

Enantiomeric haloruthenocenium salts: synthesis of the first representatives with the use of asymmetric reduction and asymmetric cyclopalladation

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Received 10 March 1996

Abstract

Optically active substituted ruthenocenes, (+)-RcCH(OH)Ph (**I**), (–)-RcCH(Me)Ph (**II**) and (+)-1-hydroxymethyl-2-methylruthenocene (**VIII**) react with molecular iodine to yield the corresponding iodoruthenocenium salts **Ia**, **IIa**, **VIIIa** with I₃[−] anions. Reduction of these salts using, for example, NaBH₄ regenerates the optically active starting compounds. Ruthenocenes with electron-withdrawing substituents (COMe, CPh, COOMe) remain intact when treated with I₂, Fe(III), or Ce(IV). Asymmetric cyclopalladation of RcCH₂NMe₂ is described for the first time as the initial step of the reaction sequence leading to (+)-**VIII**.

Keywords: Ruthenocene; Asymmetric reduction; Asymmetric cyclopalladation; Haloruthenocenium salts

1. Introduction

The chemistries of ferrocene and ruthenocene are very similar, with one notable exception. They differ considerably in their behavior under oxidation conditions: known ferrocenes lose one electron to give the ferrocenium ion, whereas ruthenocenes provide two electrons but adding at the same time one positively charged halogen atom [1,2].

The transition from neutral metallocenes to metallocenium cations changes dramatically the electronic structure, as reflected in the properties of chromophors. In previous papers we have reported on the synthesis of enantiomeric ferrocenium salts with either central or planar chirality [3]. The circular dichroism spectrum had been observed for the first time for the optically active salt of 1-carbomethoxy-2-methyl ferrocenium ion [4]. In this work we describe the synthesis of enantiomeric salts of iodoruthenocenium cations with central and planar chirality. The optically active starting ruthenocenes were prepared by asymmetric reactions, either reduction or cyclopalladation. To prepare the

haloruthenocenium salts we used a mild oxidizing agent, molecular iodine [1].

2. Results and discussion

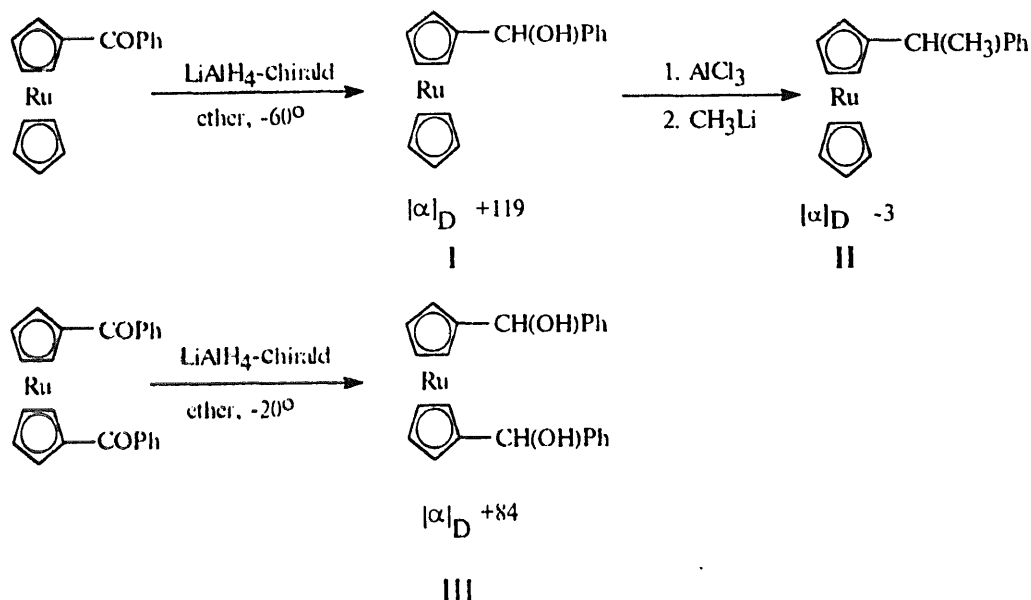
2.1. Ruthenocenes with a chiral center in the substituent via asymmetric reduction

