Stereospecific Reduction of 2,3-Epoxybutanoic Acid. Synthesis of (*R*,*R*)- and (*S*,*S*)-3-Hydroxybutanoic-*2*-*d* Acid and *S*-*tert*-Butyl 3-Acetoxythiobutanoate-*2*-*d*[1a]

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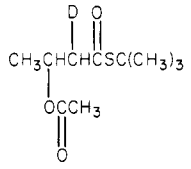
Reduction of 2,3-epoxybutanoic acid (**2**) with sodium borodeuteride provides a stereospecific synthesis of 3-hydroxybutanoic-2-*d* acid (**3**). This route should be of general utility in stereospecific syntheses of metabolically important 3-hydroxyalkanoic acid derivatives labeled at C-2. Metal ions seem to play an important role in the relative rates of nucleophilic attack at the α- and β-carbon atoms of **2**. Compound **3** was converted to *S*-*tert*-butyl 3-acetoxythiobutanoate-2-*d* (**1**) with virtually no H-D exchange; the mixed anhydride method proved more effective than the DCC method for the thioester synthesis.

Base-catalyzed addition–elimination reactions that involve carbon–carbon double bonds conjugated to carbonyl groups are important both in organic and biochemistry. Although the stereochemistry of such reactions has been elucidated for a few enzyme-catalyzed systems,[2] we found to our surprise that almost nothing is known about the stereochemistry of simple base-catalyzed elimination reactions leading to conjugated thioesters or ketones. In order to discover the stereochemistry of such a reaction in a conformationally mobile acyclic system, we have synthesized *S*-*tert*-butyl 3-acetoxythiobutanoate-2-*d* (**1**) in which the relative configurations at C-2 and C-3 are known.



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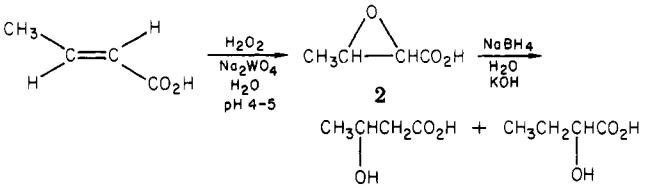
Since the synthesis of **1** from suitably labeled 3-hydroxybutanoic acid should be straightforward, we chose to concentrate our initial efforts on this route. Surprisingly, the literature contains no general methods for the synthesis of stereospecifically labeled 3-hydroxybutanoate-2-*d* or any analogous 3-hydroxyalkanoates, in spite of their metabolic importance.

Willadsen and Eggerer utilized the hydroboration of ethyl crotonate for their synthesis of the stereospecificity tritiated 3-hydroxy acid, but the yield was low (~4%).[2] We were unable to increase this yield, despite a number of attempts. Even the hydroboration of *tert*-butyl crotonate with the hindered disiamylborane led to less than 10% yield. The difficulty arises from the strong directive influence of the carboalkoxy group upon the regiospecificity of hydroboration. The boron adds at C-2 and this eventually leads to net hydrogenation of the carbon–carbon double bond.[3]

Another possible synthetic route was the reduction of epoxides of crotonic acid derivatives. Although epoxides are reported to reduce faster than esters with BH_3/BH_4^-,[4] we were unable to reduce the epoxy group preferentially in ethyl 2,3-epoxybutanoate with either BH_3/BH_4^- in THF or disiamylborane/BH_4^- in THF. The major problem is concurrent reduction of the epoxide and carbonyl functional groups. Reduction of α,β-epoxy esters with $NaBH_4$ and $LiBH_4$ also leads primarily to reduction of the carbonyl group.[5]

In an attempt to reduce the electrophilic character of the carbonyl group, we synthesized 2,3-epoxybutanoic acid (**2**) by the epoxidation of crotonic acid and examined its reduction with $NaBH_4$ in alkaline solutions. Although the reaction must be done under carefully controlled conditions, it works quite smoothly and in good yields. Nucleophilic attack by BH_4^- or BD_4^- occurs at both the α and β positions; however, reaction at the α position is favored as expected.[6]



The synthesis of thioesters has received a good deal of attention in the last few years, especially in syntheses of macrolide antibiotics.[7] We, of course, needed a synthetic route for the thioester in which no proton exchange would occur at C-2. In this light, we examined the catalytic activity of dicyclohexylcarbodiimide (DCC)[7b] and of trifluoroacetic anhydride.[8] The mixed anhydride method proved to be superior.

