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Enantioselective reduction of benzoyl derivatives of ferrocene and ruthenocene; optically active carbinols and carbenium ions

Marina N. Nefedova, Irina A. Mamedyarova, Pavel P. Petrovski
and Viatcheslav I. Sokolov *

Institute of Organo-Element Compounds, Academy of Sciences, 28 Vavilov Street, 117813 Moscow (USSR)

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Abstract

Mono- and 1,1′-disubstituted metallocenes, $XC_5H_4MC_5H_4Y$, M = Fe, Ru, X = H, Y = COPh, or X = Y = COPh, have been reduced using the $LiAlH_4$–Chirald complex to afford the corresponding carbinols and diols enantiomerically enriched. Optical yield was 53% for benzoylferrocene and 86% for benzoylruthenocene, (*R*)-configuration being predominant. Monocations had an opposite sign of rotation and were stable in CF_3COOH. On the contrary, diols have lost optical rotation in the same acid that has been explained by formation of the achiral ether intermediate. Dication has been formed in DSO_3F as evidenced by the ^1H NMR spectrum but it is completely racemized even at low temperature.

Introduction

In the metallocene series, the most common starting materials for optically active compounds having α-carbon atom as a chiral centre are usually α-amino derivatives resolved through diastereomeric salts [1]. For organic ketones, the widespread procedure is asymmetric reduction using lithium alumohydride modified by optically active amines or aminoalcohols [2]. We have now used this facile procedure for preparing enantiomerically enriched alcohols and diols starting from benzoylferrocene, benzoylruthenocene, 1,1′-dibenzoylferrocene, and 1,1′-dibenzoylruthenocene reduced with $LiAlH_4$ modified by (2*S*,3*R*)-4-dimethylamino-3-methyl-1,2-diphenylbutanol-2 (Chirald).

Results and discussion

Reduction of monobenzoylmetallocenes following [3] gave rise to optically active corresponding carbinols I and II in about 90% yield. (+)-I is known to have (*R*)-configuration and optical rotation of pure enantiomer 92° [4], and therefore enantioselectivity is 53%. The ratio of both enantiomers in II has been determined as 93:7 using PMR spectroscopy in the presence of tris(3-trifluoroacetyl-*d*-

Table 1

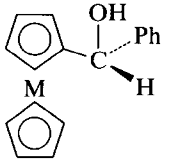
^1H spectra of monosubstituted metallocenes I–IV (δ ppm)

Compounds	OH	C_5H_5	C_5H_4		$>CH$	C_6H_5
			2,5-Protons	3,4-Protons		
Carbinols						
I [a]	2.47 (d, $J = 3.6$ Hz)	4.20 (s)	4.15 (m)		5.44 (d, $J = 3.6$ Hz)	7.2–7.4 (m)
II [a]	2.05 (d, $J = 3.4$ Hz)	4.65 (s)	4.75 (m) 4.42 (m)	4.55 (m) 4.49 (m)	5.18 (d, $J = 2.8$ Hz)	7.1–7.5 (m)
Carbocations						
III [b]		4.88 (s)	4.78 (m) 5.53 (m)	6.23 (m) 6.46 (m)	8.11 (s)	7.4–7.7 (m)
IV [b]		5.17 (s)	5.08 (m) 5.88 (m)	6.10 (m) 6.24 (m)	7.26 (s)	7.4–7.7 (m)

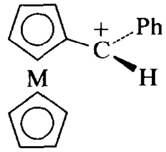
[a] In $CDCl_3$.

[b] In CF_3COOH.

camphorate)europium(III) (3–5 mol% is $CDCl_3$). In this case, enantiomeric excess amounts to 86%, and the same (*R*)-configuration can be assigned based on the same sign of rotation.



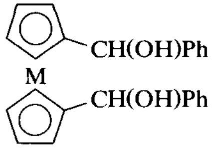
		$[\alpha]_D$
I	M = Fe	+49°
II	M = Ru	+119°



		$[\alpha]_D$
III	M = Fe	−1500°
IV	M = Ru	−2150°

When dissolved in trifluoroacetic acid, alcohols I and II formed corresponding carbocations III and IV identified by PMR spectra (Table 1). According to the literature data for similar compounds [5] the angle of rotation is enormously increased while the sign is reversed during this transformation. Cations III and IV are configurationally stable in solution exhibiting no angle decrease for at least 5 h.

Similar reduction of dibenzoyl derivatives afforded optically active diols V and VI in good yields but the presence of two structurally identical chiral fragments made a more complex picture. V and VI are formed as a mixture of two diastereomers one of which is a *meso*-form. They are difficult to separate. For VI, after several crystallizations from hexane, a fraction was obtained, $[\alpha]_D$ + 153° (*c* 0.75, benzene) which contained only small admixture of *meso*-form.



