with osmium tetroxide (0.33 g, 1.3 mmol) and pyridine (1 ml) and the mixture was stirred at room temperature for 72 hr. The insoluble complex was decomposed with mannitol (5 g) in 10% aqueous potassium hydroxide (20 ml) and stirring continued for 12 hr. The reaction mixture was extracted with methylene chloride, the organic layer washed with water and dried ($MgSO_4$), and solvents were evaporated. The residue on crystallization from benzene gave 0.34 g (63%) of II, mp 190–191° dec. This melting point was not depressed by admixture with an authentic sample,[1] mp 190–191° dec.

Reaction of I with Dinitrogen Trioxide in Benzene. Preparation of III.—A stirred and ice-cooled dry benzene solution of tetracyclone (0.5 g, 1.3 mmol, 10 ml) was treated dropwise with a dry benzene solution of dinitrogen trioxide until decolorization was complete (~10 ml). The solvent was removed *in vacuo* and without heating under rigorously dry conditions to give III as a noncrystalline solid: mp 95° dec; ir [λ_{max}^{KBr} 5.7 (>C=O), 6.5, 7.5 μ; also present 2.85 (OH) 5.9 (>C=O) μ due to decomposition to II].

Anal. Calcd for $C_{29}H_{20}N_2O_4$: N, 6.08. Found: N, 6.01.

Reactions of III. A. With Aqueous THF.—Aqueous THF (3:2, 5 ml) was added to 0.1 g of III. The solution became pink owing to the formation of some I. The color disappeared on standing. The colorless reaction mixture was extracted with benzene and dried ($MgSO_4$), and solvent evaporated to yield II, mp 191–192° dec.

B. With Aqueous Acetic Acid.—Aqueous acetic acid (3:2, 5 ml) was added to 0.1 g of III. The pinkish color due to the formation of some I, disappeared immediately. The colorless reaction mixture was extracted with benzene, the organic layer was washed with water and dried ($MgSO_4$), and solvents were evaporated to yield II, mp 190–191° dec.

C. With Anhydrous Methanol.—Absolute methanol (5 ml) was added to 0.1 g of III. The solution instantly became pink owing to the formation of I. The color did not fade on long standing. Evaporation of solvents gave pure I, mp 223°.

Preparation of 3,4,5-Triphenylcyclopentadien-1-one IV (Tricyclone).—The blue tricyclone was prepared by the condensation of benzil with phenylacetone,[14] mp 292–293° dec (lit.[14] mp 292–294°).

Reactions of Tricyclone. A. With Sodium Nitrite Acetic Acid–Water–Benzene.—A stirred benzene solution of tricyclone (0.5 g, 1.62 mmol, 10 ml) was treated with acetic acid:water (3:2, 5 ml) and cooled to 0°. Solid sodium nitrite (0.5 g 7 mmol) was gradually introduced over a period of 15 min while maintaining the temperature below 5°. The brown reaction mixture was stirred for additional 30 min. The layers were separated, the organic layer was washed several times with water and dried ($MgSO_4$), and solvents were evaporated. The residue on crystallization from benzene–hexane mixture gave 0.45 g (79%) of V: mp 158–160° dec; ir [λ_{max}^{KBr} 5.8 (>C=O), 6.5 ($-NO_2$, asymmetric), 7.3 ($-NO_2$, symmetric) μ]; nmr [δ_{CDCl_3} 7.2 (aromatic protons)].

Anal. Calcd for $C_{23}H_{15}NO_3$: C, 78.18; H, 4.24; N, 3.96. Found: C, 78.08; H, 4.6; N, 3.63.

