ELECTRON TRANSFER PROCESSES. REACTIONS OF 5-NITROFURYL DERIVATIVES GOING BY ANIONRADICAL MECHANISM

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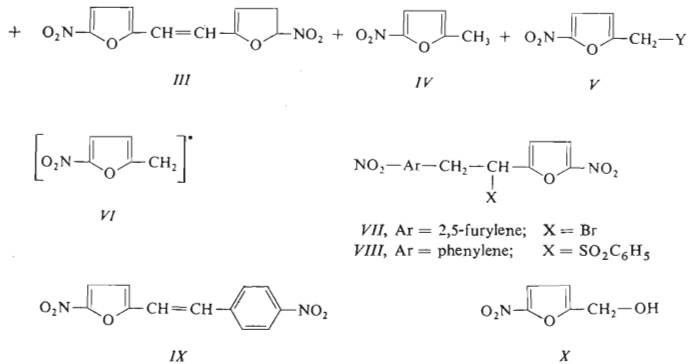
5-Nitrofurfuryl nitrate and bromide (*Ia,b*) react with electron donors to give 1,2-bis(5-nitro--2-furyl)ethane (*II*), 1,2-bis(5-nitro-2-furyl)ethylene (*III*), 5-nitro-2-methylfurane (*IV*), products of $S_{RN}1$ reactions *Va*, *Vb* and other derivatives. Formation of the derivatives *II* to *V* is discussed on the basis of anionradical mechanism. 4-Nitrobenzyl bromide reacts by a $S_{RN}1$ reaction with 5-nitrofurfuryl phenyl sulphone (*Va*) in basic medium to give 1-(5-nitro-2-furyl)-1-phenyl-sulphonyl-2-(4-nitrophenyl)ethane (*VIII*) and 1-(5-nitro-2-furyl)-2-(4-nitrophenyl)ethylene (*IX*).

According to Ingold's classification nucleophilic substitution at the saturated carbon atom can go by S_N1 and S_N2 mechanisms. Analogous mechanisms $S_{RN}1$ and $S_{RN}2$ were suggested for the substitution reactions proceeding through a radicalanion stage. Kornblum[1,2] and Russell[3,4] suggested a substitution anionradical mechanism in the aliphatic series, and, in the year 1970, Kim and Bunnett[5,6] proposed the $S_{RN}1$ mechanism (substitution, radical-nucleophilic, unimolecular) in the aromatic series. The terms "radical" and "nucleophilic" reflect the origin and the result of the reaction, respectively. As for the molecularity, the analogy with the S_N1 or S_N2 reactions consists in that splitting of —CX bond or its attack by a nucleophile does not take place in a neutral molecule but in anionradical. Many reviews[7–9] and papers[10–17] deal with the problem of the electron transfer from an electron donor to the reacting substrate and with its consequences for the reaction mechanism. These processes were also observed in nature[18,19].

In our previous work[20] we found that 5-nitrofurfuryl bromide (*Ib*) reacts in basic medium to give 1,2-bis(5-nitro-2-furyl)ethylene (*III*) and 1,2-bis-(5-nitro-2-furyl)-ethane (*II*). The present communication deals with elucidation of the reactions of 5-nitrofurfuryl nitrate (*Ia*) and bromide (*Ib*) with nucleophiles, its purpose being to deepen our knowledge of mechanism of these reactions (Scheme 1).

Ia, X = ONO_2
Ib, X = Br

II



SCHEME 1

The reaction course depends on many factors, especially on ionization potential of the electron donor, on electron affinity of the substrate, on stability and solvation of the anionradical pair and radical[21] *etc.* Besides other reaction pathways the anion-radical mechanism makes itself felt with the 5-nitrofurfuryl derivatives:

$$I + |Y^{(-)} \rightarrow [I]^{\cdot -} + [Y]^{\cdot}$$

$$[I]^{\cdot -} \rightarrow [VI]^{\cdot} + X^{(-)}$$

$$2\,[VI]^{\cdot} \rightarrow II$$

$$[VI]^{\cdot} + |Y^{(-)} \rightarrow [V]^{\cdot -}$$

$$[V]^{\cdot -} + I \rightarrow V + [I]^{\cdot -},$$

where $Y^{(-)}$ means $CN^{(-)}$, 2-furfurylthiolate, $C_6H_5SO_2^{(-)}$, $Cl_3CSO_2^{(-)}$, $OH^{(-)}$, $CH_3CH_2O^{(-)}$, $CH_3O^{(-)}$.

