

to be necessary only when connecting a hydrogenation flask to the Parr apparatus.

Work extending the application of borohydride reduced palladium to heterocyclic and homocyclic rings, halides, and sulfides is currently underway.

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Registry No.—Palladium chloride, 7647-10-1; sodium borohydride, 16940-66-2.

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Organic Synthesis Using Borane–Methyl Sulfide. II.¹ Reduction of Aromatic Carboxylic Acids in the Presence of Trimethyl Borate

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Borane–methyl sulfide (BMS) is a concentrated and stable source of BH_3 and we have reported its utility in the hydroboration of alkenes.¹ The stability, commercial availability in pure form, and solubility in a wide variety of solvents makes BMS an attractive alternative to borane–tetrahydrofuran (BH_3 –THF).

The approximate rates and stoichiometry for the reaction of BH_3 –THF with various organic functional groups has been reported by Brown and coworkers.² The reduction of carboxylic acids with BH_3 –THF was found to yield the corresponding alcohols rapidly and quantitatively under remarkably mild conditions. The obvious potential of this reaction for selective reductions in multifunctional molecules resulted in a detailed study of the scope of this reduction.³

As part of our continuing study on the full potential of BMS as a reagent in organic synthesis, we have investigated the use of this reagent for the reduction of carboxylic acids. Initially, the approximate rates of reduction were determined using *n*-hexanoic and benzoic acid as representative carboxylic acids. When *n*-hexanoic acid was added to a solution of BMS in THF, a quantitative yield of 1-hexanol was observed after 4 hr at 20–25°. Reversing the order of addition resulted in an apparent increase in the rate of reduction; *i.e.*, when BMS was added to a solution of *n*-hexanoic acid in THF, a quantitative yield of 1-hexanol was ob-

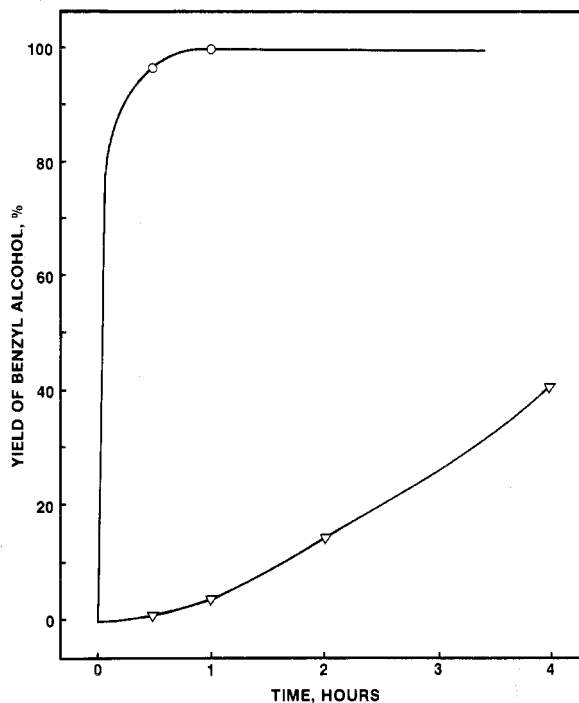
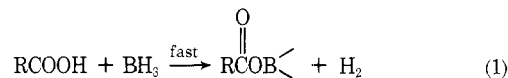


Figure 1. The effect of trimethyl borate on the reduction of benzoic acid (30 mmol) with BMS (33 mmol) at 20–25°: ∇, THF (30 ml) alone; O, THF (20 ml) plus trimethyl borate (10 ml).

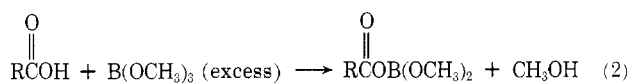
served after only 30 min at 20–25°. Surprisingly, the reduction of benzoic acid was appreciably slower and gave only a 40–50% yield of benzyl alcohol after 4 hr at 20–25°, irrespective of the order of addition. The use of either ethyl ether or hexane as the solvent in place of THF had essentially no effect upon the rate of reduction of benzoic acid. In all cases, instantaneous hydrogen evolution was observed due to the initial reaction of BH_3 with the acidic hydrogen of the carboxylic acid. The complete results of this preliminary investigation on the BMS reduction of *n*-hexanoic and benzoic acid are summarized in Table I.

