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STEREOSELECTIVE ROUTES TO ENDO- AND EXO-1,2-(α-AMINOTETRAMETHYLENE)-FERROCENE

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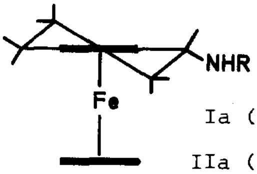
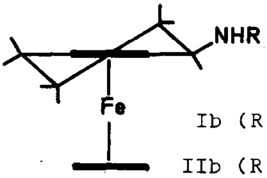
The stereochemical result from the syntheses of 1,2-(α-aminotetramethylene)-ferrocene (Ia,b) hitherto reported[1-3] has never been investigated and the products have not been unambiguously characterized. In this paper methods for the specific preparation of the endo- (Ia) and exo- (Ib) stereoisomers are described.



Ia (R = H)
IIa (R = Ac)



Ib (R = H)
IIb (R = Ac)

Oximation of 1,2-(α-ketotetramethylene)-ferrocene[4,5] (III) has recently been shown[6] to give a mixture of the anti- (IVa) and syn- (IVb) isomers of the oxime with IVa/IVb≈11. In a typical experiment, this mixture IVa,b (1.08 g, 4 mmol) was dissolved in boiling anhydrous ethanol (10 ml) and reduced with an excess of metallic sodium, the oil-bath temperature being raised to max. 130° during the reaction (3-4 hrs). After work-up (extraction of an ether-solution of the products with 0.5 M HCl), 0.81 g of crude amine (contaminated with oxime) was obtained. Chromatography on neutral Al_2O_3 with benzene-ether (2:1) removed the oxime and the remaining yellow band was eluted with ether-methanol (20:1) giving pure Ia in 55% yield. Dissolution in anhydrous ether and precipitation with HOAc gave the hydroacetate, m.p. 147-8°; N-acetylation afforded the acetamide (IIa), m.p. 145°. IIa: NMRδ_{TMS}($CDCl_3$) ppm 6.15(NH), 4.5(m,α-CH), 4.2-3.9(m,C_5H_3), 4.1(s,C_5H_5), 2.8-1.2 (m,CH_2), 2.08(s,CH_3); MS m/e (rel int) M^{+}+1 298(21), M^{+} 297(100), M^{+}-2 295 (6.4).

Reduction of IVa,b with complex metal hydrides favours the formation of Beckmann-rearranged products. Use of sodium bis-(2-methoxyethoxy)-aluminium hydride in benzene gave 1H-tetrahydro-2,3,4,5-ferroceno(b)azepine, m.p. 125-6° (lit.[2] 123-6°) in agreement with earlier results with LAH.[2,7] No primary amine was isolated, however.

Reduction of III with sodium bis-(2-methoxyethoxy)-aluminium hydride in anhydrous benzene afforded the isomeric alcohols[8,9] Va (endo-) and Vb (exo-) in a

90% over-all yield. Both Va and Vb gave the same azide upon reaction with hydrazoic acid in benzene - acetic acid at 25°. This is undoubtedly the *exo*-azide (VI), resulting in both cases from an *exo*-attack of azide-nitrogen upon the incipient common α-ferrocenylcarbonium ion. This type of stereochemical control is well documented.[9-12] 2.3 g (9 mmol) of V gave an almost quantitative yield of VI which was dissolved in methanol (150 ml) and hydrogenated[13] with 0.5 g PtO_2 added at 60 p.s.i. for 2 hrs. 2.03 g (88% from V) of the amine Ib was isolated. Hydroacetate m.p. 163-5°, acetamide (IIb) m.p. 155-5.5°. IIb: NMR δ_{TMS}($CDCl_3$) ppm 5.9(NH), 5.1(m,α-CH), 4.2-3.9(m,C_5H_3), 4.0(s,C_5H_5), 2.8-1.2(m,CH_2), 1.86(s,CH_3); MS m/e (rel int) M^++1 298(20), M^+ 297(100), M^+-2 295(6.5).

Catalytic hydrogenation of azides to primary amines are known to occur with retention of the configuration at the α-carbon atom.[14] Consequently, the assignment of Ib to the product obtained from VI is unequivocal. The NMR chemical shift values give further evidence: the *endo*-pseudo-axial α-proton in IIb, lying in the ferrocene deshielding region,[15] is 0.6 ppm more downfield than the *exo*-pseudo-axial α-proton in IIa.

The reason for the specific formation of Ia by dissolving metal reduction of IV seems to be due to a protonation at the α-carbanionic centre from the favoured *exo*-side by the solvent in a product-determining step of the reaction.

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