Intramolecular Cyclizations of *o*-Acylbenzyllithiums. Formation of Benzocyclobuten-1-ol Derivatives and Their Thermal Isomerization

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The formation of benzocyclobutenol derivatives by intramolecular cyclizations of *o*-acylbenzyllithiums is described. Treatment of *o*-(trialkylsilylmethyl)phenyl ketones with lithium diisopropylamide (LDA) followed by quenching of the resulting benzylic carbanions with chlorotrialkylsilane resulted in stereoselective formation of the corresponding 1-trialkylsiloxy-2-(trialkylsilyl)benzocyclobutenes in good yields. Subsequently, *o*-acyl-*m*-methoxybenzyllithiums were found to work well in cyclization to benzocyclobuten-1-ol derivatives. The reaction of 2-benzoyl-3,4,5-trimethoxybenzyllithium, generated in situ by deprotonation of 6-methyl-2,3,4-trimethoxybenzophenone with LDA, with chlorotrimethylsilane afforded the corresponding 1-(trimethylsiloxy)benzocyclobutene. Cyclization of 2-pivaloyl-3-methoxybenzyllithiums, generated in situ from *tert*-butyl 2-methyl-6-methoxyphenyl ketones upon deprotonation with LDA, proceeded spontaneously even at −78 °C to give the corresponding benzocyclobuten-1-ols. We also describe the results of thermal isomerization of these 1-trimethylsiloxy-2-(trialkylsilyl)benzocyclobutenes.

Introduction

In our previous reports we have described the use of reactions of *o*-acylbenzyllithiums with electrophiles, such as aldehydes, ketones, ethyl chloroformate, and furan-2(5*H*)-one, for preparing heterocycles, such as isocoumarins,[1] 3-isochromanones,[2] and arylnaphthofuranone lignans.[3] In this paper we wish to describe intramolecular cyclization reactions of *o*-acylbenzyllithiums carrying appropriate substituents, which give a very rapid access to benzocyclobuten-1-ol derivatives. These derivatives are being recognized as an important class of compounds because of their versatility in organic synthesis, e.g., for use as precursors for the generation of α-oxy-*o*-quinonedimethides,[4,5] which are useful intermediates for the synthesis of polycyclic compounds,[4−6] and for the preparation of heterocycles[7] and other useful compounds.[8] Therefore, there has been continuing interest in the development of new methods for the synthesis of benzocyclobuten-1-ol derivatives, and a number of efficient methods have been reported, most of which rely on (1) 2+2 cycloaddition of benzynes with alkenes, such as vinyl acetate,[9] 1,1-dimethoxyethene,[10] or 1,1-dichloroethene,[11] followed by the appropriate treatment of the resulting benzocyclobutene derivatives, (2) photolysis of *o*-alkylphenyl ketones,[5] or (3) intramolecular cyclization of *o*-lithiated styrene oxides[4a] and related compounds.[4b,12] The present procedure makes benzocyclobuten-1-ol derivatives available, including those carrying a trialkylsilyl group at the 2-position. They are potentially useful intermediates for organic synthesis, but their preparation is less well described,[13] although the preparation of

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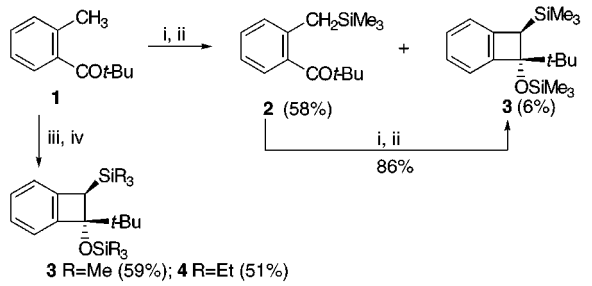
Scheme 1



Reagents and conditions: i, LDA, THF, -78 °C; ii, Me_3SiCl, -78 °C; iii, 2LDA, THF, -78 °C; iv, $2R_3SiCl$, -78 °C.

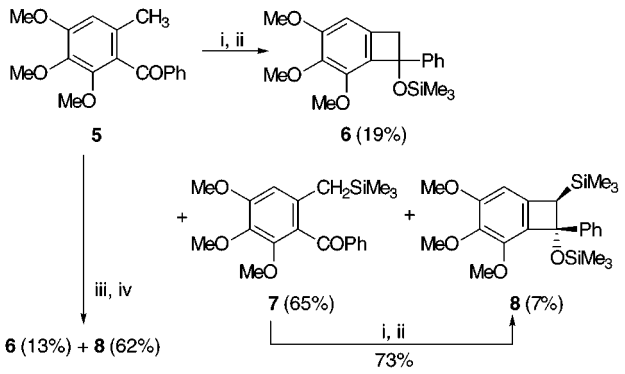
2-(trimethylsilyl)benzocyclobuten-1-ol has been recorded by Trahanovsky and Fisher.[14] We also examined thermal isomerization of some of the benzocyclobutenol derivatives prepared. The results have led to considerations on the mechanism of these cyclization reactions and the stereochemistry of the products.