		$[\alpha]_D$
V	M = Fe	+47°
VI	M = Ru	+84°

PMR spectra of diastereomeric mixtures V and VI exhibit two sets of signals, partly superimposed (Table 2). Spectra of the ferrocene compound V had been previously reported by Yamakawa and Hisatome [6] for optically inactive mixture of *meso*- and DL-diastereomers. Assignment of aromatic protons and OH groups had no complications. In the most interesting region of benzylic protons for optically active samples of V or VI, three or four signals were observed (Fig. 1) instead of two which could be expected for a mixture ot two diastereomers. Their

Table 2

^1H Spectra of 1,1′-disubstituted metallocenes V–XII [a] (δ ppm)

Compounds	C_5H_4		CH	C_6H_5
	2,5-Protons	3,4-Protons		
Dicarbinols				
V [b] racemic	4.37, 4.21	4.17, 4.11	5.38	7.0–7.4
meso	4.26, 4.21	4.17, 4.05	5.44	7.0–7.4
VI [b] racemic	4.63	4.30, 4.33	5.28	7.0–7.5
meso	4.61, 4.67	4.25, 433	5.26	7.0–7.5
Ethers				
VII [b]	4.16, 4.21	4.26, 4.38	5.05	7.0–7.6
VIII [b]	4.57, 4.64	4.62	4.37	7.1–7.7
Monocarbocations				
IX [c]	4.60, 4.65, 4.77 [e]	5.17, 5.41, 6.27 [e]	8.14, 6.12	7.2–7.8
	4.82, 4.96, 5.04	6.37, 6.45	7.87, 6.40	
X [c]	5.05, 5.07, 5.15 [e]	5.80, 6.12, 6.21 [e]	7.38, 6.35	7.3–7.6
	5.24, 5.46	6.31	7.16, 6.51	
Dicarbocations				
XI [d]	5.55, 5.78 [e]	6.25, 6.33 [e]	8.52, 7.98	7.1–8.0
XII [d]	5.57, 5.68	5.98, 6.20, 6.28	7.74, 7.61	6.8–7.6

[a] Except benzylic protons centers of multiplets are given. [b] In $CDCl_3$. [c] In CF_3COOH. [d] In FSO_3D. [e] Tentatively assigned.

intensity ratio changes at different isomeric ratio as well as chemical shifts. The feasible reason for this is probably the statistically controlled associate-diastereomerism [7].

Comparison of PMR spectra for several samples of VI with different optical activity allowed us to make the assignment of all signals in the regions of ruthenocenyl and benzylic protons. It turned out that in an optically inactive sample prepared with $LiAlH_4$ *meso*-isomer prevails: $m/r = 3.5/1$ whereas the use of the complex $LiAlH_4$–Chirald or $NaBH_4$ gave approximately equal amounts of both diastereomers.

Two sets of signals are clearly distinguished in the spectra of the ferrocene diol V (Fig. 1d,e). In an optically inactive sample prepared by reducing dibenzoylferrocene with $NaBH_4$, the isomer with a benzylic proton signal at 5.45 ppm is predominant over another which exhibits a similar signal at 5.52 ppm. In optically active samples, the portion of the former isomer is decreasing progressively with the increase of rotation angle. This may suggest that the 5.45 signal belongs to the *meso*-isomer and the 5.52 signal to another. Previous authors [6] who did not study optically active V made a reverse assignment for its isomers.

Diols V and VI are prone to intramolecular dehydration to give corresponding 7-oxa[3]metallocenophanes VII and VIII. The ferrocene compound is formed as a mixture of *cis*- and *trans*-isomers upon the treatment of diastereomeric mixture V with dilute HCl. Under these mild conditions, the ruthenocene analogue does not form in noticeable quantity. Both VII and VIII are formed, according to PMR spectra, as a single, more stable isomer under more drastic conditions, in the course of azeotropic water distillation in the presence of TsOH. This means that change of configuration of one center does occur.

