1.70 g (77%) of **5a**, mp 92–96 °C. Admixture with **5a** prepared above, mp 92–96 °C.

Attempted Michael Reaction with the Monoanions of 1a and 2b. A solution of the monoanion of **1a** (from 1.62 g, 10 mmol of **1a** with 1.76 g (9.7 mmol) of KH–oil dispersion, 8.8 mmol of H_2 evolution) in 15 mL of THF was added slowly to a solution of the monoanion of **2b** (from 2.80 g, 10 mmol, of **2b** and 1.76 g, 9.7 mmol, of KH–oil dispersion, 9.1 mmol of H_2 evolution) in 15 mL of THF. No H_2 was evolved during the addition of the monoanion of **1a** to the monoanion of **2b**. After stirring for 14 h, cold dilute HCl was added and the THF was removed. The residue was dissolved in ether and TLC showed the presence of **1a** and **2b** only.

1,15-Diphenyl-5,11-bis(*p*-methoxyphenyl)pentadecane-1,3,7,9,13,15-hexone (18). To the anion of **2b**, prepared from 1.40 g (5.0 mmol) of **2b** and 3.56 g (19.7 mmol) of KH in 40 mL of THF, was added 0.25 g (2.5 mmol) of **1b** in 5 mL of THF. H_2 evolution was rapid during the addition of **2b** and **1b**. The yellow solution turned reddish-orange during the 4-h reaction period. The mixture was poured into 200 mL of ice water. H_2 evolution occurred. After washing the clear yellow aqueous solution with two 25-mL portions of hexane, 6 M HCl was added to yield an emulsion from which an oil separated. Ether extraction, drying ($MgSO_4$), and evaporation of the solvent left a yellow oil (1.6 g). Upon standing for 2 days at room temperature, the oil partially solidified. It was recrystallized from CCl_4, followed by a rapid ether wash to yield 0.40 g of white crystals, mp 112–115 °C. Anal. Calcd for $C_{41}H_{40}O_8$: C, 74.52; H, 6.10. Found: C, 74.28; H, 5.97. Principal ^1H NMR shifts appear in Table I. The spectrum of the crude reaction mixture was identical with that of the crystallized material. When a portion of the noncrystallized material was refluxed with water, then cooled, an amorphous solid, melting from 35 to 50 °C, was obtained. Upon standing, it slowly became a viscous oil.

1,7-Bis(*p*-tolyl)-1,6-heptadiene-3,5-dione (10). Addition of 10 mmol of **1b** to 40 mmol of KH in THF yielded 11 mmol of H_2. Treatment of this mixture with 10 mmol of *p*-tolualdehyde gave vigorous H_2 evolution. After 3 h, acidification and subsequent extractions yielded *p*-toluic acid and a yellow-orange oil. Crystallization attempts were unsuccessful. Distillation yielded one fraction, bp 180–200 °C (0.4 mm), which solidified. Recrystallization from methanol yielded 0.88 g (41%) of a yellow solid: mp 203–207 °C; ^1H NMR ($CDCl_3$) δ 2.4 (s, 6), 5.78 (s, 1), 6.42 (s, 1), 6.59 (s, 1), 7.0–7.62 (m, 10), 15.5 (br s, 1).

Registry No. 1a, 93-91-4; **1b**, 123-54-6; *trans*-**2b**, 72610-53-8; *cis*-**2b**, 72610-54-9; **3**, 72610-55-0; **4**, 72610-56-1; **5a**, 72610-57-2; **5b**, 72610-58-3; **6a**, 72610-59-4; **6b**, 72610-60-7; **7**, 72610-61-8; **8**, 52393-50-7; **9**, 72610-62-9; **10**, 72610-63-0; **18**, 72610-64-1; *p*-anisaldehyde, 123-11-5; *p*-tolualdehyde, 104-87-0; *p*-anisic acid, 100-09-4; *p*-toluic acid, 99-94-5; benzophenone, 119-61-9; benzyl chloride, 100-44-7.