A known strategy has been chosen for synthesis of these models, that is formation of chiral α -carbinol in the course of asymmetric reduction of phenylruthenocetyl ketones with the system lithium aluminum hydride–ChiralD [5], as shown in Scheme 1. Carbinol **I** has been further converted into a “hydrocarbon” **II** when treated with AlCl₃ in ether and then with MeLi, similar to the reaction described for a ferrocene analogue [6].

2.2. Ruthenocenes with a chiral plane via asymmetric cyclopalladation

Optically active 1,2-disubstituted ruthenocenes have been prepared using the reaction shown in Scheme 2, which is an extension of our approach, elaborated in

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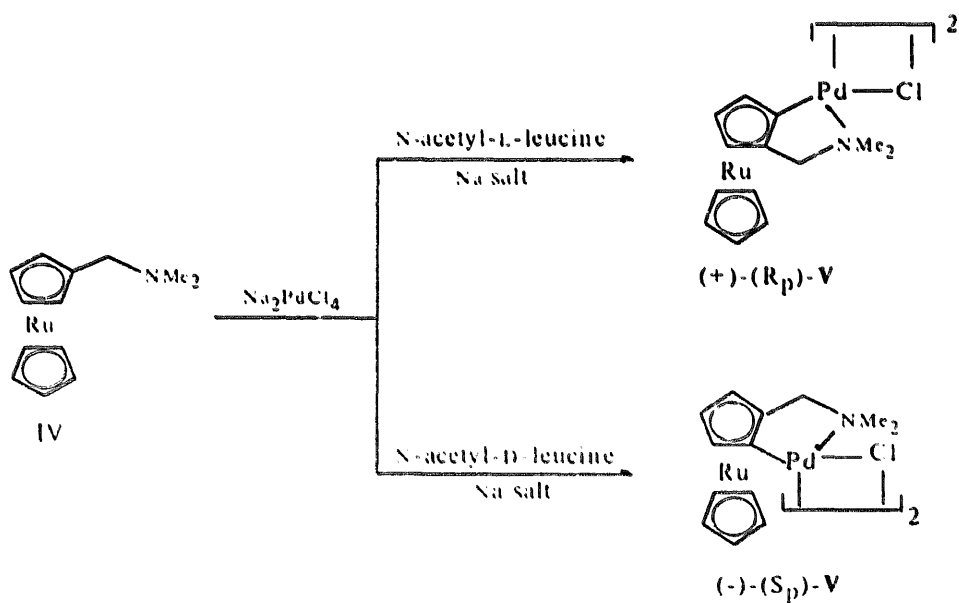


Scheme 1.