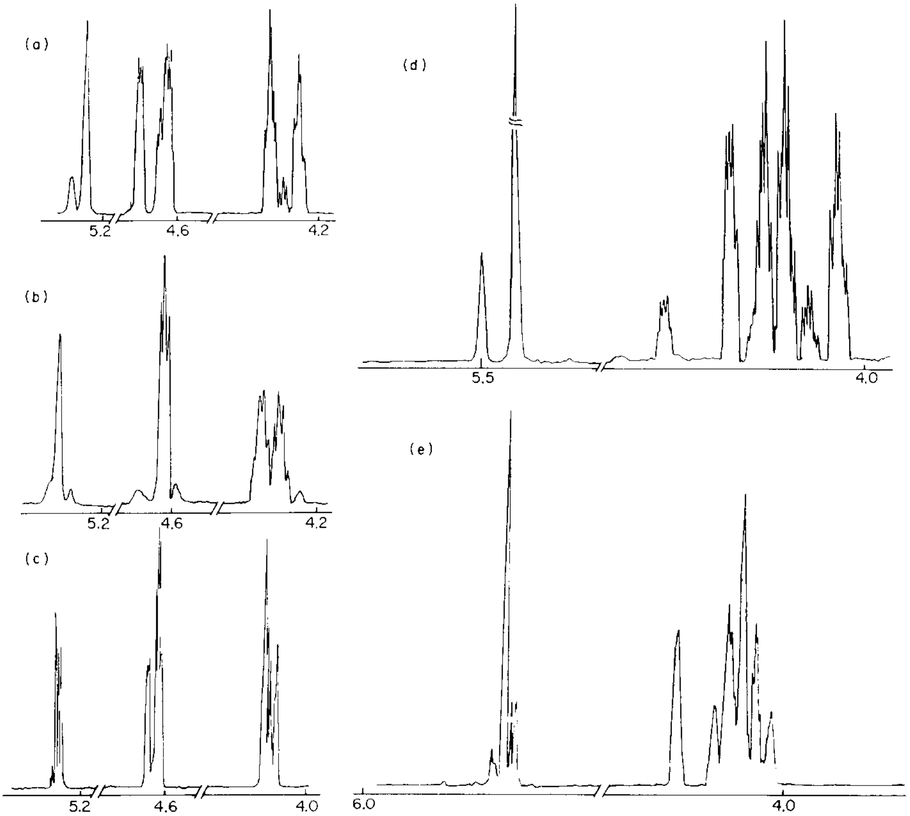
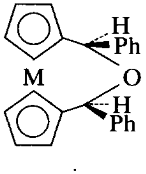
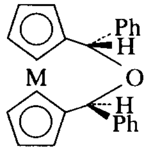


Fig. 1. ^{1}H spectra of dicarbinols V, VI in $CDCl_3$: (a) optically inactive VI; (b) VI, $[\alpha]_D$ 153; (c) VI, $[\alpha]_D$ 54; (d) optically inactive V; (e) V, $[\alpha]_D$ 47.

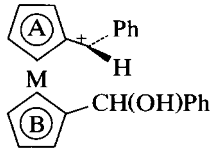
Diols or corresponding ethers in CF_3COOH at room temperature form monocarbocations IX and X. PMR spectra (Fig. 2) show the presence of two sets of signals, close (A) and remote (B) to the positively charged moiety.



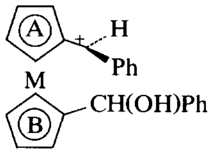
cis
(VII, M = Fe)



trans
(VIII, M = Ru)



(IX, M = Fe)



(X, M = Ru)

Starting from the mixture of diastereomers VI results in a diastereomeric mixture of monocations IX which possess both chiral center and planar chiral moiety involving Cp–$\overset{+}{C}$(Ph)H. In fact, optically inactive VI in CF_3COOD exhibited two pairs of singlets due to benzylic protons at δ 7.31 and 6.21 vs. 7.09 and 6.42 with intensity ratio 1 : 2 and 8 multiplets due to inequivalent Cp ring protons. It is remarkable that a similar pattern has been observed for a single diastereomer of 2-oxa[3]ruthenocenophane VIII in CF_3COOD, signal intensities being reversed (Fig. 2), 2.5 : 1. It seems that in solution interconversion of diastereomeric IX occurs as was previously observed for the ferrocene analogues V and VII [6].

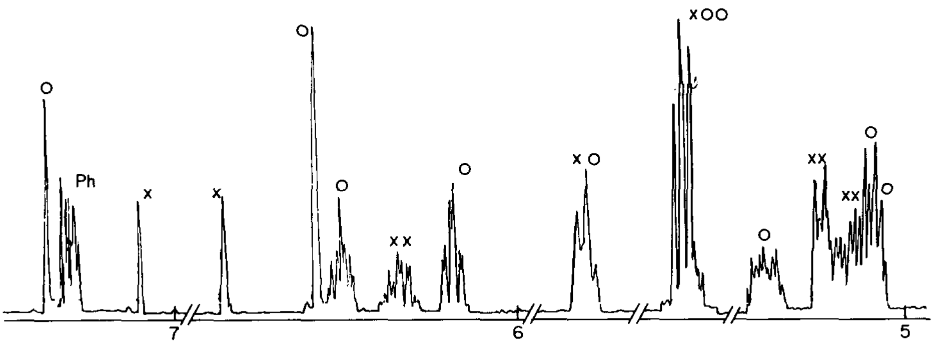
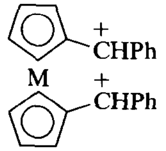


Fig. 2. ^{1}H spectrum of monocation X in CF_3COOD, signals due to different diastereomers are marked × and ○.