B. With Dinitrogen Trioxide under Anhydrous Conditions and Treatment with Absolute Methanol.—A stirred and ice-cooled dry benzene solution of tricyclone (0.5 g, 1.62 mmol, 10 ml) was treated dropwise with a dry benzene solution of dinitrogen trioxide (10 ml). Tricyclone color disappeared rapidly and the solution became chocolate brown. Solvents were removed *in vacuo* without heating and under rigorously dry conditions. Absolute methanol (10 ml) was added. No tricyclone color reappeared even on standing. Solvents were removed and the residue on crystallization from benzene–hexane mixture gave 0.46 g (80%) of V, mp 159–160° dec.

Reaction of Methyl Methacrylate with Sodium Nitrite Acetic Acid–Water–Benzene.—A stirred benzene solution of methyl methacrylate (5 g, 50 mmol, 10 ml) was treated with acetic acid:water (3:2, 20 ml) and the mixture was cooled to 0°. Solid sodium nitrite (5 g, 70 mmol) was gradually introduced over a period of 15 min while maintining the temperature below 5°. The reaction mixture was stirred for additional 6 hr. The layers were separated, the organic layer was washed several times with water and dried ($MgSO_4$), and solvents were evaporated. The residue on distillation gave 3.6 g (45%) of VI: bp 90° (4 mm);[5] ir [$\lambda_{max}^{CHCl_3}$ 5.78 (>C=O), 6.1 (C=C), 6.5 ($-NO_2$, asymmetric), 7.4 ($-NO_2$, symmetric) μ]; nmr [δ_{CCl_4} 2.2 (d, $-CH_3$), 3.8 (s, $-OCH_3$) 7.6 (q, H)].

Anal. Calcd for $C_5H_7NO_4$: C, 41.37; H, 4.82; N, 9.64. Found: C, 41.4; H, 4.9; N, 9.4.

Registry No.—Nitrous acid, 7782-77-6; II, 25716-03-4; III, 25662-49-1; V, 25665-22-9; VI, 25662-50-4.

Acknowledgments.—We thank Dr. Nitya Nand, CDRI, Lucknow, for providing nmr facilities. Financial assistance by way of a Lady Tata Memorial Trust Scholarship (SKK) is gratefully acknowledged.

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Preparation of Optically Pure Diastereomeric 2-Methyl-2,3-dihydrobenzothiophene 1-Oxides and Comments on the Mechanism of Reduction of Cyclic Sulfones[1]

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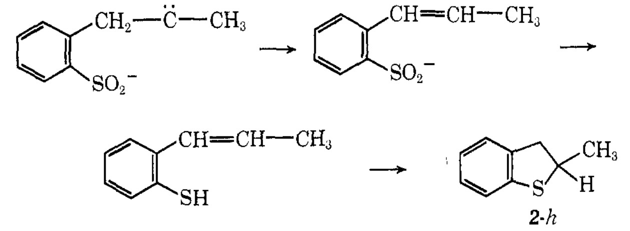
As a part of the study of electrophilic substitution at saturated carbon,[3] the title compounds were prepared as follows. Optically pure 2-methyl-2,3-dihydrobenzothiophene-2-*d* (or -2-*h*) 1-dioxide [*e.g.*, (+)-**1**-*h*] was reduced with lithium aluminum hydride to (−)-**2**-*h*, which was oxidized under controlled conditions to give a mixture of optically pure diastereomers (+)-**3**-*h* and (−)-**3**-*h*, separable by column chromatography. Although the 2,3-dihydrobenzothiophene 1-oxide system was found to be unstable toward *tert*-butyl alcohol–potassium *tert*-butoxide (thus precluding study of the stereochemistry of electrophilic substitutions), the reactions involved in the preparation of the compounds provide insight into the mechanism of the reduction of cyclic five-membered ring sulfones to sulfides.

Bordwell and McKellin[4] investigated the behavior of a variety of sulfones with lithium aluminum hydride and found that generally only cyclic four- and five-



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[1] This investigation was supported by the U. S. Public Health Service Research Grant No. GM 12640-04 from the Department of Health, Education and Welfare.

