

Furan derivatives. CXX.

Synthesis and properties of 5-nitro-2-furylbenzyl sulfones

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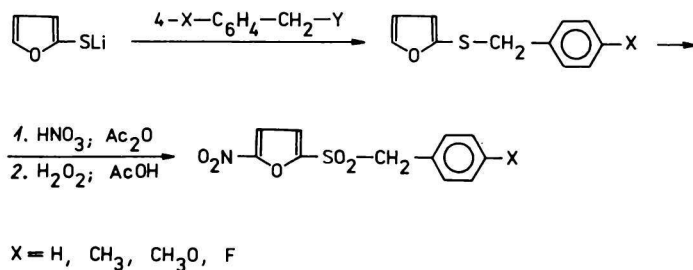
The reaction of lithium 2-furanthiolate with 4-X-benzyl halides ($X = H, CH_3, CH_3O, F$) gave the corresponding sulfides. Their nitration with an acetic acid—nitric acid system followed by hydrogen peroxide oxidation afforded the corresponding sulfones. The u.v. spectra and the stability towards treatment with base of the prepared sulfones have been studied.

Реакцией 2-фурантиолата лития с 4-Х-бензилгалогенидами, где $X = H, CH_3, CH_3O$ и F были приготовлены соответствующие сульфиды. Последние нитровались в системе ацетангидрид— HNO_3 и окислялись перекисью водорода в соответствующие нитросульфоны. Изучались УФ спектры и устойчивость приготовленных сульфонов в щелочной среде.

The synthesis and properties of 5-nitrofurfurylheteroaryl sulfides [1], 5-nitrofurfurylaryl sulfides and sulfones [2] have been previously described. It follows from the pK values and the rates of the formation of carbanions found for these systems that through the SO_2 group there exists a transfer of the electronic effects due to which substances of these classes can be considered strong C-acids.

The present work describes the synthesis of isomeric 5-nitro-furylbenzyl sulfones needed for studies of their physicochemical properties, mainly the acidity of the methylene hydrogen atoms. The starting material for the synthesis was lithium 2-furanthiolate. The obtained sulfides were nitrated with acetyl nitrate and the products obtained were oxidized to give 5-nitro-2-furylbenzyl sulfones (Scheme 1).

Alkylations of lithium 2-furanthiolate with 4-X-benzyl halides gave good yields of the corresponding 2-furylbenzyl sulfides *I* and *II* (Table 1). The relatively lower yields of *III* and *IV* (Table 1) were due to losses (up to 30%) during the process of isolation rather than incomplete reactions. The latter two substances are high boiling liquids which partially decomposed during distillation, although this operation was performed under high vacuum. The S_N reactions of lithium 2-furanthiolate with dry, crystalline 4-X-benzyl halides ($X = NO_2, CN, Cl$) in ether, acetone or sulfolane were unsuccessful even after prolonged reaction time (9 instead of 5 h). When the reaction was performed in ether only the unreacted starting 4-X-benzyl halide could be isolated from the worked-up reaction mixture. On conducting the alkylation in acetone or sulfolane (3—5 h, 55—60°C) considerable discolouration

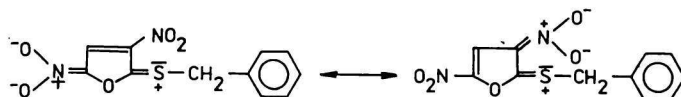


Scheme 1

of the reaction mixture was observed and no pure substance could be isolated from the resinous products.

The nitration of furan type sulfides having the sulfur atom linked directly to the furan ring has not been described in the literature as yet. We have nitrated 2-furylbenzyl sulfides with fuming nitric acid—acetic anhydride mixture under various conditions (temperature, reaction time, different — 1 1—1 5 — substrate—nitric acid ratio) but a pure 5-nitro derivative could not be isolated. After the addition intermediate was decomposed with sodium phosphate dark oily materials were obtained which would not crystallize even after prolonged standing and they evidently decomposed during vacuum distillation. Therefore, the oily products were partially purified by percolating their solutions in benzene through a column of alumina and subsequently oxidized with hydrogen peroxide in glacial acetic acid to the corresponding sulfones. To obtain the mononitro derivatives the best experimentally found ratio of nitric acid—sulfide was 1 1. When 2—3-fold molar excess of nitric acid was used the 3,5-dinitro derivative was formed exclusively. Its structure was determined by i.r. and u.v. spectroscopy and mass spectrometry. Of the prepared sulfides only the benzyl and 4-fluorobenzyl derivatives could be nitrated without difficulties. The nitration of the analogous 4-methyl and 4-methoxybenzyl sulfides was accompanied by opening of the furan ring.

