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Amine-substituted cyclobutanes and cyclopropanes are important substructures in biologically active compounds. Moreover, many of the cycloalkane units bear multiple substituents and stereocenters. Therefore, synthetic methods that produce polysubstituted aminocyclobutanes and aminocyclopropanes in a highly diastereo- and enantioselective manner are of importance. Herein, we describe the diastereo- and enantioselective synthesis of various types of polysubstituted aminocyclobutanes and aminocyclopropanes through CuH-catalyzed hydroamination of 1-substituted cyclobutenes and cyclopropenes. These strained trisubstituted alkenes exhibit much higher reactivity compared to their unstrained analogues in the initial hydrocupration step of the reaction. Moreover, an interesting reversal of regioselectivity was observed in the hydroamination of 1-aryl-substituted cyclobutenes compared to the cyclopropene analogues. The origins of the enhanced reactivity of strained trisubstituted alkenes as well as the differences in the regio- and enantioselectivity between reactions with cyclobutenes and cyclopropenes were investigated computationally.

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Diastereo- and Enantioselective CuH-Catalyzed Hydroamination of Strained Trisubstituted Alkenes

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ABSTRACT: Amine-substituted cyclobutanes and cyclopropanes are important substructures in biologically active compounds. Moreover, many of the cycloalkane units bear multiple substituents and stereocenters. Therefore, synthetic methods that produce polysubstituted aminocyclobutanes and aminocyclopropanes in a highly diastereo- and enantioselective manner are of importance. Herein, we describe the diastereo- and enantioselective synthesis of various types of polysubstituted aminocyclobutanes and aminocyclopropanes through CuH-catalyzed hydroamination of 1-substituted cyclobutenes and cyclopropenes. These strained trisubstituted alkenes exhibit much higher reactivity compared to their unstrained analogues in the initial hydrocupration step of the reaction. Moreover, an interesting reversal of regioselectivity was observed in the hydroamination of 1-aryl-substituted cyclobutenes compared to the cyclopropene analogues. The origins of the enhanced reactivity of strained trisubstituted alkenes as well as the differences in the regio- and enantioselectivity between reactions with cyclobutenes and cyclopropenes were investigated computationally.

INTRODUCTION

Cyclobutylamine and cyclopropylamine substructures are found in a variety of bioactive molecules and pharmaceutical compounds (Figure 1a).† Moreover, the stereoisomers of these compounds can exhibit remarkable differences in bioactivity.‡ Thus, considerable effort has been expended to developing methods for the stereoselective construction of these structural units. Currently, most synthetic approaches to enantioenriched cyclobutylamines are based on [2+2] cycloadditions§ and the Amadori–Heyns rearrangement.¶ Among these methods, few are catalytic and effective in an intermolecular context.¶ †‡ In contrast, for the catalytic, enantioselective synthesis of cyclobutylamines, a number of elegant methods have been developed.¶ The most well-known processes include intramolecular C–H activation of prochiral aminocyclopropanes,¶ cyclopropanation of vinylcarbamates,¶ carboamination of cyclopropanes,¶ and rare-earth-metal-catalyzed hydroamination of cyclopropanes.¶ Despite these advances, the development of a unified synthetic strategy that allows for the stereoselective formation of multiple types of polysubstituted cyclobutyl- and cyclopropylamines would be desirable. We proposed that a general, enantioselective hydroamination of cyclic alkenes could address this challenge.

Our group and others have reported copper-hydride(CuH)-catalyzed enantioselective hydrofunctionalization reactions of various unsaturated substrates.¶ †² In particular, CuH-catalyzed hydroamination has been applied on a broad range of olefins,¶ †² such as styrene derivatives,¶ †²−⁷ 1,1-disubstituted alkenes,¶ †²−⁹ and unactivated trans-1,2-disubstituted alkenes¶ †². These reactions proceed through enantioselective hydrocupration of the alkene to form a chiral alkylcopper species, which is then trapped by an electrophile such as a hydroxylamine ester.¶ †³ We postulated that the CuH-catalyzed stereoselective hydroamination of 1-substituted cyclobutenes and cyclopropenes could potentially furnish cyclobutyl- and cyclopropylamines bearing various types of substituents and with adjacent stereocenters (Figure 1b).

Despite the generality and broad utility of published CuH-catalyzed approaches, a common obstacle has been the unwanted CuH-catalyzed reduction of the electrophile, a side reaction that depletes the electrophilic reagent.¶ †³,¶ †²,¶ †⁴ For unactivated substrates with high barriers for reaction with CuH (hydrocupration), the reduction of the electrophile is a significant side reaction, resulting in greatly diminished yields or even no product formation. For instance, CuH-catalyzed hydrofunctionalization of unactivated trisubstituted alkenes has been extremely challenging in general. However, the hydroamination of certain activated trisubstituted alkenes such as allylic alcohol derivatives¶ †²,¶ †⁵ and β,β-disubstituted styrenes¶ †² have been achieved. Activation of olefins through ring strain is a strategy that has long been utilized by organic chemists to achieve new strain-enabled reactivities.¶ †⁶ Thus, we wondered whether the partial release of the ring strain energy of 1-substituted cyclobutenes and cyclopropenes in the hydrocupration step would help lower their hydrocupration barriers, and thereby allow the hydroamination of these strained trisubstituted alkenes to proceed faster than competing reduction of the electrophile.
RESULTS AND DISCUSSION

Hydroamination of 1-Substituted Cyclobutenes. We initiated our study by examining the CuH-catalyzed hydroamination reaction of 1,3-diphenyl-3-methylcyclobut-1-ene (2a) using Bn$_2$NOBz (3a). In previous CuH-catalyzed hydroamination reactions, simple styrene derivatives were generally converted selectively to the Markovnikov isomers of products$^{12a,b}$ (Figure 2a). However, when α-methyl-styrene$^{22}$ was employed, the anti-Markovnikov isomer was instead favored by a 7:1 ratio (Figure 2b), indicating that tertiary alkyl copper species are perhaps hard to form by hydrocupration or react slowly with the electrophile. In contrast to this observation, we found that, using Cu(OAc)$_2$ as the pre-catalyst and DTBM-SEGPHOS (L1) as the ligand, the reaction of phenylcyclobutene (2a) with Bn$_2$NOBz (3a) afforded the Markovnikov product exclusively in 85% yield (Figure 2c). The reaction not only generated a fully substituted carbon center on the cyclobutane ring, but also formed the 1,1,3,3-tetrasubstituted aminocyclobutene product with a 13:1 cis/trans ratio. 3-Substituted 1-arylcyclobutylamine subunits, though found in a number of interesting molecules,$^{18,19}$ have been difficult to prepare through the diastereoselective installation of 3-substituents, and highly stereoselective approaches to directly access these structures are rare.$^{21}$ Our CuH-catalyzed hydroamination approach on 3,3-disubstituted 1-cyclobutenes can provide a method to rapidly construct a diverse range of 3,3-disubstituted 1-aryl-1-aminocyclobutanes in good stereoselectivities.

Figure 1. Proposed CuH-catalyzed hydroamination of 1-substituted cyclobutenes and cyclopropenes. (a) Representa-
biologically active cyclobutylamines and cyclopropylamines. (b) Proposed catalytic strategy. (c) DFT-computed ac-
tivation barriers of the hydrocupration of 1a-1c. Geometries were optimized at the B3LYP/SDD-6-31G(d) level of theory.
Single point energies were calculated at the M06/SDD-6-311+G(d,p)/SMD(THF) level.

At the outset, it was unclear to us whether these strained trisubstituted alkenes$^{17}$ would be reactive enough to un-
dergo CuH-catalyzed hydroamination reactions. Thus, we per-
dformed DFT calculations on the hydrocupration bar-
ers of strained and unstrained trisubstituted alkenes (Fig-
ure 1c). The DTBM-SEGPHOS(L1)-based CuH catalyst sys-
tem has been shown to exhibit high levels of enantioselect-
ivity as well as enhanced reactivity in hydroamination reac-
tions$^{12,18}$ and was therefore chosen in our calculations. Our results indicated that the hydrocupration barriers of 1-methylcyclobutene (1b) and 1-methylcyclopropene (1a) are 3.5 and 11.0 kcal/mol lower, respectively, than that of the acyclic trisubstituted olefin 2-methylbut-2-ene (1c). Based on these promising results, we proceeded to exper-
imentally investigate the CuH-catalyzed hydroamination of 1-substituted cyclobutenes and cyclopropenes.

Figure 2. Regioselectivity of the CuH-catalyzed hydroamination using different phenyl-substituted alkenes.

After identifying the optimal reaction conditions (shown in Figure 2c),$^{22}$ we investigated the substrate scope for the hydroamination of 1-arylcyclobutenes (Table 1). In all cases, the Markovnikov products were formed exclusively. We found that 1-arylcyclobutenes bearing para- (4b, 4h), meta- (4c), and ortho- (4d) substituents were all suitable for the hydroamination reaction. An electron-withdrawing group on the arene (4e) greatly improved the stereoselectivity of the reaction, while electron-donating substituent (4b) led to a slightly diminished yield and diastereomer ratio. A 1-pyrrolid cyclobutene was also well tolerated (4f). Moreover, arylicyclobutenes without any substituents at the 3-position were also able to undergo the hydroamination reaction to selectively form the Markovnikov products (4d, 4e) in good yields, suggesting that the regioselectivity was not a result of the steric repulsion from the 3-
substituents. A 1-phenylcyclobutene with a spiro-fused cyclohexyl group at the 3-position also reacted efficiently (4f).

We next evaluated a range of hydroxylamine esters in this reaction. It was found that a number of functional groups such as an alcohol (4h), an ester (4i), and a phenol (4j) were tolerated under the hydroamination reaction conditions. Moreover, heterocycles such as pyrimidine (4g) and furan (4h) were shown to be compatible in the reaction.
clobutene substrates is consistent with what we observed.

We also examined the hydroamination of 1-alkylcyclobutenes, which lack the activating influence of an aryl substituent on the alkene. We chose (3-(cyclobut-1-en-1-yl)propyl)benzene (5a) as our model substrate, for which a series of amination reagents were evaluated. We found that the use of the mesityl hydroxylamine ester 6a gave the highest yield. Under the optimal reaction conditions, hydroamination of 5a provided the 1,2-disubstituted aminocyclobutane product 7a in 79% yield with >99.5:0.5 er and >20:1 dr (Table 2). That the regioselectivity is totally opposite of that observed with the aryl-substituted cyclobutene substrates is consistent with what we observed in, e.g., a comparison of the hydroamination of styrene and 1-dodecene.

Table 2. Substrate Scope for the CuH-Catalyzed Hydroamination of 1-Alkylcyclobutenes

A range of functional groups and heterocycles were found to be compatible with the reaction conditions (Table 2). For example, amination reagents containing a thiophene (7b) and an acetal (7c) as well as 1-alkylcyclobutenes bearing a silyl ether (7d) and a pyridine (7e) were all suitable coupling partners in this hydroamination reaction, each providing the corresponding product in good yield with >99:0.5 er and >20:1 dr (Table 2).

To demonstrate that our hydroamination method is also applicable to 1-silyl substituted four-membered cycloalkenes, we carried out the hydroamination reaction of 1-silyl-4-azacyclobutene (5d) with the amination reagent (6a), which resulted in the formation of an ammocetadizidine product (7f) in excellent yield, enantio- and diastereoselectivity (Table 2).

Hydroamination of 1-Substituted Cyclopropanes. We were also interested in applying the hydroamination chemistry to other strained trisubstituted olefins, and thus we turned our attention to the hydroamination of 1-substituted cyclopropanes. While exploring different types of cyclopropanes, we had two interesting observations regarding the selectivity of these reactions. First, in contrast to the regioselectivity observed with 1-arylcylobutenes (2) (Scheme 1b), the formation of the anti-Markovnikov hydroamination product was found to be preferred when using 1-phenylcyclopropane derivative 8 as the substrate (Scheme 1a). Second, while the hydroamination of 1-alkylcyclobutenes were able to proceed with excellent enantioselectivity (Scheme 2b), the reaction with 1-alkylcyclobutene 11 provided the hydroamination product 12 with only 55:44.5 er (Scheme 2a).

Scheme 1. Comparison of the regioselectivity in CuH-catalyzed hydroamination of 1-phenylcyclopropane and 1-arylcylobutenes
We reasoned that installation of a bulky group at the 1-position of the cyclopropane may help restore the enantioselectivity due to increased ligand-substrate repulsion in the disfavored hydrocupration transition state. Thus we investigated the hydroamination of 1-silylcyclopropene. First, we examined the hydroamination reaction with 1-silyl-3,3-dimethylecyclopropene (13a) and Br₂NOPiv (9) (Table 3), finding that the reaction proceeded smoothly to give the 1,2-disubstituted aminocyclopropane product (15a) in 70% yield, with 98.5:1.5 er and >20:1 dr. As previously shown by our DFT calculations, cyclopropanes hydrocuprate much faster than cyclobutenes. As a result, we discovered that 1-silylcyclopropene (13a) was even able to react with 1,2-benzisoxazole (14), an electrophile that is highly susceptible to competing Kemp elimination in the presence of CuH and therefore couples only with the most activated olefins. 12c,30 The protected primary amine product 15b was obtained in 63% yield with excellent enantio- and diastereoselectivity. Moreover, 1-silylcyclopropanes bearing 3-spirocycloalkyl substituents were also capable of reacting with 1,2-benzisoxazole (14) to give the corresponding hydroamination products (15c, 15d) in moderate or good yields and with high stereoselectivities. The latter is related to a key intermediate for the synthesis of a T-type Cav₃ channel inhibitor (Table 3). 13

Table 3. Substrate Scope for the CuH-Catalyzed Hydroamination of 1-Silylcyclopropenes

| Scheme 2. Comparison of the enantioselectivity in the CuH-catalyzed hydroamination of 1-alkylcyclopropene and 1-alkylcyclobutene |
|---|
| (a) | Ph<sup>3</sup>Ar<sup>2</sup>Si<sup>3</sup>Me<sub>2</sub> + Br<sub>2</sub>NOPiv (1.2 equiv) |
| Cu(OAc)<sub>2</sub> (5 mol%), (R)-DTBM-SEGPHOS (5.5 mol%) |
| MeO<sup>2</sup> | ThF (0.5 M), rt, 12 h |
| 8 | 9 |
| 10a | 10b |
| 58% yield, 69:31 er |
| r.r. (10a:10b) = 8:1 |

| Scheme 2. Comparison of the enantioselectivity in the CuH-catalyzed hydroamination of 1-alkylcyclopropene and 1-alkylcyclobutene |
|---|
| (b) | Ph<sup>3</sup>Ar<sup>2</sup>Si<sup>3</sup>Me<sub>2</sub> + Br<sub>2</sub>NOPiv (1.2 equiv) |
| Cu(OAc)<sub>2</sub> (5 mol%), (R)-DTBM-SEGPHOS (5.5 mol%) |
| MeO<sup>2</sup> | ThF (0.5 M), rt, 18 h |
| 2 | 3a |
| 10a | 10b |
| 58% yield, 69:31 er |
| r.r. (10a:10b) = 8:1 |

*Isolated yields on 0.5 mmol scale (average of two runs). *Cu(OAc)<sub>2</sub> (5 mol%), (R)-DTBM-SEGPHOS (5.5 mol%), 1,4-dioxane (0.5 M). *Cu(OAc)<sub>2</sub> (2 mol%), (R)-DTBM-SEGPHOS (2.2 mol%), THF (1.0 M). *14 was added via syringe pump over 2 h. *15c was added via syringe pump over 2.5 h.

Computational Studies

Our experimental results not only demonstrated the generality of the CuH-catalyzed hydroamination of cyclopropanes and cyclobutenes, but also led to several interesting mechanistic questions regarding reactivity and selectivity. First, what is the origin of the enhanced reactivities of 1-substituted cyclobutenes and cyclopropanes as compared to acyclic trisubstituted alkenes? Second, why do the hydroamination reactions with 1-phenylcyclobutene (2a) and 1-phenylcyclopropene (8) form opposite regioisomers? Lastly, why is the hydroamination with 1-alkylcyclobutene (5a) highly enantioselective, while the reaction with 1-alkylcyclopropane (11) occurs with low enantioselectivity? To address these questions, we performed density-functional theory (DFT) calculations to reveal factors that control reactivity, regio-, and enantioselectivity in the CuH-catalyzed hydroamination of strained cyclic alkenes. We surmised that the angular strain, the ease to distort the alkylidene carbon to a pyramidalized transition state geometry, and the diminished steric repulsions with the DTBM-SEGPHOS ligand may all affect the reactivity and selectivity of cyclopropanes and cyclobutenes. Therefore, we employed the distortion/interaction model to analyze the effects of catalyst/substrate distortion and the interaction energies between the CuH catalyst and the alkene in the hydrocupration transition state.

**Computational Details.** Geometries were optimized in the gas phase using the B3LYP functional and a mixed basis set of SDD for Cu and 6-31G(d) for other atoms. Single point energies were calculated with the M06 functional and a mixed basis set of SDD for Cu and 6-311+G(d,p) for other atoms. Solvation energy corrections were considered in tetrahydrofuran (THF) solvent using the SMD solvation model. All geometry optimizations and
single-point energy calculations were performed using Gaussian 09.29

A modified version18 of the distortion/interaction model (or activation strain model),29 namely the ligand-substrate interaction model, was employed to decompose the activation energy (ΔE‡) using Eq. 1.

\[
ΔE^f = ΔE_{\text{sub-dist}} + ΔE_{\text{cat-dist}} + ΔE_{\text{int-space}} + ΔE_{\text{int-bond}} \quad \text{(Eq. 1)}
\]

where ΔE‡ is the gas-phase electronic energy of the hydrocupration transition state with respect to the separated alkene substrate and the L*CuH catalyst; ΔE_{sub-dist} and ΔE_{cat-dist} are the energies to distort the alkene substrate and the catalyst into the transition state geometries, respectively; ΔE_{int-space} is the through-space interaction energy between the (R)-DTBM-SEGPHOS ligand and the substrate calculated from the interaction energy of a supramolecular complex of the ligand and the substrate at the transition state geometry in the absence of the CuH moiety; ΔE_{int-bond} is the through-bond interaction energy between the catalyst and the substrate calculated from ΔE_{int-bond} = ΔE‡ - ΔE_{sub-dist} - ΔE_{cat-dist} - ΔE_{int-space}. The overall distortion energy of the catalyst and the substrate (ΔE_{dist}) is calculated from ΔE_{dist} = ΔE_{sub-dist} + ΔE_{cat-dist}.

Origin of the Enhanced Reactivity of Strained Trisubstituted Alkenes. We performed the ligand-substrate interaction model analysis to investigate the origin of the enhanced reactivities of 1-methylcyclopentene (1a) and 1-methylcyclobutene (1b) in hydrocupration as compared to the acyclic trisubstituted alkene, 2-methylbut-2-ene (1c) (Figure 3). Using this approach, the computed activation energy (ΔE‡) is dissected to distortion energies of the substrate and the catalyst [ΔE_{sub-dist} and ΔE_{cat-dist}], and the through-space and through-bond interaction energies between the L*CuH catalyst and the substrate (ΔE_{int-space} and ΔE_{int-bond}) (Figure 3b). Among the four different energy components, the main factor that promotes the hydrocupration of 1-methylcyclopentene (1a) is the highly favorable through-bond interaction energy (ΔE_{int-bond} = -33.9 kcal/mol). The strong catalyst-substrate interaction in TS-1a is due to the prominent pyramidalization of both sp² carbons of 1a as evidenced by the out-of-plane dihedral angles of the C1-Me and C2-H groups (α_{Me} and α_{H}, Figure 3a). Frontier molecular orbital (FMO) theory analysis indicates the pyramidalization of 1-methylcyclopentene decreases its LUMO energy, and thus promotes the FMO interactions between the alkene π* orbital and the HOMO of CuH (σ_{CuH}, see SI for details). Interestingly, although the pyramidalization of 1a in TS-1a is much more significant than that of 1b and 1c in TS-1b and TS-1c, the energies to distort these substrates are comparable (ΔE_{sub-dist} = 22.4, 22.2, and 23.0 kcal/mol, respectively). This observation is consistent with previous reports that indicated easier distortion of cyclopentene as compared to cyclobutene and acyclic alkynes. Because the sp² carbons of cyclopentene have significant angular strain,23 pyramidalization of cyclopentene is promoted by strain release. The propensity of out-of-plane distortion of 1-methylcyclopentene 1a is further demonstrated in Figure 3c, where the distortion energies of three alkenes (1a, 1b, and 1c) are plotted against the out-of-plane dihedral angle of the alkynyl Me and H groups. In the transition state region (α = 120°-140°), 1-methylcyclopentene (1a) requires much smaller distortion energy than 1-methylcyclobutene (1b) and 2-methylbut-2-ene (1c). The ligand-substrate interaction model analysis also revealed the impact of catalyst distortion energy (ΔE_{cat-dist}) on the reactivity. TS-1a and TS-1b both have smaller catalyst distortion energies than TS-1c. This indicates the smaller sizes of the strained cyclic alkenes as compared to 2-methylbut-2-ene (1c) also contribute to the reactivities of these substrates through decreasing steric repulsions with the L*CuH catalyst.

Taken together, the above analysis indicates the greater reactivities of 1-methylcyclopentene (1a) and 1-methylcyclobutene (1b) in hydrocupration are due to the combination of two effects. First, the ease to distortion of strained cyclic alkenes leads to greater pyramidalization of the alkynyl carbons in 1-methylcyclopentene, which in turn promotes the bonding interactions with the CuH catalyst. Second, the smaller sizes of cyclopentene and cyclobutene than the acyclic analogues decrease the catalyst-substrate steric repulsions in the hydrocupration transition state.

![Figure 3. Origin of enhanced hydrocupration reactivity of strained cyclic alkenes 1a and 1b. All energies are in kcal/mol.](image-url)
Origin of the Regioselectivity Reversal in the Hydroamination Reactions with 1-Phenylcyclobutene and 1-Phenylcyclopropene Derivatives. Next, we computed the regioisomeric hydrocupration transition states with 1-phenylcyclobutene and 1-phenylcyclopropene derivatives 2a and 8 (Figure 4). These substrates were chosen in the computational study because their hydroamination reactions lead to opposite regioisomers (Table 1 and Scheme 1). Our DFT calculations indicated that the hydrocupration of 2a favors the formation of the tertiary benzylic copper intermediate 16a by 1.9 kcal/mol. By contrast, in the reaction with 8, hydrocupration to form the secondary alkylcopper intermediate 17b is favored by 0.8 kcal/mol. These computed regioselectivities of hydrocupration are consistent with the experimentally observed hydroamination regioselectivities with these substrates. Although we have not yet computationally confirmed the regioselectivity-determining step in the catalytic cycle, the exergonicity of the hydrocupration of strained cyclic alkenes 2a and 8 (−13.9 and −29.5 kcal/mol, respectively, see SI for details) suggests that the hydrocupration is most likely irreversible and thus regioselectivity-determining.

The origin of the regioselectivity reversal was analyzed using the ligand-substrate interaction model, as shown in Figure 4b. In the hydrocupration of 1-phenylcyclopropene derivative 8, regioisomer TS8-b is more favorable because of the strongly stabilizing through-bond interactions between the L*CuH catalyst and the substrate (ΔE_{int-bond} = −34.5 kcal/mol). At first glance, these results are counter-intuitive because TS8-b forms a secondary alkyl-copper bond which is expected to be less electronically favorable than the formation of the benzyllic copper bond via TS8-a. Closer examination of the four-membered cyclic hydrocupration transition states (TS8-a and TS8-b) revealed an unusual rhombus-shaped geometry, in which the diagonal Cu–C bond is shorter than the forming Cu–C bond. Therefore, TS8-b is stabilized by the favorable bonding interaction between the Cu center and the benzyl carbon due to the short Cu–Cα distance (2.08 Å). By contrast, TS8-a has a much longer distance between Cu and the benzyl carbon (2.20 Å) that leads to a less favorable through-bond interaction energy. In the hydrocupration with 1-phenylcyclobutene derivative 2a, the through-bond interactions in both regioisomeric transition states are weaker than those in the transition states with 1-phenylcyclopropene derivative 5 because of smaller degrees of pyramidalization of 2a (vide supra). Nonetheless, TS2a-b still has more favorable through-bond interactions than TS2a-a (ΔE_{int-bond} = −3.2 kcal/mol) because of the shorter Cu–Cα distance (2.18 and 2.24 Å in TS2a-b and TS2a-a, respectively). However, TS2a-b requires a much higher energy (ΔE_{dist} = 34.8 kcal/mol) to distort the cyclobutene derivative 2a to facilitate the through-bond interactions with CuH. Therefore, the regioselectivity in the reaction with 2a is distortion-energy controlled (ΔE_{dist} = 5.2 kcal/mol) and favors the formation of the benzyllic copper intermediate (16a) via TS2a-a.

Enantioselectivity of the Hydroamination Reactions with 1-Alkylcyclobutene and 1-Alkylcyclopropene. Finally, we investigated the origin of the notably different enantioselectivities in the hydroamination of 1-alkylcyclobutene and 1-alkylcyclopropene (Table 2 and Scheme 2). We computed the hydrocupration transition states with the two different π faces of 1-methylcyclobutene 1b and 1-methylcyclopropene 1a (Figure 5). In the reaction with 1b, DFT calculations predicted strong preference for TS1b that leads to the experimentally observed (1R,2R)-aminocyclobutene. The computed enantioselectivity (ΔG^* = 2.7 kcal/mol) is comparable to the difference between the distortion energies of the hydrocupration transition states (ΔE_{dist} = 2.6 kcal/mol), indicating the enantioselectivity is controlled by steric effects that lead to distortions of the catalyst and the substrate. Indeed, the less favorable transition state TS1b' is destabilized due to steric repulsions between the cyclobutene moiety and the P-aryl group in the more-occupied quadrant (quadrant II). The ligand-substrate steric repulsions in TS1b' are evidenced by the short C...H distance of 2.52 Å between the P-aryl group and the methylene group on cyclobutene. The C...H distance between the P-aryl group and the 1-methyl substituent is much longer (2.79 Å in TS1b"), indicating that the steric repulsions with the

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**Figure 4.** Origin of the reversed regioselectivities of the hydroamination of 1-phenylcyclobutene derivative (2a) and 1-phenylcyclopropene derivative (5). All energies are in kcal/mol.
cyclobutene moiety, rather than the 1-substituent, dictate the enantioselectivity.

In the hydrocupration of 1-methylcyclopropene (1a), the two enantiomeric transition states TS-1a and TS-1a' have comparable activation energies. This is consistent with the low e.r. observed in the hydroamination of 1-alkycyclopropene 11. Their similar distortion energies (30.1 and 30.9 kcal/mol for TS-1a and TS-1a', respectively) indicate that the ineffective stereoinduction is due to comparable ligand-substrate steric repulsions in both enantiomeric transition states. The transition state quadrant diagrams in Figure 5b show that due to the smaller size of the cyclopropene moiety compared to the cyclobutene, steric repulsions with the P-aryl group in quadrant II of TS-1a' are diminished. This is evidenced by the much longer C...H distance (2.82 Å) between the P-aryl group and the methylene on the cyclopropene in TS-1a'.

**Figure 5.** Origin of enantioselectivities in the hydroamination of 1-alkycyclobutene and 1-alkycyclopropene. All energies are in kcal/mol.

**CONCLUSION**

In summary, we have developed the diastereo- and enantioselective CuH-catalyzed hydroamination reactions of 1-substituted cyclobutenes and cyclopropenes. DFT studies showed that strained trisubstituted olefins exhibit enhanced rates of hydrocupration compared to unstrained trisubstituted analogues, which allows for the effective hydroamination reactions of these substrates. For 1-aryl-cyclobutenes, Markovnikov products were selectively formed in the hydroamination reactions and a tetrasubstituted carbon center was generated in the cyclobutane product. By contrast, the opposite regioselectivity was observed for the hydroamination of 1-phenylcyclopropene derivatives. DFT studies revealed the Markovnikov-selectivity with 1-aryl-cyclobutenes is due to a smaller distortion energy in the hydrocupration transition state to form the benzylic copper intermediate, while the anti-Markovnikov-selectivity with 1-aryl-cyclopropenes is controlled by catalyst-substrate through-bond interactions. Moreover, the hydroamination reactions of 1-alkycyclobutenes as well as 1-silyl substituted three- and four-membered cycloalkenes were shown to produce a variety of aminocyclobutenes and aminocyclopropanes bearing contiguous stereocenters in excellent enantio- and diastereoselectivity. We also showed that the small size of the cyclopropene moiety in 1-alkylcyclopropenes leads to insufficient ligand-substrate steric interactions for the chiral induction in hydrocupration. Accordingly, the hydroamination of 1-alkylcyclobutenes proceeds with considerably higher levels of enantioselectivity compared to 1-alkylcyclopropenes. We anticipate that our studies on the scope, regio-, and enantioselectivity of CuH-catalyzed hydroamination using various types of strained trisubstituted alkenes can facilitate further developments in asymmetric hydrofunctionalization of strained alkenes.

**ASSOCIATED CONTENT**

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental details and computational data (PDF)

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**Notes**

The authors declare no competing financial interest.

