J. Chem. Research (S), 1999, 578–579†

Preparative-scale HPLC Resolution of Metallacyclic η^3-Allyltricarbonyliron Complexes and Determination of the Absolute Configuration by X-Ray Crystal Structure Analysis†

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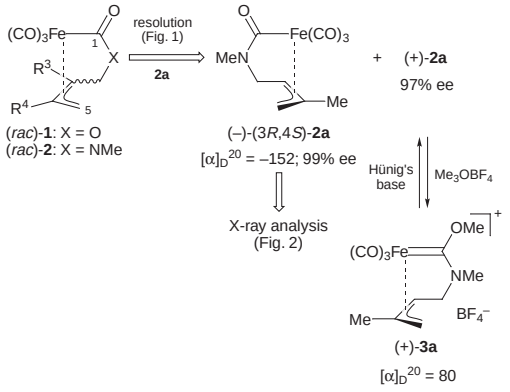
Racemates of (η^3-allyl)tricarbonyliron lactone complex $Fe(CO)_3\{\eta^1{:}\eta^3\text{-}C(O)XCH_2CHCMeCH_2\}$ **1a** (X = O) and (η^3-allyl)tricarbonyliron lactam complex **2a** (X = NMe) are resolved on a preparative scale by HPLC on cellulose tris(3,5-dimethylphenyl)carbamate/silica gel RP-8 and the absolute configuration of (−)-**2a** is determined by X-ray crystal structure analysis.

Iron complexes bearing an unsymmetrically substituted η^3-allyl ligand exhibit planar chirality. Tethering the π-ligand to the metal gives rise to metallacyclic complexes of particularly high conformational rigidity, which is a prerequisite for their use as effective stereocontrolling reagents. Ferralactones **1**,[1–4] which can be prepared from iron carbonyls and either vinyl oxiranes, or vinyl cyclic sulfites



Scheme 1

or but-2-ene-1,4-diols, have been extensively used for the establishment of new stereogenic centres during reactions of prochiral functional groups in suitable side-chains.[5] The congenerous ferralactams **2** are available by aminolysis of **1**, or from vinyl aziridines, or from 1-aminobut-2-en-4-ols.[3,4] By O-alkylation of **1** and **2**, the corresponding carbene complexes are obtained, for example the aminooxo complexes **3** from **2**. These can also undergo diastereoselective reactions, for instance with prochiral enolates which attack at the end of the allyl ligand (*i.e.* on C5).[6] To fully exploit the stereoinductive power of these ferracyclic auxiliaries it is necessary to obtain them in optically pure form. Ley *et al.*[7] described the preparation of enantiomerically pure derivatives of **1** from chiral epoxides and diiron nonacarbonyl by subsequent chromatographic separation of the resulting diastereoisomers, as well as their application in organic synthesis.[7] This procedure, however, is limited to epoxides bearing additional stereogenic centres at certain positions. Although chromatography on chiral stationary phases has been employed only more recently for the enantioseparation of organometallic compounds,[8] ferracycles **1**–**3** are predicted to be ideal candidates, as they are air- and moisture-stable and can be subjected to normal chromatography on silica gel without noticeable decomposition.

We obtained best results for the preparative resolution of racemic ferra-lactone **1a** and -lactam **2a** on microcrystalline cellulose tris(3,5-dimethylphenyl)carbamate on spheric silica gel RP-8 (30 μm)[9] which is similar to Chiralcel-OD phases. The HPLC column (25 × 300 mm) was thermostated at 15 °C and eluted with 5% propan-2-ol in hexane at a flow rate of 0.5–2 mL min^{-1}. The system was used in cyclic mode, *i.e.* the eluate from the column was repeatedly fed on it again. The progress of the enantioseparation was monitored by UV (absorption at 254 nm) using a polarimeter with a flow cell. The enantiomeric purity was deduced from analytical HPLC on Daicel Chiralcel-OD-H.

