Acknowledgment.—We thank Mr. J. J. Kobliska and his staff for the analyses report herein.

Synthetic Approaches to Oxygen-Bridged Cyclooctyl Compounds[1]

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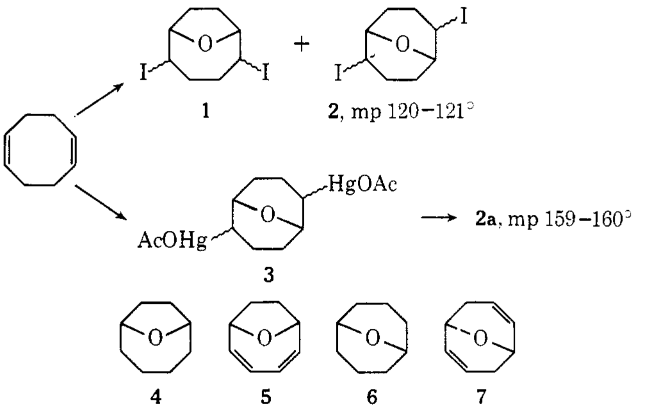
Received October 22, 1968

During our studies on transannular reactions in cyclooctyl compounds we observed that treatment of *cis,cis*-1,5-cyclooctadiene with mercuric oxide and iodine produced two new substituted 9-oxabicyclononanes. Since this structural feature is common to several products isolated from other transannular reactions,[3] we have investigated this reaction as a synthetic route to various substituted 9-oxabicyclononanes.

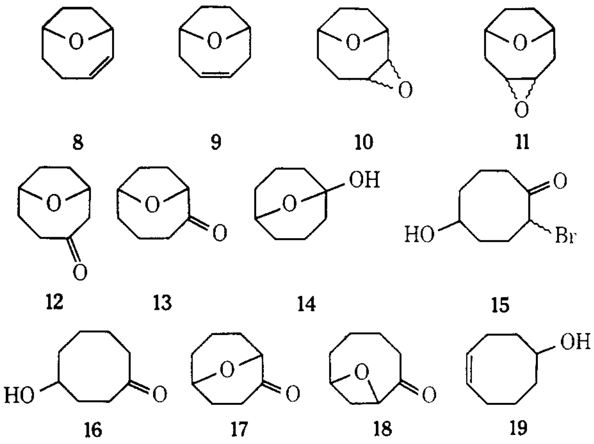
Addition of iodine to a mixture of the diene and mercuric oxide in chloroform at 35–45° led to the formation of mercuric iodide and a crystalline solid. Elemental and mass spectral analysis of the solid indicated the molecular formula $C_8H_{12}I_2O$. The molecular ion peak at *m/e* 378 in the mass spectrum was followed by intense peaks at *m/e* 251 and 124, indicating the successive loss of two iodine atoms. Glpc analysis showed the presence of two components in the ratio 2:3. Attempts to obtain pure samples of the individual components by preparative glpc were not successful although a pure sample of one was eventually obtained by selectively removing the other. Thus treatment of the mixture with potassium *t*-butoxide in ether gave a liquid and a crystalline solid. Support for structure **5** for the liquid product was obtained from spectroscopic measurements (see the Experimental Section) and from its transformation into 9-oxabicyclo[4.2.1]nonane (**4**)[4] on catalytic hydrogenation. The crystalline product, mp 120–121°, which had a glpc retention time identical with that of one of the components of the original mixture, gave (a) 9-oxabicyclo[3.3.1]nonane (**6**)[5] on exposure to tri-*n*-butyltin hydride and (b) 9-oxabicyclo[3.3.1]nona-2,6-diene (**7**)[6] on heating with potassium *t*-butoxide in tetrahydrofuran. From these experiments it was concluded that the products of the initial reaction were 2,5-diiodo-9-oxabicyclo[4.2.1]-nonane (**1**) and 2,6-diiodo-9-oxabicyclo[3.3.1]nonane (**2**) (Scheme I). Stetter and Meissner[6] have prepared an isomer of **2**, mp 159–160°, starting also with 1,5-cyclooctadiene. Treatment with aqueous mercuric acetate gave the bisacetoxymercuri compound **3** which yielded diiodide **2a** on exposure to iodine in chloroform.