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\[ n = 0, \text{R = Aryl} \]

\[ n = 0, 1, \text{R = Alkyl, Silyl} \]

9 examples
up to 90% yield, 29:1 dr

11 examples
up to 92% yield, > 20:1 dr, 99.5:0.5 er
Diastereo- and Enantioselective CuH-Catalyzed Hydroamination of Strained Trisubstituted Alkenes

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1. General Information

1.1 General Analytical Information
All new compounds were characterized by NMR spectroscopy, IR spectroscopy, elemental analysis or high resolution mass spectrometry, optical rotation (if chiral and non-racemic) and melting point analysis (if solids). \(^3\)H, \(^{13}\)C and \(^{19}\)F NMR spectra were recorded in CDCl\(_3\) on a Bruker 400 or 500 MHz spectrometer. Chemical shifts for \(^1\)H NMR are reported as follows: chemical shift in reference to residual CHCl\(_3\) at 7.26 ppm (\(\delta\) ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, sex = sextet, sep = septet, dd = double of doublets, td = triplet of doublets, m = multiplet), coupling constant (Hz), and integration. Chemical shifts for \(^{13}\)C NMR are reported in terms of chemical shift in reference to the CDCl\(_3\) solvent signal (77.16 ppm). Chemical shifts for \(^{19}\)F NMR are reported in ppm relative to CFCl\(_3\) (0.00 ppm). IR spectra were recorded on a Thermo Scientific Nicolet iS5 spectrometer (iD5 ATR, diamond) and are reported in terms of frequency of absorption (cm\(^{-1}\)). Melting points were measured on a Mel-Temp capillary melting point apparatus. Optical rotations were measured using a Jasco P-1010 digital polarimeter. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA. High-resolution mass spectra were recorded on a JEOL AccuTOF LC-Plus 46 DART system. Enantiomeric excesses (ee’s) were determined by chiral SFC analysis using a Waters Acquity UPC2 instrument; specific columns and analytical methods are provided in the experimental details for individual compounds; the wavelengths of light used for chiral analyses are provided with the associated chromatograms. Thin-layer chromatography (TLC) was performed on silica gel 60Å F\(_{254}\) plates (SiliaPlate from Silicycle) and visualized with UV light, iodine or potassium permanganate stain. Preparatory thin-layer chromatography (Prep-TLC) was performed on silica gel GF with UV 254 (20 x 20 cm, 1000 microns, catalog # TLG-R10011B-341 from Silicycle) and visualized with UV light. Isolated yields reported reflect the average values from two independent runs.

1.2 General Reagent Information
All reactions were performed under a nitrogen atmosphere using the indicated method in the general procedures. Tetrahydrofuran (THF) was purchased from J.T. Baker in CYCLE-TAINER\textsuperscript{®} solvent delivery kegs and purified by passage under argon pressure through two packed columns of neutral alumina and copper(II) oxide. Anhydrous 1,4-dioxane was purchased from Aldrich Chemical Company in a Sure-Seal\textsuperscript{TM} bottle and used as received. Copper(II) acetate was purchased from Strem and was used as received. 1,2-Bis((2S,5S)\_2,5-diphenylphospholano)ethane, 1,2-Bis((2R,5R)\_2,5-diphenylphospholano)ethane (Ph-BPE) ligands were purchased from Namena Corp. and stored in a nitrogen-filled glove box. DTBM-SEGPHOS was purchased from Takasago International Co. and used as received. Diethoxymethylsilane was purchased from TCI America. Dimethoxy(methyl)silane (DMMS) was purchased from Tokyo Chemical Industry Co. (TCI). Both silanes were stored in a nitrogen-filled glove box at \(-20 \degree C\) for long-term storage. (Caution: Dimethoxy(methyl)silane (DMMS, CAS#16881-77-9) is listed by several vendors (TCI, Alfa Aesar) SDS or MSDS as a H318, a category I Causes Serious Eye Damage Other vendors (Sigma-Aldrich, Gelest) list DMMS as a H319, a category II Eye Irritant. DMMS should be handled in a well-ventilated fumehood using proper precaution as outlined for the handling of hazardous materials in prudent practices in the laboratory\textsuperscript{1}. At the end of the reaction either ammonium fluoride in methanol, aqueous sodium hydroxide (1 M) or aqueous hydrochloric acid (1 M) should be carefully added to the reaction mixture. This should be allowed to stir for at least 30 min or the time indicated in the detailed
1,2-Benzisoxazole was purchased from Tokyo Chemical Industry Co. (TCI) and stored in a refrigerator at 4 °C. All other solvents and commercial reagents were used as received from Sigma Aldrich, Alfa Aesar, Acros Organics, TCI and Combi-Blocks, unless otherwise noted. Flash column chromatography was performed using 40-63 µm silica gel (SiliaFlash® F60 from Silicycle), or with the aid of a Biotage Isolera Automated Flash Chromatography System using prepacked SNAP silica cartridges (10-100 g). Organic solutions were concentrated in vacuo using a Buchi rotary evaporator.

2. Optimization and General Procedures for Hydroamination Reactions

2.1 Optimization of CuH-Catalyzed Hydroamination of 1-Arylcyclobutenes

Table S1. Effect of Solvent and Temperature on Hydroamination of 1-Arylcyclobutenes

| solvent      | T (°C) | yield (major + minor) |
|--------------|--------|-----------------------|
| MTBE         | 40     | 70% + 10%             |
| dioxane      | 40     | 70% + 8%              |
| CyH          | 40     | 63% + 10%             |
| toluene      | 40     | 68% + 9%              |
| THF          | 40     | 80% + 8%              |
| THF          | 50     | 80% + 8%              |
| THF          | 30     | 80% + 6%              |
| THF          | rt     | 61% + 5%              |
| THF          | 0      | <10%                  |

Reactions were conducted on 0.1 mmol scale. Yields were determined by ¹H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as the internal standard.

Table S2. Evaluation of Different Amination Reagents and Concentrations

| R = Ph | Concentration: 0.25 M (yield: 65% + 4%), 1.0 M (yield: 82% +7%) |
|--------|---------------------------------------------------------------|
| yield (major + minor): | 80% + 6% | 65% + 5% | 74% + 6% | 76% + 6% |

Reactions were conducted on 0.1 mmol scale. Yields were determined by ¹H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as the internal standard.

2.2 Optimization of CuH-Catalyzed Hydroamination of 1-Arylcyclobutenes

Table S3. Evaluation of Different Amination Reagents
Reactions were conducted on 0.1 mmol scale. Yields were determined by $^1$H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as the internal standard.

2.3 General Procedures for CuH-Catalyzed Hydroamination Reactions

General Procedure A

An oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was charged with Cu(OAc)$_2$ (5.9 mg, 0.033 mmol), (R)-DTBM-SEGPHOS (21.1 mg, 0.018 mmol), and (S)-DTBM-SEGPHOS (21.1 mg, 0.018 mmol). The reaction tube was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into a nitrogen-filled glovebox. Anhydrous THF (0.65 mL) was added to the tube via a 1 mL syringe. The tube was capped and the mixture was stirred for 15 min at rt. Then dimethoxymethylsilane (DMMS) (0.24 mL, 1.95 mmol) was added in one portion via a 1 mL syringe and the stirring was continued for another 10 min at rt to prepare an orange CuH stock solution.

A separate oven-dried screw-cap reaction tube (Fisherbrand, 16*125 mm, part no. 1495935A) containing a magnetic stir bar was loosely capped (cap: Kimble Chase Open Top S/T Closure catalog no. 73804-15425; Septum: Thermo Scientific B7995-15), and then transferred into the glovebox. The alkene (0.5 mmol, 1.0 equiv) and the amine electrophile (0.6 mmol or 0.75 mmol, as indicated for each substrate) were added to the reaction tube. Then the CuH stock solution (0.68 mL) was added via a 1 mL syringe to the reaction tube in one portion. The reaction tube was capped and then removed from the glove box. The reaction mixture was allowed to stir at 30 °C for 36 h.

General Procedure B

An oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was charged with Cu(OAc)$_2$ (5.4 mg, 0.030 mmol) and (R)-DTBM-SEGPHOS (38.9 mg, 0.033 mmol). The reaction tube was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into a nitrogen-filled glovebox. Anhydrous THF (1.20 mL) was added to the tube via syringe. The tube was capped and the mixture was stirred for 15 min at rt. Then DMMS (0.22 mL, 1.80 mmol) was added in one portion via a 1 mL syringe and the stirring was continued for another 10 min at rt to prepare an orange CuH stock solution.

A separate oven-dried screw-cap reaction tube (Fisherbrand, 16*125 mm, part no. 1495935A) containing a magnetic stir bar was loosely capped (cap: Kimble Chase Open Top S/T Closure catalog no. 73804-15425; Septum: Thermo Scientific B7995-15), and then transferred into the glovebox. The alkene (0.5 mmol, 1.0 equiv) and the amine electrophile (0.6 mmol or 0.75 mmol, as indicated for each substrate) were added to the reaction tube. Then the CuH stock solution (1.2 equiv) was added via a 1 mL syringe to the reaction tube in one portion. The reaction tube was capped and then removed from the glove box. The reaction mixture was allowed to stir at 30 °C for 36 h.
solution (1.18 mL) was added via syringe to the reaction tube in one portion. The reaction tube was capped and then removed from the glove box. The reaction mixture was allowed to stir at 40 °C for 36 or 46 h as indicated for each substrate.

General Procedure C
An oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was charged with Cu(OAc)$_2$ (5.4 mg, 0.030 mmol) and (R)-DTBM-SEGPHOS (38.9 mg, 0.033 mmol). The reaction tube was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into a nitrogen-filled glovebox. Anhydrous 1,4-dioxane (0.60 mL) was added to the tube with a 1 mL syringe. The tube was capped and the mixture was stirred for 10 min at rt. Then DMMS (0.22 mL, 1.80 mmol) was added in one portion via a 1 mL syringe and the stirring was continued for another 15 min at rt to prepare a dark red CuH stock solution.

A separate oven-dried screw-cap reaction tube (Fisherbrand, 16*125 mm, part no. 1495935A) containing a magnetic stir bar was loosely capped (cap: Kimble Chase Open Top S/T Closure catalog no. 73804-15425; Septum: Thermo Scientific B7995-15), and then transferred into the glovebox. The alkene (0.5 mmol, 1.0 equiv), the amine electrophile (0.6 mmol, 1.2 equiv), and anhydrous 1,4-dioxane (0.50 mL) were added to the reaction tube. Then the CuH stock solution (0.68 mL) was added via a 1 mL syringe to the reaction tube in one portion. The reaction tube was capped and then taken out of the glove box. The reaction mixture was allowed to stir at rt for 18 h.

General Procedure D
An oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was charged with Cu(OAc)$_2$ (5.4 mg, 0.030 mmol) and (R)-DTBM-SEGPHOS (38.9 mg, 0.033 mmol). The reaction tube was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into a nitrogen-filled glovebox. Anhydrous 1,4-dioxane (0.60 mL) was added to the tube with a 1 mL syringe. The tube was capped and the mixture was stirred for 10 min at rt. Then DMMS (0.22 mL, 1.80 mmol) was added in one portion via a 1 mL syringe and the stirring was continued for another 15 min at rt to prepare a dark red CuH stock solution.

A second oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into the glovebox. 1,2-Benzisoxazole (92 µL) and anhydrous 1,4-dioxane (0.35 mL) were added to the tube to prepare the 1,2-benzisoxazole stock solution. The tube was capped and then gently stirred to mix the solution.

A third oven-dried screw-cap reaction tube (Fisherbrand, 16*125 mm, part no. 1495935A) containing a magnetic stir bar was loosely capped (cap: Kimble Chase Open Top S/T Closure catalog no. 73804-15425; Septum: Thermo Scientific B7995-15), and then transferred into the glovebox. The alkene (0.5 mmol, 1.0 equiv) and anhydrous 1,4-dioxane (0.50 mL) were added to the reaction tube. Then the CuH stock solution (0.68 mL) was added via a 1 mL syringe to the reaction tube in one portion. (Note: The CuH solution should be added directly into the alkene solution instead of along the wall of the reaction tube, otherwise the remaining CuH solution on the wall of the reaction tube may cause decomposition of the 1,2-benzisoxazole that was subsequently added slowly along the wall of the reaction tube.) The reaction mixture was stirred at rt for 30 s. Then while the reaction mixture was stirred at rt, 1,2-benzisoxazole (10 µL)
was added over 1 min via microsyringe. The reaction tube was capped and the septum was punctured with a long needle attached to a 1 mL syringe containing the 1,2-benzisoxazole stock solution (0.32 mL). The reaction tube was then taken out of the glove box. While the reaction mixture was stirred at rt, the 1,2-benzisoxazole solution was added slowly via syringe pump at a rate of 0.13 or 0.16 mL/h (as indicated for each substrate). (Note: The tip of the needle should touch the wall of the reaction tube during the slow addition of 1,2-benzisoxazole.) The reaction mixture was allowed to stir at rt for 18 h.

**Workup A**

After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred at rt, sat. NH₄F in MeOH (1 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at rt for 30 min and transferred to a 100 mL round bottom flask with the aid of EtOAc. A small aliquot of the solution was transferred to a 20 mL scintillation vial, concentrated in vacuo, analyzed by ¹H NMR in CDCl₃ to determine the diastereomeric ratio (Dr), and then the NMR sample was transferred back to the 100 mL round bottom flask. The combined solution was concentrated in vacuo. The resulting mixture was dissolved in EtOAc, filtered through a short plug of Celite, and washed with additional EtOAc. The collected EtOAc solution was concentrated in vacuo, and the crude material was immediately purified by silica gel column chromatography (~ 30 g silica gel, diameter of the column ~ 2 cm, length of the packed column ~ 18 cm).

**Workup B**

After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred at rt, sat. NH₄F in MeOH (1 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at rt for 30 min, and then transferred to a 20 mL scintillation vial. The reaction tube was rinsed four times with additional EtOAc (5-10 mL in total). The combined EtOAc solution was concentrated in vacuo, and the crude material was immediately purified by silica gel column chromatography (~ 30 g silica gel, diameter of the column ~ 2 cm, length of the packed column ~ 18 cm).

**Workup C**

After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred vigorously at rt, sat. LiOH in MeOH (2.5 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at rt for 1 h, transferred to a 100 mL round bottom flask with the aid of EtOAc, and concentrated in vacuo. The resulting mixture was dissolved in EtOAc, sonicated for 5 min, filtered through a pad of Celite, and washed with additional EtOAc. The collected EtOAc solution was concentrated in vacuo, and the crude material was immediately purified by silica gel column chromatography (~ 30 g silica gel, diameter of the column ~ 2 cm, length of the packed column ~ 18 cm).

**Workup D**

After the reaction was completed, the cap of the reaction tube was removed, and the reaction mixture was diluted with EtOAc (1.5 mL). While the reaction mixture was stirred at 0 °C, sat. aq. NaHCO₃ (2 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at 0 °C for 5 min, and then at rt for 30 min. The mixture was transferred with the aid of EtOAc to a 125 mL separatory funnel containing brine
(30 mL) and EtOAc (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10-15 mL). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated in vacuo. The resulting residue was transferred to a 20 mL scintillation vial with the aid of EtOAc, and then concentrated in vacuo. The crude material was immediately purified by silica gel column chromatography (~ 30 g silica gel, diameter of the column was ~ 2 cm, length of the packed column was ~ 18 cm).

2.4 Structural Determination of the Hydroamination Products

**Single Crystal X-ray Diffraction Data for Compound 7b (P19056)**

A crystal of 7b was obtained by slowly evaporating the EtOH solution of 7b at 0 °C (in air). The absolute configuration of 7b was determined by X-ray crystallographic analysis. The absolute configuration of 10a, 7a-e, 12, and 15a-d was assigned by analogy to 7b.

CCDC 1945177 contains the supplementary crystallographic data for 7b. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

![Crystal Structure](image)

**Table S4. Crystal data and structure refinement for 7b (P19056)**

| Property                  | Value       |
|---------------------------|-------------|
| Identification code       | P19056      |
| Empirical formula         | C25 H29 N S |
| Formula weight            | 375.55      |
Temperature 99(2) K
Wavelength 0.71073 Å
Crystal system Monoclinic
Space group P2₁
Unit cell dimensions
\[ a = 13.0414(11) \text{ Å} \]
\[ b = 5.7208(4) \text{ Å} \]
\[ c = 14.1145(12) \text{ Å} \]
a= 90°.
b= 93.997(4)°.
g = 90°.
Volume 1050.48(15) Å³
Z 2
Density (calculated) 1.187 Mg/m³
Absorption coefficient 0.163 mm⁻¹
F(000) 404
Crystal size 0.570 x 0.165 x 0.160 mm³
Theta range for data collection 1.446 to 30.541°.
Index ranges -18<=h<=18, -8<=k<=8, -20<=l<=20
Reflections collected 89778
Independent reflections 6421 [R(int) = 0.0653]
Completeness to theta = 25.242° 99.9 %
Absorption correction Semi-empirical from equivalents
Refinement method Full-matrix least-squares on F²
Data / restraints / parameters 6421 / 366 / 309
Goodness-of-fit on F² 1.125
Final R indices [I>2sigma(I)] R1 = 0.0440, wR2 = 0.1092
R indices (all data) R1 = 0.0454, wR2 = 0.1098
Absolute structure parameter 0.04(2)
Extinction coefficient 0.192(12)
Largest diff. peak and hole 0.365 and -0.438 e.Å⁻³

**1D-NOESY Analysis of 4b (a 5:1 mixture of major and minor diastereomers)**
The configuration of the major and minor diastereomers in 4b was determined by 1D-NOESY analysis of 4b (a 5:1 mixture of major and minor diastereomers). The configuration of the major diastereomers in 4a, 4c, 4g-i was assigned by analogy to 4b.
3. Characterization Data for the Hydroamination Products

(1r,3r)-N,N-dibenzyl-3-methyl-1,3-diphenyloclobutan-1-amine (4a)

Following general procedure A. (3-methylcyclobut-1-ene-1,3-diyl)dibenzene (110 mg, 0.50 mmol, 1.0 equiv) and Bn2NOBz (190 mg, 0.60 mmol, 1.2 equiv) were used. After Workup A and purification by column chromatography [hexanes (80 mL) followed by hexanes/EtOAc = 100:1], the title compound was obtained as a white solid (1st run: 181 mg, 87% yield, 13:1 dr; 2nd run: 174 mg, 83% yield, 13:1 dr). 1H NMR analysis of the crude reaction mixture indicated 13:1 dr. 1H NMR (major diastereomer, 400 MHz, CDCl3) δ 7.29-7.25 (m, 2H), 7.19-6.94 (m, 18H), 3.39 (s, 4H), 2.77 (d, J = 12.6 Hz, 2H), 2.64 (d, J = 12.7 Hz, 2H), 1.70 (s, 3H). 13C NMR (major diastereomer, 101 MHz, CDCl3) δ 152.22, 141.73, 141.14, 128.93, 128.01, 127.79, 127.48, 126.37, 126.28, 125.12, 125.02, 55.02, 44.97, 36.07, 33.25. m.p. 128.0-129.7 °C. IR (thin film): 3063, 3024, 2842, 1605, 1511, 1280, 1179, 1029, 908, 692 cm⁻¹. EA Calcd. for C31H31N: C, 89.16; H, 7.48. Found: C, 88.96; H, 7.45.

(1r,3r)-N,N-dibenzyl-1-(4-methoxyphenyl)-3-methyl-3-phenyloclobutan-1-amine (4b)

Following general procedure A. 1-methoxy-4-(3-methyl-3-phenyloclobut-1-en-1-yl)benzene (125 mg, 0.50 mmol, 1.0 equiv) and Bn2NOBz (190 mg, 0.60 mmol, 1.2 equiv) were used. After the reaction was completed, the reaction mixture was transferred to a 100 mL round bottom flask, and the reaction tube was rinsed with additional EtOAc. Then HCl in MeOH (1.25 M, 15 mL) was added to the flask to quench the reaction mixture and acidify the mixture. The flask was swirled gently to mix the components, allowed to sit for 30 min, and then the resulting mixture was concentrated in vacuo. Hexanes (~ 20 mL) was added. The precipitate was filtered into small pieces using a spatula, and the resulting suspension was sonicated for 5-10 min. The suspension was filtered through a Buchner funnel (porosity: fine) under reduced pressure. The 100 mL flask was rinsed with hexane (~20 mL) and the suspension was poured into the funnel. The solid in the funnel was washed with additional hexanes (~10 mL). Then the solid in the above 100 mL round bottom flask and Buchner funnel was dissolved with 1 M NaOH (~50 mL in total) and CH2Cl2 (~50 mL in total). The resulting mixture was transferred to a separatory funnel, and the layers were separated. The aqueous layer was extracted with CH2Cl2 (3 x 50 mL). The combined organic layers were dried over Na2SO4, filtered, and the solution was collected in a 500 mL round bottom flask. A small aliquot of the solution was transferred to a 20 mL scintillation vial, concentrated in vacuo, analyzed by 1H NMR in CDCl3 to determine the diastereomeric ratio (dr), and then the NMR sample was concentrated and purified by column chromatography (~30 g silica gel) with a gradient of hexanes (100 mL) → hexanes/Et2O = [30:1 (90 mL) → 20:1 (160 mL)]. The title compound was obtained as a white solid (1st run: 140 mg, 62% yield, 5:1 dr; 2nd run: 150 mg, 67% yield, 5:1 dr). 1H NMR analysis of the crude reaction mixture indicated 5:1 dr. 1H NMR (major diastereomer, 400 MHz, CDCl3) δ 7.30-7.28 (m, 1H), 7.25-7.07 (m, 13H), 6.94-6.90 (m, 2H), 3.86 (s, 3H), 3.50 (s, 4H), 2.87 (d, J = 12.6 Hz, 2H), 2.74 (d, J = 12.7 Hz, 2H), 1.80 (s, 3H). 13C NMR (major diastereomer, 101 MHz, CDCl3) δ 157.91, 152.16, 141.23, 134.16, 128.92, 128.62, 127.98, 127.78, 126.34, 125.13, 124.99, 112.66, 62.21, 55.25, 55.02, 45.26, 35.87, 33.27. m.p. 134.5-136.8 °C. IR (thin film): 3059, 3025, 2931, 2834, 1605, 1511, 1247, 1179, 1028, 698 cm⁻¹. HRMS Calcd. m/z for C32H34NO⁺ [M+H]+: 448.2635; found 448.2655.
(1r,3r)-N,N-dibenzyl-1-(3-chlorophenyl)-3-methyl-3-phenylcyclobutan-1-amine (4c)

Following general procedure A, 1-chloro-3-(3-methyl-3-phenylcyclobut-1-en-1-yl)benzene (127 mg, 0.50 mmol, 1.0 equiv) and Bn₂NOBz (190 mg, 0.60 mmol, 1.2 equiv) were used. After Workup A and purification by column chromatography [hexanes (200 mL) followed by hexanes/EtOAc = 100:1], the title compound was obtained as a white solid (1st run: 180 mg, 80% yield, 29:1 dr; 2nd run: 178 mg, 78% yield, 29:1 dr). ¹H NMR analysis of the crude reaction mixture indicated 29:1 dr. ¹H NMR (major diastereomer, 400 MHz, CDCl₃) δ 7.34-7.09 (m, 19H), 3.50 (s, 4H), 2.88-2.85 (m, 2H), 2.78-2.74 (m, 2H), 1.80 (s, 3H). ¹³C NMR (major diastereomer, 101 MHz, CDCl₃) δ 151.75, 143.88, 140.75, 133.60, 128.92, 128.70, 128.09, 127.90, 127.63, 126.54, 126.52, 125.64, 125.19, 125.10, 62.61, 54.91, 44.95, 36.12, 33.27. m.p. 142.6-144.0 °C. IR (thin film): 3061, 3025, 2933, 2838, 1592, 1494, 1262, 1172, 1027, 695 cm⁻¹. HRMS Calcd. m/z for C₃₁H₃₁NCl⁺ [M+H]⁺: 452.2140; found 452.2143.

N,N-dibenzyl-1-(2-fluorophenyl)cyclobutan-1-amine (4d)

Following general procedure B, 1-(cyclobut-1-en-1-yl)-2-fluorobenzene (74 mg, 0.50 mmol, 1.0 equiv) and Bn₂NOPiv (178 mg, 0.60 mmol, 1.2 equiv) were used. The reaction was run at 40 °C for 36 h. After Workup B and purification by column chromatography with a gradient of hexanes (150 mL) → hexanes/Et₂O = [100:1 (100 mL) → 80:1 (240 mL) → 60:1 (60 mL)], the title compound was obtained as a colorless oil (1st run: 124 mg, 72% yield, 2nd run: 123 mg, 71% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.36-7.21 (m, 8H), 7.19-7.15 (m, 4H), 7.13-7.08 (m, 2H), 3.57 (s, 4H), 2.47-2.44 (m, 4H), 2.28-2.18 (m, 1H), 1.80-1.71 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 161.36 (d, J = 246.4 Hz), 141.51, 130.24 (d, J = 5.8 Hz), 129.04 (d, J = 14.6 Hz), 128.61, 128.53, 127.69, 126.22, 123.26 (d, J = 3.5 Hz), 116.28 (d, J = 24.6 Hz), 67.34 (d, J = 2.4 Hz), 54.76 (d, J = 2.9 Hz), 33.23 (d, J = 1.5 Hz), 16.30. ¹⁹F NMR (376 MHz, CDCl₃) δ -109.85. IR (thin film): 3062, 3027, 2943, 2839, 1483, 1446, 1212, 1141, 1028, 695 cm⁻¹. EA Calcd. for C₂₄H₂₄NF: C, 83.44; H, 7.00. Found: C, 83.31; H, 7.14.

N,N-dibenzyl-1-(6-methoxypyridin-3-yl)cyclobutan-1-amine (4e)

Following general procedure B, 5-(cyclobut-1-en-1-yl)-2-methoxypyridine (81 mg, 0.50 mmol, 1.0 equiv) and Bn₂NOPiv (178 mg, 0.60 mmol, 1.2 equiv) were used. The reaction was run at 40 °C for 36 h. After Workup B and purification by column chromatography with a gradient of hexanes (100 mL) → hexanes/Et₂O = [50:1 (100 mL) → 40:1 (40 mL) → 30:1 (90 mL) → 20:1 (100 mL) → 15:1 (90 mL) → 10:1 (100 mL)], the title compound was obtained as a colorless oil (1st run: 134 mg, 75% yield; 2nd run: 136 mg, 76% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.38 (dd, J = 2.6, 0.8 Hz, 1H), 7.76 (dd, J = 8.6, 2.6 Hz, 1H), 7.34-7.28 (m, 4H), 7.25-7.22 (m, 4H), 7.18-7.14 (m, 2H), 6.88 (dd, J = 8.6, 0.7 Hz, 1H), 4.04 (s, 3H), 3.42 (s, 4H), 2.35 (qd, J = 9.3, 2.4 Hz, 2H), 2.22 (tt, J = 8.4, 2.9 Hz, 2H), 1.86-1.78 (m, 1H), 1.60-1.49 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 163.13, 146.23, 141.02, 138.71, 129.58, 128.82, 128.03, 126.67, 110.07, 66.31, 53.91, 53.56, 33.25, 14.80. IR (thin film): 3024, 2943, 2840, 1599, 1488, 1368, 1285, 1132, 1023, 696 cm⁻¹. EA Calcd. for C₂₄H₂₆N₂O: C, 80.41; H, 7.31. Found: C, 80.71; H, 7.08.

N,N-dibenzyl-2-phenylspiro[3.5]nonan-2-amine (4f)
Following general procedure A, instead of using (R)-DTBM-SEGPHOS (21.1 mg) and (S)-DTBM-SEGPHOS (21.1 mg) to prepare the CuH stock solution, (R)-DTBM-SEGPHOS (42.2 mg) was used. 2-Phenylspiro[3.5]non-1-ene (99 mg, 0.50 mmol, 1.0 equiv) and Bn2NOBz (190 mg, 0.60 mmol, 1.2 equiv) were also used. After Workup A and purification by column chromatography with a gradient of hexanes (150 mL) → hexanes/EtOAc = [100:1 (100 mL) → 80:1 (240 mL) → 60:1 (60 mL)], the title compound was obtained as a white solid (1st run: 177 mg, 89% yield; 2nd run: 179 mg, 91% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.49-7.45 (m, 2H), 7.42-7.40 (m, 2H), 7.35 (tt, \(J = 6.5, 1.4\) Hz, 1H), 7.24-7.22 (m, 4H), 7.17-7.13 (m, 4H), 7.11-7.07 (m, 2H), 3.39 (s, 4H), 2.30 (d, \(J = 12.4\) Hz, 2H), 2.22 (d, \(J = 12.4\) Hz, 2H), 1.72-1.70 (m, 2H), 1.43 (p, \(J = 5.7\) Hz, 2H), 1.33-1.28 (m, 4H), 1.18-1.15 (m, 2H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 142.49, 141.36, 128.96, 127.92, 127.78, 127.59, 126.33, 62.86, 54.65, 44.26, 40.60, 38.66, 31.81, 26.10, 22.95, 22.85. m.p. 81.8-82.5 °C. IR (thin film): 3060, 3025, 2932, 2853, 1584, 1493, 1357, 1261 cm\(^{-1}\). HRMS Calcd. m/z for C\(_{29}\)H\(_{34}\)N\(_4^+\) [M+H]\(^+\): 396.2686; found 396.2690.

