

## PHASE TRANSFER-CATALYSED TRANSFER HYDROGENATION OF KETONES USING IRON CARBONYLS AS CATALYSTS

K. JOTHIMONY, S. VANCHEESAN\* and J. C. KURIACOSE

*Department of Chemistry, Indian Institute of Technology, Madras 600 036 (India)*

(Received June 13, 1984; accepted March 7, 1985)

### Summary

Transfer hydrogenation of ketones to alcohols using iron carbonyls as catalysts in liquid-liquid phase occurs in the presence of phase transfer catalysts (PTC). Based on the percentage yield of the products, the efficiencies of the phase transfer agent, iron carbonyls and the donors are compared. Benzyltriethylammonium chloride and 18-crown-6 are equally effective and better than tricaprilmethylammonium chloride (Aliquat® 336). Among the three iron carbonyls the order of efficiency is  $\text{Fe}_3(\text{CO})_{12} > \text{Fe}_2(\text{CO})_9 \gg \text{Fe}(\text{CO})_5$ . 1-Phenylethanol is a better donor than isopropanol. The relative ease of reducibility of various ketones increases with increasing reduction potential. The stereochemistry of reduction of 4-t-butylcyclohexanone is discussed.

### Introduction

We have reported [1 - 4] the transfer hydrogenation of ketones and aldehydes using isopropanol, 1-phenylethanol and a few natural products as donors and using  $\text{RuCl}_2(\text{PPh}_3)_3$  as catalyst. Transfer hydrogenation by polymer-anchored Ru, Rh and Ir complexes has been reported recently [5]. However transfer hydrogenation under phase transfer conditions has not been described thus far. We report here the first examples of such a reaction using benzyltriethylammonium chloride, tricaprilmethylammonium chloride and 18-crown-6 as phase transfer agents. Isopropanol and 1-phenylethanol act as donors and several ketones are used as acceptors (Table 1).  $\text{Fe}(\text{CO})_5$ ,  $\text{Fe}_2(\text{CO})_9$  and  $\text{Fe}_3(\text{CO})_{12}$  are compared for their efficiency as catalysts for reduction of various ketones. The reaction mixture consists of the following:

25 mg of PTC, 10 ml 1 N NaOH		(aq)
0.5 mM of $\text{Fe}_x(\text{CO})_y$		(org)
D:A (1:1) and benzene 15 ml		
D = Donor; A = Acceptor		

\*Author to whom correspondence should be addressed.

TABLE 1

Transfer hydrogenation of various ketones to alcohols<sup>a</sup>

Sl. No.	Substrate	PTC	Product	Yield (%)
1	cyclohexanone	A	cyclohexanol	60
2	cyclohexanone	B	cyclohexanol	48
3	<i>p</i> -chloroacetophenone	A	<i>p</i> -chloro-1-phenylethanol	42
4	acetophenone	A	1-phenylethanol	36
5	<i>p</i> -methylacetophenone	A	<i>p</i> -methyl-1-phenylethanol	28
6	2-butanone	A	2-butanol	20

<sup>a</sup>PTC = (A)  $\text{BzEt}_3\text{N}^+\text{Cl}^-$ ; (B) Aliquat<sup>®</sup> 336; donor = isopropanol; catalyst =  $\text{Fe}_3(\text{CO})_{12}$ ; time = 2.5 - 3 h;  $T = 28^\circ\text{C}$ ; [cat]:[sub] = 1:25.

The reaction mixture was stirred under nitrogen for 2.5 h at a temperature varying between 25 and 45 °C. At the end of the reaction the organic phase in which the products are found is distilled under vacuum and analysed by GLC, IR and <sup>1</sup>H NMR spectroscopy. Results show the formation of acetone and acetophenone respectively when isopropanol and 1-phenylethanol were used as donors. The acceptor is converted to the corresponding alcohol.

Reaction of iron carbonyls with OH<sup>-</sup> results in the formation of the corresponding carbonylate anions,  $[\text{HFe}_x(\text{CO})_{y-1}]^-$  ( $x = 1, 2, 3; y = 5, 9, 12$ ) [6]. The hydridocarbonylate anions are potential reducing agents and are employed extensively in organic synthesis for the reduction of nitroarenes [7], Schiff bases [8], conjugated dienes to monoenes [9] and alkylation and arylation of amines with aldehydes [10]. Selective hydrogenation of  $\alpha,\beta$ -unsaturated ketones is also reported [11, 12] using the anions. In these cases  $\text{HFe}_x(\text{CO})_{y-1}^-$  and the substrate must be taken in equimolar quantities. By employing phase transfer catalysts [12, 14] such as benzyltriethylammonium chloride, Aliquat<sup>®</sup> 336 or 18-crown-6, the reduction occurs under mild conditions and the yield of the product is good. In the reduction of cyclohexanone using isopropanol as the donor and  $\text{Fe}_3(\text{CO})_{12}$  as the catalyst, the percentage yields of cyclohexanol obtained are 60 and 20 when the reactions were carried out under conditions with and without the phase transfer agent respectively. Part of this work has been reported earlier [15].

