SYNTHESIS OF 2,3-TETRAMETHYLENE-5-ARENESULFONAMIDOBENZOFURANS

E. A. Titov and A. S. Grishchenko

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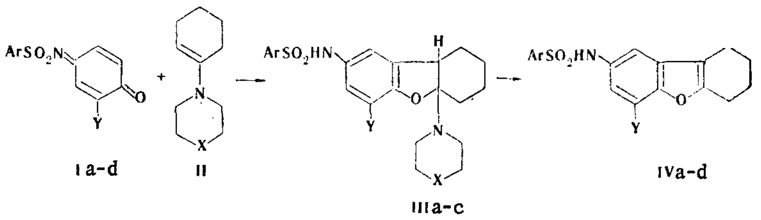
The reaction of N-arenesulfonyl-1,4-benzoquinonimines with 1-morpholino(piperidino)-1-cyclohexene gives 2,3-dihydro-2-morpholino(piperidino)-2,3-tetramethylene-5-arenesulfonamidobenzofurans. Refluxing of the latter in dilute hydrochloric acid gave 2,3-tetramethylene-5-arenesulfonamidobenzofurans, the structure of which was proved by hydrolysis to 2,3-tetramethylene-5-aminobenzofuran and conversion of it to the previously described 2,3-tetramethylene-5-hydroxybenzofuran.

In a continuation of our research on the synthesis and study of the reactions of N-arenesulfonyl-1,4-benzoquinonimines [1-4], we have accomplished the reaction of these compounds with 1-morpholino(piperidino)-1-cyclohexene. The results of Ia-c with IIa (X = O) yielded 2,3-dihydro-2-morpholino-2,3-tetramethylene-5-arenesulfonamidobenzofurans (IIIa-c), the cyclic structure of which was confirmed by the negative results obtained when the indophenol reaction was carried out [1,2] and by the absence in the IR spectra of the absorption at 3400 cm^{-1} that is characteristic for the OH group of N-arenesulfonyl-1,4-aminophenols (see Fig. 1) and of absorption bands of C=O and C=N bonds at 1565-1655 cm^{-1}.

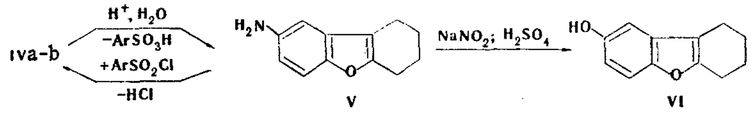


I a-d II IIIa-c IVa-d

a Ar = C_6H_5, Y = H; b Ar = p-$CH_3C_6H_4$, Y = H; c Ar = p-ClC_6H_4, Y = H; d Ar = C_6H_5, Y = Cl

Refluxing of III in 10% hydrochloric acid is accompanied by splitting off of amine and the formation of 2,3-tetramethylene-5-arenesulfonamidobenzofurans (IV), the structure of which as benzofuran derivatives [5,6] was confirmed by the presence of absorption bands at 1170 and 885 cm^{-1} in the IR spectra. The products of the reaction of Ia with IIb (X = CH_2) and of Id with IIa are dark-brown oils that are difficult to crystallize, and they were therefore converted to IVa,d without isolation in pure form.

Unambiguous experimental proof of the structure of the synthesized compounds was obtained by replacement of the arenesulfonamido group in them by a hydroxyl group to give substances with genuinely known and previously proved structures. For this, IVa,b were subjected to acid hydrolysis to 2,3-tetramethylene-5-aminobenzofuran (V) with subsequent diazotization of it and replacement of the diazo group by a hydroxyl group. As expected, the product synthesized by this route proved to be identical to the previously described 2,3-tetramethylene-5-hydroxybenzofuran (VI) [7].