2-(4-((1R,3R)-3-methyl-1,3-diphenylocyclobutyl)piperazin-1-yl)pyrimidine (4g)

Following general procedure A, (3-methylcyclobut-1-ene-1,3-diyl)dibenzene (110 mg, 0.50 mmol, 1.0 equiv) and 4-(pyrimidin-2-yl)piperazin-1-yl benzoate (171 mg, 0.60 mmol, 1.2 equiv) were used. After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred at rt, sat. NH\(_4\)F in MeOH (1 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at rt for 30 min and transferred to a 100 mL round bottom flask with the aid of CH\(_2\)Cl\(_2\). A small aliquot of the solution was transferred to a 20 mL scintillation vial, concentrated in vacuo, analyzed by \(^1\)H NMR in CDCl\(_3\) to determine the diastereomeric ratio (dr), and then the NMR sample was transferred back to the 100 mL round bottom flask. The combined solution was concentrated in vacuo. The resulting mixture was dissolved in CH\(_2\)Cl\(_2\), filtered through a short plug of basic activated alumina, and washed with additional CH\(_2\)Cl\(_2\). The CH\(_2\)Cl\(_2\) solution was collected in a 20 mL scintillation vial, concentrated in vacuo, and the crude material and immediately purified by column chromatography (~30 g silica gel, diameter of the column ~2 cm, length of the packed column ~18 cm) with a gradient of hexanes/EtOAc = [20:1 (60 mL) → 15:1 (150 mL) → 12:1 (60 mL) → 10:1 (200 mL) → 8:1 (80 mL) → 5:1 (100 mL) → 4:1 (100 mL) (the above volumes refer to the volume of hexanes used)]. The resulting material was redissolved in CH\(_2\)Cl\(_2\) (3 mL), filtered through a short plug of basic activated alumina, and washed with additional EtOAc. The collected EtOAc solution was concentrated in vacuo to afford the pure product as a white solid (1st run: 128 mg, 66% yield, 13:1 dr; 2nd run: 128 mg, 66% yield, 13:1 dr). \(^1\)H NMR analysis of the crude reaction mixture indicated 13:1 dr. \(^1\)H NMR (major diastereomer, 400 MHz, CDCl\(_3\)) \(\delta\) 8.26 (d, \(J = 4.7\) Hz, 2H), 7.28-7.24 (m, 4H), 7.19-7.10 (m, 4H), 7.06-7.04 (m, 2H), 6.43 (t, \(J = 4.8\) Hz, 1H), 3.88 (br, 4H), 2.81 (d, \(J = 11.4\) Hz, 2H), 2.77 (d, \(J = 11.5\) Hz, 2H), 2.42 (br, 4H), 1.77 (s, 3H). \(^{13}\)C NMR (major diastereomer, 101 MHz, CDCl\(_3\)) \(\delta\) 151.75, 143.88, 140.75, 133.60, 128.92, 128.70, 128.09, 127.90, 127.63, 126.54, 126.52, 125.64, 125.19, 125.10, 62.61, 54.91, 44.95, 36.12, 33.27. m.p. 197.0-198.9 °C. IR (thin film): 3021, 2932, 2853, 1584, 1493, 1357, 1261, 1181, 1012, 700 cm\(^{-1}\). HRMS Calcd. m/z for C\(_{25}\)H\(_{29}\)N\(_4^+\) [M+H]\(^+\): 385.2387; found 385.2396.
General procedure A was followed, except DMMS (0.32 mL, 2.60 mmol) (Note: An extra equivalence of DMMS was used in order to silylate the alcohol in the amination reagent.) was used to prepare the CuH stock solution. The stock CuH solution (0.74 mL) was added to the reaction tube containing 1-fluoro-4-(3-methyl-3-phenylcyclobut-1-en-1-yl)benzene (119 mg, 0.50 mmol, 1.0 equiv) and 5-(((benzoyloxy)(benzyl)amino)methyl)furan-2-yl)methanol (202 mg, 0.60 mmol, 1.2 equiv). After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred at rt, sat. NH₄F in MeOH (5 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at rt for 1 h and transferred to a 100 mL round bottom flask with the aid of a cotton ball that was stuck in a pipette, and washed with additional CH₂Cl₂. The CH₂Cl₂ solution was collected in a 20 mL scintillation vial, concentrated in vacuo, and the crude material was immediately purified by column chromatography (~ 30 g silica gel, diameter of the column ~ 2 cm, length of the packed column ~ 18 cm) with a gradient of hexanes/EtOAc = [20:1 (60 mL) → 15:1 (150 mL) → 12:1 (60 mL) → 10:1 (200 mL) → 8:1 (80 mL) → 5:1 (100 mL) → 4:1 (100 mL) (the above volumes refer to the volume of hexanes used)]. The resulting material was redissolved in CH₂Cl₂ (3 mL), filtered through a short plug of basic activated alumina, and washed with additional EtOAc. The collected EtOAc solution was concentrated in vacuo to afford the pure product as a white solid (1st run: 173 mg, 76% yield, 11:1 dr; 2nd run: 182 mg, 80% yield, 11:1 dr). H NMR analysis of the crude reaction mixture indicated 11:1 dr. H NMR (major diastereomer, 400 MHz, CDCl₃) δ 7.33-7.30 (m, 2H), 7.28-7.10 (m, 10H), 7.06-7.00 (m, 2H), 5.96 (d, J = 3.1 Hz, 1H), 5.78 (d, J = 3.1 Hz, 1H), 4.43 (d, J = 6.0 Hz, 2H), 3.54 (s, 2H), 3.49 (s, 2H), 2.92-2.88 (m, 2H), 2.82-2.78 (m, 2H), 1.84 (s, 3H), 1.43 (t, J = 6.0 Hz, 1H). C NMR (major diastereomer, 101 MHz, CDCl₃) δ 161.33 (d, J = 245.2 Hz), 153.72, 152.58, 151.96, 140.79, 137.56 (d, J = 3.1 Hz), 128.68, 128.60, 128.27, 128.11, 127.77, 126.28, 125.17, 125.07, 114.28 (d, J = 21.0 Hz), 108.49 (d, J = 19.7 Hz), 61.82, 57.55, 54.73, 46.93, 44.80, 35.81, 32.99. F NMR (major diastereomer, 376 MHz, CDCl₃) δ -116.55. m.p. 124.3-125.9 °C. IR (thin film): 3359, 3025, 2932, 2866, 1601, 1508, 1224, 1157, 1010, 699 cm⁻¹. EA Calcd. for C₃₀H₃₀FNO₂: C, 79.09; H, 6.64. Found: C, 79.01; H, 6.62.

General procedure A was followed, except DMMS (0.32 mL, 2.60 mmol) was used to prepare the CuH stock solution. The stock CuH solution (0.74 mL) was added to the reaction tube containing 3-methylcyclobut-1-en-1,3-diyl) dibenzene (110 mg, 0.50 mmol, 1.0 equiv) and methyl 5-(((benzoyloxy)(benzyl)amino)methyl)-2-hydroxybenzoate (235 mg, 0.60 mmol, 1.2 equiv). After Workup A (5 mL sat. NH₄F in MeOH was used to quench the reaction mixture) and purification by column chromatography with a gradient of hexanes (200 mL) → hexanes/Et₂O = [50:1 (100
(1S,3R)-N,N-dibenzyl-2,2-dimethyl-3-phenylcyclopropan-1-amine (10a) + N,N-dibenzyl-2,2-dimethyl-1-phenylcyclopropan-1-amine (10b)

Following general procedure C, 1,4-dioxane was replaced with an equal volume of THF, and (3,3-dimethylcycloprop-1-en-1-yl)benzene (72 mg, 0.50 mmol, 1.0 equiv, freshly prepared) and Bn2NOPiv (178 mg, 0.60 mmol, 1.2 equiv) were used. After Workup A and purification by column chromatography with a gradient of hexanes (150 mL) → hexanes/Et2O = [120:1 (180 mL) → 100:1 (150 mL) → 80:1 (80 mL)] (the product on TLC was visualized with I2), a 8:1 mixture of the title compound (a mixture of 10a and 10b, 8:1 ratio) was obtained as a colorless oil (1st run: 101 mg, 59% yield, 69:31 er for 10a; 2nd run: 98 mg, 57% yield, 69:31 er for 10a). EA Calcd. for C25H27N: C, 87.93; H, 7.97. 1H NMR analysis of the crude reaction mixture indicated an 8:1 ratio of 10a and 10b. To separately obtain characterization data and confirm the structure of 10a and 10b, a small aliquot of the title compound was purified with preparative thin-layer chromatography (20 x 20 cm, 250 microns, catalog # TLG-R10014B-323 from Silicycle) eluting with hexane/EtOAc = 80:1 to give pure 10a and 10b.

Major regioisomer 10a: White solid. mp 48.0-49.4 °C. 1H NMR (400 MHz, CDCl3) δ 7.35-7.30 (m, 8H), 7.29-7.25 (m, 4H), 7.19-7.16 (m, 1H), 7.13-7.11 (m, 2H), 3.77 (d, J = 13.6 Hz, 2H), 3.68 (d, J = 13.6 Hz, 2H), 2.20 (d, J = 4.6 Hz, 1H), 1.76 (d, J = 13.6 Hz, 1H), 1.19 (s, 3H), 0.79 (s, 3H). 13C NMR (101 MHz, CDCl3) δ 139.52, 138.72, 129.68, 128.66, 128.14, 127.93, 126.97, 125.58, 58.41, 53.80, 36.76, 27.80, 21.41, 20.58. DEPT-135 NMR (101 MHz, CDCl3) δ 129.66, 128.64, 128.12, 127.92, 126.96, 125.57, 58.41 (CH2), 53.80, 36.76, 21.40, 20.57. SFC analysis: OJ-H (5:95 IPA: scCO2 to 30:70 IPA: scCO2 linear gradient over 6 min with 1 min hold time, 2.50 mL/min, 3.96 min (minor), 4.84 min (major), 69:31 er. Specific rotation [α]D25: +13.8 (c = 1.0, CHCl3). IR (thin film): 3061, 3026, 2919, 1602, 1494, 1454, 1373, 1029, 745, 697 cm⁻¹. EA Calcd. for C25H27N: C, 87.93; H, 7.97. Found: C, 87.64; H, 8.04.

Minor regioisomer 10b: White solid. mp 88.4-90.8 °C. 1H NMR (400 MHz, CDCl3) δ 7.47-7.17 (m, 15H), 4.13 (br, 1H), 3.43-3.40 (m, 3H), 1.61 (s, 3H), 0.85 (s, 3H), 0.53-0.50 (m, 2H). 13C NMR (101 MHz, CDCl3) δ 136.31, 132.14, 129.22, 128.00, 127.63, 126.87, 126.63, 70.74, 56.33, 27.84, 25.25, 22.80, 21.43. DEPT-135 NMR (101 MHz, CDCl3) δ 132.15, 129.22, 128.04, 127.63, 126.87, 126.57, 70.74 (CH2), 27.85(CH2), 25.25, 21.43. IR (thin film): 3026, 2925, 2865, 1494, 1454, 1377, 1122, 1027, 740, 697 cm⁻¹. HRMS Calcd. m/z for C25H28N⁺ [M+H]⁺: 342.2216; found 342.2228.
Following general procedure B, (3-cyclobut-1-en-1-yl)propylbenzene (86 mg, 0.50 mmol, 1.0 equiv) and Bn₂NOC(O)Mes (270 mg, 0.75 mmol, 1.5 equiv) were used. The reaction was run at 40 °C for 46 h. After Workup C and purification by column chromatography with a gradient of hexanes (80 mL) → hexanes/Et₂O = [100:1 (100 mL) → 80:1 (until the majority of the product is eluted) → 40:1 (40 mL)] (the product on TLC was visualized with I₂), the title compound was obtained as a colorless oil (1st run: 145 mg, 78% yield, > 99.5:0.5 er, > 20:1 dr; 2nd run: 147 mg, 80% yield, > 99.5:0.5 er, > 20:1 dr). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.38-7.16 (m, 15H), 3.64 (d, \(J = 13.9\) Hz, 2H), 3.54 (d, \(J = 14.0\) Hz, 2H), 2.93 (q, \(J = 7.9\) Hz, 1H), 2.61-2.48 (m, 2H), 2.35-2.26 (m, 1H), 1.92-1.75 (m, 3H), 1.67-1.6 (m, 3H), 1.36-1.26 (m, 1H), 1.19-1.09 (m, 1H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 142.91, 140.13, 128.91, 128.49, 128.35, 128.18, 126.76, 125.70, 63.46, 54.88, 41.10, 36.10, 35.66, 29.22, 23.04, 21.16. SFC analysis: OJ-H (5:95 IPA: scCO\(_2\) to 40:60 IPA: scCO\(_2\) linear gradient over 6 min with 2 min hold time, 2.50 mL/min), 5.27 min (major), 7.14 min (minor), > 99.5:0.5 er. Specific rotation \([\alpha]_D^{23}\) = -37.1 (c = 1.0, CHCl\(_3\)). IR (thin film): 3060, 3025, 2929, 2854, 1602, 1493, 1452, 1143, 1028, 744 cm\(^{-1}\). EA Calcd. for C\(_{27}\)H\(_{31}\)N: C, 87.75; H, 8.46. Found: C, 87.49; H, 8.48.

Following general procedure B, (3-cyclobut-1-en-1-yl)propylbenzene (86 mg, 0.50 mmol, 1.0 equiv) and N-benzyl-N-(thiophen-2-ylmethyl)-O-(2,4,6-trimethylbenzoyl)hydroxylamine (274 mg, 0.75 mmol, 1.5 equiv) were used. The reaction was run at 40 °C for 46 h. After the reaction was completed, the reaction mixture was filtered through a short plug of silica gel, and washed with additional EtOAc. The EtOAc solution was collected in a 20 mL scintillation vial, and then solvent was carefully removed under high vacuum by fitting a red septum onto the vial, inserting a needle into the septum, connecting the needle to a liquid N\(_2\) trap, connecting the first liquid N\(_2\) trap to a second liquid N\(_2\) trap, and then connecting the second trap to the vacuum line on a Schlenk dual-manifold (Note: The liquid N\(_2\) traps are necessary to insure that DMMS is completely trapped). After the evaporation process, the traps were maintained inside a fumehood. After their contents were thawed, the traps were washed thoroughly with acetone and the waste was poured into a container designated for organic liquid waste). The crude material was immediately purified by column chromatography (~ 30 g silica gel, diameter of the column ~ 2 cm, length of the packed column ~ 18 cm) with a gradient of hexanes (100 mL) → hexanes/Et₂O = [50:1 (100 mL) → 40:1 (40 mL) → 30:1 (150 mL) → 20:1 (80 mL) → 15:1 (60 mL) → 10:1 (200 mL) (the above volumes refer to the volume of hexanes used)] (the product on TLC was visualized with I₂). The title compound was obtained as a white solid (1st run: 146 mg, 78% yield, > 99.5:0.5 er, > 20:1 dr; 2nd run: 151 mg, 80% yield, > 99.5:0.5 er, > 20:1 dr). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.44-7.42 (m, 2H), 7.37-7.19 (m, 9H), 6.98 (dd, \(J = 5.1, 3.4\) Hz, 1H), 6.88 (dd, \(J = 3.4, 1.0\) Hz, 1H), 3.85 (d, \(J = 14.8\) Hz, 1H), 3.79 (d, \(J = 14.8\) Hz, 1H), 3.68 (d, \(J = 14.0\) Hz, 1H), 3.58 (d, \(J = 14.0\) Hz, 1H), 2.99 (q, \(J = 7.8\) Hz, 1H), 2.65-2.52 (m, 2H), 2.37-2.28 (m, 1H), 2.00-1.77 (m, 3H), 1.67-1.52 (m, 3H), 1.41-1.33 (m, 1H), 1.26-1.16 (m, 1H). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 143.03, 142.86, 139.73, 128.95, 128.50, 128.35, 128.25, 126.88, 126.41, 125.74, 125.70, 124.65, 62.95, 54.20, 48.71, 41.33, 36.09, 35.73, 29.16, 23.32, 21.08. m.p. 50.6-51.3 °C. SFC analysis: CEL-1 (1:99 MeOH: scCO\(_2\) to 3:97 MeOH: scCO\(_2\) linear gradient over 6 min with 1 min hold time, 2.50 mL/min), 5.18 min (minor), 5.46 min (major), > 99.5:0.5 er.
Specific rotation $[\alpha]_D^{23}: -39.9$ (c = 1.0, CHCl$_3$). IR (thin film): 3025, 2927, 2852, 1602, 1494, 1452, 1335, 1142, 1028, 694 cm$^{-1}$. EA Calcd. for C$_{25}$H$_{29}$NO: C, 79.95; H, 7.78. Found: C, 79.67; H, 7.79.

(1R,2R)-N-benzyl-N-(2,2-dimethoxyethyl)-2-(3-phenylpropyl)cyclobutan-1-amine (7c)
Following general procedure B, (3-(cyclobut-1-en-1-yl)propyl)benzene (86 mg, 0.50 mmol, 1.0 equiv) and N-benzyl-N-(2,2-dimethoxyethyl)O-(2,4,6-trimethylbenzoyl)hydroxylamine (268 mg, 0.75 mmol, 1.5 equiv) were used. The reaction was run at 40 °C for 46 h. After Workup C and purification by column chromatography with a gradient of hexanes (100 mL) → hexanes/Et$_2$O = [50:1 (100 mL) → 40:1 (40 mL) → 30:1 (90 mL) → 20:1 (100 mL) → 15:1 (150 mL) → 10:1 (until the product is purified by column chromatography (m, 7H), 7.22 2 3.8 Hz, 1H), 1.95 (q, J = 8.9, 8.1 Hz, 1H), 1.90-1.74 (m, 2H), 1.69-1.53 (m, 3H), 1.40-1.32 (m, 1H), 1.18 (p, J = 8.9, 8.1 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 142.87, 140.24, 128.99, 128.47, 128.34, 128.18, 126.82, 125.70, 104.06, 64.56, 56.35, 53.84, 53.78, 53.17, 41.42, 36.08, 35.61, 29.18, 23.68, 20.89. SFC analysis: OJ-H (5:95 IPA (0.15% DEA): scCO$_2$ to 15:85 IPA (0.15% DEA): scCO$_2$ linear gradient over 6 min with 1 min hold time, 2.50 mL/min), 4.36 min (major), 4.81 min (minor), > 99.5:0.5 er. Specific rotation $[\alpha]_D^{23}: -50.5$ (c = 1.0, CHCl$_3$). IR (thin film): 3025, 2930, 2828, 1495, 1452, 1368, 1191, 1123, 1073, 735 cm$^{-1}$. EA Calcd. for C$_{24}$H$_{33}$NO$_2$: C, 78.43; H, 9.05. Found: C, 78.23; H, 9.16.

(1R,2S)-N,N-dibenzyl-2-(3-(tert-butyldiphenylsilyl)oxy)propyl)cyclobutan-1-amine (7d)
Following general procedure B, tert-butyl(3-(cyclobut-1-en-1-yl)propoxy)diphenylsilane (175 mg, 0.50 mmol, 1.0 equiv) and Bn$_2$NOC(O)Mes (270 mg, 0.75 mmol, 1.5 equiv) were used. The reaction was run at 40 °C for 46 h. After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred at rt, sat. aq. NaHCO$_3$ (1 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred uncapped at rt for 30 min. The mixture was transferred with the aid of EtOAc to a 125 mL separatory funnel containing brine (30 mL) and EtOAc (30 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10-15 mL). The combined organic layers were concentrated in vacuo. The residue was redissolved in EtOAc, filtered through a short plug of Na$_2$SO$_4$, washed with additional EtOAc, and concentrated in vacuo. The crude material was immediately purified by column chromatography (~ 30 g silica gel, diameter of the column ~ 2 cm, length of the packed column ~ 18 cm) with a gradient of hexanes (100 mL) → hexanes/Et$_2$O = [60:1 (120 mL) → 50:1 (150 mL) → 40:1 (80 mL)] (the product on TLC was visualized with I$_2$), the title compound was obtained as a colorless oil (1$^\text{st}$ run: 205 mg, 75% yield, > 99.5:0.5 er, > 20:1 dr; 2$^\text{nd}$ run: 199 mg, 73% yield, > 99.5:0.5 er, > 20:1 dr). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.71-7.69 (m, 4H), 7.46-7.37 (m, 10H), 7.33-7.29 (m, 4H), 7.26-7.22 (m, 2H), 3.65-3.60 (m, 4H), 3.56 (d, J = 14.0 Hz, 2H), 2.94 (q, J = 8.1 Hz, 1H), 2.32-2.22 (m, 1H), 1.92-1.84 (m, 1H), 1.82-1.75 (m, 2H), 1.65-1.57 (m, 1H), 1.56-1.46 (m, 2H), 1.35-1.29 (m, 1H), 1.17-1.13 (m, 1H), 1.09 (s, 9H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 140.18, 135.72, 134.31, 129.62, 128.89, 128.17, 127.71,

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Following general procedure B, 2-(3-(cyclobut-1-en-1-yl)propoxy)-5-(trifluoromethyl)pyridine (129 mg, 0.50 mmol, 1.0 equiv) and \( \text{Bn}_2\text{NO(O)Mes} \) (216 mg, 0.60 mmol, 1.2 equiv) were used. The reaction was run at 40 °C for 46 h. After Workup B and purification by column chromatography with a gradient of hexanes (100 mL) → hexanes/Et₂O = [50:1 (100 mL) → 30:1 (90 mL) → 20:1 (160 mL) → 15:1 (120 mL) → 10:1 (80 mL) → 8:1 (80 mL)] (the above volumes refer to the volume of hexanes used)] (the product on TLC was visualized with \( \text{I}_2 \)), the title compound was obtained as a colorless oil (1st run: 157 mg, 69% yield, > 99.5:0.5 er, > 20:1 dr; 2nd run: 161 mg, 71% yield, > 99.5:0.5 er, > 20:1 dr). ¹H NMR (400 MHz, CDCl₃) δ 8.44 (br, 1H), 7.77 (dd, \( J = 8.7, 2.4 \text{ Hz} \), 1H), 7.38-7.36 (m, 4H), 7.25-7.21 (m, 2H), 7.31 (t, \( J = 7.4 \text{ Hz} \), 4H), 6.80 (d, \( J = 8.7 \text{ Hz} \), 1H), 4.29 (t, \( J = 6.5 \text{ Hz} \), 2H), 3.66 (d, \( J = 14.0 \text{ Hz} \), 2H), 3.55 (d, \( J = 14.0 \text{ Hz} \), 2H), 2.97 (q, \( J = 8.1 \text{ Hz} \), 1H), 2.38-2.29 (m, 1H), 1.96-1.80 (m, 3H), 1.79-1.62 (m, 3H), 1.46-1.36 (m, 1H), 1.23-1.12 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 166.15, 145.06 (q, \( J = 4.5 \text{ Hz} \)), 140.08, 135.62 (q, \( J = 3.1 \text{ Hz} \)), 128.88, 128.20, 126.81, 124.23 (q, \( J = 271.2 \text{ Hz} \)), 119.81 (q, \( J = 32.9 \text{ Hz} \)), 111.34, 66.90, 63.52, 54.94, 40.92, 32.21, 26.80, 22.92, 21.16. ¹⁹F NMR (376 MHz, CDCl₃) δ -61.47. SFC analysis: AD-H (8:92 IPA (0.15% DEA): scCO₂, 2.50 mL/min), 5.19 min (major), 5.81 min (minor), > 99.5:0.5 er. Specific rotation \( [\alpha]_D^{27 \text{°C}} \) = -31.5 (c = 1.0, CHCl₃). IR (thin film): 3028, 2938, 2856, 1613, 1500, 1315, 1291, 1122, 1077, 698 cm⁻¹. EA Calcd. for C₂₇H₂₉F₃N₂O: C, 71.35; H, 6.43. Found: C, 71.35; H, 6.37.

(1R,2R)-N,N-dibenzyl-2-(4-methoxybenzyl)cyclopropan-1-amine (12)

An oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was charged with Cu(OAc)₂ (5.4 mg, 0.030 mmol) and (R)-DTBM-SEGPHOS (38.9 mg, 0.033 mmol). The reaction tube was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into a nitrogen-filled glovebox. Anhydrous THF (0.60 mL) was added to the tube via a 1 mL syringe. The tube was capped and the mixture was stirred for 15 min at rt. Then DMMS (0.22 mL, 1.80 mmol) was added in one portion via a 1 mL syringe and the stirring was continued for another 10 min at rt to prepare a dark red CuH stock solution.

A separate oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into the glovebox. 1-(Cycloprop-1-en-1-ylmethyl)-4-methoxybenzene (53 mg, 73% purity⁸, 0.24 mmol, 1.2 equiv, freshly prepared), \( \text{Bn}_2\text{NO} \text{Piv} \) (60 mg, 0.2 mmol, 1.0 equiv), and anhydrous THF (0.20 mL) were added to the reaction tube. Then the CuH stock solution (0.27 mL) was added via a 1 mL syringe to the reaction tube in one portion. The reaction tube was capped and then removed from the glove box. The reaction mixture was allowed to stir at rt for 18 h.
After the reaction was completed, the cap of the reaction tube was removed. While the reaction mixture was stirred at rt, sat. NH$_4$F in MeOH (0.4 mL) was added slowly to quench the reaction mixture (Caution: gas evolution observed). The mixture was stirred at rt for 30 min, and then transferred to a 20 mL scintillation vial with EtOAc. The solution was concentrated in vacuo, redissolved in hexane/EtOAc=2:1, and then passed through a short plug of silica gel eluting with hexane/EtOAc=2:1. The resulting solution was collected in another 20 mL scintillation vial, and then CDCl$_3$ and 1,1,2,2-tetrachloroethane (16.8 mg, 0.1 mmol) were added. $^1$H NMR analysis of the crude reaction mixture was carried out to determine the NMR yield. Then the solution in the NMR tube was transferred back to the 20 mL vial with CH$_2$Cl$_2$. The solution was concentrated in vacuo. The residue was purified by preparative thin layer chromatography (20 x 20 cm, 1000 microns, catalog # TLG-R10011B-341 from Silicycle) eluting with hexane/EtOAc = 20:1, followed by another purification with preparative thin layer chromatography (20 x 20 cm, 250 microns, catalog # TLG-R10014B-323 from Silicycle) eluting with hexane/EtOAc = 15:1 to give the product. The title compound was obtained as a light yellow oil (1$^{st}$ run: 15.7 mg, 22% yield, 55.5:44.5 er, > 20:1 dr; 2$^{nd}$ run: 15.6 mg, 22% yield, 55.5:44.5 er, > 20:1 dr). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.36-7.26 (m, 10H), 7.04 (m, 2H), 7.04 (m, 2H), 2.22 (dd, $J$ = 13.5 Hz, 2H), 3.60 (d, $J$ = 13.5 Hz, 2H), 2.50 (dd, $J$ = 14.5, 5.9 Hz, 1H), 2.22 (dd, $J$ = 14.5, 8.1 Hz, 1H), 1.73 (dt, $J$ = 6.7, 3.4 Hz, 1H), 0.97-0.92 (m, 1H), 0.60 (dt, $J$ = 8.6, 4.2 Hz, 1H), 0.41 (q, $J$ = 5.4 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 157.88, 139.07, 133.84, 129.51, 129.37, 128.10, 126.89, 113.77, 58.51, 55.36, 43.56, 37.59, 23.51, 14.67. SFC analysis: CEL-1 (1:99 MeOH: scCO$_2$ to 2:98 MeOH: scCO$_2$ linear gradient over 16 min with 1 min hold time, 2.50 mL/min), 7.67 min (major), 10.17 min (minor), > 99.5:0.5 er. Specific rotation [α]$_D$ $^{23}$: -6.8 (c = 1.0, CHCl$_3$). IR (thin film): 3027, 2914, 2832, 1611, 1510, 1452, 1244, 1175, 1036, 747 cm$^{-1}$. HRMS Calcd. m/z for C$_{25}$H$_{28}$NO$^+$ [M+H]$^+$: 358.2165; found 358.2177.

(1R,3R)-N,N-dibenzyl-3-(dimethyl(phenyl)silyl)-2,2-dimethylcyclopropan-1-amine (15a)

Following general procedure C, (3,3-dimethylcycloprop-1-en-1-yl)dimethyl(phenyl)silane (101 mg, 0.50 mmol, 1.0 equiv) and Bn$_2$NOPiv (178 mg, 0.60 mmol, 1.2 equiv) were used. After Workup D and purification by column chromatography with a gradient of hexanes (100 mL) → hexanes/Et$_2$O = [100:1 (100 mL) → 80:1 (240 mL) → 60:1 (60 mL)] (the product on TLC was visualized with I$_2$), the title compound was obtained as a white solid (1$^{st}$ run: 139 mg, 70% yield, 98.5:1.5 er, > 20:1 dr; 2$^{nd}$ run: 139 mg, 70% yield, 98.5:1.5 er, > 20:1 dr). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.54-7.04 (m, 10H), 7.54 (m, 1H), 1.04 (s, 3H), 0.91 (s, 3H), 0.28 (s, 3H), 0.26 (s, 3H), -0.22 (d, $J$ = 6.0 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 140.21, 139.16, 133.89, 129.52, 128.82, 128.10, 127.81, 126.90, 58.88, 54.76, 25.87, 23.77, 22.87, 19.43, -0.92, -1.20. m.p. 57.5-58.3 °C. SFC analysis: AD-H (5:95 IPA: scCO$_2$ to 20:80 IPA: scCO$_2$ linear gradient over 6 min with 1 min hold time, 2.50 mL/min), 2.68 min (major), 2.88 min (minor), 98.5:1.5 er. Specific rotation [α]$_D$ $^{23}$: +6.6 (c = 1.0, CHCl$_3$). IR (thin film): 3063, 3027, 2947, 1453, 1369, 1247, 1113, 1072, 812, 728 cm$^{-1}$. EA Calcd. for C$_{27}$H$_{33}$NSi: C, 81.14; H, 8.32. Found: C, 81.18; H, 8.31.