The u.v. spectra of 2-furyl-4-X-benzyl sulfides (Table 1) show absorption maxima at 216—230 and 255—256 nm. These are, respectively, attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electron transitions, localized in the furan and benzene part of the molecule [3]. In the case of 3,5-dinitro-2-furylbenzyl sulfide the u.v. spectrum showed two additional absorption bands with maxima at 220 and 345 nm. The one at the shorter wavelength corresponds to the electron transitions localized in the



Scheme 2

furan or benzene ring and the one at the longer wavelength, with a considerable bathochromic shift, corresponds to the extended conjugation through a lone electron pair of sulfur (Scheme 2).

It follows from the comparison of the u.v. spectra of 5-nitro-2-furylbenzyl and the isomeric 5-nitrofurfurylphenyl sulfone [2] that in the case of 5-nitro-2-furylbenzyl sulfone the exchange of the SO_2 group for a CH_2 group resulted in a hypsochromic shift of the absorption band.

In basic media (0.01 and 0.1 M sodium hydroxide) the u.v. spectra of the sulfones altered considerably. The disappearance of the absorption band at 288, resp. 287 nm indicates that, as a result of an attack of OH^- ions a destruction of the 5-nitrofuran ring occurred. It follows from the kinetic measurements that a carbanion at the methylene position is formed in the first (fast) stage of this reaction, followed by a slow disintegration of the furan ring. The rate constants k' found for the disintegration of 5-nitro-2-furylbenzyl sulfone and the corresponding 4-fluoro derivative in 0.01 M sodium hydroxide were 0.305 and $0.107 \times 10^{-3} \text{ s}^{-1}$, respectively. The rate of the formation of the carbanion and the disintegration of the furan system is a function of the concentration of OH^- ions, as found in the case of 5-nitro-2-furylbenzyl sulfone ($k'_{0.1 \text{ M-NaOH}} = 0.208 \times 10^{-3} \text{ s}^{-1}$; $k'_{0.01 \text{ M-NaOH}} = 0.107 \times 10^{-3} \text{ s}^{-1}$). The described phenomena made it impossible to determine the $\text{p}K$ values of the methylene group in the described sulfones.

Experimental

The u.v. spectra (200–400 nm) for solutions ($5\text{--}7 \times 10^{-5} \text{ M}$) in methanol were taken with a Specord UV VIS (Zeiss, Jena) instrument using 1 cm cells. The accuracy of the wavelength reading was $\pm 1 \text{ nm}$. The kinetic measurements of the first-order type disintegration of the substances in 0.1 and 0.01 M sodium hydroxide were run using the same spectrometer.

Lithium 2-furanthiolate was prepared [4] by treatment of furan in ether with *n*-butyllithium and the formed furyllithium was allowed to react with elemental sulfur.

2-Furyl-4-X-benzyl sulfides (I–IV)

Dry furan (10 g; 0.147 mol) was added dropwise under nitrogen and with stirring to a cold ethereal *n*-butyllithium (prepared from lithium metal (1.5 g; 0.216 mol) and *n*-butylbromide (14.7 g; 0.168 mol)) over a period of 10–15 min. After heating under reflux for 5 h the solution was cooled (-5°C) and powdered sulfur (3.5 g; 0.11 mol) was added portionwise at such a rate as to keep the temperature of the reaction mixture below 0°C . Immediately upon the addition of the first portion of sulfur lithium 2-furanthiolate started to separate in the form of a yellow precipitate. The corresponding benzyl halide (0.1 mol) was added to the thus prepared lithium 2-furanthiolate and the mixture was refluxed for 5 h. The mixture was cooled and poured into aqueous ammonium chloride

