REDUCTION OF SUBSTITUTED CYCLOHEXANONES BY 2-PROPANOL IN THE PRESENCE OF AMINOPHOSPHINE–RHODIUM(I) COMPLEXES*

P. SVOBODA and J. HETFLEJŠ

Institute of Chemical Process Fundamentals,
Czechoslovak Academy of Sciences, 165 02 Prague 6 - Suchdol

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Aminophosphine–rhodium(I) complexes prepared *in situ* from $[Rh(1,5\text{-cyclooctadiene})Cl]_2$ or $[Rh(ethylene)_2Cl]_2$ and $P(C_6H_5)_{3-n}R$ ($n = 1$, $R = N(CH_3)_2$, $N(i\text{-}C_3H_7)_2$, $N(C_6H_5)_2$, NC_5H_{10}, $\alpha\text{-}CH_3C_5H_9N$; $n = 2$, $R = \alpha\text{-}CH_3C_5H_9N$; $n = 2$, $R^1 = (-)$-menthyl, $R^2 = N(C_2H_5)_2$) are moderately active and selective catalysts for the title hydrogen-transfer reaction. The reduction is accompanied by isomerisation of the alcohols to thermodynamically more stable isomers.

Since the first report by Henbest and coworkers[1] about reduction of ketones to secondary alcohols by hydrogen transfer from alcohols catalysed by the soluble iridium complex, $HCl_2Ir[CH_3)_2SO]_3$, a variety of Group VIII transition metal complexes have been found to be effective, such as other iridium compounds (*cf.*[2]), some complexes of cobalt(I) (ref.[3]), ruthenium(II) (refs[4–6]) and rhodium(I) (*cf.*[7]). In the case of rhodium the effect of anionic ligands on activity and selectivity has been demonstrated by Sharf and coworkers[8]. However, little is known about the effect of neutral ligands. This, together with our interest in synthesis of optically active alcohols by reduction of ketones catalysed by rhodium(I) complexes containing aminophosphines as ligands[9], led us to examine them also as catalysts for this hydrogen transfer reaction. In order to ensure sufficient variability in the structure of complexes, instead of isolated defined compounds we have used catalytic systems in which the catalyst was formed *in situ* by ligand exchange[10] from several alkene–rhodium(I) complexes ($[RhCl(1,5\text{-cyclooctadiene})]_2$, $[RhCl(ethylene)_2]_2$, and $[RhCl(cyclooctene)_2]_2$) as precursors. The results obtained in the reduction of cyclohexanone by 2-propanol using the above complexes with triphenylphosphine and several aminophosphines as ligands confirmed that both activity and selectivity of the resulting catalytic system do not depend for a given ligand upon the catalyst precursor. The best yields of cyclohexanol were obtained with the R_h : ligand molar ratio ranging from 1 : 2 to 1 : 3.

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Further increase had rate-retarding effect, which was most distinct for triphenylphosphine used as reference ligand (*e.g.* under conditions described in Table I, reaction time 1 h, the yield of cyclohexanol was 85% for Rh : L = 1 : 2, 82% for Rh : L = 1 : 3 and only 12% for Rh : L = 1 : 6). Optimal reaction conditions found by preliminary experiments are shown in Table I. In accordance with the earlier observation[8], rhodium complexes tested in this work catalysed the reduction of cyclohexanone only in the presence of alkali metal hydroxide. Our attempts to replace it by a strong organic base such as tertiary aliphatic amine have been unsuccessful. On the other hand, the use of 2-methyl-2-propanol as solvent, recommended by the above authors[8], has turned out to be unnecessary. Although the reduction can be effected with dry reactants, the presence of water proved to be advantageous in ensuring the reproducibility of the results.