2-((E)-(((1R,3R)-3-(dimethyl(phenyl)silyl)-2,2-dimethylcyclopropyl)imino)methyl)phenol (15b)
An oven-dried screw-cap reaction tube (Fisherbrand, 13*100 mm, part no. 1495935C) containing a magnetic stir bar was charged with Cu(OAc)$_2$ (2.2 mg, 0.012 mmol) and (R)-DTBM-SEGPHOS (15.6 mg, 0.013 mmol). The reaction tube was loosely capped (cap: Thermo Scientific C4015-66; Septum: Thermo Scientific C4015-60), and then transferred into a nitrogen-filled glovebox. Anhydrous THF (0.60 mL) was added to the tube via a 1 mL syringe. The tube was capped and the mixture was stirred for 15 min at rt. Then DMMS (0.22 mL, 1.80 mmol) was added in one portion via a 1 mL syringe and the stirring was continued for another 10 min at rt to prepare an orange CuH stock solution. A second oven-dried screw-cap reaction tube (Fisherbrand, 16*125 mm, part no. 1495935A) containing a magnetic stir bar was loosely capped (cap: Kimble Chase Open Top S/T Closure catalog no. 73804-15425; Septum: Thermo Scientific B7995-15), and then transferred into the glovebox. To the second reaction tube, (3,3-Dimethylcycloprop-1-en-1-yl)dimethyl(phenyl)silane (101 mg, 0.5 mmol, 1.0 equiv) was added, and then the CuH stock solution (0.68 mL) was added via a 1 mL syringe in one portion. The reaction mixture was stirred at rt for 0.5 min, and then 1,2-benzisoxazole (76 µL) was added slowly over 2 min via microsyringe while the reaction mixture was stirred at rt. The reaction tube was capped and then removed from the glove box. The reaction mixture was allowed to stir at rt for 18 h. After Workup D and purification by column chromatography (silica gel was pretreated with hexanes containing 1% NEt$_3$) with a gradient of hexanes (contain 0.1% NEt$_3$) (100 mL) → hexanes (contain 0.1% NEt$_3$)/Et$_2$O = [150:1 (75 mL) → 100:1 (100 mL) → 70:1 (70 mL) → 60:1 (60 mL) → 50:1 (100 mL)], the title compound was obtained as a yellow oil (1$^{st}$ run: 103 mg, 63% yield, 99.5:0.5 er, > 20:1 dr; 2$^{nd}$ run: 100 mg, 62% yield, 99.5:0.5 er, > 20:1 dr). $^1$H NMR (400 MHz, CDCl$_3$) δ 13.09 (s, 1H), 8.49 (s, 1H), 7.58-7.55 (m, 2H), 7.42-7.39 (m, 3H), 7.33-7.26 (m, 2H), 6.98 (d, J = 8.2 Hz, 1H), 6.92 (td, J = 7.5, 1.1 Hz, 1H), 2.84 (d, J = 5.3 Hz, 1H), 1.39 (s, 3H), 1.14 (s, 3H), 0.46 (d, J = 5.3 Hz, 1H), 0.40 (s, 3H), 0.39 (s, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 161.97, 160.57, 139.34, 133.86, 130.62, 129.13, 127.99, 119.48, 118.80, 116.88, 57.25, 26.74, 24.36, 23.74, 23.62, -1.10, -1.18. SFC analysis: OJ-H (2:98 MeOH (0.1% DEA): scCO$_2$ to 7:93 MeOH (0.1% DEA): scCO$_2$: linear gradient over 10 min with 1 min hold time, 2.50 mL/min), 4.89 min (major), 7.50 min (minor), 99.5:0.5 er. Specific rotation [a]$_D^{23}$ -107.2 (c = 1.0, CHCl$_3$). IR (thin film): 2948, 1620, 1495, 1414, 1277, 1200, 1113, 955, 905, 698 cm$^{-1}$. EA Calcd. for C$_{20}$H$_{25}$NOSi: C, 74.25; H, 7.79. Found: C, 74.42; H, 7.98.

2-((E)-(((2R,3R)-2-(dimethyl(phenyl)silyl)-1',3'-dihydrospiro[cyclopropane-1,2'-inden]-3-yl)imino)methyl)phenol (15c)

Following general procedure D, (1',3'-dihydrospiro[cyclopropane-1,2'-inden]-2-en-2-yl)dimethyl(phenyl)silane (138 mg, 0.50 mmol, 1.0 equiv) was used, and the 1,2-benzisoxazole solution was added slowly via syringe pump at a rate of 0.16 mL/h. After Workup D and purification by column chromatography (silica gel was pretreated with hexanes containing 1% NEt$_3$) with a gradient of hexanes (contain 0.1% NEt$_3$) (100 mL) → hexanes (contain 0.1% NEt$_3$)/Et$_2$O = [80:1 (80 mL) → 60:1 (60 mL) → 40:1 (80 mL) → 30:1 (60 mL) → 20:1 (40 mL) → 15:1 (60 mL) → 10:1 (40 mL)], the title compound was obtained as a yellow solid (1$^{st}$ run: 145 mg, 73% yield, 99.5:0.5 er, > 20:1 dr; 2$^{nd}$ run: 149 mg, 75% yield, 99.5:0.5 er, > 20:1 dr). $^1$H NMR (400 MHz, CDCl$_3$) δ 12.96 (s, 1H), 8.48 (s, 1H), 7.60-7.58 (m, 2H), 7.40-7.36 (m, 3H), 7.34-7.30 (m, 1H), 7.26-7.24 (m, 2H), 7.20-7.16 (m, 3H), 7.00 (d, J = 8.2 Hz, 1H), 6.91 (td, J = 7.5, 1.0 Hz, 1H), 3.40 (d, J = 16.7 Hz, 1H), 3.29-3.21 (m, 2H), 3.05 (d, J = 5.5 Hz,
Following general procedure D, 1-(dimethyl(phenyl)silyl)-6-tosyl-6-azaspiro[2.5]oct-1-ene (199 mg, 0.50 mmol, 1.0 equiv) was used, and the 1,2-benzisoxazole solution was added slowly via syringe pump at a rate of 0.13 mL/h. After Workup D and purification by column chromatography with a gradient of hexanes (contain 0.1% NEt₃)/CH₂Cl₂ = 50:1 (100 mL) → hexanes (contain 0.1% NEt₃)/EtOAc = [30:1 (60 mL) → 25:1 (50 mL) → 20:1 (40 mL) → 15:1 (60 mL) → 12:1 (60 mL) → 10:1 (80 mL) → 8:1 (80 mL) → 7:1 (140 mL) → 6:1 (60 mL) → 5:1 (100 mL) → 4:1 (40 mL) (the above volumes refer to the volume of hexanes used)], the title compound was obtained as a yellow solid (1st run: 163 mg, 63% yield, 98:2 er, > 20:1 dr; 2nd run: 147 mg, 57% yield, 98:2 er, > 20:1 dr). ¹H NMR (400 MHz, CDCl₃) δ 12.62 (s, 1H), 8.42 (s, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.48-7.46 (m, 2H), 7.40-7.28 (m, 6H), 7.23 (dd, J = 7.6, 1.6 Hz, 1H), 6.96 (d, J = 8.1 Hz, 1H), 6.91 (td, J = 7.5, 1.0 Hz, 1H), 3.35 (dt, J = 9.8, 4.1 Hz, 1H), 3.23 (dt, J = 9.7, 4.0 Hz, 1H), 2.82 (d, J = 5.4 Hz, 1H), 2.71-2.63 (m, 2H), 2.43 (s, 3H), 2.04 (dd, J = 13.5, 9.5, 3.9 Hz, 1H), 1.83 (dt, J = 13.8, 3.7 Hz, 1H), 1.76 (ddd, J = 13.4, 9.5, 3.9 Hz, 1H), 1.33 (dt, J = 13.4, 3.7 Hz, 1H), 0.43 (d, J = 5.4 Hz, 1H), 0.33 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 162.95, 160.38, 143.42, 138.28, 133.70, 133.61, 132.05, 130.82, 129.77, 129.42, 128.12, 127.68, 119.16, 119.00, 116.92, 55.55, 46.15, 45.80, 32.66, 32.62, 31.02, 23.21, 21.65, -1.24, -1.36. m.p. 60.1-62.8 °C. SFC analysis: AD-H (20:80 MeOH (0.1% DEA): scCO₂, 250 mL/min), 4.60 min (major), 5.80 min (minor), 98:2 er. Specific rotation [α]D²³: +13.8 (c = 1.0, CHCl₃). IR (thin film): 2953, 2844, 1619, 1427, 1334, 1276, 1163, 1090, 908, 722 cm⁻¹. EA Calcd. for C₂₉H₂₇NO₃Si: C, 76.56; H, 6.61; Found: C, 76.54; H, 6.65.

tert-butyl (2S,3R)-3-(dibenzylamino)-2-(dimethyl(phenyl)silyl)azetidine-1-carboxylate (7f)

Following general procedure B, tert-butyl 4-(dimethyl(phenyl)silyl)azete-1(2H)-carboxylate (145 mg, 0.50 mmol, 1.0 equiv) and Bn₂NOC(O)Mes (270 mg, 0.75 mmol, 1.5 equiv) were used. The reaction was run at 40 °C for 46 h. After Workup D and purification by column chromatography with a gradient of hexanes (100 mL) → hexanes/acetone = [80:1 (80 mL) → 70:1 (70 mL) → 50:1 (100 mL) → 30:1 (180 mL)] (the product on TLC was visualized with I₂), the title compound was obtained as a colorless oil (1st run: 223 mg, 92% yield, > 99.5:0.5 er, > 20:1 dr; 2nd run: 223 mg, 92% yield, > 99.5:0.5 er, > 20:1 dr). ¹H NMR (400 MHz, CDCl₃) δ 7.43-7.39 (m, 3H), 7.36-7.20 (m, 12H), 4.16 (d, J = 5.7 Hz, 1H), 3.94-3.92 (m, 1H), 3.63-3.45 (m, 6H), 1.43 (s, 9H), 0.40 (s, 3H), 0.36 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 156.64, 138.99, 136.27, 134.30, 129.42, 128.76, 128.33, 127.90, 127.09, 79.38, 57.41, 53.94, 52.87, 52.61, 28.56, -4.15, -4.68. SFC analysis: OJ-H (5:95 IPA:
scCO$_2$ to 20:80 IPA: scCO$_2$ linear gradient over 6 min with 1 min hold time, 2.50 mL/min), 2.87 min (major), 3.17 min (minor), > 99.5:0.5 er. **Specific rotation** $\alpha_{D}^{23}$: +11.1 (c = 1.0, CHCl$_3$). **IR** (thin film): 2973, 1691, 1408, 1364, 1248, 1154, 1111, 1028, 832, 696 cm$^{-1}$. **EA** Calcd. for C$_{30}$H$_{38}$N$_2$O$_2$Si: C, 74.03; H, 7.87. Found: C, 73.75; H, 8.04.
4. Preparation of Alkene Substrates and Amination Reagents

4.1 Synthesis of 1-Arylcyclobutenes

All the 1-arylcyclobutenes used in this paper are listed below. 2a-c, 2f-g are known compounds and were prepared by following previously reported procedures.

\[
\begin{align*}
2a & \quad 2b & \quad 2c & \quad 2d \\
2e & \quad 2f & \quad 2g
\end{align*}
\]

Synthesis of 2d, 2e.

General Procedure E

A 250 mL round bottom flask containing a magnetic stir bar was charged with the corresponding aryl bromide (21.0 mmol, 1.05 equiv) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (63 mL) was added, and then the mixture was cooled to -78 °C. \(\text{nBuLi} \) (2.5 M in hexane, 1.1 equiv, 8.8 mL) was added dropwise at -78 °C. The reaction mixture was stirred at -78 °C for 15 min, and then cyclobutanone (20.0 mmol, 1.0 equiv, 1.40 g) was added dropwise at -78 °C. The mixture was stirred at -78 °C for 30 min, and was allowed to warm to rt and stirred for an additional 30 min. Then the reaction mixture was cooled to -78 °C, and Ac\(_2\)O (40.0 mmol, 2.0 equiv, 4.08 g) was added dropwise. The reaction mixture was allowed to warm to rt and stirred for 2 h. The septum was removed, and the reaction mixture was concentrated in vacuo. Et\(_2\)O and aq. NaHCO\(_3\) were added. The layers were separated, and the organic layer was extracted with Et\(_2\)O. The combined organic layers were washed with brine, dried over Na\(_2\)SO\(_4\), filtered, concentrated in vacuo, and then purified by column chromatography on silica gel to afford the corresponding 1-arylcyclobutyl acetate.

A 50 mL round bottom flask containing a magnetic stir bar was charged with the corresponding 1-arylcyclobutyl acetate (1.0 equiv) and LiBr (10.0 equiv), and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous DMF (13 mL) was added, and then the reaction mixture was stirred at 100 °C for 1 h or overnight (as indicated for each substrate). The mixture was allowed to cool to rt, and was immediately quenched with water. Et\(_2\)O and aq. NaHCO\(_3\) were added. The layers were separated, and the organic layer was extract with Et\(_2\)O. The combined organic layers were washed with brine, dried over Na\(_2\)SO\(_4\), filtered, concentrated in vacuo, and then purified by column chromatography on silica gel to afford the corresponding 1-arylcyclobutene (Note: 2d and 2e are very air-sensitive, and therefore need to be immediately stored under nitrogen in the glovebox freezer at -30 °C once prepared).
1-(cyclobut-1-en-1-yl)-2-fluorobenzene (2d)

Following general procedure E, 1-(2-fluorophenyl)cyclobutyl acetate (6.60 mmol, 1.46 g) was used. The title compound was obtained as a colorless oil (0.47 g, 36% yield over two steps) after purification by column chromatography on silica gel (eluting with pentane). \( ^{1}\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 7.28-7.19 (m, 2H), 7.14-7.03 (m, 2H), 6.42-6.40 (m, 1H), 2.91-2.89 (m, 2H), 2.64-2.63 (m, 2H). \( ^{13}\text{C} \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta \) 161.25 (d, \( J = 251.3 \) Hz), 140.96, 133.13 (d, \( J = 7.3 \) Hz), 128.66 (d, \( J = 8.4 \) Hz), 127.01 (d, \( J = 4.4 \) Hz), 123.97 (d, \( J = 3.5 \) Hz), 123.04 (d, \( J = 14.3 \) Hz), 115.61 (d, \( J = 21.0 \) Hz), 30.00, 27.96. \( ^{19}\text{F} \text{NMR} \) (376 MHz, CDCl\(_3\)) \( \delta \) -114.94. IR (thin film): 3070, 2918, 2834, 1490, 1446, 1237, 1214, 1176, 1031, 747 cm\(^{-1}\). HRMS Calcd. m/z for C\(_{10}\)H\(_{10}\)F\(^{+}\) [M+H]\(^{+}\): 149.0761; found 149.0757.

5-(cyclobut-1-en-1-yl)-2-methoxypyridine (2e)

Following general procedure E, 1-(6-methoxypyridin-3-yl)cyclobutyl acetate (6.60 mmol, 1.46 g) was used. The title compound was obtained as a white solid (0.26 g, 18% yield over two steps) after purification by column chromatography on silica gel (eluting with pentane/Et\(_2\)O = 30:1). \( ^{1}\text{H} \text{NMR} \) (400 MHz, CDCl\(_3\)) \( \delta \) 8.11 (d, \( J = 2.3 \) Hz, 1H), 7.57 (dd, \( J = 8.6, 2.4 \) Hz, 1H), 6.68 (dd, \( J = 8.6, 0.7 \) Hz, 1H), 6.20 (t, \( J = 1.2 \) Hz, 1H), 3.93 (s, 3H), 2.80-2.78 (m, 2H), 2.56-2.54 (m, 2H). \( ^{13}\text{C} \text{NMR} \) (101 MHz, CDCl\(_3\)) \( \delta \) 163.50, 143.39, 143.12, 134.78, 126.64, 124.65, 110.69, 77.48, 77.16, 76.84, 53.60, 28.90, 26.91. m.p. 46.7-48.0 °C. IR (thin film): 2948, 2840, 1723, 1681, 1601, 1492, 1372, 1288, 1020, 832 cm\(^{-1}\). HRMS Calcd. m/z for C\(_{10}\)H\(_{12}\)NO\(^+\) [M+H]\(^{+}\): 162.0913; found 162.0905.

4.2 Synthesis of 1-Arylcyclopropene

(3,3-dimethylcycloprop-1-en-1-yl)benzene (8)

A 25 mL round bottom flask containing a magnetic stir bar was charged with (1-bromo-2-methylprop-1-en-1-yl)benzene\(^{7}\) (5.05 mmol, 1.0 equiv, 1.07 g), BnEt\(_3\)NCl (0.505 mmol, 0.1 equiv, 115 mg), and bromoform (40.4 mmol, 8.0 equiv, 3.5 mL). While the reaction mixture was stirred vigorously at rt, NaOH (40.4 mmol, 8.0 equiv, 1.62 g) in water (1.6 mL) was added dropwise. Then the flask was capped with a septum and attached to a balloon filled with air. The reaction mixture was stirred vigorously at 60 °C for 36 h. The reaction mixture was allowed to cool to rt, and diluted with CH\(_2\)Cl\(_2\) (100 mL) and water (50 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (2 x 70 mL). The combined organic layers were filtered through a short plug of silica gel and washed with Et\(_2\)O. The resulting solution was concentrated in vacuo, and then purified by column chromatography on silica gel eluting with hexanes to give (1,2,2-tribromo-3,3-dimethylcyclopropyl)benzene. A 25 mL round bottom flask containing a magnetic stir bar was charged with (1,2,2-tribromo-3,3-dimethylcyclopropyl)benzene (2.0 mmol, 1.0 equiv, 766 mg) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous Et\(_2\)O (4 mL) was added, and then the mixture was cooled to -78 °C. \(^{6}\)BuLi (2.5 M in hexane, 2.1 equiv, 1.68 mL) was added dropwise at -78 °C. The reaction mixture was allowed to slowly warmed to rt over 2 h while being stirred. Then the reaction mixture was cooled to 0 °C, and water (0.2 mL) was added dropwise. The reaction mixture was allowed to warm to rt and was stirred at rt for 10 min. Then
saturated aqueous NH₄Cl (2 mL) was added dropwise, and the reaction mixture was stirred at rt for 5 min. The septum on the flask was removed. The reaction mixture was diluted with pentane (50 mL) and water (20 mL). The layers were separated, and the aqueous layer was extracted with pentane (50 mL). The combined organic layers were dried over Na₂SO₄, filtered, concentrated in vacuo and purified by column chromatography on silica gel (eluting with pentane) to give the title compound as a colorless oil (0.25 g, 53% yield over two steps) (Note: 8 was stored under nitrogen in the glovebox freezer at -30 °C once prepared). ¹H NMR (400 MHz, CDCl₃) δ 7.52-7.49 (m, 2H), 7.42-7.39 (m, 2H), 7.34-7.30 (m, 2H), 1.35 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 132.23, 129.58, 128.87, 128.73, 128.52, 115.19, 115.02, 21.41. IR (thin film): 2924, 2861, 1765, 1598, 1493, 1444, 1371, 1308, 1024, 700 cm⁻¹. HRMS Calcd. m/z for C₁₁H₁₃⁺ [M+H]⁺: 145.1012; found 145.1022.

4.2 Synthesis of 1-Alkylcyclobutanes³⁹

(3-(cyclobut-1-en-1-yl)propyl)benzene (5a)

A 100 mL round bottom flask containing a magnetic stir bar was transferred into a nitrogen-filled glovebox. Cp₂ZrCl₂ (1.2 mmol, 0.1 equiv, 351 mg) was added to the flask. The flask was capped with a septum, removed from the glovebox, and then attached to a balloon filled with argon. Anhydrous THF (24 mL) was added. While the reaction mixture was stirred at rt, EtMgBr (1 M in THF, 36 mmol, 3.0 equiv, 36 mL) was added dropwise. Then (5-chloropent-4-yn-1-yl)benzene¹⁰ (12 mmol, 1.0 equiv, 2.14 g) was added dropwise at rt. The reaction mixture was stirred at rt for 48 h. The reaction mixture was cooled to 0 °C in an ice bath, and water was added slowly to quench the reaction mixture. The mixture was diluted with water (50 mL) and pentane (50 mL). The layers were separated and the aqueous layer was extracted with pentane (50 mL). The combined organic layers were washed with water (50 mL), dried over Na₂SO₄, filtered, concentrated in vacuo, and purified by column chromatography on silica gel eluting with pentane (Note: (5-chloropent-4-yn-1-yl)benzene was not fully consumed in the reaction, and it could poison the CuH catalyst in the subsequent hydroamination reactions. Therefore, the last few product-containing fractions from the column chromatography were analyzed by GC to determine whether they contained (5-chloropent-4-yn-1-yl)benzene, and only the clean fractions were collected.) to afford the title compound as a colorless oil (0.58 g, 28% yield) (Note: 5a was stored under nitrogen in the glovebox freezer at -30 °C once prepared). ¹H NMR (400 MHz, CDCl₃) δ 7.32-7.28 (m, 2H), 7.21-7.18 (m, 3H), 5.71 (br, 1H), 2.67-2.63 (m, 2H), 2.44-2.42 (m, 2H), 2.37-2.35 (m, 2H), 2.06-2.03 (m, 2H), 1.81-1.74 (m, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 150.47, 142.65, 128.61, 128.41, 127.15, 125.82, 35.76, 31.31, 30.80, 28.72, 26.71. IR (thin film): 3028, 2922, 2842, 1630, 1604, 1496, 1453, 1171, 1030, 698 cm⁻¹. HRMS Calcd. m/z for C₁₃H₁₇⁺ [M+H]⁺: 173.1325; found 173.1315.

t-butyl(3-(cyclobut-1-en-1-yl)propoxy)diphenylsilane (5b)

A 100 mL round bottom flask containing a magnetic stir bar was charged with NCS (22.0 mmol, 2.0 equiv, 2.95 g), K₂CO₃ (5.5 mmol, 0.5 equiv, 0.76 g), and 1
Ag₂CO₃ (0.11 mmol, 0.1 equiv, 0.30 g) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous PrOH (22 mL) was added. Then tert-butyl(pent-4-yn-1-yl)oxy)diphenylsilane¹¹ (11.0 mmol, 1.0 equiv, 3.55 g) was added dropwise at rt. The reaction mixture was stirred at 50 °C for 48 h. Then the reaction mixture was cooled to 0 °C, and brine was added. The resulting mixture was extracted with Et₂O, and the combined organic layers were washed with water (100 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel to give tert-butyl((5-chloropent-4-yn-1-yl)oxy)diphenylsilane.

A 100 mL round bottom flask containing a magnetic stir bar was transferred into a nitrogen-filled glovebox. Cp₂ZrCl₂ (1.2 mmol, 0.1 equiv, 351 mg) was added to the flask. The flask was capped with a septum, removed from the glovebox, and then attached to a balloon filled with argon. Anhydrous THF (24 mL) was added. While the reaction mixture was stirred at rt, EtMgBr (1 M in THF, 36 mmol, 3.0 equiv, 36 mL) was added dropwise. Then tert-butyl((5-chloropent-4-yn-1-yl)oxy)diphenylsilane (12 mmol, 1.0 equiv, 4.28 g) was added dropwise at rt. The reaction mixture was stirred at rt for 72 h. The reaction mixture was cooled to 0 °C in an ice bath, and water was added slowly to quench the reaction mixture. The mixture was diluted with water (50 mL) and Et₂O (50 mL). The layers were separated and the aqueous layer was extracted with Et₂O (50 mL). The combined organic layers were washed with water (50 mL), dried over Na₂SO₄, filtered, and concentrated in vacuo, and purified by column chromatography on silica gel eluting with 0-2% EtOAc in hexanes to give a mixture of the title compound and the 1-chloroalkyne starting material. The isolated material contains 24% (w/w) tert-butyl((5-chloropent-4-yn-1-yl)oxy)diphenylsilane impurity, which was removed by carrying out a further transformation.

A 25 mL round bottom flask containing a magnetic stir bar was charged with the material isolated from the previous step (1.69 g material, contains 1.14 mmol of tert-butyl((5-chloropent-4-yn-1-yl)oxy)diphenylsilane, 1.0 equiv) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (5.7 mL) was added, and then the mixture was cooled to -78 °C. BuLi (2.5 M in hexane, 2.28 mmol, 2.0 equiv, 0.91 mL) was added dropwise at -78 °C. The reaction mixture was stirred at -78 °C for 1 h, and then anhydrous PhCHO (4.56 mmol, 4.0 equiv, 484 mg) was added dropwise at -78 °C. The mixture was stirred at -78 °C for 30 min, and was allowed to warm to rt and stirred for 30 min. Water was slowly added to quench the reaction mixture. The resulting mixture was extracted with hexane (2x). The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel eluting with 0-2% EtOAc in hexanes to give the title compound as a colorless oil (1.21 g, 13% overall yield) (Note: 8b was stored under nitrogen in the glovebox freezer at -30 °C once prepared). ¹H NMR (400 MHz, CDCl₃) δ 7.69-7.66 (m, 4H), 7.45-7.36 (m, 6H), 5.63 (tt, J = 1.7, 0.9 Hz, 1H), 3.68 (t, J = 6.4 Hz, 2H), 2.39-2.37 (m, 2H), 2.32-2.29 (m, 2H), 2.11-2.07 (m, 2H), 1.74-1.67 (m, 2H), 1.05 (s, 9H). ¹³C NMR (101 MHz, CDCl₃) δ 150.39, 135.74, 134.25, 129.65, 127.73, 126.99, 63.70, 31.31, 29.90, 27.55, 27.03, 26.61, 19.40. IR (thin film): 3071, 2929, 2856, 1472, 1427, 1105, 953, 822, 737, 699 cm⁻¹. EA Calcd. for C₂₁H₃₀OSi: C, 78.80; H, 8.63. Found: C, 78.91; H, 8.63.
2-(3-(cyclobut-1-en-1-yl)propoxy)-5-(trifluoromethyl)pyridine (5c)

A 25 mL round bottom flask containing a magnetic stir bar was charged with 5b (2.4 mmol, 1.0 equiv, 843 mg) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (4.8 mL) was added, and then the mixture was cooled to 0 °C. TBAF (1 M in THF, 2.0 equiv, 4.8 mL) was added dropwise at 0 °C. The reaction mixture was allowed to warm to rt and was stirred at rt for 3 h. Then the reaction mixture was diluted with saturated aqueous NH₄Cl and Et₂O. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layer was dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with 0-40% EtOAc in pentane) to afford 3-(cyclobut-1-en-1-yl)propan-1-ol. A 25 mL round bottom flask containing a magnetic stir bar was charged with 3-(cyclobut-1-en-1-yl)propan-1-ol (2.24 mmol, 1.12 equiv, 251 mg) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (4.5 mL) was added, and then the mixture was cooled to 0 °C. NaH (2.7 mmol, 1.35 equiv, 65 mg) was added in several portions at 0 °C. The mixture was allowed to warm to rt and was stirred at rt for 15 min. Then 2-chloro-5-(trifluoromethyl)pyridine (2.0 mmol, 1.0 equiv, 364 mg) was added and the reaction mixture was stirred at rt overnight. The reaction mixture was diluted with water and EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with 0-3% EtOAc in hexanes) to give the title compound as a colorless oil (0.50 g, 93% yield over two steps) (Note: 5c was stored under nitrogen in the glovebox freezer at -30 °C once prepared). ¹H NMR (400 MHz, CDCl₃) δ 8.44-8.41 (m, 1H), 7.75 (dd, J = 8.7, 2.5 Hz, 1H), 6.80 (d, J = 8.7 Hz, 1H), 5.72 (br, 1H), 4.37 (t, J = 6.6 Hz, 2H), 2.44 (ddd, J = 4.2, 2.7, 1.1 Hz, 2H), 2.36-2.33 (m, 2H), 2.16 (dt, J = 7.7, 3.7 Hz, 2H), 1.93 (tt, J = 7.2, 6.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 166.13, 149.53, 145.07 (q, J = 33.0 Hz), 111.37, 66.50, 31.29, 27.65, 26.68, 26.25. ¹⁹F NMR (376 MHz, CDCl₃) δ -61.52. IR (thin film): 2924, 2844, 1614, 1501, 1315, 1160, 1123, 1078, 1011, 834 cm⁻¹. EA Calcd. for C₁₁H₁₃F₃NO: C, 60.70; H, 5.49. Found: C, 60.72; H, 5.66.

4.4 Synthesis of 1-Alkylcyclopropene¹²

1-(cycloprop-1-en-1-ylmethyl)-4-methoxybenzene (11)

A 250 mL round bottom flask containing a magnetic stir bar was capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (4.5 mL) was added, and then the mixture was cooled to 0 °C. NaH (2.7 mmol, 1.35 equiv, 65 mg) was added in several portions at 0 °C. The mixture was allowed to warm to rt and was stirred at rt for 15 min. Then 2-chloro-5-(trifluoromethyl)pyridine (2.0 mmol, 1.0 equiv, 364 mg) was added and the reaction mixture was stirred at rt overnight. The reaction mixture was diluted with water and EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na₂SO₄, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with 0-3% EtOAc in hexanes) to give the title compound as a colorless oil (0.50 g, 93% yield over two steps) (Note: 5c was stored under nitrogen in the glovebox freezer at -30 °C once prepared). ¹H NMR (400 MHz, CDCl₃) δ 8.44-8.41 (m, 1H), 7.75 (dd, J = 8.7, 2.5 Hz, 1H), 6.80 (d, J = 8.7 Hz, 1H), 5.72 (br, 1H), 4.37 (t, J = 6.6 Hz, 2H), 2.44 (ddd, J = 4.2, 2.7, 1.1 Hz, 2H), 2.36-2.33 (m, 2H), 2.16 (dt, J = 7.7, 3.7 Hz, 2H), 1.93 (tt, J = 7.2, 6.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 166.13, 149.53, 145.07 (q, J = 33.0 Hz), 111.37, 66.50, 31.29, 27.65, 26.68, 26.25. ¹⁹F NMR (376 MHz, CDCl₃) δ -61.52. IR (thin film): 2924, 2844, 1614, 1501, 1315, 1160, 1123, 1078, 1011, 834 cm⁻¹. EA Calcd. for C₁₁H₁₃F₃NO: C, 60.70; H, 5.49. Found: C, 60.72; H, 5.66.
argon. Anhydrous Et₂O (53 mL) and Ti(O\text{^4}Pr)₃Cl (7.50 mmol, 1.5 equiv, 1.95 g) were added, and then the mixture was cooled to -60 °C. PrMgCl (2.0 M in Et₂O, 2.9 equiv, 7.25 mL) was added dropwise at -60 °C. The reaction mixture was stirred at -60 °C for 10 min, and then a mixture of methyl 2-(4-methoxyphenyl)acetate (5.0 mmol, 1.0 equiv, 0.90 g) and trimethyl(vinyl)silane (7.5 mmol, 1.5 equiv, 0.75 g) in anhydrous Et₂O (0.27 mL) was added dropwise. The reaction mixture was allowed to warm to -25 °C over 30 min, stirred at -25 ~ -20 °C for 1 h, and then warmed to 0 °C and stirred for 2 h. Water (2.5 mL) in THF (10 mL) was added slowly, and then the reaction mixture was allowed to warm to rt and stirred for 30 min. The reaction mixture was passed through a short plug of Celite, washed with Et₂O, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (pretreated with 1% Et₃N in hexanes) and eluted with a gradient of hexanes/Et₂O = 8:1~3:1 to afford 1-(4-methoxybenzyl)-2-(trimethylsilyl)cyclopropan-1-ol.