Ionization of optically active diols in CF_3COOH is accompanied by a fast loss of optical activity. Just after dissolving, the $[\alpha]_D$ magnitudes are less than those expected for carbocations (*vide supra* for comparison): for V +19.5° in benzene, −267° in acid; for VI +43° and −160° correspondingly. Optical rotation is decreasing gradually and vanishes completely after about 4 h.

The reason for racemization of IX and X might be reversible formation of achiral *cis*-ethers VII and VIII. This process can explain interconversion of enantiomers only, that is racemization, but occurrence of the second diastereomer in the solution of VIII in CF_3COOH suggests that in monocation X a rotation around the C_α–Cp bond is possible, a proposition that has previously been made for racemic ferrocene analogues [6].

We were able to observe the formation of dicarbocations XI and XII by dissolving diols V and VI in strong acid DSO_3F at −70 °C.



XI M = Fe
XII M = Ru

These species have been characterized by ^{1}H NMR spectra which are shown in Fig. 3 and chemical shifts are presented in Table 2. Spectra are less complicated than those for IX and X, and signals are generally down field shifted. The signals in the region δ 5.5–6.5 corresponding to the Cp ring protons demonstrate the

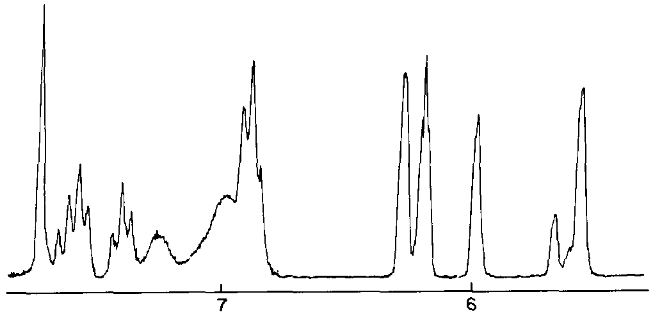


Fig. 3. ^{1}H spectrum of dication XII in FSO_3D.

presence of two isomeric dications for which the chemical shifts of only one α-proton (sterically encumbered by a close phenyl group) are markedly different. α-H in one isomer is mostly unshielded (δ 8.52 for XI and δ 7.74 for XII), whereas in another one (minor) it is superimposed on the aryl protons region (8.0 and 7.6 correspondingly).

Interestingly enough, dications turned out to be optically inactive in DSO_3F solution. Racemization took place very rapidly, presumably according to the same mechanism involving equilibria with achiral ether intermediate.

Experimental

All experiments were performed under purified argon. ^1H NMR spectra were taken using a Bruker WP-200 SY instrument (200.13 MHz) with TMS as internal standard. Optical rotations were measured with a Vniiprodmash polarimeter on the sodium D line.

Optically inactive I and V have been prepared from ketones using $NaBH_4$ in aqueous methanol [8] and crystallized from hexane. Benzoylruthenocene has been reduced with $LiAlH_4$ in ether [9]. Diol VI has been obtained similarly, after crystallization from hexane, m.p. 121 °C. Found: C, 64.73, 65.08; H, 4.69, 4.73. $C_{24}H_{22}O_2Ru$ calc.: C, 65.01; H, 4.99%.

Enantioselective reduction of benzoylmetallocenes

A solution of 1.6 g (5.6 mmol) of Chirald in 15 ml of diethyl ether was added on stirring at 0 °C to 0.1 g (2.5 mmol) of $LiAlH_4$ dissolved in abs. ether, cooled to −70 °C and then an ethereal solution of 1 mmol of dibenzoylmetallocene or 2 mmol of monobenzoylmetallocene was added dropwise. Temperature was maintained at −70 °C for FcCOPh, −50 °C for RcCOPh and −20 °C for diketones. Enantioselectivity decreased strongly at higher temperatures. After the reaction was completed, the mixture was treated with wet ether, then aqueous NH_4Cl. Ethereal extracts were treated with 1 *N* HCl (except diol V) to remove Chirald. In the case of V this procedure resulted in the complete formation of ferrocenophane VII, so the product was isolated using rapid chromatography on Al_2O_3 with ether as eluent. On prolonged contact with Al_2O_3, carbinols are oxidized to ketones. I and II were crystallized from hexane, V and VI from heptane. Chemical yields are close to quantitative, optical yields are given in the text.

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