New Syntheses of Benzobarrelenes

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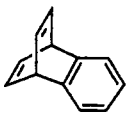
New syntheses of both substituted and unsubstituted benzobarrelenes are described. Treatment of 3,5-cyclohexadiene-*cis*-1,2-diol with benzaldehyde dimethyl acetal in the presence of a catalytic amount of *p*-toluenesulfonic acid gave 1,2-(benzylidenedioxy)-3,5-cyclohexadiene (2). Addition of benzynes to 2 provided 3 and 4. Treatment of 3 and 4 with excess LDA and potassium *tert*-butoxide afforded benzobarrelenes 1 and 5 in good yields.

Benzobarrelene (1) represents an interesting class of bicyclic strained olefins. Although a number of studies



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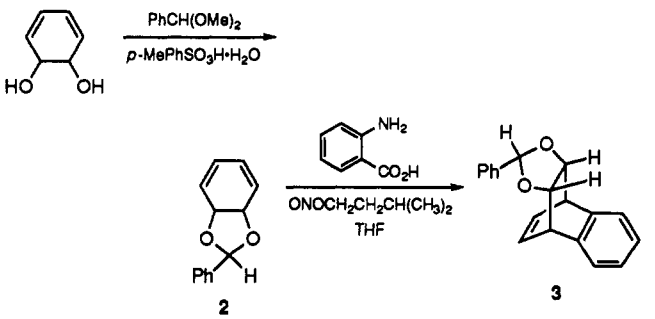
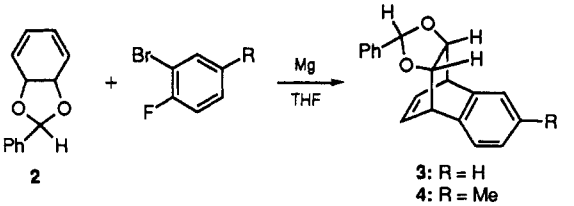
on the reactivity of this interesting molecule have been carried out,[1] many aspects of the chemistry of benzobarrelenes remain to be explored. This situation may be due to difficulties in the existing methods for the synthesis of benzobarrelene and its derivatives.[2,3] We wish to report a new method for the syntheses of both substituted and unsubstituted benzobarrelenes through benzyne cycloaddition.

3,5-Cyclohexadiene-*cis*-1,2-diol, produced by the biological dihydroxylation of benzene and provided by ICI, was reacted with benzaldehyde dimethyl acetal in the presence of a catalytic amount of *p*-toluenesulfonic acid to generate 1,2-benzylidenedioxy-3,5-cyclohexadiene (2). Although this reaction can give two stereoisomers, only one isomer of 2 was observed as shown by NMR spectroscopy. After the formation of 2, a small amount of $NaHCO_3$ was added to neutralize the acid catalyst. Without isolation of 2, this solution was heated at 70 °C under argon, and THF solutions of anthranilic acid and isoamyl nitrite were simultaneously added to it from two separate syringes using a syringe pump. The *in situ* generated benzyne[4] underwent [2 + 4] cycloaddition with 2 to give 1,2,3,4-tetrahydro-2,3-(benzylidenedioxy)-1,4-ethenonaphthalene (3). After chromatography and recrystallization, 3 was isolated in 67% yield based on 3,5-cyclohexadiene-*cis*-1,2-diol (Scheme 1). Besides anthranilic acid, 1-bromo-2-fluorobenzene can be also used as the benzyne precursor to react with isolated 2. To a mixture of 2 and Mg in THF at ~65 °C was added slowly a THF solution of 1-bromo-2-fluorobenzene. After the reaction was complete, 3 was isolated in 65% yield. When 3-bromo-4-fluorotoluene was used as the benzyne precursor, 6-methyl-1,2,3,4-tetrahydro-2,3-(benzylidenedioxy)-1,4-ethenonaphthalene (4) was isolated in 78% yield. Formation of the acetal ring in 2 before the benzyne addition is necessary. Other derivatives of 3,5-cyclohexadiene-*cis*-1,2-diol without this additional five-member ring gave low yields in the Diels–Alder reaction. For example, when dimethyl 3,5-cyclohexadiene-*cis*-1,2-dicarboxylate was treated with anthranilic acid and isoamyl nitrite, no benzyne adduct was isolated. Most of the starting dimethyl 3,5-cyclohexadiene-cis-1,2-dicarboxylate molecules remained unreacted. Presumably, the acetal ring locks the cyclohexadiene ring into the proper conformation for cycloaddition. The addition of benzynes to

