

NEW METHOD OF PREPARATION OF 5-(N,N-DIMETHYLAMINO)-2-FURYLETHYLENES *via* FURAN VINAMIDINIUM SALTS

Tibor GRACZA^a, Zdeněk ARNOLD^b and Jaroslav KOVÁČ^a

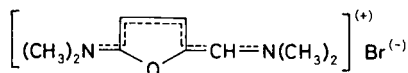
^a Department of Organic Chemistry,
Slovak Institute of Chemical Technology, 812 37 Bratislava and

^b Institute of Organic Chemistry and Biochemistry,
Czechoslovak Academy of Sciences, 166 10 Prague 6

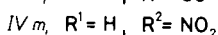
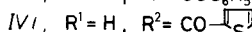
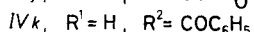
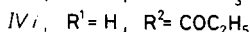
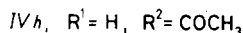
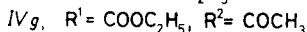
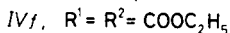
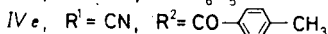
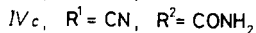
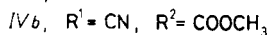
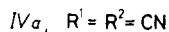
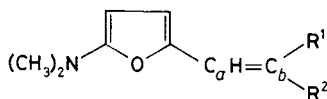
Received July 8th, 1985

Reaction of the vinamidinium system in 5-(N,N-dimethylamino)-2-furfurylidene-N,N-dimethyliminium bromide (*I*) and its 4-formyl derivatives *II* and *III* with methylene compounds has been utilized for the preparation of furylethylenes.

Condensation reactions of 5-X-2-furaldehydes with compounds containing active methylene group have been thoroughly investigated¹⁻⁷. 5-(N,N-Dimethylamino)-2-furaldehyde reacts only with strongly activated methylene groups in methylenenitriles⁶⁻⁸ to give 5-(N,N-dimethylamino)-2-furfurylidenes *IVa, b* and *d*. Compounds of this type (*IVa, b, c, f, g*) were prepared also by condensation of 5-bromo-2-fural-



I



dehyde with methylene compounds, followed by nucleophilic substitution with dimethylamine, or by condensation of 5-trimethylammonium-2-furaldehyde and subsequent thermal demethylation⁹⁻¹¹. With substituted methylenitriles, both these methods gave products *IVa-c* in yields of 73–97% whereas enolates afforded compounds *IVf, g* only in low yields (16–30%). We have now prepared 5-(N,N-di-

TABLE I
5-(N,N-Dimethylamino)-2-furylethylenes *IV*

Compound	Formula mol.wt.	M.p., °C yield, %	Method reaction time, h	Calculated/Found		
				% C	% H	% N
<i>IVa</i>	C ₁₀ H ₉ N ₃ O (187·2)	190–192 (97)	A	64·16	4·84	22·44
			—	64·50	4·81	22·45
<i>IVb</i>	C ₁₁ H ₁₂ N ₂ O ₃ (220·2)	163–164 (98)	A	59·99	5·49	12·72
			—	60·13	5·47	12·79
<i>IVc</i>	C ₁₀ H ₁₁ N ₃ O ₂ (205·2)	226–227 (78)	A	58·52	5·40	20·47
			—	58·17	5·43	20·39
<i>IVd</i>	C ₁₅ H ₁₄ N ₂ O (238·3)	105–106 (67)	A	75·60	5·92	11·75
			—	75·52	5·88	11·83
<i>IVe</i>	C ₁₇ H ₁₆ N ₂ O ₂ (280·4)	108–109 (99)	A	72·80	5·75	10·03
			—	72·74	5·79	10·11
<i>IVf</i>	C ₁₄ H ₁₉ NO ₅ (281·3)	104–106 (62)	B	59·77	6·81	4·98
			(5)	59·79	6·83	5·04
<i>IVg</i>	C ₁₃ H ₁₇ NO ₄ (251·3)	104–107 (89)	B	62·14	6·82	5·57
			(8)	61·97	6·51	5·49
<i>IVh</i>	C ₁₀ H ₁₃ NO ₂ (179·2)	oil (60)	B	67·02	7·31	7·82
			(24)	67·46	7·37	7·78
<i>IVi</i>	C ₁₁ H ₁₅ NO ₂ (193·2)	oil (57)	B	68·36	7·82	7·25
			(48)	68·43	7·81	7·29
<i>IVj</i>	C ₁₃ H ₁₃ NO ₃ (231·2)	139–140 (58)	B	67·52	5·66	6·06
			(24)	67·40	5·65	6·18
<i>IVk</i>	C ₁₅ H ₁₅ NO ₂ (241·3)	69–72 (62)	B	74·67	6·27	5·80
			(24)	74·59	6·43	5·35
<i>IVl</i>	C ₁₃ H ₁₃ NO ₂ S (247·2)	67–70 (56)	B	63·15	5·30	5·66
			(24)	63·37	5·22	5·69
<i>IVm</i>	C ₈ H ₁₀ N ₂ O ₃ (182·2)	148–152 (55)	B	52·74	5·49	15·38
			(6)	52·17	5·45	15·07