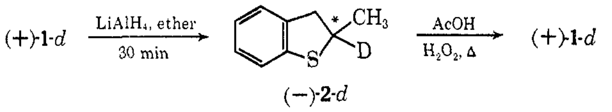
[2] National Science Foundation Predoctoral Fellow, 1962–1966.

[3] D. J. Cram and T. A. Whitney, *J. Amer. Chem. Soc.*, **89**, 4651 (1967). See also, F. A. L. Anet, L. M. Sweeting, T. A. Whitney, and D. J. Cram, *Tetrahedron Lett.*, **22**, 2617 (1968).

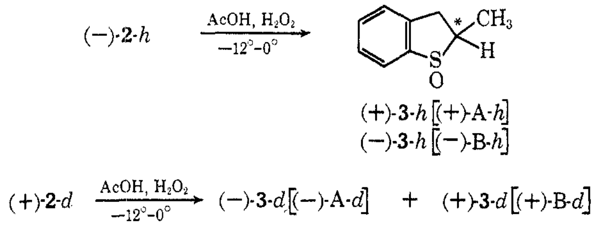
[4] F. G Bordwell and W H. McKellin, *J. Amer. Chem. Soc.*, **73**, 2251 (1951).

membered ring sulfones are readily reduced. The reduction of 2,3-dihydrobenzothiophene 1-dioxide went easily. These authors[4] suggested the mechanism involved nucleophilic attack of a donated hydride on sulfur to displace oxygen as the critical stage of the reaction. More recently, Meyers[5] suggested the mechanism (as applied to **1**-*h*) as indicated.

The results reported here are inconsistent with the Meyers, but consistent with the Bordwell–McKellin mechanism. Optically pure **1**-*d* was reduced by lithium aluminum hydride to optically active **2**-*d* *without* loss of label. Reoxidation[3] of **2**-*d* with an excess of hydrogen peroxide in acetic acid gave **1**-*d* having the same rotation and deuterium content as starting material. These results are consistent with the suggestion of Bordwell and McKellin that reduction occurs by displacement of oxygen from sulfur by hydride forming sulfide, aluminum oxide, and hydrogen gas, the evolution of which was noted previously and during the present investigation.



Partial oxidation of (−)-**2**-*h* gave nearly a quantitative yield of a mixture of diastereomers (+)-**3**-*h* and (−)-**3**-*h* [configurations (+)-A and (−)-B, respectively], which were separated chromatographically. From (−)-**2**-*d* of maximum rotation, the corresponding (−)-**3**-*d* [(−)-A-*d*)] and (+)-**3**-*d* [(+)-B-*d*)] were isolated.[6]



Experimental Section[7]

(−)-2-Methyl-2,3-dihydrobenzothiophene [(−)-2-*h*].—To a rapidly stirred suspension of 4.0 g of lithium aluminum hydride in 135 ml of anhydrous ethyl ether was added dropwise a solution of 8.14 g of (+)-**1**-*h*[3], $[\alpha]^{25}_{546}$ +23.7° (*c* 3.92), in 300 ml of 50:50 ethyl ether–benzene, and the reaction mixture was stirred at 25° for 30 min after addition of the sulfone was complete.[4] Hydrolysis was effected by dropwise addition of 100 ml of 10% aqueous hydrochloric acid. The layers were separated and the aqueous phase was extracted with two 80-ml portions of ethyl ether. The combined organic phase was dried and evaporated to a colorless oil, wt 6.53 g, $[\alpha]^{25}_{546}$ −165° (*c* 5.00). A 0.50-g portion of the product, [(−)-**2**-*h*], was chromatographed on a 2 × 30 cm column of silica gel with 5% ether–85% pentane as developer. The remainder of the sample was not purified, but was used directly in the next step.

Anal. Calcd for $C_9H_{10}S$: C, 72.00; H, 6.64; S, 21.34. Found: C, 72.15; H, 6.73; S, 21.37.