Scheme 1





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(3) A two-step synthesis of benzobarrelene from hexachlorobenzene has been reported. However, it is difficult to prepare benzobarrelene derivatives with substituents on the phenyl ring by using this method. Hales, N. J.; Heaney, H.; Hollinshead, J. H.; Sigh, P. *Org. Synth.* **1979**, *59*, 71.

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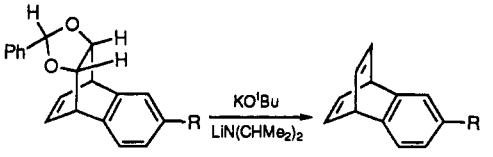
2 can give two isomers, but only one isomer was formed as shown by the ^1H NMR spectra of the crude product mixtures. It is reasonable to assume that the benzyne intermediates added from the less sterically hindered face of 2, the face opposite to the acetal ring, to form 3.

When 3 was treated with excess LDA and potassium *tert*-butoxide in THF solution under reflux,[5] benzobarrelene was produced in a 90% yield. In the ^{13}C NMR spectrum of benzobarrelene, the one-bond carbon–hydrogen coupling constant of the bridgehead carbon is 141 Hz, much larger than those observed in normal sp^3 carbons (~125 Hz). This indicates significant strain in the molecule. A similar experimental procedure was used to convert 4 to the corresponding methyl-substituted benzobarrelene, 6-methyl-1,4-dihydro-1,4-ethenonaphthalene (5) in 84% yield. In this case, a longer reaction time was needed, since the reaction was carried out in refluxing ether solution to avoid possible deprotonation of the benzylic methylene group.[6] The synthetic method described here makes both substituted and unsubstituted benzobarrelenes readily available in good yields and will facilitate further study of this class of compounds. For example, we have obtained long-chain alkyl-substituted benzobarrelenes which undergo ring-opening metathesis polymerization in the presence of metal–carbene catalysts to yield precursors to soluble conjugated polymers.



3: R = H
4: R = Me

1: R = H
5: R = Me

Experimental Section

THF solvent was dried with sodium benzophenone. Silica gel 60 (particle size 0.040–0.063 mm, 230–400 mesh, EM Science) was used for flash column chromatography.