## Results and discussion

Our studies indicate the following:

(1) the efficiency of the metal catalysts decreases in the following order under our experimental conditions (Table 2):  $\text{Fe}_3(\text{CO})_{12} > \text{Fe}_2(\text{CO})_9 \gg \text{Fe}(\text{CO})_5$ ;

(2) among the phase transfer agents the catalytic efficiency is found to be BTEAC = 18-crown-6 > Aliquat<sup>®</sup> 336;

TABLE 2

Transfer hydrogenation of cyclohexanone to cyclohexanol<sup>a</sup>

No.	Substrate	Donor	Catalyst	PTC	Product (%)
1	cyclohexanone	isopropanol	Fe <sub>2</sub> (CO) <sub>9</sub>	A	cyclohexanol (42)
	cyclohexanone	isopropanol	Fe <sub>2</sub> (CO) <sub>9</sub>	B	cyclohexanol (30)
	cyclohexanone	isopropanol	Fe <sub>2</sub> (CO) <sub>9</sub>	C	cyclohexanol (44)
2	cyclohexanone	1-phenylethanol	Fe <sub>3</sub> (CO) <sub>12</sub>	A	cyclohexanol (78)
	cyclohexanone	1-phenylethanol	Fe <sub>2</sub> (CO) <sub>9</sub>	A	cyclohexanol (64)
	cyclohexanone	1-phenylethanol	Fe(CO) <sub>5</sub>	A	no reaction
3	cyclohexanone	1-phenylethanol	Fe <sub>3</sub> (CO) <sub>12</sub>	A	cyclohexanol (78)
	cyclohexanone	isopropanol	Fe <sub>3</sub> (CO) <sub>12</sub>	A	cyclohexanol (60)

<sup>a</sup>PTC = (A) BzEt<sub>3</sub>N<sup>+</sup>Cl<sup>-</sup>; (B) Aliquat<sup>®</sup> 336; (C) 18-crown-6; time = 2.5 h; T = 28 °C; [cat]/[sub] = 1:25.

(3) 1-phenylethanol is a better donor than isopropanol;

(4) the relative ease of reducibility of various ketones increases with increasing reduction potential. Thus 2-butanone (reduction potential ≈ 100 mV) gives minimum yield of product, and cyclohexanone (reduction potential 162 mV) gives maximum yield. In Table 1 the acceptors are given in the order of decreasing reduction potential.

At temperatures up to 50 °C there is a steady increase in the yield of products and above 50 °C a steep decline. There is an induction period of 10 - 20 min, which is the time required for the formation of HFe<sub>x</sub>(CO)<sub>y</sub><sup>-1</sup>, the key intermediate and the actual catalyst for the reduction. Analysis of the reactants during the induction period indicates negligible conversion to products. At temperatures above 50 °C the anion either decomposes or is converted to Fe<sub>3</sub>(CO)<sub>12</sub>.

Reduction of nitro, keto and aldehyde compounds using Fe<sub>x</sub>(CO)<sub>y</sub> have been reported [7, 12, 13] with and without phase transfer agents. For the reduction of nitrobenzene in the presence of PTC using Fe<sub>3</sub>(CO)<sub>12</sub>, Alper has suggested [13] the removal of the oxygen from NO<sub>2</sub> as CO<sub>2</sub>. In this case the deoxygenation is not a catalytic process with respect to HFe<sub>3</sub>(CO)<sub>11</sub><sup>-</sup>, since two CO groups are lost for every molecule of aniline formed.

In the present procedure the ratio of iron carbonyls to the substrate is in the range 1:25 to 1:50. At the end of the reaction HFe<sub>3</sub>(CO)<sub>11</sub><sup>-</sup> is regenerated, as shown by a peak with λ<sub>max</sub> at 540 mμ as against λ<sub>max</sub> 602 mμ for Fe<sub>3</sub>(CO)<sub>12</sub> and ν(CO) values at 2070(vw), 1995(s), 1978(m) and 1950(w) cm<sup>-1</sup> typical of the anion.