A 25 mL round bottom flask containing a magnetic stir bar was charged with 1-(4-methoxybenzyl)-2-(trimethylsilyl)cyclopropan-1-ol (1.8 mmol, 1.0 equiv, 0.45 g), and then CH₂Cl₂ (10 mL) and Et₂N (7.2 mmol, 4.0 equiv, 0.73 g) were added. The mixture was cooled to 0 °C, and MsCl (3.6 mmol, 2.0 equiv, 0.41 g) was added dropwise. The reaction mixture was stirred at rt for 2 h. Then the reaction mixture was allowed to warm to rt, and saturated aqueous NaHCO₃ (10 mL) and Et₂O (10 mL) were added. The layers were separated, and the aqueous layer was extracted with Et₂O (2 x 30 mL). The combined organic layers were dried over Na₂SO₄, filtered, concentrated in vacuo, and used in the next step without further purification.

A 100 mL round bottom flask containing a magnetic stir bar was charged with the crude material from the last step. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (10 mL) was added, and then TBAF (1 M in THF, 9.9 mL) was added dropwise at rt. The reaction mixture was stirred at rt for 2 h, and then saturated aqueous NH₄Cl (10 mL) and Et₂O (30 mL) were added. The layers were separated, and the aqueous layer was extracted with Et₂O (2 x 20 mL). The combined organic layers were dried over Na₂SO₄, filtered, concentrated in vacuo, and immediately purified by column chromatography on silica gel (eluting with pentane and then pentane/Et₂O = 60:1) to give the title compound as a colorless oil (0.23 g, 73% purity, 21% yield over 3 steps) (Note: 11 was stored under nitrogen in the glovebox freezer at -30 °C once prepared). **¹H NMR** (500 MHz, CDCl₃) δ 7.20–7.17 (m, 2H), 6.88–6.86 (m, 2H), 6.57 (m, 1H), 3.81 (s, 3H), 3.79 (s, 2H), 1.01 (d, J = 1.8 Hz, 2H). **IR** (thin film): 2955, 2876, 2834, 1610, 1511, 1301, 1244, 1174, 1035, 840 cm⁻¹. **HRMS** Calcd. m/z for C₁₃H₁₅O⁺ [M+H]⁺: 161.0961; found 161.0972.

### 4.5 Synthesis of 1-Silyl Substituted Three- and Four-Membered Cycloalkenes

![Image of 1-Silyl Substituted Three- and Four-Membered Cycloalkenes](image)

All the 1-silyl substituted three- and four-membered cycloalkenes used in this paper are listed above. 13a is a known compound and was prepared by following previously reported procedures.
A 50 mL round bottom flask containing a magnetic stir bar was charged with 2-methylene-2,3-dihydro-1H-indene (19.0 mmol, 1.0 equiv, 2.51 g), BnEt₂NCl (1.9 mmol, 0.1 equiv, 439 mg), and bromoform (76.0 mmol, 4.0 equiv, 6.7 mL). While the reaction mixture was stirred vigorously at rt, NaOH (76.0 mmol, 4.0 equiv, 3.1 g) in water (3.1 mL) was added dropwise. Then the flask was capped with a septum and attached to a balloon filled with air. The reaction mixture was stirred vigorously at 60 °C for 24 h. The reaction mixture was allowed to cool to rt, and diluted with CH₂Cl₂ (100 mL) and water (50 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (2 x 70 mL). The combined organic layers were dried over Na₂SO₄, filtered, concentrated in vacuo, and then purified by column chromatography on silica gel eluting with hexanes/CH₂Cl₂ = 100:1 to give 2,2-dibromo-1',3'-dihydrospiro[cyclopropane-1,2'-inden]-1'-ene.

A 100 mL round bottom flask containing a magnetic stir bar was charged with 2,2-dibromo-1',3'-dihydrospiro[cyclopropane-1,2'-inden] (13.5 mmol, 1.0 equiv) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous THF (27 mL) and Ti(OPr)₄ (0.13 mmol, 0.1 equiv, 0.40 mL) were added. While the reaction mixture was stirred at rt, EtMgBr (3 M in Et₂O, 1.3 equiv, 5.8 mL) was added over 1 h via syringe pump. The reaction mixture was stirred at rt for 4 h. Then the reaction mixture was cooled to 0 °C, and 10% aq. H₂SO₄ (10 mL) was added dropwise to quench the reaction mixture. The mixture was diluted with H₂O (100 mL) and Et₂O (100 mL). The layers were separated and the aqueous layer was extracted with E₂O (100 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, filtered, and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with 0-2% Et₂O in pentane) to give 2-bromo-1',3'-dihydrospiro[cyclopropane-1,2'-inden].

A 100 mL round bottom flask containing a magnetic stir bar was charged with 2-bromo-1',3'-dihydrospiro[cyclopropane-1,2'-inden] (6.0 mmol, 1.0 equiv, 1.34 g) and then capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Anhydrous DMSO (13 mL) was added. While the reaction mixture was stirred at rt, KO'Bu (9.0 mmol, 1.5 equiv, 1.01 g) in anhydrous DMSO (3.3 mL) was added dropwise. The reaction mixture was stirred at rt overnight. Then the reaction mixture was cooled to 0 °C, and water (100 mL) was slowly added to quench the reaction mixture. Et₂O (75 mL) was added. The layers were separated and the aqueous layer was extract with Et₂O (100 mL). The combine organic layers were washed with water (3 x 75 mL), then washed with brine, dried over Na₂SO₄, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with pentane) to give 1',3'-dihydrospiro[cyclopropane-1,2'-inden]-2-ene.

A 10 mL round bottom flask with a magnetic stir bar was charged with 1',3'-dihydrospiro[cyclopropane-1,2'-inden]-2-ene (1.35 mmol, 1.0 equiv, 192 mg) and anhydrous Et₂O (1.4 mL) under nitrogen. The mixture was cooled to -78 °C, and "BuLi (2.5 M in hexane, 1.05 equiv, 0.57 mL) was added dropwise. The reaction mixture was stirred at -78 °C for 1 h, and
then at -10 °C for 1 h. The resulting solution was added over 20 min to another 25 mL round bottom flask containing PhMe2SiCl (1.48 mmol, 1.1 equiv, 263 mg) and anhydrous Et2O (2.8 mL) at -40 °C under nitrogen. The reaction mixture was stirred at -40 °C for 1 h and at rt for 2 h. The reaction mixture was quenched with saturated aqueous NH4Cl (5 mL). Then water (20 mL) and Et2O (60 mL) were added. The layers were separated and the aqueous layer was extracted with Et2O (60 mL). The combined organic layers were dried over Na2SO4, and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluted with 0-2% CH2Cl2 in hexanes) to afford the title compound as a colorless oil (0.29 g, 20% yield over 4 steps) (Note: 13b was stored under nitrogen in the glovebox freezer at -30 °C once prepared).

**1H NMR** (400 MHz, CDCl3) δ 7.96-7.95 (m, 1H), 7.56-7.53 (m, 2H), 7.41-7.32 (m, 3H), 7.16 (s, 4H), 2.87 (d, J = 17.0 Hz, 2H), 2.71 (d, J = 17.2 Hz, 2H), 0.43 (s, 6H). **13C NMR** (101 MHz, CDCl3) δ 143.63, 137.40, 133.81, 131.79, 129.44, 127.99, 126.85, 125.97, 124.27, 44.30, 26.60, -1.94. **IR (thin film)**: 3068, 2957, 2880, 2825, 1676, 1482, 1427, 1248, 1113, 733 cm⁻¹. **EA Calcd.** for C19H20Si: C, 82.55; H, 7.29. Found: C, 82.74; H, 7.45.

1-(dimethyl(phenyl)silyl)-6-tosyl-6-azaspiro[2.5]oct-1-ene (13c)

A 25 mL round bottom flask with a magnetic stir bar was charged with 6-tosyl-6-azaspiro[2.5]oct-1-ene (3.0 mmol, 1.1 equiv, 790 mg) and anhydrous THF (8.7 mL) under nitrogen. The mixture was cooled to -78 °C, and n-BuLi (2.5 M in hexane, 1.02 equiv, 1.23 mL) was added dropwise (Note: The addition process of n-BuLi needs to be terminated once the reaction mixture turns from colorless to slightly pinkish. Otherwise, disilylated byproduct, which is difficult to separate from the product, is formed). Then the reaction mixture was stirred at -10 °C for 1 h. The resulting suspension was added over 30 min to another 50 mL round bottom flask containing PhMe2SiCl (3.3 mmol, 1.1 equiv, 563 mg) and anhydrous THF (6.0 mL) at -40 °C under nitrogen. The reaction mixture was stirred at -40 °C for 1 h and at rt for 2 h. The reaction mixture was quenched with saturated aqueous NH4Cl (20 mL). Then water (30 mL) and CH2Cl2 (60 mL) were added. The layers were separated and the aqueous layer was extracted with CH2Cl2 (60 mL). The combined organic layers were dried over Na2SO4, and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluted with hexanes/EtOAc/CH2Cl2 = 30:1:2) to afford the title compound as a white solid (0.90 g, 76% yield) (Note: 13c was stored under nitrogen in the glovebox freezer at -30 °C once prepared). **1H NMR** (400 MHz, CDCl3) δ 8.05 (s, 1H), 7.64-7.62 (m, 2H), 7.41-7.39 (m, 2H), 7.37-7.27 (m, 5H), 3.11 (ddd, J = 10.8, 6.6, 3.9 Hz, 2H), 2.81 (ddd, J = 11.5, 8.5, 3.6 Hz, 2H), 2.47 (s, 3H), 1.61 (td, J = 8.6, 4.2 Hz, 2H), 1.41-1.35 (m, 2H), 0.32 (s, 6H). **13C NMR** (101 MHz, CDCl3) δ 143.29, 136.99, 136.86, 133.65, 133.51, 131.87, 129.62, 129.55, 127.99, 127.87, 47.20, 38.17, 22.52, 21.69, -2.25. **m.p.** 65.6-66.2 °C. **IR (thin film)**: 2937, 2903, 2837, 1667, 1428, 1351, 1247, 1162, 1112, 722 cm⁻¹. **EA Calcd.** for C22H27NO2SSi: C, 66.46; H, 6.84. Found: C, 66.33; H, 6.61.
tert-butyl 4-(dimethyl(phenyl)silyl)azete-1(2H)-carboxylate\textsuperscript{15} (5d)

A 100 mL round bottom flask containing a magnetic stir bar was capped with a septum. The flask was evacuated and backfilled with argon (this process was repeated for a total of three times), and then attached to a balloon filled with argon. Then tert-butyl 3-methoxyazetidine-1-carboxylate (4.0 mmol, 1.0 equiv, 749 mg) and anhydrous THF (25 mL) were added, and the mixture was cooled to -78 °C. TMEDA (10.0 mmol, 2.5 equiv, 1.16 g) was added. Then \textsuperscript{t}BuLi (1.3 M in cyclohexane, 2.5 equiv, 7.7 mL) was added dropwise over 10 min while the reaction mixture was stirred at -78 °C. The reaction mixture was stirred at -78 °C for 1 h, and then PhMe\textsubscript{2}SiCl (10.0 mmol, 2.5 equiv, 1.71 g) was added. The reaction mixture was stirred at -78 °C for 1 h, and then at rt for 1 h. The reaction mixture was quenched with saturated aqueous NaHCO\textsubscript{3} (30 mL). Then Et\textsubscript{2}O (100 mL) was added. The layers were separated and the aqueous layer was extracted with Et\textsubscript{2}O (50 mL). The combined organic layers were dried over Na\textsubscript{2}SO\textsubscript{4}, and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluted with 0-9% Et\textsubscript{2}O in hexanes). The resulting material was redissolved in Et\textsubscript{2}O (3 mL), filtered through a short plug of basic activated alumina, and washed with additional Et\textsubscript{2}O. The collected Et\textsubscript{2}O solution was concentrated in vacuo to afford the pure product as a colorless oil (0.47 g, 40% yield) (Note: 5d was stored under nitrogen in the glovebox freezer at -30 °C once prepared).

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.57 (d, J = 7.2 Hz, 2H), 7.40-7.33 (m, 3H), 5.89 (s, 1H), 4.55 (s, 2H), 1.33 (s, 9H), 0.47 (s, 6H).

\textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) δ 158.48, 152.00, 136.47, 134.23, 129.46, 127.85, 126.31, 80.34, 59.78, 28.48, -3.07.

IR (thin film): 2977, 1695, 1390, 1366, 1247, 1164, 1139, 1113, 1020, 814 cm\textsuperscript{-1}.

HRMS Calcd. m/z for C\textsubscript{16}H\textsubscript{24}N\textsubscript{2}O\textsubscript{2}Si\textsuperscript{+} [M+H]\textsuperscript{+}: 290.1571; found 290.1575.

4.6 Synthesis of Amination Reagents

All the amination reagents used in this paper are listed below. 3a\textsuperscript{16}, 3b\textsuperscript{17}, 6a\textsuperscript{18}, 9\textsuperscript{19} are known compounds and were prepared by following previously reported procedures.

Synthesis of 3c, 3d.

General Procedure F

A 100 mL round bottom flask containing a magnetic stir bar was charged with the corresponding aldehyde (1.0 equiv), BnNH\textsubscript{2} (1.0 equiv), and MeOH (2.0 M). The reaction
mixture was stirred at rt for 6 h. Then NaBH₄ (2.0 equiv) was added in several portions at rt. The reaction mixture was stirred at rt overnight, and then quenched with 5 M aq. NaOH. The resulting mixture was concentrated in vacuo, and then diluted with CH₂Cl₂ and water. The layers were separated and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with brine, dried over Na₂SO₄, concentrated in vacuo, and used in the next step without further purification.

A 100 mL round bottom flask containing a magnetic stir bar was charged with the crude material from the first step, and then DMF and K₂HPO₄ were added. BzOObz was then added in one portion at rt. The reaction mixture was stirred at rt until BzOObz was completely consumed (as indicated by TLC analysis), and then diluted with EtOAc and water. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic layers were dried over Na₂SO₄, concentrated in vacuo, and then purified by column chromatography on silica gel to give the corresponding amination reagent.

(5-(((benzoyloxy)(benzyl)amino)methyl)furan-2-yl)methanol (3c)

Following general procedure F, 5-(hydroxymethyl)furan-2-carbaldehyde (40 mmol, 5.0 g) and BnNH₂ (40 mmol, 4.4 mL) were used in the first step, and BzOObz (contains 25% water, 40 mmol, 12.9 g), K₂HPO₄ (80 mmol, 13.9 g), and DMF (50 mL) were used in the second step. The title compound was obtained as a white solid (2.83 g, 21% yield over two steps). ¹H NMR (400 MHz, CDCl₃) δ 7.92-7.90 (m, 2H), 7.54 (tt, J = 7.0, 1.3 Hz, 1H), 7.47-7.39 (m, 4H), 7.35-7.26 (m, 3H), 6.28 (d, J = 3.1 Hz, 1H), 6.23 (d, J = 3.1 Hz, 1H), 4.56 (s, 2H), 4.24 (s, 2H), 4.23 (s, 2H), 2.06 (s, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 164.87, 164.88, 161.27, 137.26, 135.81, 133.02, 131.01, 129.57, 129.41, 128.31, 128.50, 128.44, 127.85, 126.77, 117.78, 112.16, 62.17, 61.36, 52.39. m.p. 80.5-82.3 °C. IR (thin film): 3419, 3031, 2864, 1733, 1450, 1242, 1083, 1062, 1015, 698 cm⁻¹. EA Calcd. for C₂₀H₁₉NO₄: C, 71.20; H, 5.68. Found: C, 71.48; H, 5.74.

methyl 5-(((benzoyloxy)(benzyl)amino)methyl)-2-hydroxybenzoate (3d)

Following general procedure F, methyl 5-formyl-2-hydroxybenzoate (20 mmol, 3.6 g) and BnNH₂ (20 mmol, 2.2 mL) were used in the first step, and BzOObz (contains 25% water, 22 mmol, 7.1 g), K₂HPO₄ (40 mmol, 7.0 g), and DMF (25 mL) were used in the second step. The title compound was obtained as a white solid (3.31 g, 42% yield over two steps). ¹H NMR (400 MHz, CDCl₃) δ 10.70 (s, 1H), 7.87-7.83 (m, 3H), 7.56 (dd, J = 8.5, 2.2 Hz, 1H), 7.51 (tt, J = 7.0, 1.3 Hz, 1H), 7.44-7.42 (m, 2H), 7.39-7.24 (m, 5H), 6.93 (d, J = 8.5 Hz, 1H), 4.20 (s, 2H), 4.12 (s, 2H), 3.91 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 170.52, 164.88, 161.27, 137.26, 135.81, 133.02, 131.01, 129.57, 129.41, 128.31, 128.50, 128.44, 127.85, 126.77, 117.78, 112.16, 62.17, 61.36, 52.39. m.p. 111.7-112.4 °C. IR (thin film): 3032, 2953, 1739, 1674, 1595, 1489, 1441, 1241, 1086, 707 cm⁻¹. EA Calcd. for C₂₃H₂₁NO₅: C, 70.58; H, 5.41. Found: C, 70.33; H, 5.53.

Synthesis of 6b, 6c.

\[
\begin{align*}
N\text{-benzyl-N-(thiophen-2-ylmethyl)}\text{-O-(2,4,6-trimethylbenzoyl)hydroxylamine (6b)}
\end{align*}
\]
A 100 mL round bottom flask containing a magnetic stir bar was charged with N-benzyl-N-(thiophen-2-ylmethyl)hydroxylamine$^{18}$ (10.0 mmol, 1.0 equiv, 2.19 g), CH$_2$Cl$_2$ (25 mL), and Et$_3$N (14.4 mmol, 1.44 equiv, 2.0 mL). The mixture was cooled to 0°C, and 2,4,6-trimethylbenzoyl chloride (12.0 mmol, 1.2 equiv, 2.19 g) in CH$_2$Cl$_2$ (5 mL) was added dropwise. Then the reaction mixture was stirred at rt overnight. The reaction mixture was passed through a short plug of basic alumina, and washed with additional EtOAc. The resulting solution was concentrated in vacuo, and then purified by column chromatography on silica gel to give the title compound as a white solid (1.51 g, 41% yield).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.51-7.49 (m, 2H), 7.36-7.27 (m, 4H), 7.06-7.05 (m, 1H), 6.97 (dd, $J = 5.1$, 3.5 Hz, 1H), 6.76 (s, 2H), 4.43 (s, 2H), 4.16 (s, 2H), 2.25 (s, 3H), 1.95 (s, 6H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.30, 139.43, 138.16, 136.23, 135.28, 129.73, 129.41, 128.53, 128.26, 127.87, 127.51, 126.67, 126.05, 61.64, 56.74, 21.24, 19.11, 19.10. m.p. 84.3-85.4°C. IR (thin film): 3029, 2921, 1747, 1611, 1431, 1235, 1160, 1053, 851, 696 cm$^{-1}$. EA Calcd. for C$_{22}$H$_{23}$NO$_2$S: C, 72.30; H, 6.34. Found: C, 72.21; H, 6.34.

**N-benzyl-N-(2,2-dimethoxyethyl)-O-(2,4,6-trimethylbenzoyl)hydroxylamine (6c)**

A 100 mL round bottom flask containing a magnetic stir bar was charged with N-benzyl-N-(2,2-dimethoxyethyl)hydroxylamine$^{18}$ (8.0 mmol, 1.0 equiv, 1.69 g), CH$_2$Cl$_2$ (20 mL), and Et$_3$N (11.5 mmol, 1.15 equiv, 1.6 mL). The mixture was cooled to 0°C, and 2,4,6-trimethylbenzoyl chloride (8.0 mmol, 1.0 equiv, 1.82 g) in CH$_2$Cl$_2$ (4 mL) was added dropwise. Then the reaction mixture was stirred at rt overnight. The reaction mixture was passed through a short plug of basic alumina, and washed with additional EtOAc. The resulting solution was concentrated in vacuo, and then purified by column chromatography on silica gel to give the title compound as a colorless oil (1.43 g, 50% yield).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.47-7.45 (m, 2H), 7.34-7.24 (m, 3H), 6.78 (s, 2H), 4.77 (t, $J = 5.1$ Hz, 1H), 4.21 (s, 2H), 3.40 (s, 6H), 3.24 (d, $J = 5.1$ Hz, 2H), 2.25 (s, 3H), 2.06 (s, 6H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 168.43, 139.43, 135.31, 129.66, 129.49, 128.50, 128.38, 127.85, 102.05, 63.58, 60.33, 53.96, 21.24, 19.41. IR (thin film): 2921, 2833, 1748, 1612, 1454, 1238, 1127, 1054, 851, 698 cm$^{-1}$. EA Calcd. for C$_{21}$H$_{27}$NO$_4$: C, 70.56; H, 7.61. Found: C, 70.43; H, 7.49.
5. Computational Details

5.1 HOMO and LUMO Energies of Ground-State (Reactant) and Transition State Geometries of Cyclic Alkene Substrates and the CuH Catalyst

Figure S1. Frontier molecular orbital (FMO) interactions between the alkene and the L*CuH fragments. HOMO and LUMO energies were calculated at the HF/6-311G(d,p) level of theory. Although the LUMO of the alkenes have comparable energies in their ground state geometries, the greater pyramidalization of 1a in TS-1a significantly lowers the LUMO energy of 1a in its transition state geometry.

5.2 Substrate Distortion Energy versus the Out-of-Plane Dihedral Angle

Figure S2. The definition of the out-of-plane dihedral angles ($\alpha_{Me} = D(C_{Me}-C1-C2-C3')$; $\alpha_{H} = D(H-C2-C1-C3)$).

The distortion energies of 1-methylcyclopropene, 1-methylcyclobutene, and 2-methylbut-2-butene at different out-of-plane dihedral angles ($\alpha_{Me}$ and $\alpha_{H}$) (Figure 3c) were calculated at the M06/6-311+G(d,p) level of theory. The distortion energy is the single point energy difference between the distorted structures and the undistorted ground state (reactant) geometries of the alkenes. The out-of-plane angle ($\alpha$) is defined as the dihedral angle between the H(Me)-C1-C2
plane and the C1-C2-C3(C3') plane (Figure S2). The out-of-plane dihedral angle is gradually changed from $180^\circ$ to $120^\circ$ by a step of $5^\circ$ and the out-of-plane angle for Me is set to be the same as that for H in this process (i.e. Me and H are always placed in the same plane).

5.3 Dissecting the Activation Energy ($\Delta E^\ddagger$) using the Ligand-Substrate Interaction Model

$$\Delta E^\ddagger = \Delta E_{\text{sub-dist}} + \Delta E_{\text{cat-dist}} + \Delta E_{\text{int-bond}} + \Delta E_{\text{int-space}}$$  \hspace{1cm} (1)

**Table S5.** Computed energy terms to investigate the origin of regioselectivity. All energies are in kcal/mol.

|       | TS2a-a | TS2a-b | $\Delta \Delta E^\ddagger$ (TS2a-b - TS2a-a) | TS8-a | TS8-b | $\Delta \Delta E^\ddagger$ (TS8-b - TS8-a) |
|-------|--------|--------|---------------------------------------------|-------|-------|---------------------------------------------|
| $\Delta E^\ddagger$ | -10.5  | -7.9   | 2.6                                         | -13.9 | -15.5 | -1.6                                        |
| $\Delta E_{\text{sub-dist}}$ | 20.2   | 25.0   | 4.8                                         | 20.0  | 23.6  | 3.6                                         |
| $\Delta E_{\text{cat-dist}}$ | 9.4    | 9.8    | 0.4                                         | 10.8  | 9.0   | -1.8                                        |
| $\Delta E_{\text{int-bond}}$ | -22.6  | -25.8  | -3.2                                        | -31.9 | -34.5 | -2.6                                        |
| $\Delta E_{\text{int-space}}$ | -17.5  | -16.9  | 0.6                                         | -12.8 | -13.6 | -0.8                                        |

**Table S6.** Computed energy terms to investigate the origin of enantioselectivity. All energies are in kcal/mol.

|       | TS-1a  | TS-1a' | $\Delta \Delta E^\ddagger$ (TS-1a' - TS-1a) | TS-1b  | TS-1b' | $\Delta \Delta E^\ddagger$ (TS-1b' - TS-1b) |
|-------|--------|--------|---------------------------------------------|-------|-------|---------------------------------------------|
| $\Delta E^\ddagger$ | -11.1  | -11.3  | -0.2                                        | -3.7  | -1.0  | 2.7                                         |
| $\Delta E_{\text{sub-dist}}$ | 22.4   | 22.6   | 0.2                                         | 22.2  | 23.2  | 1.0                                         |
| $\Delta E_{\text{cat-dist}}$ | 7.7    | 8.3    | 0.6                                         | 7.9   | 9.5   | 1.6                                         |
| $\Delta E_{\text{int-bond}}$ | -33.9  | -35.0  | -1.1                                        | -25.4 | -26.2 | -0.8                                        |
| $\Delta E_{\text{int-space}}$ | -7.3   | -7.2   | 0.1                                         | -8.4  | -7.5  | 0.9                                         |
5.4 Free energy profiles of the alkene hydrocupration step

![Figure S3](image)

**Figure S3.** Computed activation Gibbs free energies and reaction free energies of hydrocupration with varies alkenes. All energies are in kcal/mol and are with respect to separated alkene substrate and the CuH catalyst. The hydrocupration reactions with cyclopropene and cyclobutene derivatives (1a, 1b, 2a, and 8) are all exergonic.

5.5 Cartesian Coordinates

1-methylcyclopropene (1a)
B3LYP/6-31G(d) SCF energy: -155.941626 a.u.
B3LYP/6-31G(d) Enthalpy: -155.850995 a.u.
B3LYP/6-31G(d) Gibbs free energy: -155.883360 a.u.
M06/6-311+G(d,p) SCF energy in solution: -155.864889 a.u.
M06/6-311+G(d,p) enthalpy in solution: -155.774258 a.u.
M06/6-311+G(d,p) free energy in solution: -155.806622 a.u.
Three lowest frequencies (cm$^{-1}$): 156.9522 299.9446 321.1413

**Cartesian coordinates:**

| ATOM | X      | Y      | Z      |
|------|--------|--------|--------|
| C    | -0.15681600 | 0.08709000 | -0.00023700 |
| C    | 0.91649800  | 0.81545800  | 0.00020700  |
| C    | 1.14941500  | -0.67391600 | -0.0001300  |
| H    | 1.38594900  | 1.78825800  | -0.00022200 |
1-methylcyclobutene (1b)

B3LYP/6-31G(d) SCF energy: -195.292981 a.u.
B3LYP/6-31G(d) Enthalpy: -195.292981 a.u.
B3LYP/6-31G(d) Gibbs free energy: -195.205873 a.u.

M06/6-311+G(d,p) SCF energy in solution: -195.186430 a.u.
M06/6-311+G(d,p) enthalpy in solution: -195.065079 a.u.
M06/6-311+G(d,p) free energy in solution: -195.099321 a.u.

Three lowest frequencies (cm⁻¹): 164.7382 221.6528 317.6539

Cartesian coordinates:

ATOM   X             Y             Z
C      -0.57488800  -1.04137600  -0.00011400
C      -1.62727100   0.12365500  -0.00013500
C      -0.42480100   1.04903100  -0.00013500
C       0.48155000   0.05702700  -0.00002300
H       2.26759600   0.16426000   0.89045800
H       2.26882700   0.16427900  -0.88921300
C       1.97175600  -0.01567400  -0.88934200
H       2.42173300   0.98324700  -0.00013700
H       2.34369500  -0.55689400   0.88106100
H       2.34383200  -0.55655300  -0.88103600
H       -0.59588200  -1.68451200   0.88934200
H       -0.59591800  -1.68337500  -0.89041500
H       -0.33911200   2.13356900  -0.00044500

2-methyl-2-ene (1c)

B3LYP/6-31G(d) SCF energy: -196.539826 a.u.
B3LYP/6-31G(d) Enthalpy: -196.395113 a.u.
B3LYP/6-31G(d) Gibbs free energy: -196.432626 a.u.

M06/6-311+G(d,p) SCF energy in solution: -196.428300 a.u.
M06/6-311+G(d,p) enthalpy in solution: -196.283586 a.u.
M06/6-311+G(d,p) free energy in solution: -196.321100 a.u.

