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Graphical Abstract





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Steric effects on deprotonative generation of cyclohexynes and 1,2-cyclohexadienes from cyclohexenyl triflates by magnesium amides

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ARTICLE INFO

ABSTRACT

Steric effects on the deprotonative generation of cyclohexynes and 1,2-cyclohexadienes from cyclohexenyl triflates are described. A cyclohexenyl triflate, which is readily available from nonsubstituted cyclohexanone, was selectively converted to cyclohexyne using magnesium bis(2,2,6,6-tetramethylpiperidide) as base. The generated cyclohexyne was trapped by 1,3-diphenylisobenzofuran to afford the cycloadduct. This method was also applied to a benzo-fused cyclohexenyl triflate prepared from α -tetralone. A cyclohexenyl triflate bearing two methyl substituents at the 3-position was selectively transformed into the corresponding 1,2-cyclohexadiene. This 1,2-cyclohexadiene reacted with 1,3-diphenylisobenzofuran, styrene, and nitrone to provide the corresponding cycloadducts in good yields.

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1. Introduction

As seven-membered or smaller cycloalkynes and cycloallenes are generally not isolable owing to inherent ring strain, these reaction intermediates have rarely been utilized.¹ In contrast, arynes² and relatively stable cycloalkynes³ have been used in natural product synthesis, ligand synthesis, and copper-free Huisgen cycloaddition. Among the limited approaches to generating cyclohexynes and 1,2-cyclohexadienes reported since the seminal works of Wittig and Roberts,⁴ the fluoride ioninduced generation of cyclohexyne (1) and 1,2-cyclohexadiene (2) has been synthetically reliable regarding regiochemistry and functional group compatibility⁵ (Scheme 1). The only drawback of this method is the multistep preparation of α -silyl cyclohexenyl triflates 4 and 5 from cyclohexenone. However, our group has recently reported a novel method for the preparation of these α -silvl cyclohexenvl triflates by retro-Brook rearrangement of silvl enol ether $3.^{6}$ In contrast, a deprotonative approach starting from cyclohexenyl halide 7, which would be more atomeconomical, led to the generation of a mixture of cyclohexyne 8 and 1,2-cyclohexadiene 9.7 Our group has reported that metal amides allow the deprotonative generation of cyclohexyne (1) from cyclohexenyl triflate 13a, which can be prepared from cyclohexanone (12) in one step.⁸ The present study now reports the effect of substituents of cyclohexenyl triflates on the deprotonative generation of cyclohexyne and 1,2-cyclohexadiene. The selective generation of 1,2-cyclohexadiene 16 from cyclohexenyl triflate 15 is also described as an example.

Fluoride ion-induced generation from $\alpha\mbox{-silyl}$ enol triflate (Ref. 5 and 6)





2. Results and Discussion

2.1. Deprotonative generation of cyclohexynes using metal amides 8a,8b

Initially, metal amides were investigated in the generation of cyclohexyne/1,2-cyclohexadiene for achieving high yields (Table 1). The efficacy for cyclohexyne (1) generation was evaluated by comparing the yields of the cycloadduct of cyclohexyne (1) and 1,3-diphenylisobenzofuran (18), because -cyclohexyne (1) itself was not isolable owing to ring strain. According to the seminal work of Wittig, cyclohexenyl triflate **13a** was treated with PhLi at -78 °C, which afforded no desired cycloadduct with concomitant formation of unidentified products (Table 1, entry 1).

Table 1. Generation of cyclohexyne by deprotonation of cyclohexenyl triflate.^a



Entry	Base	Triflate 13a (%) ^b	Cycloadduct 19a (%) ^b
1	PhLi	<1	_ ^c
2	LDA	<1	18
3	LiTMP	<1	14
4	TMPMgCl·LiCl	84	_ ^c
5	Mg(Ni-Pr ₂) ₂ ·2LiCl	<1	38
6	Mg(Ni-Prt-Bu)2·2LiCl	<1	24
7	Mg(Nt-Amt-Bu)2·2LiCl	91	_ ^c
8	Mg(DMP)2·2LiCl	<1	51
9	Mg(TMP)2·2LiCl	<1	56
10^{d}	$Zn(TMP)_2 \cdot 2LiCl \cdot 2MgCl_2$	56	_ ^c
11 ^e	Et ₂ Zn(TMP)Li	<1	6
12 ^e	Et ₃ Al(TMP)Li	40	32
13 ^e	<i>i</i> -Bu ₃ Al(TMP)Li	<1	48

^a Reaction conditions: cyclohexenyl triflate **13a** (1.0 equiv), base (3 equiv), 1,3-diphenylisobenzofuran (**18**) (1.5 equiv), THF, rt, 3 h. ^b Yields determined from ¹H NMR spectra using 1,1,2,2- tetrachloroethane as internal standard. ^c Not detected in the crude ¹H NMR spectra. ^d Reaction time: 19 h. ^e Reaction conditions: 60 °C, 3 h.



Fig. 1. Structure of metal amides.

Both lithium diisopropylamide (LDA)⁹ and lithium 2,2,6,6tetramethylpiperidide (LiTMP)¹⁰ resulted in complete consumption of starting cyclohexenyl triflate **13a** to afford desired cycloadduct **19a** in 18% and 14% yields, respectively (entries 2 and 3). This observation indicated that proposed lithiated intermediate **17** was reactive, causing undesired reactions. The same reaction was then performed using the corresponding magnesium amide, Knochel–Hauser base (TMPMgCl·LiCl),¹¹ as a milder base. However, cycloadduct **19a** was not observed in the ¹H NMR spectrum of the crude mixture, with recovery of starting triflate 13a (entry 4). These results prompted us to investigate more basic magnesium bisamides. The use of Mg(N*i*-Pr₂)₂·LiCl¹² led to the formation of **19a** in 38% yield (entry 5). Sterically demanding magnesium bisamides did not improve the product yield (entries 6 and 7). Magnesium bis(*cis*-2,6-dimethylpiperidide) \cdot 2LiCl (Mg(DMP)₂ \cdot 2LiCl)¹³ and $Mg(TMP)_2 \cdot 2LiCl^{14}$ bearing cyclic amide moieties provided the product in 51% and 56% yields, respectively (entries 8 and 9). In addition to magnesium bisamides, related zinc and aluminum bases were tested. The reaction using $Zn(TMP)_2 \cdot 2LiCl \cdot 2MgCl_2^{15}$ did not give the desired product, while $Et_2Zn(TMP)Li^{16}$ led to the formation of cycloadduct 19a, albeit in 6% yield at 60 °C (entries 10 and 11). Furthermore, $Et_3Al(TMP)Li$ and *i*-Bu₃Al(TMP)Li¹⁷ provided cycloadduct 19a in 32% and 48% yields, respectively, under heating (entries 12 and 13). Although cyclohexenyl triflate 13a has two allylic protons at the 6-position, no cycloadducts derived from 1,2-cyclohexadiene (2) and isobenzofuran 18 were observed.

