the value obtained by Nugteren and coworkers,[2] it was necessary to establish the optical purity of the individual optical isomers. The method of Westly and Halpern,[3] which involves the glc analysis of the *l*-menthol carbonate ester derivative of the methyl ester of (±)-**4** proved to be a facile check on the completeness of the resolution. When we applied this method to (±)-**4**, we found that the glc of (±)-**4** showed two peaks (one for each diastereoisomer) for the *l*-menthol ester derivative, while the glc of the individually resolved and derivatized acids shows only one peak indicating that each acid was >98% optically pure.

Experimental Section[4]

(±)-2-Hydroxyheptanoic Acid. Sodium metabisulfite (54 g, 0.28 mol) in water (60 ml) was added dropwise to a magnetically stirred mixture of ether (100 ml), hexanal (50 g, 0.5 mol), potassium cyanide (34.5 g, 0.53 mol), ice (50 g), and water (10 ml) at 0 to 10°. After completion of the addition, the reaction mixture was stirred for 15 min at 0° and 15 min at room temperature. The reaction was extracted with ether (4 × 100 ml), and the ether extracts were dried ($MgSO_4$) and evaporated at reduced pressure to give an oil: ir (film) 3400 (OH) and 2140 cm^{-1} (C≡N).

The crude cyanohydrin in ethanol (200 ml) was saturated at 0° with hydrogen chloride, and allowed to stand overnight. Excess ethanolic hydrogen chloride was removed at reduced pressure, and the resulting oil was stirred with ice water (50 ml), then rapidly extracted with ether (2 × 100 ml) and chloroform (2 × 100 ml). The combined extracts were dried ($MgSO_4$), then evaporated at reduced pressure to give a yellow oil. Distillation of the crude product gave 68.2 g (93%) of pure ester: bp 105–107° (17 mm); ir (film) 3480 (OH) and 1735 cm^{-1} (CO_2Et).

The pure ester (50 g, 0.287 mol) in water (70 ml) and dioxane (70 ml) was magnetically stirred while slowly adding sodium hydroxide (12.6 g, 0.315 mol). After stirring overnight, the solution was acidified with hydrochloric acid and extracted with ether (3 × 100 ml). The ether extracts were dried ($MgSO_4$), then evaporated at reduced pressure to give a solid. Recrystallization of the crude acid from benzene–hexane (1:2) gave 39.8 g (95%) of pure 2-hydroxyheptanoic acid: mp 64–65° (lit.[2] mp 64–65°); ir ($CHCl_3$) 3400 (OH) and 1710 cm^{-1} (CO_2H).

D-(−)-2-Hydroxyheptanoic Acid. Four separate but identical resolutions were performed simultaneously. Anhydrous quinine (55.75 g, 0.172 mol) and 2-hydroxyheptanoic acid (25.0 g, 0.171 mol) were combined in methanol (400 ml) and heated to boiling. Hot (70°) water (1 l.) was added with stirring, and the solution became cloudy. Enough hot methanol was added to clarify the solution. After cooling, the salt which had crystallized from solution was collected, washed (2:5 methanol–water), and dried. The collected salt weighed 38 g (47%). This and the remaining recrystallizations are shown in Table I.

Table I

Crystallization	Methanol, ml	Water, ml	Weight, g	% yield
1	400	1000	38	47
2	150	700	35	44.5
3	175	700	36	43.7
4	200	600	26	33.2

The final rotation of the salt was $[\alpha]^{27}D$ +122.53 ± 0.15 (*c* 4.0, MeOH), and the liberated acid had an average rotation of $[\alpha]^{27}D$ −5.55 ± 0.05° (*c* 5.8, $CHCl_3$), after extraction into base, washing with ether, reacidification, extraction, and recrystallization of the collected acids from hexane.

L-(+)-2-Hydroxyheptanoic Acid. The filtrates from the first crystallization were treated with acid and extracted into ether, dried, and evaporated to give 49.26 g of L-(+)-2-hydroxyheptanoic acid.