Results and Discussion

The reaction of epoxides with nucleophiles, such as BD_4^-, is an S_N2 reaction under neutral or alkaline conditions; it should proceed with clean inversion of configuration.[9] In the reduction of **2**, it is possible to confirm this by examining the NMR coupling constant of the protons at C-2 and C-3 in the reduced product. With inversion at C-2 the predicted coupling constant would be in the range 7-13 Hz; if retention had occurred, 3–5 Hz would be expected.[10,11]

(1) (a) Presented in part at the 2nd Chemical Congress of the North American Continent, Las Vegas, NV, Aug 1980, Orgn 198. (b) 3M Undergraduate Student Scholar, Summer 1980.
(2) P. Willadsen and H. Eggerer, *Eur. J. Biochem.*, **54**, 247 (1975).
(3) H. C. Brown and K. A. Keblys, *J. Am. Chem. Soc.*, **86**, 1795 (1964).
(4) H. C. Brown, "Boranes in Organic Chemistry", Cornell University Press, Ithaca, NY, 1972.
(5) (a) S. Corsano and G. Piancatelli, *J. Chem. Soc., Chem. Commun.*, 1106 (1971); (b) D. C. Bishop and W. R. N. Williamson, *J. Chem. Soc. C*, 1827 (1967).
(6) F. G. Bordwell and W. T. Brannen, Jr., *J. Am. Chem. Soc.*, **86**, 4645 (1964).
(7) (a) S. Masamune, G. S. Bates, and J. W. Corcoran, *Angew. Chem., Int. Ed. Engl.*, **16**, 585 (1977); (b) B. Neises and W. Steglich, *ibid.*, **17**, 522 (1978); (c) H.-J. Gais and T. Lied, *ibid.*, **17**, 267 (1978); (d) Y. Watanabe, S. Shoda, and T. Mukaiyama, *Chem. Lett.*, 741 (1976).
(8) L. R. Fedor, *J. Am. Chem. Soc.*, **91**, 913 (1969).
(9) (a) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959); (b) H. C. Brown and N. M. Yoon, *J. Am. Chem. Soc.*, **90**, 2686 (1968).
(10) R. A. Alberty and P. Bender, *J. Am. Chem. Soc.*, **81**, 542 (1959).
(11) O. Gawron, A. J. Glaid, III, and T. P. Fondy, *J. Am. Chem. Soc.*, **83**, 3634 (1961).

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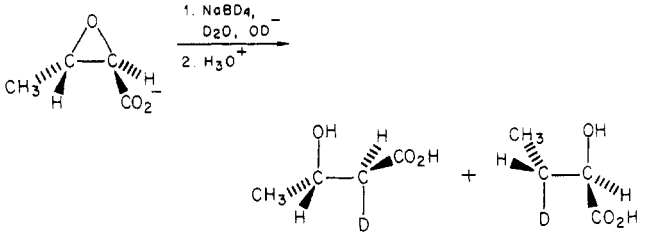
Examination of the NMR peak at 2.5 ppm, due to the proton at C-2 of the 3-hydroxybutanoic-2-*d* acid (**3**), showed a coupling constant of 9.0 Hz; this clean doublet was also somewhat broadened by H–D coupling. NMR integration showed that the product contained 1.00 deuterium atom at C-2. Thus, we can be sure of the relative configurations at C-2 and C-3. Reduction of the epoxide of *trans*-crotonic acid with $NaBD_4$ stereospecifically leads to racemic (*R,R*)- and (*S,S*)-3-hydroxybutanoate-2-*d*.

This reaction should prove to be of general utility in the stereospecific synthesis of 2-deuterio-3-hydroxy carboxylic acids. Since the parent compounds are important intermediates in biochemical pathways, our results could be quite useful to bioorganic chemists and biochemists. In addition, the deuterated hydroxy acids could serve as synthons for other useful compounds.



