Branch- and Enantioselective Allylic C–H Alkylation Works Well for Almost All Types of α-Alkenes

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Abstract

Asymmetric functionalization of alkenes represents one of the most attractive and straightforward methods to achieve precise assembly of molecular complexity from cost-effectiveness and sustainability viewpoints. Although the regio- and enantioselective transformations on the carbon-carbon double bond of alkenes have been extensively studied, those on the allylic C–H bonds of inactivated alkenes remain to be explored. Here, we report a Pd-catalyzed branch- and enantioselective allylic C–H alkylation, capable of accommodating almost all types of α-alkenes that range from feedstocks annually manufactured on million-ton scale to olefins tethering a wide scope of appended functionalities, providing unconventional access to chiral γ,δ-unsaturated amides. Notably, mechanistic studies reveal that the regioselectivity is not only governed by the coordination pattern of nucleophiles but also regulated by the ligational behaviors of ligands, highlighting the importance of the mono-ligation of chiral phosphoramidite ligands in provoking high levels of stereo- and branch-selectivity via a nucleophile-coordination enabled inner-sphere allylation pathway.

Main Text

Alkenes are among the most abundant feedstock hydrocarbons. The unparalleled reactivity and diverse range of reaction modes workable in the C–C double bond allocate the alkenes unique capacity to serve as versatile reagents in the realm of synthetic organic chemistry.[1] Indeed, the selective functionalization of alkenes based on the fundamental reactions working on the C–C double bond has long been the linchpin in synthetic chemistry,[2-4] culminating in a huge number of synthetically significant transformations (Figure 1a), some of which have exerted historical impact on the society and constitute backbones of organic chemistry. The other dimension in the historical context of synthetic organic chemistry includes the precise and concurrent control of both the regio- and stereoselectivities, which has also experienced great success over the past decades. However, no significant progresses have made on the asymmetric functionalization of allylic C–H bonds until recently, although the allylic C–H activation has been observed for more than 60 years[5] and racemic protocols have frequently emerged over the past decades (Figure 1a).[6-8] So far, three principally distinct transition metal catalyst systems are convinced to render highly stereoselective allylic C–H functionalization. Chiral bioxazoline-Cu complexes generally offer high levels of enantioselectivity for Kharasch-Sosnovsky-type reaction, but are seemingly only amenable for cyclic alkenes (Figure 1b).[9] Liu and coworkers described a Cu-catalyzed site-specific asymmetric allylic C–H cyanation (Figure 1b),[10] however, this concept has not been expanded to other nucleophiles, yet. Apart from the copper catalysis, chiral dirhodium carbenes are also efficient for regio- and stereoselective allylic C–H alkylation of internal alkenes (Figure 1c).[11,12] Very recently, a planar-chiral rhodium indenyl complex was identified to enable a branch- and enantioselective allylic C–H amidation of α-alkenes (Figure 1c),[13] but seems to be only applicable to the C–N bond-forming events. Chiral palladium complex catalysis has been a robust alternative strategy to enable the asymmetric C–H functionalization of versatile α-alkenes.[14] White and coworkers identified that aryl sulfoxide-oxazoline (ArSOX) ligands can exhibit high enantioinduction for asymmetric allylic oxidation[15] while allows the

alkylation reaction to favorably give a linear selectivity[16] (Figure 1d). Trost and our groups have convinced that chiral phosphoramidite ligands[17] are able to facilitate the Pd-catalyzed allylic C–H functionalization of α-alkenes (Figure 1d),[18,19] wherein the allylic C–H cleavage occurs via a concerted proton and two-electron transfer process (Figure 1e) to generate π-allylpalladium complexes,[20] which prefer to undergo an outer-sphere addition at the less hindered terminus (Figure 1e), except for the cases using prochiral nucleophiles, leading to the formation of achiral linear products.[21] Although nucleophile coordination to the palladium center impels the reaction to favor an inner-sphere pathway (Figure 1e), allowing for the preferable formation of branched products[22,23], α-alkene substrates remain restricted to relatively more reactive alkenes, such as allylarenes, 1,4-dienes and others (Figure 1d).[20,24-28] In sharp contrast, branch- and enantioselective allylic C–H oxidative alkylation of inactivated α-alkenes remains a longstanding formidable challenge and has not been discovered, yet, with the exception of a very few stepwise processes.[29,30] Herein, we report a chiral phosphoramidite-palladium catalyzed branch- and enantioselective allylic C–H alkylation, capable of accommodating almost all types of α-alkenes (Figure 1f).

Results And Discussion

Given that nucleophile coordination to the π-allylpalladium intermediate facilitates the branch-selectivity (Figure 1e),[20,24] our design plan was initiated with the evaluation of various carbon nucleophiles containing Lewis basic functionalities for the asymmetric allylic C–H alkylation of 1-octene **1** by using $Pd_2(dba)_3$ and chiral phosphoramidite **L1** as the catalyst, 2,5-dimethylbenzoquinone (2,5-DMBQ) as an oxidant and Na_2CO_3 as a base (Figure 2a). Although none of glycine Schiff base **2**, 2-acylimidazole **3**, and α-quinolinylacetamide **4** was able to undergo the desired reaction, to our delight, α-benzothiazylacetamide **5** was reactive enough to participate in the desired reaction and gave the branched product **7** in 78% yield with 24% ee, 12:1 dr and 18:1 b/l. Extensive evaluation of chiral ligands suggested that the incorporation of a carbazole moiety and H^8-BINOL skeleton in the chiral phosphoramidite (Figure 2b) led to superior enantioinduction, albeit with a slight decrease in the diastereo- and regioselectivities (Figure 2c, entry 1 *vs* 2). Fine-tuning of the aryl group on the H^8-BINOL skeleton (entries 3-5) revealed that the installation of *para*-trifluoromethyl phenyl substituents at 3,3'-positions turned out to be most beneficial to the control of stereo- and regioselectivities. Furthermore, enhanced results of 96% yield, 90% ee, >20:1 dr and >20:1 b/l were obtained by using piperidine-derived amide **6** as a nucleophile, NaOAc as a base, 1,4-dioxane as a solvent, and conducting the reaction at a higher concentration, a slightly lower temperature and with a prolonged time (entry 6).