Dehydroabeitylamine (50.38 g, 0.175 mol) and the partially resolved L-(+)-2-hydroxyheptanoic acid (23.45 g, 0.159 mol) were dissolved in hot methanol (250 ml), and hot water (100 ml) was added. The solution became cloudy and a small additional amount of methanol was added to clarify the solution. This and the remaining crystallization are shown in Table II.

Table II

Crystallization	Methanol, ml	Water, ml	Weight, g	% yield
1	250	100	63.4	91.6
2	450	200	62.3	89.9

The final rotation of the dehydroabeitylamine salt was $[\alpha]^{26}D$ +14.47 ± 0.06 (*c* 4.0, MeOH) while the liberated acid had a rotation of $[\alpha]^{26}D$ +5.53 ± 0.05° (*c* 5.8, $CHCl_3$).

Optical Purity Analysis. The methyl esters of individual acid samples were prepared by reaction with diazomethane in ether. One drop of the neat ester in five drops of pyridine was treated with four drops of L-menthol chlorocarbonate solution[3] (an excess). Glc analysis was performed at 180° on a 6-ft 1% QF, 1% OV-17 column with a 30-cm^3/min flow rate. Flame ionization was used for detection. The retention times for the derivatized methyl esters follow: (+), 6.57 min; (−), 7.20 min. The major components of the glc trace were identified by glc–mass spectrometry and by comparison of the individual components with authentic samples.

Acknowledgment. This work was supported under Contract NIH-NICHD-72-2712 with the Contraceptive Development Branch of the National Institutes of Child Health and Human Development.

Registry No.—(±)-4, 52358-05-1; (−)-4, 52437-20-4; (+)-4, 52437-21-5; hexanal, 66-25-1; (±)-hexanal cyanohydrin, 52358-06-2; ethyl (±)-2-hydroxyheptanoate, 52438-78-5.

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(4) Melting points were taken on a Kofler hot stage microscope and are uncorrected. Nmr spectra were determined on a Varian Associates Model HA-100 spectrophotometer in chloroform with tetramethylsilane as an internal standard. Glc–mass spectra were determined on a Varian MAT CH-7 mass spectrometer. Infrared spectra were obtained with a Perkin-Elmer Model 267 double beam spectrophotometer. Rotations were taken on a Perkin-Elmer Model 141 polarimeter.

Synthesis of 3,5-Dialkyl-1,2-dioxolanes[1]

P. M. Jacobs and A. H. Soloway*

Departments of Chemistry and of Medicinal Chemistry and Pharmacology, Northeastern University, Boston, Massachusetts 02115

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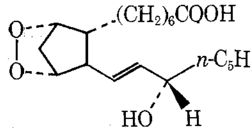
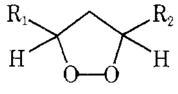
The prostaglandin endoperoxide, **1**, has been proposed as an intermediate in the biosynthesis of other prostaglandins.[2,3] Such structures have been detected in *in vitro* biosyntheses.[3] In view of the biological importance of the prostaglandins, it is pertinent to develop synthetic schemes for the chemical preparation of **1**.

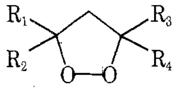


1

Saturated 1,2-dioxanorboranane have not been described in the literature. The synthesis of simple model structures may furnish necessary background for synthesis of compounds such as **1**. For this reason, we undertook to synthesize and investigate the decomposition of the 3,5-dialkyl-1,2-dioxolanes, **2**, cyclic alkyl peroxides with secondary carbon atoms adjacent to the oxygen atoms.



2

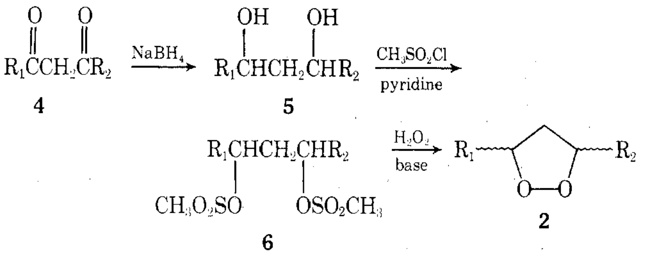


3

Compounds of the type **3**, with tertiary carbon atoms next to the peroxide linkage are known[4-7] and their thermal and photochemical decomposition have been studied.[5-7] These dioxolanes are synthesized by the acid-catalyzed reaction of the corresponding 1,3-diol with concentrated hydrogen peroxide; however, this method is feasible only with tertiary alcohols.

