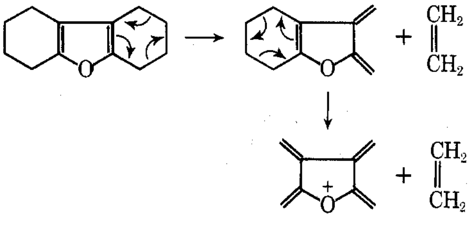
The mass spectrum of **5** proved to be of particular interest. In addition to the previously reported[4] peaks (*m/e* 176, 148, 120, etc.; see Experimental Section) two "metastables" appeared at *m/e* 125 and 97.5. These represent respectively the fragmentation of the parent peak at *m/e* 176 → 148 with loss of 28 mass units, and the *m/e* 148 peak → 120 with loss of 28 mass units. "Exact mass" measurements on the *m/e* 148 and 120 peaks suggested that ethylene is the fragment lost in each case, which leads to the fragmentation pattern indicated in Scheme III.

Scheme III



Experimental Section

Ir spectra were recorded on a Beckman IR 33 spectrometer, NMR spectra were determined on a Varian T-60 spectrometer, and the mass spectra on a Varian CH5 mass spectrometer. Microanalyses were performed on a 185 B Hewlett-Packard C, H, N analyser.

Self-condensation of Cyclohexanone.[6] Technical cyclohexanone (500 g, 5.1 mol) was condensed in the presence of 60% H_2SO_4 according to the procedure of Gault and co-workers.[6] The product was a colorless oil (290 g, 63%): ir (liquid film) 1700 (s), 1670 cm^{-1} (sh); NMR ($CDCl_3$) δ 5.4 (m, 0.8 H), 1.0–3.2 (m, 17 H); mass spectrum parent peak *m/e* 178. Separation of the mixture was attempted, without success, on the following columns: Apiezon, DEGS, XE60, and Carbowax, at temperatures ranging from 180 to 200°. A single, symmetrical peak was observed in every case.

Preparation of Ketal 9.[9] The ketone mixture (8.9 g, 0.05 mol), consisting of 80–90% (**7**), was added to 165 ml of toluene and 60 ml of freshly distilled ethylene glycol containing 0.1 g of *p*-toluenesulfonic acid, and this mixture was heated with slow distillation for 7 hr, during which time 190 ml of distillate was collected. Fresh toluene was added to maintain the original volume over this period. The organic layer was separated, and, after washing several times with saturated aqueous $NaHCO_3$ and water, the combined aqueous layers were extracted with ether, and the ether layers were washed with water and added to the organic layer. Drying ($MgSO_4$) and removal of the solvent under reduced pressure gave 11.5 g (97%) of a pale yellow oil. Distillation gave a colorless oil: bp 85–89° (0.2 mm); NMR ($CDCl_3$) δ 5.5 (m, 1 H), 3.9 (s, 4 H), 2.2–1.2 (m, 17.2 H). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.08; H, 9.82. Found: 75.38; H, 9.93.

Preparation of 2-(1,2-Epoxycyclohex-1-yl)cyclohexanone Ketal (2).[11] To 11.2 g (0.05 mol) of **7** in 70 ml of methylene chloride in a flask equipped with a thermometer, dropping funnel, stirrer, and condenser was added 11 g (0.054 mol) of *m*-chloroperbenzoic acid in 120 ml of methylene chloride over a period of 20 min. The temperature was maintained at 25° during the addition, and the stirring was continued for a further 1.5-hr period. The excess peracid was destroyed by the addition of a small amount of 10% aqueous sodium sulfite. The methylene chloride solution was then washed with 5% $NaHCO_3$, water, and saturated aqueous NaCl. Drying ($MgSO_4$) and removal of the solvent left 11.2 g (93%) of a colorless oil: mass spectrum parent peak *m/e* 238; NMR ($CDCl_3$) δ 3.9 (s, 4 H), 3.1 (m, 1 H), 2.2–1.2 (m, 17 H). Distillation in a Kugelrohr, pot temperature 145° (3 mm), gave a clear liquid. Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.59; H, 9.24. Found: C, 70.81; H, 9.21.

