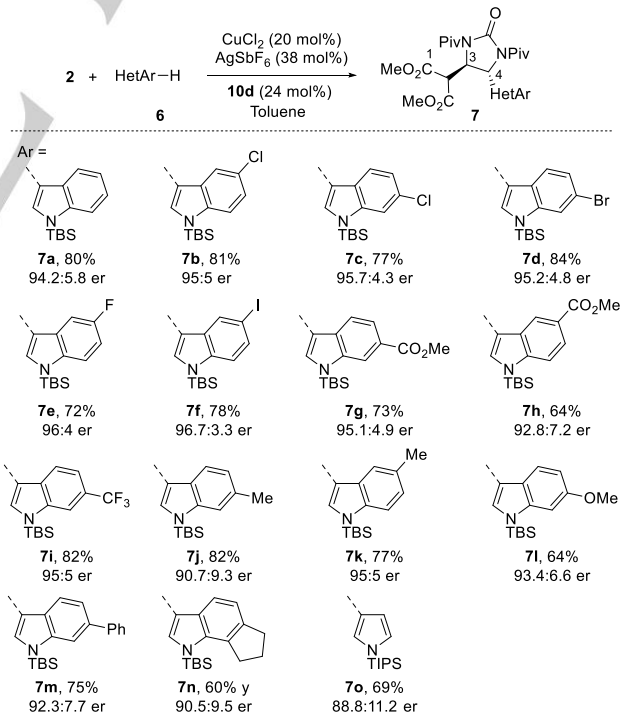

**Scheme 2.** Lead result for the enantioselective Friedel-Crafts alkylation of indole **6a** with cyclopropane **2**. Reaction conditions: 0.05 mmol **2**, 0.06 mmol **3a**, 0.05 M in Toluene, -20 °C, 48 h. TBS = *tert*-butyldimethylsilyl.

To improve further the er, we investigated ligand modification at the $\alpha$ position to the nitrogen atom. We were particularly interested in a subclass of BOX ligands bearing bulky diarylmethanol groups instead of the *tert*-butyls (Scheme 3, **A**).[9] The aryl groups can be installed by Grignard addition to the ester precursor **9**, which can be easily synthesized in two steps from serine ester.[10] Up to now, only the phenyl derivative (**10a**) has been reported.[9] It was used by Reiser and coworkers for the enantioselective 1,2- and 1,4-addition of organozincs to carbonyl compounds. The use of **10a** in the Friedel-Crafts reaction afforded a significant increase in er (Scheme 3, **B**). When the alcohol was protected as a benzyl group (**11a**), the opposite enantiomer was obtained in lower er. Subsequently, the substitution pattern on the aryl groups was investigated. Substitution in the *ortho* position could not be accessed synthetically, whereas a methyl group in *meta* gave a better er (ligand **10b**). Ligand **10c** with a methyl in *para* position led to a decrease of er. The er could be further improved to 89.5:10.5 by adding a second methyl group in *meta* position (ligand **10d**). Any further change in the *meta* positions, either by increased steric bulk (ligand **10e**) or by introducing electron-donating or withdrawing substituents (ligands **10f** and **10g**) only resulted in lower er. Replacing the benzene by a naphthalene ring was also not successful (ligand **10h**). Using 1.5 equivalents of cyclopropane **2** compared to indole **6a**, lowering the temperature to -50 °C, and diluting to 0.025 M finally afforded the desired product **7a** in 80% yield and 94.2:5.8 er on scope scale (Scheme 4).

We then investigated the scope of the reaction (Scheme 4). Indoles bearing both electron-withdrawing groups such as halides, esters, and trifluoromethyl (products **7b** to **7i**) and electron-donating groups such as methyl and methoxy (products **7j** to **7l**) delivered products in 64-84% yield and 90.7:9.3 to 96.7:3.3 er.[11] A phenyl substituent was also well-tolerated (product **7m**), as well as a fused cyclopentyl ring (product **7n**). The reaction could also be extended to pyrroles without reoptimization: TIPS-protected pyrrole **6o** gave product **7o** in good yield and promising er.[12]



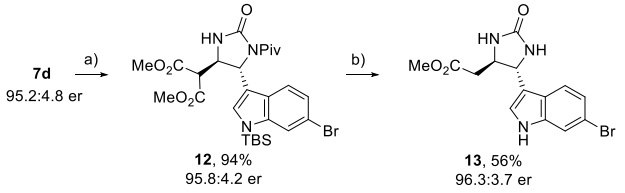

**Scheme 3.** Ligand synthesis (**A**). Reaction conditions: a) ArMgBr (6 equiv), 0.067 M in THF, -78 °C to rt, 24 h. b) NaH (2.4 equiv), BnBr (2.4 equiv), 0.5 M in DMF, 0 °C to rt, 16 h. Ligand screening for the alkylation of **6a** with **2** (**B**). Reaction conditions as in Scheme 2 but at rt for 16 h. >20:1 dr was observed in all cases. The yields and er's of **7a** are reported below each ligand. Bn = benzyl.




**Scheme 4.** Scope of the reaction. Reaction conditions: 0.15 mmol **2**, 0.1 mmol **6,** 0.025 M in Toluene, -50 °C for all the entries except **7g** and **7h** (-40 °C) and **7i** and **7o** (-30 °C). All compounds were obtained with dr > 20:1. TIPS = tri*iso*propylsilyl.

A single pivaloyl group of the product could be selectively deprotected using hydrazine to deliver **12** in excellent yield

without purification (Scheme 5). Basic hydrolysis led then to cleavage of the remaining pivaloyl group, the two methyl esters as well as the silyl protecting group, revealing the free urea. Subsequent decarboxylation/methylation of the dicarboxylic acid afforded **13** in 56% yield without erosion of enantiopurity.




**Scheme 5.** Product derivatizations. Reaction conditions: a) $N_2H_{4\ (aq)}$ 80% wt (1.5 equiv), rt. b) i. 0.5 M $LiOH_{(aq)}$ (8 equiv), rt; ii. MeOH, 80 °C; iii. $TMSCHN_2$ (10 equiv), 0 °C. 56% yield over three steps.

X-ray analysis of **7d** showed that the configuration was *3R*,*4R* (see Figure S1 in *SI*).[13] The *trans* relative configuration supports a $SN_2$-like mechanism for the ring-opening of the cyclopropane. Based on the obtained absolute configuration, a highly speculative stereochemical model can be proposed (Figure 2). We assume that the copper complex adopts a distorted square planar geometry due to hydrogen bonds between the hydroxy groups and the esters of the cyclopropane, forcing them in the more hindered quadrants and further activating them.[14,15] Indeed, rate acceleration was observed when employing ligands bearing a free hydroxy group.[16] In the resulting rigidified structure, we propose a relay of stereoinduction from the aryl groups to the pivaloyls, the latter orienting their smallest substituent (carbonyl) towards the bulky aryl groups. This results in an opposite orientation of the two carbonyl groups compared to the urea carbonyl, blocking selectively one of the electrophilic carbon of the cyclopropane with a *tert*-butyl group.

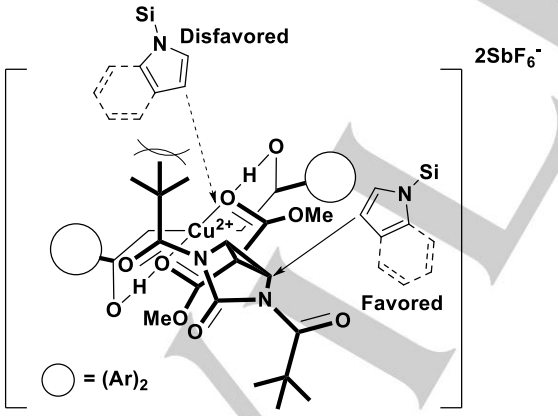



**Figure 2.** Speculative stereochemical model.

In summary, we have developed the first Lewis acid catalyzed enantioselective ring-opening desymmetrization of donor-acceptor cyclopropanes. The transformation displayed high enantioselectivity and complete diastereoselectivity, together with a broad scope of indoles as well as a pyrrole, delivering urea derivatives that are important scaffolds in natural and synthetic bioactive compounds. The use and further modification of an underexploited class of BOX ligands easily obtained in two steps from serine ester was essential to achieve high enantioselectivity. We believe that these ligands will be useful also in other new asymmetric transformations.

## Acknowledgements

We thank the Swiss National Science Foundation (SNSF, grant nos. 200021_165788 and 200020_149494) and EPFL for financial support. Dr. Johannes Preindl of LCSO is acknowledged for helping in the synthesis of **9** and **10a**. Franck Le Vaillant of LCSO is acknowledged for helping in the characterization of ligands and products.

**Keywords:** enantioselective desymmetrization • Lewis acid • BOX ligands • donor-acceptor cyclopropanes • urea

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[11] Attemps to use $C_2$, $C_3$ and $C_4$ substituted indoles led to low enantiomeric excesses or low reactivity.

[12] Only very low conversion was observed using either anisole or dimethylaniline as nucleophiles.

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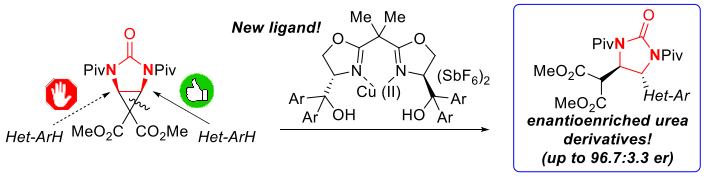
[16] When employing ligand **8**, no reactivity is observed at -30 °C, whereas with **10d**, the reaction works at -50 °C.

# COMMUNICATION




**Open carefully:** The first Lewis acid catalyzed enantioselective ring opening desymmetrization of donor-acceptor *meso*-diaminocyclopropanes is reported herein. The transformation is catalyzed by a copper(II) complex bearing a novel BOX ligand. The ring opening of an unprecedented *meso*-diaminocyclopropane is achieved *via* Friedel-Crafts alkylation of indoles and a pyrrole, and delivers diastereomerically pure and highly enantioenriched urea derivatives.

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**Lewis Acid Catalyzed Enantioselective Desymmetrization of Donor-Acceptor *Meso*-Diaminocyclopropanes**

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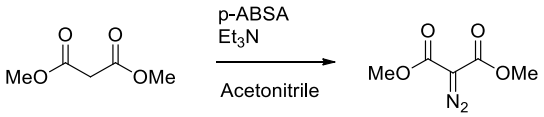
# 1. General methods

All reactions were carried out in oven- or flame- dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography, distilled technical grade solvents were used. THF, $Et_2O$, toluene, hexane and $CH_2Cl_2$ were dried by passage over activated alumina under nitrogen atmosphere ($H_2O$ content < 7 ppm, Karl-Fischer titration). All chemicals were purchased and used as received unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC plastic or aluminium plates and visualized with UV light, permanganate CAN or p-anisaldehyde stains. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. $^1$H-NMR spectra were recorded at room temperature on a Brucker DPX-400 400 MHz spectrometer in $CDCl_3$, DMSO-$d_6$ or $CD_3OD$, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm and the internal methanol signal at 3.31 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, p = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation). $^{13}$C-NMR spectra were recorded with 1H-decoupling on a Brucker DPX-400 100 MHz spectrometer in $CDCl_3$ or $CD_3OD$, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm or $CD_3OD$ signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 or a Bruker Alpha-P spectrophotometer with an ATR device and a ZnSe prism and are reported as cm-1 (w = weak, m = medium, s = strong). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. HPLC measurements were done on a Agilent 1260 Infinity autosampler using a CHIRALPAK IA, IB, IC or IF column from DAICEL Chemical. Optical rotations were measured on a polarimeter using a 10 cm cell with a Na 589 nm filter. The specific solvents and concentrations (in g/100 mL) are indicated.

# 2. Preparation of the starting materials

## 2.1 Synthesis of the cyclopropanes

### Dimethyl 2-diazomalonate (14)



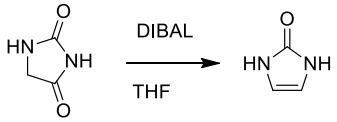

**14**

In a flame dried flask under $N_2$ atmosphere, 4-acetamidobenzenesulfonyl azide (6.82 g, 28.4 mmol, 1.5 equiv) was dissolved in acetonitrile (80 mL) and triethylamine (6.3 mL, 45 mmol, 2.4 equiv) and dimethyl malonate (2.2 mL, 19 mmol, 1 equiv) were added. The reaction mixture was stirred at room temperature for 24 hours. The solvent was evaporated and the crude product was filtered on cotton with acetonitrile (30 mL). The crude mixture was concentrated under reduced pressure and filtered on cotton one more time with DCM (30 mL) and finally purified by column chromatography (deactivated $SiO_2$, eluent pentane:ethyl acetate 9:1 + 1% of triethylamine) to give dimethyl 2-diazomalonate (**14**) (2.67 g, 16.9 mmol, 94% yield) as a slightly yellow oil (solid at 4 °C).

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 3.83 (s, 6H, C*H*$_3$).

Data match the literature report.[1]

### 1H-imidazol-2(3H)-one (15)




**15**

Following a reported procedure,[2] in a flame dried flask under $N_2$ atmosphere, hydantoin (10.0 g, 100 mmol, 1 equiv) was suspended in 100 mL of dry tetrahydrofuran. The suspension was cooled to 0 °C with an ice/water bath. A 1.2 molar solution of DIBAL in toluene (221 mL, 265 mmol, 2.65 equiv) was added dropwise over 30 minutes, and the solution was stirred for 2 hours at 0 °C. 700 mL of a solution of 9:1 methanol/water was added carefully, and the reaction was heated at 100 °C for 18 hours. After cooling to room temperature, the reaction was filtered on celite, eluting with 500 mL of methanol, and evaporated to dryness to give 1H-imidazol-2(3H)-one (**15**) (7.00 g, 83.0 mmol, 83% yield) as an off-white solid.

**$^1$H NMR** (400 MHz, DMSO-$d_6$) δ 9.75 (s, 2H, N*H*), 6.24 (s, 2H, C*H*).
Data match the literature report.[2]

### 1,1'-(2-Oxo-1H-imidazole-1,3(2H)-diyl)diethanone (16)

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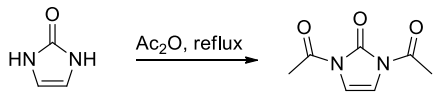
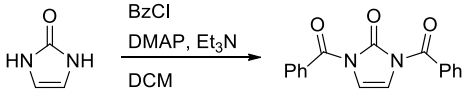



15 16

Following a reported procedure,[2] 1H-imidazol-2(3H)-one (**15**) (300 mg, 3.57 mmol, 1 equiv) was stirred in acetic anhydride (1.94 mL, 20.5 mmol, 5.8 equiv) at reflux for 90 minutes. The reaction was cooled down to room temperature and concentrated to dryness. The residue was washed with ethyl acetate to afford 1,1'-(2-oxo-1H-imidazole-1,3(2H)-diyl)diethanone (**16**) (360 mg, 2.14 mmol, 60% yield) as a white solid.

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.08 (s, 2H, C*H*), 2.65 (s, 6H, C*H*$_3$).
Data match the literature report.[3]

**(2-Oxo-1H-imidazole-1,3(2H)-diyl)bis(phenylmethanone) (17)**

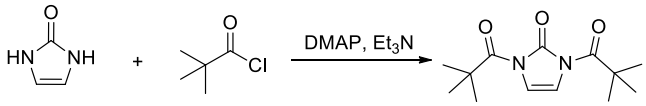



15 17

Following a reported procedure,[3] in a flame dried flask under $N_2$ atmosphere, 1H-imidazol-2(3H)-one (**15**) (1.18 g, 6.16 mmol, 1 equiv) was added, followed by 42.4 mL of dry dichloromethane, and the suspension was cooled to 0 °C. Then, DMAP (0.171 g, 1.40 mmol, 0.1 equiv) was added, followed by a solution of benzoyl chloride (3.25 mL, 28.0 mmol, 2 equiv) in dry dichloromethane (5.6 mL) dropwise. Finally, triethylamine (3.90 mL, 2.83 mmol, 2 equiv) was added dropwise. The reaction mixture was stirred at 0 °C, letting ice melt during 24 hours. 50 mL of dichloromethane were added, and the organic layer was washed with water (60 mL). The aqueous layer was separated and extracted with dichloromethane (40 mL). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$, filtered and evaporated. The residue was purified by column chromatography ($SiO_2$, eluent pentane:ethyl acetate 85:15 to 0:100), to afford (2-oxo-1H-imidazole-1,3(2H)-diyl)bis(phenylmethanone) (**17**) (1.80 g, 6.16 mmol, 44% yield) as a white solid.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 9:1) 0.21;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.81 - 7.71 (m, 4H, Ar*H*), 7.58 - 7.53 (m, 2H, Ar*H*), 7.43 (t, *J* = 7.7 Hz, 4H, Ar*H*), 7.11 (s, 2H, C*H*).
Data match the literature report.[3]

**1,1'-(2-Oxo-1H-imidazole-1,3(2H)-diyl)bis(2,2-dimethylpropan-1-one) (18)**




15 18

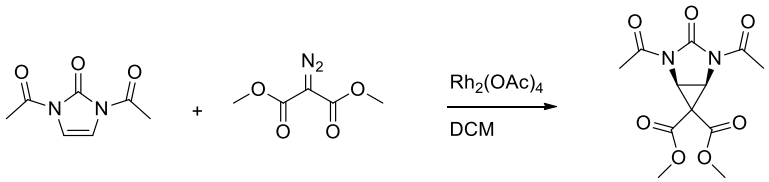
Following a modified procedure,[3] in a flame dried flask under $N_2$ atmosphere, 1H-imidazol-2(3H)-one (**15**) (3.00 g, 35.7 mmol, 1 equiv) was added, followed by 100 mL of dry dichloromethane, and the suspension was cooled to 0 °C. Then, DMAP (0.436 g, 3.57 mmol, 0.1 equiv) was added, followed by a solution of pivaloyl chloride (9.66 mL, 78.0 mmol, 2.2 equiv) in dry dichloromethane (35 mL) dropwise. Finally, triethylamine (10.4 mL, 74.9 mmol, 2.1 equiv) was added dropwise. The reaction

[3] Han, S.; Zard, S. Z., *Org. Lett.* **2014**, *16*, 5386-5389.

mixture was stirred at 0 °C, letting ice melt during 24 hours. 50 mL of dichloromethane were added, and the organic layer was washed with water (60 mL). The aqueous layer was separated and extracted with dichloromethane (40 mL). The combined organic layers were washed with brine (50 mL), dried over $Na_2SO_4$, filtered and evaporated. The residue was purified by column chromatography ($SiO_2$, eluent pentane:diethylether 9:1), to afford 1,1'-(2-Oxo-1H-imidazole-1,3(2H)-diyl)bis(2,2-dimethylpropan-1-one) (**18**) (6.93 g, 27.5 mmol, 77% yield) as a white solid.

**$R_f$:** ($SiO_2$, pentane:diethylether 94:6) 0.2;
**Mp:** 76-78 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.06 (s, 2H, C*H*), 1.44 (s, 18H, C(C*H*$_3$)$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 176.5, 149.9, 111.9, 41.6, 25.8;
**IR** (film) $\tilde{\nu}$ 2974 (w), 1705 (s), 1483 (w), 1299 (w), 1194 (w), 911 (m), 738 (s);
**HRMS** (ESI) calcd. for $C_{13}H_{20}N_2NaO_3^+$ $[M+Na]^+$ 275.1366; found 275.1120.

**Dimethyl 2,4-diacetyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (19)**

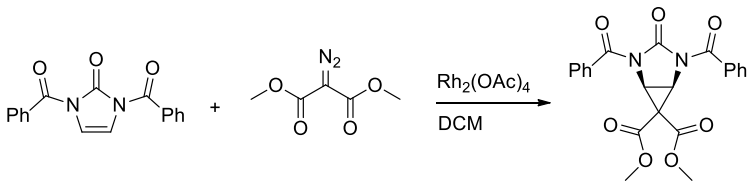



16 14 19

Following a modified procedure,[1] in a glovebox, rhodium(II) acetate dimer (32.0 mg, 71.0 µmol, 0.05 equiv) was added in a flame dried flask. The flask was closed with a septum, put under $N_2$ atmosphere, and cooled down to 0 °C. A solution of 1,1'-(2-oxo-1H-imidazole-1,3(2H)-diyl)diethanone (**16**) (240 mg, 1.43 mmol, 1 equiv) in dry dichloromethane (3.5 mL) was added in the flask. After 5 minutes, a solution of dimethyl 2-diazomalonate (**14**) (271 mg, 1.71 mmol, 1.2 equiv) in dry dichloromethane (3.5 mL) was added dropwise. The reaction mixture was stirred at 0 °C, letting ice melt during 15 hours. The solvent was then evaporated at the rotavap. The residue was purified by column chromatography ($SiO_2$, eluent pentane:ethyl acetate 65:35), to afford dimethyl 2,4-diacetyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (**19**) (210 mg, 0.704 mmol, 49% yield) as a white solid, which was stored at -20 °C in the freezer under $N_2$ atmosphere.

**$R_f$:** ($SiO_2$, pentane: ethyl acetate 7:3) 0.17;
**Mp:** 119-123 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.55 (s, 2H, NC*H*), 3.78 (s, 3H, $CO_2C$*H*$_3$), 3.71 (s, 3H, $CO_2C$*H*$_3$), 2.52 (s, 6H, C*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.0, 165.8, 163.2, 150.8, 53.4, 53.2, 38.4, 33.7, 23.7;
**IR** (film) $\tilde{\nu}$ 1769 (m), 1721 (s), 1440 (w), 1375 (w), 1339 (s), 1273 (m), 1231 (s), 1166 (w), 1088 (s), 981 (w), 915 (w);
**HRMS** (ESI) calcd. for $C_{12}H_{15}N_2O_7^+$ $[M+H]^+$ 299.0874; found 299.0882.

**Dimethyl 2,4-dibenzoyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (20)**

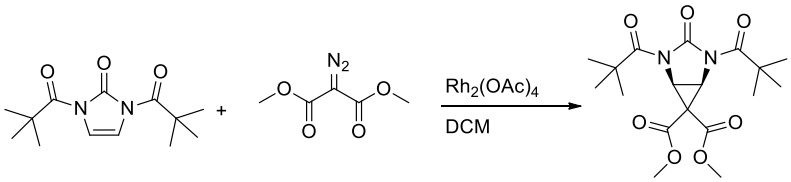



17 14 20

Following a modified procedure,[1] in a glovebox, rhodium(II) acetate dimer (113 mg, 257 µmol, 0.05 equiv) was added in a flame dried flask. The flask was closed with a septum, put under $N_2$ atmosphere, and cooled down to 0 °C. A solution of (2-oxo-1H-imidazole-1,3(2H)-diyl)bis(phenylmethanone) (**17**) (1.50 g, 5.13 mmol, 1 equiv) in dry dichloromethane (15 mL) was added in the flask. After 5 minutes, a solution of dimethyl 2-diazomalonate (**14**) (974 mg, 6.16 mmol, 1.2 equiv) in dry dichloromethane (15 mL) was added dropwise. The reaction mixture was stirred at 0 °C, letting ice melt during 14 hours. The solvent was then evaporated at the rotavap. The residue was purified by column chromatography ($SiO_2$, eluent toluene:ethyl acetate 10:1), to afford dimethyl 2,4-dibenzoyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (**20**) (1.40 g, 3.31 mmol, 65% yield) as a white solid, stored at -20 °C in the freezer under $N_2$ atmosphere.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 8:2) 0.62;
**Mp:** 119-123 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.58 (m, 4H, Ar*H*), 7.52 – 7.47 (m, 2H, Ar*H*), 7.40 – 7.35 (m, 4H, Ar*H*), 4.76 (s, 2H, NC*H*), 3.85 (s, 3H, $CO_2CH_3$), 3.79 (s, 3H, $CO_2CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 169.1, 165.9, 163.5, 149.3, 132.5, 132.4, 129.0, 127.9, 53.4, 53.1, 40.0, 34.3;
**IR** (film) $\tilde{\nu}$ 2952 (w), 1787 (m), 1733 (s), 1691 (s), 1440 (w), 1333 (s), 1279 (s), 1225 (s), 1160 (s), 1082 (w), 915 (w), 825 (w);
**HRMS** (ESI) calcd. for $C_{22}H_{18}N_2NaO_7^+$ $[M+Na]^+$ 445.1006; found 445.1008.

**Dimethyl 3-oxo-2,4-dipivaloyl-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (2)**




18 14 2

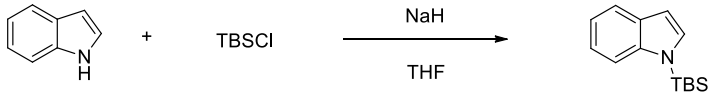
Following a modified procedure,[1] in a glovebox, rhodium(II) acetate dimer (438 mg, 991 µmol, 0.05 equiv) was added in a flame dried flask. The flask was closed with a septum, put under $N_2$ atmosphere, and cooled down to 0 °C. A solution of 1,1'-(2-oxo-1H-imidazole-1,3(2H)-diyl)bis(2,2-dimethylpropan-1-one) (**18**) (5.00 g, 19.8 mmol, 1 equiv) in dry dichloromethane (60 mL) was added in the flask. After 5 minutes, a solution of dimethyl 2-diazomalonate (**14**) (3.45 g, 21.8 mmol, 1.1 equiv) in dry dichloromethane (40 mL) was added dropwise. The reaction mixture was stirred at 0 °C, letting ice melt during 15 hours. The solvent was then evaporated at the rotavap. The residue was purified by column chromatography ($SiO_2$, eluent pentane:ethyl acetate 9:1), to afford dimethyl 3-oxo-2,4-dipivaloyl-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (**2**) (3.40 g, 8.89 mmol, 45% yield) as a white solid, stored at -20 °C in the freezer under $N_2$ atmosphere.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 7:3) 0.67;
**Mp:** 100-102 °C;

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.50 (s, 2H, NC*H*), 3.76 (s, 3H, $CO_2CH_3$), 3.67 (s, 3H, $CO_2CH_3$), 1.37 (s, 18H, $C(CH_3)_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 178.4, 166.4, 163.2, 148.4, 53.1, 52.8, 41.4, 40.8, 33.9, 26.1;
**IR** (film) $\tilde{\nu}$1742 (s), 1690 (s), 1627 (w), 1371 (s), 1287 (s), 1230 (s), 1204 (m), 1167 (w), 1125 (w), 900 (w), 869 (w);
**HRMS** (ESI) calcd. for $C_{18}H_{27}N_2O_7^+$ $[M+H]^+$ 383.1813; found 383.1825.

## 2.2 Synthesis of the protected indoles

**1-(*Tert*-butyldimethylsilyl)-1H-indole** (**6a**)

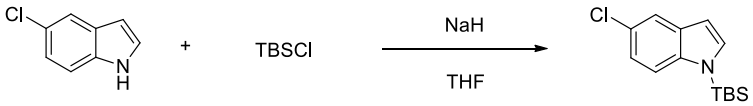


**21** **6a**

Following a modified procedure[4], a solution of 1H-indole (**21**) (0.586 g, 5.00 mmol, 1 equiv) in THF (4 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.600 g, 15.0 mmol, 3 equiv) in THF (5 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.904 g, 6.00 mmol, 1.2 equiv) was added as a solution in THF (3 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 40:1) afforded 1-(Tert-butyldimethylsilyl)-1H-indole (**6a**) (1.08 g, 4.67 mmol, 93% yield) as white solid.

**$R_f$:** ($SiO_2$, pentane) 0.42;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.9 Hz, 1H, Ar*H*), 7.52 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.19 (d, *J* = 3.2 Hz, 1H, Ar*H*), 7.18 – 7.08 (m, 2H, Ar*H*), 6.62 (d, *J* = 3.1 Hz, 1H, Ar*H*), 0.94 (s, 9H, $SiC(CH_3)_3$), 0.61 (s, 6H, 2 x $SiCH_3$).
Data match the literature report.[4]

**1-(*Tert*-butyldimethylsilyl)-5-chloro-1H-indole** (**6b**)



**22** **6b**

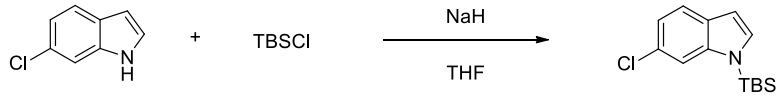
Following a modified procedure,[4] a solution of the 5-chloro-1H-indole (**22**) (0.240 g, 1.58 mmol, 1 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.190 g, 4.75 mmol, 3 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.380 g, 2.53 mmol, 1.6 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column

[4] Caramenti, P.; Nicolai, S.; Waser, J., *Chem. Eur. J.* **2017**, *23*, 14702-14706.

chromatography ($SiO_2$, eluent pentane) afforded 1-(Tert-butyldimethylsilyl)-5-chloro-1H-indole (**6b**) (0.375 g, 1.41 mmol, 89% yield) as pale yellow oil.

**$R_f$:** ($SiO_2$, pentane) 0.38;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 2.2, 0.5 Hz, 1H, Ar*H*), 7.40 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.19 (d, *J* = 3.2 Hz, 1H, Ar*H*), 7.09 (dd, *J* = 8.8, 2.2 Hz, 1H, Ar*H*), 6.55 (dd, *J* = 3.2, 0.9 Hz, 1H, Ar*H*), 0.91 (s, 9H, SiC($CH_3$)$_3$), 0.60 (s, 6H, 2 x Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.3, 132.5, 132.4, 125.5, 121.6, 120.0, 114.7, 104.4, 26.2, 19.5, -4.0;
**IR** (film) $\tilde{\nu}$ 2959 (m), 2928 (m), 2860 (m), 1510 (w), 1448 (s), 1288 (m), 1257 (m), 1201 (w), 1152 (s), 986 (m), 838 (s), 794 (s);
**HRMS** (ESI) calcd. for $C_{14}H_{21}ClNSi^+$ $[M+H]^+$ 266.1126; found 266.1126.

**1-(*Tert*-butyldimethylsilyl)-6-chloro-1H-indole** (**6c**)

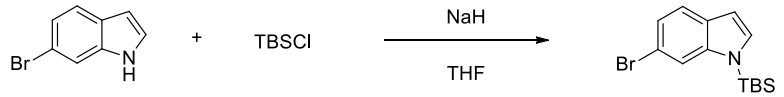


**23** **6c**

Following a modified procedure,[4] a solution of the 6-chloro-1H-indole (**23**) (0.30 g, 2.0 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.24 g, 6.0 mmol, 3.0 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0°C, tert-butylchlorodimethylsilane (0.45 g, 3.0 mmol, 1.5 equiv) was added as a solution in THF (1.5 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane: ethyl acetate 20:1) afforded 1-(Tert-butyldimethylsilyl)-6-chloro-1H-indole (**6c**) (0.46 g, 1.7 mmol, 87% yield) as yellow oil.

**$R_f$:** ($SiO_2$, pentane) 0.41;
**Mp:** 80.3-80.8 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.47 (s, 1H, Ar*H*), 7.16 (d, *J* = 3.2 Hz, 1H, Ar*H*), 7.08 (d, *J* = 8.3 Hz, 1H, Ar*H*), 6.58 (d, *J* = 3.1 Hz, 1H, Ar*H*), 0.93 (s, 9H, SiC($CH_3$)$_3$), 0.60 (s, 6H, 2 x Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.4, 131.7, 129.9, 127.2, 121.3, 120.5, 113.7, 104.8, 26.2, 19.4, -4.0;
**IR** (film) $\tilde{\nu}$ 2959 (m), 2934 (m), 2891 (w), 2860 (m), 1602 (w), 1510 (w), 1460 (m), 1436 (m), 1318 (w), 1275 (m), 1257 (m), 1152 (s), 1084 (w), 986 (m), 905 (m), 844 (s), 813 (s), 727 (m);
**HRMS** (ESI) calcd. for $C_{14}H_{21}ClNSi^+$ $[M+H]^+$ 266.1126; found 266.1123.

**6-bromo-1-(*tert*-butyldimethylsilyl)-1H-indole** (**6d**)



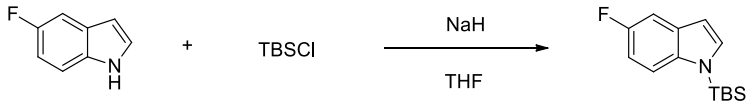
**24** **6d**

Following a modified procedure,[4] a solution of the 6-bromo-1H-indole (**24**) (0.39 g, 2.0 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.24 g, 6.0 mmol, 3.0 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling

to 0 °C, tert-butylchlorodimethylsilane (0.45 g, 3.0 mmol, 1.5 equiv) was added as a solution in THF (1.5 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane) afforded 6-bromo-1-(tert-butyldimethylsilyl)-1H-indole (**6d**) (0.56 g, 1.8 mmol, 90% yield) as white solid.

**$R_f$:** ($SiO_2$, pentane) 0.40;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.63 (s, 1H, Ar*H*), 7.48 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.21 (dd, *J* = 8.4, 1.7 Hz, 1H, Ar*H*), 7.15 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.58 (d, *J* = 3.2 Hz, 1H, Ar*H*), 0.92 (s, 9H, SiC($CH_3$)$_3$), 0.60 (s, 6H, 2 x Si$CH_3$).
Data match the literature report.[5]

**1-(*Tert*-butyldimethylsilyl)-5-fluoro-1H-indole** (**6e**)

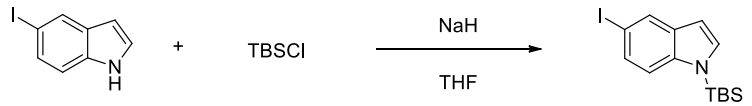


**25** **6e**

Following a modified procedure,[4] a solution of 5-fluoro-1H-indole (**25**) (0.44 g, 3.3 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.39 g, 9.8 mmol, 3.0 equiv) in THF (4 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.78 g, 5.2 mmol, 1.6 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane) afforded 1-(Tert-butyldimethylsilyl)-5-fluoro-1H-indole (**6e**) (0.75 g, 3.0 mmol, 92% yield) as white solid.

**$R_f$:** ($SiO_2$, pentane) 0.38;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.41 (dd, *J* = 9.0, 4.4 Hz, 1H, Ar*H*), 7.28 – 7.23 (m, 1H, Ar*H*), 7.21 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.89 (td, *J* = 9.1, 2.7 Hz, 1H, Ar*H*), 6.57 (d, *J* = 3.1 Hz, 1H, Ar*H*), 0.92 (s, 9H, SiC($CH_3$)$_3$), 0.60 (s, 6H, 2 x Si$CH_3$).
Data match the literature report.[6]

**1-(*Tert*-butyldimethylsilyl)-5-iodo-1H-indole** (**6f**)



**26** **6f**

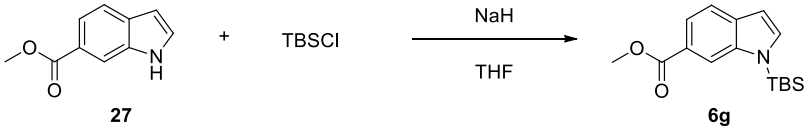
Following a modified procedure,[4] a solution of the 5-iodo-1H-indole (**26**) (0.60 g, 2.5 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.30 g, 7.4 mmol, 3.0 equiv) in THF (4 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to

[5] Kawasaki, I; Yamashita, M; Ohta, S., *Chem. Pharm. Bull*. **1996**, *44*, 1831 - 1839.
[6] F.HOFFMANN-LA ROCHE AG, WO2008/152390, 2008, A1. *Thiazoliopyrimidines and their use as inhibitors of phosphatidylinositol-3 Kinase.*

room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.56 g, 3.7 mmol, 1.5 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane) afforded 1-(Tert-butyldimethylsilyl)-5-iodo-1H-indole (**6f**) (0.78 g, 2.2 mmol, 88% yield) as white solid.

**$R_f$:** ($SiO_2$, pentane) 0.32;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.39 (dd, *J* = 8.7, 1.8 Hz, 1H, Ar*H*), 7.29 (d, *J* = 8.7 Hz , 1H, Ar*H*), 7.13 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.53 (dd, *J* = 3.2, 0.9 Hz, 1H, Ar*H*), 0.91 (s, 9H, SiC($CH_3$)$_3$), 0.59 (s, 6H, 2 x Si$CH_3$).
Data match the literature report.[7]

**Methyl 1-(*tert*-butyldimethylsilyl)-1H-indole-6-carboxylate** (**6g**)

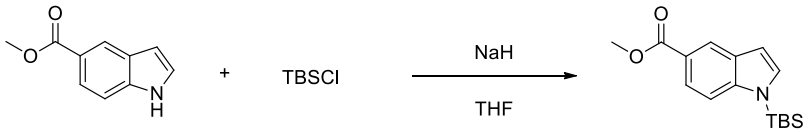


**27** **6g**

Following a modified procedure,[4] a solution of methyl 1H-indole-6-carboxylate (**27**) (0.53 g, 3.0 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.36 g, 9.0 mmol, 3.0 equiv) in THF (4 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.72 g, 4.8 mmol, 1.6 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 12:1) afforded methyl 1-(tert-butyldimethylsilyl)-1H-indole-6-carboxylate (**6g**) (0.77 g, 2.7 mmol, 89% yield) as pale yellow oil.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 20:1) 0.58;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.28 (s, 1H, Ar*H*), 7.80 (dd, *J* = 8.3, 1.4 Hz, 1H, Ar*H*), 7.63 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.34 (d, *J* = 3.1 Hz, 1H, Ar*H*), 6.65 (dd, *J* = 3.1, 0.9 Hz, 1H, Ar*H*), 3.93 (s, 3H, $CO_2CH_3$), 0.93 (s, 9H, SiC($CH_3$)$_3$), 0.65 (s, 6H, 2 x Si$CH_3$).
Data match the literature report.[8]

**Methyl 1-(*tert*-butyldimethylsilyl)-1H-indole-5-carboxylate** (**6h**)



**28** **6h**

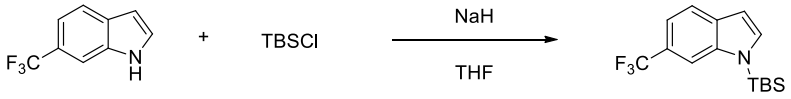
Following a modified procedure,[4] a solution of methyl 1H-indole-5-carboxylate (**28**) (0.35 g, 2.0 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil,

[7] Song, Y.-L.; Morin, C., *Synlett*, **2001**, *2*, 266–268.
[8] Islam, S., Larrosa, I., *Chem. Eur. J.* **2013**, *19*, 15093-15096.

0.24 g, 6.0 mmol, 3.0 equiv) in THF (4 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.45 g, 3.0 mmol, 1.5 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 40:1) afforded methyl 1-(tert-butyldimethylsilyl)-1H-indole-5-carboxylate (**6h**) (0.50 g, 1.7 mmol, 86% yield) as white solid.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 40:1) 0.20;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 1.2 Hz, 1H, Ar*H*), 7.85 (dd, *J* = 8.7, 1.8 Hz, 1H, Ar*H*), 7.50 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.23 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.70 (dd, *J* = 3.3, 0.9 Hz, 1H, Ar*H*), 3.92 (s, 3H, $CO_2CH_3$), 0.92 (s, 9H, $SiC(CH_3)_3$), 0.62 (s, 6H, 2 x $SiCH_3$).
Data match the literature report.[9]

**1-(*Tert*-butyldimethylsilyl)-6-(trifluoromethyl)-1H-indole** (**6i**)

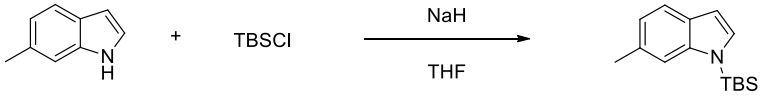


**29** **6i**

Following a modified procedure,[4] a solution of the 6-(trifluoromethyl)-1H-indole (**29**) (0.37 g, 2.0 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.24 g, 6.0 mmol, 3.0 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.45 g, 3.0 mmol, 1.5 equiv) was added as a solution in THF (1.5 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 20:1) afforded 1-(Tert-butyldimethylsilyl)-6-(trifluoromethyl)-1H-indole (**6i**) (0.54 g, 1.8 mmol, 90% yield) as colorless oil.

**$R_f$:** ($SiO_2$, pentane) 0.56;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.77 (s, 1H, Ar*H*), 7.70 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.34 (dd, *J* = 7.9, 0.9 Hz, 1H, Ar*H*), 7.32 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.67 (dd, *J* = 3.1, 0.9 Hz, 1H, Ar*H*), 0.93 (s, 9H, $SiC(CH_3)_3$), 0.63 (s, 6H, 2 x $SiCH_3$).
Data match the literature report.[10]

**1-(*tert*-butyldimethylsilyl)-6-methyl-1H-indole** (**6j**)



**30** **6j**

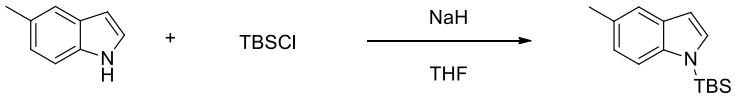
Following a modified procedure,[4] a solution of 6-methyl-1H-indole (**30**) (0.26 g, 2.0 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.24 g, 6.0

[9] Wales, S. M.; Walker, M. M.; Johnson, J. S., *Org. Lett.* **2013**, *15*, 2558 – 2561.
[10] Belley, M., Scheigetz, J., Dubé, P., Dolman, S., *Synlett* **2001**, *2*, 222 - 225.

mmol, 3.0 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.45 g, 3.0 mmol, 1.5 equiv) was added as a solution in THF (1.5 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 40:1) afforded 1-(tert-butyldimethylsilyl)-6-methyl-1H-indole (**6j**) (0.45 g, 1.8 mmol, 92% yield) as yellow oil.

**$R_f$:** ($SiO_2$, pentane) 0.37;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.29 (s, 1H, Ar*H*), 7.10 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.94 (dd, *J* = 7.7, 1.2 Hz, 1H, Ar*H*), 6.55 (dd, *J* = 3.2, 0.9 Hz, 1H, Ar*H*), 2.46 (s, 3H, C*H*$_3$), 0.93 (s, 9H, SiC(C*H*$_3$)$_3$), 0.59 (s, 6H, 2 x SiC*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 141.5, 130.9, 130.4, 129.1, 121.5, 120.1, 113.9, 104.5, 26.4, 22.1, 19.5, -3.9;
**IR** (film) $\tilde{\nu}$ 2956 (m), 2931 (m), 2888 (w), 2857 (m), 1514 (w), 1465 (m), 1286 (m), 1256 (m), 1175 (w), 1144 (s), 1009 (w), 837 (s), 800 (s), 720 (m);
**HRMS** (ESI) calcd. for $C_{15}H_{24}NSi^+$ $[M+H]^+$ 246.1673; found 246.1674.

**1-(*Tert*-butyldimethylsilyl)-5-methyl-1H-indole** (**6k**)



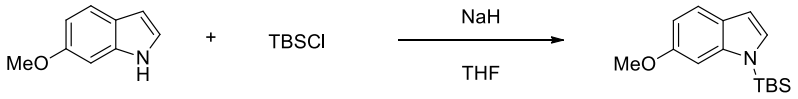
**31** **6k**

Following a modified procedure,[4] a solution of the 5-methyl-1H-indole (**31**) (0.20 g, 1.5 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.18 g, 4.5 mmol, 3.0 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.339 g, 2.25 mmol, 1.5 equiv) was added as a solution in THF (1.5 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate = 40:1) afforded 1-(Tert-butyldimethylsilyl)-5-methyl-1H-indole (**6k**) (0.33 g, 1.3 mmol, 90% yield) as colorless oil.

**$R_f$:** ($SiO_2$, pentane) 0.30;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.36 (m, 2H, Ar*H*), 7.14 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.98 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 6.53 (dd, *J* = 3.2, 0.9 Hz, 1H, Ar*H*), 2.44 (s, 3H, C*H*$_3$), 0.92 (s, 9H, SiC(C*H*$_3$)$_3$), 0.59 (s, 6H, 2 x SiC*H*$_3$).
Data match the literature report.[11]

**1-(*tert*-butyldimethylsilyl)-6-methoxy-1H-indole** (**6l**)

[11] Terada, M.; Yokoyama, S.; Sorimachi, K.; Uraguchi, D., *Adv. Synth. Catal.* **2007**, *349*, 1863–1867.

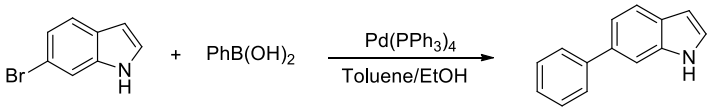



**32** **6l**

Following a modified procedure,[4] a solution of 6-methoxy-1H-indole (**32**) (0.44 g, 3.0 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.36 g, 9.0 mmol, 3.0 equiv) in THF (4 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.68 g, 4.5 mmol, 1.5 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 6 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 10:1) afforded 1-(tert-butyldimethylsilyl)-6-methoxy-1H-indole (**6l**) (0.62 g, 2.4 mmol, 79% yield) as yellow oil.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 20:1) 0.56;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.07 (d, *J* = 3.2 Hz, 1H, Ar*H*), 7.03 (d, J = 2.2 Hz, 1H, Ar*H*), 6.80 (dd, *J* = 8.6, 2.2 Hz, 1H, Ar*H*), 6.53 (d, *J* = 3.1 Hz, 1H, Ar*H*), 3.84 (s, 3H, OC*H*$_3$), 0.94 (s, 9H, SiC(C*H*$_3$)$_3$), 0.59 (s, 6H, 2 x SiC*H*$_3$).
Data match the literature report.[12]

**6-Phenyl-1H-indole (33)**



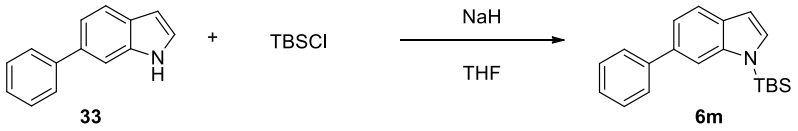

**24** **33**

Following a reported procedure,[13] a solution of 6-bromoindole (**24**) (0.47 g, 2.1 mmol, 1 equiv) in anhydrous toluene (5 mL) under an $N_2$ atmosphere was treated with $Pd(PPh_3)_4$ (0.1 equiv). After stirring the mixture for 30 minutes, phenylboronic acid (0.38 g, 3.1 mmol, 1.5 equiv) in anhydrous ethanol (2.5 mL) were added, followed by saturated $NaHCO_3$ (1.2 mL). The bi-phasic mixture was heated to reflux for 24 hours. After cooling to room temperature, the mixture was added to brine and extracted with ethyl acetate 2 times. The organic layer was dried over $MgSO_4$, filtered and concentrated in vacuo. The residue was purified by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 7:1) to give 6-Phenyl-1H-indole (**33**) (0.11 g, 0.57 mmol, 27% yield) as yellow solid.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 6:1) 0.48;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.23 (s, 1H, N*H*), 7.74 – 7.59 (m, 4H, Ar*H*), 7.48 – 7.37 (m, 3H, Ar*H*), 7.36 – 7.23 (m, 2H, Ar*H*), 6.59 (s, 1H, Ar*H*).
Data match the literature report.[14]

**1-(*Tert*-butyldimethylsilyl)-6-phenyl-1H-indole** (**6m**)

[12] Seffar, F.; Llor, N.; Bosch, J.; Amat, M., *Synthesis* **2001**, *2*, 267-275.
[13] Van Zandt, M. C.; Jones, M. L.; Gunn, D. E.; Geraci, L. S.; Jones, J. H.;Sawicki, D. R.; Sredy, J.; Jacot, J.; Dicioccio, A. T.; Petrova, T.; Mitschler, A.; Podjarny, A. D., *J. Med. Chem.* **2005**, *48*, 3141 – 3152
[14] Pascanu, V.; Hansen, P. R.; Gomez, A. B.; Ayats, C.; Platero-Prats, A. E.; Johansson, M. J.; Pericas, M. A.; Martin-Matute, B., *ChemSusChem* **2015**, *8*, 123-130.

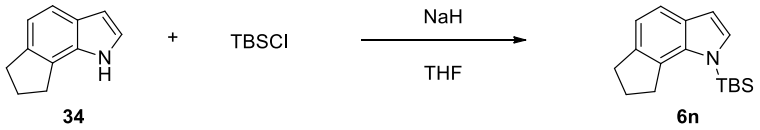



33 6m

Following a modified procedure,[4] a solution of 6-phenyl-1H-indole (**33**) (0.100 g, 0.520 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 62.0 mg, 1.55 mmol, 3.0 equiv) in THF (3 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (118 mg, 0.780 mmol, 1.5 equiv) was added as a solution in THF (1.5 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 40:1) afforded 1-(Tert-butyldimethylsilyl)-6-phenyl-1H-indole (**6m**) (118 mg, 0.380 mmol, 74% yield) as yellow solid.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 40:1) 0.21;
**Mp:** 82.8-83.4 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.73 (s, 1H, Ar*H*), 7.69 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.63 (dd, *J* = 8.3, 1.3 Hz, 2H, Ar*H*), 7.46 (dd, *J* = 8.4, 6.9 Hz, 2H, Ar*H*), 7.38 (dd, *J* = 8.2, 1.5 Hz, 1H, Ar*H*), 7.36 – 7.31 (m, 1H, Ar*H*), 7.22 (d, *J* = 3.2 Hz, 1H, Ar*H*), 6.64 (dd, *J* = 3.2, 0.9 Hz, 1H, Ar*H*), 0.98 (s, 9H, SiC($CH_3$)$_3$), 0.65 (s, 6H, 2 x Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 142.8, 141.6, 134.9, 131.7, 130.7, 128.7, 127.4, 126.4, 120.7, 119.7, 112.5, 104.6, 26.3, 19.5, -3.9;
**IR** (film) $\tilde{\nu}$ 3063 (w), 3026 (w), 2952 (m), 2934 (m), 2891 (w), 2860 (m), 1602 (w), 1503 (w), 1466 (m), 1429 (m), 1312 (m), 1263 (m), 1146 (s), 1078 (w), 986 (w), 819 (s), 788 (m), 757 (m);
**HRMS** (ESI) calcd. for $C_{20}H_{26}NSi^+$ $[M+H]^+$ 308.1829; found 308.1831.

**1-(*Tert*-butyldimethylsilyl)-1,6,7,8-tetrahydrocyclopenta[g]indole** (**6n**)




34 6n

Following a modified procedure,[4] a solution of 1,6,7,8-tetrahydrocyclopenta[g]indole (**34**) (0.47 g, 3.0 mmol, 1.0 equiv) in THF (3 mL) was added dropwise to a suspension of NaH (60% suspension in mineral oil, 0.36 g, 9.0 mmol, 3.0 equiv) in THF (4 mL) under $N_2$ atmosphere at 0 °C. The mixture was allowed to warm to room temperature with stirring over 45 minutes to give a near homogenous solution. After re-cooling to 0 °C, tert-butylchlorodimethylsilane (0.68 g, 4.5 mmol, 1.5 equiv) was added as a solution in THF (2 mL). The mixture was allowed to warm to room temperature and stirred for 12 hours. The mixture was diluted with $Et_2O$ (25 mL) and water (10 mL). The organic layer was washed with brine (10 mL), dried over $MgSO_4$, concentrated under reduced pressure. Purification by flash column chromatography ($SiO_2$, eluent pentane:ethyl acetate 20:1) afforded (**6n**) (0.74 g, 2.7 mmol, 91% yield) as white solid.

**$R_f$:** ($SiO_2$, pentane) 0.40;
**Mp:** 53.8-54.8 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 1H, Ar*H*), 7.22 (d, *J* = 3.2 Hz, 1H, Ar*H*), 7.08 (d, *J* = 7.8 Hz, 1H, Ar*H*), 6.61 (d, *J* = 3.2 Hz, 1H, Ar*H*), 3.18 (t, *J* = 7.2 Hz, 2H, $CH_2CH_2CH_2$), 3.01 (t, *J* =

7.4 Hz, 2H, C*H*$_2$CH$_2$CH$_2$), 2.12 (p, *J* = 7.3 Hz, 2H, CH$_2$C*H*$_2$ CH$_2$), 0.91 (s, 9H, SiC(C*H*$_3$)$_3$), 0.62 (s, 6H, 2 x SiC*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 139.1, 138.6, 131.8, 131.2, 126.8, 118.7, 117.3, 105.2, 34.5, 33.3, 26.6, 26.0, 19.6, -1.0;
**IR** (film) $\tilde{\nu}$ 2952 (m), 2934 (m), 2891 (w), 2860 (m), 1528 (w), 1466 (m), 1411 (m), 1294 (w), 1263 (m), 1214 (w), 1133 (m), 1084 (m), 1022 (w), 838 (m), 807 (s), 720 (m);
**HRMS** (ESI) calcd. for $C_{17}H_{26}NSi^+$ $[M+H]^+$ 272.1829; found 272.1828.

## 3. Synthesis of the ligands

**(2S,2'S)-Dimethyl 2,2'-((2,2-dimethylmalonyl)bis(azanediyl))bis(3-hydroxypropanoate) (35)**


**35**

Following a modified procedure,[15] a flame dried flask was put under $N_2$ atmosphere. Serine methylester hydrochloride (8.00 g, 51.4 mmol, 2 equiv) was added in the flask, together with 80 mL of dry dichloromethane, and the flask was cooled to 0 °C. Triethylamine (14.3 mL, 103 mmol, 4 equiv) was added dropwise over 30 minutes. Then, a solution of 2,2-dimethylmalonyl dichloride (3.40 mL, 25.7 mmol, 1 equiv) in 16 mL of dry dichloromethane was added dropwise over 1 hour. The reaction was warmed to room temperature and stirred for 16 hours. The solvent was evaporated, and the residue was purified by column chromatography ($SiO_2$, eluent pentane:ethyl acetate:tetrahydrofuran 90:10:0 to 0:0:100) to afford (2S,2'S)-dimethyl 2,2'-((2,2-dimethylmalonyl)bis(azanediyl))bis(3-hydroxypropanoate) (**35**) (8.60 g, 25.7 mmol, quantitative yield) as a colorless oil.

**$R_f$:** ($SiO_2$, ethyl acetate) 0.17;
**$[\alpha]_D^{20.0}$** = -164.5 (c = 0.03. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 6.8 Hz, 2H, N*H*), 4.58 (dt, *J* = 7.3, 3.6 Hz, 2H, NC*H*), 3.92 (d, *J* = 3.8 Hz, 4H, OC$H_2$), 3.77 (s, 6H, $CO_2CH_3$), 1.49 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 173.7, 170.9, 62.1, 55.2, 52.8, 50.1, 23.2;
**IR** (film) $\tilde{\nu}$ 3383 (m), 2955 (w), 1741 (s), 1662 (s), 1519 (s), 1464 (w), 1439 (w), 1347 (w), 1284 (w), 1224 (m), 1180 (m), 1127 (w), 1077 (w);
**HRMS (ESI)** calcd for $C_{13}H_{22}N_2NaO_8^+$ $[M+Na]^+$ 357.1268; found 357.1265.

**(4S,4'S)-Dimethyl 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4-carboxylate) (9)**


**35** **9**

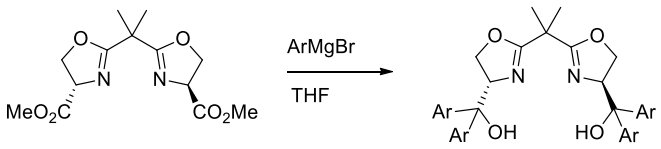
Following a modified procedure,[15] a flame dried flask was put under $N_2$ atmosphere. (2S,2'S)-dimethyl 2,2'-((2,2-dimethylmalonyl)bis(azanediyl))bis(3-hydroxypropanoate) (**35**) (3.19 g, 9.54 mmol, 1 equiv) was added to the flask, followed by 95 mL of dry tetrahydrofuran. The flask was cooled to 0 °C, and Burgess' reagent (5.00 g, 21.0 mmol, 2.2 equiv) was added portionwise. The mixture was then warmed to room temperature, and heated at reflux for 2.5 hours. The mixture was then concentrated, the residue dissolved in 60 mL of dichloromethane, washed with 20 mL of 5% aqueous solution of $NaHCO_3$, and 20 mL of brine. The organic layer was dried over $MgSO_4$, filtered and concentrated. The crude was purified by column chromatography ($SiO_2$, eluent pentane:ethyl acetate:tetrahydrofuran 20:20:1 to 0:100:0) to afford (4S,4'S)-dimethyl 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4-carboxylate) (**9**) (1.77 g, 5.94 mmol, 62% yield) as a pale yellow solid.

**$R_f$:** ($SiO_2$, ethyl acetate) 0.23;
**Mp**: 50.6-52.6 °C;

[15] Matsumoto, T.; Matsumoto, K., Tanaka, A., EP 2 781 522 A1, *optically active bisoxazoline compound, asymmetric catalyst, and method for producing optically active cyclopropane compound using said catalyst.*

**$[\alpha]_D^{20.0}$** = -33.2 (c = 0.15. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.74 (dd, *J* = 10.6, 7.8 Hz, 2H, NC*H*), 4.50 (dd, *J* = 8.7, 7.8 Hz, 2H, OC$H_2$), 4.41 (dd, *J* = 10.6, 8.7 Hz, 2H, OC$H_2$), 3.76 (s, 6H, $CO_2CH_3$), 1.53 (s, 6H, C$H_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.6, 171.3, 70.0, 67.9, 52.6, 38.8, 24.2;
**IR** (film) $\tilde{\nu}$ 2993 (w), 1736 (s), 1644 (s), 1447 (w), 1366 (w), 1286 (w), 1219 (s), 1151 (s), 1120 (m), 1046 (w), 966 (m), 917 (m), 806 (w), 744 (m) $cm^{-1}$;
**HRMS** (ESI) calcd for $C_{13}H_{18}N_2NaO_6^+$ $[M+Na]^+$ 321.1057; found 321.1058.

## Grignard addition




**9** **10**

### General procedure A:

Grignard preparation: under $N_2$ atmosphere, in a flame dried microwave vial, magnesium turnings (49 mg, 2.0 mmol, 2 equiv) were added, followed by $I_2$ (cat.) and 1.8 mL of dry tetrahydrofuran. The corresponding aryl bromide (1.00 mmol, 1 equiv) was dissolved in 0.3 mL of dry tetrahydrofuran, and added dropwise. The mixture was then heated at reflux for 30 seconds, and then allowed to reach room temperature.

Ligand synthesis: Following a modified procedure,[15] under $N_2$ atmosphere in a flame dried flask, a solution of (4S,4'S)-dimethyl 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4-carboxylate) (**9**) (50 mg, 0.17 mmol, 1 equiv) in 2.5 mL of dry tetrahydrofuran was added. The flask was cooled to -78 °C with a dry ice/acetone bath, and the freshly prepared Grignard (1.00 mmol, 6 equiv) was added dropwise over 5 minutes. The reaction was stirred at -78 °C for 24 hours allowing it to slowly reach room temperature. The reaction was then quenched at 0 °C by adding 2 mL of a saturated aqueous $NH_4Cl$ solution. The organic layer was separated and the aqueous layer was extracted with 2 mL of dichloromethane. The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated. An aliquot of the crude was purified by preparative TLC ($SiO_2$) for analysis, and the scratched silica was washed with 10 mL of ethyl acetate.

### General procedure B:

Ligand synthesis: Following a modified procedure,[15] under $N_2$ atmosphere in a flame dried flask, a solution of (4S,4'S)-dimethyl 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4-carboxylate) (**9**) (2.00 g, 6.70 mmol, 1 equiv) in 100 mL of dry tetrahydrofuran was added. The flask was cooled to -78 °C with a dry ice/acetone bath, and a 1 M solution of arylmagnesium bromide in tetrahydrofuran (13.4 mL, 40.2 mmol, 6 equiv) was added dropwise over 5 minutes. The reaction was stirred at -78 °C for 24 hours allowing it to slowly reach room temperature. The reaction was then quenched at 0 °C by adding 50 mL of saturated aqueous $NH_4Cl$ solution. The organic layer was separated and the aqueous layer was extracted with 100 mL of dichloromethane. The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated.

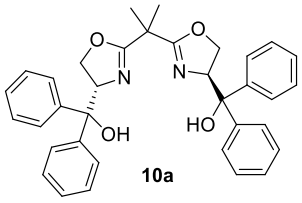
### General procedure C:

Grignard preparation: under $N_2$ atmosphere, in a flame dried flask equipped with a reflux condenser, magnesium turnings (293 mg, 12.1 mmol, 2 equiv) were added, followed by $I_2$ (cat.) and 10 mL of dry

tetrahydrofuran. The aryl bromide was then added dropwise. The mixture was then heated at reflux for 30 seconds, and then allowed to reach room temperature.

Ligand synthesis: Following a modified procedure,[15] under $N_2$ atmosphere in a flame dried flask, a solution of (4S,4'S)-dimethyl 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4-carboxylate) (**9**) (300 mg, 1.00 mmol, 1 equiv) in 15 mL of dry tetrahydrofuran was added. The flask was cooled to -78 °C with a dry ice/acetone bath, and the freshly prepared Grignard (6.03 mmol, 6 equiv) was added dropwise over 5 minutes. The reaction was stirred at -78 °C for 24 hours allowing it to slowly reach room temperature. The reaction was then quenched at 0 °C by adding 12 mL of saturated aqueous $NH_4Cl$ solution. The organic layer was separated and the aqueous layer was extracted with 30 mL of dichloromethane. The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated. The crude was purified by column chromatography.

**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(diphenylmethanol) (10a)**

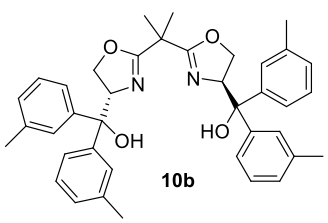


**10a**

Following general procedure **B**, using a phenylmagnesium bromide solution. The crude was purified by column chromatography, ($SiO_2$, eluent pentane:ethyl acetate 10:1 to 6:1 to 4:1) to afford ((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(diphenylmethanol) (**10a**) (1.40 g, 2.57 mmol, 38% yield) as a white solid.

**$R_f$:** ($SiO_2$, pentane: ethyl acetate 8:2) 0.28;
**Mp**: 115.0-116.5 °C;
**$[\alpha]_D^{20.0}$** = -28.8 (c = 0.3. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 7.0 Hz, 4H, Ar*H*), 7.29 (t, *J* = 7.7 Hz, 4H, Ar*H*), 7.25 (d, *J* = 6.2 Hz, 4H, Ar*H*), 7.23 – 7.12 (m, 8H, Ar*H*), 5.36 (dd, *J* = 9.8, 6.8 Hz, 2H, $OCH_2CHNR$), 4.25 (dd, *J* = 8.7, 6.8 Hz, 2H, $OCH_2CHNR$), 4.11 (t, *J* = 9.2 Hz, 2H, $OCH_2CHNR$), 3.65 (s, 2H, O*H*), 1.38 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.5, 145.4, 144.4, 128.3, 128.0, 126.7, 126.6, 125.8, 78.8, 72.0, 69.7, 39.5, 23.6 *(one aromatic carbon signal not resolved)*;
**IR** (film) $\tilde{\nu}$ 3368 (w), 3005 (w), 1650 (m), 1496 (w), 1447 (m), 1360 (w), 1249 (w), 1212 (w), 1163 (w), 1120 (m), 1071 (w), 991 (w), 898 (w), 750(s);
**HRMS** (ESI) calcd for $C_{35}H_{35}N_2O_4^+$ $[M+H]^+$ 547.2591; found 547.2598.

**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di-*m*-tolylmethanol) (10b)**



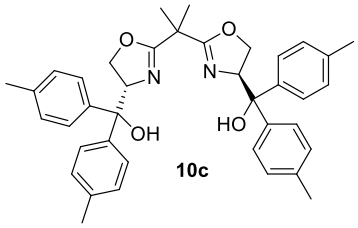
**10b**

Following general procedure **A**, using 1-bromo-3-methylbenzene (0.172 g, 1.00 mmol, 6 equiv). The weight of the crude was 125 mg. 40 mg of crude were purified for analysis by preparative TLC ($SiO_2$,

eluent toluene:ethyl acetate 9:1) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di-m-tolylmethanol) (**10b**) (16.6 mg, 28.0 µmol, 41% calculated yield) as a colorless oil.

**$R_f$:** ($SiO_2$, toluene: ethyl acetate 9:1) 0.4;
**Mp:** 119-123 °C;
**$[\alpha]_D^{20.0}$** = -36.27 (c = 0.25. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.34 (s, 2H, Ar*H*), 7.17 (d, *J* = 4.6 Hz, 6H, Ar*H*), 7.09 – 6.98 (m, 6H, Ar*H*), 6.95 (d, *J* = 7.4 Hz, 2H, Ar*H*), 5.33 (dd, *J* = 9.8, 6.8 Hz, 2H, $OCH_2CHNR$), 4.26 (dd, *J* = 8.7, 6.8 Hz, 2H, $OCH_2CHNR$), 4.12 (dd, *J* = 9.8, 8.7 Hz, 2H, $OCH_2CHNR$), 3.66 (s, 2H, O*H*), 2.34 (s, 6H, $CH_3$), 2.23 (s, 6H, $CH_3$), 1.36 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.4, 145.4, 144.6, 137.8, 137.3, 128.1, 127.9, 127.5, 127.3, 126.6, 123.7, 123.0, 78.8, 72.2, 69.8, 39.5, 23.6, 21.7, 21.6 (*one aromatic carbon signal not resolved*);
**IR** (film) $\tilde{\nu}$ 3560 (w), 3381 (w), 2966 (w), 2917 (m), 2861 (w), 2242 (w), 1661 (m), 1605 (w), 1481 (m), 1364 (w), 1302 (w), 1240 (m), 1147 (m), 1122 (m), 986 (m), 912 (S), 850 (w), 776 (m), 733 (S). IR 3557 (w), 3386 (w), 2921 (w), 2247 (w), 1738 (w), 1660 (m), 1606 (w), 1484 (w), 1363 (w), 1297 (w), 1244 (w), 1150 (m), 1120 (m), 986 (w), 911 (s), 848 (w), 780 (w), 736 (s);
**HRMS** (ESI) calcd for $C_{39}H_{43}N_2O_4^+$ $[M+H]^+$ 603.3217; found 603.3222.

**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di-*p*-tolylmethanol) (10c)**

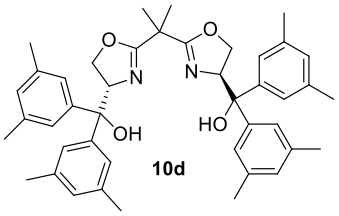


**10c**

Following general procedure **A**, using 1-bromo-4-methylbenzene (0.172 g, 1.00 mmol, 6 equiv). The weight of the crude was 107 mg. 40 mg of crude were purified by preparative TLC ($SiO_2$, eluent toluene:ethyl acetate 9:1) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di-p-tolylmethanol) (**10c**) (12.9 mg, 21.0 µmol, 34% calculated yield) as a white solid.

**$R_f$:** ($SiO_2$, toluene: ethyl acetate 9:1) 0.3;
**Mp**: 88.4-92.1 °C;
**$[\alpha]_D^{20.0}$** = 79.96 (c = 0.24. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.28 (d, *J* = 8.3 Hz, 4H, Ar*H*), 7.15 (d, *J* = 8.2 Hz, 4H, Ar*H*), 7.07 (d, *J* = 8.0 Hz, 4H, Ar*H*), 7.03 (d, *J* = 8.0 Hz, 4H, Ar*H*), 5.33 (dd, *J* = 9.8, 7.0 Hz, 2H, $OCH_2CHNR$), 4.22 (dd, *J* = 8.6, 7.0 Hz, 2H, $OCH_2CHNR$), 4.09 (dd, *J* = 9.9, 8.6 Hz, 2H, $OCH_2CHNR$), 3.72 (s, 2H, O*H*), 2.28 (s, 6H, $CH_3$), 2.26 (s, 6H, $CH_3$), 1.41 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.5, 143.1, 141.8, 136.1, 136.0, 128.9, 128.8, 126.3, 125.5, 78.4, 72.1, 69.8, 39.5, 23.7, 21.0, 20.9;
**IR** (film) $\tilde{\nu}$ 3377 (w), 2993 (w), 2924 (w), 2246 (w), 1660 (m), 1513 (m), 1470 (w), 1411 (w), 1362 (w), 1247 (w), 1171 (w), 1120 (m), 1022 (w), 986 (m), 912 (s), 818 (m), 785 (w), 736 (s);
**HRMS** (ESI) calcd for $C_{39}H_{43}N_2O_4^+$ $[M+H]^+$ 603.3217; found 603.3223.

**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-dimethylphenyl)methanol) (10d)**

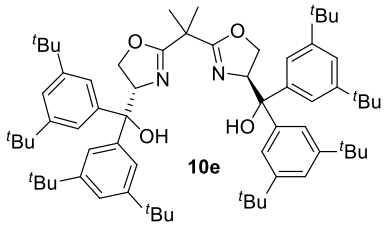



**10d**

Following general procedure **C**, using 1-bromo-3,5-dimethylbenzene (0.820 mL, 6.03 mmol, 6 equiv). The crude was purified by column chromatography (deactivated $SiO_2$, eluent pentane:ethyl acetate 9:1 + 1% of triethylamine) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-dimethylphenyl)methanol) (**10d**) (316 mg, 0.480 mmol, 48% yield) as a white solid.

**$R_f$:** ($SiO_2$, pentane: ethyl acetate 8:2) 0.5;
**Mp**: 108.1-112.6 °C;
**$[\alpha]_D^{20.0}$** = -4.46 (c = 0.5. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.10 (s, 4H, *ortho*-Ar*H*), 6.93 (s, 4H, *ortho*-Ar*H*), 6.83 (s, 2H, *para*-Ar*H*), 6.75 (s, 2H, *para*-Ar*H*), 5.27 (dd, *J* = 9.8, 6.5 Hz, 2H, $OCH_2CHNR$), 4.29 (app t, *J* = 7.7 Hz, 2H, $OCH_2CHNR$), 4.13 (app t, *J* = 9.2 Hz, 2H, $OCH_2CHNR$), 3.49 (br s, 2H, O*H*), 2.29 (s, 12H, $CH_3$), 2.12 (s, 12H, $CH_3$), 1.29 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.0, 145.0, 144.8, 137.5, 137.0, 128.5, 128.4, 124.6, 124.0, 79.0, 72.3, 69.9, 39.4, 23.4, 21.5, 21.4;
**IR** (film) $\tilde{\nu}$ 3401 (w), 2917 (w), 2246 (w), 1660 (w), 1603 (w), 1471 (w), 1366 (w), 1244 (w), 1150 (w), 1119 (m), 985 (w), 910 (m), 854 (w), 732 (s);
**HRMS** (ESI) calcd for $C_{43}H_{51}N_2O_4^+$ $[M+H]^+$ 659.3843; found 659.3846.

**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-di-*tert*-butylphenyl)methanol) (10e)**



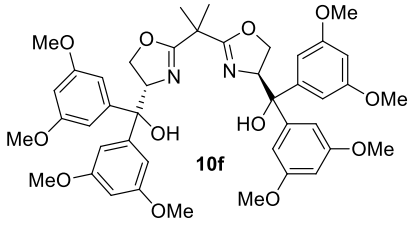

**10e**

Following general procedure **A**, using 1-bromo-3,5-di-tert-butylbenzene (0.271 g, 1.00 mmol, 6 equiv). The weight of the crude was 246 mg. 40 mg of crude were purified by preparative TLC ($SiO_2$, eluent toluene:ethyl acetate 9:1) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-di-tert-butylphenyl)methanol) (**10e**) (14.3 mg, 14.0 µmol, 53% calculated yield) as a colorless oil.

**$R_f$:** ($SiO_2$, toluene: ethyl acetate 9:1) 0.54;
**$[\alpha]_D^{20.0}$** = 8.96 (c = 0.4. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 1.8 Hz, 4H, Ar*H*), 7.23 (m, 8H, Ar*H*), 5.24 (t, *J* = 9.2 Hz, 2H, $OCH_2CHNR$), 4.15 (dd, *J* = 9.2, 1.8 Hz, 4H, $OCH_2CHNR$), 2.89 (s, 2H, O*H*), 1.45 (s, 6H, $CH_3$), 1.27 (s, 36H, $C(CH_3)_3$), 1.26 (s, 36H, $C(CH_3)_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 171.7, 150.0, 149.6, 145.3, 143.2, 121.3, 120.5, 120.4, 120.3, 79.3, 73.7, 70.4, 39.2, 34.9, 34.8, 31.5, 24.3 (*one aliphatic carbon signal is not resolved*);

**IR** (film) $\tilde{\nu}$ 3528 (w), 3071 (w), 2962 (s), 2906 (m), 2868 (m), 2246 (w), 1661 (m), 1599 (m), 1475 (m), 1393 (w), 1363 (m), 1250 (m), 1202 (w), 1178 (w), 1152 (w), 1121 (m), 1071 (w), 983 (w), 911 (m), 878 (w), 847 (w), 824 (w), 737 (s);
**HRMS** (ESI) calcd for $C_{67}H_{99}N_2O_4^+$ [M+H]$^+$ 995.7599; found 995.7595.

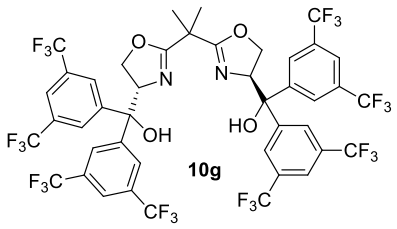
**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-dimethoxyphenyl)methanol) (10f)**




Following general procedure **A**, using 1-bromo-3,5-dimethoxybenzene (0.218 g, 1.00 mmol, 6 equiv). The weight of the crude was 154 mg. 35 mg of crude were purified by preparative TLC ($SiO_2$, eluent heptane:ethyl acetate 6:4). The obtained product was resubjected to preparative TLC ($SiO_2$, eluent heptane:ethyl acetate 6:4) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-dimethoxyphenyl)methanol) (**10f**) (11.0 mg, 14.0 µmol, 41% calculated yield) as a colorless oil.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 6:4) 0.13;
**$[\alpha]_D^{20.0}$** = -30.24 (c = 0.47. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.58 (dd, *J* = 6.0, 2.3 Hz, 8H, Ar*H*), 6.27 (dt, *J* = 9.9, 2.2 Hz, 4H, Ar*H*), 5.21 (dd, *J* = 9.8, 7.2 Hz, 2H, OCH$_2$C*H*NR), 4.24 (dd, *J* = 8.7, 7.1 Hz, 2H, OC*H*$_2$CHNR), 4.16 (dd, *J* = 9.8, 8.7 Hz, 2H, OC*H*$_2$CHNR), 3.75 (s, 12H, OC*H*$_3$), 3.70 (s, 12H, OC*H*$_3$), 1.40 (s, 6H, C*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.4, 160.5, 160.3, 147.7, 146.6, 105.2, 104.4, 98.5, 98.4, 78.9, 72.3, 69.9, 55.3, 55.1, 39.4, 23.6;
**IR** (film) $\tilde{\nu}$ 3442 (w), 3000 (w), 2942 (w), 2838 (w), 2254 (w), 1661 (w), 1600 (s), 1462 (m), 1426 (m), 1345 (w), 1294 (m), 1249 (w), 1206 (s), 1156 (s), 1121 (w), 1063 (m), 983 (w), 919 (m), 838 (w), 737 (s);
**HRMS** (ESI) calcd for $C_{43}H_{51}N_2O_{12}^+$ [M+H]$^+$ 787.3437; found 787.3433.