methylamino)-2-furylethylenes using the pentamethinium system in 5-(N,N-dimethylamino)-2-furfurylidene-N,N-dimethyliminium bromide (*I*) (ref.¹²).

In general, the α -carbon atoms in polymethinium (vinamidinium) salts¹³ exhibit an enhanced reactivity toward nucleophilic reagents. Thanks to their stability and push-pull nature, the salts react preferentially in the substitution rather than addition manner and can be used in condensation reactions. The condensation of trimethinium salts with methylenenitriles¹⁴⁻¹⁶, enolates, esters and cyclic lactones¹⁷⁻²⁰ has been utilized in the preparation of multifunctional dienamines and dienaminones.

The reaction of compound *I* with substituted methylenenitriles is quantitative and good yields are obtained also with enolates and compounds with less activated methylene groups (Table I). The use of the vinamidinium salt *I* in condensation reactions offers thus a simple route to the biologically interesting 5-substituted furylethylenes *IV*, otherwise accessible only with difficulty.

TABLE II
5-(N,N-Dimethylamino)-2,4-furandiethylenes *V*

Compound	Formula mol. wt.	M.p., °C yield, H	Method reaction time, h	Calculated/Found		
				% C	% H	% N
<i>Va</i>	C ₁₄ H ₉ N ₅ O (263.2)	233–235 (96)	A	63.87	3.44	26.60
			—	63.83	3.58	26.72
<i>Vb</i>	C ₁₆ H ₁₅ N ₃ O ₅ (329.3)	209–211 (98)	A	58.35	4.59	12.76
			—	58.22	4.52	12.81
<i>Vc</i>	C ₁₄ H ₁₃ N ₅ O ₃ (299.3)	netdo 360 (97)	A	56.18	4.37	23.39
			—	55.97	4.35	22.89
<i>Vd</i>	C ₂₄ H ₁₉ N ₃ O (365.4)	154–155 (65)	A	78.88	5.24	11.49
			—	78.21	5.39	11.78
<i>Ve</i>	C ₂₀ H ₁₇ N ₃ O ₃ (347.4)	196–198 (87)	A	69.15	4.93	12.09
			—	69.65	4.89	12.24
<i>Vf</i>	C ₂₁ H ₁₉ N ₃ O ₃ (361.4)	204–206 (89)	A	69.79	5.30	11.62
			—	69.56	5.51	11.34
<i>Vg</i>	C ₂₈ H ₂₃ N ₃ O ₃ (449.5)	210–212 (67)	A	74.82	5.16	9.35
			—	74.20	5.38	8.98
<i>Vh</i>	C ₂₂ H ₂₉ NO ₉ (451.5)	68–70 (46)	C	58.53	6.47	3.10
			(5)	58.25	6.25	2.92
<i>Vi</i>	C ₂₀ H ₂₅ NO ₇ (391.4)	oil (45)	C	61.37	6.44	3.58
			(5)	61.73	6.43	4.42

