Journal of Organometallic Chemistry, 240 (1982) 65–70
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands

ASYMMETRIC SYNTHESIS BY CHIRAL RUTHENIUM COMPLEXES

VIII *. THE ASYMMETRIC CANNIZZARO REACTION

MARIO BIANCHI, UGO MATTEOLI, GLORIA MENCHI, PIERO FREDIANI and
FRANCO PIACENTI

Istituto di Chimica Organica, Università di Firenze, Via Gino Capponi, 9, 50121 Florence (Italy)

(Received June 7th, 1982)

Summary

Disproportionation of aldehydes with formation of the corresponding acid and alcohol is catalyzed by phosphine-substituted cluster ruthenium carbonyls. The reaction takes place in the presence of water. An enantiomeric selection is shown by $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ in the disproportionation reaction of $(R)(S)$-2-methylbutanal; $(-)(S)$-2-methylbutanoic acid of 1.7% optical purity is obtained.

Introduction

Recent investigations [1–3] of the catalytic activity of cluster metal carbonyls have shown that various substitution derivatives of $H_4Ru_4(CO)_{12}$ are catalytically active in both hydrogenation under pressure and transfer hydrogenation of organic substrates, as well as in the hydroformylation of olefins. Moreover $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ catalyzes the rearrangement of diallyl ethers to γ,δ-unsaturated aldehydes [4]. In exploring the catalytic properties of such complexes towards other chemical systems we have tested their activity in the disproportionation of aldehydes to form the corresponding acid and alcohol (the Cannizzaro reaction).

Semi-sandwich mononuclear and bridged binuclear ruthenium, rhodium and iridium complexes were recently shown to have a marked catalytic activity in the disproportionation reaction of aldehydes, with total suppression of the competitive aldolization when working in the presence of water [5–7]. Disproportionation of aldehydes through a Tishchenko reaction can also be catalyzed by transition metal complexes [8,9]. We report below a study of the catalytic activity of $H_4Ru_4(CO)_8(PBu_3)_4$, $Ru_2(CO)_4(CH_3COO)_2(PBu_3)_2$ and $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ in the disproportionation of aldehydes in a dioxane/water medium at 120°C to form the corresponding acid and alcohol.

---

* For part VII see ref. 3.

Results and discussion

The results obtained with acetaldehyde as substrate are presented in Table 1. In the absence of a catalyst no reaction takes place under the conditions used. In the presence of $H_4Ru_4(CO)_8(PBu_3)_4$ there is extensive conversion of the aldehyde to acetic acid, ethyl alcohol and ethyl acetate. Analogous activity is shown by $Ru_2(CO)_4(CH_3COO)_2(PBu_3)_2$. Aldol condensation is negligible in both cases. However, when the concentration of water is drastically reduced (1% of the aldehyde), aldolization is the main reaction.

The complex $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ was previously used to catalyze the synthesis of chiral compounds either by resolution of racemic substrates [1,2] or by reaction with prochiral ones [1]. We have examined the possibility of synthesising chiral products by disproportionation of (*R*)(*S*)-2-methylbutanal in the presence of such a complex. The final optical activity of the product of this reaction arises from an enantiomeric selectivity by the catalyst, and therefore a product with a higher optical activity is more likely to be obtained by keeping the conversion of the aldehyde rather low.

Using conditions similar to those used with $H_4Ru_4(CO)_8(PBu_3)_4$ as catalyst, we obtained the results reported in Table 2. The products are 2-methylbutanoic acid and 2-methylbutan-1-ol (eq. 1).

$$2\,CH_3CH_2\overset{*}{C}H(CH_3)CHO + H_2O \xrightarrow{\text{cat}^*} CH_3CH_2\overset{*}{C}H(CH_3)COOH + CH_3CH_2\overset{*}{C}H(CH_3)CH_2OH \qquad (1)$$

A small but definite asymmetric induction is revealed in the formation of the acid. The residual aldehyde is optically active and is enriched in the enantiomer opposite to that produced in the acid.

The alcohol recovered is optically inactive. This might have been attributable to racemization of the alcohol either during the reaction or in the work-up of the products. However, experiments with (−)(*S*)-2-methylbutan-1-ol having 99.5% optical purity (o.p) showed that only 0.6% racemization takes place under the reaction conditions, and that even after working up total racemization does not exceed 1.9%.