Reaction of 2 with Boron Trifluoride Etherate.[12] The epoxide **2** (4.8 g, 0.02 mol) in 75 ml of methylene chloride at 5° was treated with 8.4 ml of boron trifluoride etherate (48%, technical) added slowly via a dropping funnel. The mixture was stirred at 5° for a further 0.5 hr, and then 75 ml of water was added rapidly. The organic layer was separated and washed with water (2 × 100 ml), saturated, aqueous $NaHCO_3$ (3 × 100 ml), and water (4 × 75 ml). Drying ($MgSO_4$) and removal of the solvent left a pink oil, which turned dark red in 0.5 hr. [The use of benzene (200 ml) as solvent, and the elimination of the 0.5-hr stirring period after the addition of the boron trifluoride etherate, did not appear to have any appreciable effect on the course of the reaction.] Examination of the crude product by TLC indicated that it contained four (or five) components, one well separated and moving very close to the solvent front. The crude red oil was then chromatographed on 400 g of neutral alumina (Woelm), dry column grade, activity III (20 mm), packed in a 2-in. plastic tube. Ether was used as eluant. The bottom ⅛th of the column, which contained the main component of the mixture, gave, on extraction with ether, 1.5 g (43%) of a pale yellow oil. Distillation [bp ~90° (2 mm), lit.[3] 88–89° (2 mm)] yielded a colorless oil: ir (liquid film) 1600 cm^{-1} (furan ring); NMR ($CDCl_3$) δ 2.0–2.6 (8 H), 1.4–2.0 (8 H); mass spectrum *m/e* 176, 148, 120, 105, 92, 91, 79, 77, 65, 51, 41, 39, and two "metastables" at 125 and 97.5. Exact mass of 148 peak. Calcd for $C_{10}H_{12}O$: 148.088. Found: 148.087. Exact mass of 120 peak. Calcd for C_8H_8O: 120.057. Found: 120.057. (Perfluoroalkane 225 was used as the reference compound.)

Anal. Calcd for $C_{12}H_{16}O$: C, 81.82; H, 9.10. Found: C, 81.62; H, 9.19.

Three other materials were isolated from the column and all were ketonic but none was obtained pure enough to warrant a definite structure assignment.

Hydrolysis of Ketal 2 to 2-(Cyclohexen-1-yl)cyclohexanone (7). Hydrolysis of **2** in 90% boiling MeOH acidified with HCl gave 2-(cyclohexen-1-yl)cyclohexanone (**7**): ir (liquid film) 1700 cm^{-1}, and very much reduced shoulder (relative to that observed in the initial mixture of ketones produced by the self-condensation of cyclohexanone) at 1670 cm^{-1}; NMR ($CDCl_3$) δ 5.4 (0.96 H), 1.0–3.2 (17.0 H). The relative areas of the proton peaks in the NMR remained unchanged when the material sat at 25° for 6 days.

Registry No.—**2**, 57090-93-4; **5**, 1010-77-1; **7**, 1502-22-3; **9**, 57090-94-5; cyclohexanone, 108-94-1; boron trifluoride etherate, 109-63-7.

References and Notes

(1) This work was supported by Research Grant NS-9399-11 from the National Institutes of Health. Also it is a pleasure to thank Dr. James D. McChesney and Dr. Richard L. Schowen for helpful suggestions.
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Demethylation of Labile Aryl Ethers

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As part of a study of structure–activity relationships of certain synthetic estrogens, the carbinols 3-hydroxy-3-(3,4-dimethoxyphenyl)-4-(4-methoxyphenyl)hexane (I) and 3-hydroxy-3,4-bis(4-methoxyphenyl)hexane (II) were prepared. We also wished to prepare the corresponding free phenols, but found conventional methods of ether cleavage[1,2] to be unsatisfactory. These generally involve heating in the presence of acid and caused dehydration of the carbinols with formation of the corresponding olefins. However, the desired compounds were prepared in good yield by reaction at low temperature with stoichiometric amounts of boron tribromide.[3-5]

Experimental Section

Melting points were taken on a Fisher-Johns apparatus. Infrared spectra (KBr pellet) were recorded on a Perkin-Elmer Model 237 spectrophotometer. Gas chromatography-mass spectrometry was performed using a Perkin-Elmer Model 990 gas chromatograph coupled to an Hitachi RMU-6E mass spectrometer by a modified Watson-Biemann separator. A 180 × 0.2 cm glass column was used, packed with 3% OV-225 on 100–120 mesh Supelcoport. Helium flow rate was 20 ml/min and the column was operated at 190°. Electron impact spectra were recorded at 70 eV.

Demethylation Procedure. A 5% w/v solution of the ether in dry dichloromethane was cooled to −80° and added to a similarly cooled 10% v/v solution of boron tribromide in dichloromethane. One mole of reagent was used for each mole of methoxyl to be cleaved, i.e., 3 mol of reagent per mole of compound I and 2 mol of reagent per mole of compound II. The mixture, protected from moisture by a calcium chloride drying tube, was allowed to warm to room temperature overnight. Water was added to hydrolyze the boron–ether complex and any excess reagent and the phenolic product was extracted into diethyl ether.

I. 3-Hydroxy-3-(3,4-dihydroxyphenyl)-4-(4-hydroxyphenyl)hexane. Crude material was crystallized from benzene–hexane, yield 80%, mp 120°. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33; O, 21.17. Found: C, 71.45; H, 7.20; O, 21.35.

Gas chromatography of the tristrimethylsilyl ether yielded a single peak, retention time 8.8 min.