Homologation of Carbonyl Compounds to Aldehydes with Lithium Bis(ethylenedioxyboryl)methide

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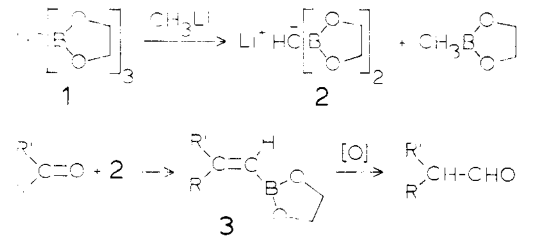
Tris(ethylenedioxyboryl)methane reacts with methyllithium at −78 °C in THF to form lithium bis(ethylenedioxyboryl)methide, which reacts with aldehydes and ketones to form 1-alkene-1-boronic esters. These need not be isolated for efficient oxidation by sodium perborate to the homologated aldehydes, which are easily purified. Systematic investigation of the reaction conditions to optimize yields at each step was undertaken. Possibly hazardous 2:1 aldehyde–hydrogen peroxide adducts were found to form under neutral conditions with dilute (5%) hydrogen peroxide. Hydrogen peroxide was also found to cause some carbon–carbon bond cleavage during oxidation of alkeneboronic acids. Both problems were avoided by the use of sodium perborate instead. Reaction of lithium bis(ethylenedioxyboryl)methide with benzoyl chloride or methyl benzoate followed by hydrolysis was found to yield acetophenone. A significant error in one previous description of the synthesis of the key starting material, tris(dimethoxyboryl)methane, is noted.

Introduction

The reaction of tris(ethylenedioxyboryl)methane (**1**) with alkyllithium to form lithium bis(ethylenedioxyboryl)methide (**2**) and condensation of aldehydes or ketones with **2** to form 1-alkene-1-boronic esters (**3**)[1] suggest the possibility of an efficient aldehyde homologation process based on this chemistry.[2]



The traditional method for accomplishing such homologations is the Darzens glycidic ester condensation, which often suffers from low yields.[3] An important exception is the efficient Darzens homologation of β-ionone, used as a step in the synthesis of vitamin A.[4] More recently developed homoloating agents include Wittig reagents bearing alkoxy[5] or phenylthio[6] substituents, though these, too, have limitations with respect to yields and convenience. After our preliminary communication appeared, a very promising aldehyde homologation based on chloro(trimethylsilyl)methyllithium was reported by Magnus and co-workers.[7]

Results

The preparation of the key starting material, tris(dimethoxyboryl)methane, in 60–80-g batches has been de-

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[2] Preliminary communication: Matteson, D. S.; Moody, R. J.; Jesthi, P. K. *J. Am. Chem. Soc.* **1975**, *97*, 5608–5609.

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[4] Isler, O.; Hüber, W.; Ronco, A.; Koffer, M. *Helv. Chim. Acta* **1947**, *30*, 1911–1927.

[5] Wittig, G.; Böll, W.; Krück, K.-H. *Chem. Ber.* **1962**, *95*, 2514–2525.

[6] Bestmann, H. J.; Angerer, J. *Tetrahedron Lett.* **1969**, 3665–3666.

[7] Burford, C.; Cooke, F.; Ehlinger, E.; Magnus, P. *J. Am. Chem. Soc.* **1977**, *99*, 4536–4537.

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scribed previously.[1,8-10] An unfortunate error in stoichiometry in one report[9] must be avoided and the correct amount of chloroform used.[8,10] Transesterification of the methoxy compound with ethylene glycol yields tris(ethylenedioxyboryl)methane [tris(1,3,2-dioxaborol-2-yl)methane] (**1**).[1,10]

Homologation of benzaldehyde to phenylacetaldehyde was chosen as the first test reaction. Methyllithium was added to **1** in tetrahydrofuran (THF) at -78 °C to form a slurry of lithium bis(ethylenedioxyboryl)methide (**2**), benzaldehyde was added, and the mixture was oxidized with alkaline hydrogen peroxide at ~25 °C and extracted with ether. Gas chromatographic analysis indicated a yield of only 50%, but this was soon increased to 98% by carrying out the oxidation in the presence of a sodium tetraborate buffer (pH 7).

The optimum conditions for production of phenylacetaldehyde gave disappointing results in the homologation of heptanal to octanal, the initial yield being only 50%. A systematic survey of reaction conditions was therefore undertaken. The oxidation with hydrogen peroxide and sodium tetraborate buffer was checked with crystalline 1-octene-1-boronic acid[1] and found to yield 95% octanal and 2% heptanal. When the boronic acid was first esterified by treatment with ethylene glycol and boron trifluoride in ether, then oxidized, the yield of octanal was 80% and that of heptanal was 2%. The formation of heptanol and other byproducts during oxidation was found later to be a significant problem, but for the time being we turned to other variables.

Variation of time and temperature for formation of the lithium diborylmethide **2** indicated that keeping the mixture at -78 °C was best. The ratio of octanal to heptanal increased systematically as the time of stirring the slurry of **2** was increased from 0.5 to 1 to 2 h and leveled off at 2.5 h. When the slurry of **2** was kept at -10 or 0 °C for 2.5 h prior to cooling to -78 °C and adding the heptanal, yields decreased slightly, but holding **2** at 25 °C for 2.5 h caused a marked decrease to 33%, indicating instability of **2** in THF at 25 °C.

