

**NEW TYPE OF ADDITION TO 5-SUBSTITUTED 4-ARYLIDENE-
-2-(4,5-DIHYDROFURFURYLIDENE)-N,N-DIMETHYLIMINIUM
BISPERCHLORATES. PREPARATION OF 4-SUBSTITUTED
5-(N,N-DIMETHYLAMINO)-2-FURANCARBALDEHYDES**

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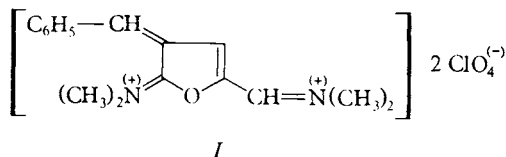
Received July 5th, 1985

4-Arylidene-5-(N,N-dimethyliminium)-2-(4,5-dihydrofurfurylidene)-N,N-dimethyliminium bisperchlorate *I* undergoes a 1,4-addition reaction with organic bases under re-formation of the furan nucleus; this behaviour has been utilized in the preparation of new 4-substituted 5-(N,N-dimethylamino)-2-furancarbaldehydes *II*, *III*. The structure of the prepared compounds has been confirmed by ¹³C and ¹H NMR spectra.

In our preceding paper¹ we described the reactions of 5-(N,N-dimethylamino)-2-furfurylidene-N,N-dimethyliminium bromide (vinamidinium salt) with aromatic aldehydes leading to 4-arylidene-5-(N,N-dimethyliminium)-2-(4,5-dihydrofurfurylidene)-N,N-dimethyliminium bisperchlorates *I*. The present communication concerns the reactions of *I* with organic bases.

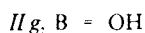
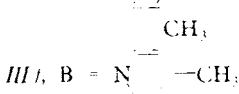
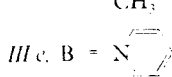
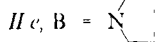
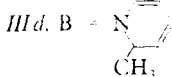
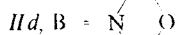
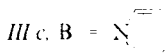
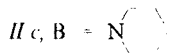
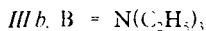
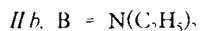
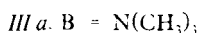
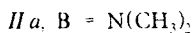
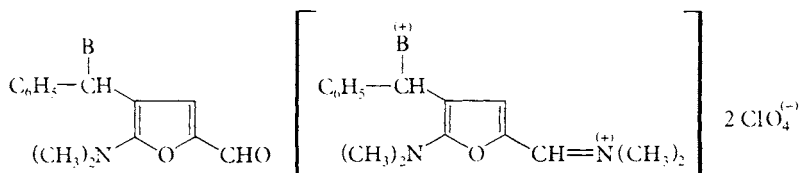
Reaction of *IV* (R = Ar) with alkoxides or hydrazines, assumed² to be a 1,2-addition to the double bond of the iminium group, affords dihydrofuran derivatives *V* (R = Ar) or, after subsequent fission and cyclization, the corresponding pyridazines. The sulfur analogue, 5-aryl-3-benzylidene-4-thiolen-2-one, reacts in a similar way with potassium hydroxide in methanol under ring opening and re-cyclization to the corresponding 3-thiophene carboxylic acid³.

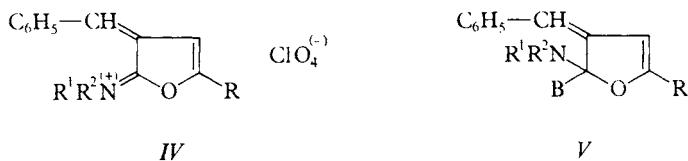
In order to study the possible use of compounds *I* for the preparation of new furan or other heterocyclic compounds by opening and closure of the furan nucleus, requiring an attack by base at the C₍₅₎ atom, we treated *I* with organic bases. In all



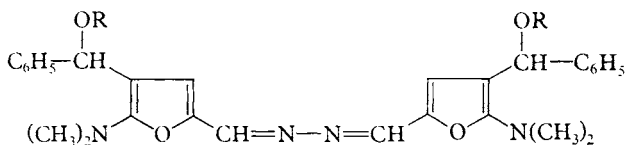
cases we obtained furan derivatives *II*, *III*, *VI*, *VII* and *X* (ref.¹), i.e. products of 1,4-addition to the conjugated benzylideneiminium system in *I*.