The nucleophile donates an electron to the substrate with formation of an anion-radical. Soft bases[22] (*e.g.* $CN^{(-)}$, $RS^{(-)}$) give by this reaction the ethane *II* as the main product resulting from recombination of two radicals $[VI]^{\cdot}$. Formation of the radical $[VI]^{\cdot}$ necessitates besides other factors[21] a sufficient stabilization by a de-activating group[23]. The other reaction product, 5-nitro-2-methylfurane (*IV*), is

formed *via* abstraction of hydrogen from medium by the radical $[VI]^{\cdot}$, *e.g.*:

$$[VI]^{\cdot} + H_3C{-}O^{(-)} \rightarrow IV + H_2C{-}O^{(-)}$$

$$H_2\dot{C}{=}O^{(-)} + I \rightarrow H_2CO + [I]^{\cdot -} .$$

The derivative *IV* was also obtained in the case of application of triphenylphosphine with *Ib* in aqueous alkaline medium of the Wittig reaction[24] and by reaction of *Ia* with NaCN in 2-methyl-2-propanol.

Carbanions represent good electron donors for the anionradical formation[10]. Application of hard bases to 5-nitrofurfuryl derivatives can convert them into carbanions in the first step, the latter acting as electron donors to the substrate. Formation of *III* as well as other ethylene derivatives (*e.g. IX*) can be explained by the following sequence:

$$I, V \rightarrow I^{(-)} + V^{(-)}$$

$$O_2N\text{-}Ar\text{-}CH_2\text{-}X + I^{(-)}, V^{(-)} \rightarrow [O_2N\text{-}Ar\text{-}CH_2\text{-}X]^{\cdot -} + [I]^{\cdot} + [V]^{\cdot}$$

$$[O_2N\text{-}Ar\text{-}CH_2\text{-}X]^{\cdot -} \rightarrow O_2N\text{-}Ar\text{-}CH_2^{\cdot} + X^{(-)}$$

$$2\,[O_2N{-}Ar{-}CH_2]^{\cdot} \rightarrow II$$

$$[O_2N\text{-}Ar\text{-}CH_2]^{\cdot} + I^{(-)}, V^{(-)} \rightarrow [VII]^{\cdot -} + [VIII]^{\cdot -}$$

$$[O_2N\text{-}Ar\text{-}CH_2]^{\cdot} + [I]^{\cdot}, [V]^{\cdot} \rightarrow VII + VIII$$

$$[VII]^{\cdot -}, [VIII]^{\cdot -} + O_2N\text{-}Ar\text{-}CH_2\text{-}X \rightarrow [O_2N\text{-}Ar\text{-}CH_2\text{-}X]^{\cdot -} + VII + VIII$$

$$VII, VIII \xrightarrow[-HX]{\text{base}} III + IX,$$

where Ar means 2,5-furylene or phenylene.

The carbanion formed by action of a hard base reacts further in the sense of the anion-radical mechanism, behaving as a soft base[22] to the substrate which can be the starting 5-nitrofurfuryl derivative or some other suitable skeleton (*e.g.* 4-O_2N—Ar—CH_2—X) Depending on the rate of formation, either the ethane derivative *II* is formed or the reaction results in formation of the ethylene derivative *III* and *IX*. The intermediate *VII*, which was isolated before[20], splits off a HBr molecule in basic medium to give the derivative *III*. The ethylene *IX* is formed in similar way. The following substances were isolated as the side reaction products: 5-nitrofurfuryl alcohol (*X*), 5-nitro-

-2-furaldehyde (*XI*) and methyl 5-nitro-2-furanecarboxylate (*XII*). These reactions were observed earlier[25]. Most often the reactions are accompanied by 5-nitrofurfuryl alcohol (*X*) which can be formed by reaction of the radical $[VI]^{\bullet}$ with air oxygen. In the presence of hard bases ($OH^{(-)}$, $CH_3O^{(-)}$) dehydrogenation to 5-nitro-2-furaldehyde (*XI*) is presumed, the latter substance being converted by bases in methanol into methyl 5-nitro-2-furanecarboxylate (*XII*). 5-Nitrofurfuryl iodide reacts in similar way[26].