Stability of the 2,3-Dihydrobenzothiophene Ring System under Conditions of Reduction with Lithium Aluminum Hydride and Oxidation with Hydrogen Peroxide.—A 0.30-g portion of sulfone (−)-**2**-*d*, $[\alpha]^{25}_{546}$ −13.30° (*c* 3.94), was dissolved in 10 ml of 50:50 benzene–ether. The solution was added dropwise to a stirred suspension of 0.3 g of lithium aluminum hydride in 7 ml of anhydrous ether. After 30 min, the product sulfide was isolated, as detailed above, wt 0.210 g (85%), $[\alpha]^{25}_{546}$ +87.0° (*c* 4.03). This sulfide [(+)-**2**-*d*] was oxidized in 2 ml of glacial acetic acid with 0.5-ml portions of 30% hydrogen peroxide being added every 10 min for 1.5 hr on a steam bath. The oxidation reaction mixture was cooled, and 10 ml of ice water was added. The sulfone (−)-**1**-*d* was isolated as described for the sulfoxides and evaporation of solvent left a white solid having absolutely no sulfide odor. The total sample was sublimed, wt 0.220 g, $[\alpha]^{25}_{546}$ −13.23° (*c* 4.44). This product sulfone [(−)-**1**-*d*] was found to have 0.970 atom of deuterium per molecule. The starting sulfone contained 0.977 atom of deuterium per molecule.

Diastereomers of 2-Methyl-2,3-dihydrobenzothiophene 1-Oxide [(+)-A-*h* and (−)-B-*h*].—The crude sulfide, (−)-**2**-*h*, wt 6.50 g, $[\alpha]^{25}_{546}$ −165° (*c* 5.00), as prepared above, was dissolved in 33 ml of glacial acetic acid. The solution was cooled in an ice-salt bath until it partially froze and 6.9 g of 30% hydrogen peroxide was added to 0.5-ml portions with constant swirling and continued cooling in the freezing mixture. When addition of hydrogen peroxide was complete, a homogeneous solution resulted which was kept at −12° for 30 min, warmed to −5°, and allowed to stand at −5–0° for 16.5 hr. The reaction mixture was poured into 175 ml of ice water, and the solution was extracted with three 100-ml portions of dichloromethane. The combined dichloromethane extracts were washed with 175 ml of water, 100 ml of cold ferrous sulfate solution, 75 ml of saturated sodium bicarbonate solution, and 175 ml of water, in that order. The dichloromethane solution of the product was dried and evaporated under reduced pressure, yielding the crude sulfoxides as an oil, wt 6.82 g. This product was purified by chromatography on a 7 × 100 cm column packed with Baker silica gel powder. Developer was 96% ethyl ether–4% anhydrous methanol. Eluate was collected in 250 ml fractions. Fractions 1–8 were empty, fractions 9–13 contained a very small amount of sulfide, fractions 14–19 contained sulfone (wt 0.113 g), and fractions 20–34 were empty. The sulfoxides were eluted in fractions 35–72. Fractions 35–45 contained only diastereomer A (wt 1.96 g), fractions 46–48 contained both diastereomers (wt 0.610 g), and the remaining fractions contained only diastereomer B (wt 3.43 g), as determined by thin layer chromatography on silica gel with 7% methanol–93% ethyl ether as developer. Diastereomer A gave $[\alpha]^{25}_{546}$ +148° (*c* 4.40), whereas diastereomer B displayed $[\alpha]^{25}_{546}$ −241° (*c* 4.01); both were oils.

Anal. Calcd for $C_9H_{10}SO$ (A): C, 65.06; H, 6.02; S, 19.30. Found: C, 65.23; H, 6.19; S, 19.09.

Anal. Calcd for $C_9H_{10}SO$ (B): C, 65.06; H, 6.02; S, 19.30. Found: C, 65.13; H, 6.21; S, 19.42.

Diastereomer A from the column had an R_f value of 0.43, while diastereomer B had an R_f value of 0.35 when both were spotted separately on silica gel and the plate was developed with 93% ethyl ether–7% methanol.