The compound *I* reacts in acetonitrile with tertiary amines, pyridines, or triphenylphosphine to give the corresponding bisperchlorates *IIIa–g*, whereas its reaction with secondary or primary amines, followed by hydrolysis with aqueous sodium hydroxide, leads to aldehydes *IIa–f*. Hydrolysis of *IIIa–f* under the same conditions affords *IIa* as the result of nucleophilic replacement of the ammonium or pyridinium group (good leaving groups) by dimethylamine, liberated in the hydrolysis of the iminium group. When the reaction of *I* with nitrogen bases is performed in an alcohol, the solvent adds preferentially under formation of 4-(1-alkoxy-1-phenylmethyl)-5-(*N,N*-dimethylamino)-2-furancarbaldehyde *X* (ref.¹) or the azine *Via, b* in the case of hydrazine hydrate. Reaction of *I* with malondinitrile or methyl cyanoacetate in methanolic sodium methoxide affords the corresponding methoxy derivative *VIIa, b*. The hydroxy derivative *IIg* was obtained in acetonitrile with aqueous solutions of amines, whereas the addition of water to *I* in aqueous alkaline solutions was unsuccessful. On the contrary, hydrolysis of *IV* (*R* = Ar) in an alkaline medium results in opening the dihydrofurfurylidene ring to the corresponding keto acid².





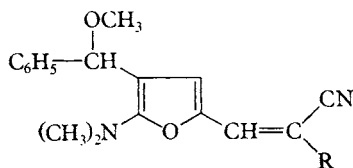
The prepared compounds were identified by elemental analyses and ^1H NMR, ^{13}C NMR, IR and UV spectra. The structure of *II*, *III*, *VII* and *X* was assigned by means of ^{13}C NMR spectra. The chemical shifts of the furan carbon atoms agree well with those in the analogous furan derivatives (Table IV). The signals of the CH carbon atoms appear in the region of alkane carbon atoms (67–78 ppm), in good agreement with the calculated values (63–87.2 ppm) for the alkane carbon atom in *II*, *III*, *VII* and *X*.



VIa, R = CH₃

VIb, R = C₂H₅

Reaction of compounds of the type *IV* with bases proceeds either as a 1,2-addition to the iminium (carbonyl) group when R = Ar (refs²⁻⁴) or as a 1,4-addition to the conjugated benzylideneiminium system when R = CH=⁽⁺⁾N(CH₃)₂. The C=C bond of the benzylidene group in *I* (*IV* when R = CH=⁽⁺⁾N(CH₃)₂) is strongly polarized by two electron-accepting substituents and, according to the Polansky concept of Lewis acids⁵⁻⁸, the system prefers an energetically more favourable attack by the base at the methylene carbon atom, combined with aromatization of the furan ring, leading to *II*, *III* and *X* but not to *V*.



VIIa, R = CN

VIIb, R = COOCH₃

EXPERIMENTAL

Melting points were measured on a Kofler block and are uncorrected. Infrared spectra were taken in 0.26 mm cells in 10^{-2} mol l $^{-1}$ chloroform solution or using the KBr technique. Ultra-violet spectra were recorded in $5 \cdot 10^{-5}$ mol l $^{-1}$ methanolic solutions on a UV-VIS (Zeiss, Jena) spectrophotometer in 10 mm cells. ^1H NMR or ^{13}C NMR spectra were taken on BS 487 C (Tesla) or on JEOL FX 60 instruments in deuteriochloroform or perdeuteriodimethyl sulfoxide with tetramethylsilane as internal standard.

