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SEPARATION AND CHARACTERIZATION OF DIASTEREOMERIC (η^4-DIENE)Fe(CO)$_3$ COMPLEXES CONTAINING CHIRAL AMIDE GROUPS

Saburo Nakanishi,* Hisashi Yamamoto, Yoshio Otsuji, and Hiroyuki Nakazumi
Department of Applied Chemistry, College of Engineering, University of Osaka Prefecture,
1-1 Gakuen-cho, Sakai, Osaka 593, Japan

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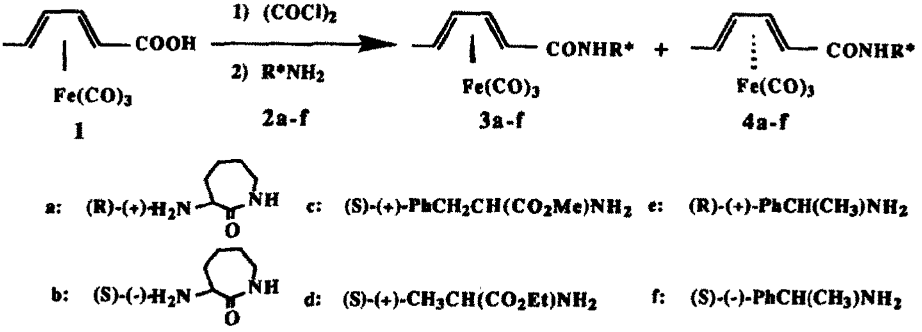
Abstract: Diastereomeric (η^4-N-substituted-2,4-hexadienamide)Fe(CO)$_3$ complexes having chiral amide groups are separated and characterized. Among the complexes, the amide complexes derived from (3R)- and (3S)-3-amino-hexahydro-2H-azepin-2-one are the most easily separated by fractional crystallization and column chromatography.

In recent years, much attention has been focused on the chemistry of planar chiral (η^4-diene) Fe(CO)$_3$ complexes because of potential applicability to asymmetric organic synthesis.[1] One of the most useful complexes as a chiral synthon is (η^4-2,4-hexadienal)Fe(CO)$_3$ which can be resolved by several methods.[2] However, utilization of (η^4-2,4-hexadienoic acid)Fe(CO)$_3$ **1** in the asymmetric synthesis has little been developed, and stereochemical features of **1** and its derivatives have little been elucidated. Further, only one resolution method of **1** has been hitherto exploited.[3] In the context of a program directed at utilizing **1** as a chiral synthon, we report here the preparation and structural characterization of (η^4-$CH_3CH{=}CHCH{=}CHCONHR^*$) Fe(CO)$_3$ complexes containing chiral amide groups. The effect of the chiral amide groups on the separation of the diastereomeric (η^4-$CH_3CH{=}CHCH{=}CHCONHR^*$) Fe(CO)$_3$ complexes is discussed.



Scheme

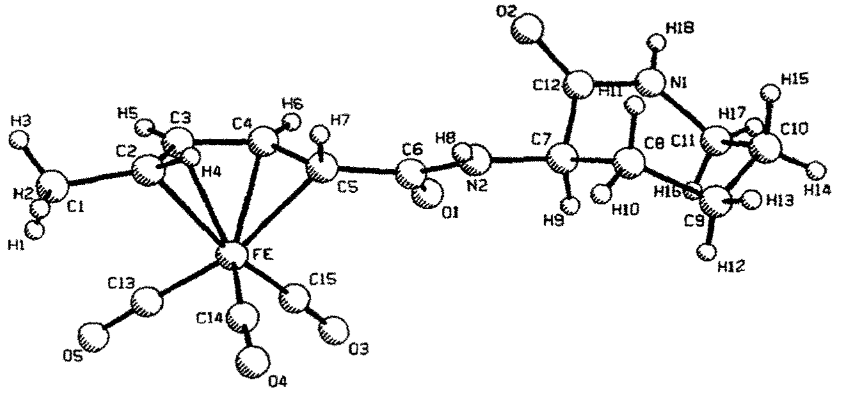
Reaction of (3R)-3-amino-hexahydro-2H-azepin-2-one **2a** with (η^4-2,4-hexadienoyl chloride) $Fe(CO)_3$, generated in situ by treatment of **1** with oxalyl chloride in dichloromethane, gave diastereomeric mixtures of amides **3a** and **4a** (1 : 1) in quantitative yields. Conversion of **1** to the acid chloride complex did not proceed by use of thionyl chloride and phosphorus trichloride in place of oxalyl chloride. The diastereomers thus obtained were separated by column chromatography on silica gel using dichloromethane and ethyl acetate as eluents. Similar treatment of **1** with chiral amines **2b-f** also afforded the corresponding diastereomeric amide complexes **3b-f** and **4b-f** which were separated in the same manner. The properties of the diastereomers are listed in Table 1. The structures of the complexes were confirmed by spectroscopy[4], X-ray analysis,[5] and optical rotation.[6] Molecular structure of **4a** is shown in Fig. 1.

