OPENING OF THE FURAN RING IN 5-AZIDO-2-FURALDEHYDE*

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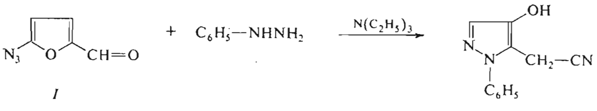
Fission of the furan ring in 5-azido-2-furaldehyde is described. α-Furylnitrene, formed from α-azido furan derivatives, is stabilized by the furan ring fission. Transformation of the intermediate to quinoxaline and pyrazole derivatives is also studied.

The behaviour of the azide group in 5-azido-2-furaldehyde has been studied on reaction of this compound with triphenylphosphine and acetylene[1]. In one of our previous papers[2] we described the reaction of 5-azido-2-furaldehyde with compounds containing an active methylene group. This reaction takes place preferentially at the carbonyl group, giving rise to 5-azido-2-furylidene derivative when the ratio of reactants is 1 : 1. When an excess of the methylene-containing agent is employed, the azide group also enters the reaction to give a 5-amino-2-furylidene derivative. In this paper we study the reaction of 5-azido-2-furaldehyde (*I*) with phenylhydrazine in the presence of a base with the aim to prepare 5-azido-2-furaldehyde phenylhydrazone. Compound *I* reacted with phenylhydrazine in the presence of triethylamine or N,N-dimethylaniline with evolution of 1 mol of nitrogen, affording a compound, identified as 1-phenyl-4-hydroxy-5-cyanomethylpyrazole (*IIa*) (Scheme 1). The presence of the hydroxy group in *IIa* was proved by acetylation to 4-acetoxy-1-phenyl-5-cyanomethylpyrazole (*IIb*).



SCHEME 1

In order to explain the transformation of a furan compound into a pyrazole derivative we studied this reaction more closely. First of all, we investitated the role of the base. In the absence of base, compound *I* reacts with phenylhydrazine to give

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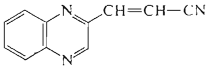
4,5-dioxo-2-pentenonitrile phenylhydrazone (*III*) in which the acrylonitrile part has *Z*-configuration. The isolated *III* on treatment with tertiary amines is transformed into *IIa*. Triethylamine or N,N-dimethylaniline catalyse intramolecular addition of the group to the acrylonitrile moiety and the arising oxo-form is transformed into the enol *IIa* by hydrogen migration. The glyoxal derivative, formed in the reaction of *I* with phenylhydrazine, was generated also in the reaction of *I* with aromatic diamines. Thus, reaction of *I* with 1,2-diaminobenzene affords 3-(2-quinoxalinyl)acrylonitrile (*IV*) in which the acrylonitrile moiety has *Z*-configuration. In the reaction of *I* with 5,6-dimethyluracil which contains amino groups of different reactivity[3], the amino group in the position 5 reacts at 60°C under formation of the acyclic derivative *V* (also with *Z*-configuration of the acrylonitrile moiety).

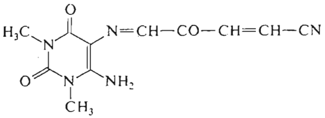
The formation of compounds *IIa*, *III*, *IV* and *V* shows that the studied transformations involve a condensation reaction at the carbonyl group in *I* and also an opening of the furan ring. One can assume that *I* is condensed with phenylhydrazine or diamines to give azomethines of the 5-azidofurylidene type which then decompose to the compounds *IIa*, *III*, *IV*, and *V*.

C_6H_5—NH—N=CH—CO—CH=CH—CN

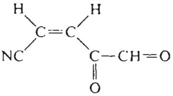
III



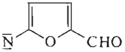
IV



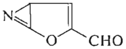
V



VI



IX



X

In order to find out whether the fission of the furan ring takes place also in the absence of bases, we studied the thermal decomposition of *I*. We anticipated that the α-azido group on the furan nucleus is decomposed on heating, affording a nitrene which is stabilized by opening of the furan ring. The compound *I* was decomposed in ethanol by hydrogen peroxide under evolution of nitrogen, oxygen and carbon dioxide. We isolated ring fission products – the monoamide *VII* and ammonium hydrogen maleate (*VIII*). Formation of these products can be explained by reaction of hydrogen peroxide with the arising 4,5-dioxo-2-pentenonitrile[4,5] (*VI*), leading either to *VII* or *VIII* by oxidation[6] of the 1,2-dicarbonyl part of *VI*. The furan ring was opened even in the absence of hydrogen peroxide when the compound *I* was decomposed in tetrachloromethane or n-hexane. In this case we isolated from the reaction mixture a product which on treatment with phenylhydrazine afforded compound *III* whereas with 1,2-diaminobenzene compound *IV* was obtained.

Structure of the products *IIa*, *III*, *IV*, *V*, *VII* and *VIII* proves that *I* is thermaly decomposed to (*Z*)-4,5-dioxo-2-pentenonitrile (*VI*).

