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A NEW APPROACH FOR THE SYNTHESIS OF PARTIALLY MIXED TRIALKYLCARBINOLS VIA THE REACTION OF DIALKYLCHLOROBORANES WITH LITHIUM ALDIMINES

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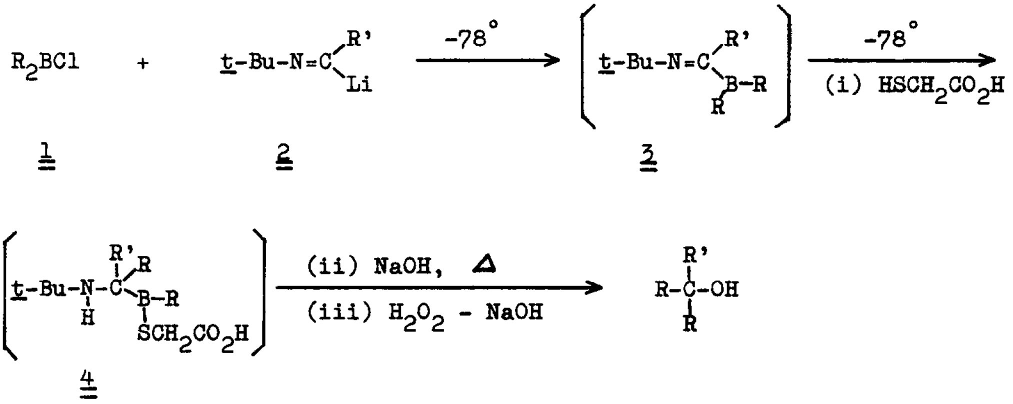
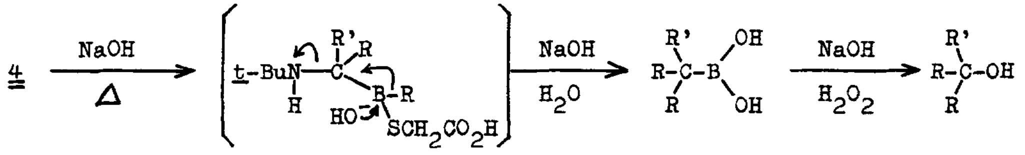
We wish to report a new approach for the synthesis of partially mixed trialkylcarbinols from dialkylchloroboranes and Walborsky's masked acyl carbanions[1] (eq 1).



(1)

We previously reported that dialkylchloroboranes (**1**), now readily available *via* hydroboration with chloroborane-ethyletherate,[2] reacted with lithium aldimines (**2**) to give unsymmetrical ketones on treatment with (i) thioglycolic acid - (ii) aqueous alkaline hydrogen peroxide.[3]

It appeared that the migration of an alkyl group (R) from boron to carbon in the initial intermediate (**3**) was induced by thioglycolic acid, leading to the intermediate borane (**4**). This was supported by the fact that the oxidation of **4** produced the alcohol (ROH) and *t*-butylamine along with the corresponding ketone (RR'C=O) and also by the previous results on the related reactions.[4] If so, partially mixed trialkylcarbinols may be obtained by achieving the migration of the second alkyl group (R) from boron to carbon in the intermediate (4). Accordingly, we undertook to examine this possibility. After tring several reactions, we found that heating 4 at 80° in diglyme containing aquous NaOH permitted the desired migration to produce the trialkylcarbinylborane derivatives. The alkaline hydrogen peroxide oxidation gave the partially mixed carbinols in good yields (eq 2).



(2)

The results are summarized in Table I. There appears no difficulty in introducing a primary and secondary alkyl groups containing a functional substituent. It is known that partially mixed trialkylcarbinols are obtained by treatment of partially mixed trialkylboranes with carbon monoxide,[5] or by treatment of trialkylboranes with 1-lithio-1,1-bis(phenylthio)alkane.[6] The present procedure offers the following advantages over the previous methods;[5,6] (i) the accommodation of the alkyl group such as *iso*-propyl or methyl, which can not be introduced *via* the hydroboration method,[5] (ii) utilization of the all three alkyl groups without loss of an alkyl group of the boranes.[6,7]

The following procedure for the synthesis of 7-*iso*-propyl-7-tridecanol is representative. In a 200-ml flask maintained under N_2 and fitted with a septum inlet, magnetic stirrer, and reflux condenser were placed *t*-butylisonitrile (3.6 ml, 30 mmol) and dry ether (60 ml). The solution was cooled to 0° and a pentane solution of *iso*-propyllithium (1.2 M, 30 mmol) was added dropwise. The mixture was stirred for 30 min at 0°, and then cooled to - 78° with a dry-ice acetone bath. Di-*n*-hexylchloroborane (7.7 ml, 30 mmol), prepared according to the described procedure,[2] was added, and the resultant mixture was kept at - 78° for 30 min. Thioglycolic acid (4.2 ml, 60 mmol)