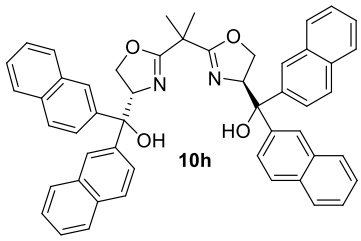
**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-bis(trifluoromethyl)phenyl)methanol) (10g)**




Following general procedure **A**, using 1-bromo-3,5-bis(trifluoromethyl)benzene (0.295 g, 1.00 mmol, 6 equiv). The weight of the crude was 239 mg. 40 mg of crude were purified by preparative TLC ($SiO_2$, eluent toluene:ethyl acetate 9:1) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-bis(trifluoromethyl)phenyl)methanol) (**10g**) (25.3 mg, 23.0 µmol, 83% calculated yield) as an off-white solid.

**$R_f$:** (silica, toluene: ethyl acetate 9:1) 0.59;
**Mp**: 53.8-58.2 °C.
**$[\alpha]_D^{20.0}$** = -99.03 (c = 0.33. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 1.6 Hz, 4H, Ar*H*), 7.82 (s, 6H, Ar*H*), 7.77 (s, 2H), 5.36 (dd, *J* = 9.8, 7.7 Hz, 2H, $OCH_2CHNR$), 4.19 (app t, *J* = 9.4 Hz, 2H, $OCH_2CHNR$), 4.10 (dd, *J* = 9.0, 7.7 Hz, 2H, $OCH_2CHNR$), 3.51 (br s, 2H, O*H*), 1.43 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 174.1, 146.3, 145.0, 132.3 (q, *J* = 33.3 Hz), 131.8 (q, *J* = 34.3 Hz), 127.0 (m), 126.0 (m), 123.0 (q, *J* = 273.7 Hz), 123.0 (q, *J* = 273.7 Hz), 122.1 (m), 122.1 (m), 77.9, 71.7, 69.3, 39.7, 23.3;
**$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -62.9, -63.0;
**IR** (film) $\tilde{\nu}$ 3381 (w), 1662 (w), 1632 (w), 1472 (w), 1375 (m), 1279 (s), 1171 (s), 1129 (s), 975 (w), 902 (m), 847 (w), 812 (w), 739 (m), 711 (m);
**HRMS** (ESI) calcd for $C_{43}H_{27}F_{24}N_2O_4^+$ $[M+H]^+$ 1091.1582; found 1091.1595.

**((4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di(naphthalen-2-yl)methanol) (10h)**

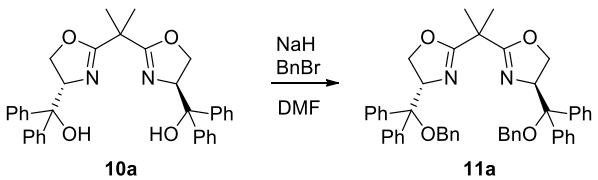


**10h**

Following general procedure **A**, using 2-bromonaphthalene (0.208 g, 1.00 mmol, 6 equiv). The weight of the crude was 194 mg. 40 mg of crude were purified by preparative TLC ($SiO_2$, eluent toluene:ethyl acetate 9:1) to afford (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di(naphthalen-2-yl)methanol) (**10h**) (12.1 mg, 16.0 µmol, 47% calculated yield) as an off-white solid.

**$R_f$:** ($SiO_2$, toluene: ethyl acetate 9:1) 0.38;
**Mp**: 139-147 °C;
**$[\alpha]_D^{20.0}$** = -246.12 (c = 0.19. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.16 (s, 2H, Ar*H*), 8.00 (s, 2H, Ar*H*), 7.95 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.84 – 7.72 (m, 4H, Ar*H*), 7.67 (dd, *J* = 8.4, 5.4 Hz, 4H, Ar*H*), 7.55 – 7.23 (m, 12H, Ar*H*), 6.98 – 6.91 (m, 2H, Ar*H*), 5.63 (dd, *J* = 9.8, 6.7 Hz, 2H, $OCH_2CHNR$), 4.40 (dd, *J* = 8.7, 6.7 Hz, 2H, $OCH_2CHNR$), 4.16 (t, *J* = 9.3 Hz, 2H, $OCH_2CHNR$), 4.11 (s, 2H, O*H*), 1.41 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.7, 142.2, 141.4, 133.0, 132.8, 132.3, 132.2, 128.6, 128.4, 128.0, 127.6, 127.4, 127.3, 126.1, 126.0, 125.8, 125.7, 125.7, 125.1, 124.5, 124.4, 79.0, 71.6, 69.8, 39.6, 23.6;
**IR** (film) $\tilde{\nu}$ 3635 (w), 3557 (w), 3363 (w), 3057 (w), 2939 (w), 2248 (w), 1923 (w), 1654 (m), 1600 (w), 1507 (w), 1472 (w), 1363 (w), 1245 (w), 1154 (w), 1120 (m), 1020 (w), 987 (w), 908 (s), 858 (w), 821 (m), 795 (m), 733 (s);
**HRMS** (ESI) calcd for $C_{51}H_{43}N_2O_4^+$ $[M+H]^+$ 747.3217; found 747.3219.

**(4S,4'S)-2,2'-(Propane-2,2-diyl)bis(4-((benzyloxy)diphenylmethyl)-4,5-dihydrooxazole) (11a)**



**10a** **11a**

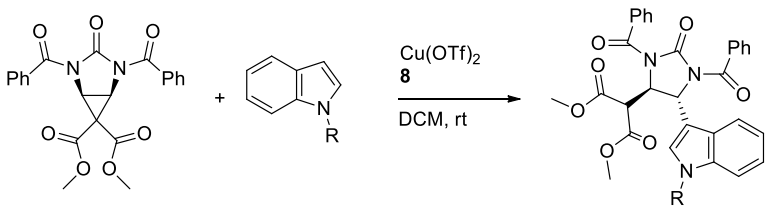
Following a modified procedure,[16] under $N_2$ atmosphere, in a flame dried flask, (2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(diphenylmethanol) (**10a**) (100 mg, 0.183 mmol, 1 equiv) was added, followed by dry dimethylformamide (0.4 mL). The flask was cooled at 0 °C, and sodium hydride (60% dispersion in mineral oil, 18.0 mg, 0.439 mmol, 2.4 equiv) was added. The reaction mixture was stirred for 1 hour at 0 °C. Then, benzyl bromide (52.0 µL, 0.439 mmol, 2.4 equiv) was added dropwise. The reaction was warmed to room temperature and stirred for 16 hours. The reaction was then quenched by the addition of 5 mL of saturated aqueous $NH_4Cl$ solution, and extracted with diethyl ether (3x5 mL). The combined organic phases were dried over $Na_2SO_4$, filtered and evaporated. The residue was purified by column chromatography ($SiO_2$, eluent pentane:ethyl acetate 49:1) to afford 2,2'-(propane-2,2-diyl)bis(4-((benzyloxy)diphenylmethyl)-4,5-dihydrooxazole) (**11a**) (73.0 mg, 0.100 mmol, 55% yield) as a white solid.

**$R_f$:** ($SiO_2$, toluene: ethyl acetate 9:1) 0.23;
**Mp**: 84.2-92.4 °C;
**$[\alpha]_D^{20.0}$** = 82.34 (c = 0.15. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.61 (m, 4H, Ar*H*), 7.44 – 7.38 (m, 4H), 7.36 – 7.26 (m, 15H, Ar*H*), 7.26 – 7.16 (m, 7H, Ar*H*), 5.26 (dd, *J* = 10.1, 7.4 Hz, 2H, $OCH_2CHNR$), 4.41 – 4.32 (m, 4H, $OCH_2CHNR$ + $OCH_2Ph$), 4.20 (d, *J* = 11.8 Hz, 2H, $OCH_2Ph$), 4.06 (dd, *J* = 10.1, 8.8 Hz, 2H, $OCH_2CHNR$), 0.98 (s, 6H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 169.7, 143.5, 141.3, 139.1, 129.0, 128.6, 128.2, 127.9, 127.3, 127.2, 127.01, 126.95, 126.91, 83.9, 70.2, 69.1, 65.6, 38.5, 23.1;
**IR** (film) $\tilde{\nu}$ 4051 (w), 3062 (w), 3030 (w), 2905 (w), 2249 (w), 1953 (w), 1741 (w), 1655 (s), 1604 (w), 1544 (w), 1495 (m), 1449 (m), 1386 (w), 1313 (w), 1261 (m), 1220 (w), 1152 (m), 1121 (m), 1063 (s), 1032 (m), 985 (m), 910 (s), 843 (w), 735 (s);
**HRMS** (ESI) calcd for $C_{49}H_{47}N_2O_4^+$ $[M+H]^+$ 727.3530; found 727.3534.

[16] Wang, S.-H.; Chein, R.-J., *Tetrahedron* **2016**, *72*, 2607-2615.

## 4. Optimization of the enantioselective desymmetrization

**General procedure D:**

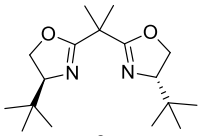



**20** | **21** (R = H), **36** (R = Me), **6a** (R = TBS) | **37a** (R = H), **37b** (R = Me), **37c** (R = TBS)

In a glovebox, an oven dried microwave vial was charged with copper(II) triflate (3.6 mg, 10 µmol, 0.2 equiv), and ligand (3.5 mg, 12 µmol, 0.24 equiv). The vial was taken out of the glovebox and put under $N_2$ atmosphere. 0.5 mL of dry dichloromethane was added and the suspension was stirred vigorously for 2 hours. Then, a solution of dimethyl 2,4-dibenzoyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (**20**) (21.1 mg, 50.0 µmol, 1 equiv) and the indole (60.0 µmol, 1.2 equiv) in 0.5 mL of dry dichloromethane was added. The reaction was stirred at room temperature for 16 hours, diluted with 0.5 mL of ethyl acetate and then filtered on a pad of $SiO_2$, eluting with 5 mL of ethyl acetate. The solution was concentrated and subjected to preparative TLC ($SiO_2$) with the specified eluent. The scratched $SiO_2$ was washed with 10 mL of ethyl acetate. The solvent was evaporated to afford the product.

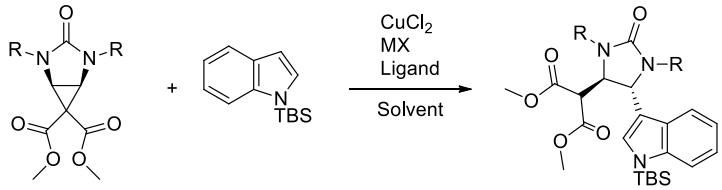
**Table S1.** Screening of N-substituents of the indole.

| entry | R | Yield (%) | er |
|---|---|---|---|
| 1 | H | 50 | 46:54 |
| 2 | Me | 65 | 46:54 |
| 3 | TBS | 60 | 42:58 |



**8**

**General procedure E:**




**2** (R = Piv), **19** (R = Ac), **20** (R = Bz) | **6a** | **7a** (R = Piv), **38** (R = Ac), **37c** (R = Bz)

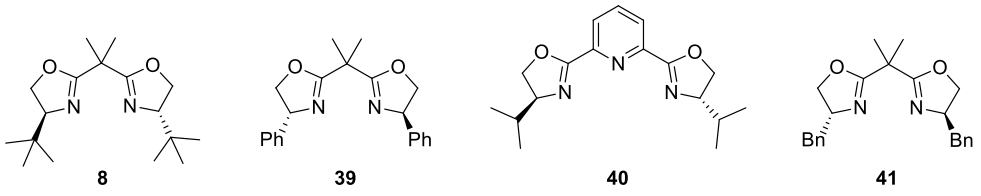
In a glovebox, an oven dried microwave vial was charged with copper(II) chloride (1.3 mg, 10 µmol, 0.2 equiv), MX (4.0 µmol, 0.4 equiv), and ligand (24 µmol, 0.24 equiv). The vial was protected from light with aluminum foil, taken out of the glovebox and put under $N_2$ atmosphere. 0.5 mL of dry solvent

was added and the suspension was stirred vigorously for 2 hours. Then, a solution of cyclopropane (50.0 µmol, 1 equiv) and 1-(tert-butyldimethylsilyl)-1H-indole (**6a**) (13.9 mg, 60.0 µmol, 1.2 equiv) in 0.5 mL of dry solvent were added. The reaction was stirred at room temperature for 16 hours, diluted with 0.5 mL of ethyl acetate and then filtered on a pad of $SiO_2$, eluting with 5 mL of ethyl acetate. The solution was concentrated and subjected to preparative TLC ($SiO_2$) with heptane:ethyl acetate 65:35 as eluent. The scratched $SiO_2$ was washed with 10 mL of ethyl acetate. The solvent was evaporated to afford the product.

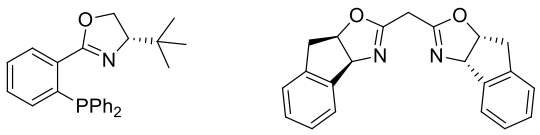
**Table S2.** Screening of protecting groups on cyclopropane, ligands, counterions and solvents.

| entry | R | Ligand | MX | Solvent | Yield (%) | er |
|---|---|---|---|---|---|---|
| 1 | PhCO | **8** | $AgSbF_6$ | DCM | 80 | 39.5:60.5 |
| 2 | PhCO | **8** | $AgSbF_6$ | $CDCl_3$ | 74 | 29:71 |
| 3 | PhCO | **8** | $AgSbF_6$ | Toluene[a] | 52 | 19.4:80.6 |
| 4 | MeCO[2] | **8** | $AgSbF_6$ | Toluene | 39 | 39.5:60.5 |
| 5 | $^t$BuCO | **8** | $AgSbF_6$ | Toluene | 70 | 25:75 |
| 6 | $^t$BuCO | **39** | $AgSbF_6$ | Toluene | 77 | 46:54 |
| 7 | $^t$BuCO | **40** | $AgSbF_6$ | Toluene | 71 | 61:39 |
| 8 | $^t$BuCO | **41** | $AgSbF_6$ | Toluene | 68 | 57:43 |
| 9 | $^t$BuCO | **42** | $AgSbF_6$ | Toluene | 91 | 42:58 |
| 10 | $^t$BuCO | **43** | $AgSbF_6$ | p-xylene | 72 | 42:58 |
| 11 | $^t$BuCO | **8** | AgOTf | p-xylene | 42 | 29:71 |
| 12 | $^t$BuCO | **8** | $AgBF_4$ | Toluene | 44 | 28:72 |
| 13 | $^t$BuCO | **8** | $AgClO_4$ | Toluene | 45 | 27.5:72.5 |
| 14 | $^t$BuCO | **8** | $AgPF_6$ | Toluene | 44 | 28:72 |
| 15 | $^t$BuCO | **8** | $AgNTF_2$ | Toluene | 25 | 37.5:62.5 |
| 16 | $^t$BuCO | **8** | NaBARF | Toluene | No conversion | - |
| 17 | $^t$BuCO | **8** | $AgSbF_6$ | $CCl_4$ | 45 | 20:80 |
| 18 | $^t$BuCO | **8** | $AgSbF_6$ | DCM | 74 | 37.5:62.5 |
| 19 | $^t$BuCO | **8** | $AgSbF_6$ | Trifluorotoluene | 83 | 34:66 |
| 20 | $^t$BuCO | **8** | $AgSbF_6$ | o-xylene | 79 | 26.5:73.5 |
| 21 | $^t$BuCO | **8** | $AgSbF_6$ | m-xylene | 87 | 25:75 |
| 22 | $^t$BuCO | **8** | $AgSbF_6$ | p-xylene | 86 | 24:76 |
| 23 | $^t$BuCO | **8** | $AgSbF_6$ | Benzene | 73 | 21.5:78.5 |
| 24 | $^t$BuCO | **8** | $AgSbF_6$ | Chlorobenzene | 75 | 30:70 |

[a]Using 5 mL of solvent. [b]The cyclopropane was added as a solid.

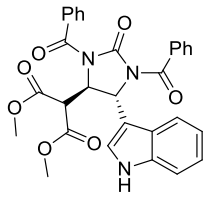


**8** **39** **40** **41**



**42** **43**

**Dimethyl 2-(1,3-dibenzoyl-5-(1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate** (**37a**)

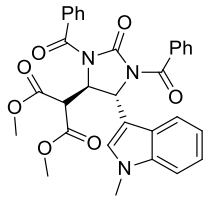


**37a**

Following general procedure **D**, using 1H-indole (**21**) (7.0 mg, 60 µmol, 1.2 equiv). Preparative TLC using eluent 1:1 heptane:ethyl acetate afforded dimethyl 2-(1,3-dibenzoyl-5-(1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (**37a**) (18.7 mg, 35.0 µmol, 69% yield) as a grey solid. Chiral HPLC conditions: er = 54:46; Chiralpak IB 80:20 Hexane/iPrOH, 1.0 mL/min, 60 min. $t_r$ (major) = 23.0 min. and $t_r$ (minor) = 31.7 min. $\lambda = 250$ cm$^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 6:4) 0.28;
**Mp:** 99.4-102.9 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.30 (s, 1H, N*H*), 7.80 – 7.75 (m, 1H, Ar*H*), 7.67 – 7.63 (m, 2H, Ar*H*), 7.56 – 7.52 (m, 2H, Ar*H*), 7.51 – 7.46 (m, 1H, Ar*H*), 7.41 – 7.34 (m, 4H, Ar*H*), 7.32 – 7.26 (m, 3H, Ar*H*), 7.25 – 7.18 (m, 2H, Ar*H*), 6.14 (d, *J* = 3.6 Hz, 1H, indole-C*H*), 5.28 (dd, *J* = 4.2, 3.6 Hz, 1H, indole-CH-C*H*), 4.46 (d, *J* = 4.2 Hz, 1H, C*H*($CO_2CH_3$)$_2$), 3.80 (s, 3H, $CO_2CH_3$), 3.64 (s, 3H, $CO_2CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.1, 169.2, 167.2, 166.9, 150.4, 136.7, 133.9, 133.7, 132.2, 131.9, 128.9, 127.9, 127.8, 124.5, 124.0, 122.6, 120.5, 118.7, 113.5, 111.8, 57.2, 53.1, 52.8, 52.5, 51.3 (*one aromatic carbon signal is not resolved)*;
**IR** (film) $\tilde{\nu}$ 3399 (w), 1758 (s), 1679 (s), 1444 (w), 1339 (m), 1277 (s), 1188 (m), 1031 (w), 910 (w);
**HRMS** (ESI) calcd for $C_{30}H_{25}N_3O_7$ [M+] 539.1687; found 539.1684.

**Dimethyl 2-(1,3-dibenzoyl-5-(1-methyl-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate** (**37b**)

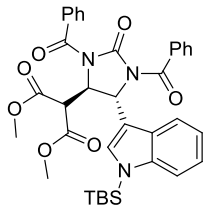


**37b**

Following general procedure **D**, using 1-methyl-1H-indole (**36**) (7.9 mg, 60 µmol, 1.2 equiv). Preparative TLC using eluent 1:1 heptane:ethyl acetate afforded dimethyl 2-(1,3-dibenzoyl-5-(1-methyl-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (**37b**) (17.0 mg, 31.0 µmol, 61% yield) as a yellow solid. Chiral HPLC conditions: er = 54:46; Chiralpak IB 80:20 Hexane/iPrOH, 1.0 mL/min, 60 min. $t_r$ (major) = 20.1 min. and $t_r$ (minor) = 26.4 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 6:4) 0.40;
**Mp:** 103.8-107.5 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.68 – 7.64 (m, 2H, Ar*H*), 7.55 – 7.52 (m, 2H, Ar*H*), 7.51 – 7.46 (m, 1H, Ar*H*), 7.42 – 7.37 (m, 3H, Ar*H*), 7.35 – 7.26 (m, 4H, Ar*H*), 7.23 – 7.17 (m, 2H, Ar*H*), 6.11 (d, *J* = 3.4 Hz, 1H, indole-C*H*), 5.28 (dd, *J* = 4.2, 3.4 Hz, 1H, indole-CH-C*H*), 4.44 (d, *J* = 4.2 Hz, 1H, C*H*($CO_2CH_3$)$_2$), 3.79 (s, 3H, $CO_2CH_3$), 3.77 (s, 3H, $CO_2CH_3$), 3.67 (s, 3H, $NCH_3$);
**$^{13}$C NMR** (101 MHz, CDCl3) δ 170.1, 169.1, 167.2, 166.9, 150.4, 137.5, 133.9, 133.7, 132.1, 131.9, 128.9, 128.5, 127.9, 127.7, 125.0, 122.1, 120.1, 118.8, 111.8, 109.9, 57.3, 53.1, 52.8, 52.5, 51.3, 32.9 (*one aromatic carbon signal is not resolved*);
**IR** (film) $\tilde{\nu}$ 2949 (w), 1758 (s), 1679 (s), 1444 (w), 1318 (m), 1266 (s), 1198 (m), 1036 (w), 916 (w);
**HRMS** (ESI) calcd for $C_{31}H_{27}N_3O_7$ [M+] 553.1844; found 553.1844.

**Dimethyl 2-(1,3-dibenzoyl-5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate** (**37c**)

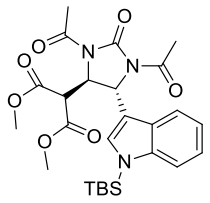



**37c**

Following general procedure **E**, using dimethyl 2,4-dibenzoyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (**20**) (21.1 mg, 50.0 µmol, 1 equiv). Preparative TLC using eluent 55:45 heptane:ethyl acetate afforded dimethyl 2-(1,3-dibenzoyl-5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (**37c**) (16.9 mg, 26.0 µmol, 52% yield) as a white solid. Chiral HPLC conditions: er = 80.6:19.4; Chiralpak IB 95:5 Hexane/iPrOH, 0.5 mL/min, 31 min. $t_r$ (major) = 15.7 min. and $t_r$ (minor) = 19.1 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate1:1) 0.62;
**$[\alpha]_D^{20.0}$** = 21.1 (c = 0.31. $CHCl_3$);
**Mp:** 87.6-88.7 °C;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 1H, Ar*H*), 7.66 – 7.62 (m, 2H, Ar*H*), 7.55 – 7.46 (m, 4H, Ar*H*), 7.42 – 7.36 (m, 3H, Ar*H*), 7.32 – 7.27 (m, 3H, Ar*H*), 7.23 – 7.17 (m, 2H, Ar*H*), 6.13 (d, *J* = 3.4 Hz, 1H, indole-C*H*), 5.26 – 5.21 (m, 1H, indole-CH-C*H*), 4.45 (d, *J* = 4.1 Hz, 1H, C*H*($CO_2CH_3$)$_2$), 3.79 (s, 3H, $CO_2CH_3$), 3.67 (s, 3H, $CO_2CH_3$), 0.92 (s, 9H, SiC($CH_3$)$_3$), 0.61 (s, 6H, Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.2, 169.0, 167.2, 166.9, 150.5, 142.0, 134.1, 133.8, 132.2, 131.8, 130.6, 128.9, 128.8, 128.0, 127.9, 127.8, 122.1, 120.5, 118.8, 115.4, 114.5, 57.2, 53.1, 52.8, 52.6, 51.4, 26.3, 19.4, -3.9 (*one $SiCH_3$ carbon signal is not resolved*);
**IR** (film) $\tilde{\nu}$ 2952 (w), 2928 (w), 1787 (m), 1733 (s), 1691 (s), 1446 (w), 1327 (s), 1279 (s), 1225 (s), 1166 (s), 1082 (w), 909 (w), 825 (w);
**HRMS** (ESI) calcd. for $C_{36}H_{39}N_3NaO_7Si^+$ $[M+Na]^+$ 676.2449; found 676.2452.

**Dimethyl 2-(1,3-diacetyl-5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate** (**38**)



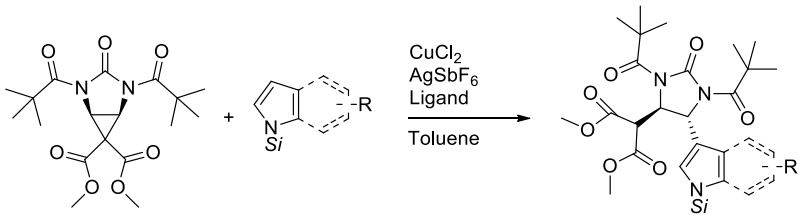

**38**

Following general procedure **E**, using dimethyl 2,4-diacetyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (**19**) (14.9 mg, 50.0 µmol, 1 equiv). Preparative TLC using eluent 65:35 heptane:ethyl acetate afforded dimethyl 2-(1,3-diacetyl-5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (**38**) (10.4 mg, 20.0 µmol, 39% yield) as a colorless oil. Chiral HPLC conditions: er = 60.5:39.5; Chiralpak IB 95:5 Hexane/iPrOH, 0.5 mL/min, 31 min. $t_r$ (major) = 8.0 min. and $t_r$ (minor) = 10.4 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 6:4) 0.67;
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48 (d, *J* = 8.2 Hz, 1H, Ar*H*), 7.42 – 7.36 (m, 1H, Ar*H*), 7.19 (s, 1H, Ar*H*), 7.18 – 7.13 (m, 1H, Ar*H*), 7.13 – 7.08 (m, 1H, Ar*H*), 5.80 (d, *J* = 1.8 Hz, 1H, indole-C*H*), 4.84 (dd, *J* = 4.1, 1.9 Hz, 1H, indole-CH-C*H*), 4.24 (d, *J* = 4.1 Hz, 1H, C*H*($CO_2CH_3$)$_2$), 3.75 (s, 3H, $CO_2C$*H*$_3$), 3.72 (s, 3H, $CO_2C$*H*$_3$), 2.66 (s, 3H, COC*H*$_3$), 2.48 (s, 3H, COC*H*$_3$), 0.90 (s, 9H, SiC(C*H*$_3$)$_3$), 0.59 (s, 3H, SiC*H*$_3$), 0.59 (s, 3H, SiC*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 170.8, 169.6, 167.1, 166.9, 152.1, 141.9, 130.7, 127.6, 121.8, 120.4, 118.4, 115.7, 114.5, 56.6, 52.9, 52.8, 51.8, 51.4, 26.2, 24.6, 24.4, 19.5, -3.9 (*one SiCH$_3$ carbon signal is not resolved*);
**IR** (film) $\tilde{\nu}$ 2958 (w), 2934 (w), 2862 (w), 1757 (s), 1703 (m), 1452 (w), 1369 (m), 1255 (s), 1166 (m), 1028 (w), 975 (w), 915 (w), 843 (w), 813 (w);
**HRMS** (ESI) calcd. for $C_{26}H_{36}N_3O_7Si^+$ $[M+H]^+$ 530.2317; found 530.2327.

## 5. Scope of the enantioselective desymmetrization

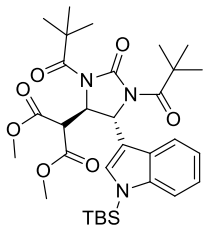
**General procedure F:**




**2** **6** **7**

In a glovebox, an oven dried microwave vial was charged with copper(II) chloride (2.7 mg, 20 µmol, 0.2 equiv) and silver hexafluoroantimonate(V) (13.1 mg, 38.0 µmol, 0.38 equiv). The vial was protected from light with aluminum foil, taken out of the glovebox and put under $N_2$. A solution of ligand **10d** (15.8 mg, 24.0 µmol, 0.24 equiv) in 2 mL of dry toluene was added in the vial, and the suspension was stirred vigorously for 2 hours. Then the vial was cooled at the indicated temperature in a cryostat. After 10 minutes, a solution of the indole/pyrrole **6** (0.100 mmol, 1 equiv) and cyclopropane **2** (57.4 mg, 0.150 mmol, 1.5 equiv) in 2 mL of dry toluene was added dropwise. The reaction was stirred at the same temperature for the indicated time, diluted with 2 mL of a mixture of pentane:ethyl acetate 1:1 and then filtered on a pad of $SiO_2$, eluting with the same mixture (15 mL). The solution was concentrated and subjected to preparative TLC ($SiO_2$) with the specified eluent. The scratched $SiO_2$ was washed with 10 mL of ethyl acetate to afford the product.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate** (**7a**)



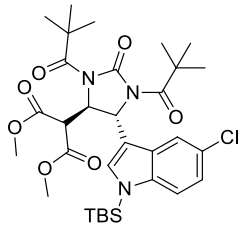

**7a**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-1H-indole (**6a**) (23.1 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 18 hours and 30 minutes. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7a**) (49.0 mg, 80.0 µmol, 80% yield) as a white solid. Chiral HPLC conditions: er = 94.2:5.8; Chiralpak IB 97:3 Hexane/iPrOH, 1.0 mL/min, 30 min. $t_r$ (minor) = 14.7 min. and $t_r$ (major) = 16.1 min. $\lambda$ = 280 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 8:2) 0.6;
**Mp:** 72.3-73.2 °C;
**$[\alpha]_D^{20.0}$** = -22.7 (c = 0.24. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.74 (m, 1H, Ar*H*), 7.48 – 7.43 (m, 1H, Ar*H*), 7.18 – 7.09 (m, 2H, Ar*H*), 7.00 (s, 1H, Ar*H*), 5.90 (s, 1H, indole-C*H*), 4.79 (dd, *J* = 4.6, 1.2 Hz, 1H, indole-CH-C*H*), 4.14 (d, *J* = 4.6 Hz, 1H, C*H*($CO_2CH_3$)$_2$), 3.75 (s, 6H, 2 x $CO_2CH_3$), 1.42 (s, 9H, C($CH_3$)$_3$), 1.35 (s, 9H, C($CH_3$)$_3$), 0.87 (s, 9H, SiC($CH_3$)$_3$), 0.56 (s, 3H, Si$CH_3$), 0.54 (s, 3H, Si$CH_3$);

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 167.2, 149.6, 141.8, 128.3, 128.2, 121.9, 120.1, 119.3, 117.1, 114.1, 58.7, 53.0, 52.8, 52.8, 51.7, 41.8, 41.8, 26.3, 26.2, 19.5, -4.0, -4.0;
**IR** (film) $\tilde{\nu}$ 2955 (w), 2934 (w), 2860 (w), 1758 (m), 1684 (w), 1454 (w), 1318 (w), 1261 (m), 1209 (w), 1156 (s), 1010 (w), 968 (w), 916 (w), 843 (w), 817 (w);
**HRMS** (ESI) calcd. for $C_{32}H_{47}N_3NaO_7Si^+$ $[M+Na]^+$ 636.3075; found 636.3077.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-chloro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7b)**

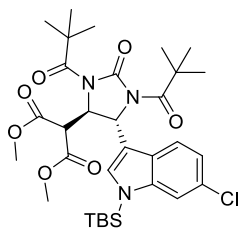



**7b**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-5-chloro-1H-indole (**6b**) (26.6 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-chloro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7b**) (52.5 mg, 81.0 µmol, 81% yield) as a white solid. Chiral HPLC conditions: er = 95:5; Chiralpak IA 98:2 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 5.9 min. and $t_r$ (major) = 7.2 min. λ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.51;
**Mp:** 131.2-132.0 °C;
**$[\alpha]_D^{20.0}$** = -29.9 (c = 0.30. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 2.0 Hz, 1H, Ar*H*), 7.35 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.10 (dd, *J* = 8.8, 2.1 Hz, 1H, Ar*H*), 7.04 (s, 1H, Ar*H*), 5.84 (s, 1H, indole-C*H*), 4.74 (d, *J* = 4.5 Hz, 1H, indole-CH-C*H*), 4.16 (d, *J* = 4.5 Hz, 1H, C*H*($CO_2Me)_2$), 3.78 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$),1.44 (s, 9H, $C(CH_3)_3$), 1.34 (s, 9H, $C(CH_3)_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.55 (s, 3H, $SiCH_3$), 0.54 (s, 3H, $SiCH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 149.4, 140.1, 129.8, 129.2, 126.0, 122.2, 118.8, 116.9, 115.0, 58.6, 52.9, 52.7, 51.6, 41.9, 41.8, 26.3, 26.3, 26.1, 19.4, -4.1 ppm (*one carbonyl and one $SiCH_3$ carbon signals are not resolved*);
**IR** (film) $\tilde{\nu}$ 2960 (w), 2933 (w), 2859 (w), 1763 (m), 1684 (m), 1440 (w), 1366 (w), 1319 (w), 1260 (m), 1202 (m), 1155 (s), 1006 (w), 969 (w), 842 (w);
**HRMS** (ESI) calcd. For $C_{32}H_{46}ClN_3NaO_7Si^+$ $[M+Na]^+$ 670.2686; found 670.2698.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-chloro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7c)**

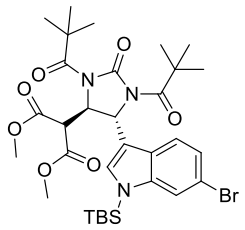



**7c**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-6-chloro-1H-indole (**6c**) (26.6 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 44 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-chloro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7c**) (49.6 mg, 77.0 µmol, 77% yield) as a white solid. Chiral HPLC conditions: er = 95.7:4.3; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 7.4 min. and $t_r$ (major) = 9.7 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.5;
**Mp:** 126.3-128.8 °C;
**$[\alpha]_D^{20.0}$** = -21.0 (c = 0.30. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.6 Hz, 1H, Ar*H*), 7.41 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.12 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 6.97 (s, 1H, Ar*H*), 5.87 (s, 1H, indole-C*H*), 4.74 (dd, *J* = 4.6, 1.1 Hz, 1H, indole-CH-C*H*), 4.13 (d, *J* = 4.6 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.75 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 1.42 (s, 9H, C(C$H_3$)$_3$), 1.35 (s, 9H, C(C$H_3$)$_3$), 0.87 (s, 9H, SiC(C$H_3$)$_3$), 0.55 (s, 3H, SiC$H_3$), 0.54 (s, 3H, SiC$H_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 167.2, 149.5, 142.1, 128.6, 128.0, 126.8, 120.8, 120.1, 117.4, 113.9, 58.6, 52.9, 52.8, 52.7, 51.5, 41.8, 41.8, 26.3, 26.1, 19.3, -4.1 (*one aliphatic and one $SiCH_3$ carbon signals are not resolved*);
**IR** (film) $\tilde{\nu}$ 2952 (w), 2866 (w), 1762 (m), 1688 (w), 1436 (w), 1331 (w), 1263 (m), 1207 (w), 1158 (s), 973 (w), 850 (w), 757 (w);
**HRMS** (ESI) calcd. For $C_{32}H_{46}ClN_3NaO_7Si^+$ $[M+Na]^+$ 670.2686; found 670.2684.

**Dimethyl 2-(5-(6-bromo-1-(*tert*-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7d)**



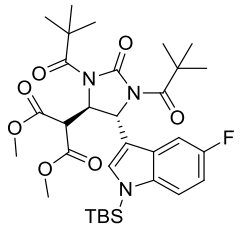
**7d**

Following general procedure **F**, 6-bromo-1-(tert-butyldimethylsilyl)-1H-indole (**6d**) (31.0 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(6-bromo-1-(tert-butyldimethylsilyl)-1H-indol-2-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7d)** (58.0 mg, 84.0 µmol, 84% yield) as a white solid. Chiral HPLC conditions: er = 95.2:4.8; Chiralpak IA 98:2 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 6.0 min. and $t_r$ (major) = 7.3 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.51;
**Mp:** 71.2-71.9 °C;
**$[\alpha]_D^{20.0}$** = -13.1 (c = 0.3. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.60 (s, 1H, Ar*H*), 7.29 (s, 1H, Ar*H*), 6.99 (s, 1H, Ar*H*), 5.89 (s, 1H, indole-C*H*), 4.76 (d, *J* = 4.4 Hz, 1H, indole-CH-C*H*), 4.16 (d, *J* = 4.3 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.77 (s, 6H, 2 x $CO_2CH_3$), 1.44 (s, 9H, C(C$H_3$)$_3$), 1.37 (s, 9H, C(C$H_3$)$_3$), 0.90 (s, 9H, SiC(C$H_3$)$_3$), 0.58 (s, 3H, SiC$H_3$), 0.57 (s, 3H, SiC$H_3$);

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 167.2, 149.5, 142.6, 128.6, 127.1, 123.4, 120.5, 117.5, 116.9, 115.7, 58.6, 52.9, 52.8, 52.7, 51.5, 41.9, 41.8, 26.3, 26.1, 19.3, -4.0 (*one aliphatic and one $SiCH_3$ carbon signals are not resolved*);
**IR** (film) $\tilde{\nu}$ 2958 (w), 2866 (w), 1760 (m), 1686 (w), 1459 (w), 1435 (w), 1367 (w), 1330 (w), 1263 (m), 1213 (w), 1152 (s), 1005 (w), 974 (w), 845 (w), 759 (w);
**HRMS** (ESI) calcd. For $C_{32}H_{46}{}^{79}BrN_3NaO_7Si^+$ $[M+Na]^+$ 714.2181; found 714.2179.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-fluoro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7e)**

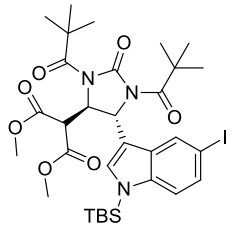



**7e**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-5-methyl-1H-indole (**6e**) (24.9 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-fluoro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7e**) (45.8 mg, 72.0 µmol, 72% yield) as a colorless oil. Chiral HPLC conditions: er = 96:4; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 8.1 min. and $t_r$ (major) = 9.2 min. λ = 280 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.58;
**$[\alpha]_D^{20.0}$** = -20.3 (c = 0.30. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 9.8, 2.6 Hz, 1H, Ar*H*), 7.35 (dd, *J* = 9.0, 4.3 Hz, 1H, Ar*H*), 7.02 (s, 1H, Ar*H*), 6.90 (td, *J* = 9.0, 2.6 Hz, 1H, Ar*H*), 5.84 (s, 1H, indole-C*H*), 4.74 (dd, *J* = 4.7, 1.1 Hz, 1H, indole-CH-C*H*), 4.13 (d, *J* = 4.6 Hz, 1H, C*H*($CO_2Me)_2$), 3.77 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 1.42 (s, 9H, C($CH_3)_3$), 1.35 (s, 9H, C($CH_3)_3$), 0.85 (s, 9H, SiC($CH_3)_3$), 0.54 (s, 3H, Si$CH_3$), 0.53 (s, 3H, Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.4, 167.2, 167.2, 157.9 (d, *J* = 235.9 Hz), 149.4, 138.2, 129.7, 128.6 (d, *J* = 9.9 Hz), 117.3 (d, *J* = 4.8 Hz), 114.5 (d, *J* = 9.7 Hz), 110.2 (d, *J* = 26.0 Hz), 104.4 (d, *J* = 24.2 Hz), 58.6, 52.8, 52.7, 51.5, 41.8, 41.7, 26.3, 26.1, 19.4, -4.1 (*one aliphatic and one $SiCH_3$ carbon signals are not resolved*);
**$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -123.7;
**IR** (film) $\tilde{\nu}$ 2953 (w), 2867 (w), 1763 (m), 1689 (w), 1479 (w), 1442 (w), 1368 (w), 1318 (w), 1263 (m), 1214 (m), 1158 (s), 1010 (w), 911 (w), 844 (w), 757 (w);
**HRMS** (ESI) calcd. For $C_{32}H_{46}FN_3NaO_7Si^+$ $[M+Na]^+$ 654.2981; found 654.2986.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-iodo-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7f)**

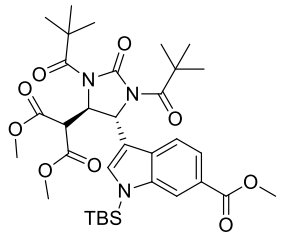



**7f**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-5-iodo-1H-indole (**6f**) (35.7 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-iodo-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7f**) (57.4 mg, 78.0 µmol, 78% yield) as a white solid. Chiral HPLC conditions: er = 96.7:3.3; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 7.1 min. and $t_r$ (major) = 10.1 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.58;
**Mp:** 71.0-71.5 °C;
**$[\alpha]_D^{20.0}$** = -31.2 (c = 0.30. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.39 (dd, *J* = 8.7, 1.7 Hz, 1H, Ar*H*), 7.22 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.00 (s, 1H, Ar*H*), 5.83 (d, *J* = 1.1 Hz, 1H, indole-C*H*), 4.73 (dd, *J* = 4.5, 1.2 Hz, 1H, indole-CH-C*H*), 4.17 (d, *J* = 4.4 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.78 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 1.45 (s, 9H, C($CH_3$)$_3$), 1.34 (s, 9H, C($CH_3$)$_3$), 0.85 (s, 9H, SiC($CH_3$)$_3$), 0.55 (s, 3H, Si$CH_3$), 0.54 (s, 3H, Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.1, 149.4, 140.8, 130.5, 130.2, 129.4, 128.0, 116.5, 116.0, 83.9, 58.6, 52.9, 52.8, 52.6, 51.6, 41.9, 41.8, 26.4, 26.3, 26.1, 19.4, -4.1 (*one $SiCH_3$ signal is not resolved*);
**IR** (film) $\tilde{\nu}$ 2955 (w), 2936 (w), 2862 (w), 1765 (m), 1684 (w), 1444 (w), 1364 (w), 1327 (w), 1259 (m), 1210 (m), 1154 (s), 846 (w), 809 (w), 759 (m);
**HRMS** (ESI) calcd. For $C_{32}H_{46}IN_3NaO_7Si^+$ $[M+Na]^+$ 762.2042; found 762.2048.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-(methoxycarbonyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate** (**7g**)



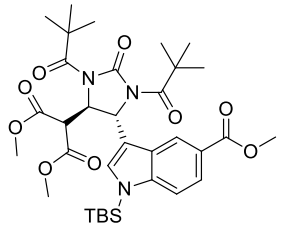

**7g**

Following general procedure **F**, methyl 1-(tert-butyldimethylsilyl)-1H-indole-6-carboxylate (**6g**) (28.9 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -30 °C for 42 hours. Preparative TLC using eluent 65:35 heptane:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-(methoxycarbonyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7g**) (49.2 mg, 73.0 µmol, 73% yield) as a white solid. Chiral HPLC conditions: er = 95.1:4.9; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 12.3 min. and $t_r$ (major) = 14.8 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 8:2) 0.5;

**Mp:** 61.7-63.9 °C;
**$[\alpha]_D^{20.0}$** = -9.1 (c = 0.35. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.21 (s, 1H, Ar*H*), 7.82 (dd, *J* = 8.4, 1.3 Hz, 1H, Ar*H*), 7.76 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.18 (s, 1H, Ar*H*), 5.90 (s, 1H, indole-C*H*), 4.76 (dd, *J* = 4.5, 1.2 Hz, 1H, indole-CH-C*H*), 4.15 (d, *J* = 4.5 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.92 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 1.43 (s, 9H, C($CH_3$)$_3$), 1.34 (s, 9H, C($CH_3$)$_3$), 0.88 (s, 9H, SiC($CH_3$)$_3$), 0.60 (s, 3H, Si$CH_3$), 0.59 (s, 3H, Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.6, 168.0, 167.2, 167.2, 149.5, 141.1, 131.7, 131.7, 123.6, 121.2, 118.8, 117.6, 116.3, 58.6, 52.9, 52.8, 52.7, 52.0, 51.5, 41.9, 41.8, 26.3, 26.3, 26.1, 19.3, -4.0 (*one $SiCH_3$ carbon signal not resolved*);
**IR** (film) $\tilde{\nu}$ 2955 (w), 2930 (w), 2861 (w), 1760 (m), 1685 (w), 1442 (w), 1355 (w), 1293 (w), 1262 (m), 1162 (s), 1001 (w), 839 (w), 758 (w);
**HRMS** (ESI) calcd. For $C_{34}H_{49}N_3NaO_9Si^+$ $[M+Na]^+$ 694.3130; found 694.3141.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-(methoxycarbonyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7h)**

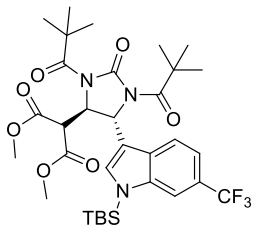



**7h**

Following general procedure **F**, methyl 1-(tert-butyldimethylsilyl)-1H-indole-5-carboxylate (**6g**) (35.7 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -40 °C for 47 hours. Preparative TLC using eluent 65:35 heptane:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-(methoxycarbonyl)-1H-indol-2-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7g**) (43.0 mg, 64.0 µmol, 64% yield) as a colorless oil. Chiral HPLC conditions: er = 92.8:7.2; Chiralpak IA 98:2 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 10.4 min. and $t_r$ (major) = 14.9 min. λ = 280 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 8:2) 0.5;
**$[\alpha]_D^{20.0}$** = -25.9 (c = 0.25. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.86 (dd, *J* = 8.8, 1.7 Hz, 1H, Ar*H*), 7.46 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.11 (s, 1H, Ar*H*), 5.92 (s, 1H, indole-C*H*), 4.78 (dd, *J* = 4.4, 1.3 Hz, 1H, indole-CH-C*H*), 4.18 (d, *J* = 4.5 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.90 (s, 3H, $CO_2CH_3$), 3.79 (s, 3H, $CO_2CH_3$), 3.76 (s, 3H, $CO_2CH_3$), 1.44 (s, 9H, C($CH_3$)$_3$), 1.34 (s, 9H, C($CH_3$)$_3$), 0.87 (s, 9H, SiC($CH_3$)$_3$), 0.58 (s, 3H, Si$CH_3$), 0.57 (s, 3H, Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.8, 167.2, 167.1, 149.4, 144.4, 129.9, 127.7, 123.3, 122.1, 121.8, 118.3, 113.7, 58.6, 52.8, 52.7, 51.7, 51.7, 41.8, 41.8, 26.3, 26.1, 19.4, -4.1 (*one aliphatic and one $SiCH_3$ carbon signals are not resolved*);
**IR** (film) $\tilde{\nu}$ 2959 (w), 2861 (w), 1757 (m), 1689 (m), 1436 (w), 1332 (m), 1264 (s), 1208 (m), 1159 (s), 968 (w), 844 (w), 814 (w), 758 (m);
**HRMS** (ESI) calcd. For $C_{34}H_{49}N_3NaO_9Si^+$ $[M+Na]^+$ 694.3130; found 694.3140.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-(trifluoromethyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7i)**

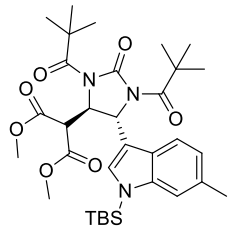


**7i**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-6-(trifluoromethyl)-1H-indole (**6i**) (29.9 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -30 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-(trifluoromethyl)-1H-indol-2-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7i**) (56.0 mg, 82.0 µmol, 82% yield) as a white solid. Chiral HPLC conditions: er = 95:5; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 7.2 min. and $t_r$ (major) = 8.8 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 8:2) 0.6;
**Mp:** 151.5-152.4 °C;
**$[\alpha]_D^{20.0}$** = -36.7 (c = 0.10. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.71 (s, 1H, Ar*H*), 7.39 (dd, *J* = 8.5, 1.4 Hz, 1H, Ar*H*), 7.15 (s, 1H, Ar*H*), 5.92 (s, 1H, indole-C*H*), 4.75 (dd, *J* = 4.5, 1.1 Hz, 1H, indole-CH-C*H*), 4.15 (d, *J* = 4.5 Hz, 1H, C*H*($CO_2Me)_2$), 3.76 (s, 3H, $CO_2CH_3$), 3.76 (s, 3H, $CO_2CH_3$), 1.43 (s, 9H, $C(CH_3)_3$), 1.35 (s, 9H, $C(CH_3)_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.59 (s, 3H, $SiCH_3$), 0.58 (s, 3H, $SiCH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 167.2, 149.4, 140.6, 130.7, 130.5, 125.1 (q, *J* = 271.6 Hz), 124.0 (q, *J* = 31.7 Hz), 119.7, 117.7, 116.9 (q, *J* = 3.6 Hz), 111.3 (q, *J* = 4.2 Hz), 58.6, 52.9, 52.8, 52.6, 51.4, 41.8, 41.7, 26.3, 26.2, 26.0, 19.3, -4.1 (*one $SiCH_3$ carbon is not resolved*);
**$^{19}$F NMR** (376 MHz, $CDCl_3$) δ -60.8;
**IR** (film) $\tilde{\nu}$ 2953 (w), 2935 (w), 2867 (w), 1763 (m), 1689 (w), 1442 (w), 1337 (m), 1263 (m), 1208 (w), 1158 (s), 1121 (w), 980 (w), 838 (w), 758 (w);
**HRMS** (ESI) calcd. For $C_{33}H_{46}F_3N_3NaO_7Si^+$ $[M+Na]^+$ 704.2949; found 704.2966.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-methyl-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate** (**7j**)



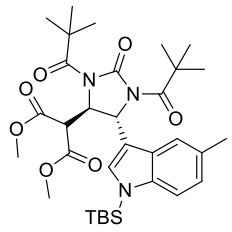
**7j**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-6-methyl-1H-indole (**6j**) (24.5 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 44 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-methyl-1H-indol-2-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7j**) (51.2 mg, 82.0 µmol, 82% yield) as a white solid. Chiral HPLC conditions: er = 90.7:9.3; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 6.7 min. and $t_r$ (major) = 9.1 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.5;

**Mp:** 65.2-67.0 °C;
**$[\alpha]_D^{20.0}$** = -12.4 (c = 0.29. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.23 (s, 1H, Ar*H*), 6.97 (d, *J* = 8.2 Hz, 1H, Ar*H*), 6.94 (s, 1H, Ar*H*), 5.86 (s, 1H, indole-C*H*), 4.78 (dd, *J* = 4.6, 1.2 Hz, 1H, indole-CH-C*H*), 4.14 (d, *J* = 4.6 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.74 (s, 6H, 2 x $CO_2CH_3$), 2.43 (s, 3H, C*H*$_3$), 1.42 (s, 9H, C(C*H*$_3$)$_3$), 1.34 (s, 9H, C(C*H*$_3$)$_3$), 0.87 (s, 9H, SiC(C*H*$_3$)$_3$), 0.55 (s, 3H, SiC*H*$_3$), 0.53 (s, 3H, SiC*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 167.2, 149.6, 142.2, 131.5, 127.7, 126.0, 121.8, 118.8, 116.9, 114.1, 58.7, 53.0, 52.8, 52.8, 51.7, 41.8, 41.8, 26.3, 26.2, 22.0, 19.4, -3.9, -4.0;
**IR** (film) $\tilde{\nu}$ 2959 (w), 2928 (w), 2860 (w), 1762 (m), 1738 (m), 1682 (m), 1442 (w), 1362 (w), 1331 (m), 1257(m), 1207 (m), 1152 (s), 1010 (w), 844 (w), 807 (m), 757 (m);
**HRMS** (ESI) calcd. For $C_{33}H_{49}N_3NaO_7Si^+$ $[M+Na]^+$ 650.3232; found 650.3234.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-methyl-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7k)**

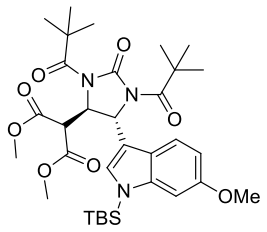



**7k**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-5-methyl-1H-indole (**6k**) (24.5 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-methyl-1H-indol-2-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7k**) (48.2 mg, 77.0 μmol, 77% yield) as a white solid. Chiral HPLC conditions: er = 95:5; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 7.2 min. and $t_r$ (major) = 8.8 min. λ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.58;
**Mp:** 68.5-69.7 °C;
**$[\alpha]_D^{20.0}$** = -18.1 (c = 0.21. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.46 (s, 1H, Ar*H*), 7.34 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.01 (s, 1H, Ar*H*), 6.97 (d, *J* = 8.5 Hz, 1H, Ar*H*), 5.86 (s, 1H, indole-C*H*), 4.79 (d, *J* = 4.5 Hz, 1H, indole-CH-C*H*), 4.16 (d, *J* = 3.9 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.75 (s, 6H, 2 x $CO_2CH_3$), 2.42 (s, 3H, C*H*$_3$), 1.44 (s, 9H, C(C*H*$_3$)$_3$), 1.34 (s, 9H, C(C*H*$_3$)$_3$), 0.87 (s, 9H, C(C*H*$_3$)$_3$), 0.55 (s, 3H, SiC*H*$_3$), 0.54 (s, 3H, SiC*H*$_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 178.9, 177.5, 167.2, 167.1, 149.6, 140.0, 129.2, 128.8, 128.3, 123.3, 118.8, 116.5, 113.7, 58.7, 53.0, 52.8, 52.7, 51.7, 41.8, 41.8, 26.3, 26.3, 26.2, 21.4, 19.4, -4.1 (*one SiCH$_3$ carbon signal is not resolved*);
**IR** (film) $\tilde{\nu}$ 2954 (w), 2861 (w), 1764 (m), 1689 (w), 1466 (w), 1367 (w), 1262 (w), 1156 (s), 1001 (w), 840 (w), 791 (w), 760 (w);
**HRMS** (ESI) calcd. For $C_{33}H_{49}N_3NaO_7Si^+$ $[M+Na]^+$ 650.3232; found 650.3232.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-methoxy-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7l)**

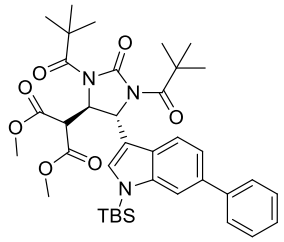



**7l**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-6-methoxy-1H-indole **6l** (26.1 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 48 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate, followed by a second preparative TLC using eluent 92:8 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-methoxy-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate **7l** (41.2 mg, 64.0 µmol, 64% yield) as a white solid. Chiral HPLC conditions: er = 93.4:6.6; Chiralpak IA 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 9.1 min. and $t_r$ (major) = 13.0 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.54;
**Mp:** 71.4-71.7 °C;
**$[\alpha]_D^{20.0}$** = -22.3 (c = 0.24. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.8 Hz, 1H, Ar*H*), 6.95 (d, *J* = 2.2 Hz, 1H, Ar*H*), 6.87 (s, 1H, Ar*H*), 6.82 (dd, *J* = 8.7, 2.2 Hz, 1H, Ar*H*), 5.85 (t, *J* = 0.8 Hz, 1H, indole-C*H*), 4.77 (dd, *J* = 4.7, 1.1 Hz, 1H, indole-CH-C*H*), 4.12 (d, *J* = 4.7 Hz, 1H, C*H*($CO_2Me)_2$), 3.82 (s, 3H, OC$H_3$), 3.75 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 1.41 (s, 9H, C(C$H_3)_3$), 1.35 (s, 9H, C(C$H_3)_3$), 0.88 (s, 9H, SiC(C$H_3)_3$), 0.54 (s, 3H, SiC$H_3$), 0.53 (s, 3H, SiC$H_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 167.2, 156.1, 149.6, 142.6, 126.8, 122.7, 119.7, 117.1, 109.1, 98.6, 58.7, 55.7, 53.0, 52.8, 52.8, 51.6, 41.8, 41.8, 26.3, 26.2, 19.5, -4.1, -4.1 (*one aliphatic carbon signal is not resolved*);
**IR** (film) $\tilde{\nu}$ 2959 (w), 2860 (w), 1756 (m), 1737 (w), 1682 (w), 1621 (w), 1559 (w), 1442 (w), 1325 (w), 1257 (m), 1207(m), 1152 (m), 1035 (w), 985 (w), 844 (w), 801 (w), 757 (m);
**HRMS** (ESI) calcd. For $C_{33}H_{49}N_3NaO_8Si^+$ $[M+Na]^+$ 666.3181; found 666.3182.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-phenyl-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7m)**

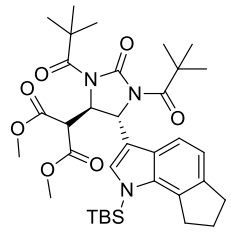



**7m**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-6-phenyl-1H-indole (**6m**) (30.8 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 48 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-phenyl-1H-indol-2-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7m**) (51.7 mg, 75.0 µmol, 75% yield) as a white solid. Chiral HPLC conditions: er = 92.3:7.7; Chiralpak IB 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 8.1 min. and $t_r$ (major) = 9.3 min. $\lambda$ = 280 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.57;
**Mp:** 155.0-156.2 °C;
**$[\alpha]_D^{20.0}$** = -9.3 (c = 0.30. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.3 Hz, 1H, Ar*H*), 7.65 (s, 1H, Ar*H*), 7.59 (d, *J* = 7.2 Hz, 2H, Ar*H*), 7.44 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.40 (dd, *J* = 8.3, 1.5 Hz, 1H, Ar*H*), 7.32 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.04 (s, 1H, Ar*H*), 5.92 (s, 1H, indole-C*H*), 4.81 (dd, *J* = 4.6, 1.2 Hz, 1H, indole-CH-C*H*), 4.16 (d, *J* = 4.6 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.77 (s, 3H, $CO_2CH_3$), 3.76 (s, 3H, $CO_2CH_3$), 1.44 (s, 9H, C($CH_3$)$_3$), 1.36 (s, 9H, C($CH_3$)$_3$), 0.91 (s, 9H, SiC($CH_3$)$_3$), 0.59 (s, 3H, $CH_3$), 0.58 (s, 3H, $CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.0, 177.5, 167.2, 149.6, 142.5, 142.3, 135.4, 128.8, 128.7, 127.5, 127.3, 126.6, 120.0, 119.4, 117.2, 112.7, 58.7, 52.9, 52.8, 52.8, 51.6, 41.8, 41.8, 26.3, 26.2, 19.4, -4.0 (*one carbonyl, one aliphatic and one $SiCH_3$ carbon signals are not resolved*);
**IR** (film) $\tilde{\nu}$ 2954 (w), 2861 (w), 1758 (m), 1690 (m), 1468 (w), 1431 (w), 1333 (w), 1258 (m), 1203 (m), 1154 (s), 975 (w), 839 (w), 759 (w);
**HRMS** (ESI) calcd. For $C_{38}H_{51}N_3NaO_7Si^+$ $[M+Na]^+$ 712.3388; found 712.3390.

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate** (**7n**)

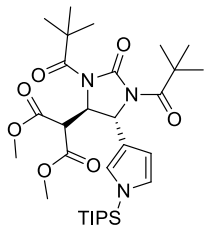


**7n**

Following general procedure **F**, 1-(tert-butyldimethylsilyl)-1,6,7,8-tetrahydrocyclopenta[g]indole (**6n**) (28.9 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -50 °C for 42 hours. Preparative TLC using eluent 9:1 toluene:ethyl acetate afforded dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7n**) (39.4 mg, 60.0 µmol, 60% yield) as a white solid. Chiral HPLC conditions: er = 90.5:9.5; Chiralpak IA 98:2 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 5.7 min. and $t_r$ (major) = 7.3 min. λ = 280 $cm^{-1}$.

**$R_f$:** ($SiO_2$, toluene:ethyl acetate 9:1) 0.51;
**Mp:** 70.7-71.1 °C;
**$[\alpha]_D^{20.0}$** = -11.7 (c = 0.20. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.12 (d, *J* = 8.0 Hz, 1H, Ar*H*), 7.05 (s, 1H, Ar*H*), 5.87 (s, 1H, indole-C*H*), 4.78 (dd, *J* = 4.5, 1.2 Hz, 1H, indole-CH-C*H*), 4.13 (d, *J* = 4.5 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.75 (s, 3H, $CO_2CH_3$), 3.75 (s, 3H, $CO_2CH_3$), 3.13 (t, *J* = 7.2 Hz, 2H, $CH_2CH_2CH_2$), 2.99 (t, *J* = 7.3 Hz, 2H, $CH_2CH_2CH_2$), 2.10 (p, *J* = 7.3 Hz, 2H, $CH_2CH_2CH_2$), 1.43 (s, 9H, C($CH_3$)$_3$), 1.35 (s, 9H, C($CH_3$)$_3$), 0.84 (s, 9H, SiC($CH_3$)$_3$), 0.58 (s, 3H, Si$CH_3$), 0.56 (s, 3H, Si$CH_3$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 178.9, 177.3, 167.2, 167.1, 149.6, 139.7, 139.4, 129.1, 128.0, 127.1, 117.6, 117.3, 117.2, 58.6, 52.9, 52.8, 52.7, 51.8, 41.8, 41.7, 34.5, 33.2, 26.5, 26.3, 25.9, 19.6, -1.1, -1.1;
**IR** (film) $\tilde{\nu}$ 2958 (w), 2860 (w), 1761 (w), 1687 (w), 1472 (w), 1435 (w), 1319 (w), 1257 (m), 1208 (m), 1153 (s), 1036 (w), 846 (w), 809 (w), 754 (w);
**HRMS** (ESI) calcd. For $C_{35}H_{51}N_3NaO_7Si^+$ $[M+Na]^+$ 676.3388; found 676.3400.

**Dimethyl 2-(2-oxo-1,3-dipivaloyl-5-(1-(triisopropylsilyl)-1H-pyrrol-3-yl)imidazolidin-4-yl)malonate** (**7o**)



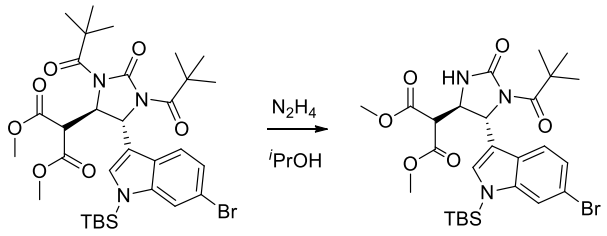

**7o**

Following general procedure **F**, 1-(triisopropylsilyl)-1H-pyrrole (**6o**) (22.3 mg, 0.100 mmol, 1 equiv) and cyclopropane **2** were stirred at -30 °C for 42 hours. Preparative TLC using eluent 65:35 heptane:ethyl acetate afforded dimethyl 2-(2-oxo-1,3-dipivaloyl-5-(1-(triisopropylsilyl)-1H-pyrrol-3-yl)imidazolidin-4-yl)malonate (**7o**) (42.1 mg, 69.0 μmol, 69% yield) as a colorless oil. Chiral HPLC conditions: er = 88.8:11.2; Chiralpak IF 99:1 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (minor) = 14.2 min. and $t_r$ (major) = 15.3 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 8:2) 0.44;
**$[\alpha]_D^{20.0}$** = -5.3 (c = 0.21. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.66 (t, *J* = 2.5 Hz, 1H, Ar*H*), 6.61 (s, 1H, Ar*H*), 6.21 (dd, *J* = 2.8, 1.5 Hz, 1H, Ar*H*), 5.55 (s, 1H, pyrrol-C*H*), 4.76 (dd, *J* = 4.8, 1.1 Hz, 1H, pyrrol-CH-C*H*), 4.08 (d, *J* = 4.8 Hz, 1H, C*H*($CO_2Me$)$_2$), 3.74 (s, 3H, $CO_2CH_3$), 3.70 (s, 3H, $CO_2CH_3$), 1.40-1.32 (m, 21H, 2 x C(C$H_3$)$_3$ + 3 x SiC*H*), 1.07-1.01 (m, 18H, CH(C$H_3$)$_2$);
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 179.4, 177.5, 167.3, 167.2, 149.4, 125.0, 124.9, 121.0, 108.1, 59.6, 53.5, 52.7, 52.7, 51.7, 41.8, 41.7, 26.4, 26.3, 17.8, 11.6;
**IR** (film) $\tilde{\nu}$ 2952 (w), 2869 (w), 1755 (m), 1736 (m), 1682 (m), 1464 (w), 1436 (w), 1354 (w), 1315 (w), 1260 (m), 1206 (m), 1152 (s), 1099 (m), 1011 (w), 856 (w), 749 (w), 691 (w);
**HRMS** (ESI) calcd. For $C_{31}H_{51}N_3NaO_7Si^+$ $[M+Na]^+$ 628.3388; found 628.3396.

## 6. Derivatizations of the products

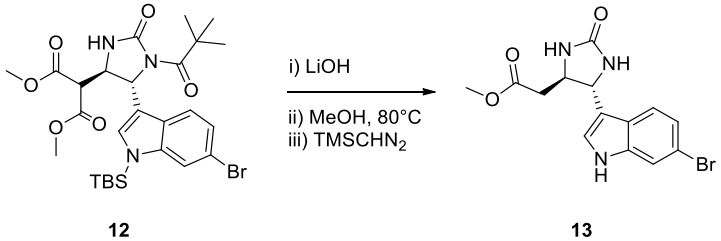
**Dimethyl 2-(5-(6-bromo-1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1-pivaloylimidazolidin-4-yl)malonate (12)**




In a microwave vial, a solution of dimethyl 2-(5-(6-bromo-1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (**7d**) (111 mg, 0.160 mmol, 1 equiv) in 2.8 mL of isopropanol was added, followed by hydrazine (80% wt in water, 14.6 µL, 0.240 mmol, 1.5 equiv) and stirred for 20 minutes. Then, 1 mL of a 1 M HCl aqueous solution was added, followed by 2 mL of water. The aqueous phase was extracted with 3x5 mL of dichloromethane, dried over $Na_2SO_4$, filtered and evaporated, to afford dimethyl 2-(5-(6-bromo-1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1-pivaloylimidazolidin-4-yl)malonate (**12**) (92.0 mg, 0.151 mmol, 94% yield) as a white solid. Chiral HPLC conditions: er = 95.8:4.2; Chiralpak IA 90:10 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (major) = 12.3 min. and $t_r$ (minor) = 15.3 min. $\lambda$ = 260 $cm^{-1}$.

**$R_f$:** ($SiO_2$, pentane:ethyl acetate 2:1) 0.52;
**Mp:** 68.8 °C (degradation);
**$[\alpha]_D^{20.0}$** = 25.7 (c =0.15. $CHCl_3$);
**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 1.8 Hz, 1H, Ar*H*), 7.51 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.23 (dd, *J* = 8.5, 1.7 Hz, 1H, Ar*H*), 7.06 (s, 1H, Ar*H*), 5.69 (s, 1H, N*H*), 5.63 (d, *J* = 3.0 Hz, 1H, indole-C*H*), 4.16 (ddd, *J* = 7.5, 3.1, 1.4 Hz, 1H, indole-CH-C*H*), 3.78 (s, 3H, $CO_2CH_3$), 3.71 (s, 3H, $CO_2CH_3$), 3.67 (d, *J* = 7.4 Hz, 1H, $CH(CO_2CH_3)_2$), 1.28 (s, 9H, $C(CH_3)_3$), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.58 (s, 3H, $SiCH_3$), 0.57 (s, 3H, $SiCH_3$).
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 178.3, 167.2, 167.0, 154.1, 142.5, 129.7, 126.9, 123.4, 119.9, 117.1, 116.9, 115.5, 56.1, 55.7, 55.0, 53.2, 53.0, 41.5, 26.4, 26.1, 19.3, -4.0, -4.0.
**IR** (film) $\tilde{\nu}$ 3291 (w), 2955 (w), 2931 (w), 2860 (w), 1734 (s), 1675 (w), 1460 (w), 1434 (w), 1286 (w), 1194 (m), 1152 (m), 973 (w), 838 (w), 805 (w), 756 (w);
**HRMS** (ESI) calcd. For $C_{27}H_{39}{}^{79}BrN_3O_6Si^+$ $[M+H]^+$ 608.1786; found 608.1789.

**Methyl 2-(5-(6-bromo-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)acetate (13)**




i) dimethyl 2-(5-(6-bromo-1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1-pivaloylimidazolidin-4-yl)malonate (**12**) (64.0 mg, 0.105 mmol, 1 equiv) was dissolved in 0.7 mL of tetrahydrofuran in a microwave vial, and a 0.5 M aqueous solution of LiOH (1.7 mL, 0.84 mmol, 8 equiv) was added, and the mixture stirred for 13 hours at room temperature. The reaction was acidified to pH 1 using a 1 M

aqueous HCl solution. The aqueous layer was extracted with 3x3 mL of ethyl acetate. The combined organic layers were washed with 7 mL of 1 M aqueous NaOH solution. The aqueous layer was extracted with 5 mL of ethyl acetate, and then acidified to pH 1 using 1 M aqueous HCl solution, and finally extracted with 3x10 mL of ethyl acetate. The combined organic layers were dried over $Na_2SO_4$, filtered and concentrated to afford crude product.

ii) The crude product was dissolved in 2.1 mL of methanol, and heated to 80 °C for 16 hours, then cooled to rt.

iii) The solution was cooled to 0 °C, and a 2 M solution of TMSdiazomethane in diethyl ether (0.53 mL, 1.1 mmol, 10 equiv) was added until gas evolution ceased. The solution was then evaporated and subjected to column chromatography ($SiO_2$, eluent dichloromethane:methanol 100:0 to 98:2 to 95:5) to afford methyl 2-(5-(6-bromo-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)acetate (**13**) (20.9 mg, 59.0 µmol, 56% yield over three steps) as a pale brown solid. Chiral HPLC conditions: er = 96.3:3.7; Chiralpak IC 50:50 Hexane/iPrOH, 1.0 mL/min, 31 min. $t_r$ (major) = 9.7 min. and $t_r$ (minor) = 13.4 min. $\lambda$ = 210 $cm^{-1}$.

**$R_f$:** ($SiO_2$, dichloromethane:methanol 9:1) 0.28;
**Mp:** 87.0 - 88.9 °C;
**$[\alpha]_D^{20.0}$** = 97.4 (c = 0.24. MeOH);
**$^1$H NMR** (400 MHz, $CD_3OD$) δ 7.60 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.54 (d, *J* = 1.7 Hz, 1H, Ar*H*), 7.27 (s, 1H, Ar*H*), 7.15 (dd, *J* = 8.5, 1.8 Hz, 1H, Ar*H*), 4.76 (d, *J* = 6.5 Hz, 1H, Indole-C*H*), 4.15 – 4.06 (m, 1H, indole-CH-C*H*), 3.63 (s, 3H, C$H_3$) 2.73 – 2.63 (m, 2H).
**$^{13}$C NMR** (101 MHz, $CD_3OD$) δ 172.9, 165.2, 139.6, 125.6, 125.1, 123.3, 121.5, 116.3, 116.1, 115.5, 58.3, 56.9, 52.2, 40.4.
**IR** (film) $\tilde{\nu}$ 3249 (w), 2952 (w), 2924 (w), 2854 (w), 1691 (s), 1614 (w), 1546 (w), 1440 (w), 1360 (w), 1332 (w), 1213 (w), 1176 (w), 1106 (w), 1050 (w), 896 (w), 804 (w), 759 (w);
**HRMS** (ESI) calcd. For $C_{14}H_{15}{}^{79}BrN_3O_3^+$ $[M+H]^+$ 352.0291; found 352.0292.