SCHEME I



Diene **5** was a useful intermediate for the synthesis of other substituted 9-oxabicyclo[4.2.1]nonanes. Hydrogenation in aqueous potassium pentacyanocobaltate[7] gave a mixture of **8** and **9** in the ratio of 4:1 (Chart I). These olefins were separated by preparative glpc and their nmr spectra confirmed the assigned structures. Epoxidation of the olefin mixture with *m*-chloroperbenzoic acid in methylene chloride gave the isomeric epoxides **10** and **11** which on reduction with lithium aluminum hydride followed by chromic acid oxidation gave 9-oxabicyclo[4.2.1]nonan-3-one (**12**) and 9-oxabicyclo[4.2.1]nonan-2-one (**13**) in the ratio 1:3. Partial separation of these ketones was achieved by adsorption chromatography over alumina and subsequent preparative glpc gave the pure isomers.

CHART I



In an attempt to find a more direct route to ketone **13** we investigated the bromination of 5-hydroxycyclooctanone.[8] This compound, which exists almost exclusively in the hemiketal form **14** (the infrared spectrum shows no carbonyl absorption), on treatment with pyridinium bromide perbromide in aqueous acetic acid at 60° gave a brominated product which showed a strong carbonyl absorption in the infrared spectrum and is therefore formulated as **15**. When this com-

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(1) Supported in part by Research Grant GP-1587 of the National Science Foundation.

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(3) (a) A. C. Cope, M. Gordon, S. Moon, and C. H. Park, *J. Amer. Chem. Soc.*, **87**, 3119 (1965); (b) A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *ibid.*, 2932 (1967); (c) A. C. Cope, B. S. Fisher, W. Funke, J. M. McIntosh, and M. A. McKervey, *J. Org. Chem.*, **34**, 2231 (1969); (d) A. C. Cope, R. B. Kinnel, M. A. McKervey, and N. M. Weinshenker, to be published.

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(5) A. C. Cope and A. Fournier, *ibid.*, **79**, 3896 (1957).

(6) H. Stetter and H. J. Meissner, *Tetrahedron Lett.*, 4599 (1966).

(7) J. Kwiatek, I. L. Mador, and J. K. Seyler, Advances in Chemistry Series, No. 37, American Chemical Society, Washington, D. C., 1963, p 201.

(8) We thank Badische Anilin und Soda Fabrik, Ludwigshafen, Germany, for this material.

pound (without purification) was dissolved in methanol containing potassium hydroxide ketone **13** was obtained (47% yield from **14**). The structural assignment follows from the infrared spectrum of **13** and from its transformation by the Wolff–Kishner method into a mixture of 9-oxabicyclo[4.2.1]nonane (**4**) and 4-cycloocten-1-ol (**19**) in the ratio 4:1. The formation of the latter compound in this reaction confirms the position of the carbonyl group since it is an example of an eliminative reduction of an α-substituted ketone.[9] The above synthetic sequence was also applied successfully to two other oxygen-bridged cyclooctanones. Thus bromination of 4-hydroxycyclooctanone (**16**)[8] with pyridinium bromide perbromide followed by treatment of the mixture of crude bromo ketones with potassium hydroxide in methanol gave 9-oxabicyclo[3.3.1]nonane-2-one (**17**) and 9-oxabicyclo[5.1.1]nonan-2-one (**18**) in the ratio 1:2.5 (30% yield from **16**). Wolff–Kishner reduction of **17** yielded 9-oxabicyclo[3.3.1]nonane (**6**) and 4-cycloocten-1-ol (**19**) in the ratio 3:1. A similar reaction with **18** failed to give 9-oxabicyclo[5.1.1]nonane; attempts to reduce the carbonyl group of **18** with sodium borohydride gave a mixture containing at least seven components.