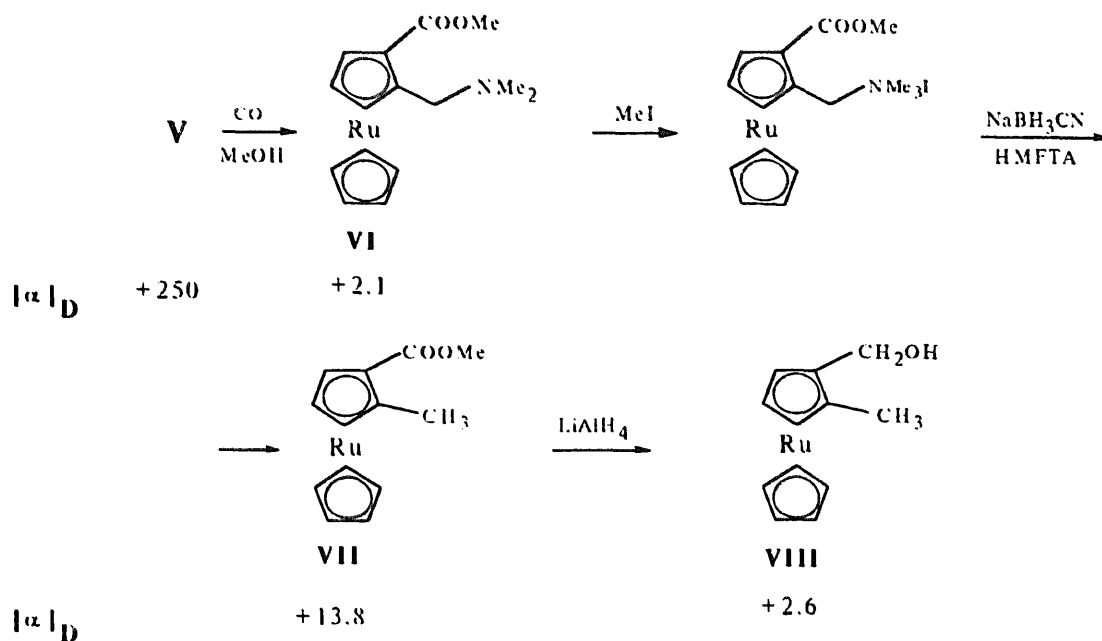
detail for the ferrocene series [7]. Now asymmetric cyclopalladation is shown to occur successfully with dimethylaminomethylruthenocene (IV). *N*-acetyl-L-leucine induces the preferential formation of the (+)-(*R_p*)-dimer V, $[\alpha]_D +250$, in chemical yield 75%, whereas *N*-acetyl-D-leucine affords the (-)-(*S_p*)-enantiomer.

Carbonylation of (+)-V in methanol affords 1-carbomethoxy-2-dimethylaminomethylruthenocene,

(+)-VI, whose methiodide is reduced with NaBH_3CN [8] to (+)-VII. Reduction of methiodide with Na/Hg has been unsuccessful, giving a mixture of products. Subsequent reduction of VII with LiAlH_4 leads to (+)-carbinol VIII (Scheme 3). The (*R_p*)-configuration for (+)-VII and (+)-VIII had been assigned earlier by Hofer and Schlogl [9]; based on the values of $[\alpha]_D$, given in this report, the enantiomeric excess for (+)-VII and (+)-VIII may be determined as about 50%.



Scheme 2.

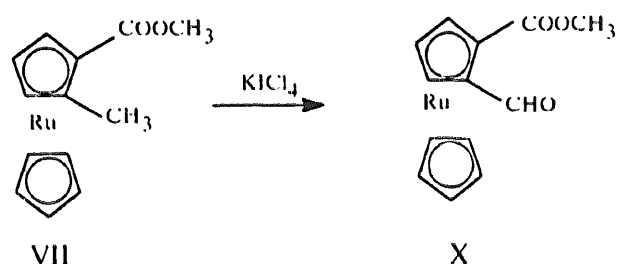


2.3. Iodoruthenocenium salts with substituents in a cyclopentadienyl ring

We have found that **I**, **II**, **VIII** and RcCH_2Ph (**IX**) react with molecular iodine to give the corresponding iodoruthenocenium salts **Ia**, **IIa**, **VIIIa**, **IXa** as triiodides.

On the contrary, the presence of electron-withdrawing substituents prevents the formation of these salts. Acetyl- and benzoylruthenocenes and 1-methoxycarbonyl-2-methylruthenocene (**VII**) remain intact during the treatment with either iodine or $\text{Ce}(\text{NH}_4)_2(\text{NO}_3)_6$ as well as the system $\text{FeCl}_3 + \text{HCl}$. The potential for electrochemical oxidation is known [10] to increase by ca. 0.3 V owing to the introduction of CH_3CO or COOCH_3 substituents into the ruthenocene core. Interestingly, under oxidation of **VII** with KICl_4 the methyl group was smoothly converted into a formyl group to give aldehyde **X** (Scheme 4).

