C), 165.7 (CO). **4b** ^{13}C NMR ($CDCl_3$): δ 45.9 (CH_2Cl), 55.4 (OMe), 84.8 (quart C), 165.6 (CO). ^{13}C NMR (C_6D_6): δ 46.0 (CH_2Cl), 55.5 (OMe), 77.4 (CHO), 85.5 (quart C), 165.9 (CO).

Polymer-Supported Amino Alcohols 5. The polymer-supported epoxide **3b** (248 mg, 0.87 mmol) and (*S*)-1-phenylethylamine (333 mg, 2.75 mmol) were reacted in 2 mL of refluxing MeOH under nitrogen for 96 h. The polymer was filtered off, washed with MeOH (3 × 20 mL), CH_2Cl_2 (2 × 20 mL), THF (20 mL), and MeOH (3 × 20 mL), and dried under vacuum at 60 °C overnight to yield 289 mg of a yellow polymer (**5b**). Similar treatment of **3a** yielded amino alcohol **5a**. The ^{13}C NMR spectra of **5a** and **5b** were in agreement with that of the amino alcohol prepared from (*S*)-1-phenylethylamine and racemic polymer-bound styrene oxide.[8] Anal. Found: N, 2.71 and 2.60 for polymers prepared from **3a** and **3b**, respectively.

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Effect of Temperature on Borane Reduction of Representative Malonic Acids

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The controlled reaction of phenylmalonic acid (**1a**) with borane–THF at appropriate temperature makes available (phenylmalonyldioxy)borane [**2a**, $PhCH(CO_2)_2BH$], which has been characterized. Reduction of **2a** or of the corresponding acid **1a** proceeds at 0 °C at the same rate. The reaction, however, is incomplete, showing only 33% product formed in 4 h. Diethylmalonic acid (**1b**), which possesses no α-hydrogen, and the (diethylmalonyldioxy)borane (**2b**) are reduced at the same rate to the corresponding cyclic dialkoxyborane **5b**. These results suggest that the reduction proceeds through intermediate formation of **2**. The rates of the borane reduction for a series of malonic acids (**1a–h**) have been systematically studied and compared at 0 °C and at −20 °C. The reductions of aromatic substituted malonic acids (**1f–h**) are quite sluggish with substantial (46–72%) α-metalation occurring at 0 °C. Aliphatic alkylmalonic acids (**1d–e**) are reduced in 24 h with 34–40% of α-metalation. At −20 °C, most malonic acids are completely reduced in times ranging from 24 h for aliphatic (**1c–e**) to 3 days for aromatic (**1f–h**) compounds, with only 2–24% α-metalation. The reduction of **1a** requires −30 °C for 6 days to avoid α-metalation. The reduction of **1b** at either 0 °C or −20 °C is completed in 8 h. At an appropriate lower temperature the reduction successfully competes with the α-metalation.

Previously, Brown and co-workers described the remarkable ease with which carboxylic acids, both aliphatic and aromatic, are reduced by borane.[1-3] They have also established the details of the borane reduction mechanism, which proceeds through a mono(acyloxy)borane intermediate, formed either directly from the carboxylic acid and borane or by a redistribution reaction of bis(acyloxy)borane with borane.[4]

$$RCOOH + BH_3\text{–}THF \rightarrow RCH_2OH + ...$$

R = alkyl or aryl

Recently, we found the reduction of phenylmalonic acid (**1a**) by borane–THF to be unusually slow.[5] The reaction proceeded sluggishly at 0 °C, requiring 16 h to yield only 35% of 2-phenyl-1,3-propanediol, along with unreacted starting material.[5] Moreover, the yield was not enhanced by the use of borane dimethyl sulfide,[6,7] which led to only 23% of the product. Subsequently an initial systematic study was made of the approximate rates and stoichiometries of the reaction of **1a** with borane–THF.[8] We have continued to study the reduction and have extended our study to a set of representative malonic acids. The results of these investigations are reported in the present paper.