Three lowest frequencies (cm⁻¹): 126.9722 154.1021 188.5166

Cartesian coordinates:

ATOM   X             Y             Z
C      -0.73459300  -0.67178700  -0.00013700
H      -0.71444600  -1.76306000  -0.00104500
C       0.44964300  -0.04035700   0.00012600
C       1.74146800  -0.82442300   0.00006300
H       1.56392800  -1.90466200  -0.00019000
1,3-diphenyl-3-methylcyclobut-1-ene (2a)
B3LYP/6-31G(d) SCF energy: -657.390971 a.u.
B3LYP/6-31G(d) Enthalpy: -657.098276 a.u.
B3LYP/6-31G(d) Gibbs free energy: -657.156364 a.u.
M06/6-311+G(d,p) SCF energy in solution: -657.051858 a.u.
M06/6-311+G(d,p) enthalpy in solution: -656.759163 a.u.
M06/6-311+G(d,p) free energy in solution: -656.817251 a.u.
Three lowest frequencies (cm$^{-1}$): 22.1352 35.7525 39.0999
Cartesian coordinates:

| ATOM | X     | Y     | Z     |
|------|-------|-------|-------|
| C    | 1.03547700 | -0.72847000 | 0.76961500 |
| C    | -0.02497000 | -1.28479300 | -0.26898900 |
| C    | -0.98987500 | -0.27046300 | 0.32698000 |
| C    | -0.98260700 | 0.21804200 | 1.19635900 |
| H    | -0.29234600 | -2.33957600 | -0.12661400 |
| H    | 0.24125900 | -1.12372300 | -1.31993300 |
| H    | -0.12387900 | 0.98569800 | 1.96563000 |
| C    | -2.39095200 | 0.00624900 | 0.02120500 |
| C    | -3.11102500 | 0.99819400 | 0.71378900 |
| C    | -3.05288200 | -0.72223200 | -0.98170400 |
| C    | -4.44583500 | 1.24998800 | 0.41189400 |
| H    | -2.61509800 | 1.57203400 | 1.49231900 |
| C    | -4.39093700 | -0.46959700 | -1.28402300 |
| H    | -2.51087600 | -1.49075200 | -1.52656900 |
| C    | -5.09254400 | 0.51671700 | -0.58886400 |
| H    | -4.98611800 | 2.01971700 | 0.95693600 |
| H    | -4.88553200 | -1.04358200 | -2.06328700 |
| H    | -6.13495400 | 0.71467100 | -0.82340100 |
| C    | 2.27247500 | -0.93709000 | 0.14788100 |
| C    | 3.06934900 | -0.82787900 | -0.74447000 |
| C    | 2.66989400 | 1.21005800 | 0.46922100 |
| C    | 4.22441500 | -0.27698000 | -1.29885300 |
| H    | 2.77922100 | -1.84205000 | -1.01073900 |
| C    | 3.82769300 | 1.76559900 | -0.08130400 |
| H    | 2.06660500 | 1.80236900 | 1.15173200 |
C  4.60928300  1.02469500 -0.96795900  
H  4.82310300 -0.86305500 -1.99168700  
H  4.11501100  2.78062700  0.18149500  
H  5.50810800  1.45676900 -1.39980300  
C  1.43809700 -1.75048800  1.84933100  
H  2.08976500 -2.52870200  2.66231400  
H  1.98504500 -1.25851300  2.66231400  
H  0.55035700 -2.23151900  2.27625100  

1-phenylcyclopropene (8)  
B3LYP/6-31G(d) SCF energy: -426.320456 a.u.  
B3LYP/6-31G(d) Enthalpy: -426.114875 a.u.  
B3LYP/6-31G(d) Gibbs free energy: -426.162512 a.u.  
M06/6-311+G(d,p) SCF energy in solution: -426.093100 a.u.  
M06/6-311+G(d,p) enthalpy in solution: -425.887519 a.u.  
M06/6-311+G(d,p) free energy in solution: -425.935156 a.u.  
Three lowest frequencies (cm⁻¹): 46.7760  85.3581  98.9093  
Cartesian coordinates:  
ATOM X     Y     Z  
C  1.77324100  1.48287300 -0.00123400  
C  0.81779600  0.59200100 -0.00045100  
C  2.23138000  0.04570300 -0.00011000  
H  2.07749900  2.52057000 -0.00313600  
C -0.58837400  0.25099600 -0.00020300  
C -0.99243700 -1.09521200  0.00011900  
C -1.57445800  1.25573000 -0.00013800  
C -2.34568100 -1.42824700  0.00027900  
H -0.23497200 -1.87384500 -0.000021200  
C -2.92484400  0.91987900  0.00003100  
H -1.26764200  2.29816900 -0.00025400  
C -3.31516100 -0.42317300  0.00018200  
C -2.64482300 -2.47306000  0.00046800  
H -3.67678000  1.70464400  0.00004900  
H -4.37023700 -0.68345100  0.00034600  
C  2.81595200 -0.56449700 -1.27437200  
H  3.90107900 -0.40012300 -1.32624500  
H  2.65319400 -1.65041300 -1.31055000  
H  2.36406100 -0.12366200 -2.16898800  
C  2.81598500 -0.56184000  1.27553800  
H  2.65324800 -1.64768500  1.31389100  
H  3.90108800 -0.39729200  1.32725400  
H  2.36388400 -0.11913400  2.16911100  

DTBM-SEGPHOS-based CuH catalyst  
B3LYP/6-31G(d) SCF energy: -4362.402757 a.u.  
B3LYP/6-31G(d) Enthalpy: -4360.703810 a.u.  

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B3LYP/6-31G(d) Gibbs free energy: -4360.930343 a.u.
M06/6-311+G(d,p) SCF energy in solution: -4360.93433998 a.u.
M06/6-311+G(d,p) enthalpy in solution: -4359.23539398 a.u.
M06/6-311+G(d,p) free energy in solution: -4359.46192698 a.u.

Three lowest frequencies (cm$^{-1}$): 5.8740 11.1992 12.4341

**Cartesian coordinates:**

| ATOM | X (Å) | Y (Å) | Z (Å) |
|------|-------|-------|-------|
| Cu   | 0.001061 | -0.341948 | 1.784810 |
| H    | -0.093750 | -0.783801 | 3.278353 |
| P    | -1.713564 | 0.170594 | 0.300593 |
| C    | -1.205215 | 0.962704 | -1.297505 |
| C    | -2.950756 | 1.329812 | 1.031067 |
| C    | -2.740010 | -1.278065 | -0.187076 |
| C    | -0.280691 | 2.249050 | -1.616966 |
| C    | -4.228997 | 1.525817 | 0.509403 |
| C    | -2.579842 | 2.041039 | 2.177910 |
| C    | -2.776298 | -2.356690 | 0.695485 |
| C    | -3.493011 | -1.344773 | -1.365634 |
| C    | 0.032246 | 0.987058 | -3.336044 |
| C    | 0.308721 | -1.066846 | -2.005920 |
| C    | -1.290178 | 2.931303 | -2.787581 |
| H    | -2.353022 | 2.742717 | -0.941542 |
| C    | -5.173312 | 2.366410 | 1.119787 |
| H    | -4.502494 | 1.005379 | -0.401185 |
| C    | -3.474848 | 2.871561 | 2.861499 |
| H    | -1.576138 | 1.901232 | 2.560141 |
| C    | -3.600778 | -3.475068 | 0.486331 |
| H    | -2.135741 | -2.319931 | 1.570942 |
| C    | -4.372508 | -2.402854 | -1.617200 |
| H    | -3.384248 | -0.551220 | -2.093594 |
| C    | -0.445391 | 2.259113 | -3.641883 |
| O    | 0.865601 | 0.566080 | -4.352167 |
| C    | -0.058511 | -2.030509 | -2.934722 |
| C    | 1.314033 | -1.469395 | -1.063703 |
| H    | -1.662383 | 3.924661 | -3.013249 |
| C    | -4.802671 | 2.937275 | 2.361653 |
| C    | -4.480881 | -3.409625 | -0.617790 |
| O    | 0.074956 | 2.673325 | -4.845851 |
| C    | 0.640287 | 1.491047 | -5.418095 |
| C    | 0.459387 | -3.323417 | -2.959203 |
| O    | -0.980343 | -1.898393 | -3.952443 |
| C    | 1.812374 | -2.780436 | -1.098277 |
| P    | 1.833459 | -0.364816 | 0.333641 |
| H    | 1.590521 | 1.736092 | -5.893966 |
| H    | -0.071667 | 1.055524 | -6.135194 |
|   |    X       |     Y       |     Z       |
|---|-----------|-----------|-----------|
| Cu | 0.04614100| 0.10743000| -1.63678500|
| H  | 0.28762400| -1.12019600| -2.63592800|
| P  | 1.77496700| 0.36613800| -0.10195400|
| C  | 1.22884600| 1.21382800| 1.45893100 |
| C  | 3.18210300| 1.39339000| -0.73539300|
| C  | 2.61557500| -1.17126400| 0.47479100 |
| C  | 0.23052600| 0.62092000| 2.29972500 |
| C  | 1.73368300| 2.48453400| 1.76980700 |
| C  | 4.51367100| 0.99742600| -0.63348900|
| C  | 2.89789300| 2.60120500| -1.39330800|
| C  | 2.51790200| -2.30471200| -0.32829400|
| C  | 3.36081100| -1.24639400| 1.65970400 |
| C  | -0.14020100| 1.37437900| 3.40548500 |
| C  | -0.32858700| -0.76708400| 2.20634500 |
| C  | 1.31365600| 3.22875100| 2.88507200 |
| H  | 2.49738100| 2.91620200| 1.13463300 |
| C  | 5.56916100| 1.71637100| -1.22281100|
| H  | 4.74358000| 0.09501600| -0.08272700|
| C  | 3.89346300| 3.36836500| -2.00543900|
| H  | 1.86781300| 2.93299000| -1.42801500|
| C  | 3.20856500| -3.49559800| -0.04153500|
| H  | 1.86985800| -2.24988700| -1.19715400|
| C  | 4.10141300| -2.38510300| 1.99234000 |
| H  | 3.36146900| -0.39157000| 2.32379900 |
| C  | 0.36882600| 2.63782000| 3.69324700 |

**TS-1a**

B3LYP/SDD-6-31G(d) SCF energy: -4518.336577 a.u.

B3LYP/SDD-6-31G(d) Enthalpy: -4516.546301 a.u.

B3LYP/SDD-6-31G(d) Gibbs free energy: -4516.781822 a.u.

M06/SDD-6-31+G(d,p) SCF energy in solution: -4516.803780 a.u.

M06/SDD-6-31+G(d,p) Enthalpy in solution: -4515.013505 a.u.

M06/SDD-6-31+G(d,p) Gibbs free energy in solution: -4515.249026 a.u.

Three lowest frequencies (cm\(^{-1}\)): -607.2594 8.4633 10.5981

Imaginary frequency: -607.2594 cm\(^{-1}\)

**Cartesian coordinates:**

| ATOM | X         | Y         | Z         |
|------|-----------|-----------|-----------|
| Cu   | 0.04614100| 0.10743000| -1.63678500|
| H    | 0.28762400| -1.12019600| -2.63592800|
| P    | 1.77496700| 0.36613800| -0.10195400|
| C    | 1.22884600| 1.21382800| 1.45893100 |
| C    | 3.18210300| 1.39339000| -0.73539300|
| C    | 2.61557500| -1.17126400| 0.47479100 |
| C    | 0.23052600| 0.62092000| 2.29972500 |
| C    | 1.73368300| 2.48453400| 1.76980700 |
| C    | 4.51367100| 0.99742600| -0.63348900|
| C    | 2.89789300| 2.60120500| -1.39330800|
| C    | 2.51790200| -2.30471200| -0.32829400|
| C    | 3.36081100| -1.24639400| 1.65970400 |
| C    | -0.14020100| 1.37437900| 3.40548500 |
| C    | -0.32858700| -0.76708400| 2.20634500 |
| C    | 1.31365600| 3.22875100| 2.88507200 |
| H    | 2.49738100| 2.91620200| 1.13463300 |
| C    | 5.56916100| 1.71637100| -1.22281100|
| H    | 4.74358000| 0.09501600| -0.08272700|
| C    | 3.89346300| 3.36836500| -2.00543900|
| H    | 1.86781300| 2.93299000| -1.42801500|
| C    | 3.20856500| -3.49559800| -0.04153500|
| H    | 1.86985800| -2.24988700| -1.19715400|
| C    | 4.10141300| -2.38510300| 1.99234000 |
| H    | 3.36146900| -0.39157000| 2.32379900 |
| C    | 0.36882600| 2.63782000| 3.69324700 |
O -1.05236000 1.02784800 4.38103800
C 0.00163100 -1.63485800 3.23991600
C -1.23979000 -1.29054800 1.23255100
H 1.72563700 4.20743000 3.10577900
C 5.21381000 -2.00105100 -3.46149300
C -3.40920000 -4.92452300 1.06110900
O -0.21220100 3.12422100 4.84059000
C -0.87031800 1.37680800 5.41794200
C -0.45838000 -2.94523000 3.33438000
O 0.83487200 -1.37680800 4.31030700
C -1.68586900 -2.61641400 1.34199900
P -1.75531400 -0.29600900 -0.24849600
H -1.84336500 2.29838900 5.80629400
H -0.23618900 1.56577700 6.20862300
C -1.30261800 -3.47606000 2.38496500
O 0.07078300 -3.54511700 4.45325000
C -1.68586900 -2.61641400 1.34199900
C -3.09829800 -1.30630900 -1.02999500
C -2.68490000 1.14470400 0.43472900
H -1.66668000 -4.49582600 2.44645300
H -0.09907900 -2.15954500 5.98670600
H 1.57216600 -2.77096200 5.64542600
C -4.40128100 -1.38145400 -0.52017300
C -2.78974000 -2.04034900 -2.17405900
C -2.65432200 2.32348900 -0.30692900
C -3.43218700 1.11264900 1.62020200
C -5.41321600 -2.09065700 -1.17271000
H -4.62761300 -0.85777800 0.39790000
C -3.74629300 -2.80173000 -2.86971900
H -1.76678700 -2.00668100 -2.53271800
C -3.41348000 3.45381200 0.04169500
H -2.00593100 2.35418800 -1.17721200
C -4.24675300 2.18327800 2.00522200
H -3.37209300 0.23130100 2.24586800
C -5.07843800 -2.71508600 -2.40703700
C -4.29515800 3.30805800 1.13528400
C 4.81871200 -2.48631100 3.36387600
C 4.28540400 -3.73120400 4.11714700
H 4.52758200 -4.65264900 3.58402700
H 4.73027200 -3.78469900 5.11913800
H 3.19610700 -3.68112000 4.22794000
C 6.35651800 -2.59163300 3.23182600
H 6.81880700 -2.50956100 4.22346000
H 6.66515700 -3.54622500 2.80513200
H 6.75916200 -1.78163700 2.61185100
C  4.52605600 -1.25099200  4.24422400
H  4.94713000 -0.33148100  3.82073400
H  3.45279000 -1.09725800  4.39555200
H  4.98932300 -1.39620800  5.22690200
C  2.88400300 -4.72661700 -0.93416000
C  3.44400500 -4.50831400 -2.35999700
H  4.53726800 -4.42788100 -2.35826600
H  3.17198500 -5.35148100 -3.00717200
C  1.33788700 -4.85648400 -1.02770400
H  0.89734300 -4.98678300  0.03276100
H  0.86331600 -3.98864500 -1.49222800
C  3.38163400 -6.08890900 -0.39831600
H  4.46348300 -6.21325700 -0.45837400
H  3.08022800 -6.25070300  0.64045000
C  1.92734400 -4.39120600  3.60630200
H  1.11273500 -3.69886400  3.37918000
H  2.10363500 -5.01176400 -1.5722020
H  1.58023800 -5.04626500  4.41397400
C  4.18976000 -4.79687300  4.50372800
H  3.65139500 -5.45059000 -5.20069200
H  4.52132700 -5.07765000  3.65829900
H  5.07766400 -4.43492500  5.02196100
C  6.81022700 -2.24183100  0.51572200
C  7.13450100 -3.74695800  0.34236800
H  8.11714500 -3.86679100  0.13142900
H  7.14982800 -4.26465000 -3.10324600
H  6.39110300 -4.23203500  0.30142400
C  7.93301000 -1.56479700 -1.33785900
H  7.67980500 -0.52393000 -1.57251100
H  8.13494300 -2.09415900 -2.26925600
H  8.86334100 -1.55775100 -0.75633700
C  6.84454700 -1.60471400  0.89137800
H  6.09001500 -2.03624100  1.55850800
H  6.69490600 -0.51932900  0.85877000
H  7.82638400 -1.78787300  1.34194000
C  3.15669400  4.74819000 -0.78007200
C  1.62127500  4.98374300 -0.83139600
H  1.21507300  5.11682200  0.17796200
H  -1.08134100  4.16040400  -1.30471500
H  -1.40811800  5.89344000  -1.40555600
C  -3.75242000  6.04752300  -0.19108600
H  -4.83887400  6.10317000  -0.26747300
H  -3.48051200  6.17952000  0.85987200
H  -3.34646900  6.89651100  -0.75416100
C  -3.67408600  4.56561400  -2.22703300
H  -4.75779700  4.40151600  -2.25031200
H  -3.45890600  5.46222000  -2.82181200
H  -3.19673400  3.71193300  -2.71969600
C  -4.98027700  2.16500100  3.37231500
C  -4.49695600  3.37447800  4.21159300
H  -4.75171100  4.31987600  3.72798200
H  -4.96613000  3.35755000  5.20385400
H  -3.40948100  3.34136000  4.34660300
C  -6.56330000  0.88333700  4.17092200
H  -5.03624800  -0.01769200  3.67483700
H  -3.58174900  0.75699300  4.33904000
C  -5.14279600  0.94265000  5.15150700
C  -6.52028000  2.22605000  3.23436000
H  -6.98366400  2.06010500  4.21492800
H  -6.85977000  3.19566000  2.87066100
H  -6.88991200  1.44508500  2.55894500
C  -7.01059600  1.22315100  -0.90725800
C  -7.13453900  1.04528500  0.63174200
H  6.96363900  1.99666600  1.14827300
H  6.43018200  0.31324000  1.03560100
C  8.14529400  0.70160300  0.88214000
H  7.25864500  -0.14684600  -1.58301800
H  6.52105500  -0.89252700  -1.26640300
H  7.20596500  -0.07256400  -2.67526500
H  8.25515000  -0.52419200  -1.32105900
C  8.15317300  2.18809200  -1.29999000
H  9.08604600  1.81141100  -0.86284200
H  8.31098900  2.25987200  -2.37658300
H  7.98426000  3.19750200  -0.91535100
C  3.56628800  4.76975500  -2.58511400
C  2.10830000  5.18020700  -2.28545300
H  1.38165900  4.54306900  -2.80138800
H  1.88290700  5.15989500  -1.21369200
H  1.94776800  6.20564800  -2.63670600
C  3.74550200  4.83883100  -4.12029200
H  4.79474100  4.78429700  -4.41197400
H  3.19710500  4.03145200  -4.62006900
H  3.34972800  5.79081800  -4.49516000
C  4.48189800  5.82291800  -1.91149300
TS-1b
B3LYP/SDD-6-31G(d) SCF energy: -4557.668218 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -4555.847183 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -4556.083737 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -4556.114176 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -4554.293141 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -4554.529695 a.u.
Three lowest frequencies (cm\(^{-1}\)): 779.5168 8.7874 11.4216
Imaginary frequency: -779.5168 cm\(^{-1}\)

Cartesian coordinates:
ATOM  X        Y        Z
Cu    0.00273400 0.03339700 -1.53417100
|   | X           | Y           | Z           |
|---|-------------|-------------|-------------|
| C | 2.15905000  | 5.41382300  | -1.77953400 |
| H | 1.31995500  | 4.79277000  | -1.45665400 |
| H | 2.75335000  | 5.66652600  | -0.89352100 |
| H | 1.74248800  | 6.34481800  | -2.18215000 |
| C | 4.09225200  | 5.79005700  | -3.26002200 |
| H | 3.56414000  | 6.72372100  | -3.48951300 |
| H | 4.79763800  | 5.99351400  | -2.44951200 |
| H | 4.66714600  | 5.52208900  | -4.14716400 |
| C | 6.94225400  | 1.74290200  | -1.08623600 |
| H | 8.65286400  | 2.88368400  | -0.35203300 |
| H | 7.49658900  | 3.86068000  | -1.27859800 |
| H | 7.11145200  | 3.36136900  | 0.38147400  |
| C | 7.69855500  | 1.27388900  | -2.35219400 |
| H | 7.20286300  | 0.41149100  | -2.81379900 |
| H | 7.78036700  | 2.06890400  | -3.09352500 |
| H | 8.71727300  | 0.96807400  | -2.08284800 |
| C | 7.15802500  | 0.65789300  | -0.00831700 |
| H | 6.67216500  | 0.91621700  | 0.93909500  |
| H | 6.78896100  | -0.32403200 | -0.32634000 |
| H | 8.23149400  | 0.55904800  | 0.18778700  |
| C | 3.18583500  | -4.67859100 | -0.80931900 |
| C | 1.65005900  | -4.88911400 | -0.91632900 |
| H | 1.20025000  | -4.99551300 | 0.07748400  |
| H | 1.14203000  | -4.06887900 | -1.42901700 |
| H | 1.44482400  | -5.80530800 | -1.48245300 |
| C | 3.73970200  | -5.99126000 | -0.20795800 |
| H | 4.82661200  | -6.06530100 | -0.24743900 |
| H | 3.43065000  | -6.12166500 | 0.83323300  |
| H | 3.33746800  | -6.83166600 | -0.78679200 |
| C | 3.75255900  | -4.49508000 | -2.23743700 |
| H | 4.84045900  | -4.36244600 | -2.22831200 |
| H | 3.52892300  | -5.37751600 | -2.84996400 |
| H | 3.31570400  | -3.62148000 | -2.73285200 |
| C | 5.04773200  | -2.16707400 | 3.37025100  |
| C | 4.58867200  | -3.40208200 | 4.18547500  |
| H | 4.85867900  | -4.33322700 | 3.68348600  |
| H | 5.05855400  | -3.39509900 | 5.17737700  |
| H | 3.50107500  | -3.39259000 | 4.32186000  |
| C | 4.70753600  | -0.91083100 | 4.20221700  |
| H | 5.07144900  | 0.00897600  | 3.72925000  |
| H | 3.63104100  | -0.80666900 | 4.37094800  |
| H | 5.19739500  | -0.98768800 | 5.17977300  |
| C | 6.58672500  | -2.20039100 | 3.21664900  |
| H | 7.05764900  | -2.05721400 | 4.19725400  |
| H | 6.93740000  | -3.15378600 | 2.82123900  |
| Atomic Symbol | X-Coordinate | Y-Coordinate | Z-Coordinate |
|---------------|--------------|--------------|--------------|
| H             | 6.93764100   | -1.39526900  | 2.56015400   |
| C             | -6.92637300  | -1.38323100  | -1.13313300  |
| C             | -7.10347900  | -1.27517200  | 0.40733400   |
| H             | -6.90979700  | -2.23995700  | 0.88980600   |
| H             | -6.44265900  | -0.53330200  | 0.86385200   |
| H             | -8.13470600  | -0.98251200  | 0.63832600   |
| C             | -7.20440000  | 0.00471600   | -1.75838200  |
| H             | -6.50297900  | 0.76098100   | -1.38994000  |
| H             | -7.11823600  | -0.02095700  | -2.85064300  |
| H             | -8.22082400  | 0.33634400   | -1.51093500  |
| C             | -8.01934900  | -2.37209000  | -1.60067800  |
| H             | -8.97836700  | -2.05085000  | -1.17583900  |
| H             | -8.14319800  | -2.40341900  | -2.68356300  |
| H             | -7.82145600  | -3.39013500  | -1.25422300  |
| C             | -3.30903300  | -4.72282200  | -2.86962800  |
| C             | -1.84362500  | -5.09326600  | -2.55505200  |
| H             | -1.13018700  | -4.39899600  | -3.01267900  |
| H             | -1.64625100  | -5.12834000  | -1.47817900  |
| H             | -1.63427300  | -6.08935200  | -2.96086400  |
| C             | -3.44994700  | -4.72002500  | -4.41043400  |
| H             | -4.49367800  | -4.68871200  | -4.72376400  |
| H             | -2.92040600  | -3.86928200  | -4.85546900  |
| H             | -3.01059100  | -5.63703100  | -4.82223600  |
| C             | -4.20095700  | -5.84120500  | -2.27374400  |
| H             | -4.06786500  | -5.90654300  | -1.18725900  |
| H             | -5.25778900  | -5.66399100  | -2.48281600  |
| H             | -3.92175400  | -6.81129300  | -2.70392100  |
| O             | -5.26596400  | 4.19091400   | 1.51200400   |
| O             | -5.94553900  | -3.51126200  | -3.08696300  |
| O             | 5.90782300   | 3.68300100   | -2.98818800  |
| O             | 5.26641700   | -4.26998900  | 1.38141900   |
| C             | -6.19686200  | -2.79628700  | -4.29750600  |
| H             | -6.88575800  | -3.41209000  | -4.88166200  |
| H             | -6.65843800  | -1.82138400  | -4.10529500  |
| H             | -5.27382500  | -2.63955800  | -4.86748000  |
| C             | -6.43373600  | 4.12562800   | 0.69391800   |
| H             | -7.12071100  | 4.88571300   | 1.07550000   |
| H             | -6.20835100  | 4.34035300   | -0.35640300  |
| H             | -6.90979500  | 3.13983300   | 0.75651700   |
| C             | 6.41932900   | -4.22070900  | 0.54120000   |
| H             | 7.09904300   | -4.99598800  | 0.90478600   |
| H             | 6.16996300   | -4.42409800  | -0.50595100  |
| H             | 6.91468300   | -3.24433600  | 0.60132800   |
| C             | 5.88647300   | 3.28178700   | -4.35883400  |
| H             | 4.92867900   | 3.51487400   | -4.83624200  |
| H             | 6.68291000   | 3.84182800   | -4.85592300  |
TS-1c
B3LYP/SDD-6-31G(d) SCF energy: -4558.907393 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -4557.063276 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -4557.301806 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -4555.351417 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -4555.507301 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -4555.745830 a.u.
Three lowest frequencies (cm$^{-1}$): -799.1215 10.7229 12.6260
Imaginary frequency: -799.1215 cm$^{-1}$

Cartesian coordinates:

| ATOM | X     | Y     | Z     |
|------|-------|-------|-------|
| Cu   | 0.00424700 | 0.05103400 | -1.56951500 |
| H    | -0.30199500 | 1.40997000 | -2.44887200 |
| P    | -1.76043300 | -0.37489600 | -0.14904500 |
| C    | -1.21615600 | -1.31290300 | 1.36041880 |
| C    | -3.10816800 | -1.41943600 | -0.87905400 |
| C    | -2.69798500 | 1.06549500 | 0.53201000 |
| C    | -0.25509700 | -0.75091200 | 2.26216400 |
| C    | -1.69916600 | -2.61103500 | 1.58043600 |
| C    | -4.46225500 | -1.11267900 | -0.76568300 |
| C    | -2.74675000 | -2.55308200 | -1.62430800 |
| C    | -2.66421200 | 2.25794900 | -0.18547700 |
| C    | -3.45408500 | 1.01080000 | 1.71107000 |
| C    | 0.10463500 | -1.56328700 | 3.33048900 |
| C    | 0.29116400 | 0.64609500 | 2.27477000 |
| C    | -1.29393300 | -3.41216600 | 2.66103200 |
| H    | -2.43403300 | -3.01982900 | 0.89808000 |
| C    | -5.46692000 | -1.84860300 | -1.42010200 |
| H    | -4.75172900 | -0.27009300 | -0.15175200 |
| C    | -3.68613100 | -3.32550600 | -2.31302600 |
| H    | -1.69807400 | -2.81668300 | -1.67075400 |
C  -3.42709400  3.38176800   0.17665100
H   -2.00656000  2.30500200  -1.04770900
C   -4.26208700  2.07796600   2.11797500
H   -3.40860000  0.11149700  2.31202700
C   -0.38650600  -2.85050200  3.53082100
O    0.98539600  -1.25954600  4.34945800
C   -0.06439500  1.43243700   3.36594000
C    1.24422800  1.23190100   1.37829900
H    1.69102900  -4.41010800  2.81185900
C    0.42526900  2.71509700   5.39321900
O    0.16980600  -3.91001000   4.66598300
C    0.78311600  -2.28190000   5.32660700
C    0.42526900  2.71509700   5.39321900
O    0.16980600  -3.91001000   4.66598300
C    0.78311600  -2.28190000   5.32660700
H    0.11034200  -1.90689800   6.11290800
C    1.33126800   3.29611700   2.73546000
O   -0.13068600   3.22900200   4.74095200
C   -0.74651500  2.10627600   5.37548500
H    2.46103300  2.95005700   0.95830100
C    3.11423400  1.40582900   0.95830100
C    2.71652300  -1.11165600   0.48955300
H    1.72993100   4.28977500   2.90855200
H   -0.07848800   1.71668700   6.15862900
H   -1.71249000   2.40371300   5.78596600
C    4.47134600  1.06703400  -0.82973900
C    2.75520700   2.59591800  -1.52354200
C    2.66484200  -2.31281800  -0.21355000
C    3.48639800  -1.04980300   1.65906900
C    5.45470100  1.82000000  -1.48271400
H    4.76029200   0.18440600  -0.27878900
C    3.69796900   3.44923000  -2.12136600
H    1.70457800   2.86832100  -1.54470100
C    3.42226800  -3.43926400   0.15648300
H    2.00202000  -2.36523400  -1.06988900
C    4.28849800  -2.11759200   2.07259100
H    3.45532500  -0.14245000   2.24826700
C    5.02566000   2.96628200  -2.20077700
C    4.31736900  -3.26849700   1.23703100
C   -4.99134000   2.03490900   3.48672500
C   -4.53515600   3.24835900   4.33534100
H   -4.81507700   4.19240300   3.86392800
H   -4.99742900   3.20806900   5.32997500
C  -3.44095800  -4.59835700  -4.54370700
H  -4.49250300  -4.59338900  -4.83189600
H  -2.95156500  -3.71607700  -4.97319200
H  -2.98114000  -5.48604200  -4.99553400
C  -4.09643200  -5.81476500  -2.42748300
H  -3.92853300  -5.91401800  -1.34837100
H  -5.16454900  -5.66776600  -2.59924900
H  -3.79721600  -6.75852200  -2.90068900
O       5.24159300  -4.25624200  1.54642000
O       5.94307300  -3.52044900  3.11547200
O       5.96454800  -3.63216300  2.97507200
C       6.25068900  -2.78589700  4.30103500
H       6.91567200  -3.42071600  4.89254400
H       6.76037600  -1.84261600  4.07504100
H       5.34635600  -2.56488300  4.87941100
C       6.40109300  -4.17283200  0.73771800
H       7.08412100  -4.92900500  1.13390600
H       6.16228200  -4.41488300  0.30367600
H       6.88798900  -3.19070100  0.76701800
C       6.39831600  -4.25497000  0.71014100
H       7.08194500  -4.99817300  1.12915600
H       6.15579200  -4.53209800  0.32133800
H       6.88603900  -3.27301600  0.70504500
C       5.83866800  -3.38299800  4.37565400
H       4.87668600  -3.73129400  4.76663000
H       6.64679600  -3.93680600  4.86068500
H       5.94121300  -2.31492600  4.60103400
C       0.11182500  -0.98460600  3.42762500
C       0.27568600  -0.36714400  3.73154500
C       0.68095900  1.22732400  4.54611800
H       0.33777200  2.26594700  4.59104400
H       0.72752300  0.83891900  5.75333000
C       1.73321400  0.57917700  4.12501300
H       2.40717000  -0.00640000  4.25070600
H       1.87371800  0.25616500  5.16803400
H       2.02586100  1.63328700  4.05070600
H       -0.71233800  1.69761700  3.44137200
H       1.69483800  1.22237700  4.13928500
C       1.43897400  1.56425300  3.88862300
H       2.30140100  -0.95744300  3.58739500
H       1.59066600  -2.56328900  3.46256900
H       1.50247000  -1.68120600  4.98524600

TS2a-a
B3LYP/SDD-6-31G(d) SCF energy:  -5019.762672 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -5017.770106 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -5018.028114 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -5017.988094 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -5015.995528 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -5016.253536 a.u.