The reduction of both *n*-hexanoic and benzoic acid with BH_3 –THF at 25° has been reported to give the corresponding alcohols rapidly and nearly quantitatively.³ We have duplicated these results.

Although many questions exist concerning the mechanism of the reduction of carboxylic acids with BH_3 –THF,^{3,4} the first step probably involves the formation of an acyloxyborane (eq 1). The carbonyl group of this acyloxyborane



has been postulated to be "activated" toward attack by borane because of possible resonance interaction of the electron pairs on the acyloxy oxygen with the electron-deficient boron atom.³ We reasoned that a similar activation might be possible in the presence of excess trimethyl borate as a result of a disproportionation reaction (eq 2).



Irrespective of the precise reasons, a pronounced increase in the rate of reduction of benzoic acid with BMS was observed when the reaction was conducted in the presence of excess trimethyl borate, as illustrated in Figure 1.

Triacyloxyboranes are unstable and are known to undergo a dismutation to acid anhydride and an oxybisdiacyloxyborane (eq 3).⁴ Pelter has shown that for both *n*-hexanoic

Table I
Reduction of Carboxylic Acids with BMS. Effect of Order of Addition and Solvent

Acid	Solvent	Procedure ^a	Reduction, ^b %			
			0.5 hr	1.0 hr	2.0 hr	4.0 hr
<i>n</i> -Hexanoic	Tetrahydrofuran	A	59	87	96	100
<i>n</i> -Hexanoic	Tetrahydrofuran	B	100			
Benzoic	Tetrahydrofuran	C	2.6	5.2	13	41
Benzoic	Tetrahydrofuran	B	1.9	3.7	14	48
Benzoic	Ethyl ether	C ^c				54 ^d
Benzoic	Ethyl ether	B				53 ^d
Benzoic	Hexane	B				43

^a Procedure A: *n*-hexanoic acid (30 mmol) was added dropwise to BMS (33 mmol) in 30 ml of THF at 0–5° over a 5-min period. The reaction mixture was then allowed to stir in a 20–25° water bath. Procedure B: BMS (33 mmol) was added dropwise to the acid (30 mmol) in 30 ml of solvent with stirring in a 20–25° water bath. Procedure C: benzoic acid (30 mmol) dissolved in 15 ml of solvent was added dropwise to BMS (33 mmol) in 15 ml of solvent at 0–5° over a 5-min period. The reaction mixture was then allowed to stir in a 20–25° water bath. ^b Yield of 1-hexanol or benzyl alcohol by gc analysis using an internal standard. Aliquots of reaction mixture were removed, after stirring for time indicated at 20–25°, and hydrolyzed with water prior to analysis. ^c Benzoic acid dissolved in 25 ml of ethyl ether. ^d Solid material precipitated and the rate could not be followed by removal of a homogeneous aliquot. Entire reaction mixture was hydrolyzed after 4 hr.

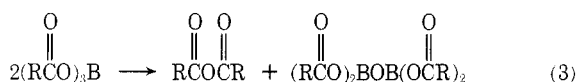
Table II
Reduction of Substituted Benzoic Acids with BMS in the Presence of Trimethyl Borate

