ALKYLATION REACTIONS OF 5-NITROFURFURYL DERIVATIVES AS C-ACIDS

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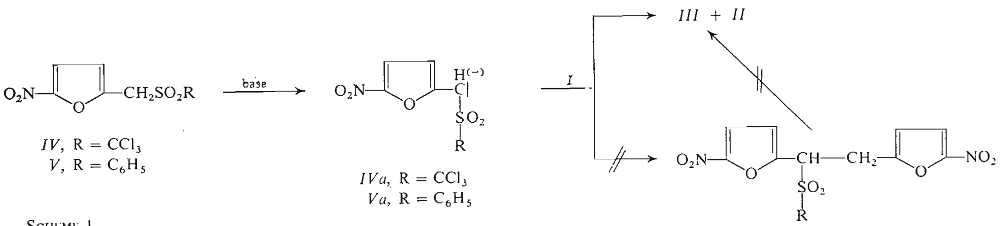
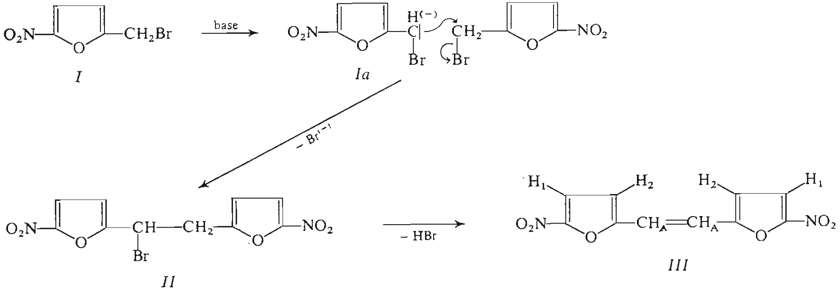
5-Nitrofurfuryl bromide (*I*) and 4-nitrobenzyl bromide (*VI*) were investigated as possible alkylation reagents in reaction with 5-nitrofurfuryl trichloromethyl sulfone (*IV*) and 5-nitrofurfuryl phenyl sulfone (*V*). 1,2-Bis(5-nitro-2-furyl)ethylene (*III*) was formed from *I* in an alkaline medium and 1,2-bis(5-nitro-2-furyl)ethane (*X*) in the presence of furfuryl mercaptan. Products of this reaction were identified by IR, UV, ^{1}H-NMR and mass spectrometries.

5-Nitrofurfuryl sulfones are characterized by an active methylene group, which undergoes an easy condensation reaction with aromatic aldehydes to afford the appropriate olefins[1]. In general, sulfones with an active CH_2 group are used for alkylation and similar reactions[2-6]. In connection with investigation of 5-nitrofurfuryl derivatives as C-acids we investigated the possibility to alkylate 5-nitrofurfuryl trichloromethyl sulfone (*IV*) and 5-nitrofurfuryl phenyl sulfone (*V*) with 5-nitrofurfuryl bromide (*I*) and 4-nitrobenzyl bromide (*VI*). As we have already shown[7], derivative *I* reacted with sulfones *IV* and *V* to give 1,2-bis(5-nitro-2-furyl) ethylene (*III*) as a main product in addition to unreacted sulfones and a smaller amount of 1-(5-nitro-2-furyl)-1-bromo-2-(5-nitro-2-furyl)ethane (*II*). The structure of the latter was corroborated by mass spectrometry. Surprisingly enough, no products of alkylation (Scheme 1) were obtained when reacting 5-nitrofurfuryl bromide (*I*) with sulfones *IV* and *V*. The more detailed study of this reaction revealed a concurrent alkylation reaction under formation of *III*. Derivative *I* gave rapidly, upon standing in an alkaline medium, *III* in a high yield. This finding provided evidence that derivative *III* was not formed as a result of alkylation of sulfones and subsequent elimination of the proper sulfinic acid (Scheme 2). The generation of *III* is rationalized as follows: in the first step, the base forms a carbanion, which attacks as a C-anion 5-nitrofurfuryl bromide (*I*) to furnish the intermediate *II*; the latter splits off HBr under formation of 1,2-bis(5-nitro-2-furyl)ethylene (*III*).

5-Nitrofurfuryl nitrate and 5-nitrofurfuryl sulfones *IV* and *V* did not react under the same conditions. The advantage to prepare derivative *III* by this method, when contrasted with Wittig reaction[8], is a quite short reaction time and a substantial increase in yield.