Three lowest frequencies (cm$^{-1}$): -733.6981 7.1722 8.8518
Imaginary frequency: -733.6981 cm$^{-1}$

**Cartesian coordinates:**

| ATOM | X        | Y        | Z        |
|------|----------|----------|----------|
| Cu   | 0.10724900 | 1.11312800 | -0.01884300 |
| H    | 0.36950500 | 2.00652600 | -1.33949600 |
| C    | -0.16095200 | 2.94190900 | 1.23977800 |
| C    | -0.01563200 | 3.25229800 | -0.15200500 |
| H    | -0.81074300 | 3.59907700 | -0.80699000 |
| P    | 1.77857000 | -0.43992000 | 0.32609800 |
| C    | 1.15013700 | -2.08834000 | 0.91288100 |
| C    | 3.03440600 | 0.05809600 | 1.59506300 |
| C    | 2.81052800 | -0.90161100 | -1.13771100 |
| C    | 0.24738400 | -2.84839500 | 0.10040900 |
| C    | 1.55755000 | -2.58909100 | 2.15716600 |
| C    | 4.40131800 | 0.09742400 | 1.33034200 |
| C    | 2.59705000 | 0.46283500 | 2.86509000 |
| C    | 2.78793700 | -0.08745200 | -2.26681500 |
| C    | 3.60812600 | -2.05455700 | -1.15411300 |
| C    | -0.13503700 | -4.07654200 | 0.62614800 |
| C    | -0.21851400 | -2.54442700 | -1.29269500 |
| C    | 1.13227300 | -3.82791100 | 2.66561800 |
| H    | 2.25600500 | -2.01479100 | 2.75213500 |
| C    | 5.34167600 | 0.58796000 | 2.25543000 |
| H    | 4.75281300 | -0.26077800 | 0.37170600 |
| C    | 3.46751300 | 0.95398200 | 3.83749000 |
| H    | 1.53247100 | 0.39949100 | 3.08451000 |
| C    | 3.59780100 | -0.33216300 | -3.39103200 |
| H    | 2.09593800 | 0.74788800 | -2.26751100 |
| C    | 4.46763100 | -2.34203000 | -2.21838200 |
| H    | 3.55037100 | -2.73186500 | -0.31189500 |
| C    | 0.28664000 | -4.55924800 | 1.86270700 |
| O    | -0.96916900 | -5.00985100 | 0.04592100 |
| C    | 0.18055100 | -3.42990600 | -2.28601300 |
| C    | -1.14798600 | -1.53401400 | -1.70628600 |
| H    | 1.47307600 | -4.19745200 | 3.62660000 |
| C    | 4.83016400 | 1.11397800 | 3.46057500 |
| C    | 4.51808700 | -1.39937600 | -3.28395500 |
| O    | -0.26210700 | -5.79696000 | 2.09236200 |
| C    | -0.79000550 | -6.19427800 | 0.82480600 |
| C    | -0.25941700 | -3.36867800 | -3.60586800 |
| Atom | X       | Y       | Z     |
|------|---------|---------|-------|
| O    | 1.051189| -4.492862| -2.155732|
| C    | -1.575532| -1.488992| -3.040025|
| P    | -1.749843| -0.254768| -0.495331|
| H    | -1.752755| -6.685672| 0.968280|
| H    | -0.070097| -6.856755| 0.320576|
| C    | -1.141961| -2.397492| -4.020727|
| O    | 0.312144| -4.381841| -4.336503|
| C    | 0.892355| -5.247789| -3.358666|
| H    | -2.291907| -0.733649| -3.336494|
| C    | -3.047066| 0.699484| 1.416619|
| C    | -2.739439| -1.271632| 0.689033|
| H    | -1.500851| -6.094600| 0.320576|
| H    | 0.214613| -6.094600| -3.171777|
| H    | 1.868177| -5.583800| -3.707171|
| C    | -4.408330| 0.625281| -1.098593|
| C    | -2.652248| 1.579524| -2.427861|
| C    | -2.727188| -0.961276| 2.047907|
| C    | -3.498381| -2.365093| 0.254068|
| C    | -5.357871| 1.473016| -1.681877|
| H    | -4.724711| -0.977930| -0.361429|
| C    | -3.559737| 2.405360| -3.111319|
| H    | -1.600278| 1.616688| -2.691491|
| C    | -3.490327| -1.675505| 2.990506|
| H    | -2.094360| -0.146582| 2.377951|
| C    | -4.314036| -3.095207| 1.122574|
| H    | -3.447741| -2.641493| -0.790438|
| C    | -4.888094| 2.423922| -2.624922|
| C    | -4.357452| -2.674160| 2.480323|
| C    | 5.252702| -3.679951| -2.256453|
| C    | 4.904250| -4.438924| -3.560729|
| H    | 5.202164| -3.874764| -4.446013|
| H    | 5.415218| -5.409799| -3.578032|
| H    | 3.825632| -4.621396| -3.616948|
| C    | 6.784312| -3.477207| -2.180412|
| H    | 7.280084| -4.450354| -2.075497|
| H    | 7.178905| -3.004668| -3.080295|
| H    | 7.063093| -2.868388| -1.312430|
| C    | 4.857065| -4.596145| -1.077226|
| H    | 5.145720| -4.173952| -0.107696|
| H    | 3.780840| -4.798355| -1.180634|
| H    | 5.377122| -5.555238| -1.180634|
| C    | 3.364102| 0.560964| -4.642589|
| C    | 3.943464| 1.975761| -4.404992|
| H    | 5.030416| 1.956136| -4.269036|
| H    | 3.726717| 2.623377| -5.263770|
| H    | 3.506732| 2.439074| -3.514122|
| Element | X-Coordinate | Y-Coordinate | Z-Coordinate |
|---------|--------------|--------------|--------------|
| C       | 1.83247400   | 0.6988240    | -4.86876900  |
| H       | 1.36315600   | -0.2839450   | -4.98846500  |
| H       | 1.32476000   | 1.2153110    | -4.04976600  |
| H       | 1.65099600   | 1.2777560    | -5.78197600  |
| C       | 3.92809100   | -0.0084650   | -5.96529300  |
| H       | 5.01622800   | 0.0152990    | -6.02282700  |
| H       | 3.60550700   | -1.0412550   | -6.12875300  |
| H       | 3.54560900   | 1.2153110    | -6.04976600  |
| C       | 3.02084200   | 3.1571070    | -4.36264000  |
| H       | 5.01622800   | 0.0152990    | -6.02282700  |
| H       | 3.60550700   | 1.2153110    | -6.04976600  |
| H       | 3.54560900   | 1.2153110    | -6.04976600  |
| C       | -2.31096500  | 2.1166440    | -5.27289700  |
| H       | -1.47361500  | 1.6171230    | -4.77832000  |
| H       | -3.01682200  | 1.3461960    | -5.60468300  |
| H       | -1.91483100  | 2.6164720    | -6.16474600  |
| C       | -4.08944400  | 3.8236210    | -5.25932100  |
| H       | -3.60369400  | 4.1453850    | -6.18868800  |
| H       | -4.89214000  | 3.1290490    | -5.52092700  |
| C       | -6.86484100  | 1.2977910    | -1.35950800  |
| C       | -7.63554200  | 1.0100000    | -2.67236600  |
| H       | -8.70245500  | 0.8695970    | -2.45748100  |
| H       | -7.53413800  | 1.8326030    | -3.38313600  |
| H       | -7.26548300  | 0.0931370    | -3.14627900  |
| C       | -7.47639600  | 2.5402520    | -0.66892500  |
| H       | -6.88942700  | 2.8366060    | 0.20888100   |
| H       | -7.54661800  | 3.3905960    | -1.34733100  |
| H       | -8.49220400  | 2.3084960    | -0.32530200  |
| C       | -7.10680000  | 0.0994960    | -0.41562400  |
| H       | -6.72409600  | -0.8382250   | -0.83288600  |
| H       | -6.64996500  | 0.2476250    | 0.56980100   |
| H       | -8.18521500  | -0.0222420   | -0.26408100  |
| C       | -3.29279000  | -1.3494110   | 4.49796700   |
| C       | -1.84513000  | -0.8481410   | 4.74494400   |
| H       | -1.10474700  | -1.5479010   | 4.34056000   |
| H       | -1.65878500  | 0.1411420    | 4.31797900   |
| H       | -1.67646800  | -0.7631090   | 5.82450500   |
| C       | -3.46285700  | -2.5897630   | 5.40865000   |
| H       | -4.47730100  | -2.9841710   | 5.42775700   |
| H       | -2.80050300  | -3.4021750   | 5.08788100   |
| H       | -3.18619600  | -2.3174690   | 6.43413700   |
| C       | -4.24590000  | -0.2152440   | 4.94648700   |
| H       | -5.30003300  | -0.4830320   | 4.83859000   |
| H       | -4.07068800  | 0.0233660    | 6.00341000   |
H  6.43935400  3.22295900  3.00903100
H  4.96455400  3.71380700  3.87630600
C  6.61729900 -0.73063500 -4.14437200
H  7.34808900 -1.08286200 -4.87722900
H  6.35950400  0.31009500 -4.36801500
H  7.05663400 -0.77733300 -3.14084400
C -6.44180800 -2.66439600  3.68044200
H -7.23509400 -3.41578500  3.74265600
H -6.33767600 -2.18948900  4.66158600
H -6.71993700 -1.90648500  2.93985800
C -5.60957500  4.66404700 -2.49083300
H -4.62265000  5.08399600 -2.71317300
H -6.38132900  5.30847800 -2.91965900
H -5.73278500  4.61963100 -1.40263400
C  1.31775200  4.01385600  0.08799200
C -1.36251400  3.00843700  2.06499000
C -2.66601000  2.98220800  1.51444500
C -1.26189700  3.21079000  3.46060200
C -3.79219100  3.15828700  2.31139300
H -2.78941200  2.83603900  0.44556400
C -2.39403200  3.38971300  4.25558500
H -0.27725600  3.25575700  3.91864500
C -3.67145200  3.36830300  3.69082000
H -4.77729800  3.14143500  1.84931000
H -2.27453700  3.55469500  5.32427700
H -4.55315800  3.51653600  4.30837900
C  1.19395600  3.57021700  1.59338300
H  1.99210800  2.90703800  1.94327400
H  1.11069200  4.41083400  2.29359200
C  2.58359000  3.54317500 -0.64142900
H  2.51160800  3.73616000 -1.71821700
H  3.45892100  4.08463200 -0.26107700
H  2.74772400  2.47263500 -0.49516700
C  1.16639800  5.52089200 -0.13123500
C  0.48625400  6.02466000 -1.24994300
C  1.78817700  6.44337400  0.72401000
C  0.41013500  7.39694300 -1.49441800
H  0.01157600  5.33740100 -1.94436600
C  1.71774200  7.81624600  0.48325400
H  2.33875700  6.08494000  1.58951200
C  1.02299500  8.30107900 -0.62603300
H -0.12971300  7.75837200 -2.36635100
H  2.20560000  8.50766400  1.16603900
H  0.96199500  9.37013300 -0.81223700

TS2a-b
B3LYP/SDD-6-31G(d) SCF energy: -5019.757025 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -5017.765334 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -5018.023443 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -5017.984064 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -5015.992373 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -5016.250482 a.u.

Three lowest frequencies (cm⁻¹): -759.2091 10.8933 11.4513
Imaginary frequency: -759.2091 cm⁻¹

Cartesian coordinates:
| ATOM | X         | Y         | Z         |
|------|-----------|-----------|-----------|
| Cu   | 0.02373400| 0.96072000| 0.44622600|
| H    | -0.22652700| 1.21946600| 2.04226500|
| C    | -0.07755600| 3.06152500| 0.06207300|
| C    | -0.37868900| 2.84606000| 1.45621100|
| P    | -1.68199600| -0.31652400| -0.49431900|
| C    | -1.04343200| -1.47904200| -1.79915200|
| C    | -2.98720200| 0.66835100| -1.36888000|
| C    | -2.66499200| -1.41650300| 0.61954000|
| C    | -0.08054400| -2.48872000| -1.47036200|
| C    | -1.47526500| -1.33878200| -3.12579400|
| C    | -4.35039700| 0.48277400| -1.15349700|
| C    | -2.58763500| 1.68188000| -2.25470600|
| C    | -2.69044600| -1.12881300| 1.97932800|
| C    | -3.38180700| -2.52605400| 0.14776900|
| C    | 0.34068600  | -3.27949000| -2.53202800|
| C    | 0.40371300  | -2.88713600| -0.10803000|
| C    | -1.01600400| -2.15012300| -4.17722700|
| H    | -2.21610200| -0.58495000| -3.36033700|
| C    | -5.33145500| 1.31097200| -1.72958000|
| H    | -4.66524100| -0.32953900| -0.51189300|
| C    | -3.50272700| 2.55146700| -2.85542600|
| H    | -1.52993600| 1.78934100| -2.46040300|
| C    | -3.46840200| -1.86467200| 2.89134400|
| H    | -2.06736600| -0.31500300| 2.33473300|
| C    | -4.20913800| -3.27777100| 0.98759000|
| H    | -3.28894300| -2.79635600| -0.89603900|
| C    | -0.10385000| -3.12528600| -3.84260200|
| O    | 1.24216300  | -4.32373400| -2.48794500|
| C    | 0.05130000  | -4.16056500| 0.32120600|
| C    | 1.29586100  | -2.17199000| 0.75556300|
| H    | -1.37882800| -2.02799700| -5.19201600|
| C    | -4.86899200| 2.41190800| -2.48263200|
| C    | -4.31288000| 2.85612800| 2.34264200|
| O    | 0.49529400  | -4.05942300| -4.65215300|
| C    | 1.09810100  | -4.98611600| -3.74559800|
| C    | 0.48935300  | -4.72985400| 1.51389500|
| Atom | X-coordinate | Y-coordinate | Z-coordinate |
|------|--------------|--------------|--------------|
| H    | 3.33080800   | 2.87269000   | -3.28469100  |
| C    | 5.35609800   | -3.27222000  | -2.64060800  |
| C    | 5.02658500   | -3.90807500  | -4.01402400  |
| H    | 5.29687000   | -3.24642800  | -4.83838500  |
| H    | 3.95512600   | -4.85196600  | -4.13133500  |
| H    | 5.29687000   | 1.012463100  | 4.08680600   |
| C    | 6.87925600   | -3.01720300  | -2.55025400  |
| H    | 7.41373500   | -3.99300500  | -0.55366300  |
| C    | 7.24861700   | -2.43739700  | -3.96993000  |
| H    | 7.14035700   | -2.49128200  | -1.62438700  |
| C    | 6.81489300   | 0.89489700   | -1.51418400  |
| H    | 6.65938400   | 0.82438100   | 2.87337600   |
| H    | 6.33565900   | 1.25134200   | 1.18651000   |
| C    | 7.21903400   | 1.11852500   | -0.03737900  |
| H    | 6.56252100   | 0.57090600   | 0.64740200   |
| H    | 7.17301600   | 2.17844600   | 0.23735000   |
| H    | 8.24738500   | 0.77463500   | 0.13109500   |
| C    | 7.84346600   | 1.59844600   | 2.42967700   |
| H    | 8.81017300   | 1.09339000   | 2.31320400   |
| H    | 7.99836500   | 2.64907100   | 2.18348100   |
| H    | 7.55696900   | 1.53860700   | 3.48344900   |
| C    | 3.03732700   | 3.56356700   | 3.93442200   |
| H    | 1.54833100   | 3.36206600   | 4.29059100   |
| H    | 0.88224000   | 3.58265700   | 3.44889400   |
| H    | 1.33974500   | 2.34272200   | 4.63308900   |
| H    | 1.28079800   | 4.04486700   | 5.10466000   |
| C    | 3.19848600   | 5.03434100   | 3.48097900   |
| H    | 4.24639400   | 5.32831200   | 3.41487500   |
| H    | 2.72196800   | 5.20725700   | 2.50878600   |
| H    | 2.71773500   | 5.69832300   | 4.21021000   |
| C    | 3.84818800   | 3.33264700   | 5.23443700   |
| H    | 3.69311000   | 2.31536500   | 5.61349700   |
| H    | 4.91707900   | 3.48198600   | 5.07213100   |
| H    | 3.51533300   | 4.03322700   | -6.01052000  |
| O    | 5.25933300   | 3.49026900   | 3.13465700   |
| O    | 5.75310700   | 3.39153000   | 2.90907700   |
| O    | 5.79372300   | 1.47654400   | 4.44477300   |
| O    | 5.46242300   | -0.99047600  | -4.43150800  |
| C    | 6.08890200   | 4.34557600   | -1.90027400  |
| H    | 6.69881900   | 5.10934600   | -2.38975500  |
TS8-a

B3LYP/SDD-6-31G(d) SCF energy: -4788.700325 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -4786.794888 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -4787.043461 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -4787.036857 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -4785.131419 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -4785.379992 a.u.

Three lowest frequencies (cm$^{-1}$):

510.7480   8.9409   12.1263

Imaginary frequency:

510.7480 cm$^{-1}$

Cartesian coordinates:

| ATOM | X       | Y       | Z       |
|------|---------|---------|---------|
| Cu   | 0.10214500 | 0.23573800 | -1.47751600 |
| H    | 0.28580300  | -0.98164000 | -2.47256700  |
| C    | -0.38794200 | 0.56708800  | -3.41439700  |
| P    | 1.82695400  | 0.25017600  | 0.06763900   |
| C    | 1.29386700  | 0.34710200  | 1.84469100   |
| C    | 0.30195400  | 1.66057100  | -0.13025600  |
| C    | 2.93153400  | -1.23050100 | 0.03380200   |
| C    | 0.44966500  | -0.66109700 | 2.41337800   |
| C    | 1.71976000  | 1.42517600  | 2.63340000   |
| C    | 4.39444200  | 1.49178500  | -0.13541600  |
| C    | 2.49721100  | 2.95598300  | -0.29685300  |
| C    | 2.96717700  | -2.01067700 | -1.11872000  |
| C    | 3.75269900  | -1.58583500 | 1.11310100   |
| C    | 0.14230200  | -0.49060400 | 3.75736900   |
| C    | -0.03199600 | -1.92871100 | 1.77334200   |
| C    | 1.37190600  | 1.57418500  | 3.98660500   |
| H    | 2.36806700  | 2.17326400  | 2.19479200   |
| C    | 5.28804500  | 2.55085400  | -0.37630300  |
| H    | 4.79565000  | 0.50334900  | 0.04522000   |
| C    | 3.32417200  | 4.05788700  | -0.53356200  |
| H    | 1.42340900  | 3.09173800  | -0.25533500  |
| C    | 3.85635900  | -3.08854900 | -1.27407200  |
| H    | 2.25876400  | -1.77676700 | -1.90624600  |
| C    | 4.69039400  | -2.61905400 | 1.01699400   |
| H    | 3.65544600  | -1.03376000 | 2.03882700   |
| C    | 0.58307000  | 0.58834560  | 4.52674100   |
| O    | -0.62775900 | -1.31826200 | 4.54840700   |
| C    | 0.43461700  | -3.11904600 | 2.31618700   |
| C    | -1.03738300 | -2.06523600 | 0.76182500   |
| H    | 1.72626100  | 2.41164200  | 4.57758700   |
| C    | 4.71552800  | 3.80280400  | -0.68636400  |
| C    | 4.79312900  | -3.28710800 | -0.23523800  |
| O    | 0.11156800  | 0.46225700  | 5.81056900   |
| C    | -0.38548000 | -0.87634500 | 5.88547100   |
| Attrib | X-Coord | Y-Coord | Z-Coord |
|--------|---------|---------|---------|
| H      | 3.552297 | -2.253244 | -3.906984 |
| C      | 2.163552 | -4.312405 | -2.676802 |
| H      | 1.803117 | -4.844753 | -2.184612 |
| H      | 2.012814 | -4.961656 | -3.547493 |
| C      | 4.404738 | -5.333746 | -2.510419 |
| H      | 5.488052 | -5.250960 | -3.203240 |
| H      | 4.186984 | -5.890365 | -3.598666 |
| H      | 2.012814 | -4.961656 | -3.547493 |
| C      | 4.404738 | -5.333746 | -2.510419 |
| H      | 5.488052 | -5.250960 | -3.203240 |
| H      | -2.260810 | -2.626599 | -5.358866 |
| H      | -2.779550 | -1.821359 | -5.891439 |
| H      | -1.392477 | -2.189272 | -4.854471 |
| H      | -1.888799 | -3.335943 | -6.108763 |
| C      | -2.387125 | -4.478224 | -3.663879 |
| H      | -1.502098 | -4.110160 | -3.138242 |
| H      | -3.012471 | -5.016321 | -2.941804 |
| H      | -2.044791 | -5.199313 | -4.415380 |
| C      | -4.314301 | -4.070661 | -5.146163 |
| H      | -3.854855 | -4.871059 | -5.738843 |
| H      | -5.051062 | -4.527182 | -4.478933 |
| H      | -4.847634 | -3.421844 | -5.841226 |
| C      | -6.911630 | -0.978676 | -1.559242 |
| C      | -7.683168 | -2.321764 | -1.602513 |
| H      | -8.740219 | -2.150640 | -1.358106 |
| H      | -7.627457 | -2.781345 | -2.591277 |
| H      | -7.275935 | -3.026796 | -0.868097 |
| C      | -7.571945 | 0.024147 | -2.535523 |
| H      | -6.986343 | 0.948277 | -2.611934 |
| H      | -7.692571 | -0.397692 | -3.533431 |
| H      | -8.570660 | 0.292714 | -2.169204 |
| C      | -7.086506 | -0.397750 | -0.138794 |
| H      | -6.663494 | -1.052651 | 0.630739 |
| H      | -6.628399 | 0.592819 | -0.035571 |
| H      | -8.156475 | -0.289484 | 0.071028 |
| C      | -3.179883 | 3.914784 | 2.417451 |
| C      | -1.668303 | 4.226990 | 2.241669 |
| H      | -1.063015 | 3.684344 | 2.976491 |
| H      | -1.296029 | 3.978838 | 1.244529 |
| H      | -1.501364 | 5.300488 | 2.386627 |
| C      | -3.573533 | 4.535298 | 3.779181 |
| H      | -4.648408 | 4.556286 | 3.956331 |
| H      | -3.107682 | 4.001799 | 4.614000 |
| H      | -3.218336 | 5.572570 | 3.802507 |
| C      | -3.945285 | 4.632305 | 1.281026 |
| H      | -5.027884 | 4.481667 | 1.354965 |
|  | x     | y     | z      |
|---|-------|-------|--------|
| H | 6.39122100 | 5.67533700 | -2.76395100 |
| H | 6.46840200 | 3.89286900 | -2.74309200 |
| H | 4.93643200 | 4.70723000 | -3.14160800 |
| C | 6.92241400 | -3.68149800 | -1.17209300 |
| H | 7.69317100 | -4.45668300 | -1.16528400 |
| H | 6.62378000 | -3.48002500 | -2.20663000 |
| H | 7.32885800 | -2.75974700 | -0.73843700 |
| C | 6.32050400 | 2.64976700 | 3.41857000 |
| H | 7.00558400 | 2.90347500 | 4.23210400 |
| H | 6.16055400 | 3.53769400 | 2.79801800 |
| H | 6.76542800 | 1.86130700 | 2.80042000 |
| C | 5.84705000 | -1.16032900 | -5.16340800 |
| H | 4.90961000 | -1.29120100 | -5.71462900 |
| H | 6.68788400 | -1.37220800 | -5.82904500 |
| H | 5.90726500 | -0.12221000 | -4.81682000 |
| C | 0.59440400 | 1.53602400 | 4.01313700 |
| H | 1.16248000 | 0.01495600 | -3.90327600 |
| C | 1.39096200 | 2.89807100 | -2.76673800 |
| C | 1.06681000 | 4.24666600 | -3.02471800 |
| C | -2.73729800 | 2.60007700 | -2.46258200 |
| C | -2.03940400 | 5.24627800 | -2.99232700 |
| H | -0.03835800 | 4.49834800 | -3.27024800 |
| C | -3.70561500 | 3.60070900 | -2.42775400 |
| H | -3.02194400 | 1.56856600 | -2.27295400 |
| C | -3.36684700 | 4.93300200 | -2.69273300 |
| H | -1.75790500 | 6.27502400 | -3.20583900 |
| H | -4.73711500 | 3.33806500 | -2.20189500 |
| H | -4.12577000 | 5.71039000 | -2.66786500 |
| C | 2.09740000 | 1.41290400 | -3.81391000 |
| H | 2.53615500 | 0.73571200 | -4.56108600 |
| H | 2.58543300 | 2.39084200 | -3.92703200 |
| H | 2.34367400 | 1.03088600 | -2.82190300 |
| C | 0.23863500 | 2.03060500 | -5.41922200 |
| H | 0.64986300 | 3.03182100 | -5.60084100 |
| H | 0.65634000 | 1.36162900 | -6.18181900 |
| H | -0.84491500 | 2.08766100 | -5.56562500 |

**TS8-b**

B3LYP/SDD-6-31G(d) SCF energy: -4788.696962 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -4786.791425 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -4787.039335 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -4787.038901 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -4785.133365 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -4785.381274 a.u.