Experimental Section[10]

2,5-Diiodo-9-oxabicyclo[4.2.1]nonane (1) and 2,6-Diiodo-9-oxabicyclo[3.3.1]nonane (2).—A slurry of red mercuric oxide (108 g) in chloroform (500 ml) containing *cis,cis*-1,5-cyclooctadiene (54 g) was stirred in a 1-l. flask fitted with a condenser. Iodine (252 g) was added in small portions through the condenser during 2.5 hr and the addition rate was adjusted so that the internal temperature remained between 35 and 45°. The mixture was cooled and the solid (HgI_2, 230 g) was removed by filtration. The filtrate was washed with sodium thiosulfate solution and dried. Removal of the solvent gave an oil which deposited crystals on standing. Methanol (100 ml) was added and the crystals were isolated by filtration. There was obtained 119 g (63%) of a mixture of diiodides **1** and **2**, mp 62–70°. A sample recrystallized from methanol had mp 75–80°. Glpc analysis on 2-ft 20% SE-30 at 180° showed the presence of both isomers in the ratio 2:3.

Anal. Calcd for $C_8H_{12}I_2O$: C, 25.39; H, 3.20; I, 67.12. Found: C, 25.29; H, 3.26; I, 67.69.

Reaction of the Diiodides with Potassium *t*-Butoxide.—Potassium *t*-butoxide (30 g) was added to a solution of the diiodide mixture (50 g) in dry ether (500 ml). The mixture was stirred and cooled during the addition and then was heated under reflux for 1.5 hr. The mixture was cooled, filtered through Celite, and the filtrate was washed with two 300-ml portions of water and dried. Removal of the solvent gave a residue which deposited crystals on trituration with pentane. Filtration yielded **2** (15 g), mp 120–121°, after recrystallization from methanol. This material was identical in glpc retention time with the minor component of the diiodide mixture.

Anal. Calcd for $C_8H_{12}I_2O$: C, 25.39; H, 3.20; I, 67.12. Found: C, 25.55; H, 3.18.

Concentration of the pentane solution followed by distillation gave 7.6 g (79.3%) of 9-oxabicyclo[4.2.1]nona-2,4-diene (**5**), bp 50–60° (*ca.* 5 mm). A second distillation gave an analytical sample, bp 46–48° (4 mm); ir (neat) 3025 (m), 1075 (s), 1000 (s), 920 (s), 780 (s), and 700 cm^{-1} (s); uv max (EtOH) 257 mμ (ε 5650); nmr ($CDCl_3$) δ 5.6–6.35 (m, 4 H), 4.5–4.8 (m, 2 H), and 2.2 (m, 4 H).

Anal. Calcd for $C_8H_{10}O$: C, 78.57; H, 8.24. Found: C, 78.42; H, 8.16.

Catalytic Hydrogenation of 5.—A sample of **5** (100 mg) in methanol (5 ml) containing 5% palladium on carbon (15 mg) was hydrogenated at room temperature and atmospheric pressure until hydrogen uptake ceased. The catalyst was removed by filtration and the filtrate was diluted with pentane. The pentane solution was then washed with water and dried. Removal of the solvent gave an oil (*ca.* 100 mg) which was shown by glpc analysis (5 ft × 20% TCEP at 90°) to contain one component with a retention time identical with that of 9-oxabicyclo[4.2.1]nonane (**4**). The ir spectrum of a sample collected by preparative glpc was superimposable with that of an authentic sample of **4**.

Tri-*n*-butyltin Hydride Reduction of 2.—A sample of **2** (1.0 g), mp 121–121.5°, was added to tri-*n*-butyltin hydride (2.0 g) and the mixture was stirred. After gentle warming on a water bath the solid went into solution. The solution was stirred overnight and the product was then flash distilled at 25° (0.2 mm) into a receiver cooled at −78°. The yield of material, mp 48–51°, was 300 mg (83%). The ir spectrum was superimposable with that of an authentic sample of **6**.

9-Oxabicyclo[4.2.1]non-2-ene (8) and 9-Oxabicyclo[4.2.1]non-3-ene (9).—The catalyst used in the hydrogenation of **5** was prepared as follows: 50 ml of a 0.3 *M* cobalt chloride solution was placed in a 250-ml flask fitted with an efficient magnetic stirrer, a hydrogen inlet, a dropping funnel with an equilibrating side arm, and a syringe cap inlet. A solution of potassium cyanide (50 ml, 1.35 *M*) was placed in the dropping funnel and the flask was flushed three times with hydrogen. The cyanide solution was then allowed to flow rapidly into the flask with very rapid stirring. Hydrogen uptake was recorded and was complete (110–130 ml) in *ca.* 30 min.

