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BORANE REACTIONS XI[1]: THE TRANSFORMATION OF α,β-UNSATURATED KETONES INTO 3-ALKYL-TRANS-1,2-DIOLS.

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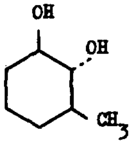
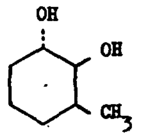
Conjugate addition of alkylmagnesium derivatives[2,3] uncatalyzed or catalyzed by cuprous salts, and that of dialkylcopper lithium[4,5] to conjugated ketones, leads to 3-alkylketones. Introduction of an acetoxy group α to the carbonyl in isophorone by conjugate addition of methylmagnesium bromide and subsequent $Pb(OAc)_4$ oxidation has been reported[6]. We wish to report a synthetic method that gives directly 3-alkyl-cyclohexane-trans-1,2-diols starting from 2-cyclohexenones.

Addition of 2-cyclohexenone to dimethylcopper lithium[5] (100% excess) in ether at -10° during 15 min. and decomposition of the reaction mixture with dilute HCl at -10° gave 3-methylcyclohexanone in 80% yield. This reaction mixture was treated, before acidification, with a solution of borane in THF (3 moles per mole ketone) for 3 hours at room temperature. After subsequent oxidation with alkaline H_2O_2[7] a 55% yield of a mixture of two diols[8] I and II in an 87:13 ratio (GLC) was obtained. A mixture (22%) of 2- and 3-methylcyclohexanols was also found. Before oxidation the hydroboration product was separated using a syringe from the black precipitate containing copper. Otherwise the yield of diols was substantially lowered.



I



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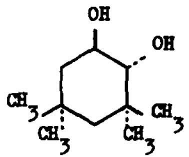

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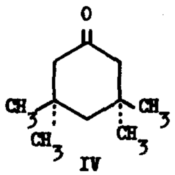


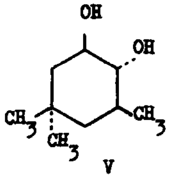
IV

Similar results were obtained by conjugate addition of 1.5 mole equiv. of methylmagnesium bromide, catalyzed by cuprous chloride, and subsequent hydroboration-oxidation. The ratio of I:II was almost identical with that above, but the yield was only 45%.

Cuprous catalyzed addition of methylmagnesium bromide to isophorone and subsequent hydroboration for 2 hours gave 3,3,5,5-tetramethylmethylcyclohexanone (IV) as the almost exclusive product. Therefore, borane attacks this enolate very slowly, probably for steric reasons. In fact, the expected diol III (35%) was obtained after hydroboration for 2 days at room temperature. The same procedure using dimethylcopper lithium and hydroboration for 2 days gave III in 53% yield (m.p. 78-80° from ethyl acetate-hexane).[9] The diol III was characterized as its diacetate, m.p. 65-69° (purified by GLC); NMR ($CDCl_3$) δ (Hz):- 5.0/t x d (J_1 = 10, J_2 = 4) 1H; 4.7/d (J = 10) 1H; 2.1/s, 3H; 2.0/s, 3H; 1.7/m, 2H; 1.3/s, 2H; 1.08/s, 3H; 1.03/s, 3H; 0.80/s, 3H; 0.73/s 3H.

The multiplicity of the hydrogens α to the OH groups at 5.0 and 4.7 ppm establish the trans-diequatorial stereochemistry of the diacetate of III. The same diol and diacetate were obtained by the previously reported method of hydroboration of enolates$^{1)}$. The enolate of IV, prepared using sodium hydride$^{10)}$, was hydroborated for 2 days and yielded 55% of III, characterized as its diacetate.

The sequence of reactions with dimethylcopper lithium, borane (2 days) and oxidation was applied also to 3,3-dimethylcyclohex-2-enone yielding 40% of the diols$^{8)}$ V and VI in a 55:45 ratio and 25% of trimethylcyclohexanols.



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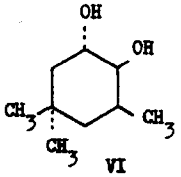

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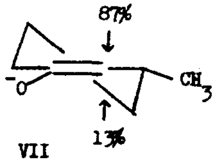
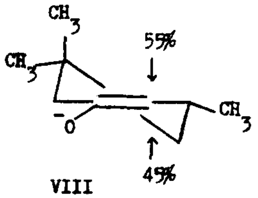


VII



VIII

Poor yields (15%) of diols were obtained from mesityl oxide by this sequence. This is the result of the facile elimination occurring during hydroboration of acyclic conjugated ketones$^{8)}$.

All the diols obtained have the two hydroxyls in a 1,2-position and in a trans-configuration like the diols obtained on hydroboration of enolates$^{1)}$. Their configuration relative to the 3-methyl is not fixed and is probably determined by steric effects. Thus, the ratio of I:II shows that attack on the enolate VII by borane is favored trans to the methyl. This effect is weakened by the two methyls in the 5 position in VIII, where the axial one interferes with borane attack trans to the 3-methyl$^{11)}$.

References.

1) Borane Reactions X. J. Klein, R. Levene and E. Dunkelblum, Tetrahedron Letters, 2845 (1972).

2) E. P. Kohler, Am. Chem. J., 31, 642 (1904).

3) R. C. Fuson, Adv. Organomet. Chem., Vol. 1, R. West and F. G. A. Stone Eds., Academic Press, New York 1964.

4) H. Gilman and J. M. Straley, Recl. Trav. Chim. Pays-Bas, 55, 821 (1936).

5) H. O. House, W. L. Respess and G. M. Whitesides, J. Org. Chem., 31, 3128 (1966).

6) J. W. Ellis, Chem. Comm., 406 (1970).

7) G. Zweifel and H. C. Brown, Org. Reactions, 13, 1 (1963).

8) J. Klein and E. Dunkelblum, Tetrahedron, 24, 5701 (1968).

9) G. W. K. Cavill and D. H. Solomon, Aust. J. Chem., 15, 764 (1962). The stereochemistry of the diol in this reference was not determined.

10) G. Stork and P. F. Hudrlik, J. Amer. Chem. Soc., 90, 4462 (1968).

11) J. Klein, E. Dunkelblum and D. Avrahami, J. Org. Chem., 32, 935 (1967).