With the optimized conditions, the scope of α-alkenes was initially evaluated for the asymmetric allylic C–H alkylation protocol (Figure 3). Significantly, 1-butene, with million ton manufactured annually from the worldwide petroleum industry, participated in the reaction to provide the branch-selective alkylation product **9** with high levels of stereo- and regioselectivity, explicating the great potential of this protocol in practical applications. Moreover, easily available 1-hexene and allylcyclohexane were both suitable

substrates to afford corresponding products **10**-**11** with excellent enantioselectivity and perfect branch-selectivity, but a moderate yield was observed for allylcyclohexane bearing a bulkier substituent at the allylic position. Other inactivated α-alkenes, bearing a γ- or β-aryl substituent, or a C-C double bond remote to the reaction site, were all nicely tolerated to give the desired products **12**-**14** in satisfactory results. In addition, a broad scope of inactivated α-alkenes bearing appended functionalities, such as C-C triple bond, halides, hydroxyl, aldehyde, silyl ether, ether, ester, sulfonamide, amide, and nitro groups, all underwent the reaction to provide the desired products **15**-**27** in moderate to excellent yields and with high levels of regio- and stereoselectivity. The introduction of homoallylic ether, substituted phenol-derived ethers and heteroarylcarboxylic acid-derived esters to substrates was also allowed to generate corresponding products **28**-**34** in moderate to high yields and with high levels of regio- and stereoselectivity. As anticipated, allylbenzene was highly reactive under the standard conditions to furnish the alkylation product **35** in an excellent yield with >20:1 dr and >20:1 b/l, but with a moderate enantioselectivity. Moreover, allyl ketone, allyl ester and allyl ether all underwent the desired reaction to deliver the branched products **36**-**38** with synthetically acceptable results. Notably, 1,1-disubstituted α-alkene was viable to afford the desired product **39** in a moderate yield and stereoselectivity, but still with an excellent regioselectivity.

The extension of the asymmetric allylic C–H alkylation protocol to the late-stage functionalization of alkene substrates derived from structurally complicated molecules appeared to be equally successful. For instance, α-alkenes tethered with coumarin, menthol, chiral vicinal diol, galactose, oestrone, cholesteryl and liquid crystal monomer were all reactive components to furnish the desired products **40**-**47** in moderate yields with good levels of regio- and stereoselectivity. More importantly, 1,11-dodecadiene was able to undergo double asymmetric allylic C–H alkylation reaction at two allylic positions, giving rise to a densely functionalized chiral diamide **48** with high levels of branch- and stereoselectivity.

Apart from the α-alkene substrates, the generality of the asymmetric allylic C–H alkylation reaction of 1-octene **1** for other carbon nucleophiles was also explored. The presence of either electron-donating or electron-withdrawing substituent at the 6-position of the benzothiazolyl moiety was allowed to cleanly undergo the branch-selective asymmetric reaction and gave the desired products **49**-**53** in high yields with excellent stereoselectivities and almost perfect regioselectivity. Unfortunately, the installation of a fluoride substituent at the 4-position led to the branched product **54** with a diminished enantioselectivity. In addition, the replacement of piperidine with morpholine on the amide moiety was allowed and the desired alkylation products **55**-**56** were produced with high levels of enantioselectivity. α-Heteroaryl ketones were another type of coordinating nucleophiles capable of smoothly undergoing the branch-selective allylic C-H alkylation. For example, α-benzothiazolyl ketone regiospecifically delivered the corresponding product **57** in good yield and enantioselectivity but with a poor diastereoselectivity. Moreover, α-quinolinyl ketone smoothly generated the branched product **58** in decent yield with perfect diastereo- and branch-selectivity, while a moderate enantioselectivity was observed.

Synthetic Applications

The presence of terminal carbon-carbon double bond and carbonyl functionality in the product enables this asymmetric allylic C–H alkylation to be highly synthetically useful. A gram-scale reaction of 1-octene **1** and α-benzothiazylacetamide **6** under the optimized reaction conditions furnished the desired product **8** in a slightly diminished yield, but with maintained branch- and stereoselectivities (Figure 4a). Interestingly, the exposure of **56** to DIBAL-H in toluene under -78 °C generated an amine **59** with maintained enantioselectivity, while the treatment of **56** with $LiAlH_4$ in THF at room temperature resulted in a deamidated product **60** (Figure 4b).[31] Following a one-pot reaction sequence involving methylation of benzothiazole moiety with Me_3OBF_4, reduction of benzothiazolium with $NaBH_4$, and hydrolysis of benzothiazoline with $AgNO_3$, **59** was converted to chiral aldehyde **61**. Treatment of aldehyde **61** with various Grignard reagents, including *n*-butyl, phenyl, alkenyl, and ethynyl magnesium, followed by oxidation of the resultant alcohols with Dess-Martin periodinane, afforded chiral ketones **62**-**65** in 87-92% yields. Notably, this protocol was also applicable to the synthesis of valuable building blocks, enabling asymmetric formal synthesis of a variety of natural products (Figure 4c). For instance, Taniguchi lactone **68**, a key chiral building block to access (+)-gelsefuranidine[32] and quninine[33], could be prepared from **22** via easily operational transformations including deamidation, conversion of benzothiazole to aldehyde, aldehyde oxidation, and debenzylation-lactonization. The similar reaction sequence smoothly converted **23** to an enantioenriched six-membered lactone **71**, which has been applied to the total synthesis of (+)-preclavulone A methyl ester as an important intermediate.[34] In addition, chiral γ,δ-unsaturated amide **10**, derived from simple 1-hexene, could be transformed into a chiral aldehyde **73** for manufacturing celery ketone.[35]