We next investigated the scope of the deprotonative generation of cyclohexynes using Mg(TMP)₂·2LiCl (Table 2). In addition to compound 19a, cvcloadducts 19b and 19c derived from cycloheptyne and cyclooctyne were obtained in 58% and 96% yields, respectively. Cyclohexenyl triflate 13d, bearing an ethyl group at the 4-position, was converted into cycloadduct 19d in 62% yield as a 1:1 diastereomeric mixture. Next, cyclohexenyl triflates bearing substituents at the α -position of the triflate group were tested. Cyclohexenyl triflate 13e, bearing a benzyl group, was transformed into corresponding cycloadduct 19e in 65% yield. Cyclohexenyl triflate 13f was also converted into compound 19f in the same manner. Cyclohexenyl triflates 13g-13i, bearing a quaternary carbon center at the 6-position, proceeded in the reaction to give corresponding cycloadducts 19g-19i in satisfactory yields. This method was also applied to benzo-fused cyclohexenyl triflate 13j to give cycloadduct 19j in 91% vield.

This deprotonative generation using TMP bases proceeded smoothly, owing to the low nucleophilicity of the anionic species bearing a bulky TMP group. However, the [4+2] cycloaddition of isobenzofuran **18** with cyclohexyne (**1**) generated by Mg(TMP)₂·2LiCl furnished corresponding cycloadduct **19a** in 56% yield, along with a substantial amount of enamine **20** that was decomposed during attempted chromatographic purification (Scheme 2). These results indicated that the nucleophilic addition of TMP base or its conjugate acid (TMPH) could not be completely suppressed.



Scheme 2. Formation of enamine through deprotonative generation of cyclohexyne.





^a Isolated yield. ^b Ratio of diastereomers determined by ¹H NMR. ^c Reaction time: 5 h. ^d Reaction time: 7 h. ^e Reaction time: 5 h.

2.2. Steric effects on deprotonative generation of cyclohexynes -2.2.2. Effect of methyl group at the 3-position on the ratio of and 1,2-cyclohexadienes from cyclohexenyl triflates cyclohexyne and 1,2-cyclohexadiene generated

2.2.1. Generation of 1,2-cyclohexadiene from cyclohexenyl triflate bearing a phenyl group at the 2-position

Cyclohexenyl triflate **21**, bearing a phenyl group at the 2position, was converted into cycloadducts *endo*-**23** and *exo*-**23** in 60% and 20% yields, respectively (Scheme 3). The corresponding ¹H NMR spectra and melting points were in good agreement with those reported by Johnson^{18a} and Ceylan.^{18b} These structures were confirmed by X-ray crystallography (Figures 2 and 3).^{19,20} These results indicated that 1,2cyclohexadiene **22** was generated through allylic deprotonation. The generated 1,2-cyclohexadiene **22** underwent [4+2] cycloaddition with isobenzofuran **18** regioselectively at the carbon–carbon double bond bearing the phenyl group, which was consistent with the reports of Johnson and Ceylan.¹⁸



Scheme 3. Generation of 1,2-cyclohexadiene 22 from cyclohexenyl triflate 21.



Fig. 2. ORTEP drawing of the molecular structure of (\pm) *endo*-23 with thermal ellipsoids at 30% probability levels.



Fig. 3. ORTEP drawing of the molecular structure of (\pm) -*exo*-23 with thermal ellipsoids at 30% probability levels.

We next investigated the reaction of cyclohexenyl triflate bearing a methyl group at the 3-position (Table 3). Under the established conditions, cyclohexenyl triflate 24 resulted in the formation of cycloadducts of both 1,2-cyclohexadiene and cyclohexyne. The ratios of cycloadducts of cyclohexyne 25 and 1,2-cyclohexadiene 26 obtained when using cyclohexenyl triflate 24 with various magnesium bisamides are summarized in Table 3. The ratios of these two intermediates were determined from the yields of corresponding cycloadducts 19f, 27, and 28 that were generated by reacting with isobenzofuran 18. We first performed the reaction at room temperature with Mg(Ni-Pr₂)₂·2LiCl,¹² but the cycloadducts were obtained in 46% combined yield with the recovery of cyclohexenyl triflate 24 (entry 1). Heating at 60 °C led to the consumption of 24 to give a 2:1 mixture of the cycloadducts in 51% yield (entry 2). Mg(NEt₂)₂·2LiCl also gave the products in lower yields (entry 3), while sterically demanding Mg(Ni-Prt-Bu)₂·2LiCl gave no conversion (entry 4). Mg(TMP)₂·2LiCl¹⁴ gave the products in 73% yields (entry 5), while the Knochel-Hauser base¹¹ gave no cycloadducts with 82% recovery of cyclohexenyl triflate 24 (entry 6). The use of LiTMP¹⁰ or LDA^{9,21} provided the cycloadducts as a mixture in comparable yields at 0 °C (entries 7 and 8).

Table 3. Effects of bases on the ratio of cycloadducts from cyclohexyne and 1,2-cyclohexadiene.^a



^a Reaction conditions: cyclohexenyl triflate **24** (0.60 mmol), base (1.8 mmol), 1,3-diphenylisobenzofuran (**18**) (0.90 mmol), THF, 60 °C, 3 h. ^b Yields determined from ¹H NMR spectra using 1,1,2,2tetrachloroethane as internal standard. ^c Reaction conditions: rt, 8 h. ^d Not observed. ^e Recovery of **24**: 10%. ^f Recovery of **24**: 8%. ^g Recovery of **24**: 82%. ^h Reaction conditions: 0 °C, 30 min.

2.2.3. Generation of 1,2-cyclohexadiene from cyclohexenyl triflate bearing two methyl groups at the 3-position

Encouraged by these results, we envisaged that cyclohexenyl triflate **15**, bearing two methyl substituents at the same allylic position, would favor the generation of 1,2-cyclohexadiene rather

than cyclohexyne. Cyclohexenyl triflate **15** was readily prepared from inexpensive 3-methyl-2-cyclohexenone (**14**) by one-pot 1,4addition using MeLi/CuI followed by triflation of the resulting enolate (Scheme 4). The starting triflate **15** was treated with Mg(TMP)₂·2LiCl in the presence of isobenzofuran **18** at 60 °C for 3 h to give cycloadducts **29** and **30** in 49% and 38% yields²² (Table 4, entry 1). These results showed that the additional methyl group led to exclusive generation of 1,2-cyclohexadiene. Using Mg(N*i*-Pr₂)₂·2LiCl resulted in a slight improvement in the yields of cycloadducts **29** and **30** (entry 2). The combined yield of cycloadducts **29** and **30** was increased to 98%, compared to Mg(TMP)₂·2LiCl (entry 3).



