

By nmr, the degree of separation achieved between the two diastereomeric deuteriosulfoxides was found to be $98 \pm 1\%$ (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 $98 \pm 1\%$ 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.

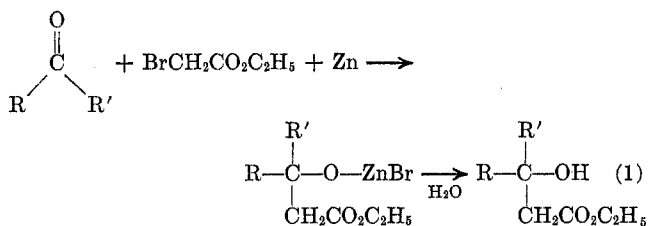
The Reformatsky Reaction at Room Temperature and in the Presence of Trimethyl Borate. Improved Procedures for the Preparation of β -Hydroxy Esters

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The Reformatsky reaction (eq 1) is normally con-



ducted 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.

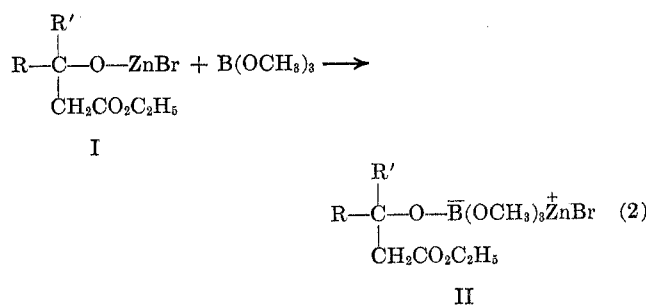
The reaction mixture in tetrahydrofuran remains homogeneous. However, in the presence of trimethyl borate a white precipitate which contains boron is formed during the reaction. Hydrolysis of the precipitate following completion of the reaction gives methanol as the sole organic product while hydrolysis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

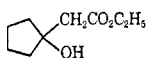
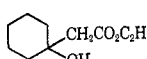


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(1) R. L. Shriner, "Organic Reactions," Vol. I, Wiley, New York, N. Y., 1942, p 20.

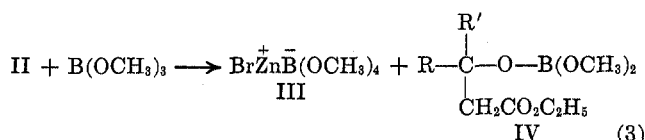
(2) Allen S. Hussey and Melvin S. Newman, *J. Amer. Chem. Soc.*, **70**, 3024 (1948).

TABLE II
REACTION OF CARBONYL COMPOUNDS WITH ZINC AND ETHYL BROMOACETATE AT 25°

Carbonyl compd	Product	Yield, % ^b		
		Tetrahydrofuran-trimethyl borate	Benzene	Lit. ^c
Acetaldehyde	CH ₃ CHOHCH ₂ CO ₂ C ₂ H ₅	95	65	
Butyraldehyde	CH ₃ (CH ₂) ₂ CHOHCH ₂ CO ₂ C ₂ H ₅	97 (90)	80	25
Isobutyraldehyde	(CH ₃) ₂ CHCHOHCH ₂ CO ₂ C ₂ H ₅	98 (89)	95	35
Crotonaldehyde	CH ₃ CH=CHCHOHCH ₂ CO ₂ C ₂ H ₅	98 (90)	89	60
Benzaldehyde	C ₆ H ₅ CHOHCH ₂ CO ₂ C ₂ H ₅	(95)	(84)	61
Phenylacetaldehyde	C ₆ H ₅ CH ₂ CHOHCH ₂ CO ₂ C ₂ H ₅	90	70	
Acetone	(CH ₃) ₂ COHCH ₂ CO ₂ C ₂ H ₅	90 (85)	90	
Cyclopentanone		93 (87)	50	40 ^d
Cyclohexanone		85 (80)	80	56

^a All products gave analytical data and spectra in accordance with the assigned structures. ^b Glpc yields. Isolated yields in parentheses. ^c Reference 1 unless otherwise noted. ^d V. N. Ipatieff, J. E. Germain, and H. Pines, *Bull. Soc. Chem. Fr.*, 259 (1951).

not isolated. Instead a precipitate assumed to be the zinc salt III is formed, presumably by reaction of II with excess trimethyl borate (eq 3). Hydrolysis of the



boron ester IV during work-up then gives the β -hydroxy ester.