After addition of the heptanal to the lithio compound **2**, stirring at -78 °C for 3 h followed by warming to 0-25 °C and immediate addition of the hyrogen peroxide gave only 10-32% yield of octanal. Stirring the mixture 0.5 h at 20-25 °C before oxidation increased the yield to 41%, 1 h at 20-25 °C, 51%; 2 h, also 51%; 3 h, 60%. Yields sometimes fluctuated, perhaps because we did not yet recognize the complexity of the oxidation step, but were seldom above 60-65% until it was found that removal of the THF by vacuum distillation prior to the oxidation step resulted in reproducible improvement to 70-75%.

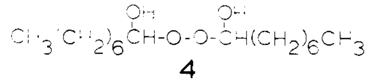
Previous work on the reaction of lithium tris(ethylenedioxyboryl)methide with an aldehyde revealed that use of dichloromethane as a cosolvent with THF improved the yields,[11] perhaps because of improved solubility of the lithio compound or its precursor. In the present work, we found that a THF/dichloromethane volume ratio of 13:2 resulted in a 60% yield of octanal, 1:1 gave 79%, 2:3 gave 82%, and pure dichloromethane gave 60%. Use of a 1:1 mixture of THF and hexane led to a 78% yield of octanal. Use of butyllithium under the optimized conditions had no measurable effect on the yield.

Table I. GLC Yields of Aldehydes from Reaction of Lithium Bis(ethylenedioxyboryl)methide (2) with Carbonyl Compounds Followed by Hydrogen Peroxide Oxidation Buffered with Sodium Bicarbonate

reactant	product	yield, %	reactant recovery, %
butanal	pentanal	85	0
heptanal	octanal	87	1
octanal	nonanal	94	7
4-penten-1-al	5-hexen-1-al	79	0
benzaldehyde	phenylacetaldehyde	97	3
acetone	isobutyraldehyde	63	1
cyclohexanone	cyclohexane-carboxaldehyde	97	4

Aldehyde Peroxides, a Potential Hazard. After the conditions had been optimized for yield of octanal by GLC analysis, isolation was tried, and a new problem surfaced. After vacuum distillation of the octanal, a variable amount of distillable white solid remained. Treatment of the solid with 2,4-dinitrophenylhydrazine gave octanal-2,4-DNP.

The same solid was readily prepared by stirring a mixture of octanal, sodium tetraborate, boric acid, water, and 30% hydrogen peroxide at 25 °C. NMR, IR, and microanalytical data supported the structure bis(1-hydroxy-1-octyl) peroxide (**4**). This compound was not found in



$CH_3(CH_2)_6CH(OH)\text{-}O\text{-}O\text{-}CH(OH)(CH_2)_6CH_3$

4

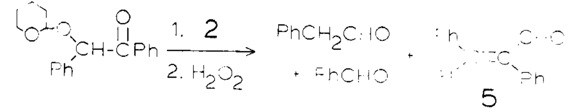
Chemical Abstracts, though it and numerous homologues have been reported in a book by Rieche[12] and reviewed by Davies.[13]

It should be noted that the hydrogen content of the solutions in which we first found the octanal peroxide **4** was only ~5%. Our attempts to detonate the material by striking it with a hammer failed, in accord with earlier reports that such peroxides are nonexplosive.[13] Compound **4** was stable for at least a year at 20 °C.

To avoid aldehyde peroxide formation, it was only necessary to increase the pH slightly during the oxidation. The use of sodium bicarbonate as the base led to isolation of octanal in 72% yield, with no visible evidence of the solid peroxide.

Generality of Procedure. The conditions just described for the preparation of octanal were tested on a short series of aldehydes and ketones, with GLC analysis. The results are summarized in Table I.

The homologation procedure proved unsuccessful with certain types of α-substituted carbonyl compounds. Reaction of benzoin with 1.15 equiv of **2** gave an 87% isolated yield of a 1:1 mixture of benzaldehyde and phenylacetaldehyde, evidently by reverse aldol cleavage of the homologation product, 2-formyl-1,2-diphenylethanol. When the hydroxyl group of the benzoin was protected with tetrahydropyran, attempted homologation yielded 63% of a 1:1 mixture of benzaldehyde and phenylacetaldehyde and 24% of (Z)-α-phenylcinnamaldehyde (**5**).



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Low yields of boronic acid and aldehyde from homologation of 1,3-dichloroacetone have been noted previously.[1,2]

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[8] Castle, R. B.; Matteson, D. S. *J. Organomet. Chem.* **1969**, *20*, 19-28.