4-(1-Dialkylamino-1-phenylmethyl)-5-(N,N-dimethylamino)-2-furancarbaldehydes *II*

The amine (0.002 mol) was added at room temperature to a stirred solution of *I* (0.002 mol) in acetonitrile (5 ml). After stirring for 30 min the mixture was concentrated under reduced pressure and hydrolyzed with 5% aqueous solution of sodium hydroxide (15 ml). The product was taken up in benzene, the solution dried and the solvent evaporated, leaving *II* as an oil which crystallized on standing. The characteristic values for compounds *II* are given in Tables I, III and IV.

4-(1-Phenyl-1-B $^{(+)}$ -methyl)-5-(N,N-dimethylamino)-2-furfurylidene-N,N-dimethyliminium Bisperchlorates *III*

The tertiary base (0.002 mol) was added at 10–15°C to a stirred solution of *I* (0.002 mol) in

TABLE I

Properties and analytical data of the carbaldehydes *II*

Compound	Formula (M.w.)	M.p., °C (yield, %)	Calculated/Found			λ_{\max} log ϵ	$\tilde{\nu}(\text{CO})^a$ cm $^{-1}$
			%C	%H	%N		
<i>Ila</i>	C $_{16}$ H $_{20}$ N $_2$ O $_2$ (272.3)	88–90 (69)	70.56 70.93	7.40 7.28	10.28 10.31	369 (3.31)	1 646
<i>Ilb</i>	C $_{18}$ H $_{24}$ N $_2$ O $_2$ (300.4)	84–86 (59)	71.97 71.92	8.05 8.07	9.32 9.27	370 (3.25)	1 646
<i>Ilc</i>	C $_{19}$ H $_{24}$ N $_2$ O $_2$ (312.4)	86–88 (82)	73.04 73.14	7.74 7.73	8.96 8.95	369 (3.63)	1 646
<i>Ild</i>	C $_{18}$ H $_{22}$ N $_2$ O $_3$ (314.4)	119–120 (72)	68.76 68.62	7.05 7.09	8.91 8.86	368 (3.32)	1 650
<i>Ile</i>	C $_{18}$ H $_{22}$ N $_2$ O $_2$ (298.4)	98–100 (85)	72.45 71.92	7.43 7.42	9.38 9.43	370 (3.26)	1 644
<i>Ilf</i>	C $_{15}$ H $_{18}$ N $_2$ O $_2$ (258.3)	79–81 (52)	69.74 69.25	7.02 7.04	10.84 10.79	368 (3.29)	1 648
<i>Ilg</i>	C $_{14}$ H $_{15}$ NO $_3$ (245.3)	126–127 (76)	68.55 68.59	6.16 6.06	5.71 5.36	367 (3.37)	1 646

^a Measured in chloroform; other IR bands: *Ilf* $\tilde{\nu}(\text{NH})$ 3 352, *Ilg* $\tilde{\nu}(\text{OH})_{\text{free}}$ 3 601, $\tilde{\nu}(\text{OH})_{\text{bonded}}$ 3 371 cm $^{-1}$.

acetonitrile (5 ml). After stirring for 1 h at this temperature, the solid *III* was collected and washed with acetonitrile and acetone (in some cases the product separated after standing overnight). Characteristic data of the compounds *III* are given in Tables II and IV.

Hydrolysis of 4-(1-Phenyl-1-B⁽⁺⁾-methyl)-5-(N,N-dimethylamino)-2-furfurylidene-N,N-dimethyliminium Bisperchlorates *IIIa-f*

Bisperchlorate *IIIa-f* (0.002 mol) was stirred with 5% aqueous solution of sodium hydroxide (15 ml) at room temperature for 30 min. The product was taken up in benzene, the solution dried and the solvent evaporated to give *IIa* (yield 52–55%).