The salts of iodoruthenoceniums **Ia**, **IIa**, **VIIIa**, **IXa** are red-brown crystalline compounds, stable in air, hardly soluble in non-polar solvents, but well soluble in



MeCN . In ^1H NMR spectra a characteristic deshielding is observed for Cp protons (ca. 1.5 ppm) compared with the neutral ruthenocenes (Table 1). The starting compounds can be obtained again when the salts are treated with reductive agents, NaBH_4 being the best.

Bis-carbinol **III**, which is a mixture of *meso*- and *d,l*-diastereomers, forms iodoruthenocenium salt in a similar way. The ^1H NMR spectrum of this salt exhibits multiplets of Cp protons in the region 6.0–6.3 ppm (8H), phenyl protons at 7.3–7.5 ppm (10H), and methine protons at 5.6–5.7 ppm (2H). However, the ratio

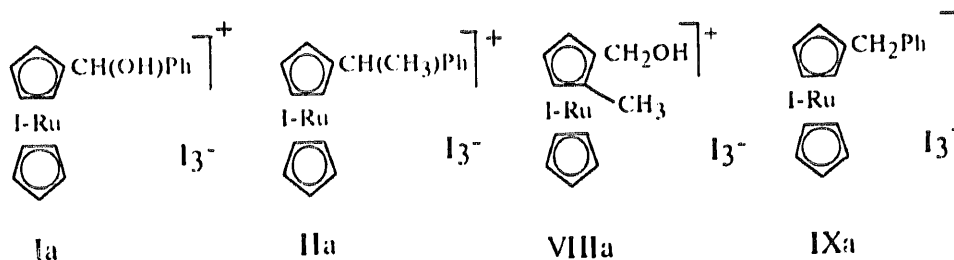


Table 1
 ^1H NMR spectra of iodoruthenocenium salts and α -ruthenocenylcarbocations ^a, δ (ppm) (J_{HH})

Compound	No.	X	C_3H_5	C_3H_4				CH or CH_2	CH_3	OH
	Ia ^b	CH(OH)Ph	6.11s	6.18m	6.18m	5.94m	5.94m	5.63d (4.1)		4.3 ^d d (4.1)
	IIa ^b	CHMePh	6.03s	6.40m	6.15m	5.99m	5.81m	4.08q (7.2)	1.46d (7.2)	
	IXa ^b	CH_2Ph	5.99s	6.15m	6.15m	5.91m	5.91m	3.89s		
	VIIIa ^b		6.01s	6.14m	6.09m	5.85		4.54, 4.37 (ABX system, ² J = 14.9, ³ J = 5.9)	2.34s	3.71t (5.9)
	XI ^c		5.17s	6.24m	6.10m	5.88m	5.08m	7.26s		
	XII ^c		5.52s	6.17m	6.11m	5.51m		5.24, 5.06 (AB system, 1.1)	1.92s	

^a Multiplets of phenyl protons are observed in the expected region 7.0–7.4 ppm.

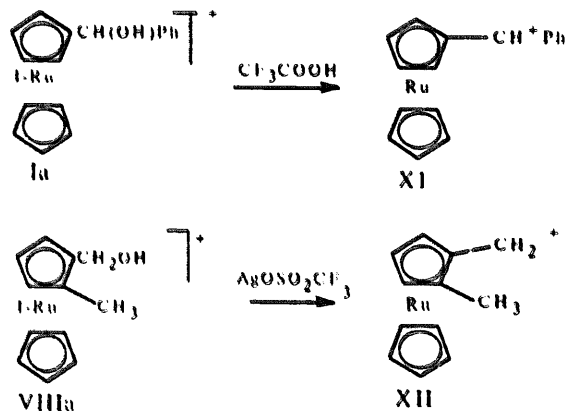
^b Ia, IIa, IXa, VIIIa in CD_3CN . ^c XI, XII in CF_3COOD .

of intensities of the latter do not correspond to the starting *meso/d,l* ratio and, for some unknown reason, change gradually with time.