By an independent experiment using Me<sub>4</sub>N<sup>+</sup>HFe<sub>3</sub>(CO)<sub>11</sub><sup>-</sup> as catalyst we have carried out homogeneous transfer hydrogenation in benzene without any phase transfer agent. As expected, there was no induction period since HFe<sub>3</sub>(CO)<sub>11</sub><sup>-</sup> is already present; after completion of the reaction the catalyst is regenerated, as evidenced by the same intensity of the absorption peak of the catalyst before and after the reaction.

The present procedure has the following advantages:

- (i) the ratio  $[\text{Fe}_x(\text{CO})_y]/[\text{substrate}]$  is very low;
- (ii)  $\text{HFe}_3(\text{CO})_{11}^-$  is regenerated;
- (iii) a variety of donors can be conveniently used to effect selective reduction; and

(iv) in a reverse sense this method can be employed for selective dehydrogenation of organic compounds using them as donors.

The following observations give a clue to the probable mechanism:

(1) the formation of ketone from the corresponding secondary alcohol (donor);

(2) the transfer of hydrogen from the anion,  $\text{HFe}_3(\text{CO})_{11}^-$  to the coordinated acceptor is evident from the formation of deuterated product,  $\text{R}^3\text{CHODR}^4$ , when  $\text{NaOD}$  is used in the aqueous phase. This gives  $\text{DFe}_3(\text{CO})_{11}^-$ , from which H (or D) is then transferred to the ketone (acceptor) in the first step.

The product is a mixture of  $\text{R}^3\text{CHODR}^4$  and  $\text{R}^3\text{CHOHR}^4$ . In the IR spectrum the  $\nu(\text{OD})$  frequency appears at a value lower than that of  $\text{OH}$  ( $\Delta\nu = 600 \text{ cm}^{-1}$ ). In the absence of the donor,  $\text{R}^1\text{CHOHR}^2$ , at optimum conditions ( $45^\circ \text{C}$  and maximum stirring) even  $\text{Fe}_3(\text{CO})_{12}$  gives less than 10% yield and  $\text{Fe}(\text{CO})_5$  gives none. This suggests that in the former case there is a definite contribution from  $\text{OH}^-$  to the product formed but  $\text{HFe}_3(\text{CO})_{11}^-$  is not regenerated. When  $\text{H}_2\text{O}$  was used in the place of  $\text{NaOH}$  or  $\text{KOH}$  in the presence of a donor, no product was formed. This suggests that  $\text{OH}^-$  is essential for the initial formation of  $\text{HFe}_3(\text{CO})_{11}^-$ . Further studies on the mechanism are in progress.

### Stereochemistry

The reduction of cyclohexanones by complex hydrides proceeds by either of the two routes, namely (i) product development-controlled or (ii) steric approach-controlled. The predominant isomer would be formed by approach of the entering group from the least hindered side of the carbonyl complex. With an unhindered ketone the predominant product is the equatorial (*trans*) isomer [16]. In the absence of steric restriction, the predominant product will be the thermodynamically more stable isomer of a series.

It was considered interesting to study the influence of the reducing agents, namely  $\text{HFe}_3(\text{CO})_{11}^-$ ,  $\text{HFe}_2(\text{CO})_8^-$  and  $\text{HFe}(\text{CO})_4^-$  (which are formed *in situ*), on the isomer ratio of the products. For this study we have chosen 1-phenylethanol as donor and benzyltriethylammonium chloride as the phase transfer agent. In 4-*t*-butylcyclohexanone, the *t*-butyl group exerts no steric influence on the reagent approaching the keto group.

In the reduction of 4-methyl- and 4-*t*-butylcyclohexanones [17, 18] using lithium aluminium hydride, sodium borohydride, aluminium isopropoxide, etc. the ratio of *cis* to *trans* isomers changes with the size of the reducing agents [16]. For  $\text{LiAlH}_4$ , since there is no steric influence, product development control is more important than steric approach control. Hence the more stable isomer *trans*-4-*t*-butylcyclohexanol is formed in larger quan-

tity than the *cis* alcohol (*trans* to *cis* ratio is 80:20 and equilibrium ratio is 88:12). With  $\text{NaBH}_4$  as reducing agent, the amount of *trans* product is slightly reduced (*trans* to *cis* ratio is 75:25). With more bulky reducing agents the yield of *trans* product is further reduced. With  $\text{HFe}_3(\text{CO})_{11}^-$  as reducing agent the ratio of *trans* to *cis* alcohol is 62:38. With  $\text{HFe}_2(\text{CO})_8^-$  and  $\text{HFe}(\text{CO})_4^-$  there is an increase in the *trans*-isomer and the product ratios are 68:32 and 75:25 respectively, in agreement with the results reported for the reduction of 4-methylcyclohexanone using  $\text{LiAlH}_4$  and  $\text{NaBH}_4$ .