Results and Discussion

Cyclization of *o*-Acylbenzyllithiums Leading to Benzocyclobutenyl Trialkylsilyl Ethers 3, 4, 6, and 8. Treatment of *tert*-butyl *o*-tolyl ketone (**1**)[1] with an equimolar amount of LDA in THF at −78 °C, followed by in situ trapping with chlorotrimethylsilane, afforded a 58% yield of the expected trimethylsilylated ketone **2**, after simple acidic workup and purification by preparative TLC on silica gel. In addition to compound **2**, an oily and very mobile product was isolated. The structure of this product was determined from spectroscopic data. The mass spectrum and elemental analysis indicated its molecular formula to be $C_{18}H_{32}OSi_2$. The infrared spectrum showed no evidence for the presence of the carbonyl group. Two singlet signals (9H each) at δ −0.11 and 0.20, which are assignable to two trimethylsilyl groups, and a singlet signal (1H) at δ 3.03 were observed in the ^{1}H NMR spectrum. These results indicated that the product was 1-(trimethylsiloxy)benzocyclobutene derivative **3**, which appears to result from the further lithiation of the silylated ketone **2**, followed by trapping of the resulting lithium intermediate with chlorotrimethylsilane. Compound **2** was similarly treated with an equimolar amount each of LDA and chlorotrimethylsilane to give the benzocyclobutene **3** in 86% yield. In addition, it was found that, when the *o*-tolyl ketone **1** was treated successively with 2 molar amounts each of LDA and chlorotrimethylsilane, compound **3** was produced in 59% yield. Similarly, treatment of **1** with 2 molar amounts each of LDA and chlorotriethylsilane resulted in the formation of 1-(triethylsiloxy)benzocyclobutene derivative **4** in 51% yield. The above-mentioned results are outlined in Scheme 1. The configuration assignments depicted for **3** and **4** rely on the considerations stated below. The production of these compounds was highly stereoselective, and the corresponding diastereomers, for example **13**, for **3** could not be obtained.

Our next object was to examine similar transformations of 2-methylbenzophenone into the corresponding benzocyclobutenol derivatives. However, lithiation of this ketone with LDA followed by treatment with chlorotrimethylsilane under conditions similar to those described above resulted in formation of an intractable mixture of the products; reactions via intermolecular condensation of the silylated ketone appeared to take place. This negative result prompted us to examine the reaction of an *o*-methylbenzophenone derivative carrying a methoxy substituent at the *o*′-position. The substrate for this purpose, 2,3,4-trimethoxy-6-methylbenzophenone (**5**), was prepared by treatment of 2-lithio-3,4,5-trimethoxytoluene with benzaldehyde, followed by the PCC oxidation of the resulting alcohol. We have found that lithiation of **5** with an equimolar amount of LDA generated 2-benzoyl-3,4,5-trimethoxybenzyllithium, treatment of which with an equimolar amount of chlorotrimethylsilane resulted in formation of 1-(trimethylsilyloxy)benzocyclobutenes **6** and **8** in 19 and 7% yields, respectively, along with silylated ketone **7** in 65% yield (Scheme 2). These products were separable from each others by means of preparative TLC on silica gel. It can be reasonably assumed from this result that the 3-methoxy group in the benzoylbenzyllithium assists in the ring closure. The stereochemistry of **8** was established on the basis of the considerations stated below. Compounds **6** and **8** were obtained from **5** by sequential treatment with 2 molar amounts each of LDA and chlorotrimethylsilane in 13 and 62% yields, respectively. Conversion of **7** to **8** was also achieved on treatment with LDA and then with chlorotrimethylsilane in 73% yield.

Scheme 2



Reagents and conditions: i, LDA, THF, -78 °C; ii, Me_3SiCl, -78 °C; iii, 2LDA, THF, -78 °C; iv, $2Me_3SiCl$, -78 °C.

Cyclization of *tert*-Butyl *o*-Tolyl Ketones Bearing an *o*′-Methoxy Group, 9 and 10, to Benzocyclobutenols 11 and 12. In view of the success of the above-mentioned reactions, we next examined the possibility in cyclization reaction of *tert*-butyl *o*-tolyl ketones bearing an *o*′-methoxy group, **9** and **10**, which were expected to provide more flexibility in terms of cyclization. *tert*-Butyl 2-methoxy-6-methylphenyl ketone (**9**) was prepared by the PCC oxidation of the alcohol which was prepared by interaction of 2-methoxy-6-methylbenzaldehyde with *tert*-butylmagnesium bromide. A procedure similar to that described above for the preparation of the trimethoxybenzophenone **5**, except for the use of pivalaldehyde in the place of benzaldehyde, gave *tert*-butyl 2,3,4-trimethoxy-6-methylphenyl ketone (**10**). As expected, the lithiated intermediates of these ketones were found to cyclize more readily than those from **1** and **5**. Thus, treatment of **9** with an equimolar amount of LDA in −78 °C resulted immediately in deep-red coloration, which turned gradually to yellow on stirring for 1 h at the same

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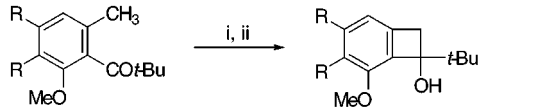
Scheme 3

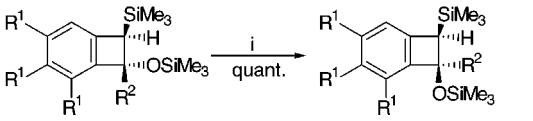


9 R=H
10 R=OMe

11 R=H (76%)
12 R=OMe (59%)

Reagents and conditions: i, LDA, THF, -78 °C; ii, aq. NH_4Cl.

