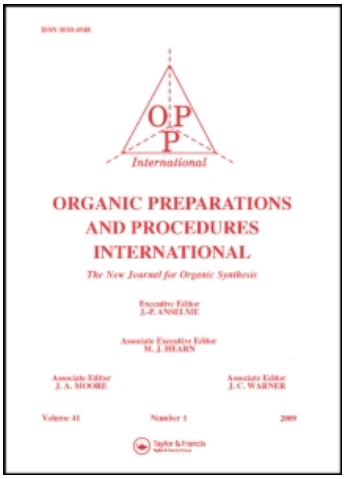

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AN IMPROVED PROCEDURE FOR THE PREPARATION OF 1-FERROCENYL-1-PHENYLMETHYLAMINE

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AN IMPROVED PROCEDURE FOR THE PREPARATION OF 1-FERROCENYL-1-PHENYLMETHYLAMINE

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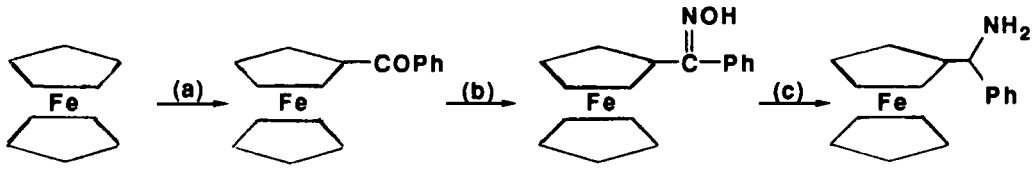
Ferrocenylalkylamines, widely recognized as useful chiral auxiliaries in organic synthesis, have been employed as starting materials for asymmetric homogenous hydrogenations[1] and used in asymmetric four-component condensations;[2] some other applications have been found as well.[3] Over the past two decades, several methods of preparation of primary ferrocenylalkylamines have been developed,[4-8] some of them leading directly to optically active products (chiral pool syntheses[9]). Resolution procedures have been also described.[4,6,7] Although several syntheses of ferrocenylalkylamines have been reported, new methods are still needed because of the great importance of these compounds. The known syntheses are either multistep, tedious procedures with low total yields or quite capricious three-component condensations, useful only in specific cases such as in the preparation of ferrocenylisobutyrylamine.[8]

1-Ferrocenyl-1-phenylmethylamine seems to be one of the most promising chiral ferrocenylalkylamines. The known syntheses of this compound all proceed via reduction of benzoylferrocene and conversion to the amine. Although they suffer either from low overall yields (59% and 25% for the last step[10,11]) or lack of experimental details,[12] the very convenient resolution procedure of Allenmark et al. prompted us to improve the procedure for the synthesis of the racemic compound.



a) $PhCOCl, AlCl_3$ b) $NH_2OH \cdot HCl, Py$ c) $NaBH_4, NiCl_2 \cdot 6H_2O$

Benzoylferrocene[4] was converted to its oxime (pure by TLC), in nearly quantitative yield (97%) and reduced with sodium borohydride-nickel(II) chloride hexahydrate in methanol[13] in 81% yield. The crude 1-ferrocenyl-1-phenylmethylamine was sufficiently pure to be resolved . Our method offers a ready access to racemic 1-ferrocenyl-1-phenylmethylamine. Cheap and easily

available reagents and starting material (ferrocene) are employed and the desired product is produced in high overall yield (63%).

EXPERIMENTAL SECTION

All reagents and solvents were commercially available (Aldrich). Melting points are uncorrected. Mass spectra (FD) were recorded on a Varian MAT 711 apparatus. IR spectra were taken on a Jena-Zeiss IR apparatus. ^{1}H NMR spectra were recorded on a Varian EM 360 instrument at 60 MHz.

Benzoylferrocene Oxime.- Hydroxylamine hydrochloride (20.85 g, 300 mmoles) was added to a solution of 8.76 g (30 mmoles) benzoylferrocene (mp. 108-110°, lit.[14] 111°) in pyridine (100 mL). The reaction mixture was stirred for 48 hrs at room temperature and poured onto crushed ice (500 g). After several hours, the product was collected, washed thoroughly with water and dried. Benzoylferrocene oxime, mp. 151-152°, was obtained in 97% yield (8.94 g). An analytically pure sample, mp. 157-158°, lit.[15] 158-159°, reported crude yield 48%, was obtained by recrystallization from benzene-hexane.

IR (KBr): 3300 cm^{-1}(OH). ^{1}H NMR ($CDCl_3$): δ 4.10-4.50 (m, 9H, C_5H_5, C_5H_4), 4.75 (s, 1H, OH), 7.50 (s, 5H, C_6H_5).

1-Ferrocenyl-1-phenylmethylamine.- Sodium borohydride (1.9 g, 50 mmoles) was added portionwise to a slurry of benzoylferrocene oxime (1.52 g, 5 mmoles) and $NiCl_2 \cdot 6H_2O$ (2.85 g, 10 mmoles) in methanol (50 mL). The reaction mixture was stirred overnight at room temperature and the solvent was removed under reduced pressure. The residue was then diluted with saturated $KHSO_4$ solution (30 mL) and the solution was stirred until the black color changed into light green. The slurry was then filtered and the filtrate washed with ether (3 x 50 mL). The aqueous phase was neutralized with aqueous ammonia and extracted with ether (3 x 50 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure to yield 1.18 g, (81%) of 1-ferrocenyl-1-phenylmethylamine as an oil, which solidified on standing; it was sufficiently pure (at least 90% by NMR) for most purposes. An analytically pure sample can be obtained using flash chromatography (silica gel, benzene-ethyl acetate 1:1), mp. 77-78°, lit.[10] 80°.

MS (FD, 70 EV): m/e 291. IR (film): 3350 cm^{-1} (NH_2). ^{1}H NMR ($CDCl_3$): δ 1.50 (s, 2H, NH_2), 3.90-4.23 (m, 9H, C_5H_5, C_5H_4), 4.73 (s, 1H, CH), 7.20 (s, 5H, C_6H_5).

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