Enantioseparation of (±)-**1a** (R^3 = Me, R^4 = H) was performed with 80 mg. Baseline separation was achieved

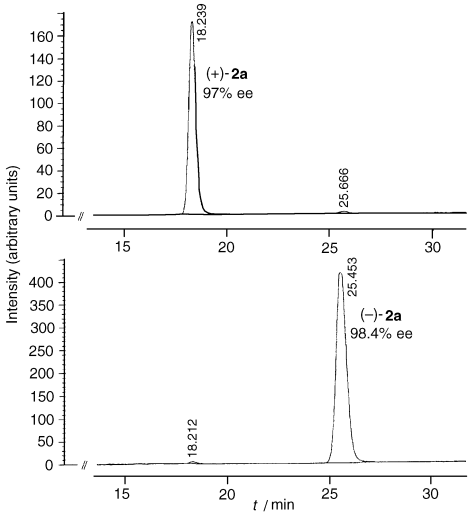


Fig. 1 Analytic HPLC of the two fractions (top: eluted first; bottom: eluted second) of **2a** obtained after two-fold preparative HPLC enantioseparations. Analytic conditions: 4.6 × 250 mm Chiralcel-OD-H (Daicel) column; eluted with 10% propan-2-ol in hexane, flow rate 0.5 mL min^{-1}; detection by UV at 230 nm. 5% of a regioisomer (two enantiomers; not shown here) were also removed in the first run.

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† This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

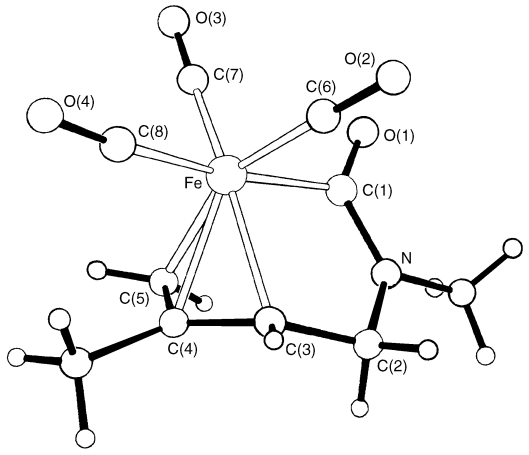

Fig. 2 Molecular structure and atom numbering of (−)-**2a**; selected bond lengths (Å) and angles (°): Fe–C1, 2.028(4), Fe–C3, 2.101(4), Fe–C4 2.089(4), Fe–C5 2.158(4), Fe–C6 1.768(5), Fe–C7 1.811(5), Fe–C8 1.827(4), C1–O1 1.231(6), C1–N 1.350(6), C3–C4 1.405(6), C4–C5 1.414(7); O1–C1–N 121.2(4), C3–C4–C5 120.1(4), C1–Fe–C3 82.8(2), C3–Fe–C4 39.2(2), C1–Fe–C8 173.1(2), Fe–C1–O1 125.0(3)

after five cycles (24 h). The enantioselectivity coefficient was $\alpha = 1.07$, the capacity factors $k'_1 = 4.21$, $k'_2 = 4.51$ and the resolution $R_S = 1.29$.[10] The laevorotatory isomer was eluted first with an enantiomeric excess of 95% and showing a specific rotation of $[\alpha]_D^{20} = -28$ ($c = 0.63$, CH_2Cl_2).

Resolution of 150 mg of (±)-**2a** ($R^3 = H$, $R^4 = Me$) was achieved after only two cycles (Fig. 1). The capacity factors were $k'_1 = 2.15$, $k'_2 = 3.40$, the selectivity factor $\alpha = 1.58$, and the resolution $R_S = 8.5$. For the enantiomer eluted second with 99% ee and showing an $[\alpha]_D^{20} = -152$ ($c = 1.0$; CH_2Cl_2), the absolute configuration could be assigned as $(3R, 4S)$[11] by an X-ray single crystal structure analysis (Fig. 2). To assure retention of the configuration during formation of the corresponding carbene complexes, the dextrorotatory enantiomer (+)-**2a**, eluted first, was alkylated with $(CH_3)_3OBF_4$ to give the aminooxocarbene complex (+)-**3a** showing a specific rotation of $[\alpha]_D^{20} = +80$ $c = 0.8$, CH_2Cl_2). (+)-**3a** was then demethylated[6a] with Hünig's base to give back identical (+)-**2a** without racemization and showing a specific rotation of $[\alpha]_D^{20} = 150$ ($c = 0.7$, CH_2Cl_2).[12]

These results show that HPLC on chiral cellulose tris(3,5-dimethylphenyl)carbamate/silica gel RP-8 phases is a suitable means for the resolution of neutral ferracyclic complexes of types **1** and **2** in preparative quantities and reasonable spells of time. These investigations are ongoing towards enantioseparations of various other types of oligonuclear and cationic ferracycles bearing π-ligands.