52% isolated yield
J = 9.0 Hz

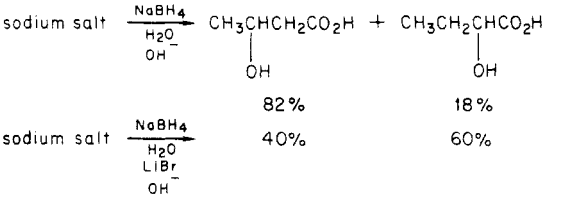
Early attempts to find a suitable organic solvent for the borohydride reduction were frustrated by poor solubility of the carboxylate salt and $NaBH_4$. The aqueous reaction environment worked very well although the reaction was quite slow. Approximately 14 days were necessary for complete reaction at 35 °C with 3 M epoxide and 1.5 M borohydride. Temperature and pH control are important in the reduction step. If the reaction mixture is too alkaline or too warm, the 2,3-diol can be formed, and this viscous compound makes product isolation very difficult. Control reactions showed that the epoxide decomposed almost completely in 6–8 days in 1.2 M KOH, whereas only 35% decomposed in 0.25 M KOH over a 14-day period. If the reaction is too acidic, decomposition of the borohydride can occur; this is especially serious when $NaBD_4$ is the reducing agent, due to its expense. We found that a KOH concentration of 0.20–0.25 M worked quite well. Progress of the reaction was conveniently monitored by NMR spectroscopy, and chromatography on silica gel gave clean separation of the α- and β-hydroxy acids. Excess heat and acid must be avoided in the workup of the hydroxy acid products, as the β-hydroxy acid readily forms a dimeric ester, which eluted on our silica gel columns between the two monomeric acids.

In an attempt to increase the rate of reduction, an excess of lithium bromide was added. Lithium salts have been reported to increase the rate of borohydride reductions in 2-propanol but not in dilute aqueous solution.[12] We thought, however, that they might do so in our concentrated aqueous reaction mixture. To our initial surprise, we found the ratio of nucleophilic attack at C-2/C-3 changed from 4.6 to 0.7 (Scheme I). We attribute this rather dramatic change to electrophilic catalysis by the lithium cation.

It seems possible that coordination of lithium at the epoxide oxygen would preferentially weaken the bond to C-3 and nucleophilic attack at C-3 would become faster as a consequence. Coordination of the lithium cation with the carboxylate oxygens would be even stronger. This

(12) H. C. Brown and K. Ichikawa, *J. Am. Chem. Soc.*, **83**, 4372 (1961).

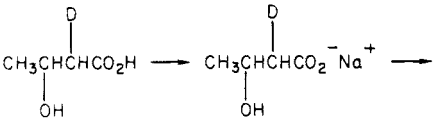
Scheme I. Borohydride Reductions of 2,3-Epoxybutanoic Acid[a]



[a] Completed reactions were acidified with HCl.

could promote hydride transfer through a cyclic transition state in which lithium is coordinated to a carboxylate oxygen and to BH_4^-. However, for this to be the case, a seven-membered transition state would have to compete effectively with the more common six-membered transition state. Our experiments thus far are of a preliminary nature, and we are continuing to investigate this interesting metal–ion control.

Conversion of **3** to **1** was achieved in two steps, modeled on the work of Fedor.[8] Acetylation of **3** with acetyl chloride in ether is a straightforward reaction; however, a certain amount of H–D exchange occurred at C-2 when the reaction was done in the usual way. This problem was avoided by the simple expedient of converting **3** to its sodium salt and reacting this under rigorously dry conditions. Production of HCl in the reaction continuously drew the carboxylate salt into solution and the reaction went smoothly. Proton NMR analysis of the 3-acetoxybutanoic-2-*d* acid (**4**) showed <1.5% H–D exchange; the α proton was a doublet, J = 7.7 Hz.



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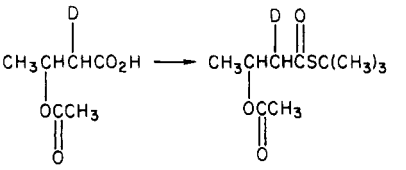

4 **1**

Reaction of **4** with trifluoroacetic anhydride, followed by addition of 2-methyl-2-propanethiol, led to **1** with <0.8% H–D exchange. Rather than the usual NMR doublet of doublets for the protons at C-2 of the unlabeled compound, **1** exhibited a somewhat broadened doublet, J = 7.7 Hz. Yields of the distilled product varied from 40% to 80%. With conservative averages for the yield in each of the three steps, the overall yield of **1** from **2** was 20%.