As expected, the advantage of using trimethyl borate is most apparent when the carbonyl compound is especially susceptible to base-catalyzed condensations. Thus the reactive aldehydes, acetaldehyde and phenylacetaldehyde, and the reactive ketone, cyclopentanone, give clearly increased yields with the trimethyl borate procedure. With less reactive carbonyl compounds, the procedure utilizing benzene at 25° gives comparable yields. With either procedure, the yields are much higher than those obtained at reflux temperatures.

Experimental Section

All experiments were conducted using unactivated 20 mesh zinc metal. Ethyl bromoacetate was distilled under reduced pressure and stored under a nitrogen atmosphere. Trimethyl borate was distilled from calcium hydride and stored under nitrogen. All carbonyl compounds were distilled shortly before use. Tetrahydrofuran and benzene, reagent grades, were used directly. Glpc analyses were performed on a SE-30 silicon oil column using appropriate internal standards.

Reactions Using Tetrahydrofuran-Trimethyl Borate Solvent.—The following procedure for the conversion of benzaldehyde into ethyl 3-phenyl-3-hydroxypropionate is representative. Zinc metal (6.54 g, 100 mg-atoms) was put in a 250-ml round-bottom flask equipped with septum inlet and magnetic stirring bar and maintained under a static nitrogen pressure. The flask was immersed in a water bath at 25° and a solution of 10.6 g (100 mmol) of benzaldehyde in 25 ml of tetrahydrofuran and 25 ml of trimethylborate was injected. Stirring was initiated and 11.1 ml (100 mmol) of ethyl bromoacetate was injected all at once. The reaction mixture was stirred for 12 hr at which time all of the zinc was consumed (with the other aldehydes and ketones studied, complete reaction was achieved in 5 hr or less). The reaction mixture was hydrolyzed by the addition of a solution containing 25 ml of concentrated ammonium hydroxide (to dissolve zinc salts) and 25 ml of glycerine (to dissolve boric acid). The organic phase was separated and the aqueous layer extracted with three 25-ml portions of ether. The combined organic ex-

tracts were dried and subjected to vacuum distillation to obtain 18.5 g (95% yield) of ethyl 3-phenyl-3-hydroxypropionate, bp 105° (0.2 mm).

Reactions Using Benzene as Solvent.—An identical procedure was utilized except an equal volume of benzene was substituted for the tetrahydrofuran-trimethyl borate solvent.

Registry No.—Trimethyl borate, 121-43-7; acetaldehyde, 75-07-0; ethyl bromoacetate, 105-36-2; tetrahydrofuran, 109-99-9.

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Cyanuric Chloride. A Novel Laboratory Hydrochlorinating Reagent for Alcohols

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This note reports on the investigation of cyanuric chloride with alcohols with the aim of extending the S_Ni type of reaction, already well known. In an attempt to prepare 2,4,6-trimethyl-*s*-triazine by the reaction of a methanolic solution of sodium methoxide with cyanuric chloride, methyl chloride was unexpectedly obtained in 92% yield along with a 100% yield of cyanuric acid.

A search of the literature revealed that only two earlier reports in 1834¹ and 1886² had briefly mentioned the occurrence of a similar reaction in the absence of sodium methoxide or other bases, but they gave no experimental details. More recent investigators³ reporting the preparation of trialkyl-*s*-triazines by similar methods

- (1) J. Liebig, *Ann. Pharm.*, **10**, 1 (1834).
- (2) P. Klason, *J. Prakt. Chem.*, **34**, 152 (1886).
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