## 7.Crystal structure of 7d

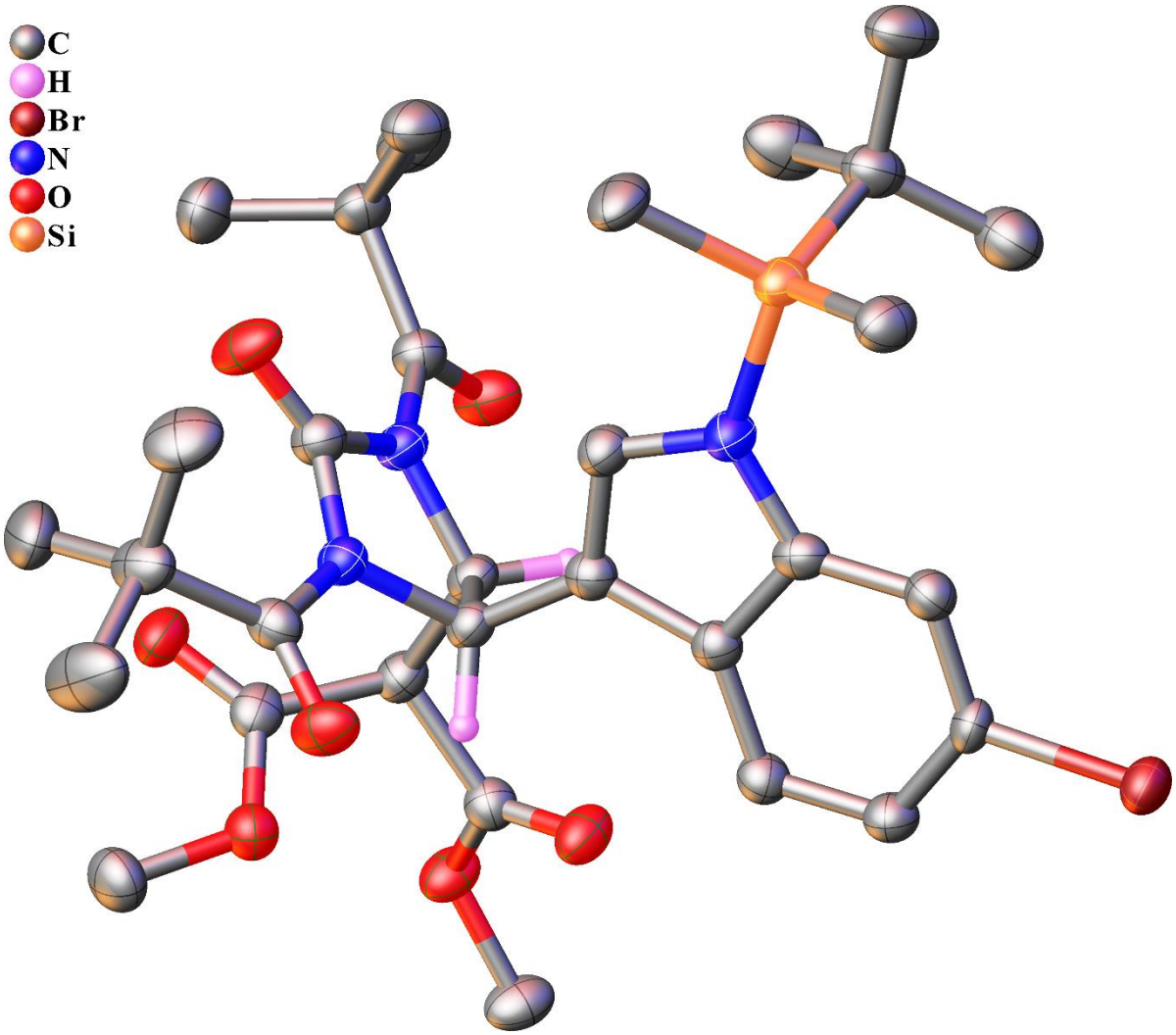


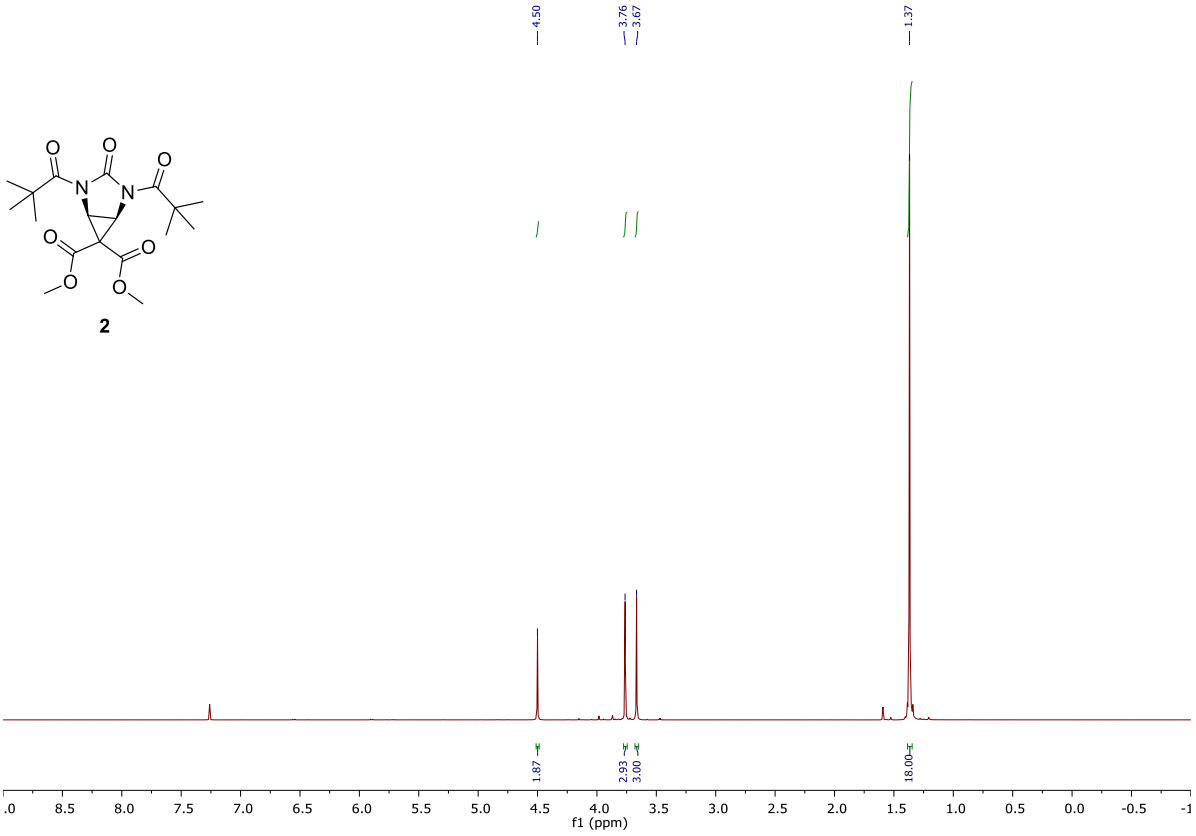

**Figure S1.** Crystal structure of **7d**.

A single crystal was grown by slow evaporation of the solution of **7d** in Methanol. Supplementary crystallographic data for this compound have been deposited at Cambridge Crystallographic Data Centre (1815214) and can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

# 8. Spectra of new compounds

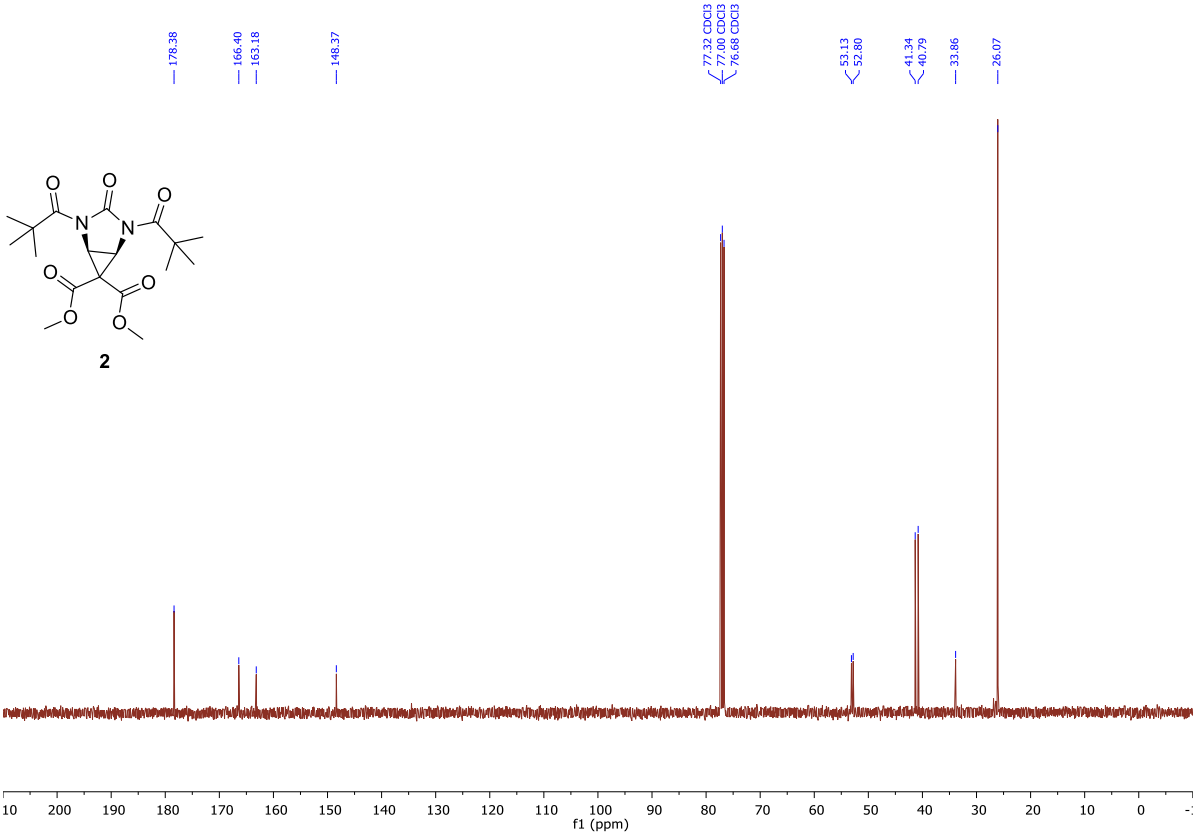
**Dimethyl 3-oxo-2,4-dipivaloyl-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (2)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



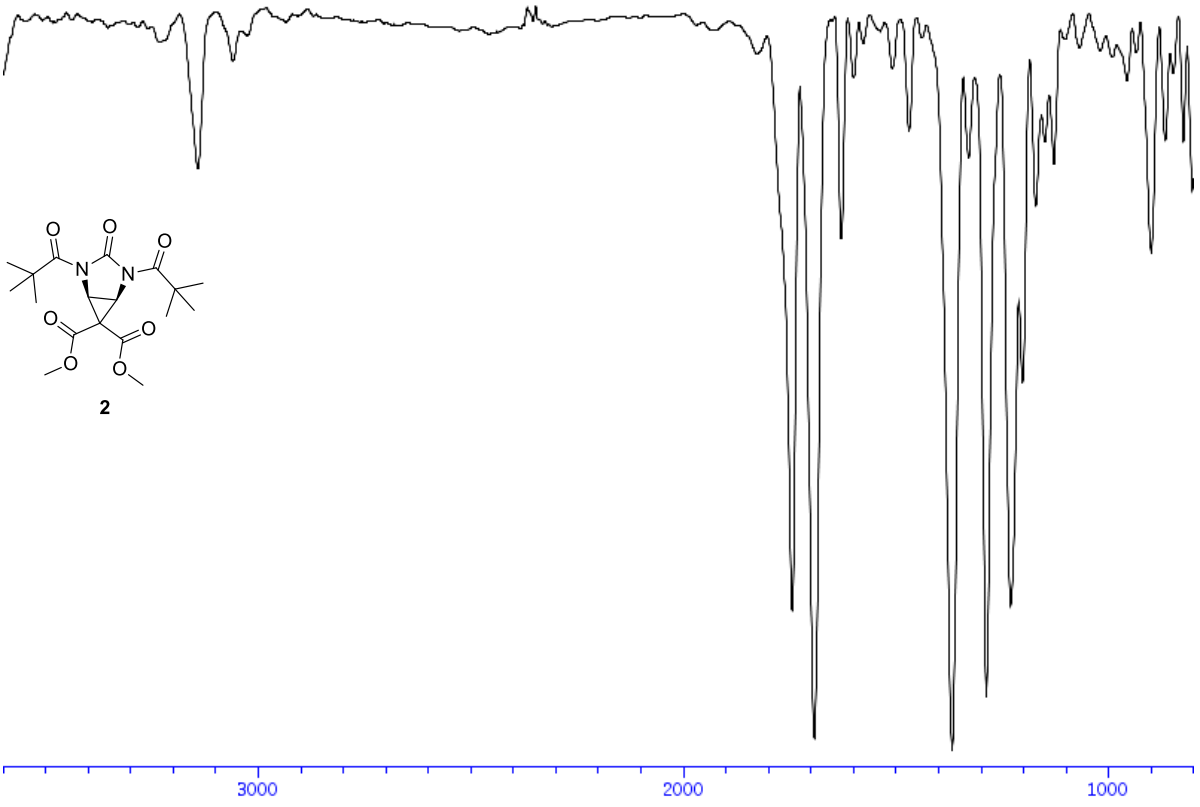

**2**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**




**2**

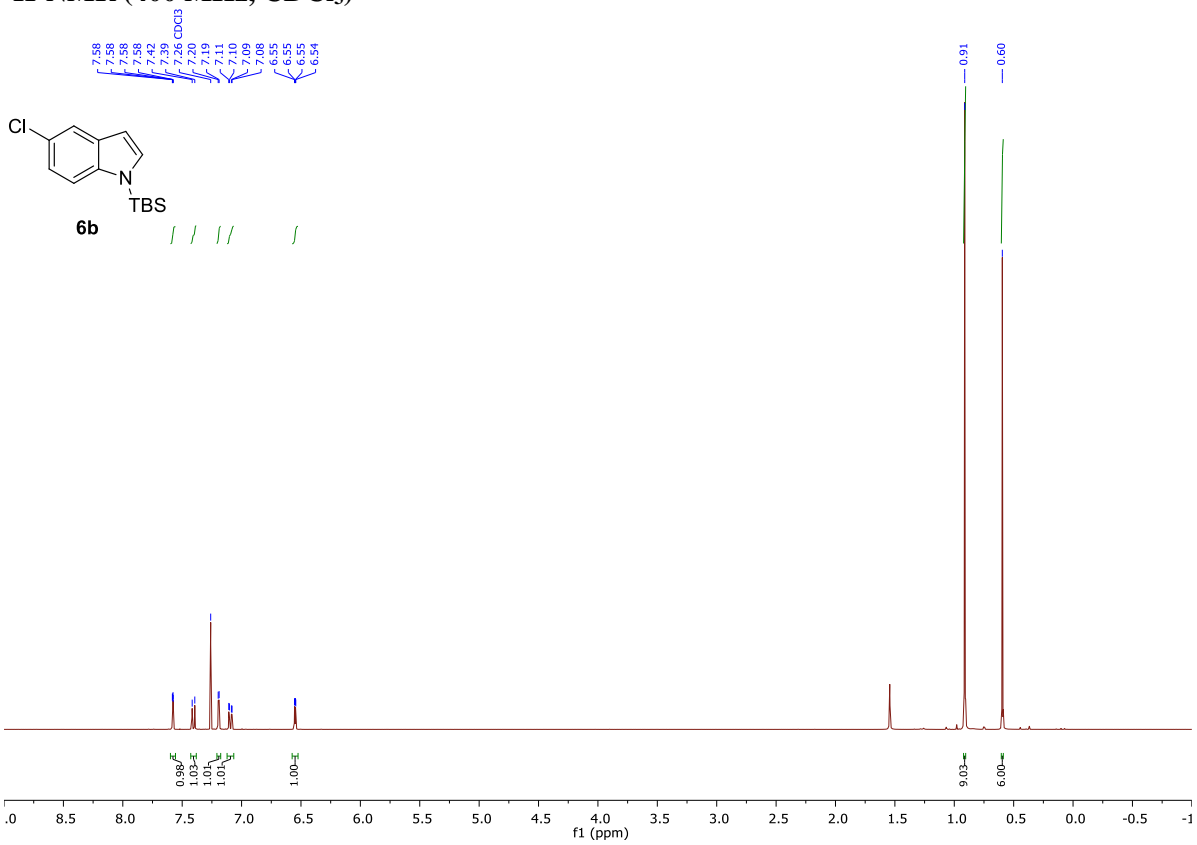
**IR**



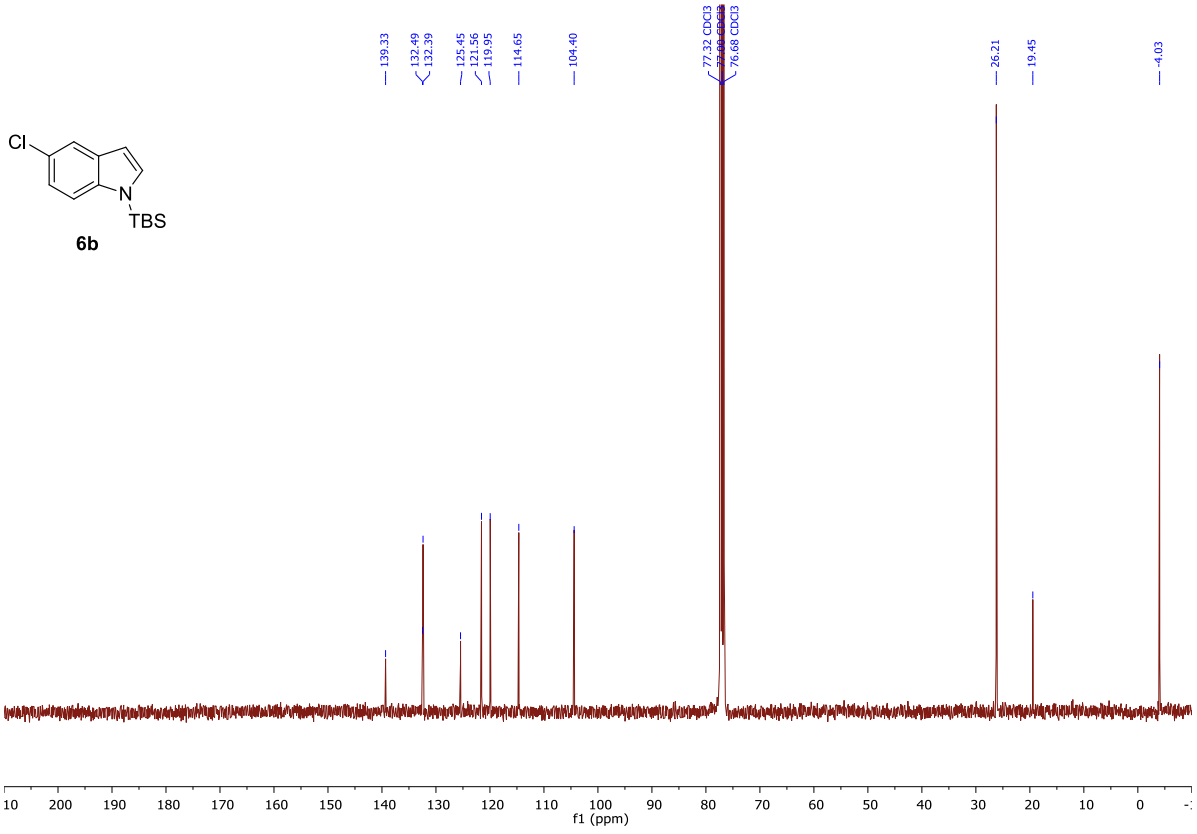

**2**

**1-(*Tert*-butyldimethylsilyl)-5-chloro-1H-indole (6b)**

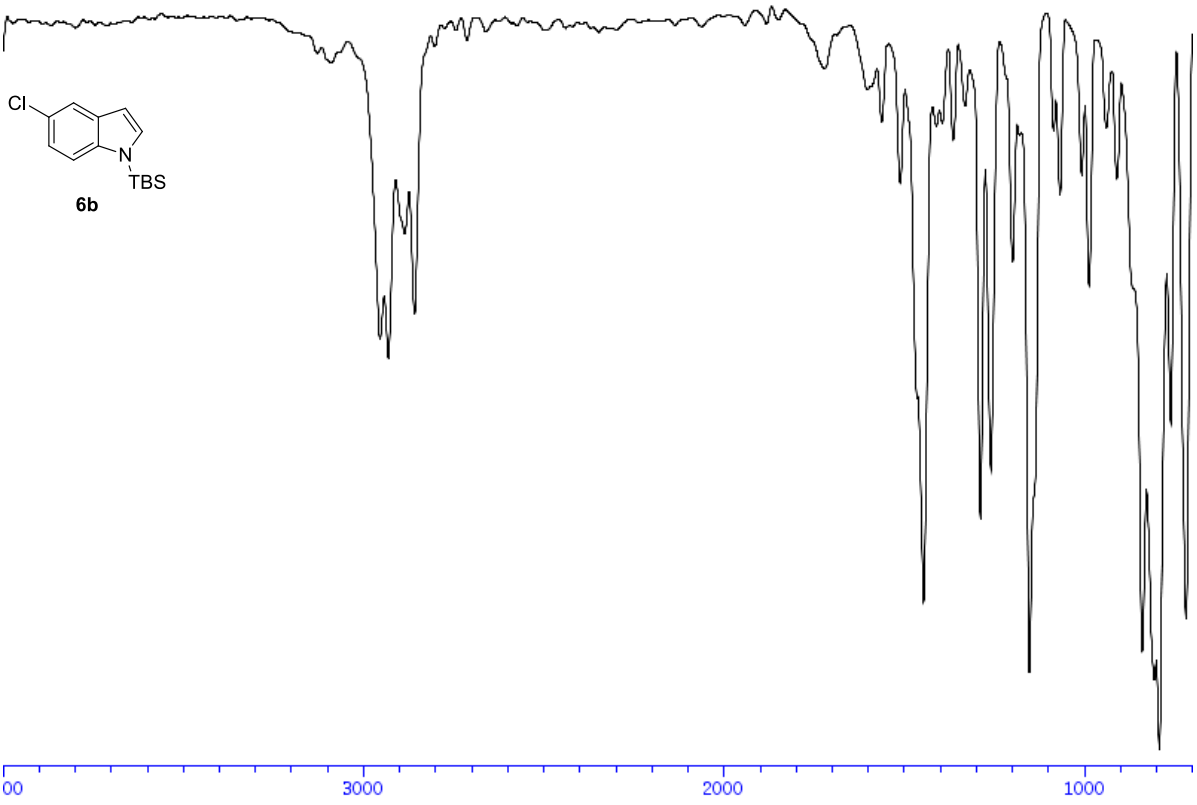
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

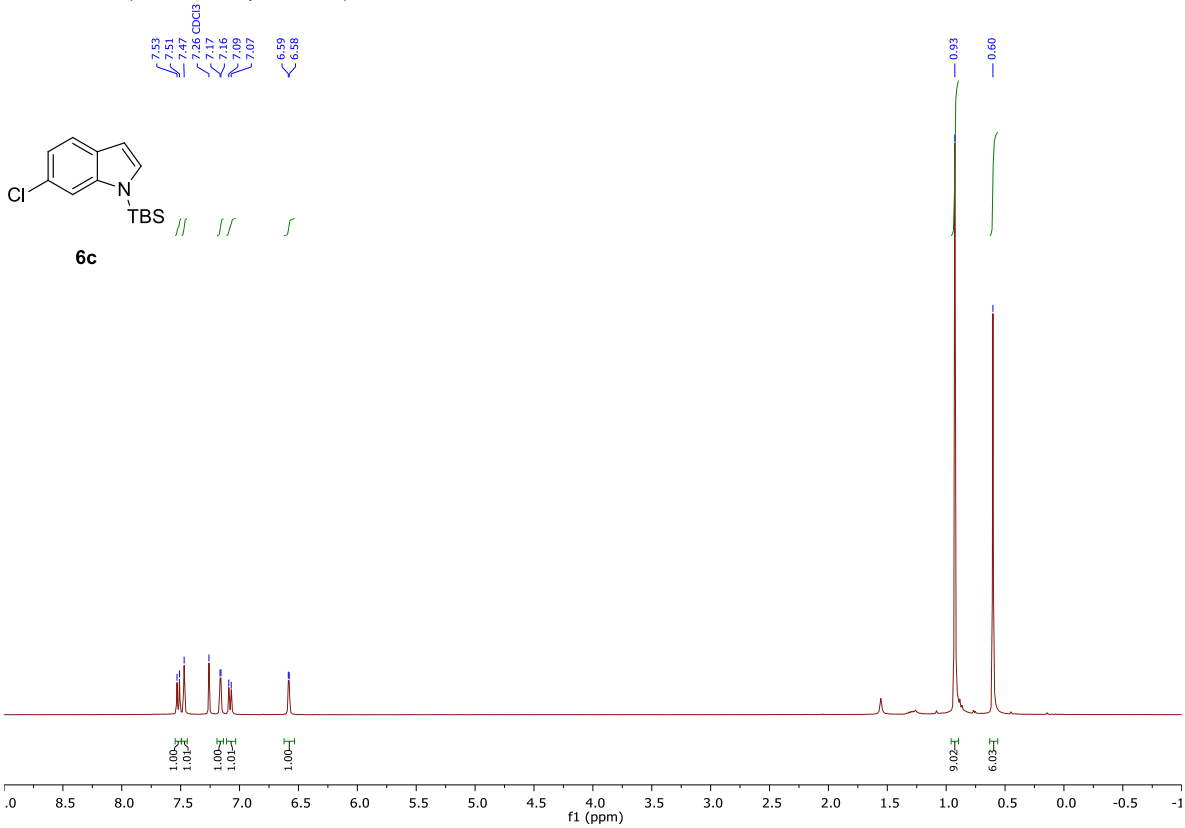


**IR**

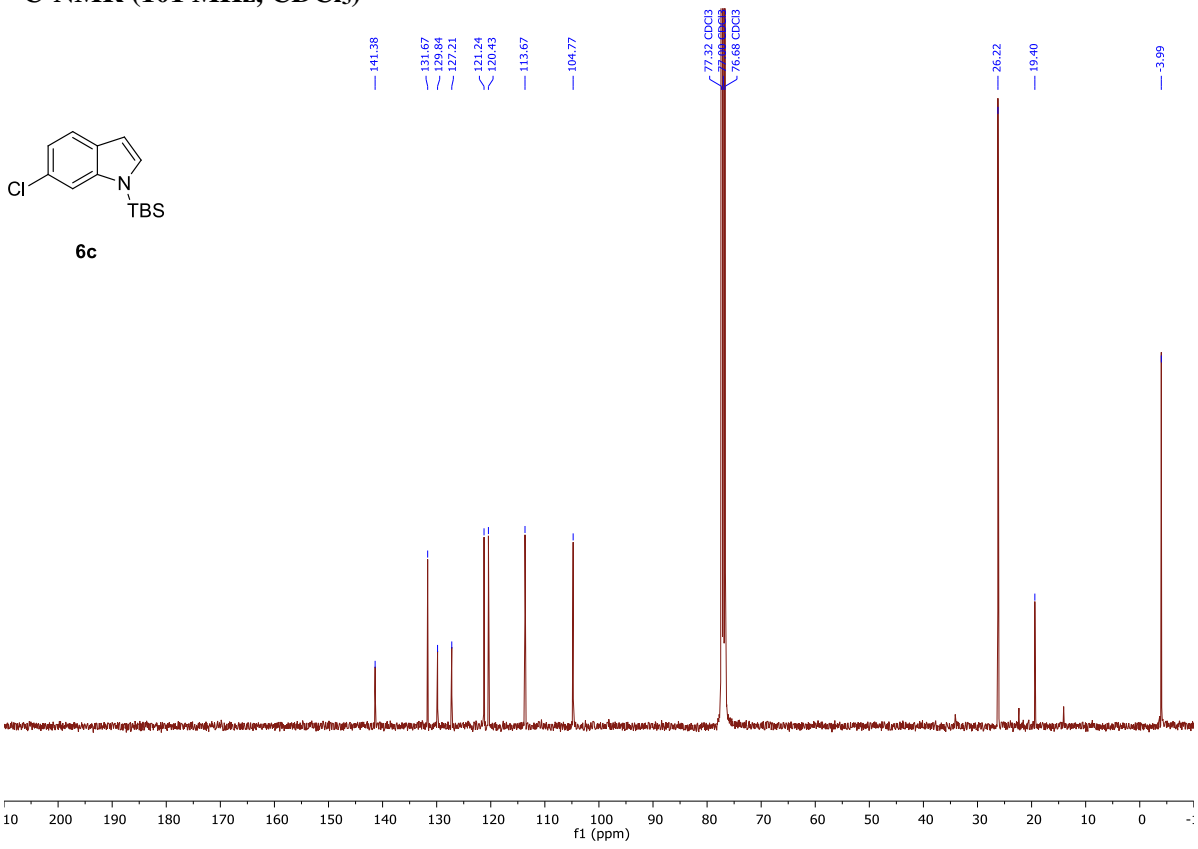


**1-(*Tert*-butyldimethylsilyl)-6-chloro-1H-indole (6c)**

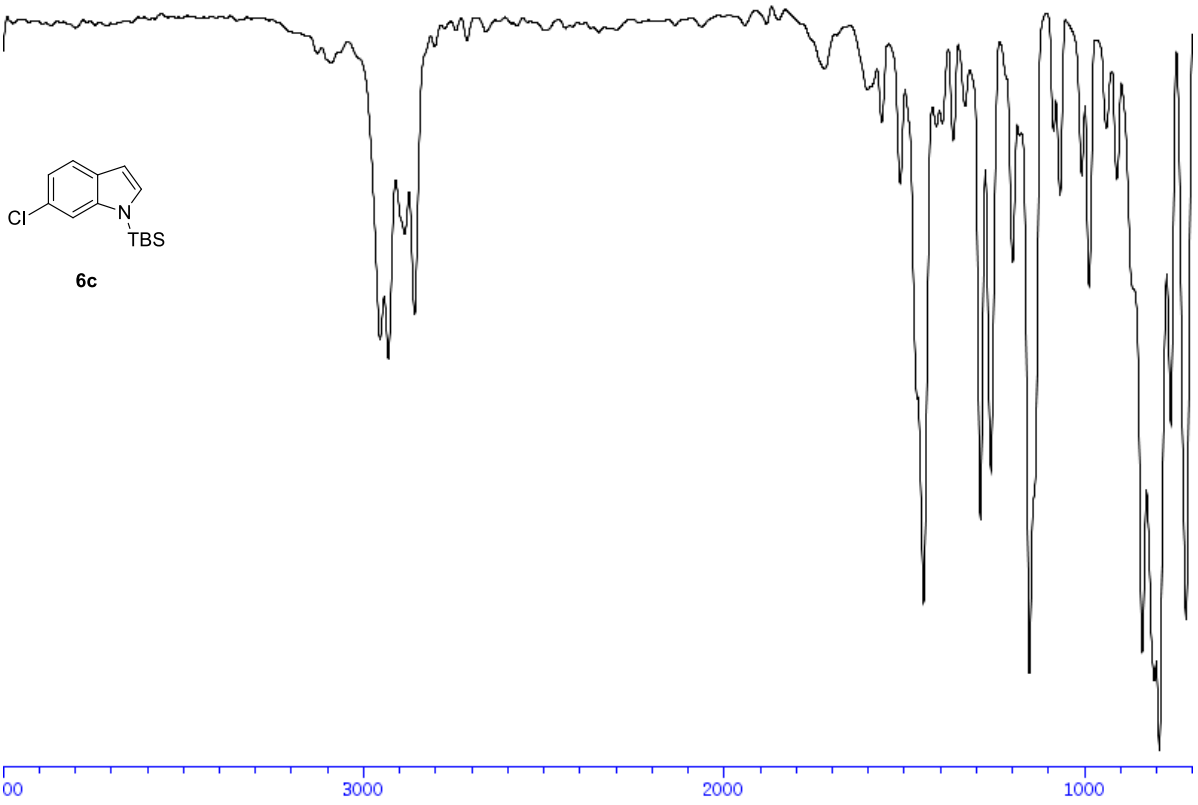
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

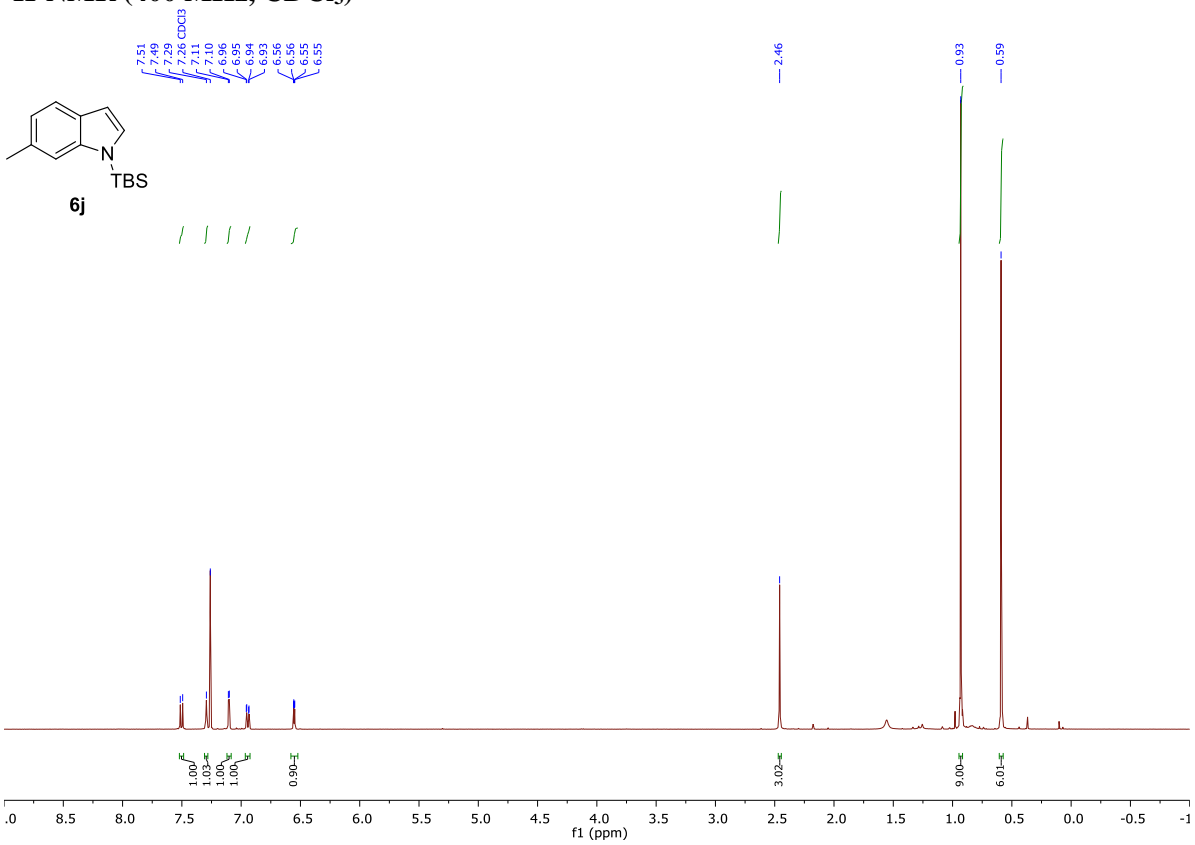


**IR**

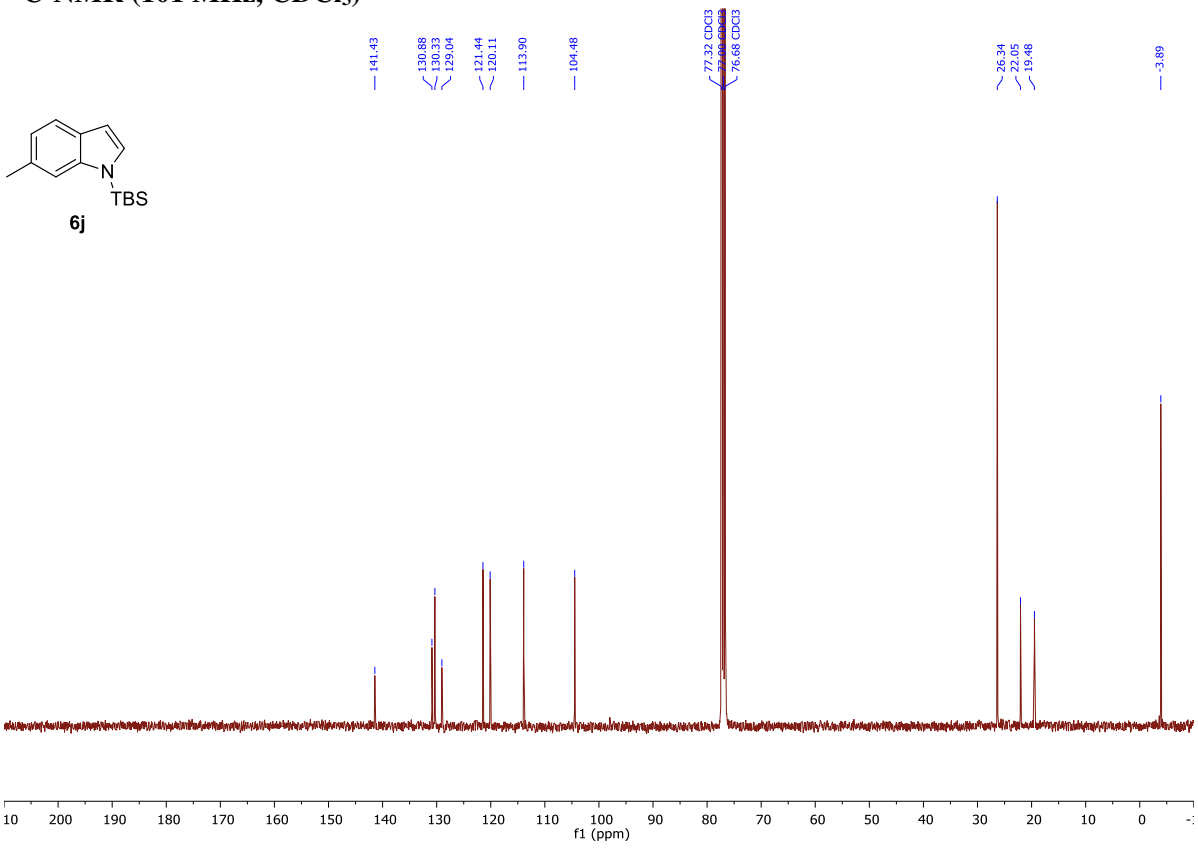


**1-(*tert*-butyldimethylsilyl)-6-methyl-1H-indole (6j)**

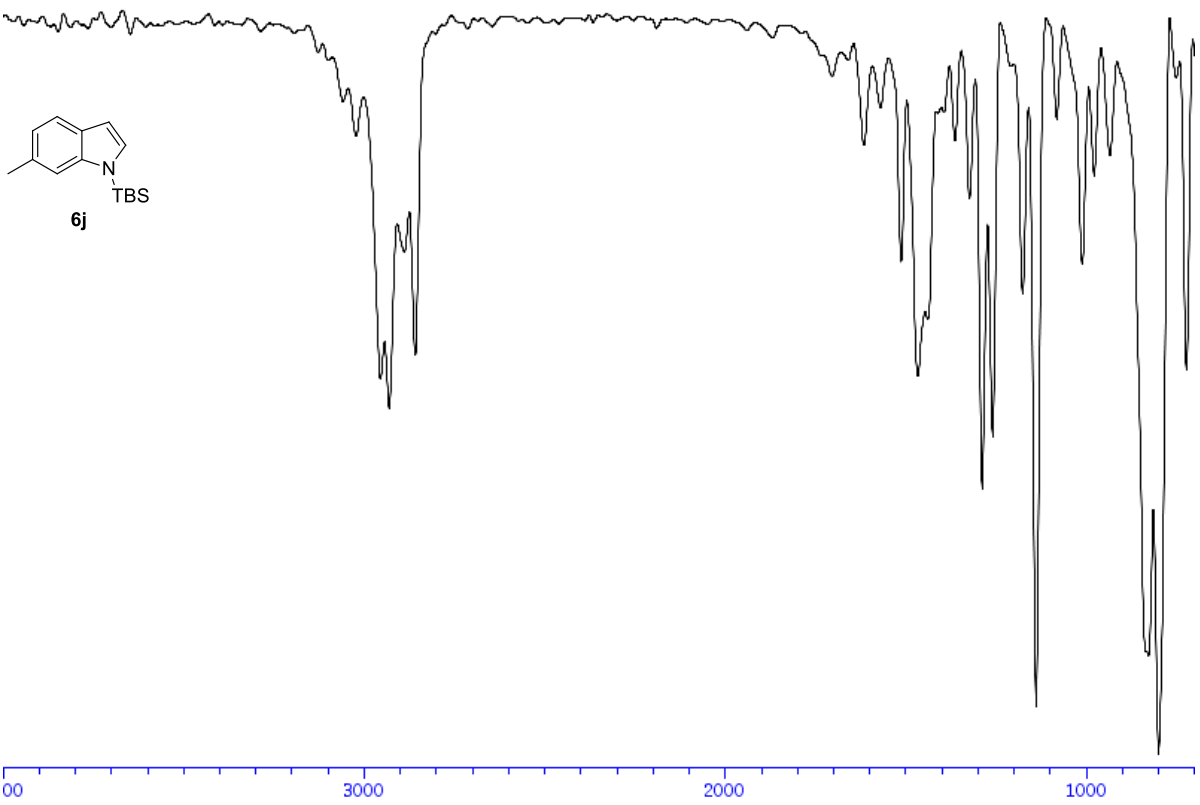
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

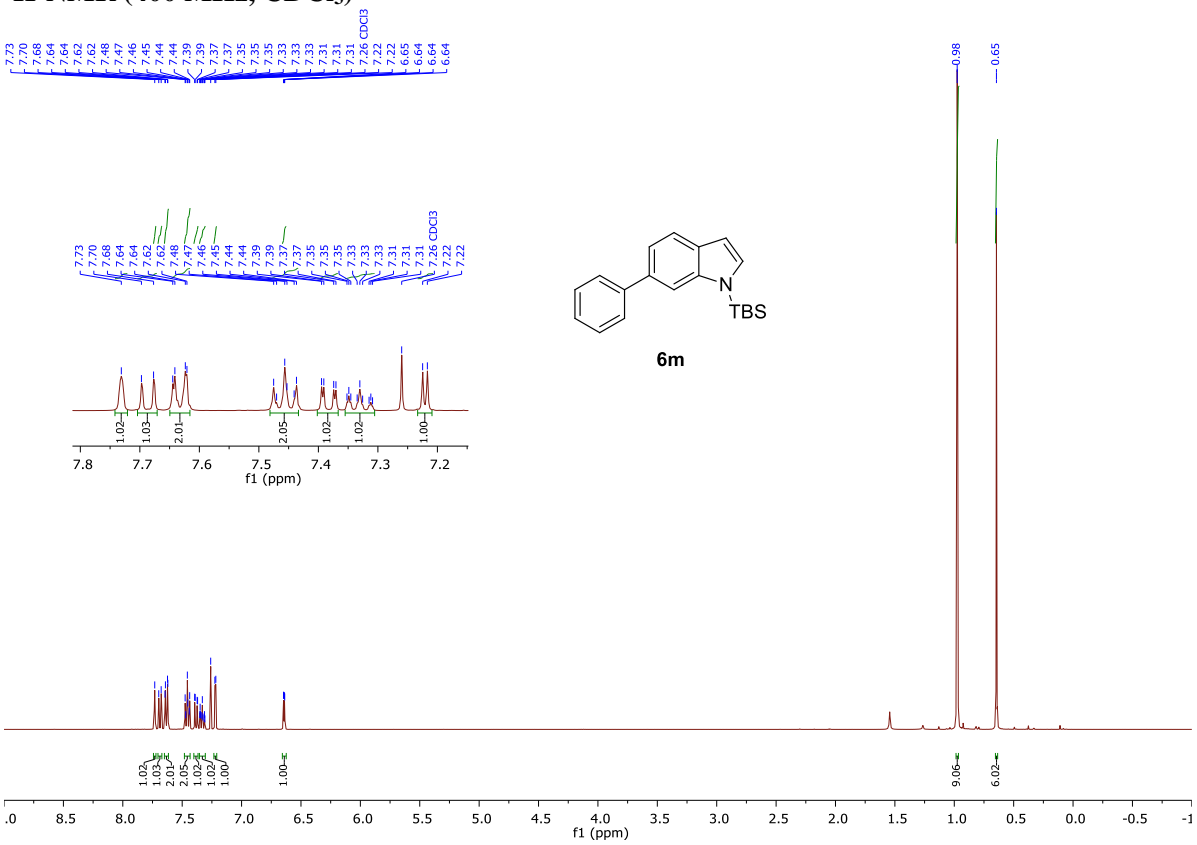


**IR**

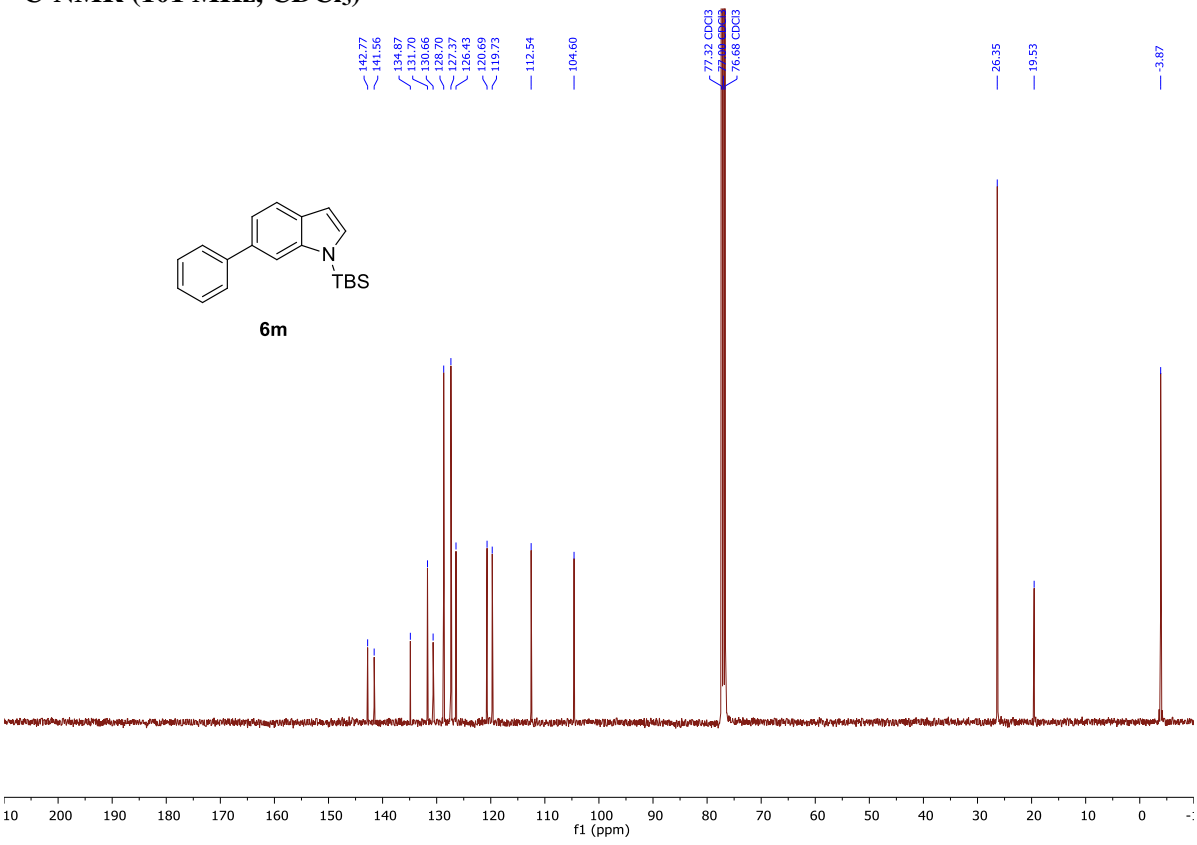


**1-(*tert*-butyldimethylsilyl)-6-phenyl-1H-indole (6m)**

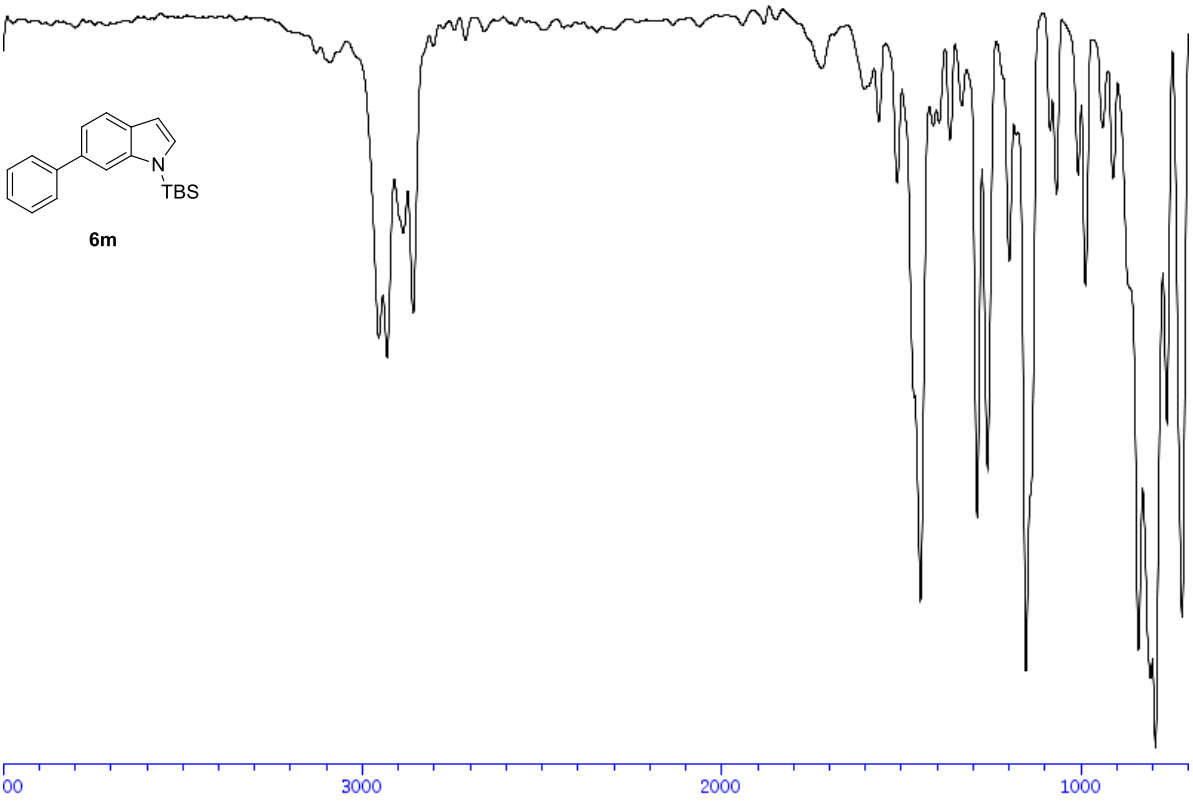
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

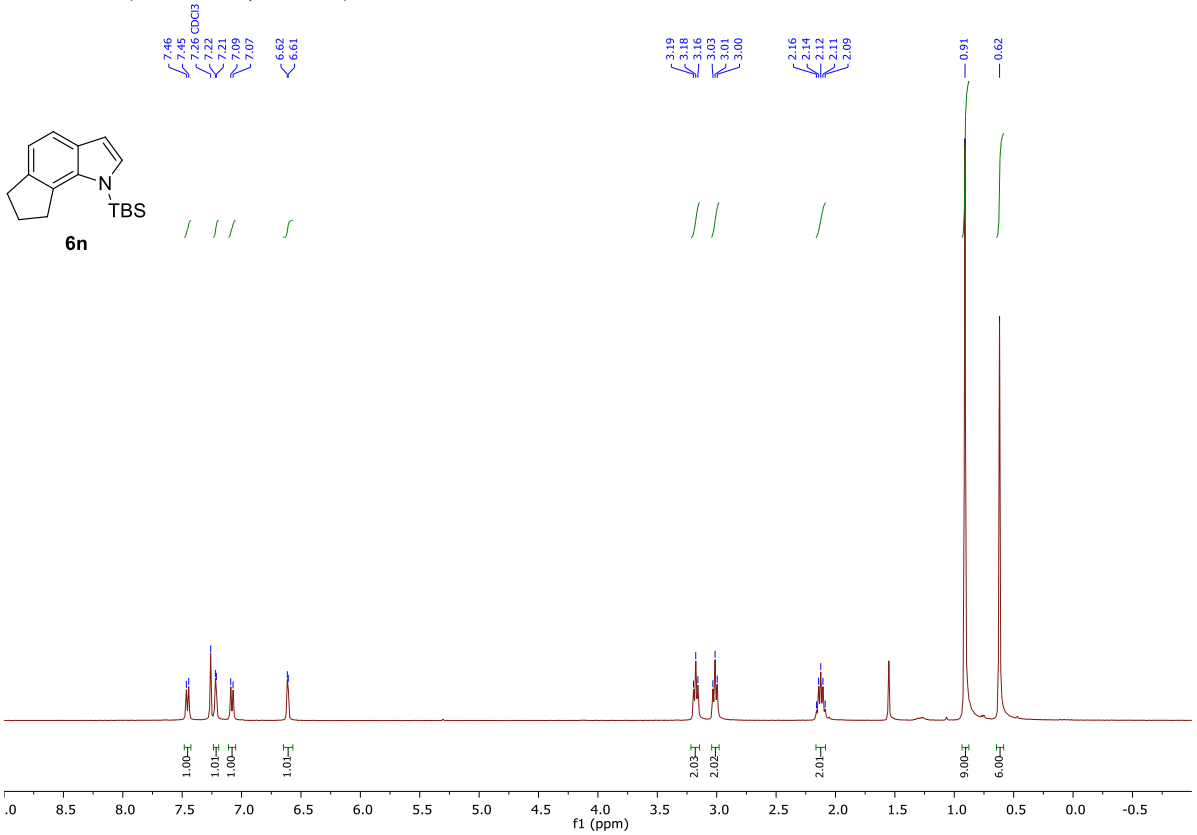


**IR**

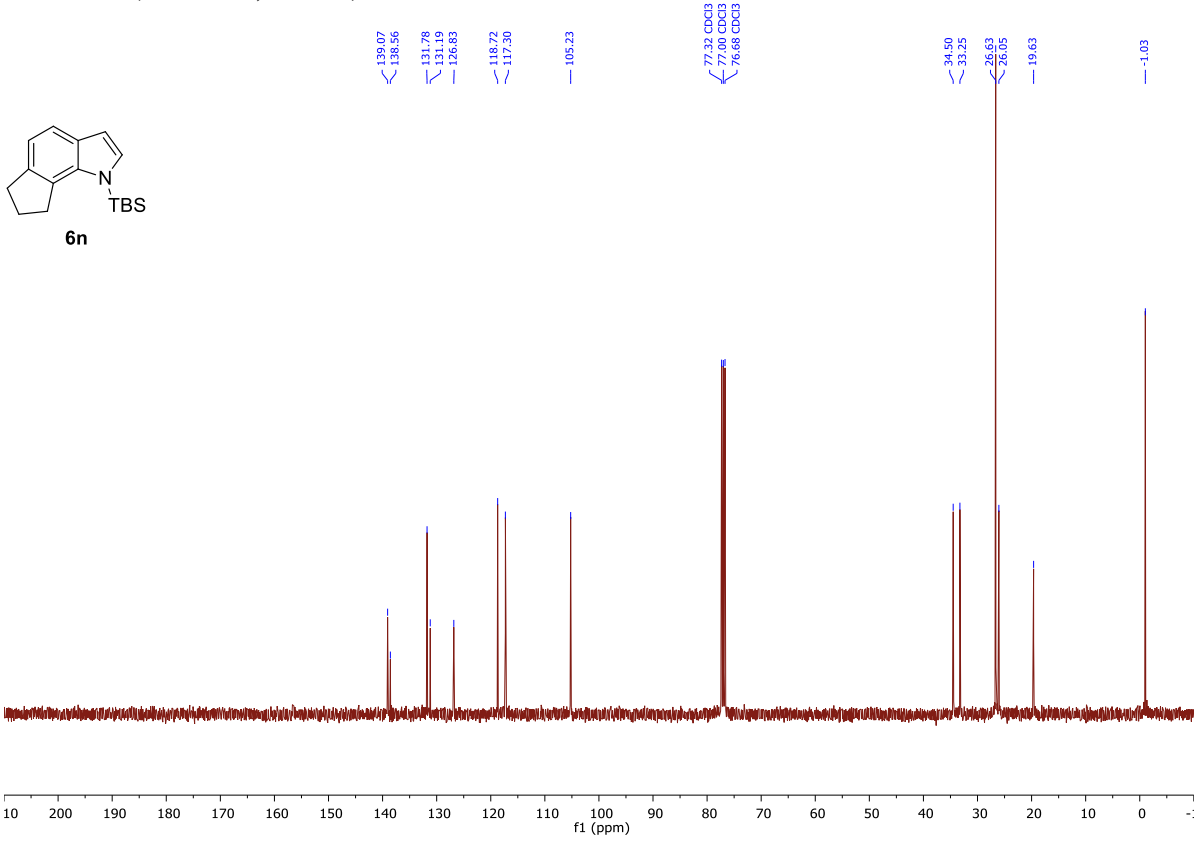


**1-(*tert*-butyldimethylsilyl)-1,6,7,8-tetrahydrocyclopenta[g]indole (6n)**

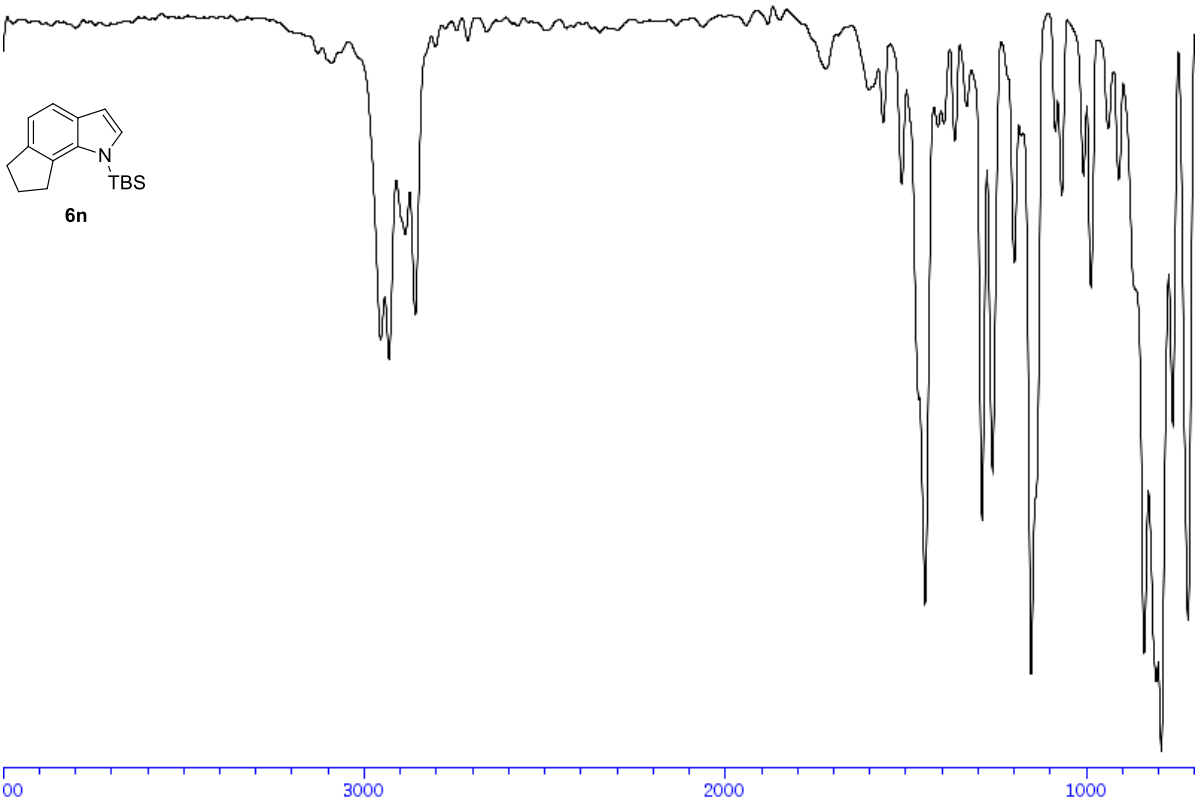
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

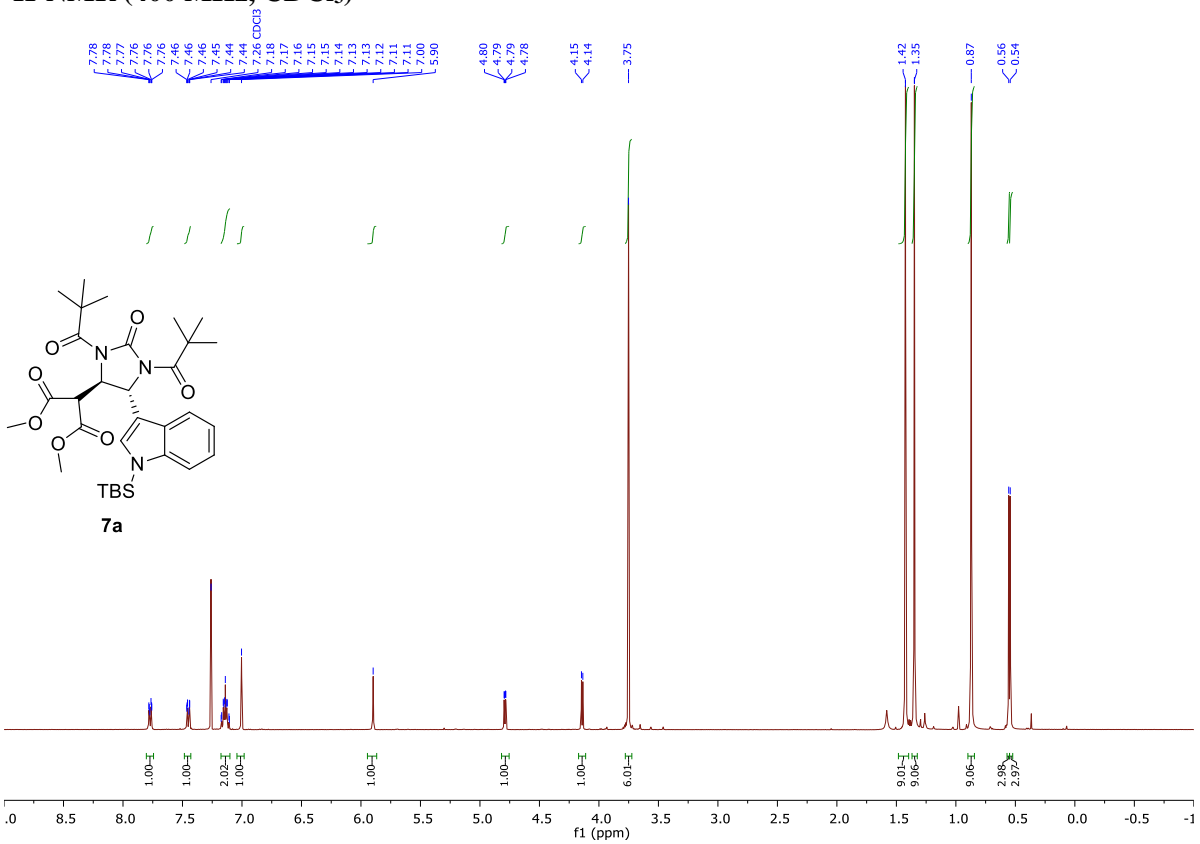


**IR**

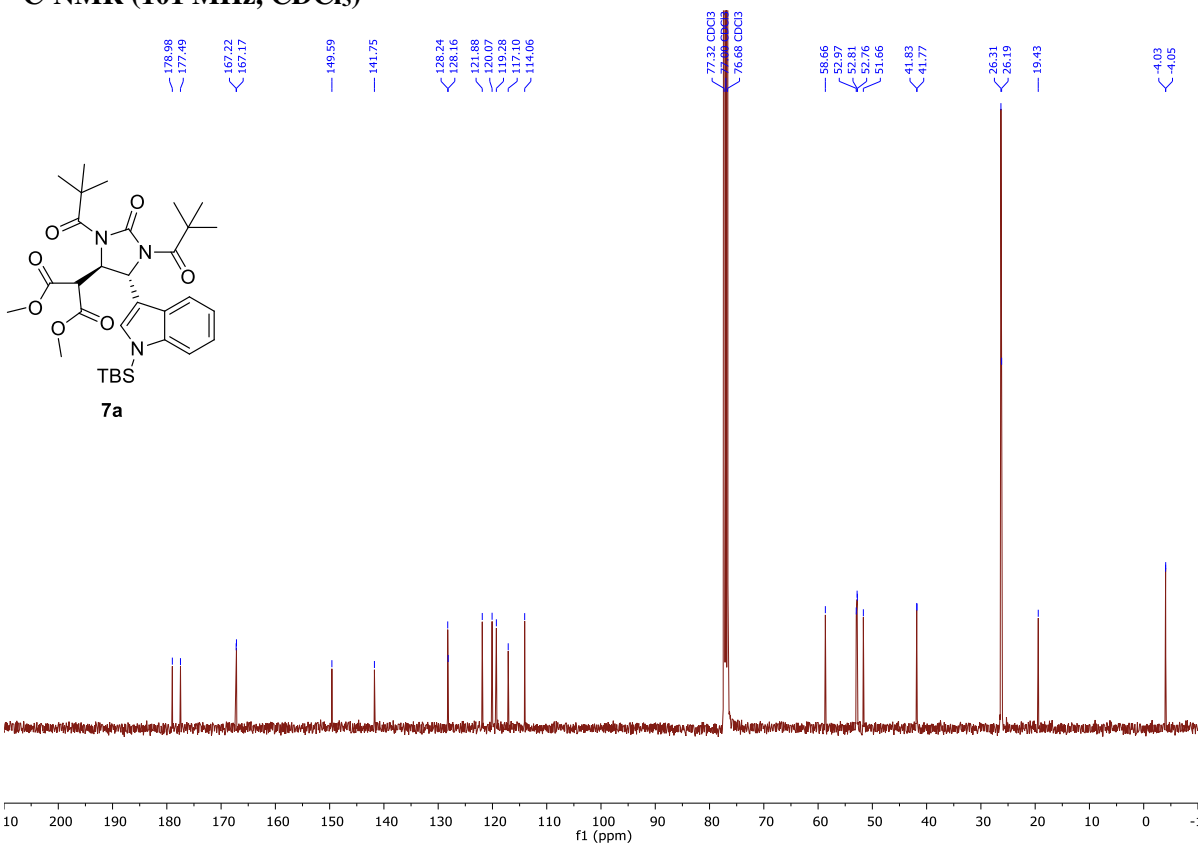


**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7a)**

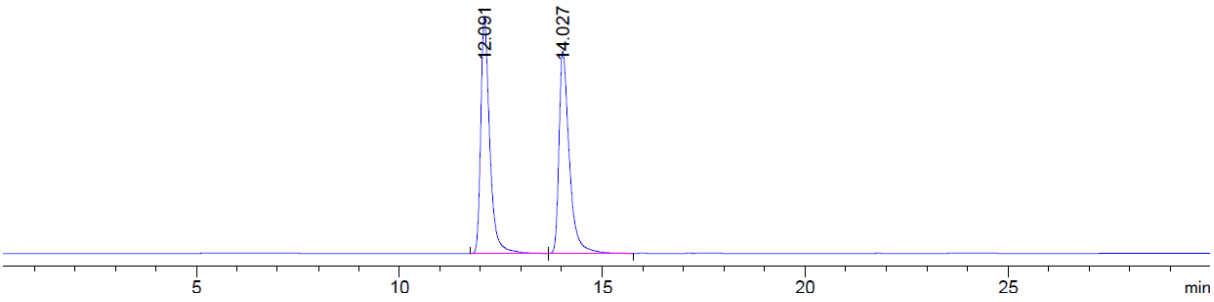
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



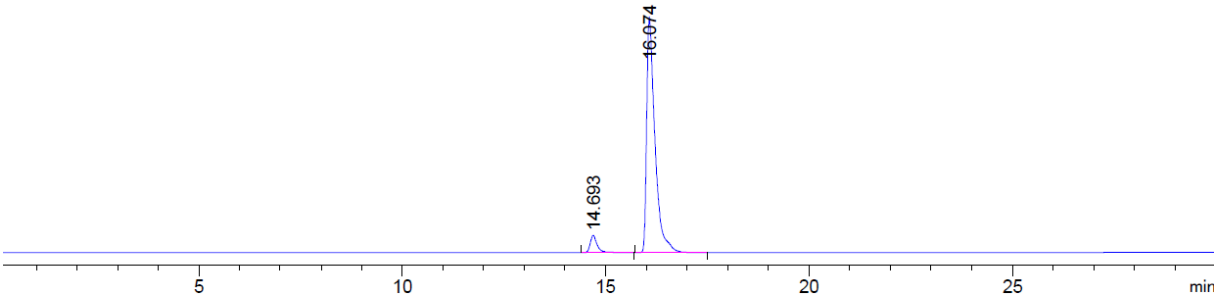

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

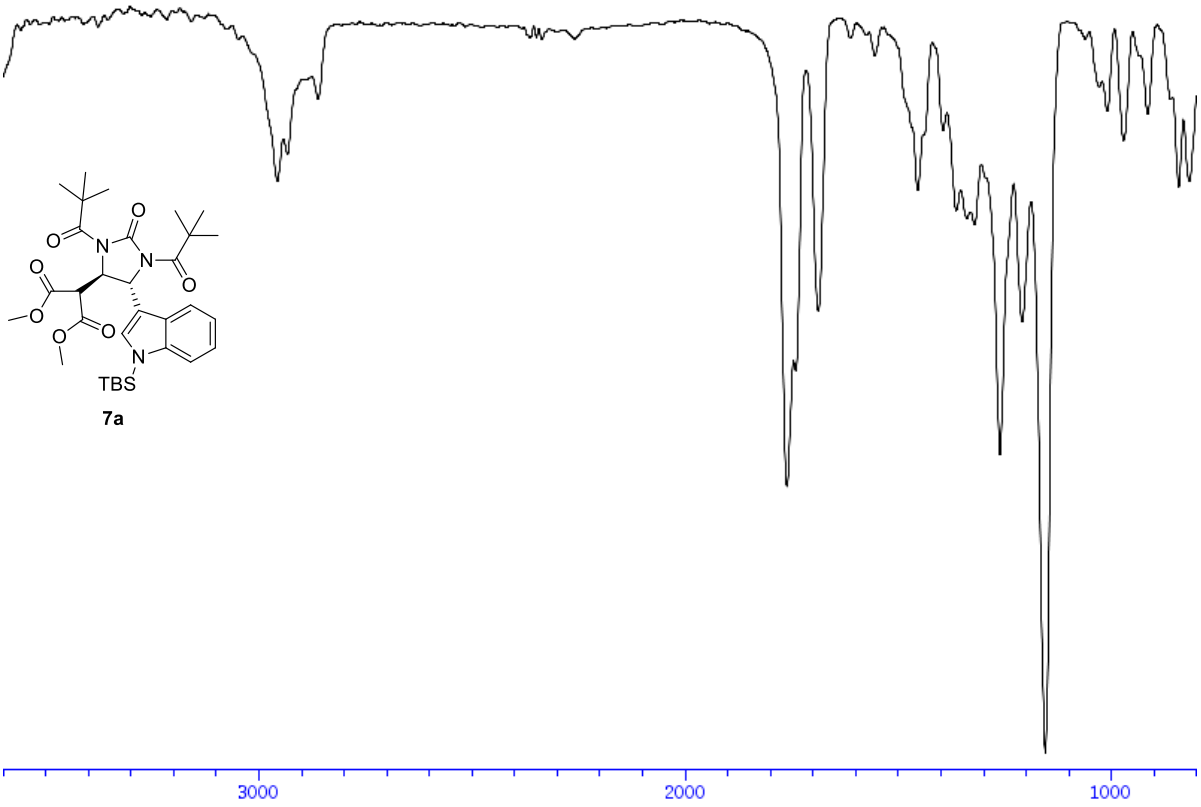



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.091 | BB | 0.2323 | 1748.08521 | 113.11364 | 50.5393 |
| 2 | 14.027 | BB | 0.2662 | 1710.77966 | 96.79921 | 49.4607 |



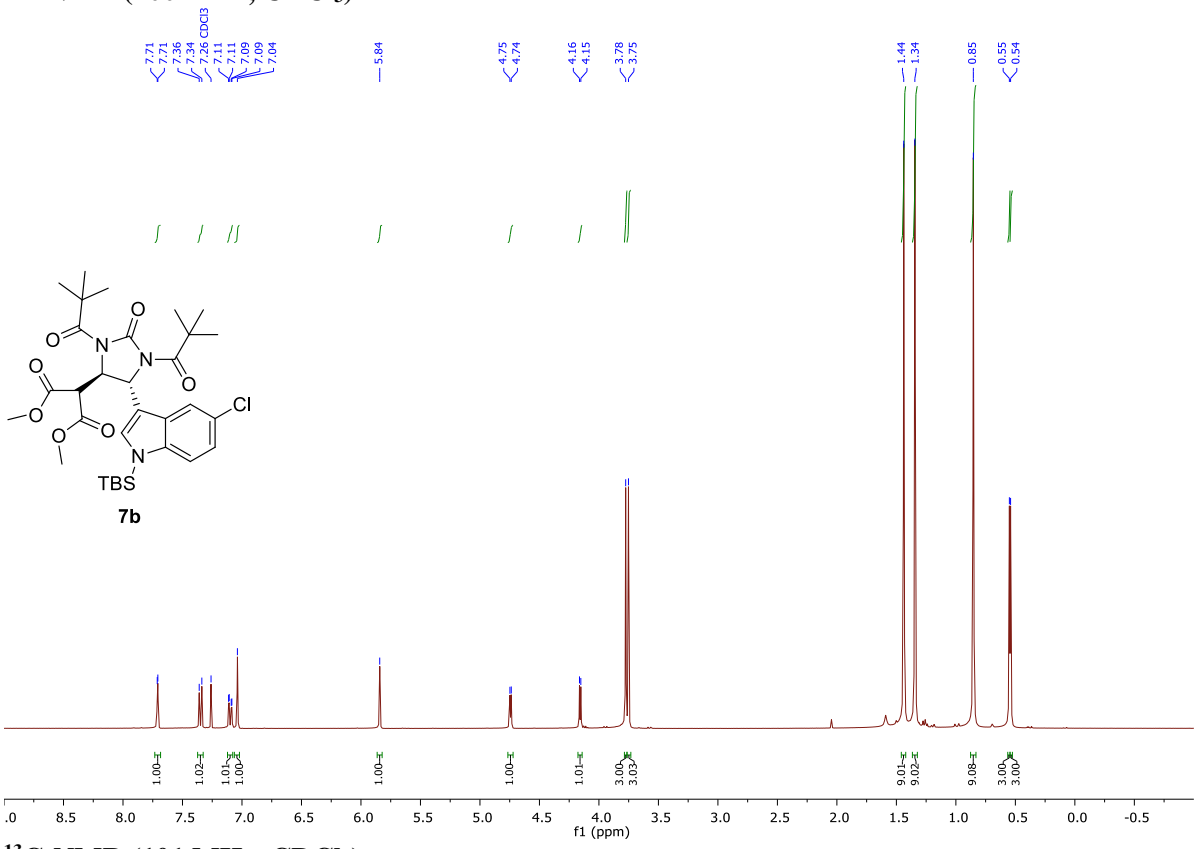

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.693 | BB | 0.1807 | 901.92865 | 74.77305 | 5.7814 |
| 2 | 16.074 | BB | 0.2107 | 1.46986e4 | 1028.92822 | 94.2186 |