V VI

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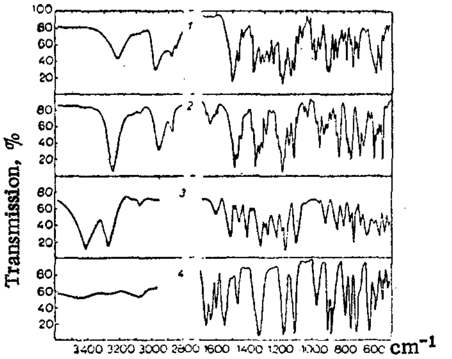

Fig. 1. IR spectra: 1) 2,3-dihydro-2-morpholino-2,3-tetramethylene-5-benzenesulfonamidobenzofuran (IIIa); 2) 2,3-tetramethylene-5-benzenesulfonamidobenzofuran (IVa); 3) N-benzenesulfonyl-4-aminophenol; 4) N-benzenesulfonyl-1,4-benzoquinonimine.

A confirmation of the fact that hydrolytic cleavage of the arenesulfonyl group is not accompanied by any other change in the in the structure of IV is the reproduction of the same compounds by acylation of the hydrolysis products with arenesulfonyl chlorides.

EXPERIMENTAL

2,3-Dihydro-2-morpholino-2,3-tetramethylene-5-benzenesulfonamidobenzofurans (IIIa). A solution of 2 g (0.012 mole) of 1-morpholino-1-cyclohexene (IIa) in 40 ml of chloroform was added with stirring at room temperature to a solution of 2.48 g (0.01 mole) of N-benzenesulfonyl-1,4-benzoquinonimine (Ia) in 40 ml of chloroform. A deep red-violet coloration appeared immediately when the reagents were mixed, and considerable warming of the reaction mass was observed. The intensity of the coloration decreased rapidly, and the solution became greenish-brown after 5 min. The reaction solution no longer gave the indophenol reaction with phenol and ammonium hydroxide [1, 2]; i.e., the starting quinonimine had reacted practically completely. The chloroform was evaporated in a stream of air, and 20-30 ml of diethyl ether was added to the residual oil. After 10-15 min, the mixture yielded a white crystalline product, which was removed by filtration, washed with ethanol, and air-dried* to give 3 g (72%) of colorless crystals with mp 168-170° (from methanol) that were insoluble in water, slightly soluble in carbon tetrachloride, more soluble in alcohol and benzene, and quite soluble in chloroform and acetone. Found: N 6.7; S 7.7%. $C_{22}H_{26}N_2O_4S$. Calculated %: N 6.8; S 7.7%.

2,3-Dihydro-2-morpholino-2,3-tetramethylene-5-(p-toluenesulfonamido)benzofuran (IIIb). This compound [3.2 g (75%)] was similarly obtained from 2.61 g (0.01 mole) of N-(p-toluenesulfonyl)-1,4-benzoquinonimine (Ib) and 2 g (0.012 mole) of IIa and had mp 120-120.5° (from ethanol). Found: C 64.9; H 6.6; N 6.6; S 7.5%. $C_{23}H_{28}N_2O_4S$. Calculated: C 64.5; H 6.6; N 6.5; S 7.5%.

2,3-Dihydro-2-morpholino-2,3-tetramethylene-5-(p-chlorobenzenesulfonamido)benzofuran (IIIc). This compound [4 g (95%)] was similarly obtained from 2.81 g (0.01 mole) of N-(p-chlorobenzenesulfonyl)-1,4-benzoquinonimine (Ic) and 2 g (0.012 mole) of IIa and had mp 121.5-122° (dec., from ethanol). Found: N 6.1; Cl 8.1%. $C_{22}H_{25}ClN_2O_4S$. Calculated: N 6.2; Cl 7.9%.

2,3-Tetramethylene-5-benzenesulfonamidobenzofuran (IVa). A. A 1-g (2.4 mmole) sample of IIIa was refluxed for 30 min in 50 ml of 10% hydrochloric acid. The mixture was cooled, and the product was removed by filtration, washed on the filter with water, and air-dried to give 0.62 g (78%) of colorless crystals with mp 191.5-192.5° (from aqueous acetic acid) that were insoluble in water, slightly soluble in carbon tetrachloride and petroleum ether, more soluble in alcohol, and quite soluble in acetone. Found: N 4.3; S 9.8%. $C_{18}H_{17}NO_3S$. Calculated: N 4.3; S 9.8%.