Experimental

(±)-**1a** and (±)-**2a** were prepared from diiron nonacarbonyl (ABCR), 2-methyl-2-vinyl-oxirane (Aldrich) and methylamine (Fluka) as described in the literature.[3b,5a] (+)-**3a**[13] was prepared by alkylation of (+)-**2a** with trimethyloxonium tetrafluoroborate (Aldrich) according to a protocol published earlier.[6a]

*Crystal Data for (−)-***2a**—Clear, pale yellow single crystals were obtained by slowly (cooling a solution of (−)-**2a** in diethyl ether to −30 °C; $C_{10}H_{11}FeNO_4$, $M = 265.05$, crystal size $0.40 \times 0.30 \times 0.30$ mm, $a = 8.704(1)$, $b = 11.233(2)$, $c = 11.405(2)$ Å, $V = 1115.1(3)$ Å^3, $T = 173$ K, $D_c = 1.579$ g cm^{-3}, $Z = 4$, orthorhombic, space group $P2_12_12_1$, Nonius Mach 3 diffractometer, $\lambda = 0.71073$ Å, θ-range 2.54–26.31 °; $\omega-\theta$-scans, index ranges $-10 \le h \le 10$, $-14 \le k \le 14$, $-14 \le l \le 14$, 2638 collected reflections, 2171 independent reflections [$I > 2\sigma(I)$], 145 refined parameters, absorption correction (Ψ-scans). Structure solution: direct methods (SHELXS 86), structure refinement: full-matrix least squares on F^2 (SHELXL93), H (riding model) not included into least-squares refinement, $R1 = 0.0600$ [$I > 2\sigma(I)$], $wR2 = 0.1530$ (all data), largest diff. peak and hole 2.305 and −0.971e Å^{-3}, absolute structure (Flack) parameter 0.04(3). Full crystallographic details, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Research (S)*, 1999, Issue 1 , Any request to the CCDC for this material should quote the full literature citation and the reference number 423/24.

See http://www.rsc.org/suppdata/jc/1999/578/ for crystallographic files in .cif format.

Received, 19th April 1999; Accepted, 11th June 1999
Paper E/9/03070K

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9 Developed by Prof. A. Werner, University of Vienna; not commercially available yet.
10 The capacity factors k'_1 and k'_2 reflect the partitioning of the substrate between the phases, the separation factor α is a measure of the separation selectivity; for a definition see: W. H. Pirkle and J. M. Finn, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1983, vol. 1, p. 87.
11 For the assignment of the descriptors of the absolute configuration each carbon atom of the allyl unit was considered to be σ-bound to the iron centre.
12 ^{1}H NMR shift analysis proved to be impracticable for the determination of enantiomeric purity of **3a**. Treatment of a racemic sample in $CDCl_3$ with $Eu(hfc)_3$ (hfc = heptafluoropropylhydroxymethylene D-camphorate) did not lead to any signal separation.
13 **3a**: mp. 121°C; R_f ($CH_2Cl_2-CH_3CN$, 1:1) 0.70; ν_{max}/cm^{-1} 3040, 2930, 2840, 2020, 1985, 1970, 1445, 1390, 1240; δ_H ($CDCl_3$, Me_4Si) 2.16 (3 H, s, 4-Me), 2.83 (3 H, s, NMe), 2.93 (1 H, d, $J_{5en,5ex}$ 2.1, 5-H^{en}), 3.63 (1 H, dd, $J_{2en,2ex}$ 13.7, $J_{2en,3}$ 2.1, 2-H^{en}), 3.89 (1 H, dd, $J_{2en,2ex}$ 1.37, $J_{2en,3}$ 8.2, 2-H^{ex}), 3.91 (1 H, d, $J_{5en,5ex}$ 2.1, 5-H^{ex}), 4.41 (3 H, s, OMe), 4.84 (1 H, dd, $J_{3,2ex}$ 8.2, $J_{2en,3}$ 2.1, 3-H); δ_C($CDCl_3$, Me_4Si) 26.9 (4-Me), 35.7 (NMe), 55.1 (C-5), 63.1 (C-2), 65.6 (OMe), 70.7 (C-3), 118.8 (C-4), 203.9, 206.3, 207.2 (FeCO), 222.3 (C-1).