Benzoic acid, 300 mmol	Registry no.	BMS, mmol	Reduction ^a		Benzyl alcohol ^b yield, %	Registry no.
			Time, hr	Temp, °C		
<i>o</i> -Chloro-	118-91-2	330	4	20–25	94	17849-38-6
<i>o</i> -Bromo-	88-65-3	330	4	20–25	88	18982-54-2
<i>o</i> -Iodo-	88-67-5	330	4	20–25	100	5159-41-1
<i>m</i> -Hydroxy- ^c	99-06-9	440	17	20–25	99	620-24-6
<i>o</i> -Amino-	118-92-3	870	2	Reflux	94	5344-90-1
<i>p</i> -Nitro-	62-23-7	330	3	Reflux	98	619-73-8
4,4'-Sulfonyldi-	2449-35-6	660	4	20–25	99 ^d	52123-62-3

^a The BMS was added dropwise to the substituted benzoic acid dissolved in THF (200 ml) and trimethyl borate (100 ml) at the temperature indicated. When addition of BMS was complete, the reaction mixture was stirred for the time indicated. The temperature necessary and time required for complete reduction were dependent upon both the position and the electron-withdrawing power of the substituent.

^b See Experimental Section for a detailed description of the isolation procedures. ^c The *m*-hydroxybenzoic acid was dissolved in THF and added to the BMS-THF-trimethyl borate. The normal order of addition (see footnote a) resulted in the formation of a polymeric precipitate.

^d Isolated product was 4,4'-sulfonyldibenzyl alcohol.



and benzoic acid, both the acid anhydride and the oxybisborane derivative are satisfactorily reduced with BH_3 -THF.⁴ A similar investigation using BMS was beyond the scope of the present study.⁵ However, interestingly, the reduction of *n*-hexanoic anhydride with BMS gave a quantitative yield of 1-hexanol after just 30 min at 20–25° while benzoic anhydride gave only a 54% yield of benzyl alcohol after 4 hr at 20–25°.

This striking rate enhancement for the BMS reduction of aromatic carboxylic acids in the presence of the trimethyl borate may eventually provide some important insight into the mechanism of borane reduction of carboxylic acids.⁵ However, since our interests are primarily directed toward developing the synthetic utility of BMS, this new method was applied to the reduction of a number of functionally substituted benzoic acids on a preparative scale. The results of this study are summarized in Table II.

The wide variety of functional groups that can be tolerated, mild conditions that are required, ease of experimental work-up, and excellent yield and high purity of the isolated product indicate that reduction of benzoic acids with BMS in the presence of trimethyl borate is a useful and convenient method for the preparation of benzyl alcohols.

Experimental Section

All starting materials were used directly as obtained from Aldrich Chemical Co. Since BMS is slowly decomposed by atmospheric moisture, all manipulations of liquid BMS and the reduction reactions were carried out in dry glassware under a nitrogen atmosphere. A detailed description of the techniques necessary in handling air-sensitive solutions has been given elsewhere.⁶

***o*-Chlorobenzyl Alcohol.** A dry, 1-l. flask equipped with a pressure-equalizing addition funnel, magnetic stirring bar, and reflux condenser vented to a bubbler was charged with 47 g (300 mmol) of *o*-chlorobenzoic acid. After flushing the system with nitrogen, 200 ml of tetrahydrofuran and 100 ml of trimethyl borate were added. The resulting solution was stirred in a 20–25° water bath as 33 ml (~330 mmol) of BMS was added dropwise over a 1-hr period. The hydrogen evolved was vented through the bubbler to a hood. Following the BMS addition, the reaction mixture was stirred for an additional 4 hr at 20–25°. Methanol (100 ml) was then added dropwise over a 1-hr period at 20–25°. After stirring for 0.5 hr, the reaction mixture was concentrated to dryness on a rotary evaporator. The residue was dissolved in 1 l. of ethyl ether and washed with 400 ml of water, 400 ml of saturated aqueous sodium bicarbonate, and 400 ml of saturated aqueous sodium chloride. The ether layer was then dried over anhydrous potassium carbonate, filtered, and concentrated to dryness on a rotary evaporator, giving 40.0 g (93.5%) of *o*-chlorobenzyl alcohol, mp 68–70° (lit.⁷ mp 70°), with an ir spectrum identical with that reported for the authentic material.⁸ Recrystallization from hexane gave colorless needles, mp 69.5–70.5°.