The given mechanisms alone need not be responsible for formation of the final products. Parallel operation of several mechanisms can be presumed. Thus the formation of the ethylene derivative can also be explained generally by the α-ElcB mechanism[12]. Formerly we presumed formation of a carbene and its dimerization:

$$I^{(-)} \xrightarrow[-X^{(-)}]{} [O_2N{-}Ar{-}CH] \xrightarrow{\text{dimerization}} III$$

The isolated intermediate[20] *VII* made us to consider the substitution-elimination mechanism[20]. With respect to considerable velocity of this reaction (the order of magnitude in seconds) the carbene mechanism can be considered most probable. The possibility of α-ElcB mechanism for longer reaction times is indicated by the fact that the ethylene derivative *III* is also obtained, if the ethane derivative *II* is let to react in basic medium for a longer time (hours).

Closer examination showed that these are general reactions of 5-nitrofurfuryl derivatives. From the abovementioned facts and from experimental data it follows that the reactions going by the anionradical mechanism have little time and energy requirements and approach the character of some fundamental processes taking place in biosystems. Their synthetic utilization consists in the possibility to obtain high yields of compounds otherwise unavailable by proper adjusting the reaction conditions. From theoretical viewpoint the $S_{RN}1$ and $S_{RN}2$ mechanisms contribute to elucidation of known but theoretically unexplained reactions and, on the other hand, they indicate the impossibility to obtain a substitution product under the chosen conditions, if formation of some other derivative predominates. Thus *e.g.* the reaction of *Ib* with $CN^{(-)}$ is explained by so-called anomaly, but the problem becomes quite clear from the viewpoint of the $S_{RN}1$ mechanism. Perhaps the most important application of this theory is its elucidation of biological properties of nitrofurane derivatives (generally of nitroaromatic derivatives). Hence it can be presumed that besides the biological effects ascribed to easy reducibility of nitro group (especially the hydroxylamine derivative) there are effects due to strong electron-acceptor character of nitrofurane derivatives. By their electron-acceptor properties they can fundamentally influence the electron transfer in biosystems and thus eliminate some vitally important processes of the cell. Generally the $S_{RN}1$ mechanism can also be presumed with further 5-nitrofurane derivatives.

EXPERIMENTAL

Melting temperatures were not corrected. The thin-layer chromatography was carried out on Silufol UV 254 plates (Kavalier) with benzene as eluent. The column chromatography was carried out on a 3 × 30 cm column of silica gel (150/250) with benzene or benzene–ethyl acetate as eluent. The ^{1}H-NMR spectra were measured with a Tesla BS 487 B apparatus (80 MHz), the IR and UV spectra were measured with a UR-20 and a Specord UV VIS apparatus (Zeiss, Jena), respectively.

Nitration of furfuryl alcohol with acetyl nitrate gave *Ia* which on refluxing with acetone and sodium bromide gave *Ib* (ref.[27]). The derivative *VIII* was prepared and described in our previous work[20], m.p. 150—151°C. The ethylene derivative *IX* was obtained as a side product of the reaction of the sulphone *Va* with 4-nitrobenzyl bromide in dimethylformamide using sodium hydride as base[20], m.p. 177°C (ref.[28] m.p. 178—180°C). 5-Nitrofurfuryl alcohol (*X*), 5-nitro-2-furaldehyde[29] (*XI*) and methyl 5-nitrofurane-2-carboxylate (*XII*) were isolated as further side products.