Scheme 4. Synthesis of 3,3-dimethylcyclohexenyl triflate (15) from commercially available enone 14.

Table 4. Exclusive generation of 1,2-cyclohexadiene fromcyclohexenyl triflate 15.ª



^a Reaction conditions: cyclohexenyl triflate **15** (0.30 mmol), base (0.90 mmol), 1,3-diphenylisobenzofuran (**18**) (0.45 mmol), THF (1.3 mL), 60 °C, 3 h. ^b Isolated yield. ^c Reaction conditions: 0 °C, 30 min. ^d Yields determined from ¹H NMR spectra using 1,1,2,2-tetrachloroethane as internal standard.

As shown in Table 2, cyclohexenyl triflate 13g, in which the allylic carbon was substituted with two methyl groups, was treated with Mg(TMP)₂·2LiCl at room temperature in the presence of 1,3-diphenylisobenzofuran (18), affording corresponding cycloadduct 19g in 75% yield.²³ In contrast, cyclohexenyl triflate 15 was exclusively converted to 1,2cyclohexadiene 16, despite bearing an olefinic proton. Subsequent cycloaddition gave a mixture of cycloadduct 29 and 30 in 87% combined yield. Careful inspection of the ¹H NMR spectrum of the crude product indicated no formation of cycloadduct 19g derived from the corresponding cyclohexyne and isobenzofuran 18. These contrasting results were attributed to the steric effect of the two methyl substituents, which prohibited access of the sterically demanding amide base to the congested olefinic proton. Furthermore, these results excluded the possibility of in-situ isomerization between 1.2cyclohexadiene 16 and cyclohexyne.

2.3. [3+2] and [2+2] cycloadditions of cycloallene.

-pr The generated 4,4-dimethyl-1,2-cyclohexadiene (**16**) also underwent [3+2] cycloaddition with nitrone **31** under heating to give a mixture of isoxazolidines *endo*-**32** and *endo*-**33** in 57% combined yield (Scheme 5). The regioisomers were identified from the coupling pattern of the alkenyl proton in the ¹H NMR spectrum. The *endo* stereochemistry was confirmed by nuclear Overhauser effect (NOE) experiments, with an NOE observed between the allylic methine proton on the cyclohexene ring and the proton on the phenyl group, in accordance with a previous report^{lai} by the Garg group.



Scheme 5. [3+2] Cycloaddition of 1,2-cyclohexadiene 16 and nitrone 31.

These results prompted us to conduct [2+2] cycloaddition using styrene. Mg(TMP)₂·2LiCl was added to a THF solution of cyclohexenyl triflate 15 and styrene (34), and the resulting solution was heated at 60 °C for 3 h to provide a mixture of four diastereomers 35 and 36 in 82% combined yield (Scheme 6). The structures of the four cycloadducts were assigned using ¹H NMR spectra, according to a previous report^{24a} of Moore and Moser that describes the reaction of nonsubstituted 1,2-cyclohexadiene and styrene. First, regioisomers 35 and 36 were identified from their alkenyl proton coupling patterns. Both exo-35 and endo-35 showed a singlet signal corresponding to the alkenyl proton, while exo-36 and endo-36 showed a multiplet signal in the olefinic region. The exo/endo stereochemistry was determined by the chemical shift of the benzylic proton, with endo isomers showing signals at δ 3.90 and 3.65 ppm (ddd). The downfield chemical shift was attributed to the deshielding effect of the carbon-carbon double bond. The ratio of exo- to endo-isomers was 1.7:1.0.



Scheme 6. [2+2] Cycloaddition of 1,2-cyclohexadiene 16 and styrene (34).

The 1,2-cyclohexadiene 16 generated using this deprotonative method underwent various cycloaddition reactions, although the corresponding cyclohexyne (1) from cyclohexenyl triflate 13a only reacted smoothly with 1,3-diphenylisobenzofuran (18) under these conditions. In contrast, a cyclohexyne generated by a combination of a silylated cyclohexenyl triflate and fluoride ion underwent [3+2] cycloaddition with nitrone 31 based on the report of Garg.1ai These results implied that the cycloaddition of cyclohexynes with various ynophiles, except for 18, was inhibited by the faster formation of enamine $\mathbf{20}$ in our magnesium bisamide-mediated deprotonative method. In the case of 1,2-cyclohexadiene 16, cyclohexenyl triflate 15 was converted into cycloadducts 29 and 30 in 87% yield without detection of the corresponding enamines. These observations indicated that 1,2-cyclohexadienes were not susceptible to nucleophilic attack by the amide base, and that the deprotonative

generation of 1,2-cyclohexadienes has applications in the r construction of such fused cyclic systems.

3. Conclusions

In conclusion, we have developed a deprotonative generation of highly strained cyclohexyne and 1.2cyclohexadiene using magnesium bisamides. When the reaction was conducted using nonsubstituted cyclohexenyl triflate or cyclohexenyl triflates bearing substituents at the 6-position, cyclohexynes were generated. We have also reported the steric effects of substituents at the 2- and 3-positions of the cyclohexenyl triflate. Selective allylic deprotonation was accomplished by introducing two methyl groups at the α -position of the alkenyl proton in the starting triflate. The resultant 1,2cyclohexadiene reacted with nitrone or styrene to afford the corresponding cycloadducts, apart from cyclohexyne, under the same reaction conditions. This method allows cyclohexynes and 1,2-cyclohexadienes to be generated in a two-pot conversion from readily available ketones or enones. Further synthetic applications of this method will be reported in due course.