SCHEME 1



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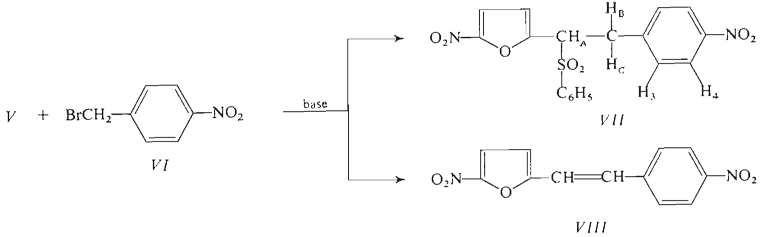
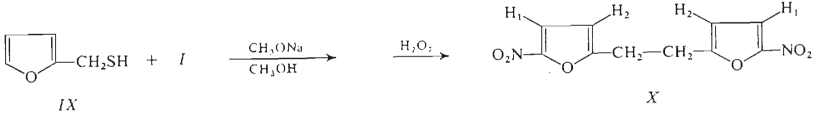


SCHEME 3



SCHEME 4

The main alkylation product of sulfone *V* with 4-nitrobenzyl bromide (*VI*) was, in addition to the unreacted *V*, 1-(5-nitro-2-furyl)-1-phenylsulfonyl-2-(4-nitrophenyl)-ethane (*VII*) together with a little amount of 1-(5-nitro-2-furyl)-2-(4-nitrophenyl)-ethylene (*VIII*, Scheme 3). 4-Nitrobenzyl bromide (*VI*), in contrast to 5-nitrofurfuryl bromide (*I*), alkylated 5-nitrofurfuryl phenyl sulfone (*V*). Derivative *VIII* can be a product of elimination reaction of *VII*.

5-Nitrofurfuryl bromide (*I*) led, upon reaction with furfuryl mercaptan (*IX*), to 1,2-bis(5-nitro-2-furyl)ethane (*X*) and not to the corresponding sulfide or, after oxidation, sulfone (Scheme 4). A like reaction was observed with 5-nitrofurfuryl iodide under another conditions[9]. The mechanism of formation of derivative *X* has so far not been elucidated.

IR, UV, ^{1}H-NMR and mass spectra were the tools for structure determination of products; the obtained data are given in the experimental section. Chemical shift of ethylene protons H_A of derivative *III* is seen as a singlet at $\delta = 7{\cdot}25$ ppm. The ^{1}H-NMR spectra of similar derivatives[10], and also the absorption band in the IR region at 975 cm^{-1} indicated this compound to have *trans* configuration.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage, the ^{1}H-NMR spectra were recorded with a Tesla BS 487 B apparatus operating at 80 MHz in hexadeuterioacetone and hexadeuteriodimethyl sulfoxide with hexamethyldisiloxane as an internal reference substance at 25 and 70°C. Mass spectra were measured with an AEI MS 902 S spectrometer, IR spectra with a UR-20 (Zeiss, Jena) spectrophotometer both in KBr discs and chloroform, UV spectra with a Specord UV VIS (Zeiss, Jena) instrument in methanol at the concentration 3—5 . 10^{-5}M in a 1 cm-cell; reading accuracy ±1 nm.

Starting materials and intermediates were prepared as follows: 5-nitrofurfuryl nitrate, obtained by nitration of furfuryl alcohol, reacted with KBr to furnish 5-nitrofurfuryl bromide (*I*) ref.[11]. Derivative *I* gave with sodium phenyl sulfinate and sodium trichloromethyl sulfinate 5-nitrofurfuryl phenyl sulfone (*V*) and 5-nitrofurfuryl trichloromethyl sulfone (*IV*) ref.[1], respectively. A photochemical bromination of 4-nitrotoluene with N-bromosuccinimide in tetrachloromethane afforded 4-nitrobenzyl bromide (*VI*).

1,2-Bis(5-nitro-2-furyl)ethylene (*III*)

a) To a solution of 5-nitrofurfuryl bromide (*I*, 2·06 g, 10 mmol) in dimethylformamide (20 ml) NaH (0·24 g) was stepwise added at room temperature. This mixture was after 1 h vacuum dried and the residue extracted with chloroform was chromatographed (alumina Brockmann-II column); the first eluates gave *III*, m.p. 244°C in a 20—30% yield.

b) Bromide *I* (2·06 g, 10 mmol) was gradually added to a cooled (15—20°C) and stirred solution of sodium metal (0·25 g) in ethanol (20 ml). The first addition of *I* turned the colour to yellow. The slightly exothermic reaction was carried out without cooling. The mixture was after 10—15 min evaporated, the residue extracted with acetone–chloroform and chromatographed (alumina Brockmann-II column, eluent chloroform–acetone). Yield of *III* 0·95 g (78·5%), m.p. 245°C (m.p. 243—245°C, ref.[8]). For $C_{10}H_6N_2O_6$ (250·2) calculated: 48·00% C, 2·41% H, 11·20% N; found: 48·02% C, 2·40% H, 11·32% N. IR spectrum (chloroform, cm^{-1}): $\nu(C{=}C)$ 1 610, $\nu_{as}(NO_2)$

1 540, $\nu_s(NO_2)$ 1 356, ν_{fur}(C—O—C) 1 028, 975. UV spectrum (methanol, nm, (log ε)): 245 (4·23), 288 (3·94), 415 (4·54). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide, 70°C, δ, ppm): 7·64, H_1 (2 H, d), 7·09, H_2 (2 H, d, $J_{1,2}$ = 4·0 Hz), 7·25, H_A (2 H, s, *trans*-derivative). Mass spectrum (*m/e*, (%)): 250 (100), 220 (11·2), 186 (37·5), 146 (19·5), 118 (19·5), 102 (50), 92 (12·2), 90 (25), 89 (17·5), 80 (14), 76 (31), 75 (12), 64 (14), 63 (19), 52 (12·5), 51 (25), 50 (17·5), 44 (31), 39 (11).