Table I. Reduction of Carboxylic Acids with Borane–THF in Tetrahydrofuran at 0 °C[a]

carboxylic acid	time, h	H_2 evolved, mmol/mmol of FG	total H^- consumed, mmol/mmol of FG	H^- used for reduction, mmol/mmol of FG
benzoic	0.25	1.00	1.08	0.08
	1.0	1.00	1.98	0.98
	3.0	1.00	2.46	1.46
	12.0	1.00	2.95	1.95
	24.0	1.00	3.00	2.00
phenylacetic	0.25	1.09	3.09	2.00
	0.5	1.09	3.09	2.00
	1.0	1.09	3.09	2.00

[a] 0.25 M in functional group (FG) in substrate in 1.0 M in hydride in BH_3–THF unless otherwise indicated.

Results and Discussion

Procedure for Rate and Stoichiometry Studies. The reaction mixtures were 0.33 M in BH_3 and 0.25 M in the functional group (FG) in substrate in THF as solvent. The

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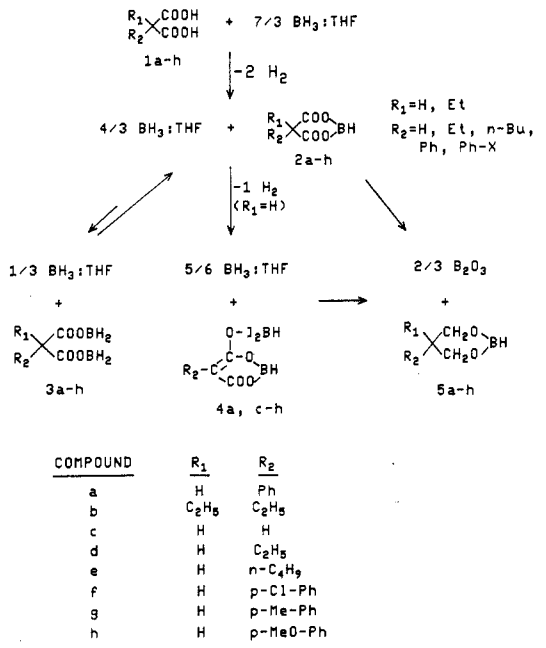
0022-3263/89/1954-1194$01.50/0

Scheme I



COMPOUND	R_1	R_2
a	H	Ph
b	C_2H_5	C_2H_5
c	H	H
d	H	C_2H_5
e	H	n-C_4H_9
f	H	p-Cl-Ph
g	H	p-Me-Ph
h	H	p-MeO-Ph

reactions were carried out at 0 °C and −20 °C unless otherwise indicated. Aliquots were removed at timed intervals and analyzed for residual hydride by hydrolysis. This established both the reduction rate and the stoichiometry of the reaction; for example, the number of hydrides utilized per mole of compound when the reaction stops. A blank experiment was carried out under the same conditions except that solvent was added instead of substrate.

Mechanism. During early investigations of diborane as an acid-type reducing agent toward organic carboxylic acids, benzoic acid reacted with borane–THF in the stoichiometric ratio to liberate the theoretical amount of hydrogen, assuming a potential synthesis of tris(benzoxyloxy)borane.[9] On the other hand, tris(acyloxy)borane, if formed momentarily, has been demonstrated to undergo a rapid dismutation.[2,10] Recently, Brown and Stocky undertook a study of the controlled reaction of carboxylic acids with borane–THF at appropriate temperatures making available mono-, bis-, and tris(acyloxy)boranes.[4] Treatment of the carboxylic acids with borane–THF (1:1), the bis(acyloxy)borane with borane–THF, or the tris(acyloxy)borane with borane–THF (1:2) produced at the same rate the corresponding trialkoxyboroxines.[4] These results established that no matter which (acyloxy)borane is initially formed, the essential intermediate is the mono(acyloxy)borane.

As shown in Table I, benzoic acid, the most inert among the acids, reacted with a solution of borane–THF in THF with evolution of 1 equiv of hydrogen in 0.25 h and complete reduction in 24 h. The corresponding reaction of phenylacetic acid, which contains acidic α-hydrogen was complete in 0.25 h, at which time 1.09 equiv of hydrogen had been released (Table I). With phenylacetic acid the reduction successfully competes with active α-hydrogen abstraction (metalation) for the borane intermediate. The reaction of **1a**, however, was quite slow. It stopped in 4 h with 33% of the expected uptake of hydride. The hydrogen evolution was 2.8 equiv in 0.25 h and 3 equiv in 0.5 h (Tables II and III), suggesting substantial metalation.