Table 1. Properties of Iron Complexes

Iron complex	Yield/%$^{a)}$	mp/°C	$[\alpha]_D^{25b)}$	Rf value$^{c)}$
3a	41	240(dec)	-140.0	0.38
4a	33	176-177	+225.0	0.24
3b	42	175-176	-126.0	0.22
4b	31	240(dec)	+228.0	0.39
3c	36	106-107	-111.0	0.64
4c	34	157-158	+78.0	0.76
3d	32	93-94	-18.5	0.46
4d	31	100-102	+11.4	0.32
3e	30	oil	-98.9	0.45$^{d)}$
4e	38	164-166	+111.0	0.65$^{d)}$
3f	37	165-166	-108.0	0.65$^{d)}$
4f	32	oil	+97.7	0.45$^{d)}$

a) Isolated yield. b) Measured in methanol (c: 0.3-1.0).
c) Silica gel, CH_2Cl_2 : Ethyl acetate = 1 : 1. d) Silica gel, CH_2Cl_2 : Ethyl acetate = 9 : 1.

Some significant features of the diastereomeric complexes are worthy of remark: 1) Two pairs of diastereomers derived from **2a** and **2b** are air stable solid compounds which can be easily separated by usual fractional crystallization because of the large differences in their solubility, i.e., the isomers having higher melting points are less soluble. Further, the diastereomers **3a** and **4a** can be clearly characterized by the proton signals of H^5, H^6 and H^9 in their ^1H NMR spectra as shown in Fig. 2. **3b** and **4b** are also similarly discriminated. 2) The diastereomers derived from **2c** and **2d** were separated from each other by column chromatography with difficulty since there is only small difference in their Rf values. No remarkable differences were observed in their ^1H NMR spectra of **3c** and **4c**. 3) The diastereomers from **2e** and **2f** consist of a mixture of solid and oily compounds which were easily separated by chromatography, but it was difficult to further purify the oily compounds by distillation. 4) The optical rotations of **3a-f** all have negative values while those of **4a-f** all have positive values, regardless of the amines employed.



Selected bond lengths (l/Å) and angles (l/°): Fe-C(2) 2.169 (9), Fe-C(3) 2.059 (7), Fe-C(4) 2.044 (8), Fe-C(5) 2.130 (6), Fe-C(13) 1.771 (9), Fe-C(14) 1.797 (9), Fe-C(15) 1.790 (9), C(5)-C(6) 1.506 (9), C(6)-O(1) 1.217 (8), C(6)-N(2) 1.360 (8), C(13)-O(5) 1.163 (9), Fe-C(2)-C(3) 66.3 (4), C(2)-C(3)-C(4) 118.6 (8), C(3)-C(4)-C(5) 118.9 (6), C(4)-C(5)-C(6) 116.5 (6), C(5)-C(6)-N(2) 114.3 (6), C(5)-C(6)-O(1) 122.3 (7).

Fig. 1 Molecular structure of **4a**.

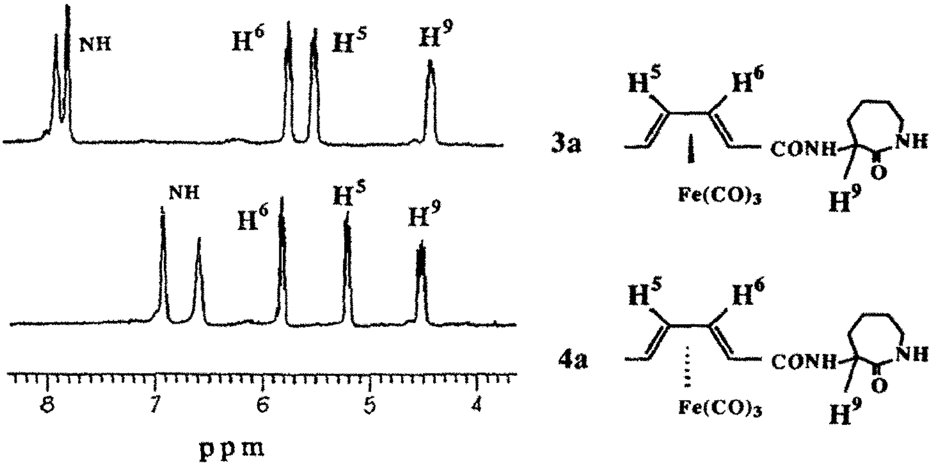


Fig. 2 ^{1}H NMR spectra of **3a** and **4a** in dimethylsulfoxide-d$_6$

References and Notes

1) Gree, R., *Synthesis*, **1989**, *5*, 341.

