Tetrahedron. Vol 26, pp. 4483 to 4489. Pergamon Press 1970. Printed in Great Britain

ORGANOMETALLIC COMPOUNDS—VIII

THE STEREOCHEMISTRY OF ACYLFERROCENE OXIME DERIVATIVES[*][†]

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(*Received in Japan 24 January 1970; Received in the UK for publication 26 June 1970*)

Abstract—Four acylferrocene oximes have been prepared and each separated into *anti* and *syn* isomers. They are formylferrocene oxime (m.p. *anti* 115–116°, *syn* 150–151°), acetylferrocene oxime (m.p. *anti* 174–175°, *syn* 144–145°), benzoylferrocene oxime (m.p. *anti* 165–166°, *syn* 164–165°), and 1,2-(α-ketotetramethylene)ferrocene oxime (m.p. *anti* 132–133°, *syn* 110–111°). The assignment of *anti* and *syn* was made by means of NMR and IR spectrometry.

IN STUDYING the stereochemistry or reactions of ferrocene derivatives, it is necessary to take into consideration the spacial bulk of ferrocene, the effects of two aromatic 5-membered rings and participation of the Fe atom. This paper deals mainly with the stereochemistry and spectrometry of the oxime derivatives of acylferrocene.

Some acylferrocene oximes have been reported.[1,2] In these studies the Beckmann rearrangement of the oximes was attempted but without separation into *syn* or *anti*-isomers. Separation into *syn* or *anti*-isomers of formylferrocene oxime and 1,2-(α-ketotetramethylene)ferrocene oxime has been described[3,4] but without spectrometric investigation. The configuration of the oximes was not based on accurately recorded physical properties, and therefore the purity and identity of the *syn* or *anti*-isomers are questionable.

On the other hand, the NMR spectra of some oxime derivatives and hydrazones have been studied in considerable detail. The signals were assigned to each isomer[5-20] and the anisotropic effect of the oximino group was qualitatively or quantitatively considered,[5,7-12,16] or the conformations were related to solvent effects in NMR spectra.[9b,18]

In the present study, formylferrocene oxime (I), acetylferrocene oxime (II), benzoylferrocene oxime (III), and 1,2-(α-ketotetramethylene)ferrocene oxime (IV) were each separated into their isomeric *syn* and *anti* configurations by means of NMR and IR spectrometry.

[Ia, b—IVa, b]

RESULTS AND DISCUSSION

In the *syn* configuration, the OH group lies near the ferrocene moiety while it is opposite in the *anti* isomer in this paper.

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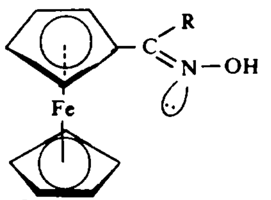
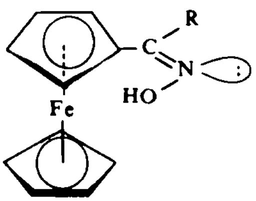
[*] Part VII. K. Yamakawa and M. Moroe, *Tetrahedron* **24**, 3615 (1968).

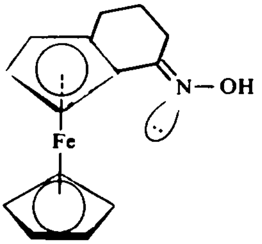
[†] Presented in part at the 2nd Symposium on Non-Benzenoid Aromatic Chemistry; Symposium papers, pp. 62–64, Kyoto. November 22–23 (1968).



Ia: R=H
IIa: $R=CH_3$
IIIa: R=Ph

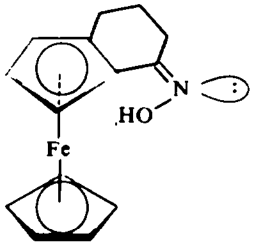


Ib: R=H
IIb: $R=CH_3$
IIIb: R=Ph



IVa

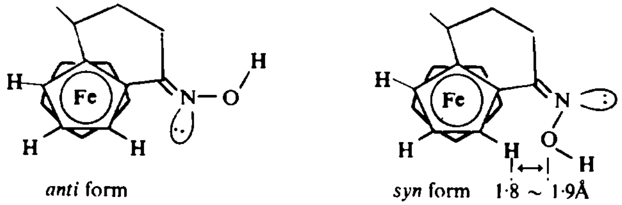
anti form



IVb

syn form

When the structure of IV, in which rotation of the Cp-C bond is rigid, is examined with a molecular model, the O atom of the OH group and the α-H atom of the Cp ring are found in the van der Waals radius of each other in the *syn* form (Fig. 1).



cf van der Waals radii[21]
O: 1·40Å, H: 1·2Å

FIG 1. The plane figures of the oxime IV.