Our present results show that the transformations of compounds *I* to *IIa*, *III*, *IV*, *V* and *VI* proceed *via* α-azido-furan derivatives which decompose to give an α-furylnitrene derivative *IX* or the product *X*, which is formed by intramolecular cyclisation[7]. The furan nucleus is opened, analogously as in the case of 2-furylcarbene, to afford the compound *VI* (ref.[8]) or its derivatives which are then transformed into compounds *IIa*, *IV*, *VII* or *VIII*.

EXPERIMENTAL

The IR spectra were measured on a UR 20 (Zeiss, Jena) spectrophotometer, UV spectra on a UV-VIS Specord instrument, and ^{1}H-NMR spectra on a BS 487C (80 MHz) spectrometer. Melting points were determined on a Kofler block.

1-Phenyl-4-hydroxy-5-cyanomethylpyrazole (*IIa*)

A) Phenylhydrazine (10·8 g; 100 mmol) and N,N-dimethylaniline (5 ml) were added at −10°C to a solution of 5-azido-2-furaldehyde (13·7 g; 100 mmol) in diethyl ether (250 ml) and the mixture was kept at −20°C for 3 days. The separated red crystals were filtered, dissolved in dimethyl sulfoxide (50 ml) and the solution was heated to 60°C for 15 min. Water (500 ml), slightly acidified with hydrochloric acid, was added. The precipitated product was crystallized from ethanol, yielding 6·4 g (32%) of *IIa*, m.p. 155−6°C.

B) Triethylamine (3 ml) was added to a mixture of 4,5-dioxo-2-pentenonitrile phenylhydrazone (4 g; 20 mmol) and dimethyl sulfoxide (30 ml). The mixture warmed spontaneously to 40°C. After stirring for 40 min it was poured into acidified water and the product taken up in ethyl acetate. Evaporation of the solvent afforded 3·3 g (83%) of *IIa*, m.p. 155−6°C. For $C_{11}H_9N_3O$ (199·8) calculated: 66·12% C, 4·54% H, 21·03% N; found: 66·20% C, 4·58% H, 21·02% N. IR spectrum (KBr): 3200−2600 cm^{-1} (several bands; bonded OH), 2252 (C≡N), 1622, 1603 (HC=N, C=C). UV spectrum (methanol): λ_{max} 261 nm (log ε 3·93), 220 (3·90), 204 (4·17). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide): 7·50 (s, 5 H, arom. hydrogens), 7·40 (s, 1 H, $C_{(3)}$—H pyrazole), 4·67 (s, broad, OH), 4·03 (s, 2 H, CH_2).

4-Acetoxy-1-phenyl-5-cyanomethylpyrazole (*IIb*)

A mixture of 4,5-dioxo-2-pentenonitrile phenylhydrazone (4 g; 20 mmol), triethylamine (3 ml) and dimethylsulfoxide (30 ml) was stirred for 30 min. After cooling to 10°C, acetic anhydride (2 g, 20 mmol) was added and the stirring was continued for 15 min. The mixture was poured into water, extracted with ethyl acetate, the extract taken down and the residue crystallized from ethanol, affording 4 g (85%) of *IIb*, m.p. 103−104°C. For $C_{13}H_{11}N_3O_2$ (241·2) calculated: 64·73% C, 4·60% H, 17·42% N; found: 64·70% C, 4·57% H, 17·35% N. IR spectrum (KBr)

2951, 2927 cm^{-1} (CH_2), 2260 (C≡N), 1763 ($COOCH_3$), 1600 (CH=N, C=C); UV spectrum (methanol): λ_{max} 243 nm (log ε 3·95), 205 (4·17); ^{1}H-NMR spectrum (hexadeuterioacetone): 7·67 ppm (s, 1 H, $C_{(3)}$—H pyrazole), 7·49 (s, 5 H, aromatic hydrogens), 4·02 (s, 2 H, CH_2), 2·28 (s, 3 H, CH_3).

4,5-Dioxo-2-pentenonitrile Phenylhydrazone (*III*)

A) Phenylhydrazine (3·2 g; 30 mmol) was added at 0°C to a stirred solution of 5-azido-2-furaldehyde (4·3 g; 30 mmol) in diethyl ether (50 ml). After standing for 5 h at −25°C, the yellow crystals were filtered and crystallized from diethyl ether; yield 5·4 g (90%) of *III*, m.p. 148°C. For $C_{11}H_9N_3O$ (199·8) calculated: 66·12% C, 4·54% H, 21·03% N; found: 66·07% C, 4·48% H, 21·08% N. IR spectrum (KBr): 3285 cm^{-1}, 3123, 3217 (N—H), 2221 (C≡N), 1723 (C=O), 1627 (CH=N). UV spectrum (methanol): λ_{max} 399 nm (log ε 4·29), 278 (3·78), 251 (4·09), 202 (4·21). ^{1}H-NMR spectrum (hexadeuterioacetone): 7·98 ppm (d, J = 12 Hz, 1 H, CH=C—CN), 7·55—6·88 (m, 6 H, CH=N, aromatic hydrogens), 6·10 (d, J = 12 Hz, 1 H, C=CH—CN), 10·9 (s, broad, 1 H, NH).