The behaviour of catalytic systems under study is illustrated by the results obtained in the reduction of 4-methyl- and 3-ethylcyclohexanones which are presented in Tables I and II. The results given in the first line of both Tables show that the reduction proceeds to a limited extent in the absence of phosphorus-containing ligand. This fact does not affect, however, the results obtained with the other systems, because of transformation of the catalyst precursor by ligand exchange. Before entering into a discussion of the selectivity of studied systems, several comments should be made concerning their catalytic activity. On examining the effect of the number

TABLE I

Reduction of 4-Methylcyclohexanone by 2-Propanol Catalysed by [Rh (1,5-Cyclooctadiene)Cl]$_2$ + Ligand

Reaction conditions: [Rh(1,5-C_8H_{12})Cl]$_2$ ($1 \cdot 10^{-5}$ mol), ligand ($6 \cdot 10^{-5}$ mol), KOH ($6{\cdot}4 \cdot 10^{-5}$ mol), 4-methylcyclohexanone ($8 \cdot 10^{-3}$ mol), 2-propanol ($1{\cdot}3 \cdot 10^{-1}$ mol), benzene ($1 \cdot 10^{-2}$ mol), water ($1{\cdot}4 \cdot 10^{-2}$ mol), temperature 80°C (the experiments were carried out under argon).

Ligand	Yields of *cis*/*trans* isomers at reaction time, h				Final *cis*:*trans* mol. ratio
	0·5	1	2	4	
None	2/5	4/7	6/10	6/10	0·6
$P(C_6H_5)_3$ (*1*)	10/5	37/15	50/22	61/24	2·5
$P(C_6H_5)_2N(CH_3)_2$ (*2*)	5/14	9/22	9/24	10/27	0·4
$P(C_6H_5)_2N(i\text{-}C_3H_7)_2$ (*3*)	6/17	12/32	12/34	14/40	0·4
$P(C_6H_5)_2N(C_6H_5)_2$ (*4*)	3/7	—	—	5/9)	0·6
$P(C_6H_5)_2NC_5H_{10}$ (*5*)	13/36	15/52	19/64	20/69	0·3

of amino groups in aminophosphines with a series of compounds of the type $P(C_6H_5)_{3-n}(NR_2)_n$ ($n = 1-3$) we have found that both tris-amino-($R = CH_3$, C_2H_5) and bis-aminophosphines ($R = CH_3$, C_2H_5, i-C_3H_7, C_6H_5; $NR_2 = C_5H_5N$ and α-$CH_3C_5H_5N$) give in general the systems of only low activity (6–12% yields of the corresponding alcohols were obtained for both ketones after 4 h under conditions specified in Table I). Efficient catalysts were obtained by using monoaminophosphines (Table I and II). The influence of the nature of the amino group in phosphines upon catalytic activity can be characterized by the following reactivity order: $P(C_6H_5)_3 \approx NC_5H_{10} \gg N(i\text{-}C_3H_7)_2 > N(CH_3)_2 \gg N(C_6H_5)_2$ for the reduction of 4-methylcyclohexanone and $N(i\text{-}C_3H_7)_2 > P(C_6H_5)_3 \approx \alpha\text{-}CH_3H_5C_9N > C_5H_{10} \cdot > N(CH_3)_2 \gg N(C_6H_5)_2$ for that of the 3-ethyl derivative. Because of limited number and qualitative nature of the data obtained so far, it is premature to discuss the above differences in terms of either electronic or steric effects of the groups[11]. Nevertheless, the data show that with several aminophosphines the activity of catalysts is comparable with the phosphine–rhodium complex, so far the most efficient rhodium catalyst[8] for this reduction. The replacement of one of the phenyl groups by a bulky alkyl group enhances the activity (see the last line in Table II). With most of the ligands tested (except(−)-menthylphenyl(diethylamino)- and (α-methylpiperidyl)diphenylphosphine) the reaction exhibited an induction period (10–15 min), which could be shortened by carrying out the reaction in an atmosphere of hydrogen.

TABLE II

Reduction of 3-Ethylcyclohexanone by 2-Propanol Catalysed by [Rh(1,5-Cyclooctadiene)Cl]$_2$ + + Ligand

For reaction conditions and numbering of ligands see Table I.

Ligand	Yields of *trans*/*cis* isomers at time, h				*trans* : *cis* molar ratio[a]
	0·5	1	2	4	
None	—	12/9	—	12/9	—
1	34/9	70/15	66/27	52/46	4·7
2	18/11	56/17	59/22	61/24	2·5
3	62/26	62/30	63/32	63/32	2·4
4	—	3/2	—	8/7	—
5	10/6	31/15	58/27	59/25	2·2
$P(C_6H_5)_2\alpha$-$CH_3C_5H_9N$	54/14	62/16	71/23	71/28	3·1
$P(C_6H_5)$((−)-menthyl) $N(C_2H_5)_2$	63/20	70/25	55/39	50/45	3·2

[a] At c. 85% conversion of the ketone.