It has been previously reported that the reactions of carboxylic acids that are not reduced by borane–THF stop at the bis(acyloxy)borane stage.[10,11] Addition of borane–THF to **1a** in a 1:1 molar ratio resulted in the evolution of 2 equiv of hydrogen and the expected formation of a cyclic (phenylmalonyldioxy)borane (**2a**) as indicated in Scheme I. This compound had been previously made and characterized by ^{1}H and ^{11}B-FT NMR and FT-IR.[8] The chemical ionization mass spectrum has now been studied and a clear M + 1 ion appeared at m/z 191, with other major fragments corresponding to the loss of BH (179), BHO (163), BHO_2 (147), $BHCO_3$ (119), and BHC_2O_4 (91), respectively. This compound is remarkably stable, as indicated by ^{11}B NMR and mass spectral data, when stored in the solid state at room temperature.

Reduction of the intermediate **2a** with 5 H^- equiv in BH_3–THF or of the acid **1a** with 8 H^- equiv both proceeded at 0 °C with approximately the same rate (Table II). After 24 h, analysis of the filtered reaction aliquots in THF by ^{11}B NMR revealed two major resonances at −0.9 and +25.9 ppm, corresponding to the unreacted BH_3–THF and the reduced product **5a**, respectively.[12,13] Apparently the reduction proceeded through the intermediate **2a** without an exchange with free BH_3–THF to form **3a** (Scheme I), which would be rapidly reduced as shown in Table I by the reduction of phenylacetic acid with borane–THF. Treatment of **2a** with $^1/_3$ mol of BH_3–THF resulted in evolution of 0.52 equiv of hydrogen and only 5% reduction in 2 h (by analysis of residual hydride by hydrolysis). The ^{11}B NMR spectrum of the reaction mixture showed three compounds: unreacted starting material **2a** (+2.9 ppm), **5a** (+25.7 ppm) as a reduction product, and **4a** (+2.9 and +19.8 ppm) as the second intermediate. Furthermore, by treatment of **1a** with borane–THF in a 1:2 ratio, 3 equiv of hydrogen were evolved, achieving only 19% of hydride uptake in 0.5 h and 23% of reduction in 1 h (Table II and Scheme I). The ^{11}B NMR of the filtered reaction aliquot showed two compounds corresponding to **5a** (+26.1 ppm) and **4a** (+2.9 and +19.2 ppm).[13] These experiments clearly indicate that at 0 °C metalation is faster than the reduction. The reduction of **4a** is slow,[14] and the reaction stops.

To control **1a** metalation by borane–THF, the reaction was carried out at a lower temperature. Addition of BH_3–THF to **1a** in a ratio of 8:3 at −20 °C resulted in the evolution of 2 equiv of hydrogen and consumption of 37% active hydride for reduction in 5 min. It appeared that at −20 °C the reduction was significantly faster in the first 5 min than at 0 °C. It was then decided to carry out the reduction of **1b**, which possesses no active α-hydrogen, with borane–THF. Treatment of borane–THF to **1b** in a 1:1 molar ratio resulted in the evolution of only 2 equiv of hydrogen in 0.25 h and the expected formation of cyclic (diethylmalonyldioxy)borane (**2b**) as indicated at +5.4 ppm relative to BF_3–OEt_2[9] by ^{11}B-FT NMR spectrum.[4,8,11] Furthermore, by treatment of **1b** with hydride in a 1:8 ratio or **2b** with hydride in a 1:5 ratio at 0 °C, consumption of

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(12) Eaton, G. R.; Lipscomb, W. N. *NMR Studies of Boron Hydrides and Related Compounds*; W. A. Benjamin: New York, 1969. The ^{11}B NMR chemical shift of the reduced product, **5**, is identical with that (+23.3 ppm) of the prepared sample by the stoichiometric reaction of 2-phenyl-1,3-propanediol with borane–THF.
(13) It appears that the second intermediate, **4a**, slowly precipitates out of the solution during the course of the reaction, as indicated by the decrease in the ^{11}B NMR resonances of **4a** and the increase in the amount of precipitate present.
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Table II. Reduction of Representative Malonic Acids with Borane–THF in Tetrahydrofuran at Selected Temperatures[a]