Three lowest frequencies (cm$^{-1}$): -651.7995 9.6475 12.1776
Imaginary frequency: -651.7995 cm$^{-1}$
### Cartesian coordinates:

| ATOM | X       | Y       | Z       |
|------|---------|---------|---------|
| Cu   | 0.031369| 0.35949 | -1.350868 |
| H    | -0.168640 | 1.885878 | -1.786863 |
| P    | -1.614912 | -0.484344 | 0.148852 |
| C    | -0.937443 | -1.72118 | 1.365626 |
| C    | -3.010361 | -1.395081 | -0.669444 |
| C    | -2.502898 | 0.751549 | 1.192126 |
| C    | 0.080655  | -1.348435 | 2.301822 |
| C    | -1.381655 | -3.051243 | 1.323055 |
| C    | -4.348618 | -1.115575 | -0.403991 |
| C    | -2.718828 | -2.384299 | -1.623492 |
| C    | -2.559012 | 2.064008 | 0.728967 |
| C    | -3.143047 | 0.433215 | 2.397677 |
| C    | 0.532413  | -2.366443 | 3.131572 |
| C    | 0.599035  | 0.027646 | 2.587034 |
| C    | -0.880523 | -4.061718 | 2.160627 |
| H    | -2.165039 | -3.321560 | 0.626929 |
| C    | -5.408383 | -1.730201 | -1.095440 |
| H    | -4.582867 | -0.394226 | 0.367358 |
| C    | -3.717334 | -3.027283 | -2.362069 |
| H    | -1.681567 | -2.644963 | -1.789820 |
| C    | -3.297261 | 3.065798 | 1.383806 |
| H    | -1.997481 | 2.307864 | -0.166591 |
| C    | -3.925567 | 1.367190 | 3.084604 |
| H    | -3.028077 | -0.567205 | 2.794310 |
| C    | 0.083288  | -3.681990 | 3.066791 |
| O    | 1.478700  | -2.267449 | 4.131330 |
| C    | 0.313757  | 0.544165 | 3.844853 |
| C    | 1.451266  | 0.835324 | 1.767328 |
| H    | -1.249269 | -5.080294 | 2.107839 |
| C    | -5.057634 | -2.597326 | -2.152428 |
| C    | -4.065978 | 2.655641 | 2.495994 |
| O    | 0.737478  | -4.444910 | 4.005323 |
| C    | 1.372844  | -3.491953 | 4.860470 |
| C    | 0.770834  | 1.775921 | 4.303396 |
| O    | -0.459603 | -0.038392 | 4.828805 |
| C    | 1.899258  | 2.075082 | 2.248683 |
| P    | 1.899039  | 0.334901 | 0.031366 |
| H    | 2.370441  | -3.846175 | 5.122940 |
| H    | 0.751963  | -3.331495 | 5.754798 |
| C    | 1.566443  | 2.578269 | 3.517013 |
| O    | 0.299033  | 2.004891 | 5.574249 |
| C    | -0.206234 | 0.737759 | 6.001349 |
| H    | 2.544895  | 2.678165 | 1.623382 |
| C    | 3.197780  | 1.570871 | -0.447815 |
C    2.86587400  -1.22619900  0.20700100
H    1.93257500  3.53888100  3.86246400
H    0.55144900  0.23089400  6.61811700
H   -1.13772300  0.88258900  6.54972100
C    4.56911100  1.34771800  0.27359400
C    2.78872500  2.79027100  0.99047200
C    2.79663100  2.13726700  0.84461600
C    3.67474900  1.52873500  1.31064500
C    5.53256000  2.25971700  0.71768500
H    4.88775100  0.43240300  0.20355400
C    3.69662800  3.77535100  1.41426400
H    1.72316000  2.96407900  6.61811700
C    3.56990300  3.31075400  0.87878500
H    2.10798700  1.92046300  6.54972100
C    4.50148000  2.65736300  1.33005400
C    3.97550400  2.03436000  5.51353800
C    4.33412500  1.77547900  6.51809300
H    2.87957900  2.02193500  5.52648700
C    6.06901400  1.05779800  4.49668900
H    6.43189900  0.66826600  5.45600300
H    6.45688100  2.07035000  4.38661200
H    6.49257800  0.42909600  3.70424100
C    4.10239200  0.39086200  4.93478900
H    4.51420900  1.17436800  4.28769300
H    3.01501700  0.51025300  4.96749600
H    4.49168700  0.56674400  5.94424100
C    3.15056600  4.51583700  0.84239800
C    3.87993500  4.65234100  0.51583800
H    4.95714700  4.47464300  0.41876400
H    3.74480800  5.66522400  0.91588400
H    3.49200400  3.94539700  1.25647400
C    1.63963700  4.79859300  0.61357600
H    1.07369300  4.67838200  1.54442500
H    1.19223000  4.14426400  0.13902600
H    1.51024300  5.83103700  0.26804000
C    3.63808100  5.63011700  1.79776000
H    4.72273800  5.67657400  1.89814900
H    3.21152700  5.52079400  2.79921700
H    3.30957200  6.59602500  1.39507700
C    3.09956600  5.14619200  1.84304100
C    2.34356700  4.99956800  3.18517000
H  3.01742500  4.71387500 -4.00074200
H  1.55998900  4.23716000 -3.12037800
H  1.87089000  5.95099500 -3.46003100
C  2.08309000  5.59295800 -0.75598600
H  1.24736200  4.89898400  0.21808600
H  2.57503500  5.69788200 -1.02680500
C  4.11422800  6.30766500 -1.95438400
H  3.55398400  7.24331600 -2.07196600
H  4.72991100  6.39538900 -1.05446300
H  4.78281400  6.22449500 -2.81142200
C  7.03451500  2.02149900 -0.41188100
H  8.64957800  3.06286100  0.62430700
H  7.50658100  4.15493600 -0.18296900
H  7.04982000  3.34933100  1.33188800
C  7.87910900  1.81827900 -1.69248900
H  7.44543800  1.04238000 -2.33472700
H  7.97413200  2.73804000 -2.27016700
H  8.89196900  1.49673600 -1.41948700
C  7.24184700  0.76473800  0.46245800
H  6.69342100  0.82563300  1.40908500
H  6.93867400 -0.15525600 -0.05052700
H  8.30660900  0.67118400  0.70409400
C  3.28624200 -4.30746000 -2.03802400
C  1.74704100 -4.47509300 -2.16824700
H  1.31347700 -4.83865000 -1.22958900
H  1.23853400 -3.54626900 -2.43741300
H  1.52412100 -5.20830100 -2.95217700
C  3.84038700 -5.73647400 -1.83384700
H  4.92542300 -5.80244400 -1.91677200
H  3.55201400 -6.14595500 -0.86125300
H  3.41697800 -6.38394000 -2.61132200
C  3.82377200 -3.73502600 -3.37190600
H  4.91307800 -3.61620500 -3.35504200
H  3.57429900 -4.40827600 -4.20159400
H  3.38535300 -2.75512900 -3.58964900
C  5.29887100 -3.02740000  2.60821700
C  4.82926900 -4.42076000  3.09737000
H  5.04773300 -5.19413800  2.35775200
H  5.34048800 -4.68470800  4.03224200
H  3.74914500 -4.42546200  3.28357700
C  5.04109800 -2.01690800  3.74769100
H  5.41441100 -1.01585500  3.50012400
H  3.97945700 -1.93389200  3.99818100
H  5.57523700 -2.34913500  4.64529200
TS-1a'

B3LYP/SDD-6-31G(d) SCF energy: -4518.335229 a.u.
B3LYP/SDD-6-31G(d) Enthalpy: -4516.544833 a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: -4516.778987 a.u.
M06/SDD-6-311+G(d,p) SCF energy in solution: -4516.804310 a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: -4515.013914 a.u.
M06/SDD-6-311+G(d,p) free energy in solution: -4515.248068 a.u.

Three lowest frequencies (cm⁻¹): -572.7360 8.4966 12.3222
Imaginary frequency: -572.7360 cm⁻¹

Cartesian coordinates:

| ATOM | X     | Y     | Z     |
|------|-------|-------|-------|
| Cu   | 0.03061700 | 0.08233500 | -1.67586300 |
| H    | -0.18403100 | 1.41707100  | -2.52906600 |
| C    | 0.30846700  | -1.27247800 | -3.26082600 |
| C    | 0.35995200  | 0.04782100  | -3.72320500 |
| P    | -1.75155400 | -0.32789700 | -0.25235000 |
| C    | -1.23120300 | -1.28573500 | 1.25564300  |
| C    | -3.12757400 | -1.34340500 | -0.96830700 |
| Element | X      | Y      | Z      |
|---------|--------|--------|--------|
| C       | -2.64507200 | 1.14946500 | 0.40094200 |
| C       | -0.29173800  | -0.75140300 | 2.19618400 |
| C       | -1.70536500  | -2.59597000  | 1.42012700 |
| C       | -4.46953600  | -1.14083100  | 0.65129100 |
| C       | -2.80135200  | -2.37185800  | -1.86415100 |
| C       | -2.61592400  | 2.30770900  | -0.37183800 |
| C       | -3.37989600  | 1.15485500  | 1.59467900 |
| H       | -2.41566000  | -2.98985600  | 0.70393800 |
| C       | -5.50865700  | -1.87573200  | -1.24724600 |
| H       | -4.72210400  | 0.07837800  | 1.63047500 |
| C       | -3.78212700  | -3.13390100  | 2.50812800 |
| H       | -1.75364500  | 2.54522000  | -2.07664600 |
| C       | -3.35947400  | -4.05766500  | -0.04486400 |
| H       | -1.97835200  | 2.30888600  | -1.24986200 |
| C       | -4.17728500  | 2.24418500  | 1.96341300 |
| H       | -3.32940000  | 0.28386600  | 2.23559400 |
| O       | 0.91033700  | -1.32228300  | 4.28927200 |
| C       | -0.08946700  | 1.40900500  | 3.35139900 |
| C       | 1.25068700  | 1.21883100  | 1.38760700 |
| H       | -1.70618900  | -4.43804300  | 2.58521000 |
| C       | -5.13814300  | -2.78822900  | -2.26038700 |
| C       | -4.22517300  | 3.34820200  | 1.06649900 |
| O       | 0.10367800  | -3.46865100  | 4.51701300 |
| C       | 0.69892300  | -2.37970400  | 5.22639200 |
| C       | 0.41503200  | 2.68073500  | 3.60779500 |
| O       | -0.98573300  | 1.07564300  | 4.34674200 |
| C       | 1.75194300  | 2.49818100  | 1.66762000 |
| P       | 1.79395400  | 0.33112400  | -0.15414000 |
| H       | 1.65715700  | -2.69504200  | 5.64126600 |
| H       | 0.01109800  | -2.03701100  | 6.01434700 |
| C       | 1.34389400  | 3.26150100  | 2.77438400 |
| O       | -0.15363200  | 3.18579900  | 4.75346600 |
| C       | -0.79288100  | 2.06201500  | 5.36270200 |
| H       | 2.50227900  | 2.92314000  | 1.01305900 |
| C       | 3.15496100  | 1.38884500  | -0.83629500 |
| C       | 2.69081400  | -1.15558100  | 0.46940500 |
| H       | 1.75253900  | 4.24705900  | 2.96902000 |
| H       | -0.14154200  | 1.65239900  | 6.14951200 |
| H       | -1.76120000  | 2.36595600  | 5.76262100 |
| C       | 4.51049100  | 1.05122400  | -0.74506700 |
| C       | 2.81147700  | 2.57177700  | -1.49614900 |
| C       | 2.60394900  | -2.32423500  | -0.28352700 |
| At. | X     | Y     | Z     |
|-----|-------|-------|-------|
| C   | 3.4507900 | -1.16747300 | 1.64449700 |
| C   | 5.50874700 | 1.79863600 | -1.38169000 |
| H   | 4.78577600 | 0.17346800 | -0.17896400 |
| C   | 3.76571000 | 3.41343200 | -2.09137000 |
| H   | 1.76251000 | 2.84511700 | -1.54449500 |
| C   | 3.32301600 | -3.48828600 | 0.03961100 |
| H   | 1.93987000 | -2.32169900 | -1.40994000 |
| C   | 4.21867200 | -2.27821000 | 2.01480000 |
| H   | 3.44805100 | -0.28536200 | 2.27175700 |
| C   | 5.09529900 | 2.93182800 | -2.13033200 |
| C   | 4.21727600 | -3.39201500 | 1.12912400 |
| C   | -4.89608100 | 2.26491100 | 3.33826600 |
| C   | -4.38843900 | 3.48558100 | 4.14652700 |
| H   | -4.63683900 | 4.42378500 | 3.64599100 |
| H   | -4.84707300 | 3.49502400 | 5.14380400 |
| H   | -3.30002300 | 3.44486900 | 4.27084400 |
| C   | -6.43672100 | 2.34198400 | 3.21437300 |
| H   | -6.89229000 | 2.19676000 | 4.20184000 |
| H   | -6.76924200 | 3.30970300 | 2.83924900 |
| C   | -6.82245600 | 1.55541200 | 2.55465200 |
| C   | -4.58016700 | 0.99639100 | 4.16090200 |
| H   | -4.97737300 | 0.08944900 | 3.68947900 |
| H   | -3.50573300 | 0.85840600 | 4.31469900 |
| H   | -5.05486100 | 1.08352200 | 5.14514300 |
| C   | -3.11279600 | 4.72152500 | -0.91198700 |
| C   | -3.71811100 | 4.52367500 | -2.32242100 |
| H   | -4.80657200 | 4.40165900 | -2.28407400 |
| H   | -3.50146000 | 5.39470100 | -2.95350600 |
| H   | -3.30142300 | 3.63856000 | -2.81515300 |
| C   | -1.57800800 | 4.91450800 | -1.06362700 |
| H   | -1.10217100 | 5.03171800 | -0.08323800 |
| H   | -1.09175900 | 4.08119600 | -1.57748400 |
| H   | -1.38002000 | 5.82088200 | -1.64801800 |
| C   | -3.63732500 | 6.04737800 | -0.31350000 |
| H   | -4.72410100 | 6.13274800 | -0.32604800 |
| H   | -3.30036900 | 6.18672300 | 0.71784400 |
| H   | -3.24146900 | 6.87662900 | -0.91246500 |
| C   | 3.26913200 | 4.80354300 | -2.58479800 |
| C   | 2.33031900 | 4.64017600 | -3.80307800 |
| H   | 2.85576300 | 4.20654900 | -4.66167700 |
| H   | 1.47811300 | 3.99196000 | -3.57421200 |
| H   | 1.93789100 | 5.61750500 | -4.11092800 |
| C   | 2.46436400 | 5.45883500 | -1.42781500 |
| H   | 1.59708900 | 4.86876700 | -1.12105900 |
| H   | 3.10083400 | 5.60805500 | -0.54753600 |
| H   | 2.09595100 | 6.44110500 | -1.74647700 |
$\begin{array}{cccc}
H & 1.60080600 & 0.30194500 & -5.42727500 \\
H & 0.93041300 & 1.82737800 & -4.80775700 \\
H & 1.04274900 & -2.06098000 & -3.39106200 \\
H & -0.73381600 & -1.08454800 & -5.26865800 \\
H & -1.79164000 & -0.64195200 & -3.84749900 \\
\end{array}$

$\begin{array}{cccc}
H & 0.93041300 & 1.82737800 & -4.80775700 \\
H & 1.04274900 & -2.06098000 & -3.39106200 \\
H & -0.73381600 & -1.08454800 & -5.26865800 \\
H & -1.79164000 & -0.64195200 & -3.84749900 \\
\end{array}$

$\begin{array}{cccc}
H & -0.73381600 & -1.08454800 & -5.26865800 \\
H & -1.79164000 & -0.64195200 & -3.84749900 \\
\end{array}$

$\begin{array}{cccc}
\end{array}$

**TS-1b'**

B3LYP/SDD-6-31G(d) SCF energy: $-4557.663502$ a.u.
B3LYP/SDD-6-31G(d) Enthalpy: $-4555.842368$ a.u.
B3LYP/SDD-6-31G(d) Gibbs free energy: $-4556.078787$ a.u.

M06/SDD-6-311+G(d,p) SCF energy in solution: $-4556.110096$ a.u.
M06/SDD-6-311+G(d,p) enthalpy in solution: $-4554.288962$ a.u.
M06/SDD-6-311+G(d,p) free energy in solution: $-4554.525382$ a.u.

Three lowest frequencies (cm$^{-1}$): $-753.1673$  $8.9276$  $11.8897$

Imaginary frequency: $-753.1673$ cm$^{-1}$

**Cartesian coordinates:**

| ATOM | X       | Y       | Z       |
|------|---------|---------|---------|
| Cu   | -0.00356400 | 0.03119000 | -1.59636300 |
| H    | -0.14829700 | 1.38179300 | -2.51004400 |
| C    | 0.37542100  | -1.12778200 | -3.36309400 |
| C    | 0.29283000  | 0.25992600  | -3.73533300 |
| P    | -1.76181500 | -0.36315900 | -0.17838600 |
| C    | -1.24217200 | -1.28629000 |  1.35627100 |
| C    | -3.14764400 | -1.39138000 | -0.86155200 |
| C    | -2.65183000 |  1.12591300 |  0.45779000 |
| C    | -0.27058900 | -0.74025200 |  2.25649000 |
| C    | -1.74966100 | -2.57316300 |  1.58981200 |
| C    | -4.48369300 | -1.00535100 | -0.78922100 |
| C    | -2.84276900 | -2.60467900 | -1.49806100 |
| C    | -2.59189600 |  2.29072500 | -0.30238100 |
| C    | -3.40813200 |  1.12918700 |  1.63802700 |
| C    |  0.08815600 | -1.56010500 |  3.31968500 |
| C    |  0.28983100 |  0.64996500 |  2.28543700 |
| C    | -1.35213100 | -3.37978900 |  2.66891300 |
| C    | -2.49895800 | -2.97238400 |  0.91903800 |
| C    | -5.52314000 | -1.74445800 | -1.38267200 |
| H    |  4.73205000 | -0.09889300 | -0.25378800 |
| C    |  3.81993500 | -3.38997400 | -2.11665900 |
| H    |  1.80845900 | -2.92551600 | -1.51334400 |
| C    | -3.32661300 |  3.44473600 |  0.02221500 |
| H    | -1.93710000 |  2.29078400 | -1.16836100 |
| C    | -4.18868400 |  2.22920500 |  2.00919500 |
| H    | -3.38742300 |  0.24833700 |  2.26678600 |
| C    | -0.42148300 | -2.83832200 |  3.52616000 |
| O    |  0.98421600 | -1.26926200 |  4.32888800 |
| C    | -0.06740400 |  1.42953900 |  3.37835700 |
|   |     x     |     y     |     z     |
|---|---------|---------|---------|
| H | -3.53782600 | 0.83482900 | 4.35674700 |
| H | -5.08630700 | 1.07083700 | 5.18540200 |
| C | -3.05350800 | 4.71421300 | -0.83300300 |
| C | -3.63967100 | 4.53035800 | -2.25332400 |
| H | -4.72983800 | 4.41939500 | -2.23144600 |
| H | -3.40499500 | 5.40248300 | -2.87635900 |
| H | -3.22465300 | 3.64376300 | -2.74478800 |
| C | -1.51459000 | 4.89176600 | -0.96018200 |
| H | -1.05260200 | 4.99960800 | 0.02794400 |
| H | -1.02958800 | 4.05522500 | -1.47029300 |
| H | -1.29808900 | 5.79873700 | -1.53709200 |
| C | -3.57413000 | 6.04215300 | -0.23583600 |
| H | -4.65983600 | 6.13790400 | -0.26392500 |
| H | -3.25099000 | 6.17378700 | 0.80088900 |
| H | -3.16172600 | 6.87020700 | -0.82523100 |
| C | 3.30154900  | 4.93142500 | -2.33509500 |
| C | 2.30035100  | 4.92217300 | -3.51360900 |
| H | 2.74836000  | 4.53954500 | -4.43258000 |
| H | 1.42669300  | 4.29975900 | -3.29488800 |
| H | 1.94653300  | 5.94081200 | -3.71648800 |
| C | 2.58272700  | 5.51669200 | -1.08754800 |
| H | 1.69183400  | 4.95171800 | -0.80145800 |
| H | 3.25962000  | 5.54170100 | -0.22565100 |
| H | 2.26422800  | 6.54154000 | -1.29473500 |
| C | 4.44175100  | 5.92744100 | -2.65060300 |
| H | 4.01570400  | 6.93779000 | -2.67988200 |
| H | 5.21899600  | 5.91191500 | -1.88134600 |
| H | 4.91958000  | 5.75373200 | -3.61494500 |
| C | 6.94269200  | 1.28723200 | -1.48853400 |
| C | 7.79812600  | 2.40502300 | -0.84126100 |
| H | 8.84856900  | 2.09147700 | -0.78940900 |
| H | 7.74395000  | 3.33152000 | -1.41619600 |
| H | 7.45874700  | 2.61046400 | 0.18093700 |
| C | 7.50687400  | 0.95519700 | -2.89083700 |
| H | 6.85982600  | 0.24614200 | -3.42109000 |
| H | 7.62557400  | 1.84819200 | -3.50473600 |
| H | 8.49630800  | 0.49180200 | -2.79041700 |
| C | 7.12238000  | 0.01805200 | -0.62622100 |
| H | 6.76881100  | 0.16126800 | 0.40067700 |
| H | 6.60230600  | -0.84922900 | -1.04937600 |
| H | 8.18992400  | -0.22922400 | -0.57674700 |
| C | 3.10915500  | -4.74861200 | -0.74192700 |
| C | 1.56938100  | -4.94245100 | -0.82116500 |
| H | 1.13395500  | -5.02663500 | 0.18104100 |
| H | 1.06239600  | -4.12508700 | -1.33969600 |
| H | 1.34399000  | -5.86540500 | -1.36828000 |
H  -4.10460200  -6.85355700  -2.35809500
O  -5.11123100  4.35983400  1.39215900
O  -6.08301000  -3.54168500  -2.91424000
O  5.98811500  3.61694500  -2.93848400
O  5.22844000  -4.33462000  1.41776700
C  -6.34299400  -2.90534300  -4.16641300
H  -7.06139800  -3.54032900  -4.69151400
H  -6.77338900  -1.90664200  -4.03289400
H  -5.42955700  -2.81417900  -4.76509500
C  -6.27606900  4.33330000  0.56747700
H  -6.93201200  5.12724400  0.93437500
H  -6.03556200  4.52353000  -0.48420300
H  -6.79416700  3.36967800  0.64033800
C  6.36641800  -4.31142400  0.56347900
H  7.03847600  -5.09328100  0.92712400
H  6.10120500  -4.52192100  -0.47844600
H  6.87690400  -3.34207800  0.60676700
C  5.79127100  3.45772100  -4.34405600
H  4.84043500  3.88963100  -4.67403900
H  6.61502800  3.98554300  -4.83185700
H  5.81344400  2.40010200  -4.63171500
C  -1.01735400  0.01925600  -4.50847500
C  -0.87304600  -1.49919800  -4.17890800
H  -1.72219100  -1.95592200  -3.66232300
H  -0.65831600  -2.10152200  -5.07420700
H  -1.90890300  0.52276700  -4.12281200
H  -0.91665100  0.25058800  -5.57689600
C  1.41372600  1.10347000  -4.29131700
H  2.29883600  1.07072300  -3.65015800
H  1.69538600  0.70835300  -5.27980800
H  1.11867000  2.15132900  -4.41242000
H  1.29883200  -1.70264800  -3.30513800
6. References and Notes

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(2) The cyclobutene and cyclopropene substrates are air-sensitive, and therefore have to be stored in the glovebox. For this reason, the hydroamination reactions are set up in the glovebox.

(3) Cyclopropenes bearing 3-hydrogen polymerize through ene-reaction when in their liquid phase. For this reason, characterization data of compound 12 by $^{13}$C NMR was not provided. The purity of 12 was determined by $^1$H NMR analysis with 1,1,2,2-tetrachloroethane as the internal standard.

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7. Spectroscopic Data

4a (1H NMR, 400 MHz, CDCl₃)

4a (13C NMR, 101 MHz, CDCl₃)
$4b$ ($^1$H NMR, 400 MHz, CDCl$_3$)

$4b$ ($^13$C NMR, 101 MHz, CDCl$_3$)
$4c$ ($^1$H NMR, 400 MHz, CDCl$_3$)

$4c$ ($^{13}$C NMR, 101 MHz, CDCl$_3$)
$^{1}H$ NMR, 400 MHz, CDCl$_3$.

$^{13}C$ NMR, 101 MHz, CDCl$_3$. 

$4d$
4e \((^{1}H\text{ NMR, 400 MHz, CDCl}_3)\)

4e \((^{13}C\text{ NMR, 101 MHz, CDCl}_3)\)
4g \((^1\text{H NMR, 400 MHz, CDCl}_3)\)

4g \((^{13}\text{C NMR, 101 MHz, CDCl}_3)\)
(11:1 ratio)
$\text{MeO}_2\text{C}$

$\text{Me}$

$\text{Br}$

$\text{Ph}$

$\text{H}$

$\text{N}$

$\text{C}$

$\text{MeO}_2\text{C}$

$\text{Me}$

$\text{Br}$

$\text{Ph}$

$\text{H}$

$\text{N}$

$\text{C}$

(13:1 ratio)

$\text{MeO}_2\text{C}$

$\text{Me}$

$\text{Br}$

$\text{Ph}$

$\text{H}$

$\text{N}$

$\text{C}$

$\text{MeO}_2\text{C}$

$\text{Me}$

$\text{Br}$

$\text{Ph}$

$\text{H}$

$\text{N}$

$\text{C}$

$\text{H}^1$ NMR, 400 MHz, CDCl$_3$

$\text{C}^13$ NMR, 101 MHz, CDCl$_3$
$^{13}$C NMR, 101 MHz, CDCl$_3$
10a (1H NMR, 400 MHz, CDCl₃)

10a (13C NMR, 101 MHz, CDCl₃)
10a (DEPT-135 NMR, 101 MHz, CDCl$_3$)

10b (1$^\text{H}$ NMR, 400 MHz, CDCl$_3$)
10b ($^{13}$C NMR, 101 MHz, CDCl$_3$)

10b (DEPT-135 NMR, 101 MHz, CDCl$_3$)
7a (1H NMR, 400 MHz, CDCl₃)

7a (13C NMR, 101 MHz, CDCl₃)
7d (1H NMR, 400 MHz, CDCl₃)

7d (13C NMR, 101 MHz, CDCl₃)
7e (1H NMR, 400 MHz, CDCl₃)

7e (13C NMR, 101 MHz, CDCl₃)
$1^{1}H$ NMR, 400 MHz, CDCl$_3$

$13^{13}C$ NMR, 101 MHz, CDCl$_3$
15b (\(\text{H NMR, 400 MHz, CDCl}_3\))

15b \(\text{(}^{13}\text{C NMR, 101 MHz, CDCl}_3\))
15d (1H NMR, 400 MHz, CDCl₃)

15d (13C NMR, 101 MHz, CDCl₃)
$7f$ ($^1$H NMR, 400 MHz, CDCl$_3$)

$7f$ ($^13$C NMR, 101 MHz, CDCl$_3$)
$2d$ (¹H NMR, 400 MHz, CDCl₃)

$2d$ (¹³C NMR, 101 MHz, CDCl₃)
$N\text{MeO}_2e$ ($^1\text{H NMR, 400 MHz, CDCl}_3$)

$N\text{MeO}_2e$ ($^{13}\text{C NMR, 101 MHz, CDCl}_3$)
8 (\(^1\)H NMR, 400 MHz, CDCl\(_3\))

8 (\(^{13}\)C NMR, 101 MHz, CDCl\(_3\))
$\text{Ph}$

$5a$ ($^1\text{H NMR, 400 MHz, CDCl}_3$)

$5a$ ($^{13}\text{C NMR, 101 MHz, CDCl}_3$)
5c (1H NMR, 400 MHz, CDCl₃)

5c (13C NMR, 101 MHz, CDCl₃)
MeO

11 (1H NMR, 500 MHz, CDCl₃)
13b \(^{(1}H \text{ NMR, } 400 \text{ MHz, CDCl}_3\))

\(13b \(^{(13}C \text{ NMR, } 101 \text{ MHz, CDCl}_3\))
13c ($^1$H NMR, 400 MHz, CDCl$_3$)

13c ($^{13}$C NMR, 101 MHz, CDCl$_3$)
5d (1H NMR, 400 MHz, CDCl₃)

5d (13C NMR, 101 MHz, CDCl₃)
$3d$ ($\text{H NMR, 400 MHz, CDCl}_3$)

$3d$ ($\text{C NMR, 101 MHz, CDCl}_3$)
6b (¹H NMR, 400 MHz, CDCl₃)

6b (¹³C NMR, 101 MHz, CDCl₃)
8. SFC Traces

\((1S,3R)-N,N\text{-dibenzyl-2,2-dimethyl-3-phenylcyclopropan-1-amine (10a)} + N,N\text{-dibenzyl-2,2-dimethyl-1-phenylcyclopropan-1-amine (10b)}\)

Racemic:

\[ \text{Enantioenriched:} \]

\[ \text{Racemic:} \]

\[ \text{Enantioenriched:} \]
(1R,2R)-N,N-dibenzyl-2-(3-phenylpropyl)cyclobutan-1-amine (7a)

Racemic:

Enantioenriched:
(1R,2R)-N-benzyl-2-(3-phenylpropyl)-N-(thiophen-2-ylmethyl)cyclobutan-1-amine (7b)

Racemic:

Enantioenriched:
(1R,2R)-N-benzyl-N-(2,2-dimethoxyethyl)-2-(3-phenylpropyl)cyclobutan-1-amine (7c)

Racemic:

Enantioenriched:
(1R,2S)-N,N-dibenzyl-2-(3-((tert-butyldiphenylsilyl)oxy)propyl)cyclobutan-1-amine (7d)

Racemic:

Enantioenriched:
(1R,2S)-N,N-dibenzyl-2-(3-((5-(trifluoromethyl)pyridin-2-yl)oxy)propyl)cyclobutan-1-amine (7e)

Racemic:

Enantioenriched:
(1R,2R)-N,N-dibenzyl-2-(4-methoxybenzyl)cyclopropan-1-amine (12)

Racemic:

Enantioenriched:
(1R,3R)-N,N-dibenzyl-3-(dimethyl(phenyl)silyl)-2,2-dimethylcyclopropan-1-amine (15a)

Racemic:

Enantioenriched:
2-((E)-(((1R,3R)-3-(dimethyl(phenyl)silyl)-2,2-dimethylcyclopropyl)imino)methyl)phenol (15b)

Racemic:

Enantioenriched:
2-((E)-((2R,3R)-2-(dimethyl(phenyl)silyl)-1',3'-dihydrospiro[cyclopropane-1,2'-inden]-3-ylimino)methyl)phenol (15c)

Racemic:

Enantioenriched:
2-((E)-(((1R,2R)-2-(dimethyl(phenyl)silyl)-6-tosyl-6-azaspiro[2.5]octan-1-yl)imino)methyl)phenol (15d)

Racemic:

Enantioenriched:
tert-butyl (2S,3R)-3-(dibenzylamino)-2-(dimethyl(phenyl)silyl)azetidine-1-carboxylate (7f)

Racemic:

Enantioenriched:
