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REACTION OF ORGANOBORANES WITH THE DIANION OF PHENOXYACETIC ACID. THE FIRST DIRECT SYNTHESIS OF CARBOXYLIC ACIDS FROM ORGANOBORANES

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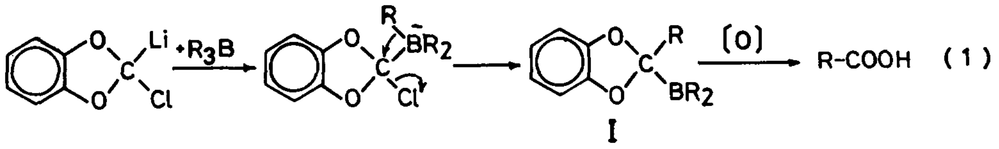
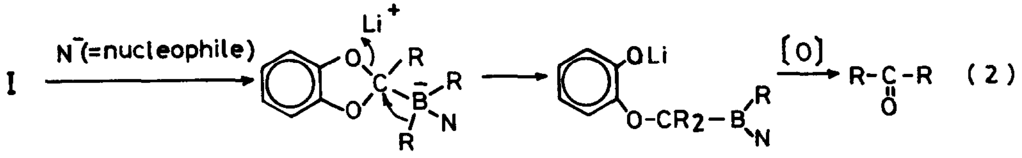
In recent years, many reports have been published dealing with new syntheses of many types of organic compounds from organoboranes.[1,2] However, there is no successful report on the direct preparation of carboxylic acids *via* organoboranes, although various attempts have been made utilizing the reactions of organoboranes, for example, with cyanide ion followed by protonolysis,[3] and with 1,1-dichloromethyl methyl ether in the presence of bases.[6] In the course of our studies, we recently tried the reaction of trialkylboranes with catechol dichloromethylene ether[7] in the presence of methyllithium with the expectation of a successful synthesis of carboxylic acids. It was not certain whether the reaction would involve the carbenoid or the corresponding carbene. Assuming the carbenoid, the reaction would undergo the following transformation (eq. 1). The products actually obtained after alkaline hydrogen peroxide oxidation were not the expected acids but were corresponding ketones,[8] which would be explained by the reaction route depicted in eq. 2. This suggests that the phenoxy group placed at the α-carbon to boron atom of an organoborane, is a good leaving group under such reaction conditions.



(1)



(2)

We now wish to report that trialkylboranes readily react with the dianion of phenoxyacetic acid in tetrahydrofuran to give the corresponding carboxylic acids in satisfactory yields (eq. 3).

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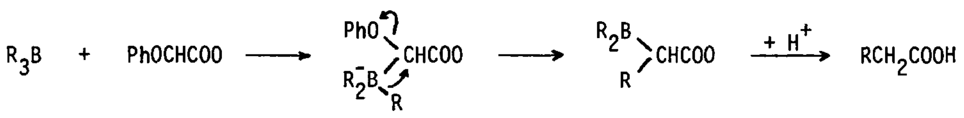
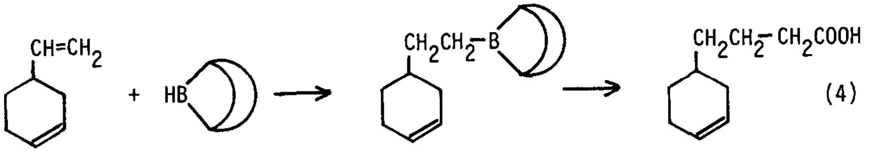


(3)

The reaction is exceedingly simple. The dianion of phenoxyacetic acid can be readily prepared by treatment of 2 equivalents of lithium diisopropylamide in tetrahydrofuran at 0°. This dianion is unusually soluble in tetrahydrofuran and can be prepared without any polar solvent such as HMPA[9] or any heating of the system.[10] Tributylborane reacts with the anion at 66° in 2 h followed by the usual alkaline hydrogen peroxide oxidation and acidification with hydrochloric acid to give hexanoic acid in an essentially quantitative yield.