4-(1-Phenyl-2-hydroxymethyl)-5-(N,N-dimethylamino)-2-furancarbaldehyde *IIg*

A 30% aqueous solution of an amine (ammonia, methylamine or dimethylamine) was added at room temperature to a stirred solution of *I* (0.002 mol) in acetonitrile (5 ml). After stirring for 1 h the mixture was concentrated under diminished pressure and hydrolyzed with 5% aqueous sodium hydroxide (15 ml). The mixture was extracted with benzene (3 × 10 ml), the benzene extract dried and concentrated to one third of the original volume to give the solid *IIg*. Its data are given in Tables I, III and IV.

TABLE II

4-(1-Phenyl-1-B⁽⁺⁾-methyl)-5-(N,N-dimethylamino)-2-furfurylidene-N,N-dimethyliminium bisperchlorates *III*

Compound	Formula (M.w.)	M.p., °C (yield, %)	Calculated/Found				$\nu(\text{C}=\text{N}(\text{CH}_3)_2)^a$ cm ⁻¹
			%C	%H	%N	%Cl	
<i>IIIa</i>	C ₁₉ H ₂₉ Cl ₂ N ₃ O ₉ (514.3)	137–139 (63)	44.36	5.68	8.17	13.78	1 672
			44.38	5.69	8.05	13.54	
<i>IIIb</i>	C ₂₂ H ₃₅ Cl ₂ N ₃ O ₉ (556.4)	140–142 (52)	47.49	6.34	7.55	12.74	1 672
			47.45	6.38	7.52	12.78	
<i>IIIc</i>	C ₂₁ H ₂₅ Cl ₂ N ₃ O ₉ (543.3)	198–200 (65)	47.20	4.71	7.86	13.27	1 675
			47.48	4.79	7.82	13.02	
<i>III d</i>	C ₂₂ H ₂₇ Cl ₂ N ₃ O ₉ (548.4)	148–150 (67)	48.19	4.96	7.66	12.93	1 673
			48.32	4.95	7.60	12.71	
<i>III e</i>	C ₂₂ H ₂₇ Cl ₂ N ₃ O ₉ (548.4)	179–181 (67)	48.19	4.96	7.66	12.93	1 672
			48.17	4.97	7.44	12.67	
<i>III f</i>	C ₂₂ H ₂₇ Cl ₂ N ₃ O ₉ (548.4)	174–176 (68)	48.19	4.96	7.66	12.93	1 673
			48.75	4.92	7.69	12.68	
<i>III g</i>	C ₃₄ H ₃₅ Cl ₂ N ₂ O ₉ P (717.5)	230–231 (86)	56.91	4.92	3.90	9.88	1 678
			56.79	4.91	3.87	9.79	

^a Measured by the KBr technique (1 mg compound/300 mg KBr).

TABLE III
Some ^1H NMR spectral parameters of carbaldehydes *II* (in deuteriochloroform)

Compound	CHO	H _{furan}	H _{benzene}	CH	N(CH ₃) ₂	Other signals
<i>IIa</i>	9.05 s	7.40 s	7.32 s	4.27 s	3.07 s	2.35 (s, 6 H, CH ₃)
<i>IIb</i>	9.05 s	7.40 s	7.32 s	4.28 s	3.10 s	2.57 (q, $J = 6, 8$ Hz, 4 H, CH ₂) 0.97 (t, $J = 6, 8$ Hz, 6 H, CH ₃)
<i>IIc</i>	9.02 s	7.27 s	7.30 s	4.41 s	3.06 s	2.35 (m, 4 H, CH ₂ —N) 1.47 (m, 6 H, CH ₂)
<i>IId</i>	9.05 s	7.40 s	7.31 s	4.36 s	3.05 s	3.66 (t, $J = 5$ Hz, 4 H, CH ₂ —O) 2.40 (t, $J = 5$ Hz, 4 H, CH ₂ —N)
<i>IIe</i>	9.07 s	7.52 s	7.30 s	4.30 s	3.06 s	2.40 (m, 4 H, CH ₂ —N) 1.72 (m, 4 H, CH ₂)
<i>IIf</i>	8.87 s	7.40 s	7.33 s	4.70 s	3.07 s	2.43 (s, 3 H, CH ₃)
<i>IIg</i>	8.77 s	6.80 s	7.35 s	5.85 s	3.17 s	—

