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DIRECT CONVERSION OF (+)-N,N-DIMETHYL-α-FERROCENYLBENZYLAMINE INTO (-)-α-FERROCENYLBENZYLALCOHOL

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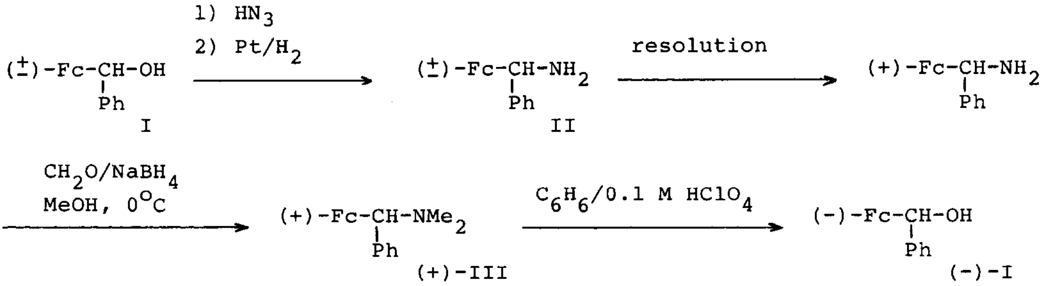
During our investigations on the chemical and stereochemical behaviour of α-ferrocenylcarbenium tetrafluoroborates as synthetic intermediates,[1,2] a simple and convenient route to optically active α-ferrocenylbenzylalcohol (I) was found. (+)-α-Ferrocenylbenzylamine (II), obtained by resolution of the racemic compound with dibenzoyl-L-(+)-tartaric acid in ethanol,[2] was converted to (+)-N,N-dimethyl-α-ferrocenylbenzylamine (III) by the use of formaldehyde/sodium borohydride in methanol at 0°C. A solution of (+)-III (1.0 mmol, $[\alpha]_D^{25}$ = +104(MeOH, c.0.5), 95% optically pure) in benzene (50 ml) was thoroughly mixed with aqueous 0.1 M perchloric acid (50 ml) at 25°C for 2.5 hrs, then the reaction mixture was made alkaline and the benzene layer evaporated. Chromatography on neutral alumina gave only two bands, consisting of (+)-III (0.59 mmol, $[\alpha]_D^{25}$ = +93.8(MeOH, c.0.7)) and (-)-I (0.37 mmol, $[\alpha]_D^{25}$ = -78.4(C_6H_6, c.0.4)), respectively. By rechromatography the optical rotation of (+)-III was increased to $[\alpha]_D^{25}$ = +102(MeOH, c.0.7), showing that no significant racemization of the starting material has occurred.

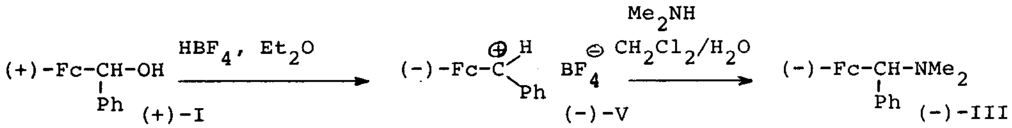


$$(\pm)\text{-Fc-}\underset{\substack{|\\ \text{Ph}}}{\text{CH}}\text{-OH}\ \ \text{I} \xrightarrow[]{\text{1) HN}_3\ \ \text{2) Pt/H}_2} (\pm)\text{-Fc-}\underset{\substack{|\\ \text{Ph}}}{\text{CH}}\text{-NH}_2\ \ \text{II} \xrightarrow{\text{resolution}} (+)\text{-Fc-}\underset{\substack{|\\ \text{Ph}}}{\text{CH}}\text{-NH}_2$$

$$\xrightarrow[\text{MeOH, 0}^\circ\text{C}]{\text{CH}_2\text{O/NaBH}_4} (+)\text{-Fc-}\underset{\substack{|\\ \text{Ph}}}{\text{CH}}\text{-NMe}_2\ \ (+)\text{-III} \xrightarrow{\text{C}_6\text{H}_6\text{/0.1 M HClO}_4} (-)\text{-Fc-}\underset{\substack{|\\ \text{Ph}}}{\text{CH}}\text{-OH}\ \ (-)\text{-I}$$

A determination of the enantiomeric purity of the product (-)-I was performed by PMR-technique. Addition of the chiral lanthanide shift reagent, tris-(3-trifluoromethylhydroxymethylene-d-camphorato)-europium (28 mg), to a deuteriochloroform solution of (-)-I (190 mg) gave a spectrum where a good separation of the resonance signals from the enantiotopic methine protons was obtained. An accurate determination of peak areas yielded a ratio 92.5/7.5 corresponding to 85% optical purity and a maximum rotation of I, $[\alpha]_D^{25} = \pm 92(C_6H_6, c.0.5)$, may be calculated. Consequently, an optical yield of 89% for the conversion (+)-III ⟶ (-)-I by this method is found. In view of the ease with which II can be resolved into enantiomers, and the fact that optically active III is recovered by chromatography without any racemization, this procedure constitutes a very convenient way to obtain optically active I.

Previously, we have used the method of quarternization of III to the corresponding methiodide (IV) with subsequent hydrolysis according to a method used by Ugi *et al.*[3] From our determination of the maximum rotation of I it follows that the procedure of converting III into I via IV has been accompanied by much more racemization than in the present case. However, if the following transformations earlier described[2] are considered, an 84% optical yield for the conversion (+)-I ⟶ (-)-III via isolation of the crystalline α-ferrocenylbenzylium tetrafluoroborate (-)-V is found.



We therefore want to call attention to the fact that optically active salts such as V, prepared from the now readily available optical isomers of I, can be used as chiral synthons from which a variety of optically active compounds may be prepared in high optical yields.

References

1. S. Allenmark, Tetrahedron Lett., 371 (1974).
2. S. Allenmark, K. Kalén and A. Sandblom, Chem. Scr., 7, 97 (1975).
3. G. Gokel, D. Marquarding and I. Ugi, J. Org. Chem., 37, 3052 (1972).