We repeated the disproportionation experiment using (+)(*S*)-2-methylbutanal having a high optical purity (91.6%). In this case, from the optical purities of the products and of the residual aldehyde we could find out at which stage racemization played a role in the Cannizzaro reaction when using this catalyst. The results (Table 3) show that there is extensive racemization of the substrate even after 34% conversion. The optical purity of the acid is fairly high, but far below that of the starting aldehyde, and therefore even lower than that expected in the light of the selectivity of the catalyst. Such a value for the optical purity of the acid can be accounted for by assuming that the optical purity of the product is high at low conversion levels but decreases as the reaction proceeds because of the increasing racemization of the substrate.

The alcohol has a low optical purity and the same configuration as the acid.

Since neither the acid or the alcohol racemize under the reaction conditions, the optical purity of both the products of this disproportionation should be the same if the catalyst showed the same enantiomer discrimination in their synthesis, but the optical purity of the alcohol is lower than that of the acid. This may be attributed to

TABLE I

DISPROPORTIONATION OF ACETALDEHYDE IN THE PRESENCE OF CLUSTER RUTHENIUM COMPLEXES (Acetaldehyde 0.5 mol, dioxane 25 ml, *T* 120°C)

Catalyst (mg)	$\frac{\text{mol water}}{\text{mol aldehyde}}$	Reaction time (h)	Conversion (%)	Reaction product composition (%)			
				Acetic acid	Ethyl alcohol	Ethyl acetate	Condensation products
$H_4Ru_4(CO)_8(PBu_3)_4$ (50)	1	148	91	36.0	36.0	27.0	~ 1
$Ru_2(CO)_4(CH_3COO)_2(PBu_3)_2$ (29)	1	87	80	37.5	38.0	24.0	≪ 1
$Ru_2(CO)_4(CH_3COO)_2(PBu_3)_2$ (29)	0.011	139	65	23.1	9.5	11.4	56.0 [a]
None	1	140	0	–	–	–	–

[a] Aldols, acetates and acetals.

TABLE 2

DISPROPORTIONATION OF (*R*)(*S*)-2-METHYLBUTANAL IN THE PRESENCE OF $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ (Aldehyde 69.7 mmol. water 69.7 mmol. dioxane 15 ml. catalyst 70 mg. *T* 120°C. reaction time 183 h)

Reaction products	Composition (%)	Configuration	o.p. (%)	e.d. [a] (%)
2-Methylbutanoic acid	18.1	(*S*)	1.70	1.7
2-Methylbutan-1-ol	18.1	(*R*)(*S*)	0.00	0.0
2-Methylbutyl 2-methylbutanoate	1.1	n.d.	n.d.	n.d.
2-Methylbutanal (residual)	62.7	(*R*)	0.23	0.6

[a] e.d.: enantiomer discrimination.

a complete absence of discrimination by the catalyst in the hydrogenation of the substrate. in contrast to that shown in the formation of the acid. The alcohol formed at any given moment has the same optical purity of the aldehyde at that time. The optical purity of the alcohol. as reported in Table 3. may therefore be taken as an indication of the average optical purity of the aldehyde which has undergone the Cannizzaro reaction. The difference between the optical purities of the acid and the alcohol in Table 3 must be attributed to the discriminating effect of the catalyst in the dehydrogenation. The optical purity of the alcohol reported in Table 2 as zero is probably significant different from zero. but was too low to be measured with our instrument.

The need for water. which is consumed. in order to initiate the Cannizzaro reaction with this catalytic system is an indication that water is a reagent. The reaction most probably proceeds through hydration of the aldehyde followed by dehydrogenation [7]. It is at this stage that the catalyst must perform the enantiomeric selection on the substrate. The complex formed releases hydrogen to the acceptor.