4. Experimental Section

4.1. General

Analytical thin layer chromatography (TLC) was performed on Merck 60 F₂₅₄ aluminum sheets precoated with a 0.25 mm thickness of silica gel. Melting points (m.p.) were measured on a Yanaco MP-J3 and are uncorrected. Infrared (IR) spectra were recorded on a Bruker Alpha with an ATR attachment (Ge) and are reported in wave numbers (cm⁻¹). ¹H NMR (400 MHz), ¹³C NMR (100 MHz), and ¹⁹F NMR (376 MHz) spectra were measured on a JEOL ECZ400 spectrometer. Chemical shifts for ¹H NMR are reported in parts per million (ppm) downfield from tetramethylsilane with the solvent resonance as the internal standard (CHCl₃: δ 7.26 ppm) and coupling constants are in Hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad. Chemical shifts for ¹³C NMR are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (CDCl₃: δ 77.16 ppm). Chemical shifts for ¹⁹F NMR are reported in ppm from CFCl₃ where C_6F_6 (δ –164.9 ppm) was used as the internal standard. High-resolution mass spectra (HRMS) were performed on a JEOL JMS-T100LP AccuTOF LC-Plus (ESI) with a JEOL MS-5414DART attachment. The experimental protocol of preparation of the metal amides and the physicochemical data of cyclic enol triflates 13a-e and 13g-j, cycloadducts 19a-e, 19g-j were described in our previous report.^{8a,8b}

4.2. Materials

Unless otherwise stated, all reactions were conducted in flame-dried glassware under an inert atmosphere of argon. All work-up and purification procedures were carried out with reagent solvents in air. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Flash column chromatography was performed on Wakogel[®] C-300 (45–75 μ m, Fujifilm Wako Pure Chemical Co.). Recycling preparative SEC-HPLC was performed with LC-9201 (Japan Analytical Industry Co., Ltd.) equipped with preparative SEC columns (JAI-GEL-1H and JAI-GEL-2H). Anhydrous THF was purchased from Wako Pure Chemical Industries, Ltd.

4.3. Preparation of cyclohexenyl triflates

4.3.1. 6-Methylcyclohex-1-en-1-yl trifluoromethanesulfonate (13f). A flame-dried two-necked 50-mL flask equipped with a Teflon-coated magnetic stirring bar and a rubber septum was charged with THF (3.0 mL). After the flask was cooled to -78 °C, LDA (1.5 M in THF/heptane/ethylbenzene, 3.7 mL, 5.6 mmol) was added. To the resulting solution was added 2methylcyclohexanone (0.61 mL, 5.0 mmol) in THF (1.0 mL) dropwise over 3 min, and the resulting solution was stirred at -78 °C for 20 min. N-Phenyl-bis(trifluoromethanesulfonimide) (1.89 g, 5.3 mmol) in THF (6.0 mL) was added, and the reaction mixture was allowed to warm to room temperature for 40 min. After the solution was treated with water and diethyl ether, the resulting mixture was extracted twice with diethyl ether (10 mL). The combined organic extracts were washed with 1 M aqueous sodium hydroxide and brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane) to afford the corresponding cyclohexenyl triflate 13f (0.638 g, 2.61 mmol, 52%) as a colorless oil. $R_f = 0.26$ (hexane); The spectroscopic data were corresponding with those reported in the literature. $^{25}\ ^1\mathrm{H}$ NMR $(400 \text{ MHz}, \text{CDCl}_3)$: δ 5.73 (td, 1H, J = 4.0, 1.2 Hz), 2.60–2.48 (m, 1H), 2.20-2.13 (m, 2H), 1.98-1.88 (m, 1H), 1.72-1.51 (m, 2H), 1.51–1.41 (m, 1H), 1.14 (d, 3H, J = 6.8 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 135.5, 118.7 (q, ${}^{1}J_{C-F}$ = 318 Hz), 118.4, 32.5, 31.6, 24.6, 19.3, 17.9; ${}^{19}F$ NMR (376 MHz, CDCl₃): δ –77.3.

4.3.2. 2-Phenylcyclohex-1-en-1-yl trifluoromethanesulfonate (21). A flame-dried two-necked 50-mL flask equipped with a Tefloncoated magnetic stirring bar and a rubber septum was charged with NaH (60% in oil, 0.234 g, 5.9 mmol) and DMF (15 mL). After the resulting suspension was cooled to 0 °C, 2phenylcyclohexanone (0.869 g, 5.0 mmol) in DMF (5.0 mL) was added dropwise. After the reaction mixture was allowed to warm to room temperature and stirred for 1 h, N-Phenylbis(trifluoromethanesulfonimide) (1.82 g, 5.1 mmol) in DMF (8.0 mL) was added to the flask, at which time the reaction was stirred for 22 h. The reaction was quenched with water and diluted with diethyl ether. After the resulting mixture was extracted twice with diethyl ether (15 mL), the combined organic extracts were washed twice with water and brine. The organic extracts were dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane/ $Et_2O = 9:1$) to afford the corresponding cyclohexenyl triflate 21 (1.00 g, 3.26 mmol, 65%) as a colorless oil. $R_f = 0.44$ (hexane/Et₂O = 9:1); The spectroscopic data were corresponding with those reported in the literature.²⁶ ¹H NMR (400 MHz, CDCl₃): δ 7.41–7.21 (m, 5H), 2.53–2.44 (m, 4H), 1.92-1.83 (m, 2H), 1.83-1.73 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 143.9, 137.1, 131.2, 128.4, 128.2, 128.0, 118.2 (q, ¹*J*_{C-} $_{\rm F}$ = 318 Hz), 31.4, 28.2, 23.1, 22.1; ¹⁹F NMR (376 MHz, CDCl₃): δ-78.3.

4.3.3. 3-Methylcyclohex-1-en-1-yl trifluoromethanesulfonate (24). A flame-dried two-necked 500-mL flat-bottomed flask equipped with a Teflon-coated magnetic stirring bar and a rubber septum was charged with CuI (1.90 g, 10 mmol) and anhydrous diethyl ether (10 mL). After the resulting suspension was cooled to 0 °C, MeLi (3.0 M in diethoxymethane, 6.7 mL, 20 mmol) was added dropwise over 3 min. The pale yellow solution was stirred for 30 min, at which time the flask was cooled to -78 °C. To the solution was added 2-cyclohexen-1-one (0.96 mL, 10 mmol) in THF (10 mL) dropwise over 3 min, and the resulting solution was stirred at -78 °C for 2 h. The reaction mixture was allowed to warm to 0 °C and stirred for 2 h. *N*-Phenylbis(trifluoromethanesulfonimide) (3.76 g, 10.5 mmol) in THF (21

mL) was added to the flask via cannula, and the reaction mixture was stirred at 0 °C for 3 h. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched with saturated aqueous ammonium chloride. To the reaction mixture was added hexane, and the mixture was transferred to a separatory funnel. After separation of the organic layer, and the aqueous layer was extracted with hexane three times. The combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane) to afford the corresponding cyclohexenyl triflate 24 (1.17 g, 4.79 mmol, 48%) as a colorless oil. $R_f = 0.22$ (hexane); IR (ATR, cm⁻¹): 2936, 2873, 1416, 1244, 1205, 1142, 978, 958, 882, 810, 609; ¹H NMR (400 MHz, CDCl₃): δ 5.62 (m, 1H), 2.47-2.21 (m, 3H), 1.93-1.83 (m, 1H), 1.82-1.62 (m, 2H), 1.23-1.12 (m, 1H), 1.05 (d, 3H, J = 6.8 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 149.3, 124.2, 118.7 (q, ¹J_{C-F} = 318 Hz), 30.0, 29.8, 27.6, 21.5, 21.0; ¹⁹F NMR (376 MHz, CDCl₃): δ -77.0; HRMS (DART⁺) m/z: calcd. for C₈H₁₂F₃O₃S, 245.0459 [M+H]⁺; found, 245.0448.