B. The reaction of 2.48 g (0.01 mole) of Ia with 2 g (0.012 mole) of IIb via the method used to synthesize IIIa gave (after evaporation of the solvent) a dark-brown, difficult-to-crystallize oil, which was converted to 1.96 g (60%) of colorless crystals of IVa with mp 190.5-191.5° by refluxing with 10% hydrochloric acid. This product did not depress the melting point of a sample of IVa obtained by method A, and their IR spectra were identical.

2,3-Tetramethylene-5-(p-toluenesulfonamido)benzofuran (IVb). This compound [0.56 g (70%)], with mp 129-130.5° (from aqueous acetic acid), was obtained from 1 g (23.4 mmole) of IIIb under the conditions used to synthesize IVa. Found: N 4.1; S 9.4%. $C_{19}H_{19}NO_3S$. Calculated: N 4.1; S 9.4%.

2,3-Tetramethylene-5-(p-chlorobenzenesulfonamido)benzofuran (IVc). This compound [0.7 g (83%)] was similarly obtained from 1 g (2.4 mmole) of IIIc as colorless plates with mp 157.5-158.5°. Found: N 3.9; Cl 9.7%. $C_{18}H_{16}ClNO_3S$. Calculated: N 3.8; Cl 9.8%.

2,3-Tetramethylene-7-chloro-5-benzenesulfonamidobenzofuran (IVd). This compound [2.26 g (60%)] was obtained via method B described for IVa from 2.81 g (0.01 mole) of N-benzenesulfonyl-2-chloro-1,4-

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*The IR spectra of this product and the material obtained after recrystallization were identical; i.e., ring formation occurred during the reaction.

benzoquinonimine (Id) and 2 g (0.012 mole) of IIa and had mp 214-215° (from glacial acetic acid). Found: N 3.8; Cl 9.6%. $C_{18}H_{16}ClNO_3S$. Calculated: N 3.9; Cl 9.8%.

2,3-Tetramethylene-5-aminobenzofuran (V). A. A 9-g (27.5 mmole) sample of IVa was heated in a sealed tube with 50 ml of concentrated hydrochloric acid at 140° for 4 h until it had dissolved completely, and the solution was cooled to room temperature. The precipitate was removed by filtration and dissolved with slight heating in 150 ml of water. A 0.1 N sodium hydroxide solution was added dropwise with stirring at room temperature until the mixture gave a distinctly alkaline reaction, and it was then allowed to stand. The precipitate was removed by filtration, washed with water, and dried at room temperature to give 3.7 g (72%) of long, colorless needles with mp 74° (from aqueous ethanol) that were slightly soluble in water and quite soluble in organic solvents. The product gave a negative qualitative reaction for sulfur but distinct qualitative reactions for a primary amino group [8]. Found: C 76.7; H 7.1; N 7.6%. $C_{12}H_{13}NO$. Calculated: C 77.0; H 7.0; N 7.5%.

B. Compound V [0.66 g (70%)] with mp 73.5° was obtained from 1.7 g (5 mmole) of IVb and 10 ml of hydrochloric acid as in method A. The product did not depress the melting point of a sample of V obtained via method A.

The acylation of V with benzenesulfonyl chloride via the method previously developed in [1] gave a white, crystalline product with mp 169°. The product did not depress the melting point of IVa.

2,3-Tetramethylene-5-hydroxybenzofuran (VI). This compound was obtained by a known method [9] by diazotization of V with sodium nitrite in sulfuric acid with subsequent heating of the diazonium sulfate in sulfuric acid solution. The crystalline precipitate was removed by filtration, dried, and sublimed under nitrogen to give colorless needles with mp 107°. The product did not depress the melting point of 2,3-tetramethylene-5-hydroxybenzofuran synthesized by a known method [7].

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