substrate	time, h	H_2 evolved, mmol/mmol of FG		total H^- consumed, mmol/mmol of FG		H^- used for reduction, mmol/mmol of FG	
		0 °C	−20 °C	0 °C	−20 °C	0 °C	−20 °C
1a	0.08		0.95		1.70		0.75
	0.25	1.44	1.08	1.95	1.84	0.51	0.76
	0.50	1.50	1.14	2.05	1.90	0.55	0.76
	1.0	1.50	1.18	2.06	2.08	0.56	0.90
	4.0	1.50	1.19	2.18	2.23	0.67	1.04
	24.0	1.50	1.19	2.31	2.37	0.81	1.18
	48.0		1.18		2.36		1.18
2a[b]	0.25	0.39		0.87		0.48	
	0.50	0.46		0.97		0.52	
	1.0	0.49		1.02		0.53	
	4.0	0.49		1.19		0.70	
	24.0	0.49		1.24		0.74	
1a[c]	0.25	1.41					
	0.50	1.49		1.86		0.37	
	1.0	1.49		1.95		0.46	
1b	0.25	1.00	1.04	1.64	1.55	0.64	0.51
	0.50	1.00	1.04	1.93	1.68	0.93	0.64
	1.0	1.00	1.04	2.32	1.95	1.32	0.91
	8.0	1.00	1.04	2.99	3.00	1.99	1.96
	24.0	1.00	1.04	2.99	3.06	1.99	2.02
2b[b]	0.25	1.00		1.57		0.57	
	0.50	1.00		1.91		0.91	
	1.0	1.00		2.31		1.31	
	4.0	1.00		2.92		1.92	
	8.0	1.00		3.00		2.00	
1c	0.25	1.30	1.10	2.07	2.24	0.77	1.14
	0.50	1.30	1.12	2.17	2.40	0.87	1.28
	1.0	1.30	1.12	2.31	2.44	1.01	1.32
	8.0		1.12		2.90		1.78
	24.0	1.30	1.12	2.76	2.96	1.46	1.84
1d	0.25	1.16	0.98	1.84	1.80	0.68	0.82
	0.50	1.17	1.01	2.16	2.00	0.99	0.99
	1.0	1.17	1.01	2.33	2.20	1.16	1.19
	8.0		1.01		2.68		1.67
	24.0	1.17	1.01	3.20	2.96	2.03	1.95
1e	0.25	1.18	0.95	1.88	1.64	0.70	0.69
	0.50	1.20	1.03	2.04	1.92	0.84	0.89
	1.0	1.20	1.03	2.32	2.18	1.12	1.15
	8.0	1.20	1.03	2.74	2.60	1.54	1.57
	24.0	1.20	1.03	3.02	3.02	1.82	1.99
1f	0.25	1.27	0.85	1.90	1.32	0.63	0.47
	0.50	1.30	1.00	2.18	1.51	0.88	0.51
	1.0	1.33	1.12	2.26	1.83	0.93	0.71
	8.0	1.33	1.12	2.57	2.35	1.24	1.23
	24.0	1.33	1.12	2.65	2.65	1.32	1.53
	48.0		1.12		2.99		1.84
	72.0		1.12		3.10		1.98
1g	0.25	1.36	0.80	2.08	1.26	0.72	0.46
	0.50	1.36	0.94	2.32	1.46	0.96	0.52
	1.0	1.36	0.98	2.39	1.62	1.03	0.64
	8.0	1.36	1.03	2.66	2.05	1.30	1.02
	24.0	1.36	1.03	2.72	2.43	1.36	1.40
	48.0		1.03		2.73		1.70
	72.0		1.03		2.99		1.96
1h	0.25	1.20	0.87	1.68	1.33	0.48	0.46
	0.50	1.22	0.95	1.77	1.45	0.55	0.50
	1.0	1.23	1.02	1.88	1.65	0.65	0.63
	8.0		1.04		2.20		1.16
	24.0	1.23	1.04	2.15	2.42	0.92	1.38

[a] See Table I. [b] 0.25 M in FG in substrate and 0.65 M in hydride in BH_3–THF. [c] 0.25 M in FG in substrate and 0.75 M in hydride in BH_3–THF.

100% active hydride (by analysis of residual hydride by hydrolysis) for reduction in 8 h was achieved (Table II). The ^{11}B NMR of a reaction aliquot showed three compounds corresponding to **5b** (+25.2 ppm), a very broad peak of boron oxide (+17.9 ppm), and borane–THF (−0.66 ppm).[15] This experiment clearly indicates that the reaction proceeds through the intermediate formation of **2b**, either formed directly from the malonic acid and borane or formed by a redistribution reaction of an acyclic (diethylmalonyldioxy)bis(borane) (**3b**). When active α-hydrogen is available in substrates, the reduction of intermediate **4** is exceptionally slow and essentially stops further reduction.