4.3.4. 3,3-Dimethylcyclohex-1-en-1-yl trifluoromethanesulfonate (15). A flame-dried 100-mL Schlenk tube equipped with a Teflon-coated magnetic stirring bar and a rubber septum was charged with CuI (2.82 g, 14.8 mmol) and anhydrous diethyl ether (15 mL). After the resulting suspension was cooled to 0 °C, MeLi (3.0 M in diethoxymethane, 9.9 mL, 30 mmol) was added dropwise over 4 min. The pale yellow solution was stirred for 30 min, at which time it was cooled to -78 °C. To the solution was added 3-methyl-2-cyclohexen-1-one (1.68 mL, 14.8 mmol) in THF (15 mL) dropwise over 10 min, and the resulting solution was stirred at -78 °C for 1.5 h. The reaction mixture was allowed to warm to 0 °C and stirred for 2.5 h. N-Phenylbis(trifluoromethanesulfonimide) (5.57 g, 15.6 mmol) in THF (21 mL) was added, and the reaction mixture was allowed to warm to room temperature for 4 h. The reaction was quenched with saturated aqueous ammonium chloride. To the reaction mixture was added hexane, and the mixture was transferred to a separatory funnel. After separation of the organic layer, and the aqueous layer was extracted with hexane three times. The combined organic extracts were washed with 1 M aqueous sodium hydroxide and brine, dried over anhydrous sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane) to afford the corresponding cyclohexenyl triflate 15 (2.03 g, 7.86 mmol, 53%) as a colorless oil. $R_f = 0.22$ (hexane); IR (ATR, cm⁻¹): 2961, 2871, 1417, 1245, 1142, 1025, 952, 880, 849, 608; ¹H NMR (400 MHz, CDCl₃): δ 5.51 (s, 1H), 2.27 (td, 2H, J = 6.4, 1.6 Hz), 1.79 (tt, 2H, J = 6.4, 6.0 Hz), 1.45–1.40 (m, 2H), 1.06 (s, 6H); ¹³C NMR (100 MHz, CDCl₃): δ 148.4, 128.1, 118.7 (q, ${}^{1}J_{C-F}$ = 318 Hz), 36.0, 33.1, 29.3, 27.7, 19.9; ${}^{19}F$ NMR (376 MHz, CDCl₃): δ –76.9; HRMS $(DART^{+})$ m/z: calcd. for C₉H₁₄F₃O₃S, 259.0616 [M+H]⁺; found, 259.0607.

4.4. [4+2] Cycloaddition with 1,3-Diphenylisobenzofuran

4.4.1. Generation of 1-phenyl-1,2-cyclohexadiene (22) from the cyclohexenyl triflate 21. A flame-dried 20-mL Schlenk tube equipped with a Teflon-coated magnetic stirring bar and a rubber septum was charged with cyclohexenyl triflate 21 (155.2 mg, 0.507 mmol), 1,3-diphenylisobenzofuran (18) (207 mg, 0.77 mmol), and anhydrous THF (1.5 mL). To the mixture was added Mg(TMP)₂·2LiCl (0.272 M, 5.6 mL, 1.5 mmol) at room temperature. After stirring at 60 °C for 3 h, the reaction mixture was treated with saturated aqueous ammonium chloride. The resulting mixture was extracted twice with diethyl ether (2 mL). The combined organic extracts were washed with brine, dried

over anhydrous sodium sulfate and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane/CH₂Cl₂ = 5:1 to 3:1, gradient) to afford the title compound the *endo*-**23** (white solid, 129 mg, 0.302 mmol, 60%) and *exo*-**23** (pale greenish yellow solid, 43.4 mg, 0.102 mmol, 20%), respectively.

4.4.2. rac - (9R, 9aS, 10S) - 9, 9a, 10-triphenyl-1,2,3,9,9a, 10hexahydro-9,10-epoxyanthracene (endo-23)^{18b} R_f = 0.12 (hexane/CH₂Cl₂ = 5:1); M.p. 192–193 °C; IR (ATR, cm⁻¹): 3060, 3034, 2941, 1601, 1494, 1456, 1306, 1001, 909, 741, 699; ¹H NMR (400 MHz, CDCl₃): δ 8.04–7.99 (m, 2H), 7.62–7.48 (m, 4H), 7.46–7.40 (m, 2H), 7.31–7.12 (m, 6H), 7.01–6.91 (m, 5H), 5.95 (dd, 1H, *J* = 4.8, 3.2 Hz), 2.67 (dt, 1H, *J* = 12.0, 3.6 Hz). 2.03–1.81 (m, 2H), 1.57–1.47 (m, 1H), 1.34–1.19 (m, 1H), 0.95 (td, 1H, *J* = 12.8, 4.0 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 150.2, 147.7, 145.3, 142.3, 137.9, 135.2, 129.7, 128.8, 128.7, 128.5, 127.9, 127.5, 127.0, 126.8, 125.7, 125.6, 125.4, 123.5, 122.1, 117.5, 93.5, 89.3, 56.7, 32.1, 24.1, 18.8; HRMS (DART⁺) *m/z*: calcd. for C₃₂H₂₇O, 427.2062 [M+H]⁺; found, 427.2063.