**IR**

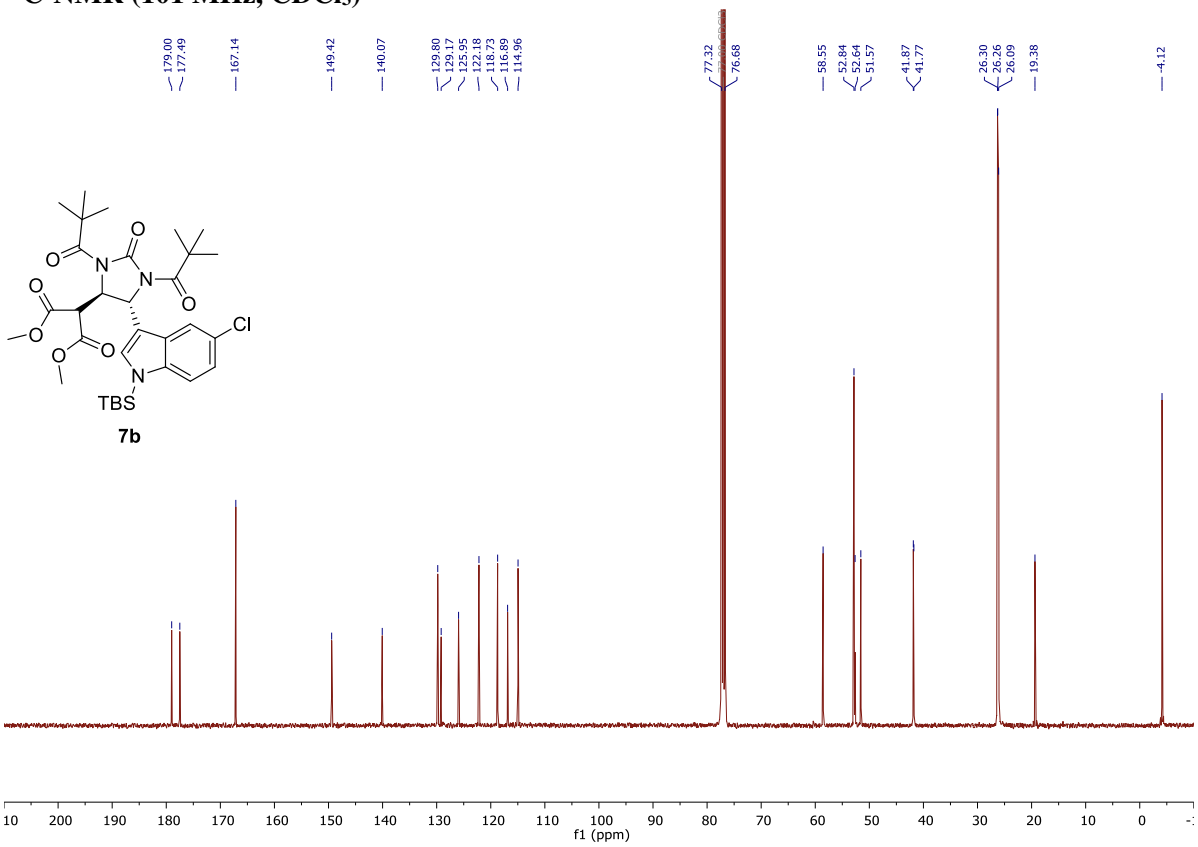


**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-chloro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7b)**

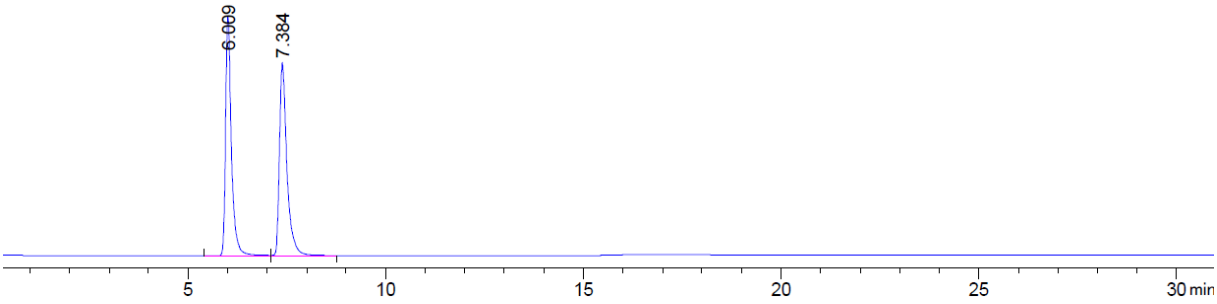
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



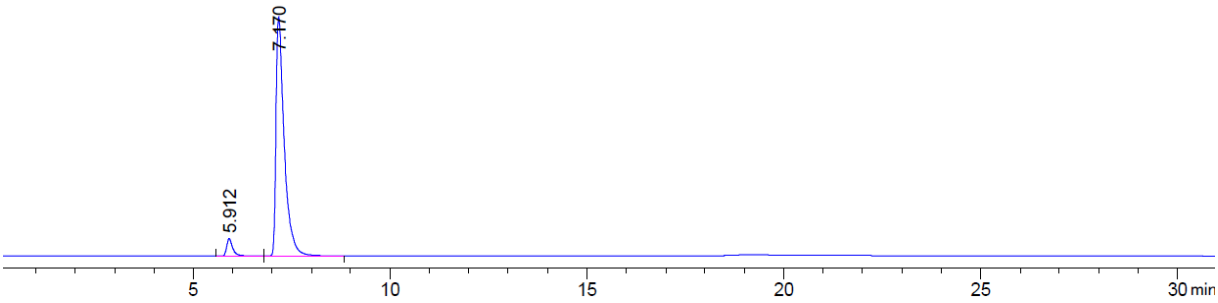

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

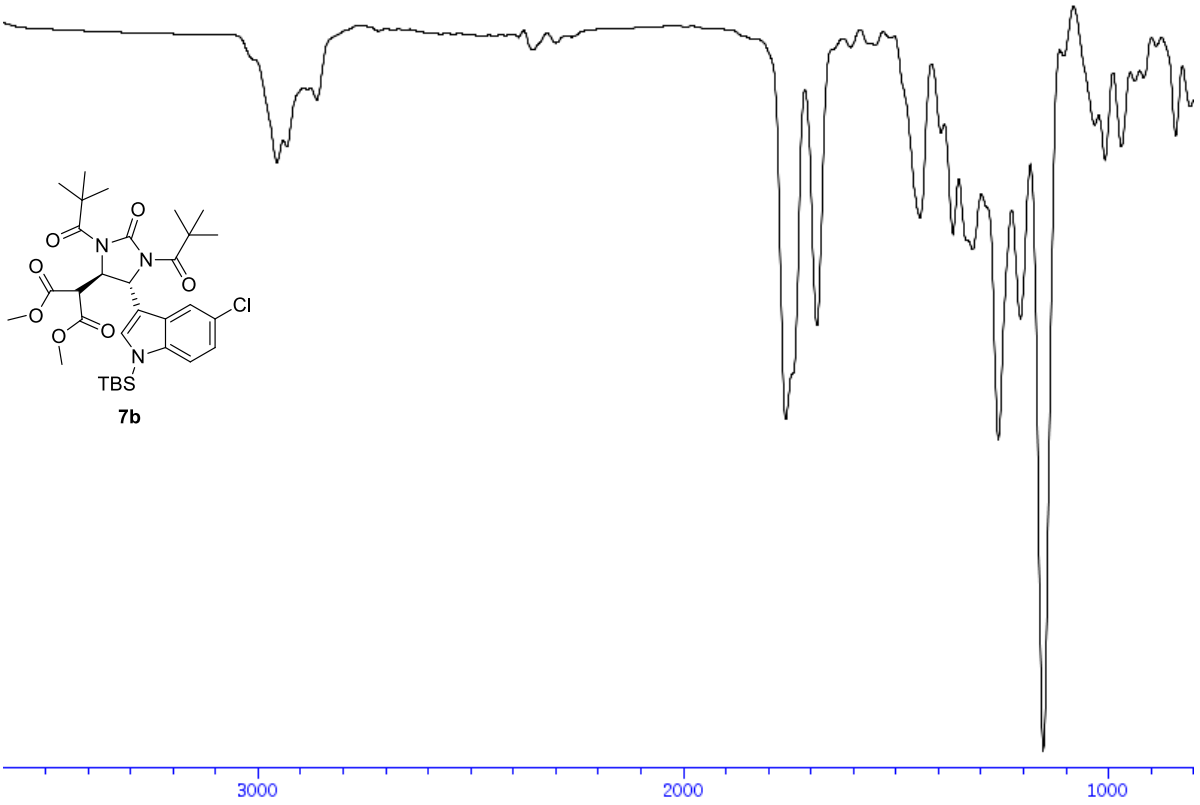



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.009 | BB | 0.1511 | 1485.86963 | 145.59550 | 49.2526 |
| 2 | 7.384 | BB | 0.1946 | 1530.96472 | 117.05157 | 50.7474 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.912 | BB | 0.1556 | 449.42056 | 43.13351 | 4.9834 |
| 2 | 7.170 | BB | 0.2155 | 8568.84375 | 589.71967 | 95.0166 |

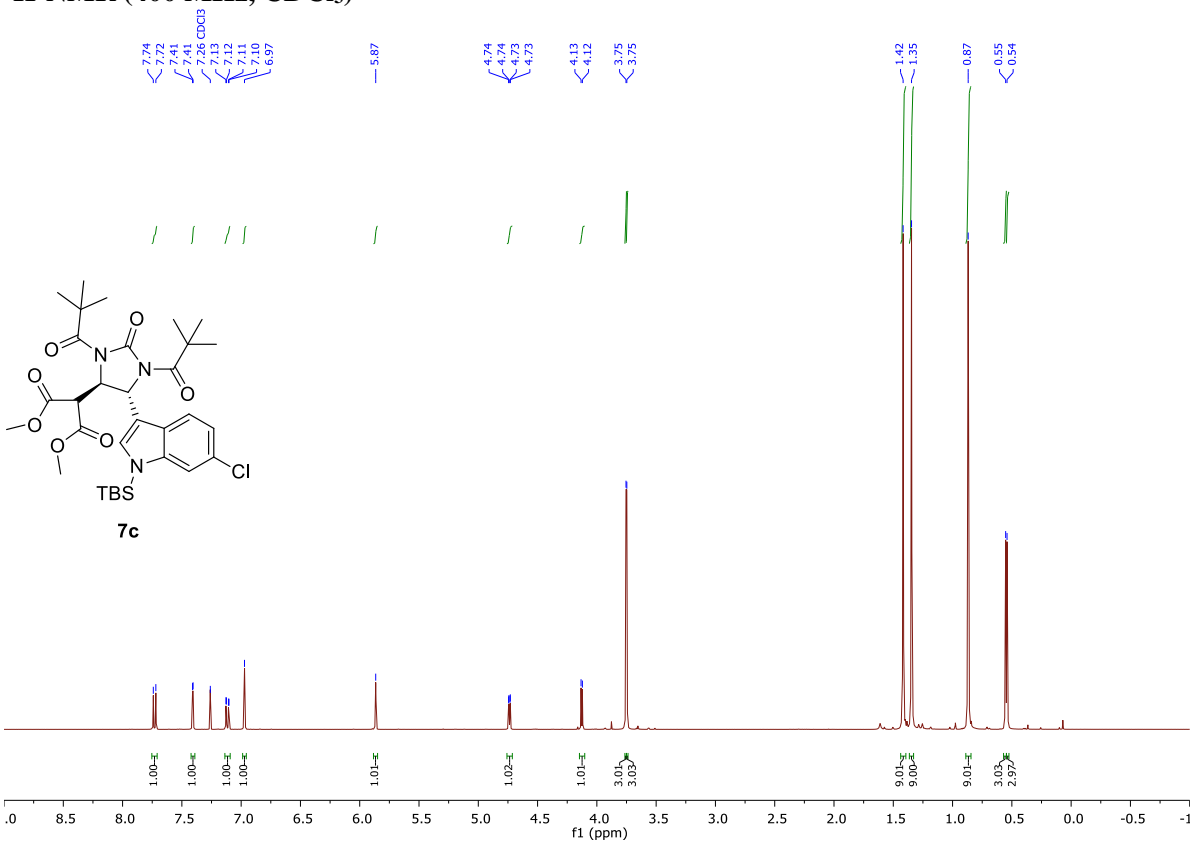
**IR**



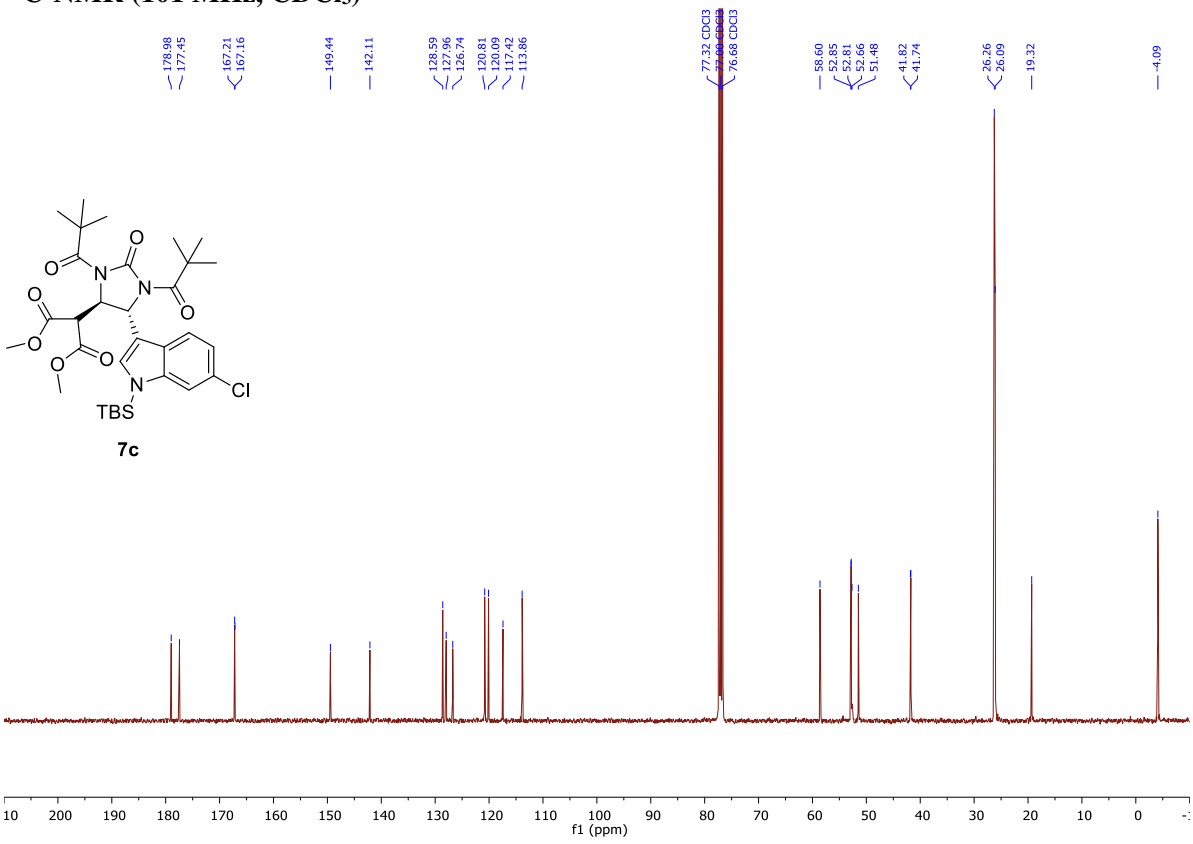

**7b**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-chloro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7c)**

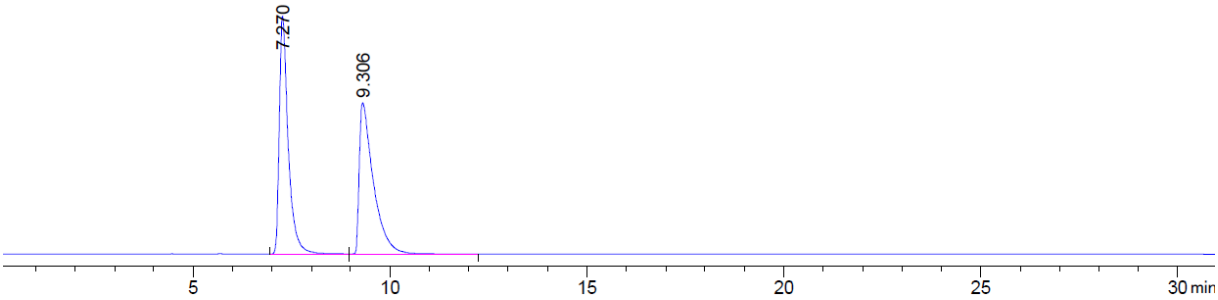
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



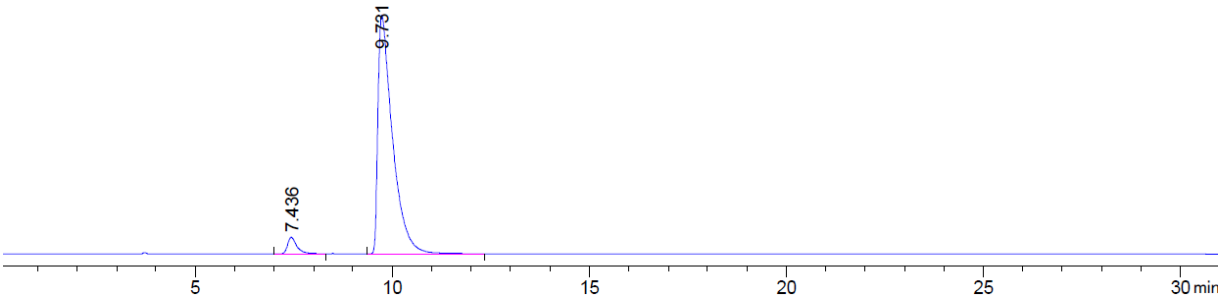

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

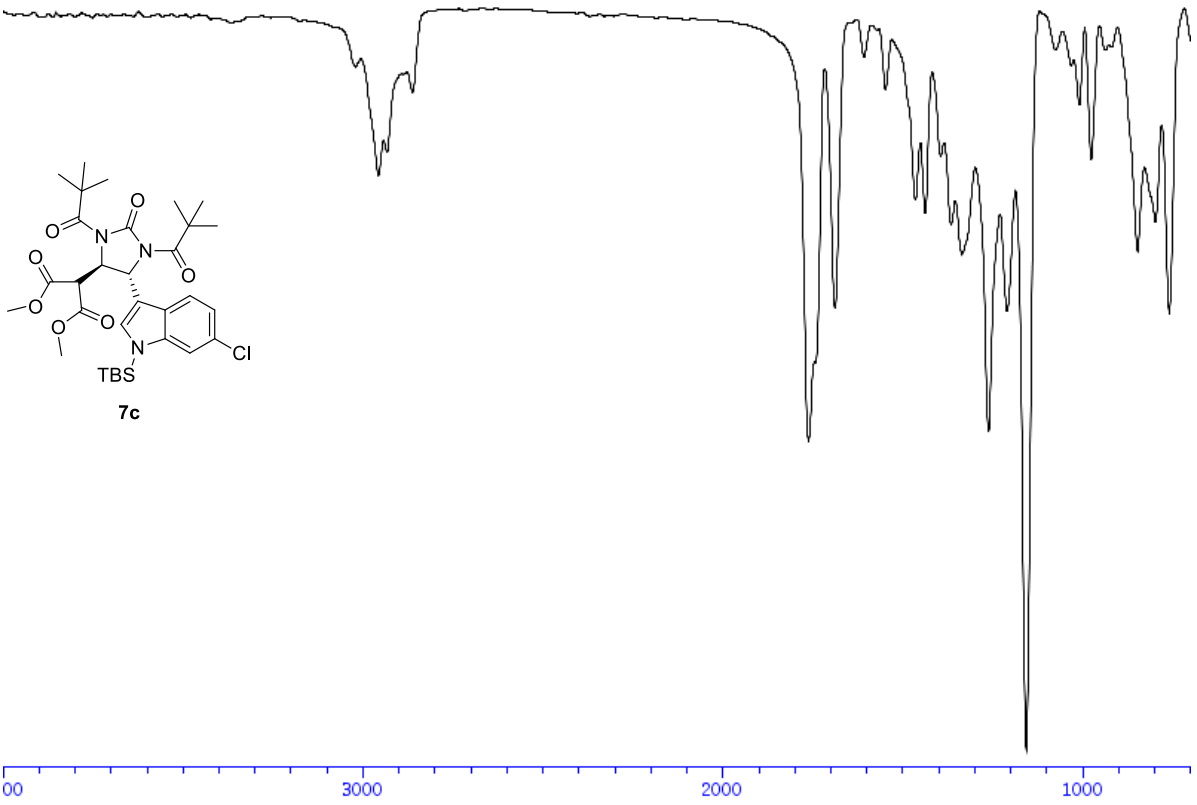



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.270 | BB | 0.2323 | 2512.69824 | 159.02888 | 50.0272 |
| 2 | 9.306 | BB | 0.3577 | 2509.96826 | 101.08558 | 49.9728 |



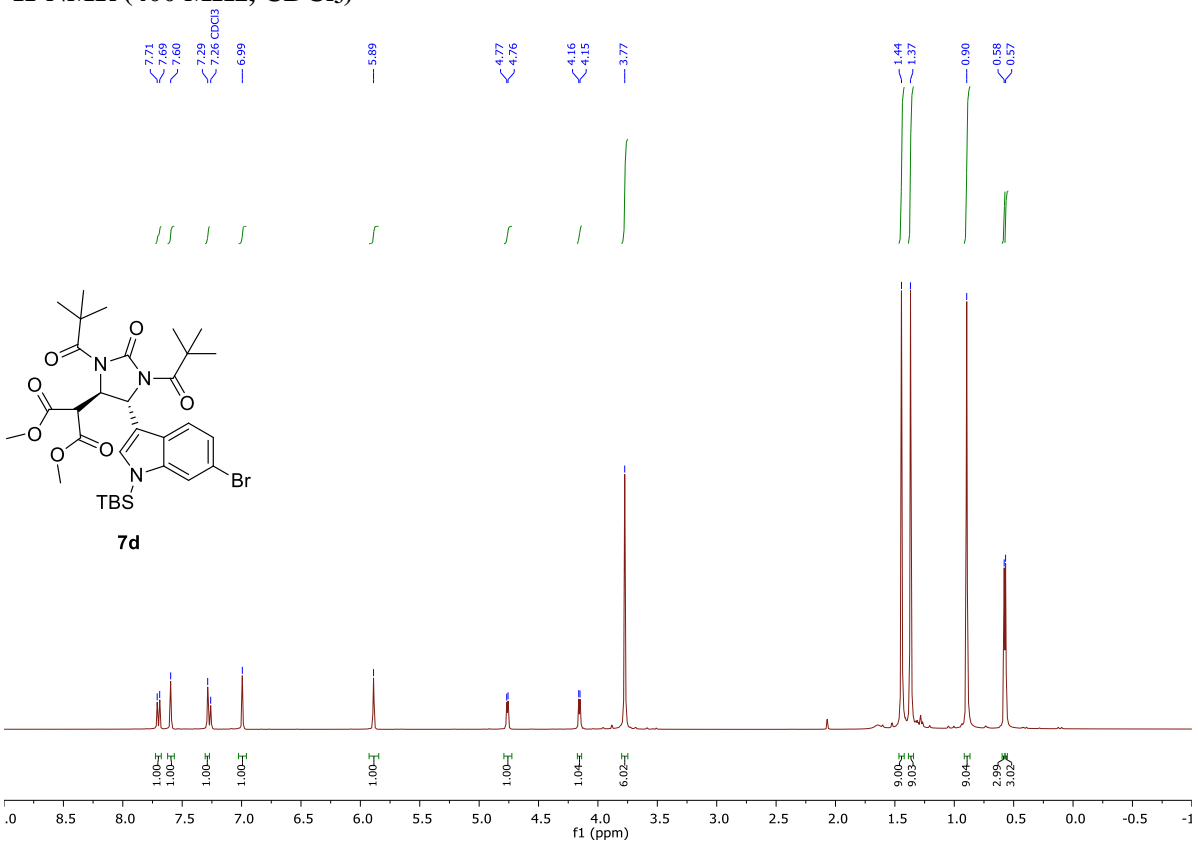

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.436 | BB | 0.2437 | 163.03163 | 9.92031 | 4.2598 |
| 2 | 9.731 | BB | 0.3714 | 3664.21167 | 142.75908 | 95.7402 |

**IR**



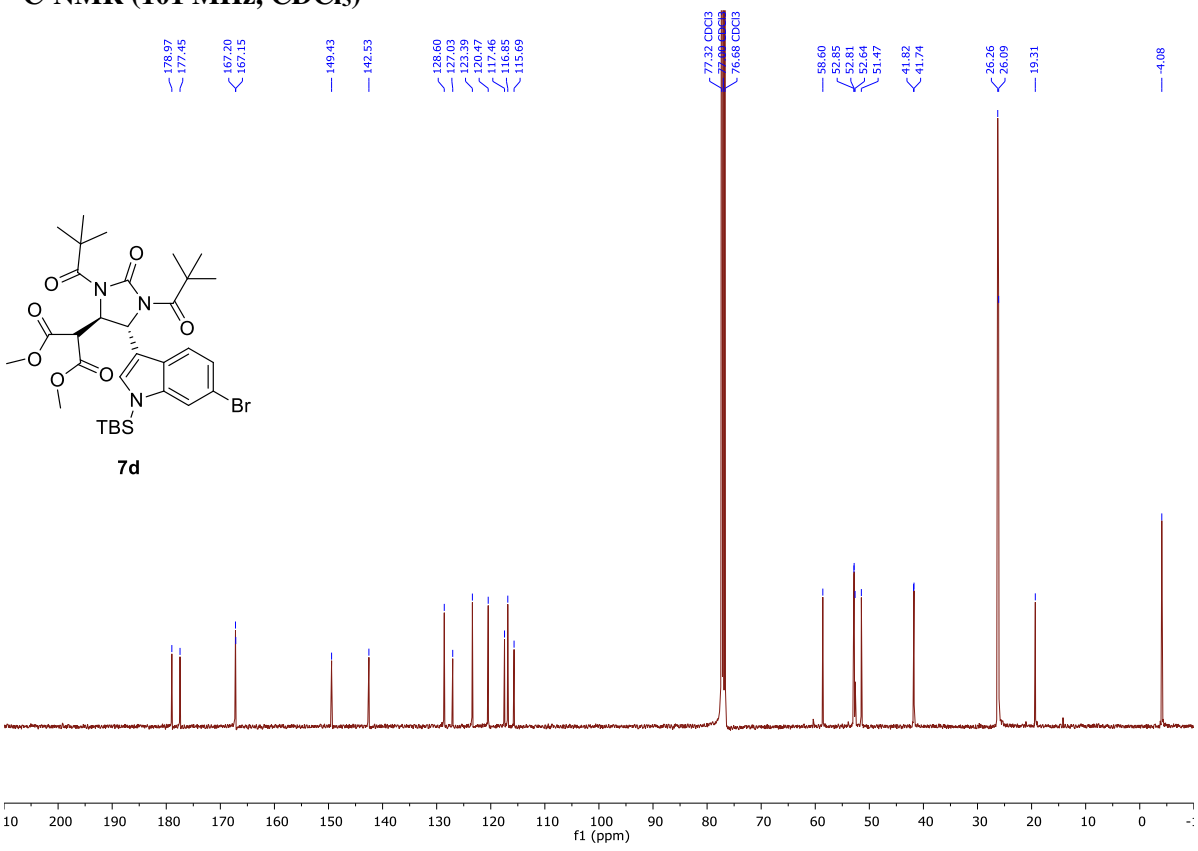
**Dimethyl 2-(5-(6-bromo-1-(*tert*-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7d)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



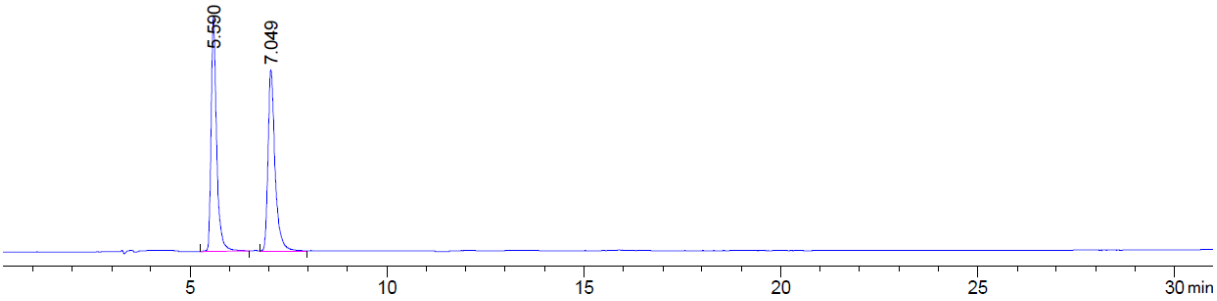

**7d**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

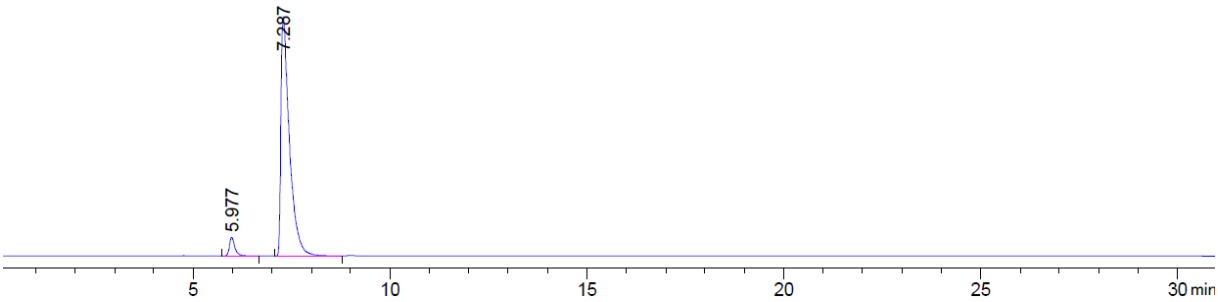



**7d**

**HPLC**

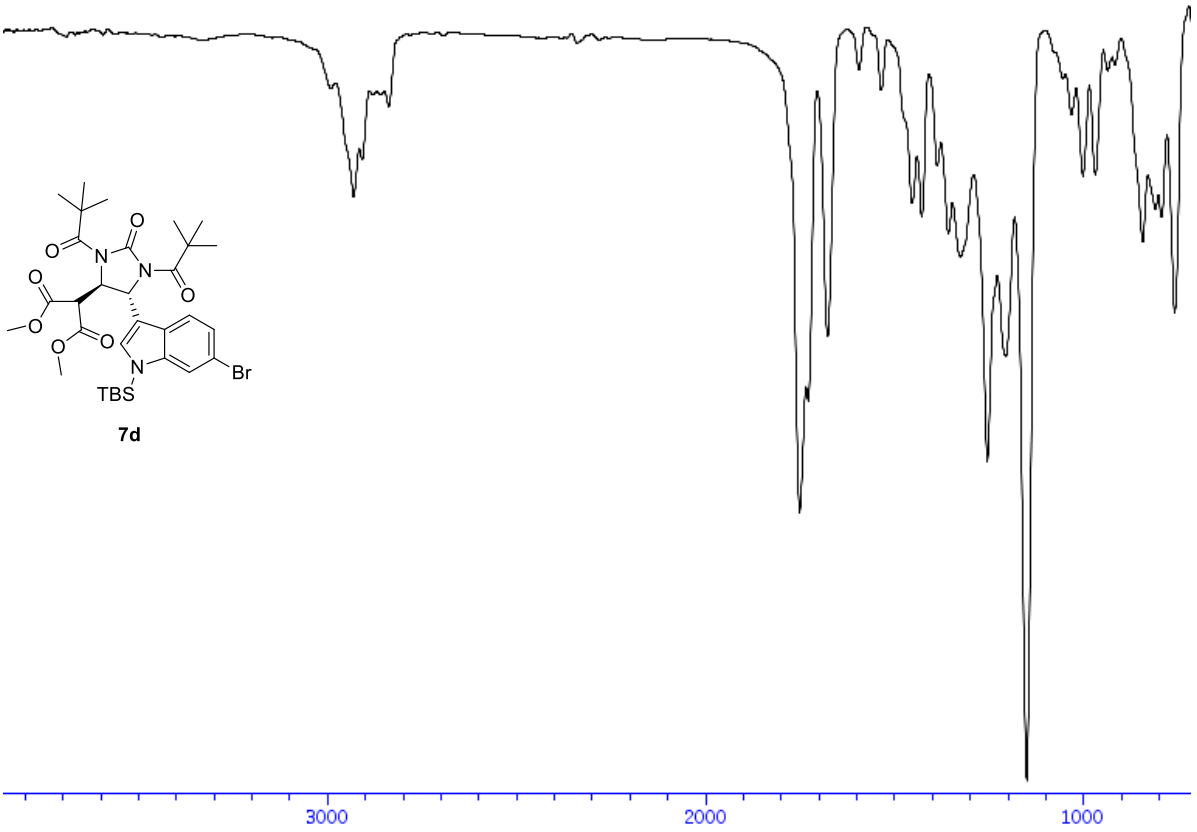



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.590 | BB | 0.1442 | 80.67544 | 8.38803 | 50.3437 |
| 2 | 7.049 | BB | 0.1841 | 79.57391 | 6.44182 | 49.6563 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.977 | BB | 0.1456 | 260.92438 | 26.78724 | 4.7736 |
| 2 | 7.287 | BB | 0.2183 | 5205.04199 | 344.46219 | 95.2264 |

**IR**



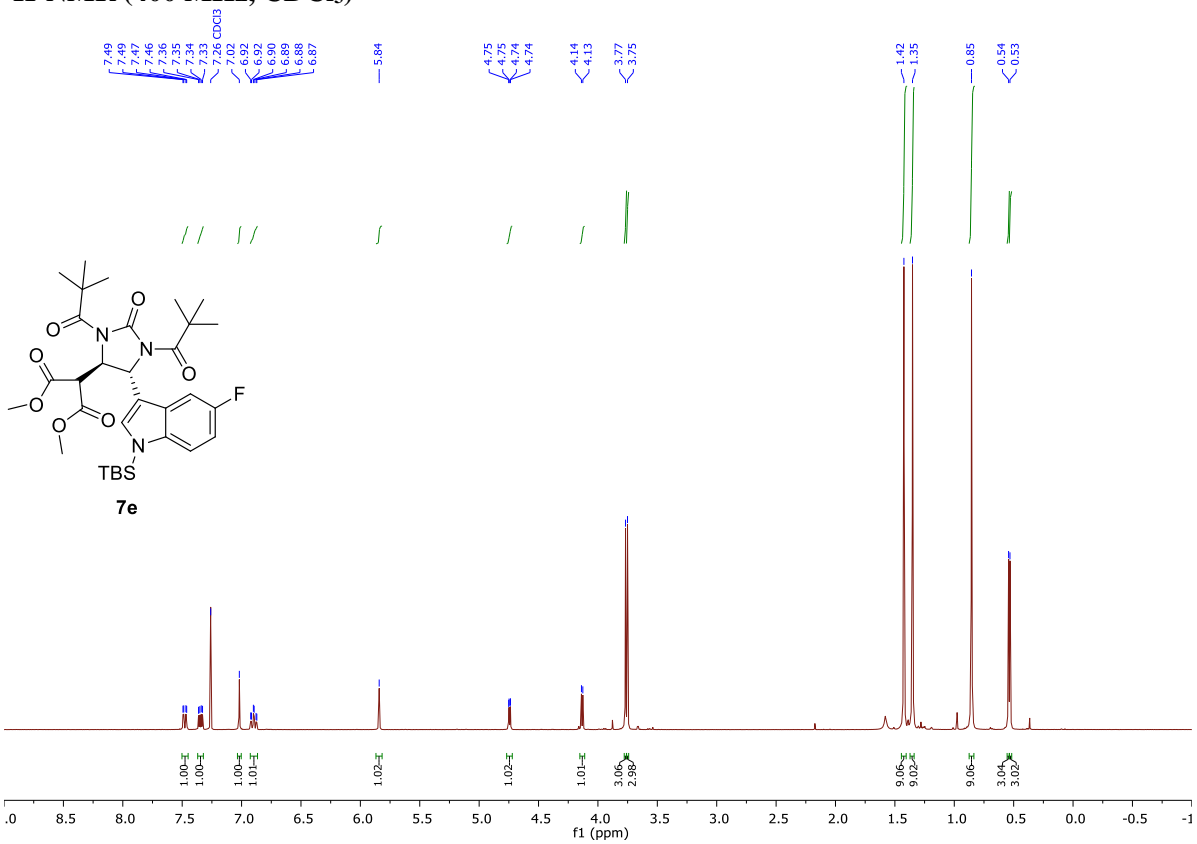




**7d**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-fluoro-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7e)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**

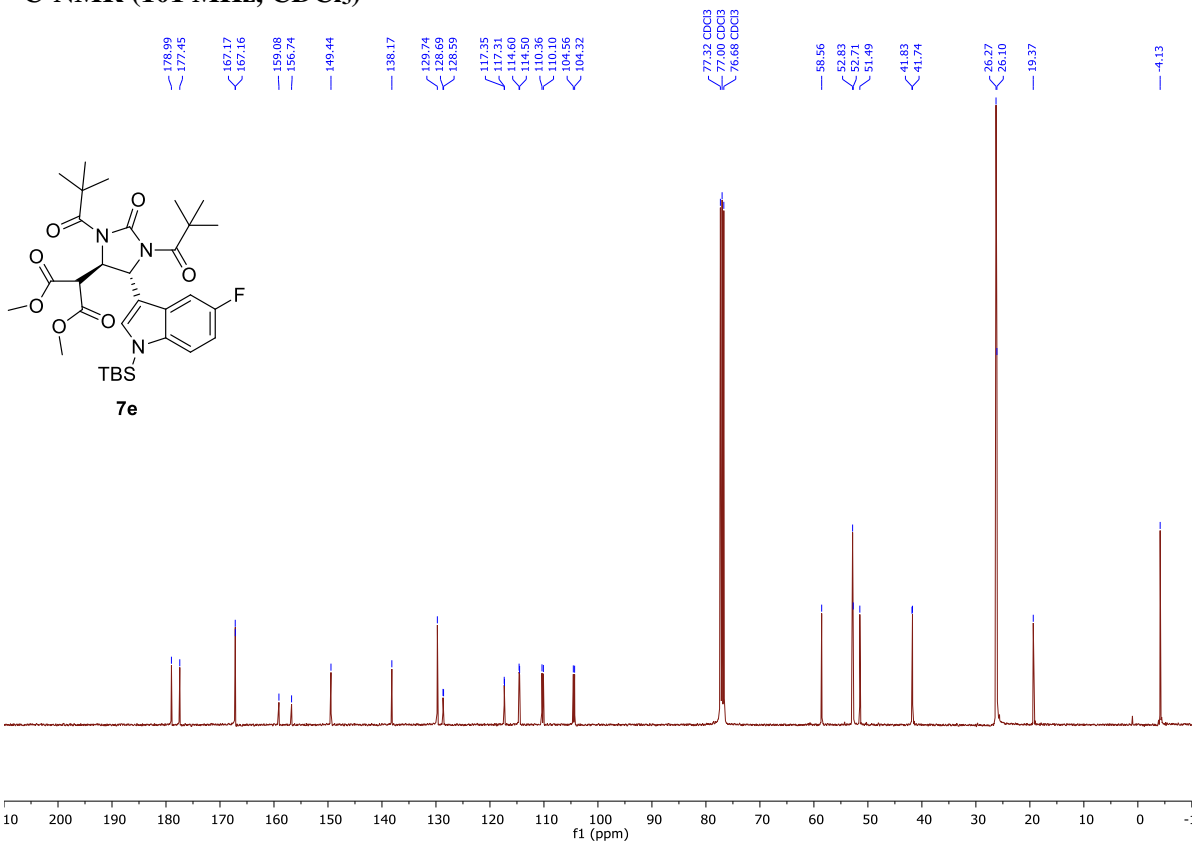






**7e**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

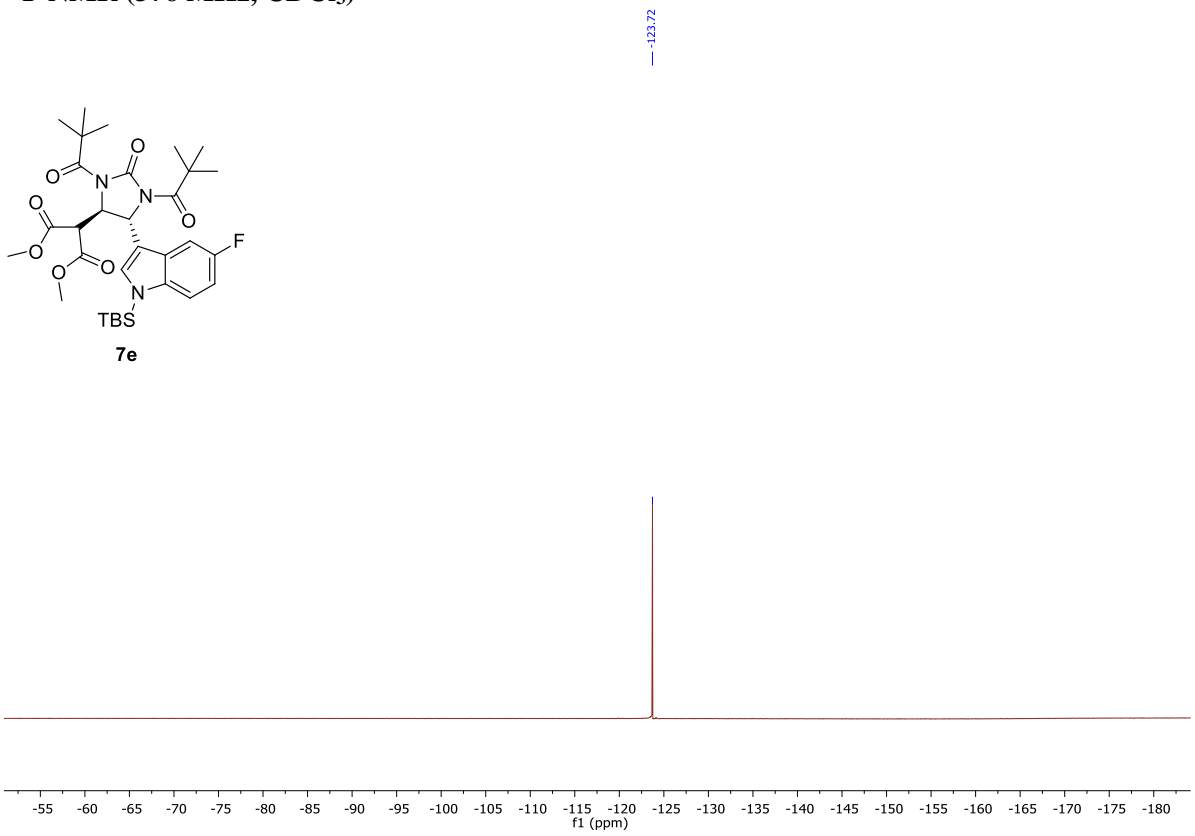






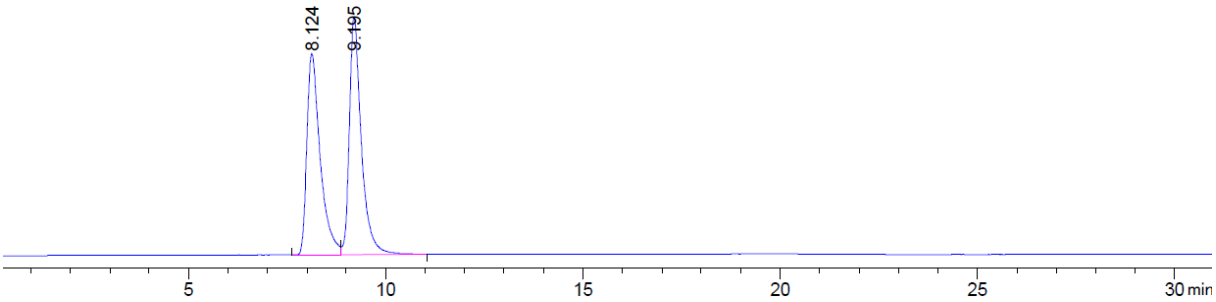
**7e**

**$^{19}$F NMR (376 MHz, $CDCl_3$)**

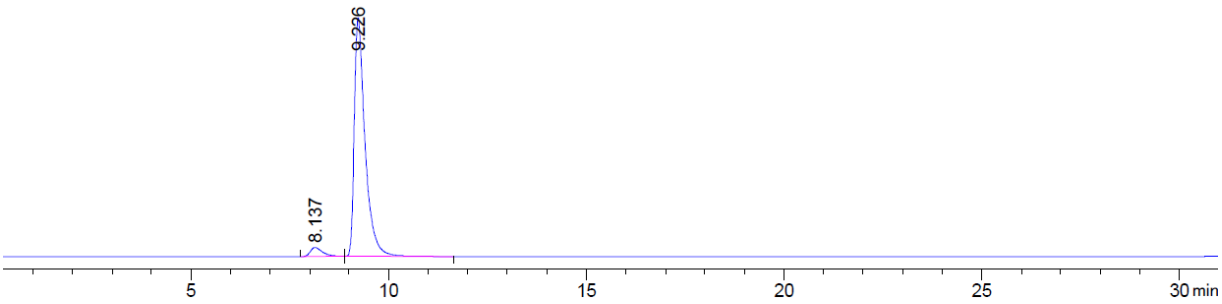



**7e**

**HPLC**

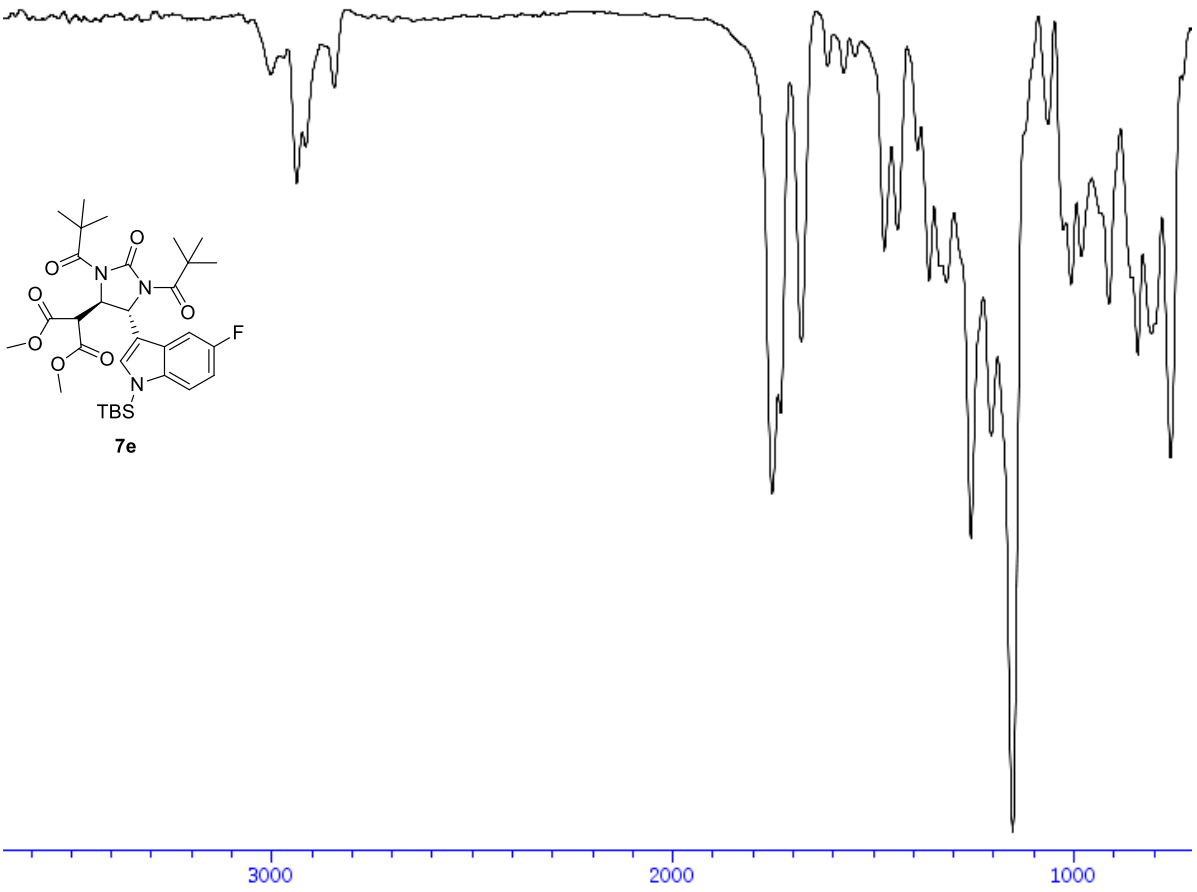



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 8.124 | BB | 0.3381 | 265.59882 | 11.82125 | 49.1117 |
| 2 | 9.195 | BB | 0.3011 | 275.20651 | 13.77244 | 50.8883 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 8.137 | BB | 0.3192 | 86.86350 | 4.09916 | 4.0819 |
| 2 | 9.226 | BB | 0.2800 | 2041.17041 | 108.23043 | 95.9181 |

**IR**



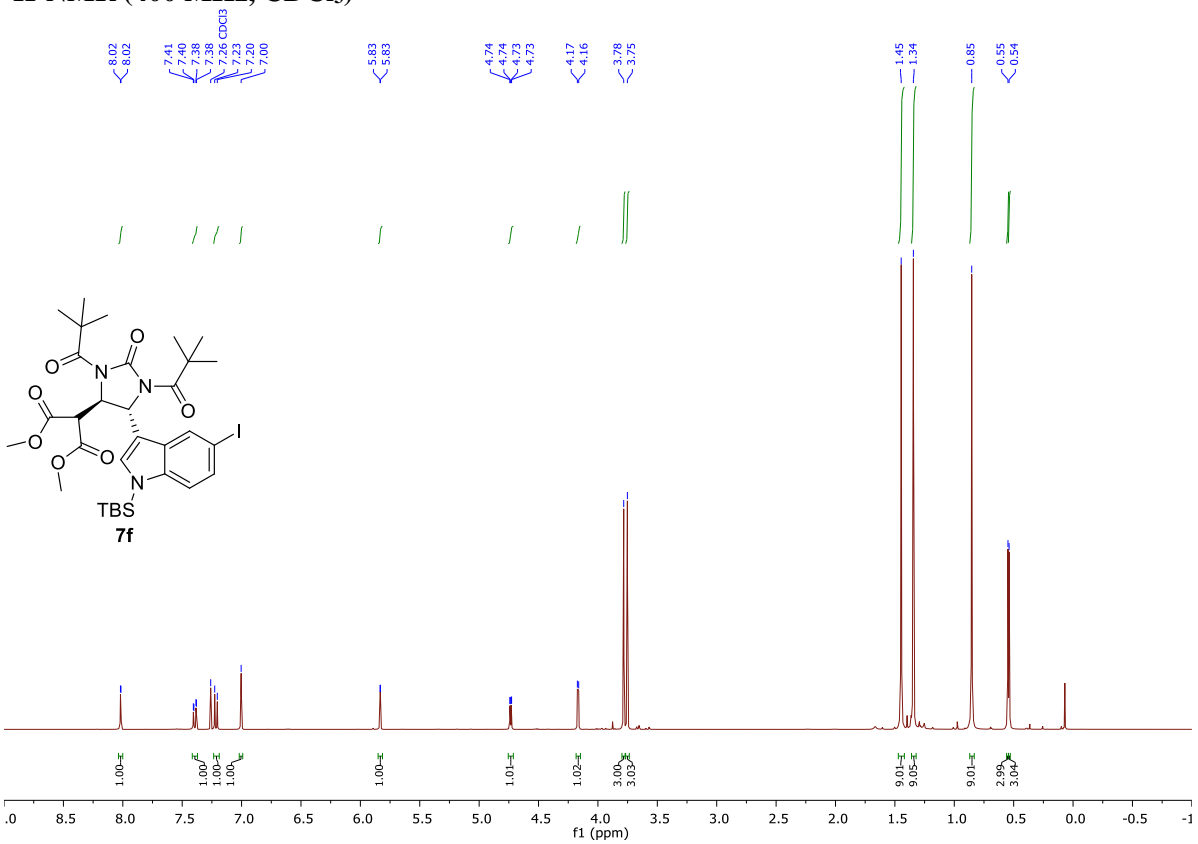




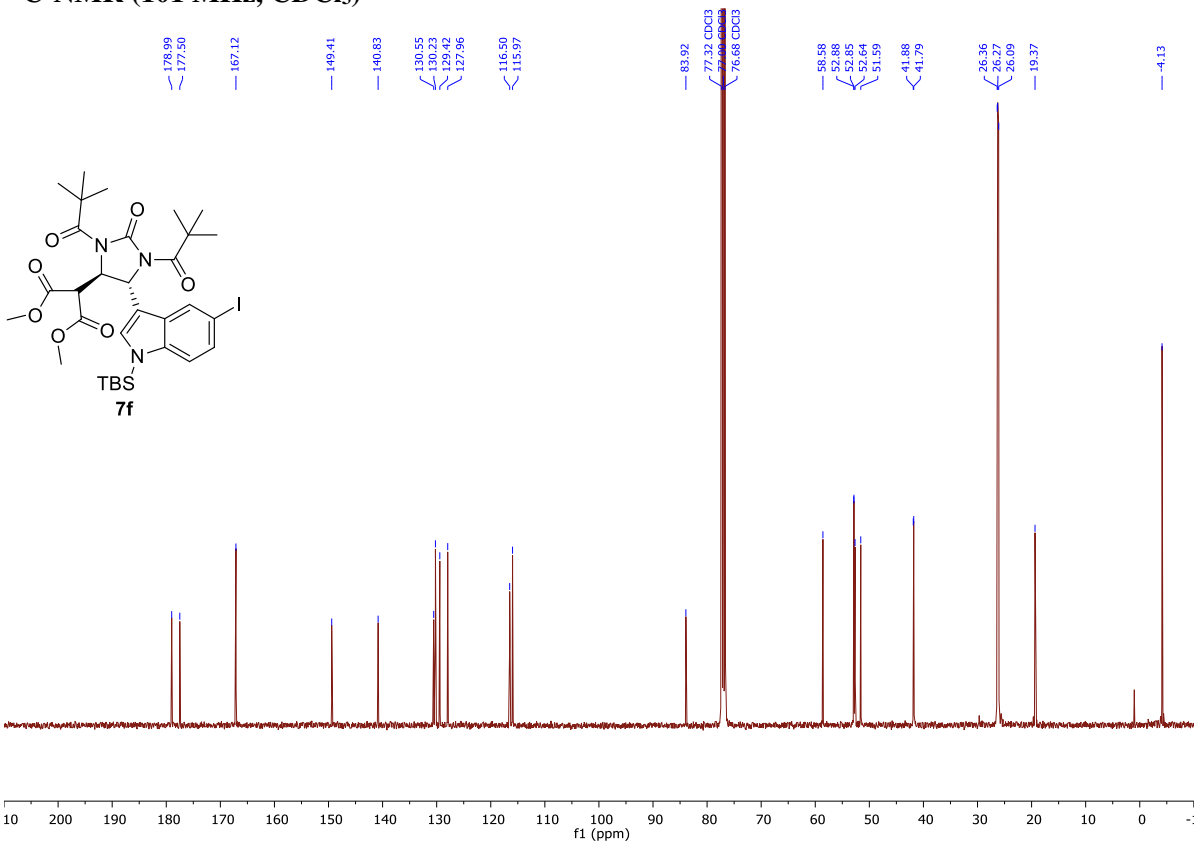
**7e**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-iodo-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7f)**

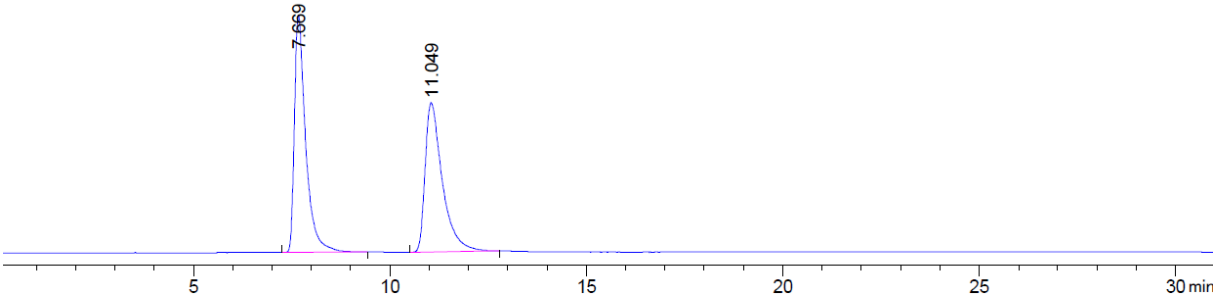
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



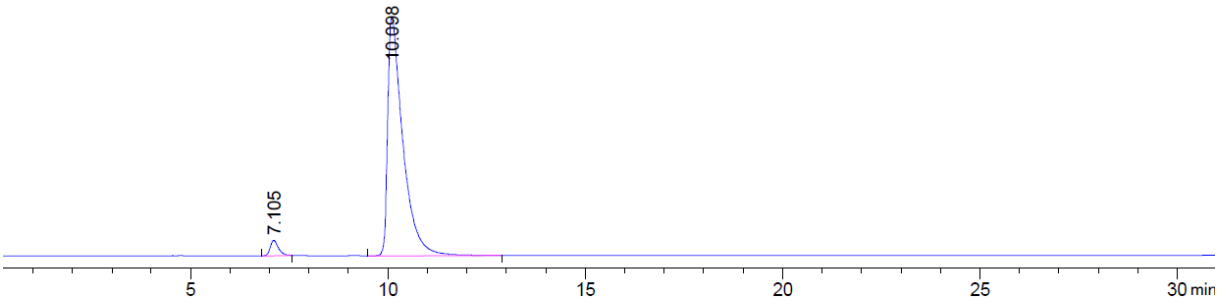

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

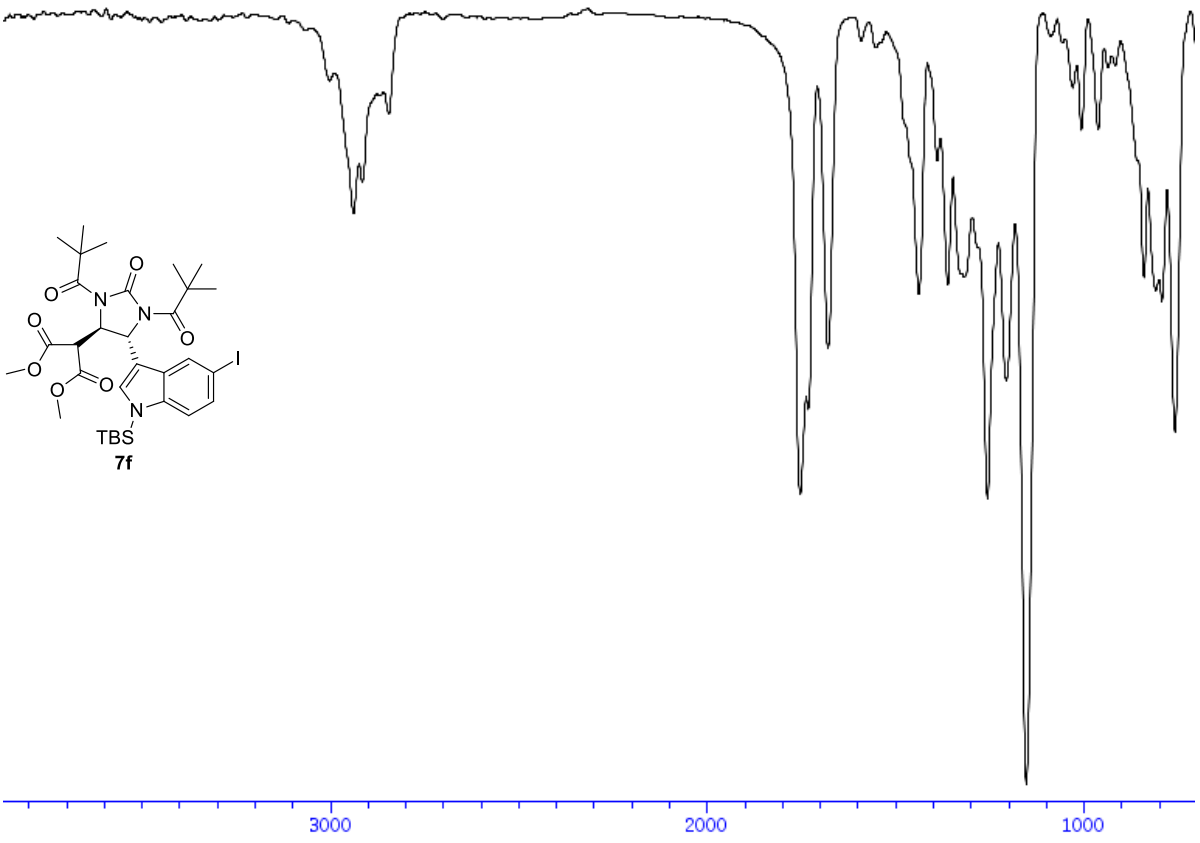



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.669 | BB | 0.2964 | 964.52948 | 47.99747 | 51.0310 |
| 2 | 11.049 | BB | 0.4520 | 925.55603 | 30.33042 | 48.9690 |



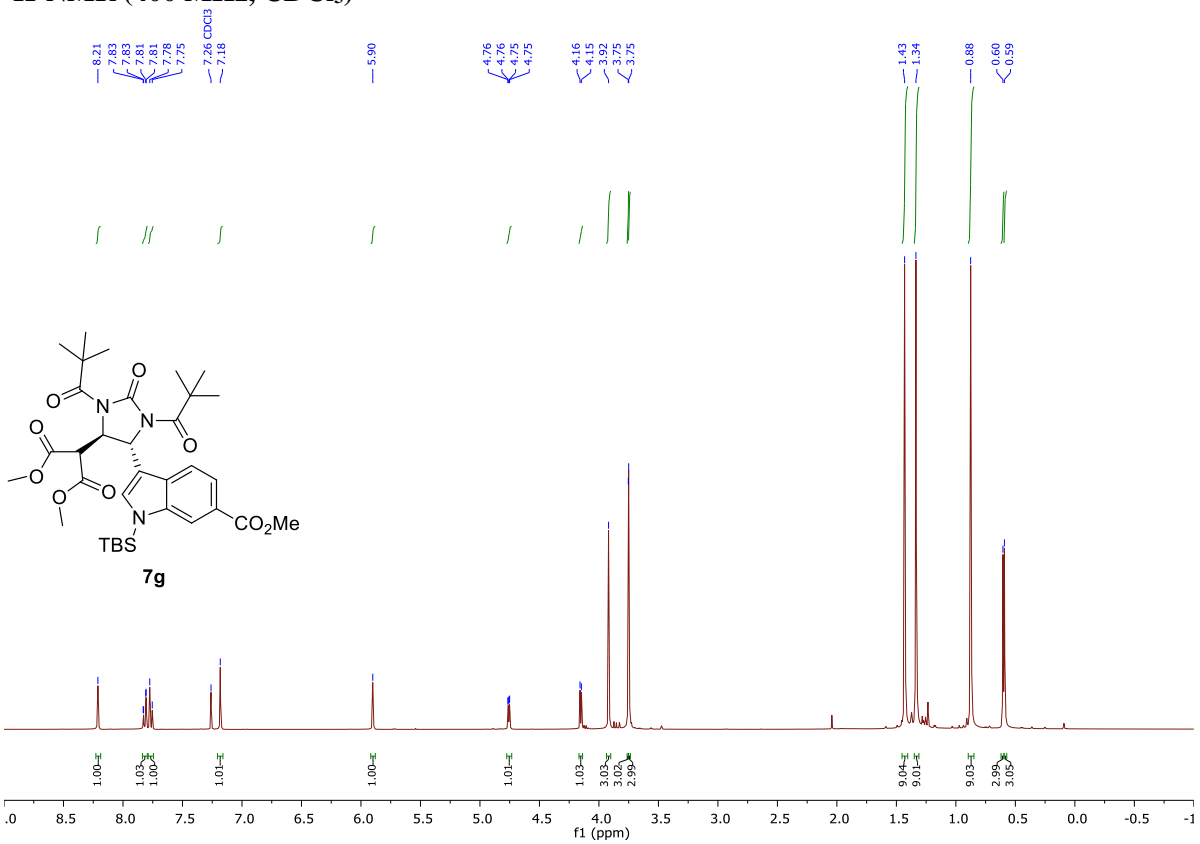

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.105 | BB | 0.2174 | 171.00633 | 11.91986 | 3.3194 |
| 2 | 10.098 | BB | 0.3886 | 4980.64990 | 185.87810 | 96.6806 |

**IR**



**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-(methoxycarbonyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7g)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**

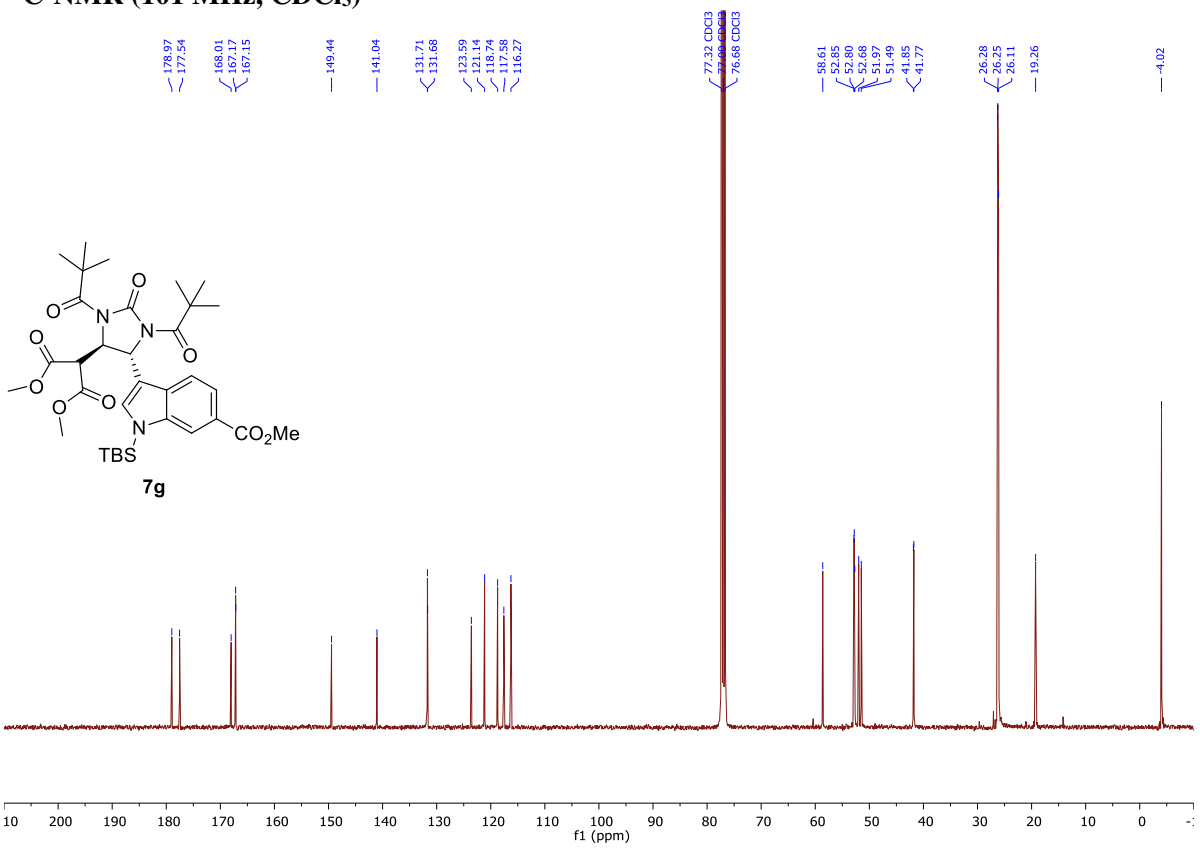






**7g**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

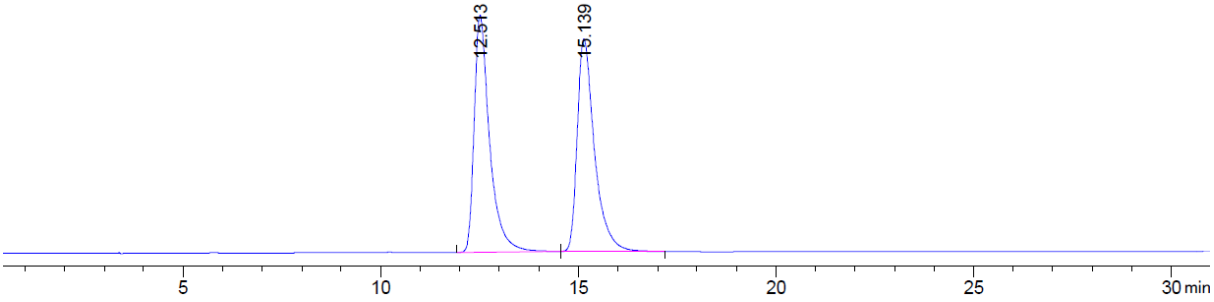




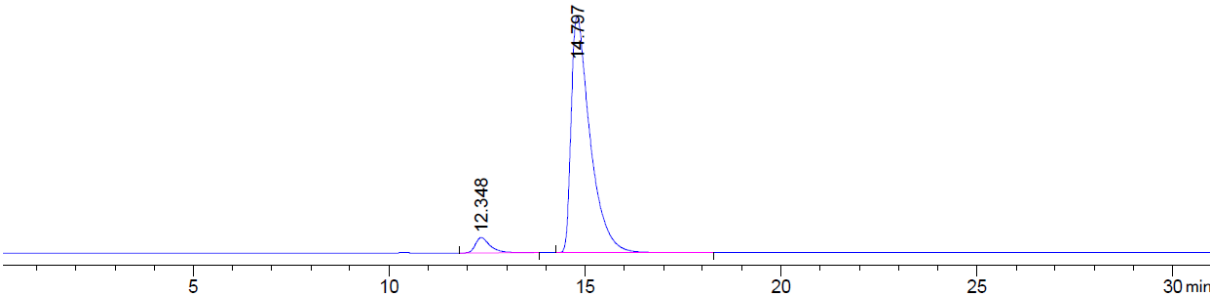


**7g**

**HPLC**

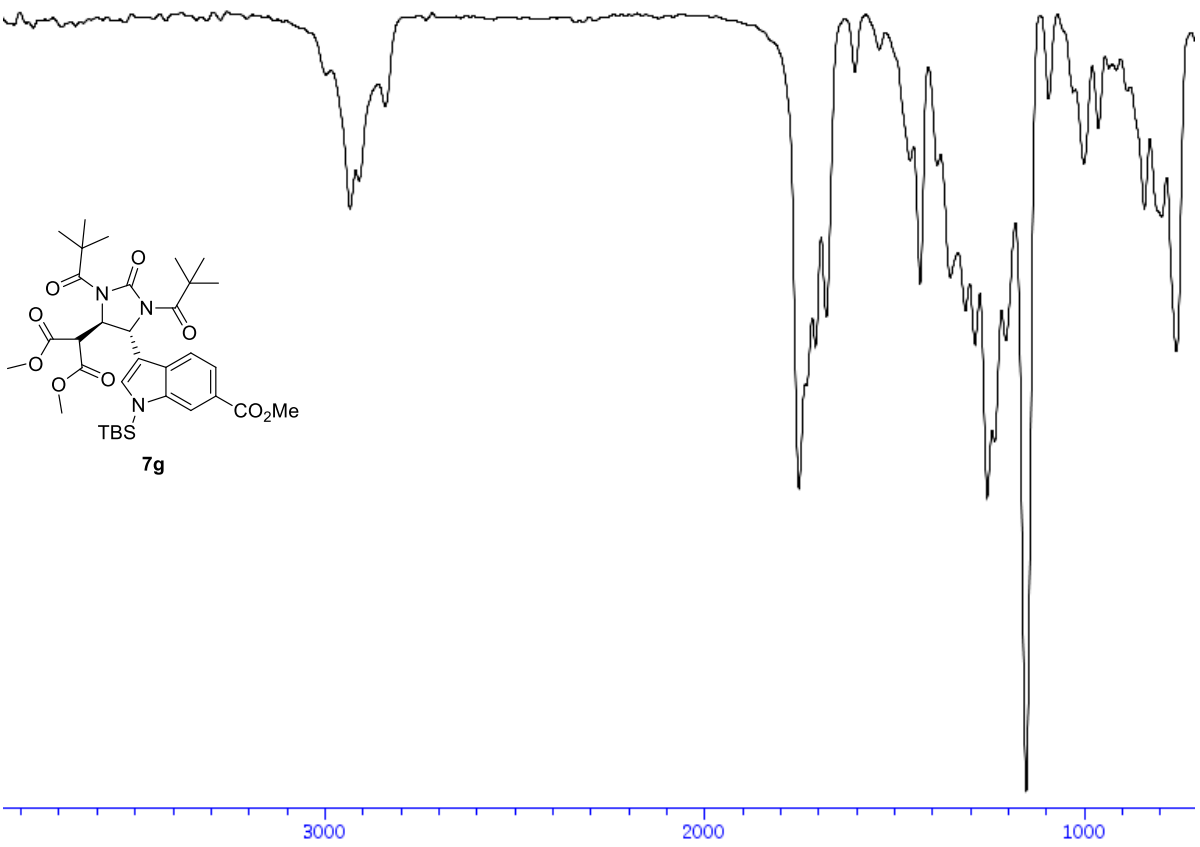



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.513 | BB | 0.4019 | 829.11749 | 30.61956 | 49.9670 |
| 2 | 15.139 | BB | 0.4549 | 830.21429 | 27.44681 | 50.0330 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.348 | BB | 0.3962 | 244.50339 | 9.19690 | 4.8755 |
| 2 | 14.797 | BB | 0.4971 | 4770.45361 | 141.57822 | 95.1245 |