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[11] Matteson, D. S.; Biernbaum, M. S.; Bechtold, R. A.; Campbell, J. D.; Wilcsek, R. J. *J. Org. Chem.* **1978**, *43*, 950-954.

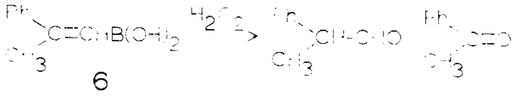
[12] Rieche, A. "Alkyl Peroxide and Ozonide", Steinkopff: Dresden, **1971**; pp 57-60.

[13] Davies, A. G., "Organic Peroxides", Butterworths: London, **1961**; pp 71-72.

Ethyl pyruvate gave ethyl 2-formylpropionate in 25% isolated yield, perhaps due to losses in workup.

Carbon–Carbon Cleavage in Alkeneboronic Acids. It was noted earlier that hydrogen peroxide oxidation of crystalline 1-octene-1-boronic acid yielded 2% heptanal in addition to octanal, as shown by GLC analysis. NMR and IR spectra showed no evidence of any heptanal contaminating the boronic acid, and the heptanal from which the boronic acid was made was not contaminated with hexanal, as shown by GLC analysis.

Conclusive proof that carbon–carbon bond cleavage can occur during oxidation of alkeneboronic acids was provided by 2-phenylpropene-1-boronic acid (**6**), prepared from acetophenone as a cis–trans mixture.[1] Application of the usual oxidation conditions to this crystalline boronic acid gave mixtures which contained 18–40 mol % acetophenone together with α-phenylpropionaldehyde, as shown by NMR analysis.



In the short series of oxidations of 2-phenylpropene-1-boronic acid (**6**) tested, no coherent trend was found as the buffer was varied from sodium tetraborate to sodium bicarbonate to sodium carbonate. With sodium hydroxide at pH 13, the proportion of acetophenone was still about 17 mol %.

Recalling that Kuivila and Armour had found a kinetic term corresponding to attack by a boron hydroperoxide anion on benzeneboronic acid in its oxidation by hydrogen peroxide,[14] we tried sodium perborate as an oxidizing agent. The amount of acetophenone from oxidation of **6** fell to 3 mol %. Purification of **6** then became significant and further reduced acetophenone production to 1 ± 0.5 mol %. Rechecking with hydrogen peroxide, in 2 M sodium hydroxide the acetophenone yield was 4%, and with some added sodium tetraborate, 3%. Although sodium perborate forms rapidly from hydrogen peroxide and borate, the separate reagents did not appear to be equivalent to preformed sodium perborate in this brief investigation.

Aldehyde Isolation. By using an extraction procedure to remove residual starting material and oxidizing the boronic ester product with sodium perborate, we found it possible to isolate pure aldehydes in high yields in most cases. The water-soluble alkenylboronic acid sodium salts survive at least brief exposure to aqueous 1 M sodium hydroxide at 20–25 °C, and the organic impurities are readily extracted from the aqueous solution with chloroform or dichloromethane. Addition of a second portion of the organic solvent followed by sodium perborate to the alkaline mixture and stirring 10 min yields a solution of aldehyde which can be purified by simple distillation.

Phenylacetaldehyde proved too sensitive to base-catalyzed aldol condensation to survive the general conditions, but was readily obtained in high purity when the pH was lowered to 7 with boric acid before the oxidation. Base precipitated the lithium salt of 1-octene-1-boronic acid, and the procedure was modified to include extraction of an ether solution of the crude boronic ester with aqueous phosphoric acid to remove the lithium salts, followed by extraction of the boronic acid in the usual manner. The homologation product from ethyl levulinate proved unstable to aqueous base at some stage, and extractive purification had to be omitted, leaving a small residue of starting material in the product. (Conventional, more laborious distillation of the boronic ester intermediate was not tried.)

Table II. Isolated Aldehyde Yields from Homologation of Carbonyl Compounds with Lithium Bis(ethylenedioxyboryl)methide (**2**) Followed by Sodium Perborate Oxidation

reactant	product	yield, %	recovered reactant, %[a]
$CH_3(CH_2)_5CHO$	$CH_3(CH_2)_6CHO$	84	0
C_6H_5CHO	$C_6H_5CH_2CHO$	77	0
CH_3CH_2-$COCH_2CH_3$	$(CH_3CH_2)_2CHCHO$	74	0
$C_6H_5COCH_3$	$C_6H_5CH(CH_3)CHO$	80	0
$(CH_3)_2C{=}CHCOCH_3$	$(CH_3)_2C{=}CHCH(CH_3)CHO$	81	0.7
EtO_2CCH_2-CH_2COCH_3	$EtO_2CCH_2CH_2$-$CH(CH_3)CHO$	65	3

[a] Estimated by GLC analysis of the first four products, NMR analysis of the last two.

