Chelate Control in the Rhodium-catalysed Homogeneous Hydrogenation of Chiral Allylic and Homoallylic Alcohols

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Chelate bisphosphine rhodium complexes afford a high degree of stereoselection in the homogeneous hydrogenation of 3-phenylbut-3-en-2-ol and 4-phenylpent-4-en-2-ol, in opposite senses.

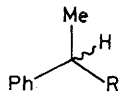
The recent surge of interest in acyclic stereoselection[1] has largely been directed towards the selectivity of carbon–carbon bond forming reactions with comparatively less emphasis on alternative approaches. It has produced remarkable control in (1,2)-asymmetric induction, but comparatively few good examples of (1,3) or more remote[2,3] asymmetric inductions exist. We report that the hydrogenation of allylic and homoallylic alcohols occurs with high stereoselectivity with simple readily available catalysts.

3-Phenylbut-3-en-2-ol (**1**) was prepared by the reaction of 1-phenylethenylmagnesium bromide with acetaldehyde [1-bromo-1-phenylethene, Mg, tetrahydrofuran (THF), −5 °C, MeCHO, 0 °C]. Hydrogenation produced a mixture of (*S**,*S**)-*erythro*- and (*R*,**S**)-*threo*-3-phenylbutan-2-ol (**2**)[4] in which the latter always predominated.[5] With catalysts derived from triphenylphosphine or diphenylpyridylphosphine a 2:1 ratio of components was formed, most likely by a pathway requiring olefin addition to a rhodium dihydride complex.[6] The reactivity of chelate rhodium bisphosphine complexes in catalytic hydrogenation is known to be very dependent on

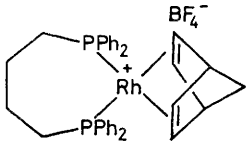
Table 1. Hydrogenation of the alcohols (**1**) and (**4**) with di- or bis-phosphine bicyclo[2.2.1]heptadiene rhodium tetrafluoroborate complexes.

Substrate	Solvent[a]	Procatalyst	$R:S$[b]	% Isomerisation
(**1**)	CH_2Cl_2	PPh_3	65:35	0
(**1**)	CH_2Cl_2	$Ph_2P[CH_2]_4PPh_2$	94: 6	60
(**1**)	CH_2Cl_2	$Ph_2P[CH_2]_4PPh_2$	97: 3[c]	23
(**1**) [1:0.25NEt_3]	CH_2Cl_2	$Ph_2P[CH_2]_4PPh_2$	50:50	44
(**4**)	CH_2Cl_2	PPh_3	38:62	—
(**4**)	MeOH	$Ph_2P[CH_2]_4PPh_2$	67:33	—
(**4**)	CH_2Cl_2	$Ph_2P[CH_2]_4PPh_2$	82:18[d]	—
(**4**)	THF	$Ph_2P[CH_2]_4PPh_2$	88:12[e]	—
(**4**)	CH_2Cl_2	$Ph_2P[CH_2]_5PPh_2$	38:62[f]	—

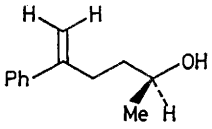
[a] Hydrogenations of substrate (**1**) in methanol were slow and/or unselective. [b] Analysed from the 300 MHz ^1H n.m.r. spectra of products in $CDCl_3$ following catalyst removal on silica: δ [(*R**,*S**)-(**2**)] 1.25 (H-1) and 1.29 (H-4); δ [(*S**,*S**)-(**2**)] 1.13 (H-1) and 1.38 (H-4); δ [(*R**,*S**)-(**5**)] 1.11 (H-1) and 1.19 (H-5); δ [(*S**,*S**)-(**5**)] 1.04 (H-1) and 1.18 (H-5). [c] At 0—2 °C. [d] Ratio of 71:29 in the presence of an equimolar quantity of NEt_3. [e] Unchanged at 0—2 °C. [f] Hydrogenation follows the 'hydride' route *cf.* J. M. Brown, P. A. Chaloner, A. G. Kent, B. A. Murrer, P. N. Nicholson, D. Parker, and P. J. Sidebottom, *J. Organomet. Chem.*, 1981, **216**, 263.