Similarly to 5-(N,N-dimethylamino)-2-furaldehyde, also its 4-formyl derivative *III* condenses with substituted methylenenitriles to give the products in good yields (Table II); on the other hand, it does not react with less active methylene groups. The bisperchlorate *II* reacts even with enolates. With one equivalent of the methylene component, compound *III* reacts selectively at its α -carbonyl group to give the deri-

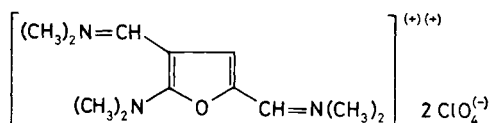
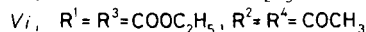
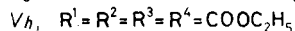
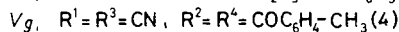
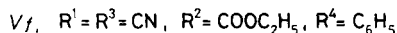
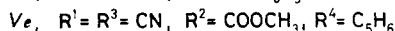
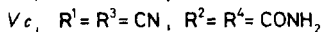
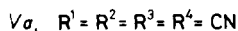
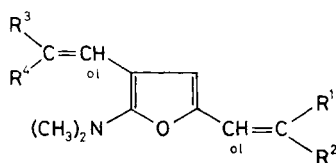
*II*

TABLE III

4-Formyl-5-(N,N-dimethylamino)-2-furylethylenes *VI*

Compound	Formula mol. wt.	M.p., °C yield, %	Method	Calculated/Found		
				% C	% H	% N
<i>VIa</i>	C ₁₁ H ₉ N ₃ O ₂ (215·2)	174–178 (88)	A	61·39 61·55	4·21 4·10	19·52 20·11
<i>VIb</i>	C ₁₂ H ₁₂ N ₂ O ₄ (248·2)	232–233 (98)	A	58·06 57·99	4·87 4·82	11·28 11·25
<i>VIc</i>	C ₁₁ H ₁₁ N ₃ O ₃ (233·2)	235–237 (87)	A	56·64 56·40	4·75 4·77	18·01 17·99
<i>VI d</i>	C ₁₆ H ₁₄ N ₂ O ₂ (266·3)	148–150 (97)	A	72·16 72·29	5·29 5·50	10·52 10·06

TABLE IV
¹H NMR spectral data for 5-(N,N-dimethylamino)-2-furylethylenes IV

Compound	H ₃ furan	H ₄ furan	C ₄ H	C ₆ H	N(CH ₃) ₂	Other ^a
IVa	7·37 d	5·92 d	7·10 s	—	3·07 s	—
IVb	7·47 d	5·81 d	7·35 s	—	3·07 s	3·62 (s, 3 H, OCH ₃)
IVc	7·27 d	5·60 d	7·42 s	—	3·01 s	7·05 (s, 2 H, NH ₂)
IVd	6·96 d	5·38 d	7·36 s	—	2·96 s	7·38 (m, 5 H, H _b)
IVe	7·60 d	5·97 d	7·57 s	—	3·12 s	7·52 (d, J = 8 Hz, 2 H, H _b) 7·20 (d, J = 8 Hz, 2 H, H _b)
IVf	7·05 d	5·37 d	7·11 s	—	2·85 s	2·30 (s, 3 H, CH ₃) 4·16 (q, J = 6·8, 2 H, CH ₂) 4·05 (q, J = 6·8, 2 H, CH ₂)
IVg	7·10 d	5·45 d	7·15 s	—	2·88 s	1·16 (t, J = 6·8, 3 H, CH ₃) 1·12 (t, J = 6·8, 3 H, CH ₃) 4·16 (q, J = 7, 2 H, CH ₂)
IVh	7·12 d	5·34 d	6·00 d (J = 15 Hz)	7·37 d (J = 15 Hz)	2·86 s	2·15 (s, 3 H, COCH ₃) 1·15 (t, J = 7, 3 H, CH ₃) 2·11 (s, 3 H, CH ₃)
IVi	6·87 d	5·30 d	6·06 d (J = 15 Hz)	7·12 d (J = 15 Hz)	2·88 s	2·08 (q, J = 7, 2 H, CH ₂) 0·92 (t, J = 7, 3 H, CH ₃)
IVj	7·05 d	5·43 d	6·76 d (J = 15 Hz)	7·33 d (J = 15 Hz)	2·97 s	7·90 (d, J = 2·5, 1 H, H ₅) 7·36 (d, J = 4, 1 H, H ₅)
IVk	7·05 d	5·41 d	5·72 d (J = 15 Hz)	7·40 d (J = 15 Hz)	2·96 s	6·66 (dd, J = 4, J = 2·5, 1 H, H ₄) 7·50 (m, 5 H, H _b)
IVl	7·06 d	5·42 d	6·86 d (J = 15 Hz)	7·45 d (J = 15 Hz)	2·97 s	7·97 (d, J = 2·5, 1 H, H ₅) 7·00 (dd, J = 4, J = 2·5, 1 H, H ₄)
IVm	7·40 d	5·76 d	7·20 d (J = 13 Mz)	7·62 d (J = 13 Hz)	3·02 s	7·35 (d, J = 4, 1 H, H ₅)

