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Graphical Abstract

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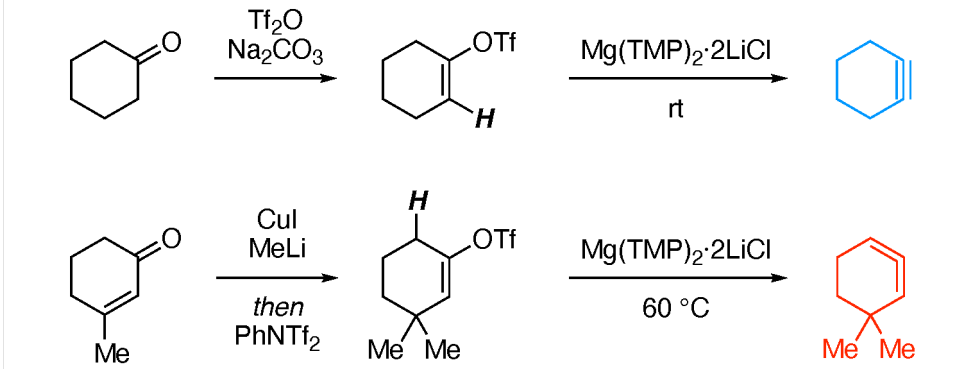

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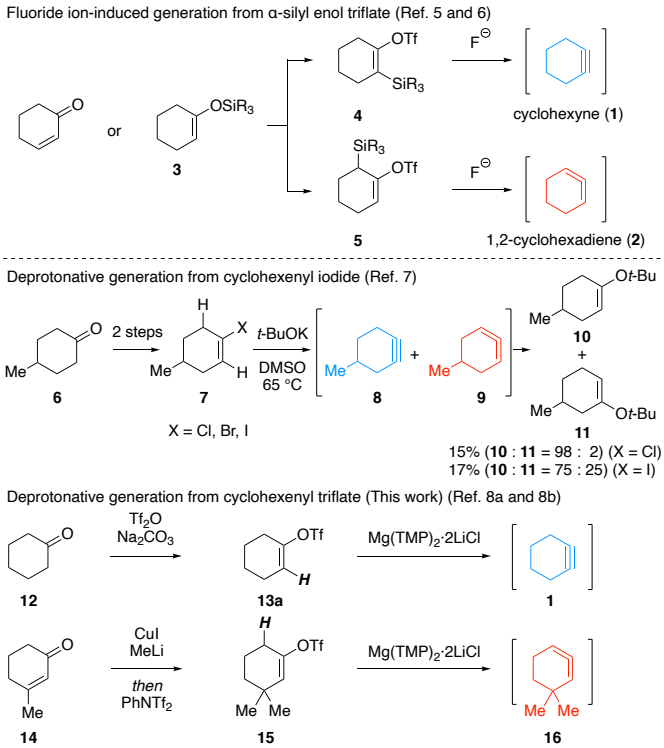
ABSTRACT

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.

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, arynes[2] and relatively stable cycloalkynes[3] 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 ion-induced generation of cyclohexyne (**1**) and 1,2-cyclohexadiene (**2**) has been synthetically reliable regarding regiochemistry and functional group compatibility[5] (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-silyl cyclohexenyl triflates by retro-Brook rearrangement of silyl enol ether **3**.[6] In contrast, a deprotonative approach starting from cyclohexenyl halide **7**, which would be more atom-economical, 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.



Scheme 1. Representative methods for generating cyclohexyne and 1,2-cyclohexadiene.

