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A NOVEL SYNTHESIS OF SYMMETRIC KETONES BY THE REACTION OF ORGANOBORANES WITH CATECHOL DICHLOROMETHYLENE ETHER IN THE PRESENCE OF METHYLLITHIUM

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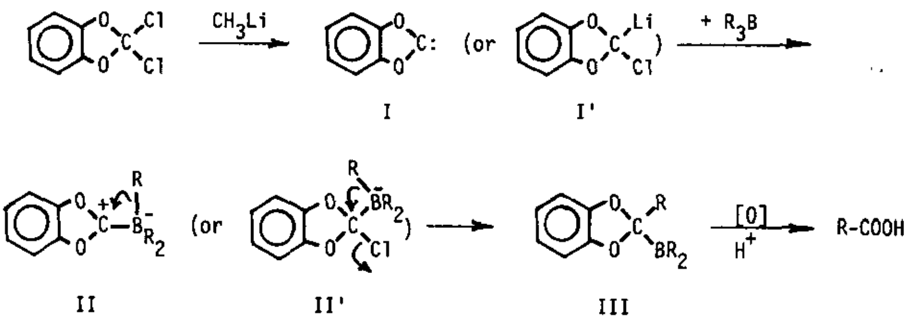
Abstract — Organoboranes readily available from alkenes via hydroboration react with catechol dichloromethylene ether in the presence of methyllithium followed by the usual alkaline hydrogen peroxide oxidation to give corresponding symmetric ketones in good yields.

Organoboranes have been recently recognized to have a high versatility for the synthesis of organic compounds with various functional groups. However, until most recently, there have been no successful reports on the direct synthesis of carboxylic acids from organoboranes.[1] Since 1967, we have made continuous efforts to find such a conversion. In the course of the study, we examined the reaction with catechol dichloromethylene ether[2] under basic conditions, in the expectation that organoboranes may react with the carbene (I) [or carbenoid (I')] formed from catechol dichloromethylene ether to yield the intermediates II or II', which are then converted to the boron derivatives (III). Finally the organoboranes (III) are changed to the corresponding carboxylic acids by the alkaline hydrogen peroxide oxidation and acidification (Scheme 1). The actually obtained products, however, were not the expected carboxylic acids, and we found that symmetric ketones were



Scheme 1

formed in good yields, the results of which are reported here.

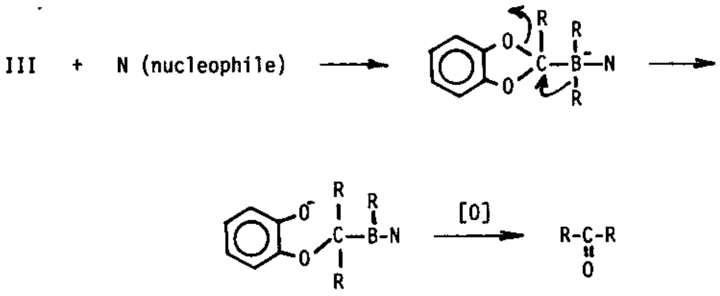
The following procedure for the preparation of 4-heptanone from tripropylborane is representative. A dry 50 ml round-bottomed flask equipped with a condenser, a septum inlet and a magnetic stirring bar was flushed with nitrogen. In the flask was placed tripropylborane (5 mmol, 2.5 ml of a 2M solution in THF) and 1.15 g (6 mmol) of catechol dichloromethylene ether (prepared from catechol carbonate by the method of Gross[2]) in nitrogen gas atmosphere. Then methyllithium (7.5 mmol, 3.8 ml of a 1.95M solution in ether) was added dropwise at 0°C under stirring. The mixture was stirred for 1 h at room temperature. After the reaction was complete, the mixture was oxidized with 3M aqueous hydroxide (4 ml) and 30% hydrogen peroxide (4 ml) at room temperature. The product thus obtained was extracted three times with ether and the combined organic layer was dried over magnesium sulfate. VPC analysis (10% SE-30, 1 m) indicated that 4.75 mmol (95%, based on tripropylborane) of 4-heptanone had been obtained. An analytically pure material was obtained by preparative VPC by using Varian Autoprep Model-2800. The representative results are summarized in Table 1.

Table 1. Synthesis of Symmetric Ketones

Organoborane R_3B, R=	Product[a]	Yield,[b] %	n_D^{20}
Ethyl	3-Pentanone	100	1.3910
Propyl	4-Heptanone	95	1.4090
Butyl	5-Nonanone	94	1.4221
Isobutyl	2,6-Dimethyl-4-heptanone	80	1.4132
Cyclopentyl	Dicyclopentyl ketone	76[c]	1.4787

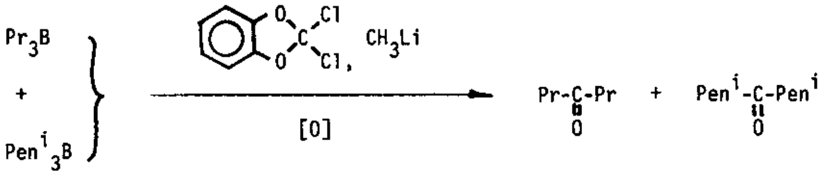
[a] The products were adequately characterized by IR, NMR and mass spectroscopy, and by elemental analysis. [b] Based on the organoborane used, and determined by VPC. [c] Reaction time, 2 h.

The reaction mechanism, although it was not explored in detail, could be considered to involve the following pathway (Scheme 2). In order to eliminate the intermolecular mechanism of the present reaction, we attempted a crossover experiment by using a mixture of tripropylborane and triisobutyl-

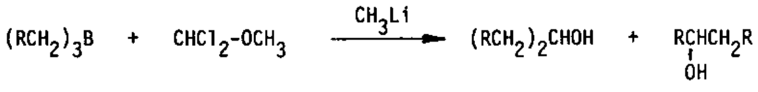


Scheme 2

borane, and found that only two ketones, 4-heptanone and 2,6-dimethyl-4-heptanone, are isolated, both of them symmetrically substituted. The nonformation of the unsymmetric ketone (2-methyl-4-heptanone) provides strong evidence that the reaction is intramolecular.



There have been many interesting reports on organic syntheses via the reactions of organoboranes with carbenes, carbenoids and related chemical species.[3] Among them, the reactions with dichloromethyl methyl ether under basic conditions were reported. Organoboranes react with dichloromethyl methyl ether in the presence of methyllithium to give dialkylmethanols (IV) and (V),[4] whereas the reaction of organoboranes with the same substrate in the presence of lithium 1,1-diethyl-1-propanolate yields, after oxidation, the corresponding trialkylmethanols.[5] On the other hand, the



$$(RCH_2)_3B + CHCl_2\text{-}OCH_3 \xrightarrow{CH_3Li} (RCH_2)_2CHOH + \underset{OH}{RCHCH_2R}$$

IV V

$$R_3B + CHCl_2\text{-}OCH_3 \xrightarrow{LiOCEt_3} R_3C\text{-}OH$$

present reaction provides a convenient synthetic procedure of symmetric ketones. In addition to that, it was noted that under basic conditions, O-C bonds, especially phenoxylic O-C bonds, the carbons of which combine with boron atoms, were readily cleaved. Based on such results, we found that the dianion derived from phenoxyacetic acid and lithium diisopropylamide, reacts smoothly with organoboranes, followed by acidification to give corresponding carboxylic acids in excellent yields.[1]

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