With the current interest in thioester syntheses, it may be useful to report our experience with DCC as a dehydration agent for the conversion of **4** to **1**.[7b] With the use of catalytic quantities of heterocyclic bases, synthesis of **1** went smoothly but, along with **1**, produced some *S-tert*-butyl thiocrotonate by elimination of acetic acid. Even more important a considerable amount of H–D exchange occurred at C-2. When the DCC-catalyzed esterification was done without base present, product yields dropped significantly and a large amount of the *N*-acylurea accompanied the desired thioester. Using a variety of solvents did not improve the situation.

In order to discover experimental conditions under which no H–D exchange takes place during synthesis of **1** and **4**, we ran large numbers of control experiments.

Especially useful in these experiments was 3-hydroxybutanoic-2-d_2 acid (5). Proton NMR integration allowed straightforward evaluation of H–D exchange. The synthesis of 5 started with methyl acetoacetate, which was deuterated, reduced, and hydrolyzed in one step by using $NaBH_4$ in alkaline D_2O solution.

Experimental Section

General Procedures. Proton NMR spectra were run on a 60-MHz Perkin-Elmer R-24B spectrometer with $CDCl_3$ or D_2O solutions and Me_4Si as the standard. IR spectra were recorded on a Perkin-Elmer Model 700 spectrophotometer. For GC analyses, 6-ft columns of 8% Carbowax 1540 and 8% SF-96 on Anakrom ABS were used on a Carle GC 8700. Glassware was oven dried and cooled in a desiccator where appropriate. Compound 2 and stereospecifically deuterated compounds were stored at −90 °C. Epoxidation of ethyl crotonate was done by the method of Kishi.[13] Borane and disiamylborane reductions were done in the usual manner.[4]

Synthesis of 2,3-Epoxybutanoic Acid (2).[14] Crotonic acid (Aldrich) was recrystallized from H_2O, which removed all traces of the cis isomer. One-half mole (43 g) of crotonic acid was added to 125 mL of 2 M NaOH solution. The solution was brought to 24 ± 0.5 °C and 17.5 g (0.053 mol) of $Na_2WO_4 \cdot 2H_2O$ was added with mixing. Over a 15–20-min period, 0.65 mol of 30% H_2O_2 was dripped into the stirred solution. The reaction was monitored by NMR spectroscopy; the characteristic doublet of crotonic acid at δ 1.75 disappeared in 24–48 h. During the entire reaction the pH was maintained at 4–5 by the addition of 50% NaOH solution.

The pH was brought to 2.4 by dropwise addition of 6 M H_2SO_4 at 24 °C and the reaction mixture saturated with $(NH_4)_2SO_4$. A total of 0.6 L of Et_2O in six equal fractions was used to extract 2. The ether solution was dried ($MgSO_4$, Drierite) and the ether removed under vacuum. The solid product (24.5 g) was recrystallized from CH_2Cl_2. Recrystallized 2 was isolated in 36% yield (18.0 g).

Reduction of 2 with $NaBH_4$. A CO_2-free 50% KOH solution was used to convert 2 to its potassium salt and 1-propanol was added to make a 28.2/71.8 (H_2O/1-propanol) mixture by volume. Removal of excess water was accomplished by rotary evaporation of the H_2O/1-propanol azeotrope (bp 88.1 °C) at less than 40 °C. Subsequent vacuum desiccation over Drierite gave solid potassium 2.

Potassium 2 (10.5 g, 0.075 mol) was added to a small volume of H_2O, and a CO_2-free 50% KOH solution (0.474 mL, 10.5 M) was added to bring the final hydroxide concentration to 0.20 M. The temperature was kept below 10 °C during the addition of alkali. Sodium borohydride (1.42 g, 0.0375 mol, Eastman) and water were added to the solution to bring the final concentration of potassium 2 to 3.0 M and $NaBH_4$ to 1.5 M; the final volume was 25 mL. The reaction vessel was flushed with N_2 and an N_2 atmosphere maintained throughout the reaction.