Introduction of bulky alkyl groups such as isobutyl and cyclopentyl is sluggish and required longer reaction times. Tri-sec-butylborane and tricyclohexylborane give low yields of the corresponding acids. In these cases, however, some improvements in yields are observed by the use of the B-alkyl-9-borabicyclo[3,3,1]nonane (B-R-9-BBN) derivatives instead of trialkylboranes.

9-BBN is well-known to exhibit high regiospecificity in hydroboration of dienes. Thus, it is possible to utilize this characteristic of 9-BBN to achieve the selective conversion of dienes such as 4-vinylcyclohexene and 1,4-hexadiene into the unsaturated carboxylic acids (eqs. 4 and 5).



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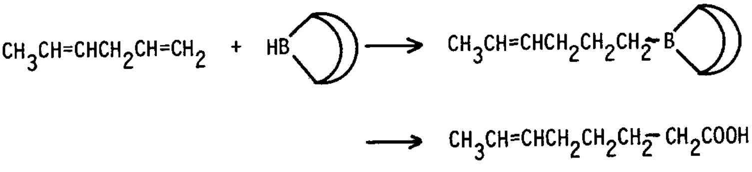


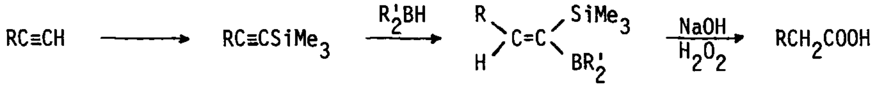
(5)

93%

Representative results are summarized in Table 1.

The following procedure for the preparation of hexanoic acid is representative. A dry 100-ml flask equipped with a magnetic stirring bar, septum inlet, and reflux condenser was flushed with nitrogen. The flask was charged under nitrogen with 1.4 ml (10 mmol) of diisopropylamine and 10 ml of dry THF, and then cooled to 0°. Butyllithium (10 mmol, 6.7 ml of a 1.5M solution in ether) was added to form the lithium diisopropylamide. After stirring for 15 min. at 0°, 760 mg (5 mmol) of phenoxyacetic acid in 3 ml of dry THF was added. The reaction mixture was stirred for 2 h at 0° to complete the formation of the dianion of phenoxyacetic acid. Tributylborane (3.25 mmol, 2.5 ml of a 1.3M solution in THF) was added and the reaction mixture was refluxed under stirring for 2 h. To the reaction mixture was then added 5 ml of 3N-NaOH, followed by dropwise addition of 5 ml of 30% hydrogen peroxide at 0°. The reaction mixture was stirred for 2 h at 0° and 30 ml of ether was added. The separated aqueous layer was acidified with 3N-HCl, saturated with sodium chloride and extracted three times with 30 ml of ether. The analysis of organic layer by GLC showed that the expected hexanoic acid had formed in quantitative yield.

Recently, Zweifel and Backlund[11] have reported a synthesis of monosubstituted acetic acids via silylation, hydroboration, and oxidation of the ethynyl group of 1-alkynes (eq. 6). However, the alkyl groups of organoboranes are not used as alkyl sources in monosubstituted acetic acids. Consequently, the present reaction provides for the first time a direct route



(6)

to the synthesis of carboxylic acids by using organoboranes.

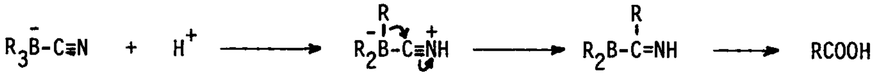
Table 1. The Synthesis of Carboxylic Acids *via* the Reaction of Organoboranes with the Dianion of Phenoxyacetic Acid[a]

Organoborane R_3B or B-R-9-BBN	Product[b]	Reaction time at 66°, h	Yield (%)[c]
Tripropyl	Pentanoic acid	2	81
Tributyl	Hexanoic acid	2	100
Triisobutyl	4-Methylpentanoic acid	4	67
Tri-*sec*-butyl	3-Methylpentanoic acid	6	17
B-*sec*-butyl	3-Methylpentanoic acid	6	39
Trihexyl	Octanoic acid	2	77
Tricyclopentyl	2-Cyclopentylacetic acid	6	97
B-cyclohexyl	2-Cyclohexylacetic acid	6	36
Tri(2-phenylpropyl)	4-Phenylpentanoic acid	6	65
B-4-hexenyl	6-Octenoic acid	6	93
Trioctyl	Decanoic acid	4	90
B-2-(3-cyclohexenyl)ethyl	4-(3-Cyclohexenyl)butanoic acid	6	60

[a] A 50% excess of the dianion was used. [b] Satisfactory IR and ^{1}H-NMR was obtained for all compounds. [c] Yield by GLC analysis based on the organoborane used.