A useful general but low-yield method for the synthesis of secondary acyclic hydroperoxides and dialkyl peroxides is that of Williams and Mosher.[8,9] In this synthesis, methanesulfonyl groups are displaced by nucleophilic attack of peroxy anions; adjustment of the proportion of hydrogen peroxide in the mixture determines whether the product is primarily hydroperoxide[8] or dialkyl peroxide.[9] This method has been used[10] to synthesize one unsubstituted six-membered ring, 1,2-dioxane, in moderate yield from a diprimary 1,4-diol bismethanesulfonate.

We adapted this method for the synthesis of two 3,5-dialkyl-1,2-dioxolanes from the bismethanesulfonates of disecondary 1,3-diols. The general synthetic scheme is shown below.



a, $R_1 = CH_3$; $R_2 = PhCH_2CH_2$
b, $R_1 = R_2 = PhCH_2CH_2$

Reduction of **4a**[11] with sodium borohydride in methanol[12] gave the diol **5a**; the bismethanesulfonate, **6a**, was prepared from **5a** and methanesulfonyl chloride in the presence of pyridine. Reaction of **6a** with an excess of hydrogen peroxide and potassium hydroxide in methanol gave **2a**. To avoid excessive base decomposition, **2a** was extracted from the reaction mixture as it was formed by an overlayer of hexane. After purification by repetitive short column chromatography, the product **2a** was homogeneous on tlc and gave a positive reaction to a peroxide spray reagent.[13] Microanalysis and molecular weight determination were in accord with structure **2a**.

The infrared spectrum of **2a** shows no alcohol, hydroperoxide, ketone, or methanesulfonate absorptions; the nmr shows no exchangeable protons and all the absorptions are in the expected regions. The protons α to the oxygen atoms are shifted downfield relative to the parent alcohol by about 0.2 ppm. The direction and magnitude of this shift is similar to that observed for dialkyl peroxides.[14] Reaction of **2a** with lithium aluminum hydride in ether gives a diol identical in all respects with diol **5a**. The dioxolane is unchanged after being stored for one year at −20° but decomposes significantly after a few days at room temperature.

Similarly, diketone **4b**[15] was transformed to diol **5b** which in turn was converted to bismethanesulfonate **6b**. The dioxolane, **2b**, was obtained by reaction of **6b** with hydrogen peroxide and solid potassium carbonate in methanol with a hexane overlayer. Analysis, spectra, and tlc data were all in accord with the structure **2b**, and reduction with lithium aluminum hydride furnished the expected diol **5b**. The thermal stability of **2b** is similar to that of **2a**.

No attempt was made to optimize the yields of these peroxides by systematically varying the temperature, the concentration of hydrogen peroxide, and the specific base used for the cyclization. The key purpose of this study was to determine the feasibility of preparing such compounds and to assess their stability.

Experimental Section

General. Melting points were taken on a Mel-Temp apparatus and are corrected. Boiling points are uncorrected. *All reactions involving 98% hydrogen peroxide (FMC Corporation) were performed behind safety shields and reasonable caution was exercised with potentially explosive products.* Elemental and molecular weight analyses were performed by Midwest Microlabs, Inc. (Indianapolis, Ind.). Nuclear magnetic resonance (nmr) spectra were recorded on a Varian T-60 instrument and are reported in parts per million downfield from tetramethylsilane. Infrared spectra were recorded on a Beckman IR-8 or IR-10 and are reported in reciprocal centimeters. Silica gel coated glass plates (E. Merck, F-254) were used for all tlc and were stored in a desiccator prior to use.