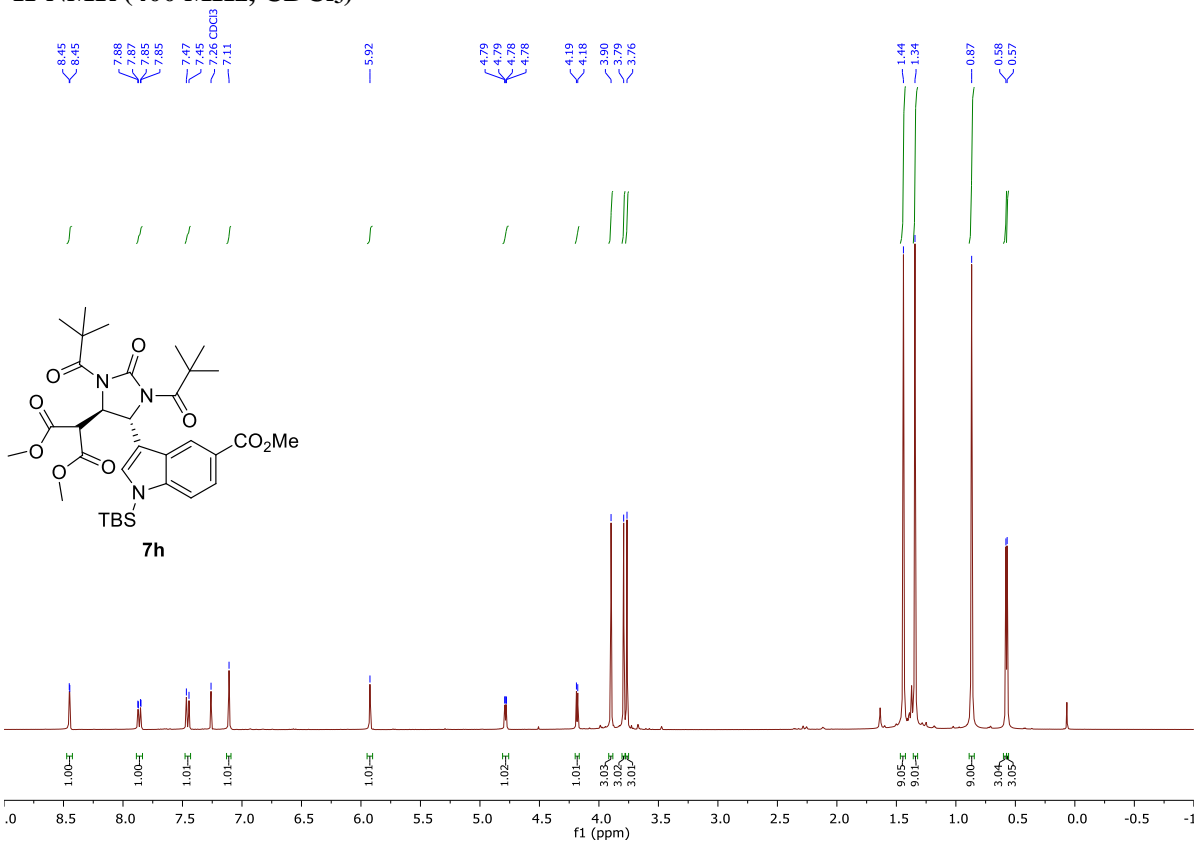
**IR**



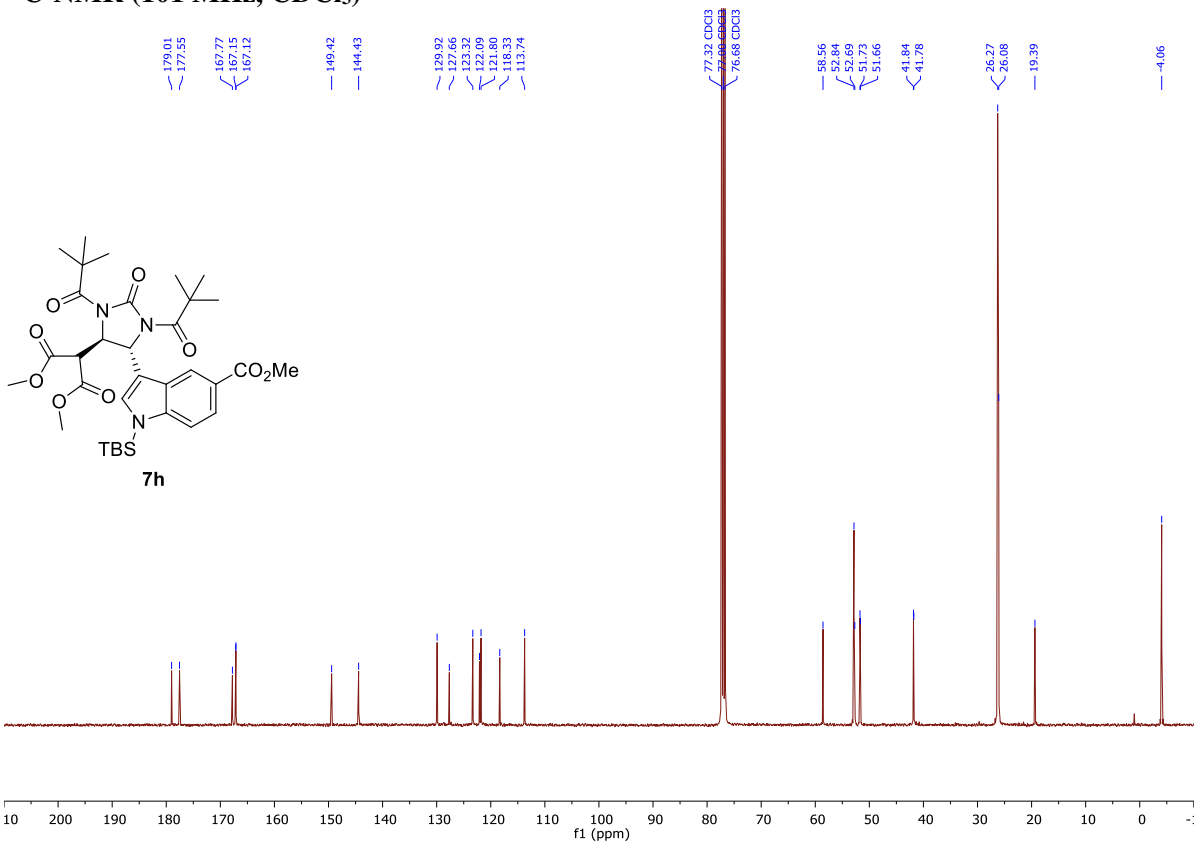

**7g**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-(methoxycarbonyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7h)**

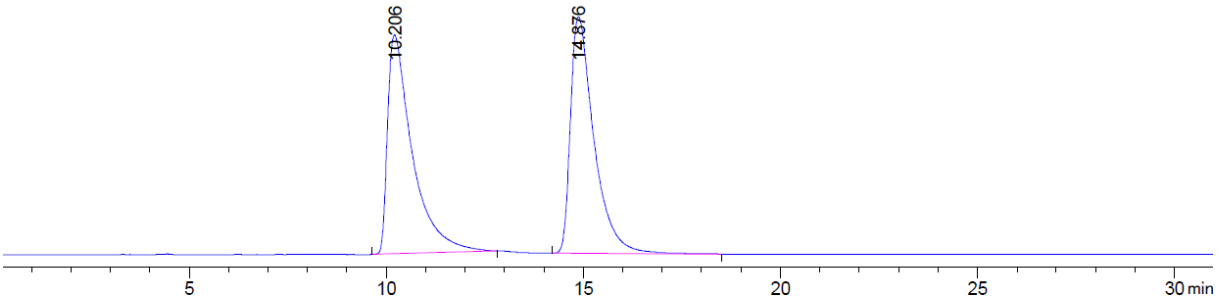
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



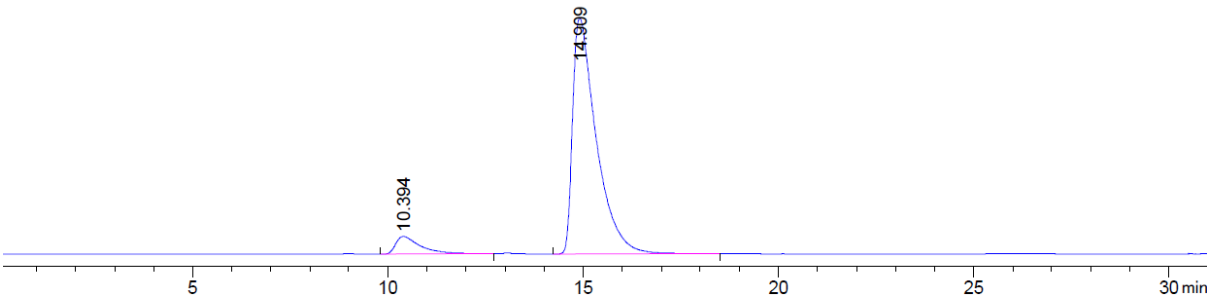

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

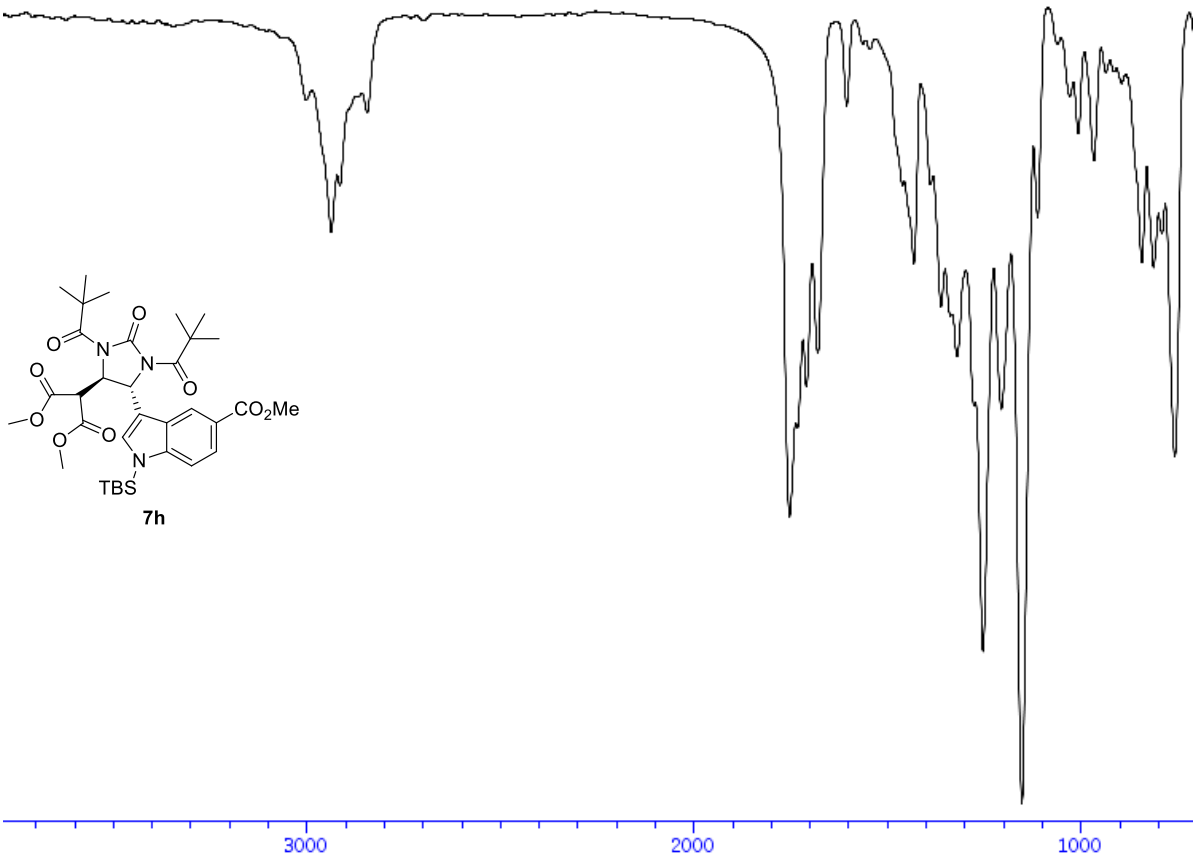



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.206 | BB | 0.6360 | 1644.50745 | 37.61931 | 49.4411 |
| 2 | 14.876 | BB | 0.6170 | 1681.68542 | 40.61745 | 50.5589 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 10.394 | BB | 0.6441 | 386.09814 | 8.76246 | 7.1864 |
| 2 | 14.908 | BB | 0.6218 | 4986.51953 | 118.29451 | 92.8136 |

**IR**



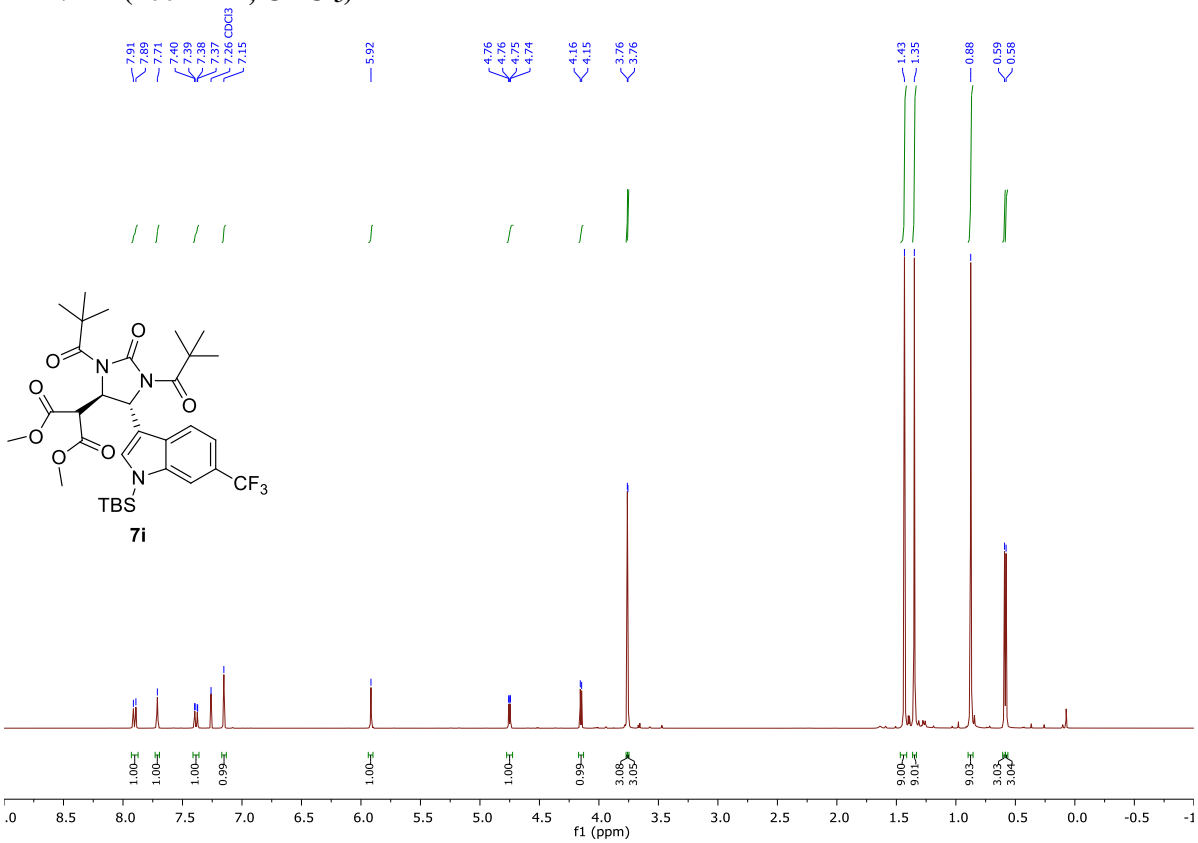




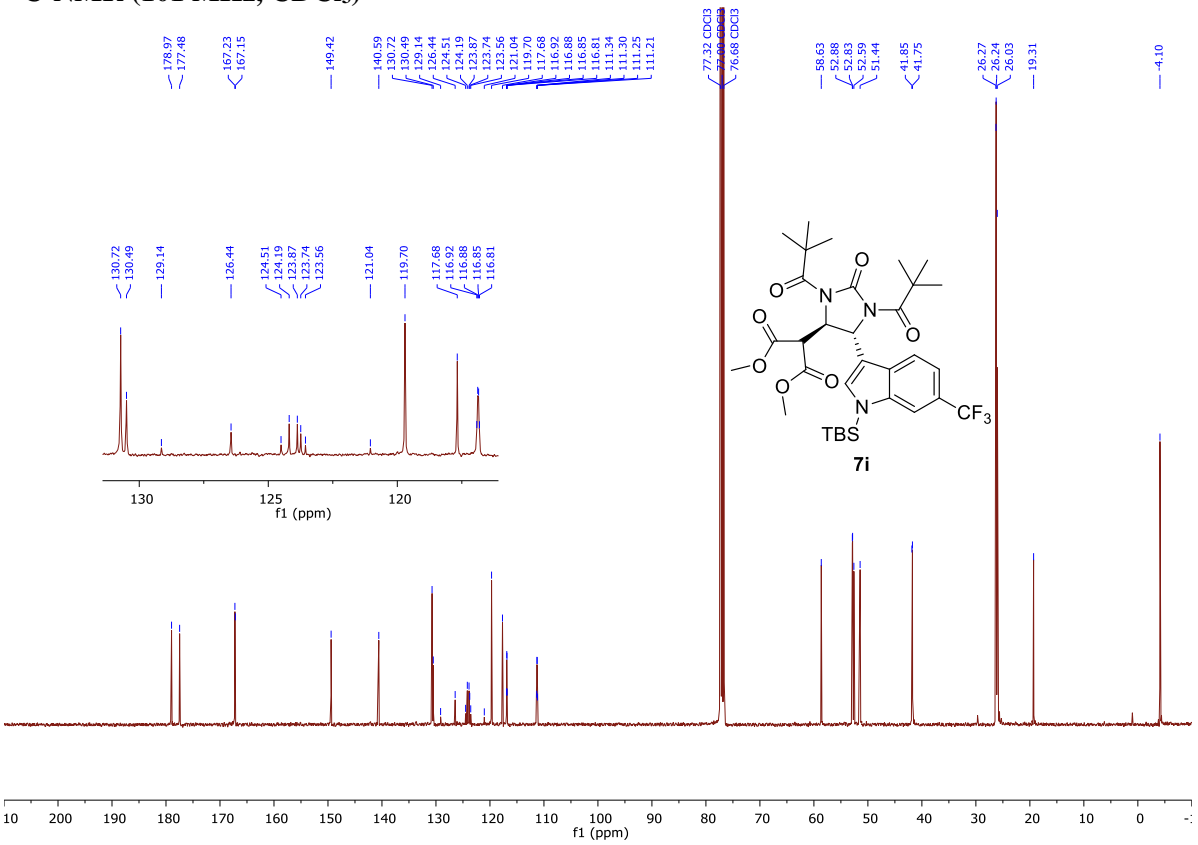
**7h**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-(trifluoromethyl)-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7i)**

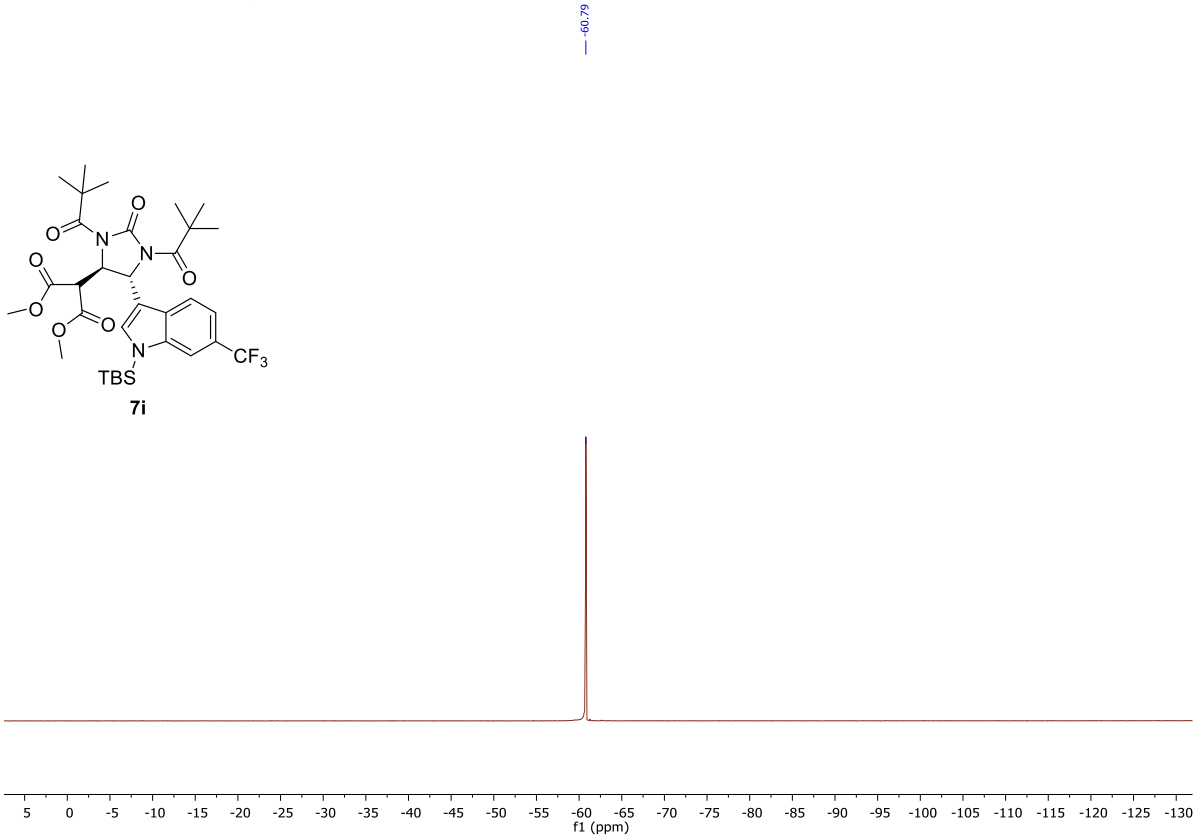
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



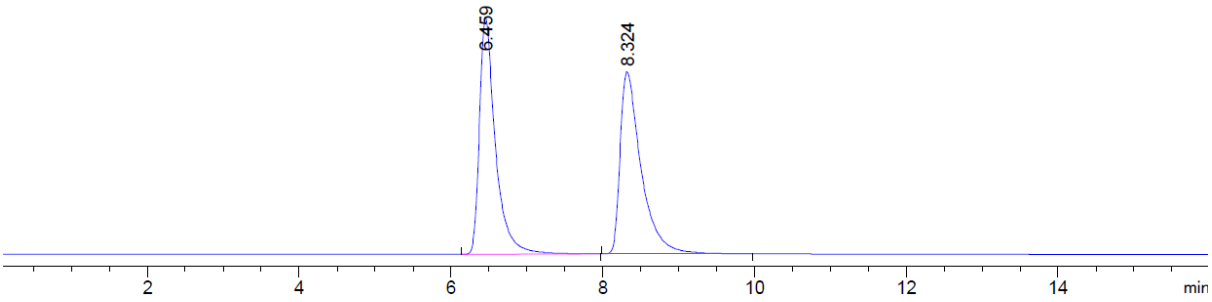

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



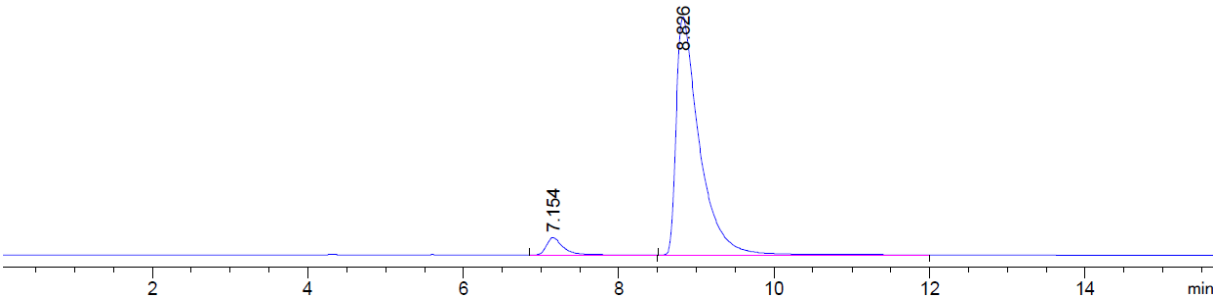
**$^{19}$F NMR (376 MHz, $CDCl_3$)**



**HPLC**

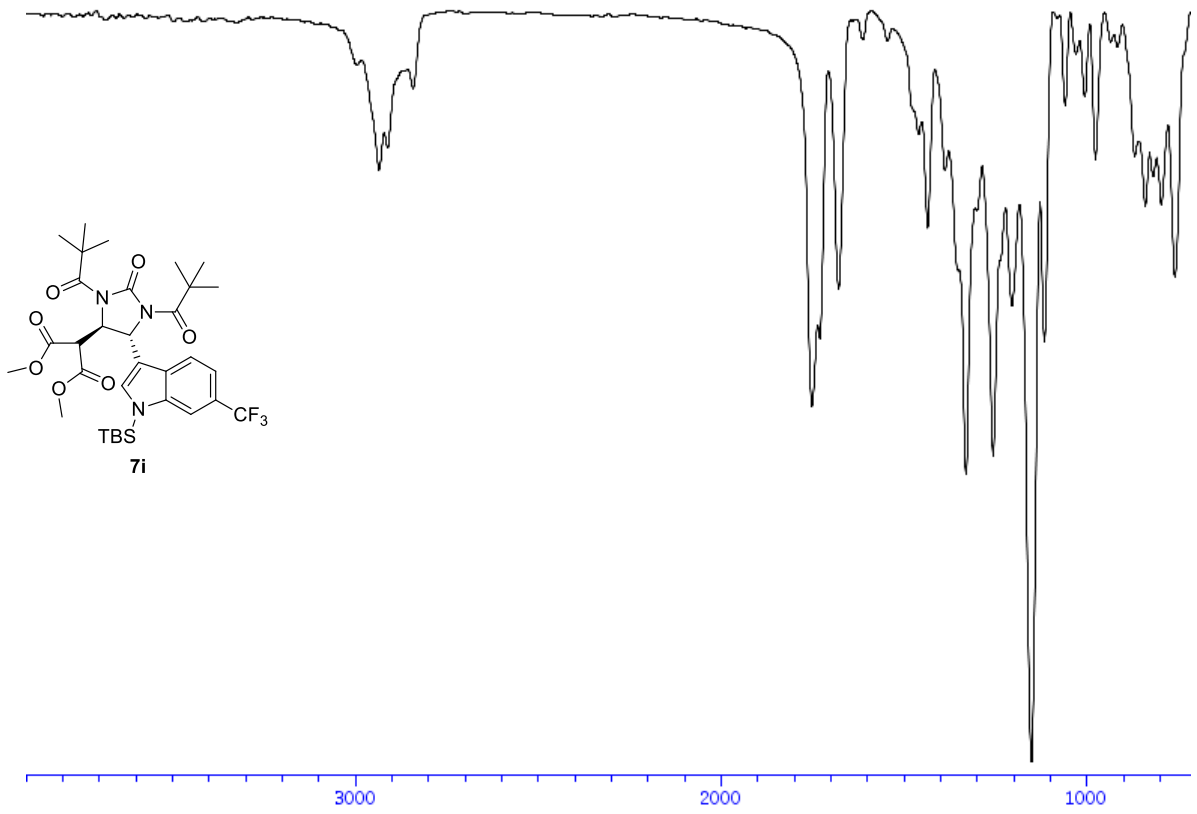



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.459 | BB | 0.2167 | 956.38446 | 65.38104 | 49.8848 |
| 2 | 8.324 | BB | 0.2832 | 960.80029 | 50.21458 | 50.1152 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.154 | BB | 0.2205 | 163.94270 | 10.96255 | 4.9705 |
| 2 | 8.826 | BB | 0.3037 | 3134.36255 | 151.32201 | 95.0295 |

**IR**



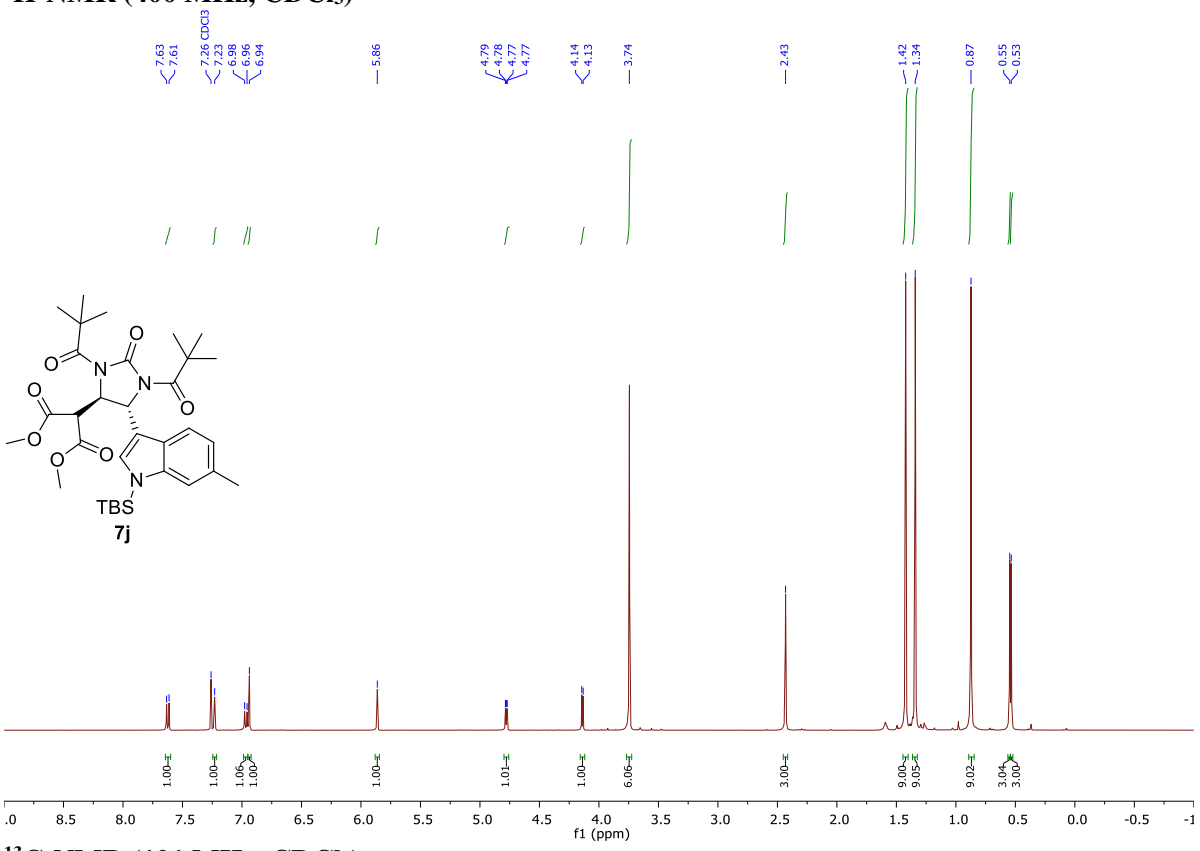




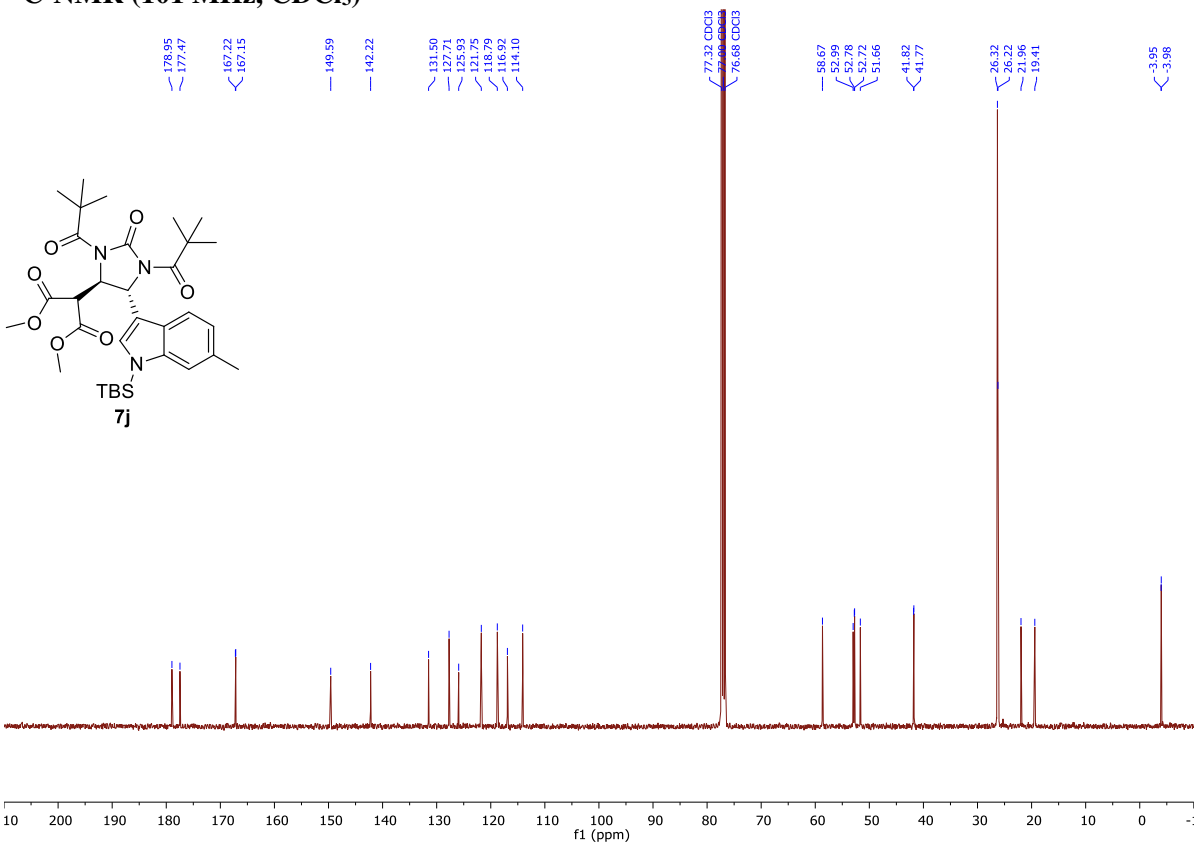
**7i**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-methyl-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7j)**

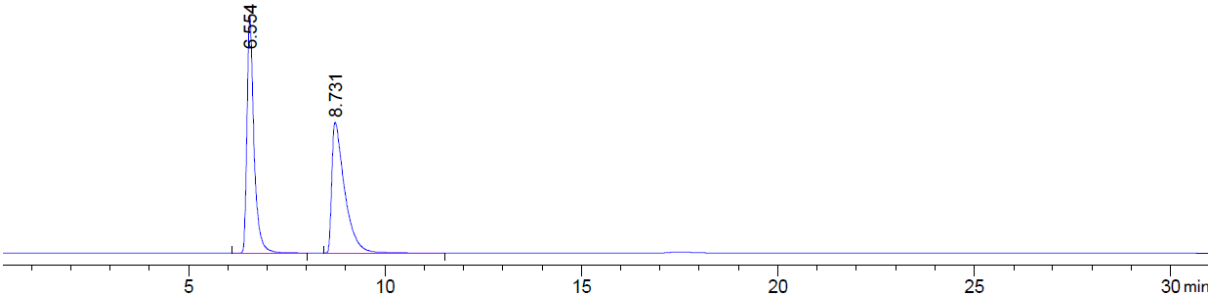
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



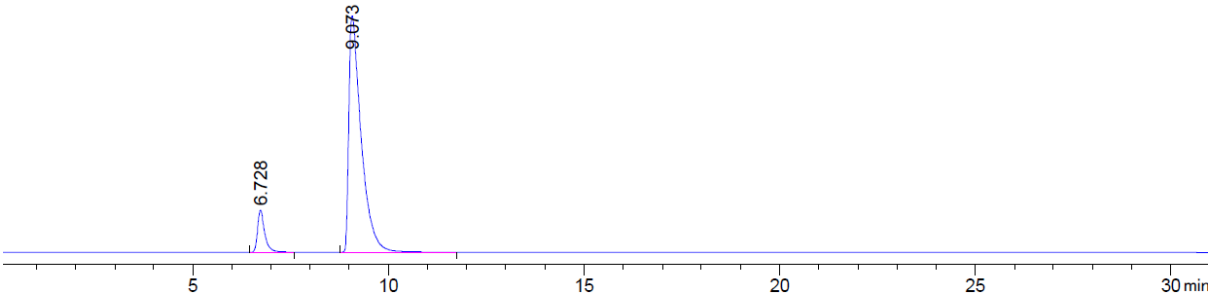

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

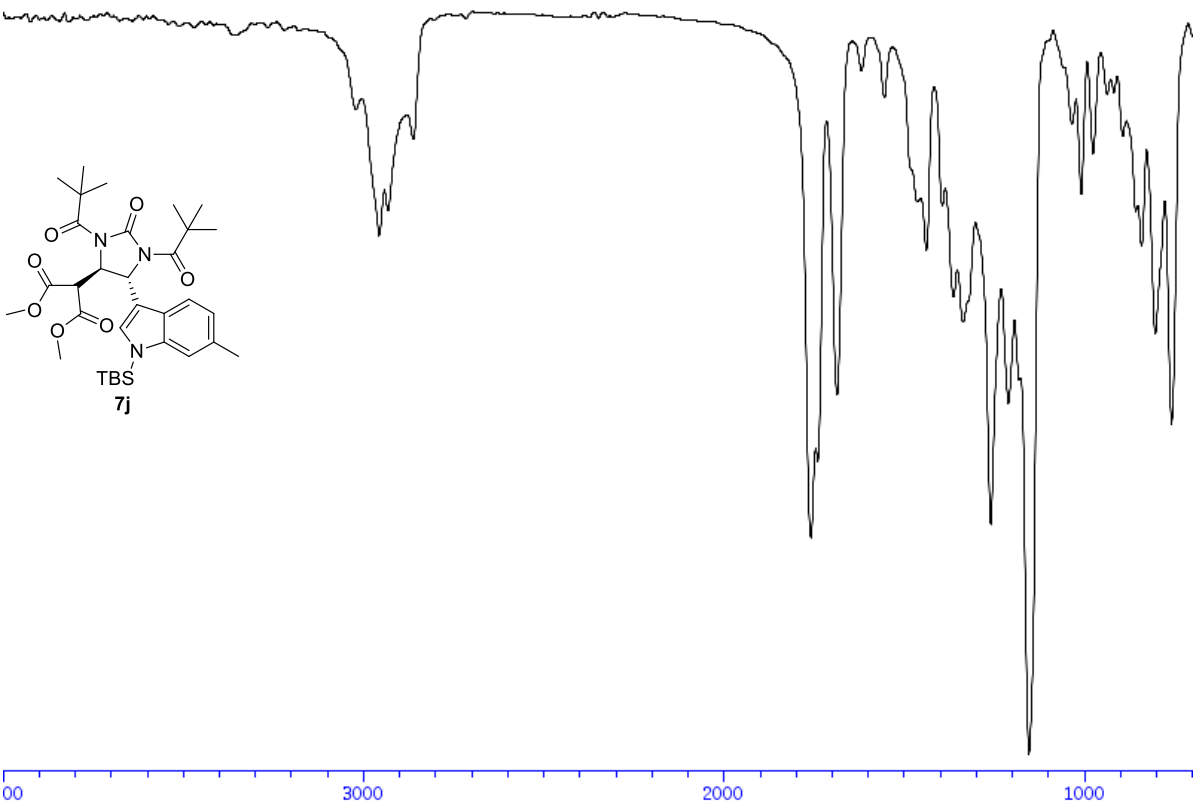



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.554 | BB | 0.1850 | 2565.46973 | 206.34976 | 49.8906 |
| 2 | 8.731 | BB | 0.3317 | 2576.72021 | 113.16083 | 50.1094 |



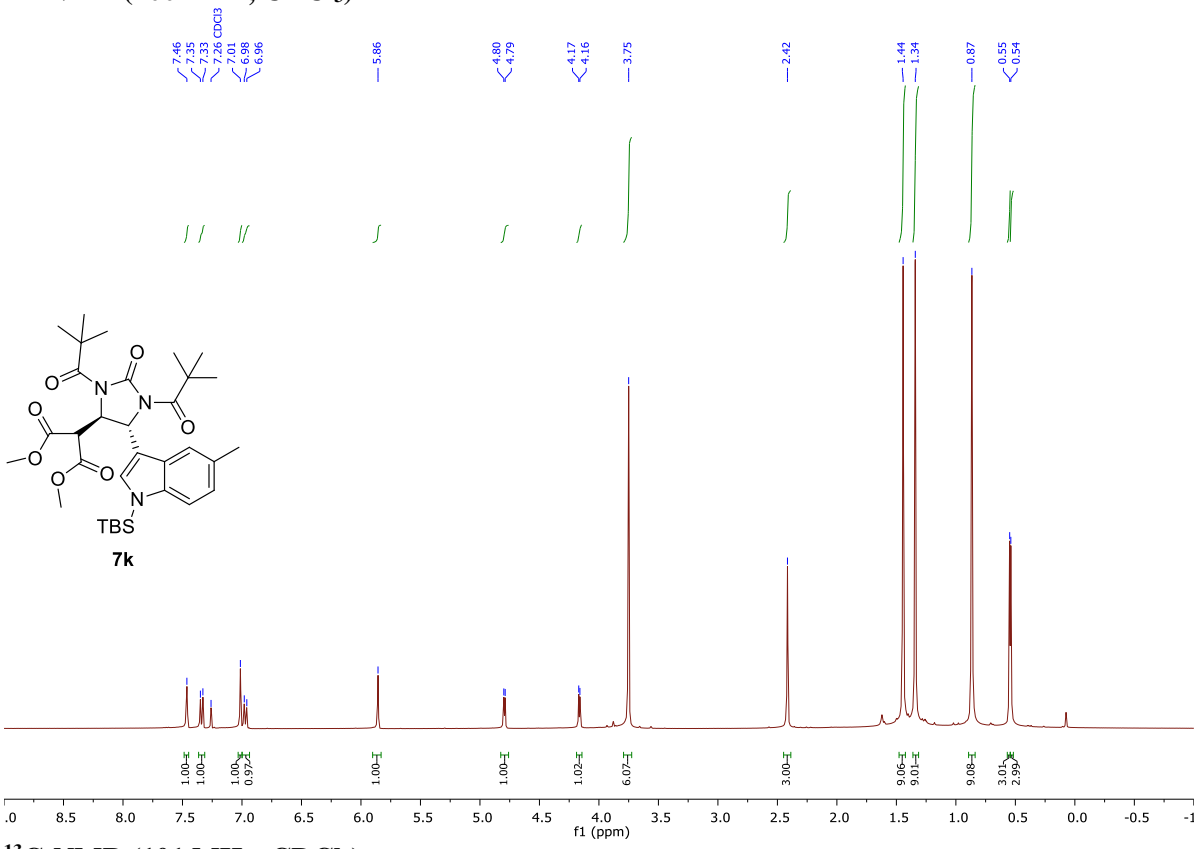

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.728 | BB | 0.1888 | 301.38214 | 23.94639 | 9.2705 |
| 2 | 9.073 | BB | 0.3242 | 2949.60498 | 134.32072 | 90.7295 |

**IR**

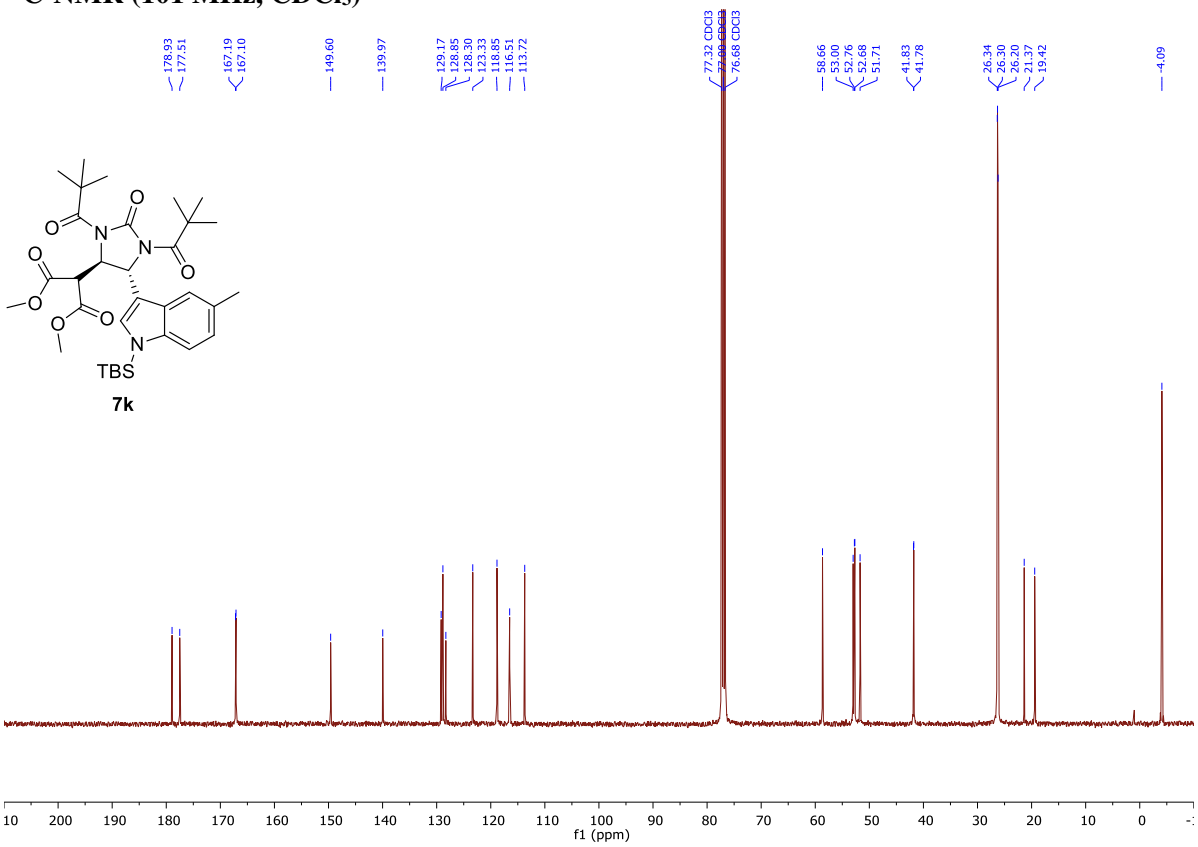


**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-5-methyl-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7k)**

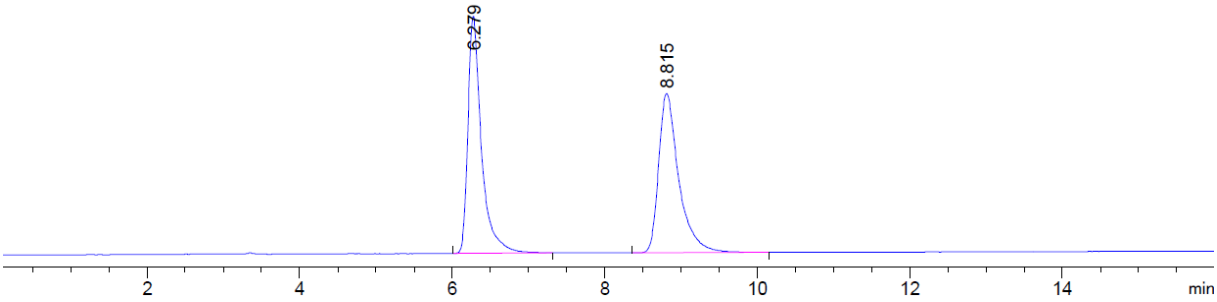
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



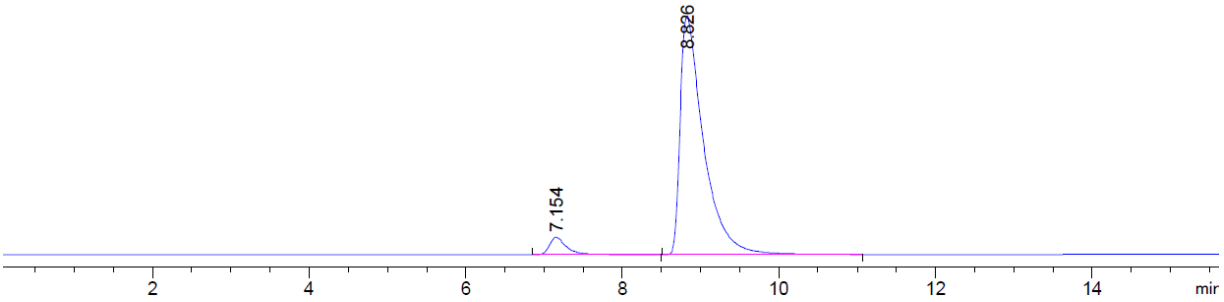

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

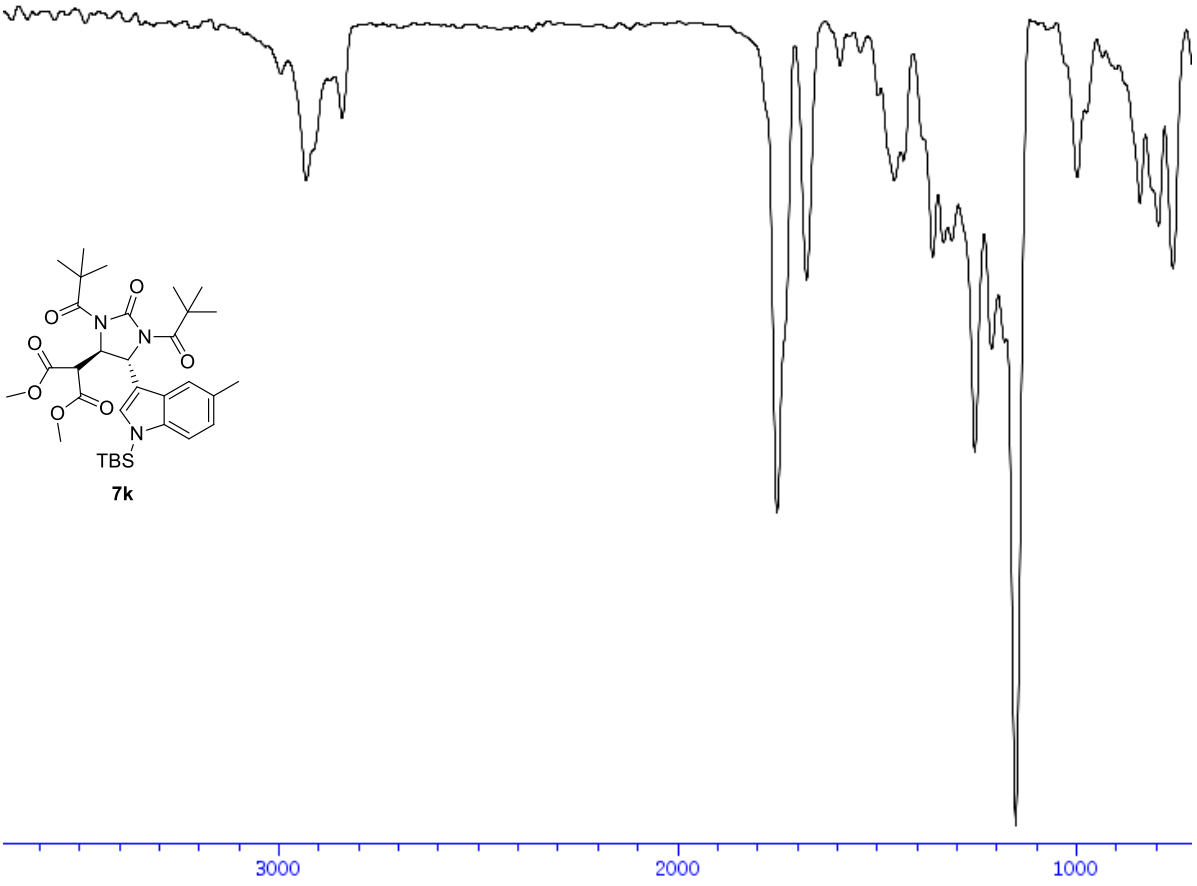



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.279 | BB | 0.1814 | 172.03889 | 13.99507 | 49.9280 |
| 2 | 8.815 | BB | 0.2743 | 172.53520 | 9.39392 | 50.0720 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.154 | BB | 0.2205 | 163.94270 | 10.96255 | 4.9705 |
| 2 | 8.826 | BB | 0.3037 | 3134.36255 | 151.32201 | 95.0295 |

**IR**



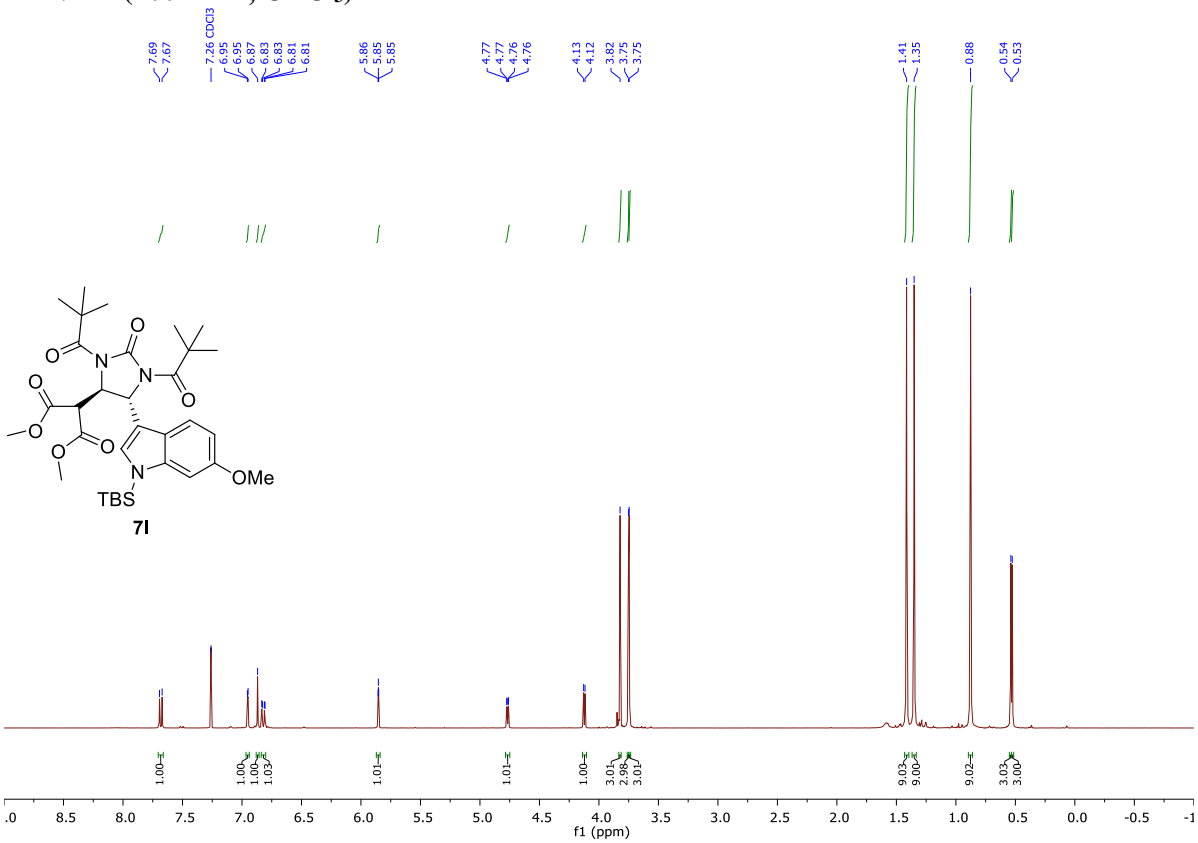




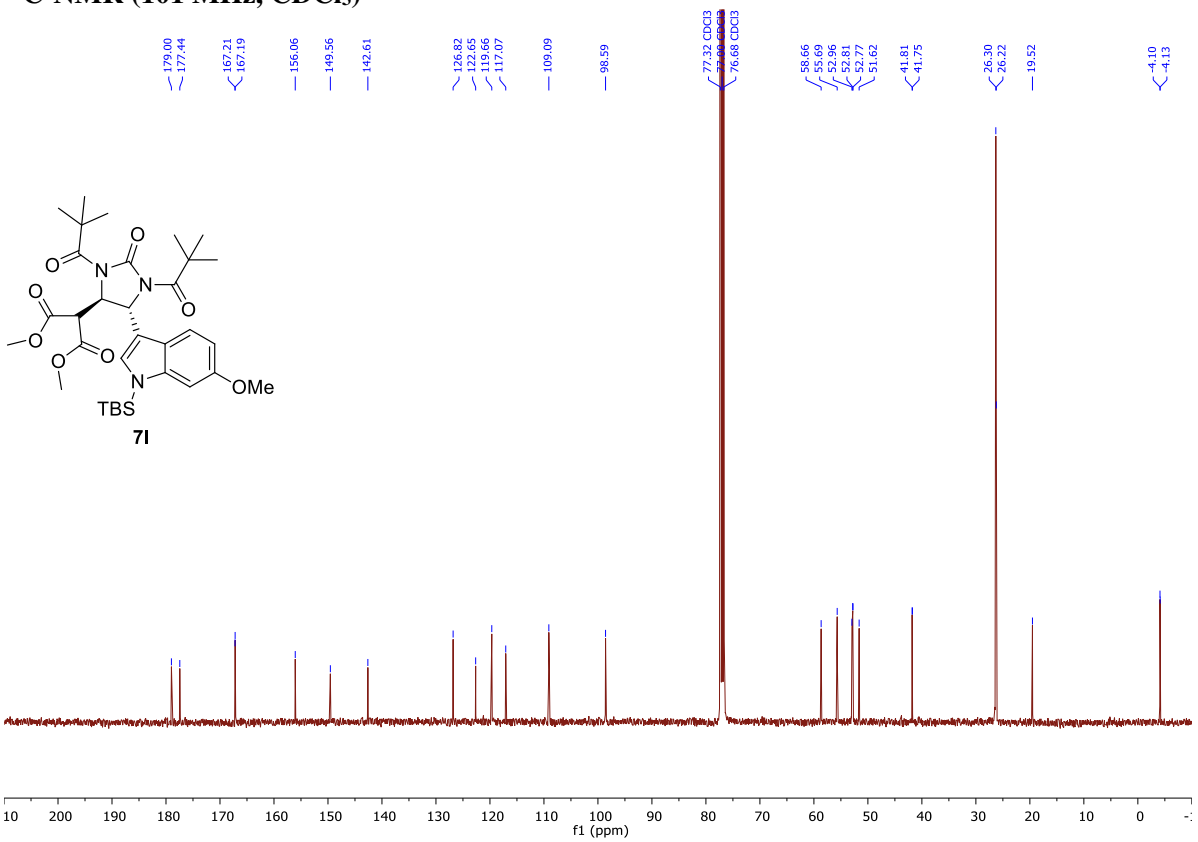
**7k**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-methoxy-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7l)**

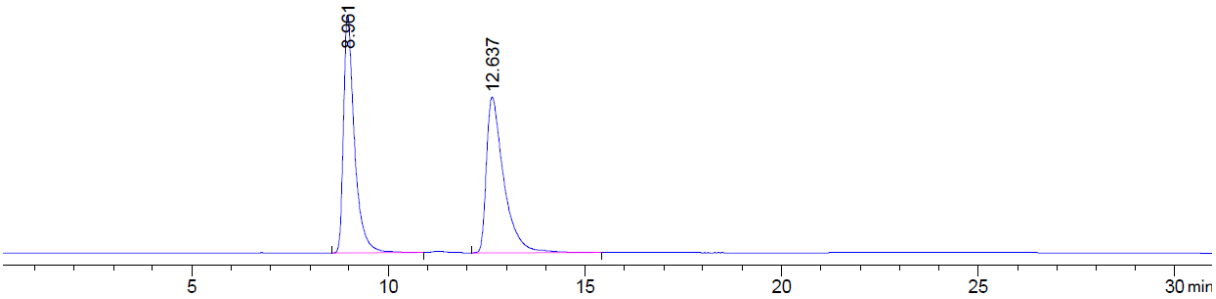
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



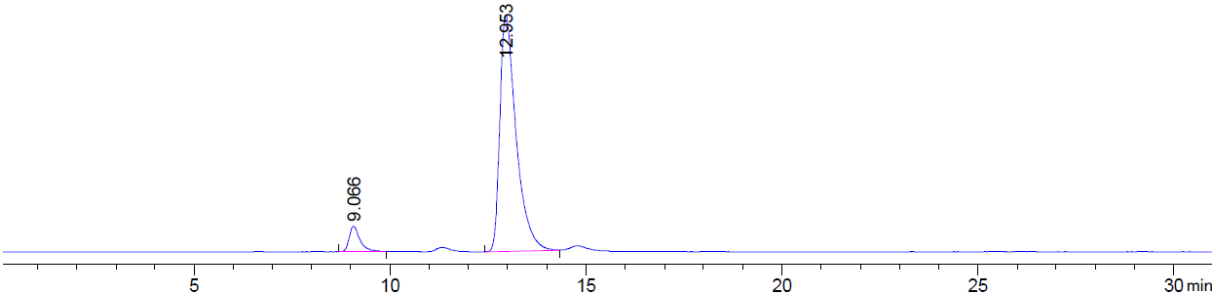

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

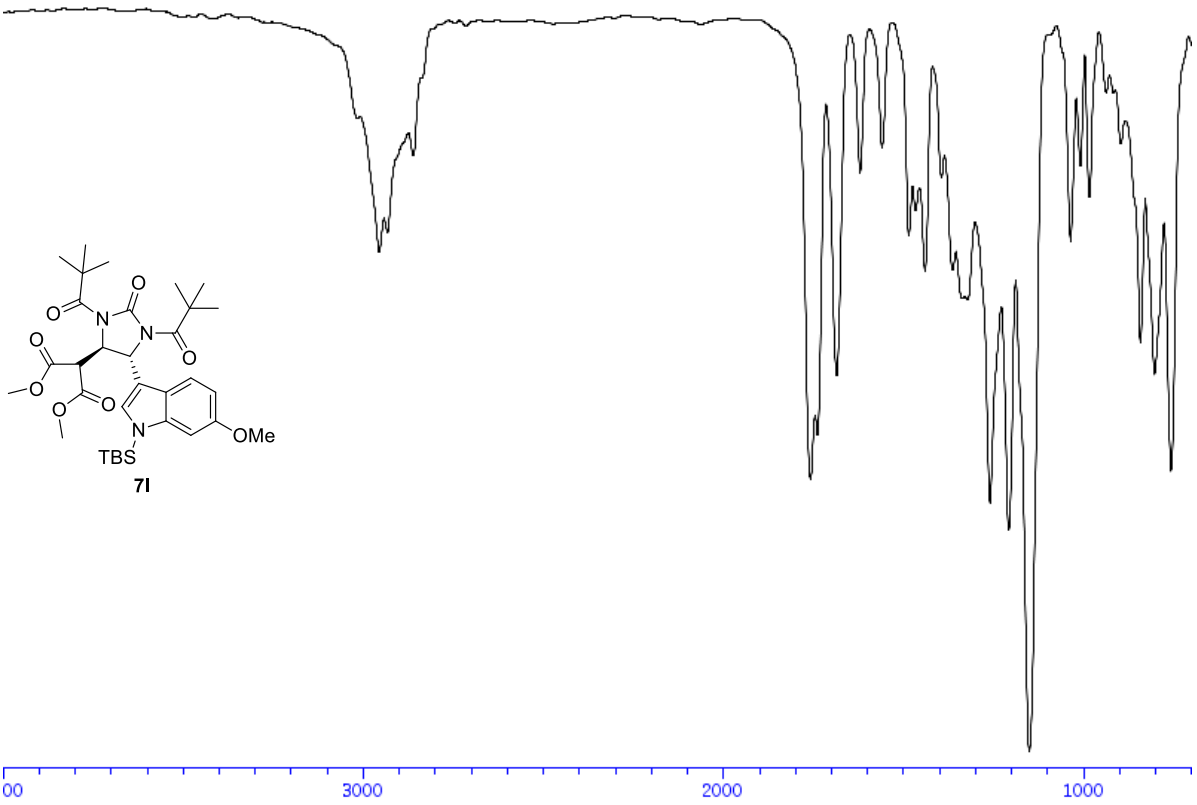



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 8.961 | BB | 0.2862 | 1095.87964 | 56.52717 | 49.1825 |
| 2 | 12.637 | BB | 0.4533 | 1132.31091 | 36.97139 | 50.8175 |



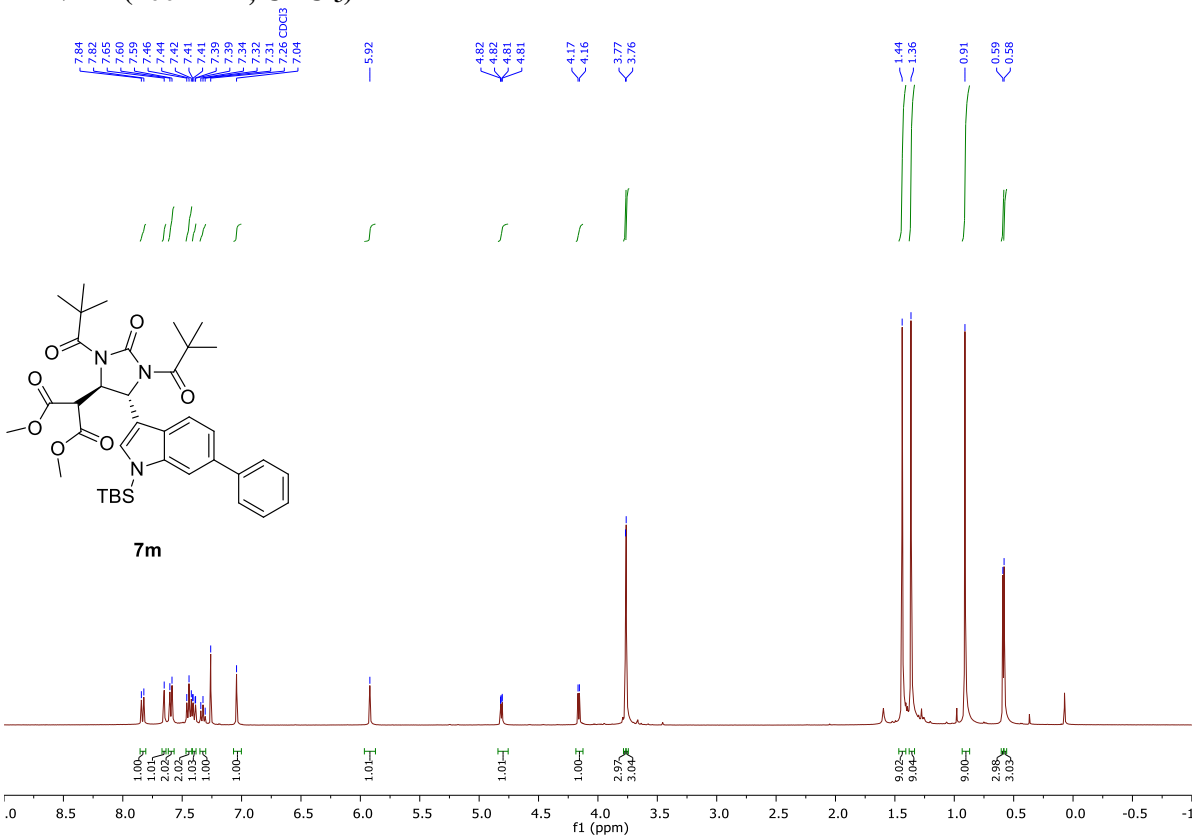

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.066 | BB | 0.2795 | 39.33647 | 2.07167 | 6.6039 |
| 2 | 12.953 | BB | 0.4297 | 556.31537 | 19.33605 | 93.3961 |

**IR**

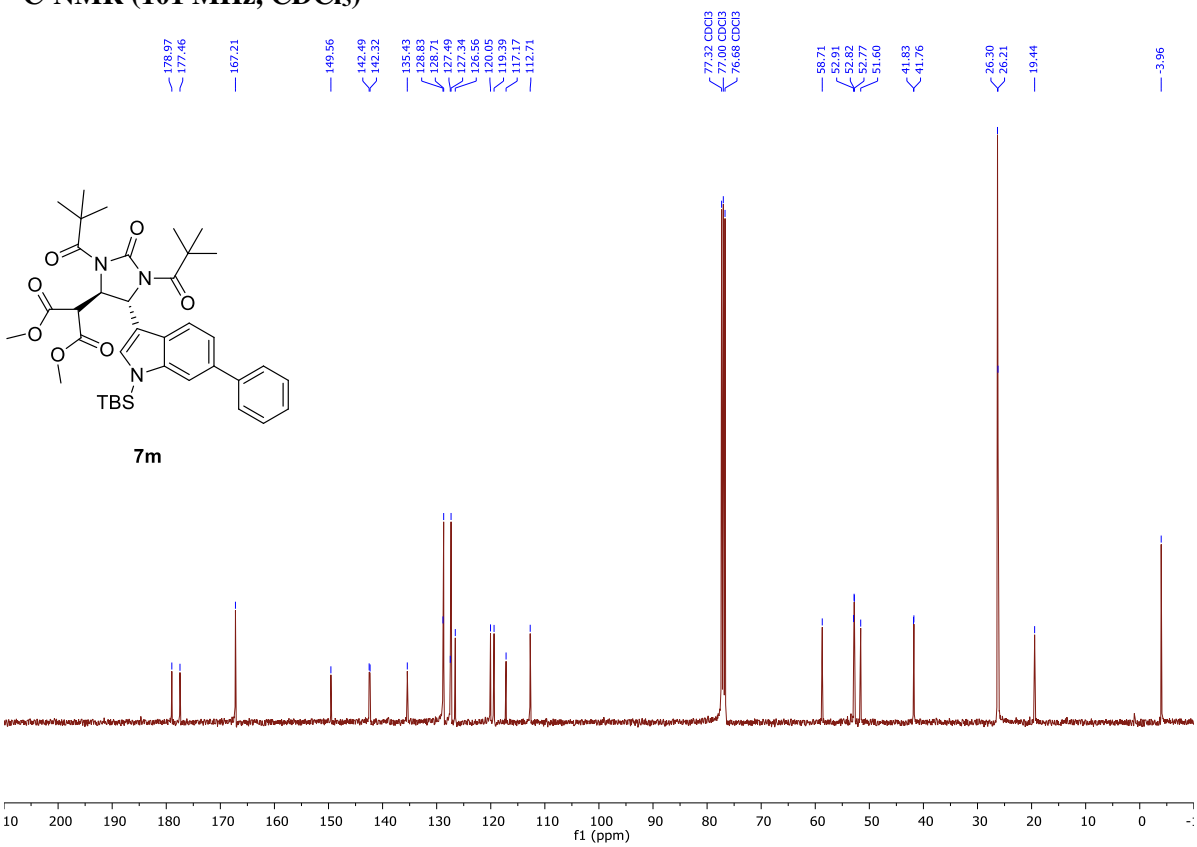


**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-6-phenyl-1H-indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7m)**

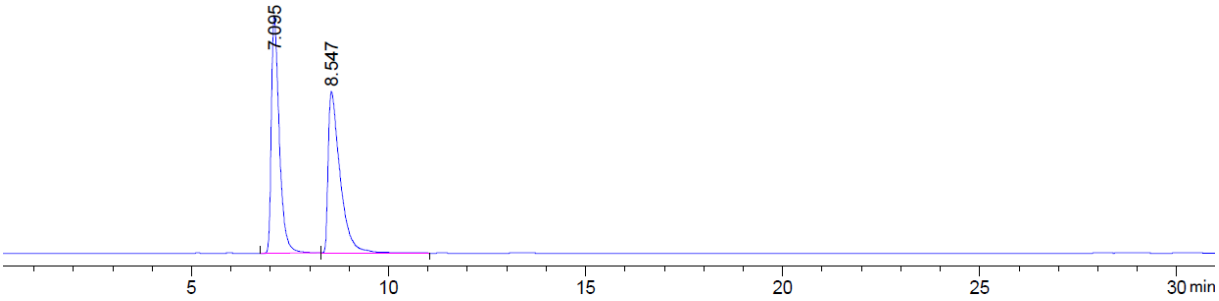
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



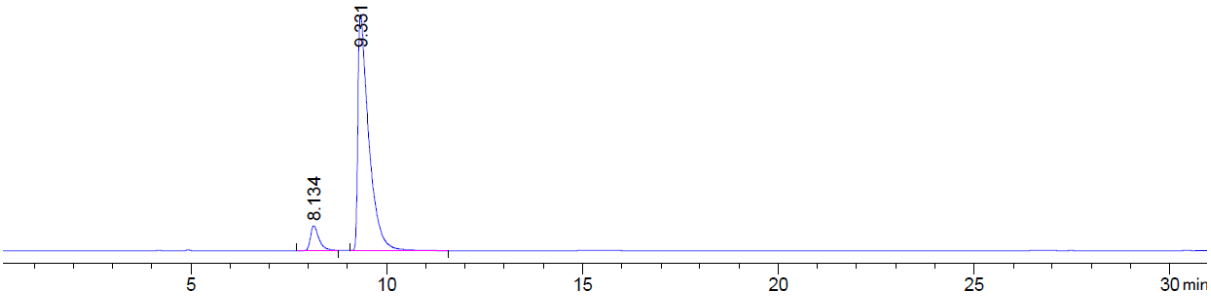

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

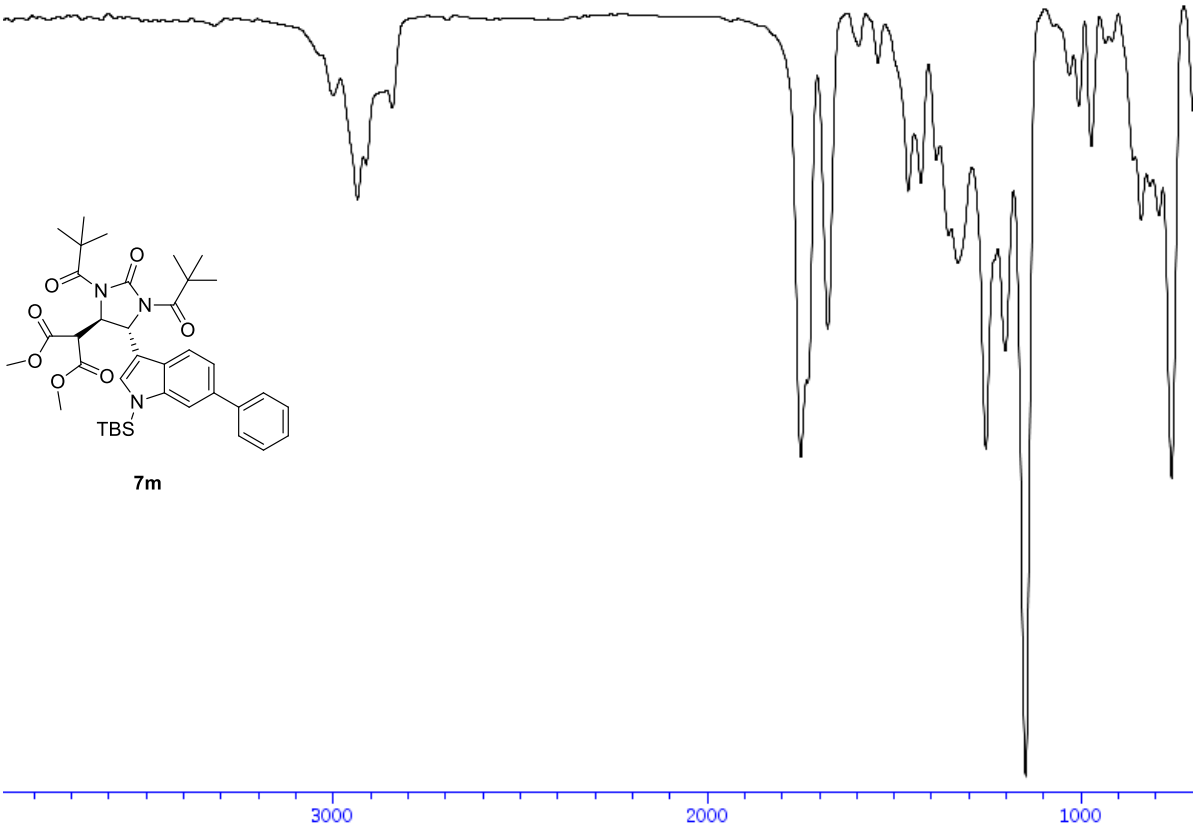



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 7.095 | BB | 0.2124 | 1829.82813 | 129.89087 | 49.5743 |
| 2 | 8.547 | BB | 0.3070 | 1861.25134 | 88.62238 | 50.4257 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 8.134 | BV | 0.2283 | 835.99512 | 54.70217 | 7.6815 |
| 2 | 9.331 | VB | 0.2763 | 1.00472e4 | 518.02020 | 92.3185 |