^a J_{H₄,H₃} = 4 Hz; H_b = H_{benzene}.

TABLE V

¹H NMR spectral data for 4-formyl-5-(N,N-dimethylamino)-2-furylethylenes VI

Compound	CHO	CH _{o1}	H ₃ furan	N(CH ₃) ₂	Other signals
<i>VIa</i>	9.67 s	7.06 s	7.45 s	3.50 s	—
<i>VIb</i>	9.67 s	7.66 s	7.45 s	3.50 s	3.90 (s, 3 H, OCH ₃)
<i>VIc</i>	9.70 s	7.71 s	7.57 s	3.37 s	7.52 (s, 2 H, NH ₂)
<i>VIId</i>	9.68 s	7.08 s	7.01 s	3.40 s	7.47 (m, 5 H, H _{benzene})

TABLE VI

¹H NMR spectral data for 5-(N,N-dimethylamino)-2-furandiethylenes V

Compound	CH _{o1(2)}	CH _{o1(4)}	H ₃ furan	N(CH ₃) ₂	Other signals
<i>Va</i>	8.01 s	8.17 s	6.82 s	3.40 s	—
<i>Vb</i>	8.01 s	8.17 s	7.63 s	3.42 s	3.83 (s, 6 H, OCH ₃)
<i>Vc</i>	7.87 s	8.02 s	7.70 s	3.30 s	7.10 (m, 4 H, NH ₂)
<i>Vd</i>	7.37 s	7.72 s	7.05 s	3.36 s	7.05 (m, 10 H, H _{benzene})
<i>Ve</i>	7.71 s	8.17 s	7.06 s	3.57 s	7.28 (m, 5 H, H _{benzene}) 3.36 (s, 3 H, OCH ₃)
<i>Vf</i>	7.72 s	8.20 s	7.07 s	3.57 s	7.23 (m, 5 H, H _{benzene}) 4.30 (q, <i>J</i> = 7, 2 H, CH ₂) 1.35 (t, <i>J</i> = 7, 3 H, CH ₃)
<i>Vg</i>	8.05 s	8.23 s	7.87 s	3.30 s	7.60 (d, <i>J</i> = 8.2; 4 H, H _{benzene}) 7.28 (d, <i>J</i> = 8.2; 4 H, H _{benzene}) 2.45 (s, 3 H, CH ₃) 2.43 (s, 3 H, CH ₃)
<i>Vh</i>	7.28 s	7.57 s	6.87 s	3.11 s	4.12; 4.08; 3.91; 3.86 alls (q, <i>J</i> = 7, 2 H, CH ₂) 1.17; 1.11; 1.07; 1.02 alls (t, <i>J</i> = 7, 3 H, CH ₃)
<i>Vi</i>	7.37 s	7.55 s	6.87 s	3.17 s	4.06 (m, 4 H, CH ₂) 2.22 (s, 3 H, COCH ₃) 2.12 (s, 3 H, COCH ₃) 1.11 (m, 6 H, CH ₃)

vative *VI* (Table III), with two equivalents both the carbonyl groups react and compound *V* is obtained. This selectivity enables the preparation of derivatives with different substituents in positions 2 and 4 of the furan ring. Contrariwise, compound *II* reacts with one equivalent of the methylene component to afford a 1 : 1 mixture of the monocondensation and bis-condensation products *VI* and *V*, respectively.