Scheme 4



3 R^1=H, R^2=*t*-Bu
8 R^1=OMe, R^2=Ph

13 R^1=H, R^2=*t*-Bu
14 R^1=OMe, R^2=Ph

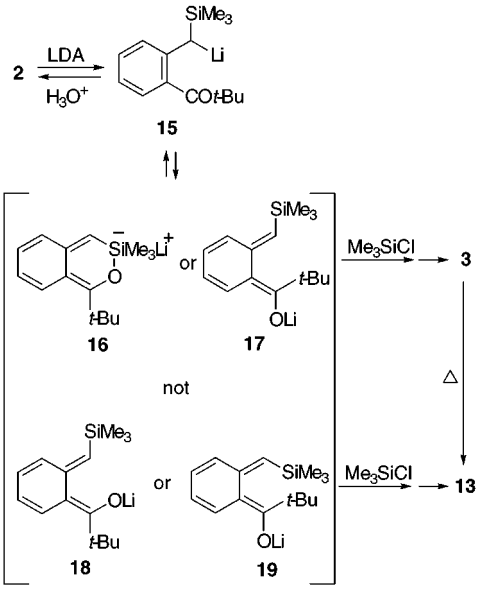
Reagents and conditions: i, *p*-cymene, reflux.

temperature, indicating that the intramolecular cyclization was complete. The usual workup gave the expected benzocyclobutenol **11** in 76% yield. The cyclization reaction of **10** was carried out similarly and gave the corresponding benzocyclobutenol **12** in 59% yield. These reactions are outlined in Scheme 3.

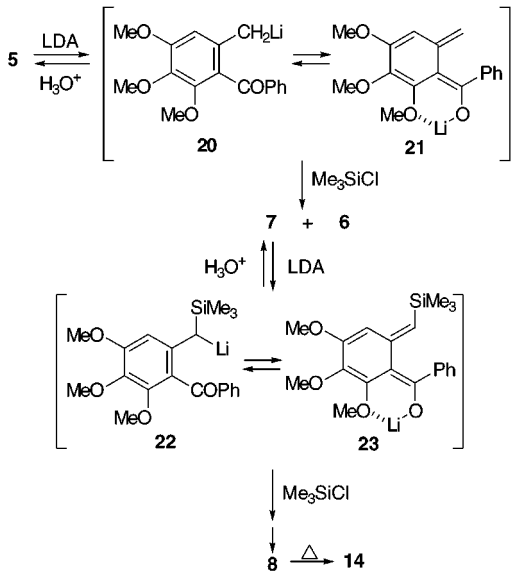
Thermal Isomerization of Trimethylsiloxybenzocyclobutenes 3 and 8. We tried thermal isomerization of the benzocyclobutenes **3** and **8** in order to examine thermodynamic behavior of these compounds. The results obtained are outlined in Scheme 4. When a solution of **3** in *p*-cymene was heated at reflux temperature for 2.5 h, an isomerization reaction took place and the stereoisomer **13** was formed in an almost quantitative yield. This result is intriguing since it indicates that **13** is thermodynamically more stable and sterically less strained than **3**. Similarly, a thermal isomerization of compound **8** proceeded smoothly to give the corresponding stereoisomer **14** quantitatively. This leads to a conclusion similar to that mentioned above for **3** and **13**. MM2 calculations with Chem3D Pro suggest that compound **13** is more stable (7.48 kcal/mol) than the corresponding stereoisomer **3** and that **14** is more stable (2.08 kcal/mol) than **8**.

Determination of the Stereochemistries of Benzocyclobutenol Derivatives 3, 8, 13, and 14. In our preliminary communication,[13] the stereochemistry of **3** was tentatively assigned as depicted in **13**. This assignment was based on consideration that the reaction could proceed via the intermediate **18** (vide infra). However, since the thermal isomerization experiment coupled with the MM2 calculations revealed that **3** is thermodynamically less stable than **13**, the previous assignment should be reversed. This revised stereochemistry was supported by the results of NOE studies of compounds **3** and **13**. Thus, irradiation of the signal at δ 0.20 due to OTMS of **3** resulted in an enhancement (6.3%) of the signal at δ 3.03 due to the cyclobutyl proton, while a large enhancement (23%) of the signal at δ 3.22 due to the cyclobutyl proton of **13** was observed on irradiation of the signal at δ 0.95 due to *t*-Bu. The stereochemistries of **8** and **14** were also established with the aid of NOE experiments. For compound **8**, irradiation of the signal at δ 0.13 due to OTMS resulted in an enhancement (11%) of the signal at δ 3.28 due to the cyclobutyl proton. On the other hand, an enhancement was observed for the signal at δ 7.27 due to the *ortho*-protons of Ph (5.5%) of **14** when the