The different discriminating ability of the catalyst in the dehydrogenation and hydrogenation steps of the reaction on the same substrate may be explained by assuming that the molecule which is dehydrogenated is the hydrated form of the substrate which may enter as a bidentate ligand in the intermediate complex. while

TABLE 3

DISPROPORTIONATION OF (+)(*S*)-2-METHYLBUTANAL (o.p. 91.6%) IN THE PRESENCE OF $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$. (Aldehyde 69.7 mmol. water 69.7 mmol. dioxane 15 ml. catalyst 70 mg. *T* 120°C. reaction time 183 h)

Reaction products	Composition (%)	Configuration	o.p. (%)
2-Methylbutanoic acid	16.7	(S)	32.6
2-Methylbutan-1-ol	16.7	(S)	22.6
2-Methylbutyl 2-methylbutanoate	0.9	n.d.	n.d.
2-Methylbutanal (residual)	65.7	(S)	1.4

the hydrogen acceptor acts as a monodentate ligand. The different coordinating abilities of these two forms of the same molecule must be associated with different reactivities, and must be responsible for the differing discriminating abilities of the complex.

Experimental

GLC analyses were performed on a Perkin–Elmer Sigma 1 system; rotatory powers were determined with a Perkin–Elmer 241 polarimeter; GC-mass spectra were recorded with a Perkin–Elmer 270B spectrometer; spinning band distillations were performed with a Perkin–Elmer 251 apparatus; IR spectra were recorded with a Perkin–Elmer 580 spectrophotometer.

Materials

(−)(*S*)-2-Methylbutan-1-ol. Fluka product. After spinning band rectification had b.p. 129°C, n_D^{25} 1.4086, $[\alpha]_D^{25}$ −5.79, o.p. 99.5% [10].

(+)(*S*)-2-Methylbutanal. Prepared according to Lardicci et al. [11] from (−)(*S*)-2-methylbutan-1-ol (o.p. 99.5%) had b.p. 91.5°C, α_D^{25} +25.682°, o.p. 91.6%.

(*R*)(*S*)-2-Methylbutanal. Prepared as described for (+)(*S*)-2-methylbutanal, starting from (*R*)(*S*)-2-methylbutan-1-ol (Fluka product).

2-Methylbutyl 2-methylbutanoate. Prepared by the procedure described by Vogel [12] for butyl butanoate, starting from (*R*)(*S*)-2-methylbutan-1-ol (Fluka product) (yield 44%) had b.p. 98–100°C/40 mmHg, n_D^{20} 1.4139.

$H_4Ru_4(CO)_8(PBu_3)_4$ [13], $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ [14] and $Ru_2(CO)_4(CH_3COO)_2(PBu_3)_2$ [15] were prepared by known procedures.

Solvents were purified by standard procedures.

Cannizzaro reactions

(a) Acetaldehyde. Reactions were carried out in a 125 ml stainless steel rocking autoclave (reaction conditions in Table 1). The composition of the product mixture was determined by GLC (2 m 5% free fatty acids phase on Chromosorb G AW-DMCS (FFAP)). Products were identified by GLC-mass spectroscopic analyses. A mixture of higher boiling products was obtained in the third experiment as a result of condensation, and aldolization products of acetaldehyde were, in fact, identified.

(b) (R)(S)-2-Methylbutanal. (*R*)(*S*)-2-Methylbutanal (6 g, 69.7 mmol), water (1.26 g, 69.7 mmol), dioxane (15 ml), $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ (70 mg) were placed in a 125 ml stainless steel rocking autoclave and heated at 120°C for 183 h. After cooling the product mixture was shown by GLC and GLC-mass spectroscopic analysis (2 m FFAP) to contain 2-methylbutanal (62.7%), 2-methylbutanoic acid (18.1%), 2-methylbutan-1-ol (18.1%) and 2-methylbutyl 2-methylbutanoate (1.1%). The product mixture was neutralized with a 5% aqueous solution of $NaHCO_3$ and then distilled to dryness under reduced pressure in nitrogen. The solid residue, after acidification and the usual work-up, gave (+)(*S*)-2-methylbutanoic acid (1.1 g) having b.p. 175°C, $\alpha_{D(l=1)}^{25}$ +0.320° (neat), o.p. 1.7% [11]. 2-Methylbutanal present in the distillate was oxidized to the corresponding acid by treatment with an Ag_2O suspension at 0°C for 48 h (30 g $AgNO_3$, 100 ml H_2O, 2 g NaOH). The mixture was extracted with diethyl ether. From the ethereal extract 2-methylbutan-1-ol was isolated by spinning band distillation, and had $\alpha_{D(l=1)}^{25}$ 0.000° (neat). The aqueous

phase after acidification gave (−)(*R*)-2-methylbutanoic acid. $\alpha^{25}_{D(l=1)}$ −0.042° (neat), o.p. 0.23% [11].