Isolated yields of aldehydes are summarized in Table II.

Acylation of 2. Reaction of lithiodiborylmethane **2** with benzoyl chloride was tested. The product after hydrolysis was found to be acetophenone, which was isolated as the 2,4-dinitrophenylhydrazone in 75% yield. GLC analysis of the crude reaction mixture indicated the absence of phenylacetylene, which was considered to be another possible product.

Methyl benzoate was then tried. Since it appeared that esters do not react under the conditions found successful with ketones, more vigorous conditions were used. Refluxing a suspension of **2** in cyclohexane with methyl benzoate for 15 h followed by hydrolysis gave 74% acetophenone as the 2,4-DNP derivative.

Discussion

The process described here for conversion of an aldehyde or ketone to the homologous aldehyde appears to be generally more efficient than older methods.[3-6] A unique feature is the ability to generate the aldehyde product without the use of acidic conditions at any stage of the process. We have not attempted homologation of an unprotected carbonyl group in the presence of a protected carbonyl, but this should be possible in view of the proven stability of the ethylene ketal function to closely related reagents.[15,16] The inherently more sensitive ester function of ethyl levulinate survives the homologation conditions well, provided only that exposure to aqueous base in the workup is avoided. Complications may be expected with α,β-unsaturated carbonyl compounds, even though the example chosen, mesityl oxide, gave a good yield of a single homologation product. Cinnamaldehyde gave only a 41% yield of the corresponding boronic ester.[1] To what extent the lithio compound **2** might undergo conjugate addition in systems prone to do so has not been explored. Although it would seem necessary to avoid unprotected hydroxyl groups in the substrate, as in all other methods except one,[6] the stoichiometry of the reaction of **2** with benzoin requires that the carbonyl group was attacked in preference to the hydroxyl, a point we have not checked further.

The major disadvantage of this new method is the inconvenience of preparing tris(ethylenedioxyboryl)methane (**1**), ~2 days' labor for ~50 g with correct directions.[8,10]

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[14] Kuivila, H. G.; Armour, A. G. *J. Am. Chem. Soc.* **1957**, *79*, 5659–5662.

[15] (a) Matteson, D. S.; Moody, R. J. *J. Am. Chem. Soc.* **1977**, *99*, 3196–3197. (b) Matteson, D. S.; Moody, R. J., to be published.

[16] Mendoza, A.; Matteson, D. S. *J. Organomet. Chem.* **1978**, *156*, 149–157.

The alternative reagent, bis(trimethylenedioxyboryl)methane,[15] requires about the same effort to prepare, though our experience indicates there is less chance of difficulty with preparation of $CH_2[B(OCH_3)_2]_2$ than with $HC[B(OCH_3)_2]_3$ because of the greater stability of diboronic esters. The triboronic ester route described in this article has the advantage of utilizing the ethylene glycol boronic ester, which hydrolyzes rapidly and permits oxidation to the aldehyde to proceed under the mildest possible conditions. The use of 1,3-propanediol boronic esters, required for the efficient production of anions from diboronic esters, results in sluggish hydrolysis of the alkeneboronic ester intermediate and consequently longer oxidation times or lower yields.[15]

A more conveniently available and generally equally efficient reagent for homologating carbonyl compounds is chloro(trimethylsilyl)methyllithium.[7] However, its use does require acidic conditions for liberating the aldehyde or acetal, and it is therefore not fully equivalent to **2** as a synthetic tool. Also, the silicon reagent appeared to suffer some lowering of yield when used with an aliphatic aldehyde (acidic α hydrogens),[7] with which **2** is fully compatible.

Even though the aldehyde peroxide byproducts which may arise in our procedure have failed to show explosive character, they must be considered potentially hazardous.[13] They do not appear to be formed under alkaline conditions, but the presence of hydrogen peroxide together with an aldehyde in ester is sufficient to give rise to these or related peroxides.[13] Thus, any oxidation of a borane with hydrogen peroxide which produces an aldehyde is potentially hazardous. The risk is minimized by the use of sodium perborate, a readily available and inexpensive reagent having excellent shelf life and which therefore need not be analyzed or used in large excess to insure sufficient oxidizing agent. In view of these considerations as well as its lower tendency to cause carbon–carbon bond cleavage, we routinely use sodium perborate for all of our peroxide oxidations of organoboron compounds.