Scheme 5



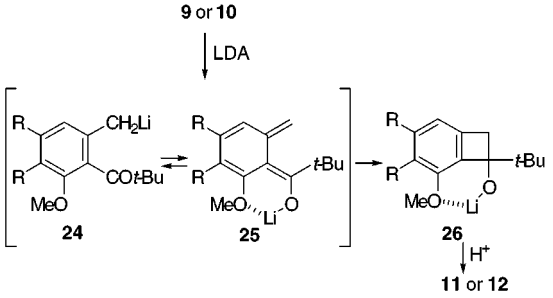
Scheme 6



signal at δ 2.84 due to the cyclobutyl proton was irradiated. A considerable upfield shift of the signal due to the cyclobutyl proton of **14** gives further support to the stereochemical assignment of **8** and **14**.

Probable Mechanisms for the Formation of Benzocyclobutenol Derivatives and Their Thermal Isomerization. Although no unambiguous explanation of the mechanisms of the present cyclizations can be offered at the present time, the probable pathways to the products are depicted in Schemes 5−7. The proposed mechanism for the highly selective formation of the sterically hindered product **3** is illustrated in Scheme 5. Thus, interaction of *tert*-butyl *o*-[(trimethylsilyl)methyl]-phenyl ketone (**2**) with LDA leads to formation of the lithiated intermediate **15**, which is trapped with chlorotrimethylsilane selectively at the oxygen of the α-oxy-*o*-quinodimethane type equilibrium form **16** (or **17**) not at the α-carbon of **15** to give the corresponding trimethylsiloxy-*o*-quinodimethane, of which conrotatory ring closure[15] gives rise to the product **3**. *o*-[Bis(trimethylsilyl)-methyl]phenyl *tert*-butyl ketone was not isolated, indicat-

Scheme 7



ing that the introduction of the second trimethylsilyl group at the oxygen is strongly favored over introduction at the carbon. The high stereoselectivity of the cyclization can be understood by comparison of relative stabilities between the intermediates **16** (or **17**) and **18** (or **19**). The formation of the silicate through a intramolecular coordination of the alkoxide to the silicon atom would result in a stabilization of **16**. The intermediacy of **17** would be supported by the large outward preference of oxy substituents in the formation of *o*-quinodimethanes, demonstrated in the work of Houk et al. on the concept of torquioselectivity.[16] It should be noted that no benzocyclobutenol derivative was isolated by quenching the lithiated intermediate **15** with aqueous ammonium chloride, and the starting ketone **2** was recovered in an almost quantitative yield. This result indicates that the corresponding benzocyclobutenoxide was not formed in the reaction mixture.

Scheme 6 shows the probable pathway to the 1-(trimethylsiloxy)benzocyclobutene **6** and **8** from the *o*-methoxy-*o*′-methylbenzophenone **5**. Presumably, the α-oxy-*o*-quinodimethane type equilibrium form **21** of the *o*-benzoylbenzyllithium **20** is somewhat stabilized due to the *o*′-methoxy group to form the 1-(trimethylsiloxy)benzocyclobutene **6**. The formation of **8** can be explained by considering the chelate-stabilized intermediate **23** (or a silicate intermediate similar to **16**). It is also worth noting that treatment of the lithiated intermediates **20** and **22** with aqueous ammonium chloride resulted in the almost quantitative recovery of the starting materials **5** and **7**, respectively.

An alternative path for the formation of these 1-(trimethylsiloxy)benzocyclobutenes may be by a chlorotrialkylsilane-induced intramolecular nucleophilic attack of the benzylic carbanions to the carbonyl groups, followed by trapping of the resulting lithium alkoxides with chlorotrimethylsilane. Although this possibility cannot be excluded, it appears even less likely considering that compounds **3** and **8**, which appear to be sterically more hindered than their corresponding isomers **13** and **14**, were exclusively formed as a single stereoisomer and that the quenching experiments of the lithiation products from the ketones **2**, **5**, and **7** with aqueous ammonium chloride gave no benzocyclobutenol derivatives.

The ease of the production of the benzocyclobutenols **11** and **12** is noteworthy and is most likely ascribed to the high stability of the α-oxy-*o*-quinodimethane type equilibrium form **25** of the *tert*-butyl *o*-(lithiomethyl)-phenyl ketone **24** and/or the lithium benzocyclobutenyl oxide **26**, as illustrated in Scheme 7.

We have no clear explanation for the mechanism of the isomerization of **3** to **13** and **8** to **14**. We attempted the isomerization of **8** to **14** in refluxing toluene. This temperature is high enough for the ring opening of benzocyclobutenes bearing an oxy substituent at the 1-position, as described by Oppolzer.[17] The isomerization, however, proceeded very sluggishly, and most of the starting material remained unchanged after 18 h. This result would indicate that the isomerization, of course, does not occur through an *o*-quinodimethane intermediate and that this is a concerted reaction.