In the course of the present work we have observed that iodoruthenocenium salts are inclined to convert into the α -carbocationic salts easily identified by their ^1H NMR spectra. So Ia upon dissolving in CF_3COOH affords RCH^+Ph (XI). Formation of this carbocation accompanies the normal reaction of I with iodine. The major product is admixed with 10% of XI when unpurified iodine is used, but with only 2–3% XI if the iodine is previously sublimed and dried. Then the attempt to exchange I_3^- for CF_3SO_3^- in VIIIa using silver triflate

leads to the formation of XI, identical to that obtained from VIII in CF_3COOH (Scheme 5). More unexpected was the formation of $\text{RCH}^+\text{Ph PF}_6^-$ as a sole product in an attempted preparation of chlororuthenocenium salt from benzylruthenocene, which yielded iodoruthenocenium salt in the normal way (Scheme 6).

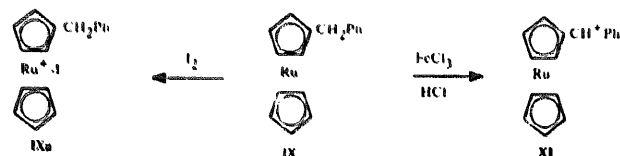
The formation of α -carbocations from haloruthenocenium ions seems to be in accord with the recent work of Watanabe et al. [11] in which a similar conversion was observed for a bimetalloenyl system $\text{Fc}-\text{CH}_2-\text{Rc}$ in the reaction with Cp_2RuCl^+ . The process might be either bimolecular or monomolecular. In the latter case it can be depicted formally through a quasi-five-membered transition state (Scheme 7).



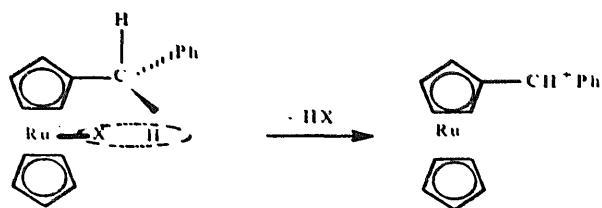
Scheme 5.

2.4. Enantiomerically enriched iodoruthenocenium salts

These salts Ia, IIa and VIIIa have been obtained by oxidation of optically active I, II, VIII with iodine in CCl_4 . The deep color of these compounds (having I_3^- or CF_3SO_3^- as counterions) does not allow their optical



Scheme 6.



Scheme 7.

rotations to be measured. However, reduction of **IIa** and **VIIIa** with NaBH_4 gives back the starting **II** and **VIII** with angles of rotation unchanged. In the case of **I** the optical rotation decreases from $+87^\circ$ to $+40^\circ$, which may be explained by the formation of some achiral by-products (RcCH_2Ph for example).

3. Experimental details

^1H NMR spectra were obtained using a Bruker WP-200 SY spectrometer (200.13 MHz), chemical shifts δ are given in ppm from TMS and J values are given in Hz. Optical rotations were measured with a Vniiprod-mash polarimeter on the sodium D line. The mass spectra were recorded on a Kratos MS890 instrument, operating at 70 eV ionizing voltage. Dimethylaminomethylruthenocene (**IV**) was prepared by the method described by Hofer and Schlogl [12].

3.1. (+)-(R)-di- μ -chloro-bis[2-(dimethylaminomethyl)ruthenoceny]dipalladium(II) (**V**)

A solution of 0.28 g (1.74 mmol) of N-acetyl-L-leucine and 0.076 g of NaOH in 9 cm^3 of water was added to a solution of 0.552 g (1.74 mmol) of Na_2PdCl_4 in 27 cm^3 of MeOH. The solution was brought to slightly alkaline reaction using 50% aq. NaOH, and 0.5 g (1.74 mmol) of **IV** in 9 cm^3 MeOH was added. The precipitate formed after 25–30 min. The reaction mixture was stirred for 4 h at room temperature, then evaporated in vacuo without heating. The dried precipitate was dissolved in benzene, filtered and evaporated to give 0.57 g (75%) of **V**, $[\alpha]_D^{20} + 250$ (c, 1.11; CH_2Cl_2). Fractional crystallization of **V** from a benzene–heptane mixture by gradual evaporation of solution gave a fraction of **V** with higher specific rotation $[\alpha]_D^{20} + 275$ (c, 1.08; CH_2Cl_2). ^1H NMR (C_6D_6) 4.70 (C_5H_5), 4.60–4.50 (C_5H_3), 4.33 and 3.51 (parts of NCH_2 quadruplet), 3.03 and 2.90 (NMe_2).