***o*-Bromobenzyl Alcohol.** The reduction of 56.2 g (300 mmol) of *o*-bromobenzoic acid was carried out using the procedure de-

scribed for *o*-chlorobenzoic acid. Isolation by the same procedure gave 49 g (88%) of *o*-bromobenzyl alcohol, mp 78–80° (lit.⁹ mp 79.5–80°), with ir and nmr spectra in accordance with the assigned structure. Recrystallization from hexane gave 46.4 g of off-white needles, mp 79–80°.

***o*-Iodobenzyl Alcohol.** The reduction of 74.5 g (300 mmol) of *o*-iodobenzoic acid was carried out using the procedure described for *o*-chlorobenzoic acid. Following methanolysis, the reaction mixture was concentrated to dryness on a rotary evaporator. The residue contained traces of boron as shown by a flame test. This boron-containing impurity was easily removed by dissolving the solid in 150 ml of methanol and concentrating to dryness on a rotary evaporator.¹⁰ Further drying in a vacuum oven gave 70 g (100%) of *o*-iodobenzyl alcohol, mp 88–89° (lit.¹¹ mp 91°), with ir and nmr spectra in accordance with the assigned structure.

***m*-Hydroxybenzyl Alcohol.** A dry, 1-l. flask equipped with a pressure-equalizing addition funnel, magnetic stirring bar, and reflux condenser was flushed with nitrogen and charged with 100 ml of THF, 100 ml of trimethyl borate, and 44 ml (440 mmol) of BMS. This solution was then stirred in a 20–25° water bath as 41.4 g (300 mmol) of *m*-hydroxybenzoic acid dissolved in 150 ml of THF was added dropwise over a 1-hr period.¹² Instantaneous hydrogen evolution occurred throughout the addition. After stirring for 17 hr at 20–25°, methanol (200 ml) was added dropwise and the solution was filtered *via* nitrogen pressure through a fritted glass funnel charged with diatomaceous earth to remove a minor amount of suspended solid. The clear, light-yellow filtrate was concentrated to dryness on the rotary evaporator, giving a brown oil. This oil was dissolved in 100 ml of methanol, concentrated to dryness, redissolved in 100 ml of methanol, and again concentrated to dryness, giving 36.9 g (99%) of *m*-hydroxybenzyl alcohol as a brown oil, which was free of boron-containing impurities by a flame test. The oil rapidly crystallized at room temperature, giving tan crystals, mp 69–71° (lit.¹³ mp 73°), with an ir spectrum identical with that reported for the authentic material.¹⁴

***o*-Aminobenzyl Alcohol.** A dry, 1-l. flask equipped as usual was charged with 41 g (300 mmol) of anthranilic acid, 200 ml of THF, and 40 ml of trimethyl borate. The resulting solution was heated at reflux as 87 ml (870 mmol) of BMS was added dropwise over a 1-hr period. Vigorous hydrogen evolution occurred during the BMS addition. The reaction mixture was maintained at reflux with stirring for an additional 2 hr. After cooling to 20–25°, the light-yellow supernate was removed *via* nitrogen pressure, leaving behind a small amount of black precipitate. Methanol (280 ml) was then added dropwise over a 1-hr period at 20–25°. The reaction mixture was then heated to a gentle reflux for a few minutes with stirring and concentrated on a rotary evaporator to a red oil. This oil was dissolved in 150 ml of ethyl ether and treated with 200 ml of 6 *N* aqueous sodium hydroxide. After heating at reflux for 2 hr and then cooling to 20–25°, the organic layer was removed and the aqueous layer was saturated with potassium carbonate and extracted with ethyl ether (3 × 50 ml). The combined organic layers were dried over anhydrous potassium carbonate, filtered, and concentrated to dryness on a rotary evaporator. Further drying in a vacuum oven gave 34.6 g (94%) of *o*-aminobenzyl alcohol as a light-tan, crystalline solid, mp 81–82° (lit.¹³ mp 84°), with an ir spectrum identical with that reported for the authentic material.¹⁵

