Tetrahedron Letters No. 44, pp 3867 - 3870, 1975. Pergamon Press. Printed in Great Britain.

STEREOSELECTIVITY IN THE HYDROBORATION OF HINDERED CYCLOHEXENES

M. H. Gordon and M.J.T. Robinson*

Dyson Perrins Laboratory, University of Oxford

(Received in UK 3 September 1975; accepted for publication 22 September 1975)

Hydroboration of a trialkylethylene is well established as a cis anti-Markovnikov addition to the double bond.[1] In norbornene and related olefins hydroboration is sensitive to the balance of steric hindrance to the two faces of the double bond[2] but little is known about systems in which steric hindrance to one face of a double bond might force addition to lead to the less stable of the possible diastereomeric products. In 1-alkylcyclohexenes and related olefins, e.g. $\Delta^{1(9)}$-octalins, the most stable diasteromeric product that can result from cis-addition is commonly the predominant or sole identified product. We have recently prepared a variety of tri- and tetra-alkylcyclohexenes, mainly by dehydrating corresponding tertiary alcohols followed by preparative g.l.c. separation of the resulting mixtures of olefins.[3] As a routine check on the position of the double bonds we converted the separated olefins via hydroboration and oxidation into secondary alcohols and observed striking substituent effects on the stereoselectivity of the addition of borane (Fig. 1). Since the addition of a second molecule of a 1-alkylcyclohexene to borane is relatively slow and borane (in tetrahydrofuran) was used in large excess we believe that the selectivity is associated with addition of borane rather than (in part) of an alkylborane to these olefins and that if mono- or di-alkylboranes were used even greater and synthetically useful selectivity leading to the formation of strained cyclohexanols might be realised.

The configurations of the products in each instance were determined from the vicinal couplings between the C-1 hydrogen, absorbing at low field in the ^{1}H NMR spectrum, and the hydrogen atoms at C-2 and C-6. When mixtures of two alcohols were obtained the low field NMR absorptions were well separated, the differences in chemical shifts being qualitatively consistent with structures derived from the coupling constants (Fig. 1), and therefore convenient for integration (± 5%).

The cis-trialkylcyclohexenes 1-3 gave the all-equatorial cyclohexanols 9 or 10 exclusively. The alternative products 15-17 are presumably considerably less stable, having two axial substituents in their less