When both diastereomers were spotted together as a 50:50 mixture, the R_f values were 0.44 and 0.38, respectively. Separate experiments demonstrated that 5% by weight of one diastereomer could be detected in a mixture with the other. Such was the case, regardless of which diastereomer predominated. Thus, each diastereomer was at least 95% free of contamination by the other.

Diastereomers of 2-*d*-2-Methyl-2,3-dihydrobenzothiophene 1-Oxide [(−)-A-*d* and (+)-B-*d*].—Reduction of 8.70 g of (−)-**1**-*d*[3], $[\alpha]^{25}_{546}$ −24.1° (*c* 3.86), as described above, with lithium aluminum hydride yielded 6.68 g of crude (+)-**2**-*d*, $[\alpha]^{25}_{546}$ +170° (*c* 4.57). The sulfide was not purified, but was oxidized in 34 ml of glacial acetic acid with 7.0 g of 30% hydrogen peroxide, as described above, and 6.96 g (94.5%) of crude sulfoxides were obtained. The two diastereomeric sulfoxides were separated *via* chromatography on silica gel by the same method utilized above to give 2.16 g of (−)-A-*d*, $[\alpha]^{25}_{546}$ −150° (*c* 4.26), and 3.92 g of (+)-B-*d*, $[\alpha]^{25}_{546}$ +248° (*c* 5.36). The nmr spectrum of diastereomer (−)-A-*d* showed the following absorptions: aromatic protons (m, 4.0 protons), τ 2.05–2.83; benzyl protons (s, 1.96 protons), τ 6.67; methyl protons (s, 2.90 protons), τ 8.50. Diastereomer (+)-B-*d* showed the following spectrum: aromatic protons (m, 4.0 protons), τ 2.10–2.81; benzyl protons (AB quartet, J_{AB} = 16 cps, ν_{AB} = 55.9 cps, 2.09 protons), centered at τ 6.64; methyl protons (s, 2.98 protons), τ 8.62.

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[5] C. Y. Meyers, Abstracts, 144th National Meeting of the American Chemical Society, Los Angles, Calif., April 1963, p 4M.

[6] Determination of the absolute configurations of A and B is in progress (W. H. Pirkle, T. A. Whitney, and S. D. Beare).

[7] Rotations were taken with a Perkin-Elmer Model 141 polarimeter with chloroform as solvent. Nmr spectra were taken with a Varian A-60 spectrometer. Deuterium analyses were performed by Dr. J. Nemeth of Urbana, Ill., using the combustion and falling drop method.

By nmr, the degree of separation achieved between the two diastereomeric deuteriosulfoxides was found to be 98 ± 1% (area of the methylene singlet for diastereomer A *vs.* area of the methylene AB quartet for diastereomer B). Thin layer chromatography was employed to determine which fractions contained both deuteriodiastereomers in exactly the same manner as in the above separation. The degree of separation of the individual protiodiastereomers was probably 98 ± 1% also.

Registry No.—(−)-**2**-*h*, 25662-51-5; (+)-**3**-*h*, 25662-52-6; (−)-**3**-*h*, 25662-53-7; (+)-**3**-*d*, 20550-30-5; (−)-**3**-*d*, 20550-31-6.

The Reformatsky Reaction at Room Temperature and in the Presence of Trimethyl Borate. Improved Procedures for the Preparation of β-Hydroxy Esters

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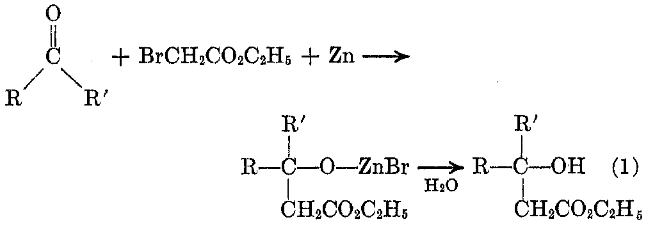
The Reformatsky reaction (eq 1) is normally conducted at reflux temperatures in benzene or benzene–ether solvents. Using such procedures, the yields of β-hydroxy esters from a wide variety of aldehydes and ketones lie in the range of 25–65%.[1] It is likely that a major factor responsible for such low yields is base-catalyzed side reactions of the starting materials.[2] This should be especially critical at the elevated temperatures utilized in the normal procedures.