Experimental Section

General. All reactions were carried out under argon. Tetrahydrofuran (THF) was freshly distilled from sodium–potassium alloy. Dichloromethane was distilled from calcium hydride. Oven-dried glassware was used, and liquid reagents and solutions were transferred by syringe. Commercial 1.6 M methyllithium in ether was stored at 0 °C and used only as long as it did not show significant visible deterioration. Aldehydes and ketones were redistilled. The 60-MHz ^1H NMR spectra were recorded with a Varian EM-360 instrument and Me_4Si internal standard, IR spectra with a Beckman IR 18A. Gas chromatographic (GLC) analyses were carried out with a Series 1700 Varian Aerograph instrument equipped with a flame ionization detector, using a 3.1 m × 3 mm column of 15% Carbowax 20 M on Chrom P. Reference compounds used as internal standards included benzene, bicyclohexyl, undecane, and dodecane, and each aldehyde product was separately calibrated against the selected internal standard. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN, and by Dave Harsch, Washington State University.

Tris(ethylenedioxyboryl)methane (**1**) was prepared as reported previously[1] from ethylene glycol and tris(dimethoxyboryl)methane, which was prepared by the previously published method as corrected.[10]

Aldehydes. General Procedure for GLC Analysis. A 2.60-g (11.5 mmol) sample of tris(ethylenedioxyboryl)methane (**1**) was placed in a 50-mL Morton flask equipped with a rubber septum, magnetic stirrer, and argon inlet, and the flask was evacuated and purged with argon. Ten milliliters of THF and 10 mL of dichloromethane were injected by syringe, the solution was cooled to −78 °C (dry ice–acetone), 7.2 mL (11.5 mmol) of 1.6 M methyllithium in ether was added dropwise in a few minutes to the stirred solution, and stirring of the resulting slurry of lithium bis(ethylenedioxyboryl)methide (**2**) was continued for 2.5 h at −78 °C. A 10-mmol portion of the aldehyde or ketone to be homologated was injected, the dry ice bath was removed, and the mixture was allowed to warm at room temperature and stirred 3 h. The solvent was removed by vacuum distillation to leave a residue of alkeneboronic ester and lithium salts. The flask was cooled with an ice bath, and 15 mL of saturated aqueous sodium bicarbonate was added, followed immediately by 3.3 mL of 30% hydrogen peroxide. The mixture was stirred for 1.5 h at 0 °C. A measured amount of the compound used for the GLC internal standard was added, followed by 100 mL of ether. The ether solution was dried over 4-Å molecular sieves and analyzed by GLC. Yields are summarized in Table I.

Phenylacetaldehyde for GLC Analysis. The general procedure was modified as follows. A suspension of 2.37 g of **1** in 35 mL of THF at −78 °C was treated with 10.5 mmol of methyllithium. After 2.5 h, 1.06 g (10 mmol) of benzaldehyde was added. Stirring at room temperature was for 1 h and the solvent was not removed before addition of 8 mL of 0.26 M sodium tetraborate and 2.3 mL of 30% hydrogen peroxide.

Reaction of Benzoin. The general procedure for GLC analysis was scaled up to 34.5 mmol of **2** and 30 mmol of benzoin was added as a solution in 10 mL of 1:1 THF/dichloromethane. Bulb-to-bulb vacuum distillation yielded 4.93 g of material shown by comparison of the ^1H NMR spectrum with known samples to be a 1:1 mixture of benzaldehyde and phenylacetaldehyde.

Reaction of Tetrahydropyranylbenzoin. The THP derivative of benzoin was used in place of benzoin in the same procedure. Bulb-to-bulb distillation yielded 5.76 g of material containing benzaldehyde and phenylacetaldehyde by NMR, from which distillation and recrystallization yielded 1.49 g (24%) of (*Z*)-α-phenylcinnamaldehyde (**5**): ^1H NMR ($CDCl_3$) δ 7.5–7.7 (m, 11, C_6H_5 and C=CH), 10.0 (s, 1, CHO); mp 93 °C (lit.[17] mp 94–95 °C). Anal. Calcd for $C_{15}H_{12}O$: C, 86.54; H, 5.77. Found: C, 86.78; H, 5.73.

Ethyl 2-Formylpropionate. The general procedure for GLC analysis was scaled up to 30 mmol with ethyl pyruvate as substrate. The product was isolated by bulb-to-bulb distillation; 0.96 g (25%). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.24; H, 8.17. It is a known compound,[18] and the IR spectrum was in accord with the assigned structure.