Mechanistic Investigations

To gain insights into the possible reaction mechanism, a series of kinetic studies and control experiments were conducted. Firstly, a non-negligible kinetic isotope effect (KIE, k_H/k_D = 2.6) was observed for the reaction of α-benzothiazylacetamide **6** and α-alkene **74**(d_2), suggesting that the allylic C–H cleavage might be involved in the rate-limiting step (Figure 5a). Secondly, the reaction of α-benzothiazylacetamide **6** and 1-octene **1** showed a linear correlation between the ee value of ligand **L6** and that of the product **9** (Figure 5b), implying that only one molecule of chiral ligand was involved in the enantio-determining event of nucleophilic addition to π-allylpalladium.[36,37] Thirdly, the first-order dependence of the initial rate on the concentration of Pd-**L6** catalyst, 1-octene **1**, and 2,5-DMBQ was identified, but a slightly negative effect on the initial rate was observed as the concentration of α-benzothiazylacetamide **6** increased (Figure 5b). Given that the allylic C–H cleavage was identified as the most possible rate-limiting step via the KIE studies, these kinetic results were consistent with a concerted proton and two-electron transfer process to cleave the allylic C–H bond, wherein a 16-electron Pd(0) complex formed from a phosphoramidite ligand, a *p*-quinone, and an α-alkene was convinced as the key intermediate[20] (Figure 1d). In this context, elevating the concentration of Pd-**L6** catalyst, 1-octene **1** or 2,5-DMBQ was able to accelerate the reaction by facilitating the formation of the catalytically active 16-electron Pd(0) complex. It is worth noting that such an accelerating effect of 2,5-DMBQ in this reaction represents a striking contrast to the inhibitory effect of benzoquinone (BQ) observed in the Pd(II)/bis-sulfoxide catalysis,[38]

wherein the Pd(II)/BQ π-acidic interactions have proven to be detrimental to the allylic C–H activation via a concerted metalation–deprotonation (CMD) mechanism. On the other hand, the inhibitory effect of the coordinating nucleophile **6** on the reaction rate was also in accordance with the concerted proton and two-electron transfer process, as the competitive coordination of **6** to Pd(0) would most probably be leveraged by increasing the concentration of **6**, being detrimental to the formation of the active 16-electron Pd(0) complex.

Furthermore, an unusual dependence of regioselectivity on the mole-ratio of ligand to Pd [**L**/Pd] was observed in the case using Tsuji-Trost allylation of α-benzothiazylacetamide **6** and allylic carbonate **75** as a model reaction (Figure 5c). In the process using PPh_3 as ligand, the increasement in the molar ratio of PPh_3 to Pd tended to gradually favor the formation of a linear product **76**.[31] In contrast, the variation of the [**L6**/Pd] molar ratio did not exhibit obvious influence on the reaction performance, always smoothly leading to a branched product **10** in >90% yield with 90% ee, >20:1 dr and >20:1 b/l. These results were almost identical to those obtained from the asymmetric allylic C–H alkylation protocol (Figure 3, **10**), indicating that these reactions might proceed via a similar C–C bond-forming transition state. The different performance of Ph_3P and **L6** in regioselective control might be attributed to the different complexation ability between PPh_3 and **L6**. In the case involving a Pd complex of monodentate ligand with a 1/1 ratio, a coordination-unsaturated [(π-allyl)Pd(**L**)] was preferentially formed, allowing the secondary coordination of the nucleophile to Pd to occur, and thereby enabled a branch-selectivity via an inner-sphere allylation pathway (Figure 5c). However, as the ratio of [**L**/Pd] increased, the complexation of [(π-allyl)Pd(PPh_3)] with excess amounts of PPh_3 might occur and tended to give a coordination-saturated [(π-allyl)Pd(PPh_3)$_2$], which had not vacant site for an additional nucleophile coordination and thus preferred an outer-sphere pathway to give a linear-selectivity (Figure 5c). In sharp contrast, the chiral phosphoramidite **L6** is relatively bulkier and less-coordinating than PPh_3,[17,39] therefore it is more difficult to form a coordination-saturated [(π-allyl)Pd(**L6**)$_2$] even with excess amounts of **L6**.[40] As a consequence, the coordination-unsaturated [(π-allyl)Pd(**L6**)] that has a vacant site open for the secondary coordination always exists in priority and allows the branch-selective bond-forming event to keep working. Moreover, bidentate phosphorus-containing ligands, commonly used in Tsuji-Trost allylation to form coordination-saturated π-allylpalladium complexes structurally analogous to [(π-allyl)Pd(PPh_3)$_2$], preferred a linear selectivity as anticipated (Figure 5c). Interestingly, DPPE and BINAP, bearing a relatively narrow bite angle ranging from 86° to 93°, preferentially delivered the linear-selectivity, presumably because these ligands were able to stabilize coordination-saturated π-allylpalladium intermediates by strong chelation.[41,42] In contrast, DPPF and Trost's ligand with **wider bite-angle** (>99°) led to low levels of regioselectivity, wherein the branch-selectivity probably resulted from the mono-P-ligational behavior[43] of these **wide bite-angle** ligands to generate coordination-unsaturated π-allylpalladium intermediates that basically preferred an inner-sphere allylation pathway. Notably, chiral phosphinooxazoline (PHOX) ligand[44] also preferentially gave a linear-selectivity, whereas chiral aryl sulfoxide-oxazoline (ArSOX) ligand, which was reported to be optimal for a linear-selective asymmetric C–H alkylation,[16] failed to facilitate the current allylic alkylation reaction. Overall, these results clearly indicate that the regioselectivity of Pd-catalyzed allylic substitution

with coordinating nucleophile is switchable by tuning the ligational behavior of ligands to alter the bond-forming pathway.