(3) R = C(O)Me
(7) R = $CH_2C(O)Me$
(8) R = CH_2CO_2H



(6)



(9)

the chelate ring-size.[7] Whilst 5-membered chelate ring complexes are unreactive, 7-membered chelate complexes effect reaction (Table 1) with some accompanying isomerisation to 3-phenylbutan-2-one (**3**). In aprotic solvents, but not in methanol, selectivity of up to 30:1 in favour of the *threo*-product may be obtained. This compares with a maximum selectivity of 4.9:1 in the hydride reduction of (**3**).[8]

The homologue 4-phenylpent-4-en-2-ol (**4**) was prepared from 1-phenylethenylcopper (RLi, Et_2O; then CuI, epoxypropane, −80 to 0 °C). This was found to be hydrogenated smoothly and quantitatively to a mixture of (*R**,*S**)-(**5**) and (*R**,*R**)-(**5**) under all conditions tried, the stereochemical outcome being strongly dependent on the catalyst. When hydrido–rhodium complexes are the primary intermediate then a weak preference for the (*R**,*R**)-diastereomer prevails, but chelate complexes in aprotic solvents favour formation of (*R**,*S**)-(**5**). Again it is 1,4-bis(diphenylphosphino)-butane which leads to the most stereoselective reaction with a predominance of up to 88:12. Since the absolute configuration of (**5**) was previously unknown, a sample of (*S*)-(**4**), $[\alpha]_{20}^{589}$ +20.55° (*c* 1.8, Me_2CO), was prepared from optically active epoxypropane and hydrogenated in dichloromethane with (**6**) as catalyst. The resulting sample of (**5**) was oxidised to the ketone (**7**) ($C_5H_5NH^+$ CrO_3HCl^-, CH_2Cl_2, 20 °C, 3 h). The value for $[\alpha]_{20}^{589}$ of −25.05 (*c* 3.86, C_6H_6) suggests that the benzyl carbon atom has the *R*-configuration.[10] The configuration of one sample was further checked by oxidation with sodium hypobromite (0 °C, aq. dioxan) giving the acid (**8**) which was compared with an authentic sample[10b] having the (*R*)-(−)-configuration.

Stereoselectivity in the reduction of (**1**) may be rationalised using a model [Scheme 1(a)] in which the non-bonded interactions experienced by the methyl group in the transition-state are minimised. The stereochemical course of the reduction of (**4**) is *opposite* to that of (**1**) and here it represents a preference for the methyl group to assume a *pseudo*-equatorial conformation [Scheme 1(b)].

Neither the acetates of (**1**) and (**4**) nor the homologue (**9**) were reduced with appreciable selectivity under our optimum conditions. Further examples are being studied and we merely comment at this stage on the paucity of cases[11] where the stereochemical course of homogeneous hydrogenation is controlled by adjacent polar substituents at a chiral centre and its obvious synthetic potential.

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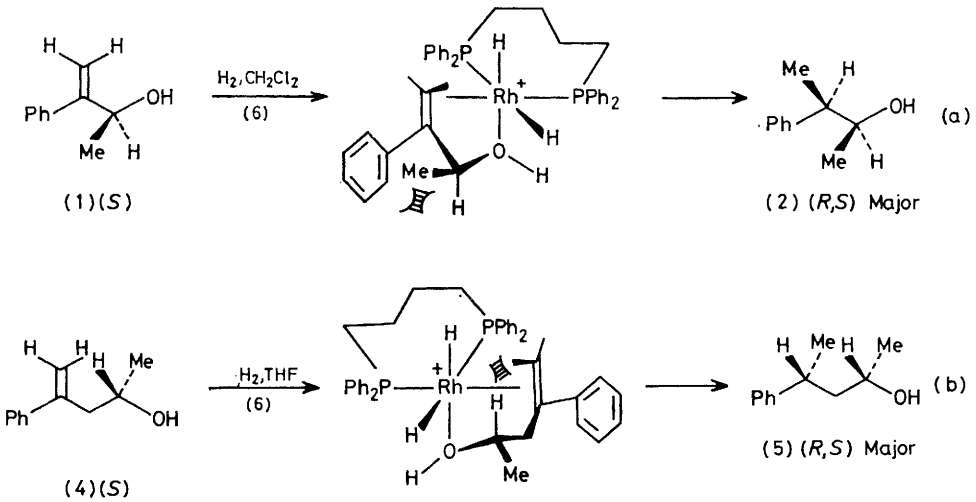

Scheme 1

Professor J. E. Baldwin kindly provided details of unpublished work.

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