***p*-Nitrobenzyl Alcohol.** The reduction of 50.2 g (300 mmol) of *p*-nitrobenzoic acid was carried out using the procedure described for *o*-chlorobenzoic acid. However, the THF solution of the acid and trimethyl borate was heated at reflux as 33 ml (330 mmol) of BMS was added dropwise over a 1-hr period. Vigorous hydrogen evolution occurred during the BMS addition. The reaction mixture was then heated at reflux with stirring for an additional 3 hr. Methanolysis and isolation of the product, using the procedure described for *o*-iodobenzyl alcohol, gave 48 g (>100% yield) of a light-yellow, crystalline solid. This solid was washed with hot hexane, filtered, and dried in a vacuum oven, giving 44.8 g (97.6%) of *p*-nitrobenzyl alcohol, mp 93–94.5° (lit.¹⁶ mp 93°), with an ir spectrum identical with that reported for the authentic material.¹⁷

4,4'-Sulfonyldibenzyl Alcohol. The reduction of 91.8 g (300 mmol) of 4,4'-sulfonyldibenzoic acid with 66 ml (660 mmol) of BMS was carried out using the procedure described for *o*-chlorobenzoic acid. Methanolysis and isolation of the product, using the procedure described for *m*-hydroxybenzyl alcohol, gave 83.3 g (99%) of 4,4'-sulfonyldibenzyl alcohol: mp 133–135°; ir (mineral oil mull) 3401 (s), 3311 (s), 2933 (vs), 2865 (vs), 1597 (w), 1458 (m), 1412 (w), 1376 (w), 1309 (m), 1290 (m), 1267 (w), 1202 (w), 1151 (s), 1103 (m), 1070 (m), 1030 (s), 1012 (m), 986 (w); nmr (CDCl₃ plus DMSO-*d*₆) δ 4.58 (s, 4 H), 5.11 (s, 2 H), 7.47 (d, 4 H), 7.76 (d, 4 H).

Registry No.—BMS, 13292-87-0; trimethyl borate, 121-43-7; hexanoic acid, 142-62-1; benzoic acid, 65-85-0.

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O-Benzylmonoperoxydicarboxylic Acid. A New Oxygenating Reagent¹

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Although the peroxydicarboxylic acids are a well known and widely used group of oxygenating agents,^{3–5} the corresponding peroxydicarboxylic acids (e.g., **2**) have been little studied. The parent member of this family, monoperoxydicarboxylic acid (H₂CO₄) has been suggested as a transient intermediate⁶ and a number of its metal salts have been reported.⁷ Dialkyl esters of monoperoxydicarboxylic acid (ROCO₂R') have been prepared.⁸

However, there seems to be no mention of an *O*-alkylmonoperoxydicarboxylic acid (ROCO₂H) in the literature, although such compounds would be expected to be reasonably stable and readily prepared by perhydrolysis of the well-known dialkyl peroxydicarbonates.^{8,9} It is possible that the active oxidizing agents formed by the reaction of hydrogen peroxide and aryl isocyanates are, in fact, *N*-arylperoxydicarboxylic acids (ArNHCO₂H), nitrogen analogs of *O*-alkylperoxydicarboxylic acids.^{10,11}

We have prepared *O*-benzylmonoperoxydicarboxylic acid (**2**) by perhydrolysis¹² of dibenzyl peroxydicarbonate (**1**),⁸ a crystalline, relatively stable peroxydicarbonate which is easily obtained from the reaction of benzyl chloroformate and alkaline hydrogen peroxide.^{8,13}

The structure of **2** is based upon its reconversion to dibenzyl peroxydicarbonate (**1**) upon reaction with benzyl chloroformate in pyridine, its high peroxide content (>97% of theoretical amount by iodometric titration), its acidic