UDC 547.722 + 542.953.5

RESEARCHES ON FURANS

XLV. Reaction of β-Chloromethylfurans with Secondary Amines*

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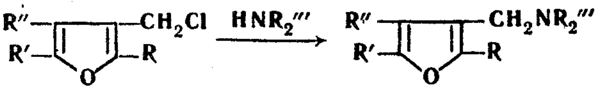
Khimiya Geterotsiklicheskikh Soedinenii, Vol. 2, No. 6, pp. 835–838, 1966

A series of hitherto undescribed 3-dialkylaminomethylfurans is obtained by reacting 3-chloromethylfuran and its homologs with secondary amines.

Unlike 2-aminomethylfurans, the β-amines are accessible with difficulty, and have been but little studied. Only some β-amines with aryl groups at positions 2 and 5 of the furan ring are known [2, 3]. We previously obtained a series of 3,4-bis(alkylaminomethyl) furans by reacting 3,4-bis(chloromethyl) furans with secondary [4] and primary [5] amines.

In the present paper a series of tertiary 3-aminomethylfurans are synthesized by reacting 3-chloromethylfurans with secondary amines in the presence of potassium hydroxide.



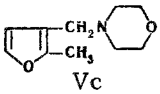
$R=R'=R''=H$ (I); $R=CH_3$, $R'=R''=H$ (II);
$R=R''=CH_3$, $R'=H$ (III); $R=R'=CH_3$, $R''=H$ (IV)

Bearing in mind the properties of 2-aminomethylfurans [6], amines with structures Va-f (Table 1), and their derivatives, are of interest on account of possible physiological activity.

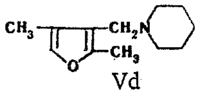
We have synthesized the most inaccessible halide, 3-chloromethylfuran (I), by the following route: diethyl furan-3,4-dicarboxylate [7], -monoethyl ester of furan-3,4-dicarboxylic acid-ethyl furan 3-carboxylate [8]-furan-3-carboxylic acid-3-furylcarbinol-3-chloromethylfuran (I) [9]. It should be mentioned that the properties of I differed somewhat from those given in the literature[9]. Chloromethylfurans II–IV were also obtained by reducing the esters of the corresponding furan-3-carboxylic acids, and then converting the 3-furylcarbinols to chlorides [10–12]. The hitherto undescribed 2,4-dimethyl-3-chloromethylfuran (III) is distinguished by its extreme instability.

Table 1

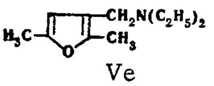
3-Aminomethylfurans



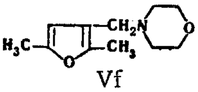
Vc



Vd



Ve



Vf

Amine	Bp, °C (pressure, mm)	n_D^{20}	d_4^{20}	MR_D Found	MR_D Calculated	Formula	Found, % C	Found, % H	Calculated, % C	Calculated, % H	Yield, %
Vc	128—130 (22)	1.4961	1.0618	49.87	50.27	$C_{10}H_{15}NO_2$	65.97 65.80	8.48 8.49	66.27	8.34	77
Vd	112—113 (6)	1.4922	0.9660	58.06	57.87	$C_{12}H_{19}NO$	74.73 74.72	10.20 10.14	74.56	9.90	78
Ve	78—79 (6)	1.4673	0.9141	55.02	55.44	$C_{11}H_{19}NO$	72.45 72.37	9.77 10.00	72.88	10.56	74
Vf	113—114 (7)	1.4930	1.0393	54.67	54.89	$C_{11}H_{17}NO_2$	67.32 67.36	8.75 8.89	67.64	8.77	96

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*For Part XLIV see [1].

Experimental

Syntheses of 3-chloromethylfurans I–IV.

3-Chloromethylfuran (I). A solution of 3.7 g $SOCl_2$ in 3 ml n-heptane was rapidly added at −10°C to a solution of 3.0 g 3-hydroxymethylfuran [bp 75–76° C (10 mm); n_D^{20} 1.4827; the literature [8] gives bp 79°–80° (17 mm); n_D^{20} 1.4842] in 20 ml dry ether containing 2.5 ml dry pyridine. During this time the temperature rose to 25–30° C, and it was held there for 15 min, with stirring, then lowered to 0° C, the products poured into ice-water, the organic layer thrice washed with dilute HCl (1 : 10), then thrice with 3% NaOH and dried over K_2CO_3. After distilling off the solvent, the residue was vacuum-distilled in a current of nitrogen to give 1.2 g (45%) I, bp 43–44°C (28 mm) n_D^{20} 1.4855, d_4^{20} 1.1582. The literature gives [8]: bp 42–43° (17 mm), n_D^{20} 1.4863, d_4^{20} 1.1855. Found: C 51.48, 51.50; H 4.47, 4.58%; MR_D 28.93. Calculated for C_5H_5OCl: C 51.52; H 4.33%; MR_D 28.67.

