MECHANISM OF FORMATION OF 2-AMINO-3-CYANO-4,5-DIPHENYLFURANE AND SOME OF ITS REACTIONS

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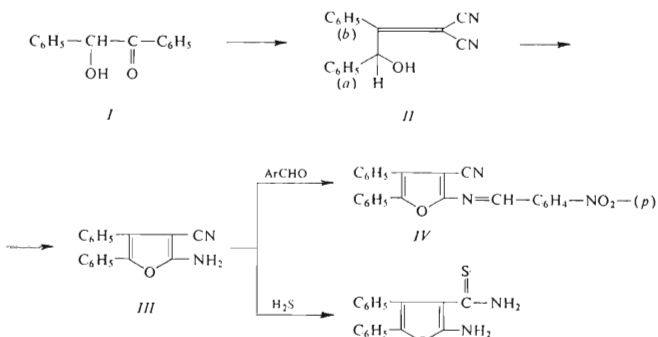
The reaction of benzoin (*I*) with propanedinitrile in dimethylformamide catalyzed with diethylamine gives directly 2-amino-3-cyano-4,5-diphenylfurane (*III*),whereas this reaction catalyzed with glycine in ethanol produces the intermediate *II* which is transformed into *III* thermally or by catalysis with diethylamine. The aminofurane *III* reacts with 4-nitrobenzaldehyde to give azomethine *IV*, and it produces 2-amino-3-thioamido-4,5-diphenylfurane (*V*) by reaction with H_2S in dimethylformamide.

One of the methods of preparation of aminofurane derivatives consists in base-catalyzed reaction of acyloins with propanedinitrile where 2-amino-3-cyano-4,5-disubstituted furane derivatives are formed as final products of intramolecular cyclization[1]. In our previous works[2-4] this procedure was used for preparation of some aminofurane derivatives.

The present communication deals with mechanism of formation of 2-amino-3-cyano-4,5-diphenylfurane (*III*) and some its reactions (Scheme 1). The authors[5] report formation of the derivative *II* in the reaction of benzoin with propanedinitrile in ethanol with catalysis by diethylamine, but from m.p. 204–206°C and from IR spectral data it follows that the authors identified incorrectly the aminofurane derivative *III*. Later this synthetic method was generalized by Gewald[6] for use in preparations of analogous aminofurane derivative. On the basis of ref.[5] the compound *II* is presumed to be the intermediate, but it has not been isolated so far. Our aim was to prove the intermediate *II* as a precursor in formation of the aminofurane *III* and to characterize reactivity of CN group in the derivative *III*.

Starting from the reports describing the Knoevenagel-type condensation reactions with glycine as the base[7-10], we prepared the compound *II* from benzoin and propanedinitrile in aqueous ethanol with glycine as the catalyst. The derivative *II* was isolated and identified by its ^{1}H NMR spectrum. By comparison with analogous derivatives[11] we could identify OH group at $\delta = 3{\cdot}05$ as a broad singlet and the

benzyl hydrogen atom as a singlet at $\delta = 6{\cdot}01$. The phenyl hydrogen atoms *a* agreed well with δ values and shape of spectrum of benzyl alcohol[11], the atoms *b* agreed well with δ values, shape of spectrum and shifts of analogous cinnamyl derivative[11]. From the derivative *II* we obtained the product *III* either thermally or at the reaction conditions described in ref.[2], and *III* reacted with 4-nitrobenzaldehyde to give the corresponding azomethine derivative *IV* (ref.[2]). The other 2-amino-3-cyano--4,5-disubstituted furane derivatives can be presumed to be formed in this way, too.



SCHEME 1

Furthermore we investigated transformation reactions of CN group of the amino-furane *III*. Generally it can be stated that the reactivity is low due to conjugation with amino group. Attempts to transform nitrile *III* into the corresponding amide or similar derivatives failed. None of usual reactions of this type[12] could change the derivative *III*. Only on the basis of ref.[13], which describes transformations of *ortho*-amino-cyano derivatives into thioamides, we could prepare 2-amino-3-thio-amido-4,5-diphenylfurane (*V*) (IR absorption band of $CSNH_2$ group at 3 422 cm^{-1}) by reaction of *III* with H_2S in dimethylformamide at 50°C. Mass spectrum of the aminofurane *III* shows $M^{+\cdot}$ as the most intensive peak (100%, ref.[2]), whereas the derivative *V* only has relative intensity of 16% for $M^{+\cdot}$. Fragmentation of the two derivatives is different, too. A common peak is that with m/z 105 whose relative intensities are 26% and 100% for the derivatives *III* and *V*, respectively. ^{1}H NMR spectrum of *V* exhibits a slight shift of signal of amino group as compared with that of *III* ($\Delta\delta = \delta_V - \delta_{III} = 7{\cdot}90 - 7{\cdot}64 = 0{\cdot}26$ ppm). 2-Amino-3-cyano-4,5-difuryl-furane and 2-amino-3-cyano-4,5-dithienylfurane react similarly[14].