2) (a) Monpert, A., Martelli, J., Gree, R., Carrie, R., *Tetrahedron Lett.*, **1981**, *22*, 1961; (b) Frank-Neumann, M., Martina, D., Heitz, M. P., *J. Organomet. Chem.*, **1986**, *301*, 61; (c) Xu, M., Tran, C. D., *J. Chromatography*, **1991**, *543*, 233.

3) Musco, A., Palumbo, R., Paiaro, G., *Inorganic Chimica Acta*, **1971**, *5*, 157.

4) All new compounds were characterized by their spectral data. Selected data: **3a:** ^1H NMR (CD_3SOCD_3) δ 7.80-7.65 (m, 2H, NH), 5.65 (dd, J=8.1, 4.8 Hz, 1H, CH=), 5.42 (dd, J=8.1, 4.9 Hz, 1H, =CH), 4.36-4.27 (m, 1H, NCHCO), 3.23-2.95 (m, 2H, CH_2N), 1.90-1.15 (m, 8H, CH_2, =CH), 1.38 (d, J=6.2 Hz, 3H, CH_3). ^{13}C NMR (CD_3SOCD_3) δ 211.67, 211.49 (CO), 174.23, 174.13 (NCO), 87.49, 82.50, 59.01, 51.67 (CH=), 51.57 ($N\underline{C}CO$), 40.61 (NCH_2), 30.91, 28.79, 27.55 (CH_2), 18.84 (CH_3); **4a:** ^1H NMR (CD_3SOCD_3) δ 6.80 (br s, 1H, NH), 6.09 (br s, 1H, NH), 5.80 (dd, J=7.8, 5.0 Hz, 1H, CH=), 5.20 (dd, J=8.4, 5.0 Hz, 1H, =CH), 4.50 (dd, J=9.8, 6.0 Hz, 1H, NCHCO), 3.30-3.20 (m, 2H, CH_2N), 2.12-1.23 (m, 7H, CH_2, =CH), 1.45 (d, J=6.0 Hz, 3H, CH_3), 1.04 (d, J=7.9 Hz, 1H, =CHCO). ^{13}C NMR (CD_3SOCD_3) δ 210.63 (CO), 175.78, 169.59 (NCO), 87.70, 82.10, 58.55, 52.19 (CH=), 49.82 ($N\underline{C}CO$), 42.12 (NCH_2), 31.44, 28.86, 27.91 (CH_2), 19.13 (CH_3).

5) Crystallographic details : for **4a**; $C_{15}H_{18}N_2O_5Fe$, F. W. =362.16. **4a** was crystallized in space group $P2_12_12_1$ with lattice parameters: a=13.361(1) Å, b=16.806(6) Å, c=7.571 (4) Å, V=1700 (2) Å^3, Z=4, Dcalc=1.415 g/cm^3. From a crystal dimensions 0.800 x 0.200 x 0.250 mm, 2630 independent reflections were measured over a 2θ range of 6-58.2° using Mo-Kα radiation (λ=0.71069 Å) at 23 °C. The Fe atom was found from a three dimensinonal Patterson map, and the nonhydrogen atoms were lacated by subsquent difference Fourier syntheses. All hydrogen atoms were included at calculated positions. Full matrix least-squares refinement using 1355 reflections with $I>3.00\ \sigma\ (I)$ converged to final agreement factors R=0.050, Rw=0.038 with GOF=1.98.

6) Acid hydrolysis of **4a** and **4b** having (2S, 5R) configuration gave the complex **1** which had a positive sign of optical rotation. However, racemization and decomposition of **1** occurred to some extent during the hydrolysis of the complexes. For example, ee of the recoverd **1** from **4a** was 82 % which was calculated based on its $[\alpha]_D$ using the literature value.[3] Structures of the other complexes were identified by the sign of the optical rotation of the recovered complex **1** and also by comparison with an authentic sample of the complex **1**.