The reduction involves the initial formation of a metallo-organic complex between the ketone and the hydride species [16, 17]. It is in this complex that hydride transfer occurs and  $\text{sp}^2$  bonding of the carbonyl group changes to  $\text{sp}^3$  bonding of the product. In the process, the intermediate stages of the reduction are governed by the steric requirements of the products. The relative stabilities of the products also become important in this early stage of the reduction. For the initial formation of the metal-substrate complex, steric approach control favours equatorial attack by the  $\text{HFe}_x(\text{CO})_{y-1}^-$  reagent. As the nuclearity of the hydrido iron complex changes from 3 to 1 (tri-iron to mono-iron) the yield of *trans* product increases. For  $\text{HFe}(\text{CO})_4^-$  the probability of axial attack becomes nearly equal to that of equatorial attack, and the yield of the resulting products is governed by their stabilities. As a result, with  $\text{HFe}(\text{CO})_4^-$  the more stable *trans*-4-t-butylcyclohexanol is formed in larger quantity.

The products were separated on a column of alumina in which the *cis*-alcohol is eluted first using pentane as eluent and the *trans*-alcohol is eluted using 20% ether in pentane.

The  $^1\text{H}$  NMR spectrum exhibits quintets for  $\text{C}_1\text{-H}$  at  $\delta$  3.9 and 4.5 for *cis* and *trans* alcohols respectively. For  $\text{C}_1\text{-OH}$  a broad signal is obtained at  $\delta$  1.8 and 3.4 for *cis* and *trans* alcohols respectively. For  $\text{C}_2\text{-H}$  and  $\text{C}_6\text{-H}$  a triplet at  $\delta$  1.4 and multiplet at  $\delta$  1.6 - 2.0 were obtained for *cis* and *trans* isomers respectively.

## Acknowledgement

One of us (K.J.) is grateful to the Council of Scientific and Industrial Research, New Delhi, for the grant of fellowship.

## References

- 1 S. Muthukumar Pillai, S. Vancheesan, J. Rajaram and J. C. Kuriacose, *J. Mol. Catal.*, **16** (1982) 349.
- 2 S. Muthukumar Pillai, S. Vancheesan, J. Rajaram and J. C. Kuriacose, *J. Mol. Catal.*, **20** (1983) 169.
- 3 S. Rajagopal, S. Vancheesan, J. Rajaram and J. C. Kuriacose, *J. Mol. Catal.*, **22** (1983) 131.
- 4 S. Rajagopal, S. Vancheesan, J. Rajaram and J. C. Kuriacose, *J. Mol. Catal.*, **22** (1983) 137.

- 5 Y. Migron, J. Blum and Y. Sasson, *J. Mol. Catal.*, **22** (1983) 187.
- 6 H. Alper, *Adv. Organometall. Chem.*, **19** (1981) 183.
- 7 J. M. Landesberg, L. Katz and C. Olsen, *J. Org. Chem.*, **37** (1972) 930.
- 8 H. Alper, *J. Org. Chem.*, **37** (1972) 3972.
- 9 Y. Takegami, Y. Watanabe, I. Kanaya, T. Mitsudo, T. Okajima, Y. Morishita and H. Masada, *Bull. Chem. Soc. Jpn.*, **41** (1968) 2990.
- 10 G. P. Boldrini, M. Paunizio and A. Umani-Ronchi, *Synthesis*, (1974) 773.
- 11 R. Noyori, I. Umeda and T. Ishigami, *J. Org. Chem.*, **37** (1972) 1542.
- 12 M. Yamashita, K. Miyoshi, Y. Okada and R. Suemitsu, *Bull. Chem. Soc. Jpn.*, **55** (1982) 1329.
- 13 H. des Abbayes and H. Alper, *J. Am. Chem. Soc.*, **99** (1977) 98.
- 14 H. Alper, D. Des Roches and H. des Abbayes, *Angew. Chem.*, **16** (1977) 41.
- 15 K. Jothimony, S. Vancheesan and J. C. Kuriacose, *Int. Symp. New Vistas in Organometallic Chemistry*, March 1984, Jaipur, India.
- 16 E. L. Eliel and Y. Senda, *Tetrahedron*, **26** (1970) 2411.
- 17 W. G. Dauben, G. J. Fonken and D. S. Noyce, *J. Am. Chem. Soc.*, **78** (1956) 2579.
- 18 S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77** (1955) 5562.