To gain more insight into the molecular origin of stereoselectivity, the competing transition states of both the inner-sphere pathways and the outer-sphere pathways were explored by density functional theory (DFT) calculations using α-benzothiazylacetamide **5** as a model nucleophile and chiral phosphoramidite **L7** as a model ligand. The computational analysis of α-benzothiazylacetamide anion suggests that a *syn*-periplanar 1,5-O···S relationship is beneficial to fix the geometry of this anion,[45] making the rigidized planar conformation **77** thermodynamically favorable than the other competing conformations (**78** and **79**) by at least 4.4 kcal/mol (Figure 6a). With respect to the inner-sphere pathways (Figure 6b), the N-coordinating transition states (**TS-N**, 0.0-4.5 kcal/mol) are energetically favored than the O-coordinating transition states (**TS-O**, 4.6-9.1 kcal/mol), suggesting that the bond-forming event proceeding via the N-coordinating mode is more feasible. The enantio- and diastereoselectivities are governed by four competing N-coordinating transition states. The transition state **(*R,S*)-TS-N** that leads to the formation of the observed enantiomer is at least 1.7 kcal/mol more favorable than the other three transition states. Both **(*R,R*)-TS-N** and **(*S,S*)-TS-N**, adopting the partially overlapped conformation in the Newman projections, suffer from the steric repulsion between the amide group of α-benzothiazylacetamide and the methyl group on the allyl moiety to make the generation of diastereomers unfavorable. These results are consistent with the experimental findings in Figure 2c, wherein the replacement of dimethylamine with a bulkier piperidine on the amide moiety (entry 5 vs 6) is able to enhance the diastereoselectivity. In addition, the length of the S−O bond in α-benzothiazylacetamide exerts considerable effect on the preferential formation of the enantio-determining transition state. In comparison with the rigidized planar conformation **67**, the favored transition state **(*R,S*)-TS-N** has a very similar S−O bond length (2.77 Å *vs* 2.73 Å), while the S-O bond is significantly elongated (2.87 Å *vs* 2.73 Å) in **(*S,R*)-TS-N**. Therefore, **(*R,S*)-TS-N** is favorably formed to generate the experimentally observed stereochemistry of the major alkylation product. In addition, the outer-sphere bond-forming pathways are also considered (see the Supporting Information for details). However, the activation energy barriers of the outer-sphere pathways turn out to be much higher than those of the inner-sphere pathways, suggesting that the outer-sphere pathways are highly disfavored.

In summary, we have established a chiral phosphoramidite-palladium complex-catalyzed branch- and enantioselective allylic C−H alkylation of α-alkenes by using α-benzothiazylacetamides as the alkylating agents. This protocol tolerates an extremely wide spectrum of α-alkenes and α-heteroaryl carbonyl compounds, providing an unconventional approach to access enantioenriched γ,δ-unsaturated carbonyl compounds in moderate to excellent yields with high levels of regio- and stereoselectivity. Experimental and computational studies suggest that aside from the coordination pattern of the nucleophiles, the ligational behaviors of ligands can also regulate the regioselectivity, highlighting that the mono-ligation of chiral phosphoramidite ligand is the key factor to keep the preference for the branch-selectivity via an inner-sphere allylation pathway. We anticipate that this report will facilitate the future development of the precise control in the Pd-catalyzed allylation reactions.

Data Availability Statement

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Declarations

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Author Contributions

Z.-S.N., T.-C.W. and L.-F.F. performed the asymmetric allylic C−H alkylation methodology and experimental mechanistic study. L.Z. performed the DFT-calculations. P.-S.W. and L.-Z.G. conceived and supervised the project. All authors analyzed the data and wrote the manuscript. All authors analyzed the data and wrote the manuscript.

Competing Interests

The authors declare no competing financial interests.

Materials & Correspondence

Supplementary Information is available in the online version of the paper. Reprints and permissions information is available online. Correspondence and requests for materials should be addressed to L.-Z.G. (gonglz@ustc.edu.cn).