TABLE IV
Some ^{13}C NMR spectral parameters of the prepared compounds

Compound	C ₍₂₎ furan	C ₍₃₎ furan	C ₍₄₎ furan	C ₍₅₎ furan	CH=X	N(CH ₃) ₂	CH
<i>IIe</i> ^{a,b}	143.75	127.99	107.81	159.89	172.65	40.49	65.88
<i>IIg</i> ^{a,c}	142.72	127.65	105.44	160.37	171.28	39.43	68.30
<i>IIIa</i> ^{d,e}	142.83	127.09	113.18	163.34	141.25	39.76	65.88
<i>IIIc</i> ^{d,f}	143.20	127.34	113.44	163.73	139.69	40.15	66.27
<i>VIII</i> ^{a,g}	143.33	128.65	105.83	162.29	174.05	40.42	—
<i>IX</i> ^{a,h}	141.86	129.56	104.15	162.62	173.61	40.69	—
<i>X</i> ^{a,i}	142.09	127.93	103.37	160.54	171.33	39.31	77.70

^a Measured in deuteriochloroform; ^b *IIe* δ_{Cbenzene} (142.18 s, 131.11 d, 128.25 d, 127.47 d), δ_{Cpyrrol} (53.51 t, 23.43 t); ^c *IIg* δ_{Cbenzene} (141.93 s, 128.57 d, 126.09 d, 131.67 d); ^d in perdeuterio-dimethyl sulfoxide; ^e *IIIa* δ_{Cbenzene} (130.85 s, 127.99 d, 125.95 d, 139.30 d), $\delta_{\text{N(CH}_3)_3}$ (43.79 q), $\delta_{\text{N(CH}_3)_2}$ (46.78 q); ^f *IIIc* δ_{Cbenzene} (131.24 s, 128.25 d, 126.30 d, 139.89 d), $\delta_{\text{Cpyridine}}$ (146.32 s, 143.03 d, 129.03 d, 129.55 d), $\delta_{\text{N(CH}_3)_2}$ (47.17 q); ^g 5-(N,N-dimethylamino)2,4-furancarbaldehyde (*VIII*) $\delta_{\text{C}_4-\text{CHO}}$ (181.13 d); ^h 4-acetyl-5-(N,N-dimethylamino)-2-furancarbaldehyde⁹ (*IX*) δ_{CO} (190.17 s), δ_{CH_3} (28.78 q); ⁱ 4-(1-phenyl-1-methoxymethyl)-5-(N,N-dimethylamino)-2-furancarbaldehyde¹ (*X*) δ_{Cbenzene} (140.12 s, 128.63 d, 126.91 d, 132.00 d), δ_{OCH_3} (56.14 q).

4-(1-Alkoxy-1-phenylmethyl)-5-(N,N-dimethylamino)-2-furalazines *VIa, b*

Hydrazine hydrate (0.001 mol) was added at 10–15 °C to a solution of *I* (0.002 mol) in the appropriate alcohol (10 ml). After stirring for 2 h the mixture was concentrated to half of its volume and poured in ice-cold water. Extraction and evaporation of the solvent gave *VI*.

4-(1-Phenyl-1-methoxymethyl)-5-(N,N-dimethylamino)-2-furalazine (VIa): For $C_{30}H_{34}N_4O_4$ (514.6) calculated: 70.01% C, 6.65% H, 10.88% N; found: 69.84% C, 6.82% H, 11.19% N. M.p. 167–168 °C, yield 51%. 1H NMR spectrum (C_2HCl_3): 8.12 (s, 1 H, CH=N), 7.35 (s, 5 H, $H_{benzene}$), 6.50 (s, 1 H, H_{furan}), 5.31 (s, 1 H, CH), 3.32 (s, 3 H, OCH_3), 3.03 (s, 6 H, CH_3).