Experimental Section

Phenyl 2,3,4-Trimethoxy-6-methylphenyl Ketone (5). To a stirred solution of *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) (20 mmol, 2.3 g) in Et_2O (50 cm^3) at 0 °C under argon was added butyllithium (20 mmol, 1.6 M in hexane) and then 1,2,3-trimethoxy-5-methylbenzene (10 mmol, 1.8 g). The mixture was refluxed for 2 h and then allowed to stand for 12 h at room temperature. To the cooled (0 °C) suspension was added benzaldehyde (20 mmol, 2.1 g) dropwise. The resulting mixture was stirred for an additional 2 h at the same temperature before it was quenched by adding 5% aqueous HCl. The organic layer was separated, and the aqueous layer was extracted with Et_2O twice (100 cm^3 each). The combined ether layers were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel to afford phenyl(2,3,4-trimethoxy-6-methylphenyl)methanol (2.3 g, 81%) as a pale yellow oil: R_f 0.41 (1:5, EtOAc−hexane); IR (neat) 3470 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 2.26 (3H, s, 6′-Me), 3.33 (3H, s, OMe), 3.5 (1H, br s, OH), 3.74 (3H, s, OMe), 3.82 (3H, s, OMe), 5.82 (1H, br d, J = 10 Hz), 6.42 (1H, s, 5′-H), 7.19 (5H, s, ArH); MS (rel intensity) *m*/*z* 288 (M^+, 100). Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.93; H, 7.06. A mixture of the foregoing alcohol (2.3 g, 8.0 mmol), pyridinium chlorochromate (PCC) (5.2 g, 24 mmol), and Celite (5.0 g) in CH_2Cl_2 (200 cm^3) was stirred for 1 h at room temperature. After this time, the mixture was filtered. The filtrate was washed successively with 5% aqueous HCl and brine and dried ($MgSO_4$). Removal of the solvent gave a residue, which was introduced at the top of a short silica gel column and eluted with CH_2Cl_2. After concentration of the eluent, the residual solid was recrystallized from hexane to afford the title compound (2.1 g, 92%) as a white solid: mp 93−94.5 °C; IR (neat) 1669 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 2.12 (3H, s, 6-Me), 3.68 (3H, s, OMe), 3.86 (3H, s, OMe), 3.90 (3H, s, OMe), 6.55 (1H, s, 5-H), 7.35−7.55 (3H, m, 3′, 4′, 5′-H), 7.81 (2H, dd, J = 7.6, 1.5 Hz, 2′, 6′-H); MS (rel intensity) *m*/*z* 286 (M^+, 71), 285 [$(M - 1)^+$, 100]. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.05; H, 6.30.

***tert*-Butyl 2-Methoxy-6-methylphenyl Ketone (9).** To a stirred solution of *tert*-butylmagnesium chloride, prepared in situ from *tert*-butyl chloride (0.46 g, 5.0 mmol) and magnesium turnings (0.15 g, 6.0 mmol) in Et_2O (5 cm^3), at 0 °C was added a solution of 2-methoxy-6-methylbenzaldehyde[18] (0.50 g, 3.3 mmol) in Et_2O (5 cm^3). The mixture was allowed to warm slowly to room temperature and poured into 5% aqueous HCl. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined extracts were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by preparative TLC on silica gel to give 2,2-dimethyl-1-(2-methoxy-6-methylphenyl)-1-propanol (0.38 g, 54%) as a yellow liquid: R_f 0.24 (1:10 EtOAc−hexane); IR (neat) 3542 cm^{-1}; ^1H NMR (60 MHz, CCl_4) δ 0.91 (9H, s, *t*-Bu), 2.31 (3H, s, 6′-Me), 3.7−4.0 (4H, m including s at 3.78, OMe, OH), 4.47

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(1H, br. d, J = 11 Hz), and 6.5−7.1 (3H, m, ArH); MS (rel intensity) m/z 208 (M^+, 0.8), 151 [$(M - C_4H_9)^+$, 100]. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.94; H, 9.70. Oxidation of the alcohol thus obtained (0.35 g, 1.7 mmol) with PCC (1.1 g, 5.1 mmol) in CH_2Cl_2 (40 cm^3) under conditions similar to those described above afforded the title compound (0.30 g, 90%) as a yellow liquid: R_f 0.33 (1:10 EtOAc−hexane); IR (neat) 1694 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ 1.16 (9H, s, *t*-Bu), 2.14 (3H, s, 6′-Me), 3.79 (3H, s, OMe), 6.63 (1H, d, J = 7.9 Hz, 3′-H), 6.72 (1H, d, J = 7.3 Hz, 5′-H), 7.09 (1H, dd, J = 7.9, 7.3 Hz, 4′-H); MS (rel intensity) m/z 206 (M^+, 1.1), 149 [$(M - C_4H_9)^+$, 100]. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.39; H, 8.55.

