Tetrahedron Letters,Vol.25,No.13,pp 1393-1396,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

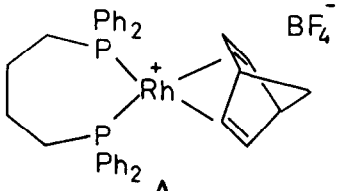
SCOPE AND LIMITATIONS OF THE STEREOSELECTIVE HOMOGENEOUS HYDROGENATION OF METHYLENECYCLOHEXANOLS BY CATIONIC RHODIUM COMPLEXES

By John M. Brown and Stephen A. Hall
(Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, U.K.)

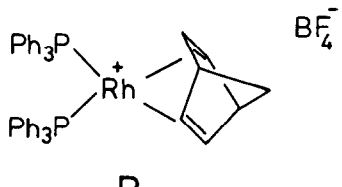
Summary Homogeneous catalytic hydrogenation of 3-methylenecyclohexanol gives trans-3-methylcyclohexanol with 98% stereoselectivity, but low selectivity is observed for 2-methylenecyclohexanol and 2-methylenecyclohexanemethanol.

Homogeneous hydrogenation of chiral acyclic allylic and homoallylic alcohols may be carried out with a high degree of [1,2] or [1,3] asymmetric induction.[1] Success requires both a cationic chelate biphosphine rhodium catalyst and an aprotic solvent, normally dichloromethane or tetrahydrofuran. Our study has now been extended to cyclic unsaturated alcohols, and results obtained are summarised in the Scheme, overleaf.

Reaction of the readily available[2] 2-methylenecyclohexanol (1a) and H_2 in the presence of 2 mol % of catalyst A in thf leads to its isomerisation to 2-methylcyclohexanone (2) in competition with reduction to 2-methylcyclohexanol (3). Isomerisation is largely suppressed by carrying out reduction with the $\bar{B}Ph_4$ salt of A but here addition of hydrogen is very slow. Under a range of conditions the selectivity to cis(3) never exceeeded 65%. The corresponding acetate (1b) was reduced cleanly but unselectively, employing A in thf.

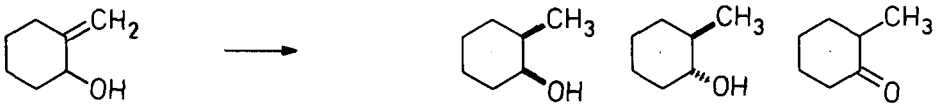


A

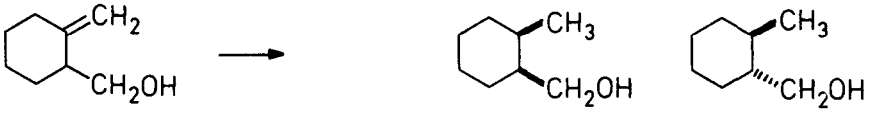


B

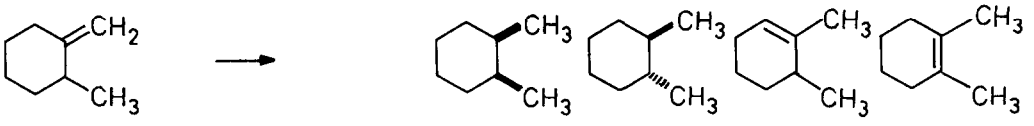
Correspondingly, 2-methylenecyclohexanemethanol[3] (4a) and its acetate (4b) show little selectivity in hydrogenation catalysed by complex A in thf, CH_2Cl_2, or MeOH. The isomer formed in reduction of (4a) is solvent-dependent,[4,5] but the hydroxyl-group nevertheless plays a significant part in determining the course of hydrogenation. This is evidenced by comparison with the reduction of 2-methylmethylenecyclohexane (6) catalysed by complex A. In thf and MeOH, reduction gives mainly 1,2-dimethylcyclohexane (7) as a 2:1 mixture of cis and trans-isomers but accompanied by significant amounts (37% and 12% respectively) of isomerisation product which is almost exclusively 2,3-dimethylcyclohexene (8).[5] In CH_2Cl_2, isomerisation is the dominant reaction course and 1,2-dimethylcyclohexene (9), is formed



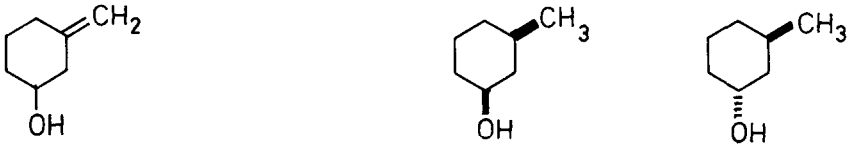
1a		cis-3	trans-3	2
	A CH_2Cl_2	minor	55:45	major
	B CH_2Cl_2	similar		



4a		cis-5	trans-5
	A CH_2Cl_2	53	47
	A thf	60	40
	A MeOH	45	55



6		cis-7	trans 7	8	9
	A CH_2Cl_2	10 [25]	6 [14]	80 [37]	4 [24]
	A thf	38	25	37	< 1
	A MeOH	60	28	12	-



10a		cis-11	trans-11
	A CH_2Cl_2, thf	$\ll 2$	$\gg 98$
	B CH_2Cl_2	9	91
	B thf	19	81

Scheme. Results of hydrogenation reactions. Values recorded in square brackets relate to runs carried out in the absence of mercury (20 μL). In other cases this had no effect on the course of reaction. Standard conditions: 1 atm; 20°; 50:1 substrate: catalyst; $[substrate]_{init} \simeq 0.1$ M.

unless mercury is added to scavenge colloidal rhodium. The competitive isomerisation here, and its absence in reduction of the homoallylic alcohol (4a) intimates that the OH-group of the latter is bound to rhodium during the catalytic cycle of reduction.