B) A solution of 5-azido-2-furaldehyde (4·30 g; 30 mmol) in methanol (150 ml) was set aside at room temperature. During the standing evolution of nitrogen was observed. After 7 days phenylhydrazine (3·2 g; 30 mmol) was added. The solvent was evaporated *in vacuo* and the residue chromatographed on a silica gel column (acetone–chloroform 1 : 6), affording 0·9 g (15%) of *III*, m.p. 146—148°C.

3-(2-Quinoxalinyl)acrylonitrile (*IV*)

A) 1,2-Diaminobenzene (1·08 g; 10 mmol) in ethanol (20 ml) was added to a stirred mixture of 5-azido-2-furaldehyde (1·38 g; 10 mmol) and ethanol (20 ml). The mixture was kept at 35 to 40°C until the evolution of nitrogen ceased. After cooling, water (10 ml) was added, the precipitated crystals were filtered and crystallized from ethanol, affording 1·1 g (54%) of *IV*, m.p. 115 to 116°C. For $C_{11}H_7N_3$ (181·2) calculated: 72·92% C, 23·19% N, 3·89% H; found: 72·89% C, 3·80% H, 23·01% N. IR spectrum (KBr): 2221 cm^{-1} (C≡N). UV spectrum (methanol): λ_{max} 336 (log ε 4·03), 265 (4·46), 205 (4·35). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide): 9·13 ppm (s, 1 H, $C_{(3)}$—H quinoxaline), 8·25—7·80 (m, 4 H, $C_{(5-8)}$—H quinoxaline), 7·75 (d, J = 12 Hz, 1 H, CH=C—CN), 6·40 (d, J = 12 Hz, 1 H, C=CH—CN).

B) A mixture of 5-azido-2-furaldehyde (1·38 g; 10 mmol) and ethanol (30 ml) was heated to 60°C. After the nitrogen evolution had ceased, 1,2-diaminobenzene (1·08 g; 10 mmol) in ethanol (20 ml) was added. The mixture was concentrated to half of its original volume and worked up as described under *A*. Yield 0·87 g (51%) of *IV*, m.p. 115—116°C.

Reaction of 5,6-Diamino-1,3-dimethyluracil with 5-Azido-2-furaldehyde

A mixture of 5,6-diamino-1,3-dimethyluracil (1·8 g; 10 mmol) and ethanol (220 ml) was stirred at room temperature and treated with a solution of 5-azido-2-furaldehyde (1·38 g; 10 mmol) in ethanol (20 ml). After addition of the azide the solution was heated to 50—60°C. The precipitated compound was collected on filter and crystallized from ethanol, affording 2·3 g (91%) of *V*, m.p. 239°C. For $C_{11}H_9N_5O_3$ (259·2) calculated: 50·97% C, 3·50% H, 27·02% N; found: 50·91% C, 3·45% H, 27·10% N. IR spectrum (KBr): 3460, 3352 cm^{-1} ($(NH)_2$), 2220 (C≡N), 1715 (C=O), 1650—1600 (CH=N, C=C). UV spectrum (methanol): λ_{max} 412 nm (log ε 4·09), 278 (3·94), 254 (4·09), 202 (4·24). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide): 9·11 ppm (s, 1 H, CH=N), 8·31 (d, J = 11 Hz, 1 H, CH=C—CN), 7·85 (s, broad, 2 H, NH_2), 6·26 (d, J = 11 Hz, 1 H, C=CH—CN), 3·44 (s, 3 H, $N_3—CH_3$), 3·18 (s, 3 H, $N_{(1)}—CH_3$).

Reaction of 5-Azido-2-furaldehyde with Hydrogen Peroxide

A mixture of 5-azido-2-furaldehyde (4·2 g; 30 mmol), 30% hydrogen peroxide (16 ml) and ethanol (50 ml) was warmed to 50°C till the evolution of gases ceased. After 24 h the mixture deposited 0·5 g (13%) of maleic acid monoamide (*VII*), m.p. 152—153°C (reported[9] m.p. 153°C). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide): 8·67, 8·25 (broad d, 3 H, COOH and $CONH_2$), 6·45 (d, J = 13 Hz, 1 H, C=CH—$CONH_2$), 6·27 (d, J = 13 Hz, 1 H, C=CH—COOH). The filtrate was concentrated *in vacuo*, treated with dioxane (150 ml) and the precipitated tetrahydrate of ammonium hydrogen maleate (*VIII*) was collected (2·7 g; 67%); decomposition above 90°C (ref.[10]). ^{1}H-NMR spectrum (hexadeuteriodimethyl sulfoxide): 7·05 (broad s, 13 H, COOH, NH_4^+, 4 H_2O), 6·10 (s, 2 H, ethylenic hydrogens).

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