The reaction temperature was maintained at 35 °C and its progress monitored by proton NMR spectroscopy. Each NMR sample was acidified with concentrated HCl, thereby eliminating the B–H peaks in the spectrum and production of H_2 gas in the NMR tube. When the epoxide peak at δ 3.5 had disappeared, the reaction was complete. Complete reaction took 12–14 days under these conditions. NMR spectroscopy showed that the reduced product was a mixture of 3-hydroxy- and 2-hydroxybutanoic acid in a 4:1 ratio. The 2-hydroxy acid had characteristic NMR peaks at δ 1.0 (t), 1.7 (m), and 3.9 (t), whereas 3-hydroxybutanoic acid had characteristic peaks at δ 1.2 (d), 2.5 (d), and 4.3 (m). NMR spectra of authentic samples were used for comparison with spectra of the reduction mixture.

After the reaction mixture was cooled to 0 °C, the pH was brought to 7.0 with concentrated HCl and the water removed by rotary evaporation with as little heat as possible. A white solid resulted. This was dissolved in a minimum, measured amount of water (10.0 mL) and the pH brought to 2.0 with 7.7 mL of concentrated HCl. Enough 1-propanol (45 mL) was added to make a 28.2/71.8 (H_2O/1-propanol) mixture by volume. The liquid was removed by rotary evaporation below 40 °C; higher temperatures led to dimerization of the hydroxybutanoic acids.

The solid was extracted with Et_2O in six thorough extractions (30 mL each). After drying the combined ether solutions ($MgSO_4$, Drierite), the ether was evaporated, giving a hygroscopic, viscous liquid. The isomeric hydroxy acids were separated on silica gel (Mallinckrodt, 100 mesh) with N_2 pressure, using 20 g of silica gel for each gram of hydroxy acid. Addition of Bromcresol green indicator and a few drops of triethylamine to the silica gel made visualization of the chromatogram straightforward. The hydroxy acids were eluted at 9 °C with a CH_2Cl_2/2-propanol mixture (95:5). The 2-hydroxy acid eluted first.

Stereospecific Reduction of 2 with $NaBD_4$. The same procedure was followed as above, except that deuterated reagents were used, and the free acid, 2, was substituted for its potassium salt. To 20 mL of D_2O (99.8% D) was added 2 (23.0 g, 0.225 mol). While this solution cooled at 10 °C, a 40% KOD/D_2O solution (22.4 mL, 10.7 M; 98+% D, Aldrich) was added dropwise with stirring to bring the final [OD^-] to 0.20 M. After addition of $NaBD_4$ (4.71 g, 0.113 mol; 98% D, Merck, Sharp & Dohme), the solution was brought to a final volume of 75 mL with D_2O. The reduction took 9 days at 35 °C. After chromatography a 52% yield of stereospecifically deuterated 3 (12.2 g) was obtained. NMR integration showed 50–51% deuterium incorporation at C-2. The coupling constant $J_{H(C\text{-}2)\text{-}H(C\text{-}3)}$ was 9.0 Hz with some line broadening of the proton at C-2 due to H–D coupling.

Synthesis of 3-Acetoxybutanoic-2-d Acid (4).[8] A 50% NaOH solution was used to convert 3 to its sodium salt. Removal of excess water by rotary evaporation at less than 40 °C and subsequent vacuum desiccation gave solid sodium 3, $J_{H(C\text{-}2)\text{-}H(C\text{-}3)}$ = 7.7 Hz.

Fifteen milliliters of Et_2O and 5.0 g (0.040 mol) of the sodium salt were slurried together in a flask provided with an N_2 atmosphere. Under cooling (ice–salt), a solution of acetyl chloride (3.1 mL, 0.044 mol) in Et_2O (6 mL) was added dropwise over a 20-min period. The reaction was stirred for 12 h at 22 °C. Ether and excess acetyl chloride were removed by evaporation. Et_2O (25 mL) was added and the mixture filtered to remove NaCl. Saturated NaCl/$NaHCO_3$ solution (2–3 mL) was added until the pH of the aqueous wash was brought up to 2.5. The ether solution was then dried and evaporated, giving a viscous, clear liquid. The yield was 5.6 g (>90%). Less than 1.5% H–D exchange occurred at carbon-2. The α proton of 4 was a doublet, J = 7.7 Hz; NMR integration showed 51% H at the α carbon. NMR analysis of nondeuterated 4 showed characteristic peaks at δ 1.1 (d), 1.8 (s), 2.4 (d of d), 5.0 (m), and 11 (s).

