UDC 547.722 + 542.955.4

RESEARCHES ON FURANS

XLIII. Effect of Solvent on the Reaction Between 2-Chloromethylfuran and Sodium Cyanide*

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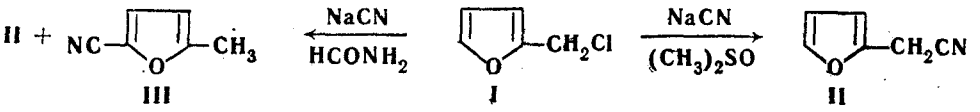
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 2, No. 6, pp. 829-831, 1966

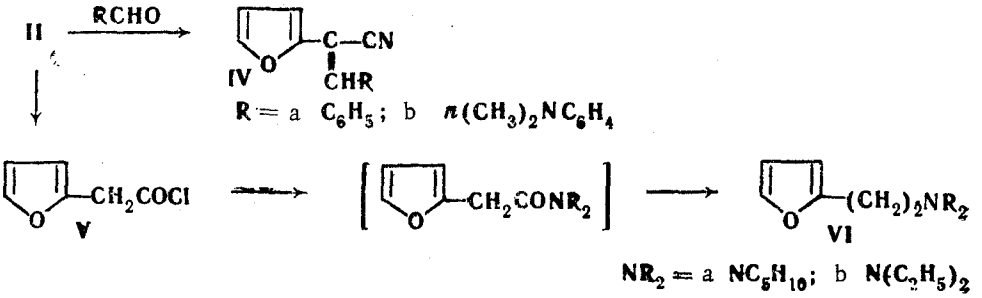
A study is made of the effect of solvent on the direction of the reaction between 2-chloromethylfuran and sodium cyanide. It is found that in dimethylsulfoxide only 2-furylacetonitrile is formed, while in formamide a mixture of 2-furylacetonitrile and 5-methyl-2-furonitrile is formed. 2-(β-Aminoethyl) furans are synthesized from 2-furylacetonitrile.

In previous papers in this series [2] it was shown that 2-chloromethylfuran (I) and sodium cyanide react in one direction only in aprotic solvents (dimethylformamide, acetonitrile, and nitromethane), and that the sole reaction product is 2-furylacetonitrile (II).

The present work showed that with dimethylsulfoxide as the aprotic solvent (the reaction products being treated with sodium chloride solution) the result is similar, the yield of 2-furylacetonitrile (II) being 75%. When the reaction is run in formamide a mixture of the two isomeric nitriles is formed, with 5-methylpyromuconitrile (III) predominating, i.e., the ratio is about the same as with water. A protonated solvent would facilitate a S_N1 reaction, and the last result can be explained by assuming that type of reaction mechanism [3, 4].



We have also established that high yields of benzylidene derivatives IV are obtained by the action of aromatic aldehydes on 2-furylacetonitrile, indicating high methylene hydrogen lability in 2-furylacetonitrile (II). Starting from 2-furylacetyl chloride (V), and using a method which we previously developed [2], we have now synthesized 2-(β-N-piperidinoethyl)-furan (VIa) in 84% yield, and 2-(β-diethylaminoethyl) furan (VIb), formed in only 20% yield by quite prolonged reduction. In this connection it should be mentioned that amine VIa is obtained in low yield (12%) by addition of piperidine to 2-vinylfuran, while it has proved impossible to obtain amine VIb from 2-vinylfuran and diethylamine [5].



Consequently our method of preparing 2-(β-aminoethyl) furans by reducing 2-furylacetamides is a general one.

Experimental

Reaction of 2-chloromethylfuran with sodium cyanide

a) In dimethylsulfoxide. 40 g 2-chloromethylfuran in 40 ml dimethylsulfoxide was added dropwise with stirring

* For Part XLII see [1].

to a suspension of 20 g NaCN in 60 ml dimethylsulfoxide bp 83–84° C at 19 mm, n_D^{20} 1.4785, the temperature not exceeding 40–45° C. Next day 150 ml benzene and 100 ml saturated brine were added, the benzene layer separated off, washed with saturated brine, dried over $MgSO_4$, run onto an alumina column, and eluted with benzene. When the solvent was distilled off, the yield of II was 26.5 g (75%): bp 86.5–88° (20 mm), n_D^{20} 1.4713, R_f 0.52.* The literature gives bp 69–73° C (10 mm) [6], n_D^{25} 1.4715 [7], n_D^{25} 1.4691 [8].