This isomer should differ from the other isomer in spectra and stability. In the NMR spectrum, an α-proton on the Cp ring of the *syn* isomer should resonance at a considerably lower field than the *anti* isomer because of a steric compression effect of the O atom. In the IR spectrum of the *syn* isomer the line of C=N stretching should appear at a higher frequency than that of the *anti* isomer, since there is a considerable strain on the C=N bond by hindrance between the α-H of the Cp ring and the OH group.

In the IR spectrum, the isomer IVb has a band of C=N stretching at a higher frequency than IVa. In the NMR spectra the absorption of substituted Cp ring protons is separated into two groups by a ratio of 2:1 in its relative intensity, while that of unsubstituted ring protons appear as a sharp singlet peak. Of the two peaks of substituted ring protons, the less intense absorption at the lower field should arise from a proton at α-position. The chemical shift of the α-proton on the Cp ring is very different in IVa and IVb; the signal of the b isomer lies at a field 0·60 ppm lower than the other isomer, and therefore IVa and IVb are *anti* and *syn* isomers, respectively.

Stoll and Troxler[19] assigned the *syn* form to the isomer of 4-oxo-4,5-6,7-tetrahydroindol oxime in which the proton at 3-position was 0·60 ppm lower than the other isomer.

In the oxime IVa, one of the six protons of the three methylene groups gave a signal isolated from the other protons at a rather low field (6·74 τ, quartet) because of an unusual deshielding effect. The isolated signal would be assigned to an equatorial proton in the methylene group at the α-position of the oximino group.[20]

The *syn* oxime should be more acidic than the *anti* oxime, due to the stereochemical environment around the H atom of the hydroximino group. In fact, the *anti* form (IVa) was eluted earlier than the *syn* form (IVb) in column chromatography on alumina, and this phenomenon was also observed in the other oximes, I and II.

The oxime I is different from the oxime IV in that rotation of the Cp—C bond is not restricted. From the IR spectra of I in KBr, however, one would be able to predict the configuration in the same manner as the case of the oxime IV, since the C=N stretching would be sensitive to the resonance effect.[22] Thus, in the *syn* oxime Ib the C=N stretching band appeared at a higher frequency than that of the *anti* oxime Ia. On the other hand, in the NMR spectra the absorption of the ring α-proton in the oxime Ib appeared at a lower field than in Ia, and the signal of the methine proton showed an opposite behaviour to the ring proton; the assignment by the NMR spectra was consistant with the result in the IR spectra.

TABLE 1. DATA OF IR SPECTRA IN FREQUENCY

Compounds	In KBr phase		In CHCl$_3$ solution	
	$\nu_{C=N}$	$\Delta\nu_{C=N}$	$\nu_{C=N}$	$\Delta\nu_{C=N}$
I-a	1628	26	1618	20
I-b	1654		1638	
II-a	1644	7	1624	3
II-b	1651		1627	
III-a	1634	0	1630	0
III-b	1634		1630	
IV-a	1624	19	1622	7
IV-b	1643		1629	

By analogy to the oximes I and IV, it was deduced that IIa and IIb were *anti*- and *syn*-form oximes, respectively, from the results of the NMR and IR spectra. There has been no detailed report on the structure of the acetylferrocene oxime (II).

The C=N stretching band of III in the IR spectra appeared at the same frequency in both isomers. This fact can be interpreted as evidence of existence of almost equal degrees of steric hindrance in the two isomers which are different in the direction of the OH group. In the NMR spectra, however, a difference is observed between IIIa and

TABLE 2. DATA OF NMR SPECTRA AT 100 MHz IN τ VALUE ($CDCl_3$ solution)

Compounds	Methyl	Methylene	Unsubstd. Cp ring	Substd. Cp ring				Methine	Ph ring
				β-position	α-position	$\Delta\delta_{\beta-\alpha}$	$\Delta\delta_{b-a}$		
I-a	—	—	5·79(5)	5·65(2)	5·46(2)	0·19	0·25	2·01(1)	—
I-b	—	—	5·80(5)	5·63(2)	5·19(2)	0·44		2·74(1)	—
II-a	7·78(3)*	—	5·80(5)	5·67(2)	5·45(2)	0·22	0·37	—	—
II-b	7·78(3)*	—	5·80(5)	5·66(2)	5·07(2)	0·59		—	—
III-a	—	—	5·78(5)	5·65(2)	5·54(2)	0·11	0·31	—	2·40–2·65(5)
III-b	—	—	5·80(5)	5·61(2)	5·19(2)	0·42		—	2·40–2·65(5)
IV-a	-	7·2–8·1(5) 6·74(1)	5·84(5)	5·71(2)	5·30(1)	0·41	0·60	—	—
IV-b	—	7·1–8·1(6)	5·86(5)	5·70(2)	4·69(1)	1·01		—	—

* The signals of methyl protons of II-a and II-b in the measurement in CS_2 showed different chemical shifts; II-a: 7·85, II-b: 7·87.