***tert*-Butyl 2,3,4-Trimethoxy-6-methylphenyl Ketone (10).** Lithiation of 1,2,3-trimethoxy-5-methylbenzene (1.8 g, 10 mmol) with *n*-BuLi-TMEDA (20 mmol) in Et_2O (40 cm^3) followed by treatment of the resulting lithium compound with 2,2-dimethylpropanal (2.4 g, 20 mmol) in THF (8 cm^3) was carried out in a manner similar to that described above for the preparation of phenyl(2,3,4-trimethoxy-6-methylphenyl)-methanol to give 2,2-dimethyl-1-(2,3,4-trimethoxy-6-methylphenyl)-1-propanol (1.6 g, 59%) as a yellow liquid: R_f 0.27 (1:5 EtOAc−hexane); bp 115−117 °C/0.1 Torr; IR (neat) 3541 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ 0.90 (9H, s, *t*-Bu), 2.25 (3H, s, 6′-Me), 3.7−4.0 (10H, m including 3s at 3.73, 3.79, 3.93, 3OMe, OH), 4.40 (1H, br d, J = 10 Hz), 6.33 (1H, s, 5′-H); MS (rel intensity) m/z 268 (M^+, 0.06), 250 [$(M - H_2O)^+$, 6.9], 212 [$(M - C_4H_8)^+$, 100]. Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.19; H, 9.12. Oxidation of the alcohol thus obtained (2.3 g, 8.0 mmol) with PCC (5.2 g, 24 mmol) in CH_2Cl_2 (200 cm^3) afforded the title compound (2.1 g, 92%) as a pale yellow solid: mp 93−94 °C (hexane); IR (neat) 1694 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ 1.16 (9H, s, *t*-Bu), 2.07 (3H, s, 6′-Me), 3.75 (3H, s, OMe), 3.80 (3H, s, OMe), 3.84 (3H, s, OMe), 6.39 (1H, s, 5′-H); MS (rel intensity) m/z 266 (M^+, 6.0), 210 [$(M - C_4H_8)^+$, 100]. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.93; H, 8.22.

Lithiation of *tert*-Butyl *o*-Tolyl Ketone (1) with an Equimolar Amount of LDA and Subsequent Treatment of the Resulting Carbanion with an Equimolar Amount of Me_3SiCl. The ketone **1**[1] (0.72 g, 4.1 mmol) was added dropwise to a stirred solution of LDA (4.1 mmol) in THF (20 cm^3) (at −78 °C under argon), which was generated from *n*-BuLi (1.6 M in hexane, 4.1 mmol) and diisopropylamine (0.40 g, 4.1 mmol) by the standard method, resulting in the production of a characteristic red solution of the carbanion. After 15 min, Me_3SiCl (0.44 g,4.1 mmol) was added dropwise, and the mixture was stirred for an additional 1 h at the same temperature, whereupon the red color gradually faded to orange. The resulting mixture was quenched by adding aqueous NH_4Cl and extracted with Et_2O three times (30 cm^3 each). The combined organic layers were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure, and the crude products were purified by preparative TLC on silica gel to afford *tert*-butyl 2-(trimethylsilylmethyl)phenyl ketone **(2)** (a pale yellow oil; 0.59 g, 58%) and *trans*-7-*tert*-butyl-8-trimethylsilyl-7-(trimethylsiloxy)bicyclo[4.2.0]octa-1,3,5-triene (**3**) (a colorless oil; 79 mg, 6.0%). **2**: R_f 0.44 (1:20 EtOAc−hexane); IR (neat) 1689, 1248, 851 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.03 (9H, s, $SiMe_3$), 1.25 (9H, s, *t*-Bu), 1.96 (2H, s, CH_2SiMe$_3$), 6.95−7.2 (4H, m, ArH); MS (rel intensity) m/z 248 (M^+, 7.3), 247 [$(M - 1)^+$, 8.9], 233 [$(M - CH_3)^+$, 99], 73 (100). Anal. Calcd for $C_{15}H_{24}OSi$: C, 72.53; H, 9.74. Found: C, 72.41; H, 9.66. **3**: R_f 0.88 (1:20 EtOAc−hexane); IR (neat) 1599, 1583, 1250, 1068, 859 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.11 (9H, s, 8-$SiMe_3$), 0.20 (9H, s, O$SiMe_3$), 0.97 (9H, s, *t*-Bu), 3.03 (1H, s, 8-H), 6.95−7.2 (4H, m, ArH); MS (rel intensity) m/z 320 (M^+, 0.83), 305 [$(M - CH_3)^+$, 1.6], 263 [$(M - t\text{-Bu})^+$, 17], 247 [$(M - SiMe_3)^+$, 18], 233 (65), 73 (100). Anal. Calcd for $C_{18}H_{32}OSi_2$: C, 67.43; H, 10.06. Found: C, 67.50; H, 9.92.

Lithiation of the Silylated Ketone 2 and Subsequent Treatment of the Resulting Carbanion with Me_3SiCl. Lithiation of **2** (0.26 g, 1.1 mmol) with LDA (1.1 mmol) in THF (5 cm^3) was followed by treatment with chlorotrimethylsilane (0.12 g, 1.1 mmol) in a manner similar to that described above for the reaction of **1** to give **3** (0.30 g, 86%).

Treatment of the Ketone 1 with 2 Molar Amounts each of LDA and Me_3SiCl. Lithiation of **1** (0.17 g, 1.0 mmol) with LDA (2.0 mmol) in THF (5 cm^3), followed by treatment with Me_3SiCl (0.22 g, 2.0 mmol), gave **3** (0.19 g, 59%).

