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A NEW SYNTHETIC METHOD FOR 1-METHOXY-2-ALKANONES FROM 1,2-DIMETHOXYETHENYLLITHIUM AND ORGANOBORANES

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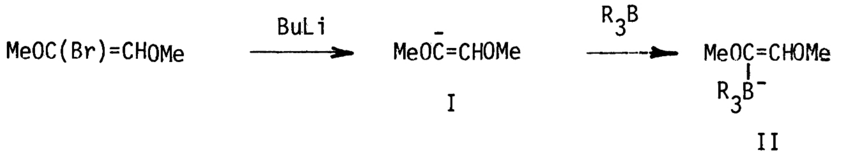
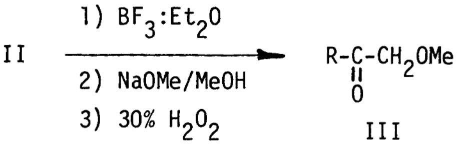
1-Methoxy-2-alkanones are prepared from ate-complexes formed from 1,2-dimethoxyethenyllithium and trialkylboranes by the reaction with BF_3:Et_2O, followed by basic hydrogen peroxide oxidation.

Recently we have reported that 1,1-dialkylethenes and unsymmetric ketones are obtaied by the reaction of ate-complexes of 1,2-dimethoxyethenyllithium[1] and trialkylboranes with electrophiles, proton or alkyl cations respectively.[2,3] In this communication, we wish to report as a subsequent investigation on the reaction of the borate complexes with BF_3:Et_2O, sodium methoxide and hydrogen peroxide, which provides a new synthesis of 1-methoxy-2-alkanones (eqs. 1 and 2).



$$\mathrm{MeOC(Br){=}CHOMe} \xrightarrow{\mathrm{BuLi}} \underset{\mathrm{I}}{\mathrm{MeO\overset{-}{C}{=}CHOMe}} \xrightarrow{R_3B} \underset{\mathrm{II}}{\mathrm{MeO}\underset{R_3B^-}{\mathrm{C}}\mathrm{{=}CHOMe}} \qquad (1)$$



$$\mathrm{II} \xrightarrow[\substack{2)\ \mathrm{NaOMe/MeOH} \\ 3)\ 30\%\ H_2O_2}]{1)\ BF_3:Et_2O} \underset{\mathrm{III}}{\mathrm{R{-}\underset{\underset{O}{\|}}{C}{-}CH_2OMe}} \qquad (2)$$

First we tried oxidation of the borate (II) (R=Bu) with aqueous sodium hydroxide and hydrogen peroxide under the usual oxidation conditions, and obtained 1-methoxy-2-hexanone in a 49% yield. During the study, we found that the α-methoxy group in the borate (II) is reluctant to be eliminated under these conditions. Therefore, we treated II with BF_3:Et_2O in expectation to promote the elimination. The best yield of 1-methoxy-2-hexanone was obtained by sequential treatments with BF_3:Et_2O and sodium methoxide in methanol.

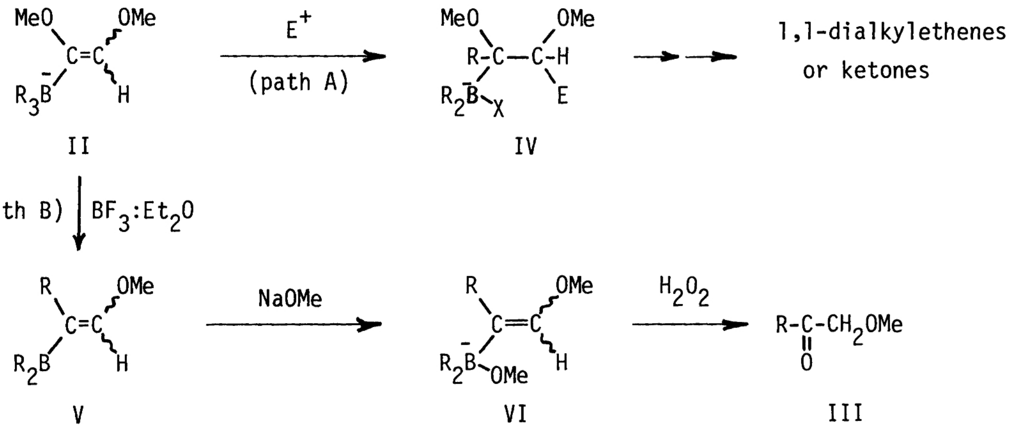
The following procedure is typical. To a solution of 1,2-dimethoxyethenyllithium,[2] prepared from 1-bromo-1,2-dimethoxyethene (342 mg, 2.05 mmol) and butyllithium (1.02 mL of a 2.01 M solution in ether) in 6 mL of ether, tributylborane (1.23 mL of a 1.39 M solution in THF, 1.71 mmol) was added at -78 C and stirred for 10 min. Then, BF_3:Et_2O (0.26 mL, 2.05 mmol) was added and the reaction mixture was warmed to 0 °C, and then stirred for 1 h. Sodium methoxide in methanol (1.3 mL, 6.15 mmol) was added to the resulting solution, followed by oxidation with 30% hydrogen peroxide. After stirring at room temperature for 2 h, the glpc analysis of the organic layer showed that 1.33 mmol of 1-methoxy-2-hexanone had formed in a yield of 65%. The representative results are shown in Tab. 1.

Although the mechanistic investigation of the reaction was not undertaken, the reaction may be considered to proceed through the following reaction path. In the syntheses of 1,1-dialkylethenes[2] and ketones,[3] the initial formation of IV was rationalized by the attack of electrophiles on II with concurrent migration of alkyl group from boron to carbon, as depicted in Scheme (path A). It has already been reported that complete elimination of the α-methoxy moiety in such a vinylborate is difficult.[4] The addition of $BF_3:Et_2O$ to II may cause elimination of the α-methoxy group to give the intermediate (V) (path B), and the sequential oxidation of the B-C bond in V may form the expected product (III). However, we could not obtain satisfactory results by the usual aqueous sodium hydroxide-hydrogen peroxide oxidation, because the boron trifluoride seems to be partly decomposed in such an aqueous solution to boric acid and hydrogen fluoride, which lead to side reactions of II.[5] Utilization of sodium methoxide in methanol free from water was found to be very effective for the preparation of 1-methoxy-2-alkanones.

Table 1. Synthesis of 1-Methoxy-2-alkanones

Organoborane R_3B, R=	Yield of 1-methoxy-2-alkanones $RCOCH_2OCH_3$, (%)[a]
Butyl	65
Isobutyl	67
sec-Butyl	47
Pentyl	62
Cyclopentyl	61
Hexyl	60

a) Glpc yield based on the organoborane used.



References

1) C. N. Skold, Synth. Commun., 6, 119 (1976).
2) T. Yogo and A. Suzuki, Chem. Lett., 1980, 591.
3) T. Yogo, J. Koshino, and A. Suzuki, Chem. Lett., 1981, 1059.
4) N. Miyaura, T. Yoshinari, M. Itoh, and A. Suzuki, Tetrahedron Lett., 21, 537 (1980).
5) Under the usual oxidation conditions with aqueous hydroxide and 30% hydrogen peroxide, II (R=Bu) gave dibutyl(methoxymethyl)methanol as a by-product together with the expected methoxyketone.

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