IIIb in the chemical shift of the α-protons of the substituted Cp ring. Since the α-proton signal of the Cp ring in IIIb appeared at a lower field than in IIIa, the former could be assigned to the *syn* form and the latter to the *anti* form. This assignment would explain the observation that in preparation of III, the *syn* form was somewhat predominant to the *anti* form whose OH group was near the Ph ring, and IIIa was converted into IIIb by acid treatment.

The bands of the C=N stretching of the four pairs of oximes shown in Table 1. From the Table it can be seen that the difference in frequency of the C=N stretching between the *anti* and *syn* isomers decreases as the bulkiness of an α-substituent the hydroximino group increases. The fact seems to indicate that there is some general stereochemical correlation between the C=N stretching band and *syn* and *anti* configurations in the oximes.

The NMR data are shown in Table 2. The difference in chemical shift of the methine proton between the two isomers of the oxime I is unusually large, while there is scarcely a difference in the methyl proton of the oxime II. Saito and Nukada[11] reported that the discrimination of signals of the α-methylene (or methine) proton between the two isomers arose mainly from a term related to lone-pair electrons of the N atom. On the other hand, Karabatsos *et al.*[9] have presented evidence that a large deshielding effect resulted from the proximity of the OH group, and other workers have also reported the same conclusion.[12, 16] If the chemical shift is due to lone-pair electrons, one could not fully explain the fact that the difference in the signal of the Cp ring α-proton between the two isomers of IV was considerably large, and that the proton in the *syn* form resonanced at an unusually low field (4·69 τ) in comparison to the chemical shift of the ring α-proton of the corresponding ketone (5·29 τ). Moreover, the Cp ring α-proton (5·30 τ) of the *anti* oxime IVa does not seem particularly to exert a diamagnetic anisotropic effect due to the lone-pair electrons. However, if the lower field shift is due to the deshielding effect of the OH group, it seems to be difficult to explain the unusual chemical shift as due to the difference of the methine proton between the two isomers of I (0·73 ppm).* Thus, the chemical shift of the protons near the hydroximino group would be competitively influenced by the deshielding effect of the OH group and by the diamagnetic anisotropic effect due to the lone-pair electrons of the N atom.

EXPERIMENTAL

All m.ps are uncorrected. NMR spectra were measured with JEOL (Nippon Denshi Co.) JNM-4H-100 spectrometer at 100 MHz using $CDCl_3$ or CS_2 as solvent and TMS as internal reference. IR spectra were taken with JASCO (Nippon Bunko Co.) IR-403-G grating spectrophotometer, and measured in KBr disk or $CHCl_3$ soln.

Preparations of ketones. Formylferrocene was prepared according to the modified method reported.[3] Acetylferrocene and benzoylferrocene were obtained by the Friedel–Crafts acylation. 1,2-(α-Ketotetramethylene)ferrocene was prepared via β-ferrocenylpropionic acid and γ-ferrocenylbutyric acid according to the modified methods described.[23, 24]

Preparations of oximes. Chromatography was carried out using Wako activated alumina (300 mesh). The isomer ratio a/b of oximes was determined from the relative intensity of ring protons in NMR spectra of the crude oximes before purification.

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* The chemical shift difference between the *syn* and *anti* α-methine protons in n-heptaldoxime was 0·68 ppm.[11c]

Formylferrocene oxime (I). A mixture of formylferrocene (1·00 g), hydroxylamine hydrochloride (0·70 g), NaOAc·$3H_2O$ (1·70 g) and 70% EtOH (17 ml) was refluxed for 3·5 hr, then evaporated, and extracted with ether. The ether layer was washed, dried and evaporated. The residue was chromatographed on alumina with EtOAc as eluent, and separated into two bands. Both were repeatedly recrystallized from hexane free from trace acid. The reddish orange needles from the first band (Ia) had m.p. 115–116°. (Found: C, 57·86; H, 4·63; N, 6·14. $C_{11}H_{11}ONFe$ requires: C, 57·68; H, 4·85; N, 6·12%); IR spectrum (KBr; cm^{-1}): 3175 (ν OH), 1628 (ν C=N), and 968 (ν NO).

The brown orange flakes from the second band (Ib) had m.p. 150–151°. (Found: C, 57·67; H, 4·76; N, 6·26. $C_{11}H_{11}ONFe$ requires: C, 57·68; H, 4·85; N, 6·12%); IR spectrum (KBr; cm^{-1}): 3230 (ν OH), 1654 (ν C=N), and 940 (ν NO). (Lit.[3] *anti*-isomer: m.p. 96–99°; *syn*-isomer: m.p. 155–157°). A ratio Ia/Ib was 1·7.