(c) (+)(S)-2-Methylbutanal (o.p. 91.6%). The reactants, conditions, and product composition are shown in Table 3. The work-up was as described in (b). The optical rotations of the products were as follows: (−)(*S*)-2-methylbutanoic acid $\alpha^{25}_{D(l=1)}$ −5.983° (neat), (−)(*S*)-2-methylbutan-1-ol $\alpha^{25}_{D(l=1)}$ −1.070° (neat), (−)(*S*)-2-methylbutanoic acid from residual 2-methylbutanal $\alpha^{25}_{D(l=1)}$ −0.257° (neat).

Racemization of (−)(S)-2-methylbutan-1-ol

A solution of (−)(*S*)-2-methylbutan-1-ol (6 g, o.p. 99.5%), water (1.26 g), dioxane (15 ml), $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ (70 mg) was heated at 120°C for 183 h. (−)(*S*)-2-Methylbutan-1-ol recovered by distillation from half of the product mixture had o.p. 98.9% (racemization 0.6%). From the other portion of the product mixture, after treatment with an Ag_2O suspension (30 g $AgNO_3$, 2 g NaOH, 100 ml water) for 48 h, (−)(*S*)-2-methylbutan-1-ol, o.p. 97.6% (racemization 1.9%), was isolated.

Acknowledgements

This research was supported in part by C.N.R. Rome. We thank Dr. Gloriano Moneti, Facoltà di Farmacia, University of Florence, for recording the GC-mass spectra.

References

1 U. Matteoli, P. Frediani, M. Bianchi, C. Botteghi and S. Gladiali, J. Mol. Catal., 12 (1981) 265 and citations therein.
2 M. Bianchi, U. Matteoli, P. Frediani, G. Menchi and F. Piacenti, J. Organometal. Chem., 236 (1982) 375.
3 M. Bianchi, U. Matteoli, P. Frediani, G. Menchi and F. Piacenti, J. Organometal. Chem., 240 (1982) 59.
4 S. Gladiali, G.A. Faedda, C. Botteghi and G. Menchi, Chim. Ind. (Milan), 63 (1981) 506.
5 J. Cook, J.E. Hamlin, A. Nutton and P.M. Maitlis, J. Chem. Soc. Chem. Commun., (1980) 144.
6 J. Cook and P.M. Maitlis, J. Chem. Soc. Chem. Commun., (1981) 924.
7 J. Cook, J.E. Hamlin, A. Nutton and P.M. Maitlis, J. Chem. Soc. Dalton, (1981) 2342.
8 M. Yamashita, Y. Watanabe, T. Mitsudo and Y. Takegami, Bull. Chem. Soc. Japan., 49 (1976) 3579.
9 T. Ito, H. Horino, Y. Koshiro and A. Yamamoto, Bull. Chem. Soc. Japan., 55 (1982) 504.
10 R.M. Ikeda, R.E. Kepner and A.D. Webb, Anal. Chem., 28 (1956) 1335.
11 L. Lardicci and R. Rossi, Atti Soc. Tosc. Sci. Nat., 68 [A] (1961) 23.
12 A.I. Vogel, Practical Organic Chemistry, Longmans, 3rd ed., 1964, p. 357.
13 F. Piacenti, M. Bianchi, P. Frediani and E. Benedetti, Inorg. Chem., 10 (1971) 2759.
14 C. Botteghi, S. Gladiali, M. Bianchi, U. Matteoli, P. Frediani, P.G. Vergamini and E. Benedetti, J. Organometal. Chem., 140 (1977) 221.
15 G.R. Crooks, B.F.G. Johnson, J. Lewis, I.G. Williams and G. Gamlen, J. Chem. Soc. A (1969) 2761.