Table I. Partially Mixed Trialkylcarbinols _via_ the Reaction of **1** with **2**.[a]

Dialkylchloroborane (R_2BCl)	Alkyllithium (R'Li)	Product[b]	Yield[c], % (isoln)
_n_-Hexyl	_n_-Butyl	7-_n_-Butyl-7-tridecanol	87
_n_-Hexyl	_iso_-Propyl	7-_iso_-Propyl-7-tridecanol	(75)
_n_-Hexyl	Methyl	7-Methyl-7-tridecanol	(45)[d]
Cyclopentyl	_iso_-Propyl	1,1-Dicyclopentyl-2-methyl-1-propanol	77
_n_-Butyl	4-_n_-Pentenyl	5-_n_-Butyl-9-decen-5-ol	(46)[d]

[a] Stoichiometric amounts of **1**, alkyllithium, and _t_-butylisonitrile were utilized. [b] Satisfactory nmr, ir, and elemental analysis data were obtained for all compounds. [c] The yields are based on glpc analysis, and not necessarily optimum. [d] The low yield must be due to the unfavorable equilibrium of the lithium aldimine.[1]

was then added, and the reaction was allowed to come to room temperature over 1 hr. The solvent was removed at reduced pressure and replaced with diglyme (60 ml) and 6 N aqueous NaOH (15 ml). The resultant mixture was refluxed for 8 hr (the temperature in the flask was at 80°). Oxidation was accomplished by the addition of 6 N aqueous NaOH (20 ml) - 30 % H_2O_2 (40 ml). Petroleum ether (60 ml) was added, and the organic phase was separated, washed with water, and dried over anhyd. K_2CO_3. 7-_iso_-Propyl-7-tridecanol was obtained by distillation under reduced pressure: 5.41 g, 75 % yield, b. p. 94 - 95°(0.2 mm), n_D^{20}1.4517.

Consequently, the present reaction provides a facile procedure for the synthesis of partially mixed trialkylcarbinols, and can even be extended to the accommodation of a functional group.[8] The reaction of Grignard reagents with ketones or esters also produces trialkylcarbinols, though such reaction is complicated in the case of sterically bulky alkyl groups and has a low functional group tolerance.[9]

References

1) G. E. Niznik, W. H. Morrison, III, and H. M. Walborsky, J. Org. Chem., 39, 600 (1974).

2) H. C. Brown and N. Ravindran, J. Amer. Chem. Soc., 94, 2112 (1972); for a reading reference, see Y. Yamamoto, J. Synth. Org. Chem. Jap., 32, 544(1974).

3) Y. Yamamoto, K. Kondo, and I. Moritani, Tetrahedron Lett., 793 (1974).

4) J. Casanova, Jr., in "Isonitrile Chemistry," I. Ugi, Ed., Academic, New York, N. Y., 1971, p. 109; the previous results indicate that the boranes similar to 3 undergo dimerization. However, in the present case, low temperature used probably suppresses such dimerization.

5) H. C. Brown, E. Negishi, and S. K. Gupta, J. Amer. Chem. Soc., 92, 6648 (1970); H. C. Brown and S. K. Gupta, ibid., 93, 1818 (1971); ibid., 93, 4062 (1971).

6) R. J. Hughes, A. Pelter, and K. Smith, Chem. Commun., 863 (1974).

7) Utilization of thexyldioctylborane overcomes this difficulty.[6] However, thexylboranes containing bulky alkyl groups are relatively labile.

8) Symmetrical trialkylcarbinols are produced from the reaction of trialkylboranes with CO, NaCN, or α,α-dichloromethyl methyl ether (DCME).[9a] On the other hand, totally mixed carbinols are available via the reaction of totally mixed hindered boranes with DCME,[9a] or via dialkylmethylvinylboronates (G. Zweifel and R. P. Fisher, Synthesis, 339 (1974)). However, it seems to us that the presently available methods for the synthesis of totally mixed carbinols are indeed the best way to specific compounds, but lack overall generality.

9) (a) H. C. Brown, "Organic Synthesis via Boranes," Wiley, New York, N. Y., 1975; (b) H. C. Brown, "Boranes in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1972, p. 351; (c) M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Non-Metallic Substances," Constable, London, 1954.