b) In formamide. 23.5 g I was added, with stirring to a solution of 15 g NaCN in 120 ml formamide, the temperature being held at 55–60° C. Next day the products were extracted with ether, the extracts washed with water, dried over $MgSO_4$, and the ether distilled off. 7.8 g of a fraction bp 60–75° C (10 mm) was obtained, and this was fractionally distilled into: 1) bp 57–62° C (9 mm), 2.4 g; 2) bp 63–69° C (9 mm), 4.1 g; 3) bp 69–71° C (9 mm), 0.5 g. The 1st fraction was 5-methyl-2-furonitrile (III): bp 57–62° (9 mm); n_D^{20} 1.4815, d_4^{20} 1.0833; MR_D 28.16. Calculated for C_6H_5NO with 2 F, 28.11. R_f 0.52. The literature gives bp 60° C (13 mm) [6], 66–68° C (15 mm) [9]; n_D^{20} 1.4848, d_4^{20} 1.0463. Hydrolysis of 0.3 g nitrile III by boiling for 1 hr 30 min with 10 ml 20% KOH, gave 0.3 g 5-methylpyromucic acid, colorless needles, mp 109–110° C (ex petrol ether). The literature gives mp 109–110° C (ex petrol ether). The literature gives mp 109–110° C [6], 107–108.5° C [10].

Fraction 2 was a mixture of nitriles II and III: hydrolysis gave a mixture of 2 furylacetic acid (mp 67° C) and 5-methylpyromucic acid (mp 109° C), which were separated mechanically.

Fraction 3 was 2-furylacetonitrile (II): bp 69–71° C (9 mm); n_D^{20} 1.4720. R_f 0.52. Hydrolysis gave a quantitative yield of 2-furylacetic acid, mp 67–67.5° C (ex petrol ether). The literature gives mp 67.3–67.5° C [7], 66.8–67.5° C [7], 66.8–67.5° C [8], 68° C [9].

Benzylidenefurylacetonitrile (IVa). 2.5 ml of a 20% solution of NaOEt was added to a mixture of 5.3 g II and 5.3 g benzaldehyde, the mixture left 1 hr, dissolved in benzene, washed with water till neutral, dried over $MgSO_4$, and the benzene distilled off. Yield 7.3 g (75%), bp 108–108.5° C (1 mm); R_f 0.79, colorless thick liquid, rapidly discoloring in air, and turning red. Found: C 79.93, 80.15; H 4.86, 4.81%. Calculated for $C_{13}H_9NO$: C 79.98; H 4.65.

p-Dimethylaminobenzylidenefurylacetonitrile (IVb).

a) A mixture of 7.5 g p-dimethylaminobenzaldehyde and 5.3 g 2-furylacetonitrile was heated until solution was complete, and 2.5 ml 20% NaOEt added. On cooling yellow flaky crystals separated, yield 10.9 g (92%), mp 124–124.5° C (ex EtOH), R_f 0.65.

b) A few drops of 20% NaOEt solution were added to a mixture of 200 mg 2-furylacetonitrile and 4 ml saturated ethanolic solution of p-dimethylaminobenzaldehyde. Yield 440 mg (quantitative), mp 124–124.5° C. Found: C 75.50, 75.56; H 6.15, 6.16%. Calculated for $C_{15}H_{14}N_2O$: C 75.64; H 5.93%.

2-(β-N-piperidinoethyl) furan (VIa). 4.8 g piperidine in 30 ml dry benzene was added to 4.0 g acid chloride V (bp 53–54° C (7 mm), n_D^{20} 1.4895) [2], and the mixture refluxed for 4 hr with 1.1 g $LiAlH_4$ in 40 ml dry ether. The complex was decomposed, the mixture extracted, and the extract distilled to give (see [2]) 4.2 g colorless liquid (84%), bp 78–80° C (1 mm); n_D^{20} 1.4948; d_4^{20} 0.9840; MR_D 53.12. Calculated for $C_{11}H_{17}NO$ with 2 F, MR_D 53.25. The literature gives bp 92–93° C (6 mm), n_D^{20} 1.4945, d_4^{20} 0.9794 [5].

Picrate: Mp 119–120° C (ex EtOH). Mixed mp with a sample of the picrate of this amine [5] undepressed.

2-(β-Diethylaminoethyl) furan (VIb). Following the procedure described above, 9.0 g acid chloride V in 90 ml dry ether, 11.2 g diethylamine in 80 ml dry benzene, and 3.5 g $LiAlH_4$ in 40 ml dry ether, were refluxed and worked up to give 2.0 g colorless liquid (20%), bp 71–72° C (6 mm), n_D^{20} 1.4650; d_4^{20} 0.9160. Found: C 71.52, 71.57; H 9.90, 10.09%; MR_D 50.47. Calculated for $C_{10}H_{17}NO$: C 71.82; H 10.25%; MR_D 50.83.

Picrate: Mp 86–87° C (ex EtOH). Found: N 14.07, 13.88%. $C_{10}H_{17}NO \cdot C_6H_2(NO_2)_3OH$: N 14.14%.

Methiodide: Mp 178–179° C (ex EtOH). Found: C 42.89, 42.76; H 6.47, 6.44%. Calculated $C_{11}H_{20}INO$: C 42.73; H 6.52%.

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* All R_f values are for a thin non-stabilized layer of alumina, activity grade 2, solvent system benzene-heptane (4:1).

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6 July 1965

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