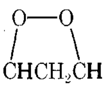
6-Phenyl-2,4-hexanediol (5a). A solution of 42.2 g (0.222 mmol) of dione **4a**[11] in 60 ml of methanol was added dropwise to a solution of 6 g (0.158 mmol) of sodium borohydride and 0.3 g sodium hydroxide in a mixture of water (60 ml) and methanol (50 ml). The solution was stirred overnight. The methanol was removed under reduced pressure and water was added. The mixture was extracted twice with chloroform. The chloroform solution was dried over magnesium sulfate and evaporated to give 43 g (100%) of a hydroscopic yellow oil. Purification of a portion of this oil on silica gel/chloroform gave diol **5a** in 65% yield: ir 3400–3600 (OH), 1610 (phenyl), 1500 (CH_3), 1050–1150 (CO); nmr ($CDCl_3$) δ 7.15 (s, 5, C_6H_5), 4.6 (br s, 2, exchangeable, two OH), 3.95 [m, 2, $\mathbf{CH}(OH)CH_2\mathbf{CH}(OH)$], 2.6 (m, 2, $C_6H_5\mathbf{CH_2}$), 1.7 [m, 4, $\mathbf{CH_2}CH(OH)\mathbf{CH_2}CH(OH)$], 1.2 (d, 3, CH_3).

A bisnitrobenzoate was prepared from the diol and had mp 115–118°; ir 3110, 3050, 3020 (aromatic H), 2980, 2930 (aliphatic H), 1720 (ester), 1600 (phenyl), 1520, 1350 (NO_2), 1270 (ester); nmr ($CDCl_3$) δ 8.2 (s, 8, two $NO_2C_6H_4$), 7.2 (s, 5, C_6H_5), 5.4 [m, 2, $\mathbf{CH}(OCOPhNO_2)CH_2\mathbf{CH}(OCOPhNO_2)$], 2.8 (m, 2, $C_6H_5\mathbf{CH_2}$), 2.2 [m, 4, $\mathbf{CH_2}CH(OCOR)\mathbf{CH_2}CH(OCOR)$], 1.5 (d, 3, CH_3).

Anal. Calcd for $C_{26}H_{24}N_2O_8$: C, 63.41; H, 4.91; N, 5.69. Found: C, 63.28; H, 4.87; N, 5.70.

The bismethanesulfonate **6a** was prepared from the diol and purified by column chromatography on silica gel/chloroform to give 84% of a clear oil: ir no alcohol, 1185 and 1350 (sulfonate); nmr ($CDCl_3$) δ 7.2 (s, 5, C_6H_5), 4.9 [m, 2, $\mathbf{CH}(OMs)CH_2\mathbf{CH}(OMs)$], 2.9 (m, 8, two OSO_2CH_3 and $C_6H_5CH_2$), 2.1 [m, 4, $CH_2CH(OMs)CH_2CH(OMs)$], 1.5 (d, 3, CH_3).

3-Methyl-5-(2-phenylethyl)-1,2-dioxolane (2a). A solution of 3.7 g (10.5 mmol) 6-phenyl-2,4-hexanebismethanesulfonate **6a**, 12 ml 30% hydrogen peroxide (0.13 mol), and a trace of thymol blue indicator in 35 ml methanol was heated to 50° and overlaid with hexane. A solution of 1 *N* potassium hydroxide in methanol–water was added dropwise to keep the indicator color blue to green. In 7 hr, one third of the required amount of base had been added. The hexane layer was removed and replaced with fresh solvent. The remainder of the base was added all at once. Another hexane extract was taken at 24 hr and again at 96 hr. The combined hexane layers were evaporated and chromatographed on silica gel/chloroform to give 280 mg (13%) peroxide positive[13] material, R_f ($CHCl_3$) 0.62, contamined with starting material. Two further column chromatographs, on silica gel with methylene chloride and with benzene, gave 140 mg (7%) pure **2a**, a yellow oil: it was homogeneous on tlc in $CHCl_3$, ethyl acetate, and 20% ethyl acetate in hexane; ir, no alcohol absorptions, 3070, 3040 (aromatic H), 2980, 2940 (aliphatic H), no carbonyl absorptions, 1600 (phenyl), 1500 (methyl); nmr ($CDCl_3$) δ 7.1 (s, 5, C_6H_5), 4.2 (m, 2, a), 2.6 (m, 2, $C_6H_5\mathbf{CH_2}$), 2.4–1.4 [m, 4, $\mathbf{CH_2}CH(OO)\mathbf{CH_2}$], 1.2 (d, 3, $\mathbf{CH_3}$). The couplings are clearly second order; irradiation at the δ 4.2 peak causes peak



$\overset{O\text{—}O}{CHCH_2CH}$

a

shape changes in the peaks at δ 2.6 (crude t), 2.4–1.4 (crude t), and 1.2 (s).