Table 1
Characteristics of the synthesized furyl-(4-X-benzyl) sulfides

Compound	X	Formula	M	Calculated/found			Yield %	B.p. °C/kPa	λ_{\max} , nm (log ϵ)	
				% C	% H	% S				
I	H	C ₁₁ H ₁₀ OS	190.2	69.45 69.28	5.29 5.08	16.85 16.43	64.5	106—109/9.33	216 (4.11)	255 (3.76)
II	CH ₃	C ₁₂ H ₁₂ OS	204.2	70.58 70.26	5.92 5.84	15.68 15.42	64	109—111/1.33	217 (4.13)	256 (3.78)
III	CH ₃ O	C ₁₂ H ₁₂ O ₂ S	220.2	69.99 69.75	5.49 5.44	14.54 14.29	30	135—137/0.33	230 (4.15)	256 (3.66)
IV	F	C ₁₁ H ₉ FOS	208.2	63.46 63.27	4.35 4.22	15.36 15.17	35	115—116/0.66	218 (4.05)	255 (3.71)

(17% ; 150 ml), the ethereal phase was separated and the aqueous solution was extracted with ether. The combined ethereal extracts were washed with 3% aqueous sodium hydroxide and water, dried with anhydrous sodium sulfate, concentrated and the residue was distilled under vacuum. The prepared substances are summarized in Table 1.

Nitration of 2-furyl-4-X-benzyl sulfides

Fuming nitric acid (1.89 g; 0.03 mol) was added at 0°C to acetic anhydride (20.4 g; 0.2 mol), the solution of the formed acetyl nitrate was cooled to -40°C and 2-furyl-4-X-benzyl sulfide (0.03 mol) dissolved in acetic anhydride (30 ml) was added dropwise over a period of 20 min. The mixture was stirred for 2 h at -45°C and poured onto crushed ice (20 g). Sodium phosphate (7.5 g; 0.043 mol) was added, the mixture was kept at 60°C for 1 h and poured onto crushed ice (25 g). The free acids were neutralized with 10% sodium hydroxide and the liberated 5-nitro-2-furyl-4-X-benzyl sulfide was extracted with benzene. The extracts were dried and concentrated to give a red, viscous oil which could not be induced to crystallize. The crude product in benzene was percolated through a column of alumina and the oil obtained on concentration of the benzene eluate was used as such to make the sulfones (see below).

3,5-Dinitro-2-furylbenzyl sulfide

Fuming nitric acid (9.47 g; 0.15 mol) was added at -5°C to acetic anhydride (25.5 g; 0.25 mol), the mixture was cooled (-10°C) and 2-furylbenzyl sulfide (5.7 g; 0.03 mol) in acetic anhydride (15 ml) was added dropwise over a period of 30 min. The mixture was stirred at -15°C for 2 h and poured onto crushed ice (30 g). When the ice melted sodium phosphate (10 g; 0.061 mol) was added and the mixture was heated at 60°C with stirring for 1 h. After cooling and neutralization, the liberated 3,5-dinitro-2-furylbenzyl sulfide was extracted with ethyl acetate, the extract dried, concentrated and the residue was crystallized from ethanol to give 3.86 g (46%) of the title substance melting at 146°C.

For $C_{11}H_8N_2O_5S$ (280.0) calculated: 47.21% C, 2.85% H, 9.98% N, 11.45% S; found: 47.15% C, 2.83% H, 9.78% N, 11.18% S.

5-Nitro-2-furylbenzyl sulfone

Hydrogen peroxide (30% ; 3 ml) was added to a solution of 5-nitro-2-furylbenzyl sulfide (0.005 mol) in glacial acetic acid (15 ml). The mixture was stirred for 30 min and left at room temperature for 5 days. The solution was concentrated to a half of the original volume and diluted with water (30 ml). The separated 5-nitro-2-furylbenzyl sulfone was crystallized from ethanol to give 47.8% of the material melting at 124—126°C.

For $C_{11}H_8NO_5S$ (267.2) calculated: 49.52% C, 3.37% H, 5.34% N, 11.98% S; found: 49.81% C, 3.45% H, 5.20% N, 11.97% S.

UV spectra: λ_{\max} , nm (log ϵ) 218 (4.08); 288 (4.05).

5-Nitro-2-furyl-4-fluorobenzyl sulfone

The title substance (m.p. 105—106°C) was obtained in a yield of 52.2% by applying the above-described procedure and crystallization of the product from ethanol.

For $C_{11}H_8FNO_5S$ (285.2) calculated: 46.38% C, 2.81% H, 4.92% N, 11.23% S; found: 46.36% C, 2.88% H, 4.91% N, 11.19% S.

UV spectra: λ_{\max} , nm (log ϵ) 220 (4.13); 287 (4.05).

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