Aldehydes. General Procedure for Isolation. The scale of the reactions for GLC analysis was doubled and the same procedure was followed until after the solvent had been evaporated. The residue was then dissolved in 30 mL of 1 M aqueous sodium hydroxide, 25 mL of chloroform was added, the mixture was stirred 5 min, the chloroform was separated, and a second 30-mL portion of chloroform or dichloromethane was added. The mixture was stirred and 3.4 g (22 mmol) of sodium perborate tetrahydrate was added in several portions. Stirring was continued 10 min after addition was complete. The product was extracted with 100 mL of chloroform or dichloromethane, dried over magnesium sulfate, and isolated by bulb-to-bulb vacuum distillation. Purity was checked by ^1H NMR and GLC analysis. Yields are summarized in Table II.

Phenylacetaldehyde Isolation. The general procedure was followed, using benzaldehyde, except that before the addition of sodium perborate, the pH was adjusted to 7 (pH paper) by addition of boric acid, and the mixture was stirred 75 min after addition of the perborate.

Octanal Isolation. The general procedure was followed using heptanal on a 10-mmol scale until after evaporation of the solvent. The residue was treated with 20 mL of 2 M phosphoric acid and the product was extracted with 100 mL of ether, partially concentrated, and extracted into 1 M sodium hydroxide. The aqueous phase was adjusted to pH 11 with boric acid, 20 mL of dichloromethane was added, and the mixture was cooled to 0 °C before 2.2 g (14 mmol) of sodium perborate tetrahydrate was added. Stirring was continued 1.5 h at 20–25 °C before extraction with dichloromethane and distillation.

Ethyl 4-Formylpentanoate. The general procedure was followed with ethyl levulinate on a 10-mmol scale through

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evaporation of the solvent. Twenty milliliters of water and 20 mL of dichloromethane were added, followed by 2.0 g (13 mmol) of sodium perborate tetrahydrate at 0 °C and stirring 1.5 h at 20–25 °C. Bulb-to-bulb distillation yielded 1.073 g of material judged by ^{1}H NMR analysis to contain 1.03 g (65% yield) of ethyl 4-formylpentanoate and the remainder was ethyl levulinate. This sample was used directly for analysis: ^{1}H NMR ($CDCl_3$) δ 1.11 (d, 3, $CHC\mathbf{H}_3$), 1.25 (t, 3, $CH_2C\mathbf{H}_3$), 1.6–2.2 (m, 3, $C\mathbf{H}C\mathbf{H}_2$), 2.35 (t, 2, $CH_2C\mathbf{H}_2CO$), 4.10 (q, 2, $CH_3C\mathbf{H}_2O$), 9.60 (d, $J \sim 1$ Hz, 1, $C\mathbf{H}O$). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 61.05; H, 8.78.

Reaction of Benzoyl Chloride with 2. To a suspension of 11.5 mmol of **2** prepared by the usual method was added 1.12 g (8 mmol) of benzoyl chloride at −78 °C. After stirring 1 h at −78 °C the mixture was allowed to warm to 0 °C and then was treated with 35 mL of 5 M hydrochloric acid, extracted with 30 mL of dichloromethane, and converted to the 2,4-dinitrophenylhydrazone of acetophenone, 1.83 g (76%).

Reaction of Methyl Benzoate with 2. The solvent was removed under vacuum at 20 °C from 22 mmol of **2** that had been prepared in the usual manner, 30 mL of cyclohexane was added followed by 2.19 g (16 mmol) of methyl benzoate, and the mixture was refluxed for 15 h. Workup as described in the preceding paragraph yielded 3.56 g (74%) of acetophenone 2,4-dinitrophenylhydrazone.

Bis(1-hydroxy-1-octyl) Peroxide (4). A solution of 0.576 g of octanal with 1.1 g of boric acid and 2.8 g of sodium tetraborate decahydrate in 15 mL of water and 35 mL of 30% hydrogen peroxide was stirred for 3 h at 20 °C followed by extraction with ether and recrystallization from ether to yield 0.594 g of **4**: mp 68–70 °C (lit.[13] mp 72 °C); ^{1}H NMR (Me_2SO-d_6) δ 0.87 and 1.27 (m, n-$C_7\mathbf{H}_{15}$), 5.13 (m, $C\mathbf{H}(OH)O$), 6.2 (br, $O\mathbf{H}$), and 9.87 (m, $C\mathbf{H}O$, integral suggests 20% dissociation to free aldehyde); IR (Nujol) 3300–3400 cm^{-1} (vs, OH), no aldehyde C=O. Anal. Calcd for $C_{16}H_{34}O_4$: C, 66.17; H, 11.79; O, 22.03. Found: C, 66.25; H, 11.73; O, 22.06.