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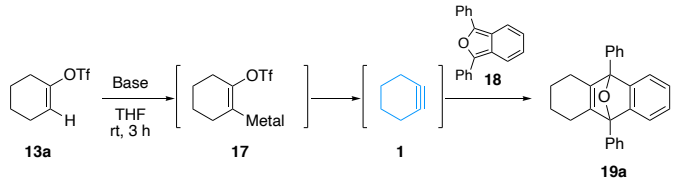
2. Results and Discussion

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(N*i*-Pr$_2$)$_2$·2LiCl	<1	38
6	Mg(N*i*-Pr*t*-Bu)$_2$·2LiCl	<1	24
7	Mg(N*t*-Am*t*-Bu)$_2$·2LiCl	91	–[c]
8	Mg(DMP)$_2$·2LiCl	<1	51
9	Mg(TMP)$_2$·2LiCl	<1	56
10[d]	Zn(TMP)$_2$·2LiCl·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*-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 ^{1}H NMR spectra using 1,1,2,2-tetrachloroethane as internal standard. [c] Not detected in the crude ^{1}H NMR spectra. [d] Reaction time: 19 h. [e] Reaction conditions: 60 °C, 3 h.

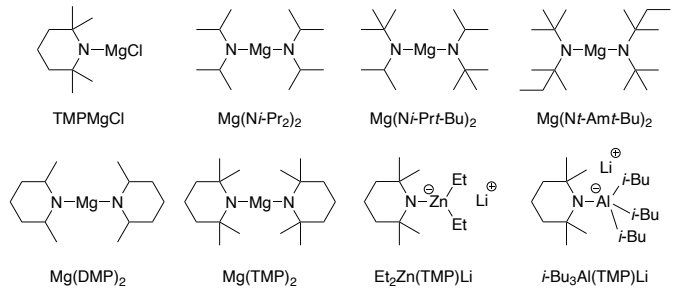
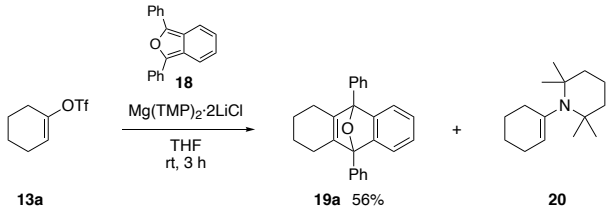


Fig. 1. Structure of metal amides.

Both lithium diisopropylamide (LDA)[9] and lithium 2,2,6,6-tetramethylpiperidide (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 ^{1}H 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*-Pr$_2$)$_2$·LiCl[12] 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)·2LiCl (Mg(DMP)$_2$·2LiCl)[13] and Mg(TMP)$_2$·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)$_2$·2LiCl·2MgCl$_2$[15] did not give the desired product, while Et$_2$Zn(TMP)Li[16] led to the formation of cycloadduct **19a**, albeit in 6% yield at 60 °C (entries 10 and 11). Furthermore, Et$_3$Al(TMP)Li and *i*-Bu$_3$Al(TMP)Li[17] 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.

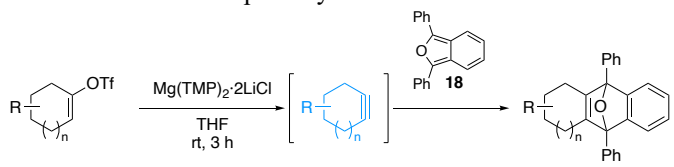
We next investigated the scope of the deprotonative generation of cyclohexynes using Mg(TMP)$_2$·2LiCl (Table 2). In addition to compound **19a**, cycloadducts **19b** and **19c** derived from cycloheptyne and cyclooctyne were obtained in 58% and 96% yields, respectively. Cyclohexenyl triflate **13d**, 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% yield.