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

a) The nitrate *Ia* (1·88 g *i.e.* 0·01 mol) was added in portions to solution of 0·49 g (0·01 mol) sodium cyanide in 30 ml methanol with stirring at 25°C. After 24 h the mixture was evaporated and purified by column chromatography using benzene as eluent. Yield 87%.

b) Solution of 2·06 g (0·01 mol) bromide *Ib* in 30 ml methanol was stirred and treated with 0·49 g (0·01 mol) sodium cyanide. After 2 h the mixture was evaporated and purified chromatographically using benzene as eluent. Yield 75%.

c) Furfuryl mercaptane (1·04 g, 0·01 mol) was added to solution of sodium methoxide (0·25 g sodium in 40 ml methanol) at 20°C, whereafter 2·06 g (0·01 mol) bromide *Ib* was added slowly. The mixture was stirred 24 h, evaporated, and purified by crystallization. Yield 65% of the derivative *II*, m.p. 163°C (ref.[26] m.p. 161—162°C). IR spectrum (KBr, cm^{-1}): $\nu_{as}(NO_2)$ 1 530, 1 509, $\nu_s(NO_2)$ 1 362, ν(C—O—C)$_{fur}$ 1 025. ^{1}H-NMR spectrum (hexadeuterioacetone, 25°C, δ, ppm): 7·45 d, 6·63 d (H-furane), 3·60, 2·92 (—CH_2CH_2—).

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

a) The bromide *Ib* (2·06 g, 0·01 mol) was added to solution of sodium ethoxide (0·25 g sodium in 20 ml ethanol) and the yellow solution was, after 10—15 min, evaporated and purified by column chromatography (Al_2O_3, Brockmann II) with ethyl acetate as eluent. Yield 75—80%.

b) The two-phase system consisting of 10% aqueous sodium hydroxide and dichloromethane was stirred and treated with 2·06 g (0·01 mol) bromide *Ib*. After 1 h the organic layer was separated, dried, evaporated, and purified on a column. Yield of *III* was 25—30%, m.p. 245°C (ref.[30] m.p. 243—245°C). Small amounts of the derivative *II* were isolated, too. IR spectrum (chloroform, cm^{-1}): ν(C=C) 1 610, $\nu_{as}(NO)_2$ 1 540, $\nu_s(NO_2)$ 1 356, ν(C—O—C)$_{fur}$ 1 028. UV spectrum (methanol, nm, (log ε)): 245 (4·23), 288 (3·94), 415 (4·54).

5-Nitro-2-methylfurane (*IV*)

The derivative *IV* was isolated as a side product after the reaction of the nitrate *Ia* with sodium cyanide in methanol (yield 8%) and after the reaction of *Ia* with sodium cyanide in 2-methyl-2-propanol (yield 41%). M.p. 43—45°C (ref.[31] m.p. 43·5°C). ^{1}H-NMR spectrum (deuteriochloroform, 25°C, σ, ppm): 7·19 d, 6·20 d (H-furane), 2·44 s (CH_3).

5-Nitro-2-furfuryl Phenyl Sulphone (*Va*)

Mixture of 6·3 g (0·03 mol) *Ia* and 4·9 g (0·03 mol) sodium benzenesulphinate in 40 ml ethanol was refluxed 2 h. The raw product was collected by suction and crystallized from acetic acid. Yield 70—75%, m.p. 196—198°C (ref.[32] m.p. 196—197°C). From the mother liquors the derivative *II* was isolated in the yield 10—15%.

5-Nitrofurfuryl Trichloromethyl Sulphone (*Vb*)

Solution of 6·3 g (0·03 mol) bromide *Ib* in 25 ml dimethylformamide was treated with 8·2 g (0·04 mol) sodium trichloromethanesulphinate dissolved in 25 ml dimethylformamide. After 12 h stirring at 40°C the raw product was collected by suction, dried and recrystallized from chloroform. Yield 40— 0% *Vb*, m.p. 139°C. For $C_6H_4Cl_3NO_5S$ (308·5) calculated: 4·54% N, 10·38% S; found: 4·63% N, 10·27% S. IR spectrum (chloroform, cm^{-1}): $_{as}(NO_2)$ 1 550, 1 507, $_{as}(SO_2)$ 1 364, $_{s}(SO_2)$ 1 167. ^{1}H-NMR spectrum (hexadeuteriodimethyl sulphoxide, 25°C, ppm): 7·68 d, 7·06 d (H-furane, $J_{3,4}$ = 3·9 Hz), 5·62 s (CH_2). The derivative *II* was obtained as a side product from the mother liquors (yield 20—30%).

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