SYNTHESIS OF FURAN β-AMINOKETONES

B. I. Ardashev and I. S. Malik

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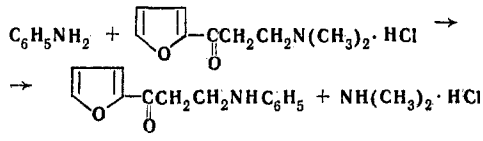
Reaction of 2-furyl(β-dimethylamino)ethylketone with aromatic amines gives ten β-arylaminoethylfurylketones, whose structures are confirmed by converting them to the corresponding quinoline derivatives.

In order to prepare, among furan derivatives, new physiologically active substances, we have prepared a series of furyl-β-aminoketones hitherto undescribed in the literature, by alkylating aromatic amines with 2-furyl(β-dimethylamino)ethylketone and 2-furyl(β-acetylfuran by the Mannich reaction. The literature describes [1–3] some cases of N-alkylation of aromatic amines by Mannich bases. The reaction products are β-aryl-aminoketones. There are papers [4, 5] describing alkylation of aromatic amines with salts of Mannich bases to give lepidine and 1-phenyllepidinium salts without the intermediate aminoketones being isolated.

We have now shown that the hydrochlorides of 2-furyl(β-dimethylamino)-ethylketone and 2-furyl(β-piperidino) ethylketone are smoothly alkylated by various amines by heating in aqueous solution.



The table gives the properties of the resultant amino ketones. Some of the aminoketones were converted to the corresponding quinoline bases. Cyclization to quinolines confirms the structures of the compounds prepared [6–8]. Tests for physiological activity showed that the compounds were nontoxic.

EXPERIMENTAL

2-Acetylfuran was prepared by acetylating furan with acetic anhydride [9, 10]. 2-Furyl(β-dimethylaminoethyl)ketone and 2-furyl(β-piperidinoethyl)-ketone hydrochlorides were prepared from 2-acetylfuran as described in [11, 12].

β-Anilinoethyl-2-furylketone. 0.75 g (0.0075 mole) aniline was dissolved with warming in 30–50 ml water, 1.02 g (0.005 mole) 2-furyl(β-dimethylamino)ethylketone added, and the mixture refluxed for 5–10 min. The condensation product separated as an oil; it solidified on cooling, and was filtered off and recrystallized from ethanol.

The other β-arylaminoketones were prepared similarly. β-(o-Tolylidino)ethylfurylketone, β-(m-tolylidino)ethylfurylketone, and β-diphenylaminethylfurylketone did not crystallize on cooling, and were isolated by extracting with ether followed by vacuum-distillation. Similar products were obtained using 2-furyl(β-piperidinoethyl)-ketone.

4-(2-Furyl)quinoline. A mixture of 2.15 g (0.01 mole) β-anilinoethylfurylketone, 2.5 g (0.02 mole) aniline hydrochloride, 2.6 g (0.01 mole) tannic chloride, 0.3 g zinc chloride, and 25 ml ethanol was refluxed for 1 hr 30 min, the ethanol vacuum-distilled off, the residue made alkaline with sodium hydroxide, and extracted with ether. The ether was distilled off, and excess aniline removed from the residue by vacuum-steam-distillation. The oil obtained was dissolved in ethanol, and 1 g picric acid added to the hot solution. Yield of picrate 0.72 g (17.2%), mp 202–203° (ex EtOH). Found: C 53.64, 53.65; H 2.91, 2.90, N 13.24, 13.22%. $C_{19}H_{12}N_4O_8$. Calculated for C 53.7; H 2.83; N 13.2%.

4-(2-Furyl)-5, 6-benzoquinoline picrate. Prepared similarly, yield 0.9 g (19.6%), mp 217–218°. Found: C 58.15, 58.18, H 5.11, 5.00, N 11.85, 11.88%. Calculated for $C_{23}H_{14}N_4O_8$: C 58.2, H 5.10, N 11.8%.

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Compound	Mp, °C	Formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
β-Anilinoethylfurylketone	52—53	$C_{13}H_{13}NO_2$	72.81, 72.60	6.23, 6.20	6.55, 6.53	72.5	6.04	6.5	2.3
β-(α-Naphthylamino)-ethylfurylketone	65—66	$C_{17}H_{15}NO_2$	77.02, 77.12	5.60, 5.56	5.32, 5.38	76.9	5.66	5.28	35.4
β-(β-Naphthylamino)ethylfurylketone	124—125	$C_{17}H_{15}NO_2$	76.52, 76.80	5.75, 5.70	5.30, 5.33	76.9	5.66	5.28	64.0
β-(m-Nitroanilino)ethylfurylketone	154—155	$C_{13}H_{12}N_2O_4$	60.51, 60.43	4.65, 4.60	10.25, 10.17	60.0	4.61	10.7	67.3
β-(p-Nitroanilino)ethylfurylketone	172—173	$C_{13}H_{12}N_2O_4$	60.2, 60.51	4.55, 4.50	10.2, 10.0	60.0	4.61	10.7	78.2
β-(p-Anisidino)ethylfurylketone	73—74	$C_{14}H_{15}NO_3$	68.91, 68.62	6.20, 6.18	5.75, 5.78	68.5	6.12	5.71	74.2
β-(o- Tolylidino)ethylfurylketone	40—41	$C_{14}H_{15}NO_2$	73.42, 73.52	6.71, 6.68	6.02, 6.00	73.3	6.55	6.11	44.1
β-(m-Tolylidino)ethylfurylketone	56—57	$C_{14}H_{15}NO_2$	73.51, 73.45	6.62, 6.60	6.18, 6.20	73.3	6.55	6.11	50.1
β-(p-Tolylidino)-ethylfurylketone	71—72	$C_{14}H_{15}NO_2$	73.35, 73.40	6.58, 6.62	6.15, 6.19	73.3	6.55	6.11	45.3
β-Diphenylaminoethylfurylketone	39—40	$C_{19}H_{17}NO_2$	78.35, 78.43	5.90, 5.96	4.85, 4.90	78.3	5.84	4.81	63.1

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