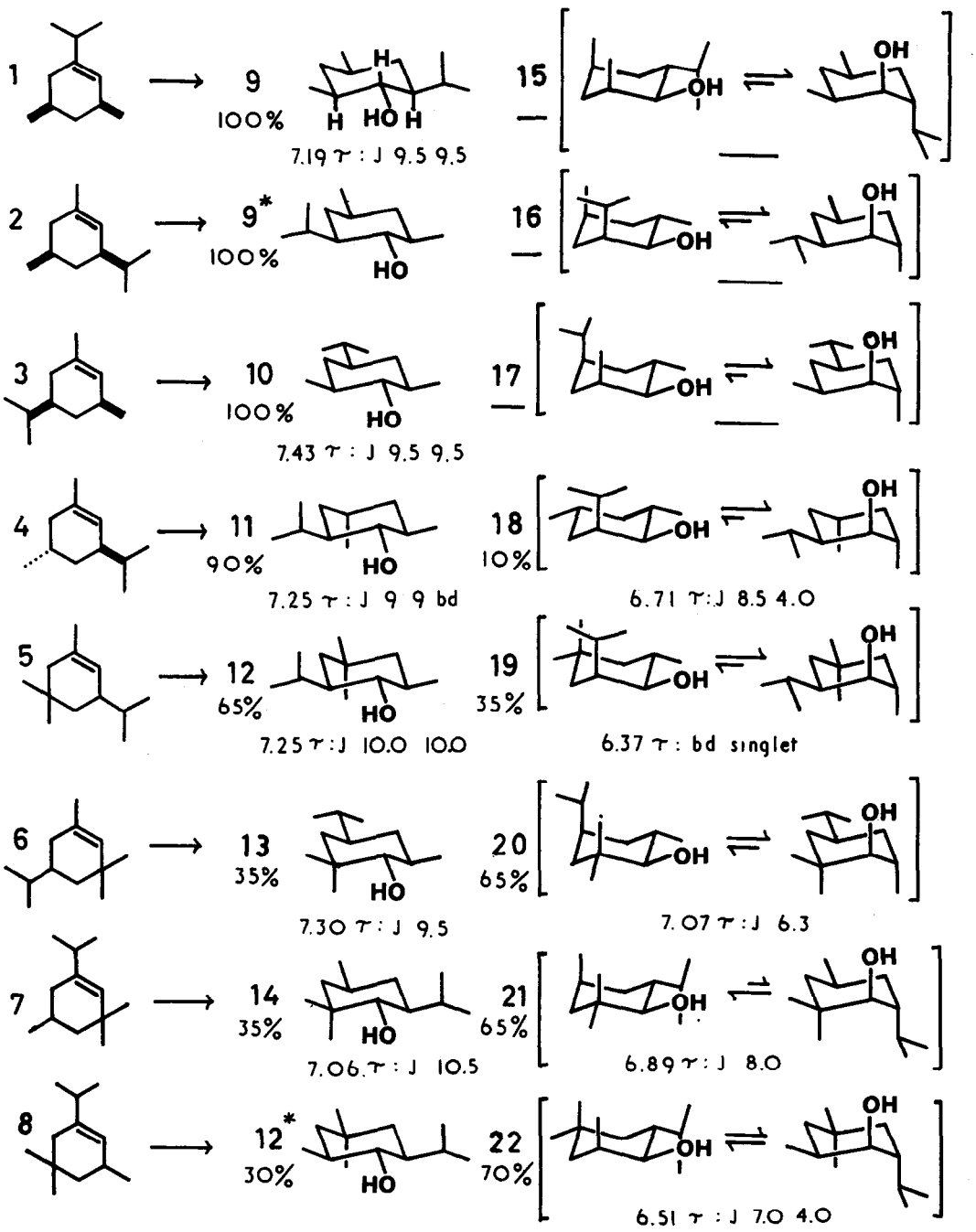

Figure 1. Hydroboration-oxidation of tri- and tetra-alkylcyclohexenes 1-8: the more stable products 9-14 have one strongly preferred chair conformer as shown, while the less stable products 15-22 have two highly strained conformers (see notes 5-7).

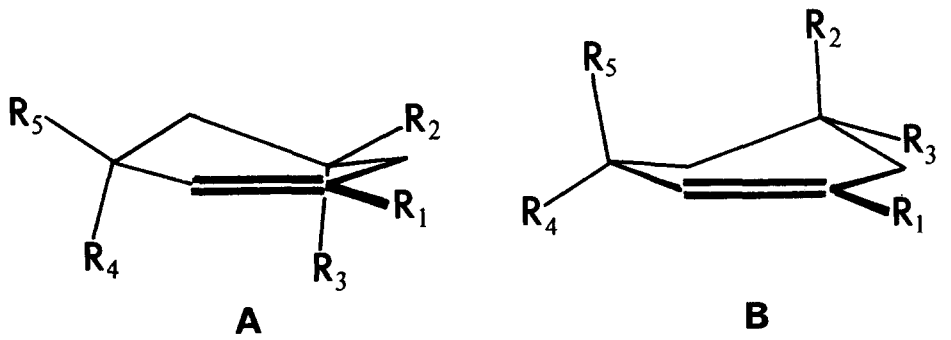

Figure 2. Half-chair conformers of the olefins 1-8. When R_3 or R_4 (or both) is hydrogen and R_2 and R_5 are alkyl groups (1-3 and 5-8) conformer A is far more stable than B. In 4 the two conformers are of comparable stability and borane probably adds mainly to the unhindered face of the double bond, trans to the (pseudo) axial 3-isopropyl group in B.

strained chair conformers. In contrast the olefins 6-8 give predominantly the less stable products 20-22, even though these all have syn-1,3-diaxial alkyl interactions in chair conformers and must be several kcal mol^{-1} less stable than 13, 14, and 12 respectively. Olefins 4 and 5, too, give substantial amounts of the less stable possible products 18 and 19. Clearly the steric strains in the products 19-22 are not reflected in the transition complexes which must more nearly resemble the original olefins sterically.

The olefins 1-3 and 5-8 each have one very strongly preferred half-chair conformation (see Fig. 2), whereas 4 has two conformations of comparable stability. Comparing the additions to 6 and 7 shows that the size of the 1-alkyl group (R_1) is not important, assuming that the equatorial 5-alkyl group (R_2) is too remote to have any direct effect. The results for the pairs 2 and 5 or 1 and 8 show that an axial 5-methyl group (R_3) strongly hinders addition from the lower face of the double bond as drawn so that attack from the upper face becomes important. An axial 3-methyl group (R_4: compare pairs 1 and 7 or 3 and 6) is at least as effective as an axial 5-methyl group and this is probably attributable to (partial) eclipsing of the developing C(2)...BH_2 and C(3)—ax-Me bonds and to steric repulsion between these vicinal groups. It is probable, therefore, that the high selectivity shown by 1-3, which give only the more stable possible diastereomers, is due more to the effect of the (pseudo) equatorial group R_5 hindering attack from the upper face of the double bond than to the relative stabilities of the products being reflected in the transition complexes. At present

it is not possible to draw any conclusion as to whether the strained products 18-22 result from additions via chair-like or twist-like transition complexes.

We thank the Science Research Council for a C.A.P.S. Studentship (to M.H.G.).

REFERENCES AND NOTES

1 H. C. Brown, Synthesis via Boranes, Wiley-Interscience, New York, 1975, p.6.

2 H. C. Brown and Kwang-Ting Liu, J.Am.Chem.Soc. 93, 7335 (1971).

3 M. H. Gordon, R. G. Peck and M.J.T. Robinson, in preparation.

4 The chemical shifts (δ, ± 0.02 p.p.m., relative to TMS for ~5% solutions of mixtures in CCl_4) and vicinal coupling constants (J, mostly ± 0.5 Hz except for multiplets, marked bd, that are seriously broadened by long range and virtual coupling) for the carbinyl protons in the cyclohexanols detected are given beneath the formulae. The relevant protons are given explicitly for 2 only.

5 Isopropyl groups that are axial or adjacent to a hydroxyl group are drawn in the most probable rotameric forms, although these still leave severe methyl-hydroxyl interactions for some axial isopropyl groups (see 16, 18 and 19).

6 All compounds are meso or racemic, with one enantiomeric form shown for the latter: 9^* = enantiomer of 9, 12^* = enantiomer of 12.