The diene (5.78 g) was then added with a syringe and hydrogen uptake was recorded. The reaction stopped after 2 hr when 38.9 mmol of hydrogen had been absorbed. Glpc analysis indicated the absence of diene. The mixture was extracted with 50-ml portions of ether and the ether solution was washed with sodium chloride solution and dried. Removal of the solvent gave 5.84 g (98%) of a mixture of **8** and **9** in the ratio 4:1, bp 40–43° (4.5 mm). Pure samples of each isomer were obtained by preparative glpc on 8-ft 20% LAC-728. **8** showed the following characteristics: ir (film) 3010 (m), 1110 (m), 1060 (vs), 1015 (m), 885 (m), 820 (m), 715 (m), and 660 cm^{-1} (m); nmr (CCl_4) 1.2–1.9 (m, 6 H), 1.9–2.3 (m, 2 H), 4.15 (bs, 2 H), and 5.2 (m, 2 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.50; H, 9.78. **9** showed the following characteristics: ir (film) 2990 (m), 1200 (m), 1085 (m), 1055 (s), 1000 (m), 960 (m), 900 (m), 860 (m), and 660 cm^{-1} (s); nmr (CCl_4) 1.3–2.0 (m, 4 H), 2.0–2.7 (m, 4 H), 4.3 (bs, 2 H), and 5.5 (m, 2 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.36; H, 9.69.

9-Oxabicyclo[4.2.1]nonan-3-one (12) and 9-Oxabicyclo[4.2.1]-nonan-2-one.—A mixture of the epoxyolefins (79% **8** and 21% **9**) (6.0 g) was dissolved in methylene chloride (30 ml) at 5° and a solution of *m*-chloroperbenzoic acid (15.0 g) in methylene chloride (150 ml) was added dropwise with stirring during 1 hr. The mixture was then allowed to stand at room temperature for 2 hr. The precipitated solid was removed by filtration and the filtrate was washed twice with 10% aqueous potassium hydroxide and dried ($MgSO_4$). Removal of the solvent gave a semisolid which, on sublimation at 70° (0.5 mm), gave 5.0 g (72%) of a mixture of epoxides **10** and **11**. Glpc analysis on an 8-ft 20% LAC-728 at 180° indicated the presence of all four isomers. A sample of the epoxide mixture was collected by preparative glpc on 2-ft 20% SE-30 at 140° and analyzed.

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.50; H, 8.76.

A solution of the epoxide mixture (4.55 g) in ether (20 ml) was added dropwise to a slurry of lithium aluminium hydride (1.5 g) in ether (75 ml). The mixture was stirred for 30 min and then treated successively with cold water and dilute hydrochloric acid. The precipitated solids were removed by filtration and the filtrate concentrated to afford 4.65 g (95%) of an oil. Glpc analysis on an 8-ft 20% LAC-728 at 120° showed the presence of three isomers. A sample of the alcohol mixture was purified by preparative glpc on a 2-ft 20% SE-30 at 140° and analyzed.

Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.58; H, 9.77.

The crude alcohol mixture (4.55 g) was dissolved in acetone (35 ml) at 0° and an excess of 8 *N* chromic acid was added drop-

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(9) N. J. Leonard and S. Gelfand, *J. Amer. Chem. Soc.*, **77**, 3272 (1955); see also P. S. Wharton and D. H. Bohlen, *J. Org. Chem.*, **26**, 3615 (1961).