3.2. (+)-Acetylacetonato[2-(dimethylaminomethyl)ruthenoceny]palladium(II)

A solution of sample **V**, $[\alpha]_D^{20} + 250$, in benzene and a double amount of $\text{Na}(\text{acac})$ in MeOH were stirred at room temperature, whereupon the color changed from

dark to light yellow. The solution was evaporated to dryness and the product extracted with pentane to give acetylacetonato [2-(dimethylaminomethyl)ruthenoceny]palladium(II), $[\alpha]_D^{20} + 217$ (c, 1.5; CH_2Cl_2), m.p. 125°C . ^1H NMR (CD_2Cl_2) 5.18 (CH of acac group), 5.13dd, 4.57t and 4.49dd (C_5H_3), 4.49s (C_5H_5), 3.58 and 3.09 (AB system, $J = 13$ Hz, RcCH_2N), 2.79 and 2.41 (NMe_2), 1.84 and 1.79 (CH_3 of acac group). Mass-spectra M^+ 495.

3.3. (+)-1-Methoxycarbonyl-2-dimethylaminomethylruthenocene (**VI**)

A flow of CO was passed for 4 h through a solution of 0.6 g (1.4 mmol) of **V**, $[\alpha]_D^{20} + 203$, in MeOH; metallic palladium was removed and MeOH evaporated. The product was extracted with benzene–triethylamine (5:1) and treated with aq. NaHCO_3 , washed with water, and dried over anhydrous K_2CO_3 . Chromatography of benzene solution (SiO_2 , eluent benzene–triethylamine 5:1) gave 0.33 g (70%) of **VI**, $[\alpha]_D^{20} + 2.1$ (c, 4; CH_2Cl_2). ^1H NMR (C_6D_6) 5.22dd ($^3J = 2.4$, $^4J = 1.37$ Hz), 4.75dd ($^3J = 2.4$, $^4J = 1.36$ Hz) and 4.44t ($^3J = 2.4$ Hz) (C_5H_3), 4.39s (C_5H_5), 4.20 and 3.23 (AB system, $J = 13.3$, $-\text{N}-\text{CH}_2-$), 3.46s (OMe), 2.28 (NMe_2).

3.4. (+)-1-Methoxycarbonyl-2-methylruthenocene (**VII**)

0.053 cm^3 (0.86 mmol) of MeI was added to a solution of 0.3 g (0.86 mmol) of **VI** in acetone and stirred for 0.5 h. The solution was decanted and the quaternary salt dried. To a suspension of this salt in 6 cm^3 of HMFTA under argon was added 0.105 g (1.72 mmol) of solid NaBH_3CN . This mixture was stirred for 0.5 h at 90°C , then for 0.5 h at room temperature, diluted with water and extracted with benzene. Chromatography of benzene solution (SiO_2 , eluent benzene) gave 0.14 g (56%) of **VII**, $[\alpha]_D^{20} + 13.8$ (c, 4.3; CH_2Cl_2). ^1H NMR (C_6D_6) 5.21dd ($^3J = 2.4$, $^4J = 1.37$ Hz), 4.50dd ($^3J = 2.31$, $^4J = 1.7$ Hz) and 4.35t ($^3J = 2.37$) (C_5H_3), 4.37s (C_5H_5), 3.47s (OMe), 2.37s (Me).