Reduction. The reduction of **1a** by borane–THF was reported to be incomplete at −20 °C.[8] Now we describe

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Table III. Effect of Temperature on the Rates of Reduction of Phenylmalonic Acid (1a) with Borane–THF in Tetrahydrofuran[a]

temperature, °C	time, h	H_2 evolved, mmol/mmol of FG	total H^- consumed, mmol/mmol of FG	H^- used for reduction, mmol/mmol of FG
0	0.25	1.44	1.95	0.51
	0.50	1.50	2.05	0.55
	1.0	1.50	2.06	0.56
	4.0	1.50	2.18	0.67
	24.0	1.50	2.31	0.81
−20	0.10	0.95	1.70	0.75
	0.25	1.08	1.84	0.76
	0.50	1.14	1.90	0.76
	1.0	1.18	2.08	0.90
	4.0	1.19	2.23	1.04
	24.0	1.19	2.37	1.18
	48.0	1.18	2.36	1.18
−30	0.25	0.55	1.11	0.56
	1.0	0.89	1.62	0.73
	8.0	1.00	2.01	1.01
	24.0	1.00	2.17	1.17
	72.0	1.00	2.71	1.71
	120.0	1.00	2.87	1.87
	144.0	1.00	2.97	1.97
−50	0.25	0.01	0.00	0.00
	0.50	0.02	0.20	0.18
	1.0	0.02	0.20	0.18
	4.0	0.02	0.20	0.18

[a] See Table I.

the complete study of **1a** reduction and the comparison of the rate of reduction of **1a** with other corresponding malonic acids under both 0 °C and −20 °C, unless otherwise indicated. The results are given in Tables II and III.

At −20 °C 35% of metalation of **1a** still occurred.[8] The reaction essentially stopped in 24 h and gave only 59% reduction as shown in Table III. Reduction of **1a** at −30 °C with 8 equiv of H^- in borane–THF was then carried out. The reaction at −30 °C was clean enough to be completed but took 6 days. No metalation was seen. The isolated yield after further purification was 85%. Reaction at −50 °C was quite sluggish, giving only 9% reduction in 4 h and no hydrogen evolution.

A model experiment was then carried out utilizing **1b** at both 0 °C and −20 °C (Table II). The rate of reduction at 0 °C was about the same as that at −20 °C and resulted in complete reduction in 8 h. Then we did a comparative study of the reactions of other representative malonic acids at 0 °C with the corresponding reaction at −20 °C. The results are summarized in Table II. For all aromatic α-substituted malonic acids (**1f–h**) the reductions at 0 °C showed significant metalation (46–72%), leading to incomplete reactions (46–67%). Under similar conditions, the aliphatic monoalkylmalonic acids (**1d–e**) except for malonic acid (**1c**) were reduced in 24 h with 34–40% metalation. On the other hand, at −20 °C, the corresponding reaction employing **1f–h** gave reduction in 3 days with 6–24% of metalation. With the aliphatic malonic acids (**1d–e**) at −20 °C, no metalation was found and the reduction was completed in 24 h. The data and observations indicate that (1) at −20 °C metalation is reduced and reduction occurs at the same rate as at 0 °C; (2) at −50 °C, however, neither reduction nor metalation occurred; and (3) the relative rates of reduction and metalation between aromatic and aliphatic malonic acids at 0 °C and −20 °C is presumably due to an electronic influence of the α-substituent group. No clear difference in the rate of the reduction among the substituted aromatic malonic acids (**1f–h**) was found under these reaction conditions.

Conclusion

The reaction mechanism for reduction of representative malonic acids has been investigated systematically with borane–THF. The relatively stable cyclic intermediate, **2a**, has been synthesized and characterized. It appears that the reduction occurs via the intermediate **2** and the exceptionally slow reduction seen in some cases is due to the intermediate formation of the metalation product, **4**. The data for the comparison of the rate of reduction of **1a** with other corresponding malonic acids under both 0 °C and −20 °C are summarized in Tables I–III. The data indicate that the use of a low temperature (−20 °C) prevents metalation except for **1a** which requires −30 °C. The reduction at −20 °C proceeded at approximately the same rate as at 0 °C.