***trans*-7-*tert*-Butyl-8-triethylsilyl-7-(triethylsiloxy)bicyclo[4.2.0]octa-1,3,5-triene (4).** Lithiation of **1** (0.17 g, 1.0 mmol) with LDA (2.0 mmol) in THF (5 cm^3), followed by treatment with Et_3SiCl (0.30 g, 2.0 mmol), gave the title compound (0.21 g, 51%) as a colorless oil; R_f 0.75 (hexane); IR (neat) 1582, 1238, 1069, 1006, 762, 727 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.41 [6H, q, J = 7.9 Hz, 8-Si(CH_2Me)$_3$], 0.76 [6H, q, J = 7.9 Hz, OSi(CH_2Me)$_3$], 0.84 [9H, t, J = 7.9, 8-Si-(CH$_2$*Me*)$_3$], 0.97 (9H, s, *t*-Bu), 1.01 [9H, t, J 7.9, OSi(CH$_2$*Me*)$_3$], 3.16 (1H, s, 8-H), 7.0−7.25 (4H, m); MS (rel intensity) m/z 404 (M^+, 8.9), 347 [$(M - t\text{-Bu})^+$, 55], 275 (76), 87 (100). Anal. Calcd for $C_{24}H_{44}OSi_2$: C, 71.21; H, 10.96. Found: C, 71.07; H, 10.71.

Lithiation of the Benzophenone 5 and Subsequent Treatment of the Resulting Carbanion with Me_3SiCl. Lithiation of **5** (0.29 g, 1.0 mmol) with LDA (1.0 mmol) in THF (5 mL) followed by treatment with Me_3SiCl (0.11 g, 1.0 mmol) was carried out in the same way as described above for the preparation of **2** and **3** to give 3,4,5-trimethoxy-7-phenyl-7-(trimethylsilyloxy)bicyclo[4.2.0]octa-1,3,5-triene **(6)** (a white solid; 69 mg, 19%), phenyl 2,3,4-trimethoxy-6-(trimethylsilylmethyl)phenyl ketone **(7)** (a yellow oil; 0.23 g, 65%), and *trans*-3,4,5-trimethoxy-7-phenyl-8-trimethylsilyl-7-(trimethylsiloxy)-bicyclo[4.2.0]octa-1,3,5-triene (**8**) (a white solid; 30 mg, 7%). **6**: R_f 0.30 (1:10 EtOAc−hexane); mp 97.5−98 °C (hexane); IR (KBr disk) 1252, 841 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.06 (9H, s, $SiMe_3$), 3.28 (1H, d, J = 14.0 Hz, 8-H), 3.47 (1H, d, J = 14.0 Hz, 8-H), 3.59 (3H, s, OMe), 3.71 (3H, s, OMe), 3.80 (3H, s, OMe), 6.41 (1H, s, 2-H), 7.1−7.35 (5H, m, ArH); MS (rel intensity) m/z 358 (M^+, 61), 357 [$(M - 1)^+$, 100]. Anal. Calcd for $C_{20}H_{26}O_4Si$: C, 67.00; H, 7.31. Found: C, 66.94; H, 7.29. **7**: R_f 0.27 (1:10 EtOAc−hexane); IR (neat)1668, 1276, 853 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.05 (9H, s, $SiMe_3$), 1.86 (2H, s, CH_2SiMe$_3$), 3.63 (3H, s, OMe), 3.82 (3H, s, OMe), 3.88 (3H, s, OMe), 6.33 (1H, s, 5-H), 7.2−7.55 (3H, m, ArH), and 7.65−7.9 (2H, m, ArH); MS (rel intensity) m/z 358 (M^+, 100). Anal. Calcd for $C_{20}H_{26}O_4Si$: C, 67.00; H, 7.31. Found: C, 66.97; H, 7.19. **8**: R_f 0.31 (1:10 EtOAc−hexane); mp 93−94 °C (hexane); IR (KBr disk) 1252, 840 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ −0.30 (9H, s, 8-$SiMe_3$), 0.13 (9H, s, O$SiMe_3$), 3.28 (1H, s, 8-H), 3.60 (3H, s, OMe), 3.70 (3H, s, OMe), 3.86 (3H, s, OMe), 6.23 (1H, s, 2-H), 7.2−7.35 (5H, s, ArH); MS (rel intensity) m/z 430 (M^+, 5.9), 415 [$(M - CH_3)^+$, 100]. Anal. Calcd for $C_{23}H_{34}O_4Si_2$: C, 64.14; H, 7.95. Found: C, 64.35; H, 7.66.

Treatment of the Ketone 5 with 2 Molar Amounts Each of LDA and Me_3SiCl. Lithiation of **5** (0.29 g, 1.0 mmol) with LDA (2.0 mmol) in THF (5 cm^3), followed by treatment with Me_3SiCl (0.22 g, 2.0 mmol), gave **6** (47 mg, 13%) and **8** (0.27 g, 62%).

Lithiation of the Silylated Benzophenone 7 and Subsequent Treatment of the Resulting Carbanion with Me_3SiCl. Lithiation of **7** (0.11 g, 0.32 mmol) with LDA (0.32 mmol) in THF (5 cm^3) followed by treatment with Me_3SiCl (35 mg, 0.32 mmol) gave **8** (0.10 g, 73%).