The mass spectrum of the trimethylsilyl derivative exhibited no molecular ion. Base ion was at *m/e* 500 as a result of loss of water from the molecule. Other prominent ions were at *m/e* 485 (loss of CH_3), 472 (loss of C_2H_4), 295, 205 (hydrogen transfer followed by scission of the molecule between C-3 and C-4 of the hexane chain), 281, 219 (rearrangement followed by scission), 75, 73 (from Me_4Si).

The infrared spectrum of the parent compound exhibited the expected bands due to bonded phenolic OH at ca. 3200 and 1240 cm^{-1} and substituted aromatic CH stretch in the region 1500–1600 cm^{-1}. In addition, a sharp band appeared at 3620 cm^{-1}. This band was absent in the spectrum of 3,4-bis-(4-hydroxyphenyl)hexane (diethylstilbestrol) and may, therefore, be attributed to nonbonded carbinol OH.

II. 3-Hydroxy-3,4-bis(4-hydroxyphenyl)hexane was crystallized from benzene, yield 87%, mp 137°. Anal. Calcd for $C_{18}H_{22}O_3$: C, 75.49; H, 7.74; O, 16.76. Found: C, 75.20; H, 7.80; O, 17.00.

Gas chromatography of the bistrimethylsilyl ether yielded a single peak, retention time 6.4 min.

The mass spectrum of the trimethylsilyl derivative was similar in all respects to that of compound I with ions appearing 88 amu lower. Base ion was at *m/e* 412 and other prominent ions appeared at *m/e* 397, 384, 207, 205, 219, 193, 75, and 73.

The infrared spectrum of the parent compound was also similar to that of compound I with differences attributable to the lesser degree of substitution of compound II.

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Registry No.—I, 57090-99-0; II, 5331-23-7; 3-hydroxy-3-(3,4-dihydroxyphenyl)-4-(4-hydroxyphenyl)hexane, 57091-00-6; 3-hydroxy-3,4-bis(4-hydroxyphenyl)hexane, 7504-83-8; boron tribromide, 10294-33-4.

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Stereochemistry of the Type II Elimination from 4-*tert*-Butylcyclohexyl Phenylacetate

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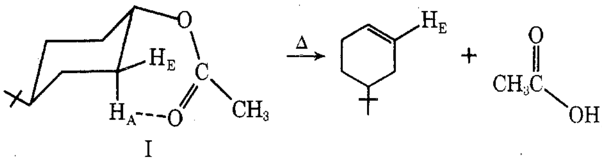
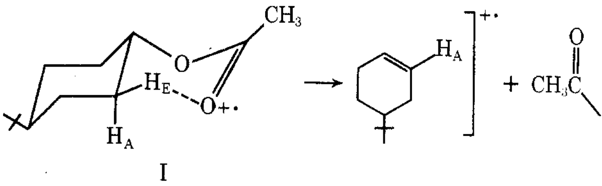
Recently, it has been observed that the stereochemistries of the electron impact induced and pyrolytic elimination of acetic acid from *trans*-4-*tert*-butylcyclohexyl acetate (I) differ.[1] The near-exclusive cis elimination observed in the pyrolysis (eq 1) is related to the greater ease of forcing cis cyclohexyl substituents toward coplanarity than trans substituents.[2] Since the pyrolysis is a concerted elimination, introduction of a double bond into the cyclohexyl ring system must involve a movement toward coplanarity of the eliminated substituents.[2,3] Conversely, it was suggested that the predominantly trans elimination observed in the electron impact induced process (eq 2) was evidence for the nonconcerted nature of this process.[4] In order to test this hypothesis, it appeared desirable to examine the stereochemistry of a bona fide stepwise unimolecular elimination occurring in an accessible phase. Because of the considerable recent interest in the type II photoelimination from phenylacetates, this reaction was an obvious choice for further investigation.

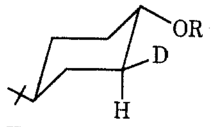


(1)



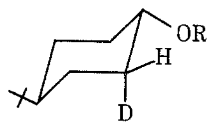
(2)

The photolytic elimination of phenylacetic acid has been suggested to be a syn intramolecular, nonconcerted process proceeding predominantly or exclusively through a singlet state.[5] Thus, the phenylacetates of the stereospecifically labeled alcohols IIa–Va were prepared and irradiated. Mass spectrometry was utilized to establish the isotopic composition of the 4-*tert*-butylcyclohexene product and thus the



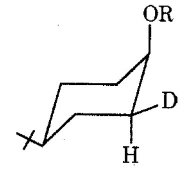
IIa, R = H

b, R = $C_6H_5CH_2\overset{\overset{O}{\|}}{C}$



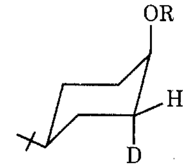
IIIa, R = H

b, R = $C_6H_5CH_2\overset{\overset{O}{\|}}{C}$



IVa, R = H

b, R = $C_6H_5CH_2\overset{\overset{O}{\|}}{C}$



Va, R = H

b, R = $C_6H_5CH_2\overset{\overset{O}{\|}}{C}$