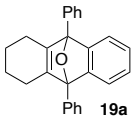
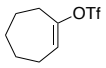
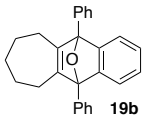
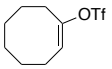
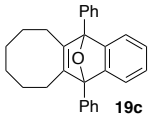
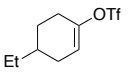
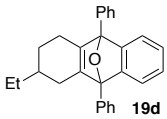
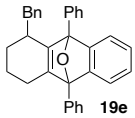
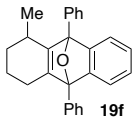
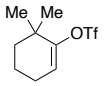
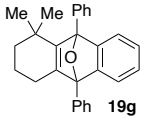
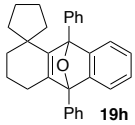
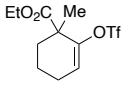
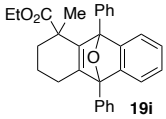
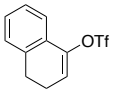
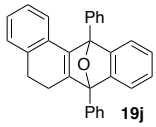
This deprotonative generation using TMP bases proceeded smoothly, owing to the low nucleophilicity of the anionic species bearing a bulky TMP group. However, the [4+2] cycloaddition of isobenzofuran **18** with cyclohexyne (**1**) generated by Mg(TMP)$_2$·2LiCl furnished corresponding cycloadduct **19a** 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.

Table 2. Substrate scope of cyclic enol triflates.



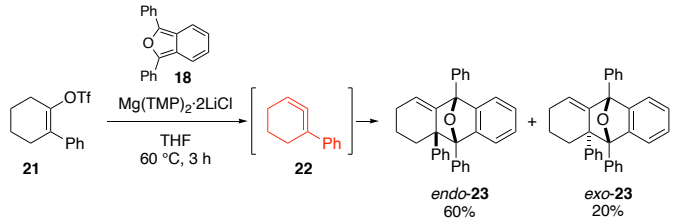
Enol triflate **13**	Cycloadduct **19**	Yield (%)[a]
 **13a**	 **19a**	55
 **13b**	 **19b**	58
 **13c**	 **19c**	96
 **13d**	 **19d**	62[c] (dr = 1:1[b])
 **13e**	 **19e**	65[d] (dr = 9:4[b])
 **13f**	 **19f**	72 (dr = 3:2[b])
 **13g**	 **19g**	75
 **13h**	 **19h**	81[e]
 **13i**	 **19i**	60 (dr = 3:2[b])
 **13j**	 **19j**	91

[a] Isolated yield. [b] Ratio of diastereomers determined by ^{1}H 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 and 1,2-cyclohexadienes from cyclohexenyl triflates

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 2-position, was converted into cycloadducts *endo*-**23** and *exo*-**23** in 60% and 20% yields, respectively (Scheme 3). The corresponding ^{1}H 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 1,2-cyclohexadiene **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**.

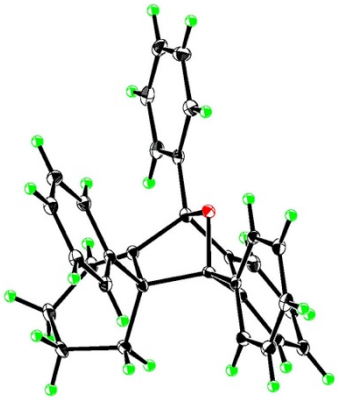


Fig. 2. ORTEP drawing of the molecular structure of (±)-*endo*-**23** with thermal ellipsoids at 30% probability levels.

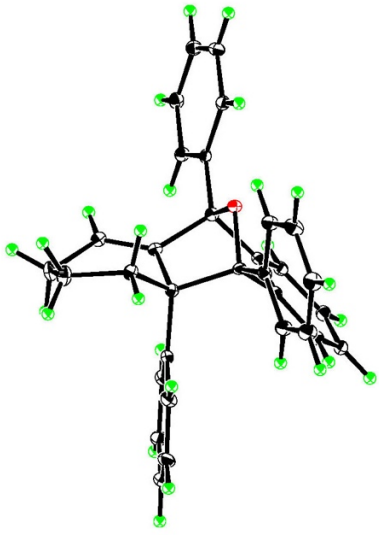
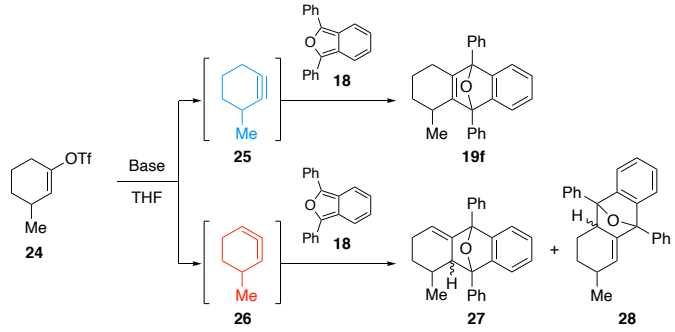