7-*tert*-Butyl-5-methoxybicyclo[4.2.0]octa-1,3,5-trien-7-ol (11). After treatment of **9** (0.21 g, 1.0 mmol) with LDA (1.0 mmol) in THF (5 cm^3) at −78 °C, the resulting red solution was allowed to stir for 1 h at the same temperature, whereupon the color faded. The mixture was worked up as usual and separated by preparative TLC on silica gel to give the title compound (0.16 g, 76%) as a pale-yellow oil: R_f 0.13 (1:10 EtOAc−hexane); IR (neat) 3456 cm^{-1}; ^{1}H NMR (60 MHz, CCl_4) δ 0.99 (9H, s, *t*-Bu), 2.00 (1H, br s, OH), 2.77 (1H, d, J = 14.3 Hz, 8-H), 3.33 (1H, d, J = 14.3 Hz, 8-H), 3.75 (3H, s, OMe), 6.56 (1H, d, J = 7.9 Hz, 4-H), 6.66 (1H, d, J = 7.3, 2-H), 7.10 (1H, dd, J = 7.9, 7.3, 3-H); MS (rel intensity) m/z 206 (M^+, 12), 191 [$(M - CH_3)^+$, 24], 150 [$(M - C_4H_8)^+$, 70], 149 [$(M - t\text{-Bu})^+$, 100]. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.65; H, 9.05.

7-*tert*-Butyl-3,4,5-trimethoxybicyclo[4.2.0]octa-1,3,5-trien-7-ol (12). Compound **10** (0.27 g, 1.0 mmol) was treated with LDA (1 mmol) in THF (5 cm^3) under conditions similar to those described above for the preparation of **11** to give the title compound (0.16 g, 59%): R_f 0.06 (1:5 EtOAc−hexane); mp 80−81 °C (hexane); IR (neat) 3482 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 0.99 (9H, s, *t*-Bu), 2.14 (1H, s, OH), 2.66 (1H, d, J = 14.3 Hz, 8-H), 3.29 (1H, d, J = 14.3 Hz, 8-H), 3.69 (3H, s, OMe), 3.76 (3H, s, OMe), 3.86 (3H, s, OMe), 6.35 (1H, s, 2-H); MS (rel intensity) *m*/*z* 266 (M^+, 5.0), 209 [$(M - t\text{-Bu})^+$, 100]. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.74; H, 8.46.

***cis*-7-*tert*-Butyl-8-trimethylsilyl-7-trimethylsiloxybicyclo[4.2.0]octa-1,3,5-triene (13).** The trimethylsiloxybenzocyclobutene **3** (0.15 g, 0.50 mmol) was dissolved in dry *p*-cymene (4 cm^3), and the solution was heated at reflux temperature for 1 h under argon, the reaction being followed by TLC. The mixture was allowed to cool to room temperature, and the solvent was removed under reduced pressure. The residue was purified by preparative TLC to give the title compound (0.15 g, quantitative) as a colorless oil: R_f 0.80 (hexane); IR (neat) 1250, 1107, 1077, 840 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 0.05 (9H, s, $SiMe_3$), 0.09 (9H, s, $SiMe_3$), 0.95 (9H, s, *t*-Bu), 3.22 (1H, s, 8-H), 6.99 (1H, d, J = 7.3 Hz, ArH), 7.05−7.1 (2H, m, ArH), 7.15−7.2 (1H, m, ArH); MS (rel intensity) *m*/*z* 320 (M^+, 5.1), 319 [$(M - 1)^+$, 6.4], 305 [$(M - Me)^+$, 6.6], 263 [$(M - t\text{-Bu})^+$, 31], 247 [$(M - SiMe_3)^+$, 46], 147 (66), 73 (100). Calcd for Anal. $C_{18}H_{32}OSi_2$: C, 67.43; H, 10.06. Found: C, 67.71; H, 9.92.

***cis*-3,4,5-Trimethoxy-7-phenyl-8-trimethylsilyl-7-trimethylsiloxybicyclo[4.2.0]octa-1,3,5-triene (14).** Isomerization of **8** (0.11 g, 0.25 mmol) in dry *p*-cymene (3 cm^3) was carried out following a procedure similar to that described above for **3** to give the title compound (0.11 g, quantitative) as a white solid; R_f 0.58 (1:10 EtOAc−hexane); mp 83−84 °C (hexane); IR (KBr disk) 1602, 1251, 1121, 840 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ −0.09 (9H, s, $SiMe_3$), 0.03 (9H, s, $SiMe_3$), 2.84 (1H, s, 8-H), 3.76 (3H, s, OMe), 3.79 (3H, s, OMe), 3.84 (3H, s, OMe), 6.30 (1H, s, 2-H), 7.15−7.2 (3H, m, Ph), 7.27 (2H, dd, J = 8.1, 1.6 Hz, Ph); MS (rel intensity) *m*/*z* 430 (M^+, 1.0), 415 [$(M - Me)^+$, 28], 73 (100). Anal. Calcd for $C_{23}H_{34}O_4Si_2$: C, 64.14; H, 7.96. Found: C, 64.37; H, 7.75.

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