1,2,3,4-Tetrahydro-2,3-(benzylidenedioxy)-1,4-ethenonaphthalene (3). Method A: In a drybox, benzaldehyde dimethyl acetal (22 g, 0.15 mol), followed by *p*-toluenesulfonic acid monohydride (4.0 mg), was added to a solution of 3,5-cyclohexadiene-*cis*-1,2-diol (3.0 g, 0.027 mol) in THF (4.2 mL). The reaction was stirred at rt for 1 h and $NaHCO_3$ (10 mg) was added to neutralize the acid catalyst. The THF solutions of anthranilic acid (11.4 g, 0.083 mol, 3.5 M) and isoamyl nitrite (9.9 g, 0.085 mol, 4.0 M) were loaded into two separate syringes. Under argon, while the solution of 2 was heated at 70 °C, the two THF solutions were added simultaneously over 4 h by a syringe pump. Gas evolved and the reaction solution turned dark brown. After the addition was complete, the solution was continuously heated at reflux for another 15 h. The resulting dark-brown solution was filtered through a plug of silica gel, and a mixture of hexane:ethyl acetate (5:1) was used to wash the silica gel. After removal of the solvent under vacuum, the residue was loaded on a silica gel column (200 g silica gel, 52 mm o.d. column). The column was washed with hexane, and the product was eluted with a solution of 5% ethyl acetate in hexane. The first yellowish band was collected and the solvent was removed to give a yellowish solid. The solid was partially dissolved in hexane and was then cooled at −50 °C for 3 h. Filtration of the cold mixture afforded a white solid (4.5 g). The filtrate was concentrated and heated under vacuum at 60 °C to remove the unreacted benzaldehyde dimethyl acetal. The residue was dissolved in hexane and cooled to −50 °C. After ~3 h, a second crop (0.47 g) of 3 was collected by filtration. The combined yield was 67% based on 3,5-cyclohexadiene-*cis*-1,2-diol: mp 148–149 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.28 (br, 2 H), 4.32 (br, 2 H), 5.78 (s, 1 H), 6.59 (t, J = 3.6 Hz, 2 H), 7.1–7.5 (m, 9 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 45.2, 79.5, 106.0, 124.8, 126.2, 127.4, 128.2, 129.6, 132.9, 136.4, 140.3; exact mass (EI) calcd for $C_{19}H_{16}O_2$ + H 277.1229, found 277.1217. Anal. Calcd for $C_{19}H_{16}O_2$: C, 82.58; H, 5.84. Found: C, 82.57; H, 6.09.

Method B: (1) Isolation of 2. In a drybox, to a flask containing 3,5-cyclohexadiene-*cis*-1,2-diol (1.0 g, 8.92 mmol) was added benzaldehyde dimethyl acetal (7.3 g, 48 mmol), followed by *p*-toluenesulfonic acid monohydride (4.0 mg). After the mixture was stirred at rt for 1 h, a clear solution was obtained and the reaction, as shown by ^1H NMR spectroscopy, was complete. Excess $NaHCO_3$ was added to neutralize the acid catalyst. The unreacted benzaldehyde dimethyl acetal was distilled under vacuum at ~45 °C. The residue was dissolved in THF and filtered. After removal of THF, 2 was isolated and dried under vacuum and used without purification in the next step: ^1H NMR ($CDCl_3$, 300 MHz) δ 4.72 (s, 2 H), 5.69 (s, 1 H), 5.90 (m, 4H), 7.35 (m, 3 H), 7.51 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 71.1, 98.2, 123.9, 124.2, 126.9, 128.3, 129.5, 136.5. (2) Preparation of 3. Under argon, a small portion of a THF solution of 1-bromo-2-fluorobenzene (3.24 g, 18.5 mmol, 1.85 M) was added to a mixture of 2 and Mg (1.1 g, 0.045 g-atoms) in THF (5 mL) at ~65 °C (oil bath temperature). After ~20 min, the reaction initiated (boiling of the THF solution) and the remaining THF solution of fluorobromobenzene was continuously added slowly over 1 h. The reaction mixture was then maintained at ~65 °C with stirring for 10 h. After the reaction was complete, the solution was filtered through a plug of silica gel and washed with ethyl acetate. After removal of the solvent, the residue was dissolved in hexanes and cooled at −50 °C for more than 5 h. 3 was isolated by filtration in 65% yield (1.32 g) based on 3,5-cyclohexadiene-*cis*-1,2-diol.