EXPERIMENTAL

The melting points were measured with a Kofler apparatus and are not corrected. The ^{1}H NMR spectra were measured with a Tesla BS 487 B apparatus (80 MHz) in hexadeuterioacetone at 25 and 50°C using hexamethyldisiloxane as internal standard. The IR spectra were obtained with a UR-20 apparatus (Zeiss, Jena), and the mass spectra were measured with AEI MS 902 S.

[(1,2-Diphenyl-2-hydroxy)ethylidene]propanedinitrile (*II*)

Aqueous-ethanolic (80 ml 98% ethanol and 3 ml water) solution of 10·5 g (0·05 mol) benzoin and 4·25 g (0·064 mol) propanedinitrile was treated with catalytic amount of glycine at 50°C. After 10 min, the solution was refluxed 1 h. On cooling we obtained compound *II*, m.p. 123 to 125°C, yield 11·5 g (88%), contaminated with aminofurane *III*. ^{1}H NMR spectrum of *II* (hexadeuterioacetone, δ, ppm): 3·05 bs (1 H, OH), 6·01 s (1 H, C—H), 7·34 s (5 H, the phenyl protons *a*), 7·16—7·40 m, 7·90 d, 7·93 d (5 H, the phenyl protons *b*).

2-Amino-3-cyano-4,5-diphenylfurane (*III*)

a) 1 g derivative *II* was melted at 140—150°C. Crystals of *III* were obtained by cooling of the melt. M.p. 206—207°C (ref.[2] m.p. 206°C).

b) 2·6 g (0·01 mol) *II* was dissolved in 30 ml dimethylformamide, and the solution was treated with 4 ml diethylamine. After 12 h stirring, the solution was poured in water, the precipitate formed was collected by suction and recrystallized from ethanol to give 2·1 g (81%) *III*, m.p. 204—206°C (ref.[2] m.p. 206°C).

2-(4-Nitrophenylmethyleneimino)-3-cyano-4,5-diphenylfurane (*IV*)

Solution of 2·6 g (0·01 mol) *III* and 1·51 g (0·01 mol) 4-nitrobenzaldehyde in 30 ml ethanol was refluxed 2 h to give an orange colouration. The solvent was evaporated, and the residue was purified by column chromatography (Al_2O_3, Brockmann II, chloroform as eluent). Recrystallization of the main fraction gave 3·25 g (83%) azomethine *IV*, m.p. 186—188°C (ref.[2] m.p. 187—189°C).

2-Amino-3-thioamido-4,5-diphenylfurane (*V*)

Hydrogen sulphide was bubbled through solution of 2·6 g (0·01 mol) *III* and 10 g triethylamine in 100 ml dimethylformamide at 50—60°C 48 h. Then the mixture was poured in 150 ml water and the precipitate formed was collected by suction. The raw product was separated by column chromatography (silica gel 150/250) using benzene–acetone (1 : 1) as eluent. From the first portions of the eluate we obtained 0·65 g (22%) thioamide *V*, m.p. 177—178°C. For $C_{17}H_{14}N_2OS$ (294·4) calculated: 69·36% C, 4·79% H, 9·52% N; found: 69·91% C, 4·87% H, 9·24% N. IR spectrum (KBr, cm^{-1}): 3 275, 3 170, 1 643 (NH_2), 3 422, 1 620 (NH_2 of thioamide), 1 032 (C—O—C), 1 488, 1 403, 1 320, 1 081, 960, 770, 708. ^{1}H NMR spectrum (hexadeuterioacetone, δ, ppm): 7·45 s (5 H, H-phenyl), 7·06 s (5 H, H-phenyl), 7·90 bs (NH_2), 8·33 bs ($CSNH_2$). Mass spectrum *m/z* (rel. intensity, %): 296 (0·6) [M+2], 295 (1·7) [M+1], 294 (16) $M^{+\cdot}$, 279 (10), 277 (12), 260 (9), 255 (11), 192 (8), 167 (16), 160 (7), 150 (10), 149 (68), 128 (10), 122 (7), 113 (9), 106 (11), 105 (1000), 101 (11), 97 (11), 95 (9), 85 (8), 84 (7), 83 (16), 82 (7), 81 (10), 78 (13), 77 (50), 71 (18), 70 (13), 69 (13), 67 (8), 66 (6), 65 (7), 64 (16), 59 (18), 58 (12), 57 (26), 56 (15), 55 (20), 51 (16), 49 (8), 44 (34) 43 (58), 42 (8), 41 (26), 39 (13), 34 (11), 32 (10).

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