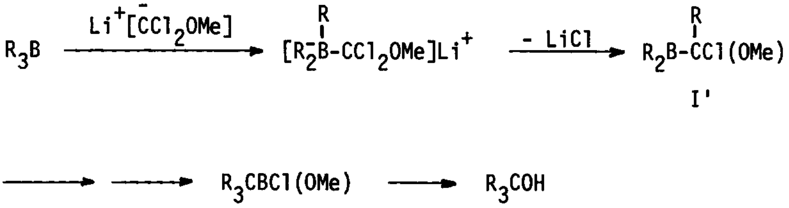
References and Notes

1. H. C. Brown, "Organic Syntheses *via* Organoboranes", John Wiley, New York, 1975.
2. For recent reviews, see (a) G. W. Kabalka, J. D. Baker, and G. W. Neal, *J. Chem. Educ.*, **53**, 549 (1976). (b) E. Negishi, *J. Organometal. Chem.*, **108**, 281 (1976). (c) J. Weill-Raynal, *Synthesis*, 633 (1976).
3. In 1970, we examined the reaction of cyanotrialkylborates with Brønsted acid in an attempt to synthesize carboxylic acids as shown in the following reaction route.[4] However, the expected products were not obtained, and it was found that treatment of the cyanoborates



$$R_3\overset{-}{B}-C\equiv N + H^+ \longrightarrow R_2\overset{R}{\overset{-}{B}}-C\equiv\overset{+}{N}H \longrightarrow R_2B-\overset{R}{C}=NH \longrightarrow RCOOH$$

with suitable electrophiles such as benzoyl chloride gives corresponding ketones, as reported by Pelter and his co-workers.[4,5]
4. A. Suzuki, N. Miyaura, and M. Itoh, *Abstracts of the Fall Annual Meeting 1970 of the* Chemical Society of Japan, p.153 (1970).
5. A. Pelter, M. G. Hutchings, and K. Smith, *J. C. S. Chem. Commun.*, 1529 (1970); 1048 (1971); *J. C. S. Perkin I*, 129 (1975).
6. Organoboranes undergo a facile reaction with 1,1-dichloromethyl methyl ether in the presence of strong bases. Assuming the carbanion, the reaction may be considered to proceed through the following reaction paths. If the monoalkyl group migration from boron to carbon is predominant, the resultant intermediate (I') should give the corresponding



$$R_3B \xrightarrow{Li^+[\overset{-}{C}Cl_2OMe]} [R_2\overset{R}{\overset{-}{B}}-CCl_2OMe]Li^+ \xrightarrow{-\,LiCl} R_2B-\overset{R}{C}Cl(OMe)$$

I'

$$\longrightarrow \longrightarrow R_3CBCl(OMe) \longrightarrow R_3COH$$

acid by alkaline hydrogen peroxide oxidation. However, the migration of three alkyl groups to carbon occurs mainly to give corresponding trialkylmethanol, as reported by Brown and Carlson. H. C. Brown and B. A. Carlson, *J. Org. Chem.*, **38**, 2422 (1973).
7. H. Gross, J. Rusche, and M. Mirsch, *Chem. Ber.*, **96**, 1382 (1963).
8. M. Ishidoya, T. Kawaguchi, and A. Suzuki, *Abstracts of the 34th Annual Meeting of the Chemical Society of Japan, Part II*, p.817 (1976).
9. P. E. Pfeffer, E. Kinsel, and L. S. Silbert, *J. Org. Chem.*, **37**, 1256 (1972).
10. A. P. Krapcho and E. G. E. Jahngen, Jr., *J. Org. Chem.*, **39**, 1322, 1650 (1974).
11. G. Zweifel and S. J. Backlund, *J. Am. Chem. Soc.*, **99**, 3184 (1977).