Synthesis of (*R*,*R*)- and (*S*,*S*)-*S*-*tert*-Butyl 3-Acetoxythiobutanoate-2-d (1). Trifluoroacetic anhydride (Aldrich) in 35% excess was added dropwise to stirred, cooled (ice–salt) viscous 4 over a 30-min period; the reaction was allowed to proceed for 1.5 h. 2-Methyl-2-propanethiol (Aldrich) in 50% excess was added dropwise to the cooled reaction mixture and the reaction allowed to go on at 22 °C for 15 h (stench, rinse glassware with 5% $KMnO_4$ before routine cleaning). Addition of Et_2O followed by washing with saturated $NaHCO_3$ and saturated NaCl, drying, and gentle rotary evaporation led to a yellow liquid. Vacuum distillation at 10 mtorr through a Vigreaux column gave a 40–80% yield of 1, bp 48 °C (0.01 mm). Less than 0.8% H–D exchange took place under these conditions; 49–52% H was present at C-2; $J_{H(C\text{-}2)\text{-}H(C\text{-}3)}$ was 7.7 Hz. NMR analysis of nondeuterated 1 showed peaks at δ 1.3 (d, 3 H), 1.4 (s, 9 H), 1.9 (s, 3 H), 2.7 (d of d, 2 H), and 5.2 (m, 1 H).

Synthesis of 3-Hydroxybutanoic-2-d_2 Acid (5). Methyl acetoacetate (20 mL, 0.185 mol, Aldrich) was mixed with 40 mL of D_2O (99.8% D, Aldrich) and a calculated volume of 40% NaOD/D_2O (99+% D, Aldrich) added dropwise with cooling to give a [OD^-] of 0.50 M. $NaBH_4$ (7.01 g, 0.185 mol) was added and the mixture stirred for 24–48 h. Workup followed the same procedure given for the reduction of 2. An 80% yield of 5 with 90% deuteration at C-2 resulted.

Use of DCC in the Synthesis of 1.[7b] To a stirred solution of 50 mmol of 3-acetoxybutanoic-2-d_2 acid in 25 mL of dried CH_2Cl_2 *or* 25 mL of hexane were added 50 mmol of DCC (Aldrich) and 200 mmol of 2-methyl-2-propanethiol (stench). After 1 h, 25 mg of 4-(dimethylamino)pyridine (DMAP, Aldrich) was added

(13) (a) Y. Kishi et al., *J. Chem. Soc., Chem. Commun.*, 64 (1972); (b) N. N. Schwartz and J. H. Blumbergs, *J. Org. Chem.*, **29**, 1976 (1964).
(14) G. B. Payne and P. H. Williams, *J. Org. Chem.*, **24**, 54 (1959).

and the reaction stirred further for 9 days. The disappearance of IR peaks at 2130 and 1820 cm^{-1} was used as evidence for complete reaction. After removal of dicyclohexylurea by filtration, the solvent and excess thiol were removed by rotary evaporation. Et_2O (35 mL) was added and the solution washed sequentially with $NaHCO_3$, with 1 M H_2SO_4, and again with saturated $NaHCO_3$. After drying and rotary evaporation, the thioester product was vacuum distilled as reported above. GC analysis showed that the crude product (85% yield) contain 19% *N*-acylurea and <2% *tert*-butyl thiocrotonate. Approximately 1% H-D exchange occurred at C-2. Even at 10 mtorr, thermal decomposition (presumably of the *N*-acylurea) made it impossible to obtain pure 1-d_2, even by repeated vacuum distillation.

Increasing amounts of DMAP led to product uncontaminated by *N*-acylurea but which contained substantial amounts of *tert*-butyl thiocrotonate and an increasing degree of H-D exchange at C-2. When no DMAP was used, the reaction became sluggish and *N*-acylurea accounted for 35% of the crude product. Using Et_2O or excess thiol as solvent did not produce a more successful reaction.

