

SYNTHESIS OF CHIRAL *N*-(FERROCENYLALKYL)HYDROXYLAMINES

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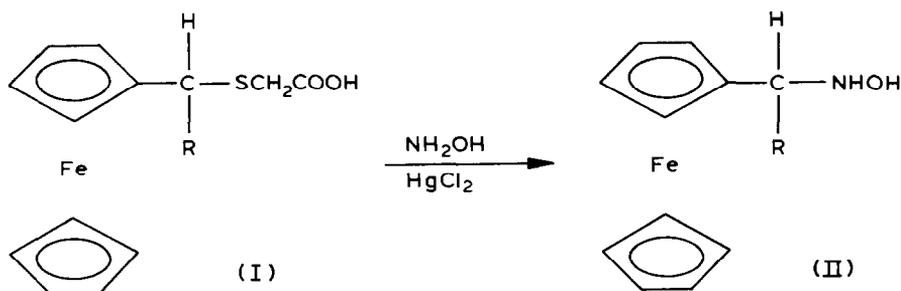
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Summary

The preparation of chiral *N*-(ferrocenylalkyl)hydroxylamines from *S*-(ferrocenylalkyl)mercaptoethanoic acids is reported. They are the first hydroxylamine derivatives with an asymmetric carbon atom directly attached to the nitrogen atom, and are potentially useful as chiral templates in asymmetric synthesis.

Introduction

To our knowledge no chiral hydroxylamine derivatives have previously been reported in which a hydroxylamine group is attached to an asymmetric carbon. Such compounds are potentially useful in the construction of chiral templates for asymmetric syntheses. We now describe the preparation of the chiral hydroxylamine derivatives IIa–IIc from the corresponding mercaptoethanoic acid derivatives Ia–Ic.



(Ia, IIa : R = Me ;
 Ib, IIb : R = Prⁱ ;
 Ic, IIc : R = Bu^t)

Results

The racemic *S*-1-ferrocenylalkylmercaptoethanoic acids (I) are readily made by the method of Herrmann and Ugi [1]. The resolution of Ia with ephedrine has been described by Misterkiewicz and Ratajczak [2], while Ib [1,3] and Ic are best resolved with 1-phenylethylamine.

The conversion of Ia–Ic into IIa–IIc was achieved by reaction with NH_2OH and mercuric chloride in aqueous acetonitrile. Analogous syntheses of the corresponding alcohols and amines have been described previously [2,4]. Such $\text{S}_{\text{N}}1$ reactions via an α -ferrocenyl carbocation proceed with complete retention of configuration [5].

The hydroxylamine derivatives IIa–IIc may be used as chiral templates for various asymmetric syntheses.

Experimental

S-[1-Ferrocenyl-2,2-dimethylpropyl]mercaptoethanoic acid (Ic)

Racemic Ic was prepared by the procedure described for the synthesis of Ia and Ib [1]. Yield: 82%, m.p. 108–110°C. Found: C, 59.17; H, 6.52. $\text{C}_{17}\text{H}_{22}\text{FeO}_2\text{S}$ (346.25) calcd.: C, 58.97; H, 6.40%.

$^1\text{H-NMR}$ (δ (ppm) in CDCl_3 , 60 MHz) 0.91 (s, 9H) 3.34 (s, 1H) 3.50 (s, 2H) 4.05 (m, 4H) 4.18 (s, 5H) 9.50 (s, br, 1H).

Resolution of Ib and Ic

R-(+)-1-Phenylethylamine (200 mmol) was added to a solution of 200 mmol of racemic acid Ib or Ic in 200 ml of methanol at 30°C. The mixture was allowed to cool to room temperature overnight, the crystals were filtered off, and the acid liberated from the salt with 10% aqueous NaOH. The procedure was repeated with appropriate quantities of amine until the final value of the optical rotation was reached. Ib: $[\alpha]_{\text{D}}^{25} - 68.2^\circ$ ($c = 1$, methanol); Ic: $[\alpha]_{\text{D}}^{25} - 11.0^\circ$ ($c = 1$, methanol).

Ferrocenylalkylhydroxylamines (II)

A solution of 4.0 mmol of the mercaptoethanoic acid derivative I and 90.0 mmol (6.25 g) of hydroxylamine hydrochloride in 25 ml of a mixture of acetonitrile and 2.5% aqueous NaOH (5/1) was cooled to -10°C , and 8.0 mmol (2.17 g) of finely powdered HgCl_2 were added. The mixture was stirred at -10°C for 10 minutes, then the precipitate was filtered off and the filtrate extracted with 50 ml of Et_2O . The ether extract was washed successively with 10% aqueous NH_4Cl , water and saturated sodium carbonate solution, then dried (Na_2SO_4) and evaporated. The residue was recrystallized from hexane.

IIa: yield 26%; m.p. 100°C, $[\alpha]_{\text{D}}^{25} - 15.9^\circ$ ($c = 1$, benzene). Found: C, 60.04; H, 6.22; N, 5.12. $\text{C}_{12}\text{H}_{15}\text{FeNO}$ (245.10) calcd.: C, 58.80; H, 6.17; N, 5.71%. $^1\text{H NMR}$ (δ (ppm), in CDCl_3 , 60 MHz): 1.47 (d, 3H) 4.10 (m, 9H) 4.57 (qua, 1H) 5.28 (s, 2H).

IIb: yield 37%; m.p. 112°C, $[\alpha]_{\text{D}}^{25} - 80.3^\circ$ ($c = 1$, benzene). Found: C, 61.71; H, 7.19; N, 5.00. $\text{C}_{14}\text{H}_{19}\text{FeNO}$ (273.16) calcd.: C, 61.60; H, 7.01; N, 5.13%. $^1\text{H NMR}$ (δ (ppm) in CDCl_3 , 60 MHz): 0.78 (dd, 6H) 2.23 (m, 1H) 3.58 (d, 1H) 4.12 (m, 4H) 4.17 (s, 5H) 5.32 (s, 2H).

IIc: yield 43%; m.p. 119–120°C $[\alpha]_{\text{D}}^{25} - 106.4^\circ$ ($c = 1$, benzene). Found: C, 62.88; H, 7.40; N, 4.61. $\text{C}_{15}\text{H}_{21}\text{FeNO}$ (287.18) calcd.: C, 62.74; H, 7.37; N, 4.88%.

^1H NMR (δ (ppm) in CDCl_3 , 60 MHz): 0.85 (s, 9H) 3.28 (s, 1H) 4.10 (m, 4H) 4.24 (s, 5H) 5.30 (s, 2H)

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