(10) Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected; boiling points are uncorrected. Glpc analyses were carried out using an F & M Model 720 instrument. Liquid phases are abbreviated in the following way: SE-30, silicone gum rubber; XF-1150, GE-fluorosilicone, TCEP, 1,2,3-tris(2-cyanoethoxy)propane; LAC-728, diethyleneglycol succinate. Nmr spectra were recorded on a Varian Associates A-60 spectrometer. Microanalyses were performed by Dr. S. M. Nagy and his associates.

wise. The mixture was allowed to stand overnight and then the solvent was removed at reduced pressure. The residue was dissolved in ether and washed with water. The aqueous layer was saturated with sodium chloride and extracted with ether. The combined ether extracts were dried and concentrated to give 3.98 g (88.5%) of an oil. Glpc analysis on 8-ft 20% LAC-728 at 190° indicated the presence of two components in the ratio 1:3. Analytical samples of the individual ketones were obtained by preparative glpc on the same column. The minor component **12** had mp 29.5–32°; ir (KBr) 1700 (vs), 1190 (m), 1140 (w), 1105 (m), 1090 (s), 1060 (m), 1035 (s), 1005 (w), 960 (w), 945 (m), 860 (w), and 760 cm^{-1} (w); nmr (CCl_4) 1.1–2.3 (m, 6 H), 2.4–3.0 (m, 4 H), 4.15–4.65 (bs, 2 H).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.32; H, 8.61.

The major component **13** was identical in every respect with the material described below.

9-Oxabicyclo[4.2.1]nonan-2-one (**13**).—5-Hydroxycyclooctanone (**14**, 7.8 g) was dissolved in glacial acetic acid (75 ml) containing water (25 ml). The solution was heated to 60° and pyridinium bromide perbromide (19.5 g) was added slowly with stirring during 1 hr. When the addition was complete, the solution was left overnight at room temperature. It was then poured into cold water (700 ml) and extracted six times with methylene chloride. The combined extracts were washed twice with water and dried. Removal of the solvent left a viscous brown oil (12.8 g) which was dissolved in methanol and added to a solution of potassium hydroxide (3.0 g) in methanol (20 ml). After 5 min, the solution was poured into cold water (700 ml) and extracted with methylene chloride. The combined extracts were washed with water and dried. Removal of the solvent followed by fractional distillation gave **13**, 3.7 g (47%), bp 76–77.5° (3 mm). A sample of >99% purity was obtained by adsorption chromatography over alumina.

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.63; H, 8.57.

Wolff–Kishner Reduction of 9-Oxabicyclo[4.2.1]nonan-2-one (**13**).—The ketone (1.0 g), potassium hydroxide (1.5 g), hydrazine hydrate (1.0 ml), and diethylene glycol (10 ml) were placed in a flask fitted with a reflux condenser. The mixture was heated in an oil bath at 160° for 2 hr. After cooling, cold water was added and the solution was extracted with ether. The ether solution was washed with water and dried ($MgSO_4$). Cautious removal of the solvent left an oil which was shown by glpc on 2-ft 20% SE-30 to contain components in the ratio 4:1. The individual components were isolated by preparative glpc and identified as 9-oxabicyclo[4.2.1]nonane (**4**) and 4-cycloocten-1-ol (**19**) by comparison of their ir spectra and glpc retention times with those of authentic samples.

Wolff–Kishner Reduction of 9-Oxabicyclo[4.2.1]nonan-3-one (**12**).—A sample of **12** (24.5 mg) was dissolved in ethylene glycol (0.5 ml) containing 85% hydrazine hydrate (50 μl) and potassium hydroxide (10 mg). The mixture was heated under reflux for 1 hr and then cooled, diluted with water, and extracted with pentane. The pentane solution was dried ($MgSO_4$) and concentrated. The ir spectrum of the residue was identical with that of an authentic sample of 9-oxabicyclo[4.2.1]nonane (**4**). Glpc analysis on a 2-ft 20% SE-30 showed only one component. A sample obtained by preparative glpc had mp 28–30° (lit.[4] mp 31°).