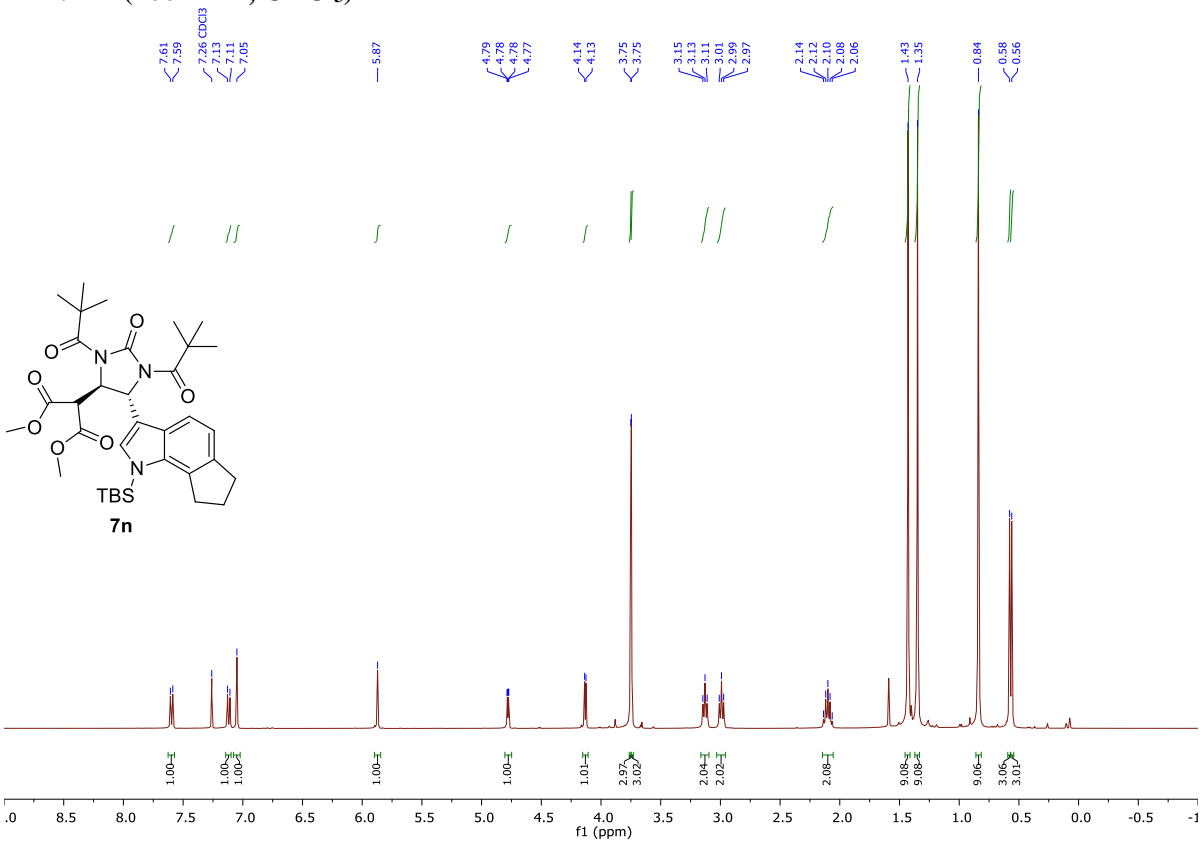
**IR**



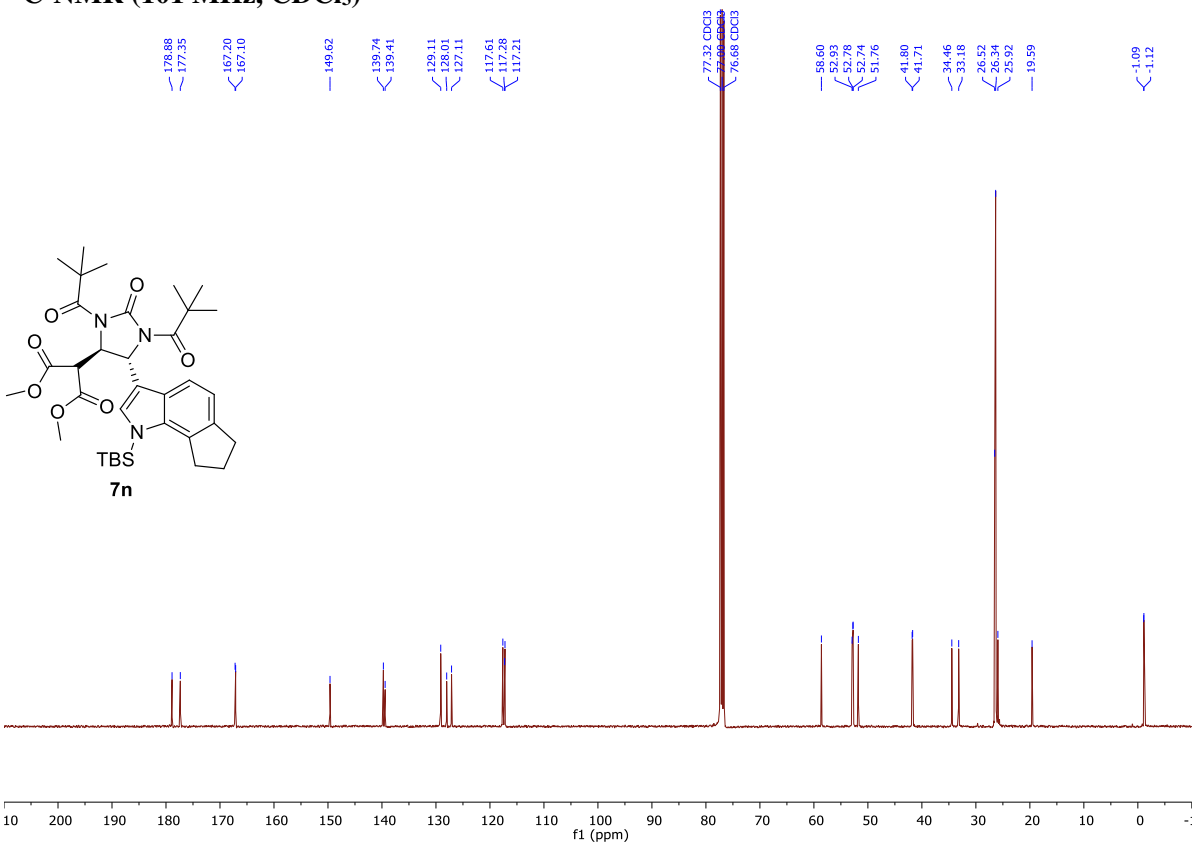

**7m**

**Dimethyl 2-(5-(1-(tert-butyldimethylsilyl)-1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)-2-oxo-1,3-dipivaloylimidazolidin-4-yl)malonate (7n)**

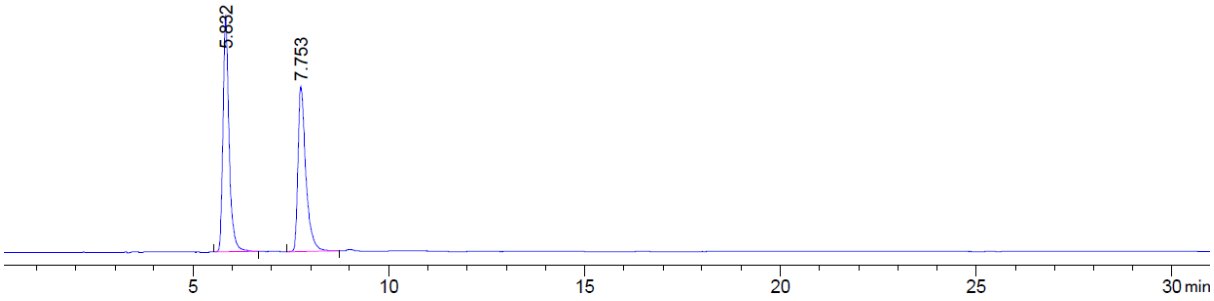
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



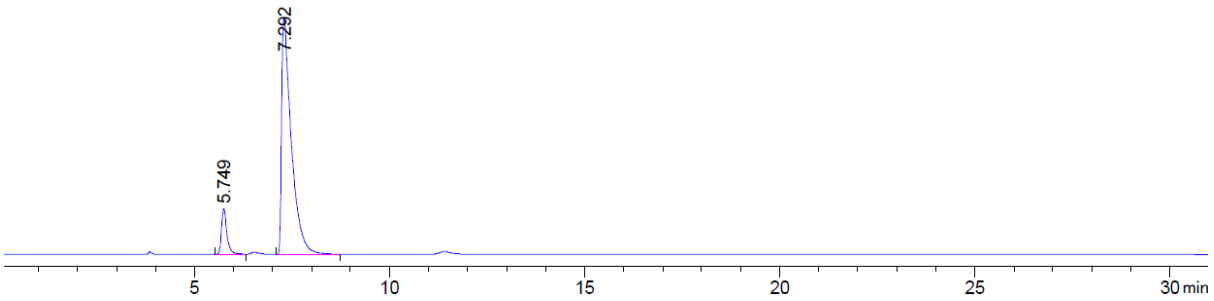

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

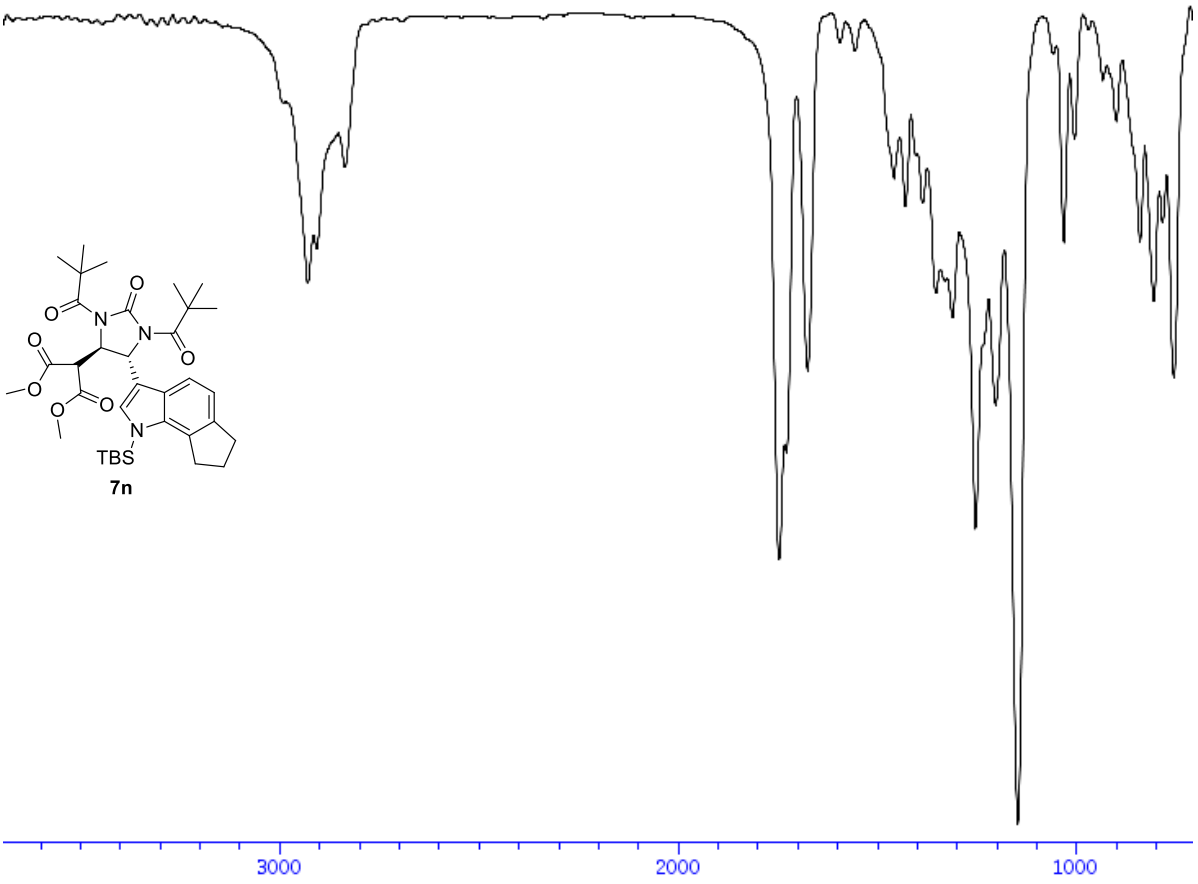



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.832 | BB | 0.1618 | 243.42946 | 22.57959 | 52.5208 |
| 2 | 7.753 | BB | 0.2087 | 220.06186 | 15.77604 | 47.4792 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.749 | BB | 0.1427 | 818.25580 | 86.23480 | 9.5457 |
| 2 | 7.292 | BB | 0.2437 | 7753.75977 | 448.58212 | 90.4543 |

**IR**



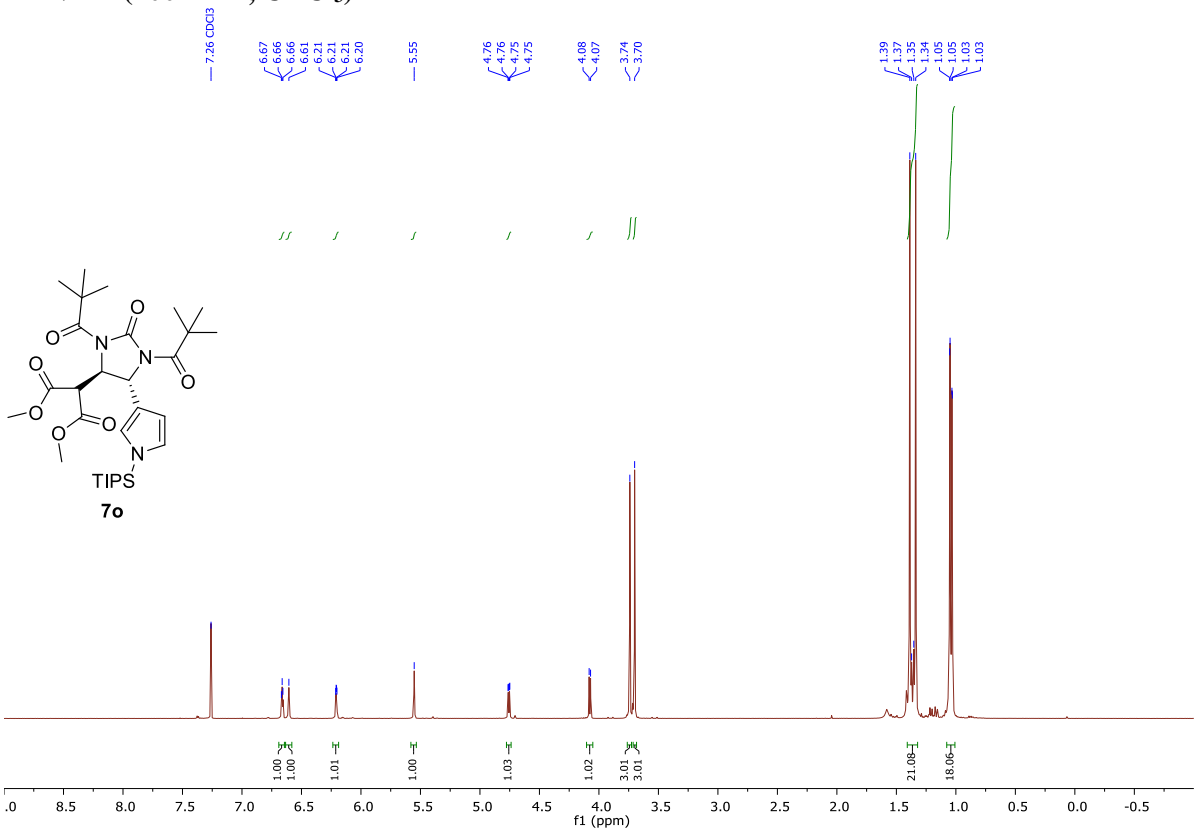


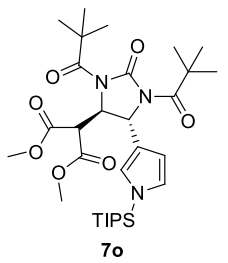


**7n**

**Dimethyl 2-(2-oxo-1,3-dipivaloyl-5-(1-(triisopropylsilyl)-1H-pyrrol-3-yl)imidazolidin-4-yl)malonate (7o)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**7o**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

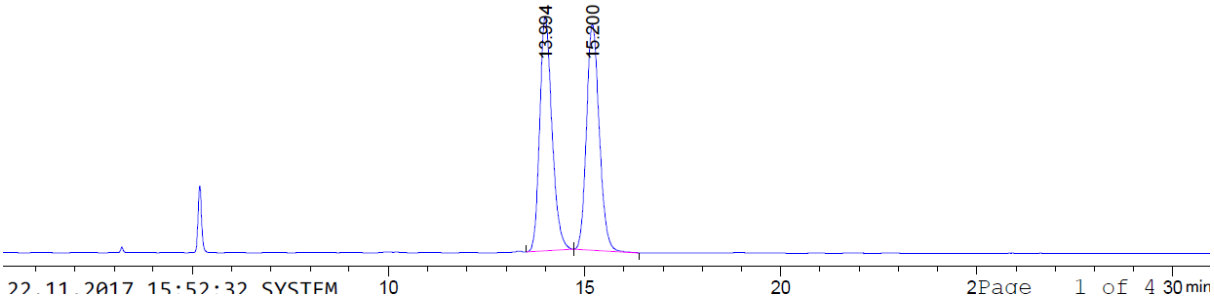




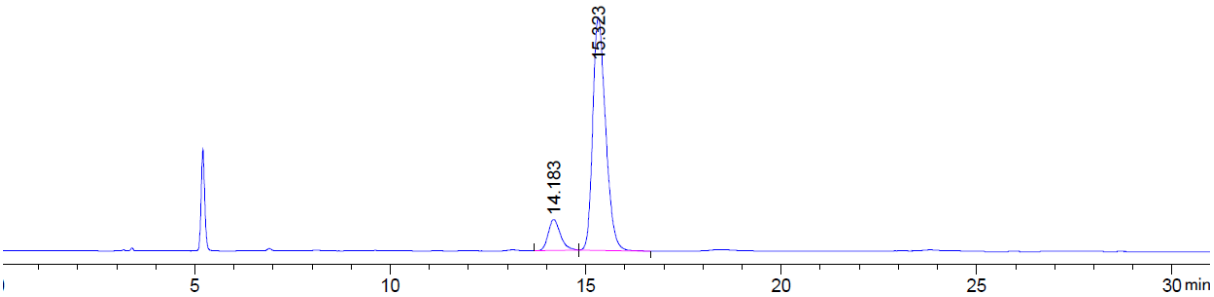


**7o**

**HPLC**

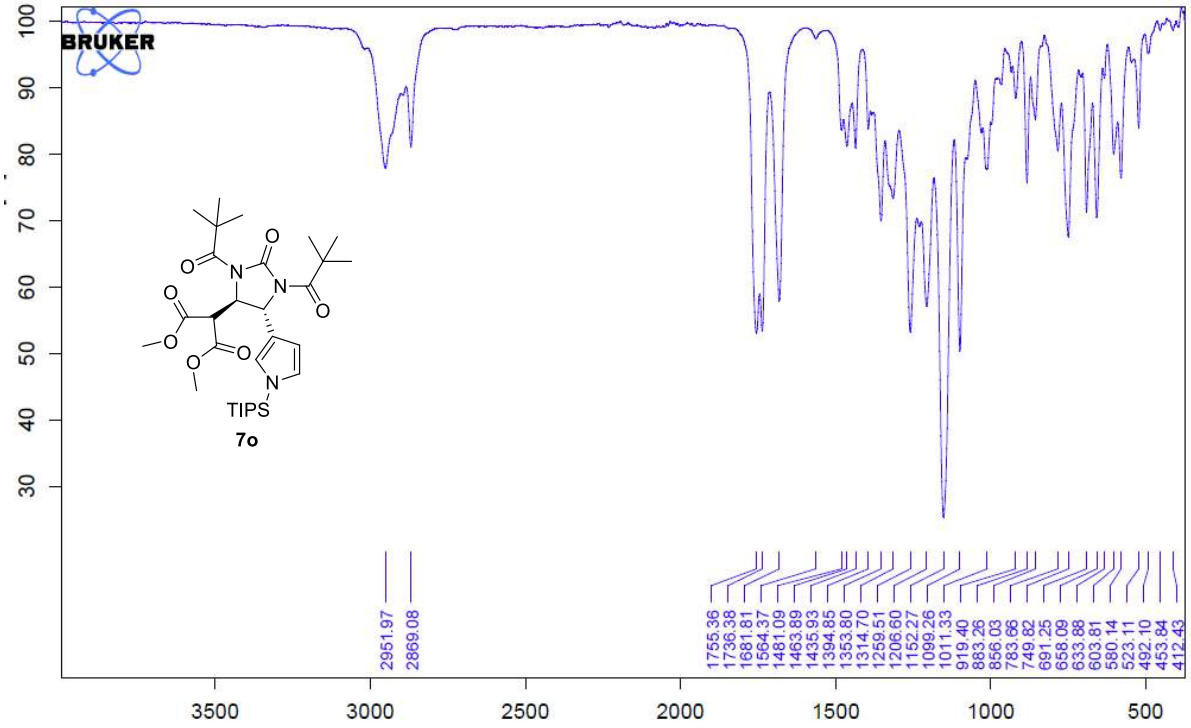



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.994 | BB | 0.3338 | 1418.42273 | 65.21094 | 49.9431 |
| 2 | 15.200 | BB | 0.3489 | 1421.65637 | 63.08244 | 50.0569 |



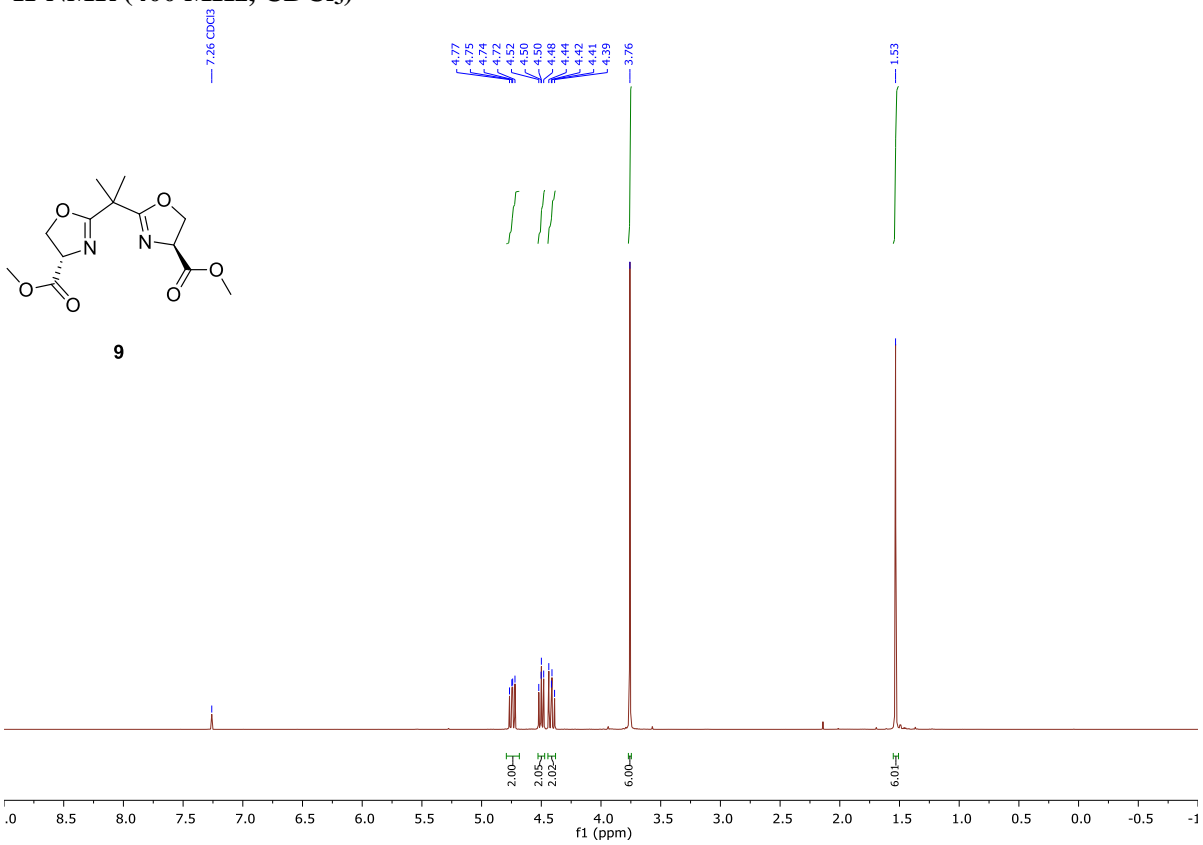

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 14.183 | BB | 0.3342 | 50.63592 | 2.34280 | 11.1984 |
| 2 | 15.323 | BB | 0.3518 | 401.53619 | 17.62564 | 88.8016 |

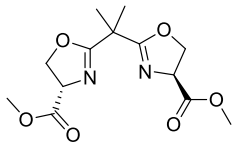
**IR**


BRUKER
TIPS
7o
2951.97
2869.08
1755.36
1736.38
1681.81
1564.37
1481.09
1463.89
1435.93
1394.85
1353.80
1314.70
1259.51
1206.60
1152.27
1099.26
1011.33
919.40
883.26
856.03
783.66
749.82
691.25
658.09
633.88
603.81
580.14
523.11
492.10
453.84
412.43
100
90
80
70
60
50
40
30
3500
3000
2500
2000
1500
1000
500

**(4S,4'S)-dimethyl 2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4-carboxylate) (9)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



**9**

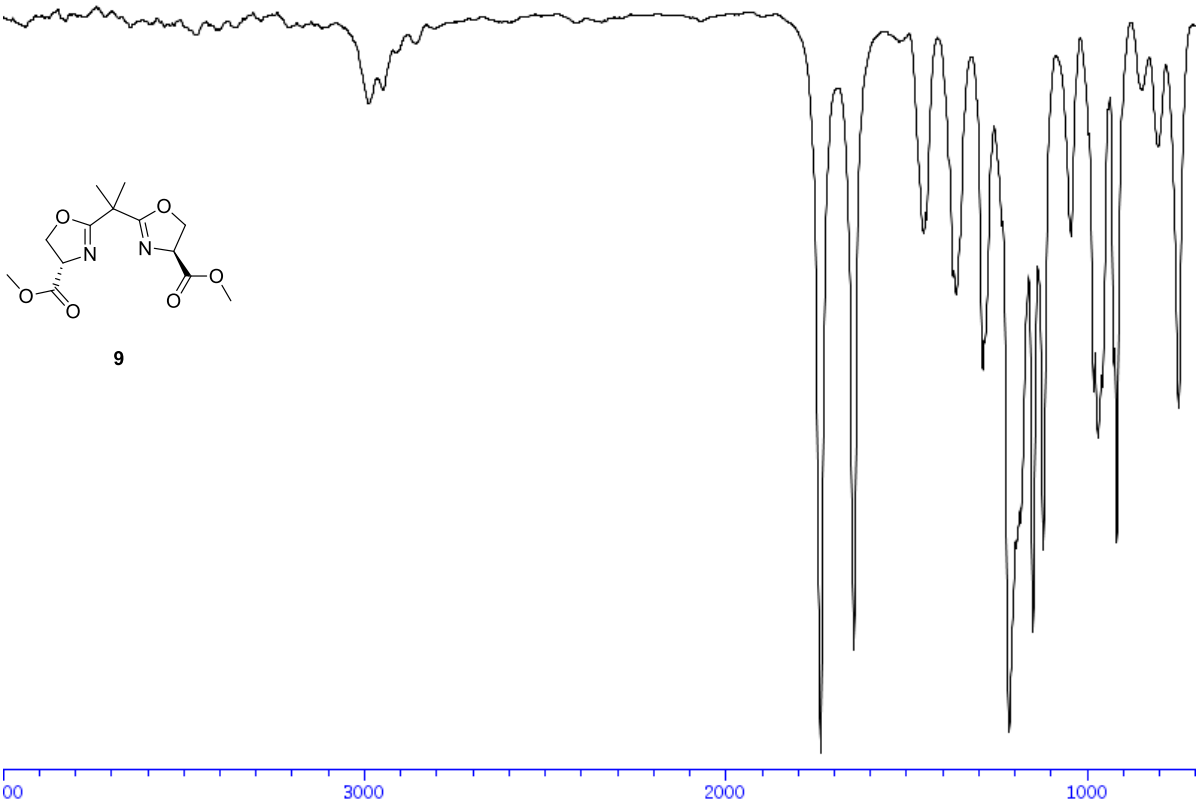
**$^{13}$C-NMR (101 MHz, $CDCl_3$)**






**9**

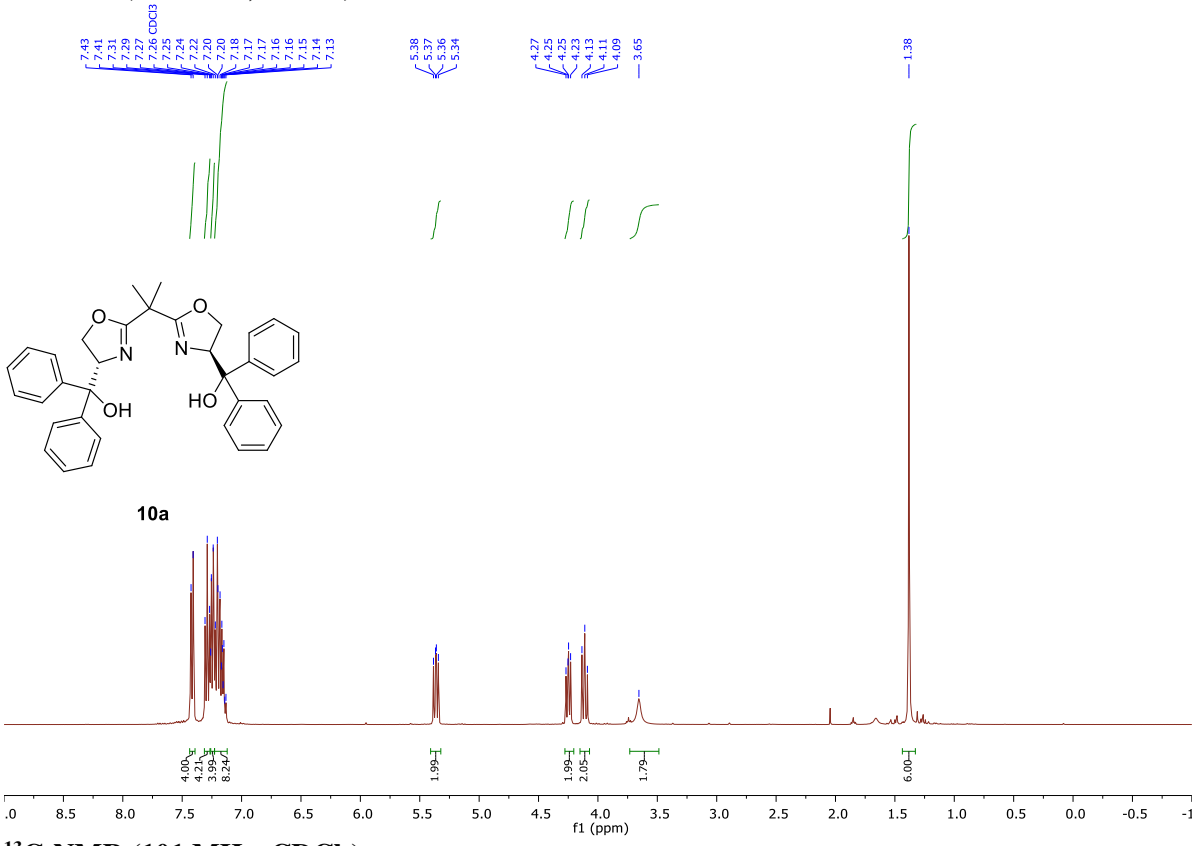
**IR**



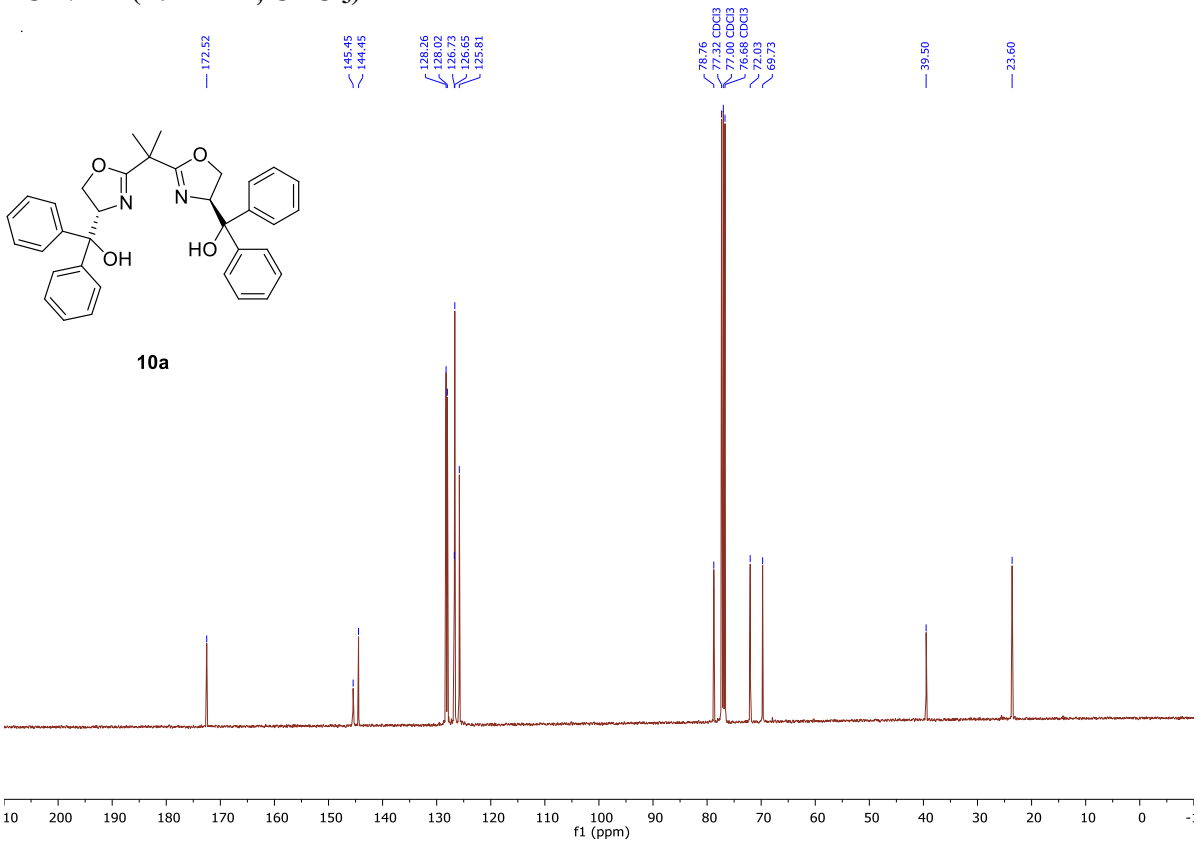

**9**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(diphenylmethanol) (10a)**

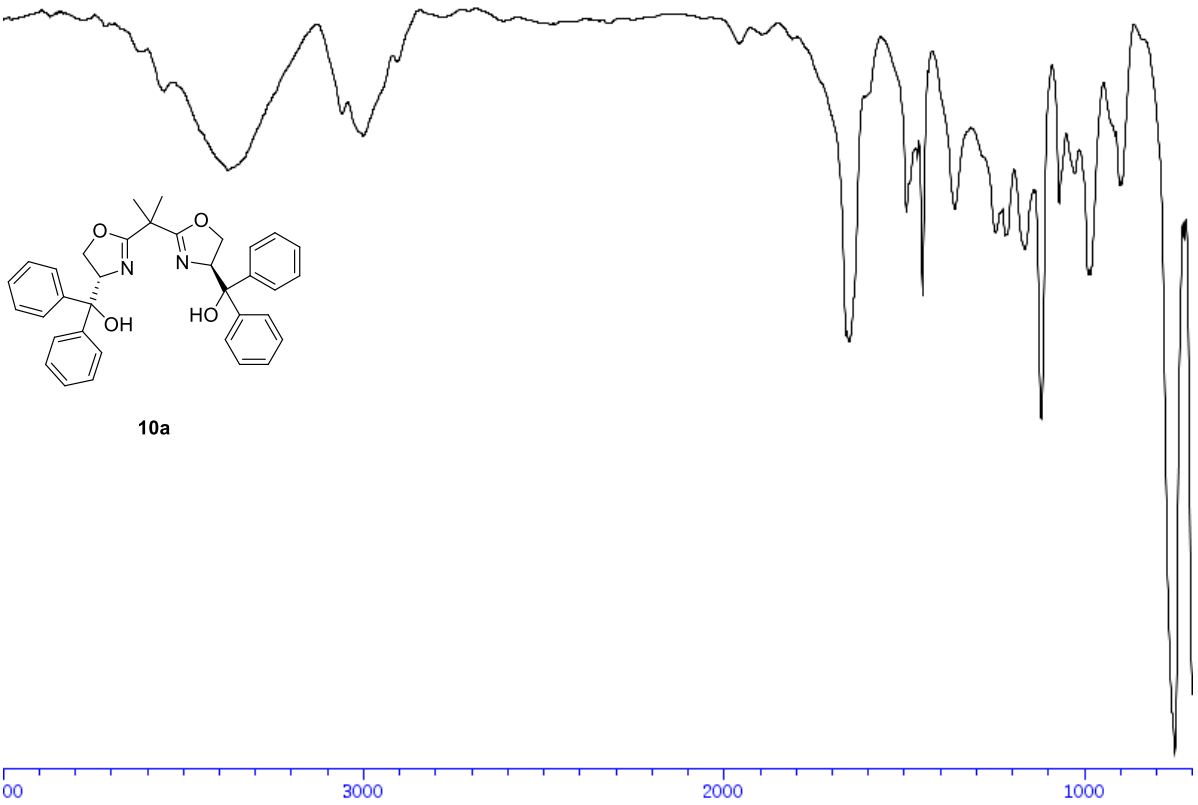
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



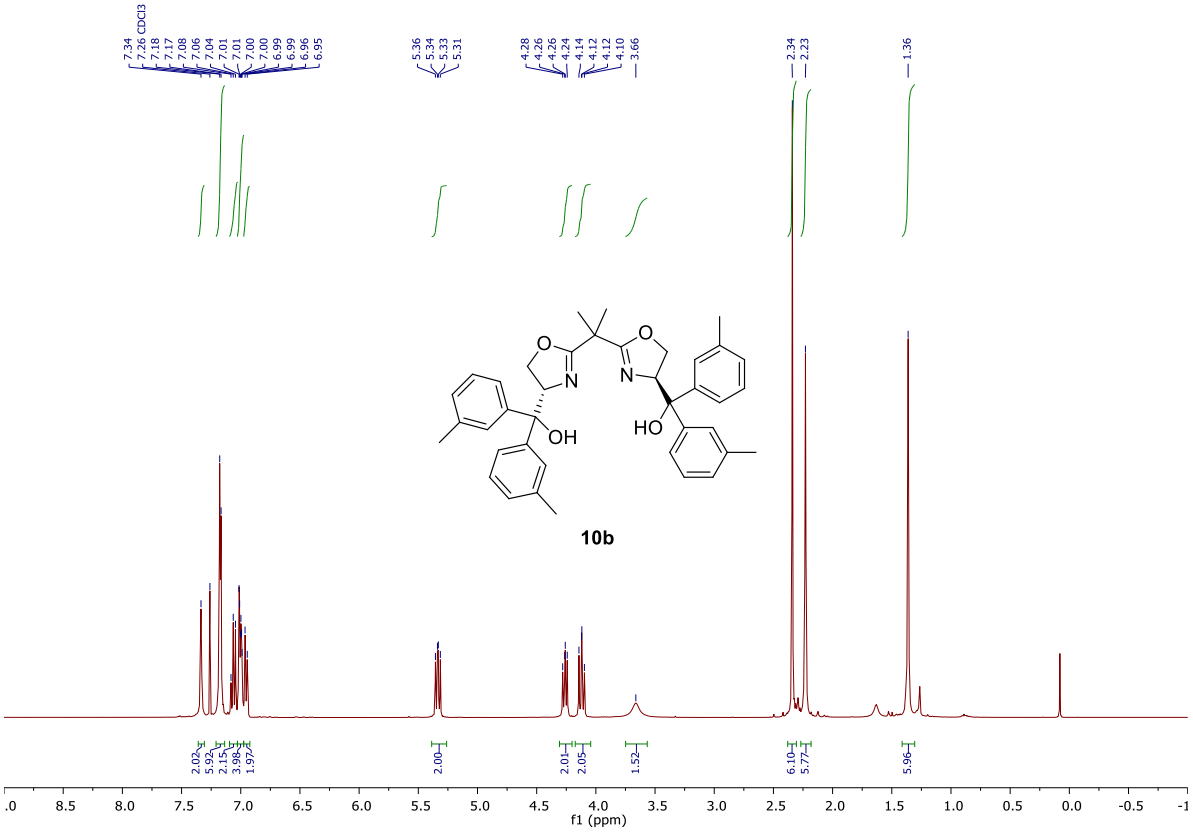
**IR**



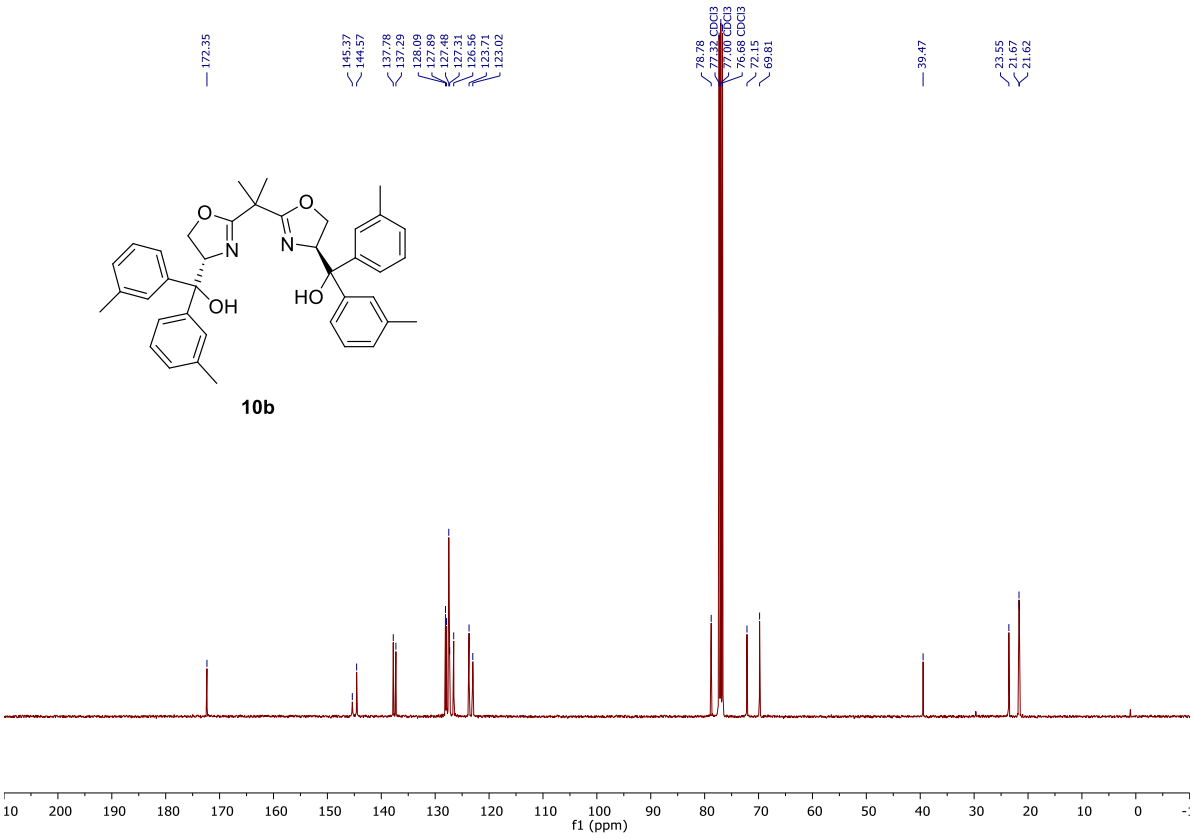

**10a**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di-*m*-tolylmethanol) (10b)**

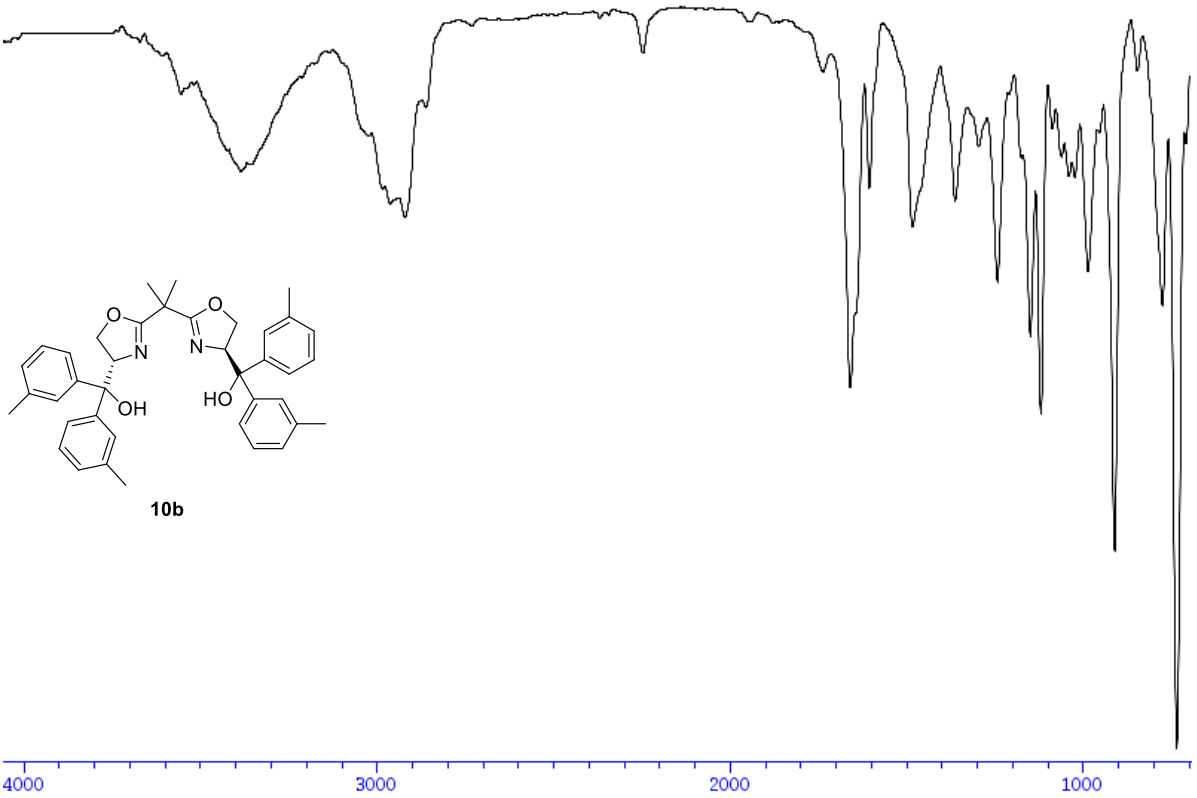
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**IR**



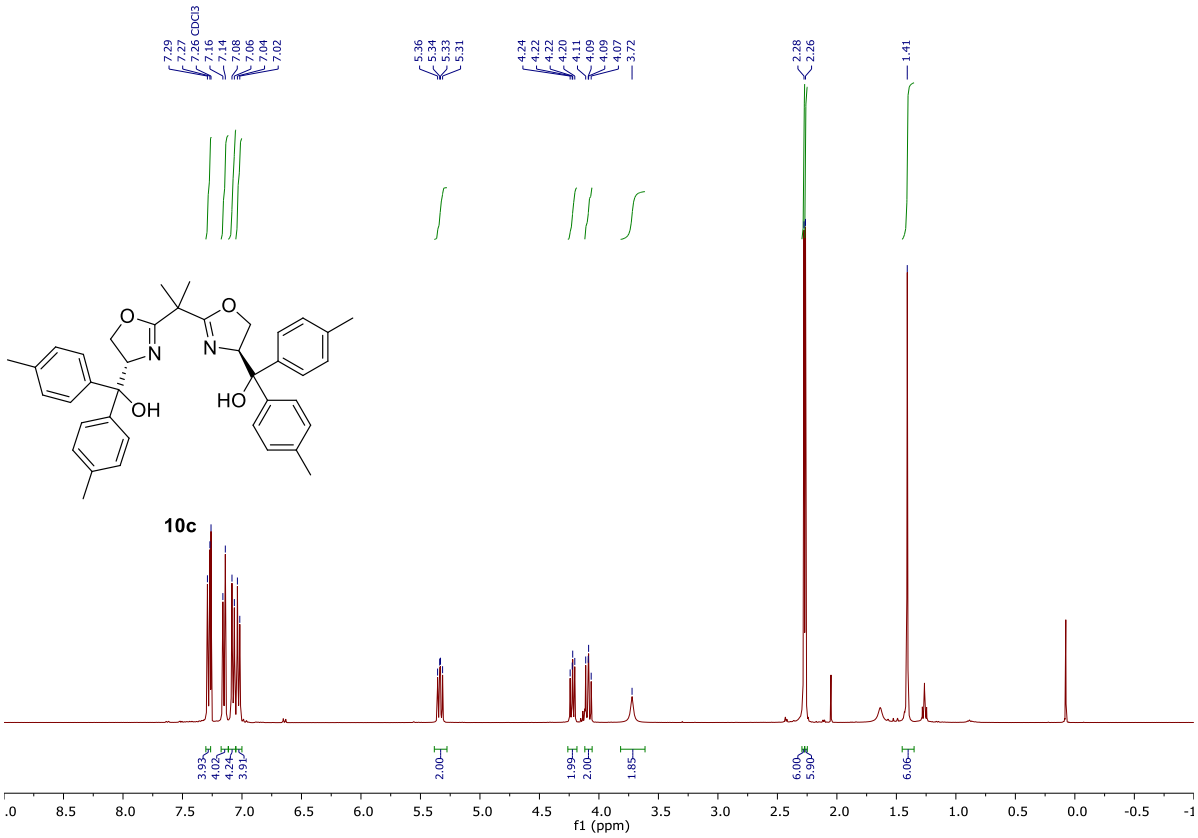




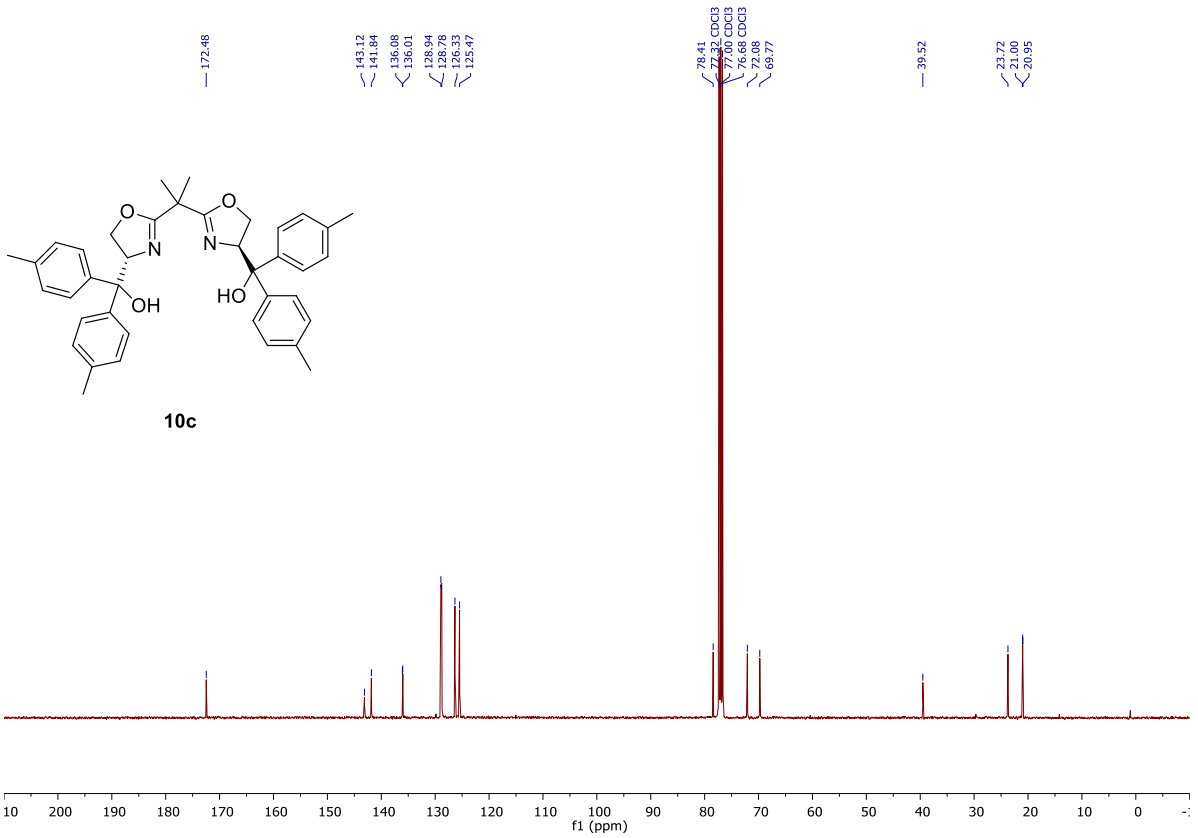
**10b**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di-*p*-tolylmethanol) (10c)**

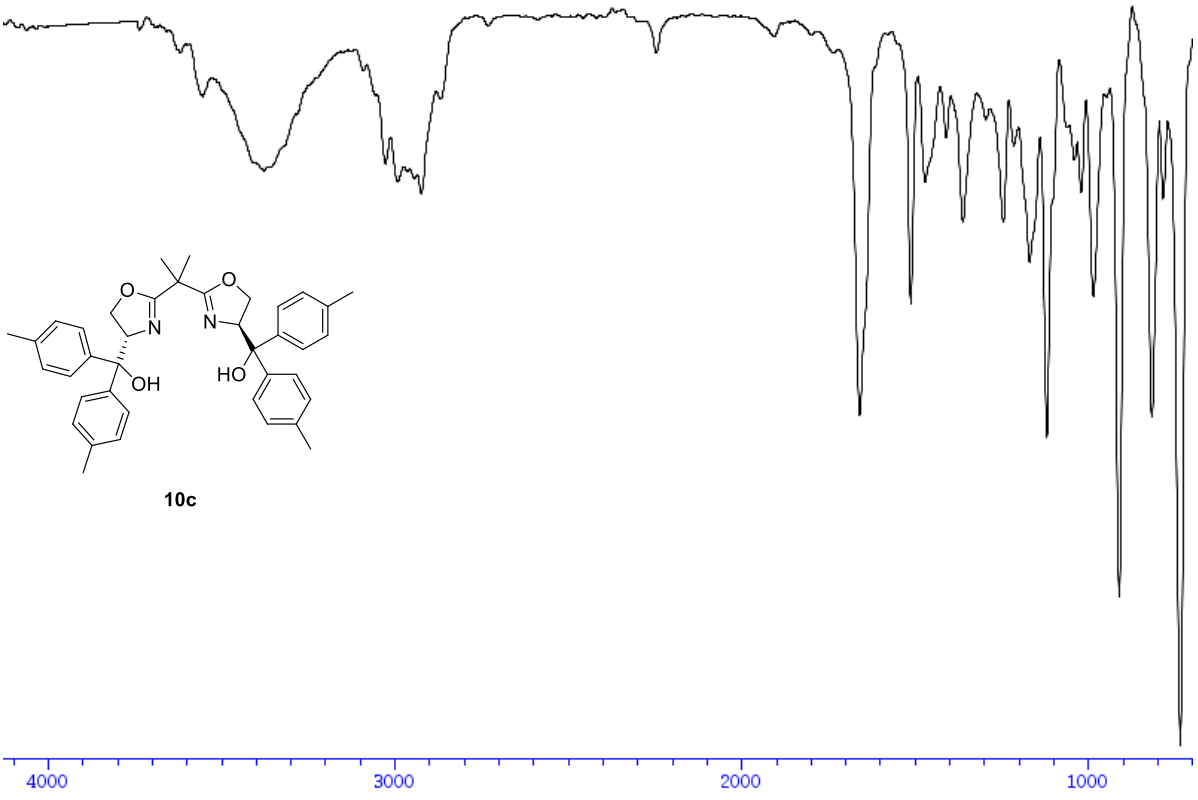
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**IR**



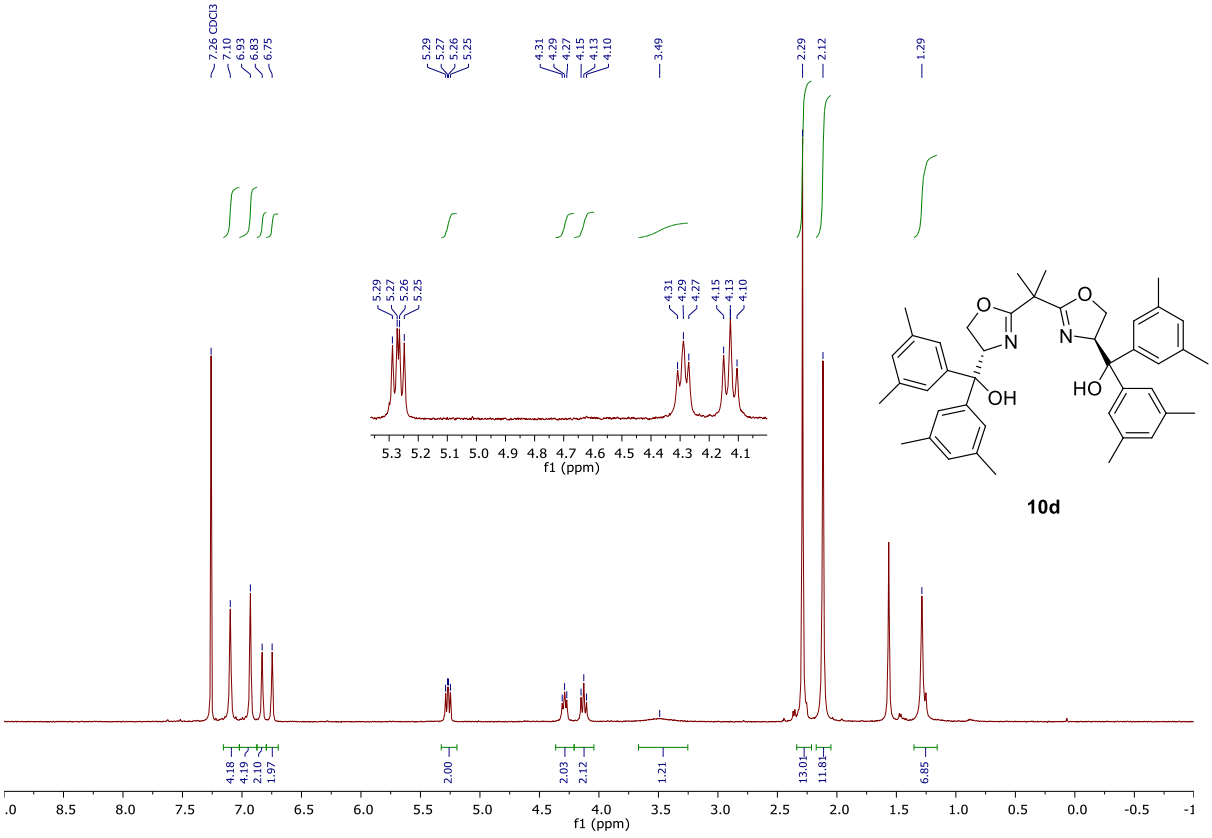




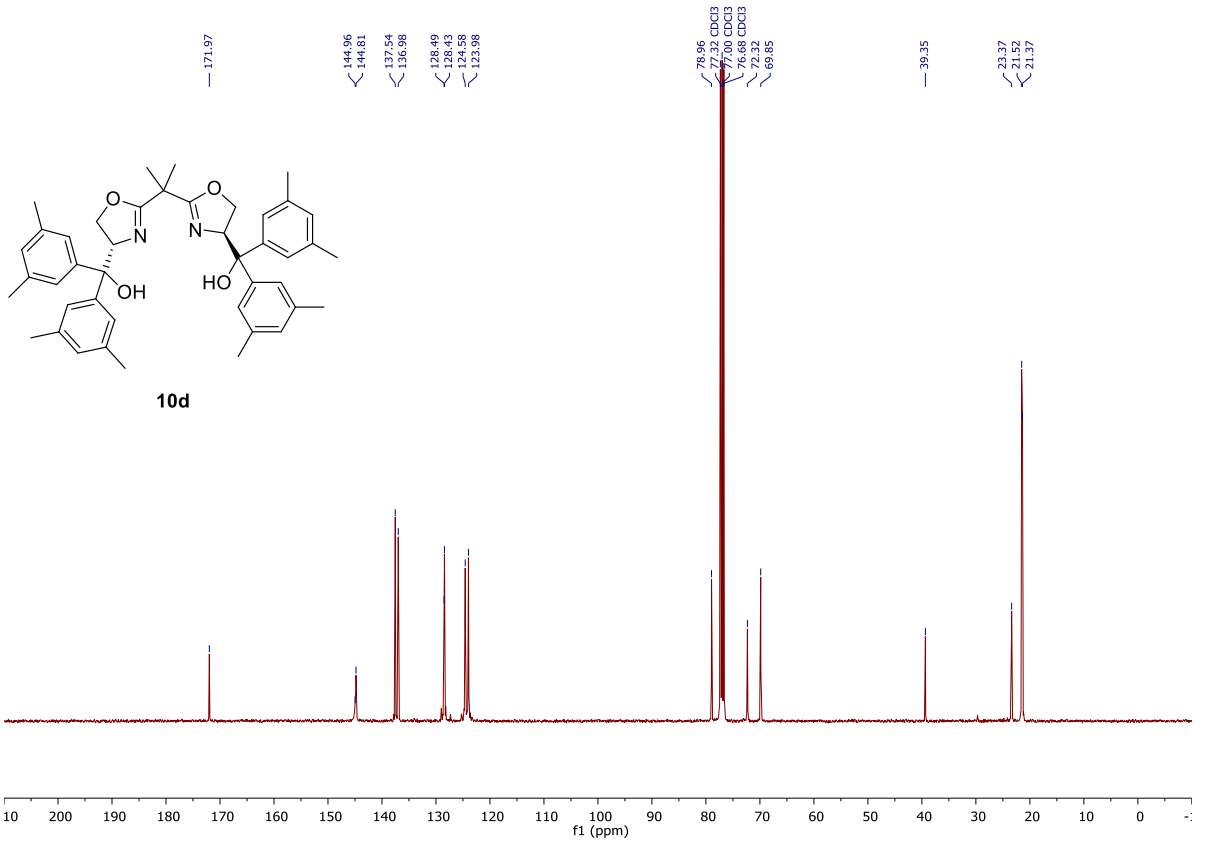
**10c**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-dimethylphenyl)methanol) (10d)**

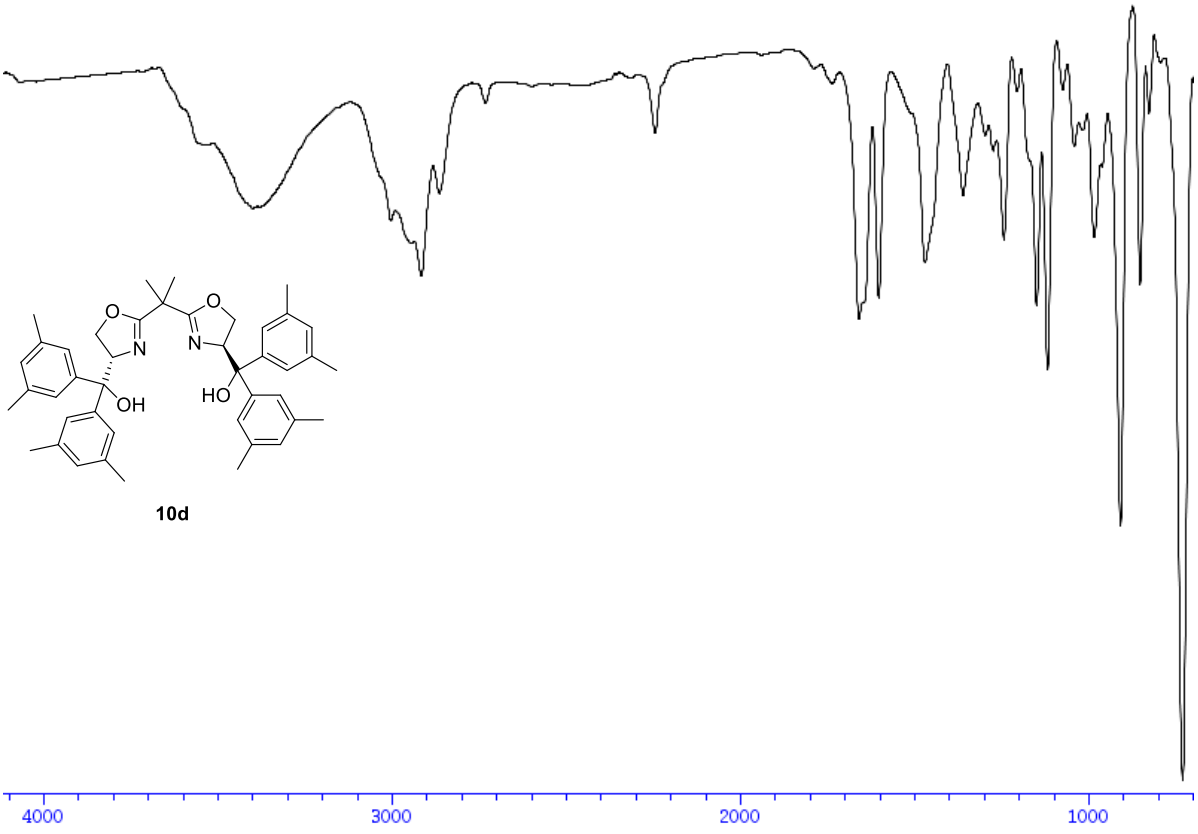
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**IR**



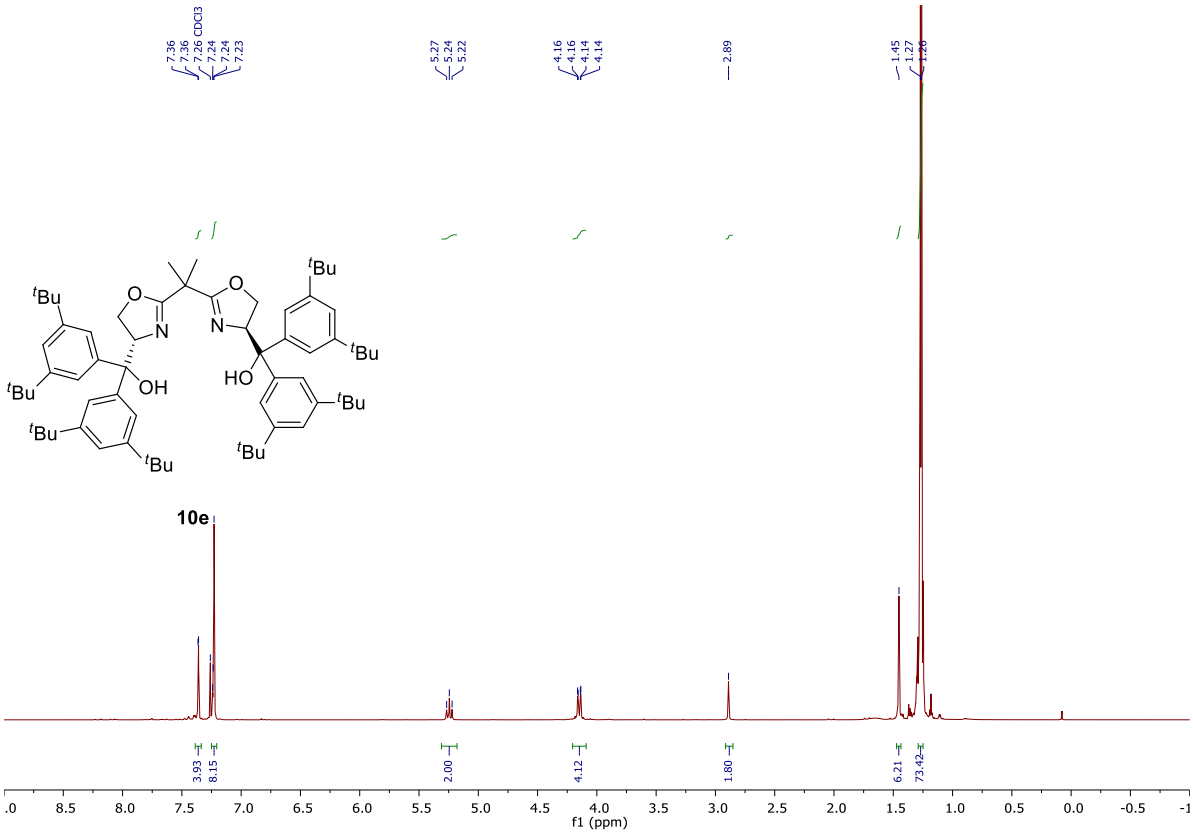




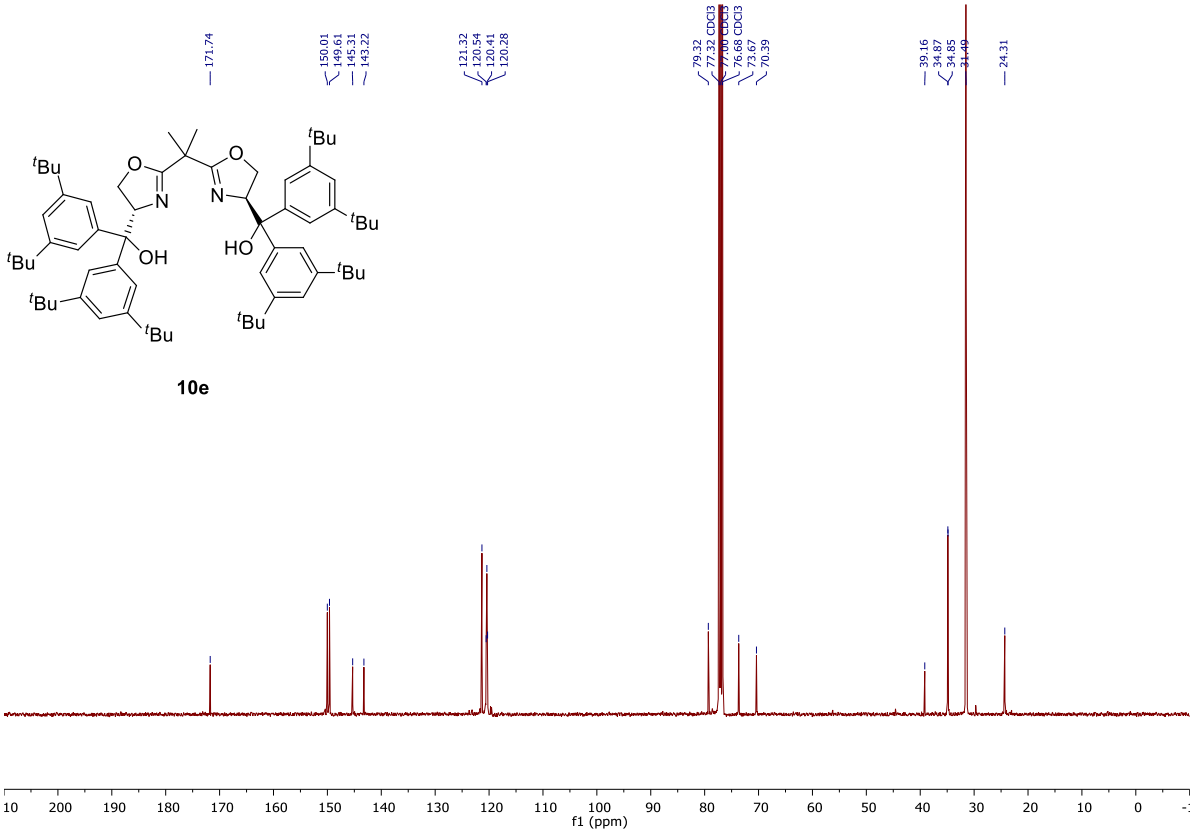
**10d**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-di-*tert*-butylphenyl)methanol) (10e)**

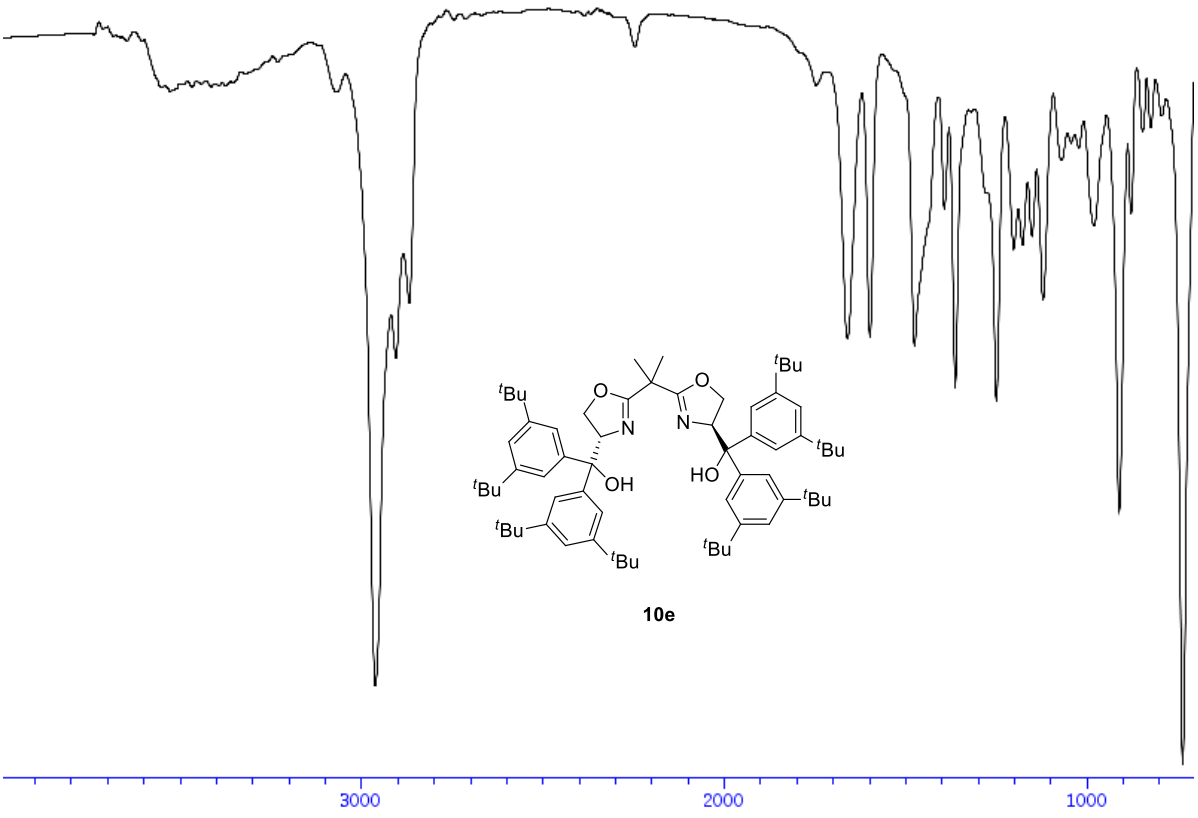
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