2-Methyl-3-chloromethylfuran (II), was prepared by the method of [9], starting from 2-methyl-3-hydroxymethyl furan and thionyl chloride.

2,4-Dimethyl-3-chloromethylfuran (III), a solution of 27.3 g 2,4-dimethylfuran-3-carboxylic acid [10] in 200 ml dry ether was added dropwise to a solution of 15 g $LiAlH_4$ in 450 ml dry ether which was refluxing steadily, refluxing continued for an hour after addition was complete, and the products then left overnight. They were then decomposed with 350 ml 20% solution of Seignette's salt, the ether layer separated off, and the water layer extracted with ether. The bulked ether extracts were dried over $MgSO_4$, and the ether distilled off to give 22.5 g (91.5%) 2,4-dimethyl-3-hydroxymethylfuran, bp 47–48°C (ex petrol ether), as hygroscopic crystals. Found: C 66.17, 66.16; H 8.27, 7.96%. Calculated for $C_7H_{10}O_2$: C 66.64; H 7.99%.

A solution of 16.8 g 2,4-dimethyl-3-hydroxymethylfuran in 36 ml dry ether plus 13 ml dry pyridine was cooled to −10°C, and to it added 10.5 ml $SOCl_2$ in 15 ml dry n-pentane, at 8–10° C, the cooling bath was removed, and the products stirred for 10 min. As soon as the temperature rose to 20–22° C, the solution was quickly cooled to 0° C and poured into ice-water, after which the products were worked up as previously described for I, all operations being carried out at 0° C. Yield of III 5.3 g (28%) bp 63–64°C (10 mm) n_D^{20} 1.4905.*

The synthesis of 2,5-dimethyl-3-chloromethylfuran (IV) has previously been described [2].

Reaction of 3-chloromethylfurans with secondary amines

3-Morpholinofuran (Va). A solution of 0.7 g I in 20 ml dry benzene was added to a mixture of 0.4 g finely powdered KOH, 2.1 g morpholine, and 20 ml dry ether, and the mixture refluxed for 8 hr. The precipitate was then filtered off, the solvent distilled off, and the residue vacuum-distilled. Yield 0.8 g (80%), bp 112–113°C (20 mm). n_D^{20} 1.4918, d_4^{20} 1.0774. Found: C 64.72, 64.40; H 7.99, 8.01%; MR_D 45.02. Calculated for $C_9H_{13}NO_2$: C 64.64; H 7.85%; MR_D 45.65.

Table 2

Picrates and Methiodides of Amines Vb-f

Amine	Picrates					Methiodides				
	Mp, °C (ex EtOH)	Found, %		Calculated, %		Mp, °C (ex dry EtOH)	Found, %		Calculated, %	
		C	H	C	H		C	H	C	H
Vb	97—98	48.58 48.72	5.16 5.18	48.48	5.09	—	—	—	—	—
Vc	168—169	46.90 46.70	4.50 4.31	46.83	4.42	—	—	—	—	—
Vd	153—154	50.84 50.92	5.32 5.37	51.17	5.24	177—178	46.44 46.49	6.57 6.67	46.56	6.61
Ve	96—97	49.61 49.56	5.48 5.57	49.76	5.40	180—180,5	44.41 44.53	6.98 7.06	44.59	6.85
Vf	172,5—173	47.87 48.14	4.76 4.79	47.99	4.73	192—193	43.01 43.19	6.49 6.48	42.74	5.97

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* The density and elementary composition of the chloride III were not determined because it was extremely unstable.

Picrate: mp 144–145° C (ex EtOH). Found: C 45.26, 45.49; H 4.11, 4.01%. Calculated for $C_{15}H_{16}N_4O_9$: C 45.46; H 4.07%.

Hydrochloride: mp 183–184° C (washed with dry ether), white hygroscopic crystals. Found: C 52.84, 53.02; H 6.78, 6.81%. Calculated for $C_9H_{14}NO_2Cl$: C 53.07; H 6.93%.

2-Methyl-3-diethylaminomethylfuran (Vb), yield 40%, bp 86–88° C (22 mm), n_D^{20} 1.4712, rapidly forms the carbonate in air.

Hydrochloride: mp 149–150° C (washed with dry ether). Found: C 59.00, 58.74; H 8.78, 8.75%. Calculated for $C_{10}H_{18}NOCl$: C 58.96; H 8.91% .

The rest of the amines of this series (Vc-f) were synthesized similarly. Table 1 gives their yield and properties, while Table 2 gives analytical data for picrates and methiodides of amines Vb-f.

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25 March 1966

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