3.5. (+)-(R)-1-hydroxymethyl-2-methylruthenocene (**VIII**)

To the filtered solution of 0.15 g of LiAlH_4 in 15 cm^3 of abs. ether, 0.13 g (0.32 mmol) of (+)-**VII** in 15 cm^3 of abs. ether was added dropwise. After 0.5 h stirring the mixture was quenched with 10% aq. NH_4Cl . Extraction with ether gave 0.11 g (95%) of **VIII**, $[\alpha]_D^{20} + 2.6$ (c, 2.4; CH_2Cl_2). ^1H NMR (C_6D_6) 4.53m, 4.42m and 4.29m (C_5H_3), 4.35s (C_5H_5), 4.07m (CH_2), 1.89s (Me), 1.19br.s (OH).

3.6. (-)-(R)-(1-phenylethyl)ruthenocene (**II**)

0.35 g (0.25 mmol) of AlCl_3 was added at -60°C to a solution of 0.6 g (1.8 mmol) of (+)-phenyl-

ruthenocencylcarbinol (I) in abs. ether, then a stoichiometric amount of MeLi in hexane was added and the reaction mixture was stirred for 0.5 h at -40°C . This mixture was then quenched with aq. NH_4Cl , extracted with ether and chromatographed (SiO_2 , eluent hexane), to yield 0.42 g of II (66%), $[\alpha]_{\text{D}}^{20} -3$ (c, 1.6; C_6H_6). Mass-spectra m/z 336 (M^+), 321 ($\text{M}^+ - \text{Me}$), 259 ($\text{M}^+ - \text{Ph}$), 244 ($\text{M}^+ - \text{Me} - \text{Ph}$). $^1\text{H NMR}$ (C_6D_6) 7.0–7.2 m (Ph), 4.48m 4.41m 4.40m and 4.36m (C_5H_4), 4.45s (C_5H_5), 3.54q ($^3J = 7.17$ Hz, CH), 1.38d ($^3J = 7.17$ Hz, CH_3).

3.7. Preparation of iodoruthenocenium salts: a typical procedure

A solution of 0.28 g (1.1 mmol) of I_2 (purified by sublimation and dried over H_2SO_4) in 50 cm^3 of CCl_4 was added dropwise to 0.10 g (0.34 mmol) of VIII, $[\alpha]_{\text{D}}^{20} +3$, in 20 cm^3 of CCl_4 under stirring. A dark precipitate formed slowly. The reaction mixture was stirred for 2 h, then the solution was decanted and the residual solid washed with CCl_4 to remove unreacted I_2 and dried under vacuo. The yield of VIIIa was quantitative.

To a stirred solution of iodoruthenocenium salt was added NaBH_4 until the mixture was colorless. Then the mixture was filtered and MeCN removed in vacuo. The residue was dissolved in benzene, washed with water and dried over MgSO_4 , benzene was evaporated to yield 0.04 g of VIII, $[\alpha]_{\text{D}}^{20} +3$.

Iodoruthenocenium salts were alternatively obtained by an exposition of the powdered substance with I_2 vapor.

3.8. 1-Carbomethoxy-2-formylruthenocene (X)

0.12 g of KICl_4 was dissolved in 10 cm^3 of a mixture of MeCN and CCl_4 (9:1), added dropwise to a solution

of 0.04 g (0.01 mmol) of (+)-VII in MeCN and stirred at room temperature for 1 h. The solution was evaporated and the solid extracted with benzene. After chromatography on SiO_2 , 0.015 g (36%) of X, $[\alpha]_{\text{D}}^{20} -220$, was obtained (c, 1; CH_2Cl_2). Mass-spectra m/z 318 (M^+). $^1\text{H NMR}$ (C_6D_6) 10.92s (CHO), 5.35dd ($^3J = 2.55$, $^4J = 1.49$ Hz), 5.18dd ($^3J = 2.58$, $^4J = 1.49$ Hz) and 4.37t ($^3J = 2.6$ Hz, C_5H_3), 4.24s (C_5H_5), 3.35s (CH_3).

Acknowledgements

The authors acknowledge financial support from the Russian Foundation for Fundamental Research (Grant 93-03-05827) and INTAS-94-1716.

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