4.4.3. rac-(9R,9aR,10S)-9,9a,10-triphenyl-1,2,3,9,9a,10hexahydro-9,10-epoxyanthracene (exo-23)^{18b} $R_f = 0.21$ (hexane/CH₂Cl₂ = 5:1); M.p. 230–231 °C; IR (ATR, cm⁻¹): 3031, 2947, 1602, 1497, 1447, 1305, 998, 909, 743, 700; ¹H NMR (400 MHz, CDCl₃): δ 7.88–7.83 (m, 2H), 7.77–7.72 (m, 2H), 7.58 (dd, 2H, J = 7.6, 7.6 Hz), 7.49 (dd, 2H, J = 7.6, 7.6 Hz), 7.47–7.34 (m, 4H), 7.32-7.27 (m, 1H), 7.13-7.04 (m, 2H), 6.90-6.82 (m, 2H), 6.76 (brs, 1H), 6.01 (brs, 1H), 5.78 (dd, 1H, J = 6.8, 2.8 Hz), 2.01–1.83 (m, 2H), 1.55–1.35 (m, 3H), 1.32–1.15 (m, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 148.9, 146.9, 144.8, 141.3, 137.6, 136.6, 128.6, 128.1, 127.6, 127.5, 127.0, 126.7, 126.5, 126.4, 126.1, 126.0, 120.9, 119.7, 119.2, 92.1, 89.9, 56.3, 30.5, 21.3, 17.6 (one aromatic signal is missing due to overlapping); HRMS $(DART^{+})$ m/z: calcd. for C₃₂H₂₇O, 427.2062 [M+H]⁺; found, 427.2053.

4.4.4. Generation of cyclohexyne 25 and cycloallene 26 from cyclohexenyl triflate 24. A flame-dried 20-mL Schlenk tube equipped with a Teflon-coated magnetic stirring bar and a rubber septum was charged with cyclohexenyl triflate 24 (146.5 mg, 0.600 mmol), 1,3-diphenylisobenzofuran (18) (246 mg, 0.91 mmol), and anhydrous THF (2.3 mL). To the mixture was added Mg(TMP)₂·2LiCl (0.305 M, 5.9 mL, 1.8 mmol, 3.0 equiv) at room temperature. After stirring at 60 °C for 3 h, the reaction mixture was treated with saturated aqueous ammonium chloride. The resulting mixture was extracted twice with diethyl ether (2 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane/ $CH_2Cl_2 = 5:1$ to 1:1, gradient) to afford a mixture of cycloadducts with cyclohexyne (19f: 38%) and 1,2cyclohexadiene (27 and 28: 35%). The yields of cycloadducts 19f, 27 and 28 were determined by ¹H NMR analysis using 1,1,2,2-tetrachloroethane (50.2 mg, 0.299 mmol) as an internal standard by comparing relative values of integration for the peaks observed at 0.73 ppm and 0.60 ppm (19f: 3 protons) and 5.74-5.45 ppm 27 and 28: 1 proton) with that of 1,1,2,2tetrachloroethane observed at 5.96 ppm. Cycloadducts endo-19f and exo-19f were prepared by the same reaction of 6methylcyclohex-1-en-1-yl trifluoromethanesulfonate (13f) and isobenzofuran 18.

4.4.5. *1-Methyl-9,10-diphenyl-1,2,3,4,9,10-hexahydro-9,10-epoxyanthracene (19f)*. The title compound was synthesized in 72% yield as a 3:2 diastereomeric mixture from cyclohexenyl triflate **13f** and isobenzofuran **18**. $R_f = 0.15-0.10$ (hexane/CH₂Cl₂ = 5:1); IR (ATR, cm⁻¹): 2931, 2869, 1451, 1307, 998, 909, 745,

733, 702; ¹H NMR (400 MHz, CDCl₃): δ 7.88–7.79 (m, 2H), r 7.75–7.70 (m, 1H), 7.68–7.63 (m, 1H), 7.55–7.31 (m, 7H), 7.24– 7.15 (m, 1H), 7.05–6.91 (m, 2H), 2.88–2.76 (m, 0.6H), 2.53–2.43 (m, 0.4H), 2.32–2.21 (m, 1H), 2.06–1.88 (m, 1H), 1.82–1.70 (m, 0.6H), 1.66–1.55 (m, 2H), 1.44–1.32 (m, 0.8H), 1.11–1.01 (m, 0.6H), 0.73 (d, 1.8H, *J* = 6.8 Hz), 0.60 (d, 1.2H, *J* = 7.2 Hz); ¹³C NMR (100 MHz, CDCl₃): δ 153.9, 153.1, 152.7, 152.1, 151.7, 151.5, 149.7, 136.7, 135.8, 135.6, 135.5, 128.9, 128.7, 128.5, 128.44, 128.41, 127.73, 127.66, 127.5, 126.4, 126.1, 125.3, 124.74, 124.68, 124.5, 120.9, 119.2, 118.93, 118.89, 93.2, 92.01, 91.98, 91.6, 31.7, 30.6, 29.5, 27.1, 24.2, 24.0, 20.5, 19.3, 18.3, 17.4; HRMS (DART⁺) *m*/z: calcd. for C₂₇H₂₅O, 365.1905 [M+H]⁺; found, 365.1899.

4.4.6. The mixture of cycloadducts **27** and **28** from 1,2cyclohexadiene **26**. IR (ATR, cm⁻¹): 2931, 2853, 1452, 1339, 997, 745, 702, 633; HRMS (DART⁺) m/z: calcd. for C₂₇H₂₅O, 365.1905 [M+H]⁺; found, 365.1896.

4.4.7. Generation of 1,2-cyclohexadiene 16 from cyclohexenyl triflate 15. A flame-dried 20-mL Schlenk tube equipped with a Teflon-coated magnetic stirring bar and a rubber septum was charged with cyclohexenyl triflate 15 (77.2 mg, 0.299 mmol), 1,3-diphenylisobenzofuran (18) (123.6 mg, 0.457 mmol), and anhydrous THF (1.27 mL). To the mixture was added Mg(Ni-Pr-2)2·2LiCl (0.319 M, 2.81 mL, 0.90 mmol, 3.0 equiv) at room temperature. After stirring at 60 °C for 3 h, the reaction mixture was treated with saturated aqueous ammonium chloride. The resulting mixture was extracted twice with diethyl ether (2 mL). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated under reduced pressure to give a crude material. The yields of cycloadducts 29 and 30 were determined by ¹H NMR analysis using 1,1,2,2-tetrachloroethane (37.8 mg, 0.225 mmol) as an internal standard by comparing relative values of integration for the peaks observed at 5.70-5.66 ppm (endo) and 5.66-5.61 ppm (exo) (29: 1 proton), and 5.38 ppm (endo) and 5.32-5.30 ppm (exo) (30: 1 proton) with that of 1,1,2,2tetrachloroethane observed at 5.96 ppm. Silica gel chromatography (hexane/ $CH_2Cl_2 = 5:1$ to 1:1, gradient) of the crude material provided analytically pure exo-29 (16%), exo-30 (15%), and a mixture of endo-29 and endo-30.