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Figures

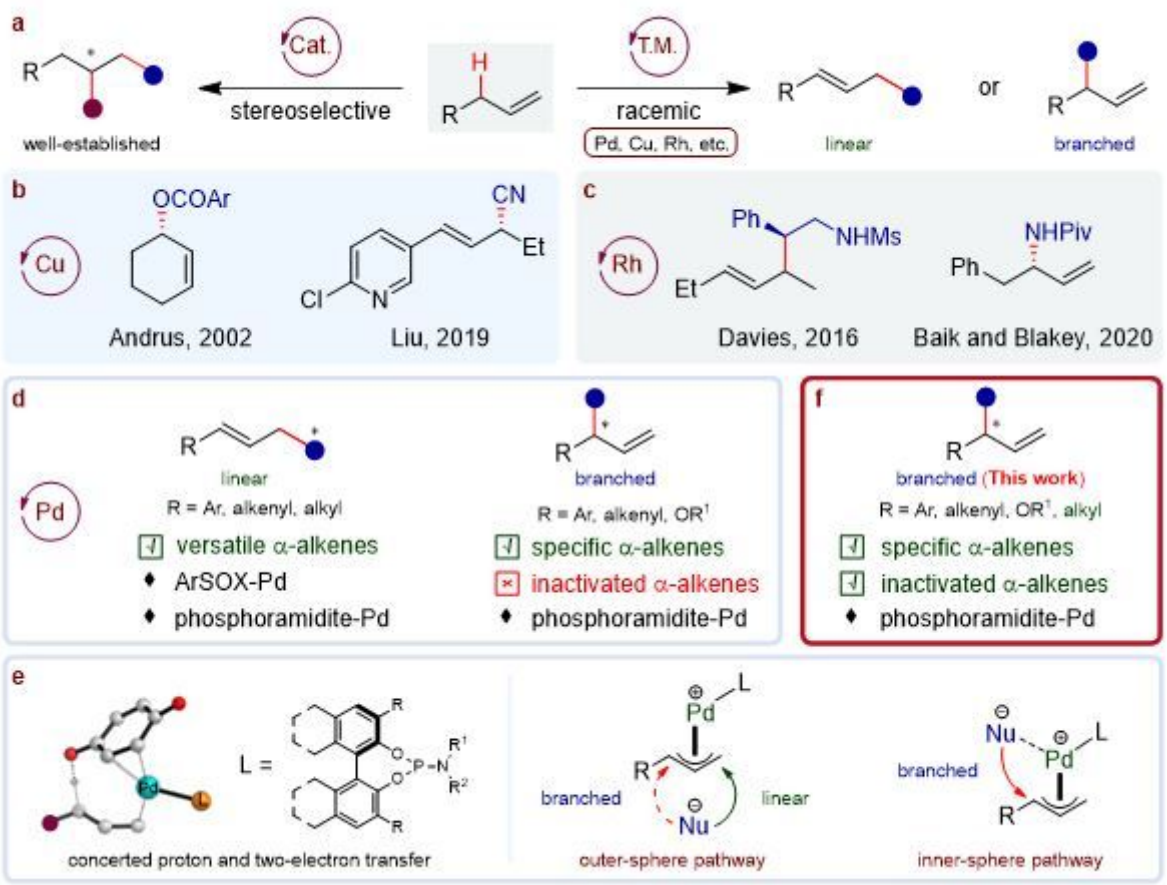
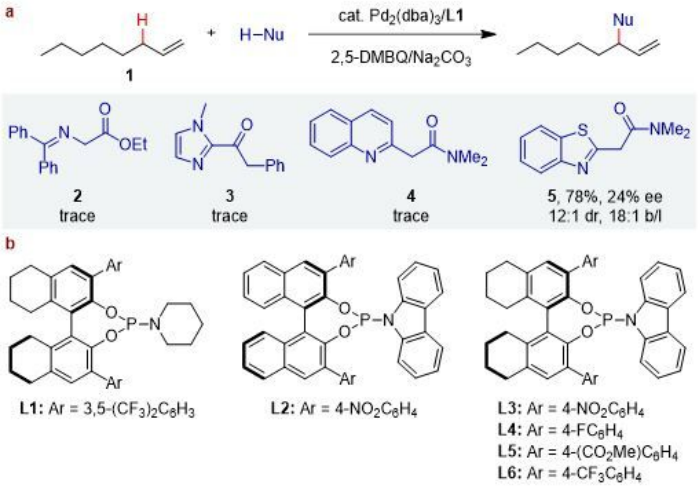
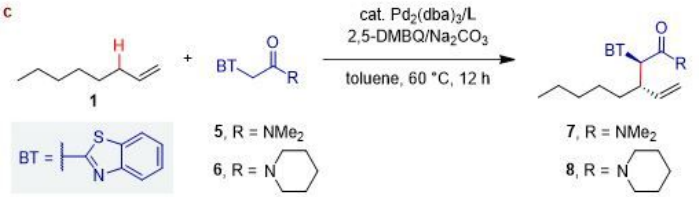


Figure 1

Asymmetric functionalization of α-alkenes. a, Stereoselective functionalization of C–C double bonds and transition metal catalyzed allylic C–H functionalization. b, Limited examples of Cu-catalyzed asymmetric allylic C–H functionalization. c, The only example of Rh-catalyzed regio- and enantioselective allylic C–H amidation. d, Pd-catalyzed regio- and enantioselective allylic C–H functionalization. e, Concerted proton and two-electron transfer process for allylic C–H cleavage and possible bond-forming pathways. f. Pd-catalyzed branch- and enantioselective allylic C–H alkylation tolerating almost all types of α-alkenes. T.M. = transition metal.





entry	L	yield (%)	ee (%)	dr	b/l
1	**L2**	90	67	12:1	>20:1
2	**L3**	77	77	10:1	15:1
3	**L4**	71	68	12:1	18:1
4	**L5**	90	79	12:1	>20:1
5	**L6**	75	84	15:1	>20:1
6[i]	**L6**	96(93[ii])	90	>20:1	>20:1

Figure 2

Asymmetric allylic C–H alkylation catalyzed palladium-phosphoramidite complex. a, Initial screening of nucleophiles. b, Chiral phosphoramidites evaluated. c, Unless indicated otherwise, reactions of 1 (0.20 mmol), 5 (0.10 mmol), Pd2(dba)3 (0.0025 mmol), L (0.0075 mmol), 2,5-DMBQ (0.12 mmol) and Na2CO3 (0.10 mmol) were carried out in toluene (1.0 mL) at 60 °C for 12 h. The yield, diastereo- and regioselectivity were determined via 1H NMR analysis using 1,3,5-triacetylbenzene as an internal standard, and the ee value was determined by HPLC using a chiral stationary phase. The absolute configuration of 8 was assigned by X-ray crystallography. iThe reaction of 1 (0.15 mmol) and 6 (0.10 mmol) was conducted with NaOAc (0.10 mmol) in 1,4-dioxane (0.5 mL) at 50 °C for 36 h. iiIsolated yield. DMBQ = dimethyl-p-benzoquinone.

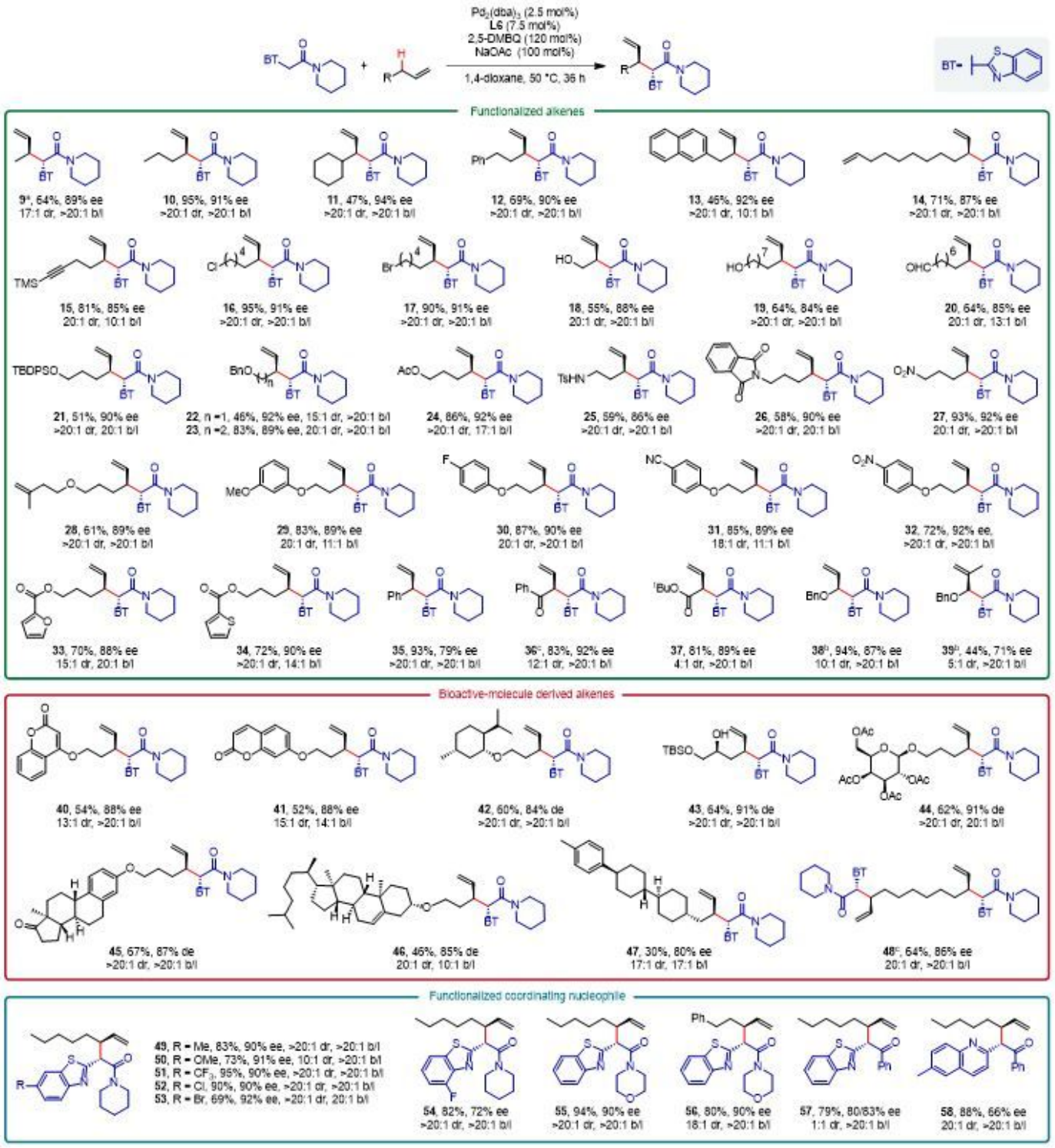


Figure 3

Scope of the asymmetric allylic C–H alkylation. Reaction conditions: α-alkene (0.15 mmol), the nucleophile (0.10 mmol), Pd2(dba)3 (0.0025 mmol), L6 (0.0075 mmol), 2,5-DMBQ (0.12 mmol) and NaOAc (0.10 mmol) and 1,4-dioxane (0.5 mL) under N2, 50 °C, 36 h. Isolated yield, dr and b/l were determined by 1H NMR analysis, and ee was determined by HPLC using a chiral stationary phase. The absolute stereochemistry was assigned by analogy. aWith 10 equivalents of 1-butene. bAt 40 °C, 48 h.

cWith 1,11-dodecadiene (0.10 mmol), 6 (0.30 mmol), Pd2(dba)3 (0.005 mmol), L6 (0.015 mmol), 2,5-DMBQ (0.24 mmol) and NaOAc (0.20 mmol) and 1,4-dioxane (1.0 mL), 72 h.