Fig. 3. ORTEP drawing of the molecular structure of (±)-*exo*-**23** with thermal ellipsoids at 30% probability levels.

2.2.2. Effect of methyl group at the 3-position on the ratio of cyclohexyne and 1,2-cyclohexadiene generated

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(N*i*-Pr$_2$)$_2$·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(NEt$_2$)$_2$·2LiCl also gave the products in lower yields (entry 3), while sterically demanding Mg(N*i*-Pr*t*-Bu)$_2$·2LiCl gave no conversion (entry 4). Mg(TMP)$_2$·2LiCl[14] gave the products in 73% yields (entry 5), while the Knochel–Hauser base[11] gave no cycloadducts with 82% recovery of cyclohexenyl triflate **24** (entry 6). The use of LiTMP[10] 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]

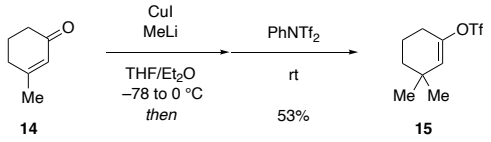


Entry	Base	**19f** (%)[b]	**27**+**28** (%)[h]
1[c,e]	Mg(N*i*-Pr$_2$)$_2$·2LiCl	36	10
2	Mg(N*i*-Pr$_2$)$_2$·2LiCl	34	17
3	Mg(NEt$_2$)$_2$·2LiCl	22	12
4[f]	Mg(N*i*-Pr*t*-Bu)$_2$·2LiCl	–[d]	–[d]
5	Mg(TMP)$_2$·2LiCl	38	35
6[g]	TMPMgCl·LiCl	–[d]	–[d]
7[h]	LiTMP	13	33
8[h]	LDA	48	14

[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 ^{1}H NMR spectra using 1,1,2,2-tetrachloroethane 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.

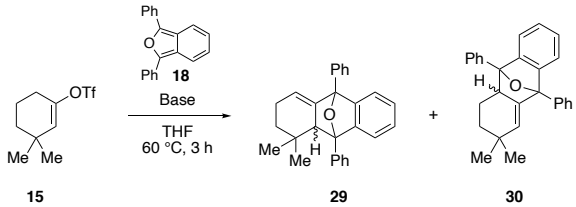
2.2.3. Generation of 1,2-cyclohexadiene from cyclohexenyl triflate bearing two methyl groups at the 3-position

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 1,4-addition 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% yields[22] (Table 4, entry 1). These results showed that the additional methyl group led to exclusive generation of 1,2-cyclohexadiene. Using Mg(N*i*-Pr$_2$)$_2$·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 from cyclohexenyl triflate **15**.[a]



Entry	Base	**29** (%)[b] (*endo*:*exo*)	**30** (%)[b] (*endo*:*exo*)
1	Mg(TMP)$_2$·2LiCl	49 (34:15)	38 (28:10)
2	Mg(N*i*-Pr$_2$)$_2$·2LiCl	55 (36:19)	45 (26:19)
3[c]	LiTMP	60 (44:16)[d]	38 (28:10)[d]