1-(5-Nitro-2-furyl)-1-bromo-2-(5-nitro-2-furyl)ethane (*II*)

Natrium hydride (144 mg) was added to a stirred solution of 5-nitrofurfuryl trichloromethyl sulfone (*IV*, 2 g, 6 mmol) in dimethylformamide (20 ml) at 20°C. The carbanion *IVa*, thus being formed, turned the colour of the solution red. After 3 min the bromide *I* (1·24 g, 6 mmol) in dimethylformamide (5 ml) was added; the mixture was stirred 12 h at 50—60°C and it was allowed to stand for 12 h at 20°C. The residue, obtained after drying in a high vacuum at 50°C, was crystallized from chloroform with a little amount of acetone. Derivative *III* crystallized as the first, whereas *II* (m.p. 128—129°C) was obtained from mother liquors of the second fraction. Yield 30 mg, M^+ 330 ($C_{10}H_7BrN_2O_6$ for ^{79}Br).

1-(5-Nitro-2-furyl)-1-phenylsulfonyl-2-(4-nitrophenyl)ethane (*VII*)

Natrium hydride (0·3 g) was added to a solution of 5-nitrofurfuryl phenyl sulfone (*V*, 2·67 g, 10 mmol) in dimethylformamide (35 ml) at —20°C. 4-Nitrobenzyl bromide (*VI*, 2·16 g, 10 mmol) was added during 15 min; after 2 h, this mixture was poured into cold water and extracted with benzene from which *VII* was obtained in a low yield. M.p. 150—151°C; for $C_{18}H_{14}N_2SO_7$ (402·4) calculated: 53·72% C, 3·50% H, 6·96% N, 7·97% S; found: 51·40% C, 3·50% H, 6·58% N, 8·92% S. ^{1}H-NMR (hexadeuteriodimethyl sulfoxide, 25°C, δ, ppm): 5·62, H_A (1 H, dd), 3·55, H_B, H_C (2 H, t), 7·57, H_1 (1 H, d), 6·63, H_2 (1 H, d, $J_{1,2}$ = 4·0 Hz), 7·51, H_3 (2 H, d), 8·02, H_4 (2 H, d, $J_{3,4}$ = 8·9 Hz), 7·74—7·65, H_{phenyl} (5 H, m).

The residue after extraction was separated chromatographically (alumina Brockmann-II) with chloroform–acetone as eluent. Evaporation of the orange-coloured fraction gave 1-(5-nitro-2-furyl)-2-(4-nitrophenyl)ethylene (*VIII*), m.p. 177°C (178—180°C, ref.[12]).

1,2-Bis(5-nitro-2-furyl)ethane (*X*)

Furfuryl mercaptan (*IX*, 10·4 g, 10 mmol) was dropwise added to a stirred solution of sodium methylate (2·5 g of Na in 60 ml of methanol) at 15°C. Sodium salt of *IX*, obtained after evaporation, was added to a stirred solution of *I* (20·6 g, 10 mmol) in benzene (60 ml) and the mixture was allowed to stand for 48 g. Hydrogen peroxide (40 ml, 30%) was gradually added to a cooled solution (an exothermic reaction) of the residue resulting from evaporation of the reaction mixture dissolved in glacial acetic acid (60 ml). Within some days, *X* crystallized as a yellow substance. Yield 1·5 g, m.p. 155—158°C (161—162°C, ref.[9]). For $C_{10}H_8N_2O_6$ (252·2) calculated: 47·62% C, 3·19% H, 11·11% N; found: 47·41% C, 3·17% H, 11·30% N. IR spectrum (KBr, cm^{-1}): $\nu(CH_2)$ 3 148, 3 120, $\nu_{as}(NO_2)$ 1 530, 1 509, $\nu_s(NO_2)$ 1 362, ν_{fur}(C—O—C) 1 025. UV spectrum (methanol, nm, (log ε)): 206 (4·13), 228 (3·99), 321 (4·40). ^{1}H-NMR spectrum (hexadeuterioacetone, 25°C, δ, ppm): 7·45, H_1 (2 H, d), 6·63, H_2 (2 H, d, $J_{1,2}$ = 4·0 Hz), 3·60, CH_2 (2 H, s), 2·92 CH_2, (2 H, s). Mass spectrum (*m/e*, (%)): 252 (32·7), 206 (44·8), 126 (100), 110 (56·9), 96 (13·1), 80 (31), 79 (10·7), 68 (21), 52 (79), 51 (31), 50 (11), 44 (24), 39 (21).

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