Structure elucidation of four regio- and stereoisomers. We identified the structure of the four cycloadducts by ¹H NMR spectra, according to the Guitián's report.^{5b} The regioisomers **29** and **30** were determined by their coupling pattern of the alkenyl proton (**29**: multiplet, **30**: doublet). In addition, the *exo/endo* stereochemistry was determined by chemical shifts of the allylic methine proton. Guitián reported that the chemical shifts of the allylic methine proton of the cycloadducts with 1,2-cyclohexadiene and isobenzofuran **18** was observed at 3.05 ppm (*endo*) and 2.52 ppm (*exo*). They also determined the structure of *endo*-isomer absolutely by X-ray crystallography. In this case, the peaks of methine proton of **29** were observed at 3.32–3.27 ppm and 2.61–2.56 ppm. We assigned the former one is *endo*-isomer and the latter one is *exo*-isomer by comparing these chemical shifts.

4.4.8. rac-(9R,9aS,10R)-1,1-Dimethyl-9,10-diphenyl-1,2,3,9,9a,10-hexahydro-9,10-epoxyanthracene (exo-**29**). The title compound was obtained as a colorless solid in 16% yield (18.6 mg, 0.049 mmol) from cyclohexenyl triflate **15** (0.299 mmol) according to the above procedure. $R_f = 0.19$ (hexane/CH₂Cl₂ = 5:1); M.p. 149–152 °C; IR (ATR, cm⁻¹): 2917, 2871, 1448, 1017, 979, 741, 704, 644, 555; ¹H NMR (400 MHz, CDCl₃): δ 7.87–7.83 (m, 2H), 7.82–7.77 (m, 2H), 7.55 (t, 2H, J =7.6 Hz), 7.48 (t, 2H, J = 7.6 Hz), 7.46–7.41 (m, 2H), 7.38–7.34 (m, 2H), 7.20–7.11 (m, 2H), 5.66–5.61 (m, 1H), 2.61–2.56 (m, -1H), 2,12–2.01 (m, 1H), 1.99–1.84 (m, 1H), 1.39–1.28 (m, 1H), 1.18–1.14 (m, 1H), 0.78 (s, 3H), 0.64 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 150.1, 145.2, 139.9, 137.8, 136.8, 128.5, 127.7, 127.5, 127.32, 127.27, 126.8, 126.6, 126.2, 119.6, 118.5, 118.3, 89.1, 88.6, 56.4, 38.9, 33.9, 31.0, 23.2, 18.5; HRMS (DART⁺) *m/z*: calcd. for C₂₈H₂₇O, 379.2062 [M+H]⁺; found, 379.2044.

4.4.9. rac-(9S,9aR,10S)-3,3-Dimethyl-9,10-diphenyl-1,2,3,9,9a,10-hexahydro-9,10-epoxyanthracene (exo-**30**). The title compound was obtained as a colorless solid in 15% yield (16.9 mg, 0.045 mmol) from cyclohexenyl triflate 15 (0.299 mmol) according to the above procedure. $R_f = 0.15$ (hexane/CH₂Cl₂ = 5:1); M.p. 101–104 °C; IR (ATR, cm^{-1}): 2954, 2930, 2860, 1457, 1449, 1211, 1020, 872, 739, 702, 666; ¹H NMR (400 MHz, CDCl₃): δ 7.77-7.72 (m, 2H), 7.70-7.64 (m, 2H), 7.58–7.47 (m, 4H), 7.45–7.35 (m, 2H), 7.31–7.26 (m, 1H), 7.18–7.10 (m, 3H), 5.32–5.30 (m, 1H), 2.53 (ddd, 1H, J = 12.0, 4.0, 0.8 Hz), 1.71-1.62 (m, 1H), 1.37-1.23 (m, 2H), 0.97 (s, 3H), 0.95–0.85 (m, 1H), 0.77 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 150.2, 144.7, 139.9, 137.1, 136.3, 128.8, 128.5, 127.5, 127.3, 126.9, 126.6, 126.1, 125.9, 120.1, 117.8, 89.7, 88,8, 48.5, 37.8, 33.0, 31.1, 30.1, 24.6 (one aromatic signal is missing due to overlapping); HRMS (DART⁺) m/z: calcd. for C₂₈H₂₇O, 379.2062 [M+H]⁺; found, 379.2061.

*rac-(9R,9aR,10R)-1,1-Dimethyl-9,10-diphenyl-*4.4.10. 1,2,3,9,9a,10-hexahydro-9,10-epoxyanthracene (endo-29) and rac-(9S,9aS,10S)-3,3-Dimethyl-9,10-diphenyl-1,2,3,9,9a,10hexahydro-9,10-epoxyanthracene (endo-30). The title compounds were obtained as a pale green solid in 62% ¹H NMR yields (endo-29/endo-30 = 36:26) (71.0 mg, 0.187 mmol) from cyclohexenyl triflate 15 (0.299 mmol) according to the above procedure. $R_f = 0.27$ (endo-30), 0.24 (endo-29) (hexane/CH₂Cl₂ = 1:1); IR (ATR, cm⁻¹): 2953, 2931, 1455, 1355, 1303, 988, 904, 753, 700, 562; ¹H NMR (400 MHz, CDCl₃): δ 8.00–7.93 (m, 2H), 7.90-7.81 (m, 4H), 7.73-7.68 (m, 2H), 7.62-7.58 (m, 1H), 7.53-7.35 (m, 12H), 7.26-7.17 (m, 5H), 7.17-7.08 (m, 2H), 5.70–5.66 (m, 1H (endo-29)), 5.38 (d, 1H, J = 2.8 Hz (endo-30)), 3.32-3.27 (m, 1H), 3.11-3.02 (m, 1H), 2.20-2.02 (m, 2H), 1.91-1.77 (m, 1H), 1.60-1.41 (m, 3H), 1.21-1.13 (m, 1H), 1.05 (s, 3H), 0.98 (s, 3H), 0.66–0.56 (m, 1H), 0.55 (s, 3H), 0.08 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 148.6, 148.5, 144.5, 143.8, 142.10, 142.05, 138.2, 138.0 135.4, 134.9, 130.8, 129.0, 128.8, 128.6, 128.52, 128.46, 128.4, 128.2, 128.1, 127.3, 127.1, 127.0, 125.9, 125.7, 123.8, 121.5, 118.7, 118.3, 118.0, 90.5, 90.4, 89.9, 89.4, 58.0, 49.1, 39.8, 37.8, 33.6, 32.7, 31.1, 30.7, 29.4, 24.6, 23.9, 19.2; HRMS (DART⁺) m/z: calcd. for C₂₈H₂₇O, 379.2062 [M+H]⁺; found, 379.2055.