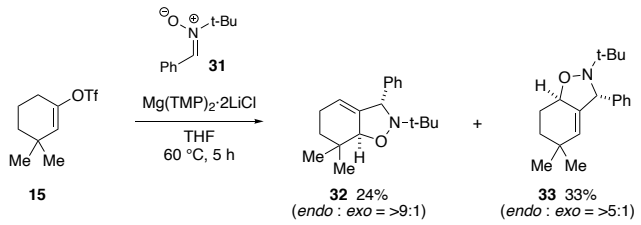
[a] Reaction conditions: cyclohexenyl triflate **15** (0.30 mmol), base (0.90 mmol), 1,3-diphenylisobenzofuran (**18**) (0.45 mmol), THF (1.3 mL), 60 °C, 3 h. [b] Isolated yield. [c] Reaction conditions: 0 °C, 30 min. [d] Yields determined from ^{1}H NMR spectra using 1,1,2,2-tetrachloroethane as internal 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 1,2-cyclohexadiene **16**, despite bearing an olefinic proton. Subsequent cycloaddition gave a mixture of cycloadduct **29** and **30** in 87% combined yield. Careful inspection of the ^{1}H 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 1,2-cyclohexadiene **16** and cyclohexyne.

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

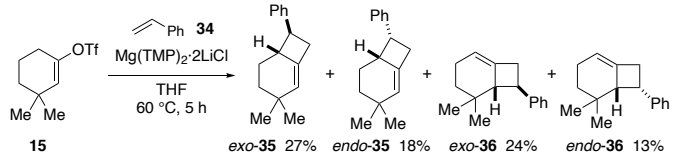
The generated 4,4-dimethyl-1,2-cyclohexadiene (**16**) also underwent [3+2] cycloaddition with nitrone **31** under heating to

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 ^{1}H 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[1ai] 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 ^{1}H 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 **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 construction of such fused cyclic systems.

3. Conclusions

In conclusion, we have developed a deprotonative generation of highly strained cyclohexyne and 1,2-cyclohexadiene 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 1,2-cyclohexadiene 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 F_{254} 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}). ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and ^{19}F NMR (376 MHz) spectra were measured on a JEOL ECZ400 spectrometer. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) downfield from tetramethylsilane with the solvent resonance as the internal standard ($CHCl_3$: 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 ^{13}C NMR are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 77.16 ppm). Chemical shifts for ^{19}F NMR are reported in ppm from $CFCl_3$ 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 μm, 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 2-methylcyclohexanone (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}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.5, 118.7 (q, $^1J_{C–F}$ = 318 Hz), 118.4, 32.5, 31.6, 24.6, 19.3, 17.9; ^{19}F NMR (376 MHz, $CDCl_3$): 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 Teflon-coated 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, 2-phenylcyclohexanone (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*-Phenyl-bis(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/Et_2O = 9:1); The spectroscopic data were corresponding with those reported in the literature.[26] ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 137.1, 131.2, 128.4, 128.2, 128.0, 118.2 (q, $^1J_{C–F}$ = 318 Hz), 31.4, 28.2, 23.1, 22.1; ^{19}F NMR (376 MHz, $CDCl_3$): 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*-Phenyl-bis(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; ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 124.2, 118.7 (q, $^1J_{C–F}$ = 318 Hz), 30.0, 29.8, 27.6, 21.5, 21.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ –77.0; HRMS ($DART^+$) *m/z*: calcd. for $C_8H_{12}F_3O_3S$, 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*-Phenyl-bis(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; ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 128.1, 118.7 (q, $^1J_{C–F}$ = 318 Hz), 36.0, 33.1, 29.3, 27.7, 19.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ –76.9; HRMS ($DART^+$) *m/z*: calcd. for $C_9H_{14}F_3O_3S$, 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/CH_2Cl_2 = 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,10-hexahydro-9,10-epoxyanthracene (endo-**23**)*[18b] R_f = 0.12 (hexane/CH_2Cl_2 = 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, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{32}H_{27}O$, 427.2062 $[M+H]^+$; found, 427.2063.