A much more clear-cut result was obtained when 3-methylenecyclohexanol (10a) was employed.[6,7] Hydrogenation in CH_2Cl_2 or thf catalysed by complex A gave 98% selectivity to the trans-isomer of 3-methylcyclohexanol (11) accompanied by ca. 5% of an unidentified impurity. Even the triphenylphosphine complex B effected reduction with appreciable stereoselectivity giving 81% and 91% of trans-(11) in thf and CH_2Cl_2 respectively. Like other examples the acetate (10b) was reduced to a near-equal mixture of the cis- and trans- isomers of (11b).

The reduction of homoallylic alcohols (10a) and (4a) may be rationalised if both the olefin and hydroxyl-groups are bound to rhodium at some intermediate stage in the catalytic cycle. In the former case, this leads to a transition-state in which an axial hydroxyl-group controls the delivery of hydrogen from the axial-direction so that the methyl-group in the initially formed product is equatorial (Figure). In the latter case, the stereoelectronically preferred transition-state leads to a product in which both the hydroxymethyl and methyl-groups are axial.

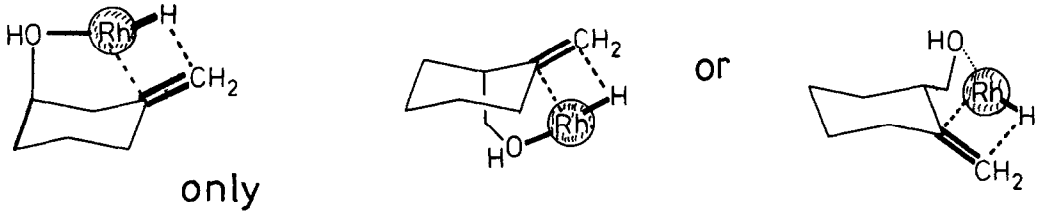


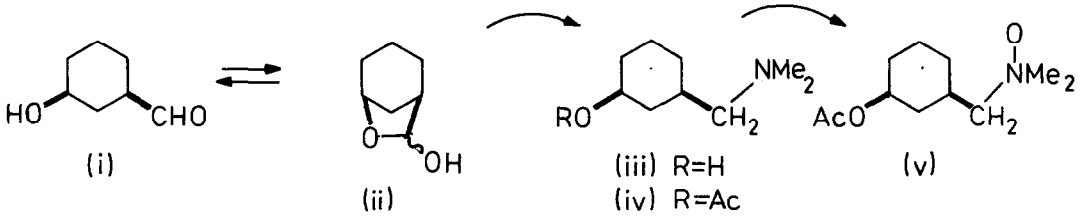
Figure Hydroxyl-group binding to control the stereochemistry of hydrogen delivery.

These results may be compared with the highly selective reductions of endocyclic unsaturated alcohols reported by Crabtree, Stork and their respective co-workers.[8,9] It may be that iridium catalysts perform better in the reduction of hindered double bonds,[10] but that rhodium complexes (which give clean hydrogenation at a reasonable rate when 2 mol % catalyst is employed) are to be preferred for the hydrogenation of exocyclic olefins. The stereoselectivity obtained in reduction of (10a) is comparable to that obtained in reduction of 3-methylcyclohexanone by the most hindered tralkylborohydride reducing agents.[11]

Acknowlegment We thank BP Research and Dr. David J.H. Smith for a CASE studentship (to SAH) and Johnson-Matthey for a generous loan of rhodium trichloride.

References

1. J.M. Brown and R.G. Naik, J. Chem. Soc. Chem. Commun. 1982, 348; H.W. Thompson J. Amer. Chem. Soc., 1974, 96, 6232.
2. A.S. Dreiding and J.A. Hartmann, J. Amer. Chem. Soc., 1953, 75, 939.
3. G. Ohloff, Liebigs Ann. 1959, 627, 79, and references therein.
4. C.f. H.C. Brown, R. Liotta and L. Breuer, J. Amer. Chem. o , 1977, 99, 3427.
5. Products of hydrogenation reactions were identified by preparative GLC (Pye Unicam 105, 15'OV-17, 120°) with direct collection of eluted fractions in $CDCl_3$ at -30° followed by ^1H NMR analysis (Bruker WH 300).
6. J.B. Lambert and R.R. Clikeman J. Amer. Chem. Soc., 1976, 98, 4203.
7. The compound was prepared from endo-4-iodo-6-oxabicyclo[3,2,1]octan-7-one (R. Grewe, A. Heinke and C. Sommer, Chem. Ber. 1956, 89, 1978). Successive treatment with tributyltin hydride (C-I → C-H), and diisobutylaluminium hydride in C_7H_8 at -60° gave cis 3-formylcyclohexanol (i) in equilibrium with the cyclic lactol tautomer (ii) in 58% overall yield. Reductive amination by $NaBH_3CN$ and $(CH_3)_2\overset{+}{N}H_2Cl^-$ gave cis-3-(N,N--dimethylamino)methylcyclohexanol (iii) (63% distilled), which was acetylated with Ac_2O giving (iv) in 78% yield. Oxidation with m-chloroperoxybenzoic acid and thermolysis of neat liquid (v) at 150° gave analytically pure (10b) in 43% yield, hydrolysed to (10a) by 5M KOH.



8. R.H. Crabtree and M.W. Davis, Organometallics, 1983, 2, 681.
9. G. Stork and D.E. Kahne, J. Amer. Chem. Soc., 1983, 105, 1072
10. R. Crabtree, Accounts Chem. Res., 1979, 12, 331.
11. S. Krishnamurthy and H.C. Brown, J. Amer. Chem. Soc., 1976, 98, 338.

(Received in UK 10 January 1984)