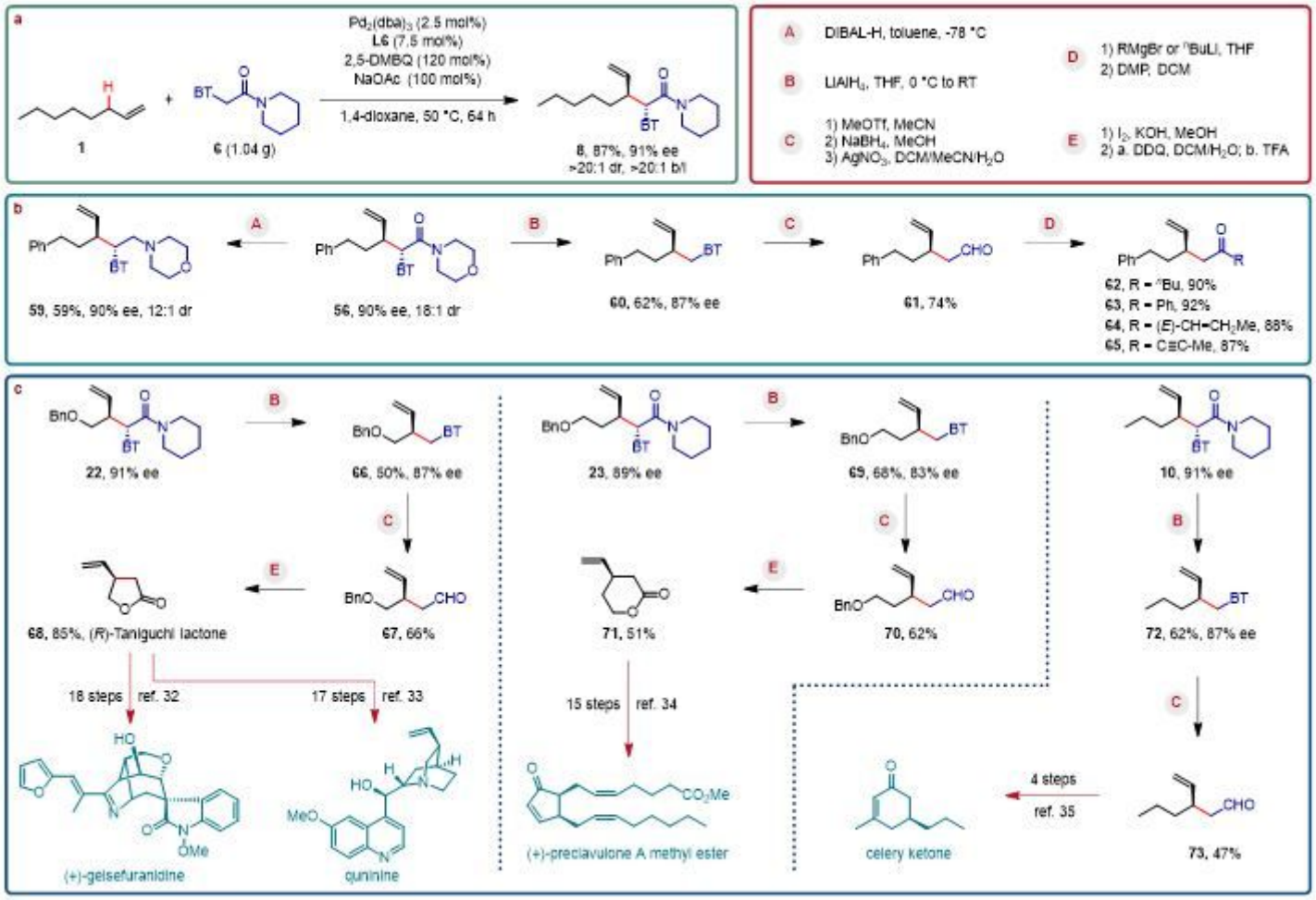


Figure 4

Synthetic applications. a, A gram-scale synthesis of 8. b, Synthetic transformation of α-benzothiazylacetamide. c, Asymmetric formal synthesis of natural products. DIBAL-H = diisobutylaluminium hydride. DMP = Dess-Martin periodinane. DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. DMAP = 4-dimethylaminopyridine.