*4.4.3. rac-(9R,9aR,10S)-9,9a,10-triphenyl-1,2,3,9,9a,10-hexahydro-9,10-epoxyanthracene (exo-**23**)*[18b] R_f = 0.21 (hexane/CH_2Cl_2 = 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, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{32}H_{27}O$, 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 $Mg(TMP)_2 \cdot 2LiCl$ (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 1,2-cyclohexadiene (**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 1,1,2,2-tetrachloroethane observed at 5.96 ppm. Cycloadducts *endo*-**19f** and *exo*-**19f** were prepared by the same reaction of 6-methylcyclohex-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/CH_2Cl_2 = 5:1); IR (ATR, cm^{-1}): 2931, 2869, 1451, 1307, 998, 909, 745, 733, 702; ^1H NMR (400 MHz, $CDCl_3$): δ 7.88–7.79 (m, 2H), 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{27}H_{25}O$, 365.1905 $[M+H]^+$; found, 365.1899.

*4.4.6. The mixture of cycloadducts **27** and **28** from 1,2-cyclohexadiene **26**.* IR (ATR, cm^{-1}): 2931, 2853, 1452, 1339, 997, 745, 702, 633; HRMS ($DART^+$) *m/z*: calcd. for $C_{27}H_{25}O$, 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 $Mg(N\textit{i}\text{-}Pr\text{-}_2)_2 \cdot 2LiCl$ (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 1,1,2,2-tetrachloroethane 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/CH_2Cl_2 = 5:1); M.p. 149–152 °C; IR (ATR, cm^{-1}): 2917, 2871, 1448, 1017, 979, 741, 704, 644, 555; ^1H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{28}H_{27}O$, 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/CH_2Cl_2 = 5:1); M.p. 101–104 °C; IR (ATR, cm^{-1}): 2954, 2930, 2860, 1457, 1449, 1211, 1020, 872, 739, 702, 666; ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{28}H_{27}O$, 379.2062 $[M+H]^+$; found, 379.2061.

*4.4.10. rac-(9R,9aR,10R)-1,1-Dimethyl-9,10-diphenyl-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,10-hexahydro-9,10-epoxyanthracene (endo-**30**).* The title compounds were obtained as a pale green solid in 62% ^{1}H 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/CH_2Cl_2 = 1:1); IR (ATR, cm^{-1}): 2953, 2931, 1455, 1355, 1303, 988, 904, 753, 700, 562; ^{1}H NMR (400 MHz, $CDCl_3$): 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); ^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{28}H_{27}O$, 379.2062 $[M+H]^+$; found, 379.2055.

4.5. [3+2] Cycloaddition with nitrone

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** (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 ^{1}H NMR analysis by comparing relative values of integration for the peaks observed at 4.33–4.12 ppm, according to the report by Garg.[1ai]

*4.5.1.rac-(3S,7aS)-2-(tert-Butyl)-7,7-dimethyl-3-phenyl-2,3,5,6,7,7a-hexahydrobenzo[d]isoxazole (endo-**32**) and rac-(3R,7aR)-2-(tert-Butyl)-5,5-dimethyl-3-phenyl-2,3,5,6,7,7a-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; ^{1}H NMR (400 MHz, $CDCl_3$): 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 $C_{19}H_{28}NO$, 286.2171 $[M+H]^+$; found, 286.2167.

4.6. [2+2] Cycloaddition with styrene

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** (79.8 mg, 0.309 mmol), styrene (**34**: 106 μL, 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 ^{1}H 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 the olefinic region. The *exo/endo* stereochemistry 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; ^{1}H NMR (400 MHz, $CDCl_3$): 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 $C_{16}H_{21}$, 213.1643 $[M+H]^+$; found, 213.1636.

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Supplementary Material

Supplementary material that may be helpful in the review process should be prepared and provided as a separate electronic file. That file can then be transformed into PDF format and submitted along with the manuscript and graphic files to the appropriate editorial office.