4.5. [3+2] Cycloaddition with nitrone

A flame-dried 20-mL Schlenk tube equipped with a Tefloncoated magnetic stirring bar and a rubber septum was charged with cyclohexenyl triflate 15 (129 mg, 0.499 mmol), nitrone 31 (179 mg, 1.01 mmol), and anhydrous THF (2.1 mL). To the mixture was added Mg(TMP)₂·2LiCl (0.312 M, 6.4 mL, 2.0 mmol) at room temperature. After stirring at 60 °C for 5 h, the reaction mixture was treated with saturated aqueous ammonium chloride. The resulting mixture was extracted twice with diethyl ether (2 mL). The combined organic extracts were washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane/ethyl acetate = 9:1) to afford a mixture of cycloadducts 32 and 33 as major exo isomers (81.4 mg, 0.285 mmol, 57%) as a brown oil. The ratio of endo- and exo-isomers was determined by ¹H NMR analysis by comparing relative values of integration for

the peaks observed at 4.33–4.12 ppm, according to the report by re-JP18H04413 in the Middle Molecular Strategy, the JSPS Garg.^{1ai} predoctoral fellowship (for Y.H.), Tonen General Sekiy

4.5.1.rac-(3S,7aS)-2-(tert-Butyl)-7,7-dimethyl-3-phenyl-

2,3,5,6,7,7*a*-hexahydrobenzo[d]isoxazole (endo-**32**) and rac-(3*R*,7*aR*)-2-(tert-Butyl)-5,5-dimethyl-3-phenyl-2,3,5,6,7,7*a*hexahydro-benzo[d]isoxazole (endo-**33**). $R_f = 0.3 - 0.4$ (hexane/ethyl acetate = 9:1); IR (ATR, cm⁻¹): 2956, 2927, 2866, 1454, 1362, 1222, 1084, 703; ¹H NMR (400 MHz, CDCl₃): δ 7.50–7.44 (m, 2H), 7.33–7.26 (m, 2H), 7.24–7.18 (m, 1H), 5.31– 5.26 (m, 0.44H (endo-**32**)), 5.12 (d, 0.56H, J = 1.2 Hz (endo-**33**)), 4.49 (brs, 0.56H (endo-**33**)), 4.48–4.45 (m, 0.44H (endo-**32**)), 4.33–4.27 (m, 0.56H (endo-**33**)), 4.16–4.12 (m, 0.44H (endo-**32**)), 2.09–1.20 (m, 4H), 1.13 (s, 1.3H (endo-**32**)), 1.07 (s,

4.9H (endo-**33**)), 1.06 (s, 4.0H (endo-**32**)), 0.98 (s, 1.7H (endo-**33**)), 0.90 (s, 1.7H (endo-**33**)), 0.82 (s, 1.3H (endo-**32**)); HRMS (DART⁺) m/z: calcd. for C₁₉H₂₈NO, 286.2171 [M+H]⁺; found, 286.2167.

4.6. [2+2] Cycloaddition with styrene

A flame-dried 20-mL Schlenk tube equipped with a Tefloncoated magnetic stirring bar and a rubber septum was charged with cyclohexenyl triflate **15** (79.8 mg, 0.309 mmol), styrene (**34**: 106 μ L, 0.93 mmol), and anhydrous THF (1.3 mL). To the mixture was added Mg(TMP)₂·2LiCl (0.293 M, 3.16 mL, 0.93 mmol) at room temperature. After stirring at 60 °C for 5 h, the reaction mixture was treated with saturated aqueous ammonium chloride. The resulting mixture was extracted twice with diethyl ether (2 mL). The combined organic extracts were washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated under reduced pressure to give a crude material, which was purified by silica gel column chromatography (hexane) to afford a mixture of **35** and **36** (53.7 mg, 0.253 mmol, 82%) as a colorless oil.

Structure elucidation of four regio- and stereoisomers. The structure of the four cycloadducts was identified by ¹H NMR spectra, according to the previous report^{24a} by Moore and Moser that describes the reaction of non-substituted 1,2-cyclohexadiene and styrene. First, two regioisomers 35 and 36 were identified by their coupling pattern of the alkenyl proton. Both exo-35 and endo-35 have each singlet signal corresponding to the alkenyl proton, whereas exo-36 and endo-36 have a multiplet signal in olefinic region. The *exo/endo* stereochemistry the was determined by chemical shifts of the benzylic proton; the endo isomers have signals at δ 3.90 and 3.65 ppm (ddd). The downfield chemical shifts are attributed to the deshielding effects of the carbon-carbon double bond. The ratio of exo isomers and endo isomers was 1.7:1.0.

4.6.1. 3,3-Dimethyl-7-phenylbicyclo[4.2.0]oct-1-ene (**35**) and 5,5-Dimethyl-7-phenylbicyclo[4.2.0] oct-1-ene (**36**). $R_f = 0.50$, 0.60 (hexane); IR (ATR, cm⁻¹): 3027, 2953, 2921, 2863, 1495, 1452, 1361, 745, 697; ¹H NMR (400 MHz, CDCl₃): δ 7.34–7.14 (m, 5H), 5.38–5.30 (m, 0.15H (endo-**36**)+0.30H (exo-**36**)), 5.17 (brs, 0.21H (endo-**35**)), 5.14 (brs, 0.34H (exo-**35**)), 3.89 (ddd, 0.15H, J = 9.6, 9.6, 3.2 Hz (endo-**36**)), 3.64 (ddd, 0.21H, J = 9.6, 9.6, 2.4 Hz (endo-**35**)), 3.30–2.69 (m, 3.6H), 2.10–1.86 (m, 1.3H), 1.55–0.64 (m, 2.7H), 1.02, 1.00, 0.97 (s, total 3H), 0.92, 0.89, 0.85 (s, total 3H); HRMS (DART⁺) *m/z*: calcd. for C₁₆H₂₁, 213.1643 [M+H]⁺; found, 213.1636.

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Highlights

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Steric effects on deprotonative generation of cyclohexynes and 1,2-cyclohexadienes from cyclohexenyl triflates by magnesium amides

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- A deprotonative generation of highly strained cyclohexynes and 1,2-cyclohexadienes from cyclohexenyl triflates using magnesium bisamides.
- Substituted cyclohexenyl triflates readily prepared from ketones or enones.
- Reaction pathway determined by steric effects of substituents on the cyclohexenyl ring.
- Cycloaddition of a 1,2-cyclohexadiene with 1,3-diphenylisobenzofuran, α -phenyl-*N-tert*-butylnitrone, or styrene to afford the corresponding cycloadducts.

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Declaration of interests

 \boxtimes The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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