4-(1-Ethoxy-1-phenylmethyl)-5-(N,N-dimethylamino)-2-furalazine (VIb): For $C_{32}H_{38}N_4O_4$ (542.7) calculated: 70.82% C, 7.05% H, 10.32% N; found: 70.95% C, 7.10% H, 10.50% N. M.p. 153–155 °C, yield 60%. 1H NMR spectrum (C_2HCl_3): 8.13 (s, 1 H, CH=N), 7.36 (s, 5 H, $H_{benzene}$), 6.70 (s, 1 H, H_{furan}), 5.42 (s, 1 H, CH), 3.48 (q, $J = 7$ Hz, 2 H, OCH_2), 3.03 (s, 6 H, CH_3), 1.23 (t, $J = 7$ Hz, 3 H, CH_3).

4-(1-Phenyl-1-methoxymethyl)-5-(N,N-dimethylamino)-2-furfurylidene malondinitrile (*VIIa*) or Methyl 4-(1-Phenyl-1-methoxymethyl)-5-(N,N-dimethylamino)-2-furfurylidene cyanoacetate (*VIIb*)

Malondinitrile or methyl cyanoacetate (0.002 mol) and sodium methoxide (0.002 mol) in methanol (5 ml) were added at room temperature to a stirred solution of *I* (0.002 mol) in methanol (10 ml). After stirring for 1 h the product was collected on filter, washed with methanol and crystallized from methanol.

4-(1-Phenyl-1-methoxymethyl)-5-(N,N-dimethylamino)-2-furfurylidene malondinitrile (VIIa): For $C_{18}H_{17}N_3O_2$ (307.2) calculated: 70.37% C, 5.53% H, 13.67% N; found: 69.97% C, 5.47% H, 13.72% N. M.p. 195–197 °C, yield 92%. 1H NMR spectrum (C_2HCl_3): 7.35 (s, 5 H, $H_{benzene}$), 7.35 (s, 1 H, CH_{O1}), 6.57 (s, 1 H, H_{furan}), 5.25 (s, 1 H, CH), 3.32 (s, 3 H, OCH_3), 3.31 (s, 6 H, CH_3). ^{13}C NMR spectrum (C_2HCl_3): 162.05 (C_{f5} furan), 108.51 (C_{f4} furan), 128.51 (C_{f3} furan), 139.30 (C_{f2} furan), 134.81 (CH_{O1}), 77.70 (CH), 56.40 (OCH_3), 39.63 ($N(CH_3)_2$), 129.03, 127.08, 117.62, 132.31 (C benzene).

Methyl 4-(1-Phenyl-1-methoxymethyl)-5-(N,N-dimethylamino)-2-furfurylidene cyanoacetate (VIIb): For $C_{19}H_{20}N_2O_4$ (340.4) calculated: 67.03% C, 5.92% H, 8.22% N; found: 67.28% C, 5.86% H, 8.14% N. M.p. 105–106 °C, yield 87%. 1H NMR spectrum (C_2HCl_3): 7.38 (s, 5 H, $H_{benzene}$), 7.38 (s, 1 H, CH_{O1}), 6.65 (s, 1 H, H_{furan}), 5.32 (s, 1 H, CH), 3.80 (s, 3 H, $COOCH_3$), 3.35 (s, 3 H, OCH_3), 3.27 (s, 6 H, CH_3). ^{13}C NMR spectrum (C_2HCl_3): 166.07 (CO), 161.26 (C_{f5} furan), 108.81 (C_{f4} furan), 128.25 (C_{f3} furan), 139.82 (C_{f2} furan), 138.13 (CH_{O1}), 133.97 (CH_{O1}), 77.96 (CH), 56.39 (OCH_3), 52.36 (OCH_3), 39.63 ($N(CH_3)_2$), 128.90, 127.08, 118.38, 132.16 (C benzene).

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Translated by M. Tichý.