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Registry No. (*R*,R**)-(±)-1, 79069-05-9; (±)-1-d_2, 79069-06-0; *trans*-(±)-2, 13737-02-5; trans-(±)-2 K salt, 79069-07-1; (*R*,R**)-(±)-3, 79069-08-2; (*R*,R**)-(±) 3 Na salt, 79069-09-3; (*R*,R**)-(±)-4, 79069-10-6; (±)-5, 79069-11-7; *trans*-crotonic acid, 110-17-8; (±)-2-hydroxybutanoic acid, 600-15-7; (±)-3-hydroxybutanoic acid, 625-71-8; (±)-3-acetoxybutanoic acid, 24621-58-7; methyl acetoacetate, 105-45-3; (±)-3-acetoxybutanoic acid-2-d_2, 79069-12-8; 2-methyl-2-propanethiol, 75-66-1.

Synthetic Routes to Benz[*a*]anthracenes via Transient 1-Benzylisobenzofuran Derivatives

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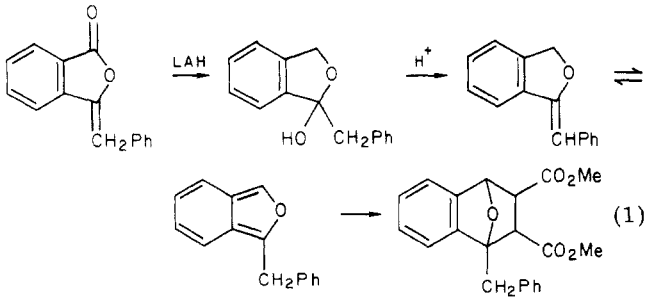
A synthetic route to 7-acetoxybenz[*a*]anthracenes is described based on the generation of 1-benzylisobenzofurans and their capture with methyl acrylate in a Diels-Alder reaction. The 1,4-epoxy-1,2,3,4-tetrahydronaphthalene derivatives so formed are aromatized to naphthoate esters under acidic conditions and hydrolyzed to the naphthoic acids, and these are cyclized to the 7-acetoxybenz[*a*]anthracenes with zinc chloride in acetic anhydride.

Lately, considerable interest has been shown[1] in the synthesis of benz[*a*]anthracene derivatives bearing methyl and/or hydroxy groups in specific locations. An interesting report[2] by Gomez described a one-step synthesis of benz[*a*]anthracene derivatives from appropriately substituted 1,4-epoxy-1,2,3,4-tetrahydronaphthalene derivatives (i.e., **1a** → **3a**, Scheme I) using polyphosphoric acid. Presumably this reaction proceeds through the naphthalene derivative **2a**.

This report interested us since compounds such as 1 are readily prepared[3] via benzylisobenzofurans (eq 1). The

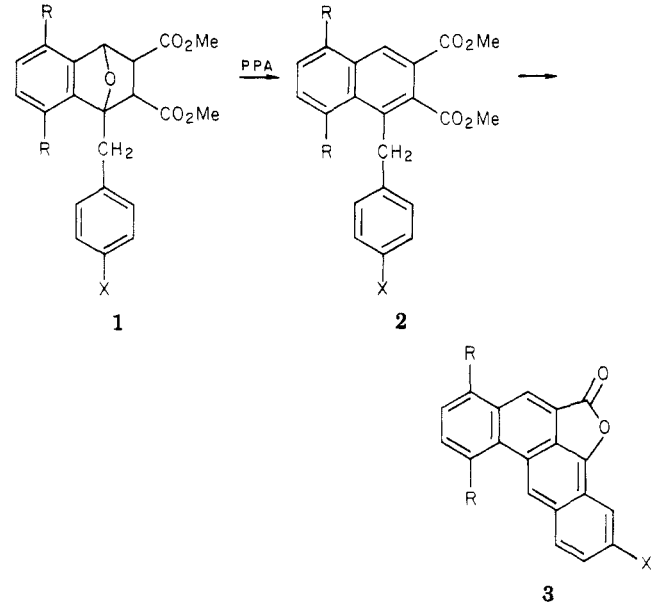


(1)

overall sequence appeared to be a direct route to benz[*a*]anthracene derivatives and therefore it was reinvestigated and confirmed. Three additional examples of the preparation of benz[*a*]anthracenes (i.e., **3b-d**) by this method are reported here. Thus this route appears to be a general one.

While the lactone ring is potentially a functional group useful for further elaborating **3**, it was decided instead to modify the synthetic route to obtain a product without this

Scheme I. Formation of Benz[*a*]anthracenes



a, R = H; X = H
b, R = Me; X = H
c, R = Ph; X = H
d, R = H; X = OMe

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