A similar favourable effect of hydrogen on the course of the reduction of cyclohexanone by 2-pentanol catalysed by $RhCl[P(C_6H_5)_3]_3$ has been described by Freidlin and coworkers[12].

As to the reactivity of substrates, 3-ethyl derivative was in some cases more readily reduced than 4-methylcyclohexanone. When compared to the reaction of cyclohexanone, this difference was caused by the lower reactivity of the former ketone (4-ethylcyclohexanone and the unsubstituted ketone were converted into alcohols at comparable rates). The reason why some catalysts under study differentiates the above ketones is at present unclear. It has been reported[8] that in the presence of $RhCl[P(_6H_5)_3]_3$ the rate of reduction of substituted cyclohexanones does not depend on the size of the alkyl substituent and is the same for 3- and 4-substituted derivatives. In the case of the system containing triphenylphosphine, it can be expected that the interaction of the ligand with the alkene–rhodium complex leads to the same catalytically active species as are formed from $RhCl[P(C_6H_5)_3]_3$ (*cf.*[11]).

Preferential formation of thermodynamically less stable isomers (*cis*-4-methylcyclohexanol and *trans*-3-ethylcyclohexanol) in the reductions catalysed by both the *in situ* prepared system (line 2 in Tables I and II) and $RhCl[P(C_6H_5)_3]_3$ (ref.[12]) supports this assumption. In contrast to the rhodium–phosphine complex, the systems containing aminophosphines direct the reduction toward the less stable isomer only in the case of 3-ethylcyclohexanone, while with 4-methyl derivative, thermodynamicaly more stable isomer is produced preferentially. From comparison of the composition of the product at different time intervals during the reaction of 3-ethylcyclohexanone it follows that the relative amount of the *cis* alcohol decreases with time. This indicates that the reduction is accompanied by isomerisation of the less thermodynamically stable isomer. An extensive isomerisation proceeds also in the presence of the triphenylphosphinerhodium complex (line 2 in Table II), and, indeed, also with $RhCl[P(C_6H_5)_3]_3$ used by the Soviet authors[12]. Thus, in a mixture of isomeric 3-ethylcyclohexanols containing 65% of the *trans* and 35% of the *cis* isomer (*trans*/*cis* ratio = 1·85) the content of the *trans* isomer decreases under the conditions described in Table I in the presence of $RhCl[P(C_6H_5)_3]_3$ to 45% in 2 h. This shows that strictly controlled conditions should be ensured to achieve high yields of the less stable isomer.

In conclusion, several monoaminophosphine–rhodium(I) complexes have turned out to be suitable catalysts for the reduction of substituted cyclohexanones. Compared to $RhCl[P(C_6H_5)_3]_3$ they are, however, less active and selective.

EXPERIMENTAL

Compounds used. Benzene was dried over sodium prior to using. 2-Propanol was dried by CaO and rectified. $[Rh(1,5\text{-cyclooctadiene})Cl]_2$, $[Rh(ethylene)_2Cl]_2$, and $[Rh(cyclooctene)_2\ Cl]_2$ were prepared by reported procedures. The aminophosphines were obtained by the reaction of the

appropriate chlorophosphines with secondary amines according to ref.[13] and their identity was checked by elemental analysis. 4-Methylcyclohexanone (b.p. 171—172°C) was prepared[14] by oxidation of the corresponding alcohol with $H_2Cr_2O_7$. 3-Ethylcyclohexanone (b.p. 196 to 197°C) was prepared analogously. The *cis* and *trans* isomers of the alcohols were obtained by preparative gas chromatography and identified by comparing their ^{1}H-NMR spectra with those reported.

Procedure. All experiments were carried out in argon atmosphere. The conditions used are listed in Table I, along with the amounts of the reaction components. The samples of the reaction mixtures taken at fixed time intervals were analysed gas chromatographically (Chrom IV instrument equipped with a flame-ionisation detector, 370 × 0·3 cm column filled with 16% poly(ethylene glycol adipate) on Chromosorb (30—60), 40 ml per min nitrogen flow rate) at 110°C (4-methylcyclohexanol) and 120°C (3-ethylcyclohexanol). The composition of the reaction products and the yields of individual isomers were calculated from corresponding peak areas by means of calibration graphs and are presented in Tables I and II.

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