Experimental Section

^{11}B-FT NMR and ^{1}H-FT NMR spectra were recorded on a JEOL FX-90Q FT NMR spectrometer. All ^{1}H chemical shifts are relative to tetramethylsilane (δ 0), and ^{11}B chemical shifts are relative to boron trifluoride etherate (δ 0). FT-IR spectra were recorded on FX-6160 FT-IR spectrometer. Mass spectra were recorded on a Finnigan TSQ-70 instrument operating in the chemical ionization (ethane) mode. All glassware was dried thoroughly in a drying oven and cooled under a stream of dry nitrogen. All reduction experiments were carried out under a dry nitrogen atmosphere. Hypodermic syringes were used to transfer the solutions. Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected.

All malonic acids were either commercially available (Aldrich Chemical Co.) or were prepared from the corresponding acetic acid by the published procedure.[5] Tetrahydrofuran (THF) was dried with excess lithium aluminum hydride and distilled under nitrogen immediately prior to use. Borane–THF was the commercial product and was standardized by hydrolyzing a 1-mL aliquot of the solution with a glycerine–water–THF mixture and measuring the hydrogen evolved.

Procedure for the Rate Study. The reaction of phenylmalonic acid is representative. Two 100-mL round-bottom side-arm flasks were dried in an oven and cooled in a dry nitrogen atmosphere. The first flask was equipped with a rubber syringe cap, a magnetic stirring bar, and a reflux condenser connected to a gas buret for the measurement of hydrogen evolved. Then 6.0 mL (3.0 mmol) of a 0.5 M solution of phenylmalonic acid was injected into the reaction flask followed by 9.0 mL of dry THF. The contents of the flask were immersed in an ice bath and cooled to 0 °C. Then 9.04 mL (24 mmol of hydride) of 0.89 M borane solution in THF was added slowly (the resulting solution contained 1.0 M in hydride and 0.25 M in functional group). The rate of hydrogen evolved was followed with time. The results are summarized in Table I–III.

The second reaction flask was prepared in the same manner for the reduction. Aliquots (2.0 mL) were withdrawn at various time intervals and analyzed by hydrolysis. A blank experiment was performed in which THF was substituted for the acid. From the difference, the number of millimoles of hydride used for reduction per millimole of acid and hence the percentage of reaction was calculated. The results are given in Tables I–III.

(Phenylmalonyldioxy)borane. The apparatus is the same as that described previously. In a 50-mL round-bottom flask was placed 3 mL (1.5 mmol) of 0.5 M solution of phenylmalonic acid followed by 4.5 mL of dry THF. The mixture was cooled to 0 °C, and then 1.68 mL of 0.89 M BH_3–THF (1.5 mmol) was slowly added. Hydrogen evolution (72 mL, 2.84 mmol) ceased in 1.5 h. The glass apparatus was weighed. A small piece of vacuum tubing was attached to the connecting tube. It was then immersed in a water bath at room temperature and connected to a vacuum setup. The flask was then opened slowly to the vacuum, and the weight change was noted with time. A white, crystalline solid whose weight corresponds to $PhCH(CO_2)_2BH$ was obtained, 0.25 g (98%), mp 159–161 °C: IR (THF) 2470 (br s), 1725 (sh), 1702 (s), 1600 (s), 1560 (w), 1502 (s), 1330 (m), 1290 (vs), 1090 (m), 990 (m), 770 (m), 690 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.61 (s, 1 H, benzylic) and 7.36 (s, 5 H, Ar); ^{11}B NMR (THF) +2.98 ppm; MS,

m/z (relative intensity) 91 (77), 119 (100), 147 (11), 163 (4), 179 (4), and 191 (3).