9-Oxabicyclo[3.3.1]nonan-2-one (**17**) **and 9-Oxabicyclo[5.1.1]-nonan-2-one** (**18**).—4-Hydroxycyclooctanone (**16**, 5.0 g) was dissolved in glacial acetic acid (19 ml) containing water (6 ml). The solution was heated to 60° and pyridinium bromide perbromide (11.1 g) was added slowly with stirring during 15 min. When the addition was complete, the solution was left overnight at room temperature. It was then diluted with cold water (200 ml) and extracted with methylene chloride. The combined extracts were washed with saturated sodium bicarbonate solution and dried. Removal of the solvent left 7.2 g of a brown oil which was then dissolved in methanol (50 ml) and added to a solution of potassium hydroxide (5.0 g) in methanol (35 ml). After 10 min, the volume of the solution was reduced and the residue was dissolved in ether and poured into water (200 ml). The ether layer was separated and the aqueous layer was extracted with an additional 100 ml of ether. The combined extracts were washed with water and dried. Removal of the solvent followed by distillation gave 1.0 g (20%) of a mixture of **17** and **18**, bp 50° (0.3 mm). Glpc analysis on a 5-ft 5% XF-1150 at 148° indicated an isomer ratio of 1:2.5. Separation of the two isomers was achieved by adsorption chromatography on alumina. Elution with methylene chloride–pentane (1:4) gave pure **17** (200 mg) in the first three fractions. Fractions 4–8 (410 mg) contained equal amounts of the two ketones. Finally, elution with 300 ml of methylene chloride gave **18** (300 mg) of 90–95% purity. Further purification was achieved by preparative glpc on an 8-ft 20% LAC-728 at 180°. Ketone **18** had principle ir bands at 1700 (vs), 1050 (s), 1020 (s), 980 (s), 940 (m), and 865 cm^{-1}; mass spectrum major peaks (*m/e*, relative intensity) 140 (17, molecular ion), 84 (45), 83 (46), 68 (45), 55 (100), 41 (100), and 39 (99).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.59; H, 8.80.

Structure Proof of 9-Oxabicyclo[3.3.1]nonan-2-one (**17**).—A sample of **17** (17 mg) was dissolved in ethylene glycol (250 μl) containing 95% hydrazine (75 μl) and potassium hydroxide (10 mg). The mixture was heated under reflux for 1 hr and then cooled, diluted with water, and extracted with ether. The ether solution was dried ($MgSO_4$) and concentrated. Glpc analysis of the residue on a 2-ft 20% SE-30 showed the presence of 9-oxabicyclo[3.3.1]nonane (**6**) and 4-cycloocten-1-ol (**19**) in the ratio 3:1.

Registry No.—**1**, 19740-73-9; **2**, 10299-46-4; **5**, 19740-75-1; **8**, 19740-76-2; **9**, 19771-17-6; **12**, 19740-77-3; **13**, 19740-78-4; **17**, 19740-79-5; **18**, 19740-80-8.

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cis,cis-1,5-Cyclooctadiene Diepoxide[1]

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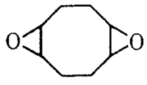
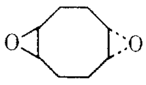
Received October 22, 1968

The epoxidation of *cis,cis*-1,5-cyclooctadiene with excess peracid can give *cis*- and/or *trans*-diepoxides **1a** and **b**. The use of perbenzoic acid in this reaction was studied by Criegee and Kerkow,[3] although no experiments concerning the configuration of the product were carried out. We have investigated the stereochemistry of this reaction and have observed some transannular reactions with the diepoxide. A study of the diepoxidation of 1,4-cyclohexadiene revealed that depending on the peracid used, *trans*-1,4-cyclohexadiene diepoxide or mixtures of the *cis* and *trans* isomers were obtained.[4] It appeared possible that changing the peracid would lead to similar effects in the case of *cis,cis*-1,5-cyclooctadiene. However, we found that peracetic acid in acetic acid gave a diepoxide identical in glpc retention time, infrared spectrum, and refractive index with that obtained using perbenzoic acid in chloroform; according to the glpc analysis, performed on various liquid phases, only one isomer of the diepoxide was obtained from both reactions.


1a


1b

The well-established mode of reaction of lithium

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[1] Supported in part by a research grant (GP-1587) from the National Science Foundation.

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[3] Unpublished results of R. Criegee and A. Kerkow. We thank Professor Criegee for an account of this work.

[4] T. W. Craig, G. R. Harvey, and G. A. Berchtold, *J. Org. Chem.*, **32**, 3743 (1967); H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 221 (1959).