INTERACTION OF O-ARYLHYDROXYLAMINES WITH PHENYLSULFONYLACETONE

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Examination of the interaction of O-arylhydroxylamines with unsymmetrical ketones, i.e., those in which the α - and α '-positions to the CO group differ in chemical properties, could clarify the reaction sequence and the elementary reaction mechanisms in the individual stages of the formation of benzofurans in the condensation of O-arylhydroxylamines with ketones (see, e.g., [1-4]).

In phenyl sulfory lacetone (I) the α - and α '-positions are dissimilar as regards both the number of hydrogen atoms (methyl and methylene groups) and the activation of these fragments, thus making it difficult to predict the course of the rearrangement of O-aryloximes of ketone (I).

We have found that the reaction of phenylhydroxylamine (IIa) with ketone (I) (reflux in 23% alcoholic hydrogen chloride) forms a mixture of isomeric benzofurans (IIIa) and (IV), which we isolated in 36 and 19% yield, respectively.

The initial formation of O-aryl ethers (Va) and (Vb) of the oximes of ketone (I) from (IIa) or (IIb) and (I) is exemplified by compound (Vb) (yield 68%; the components were heated for 1 h in 23% alcoholic hydrogen chloride). That oxime ether (Vb) exists as one geometrical isomer (probably with the syn arrangement of the methyl and aryloxy groups) can be deduced from analysis of the PMR spectra, which has only one set of signals from each of the CH₂, CH₃ (singlets), and C₆H₄ (AA'BB' system) groups. In addition to oxime ether (Vb) we isolated the intermediate (VIb) in 15\% yield (hydrolysis of ammonia from the primary rearrangement product, which contains an imino group, takes place in the reaction mixture). The IR spectrum of (VIb) (in Vaseline oil) has intense bands at 1722 (ν C=O) and 3425 cm⁻¹ (broad band; bound phenolic hydroxyl). When the reaction time was increased (15 h) hydroxy ketone (VIb) could be derived from (Vb) in 74\% yield.



IIa, IIIa, Va, VIa R=H; IIb, IIIb, Vb, VIb R=NO2

We carried out the cyclization of (IIIb) (yield 97%) in refluxing trifluoroacetic acid. We verified the structures of benzofurans (IIIa), (IIIb), and (IV) by molecular weight determination and PMR spectroscopy (see the experimental section). We did not isolate oxime ether (Va) or hydroxy ketone (VIa).

Thus we have been able to synthesize hitherto unreported benzofurans with a sulfonyl group in position 2 or 3 on the basis of the intersection of O-arylhydroxylamines with ketone (I).

EXPERIMENTAL

Spectra were recorded on: IR: a UR-10; and PMR: a Varian T-60 (on the δ scale). Mass spectra were derived with a Varian MAT-112 spectrometer at 80 eV by direct sample insertion into the ion source. The purity of the compounds was monitored by TLC (Al₂O₃, activity II, alkaline form, chloroform eluent).

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<u>2-Phenylsulfonylmethylbenzofuran (IIIa) and 2-Methyl-3-phenylsulfonylbenzofuran (IV).</u> Hydrochloride (IIa) (0.37 g, 2.5 mmole) and ketone (I) (0.5 g, 2.5 mmole) were refluxed for 1 h in 23% solution (5 ml) of hydrogen chloride in absolute alcohol (precipitating ammonium chloride). After cooling the precipitate was filtered off and washed with water and absolute alcohol to give (IIIa) (0.25 g, 36%), mp 165.5-166.5°C (from alcohol), Rf 0.45. Found: C 66.2; H 4.5; S 11.8%; M 272 (mass spectrum). $C_{15}H_{12}O_3S$. PMR spectrum (in CDCl₃): 4.6 (s, 2H, CH₂), 6.6 (s, 1H, C₃H), 7.1-8.0 ppm (C₆H₄ + C₆H₅). Evaporation of the mother liquor gave (IV) (0.13 g, 19%), mp 104.5-105°C (from alcohol), Rf 0.58. Found: C 66.4; H 4.4; S 11.9%; M 272 (mass spectrum). $C_{15}H_{12}O_3S$. PMR spectrum (in CDCl₂): 2.8 (s, 3H, CH₃), 7.3-8.3 ppm (C₆H₄ + C₆H₅).

Phenylsulfonylacetone Oxime 4-Nitrophenyl Ether (Vb) and 1-Phenylsulfonyl-3-(2-hydroxy-5-nitrophenyl)acetone (Vlb). A mixture of hydrochloride (Ilb) (0.96 g, 5 mmole) and ketone (I) (1 g, 5 mmole) was refluxed for 1 h in 23% alcoholic hydrogen chloride (16 ml). After cooling the precipitate was filtered off and washed with water and alcohol to give oxime ether (Vb) (1.15 g, 68.5%), mp 153-154°C (from alcohol), R_f 0.46. Found: C 53.8; H 4.1; N 8.3; S 10.0%; M 334 (mass spectrum). $C_{15}H_{14}N_2O_5S$. Calculated: C 53.9; H 4.2; N 8.4; S 9.6%; M 334.3. PMR spectrum (in CDCl₃): 2.3 (s, 3H, CH₃), 4.1 (s, 2H, CH₂), 6.8 and 8.0 ppm (centers of two "doublets" of an AA'BB' system, $O-C_6H_4-NO_2-4$). The mother liquor gave hydroxy ketone (VIb) (0.25 g, 15%), mp 197.5-198°C (from alcohol), as bright yellow crystals, soluble in alkali. Found: N4.2; S 9.7%; $C_{15}H_{13}NO_6S$. Calculated: N 4.2; S 9.6%.

Reflux of the isolated oxime ether (Vb) (0.55 g) in 23% alcoholic hydrogen chloride (17 ml) for 15 h formed hydroxy ketone (VIb) (0.41 g, 74%).

<u>2-Phenylsulfonylmethyl-5-nitrobenzofuran (IIIb).</u> A mixture of hydroxy ketone (VIb) (0.35 g, 1 mmole) was refluxed for 2 h in trifluoroacetic acid (7 ml). After cooling the reaction mixture was poured into water. The precipitate was filtered off and washed with water to give benzofuran (IIIb) (0.32 g, 97%), mp 185-186°C (from alcohol); Rf 0.63 (Al₂O₃, grade IV). Found: C 57.1; H 3.7; N 4.5; S 10.0%; M 317 (mass spectrum). $C_{15}H_{11}NO_5S$. Calculated: C 56.8; H 3.5; N 4.4; S 10.1%; M 317.3. PMR spectrum (in CF₃COOH): 5.1 (s, 2H, CH₂), 7.2 (s, 1H, C₃H), 7.8 (s, 1H, C₃H), 7.8 (d, J = 9 Hz, 1H, C₇H), 8.6 (q, J₁ = 9 Hz, J₂ = 3 Hz, 1H, C₆H), 8.9 (d, J = 3 Hz, 1 H, C₅H), and 7.9-8.4 ppm (C₆H₅).

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