It occurred to us that trimethyl borate would provide a mildly acidic medium for conducting the Reformatsky reaction, possibly allowing the reaction to proceed as usual, but neutralizing the basic alkoxide products. In addition, we considered the possibility of conducting the reaction at room temperature. Accordingly we carried out a brief study of the Reformatsky reaction of acetaldehyde and ethyl bromoacetate, varying both solvent and temperature. The results were applied to a representative number of aldehydes and ketones.

Results

Reaction of acetaldehyde with 1 equiv of zinc and ethyl bromoacetate in refluxing benzene is complete in 2 hr and gives a 22% yield of ethyl 3-hydroxybutanoate. The same reaction conducted at 25° is complete in 4 hr and gives a 65% yield of product. Reactions with ethyl ether or tetrahydrofuran as solvent proceed faster but give somewhat lower yields, 56 and 35%, respectively.

Attempts to use trimethyl borate or trimethyl borate–benzene mixtures as solvent were unsuccessful; no reaction occurs over a period of 2 days at 25°. However, a solvent mixture of trimethyl borate and tetrahydrofuran gives complete reaction in 2 hr at 25° and the yield of β-hydroxy ester is 95%. These results are summarized in Table I.

TABLE I
REACTION OF ACETALDEHYDE WITH ETHYL BROMOACETATE AND ZINC UNDER VARIOUS CONDITIONS[a]

Solvent	Temp, °C	Time for complete reaction, hr[b]	Yield, %[c]
Benzene	75	2	22
Benzene	25	4	65
Ethyl ether	25	2	56
Tetrahydrofuran	25	1	35
Tetrahydrofuran–trimethyl borate	25	2	95

[a] 20.0 mmol of each reactant and 10.0 ml of each solvent. [b] Judged by the disappearance of zinc metal. [c] Glpc analysis for ethyl 3-hydroxybutanoate.

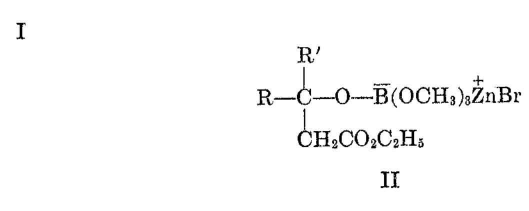
The reaction mixture in tetrahydrofuran remains homogeneous. However, in the presence of trimethyl borate a white precipitate which contains boron is formed during the reaction. Hydrolysis of the precipitate following completion of the reaction gives methanol as the sole organic product while hydrolysis of the clear supernatent gives the β-hydroxy ester.

The procedure using trimethyl borate–tetrahydrofuran as solvent at room temperature was applied to a variety of aldehydes and ketones with the results shown in Table II. For comparison, our results using benzene as solvent at room temperature are also presented, together with the yields previously reported in the literature.

Discussion

Our results show that the Reformatsky reaction proceeds readily at 25° in benzene solution and that higher yields are obtained at this temperature than at the usual reflux temperature. More important, the yields are nearly quantitative when a solvent mixture containing trimethyl borate is used.

It is likely that the function of trimethyl borate is to neutralize the zinc alkoxides, I, formed in the reaction, as illustrated in eq 2. The tetraalkylborate salt, II, is



I

II

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* Author to whom correspondence should be addressed.

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[2] Allen S. Hussey and Melvin S. Newman, *J. Amer. Chem. Soc.*, **70**, 3024 (1948).