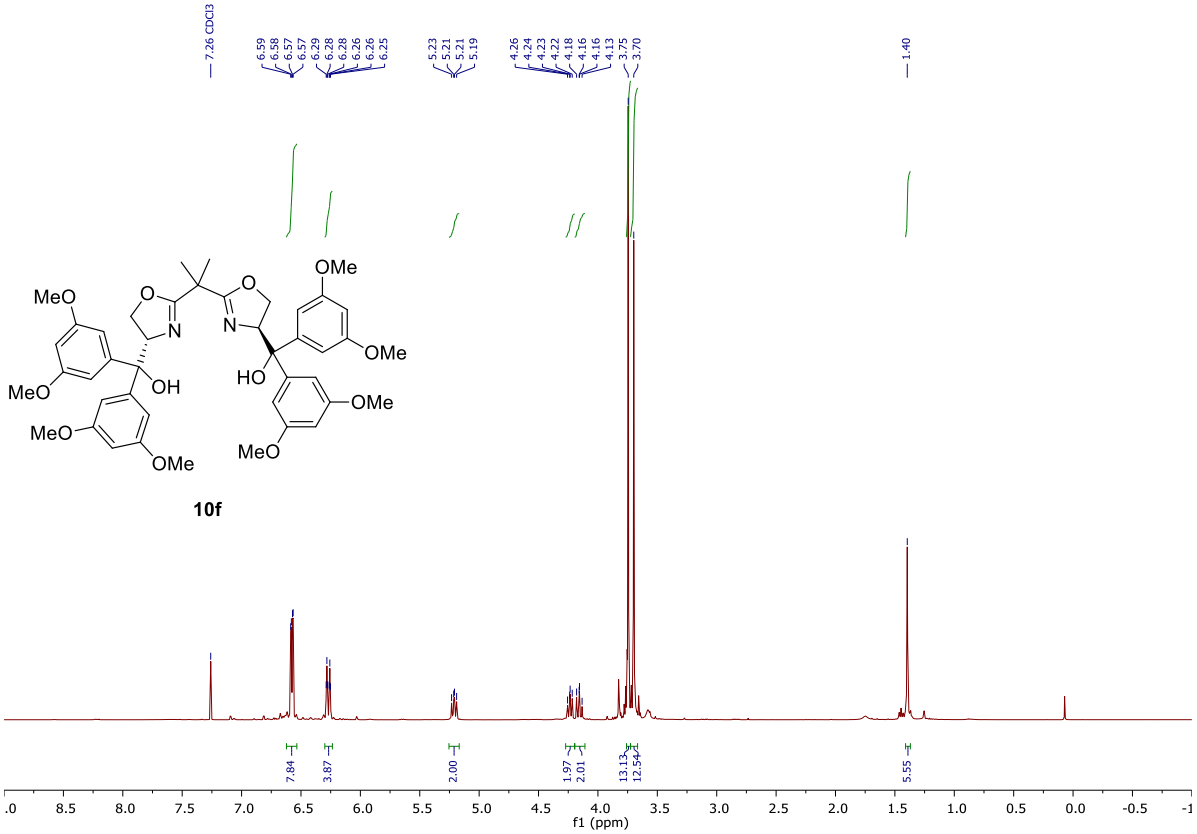
**IR**



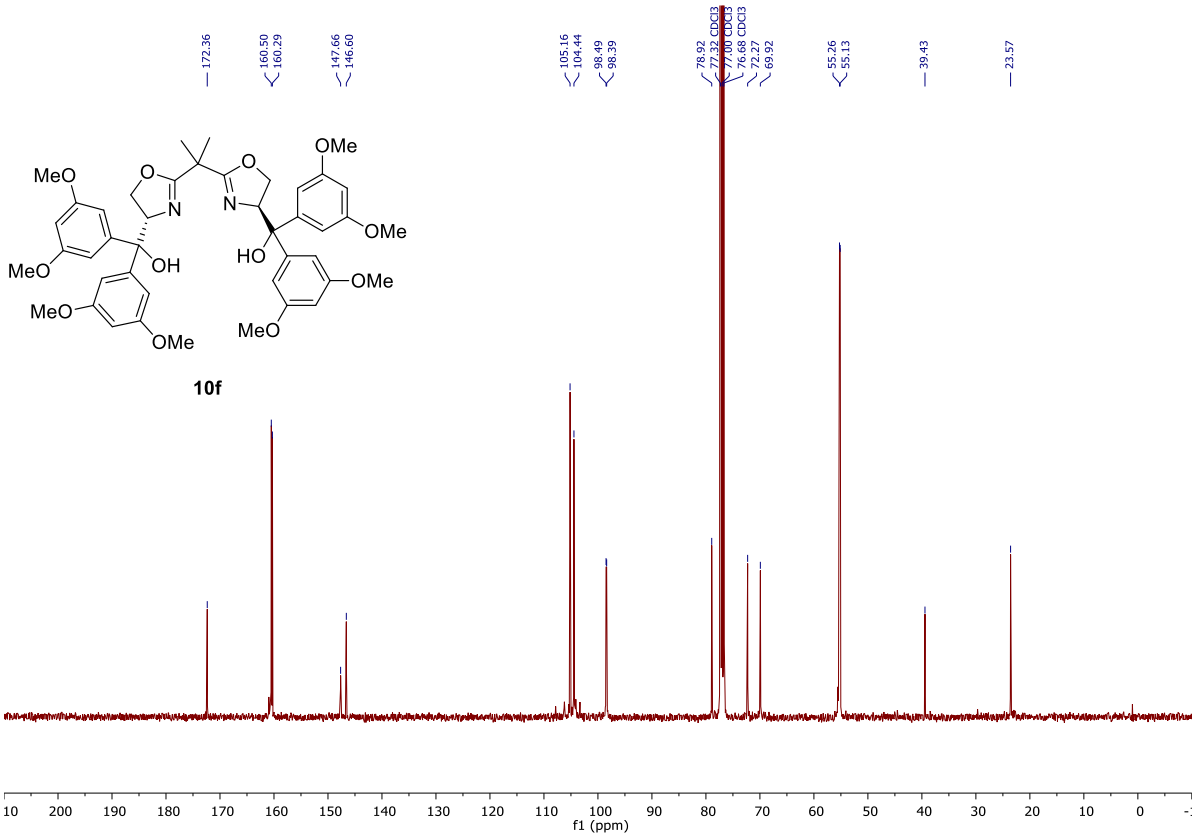

**10e**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-dimethoxyphenyl)methanol) (10f)**

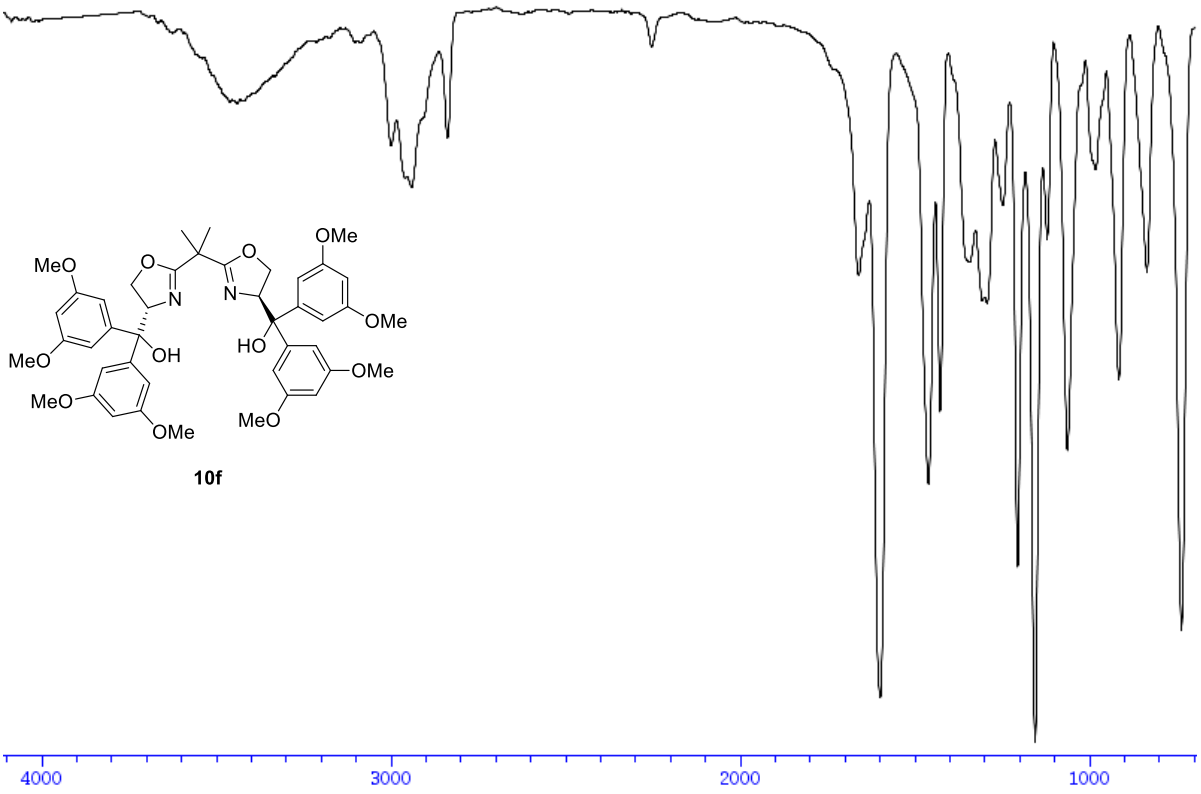
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



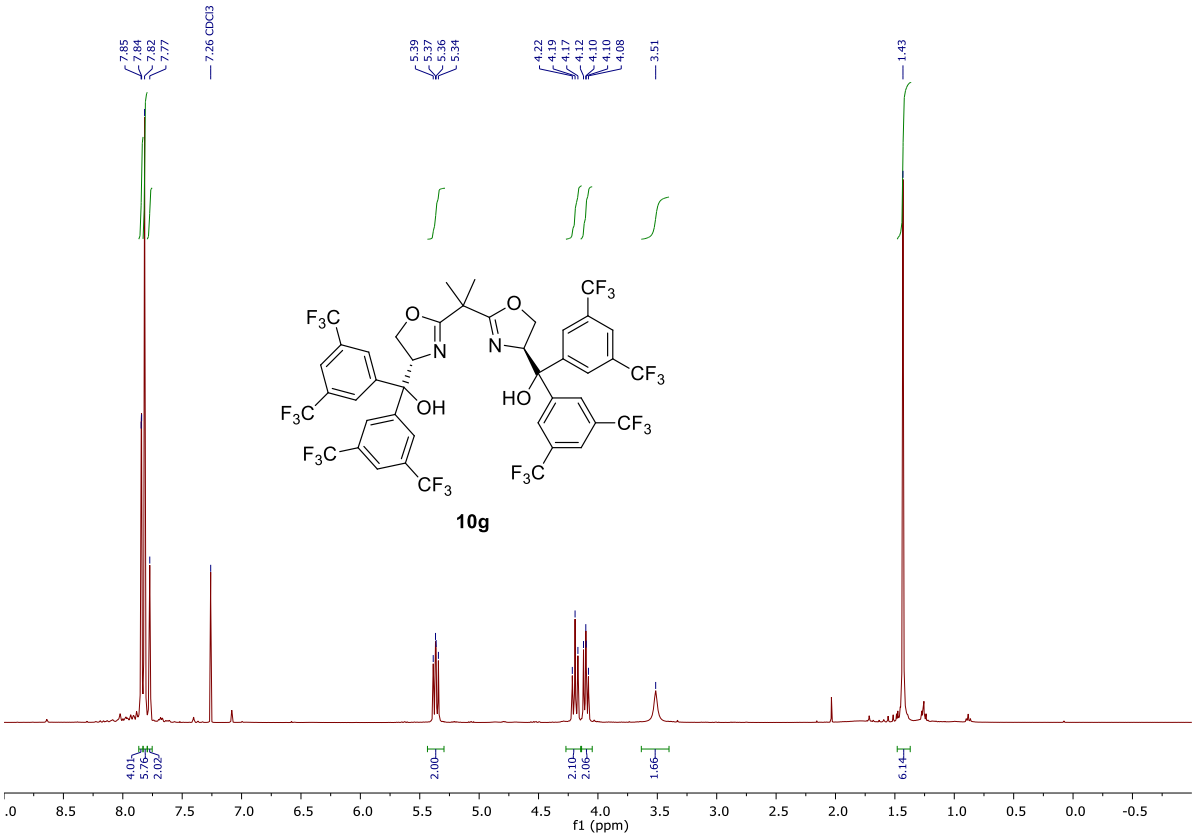
**IR**



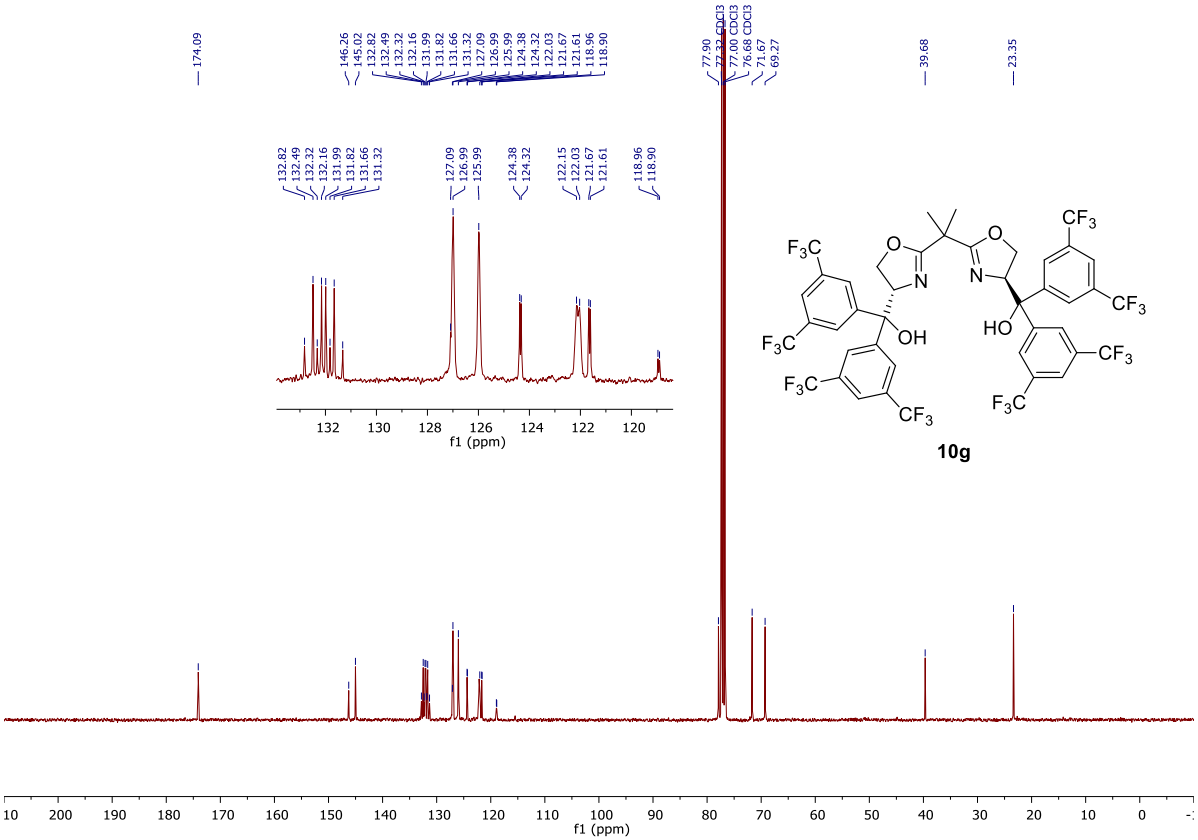

**10f**

**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(bis(3,5-bis(trifluoromethyl)phenyl)methanol) (10g)**

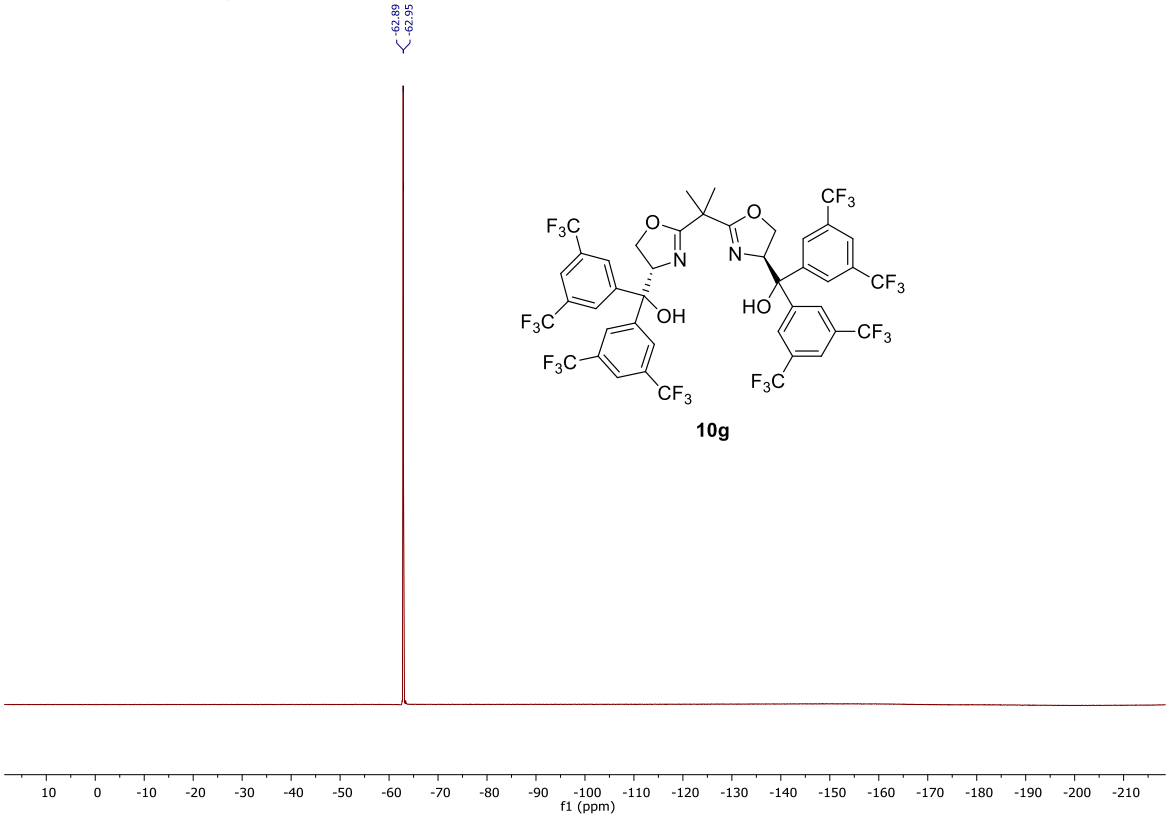
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



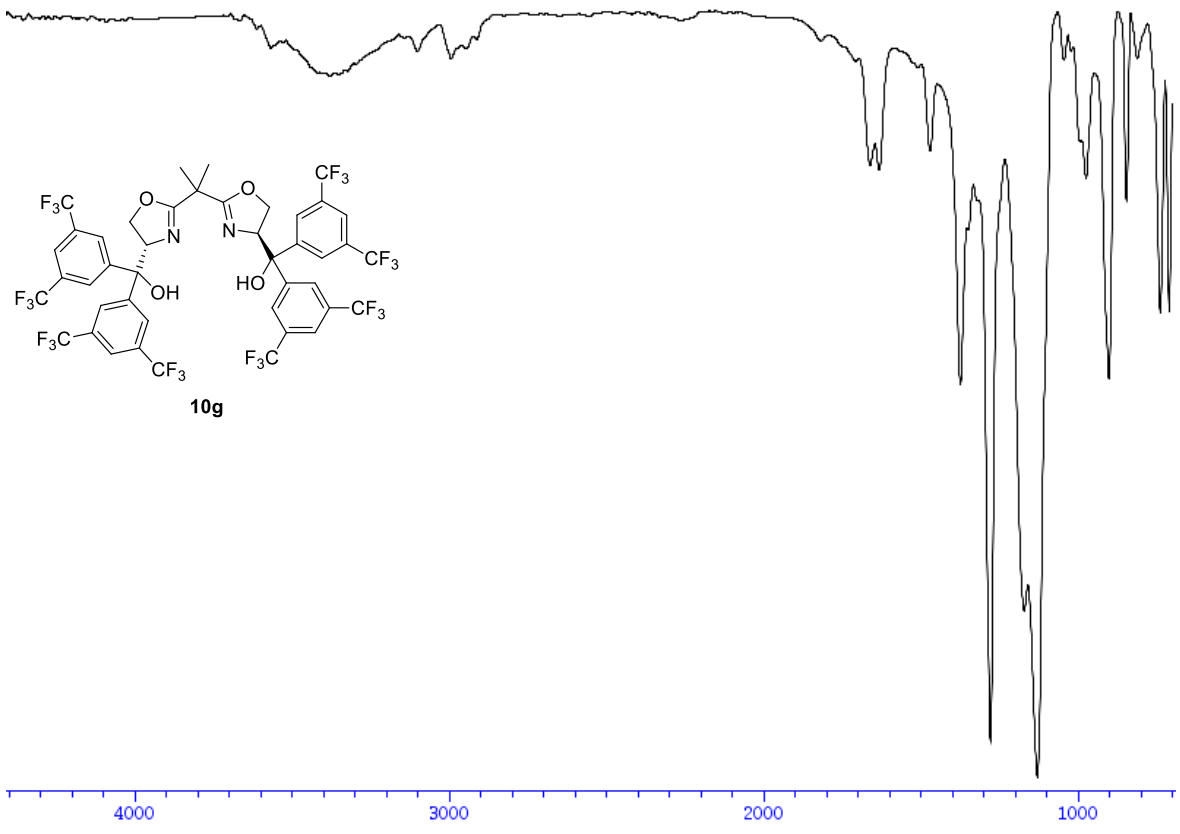

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**$^{19}$F NMR (376 MHz, $CDCl_3$)**

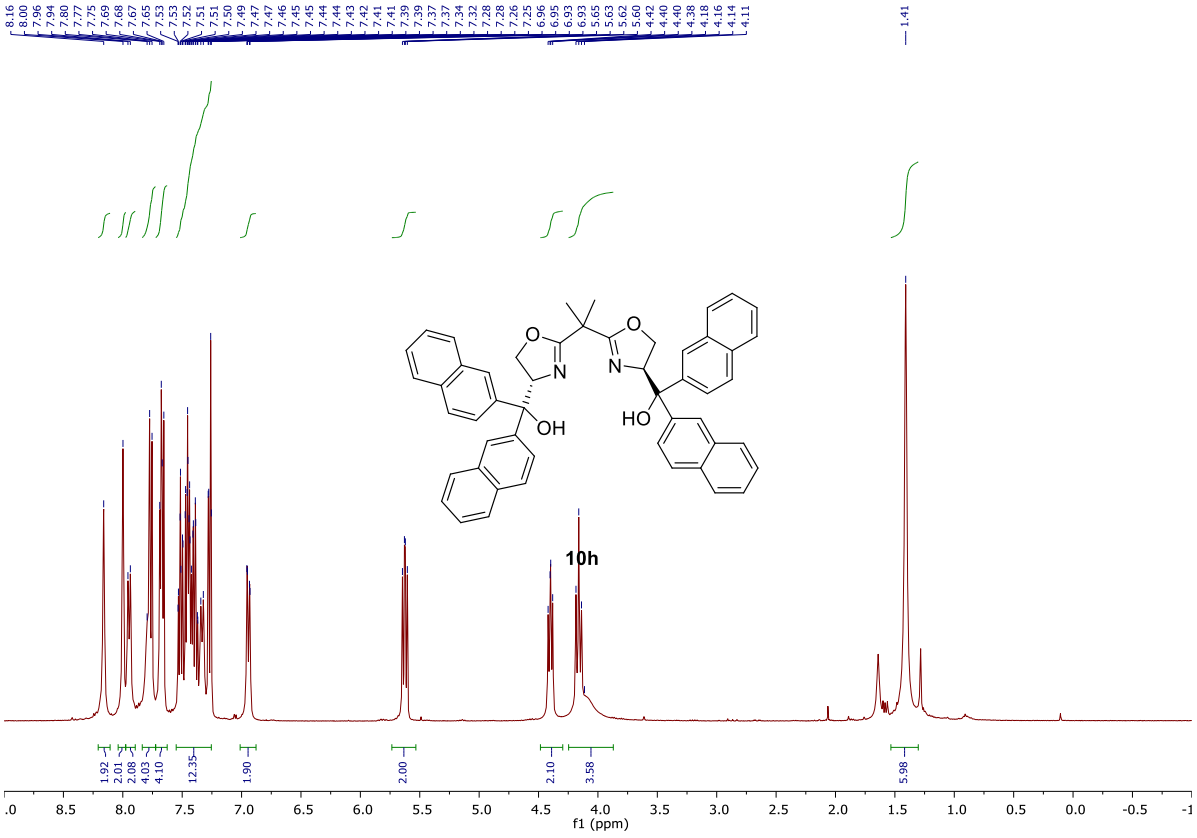



**IR**

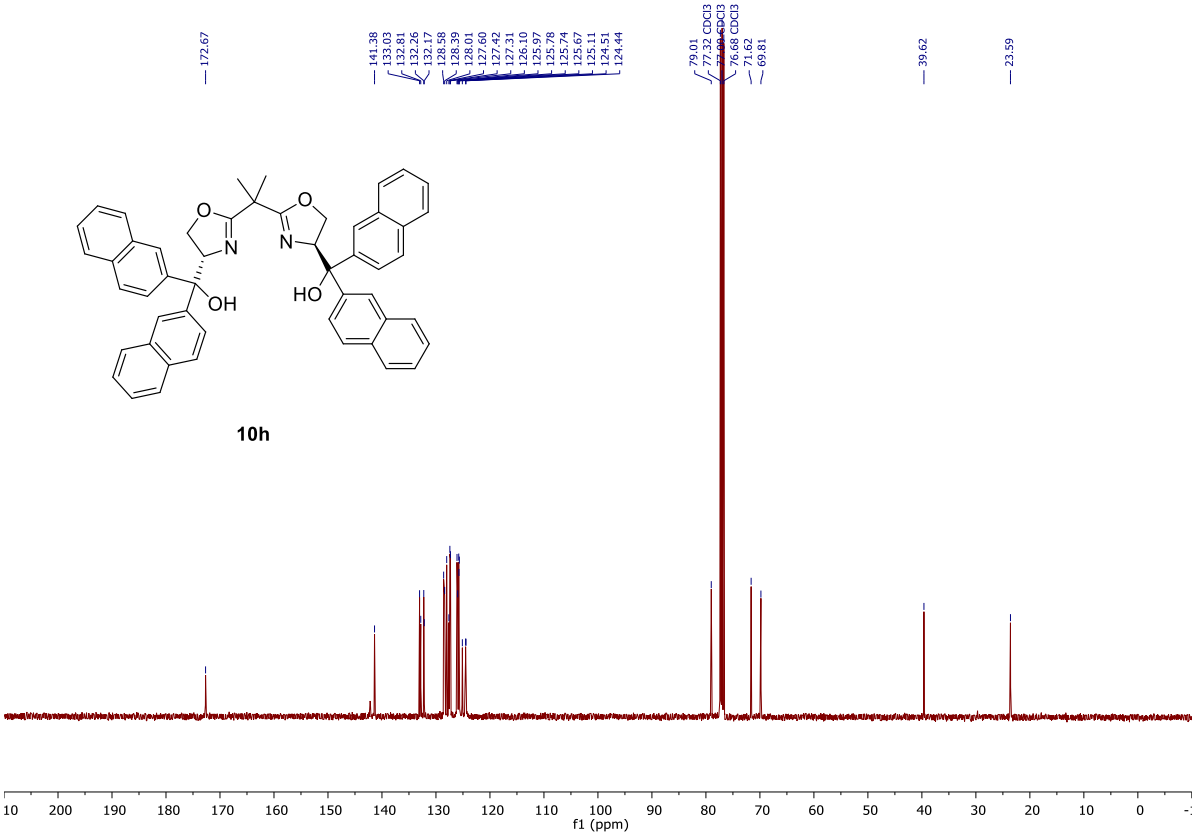


**((4S,4'S)-2,2'-(propane-2,2-diyl)bis(4,5-dihydrooxazole-4,2-diyl))bis(di(naphthalen-2-yl)methanol) (10h)**

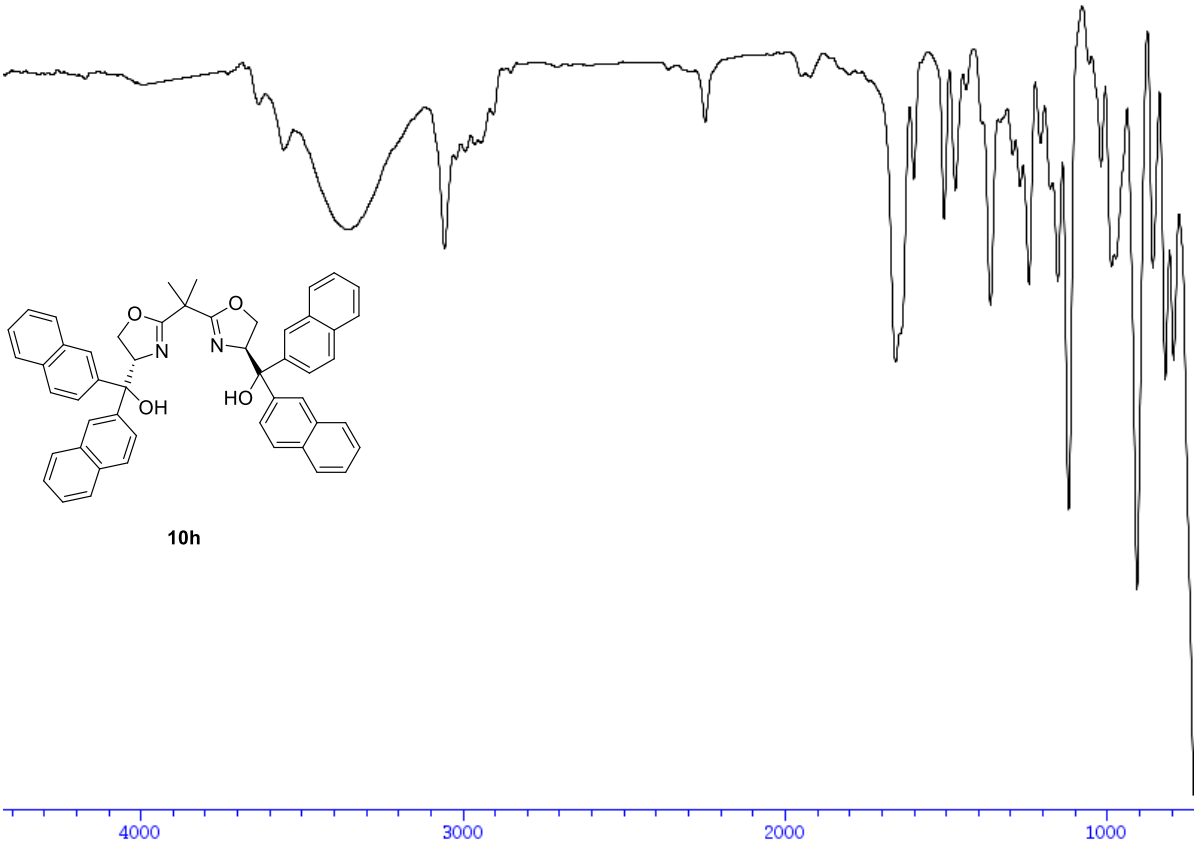
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



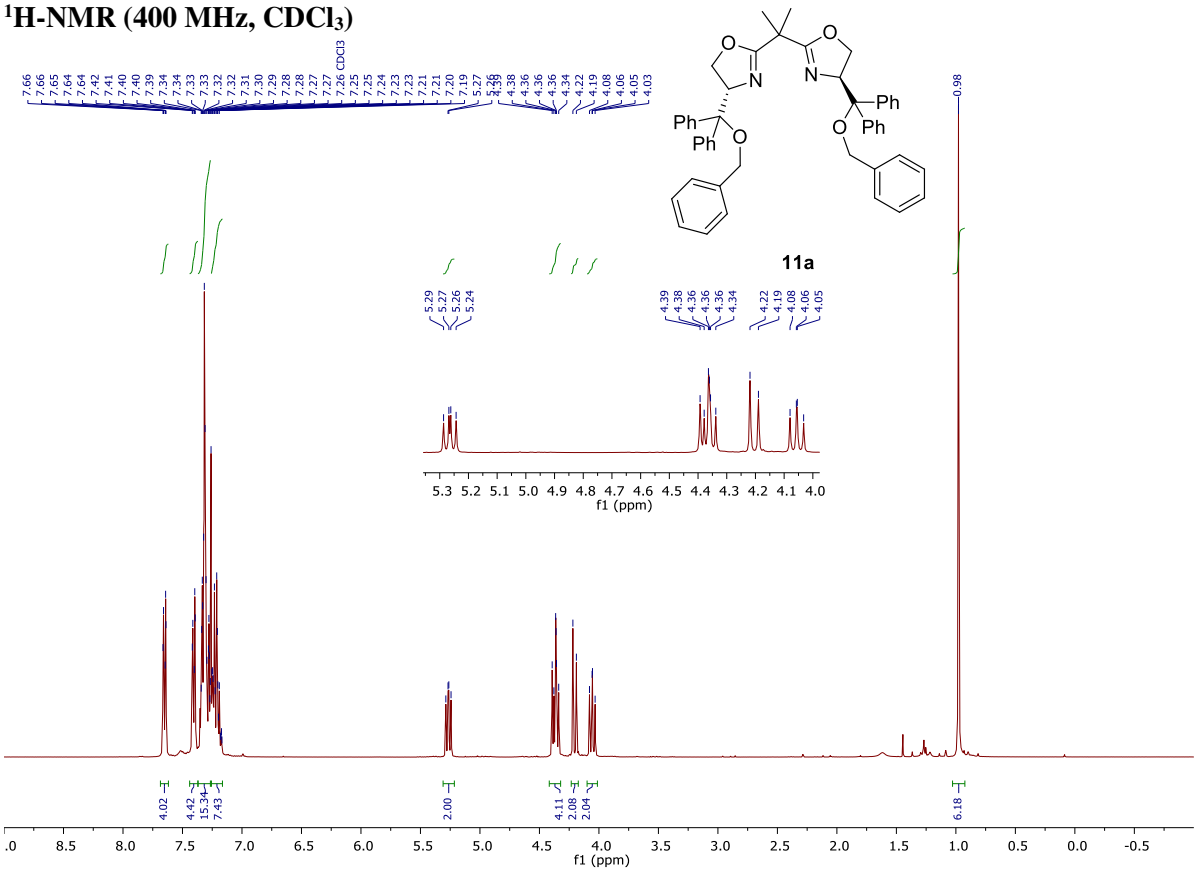
**IR**



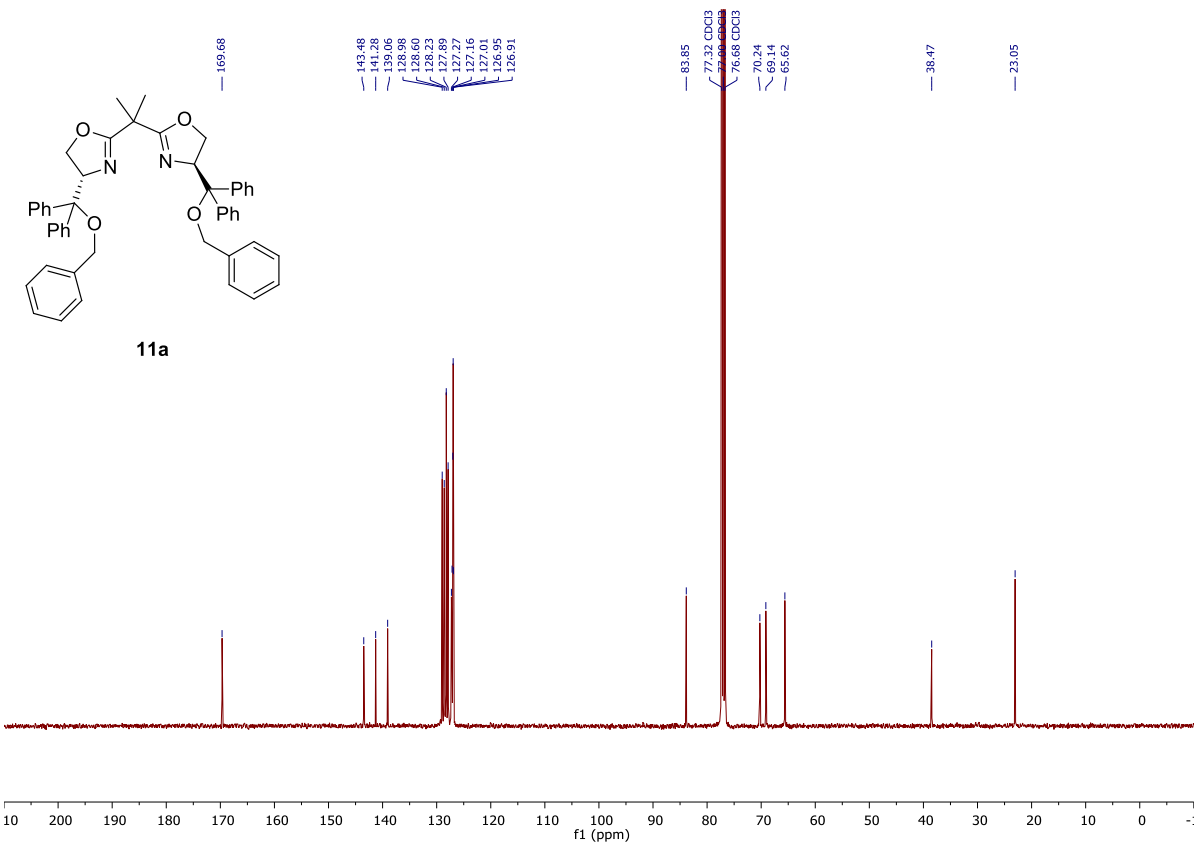

**10h**

**(4S,4'S)-2,2'-(propane-2,2-diyl)bis(4-((benzyloxy)diphenylmethyl)-4,5-dihydrooxazole) (11a)**

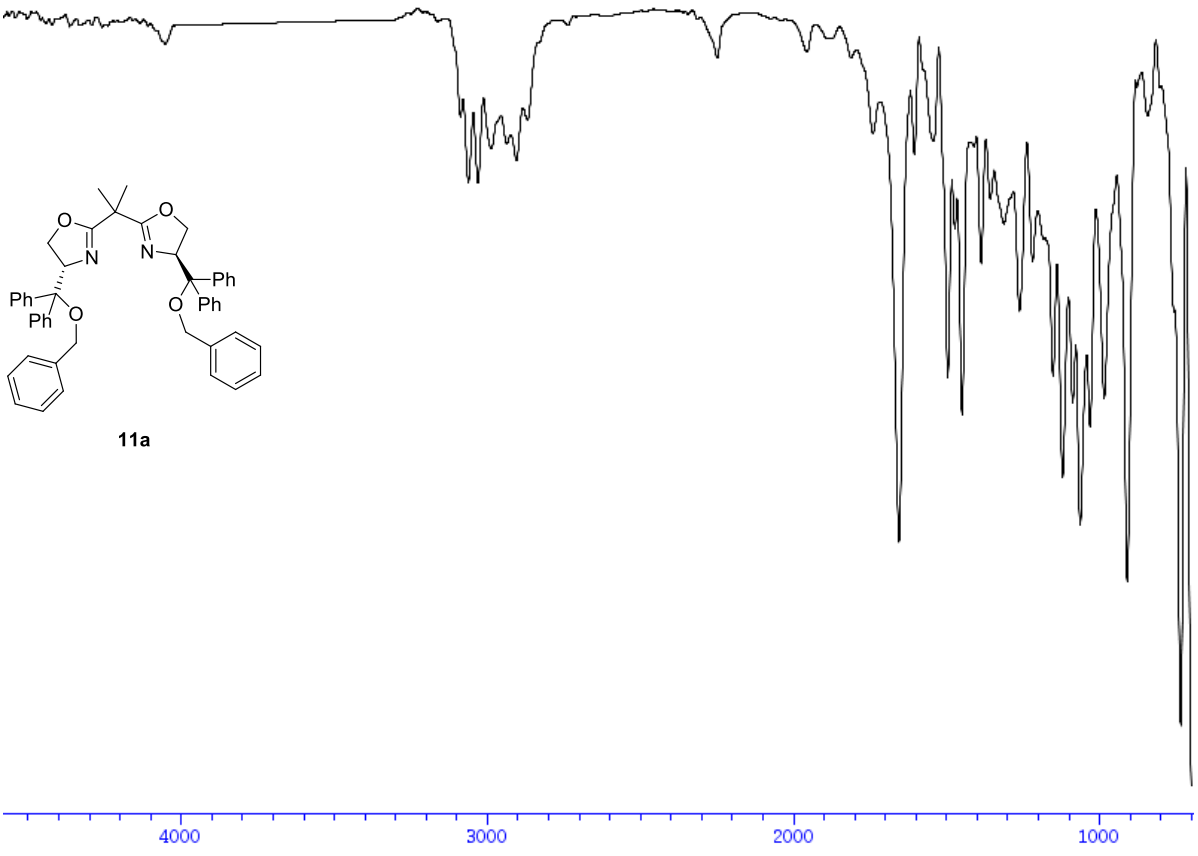
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**IR**

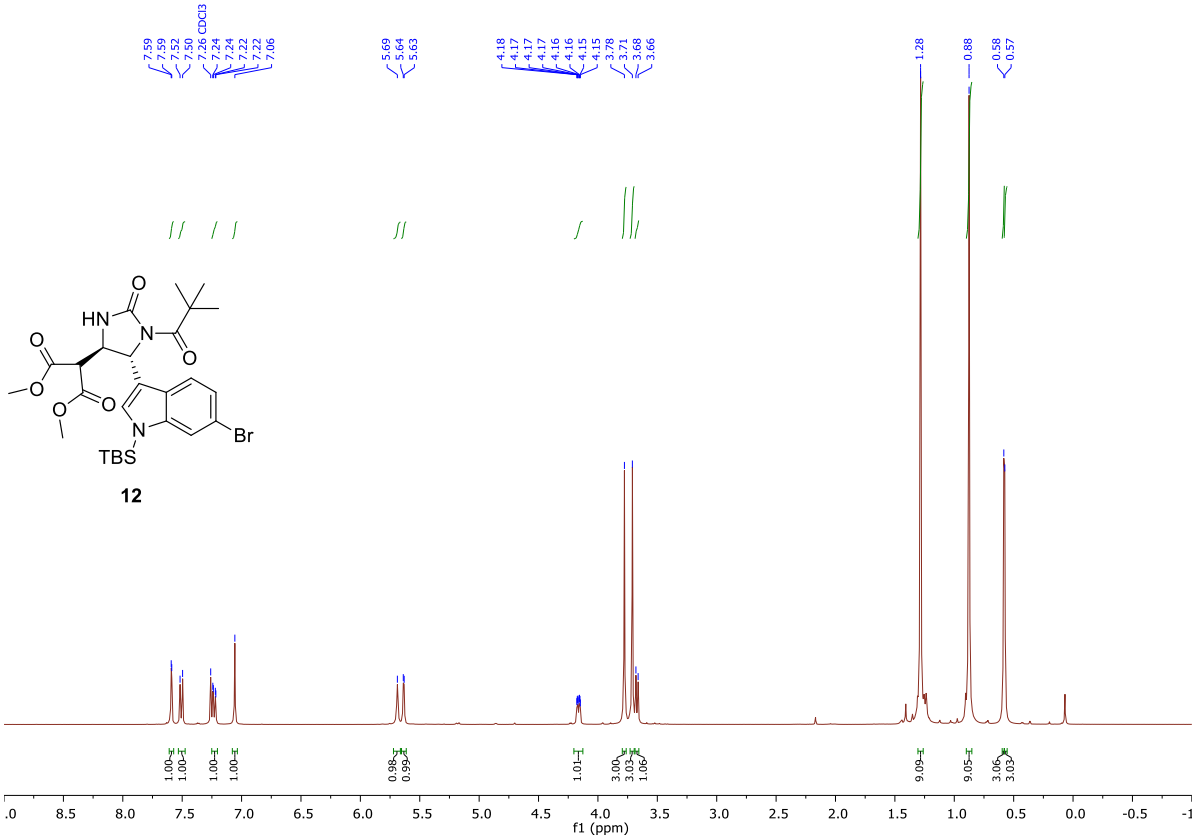


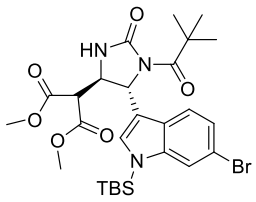



**11a**

**Dimethyl 2-(5-(6-bromo-1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxo-1-pivaloylimidazolidin-4-yl)malonate (12)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**12**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

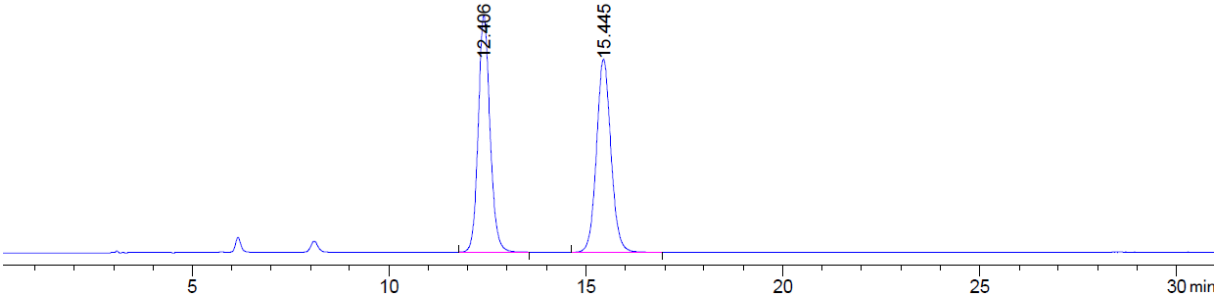




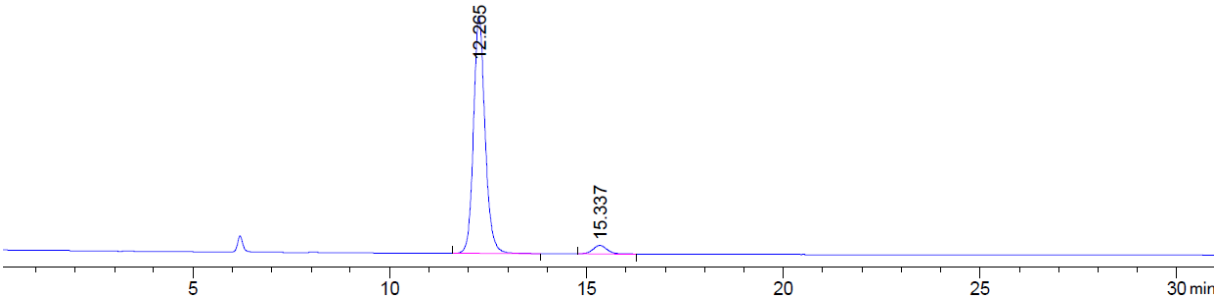


**12**

**HPLC**

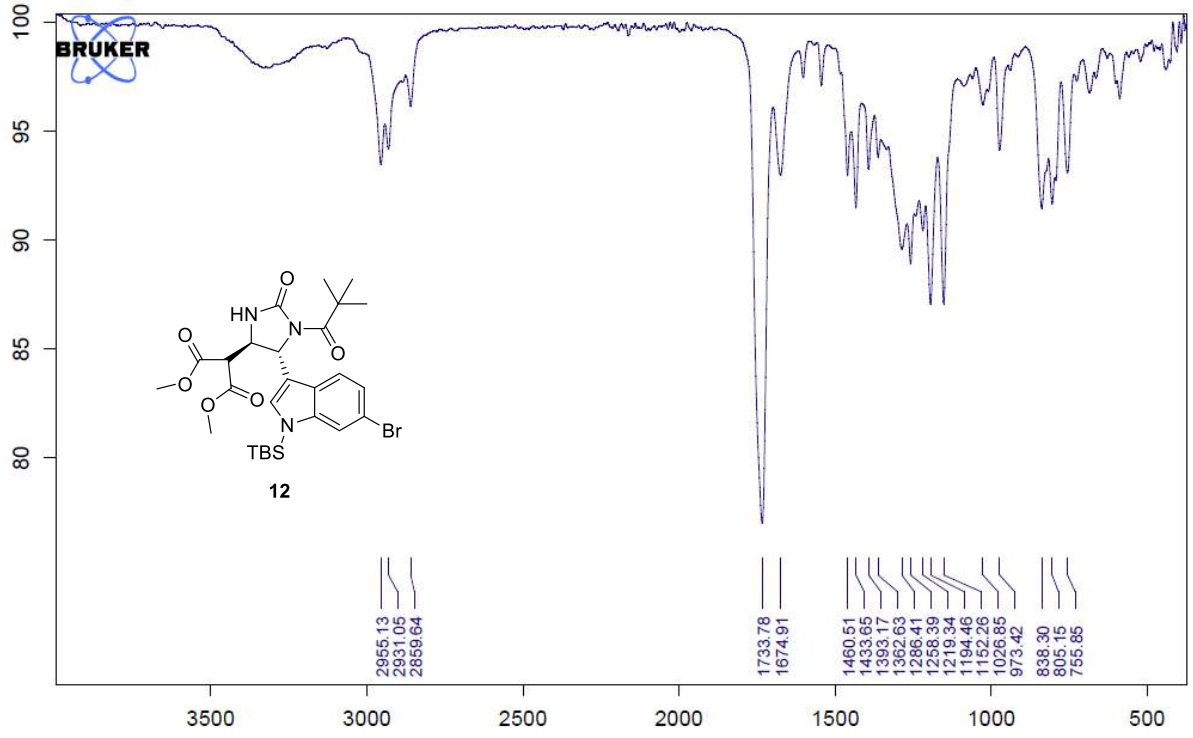



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.406 | BB | 0.3190 | 499.85181 | 23.99638 | 49.9896 |
| 2 | 15.445 | BB | 0.3949 | 500.05972 | 19.52072 | 50.0104 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 12.265 | BB | 0.3099 | 1376.40649 | 67.48692 | 95.8382 |
| 2 | 15.337 | BB | 0.3851 | 59.77117 | 2.39564 | 4.1618 |

**IR**


BRUKER
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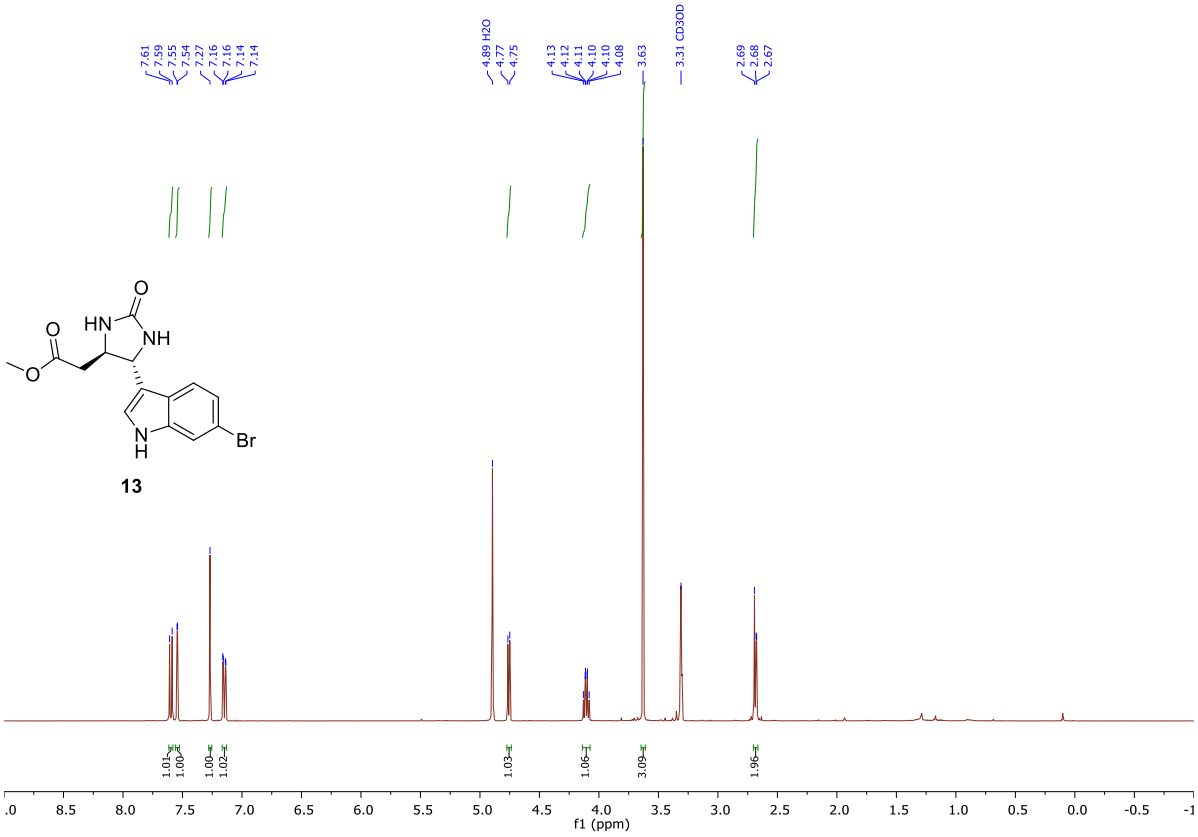
90
85
80
3500
3000
2500
2000
1500
1000
500
2955.13
2931.05
2859.64
1733.78
1674.91
1460.51
1433.65
1393.17
1362.63
1286.41
1258.39
1219.34
1194.46
1152.26
1026.85
973.42
838.30
805.15
755.85
HN
N
O
O
O
O
O
O
N
TBS
Br
12

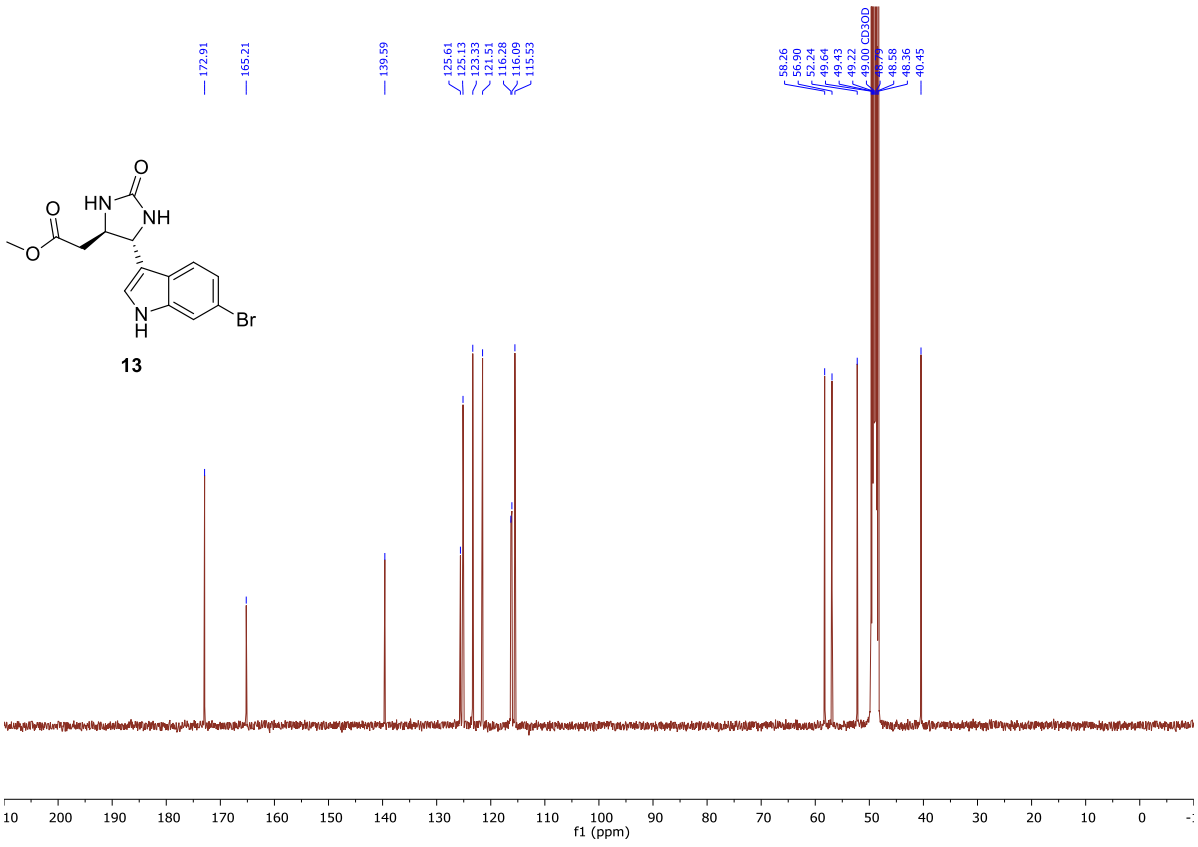
**Methyl 2-(5-(6-bromo-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)acetate (13)**

**$^{1}$H-NMR (400 MHz, $CD_3OD$)**



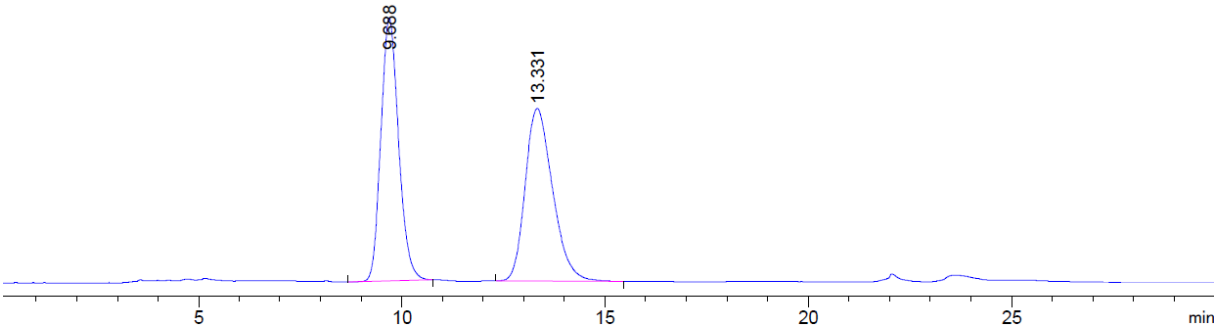

13

**$^{13}$C-NMR (101 MHz, $CD_3OD$)**

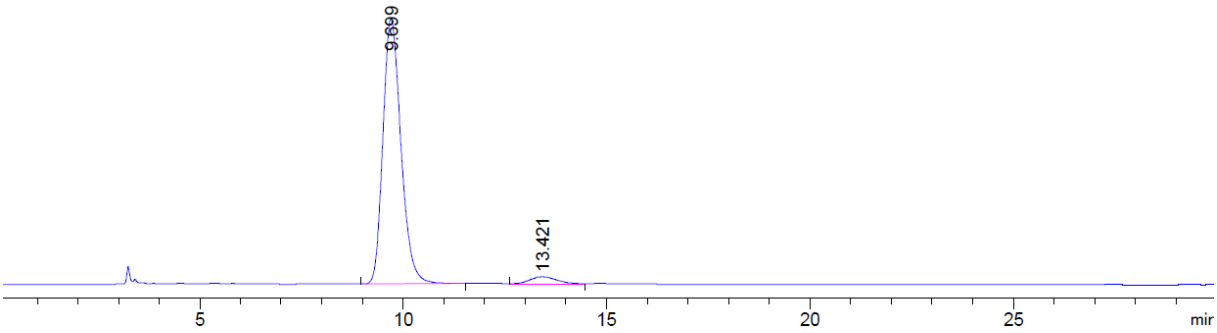



13

**HPLC**

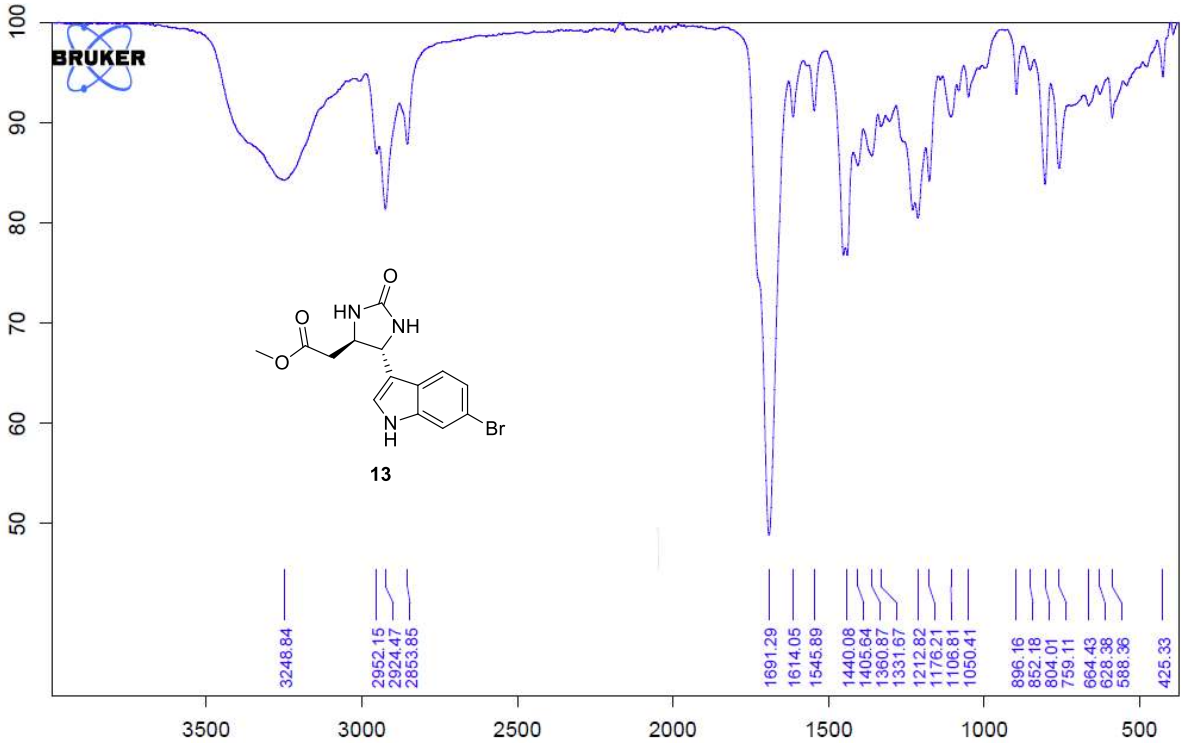



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.688 | BB | 0.4616 | 1951.05151 | 64.38180 | 49.5707 |
| 2 | 13.331 | BB | 0.7122 | 1984.84839 | 42.24086 | 50.4293 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 9.699 | BB | 0.4781 | 3.11224e4 | 1008.40546 | 96.3021 |
| 2 | 13.421 | BB | 0.7020 | 1195.05774 | 26.40552 | 3.6979 |

**IR**


BRUKER
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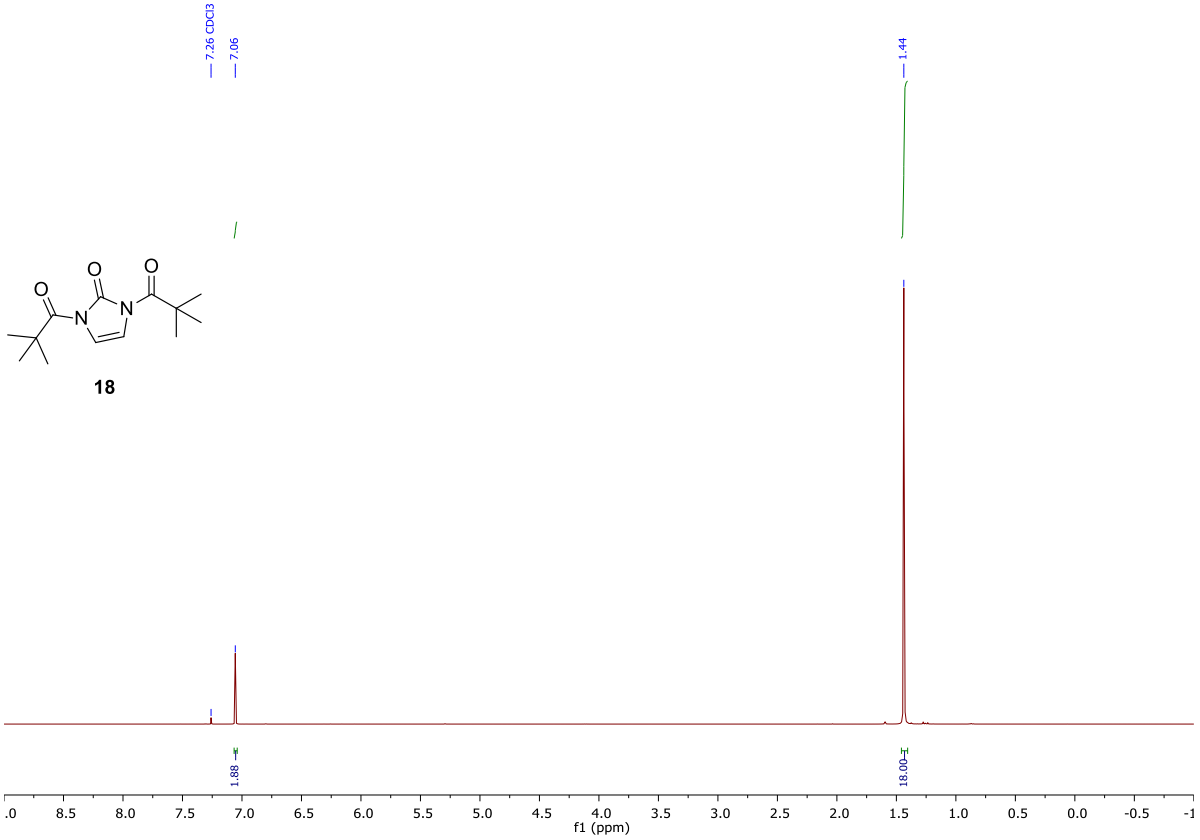
70
60
50
3500
3000
2500
2000
1500
1000
500
3248.84
2952.15
2924.47
2853.85
1691.29
1614.05
1545.89
1440.08
1405.64
1360.87
1331.67
1212.82
1176.21
1106.81
1050.41
896.16
852.18
804.01
759.11
664.43
628.38
588.36
425.33
HN
NH
O
O
N
H
Br

**13**

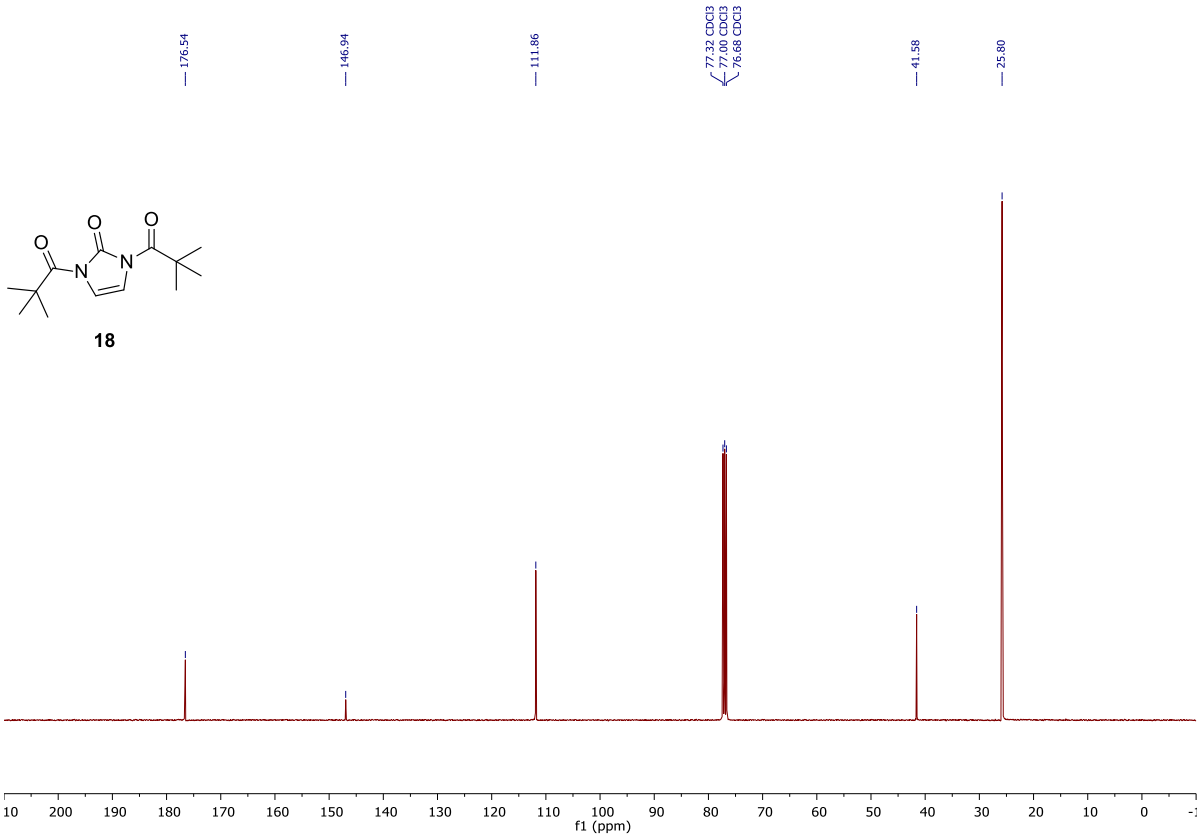
**1,1'-(2-oxo-1H-imidazole-1,3(2H)-diyl)bis(2,2-dimethylpropan-1-one) (18)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