Oxidations of 2-Phenylpropene-1-boronic Acid. The usual procedure was followed on a 10-mmol scale with acetophenone (1.23 g), until after the solvent was evaporated. The crude boronic ester was then analyzed by NMR and shown to contain no more than 1% residual acetophenone. Oxidation in the usual manner with hydrogen peroxide and sodium carbonate as buffer followed by extraction and distillation of the product yielded 0.97 g of material estimated to contain about 40 mol % acetophenone and 60 mol % α-phenylpropionaldehyde by NMR analysis. Further tests were carried out on 0.08-g samples of recrystallized 2-phenylpropene-1-boronic acid in 1 mL of deuteriochloroform with 2.5 mL of the aqueous phase. The solution was stirred with 0.1 g of sodium hydroxide and 0.08 g of sodium perborate tetrahydrate for 5 min. NMR analysis of the deuteriochloroform phase indicated about 1 mol % acetophenone in the resulting α-phenylpropionaldehyde solution. Use of 0.21 g of sodium hydroxide, 0.10 g of sodium tetraborate decahydrate, and 0.10 mL of 30% hydrogen peroxide led to 3 mol % acetophenone. Use of 0.18 g of sodium hydroxide and 0.10 mL of 30% hydrogen peroxide led to 4 mol % acetophenone.

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Registry No. **1**, 59278-44-3; **2**, 57404-82-7; **4**, 57335-83-8; **5**, 72659-45-1; **6**, 72659-46-2; butanal, 123-72-8; heptanal, 111-71-7; octanal, 124-13-0; 4-penten-1-al, 2100-17-6; benzaldehyde, 100-52-7; acetone, 67-64-1; cyclohexanone, 108-94-1; pentanal, 630-19-3; nonanal, 124-19-6; 5-hexen-1-al, 764-59-0; phenylacetaldehyde, 122-78-1; isobutyraldehyde, 78-84-2; cyclohexanecarboxaldehyde, 2043-61-0; $CH_3CH_2COCH_2CH_3$, 96-22-0; $C_6H_5COCH_3$, 98-86-2; $(CH_3)_2C{=}CHCOCH_3$, 141-79-7; $EtO_2CCH_2CH_2COCH_3$, 539-88-8; $(CH_3CH_2)_2CHCHO$, 97-96-1; $C_6H_5CH(CH_3)CHO$, 93-53-8; $(CH_3)_2C{=}CHCH(CH_3)CHO$, 14690-10-9; $EtO_2CCH_2CH_2CH(CH_3)CHO$, 57404-75-8; benzoin, 119-53-9; tetrahydropyranylbenzoin, 51706-34-4; ethyl 2-formylpropionate, 27772-62-9; ethyl pyruvate, 617-35-6; ethyl 4-formylpentanoate, 57404-75-8; ethyl levalinate, 539-88-8; benzoyl chloride, 98-88-4; acetophenone 2,4-dinitrophenylhydrazone, 2074-04-6; methyl benzoate, 93-58-3.

Phase-Transfer Synthesis of Monoalkyl Ethers of Oligoethylene Glycols

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The effects of catalyst, temperature, solvent, and reagent ratios on the phase-transfer-catalyzed Williamson ether synthesis of monoalkyl ethers of oligoethylene glycols have been studied. A convenient method has been developed which gives reproducibily high yields of pure monoethers in the presence of aqueous sodium hydroxide.

Monoalkyl ethers of oligoethylene glycols (**1**) (eq 1) are

$$RX + HO(CH_2CH_2O)_nH \rightarrow \underset{\mathbf{1}}{RO(CH_2CH_2O)_nH} + \underset{\mathbf{2}}{RO(CH_2CH_2O)_nR} \quad (1)$$

useful nonionic surfactants. They have been prepared on a laboratory scale by the Williamson ether synthesis, in which the alkoxide is formed in excess glycol using sodium metal or sodium hydride. Reaction with alkylating agents gives variable amounts of dialkylation product (**2**) which can be minimized but not entirely suppressed by the use of a large excess of glycol. On a large scale the reaction requires handling large amounts of sodium or its hydride, and the product is sometimes contaminated with lower ethoxylogues. In our hands, the reaction also gave low (30–60%) yields, and we therefore looked for ways to improve the process.

The application of phase-transfer methodology to the Williamson ether synthesis has been described.[1-5] Freedman has developed a method for the efficient preparation of asymmetrical ethers using 50% aqueous sodium hydroxide as the base and tetrabutylammonium bisulfate as the phase-transfer catalyst.[5] Under the most favorable conditions developed, which involve the use of excess alkyl halide in tetrahydrofuran, tetraethylene glycol is efficiently dialkylated to give **2** in >90% yield.[5]

Initial work using Freedman's conditions, in the presence of a 2- to 10-fold excess of glycol, was moderately successful. Yields varied widely, however, depending on conditions employed, so we decided to concentrate our efforts on a single system in order to untangle the roles

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