6-Methyl-1,2,3,4-tetrahydro-2,3-(benzylidenedioxy)-1,4-ethenonaphthalene (4). The experimental procedure was the same as method B for the preparation of 3. 3-Bromo-4-fluorotoluene (3.78 g, 0.02 mol, 2.0 M) was treated with 2 (2.0 g, 0.01 mol, 2.0 M) in the presence of magnesium (0.53 g, 0.022 g-atoms). 4 (2.26 g, 78% yield) was isolated by using a solution of 10% ethyl acetate in hexanes to elute a silica gel column: ^1H NMR ($CDCl_3$, 300 MHz) δ 2.33 (s, 3 H), 4.26 (br, 2 H), 4.34 (br, 2 H), 5.80 (s, 1 H), 6.61 (br t, J = 3 Hz, 2 H), 6.96 (d, J = 7 Hz, 1 H), 7.11 (s, 1 H), 7.15 (d, J = 7 Hz, 1 H), 7.39 (m, 3 H), 7.54 (m, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 21.1, 44.8, 45.2, 79.7, 79.7, 105.9, 124.6, 125.7, 126.7, 127.4, 128.3, 129.7, 132.9, 133.3, 135.9, 136.4, 137.4, 140.4; exact mass (FAB) calcd for $C_{20}H_{18}O_2$ + H^+ 291.1385, found 291.1403.

1,4-Dihydro-1,4-ethenonaphthalene (benzobarrelene, 1). In a drybox, LDA (8.2 g, 77 mmol) and potassium *tert*-butoxide (9.1 g, 81 mmol) were added sequentially and slowly to a THF solution of 3 (3.0 g, 11 mmol, 73.3 mM). The resulting deep-brown slurry was heated at reflux under argon for 31 h and then cooled to rt. Ice–water (100 mL) was slowly added with stirring. After ether extraction (4 × 100 mL), an orange-brown organic solution was obtained. The ether solution was dried over sodium sulfate for 1 h and concentrated. The residue was loaded to a silica gel column (250 g silica gel, 52 mm o.d. column) and was eluted first with hexane and then with 5% ethyl acetate in hexane. The first yellowish band was collected. Evaporation of the solvent gave pure benzobarrelene solid: 1.5 g (90% yield). Sublimation of the product under vacuum at ~40 °C gave very pure benzobarrelene: mp 64–65 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.92 (p, J = 3.5 Hz, 2 H), 6.86 (m, 6H), 7.14 (dd, J = 3.3, 5.1 Hz); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75 MHz) δ 48.8, 121.9, 123.0, 139.2, 147.3; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 48.8 (dd, J = 141, 4 Hz), 121.9 (d, J = 161 Hz), 123.0 (dd, J = 160, 7 Hz), 139.2 (d, J = 176 Hz), 147.3; exact mass (EI) calcd for $C_{12}H_{10}$ 154.0783, found 154.0785. Anal. Calcd for $C_{12}H_{10}$: C, 93.46; H, 6.54. Found: C, 93.21; H, 6.72.

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(6) When a hexyl-substituted analog of 4 [R = $(CH_2)_5CH_3$] was subjected to the same conditions in a refluxing THF solution, a side product was generated probably from the deprotonation of the benzylic methylene group. The chemistry of such long alkyl chain-substituted benzobarrelenes will be reported.

6-Methyl-1,4-dihydro-1,4-ethenonaphthalene (5). In a drybox, LDA (3.1 g, 28.9 mmol) and potassium *tert*-butoxide (3.0 g, 26.7 mmol) were added sequentially and slowly to an ether solution of **4** (1.0 g, 3.4 mmol, 68 mM). The resulting deep-brown slurry was heated at reflux under argon for 2 d and was then cooled to rt. Water (1 mL) was added slowly with stirring to quench the excess bases. The mixture was filtered through a plug of silica gel and washed with ether. After removal of the solvent, the residue was loaded to a silica gel column (75 g silica gel) and was eluted with hexanes. The first band was collected. Evaporation of the solvent gave **5** as a colorless liquid: 0.5 g (84% yield); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.26 (s, 3 H), 4.89 (m, 2 H), 6.69 (d, J = 7 Hz, 1 H), 6.87 (m, 4 H), 7.02 (s, 1 H), 7.05 (d, J = 7 Hz, 1 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 75 MHz) δ 20.9, 48.6, 48.9, 121.7, 123.3, 123.4, 132.7, 139.4, 139.7, 144.6, 147.6; exact mass (EI) calcd for $C_{13}H_{12}$ 168.0939, found 168.0942. Anal. Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.59; H, 7.26.

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