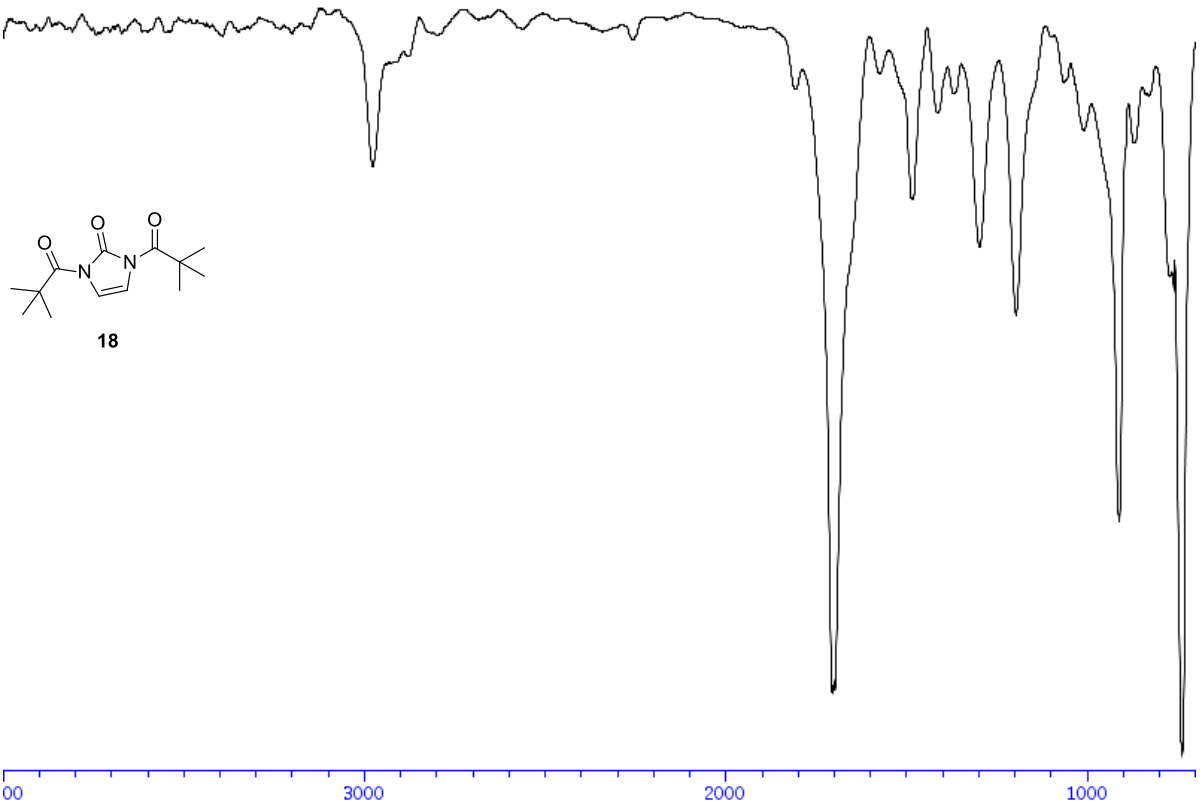

18

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



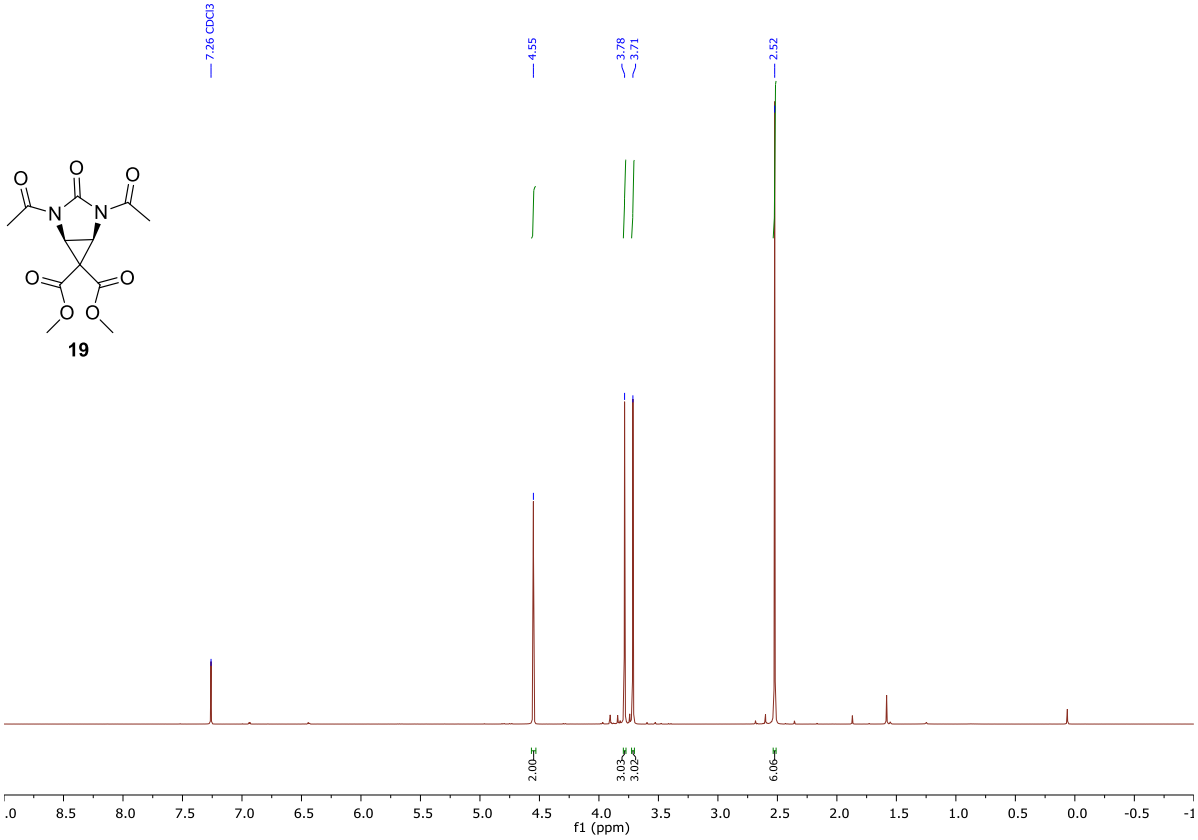

18

**IR**

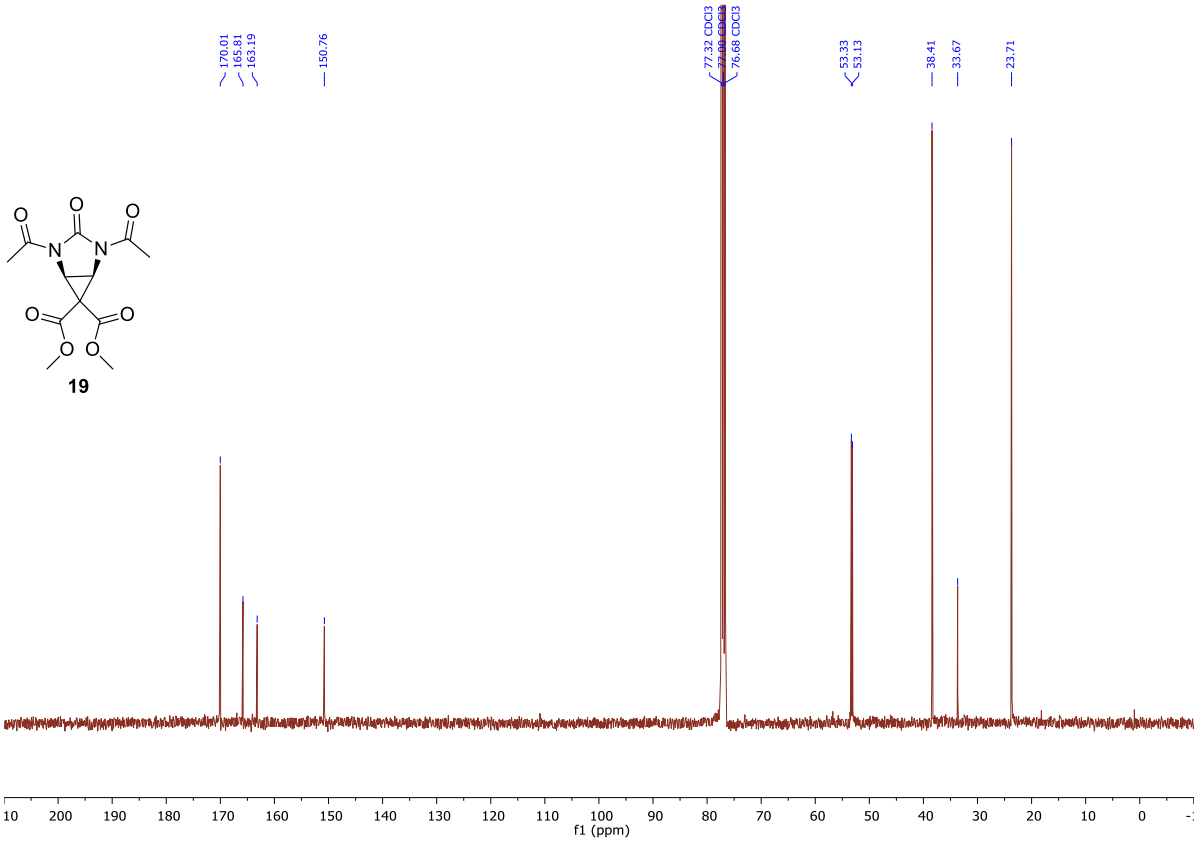


**Dimethyl 2,4-diacetyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (19)**

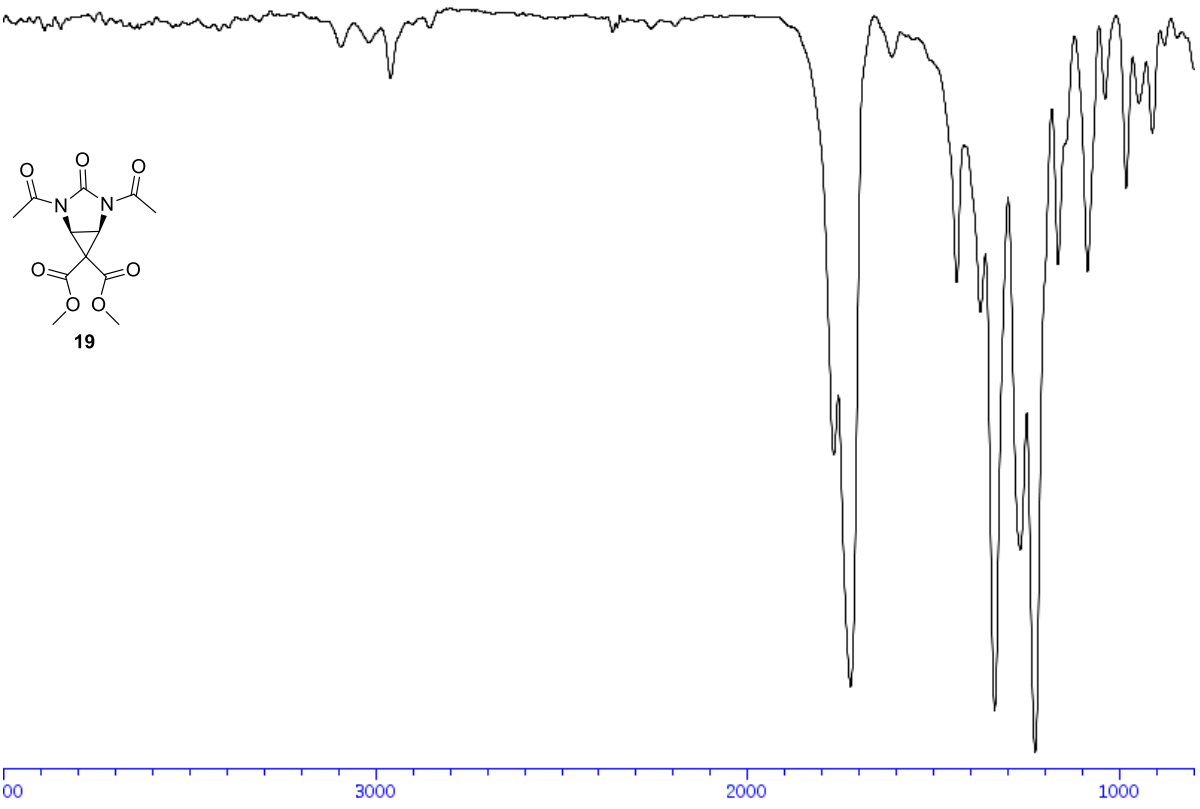
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**IR**

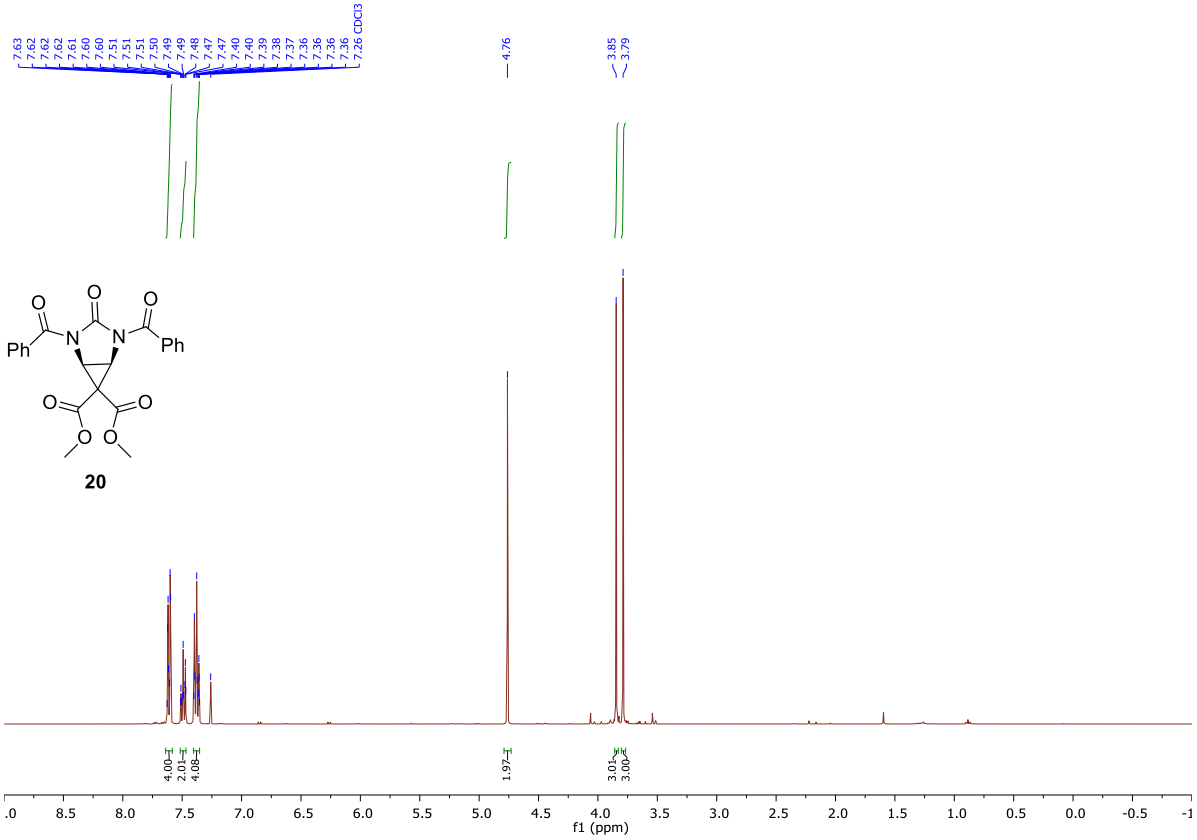




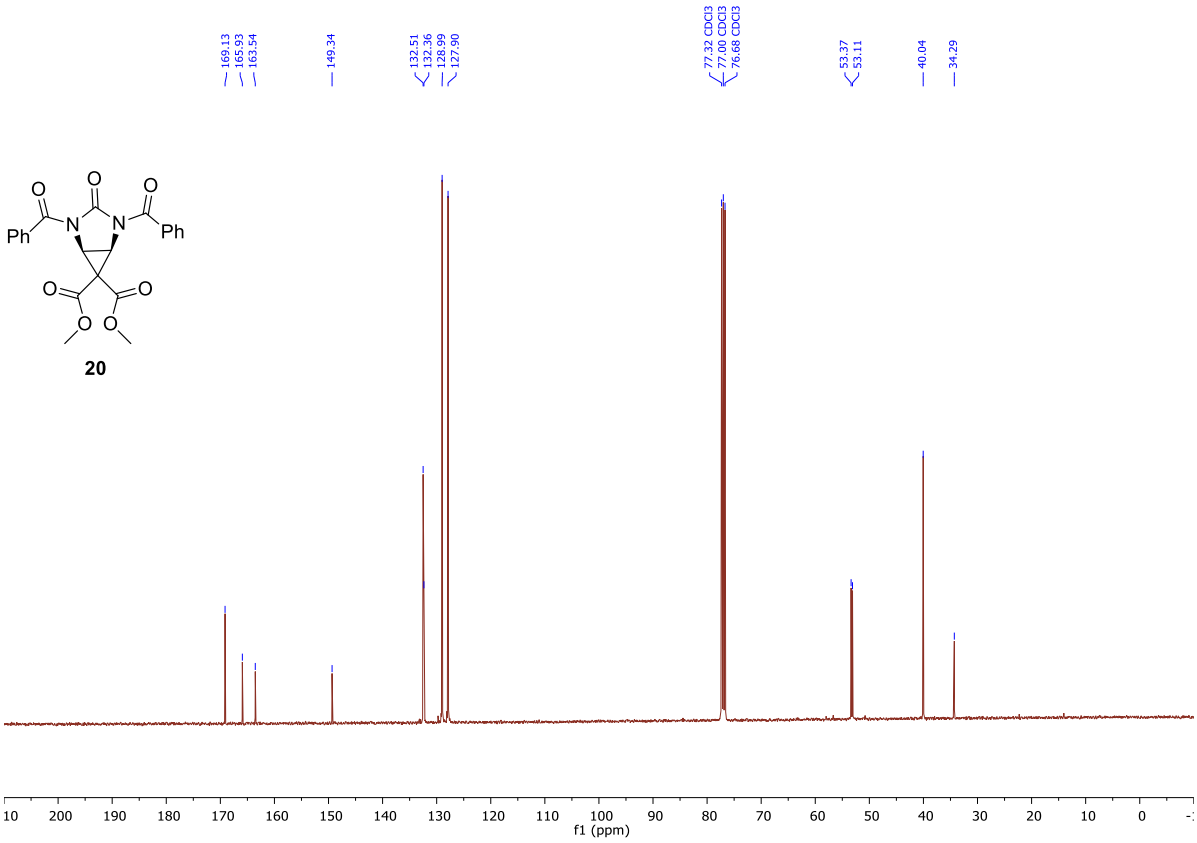

**19**

**Dimethyl 2,4-dibenzoyl-3-oxo-2,4-diazabicyclo[3.1.0]hexane-6,6-dicarboxylate (20)**

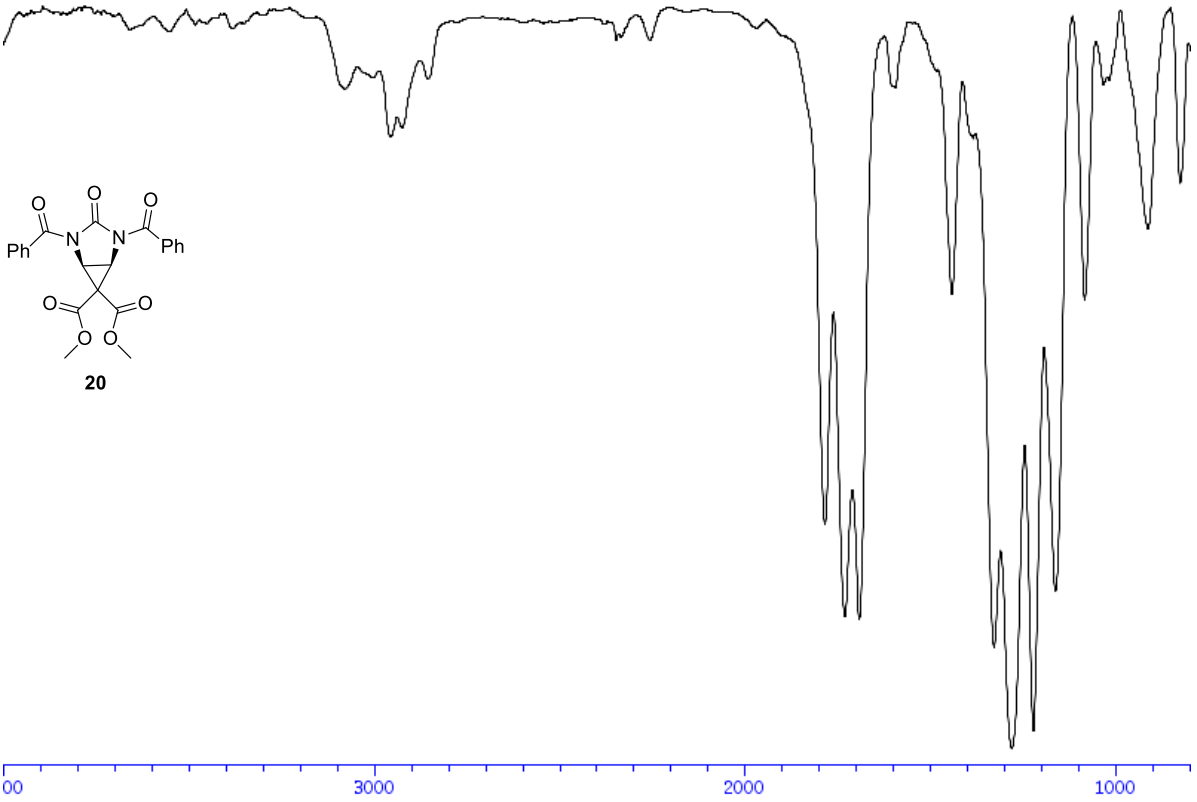
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**IR**

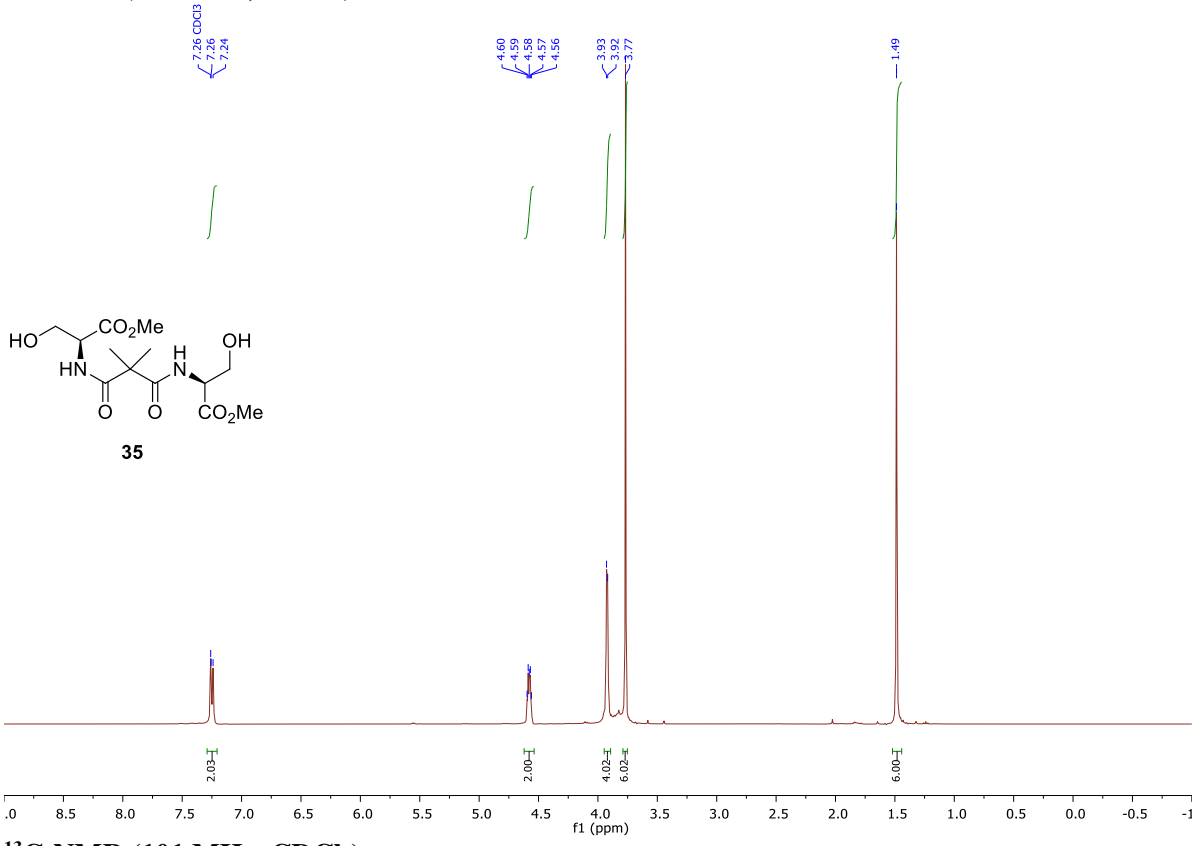




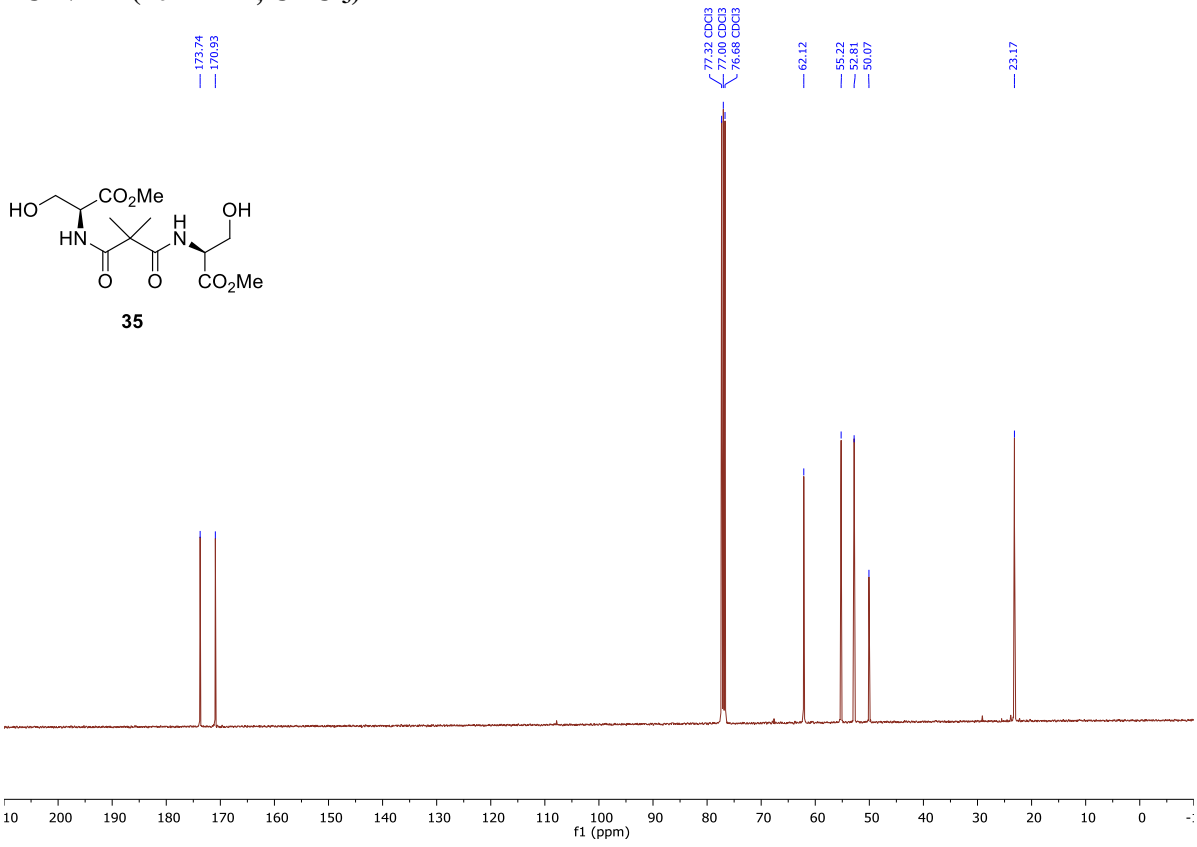

**20**

**(2S,2'S)-dimethyl 2,2'-((2,2-dimethylmalonyl)bis(azanediyl))bis(3-hydroxypropanoate) (35)**

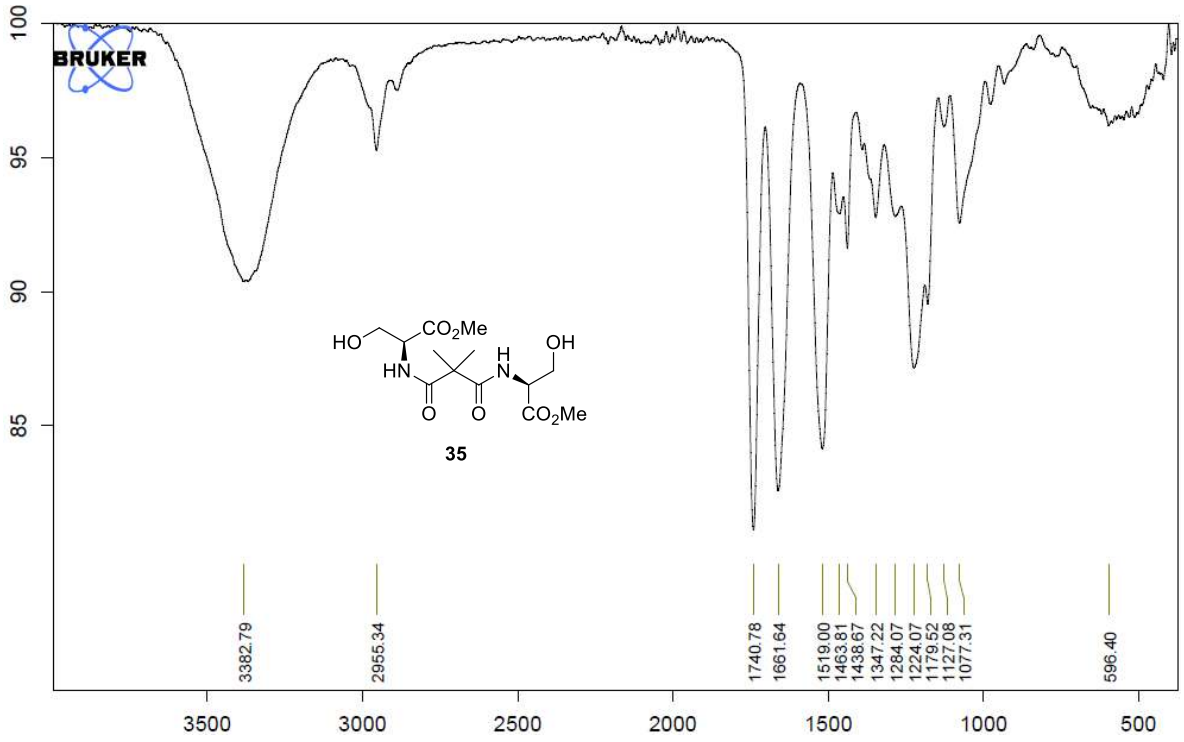
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**




**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

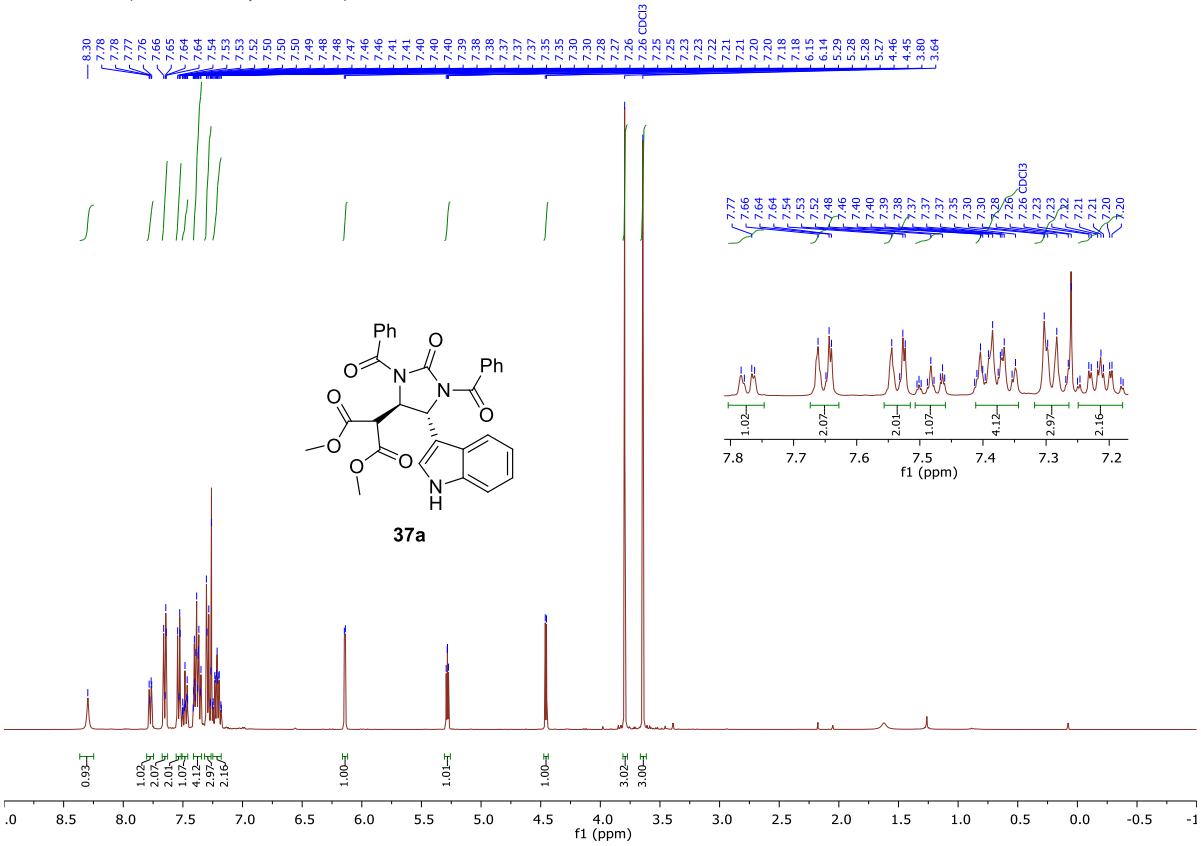


**IR**

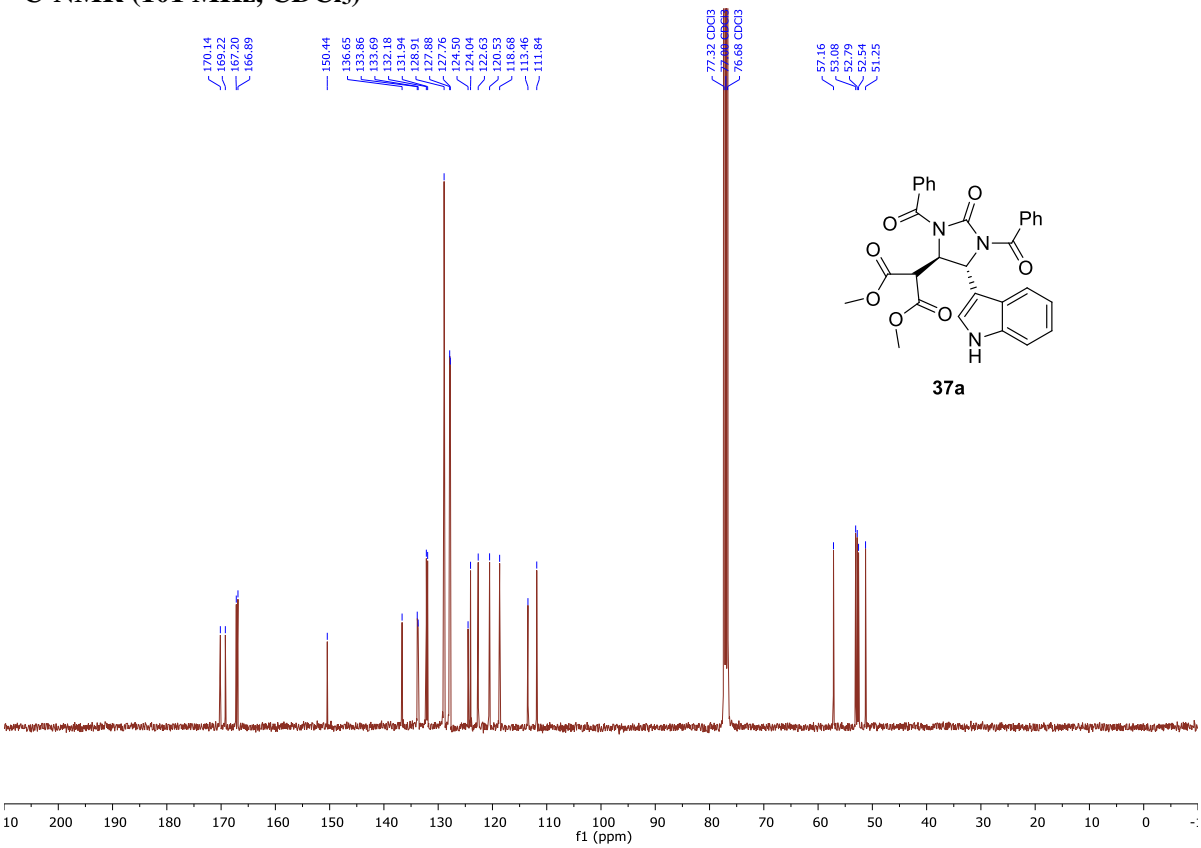

100
95
90
85
BRUKER
HO
CO2Me
HN
H
N
OH
O
O
CO2Me
35
3382.79
2955.34
1740.78
1661.64
1519.00
1463.81
1438.67
1347.22
1284.07
1224.07
1179.52
1127.08
1077.31
596.40
3500
3000
2500
2000
1500
1000
500

**Dimethyl 2-(1,3-dibenzoyl-5-(1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (37a)**

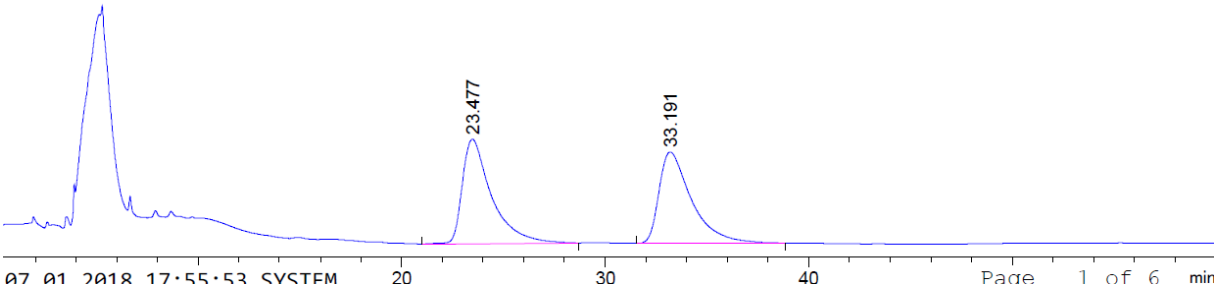
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



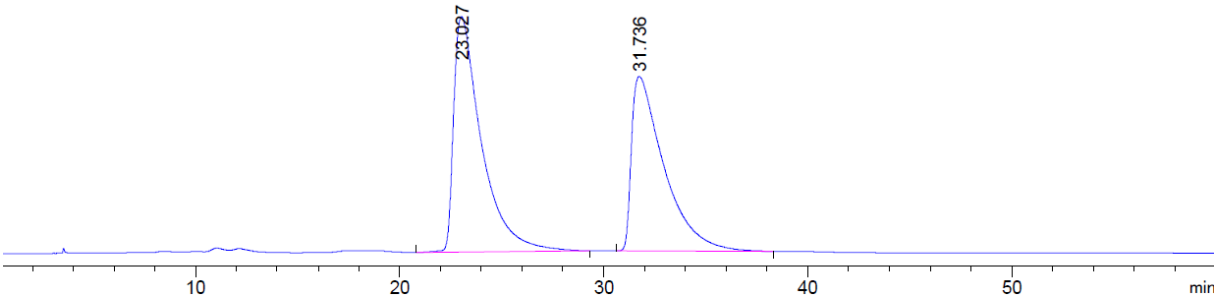

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

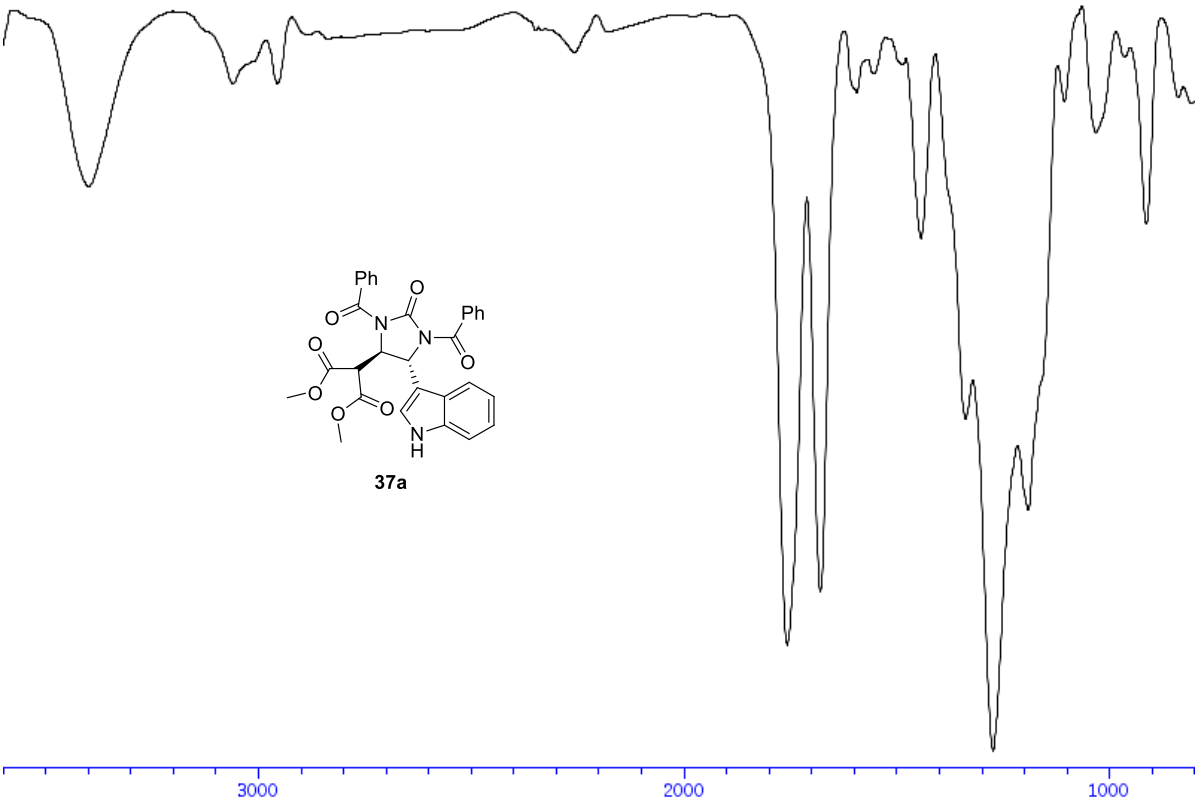



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 23.477 | BB | 1.4360 | 2106.84277 | 20.97338 | 50.8853 |
| 2 | 33.191 | BB | 1.5470 | 2033.53027 | 18.32022 | 49.1147 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 23.027 | BB | 1.3877 | 2.37098e4 | 249.72836 | 53.6806 |
| 2 | 31.736 | BB | 1.5937 | 2.04584e4 | 185.07137 | 46.3194 |

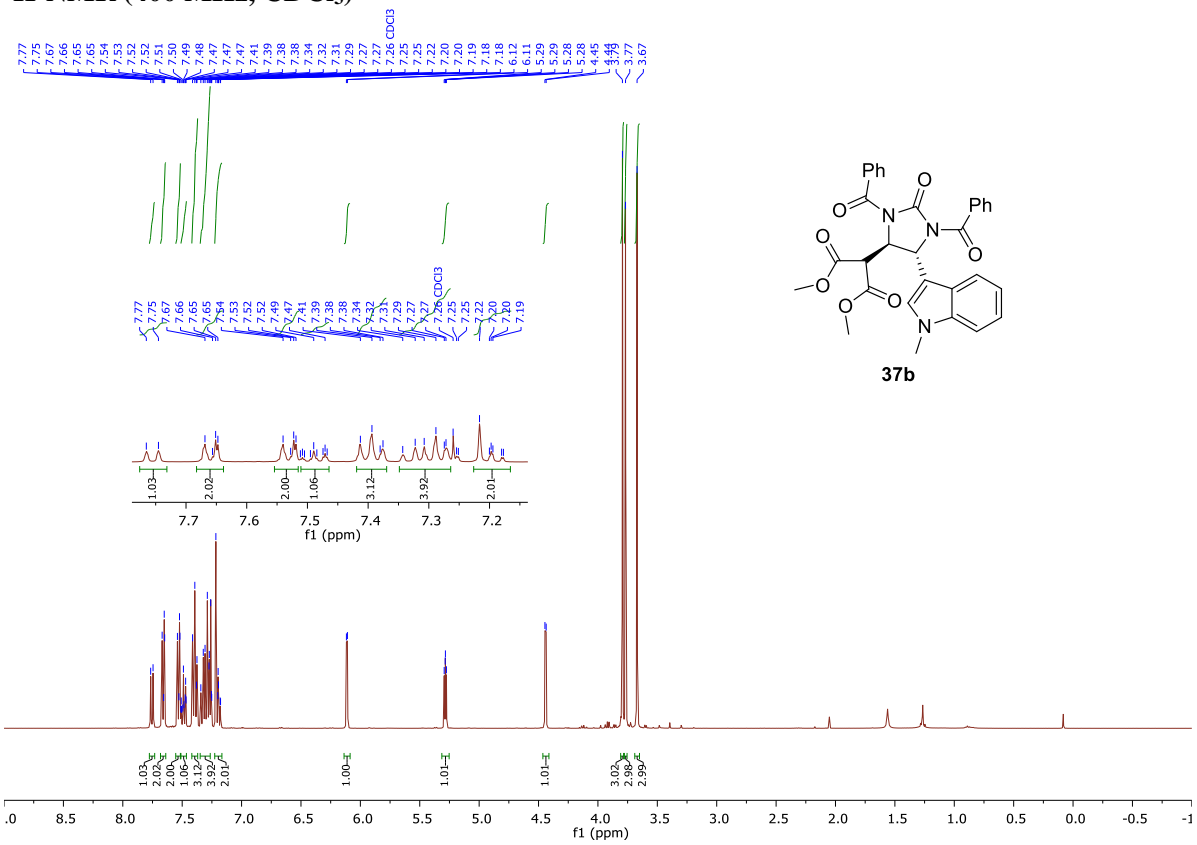
**IR**




**37a**

**Dimethyl 2-(1,3-dibenzoyl-5-(1-methyl-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (37b)**

**$^{1}$H-NMR (400 MHz, $CDCl_3$)**

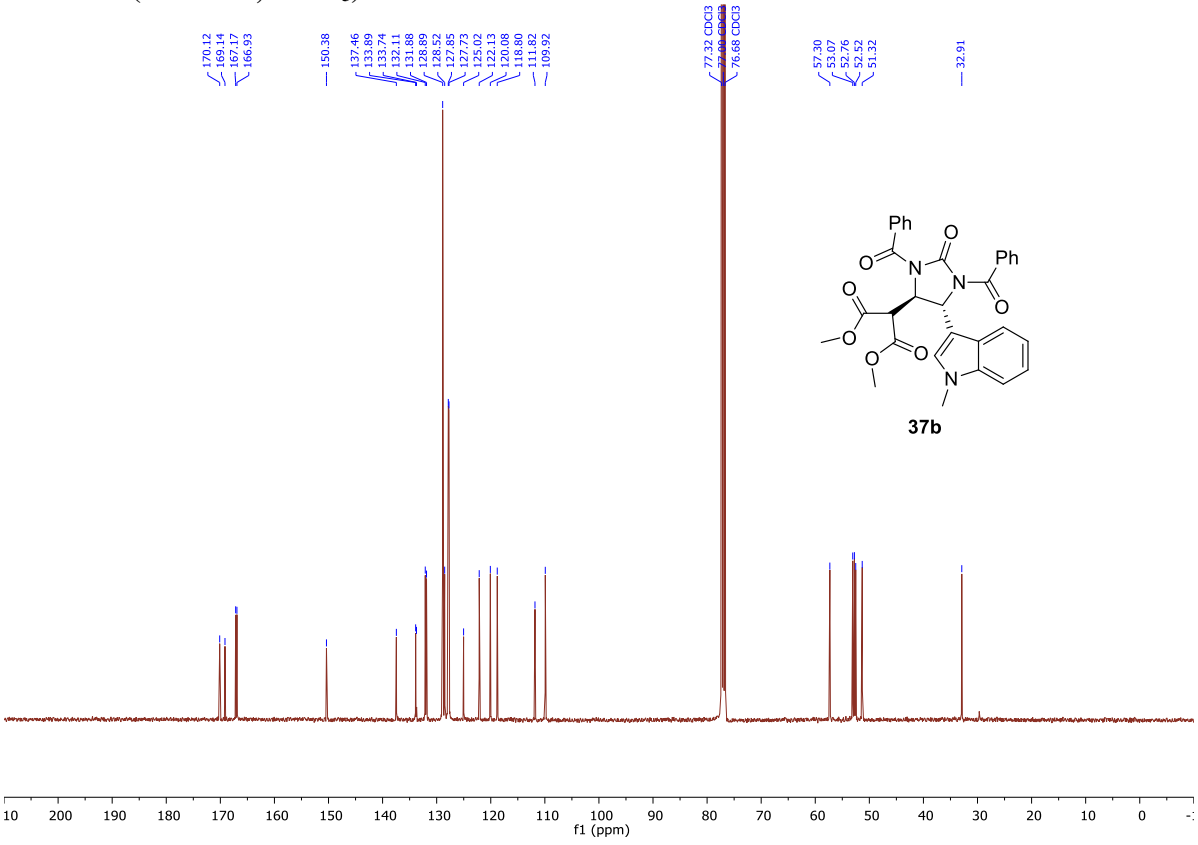






**37b**

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**

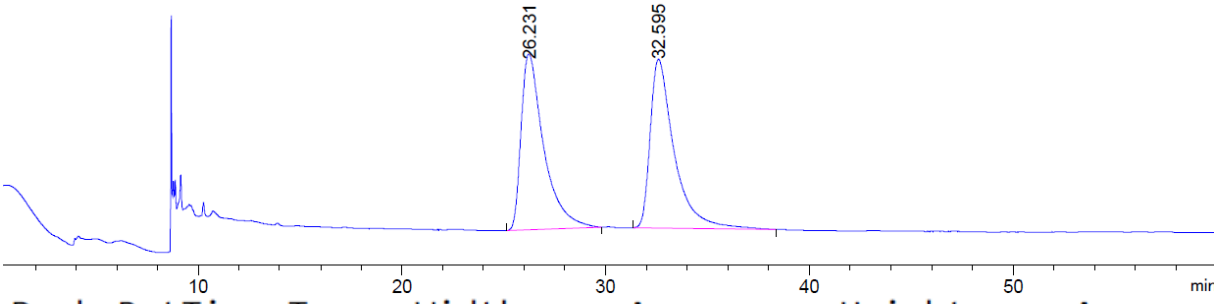




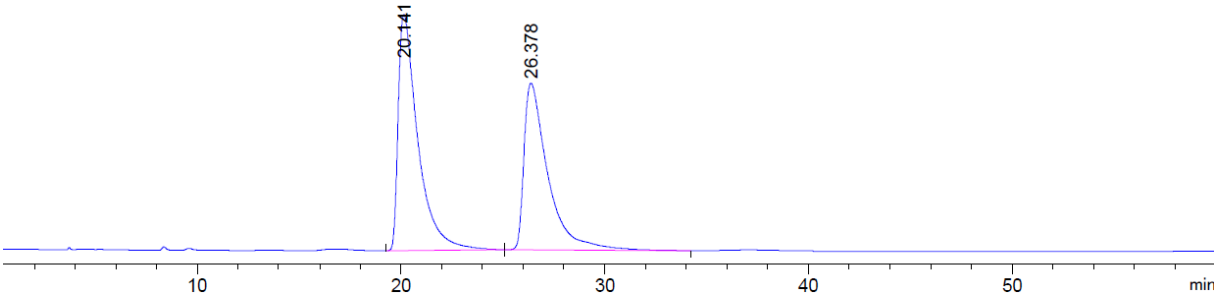


**37b**

**HPLC**

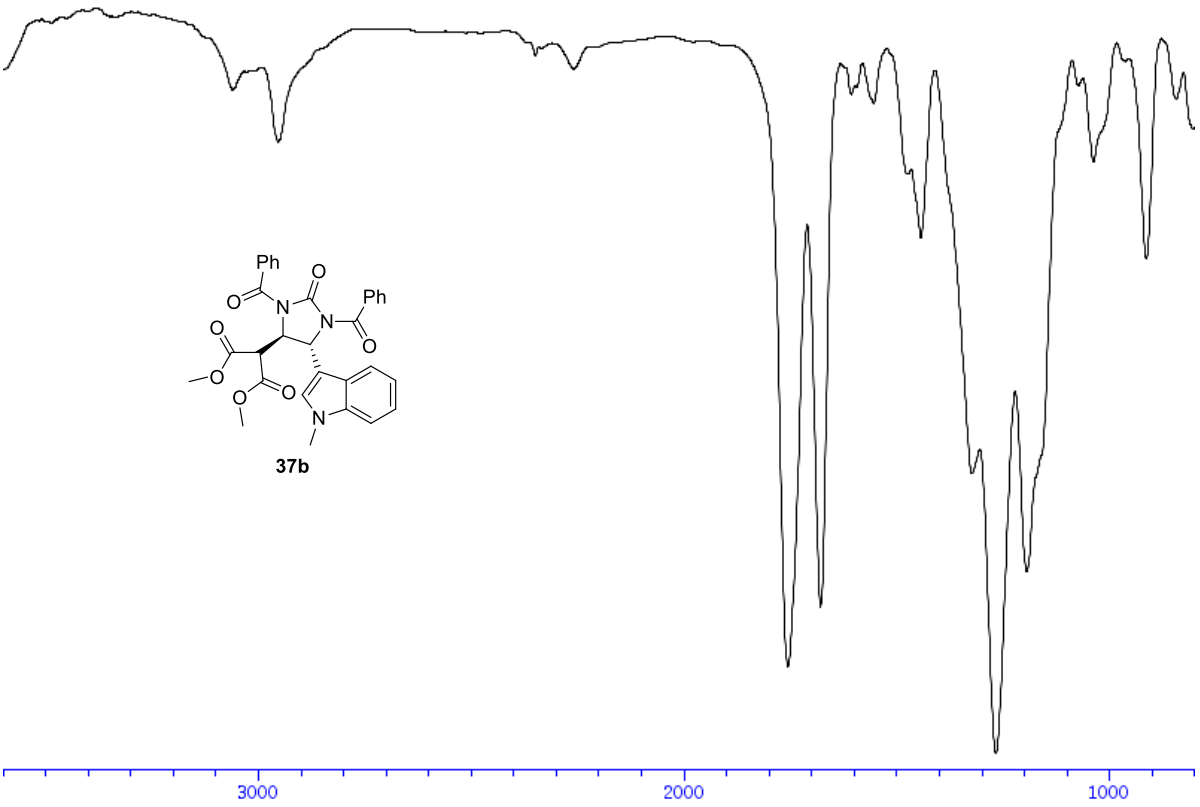



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 26.231 | BB | 1.1351 | 1276.38037 | 16.52586 | 49.5286 |
| 2 | 32.595 | BB | 1.1962 | 1300.67651 | 15.83574 | 50.4714 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 20.141 | BB | 0.9875 | 1.15441e4 | 171.90218 | 53.8875 |
| 2 | 26.378 | BB | 1.1885 | 9878.47363 | 121.24817 | 46.1125 |

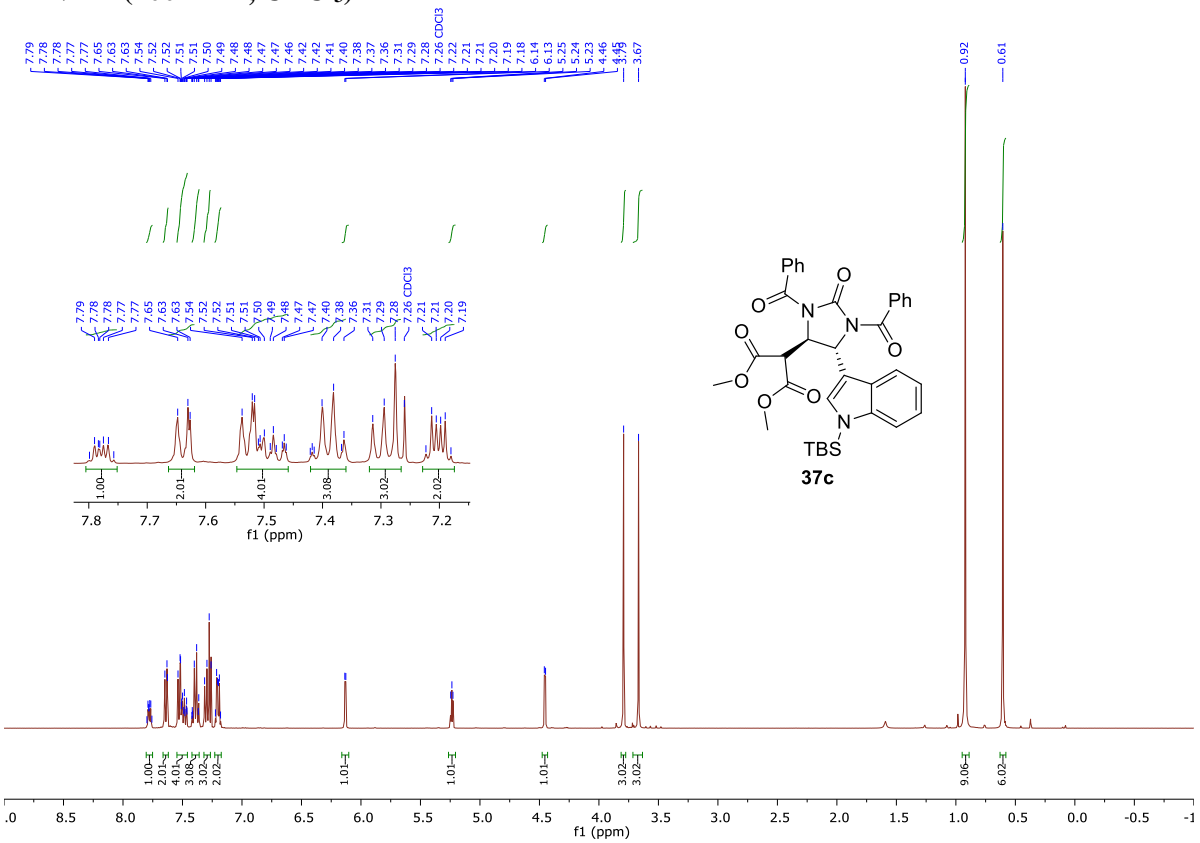
**IR**



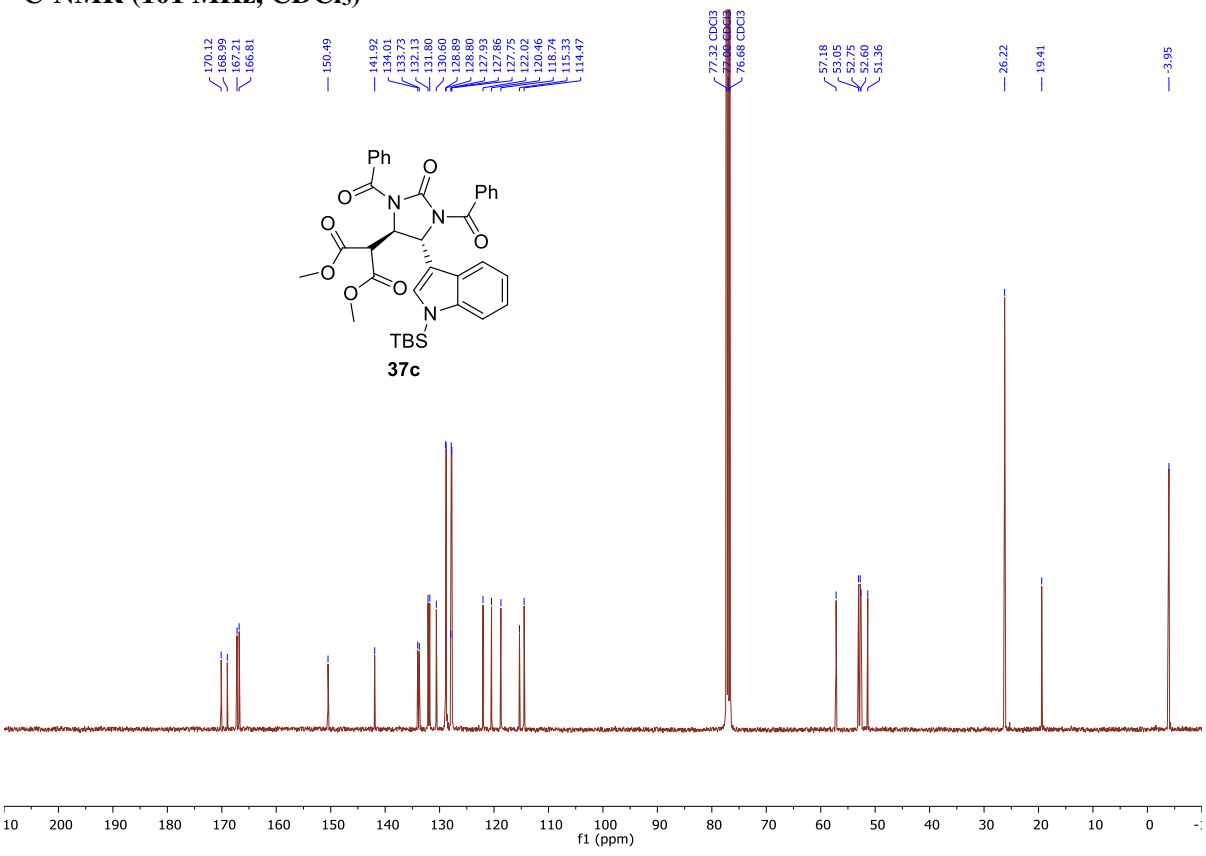

**37b**

**Dimethyl 2-(1,3-dibenzoyl-5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (37c)**

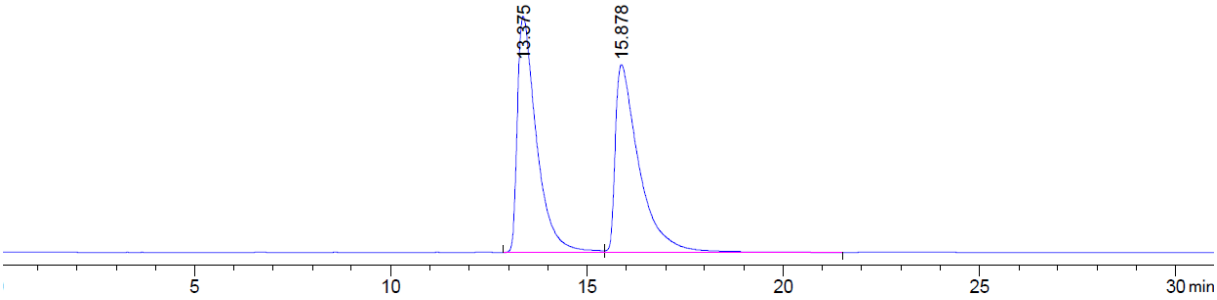
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



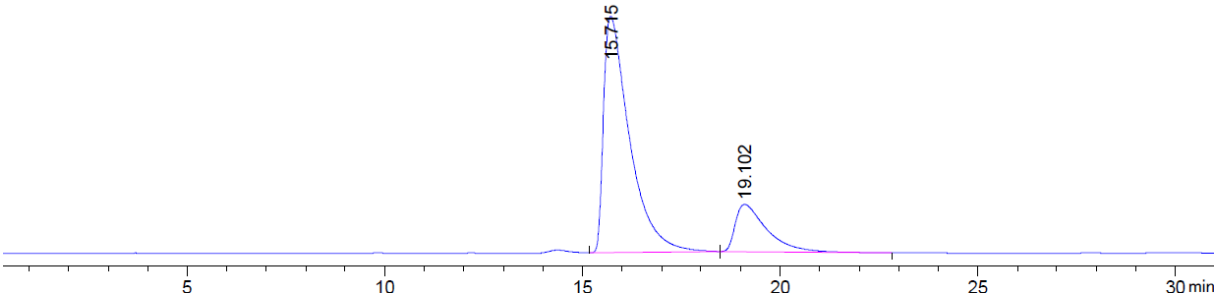

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**

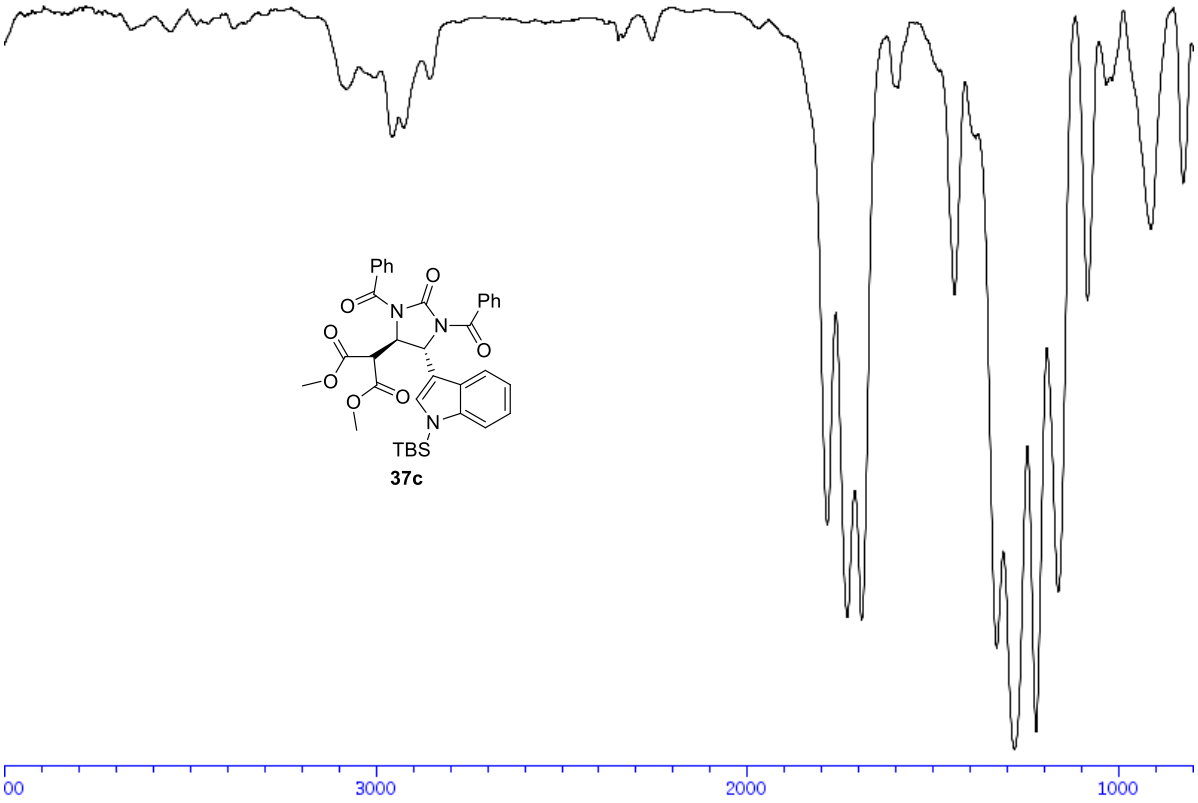



| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 13.375 | BV | 0.5039 | 1.03140e4 | 303.93405 | 50.3354 |
| 2 | 15.878 | VB | 0.6115 | 1.01766e4 | 241.56946 | 49.6646 |



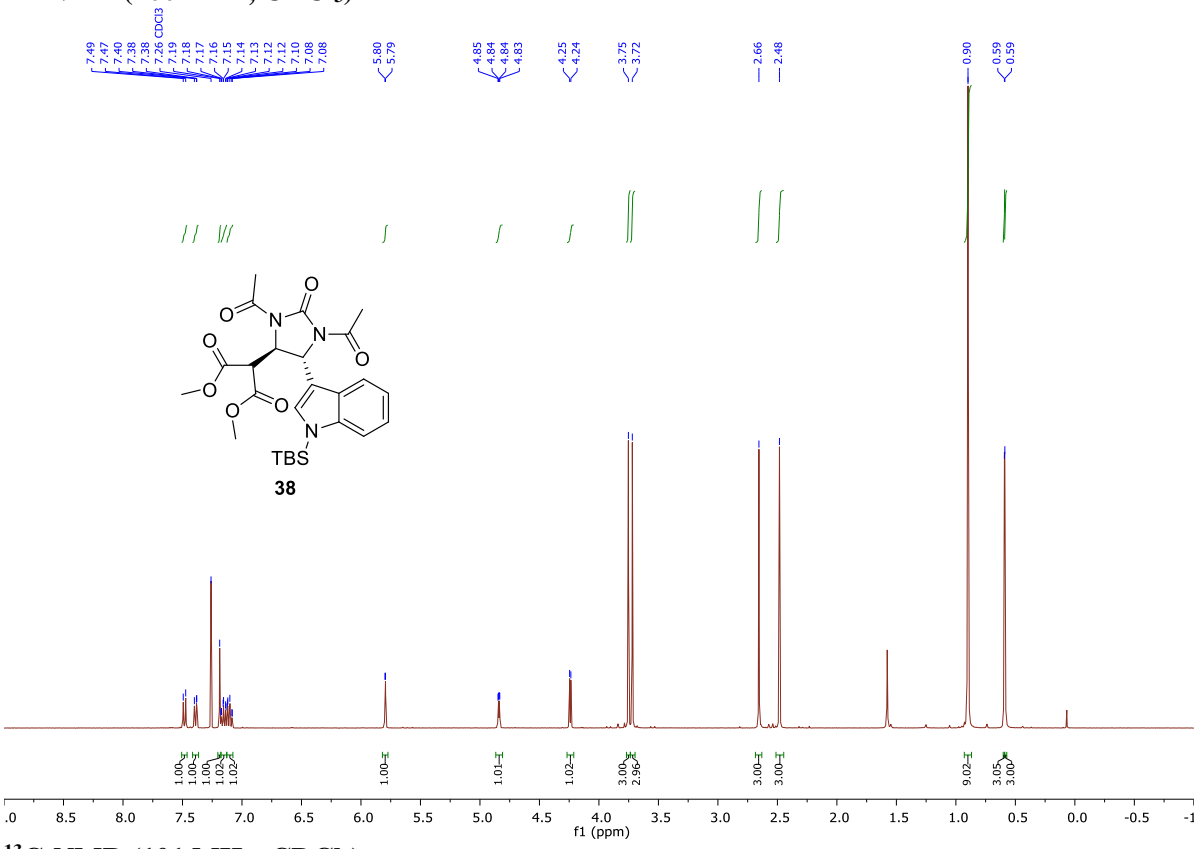

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 15.715 | BB | 0.6740 | 1.80448e4 | 394.22021 | 80.5650 |
| 2 | 19.102 | BB | 0.8102 | 4353.02441 | 78.83581 | 19.4350 |

**IR**

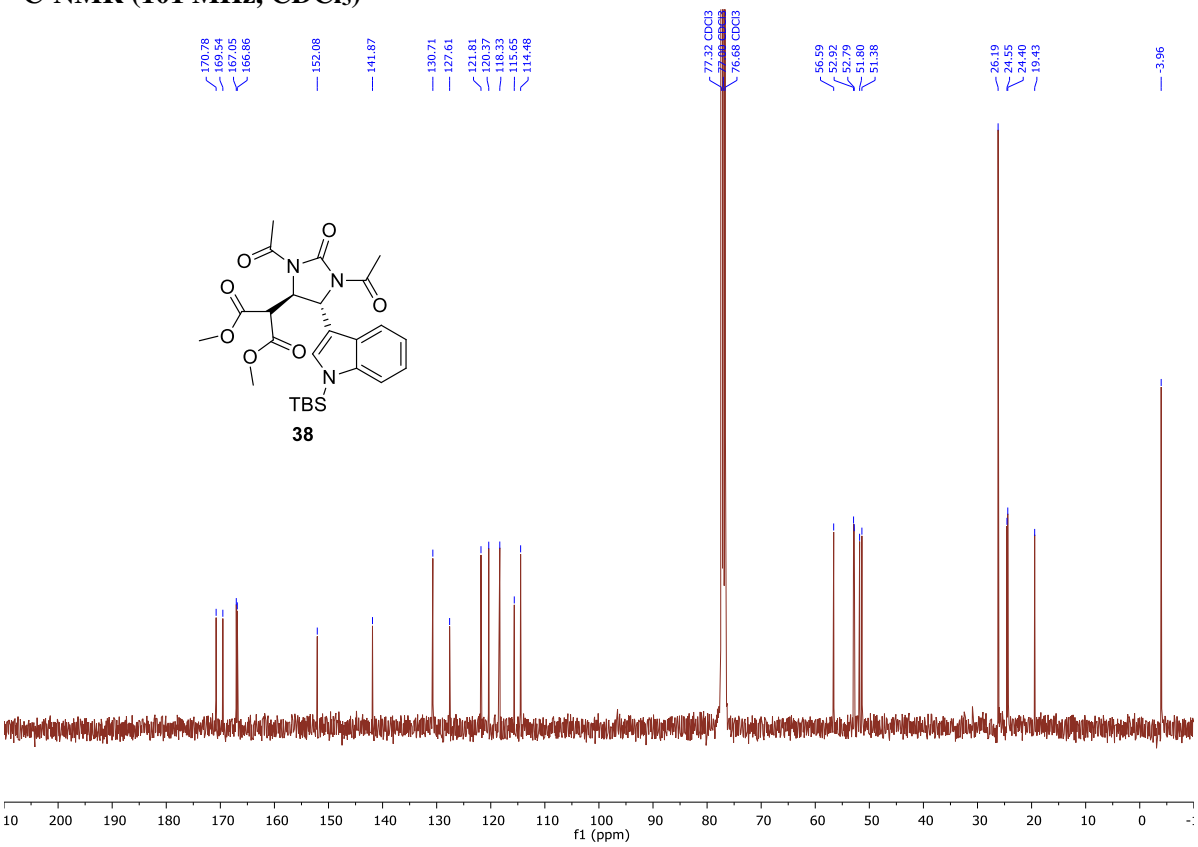


**Dimethyl 2-(1,3-diacetyl-5-(1-(tert-butyldimethylsilyl)-1H-indol-3-yl)-2-oxoimidazolidin-4-yl)malonate (38)**

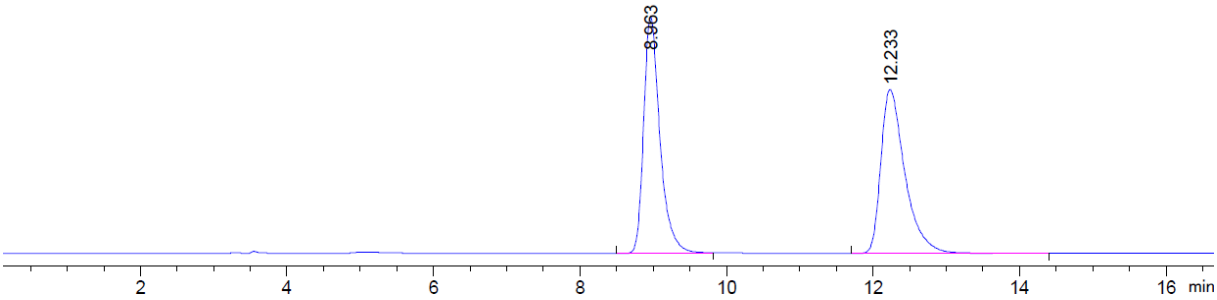
**$^{1}$H-NMR (400 MHz, $CDCl_3$)**



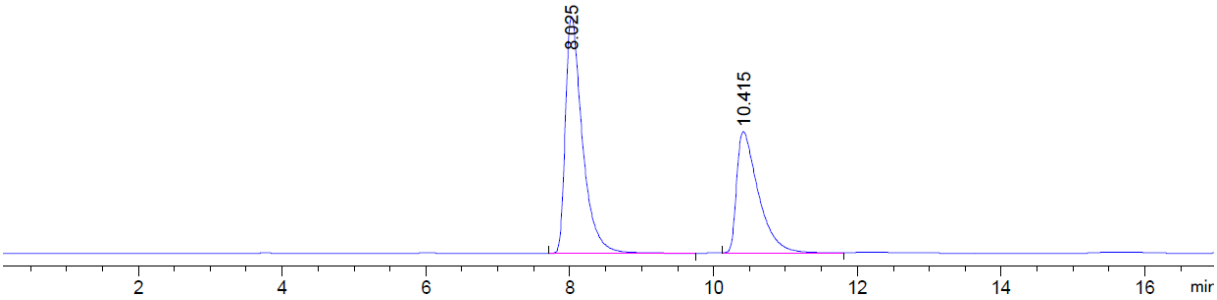

**$^{13}$C-NMR (101 MHz, $CDCl_3$)**



**HPLC**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 8.963 | BV | 0.2342 | 2.80832e4 | 1818.24341 | 49.4899 |
| 2 | 12.233 | BB | 0.3440 | 2.86622e4 | 1257.33997 | 50.5101 |




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 8.025 | BB | 0.2452 | 4161.33301 | 253.93781 | 60.5109 |
| 2 | 10.415 | BB | 0.3101 | 2715.66553 | 129.78133 | 39.4891 |

**IR**