2-Phenyl-1,3-propanediol. A 250-mL round-bottom flask with a side-arm was dried in an oven and cooled under a stream of dry nitrogen. The flask was fitted with a rubber syringe cap, a magnetic stirring bar, and a nitrogen outlet connecting tube. Then 1.80 g (10 mmol) of phenylmalonic acid was added followed by 52.0 mL of dry THF. The rapidly stirring solution was cooled to −30 °C, and 28.0 mL (80.0 mmol of hydride) of 0.95 M borane solution in THF was added slowly. The reaction mixture was maintained at −30 °C for 6 days. Then 40 mL of methanol was slowly added, and the solution was slowly warmed to room temperature overnight. The solvents were removed at reduced pressure, and the residue was dissolved in 125 mL of diethyl ether. The ethereal solution was washed with saturated potassium carbonate (2 × 30 mL), which was then extracted with diethyl ether (2 × 100 mL). The combined organic phases were dried with potassium carbonate and concentrated at reduced pressure to give 1.38 g (91%) of a white oily material, which was reprecipitated from a mixture of diethyl ether–hexane–toluene (5:150:30) to give the purified diol, 1.29 g (85%), mp 51–53 °C (lit.[16] mp 51–53 °C).

Registry No. **1a**, 2613-89-0; **1b**, 510-20-3; **1c**, 141-82-2; **1d**, 601-75-2; **1e**, 534-59-8; **1f**, 118459-48-6; **1g**, 118459-49-7; **1h**, 53181-45-6; **2a**, 109306-89-0; **2b**, 118459-50-0; 2-phenyl-1,3-propanediol, 1570-95-2; benzoic acid, 65-85-0; phenylacetic acid, 103-82-2.

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Notes

A Simple Conversion of Diethyl Phenylmalonate with Metal Hydride to the Corresponding Primary Diol: A Competing Reaction between Reduction and Metalation

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2-Phenyl-1,3-propanediol (**2**) has been used as an important intermediate in the synthesis of 2-phenyl-1,3-propanediol dicarbamate (felbamate), an antiepileptic drug under development in our laboratories.[1,2] The preparation of **2** from diethyl phenylmalonate (**1**) by reduction with excess lithium aluminum hydride (LAH) in refluxing ethyl ether has been described.[1] However, the procedure was not detailed, and the reported yield of **2** was only 30–50%.[1,3] Furthermore, we observed hydrogen evolution during the reaction,[3] probably due to α-proton abstraction[4,5] (metalation) by the reagent, with formation of the malonic enolate **3** (Scheme I).

Enolizable 1,3-dicarbonyl compounds have frequently been reported to afford products of both reduction and metalation upon treatment with LAH.[6-9] Ketone enolates were found to resist reduction by the reagent.[8,10] Marshall and co-workers studied the reduction of malonic enolates with LAH in refluxing 1,2-dimethoxyethane.[11] However, the reduction gave a mixture of aldehydes and saturated or unsaturated alcohols as major products without formation of 1,3-propanediol.[11]

Accordingly, we undertook a detailed comparison of the behavior of representative Lewis basic reducing agents [$LiAlH_4$, $LiBH_4$][12a,c,13] with Lewis acidic ones [AlH_3,

Table I. Rates of Reduction of Diethyl Phenylmalonate with Metal Hydrides in Tetrahydrofuran at Room Temperature[a]

metal hydride	time, h	H_2 evolved, mmol/mmol of compd	total H^- consumed, mmol/mmol of compd	H^- used for reduction, mmol/mmol of compd
$LiAlH_4$[b]	0.25	0.05	2.05	2.00
	0.50	0.05	2.05	2.00
	1.0	0.05	2.05	2.00
$LiAlH_4$	0.25	0.18	3.51	3.33
	0.50	0.18	3.69	3.51
	1.0	0.18	3.81	3.63
	2.0	0.18	3.81	3.63
$LiBH_4$	0.25	0.57	2.27	1.70
	0.50	0.67	2.98	2.31
	1.0	0.67	3.34	2.67
	2.0	0.67	3.34	2.67
AlH_3	0.25	0.17	3.57	3.40
	0.50	0.17	3.69	3.52
	1.0	0.17	3.82	3.65
BH_3–SMe_2	0.25	0.01	0.01	0.00
	0.50	0.01	0.06	0.05
	1.0	0.01	0.06	0.05
	4.0	0.01	0.12	0.11
	8.0	0.01	0.16	0.15
	24.0	0.01	0.30	0.29
$(i\text{-}Bu)_2AlH$	0.25	0.01	2.56	2.55
	0.50	0.01	2.98	2.97
	1.0	0.01	3.53	3.52
	2.0	0.01	4.02	4.01

[a] 1.0 M in hydride in metal hydride and 0.17 M in substrate (compd). [b] Reduction of ethyl phenylacetate, 1.0 M in hydride in metal hydride and 0.33 M in compd.

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