Acetylferrocene oxime (II). Acetylferrocene (2·00 g), hydroxylamine hydrochloride (1·60 g), KOH (2·00 g) and 95% EtOH (100 ml) were used. The procedure was the same as in formylferrocene oxime. The two compounds from the first band (1·50 g) and second band (0·34 g) were repeatedly recrystallized from hexane. Then the first band oxime gave orange yellow flakes with m.p. 174–175° (IIa). (Found: C, 59·40; H, 5·56; N, 5·55. $C_{12}H_{13}ONFe$ requires: C, 59·29; H, 5·39; N, 5·76%); IR spectrum (KBr; cm^{-1}) 3200 (ν OH), 1644 (ν C=N), and 935 (ν NO).

The oxime from the second band, orange yellow flakes, had m.p. 144–145° (IIb). (Found: C, 59·01; H, 5·18; N, 5·65. $C_{12}H_{13}ONFe$ requires: C, 59·29; H, 5·39; N, 5·76%); IR spectrum (KBr; cm^{-1}): 3240 (ν OH), 1651 (ν C=N), and 937 (ν NO). (Lit. recorded: m.p. 163–166°,[2a] m.p. 173–174°,[2b] and m.p. 161–164°.[4]) A ratio IIa/IIb was 7·8.

Benzoylferrocene oxime (III). Benzoylferrocene (0·79 g), hydroxylamine hydrochloride (0·80 g), KOH (1·00 g) and 95% EtOH (50 ml) were refluxed for 3·5 hr. The procedure was the same as in formylferrocene oxime. Extraction was carried out with ether–benzene. The oxime band (0·33 g) was only one. The oxime was rechromatographed on Merk activated neutral alumina with EtOAc. The one band of oxime was separated into the first eluted portion (0·10 g) and the residual portion (0·17 g). The former was repeatedly recrystallized from EtOH to give red prisms, m.p. 165–166° (IIIa). (Found: C, 66·87; H, 4·92; N, 4·38. $C_{17}H_{15}ONFe$ requires: C, 66·91; H, 4·96; N, 4·59%); IR spectrum (KBr; cm^{-1}) 3190 (ν OH), 1634 (ν C=N), 1495 (ν C=C in Ph), 991 and 942 (ν NO).

The residual portion was recrystallized two or three times from EtOH as orange red prisms, m.p. 164–165° (IIIb). (Found: C, 66·72; H, 4·76; N, 4·37. $C_{17}H_{15}ONFe$ requires: C, 66·91; H, 4·96; N, 4·59%); IR spectrum (KBr; cm^{-1}): 3190 (ν OH), 1634 (ν C=N), 1492 (ν C=C in Ph), 988 and 920 (ν NO), (lit.[1] m.p. 164–169°). A ratio IIIa/IIIb was 0·6.

1,2-(α-*Ketotetramethylene*)*ferrocene oxime* (IV). A mixture of 1,2-(α-ketotetramethylene)ferrocene (1·00 g), hydroxylamine hydrochloride (0·85 g), KOH (0·30 g) and 95% EtOH (60 ml) was refluxed for 3·5 hr. The procedure was the same as in formylferrocene oxime. Benzene was used as solvent for extraction. The oxime band was separated into the first eluted portion (0·65 g) and residual portion (0·08 g). The former was recrystallized twice from benzene-hexane free from trace acid to give an oxime, red prisms, m.p. 132–133° (IVa). (Found: C, 62·44; H, 5·49; N, 5·08. $C_{14}H_{15}ONFe$ requires: C, 62·48; H, 5·62; N, 5·21%); IR spectrum (KBr; cm^{-1}): 3150 (ν OH), 1624 (ν C=N), and 924 (ν NO).

The oxime from the residual portion was repeatedly recrystallized from benzene-hexane free from trace acid to give orange red prisms, m.p. 110–111° (IVb). (Found: C, 62·34; H, 5·54; N, 5·16. $C_{14}H_{15}ONFe$ requires: C, 62·48; H, 5·62; N, 5·21%); IR spectrum (KBr; cm^{-1}): 3200 (ν OH), 1643 (ν C=N), and 942 (ν NO), (lit.[4] *anti*-isomer; m.p. 115–123°, *syn*-isomer; m.p. 118–124°). A ratio IVa/IVb was 11.

Acknowledgement- The authors wish to thank Mrs. Hirose of the Keio University for elemental analyses. This research was supported in part by the Grant-in-Aid for Scientific Research from the Ministry of Education (No. 387,168), which is gratefully acknowledged.

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