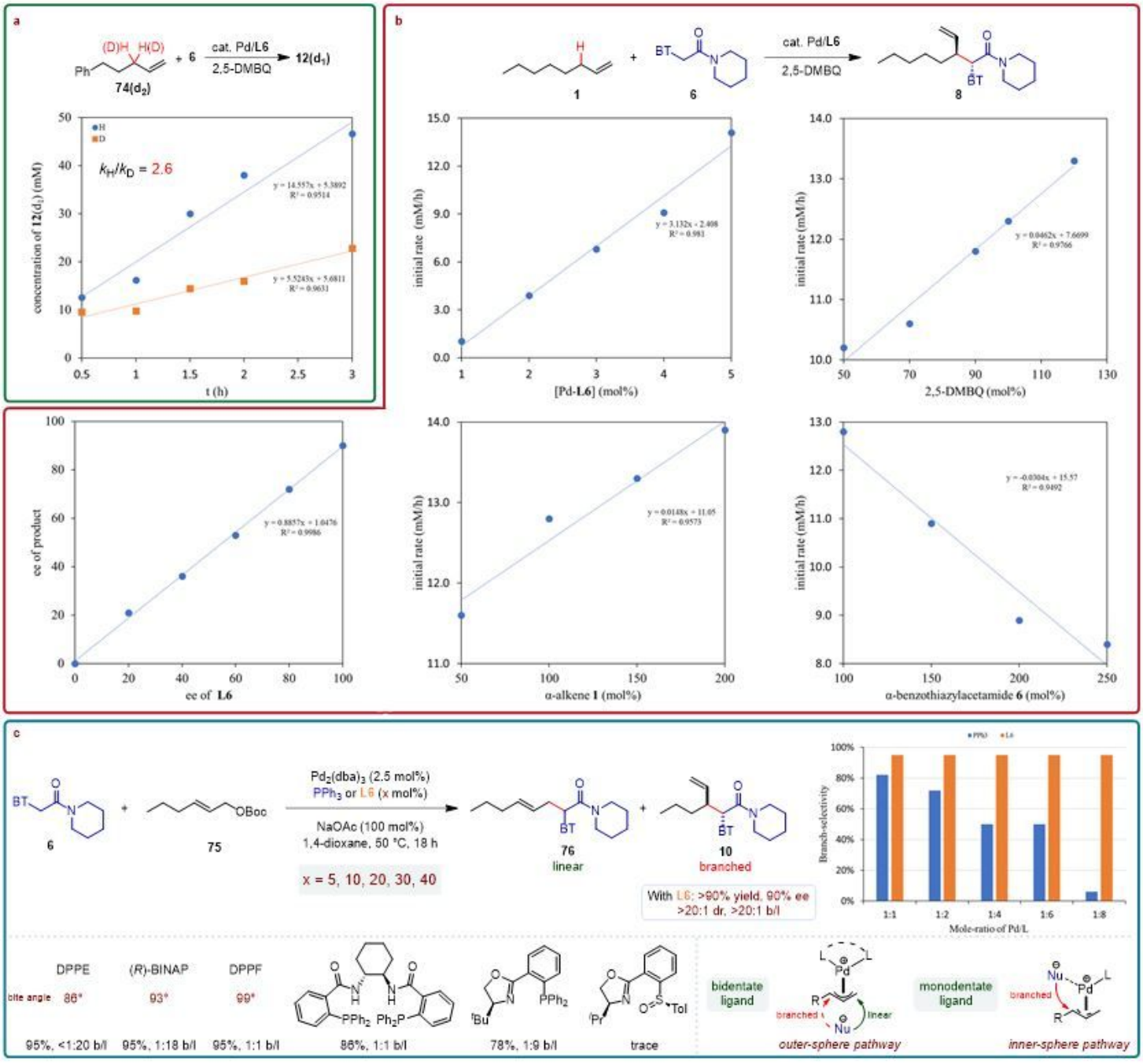


Figure 5

Mechanistic investigation. a, Deuterium kinetic isotope effect (KIE) studies. b, Nonlinear effect (NLE) studies and the dependence of the initial rate on [Pd/L6], [α-alkene 1], [α-benzothiazylacetamide 6] and [2,5-DMBQ]. c, The dependence of the regioselectivity on the mole-ratio of [Pd/L]. DPPE = 1,2-bis(diphenylphosphino)ethane. DPPF = 1,1'-bis(diphenylphosphino)ferrocene. Tol = p-tolyl.

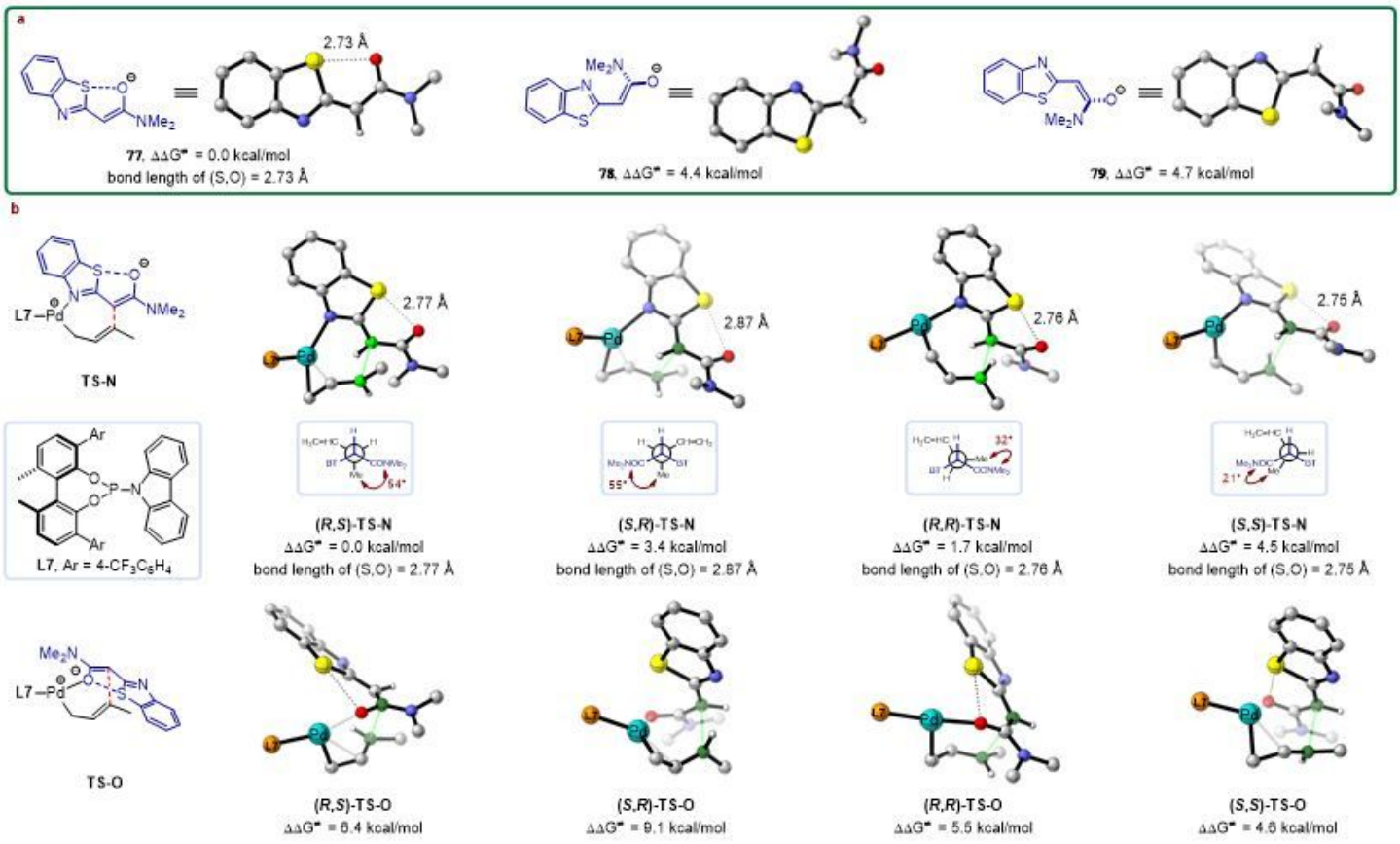


Figure 6

DFT-computed relative energy profiles of plausible inner-sphere pathways. a, Conformation analysis of α-benzothiazylacetamide anion via computational calculations. b, Computational results of N- and O-coordinating transition states.

Supplementary Files

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