Anal. Calcd for $C_{12}H_{16}O_2$ (mol wt, 192.26): C, 74.96; H, 8.39. Found [mol wt, 198 (±5%)]: C, 75.14; H, 8.35.

Treatment of a solution of dioxolane **2a** in ether with an excess of lithium aluminum hydride for 3 hr gave a quantitative yield of diol having the same R_f on tlc as 6-phenyl-2,4-hexanediol **5a**. A bisnitrobenzoate was prepared from this material, chromatographed on silica gel/chloroform, and crystallized from ethyl acetate–hexane. It had mp and mmp 115–118°, with the bisnitrobenzoate from **5a** and its ir was superimposable on that of the authentic compound.

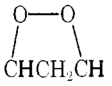
1,7-Diphenyl-3,5-heptanediol (5b). A solution of 1,7-diphenyl-3,5 heptanedione[15] (0.111 mol, 31 g) in 100 ml methanol was added dropwise to a solution of 4.6 g sodium borohydride (0.122 mol) in 150 ml methanol. The solution was refluxed overnight. The methanol was removed under vacuum. To the residue was added water and an excess of mannitol;[12] this aqueous solution was extracted three times with chloroform. A yellow oil was obtained in 98% yield and crystallized from ether–hexane to give 20 g (63%), mp 65–82°. Three fractional crystallizations failed to give any usable gradation in melting point. The highest melting point attained, after extensive crystallizations was 78–82°. The diasteromers appear to form a solid solution since spectra and analytical results are the same for the high melting as for the initially crystallized material: ir 3680, 3590, 3450 (OH), 1600 (phenyl), 1200 (CO); nmr ($CDCl_3$) δ 7.2 (s, 10, two C_6H_5), 3.9 [m, 2, $CH(OH)CH_2CH(OH)$], 3.3 (br s, exchangeable, two OH), 2.7 distorted t, 4, two $C_6H_5CH_2$), 1.7 [m, 6, $\mathbf{CH_2}CH(OH)\mathbf{CH_2}CH(OH)\mathbf{CH_2}$].

Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found; C, 80.21; H, 8.68.

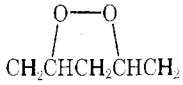
The bismethanesulfonate **6b** was prepared and crystallized from chloroform-hexane to give mp 60–69°; nmr ($CDCl_3$) δ 7.2 (s, 10, two C_6H_5), 4.8 [m, 2, $CH(OMs)CH_2CH(OMs)$], 2.9 (s, 6, two OSO_2CH_3), 2.7 (m, 4, two $C_6H_5CH_2$), 2.1 [m, 6, $\mathbf{CH_2}CH(OMs)\mathbf{CH_2}CH(OMs)\mathbf{CH_2}$].

Anal. Calcd for $C_{21}H_{28}S_2O_6$: C, 57.26, H, 6.41, S, 14.53. Found: C, 57.19, H, 6.13, S, 14.28.

3,5-Bis(2-phenylethyl)-1,2-dioxolane (2b). A mixture of 11 g of bismethanesulfonate **6b** (25 mmol), 8.3 g of potassium carbonate (60 mmol), and 10 ml of 98% hydrogen peroxide (400 mmol) in 100 ml of methanol with a hexane overlayer was heated to 40° overnight. The hexane was removed and the reaction continued with fresh hexane for an additional 12 hr. The hexane layers were combined to give 0.86 g oil (17%, corrected for 3.2 g bismethanesulfonate recovered). After two column chromatographs on silica gel/benzene, 280 mg (5.6%) of peroxide positive material was obtained. Preparation of **2b** by the method used for **2a** gave only 0.5% yield: the material was homogeneous on tlc in four solvent systems; ir, no alcohol, no carbonyl, 1880, 1810, 1740, all weak aromatic bands; no sulfonate; nmr ($CDCl_3$) δ 7.2 (s, 10, two C_6H_5), 4.2 (quintet, 2, b, 2.7 (distorted d of t, 4, two $C_6H_5CH_2$), 2.4–1.6 (m, 6, c).



b



c

Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.52; H, 8.11.

