

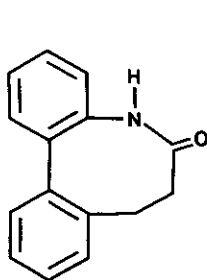
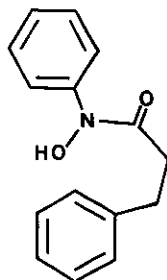
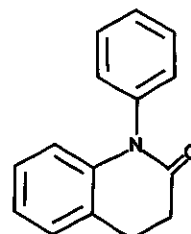
A REVISED STRUCTURE FOR THE PRODUCT OF THE ACID CATALYZED
REARRANGEMENT OF N-(1-PHENYLPROPIONYL)-N-PHENYLHYDROXYLAMINE

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Abstract - The reaction of N-(1-phenylpropionyl)-N-phenylhydroxylamine 2 with trifluoromethanesulphonic acid at 80°C gives the 1-phenyl-1,2,3,4-tetrahydroquinolin-2-one 3. For this compound a 5,6,7,8-tetrahydro-dibenz[b,d]azocin-6-one 1 has been previously reported. Spectroscopic evidences support the proposed structure.

Our interest in the structure-biological activity relationship of heterocyclic seven- and eight-membered ring compounds containing nitrogen¹⁻⁴ attracted our attention on the synthesis of azocine derivatives.

The synthesis of 5,6,7,8-tetrahydrodibenz[b,d]azocin-6-one 1 by a simple ring closure of N-(1-phenylpropionyl)-N-phenylhydroxylamine 2 catalyzed by trifluoromethanesulphonic acid (TFSA) has been reported a few years ago⁵. However in our hands the reaction of 2 with TFSA gave as main reaction product a compound whose physical characteristics were those previously reported, but whose ir and nmr spectral parameters arised severe doubts on the correctness of the proposed eight-membered ring structure.

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The reaction of 2 with TFSA was carried out as reported⁵ by dissolving the amide into the acid and raising the temperature to 80°C for 4 h. The reaction mixture, diluted with dichloromethane, was neutralized with aqueous sodium carbonate, and separated by column chromatography (SiO₂, eluant light petroleum- diethyl ether 2-8 v.v.). We obtained a compound (55% yield) with a melting point of 121-122°C that we believe is the 1-phenyl-1,2,3,4-tetrahydroquinolin-2-one 3.

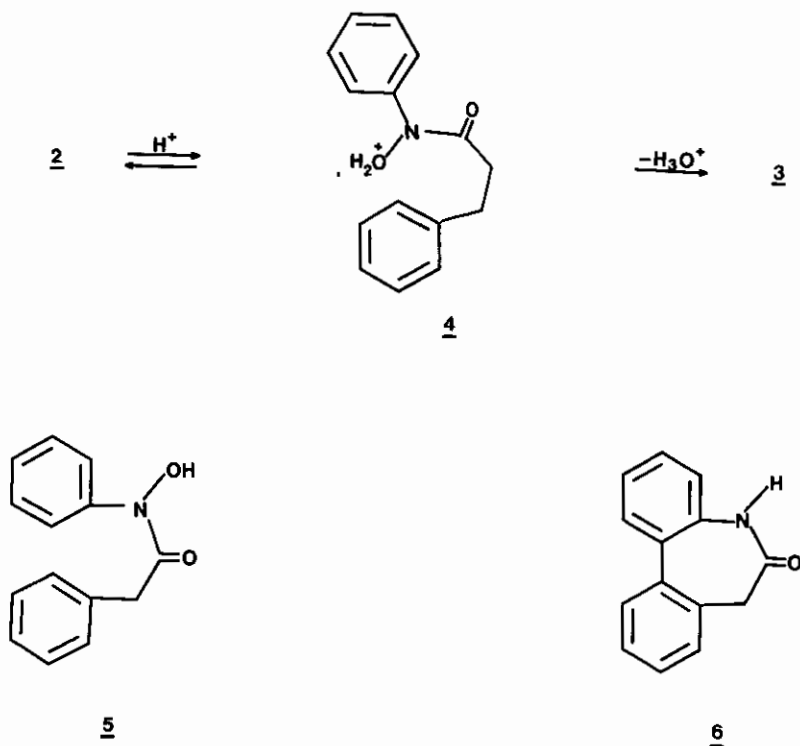
Compound 3 has a correct molecular ion (m/e = 223) in mass spectrometry and shows a 200 MHz spectrum in sim-tetrachloroethane-d₂ solution consisting of two multiplets centered at 2.85(2H) and 3.06(2H) ppm and four multiplets in the aromatic region centered at 6.35(1H), 7.04(2H), 7.24(3H), and 7.50(3H) ppm. In order to detect the presence of an amidic proton, the spectrum of 3 was recorded at different concentrations and in a different solvent (CDCl₃) also by adding D₂O. In any event no significant spectral changes were observed. Moreover no evidence for the presence of N-H stretching band was found in the ir spectrum of 3 which in turn showed an intense C=O absorbance at 1680 cm⁻¹.

Compound 3 has been synthesized by a completely different route⁶ and showed the same physical and spectroscopic characteristics of the product obtained in the acid catalyzed rearrangement of 2.

We also carefully searched for the presence of 1 in the minor components of the reaction mixture of the acid treatment of 2. Two other products (both less than 5% yield) were isolated by chromatography. They have, in ir spectra, an intense band at 3325 and 3310 cm⁻¹ respectively, probably due to an N-H stretching, but the ratio of the integrated areas of the aliphatic and aromatic protons in the nmr spectra do not correspond to the 4:8 ratio requested by compound 1.⁷

The formation of 3 from the protonated hydroxylamine 4 is straightforward since it is a simple intramolecular electrophilic substitution on the aryl-alkyl residue by the electrophilic nitrogen of 4 (Scheme). Phenyl coupling is often observed in related systems⁸⁻¹⁰ and even in the very similar hydroxylamine 5 which gives 6 upon reaction with TFSA⁵. This indicates a significant delocalization of the positive charge in the phenyl ring linked to the nitrogen atom.

Scheme



However in the system at hands the reaction seems controlled by structural and entropic factors which favour a six-membered ring closure over the formation of an eight-membered ring heterocycle.

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Received, 30th March, 1984