A solution of dioxolane **2b** in ether was treated with an excess of lithium aluminum hydride at room temperature, yielding a diol that was identical with **5b** on four tlc systems and having mp 81–82°, mmp 77–81° with **5b**.

Registry No.—**2a**, 52393-48-3; **2b**, 52393-49-4; **4a**, 52393-50-7; **4b**, 38572-30-4; **5a**, 52393-51-8; **5a** bisnitrobenzoate, 52393-52-9; *meso*-**5b**, 52393-53-0; *dl*-**5b**, 52393-54-1; **6a**, 52393-55-2; *meso*-**6b**, 52393-56-3; *dl*-**6b**, 52393-57-4; hydrogen peroxide, 7722-84-1.

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(1) This investigation was supported by Grant No. NR408-979 from the Department of the Navy. It is abstracted in part from the Ph.D. thesis of P. M. Jacobs.
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Synthesis of 1-, 2-, 3-, and 4-Phenylphenanthrenes by Photocylization of Isomeric Phenylstilbenes[1]

S. Carlton Dickerman and Isaak Zimmerman*[2]

Department of Chemistry, New York University, New York, New York 10453

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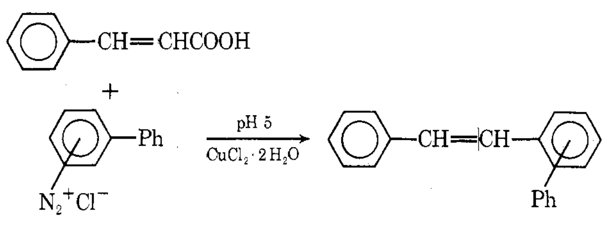
Authentic samples of 1-, 2-, 3-, 4-, and 9-phenylphenanthrenes were needed in connection with a larger study of the correlation of structure and reactivity in homolytic phenylation of polycyclic aromatic hydrocarbons.[3] At the time our investigation began, the required compounds had already been described in the literature,[4] but their synthesis involved lengthy reaction sequences. After we had prepared 1- and 4-phenylphenanthrene *via* the classical method of Haworth,[5] Mallory and coworkers described the photocyclization of substituted stilbenes to phenanthrene derivatives, including the formation of 9-phenylphenanthrene from triphenylethylene.[6] The simplicity of Mallory's method led us to extend it to the desired 1-, 2-, 3-, and 4-phenylphenanthrenes (**1–4**). Since the original report, the photolysis of a variety of stilbenes in the presence of air or iodine to form phenanthrenes has proved to be the method of choice and has been studied extensively.[7–9] The isomeric *o*-, *m*-, and *p*-phenylstilbenes (**6a–c**) were obtained by a modification of the Meerwein reaction between cinnamic acid and diazotized 2-, 3-, and 4-aminobiphenyl hydrochlorides (**5a–c**), respectively. The reaction is represented in eq 1 (see the Experimental Section).



(1)

5a, 2-N_2^+ Cl^-
b, 3-N_2^+ Cl^-
c, 4-N_2^+ Cl^-

6a, *o*-Ph
b, *m*-Ph
c, *p*-Ph

Photoconversions of **6a–c** to phenylphenanthrenes were conducted in benzene–cyclohexane solutions in the presence of iodine and air as outlined in Scheme I. Separation of **4** from **2** was easily accomplished because of the low solubility of **2** in ethanol. The slightly lower yield of **4** compared with **2** may be attributed to a steric effect in the cyclization between the phenyl and hydrogen at positions 4 and 5. Recently very low yields of photocyclization product were reported in a case where the steric effect was more pronounced.[9]