TABLE VII
Infrared and UV spectral data for 5-(N,N-dimethylamino)-2-furylethylenes *IV*

Compound	$\nu(\text{CN})$ cm^{-1}	$\nu(\text{CO})$ cm^{-1}	$\nu(\text{C}=\text{C})$ cm^{-1}	λ_{max} (log ϵ)	
<i>IVa</i>	2 203	—	1 634, 1 576	234 (3·17)	466 (3·83)
<i>IVb</i>	2 196	1 705	1 641, 1 572	230 (3·38)	461 (3·98)
<i>IVc</i>	2 189	1 724	1 635, 1 588	230 (3·10)	460 (3,35)
<i>IVd</i>	2 189	—	1 627, 1 572	242 (3·02)	463 (3·43)
<i>IVe</i>	2 177	1 701	1 614, 1 558	286 (2·22)	499 (3·60)
<i>IVf</i>	—	1 719	1 634, 1 571	231 (3·02)	422 (3·49)
<i>IVg</i>	—	1 712	1 625, 1 563	235 (2·88)	443 (3·44)
<i>IVh</i>	—	1 714	1 628, 1 580	242 (2·88)	437 (3·41)
<i>IVi</i>	—	1 716	1 628, 1 584	243 (2·95)	435 (3·38)
<i>IVj</i>	—	1 646	1 615, 1 572	285 (3·20)	499 (3·52)
<i>IVk</i>	—	1 647	1 615, 1 577	272 (2·94)	492 (3·46)
<i>IVl</i>	—	1 641	1 611, 1 541	284 (3·18)	499 (3·48)
<i>IVm</i> ^a	—	—	1 641, 1 588	—	520 (2·78)

^a $\tilde{\nu}_{\text{as}}(\text{NO}_2)$ 1 520, $\nu_{\text{s}}(\text{NO}_2)$ 1 348.

Reaction of *II* with two equivalents of the methylene compound leads to the bis-condensation product *V*.

TABLE VIII

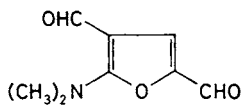
Infrared spectral data for 4-formyl-5-(*N,N*-dimethylamino)-2-furylethylenes *VI*

Compound	$\nu(\text{CN})$ cm^{-1}	$\nu(\text{CO})$ cm^{-1}	$\nu(\text{C}=\text{C})$ cm^{-1}
<i>VIa</i>	2 213	1 695	1 618, 1 588
<i>VIb</i>	2 208	1 721	1 615, 1 587
<i>VIc</i>	2 200	1 688	1 608, 1 578
<i>VIId</i>	2 202	1 678	1 639, 1 600

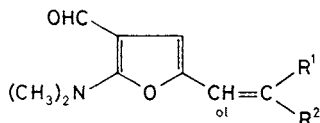
TABLE IX

Infrared and UV spectral data for 5-(*N,N*-dimethylamino)-2,4-furandiethylenes *V*

Compound	$\nu(\text{CN})$ cm^{-1}	$\nu(\text{CO})$ cm^{-1}	$\nu(\text{C}=\text{C})$ cm^{-1}	λ_{max} (log ϵ)			
<i>Va</i>	2 212	—	1 635 1 571	257 (2·87)	382 (2·88)	498 (3·42)	642 (3·34)
<i>Vb</i>	2 208	1 712	1 622 1 582	258 (2·90)	380 (3·09)	482 (3·23)	— —
<i>Vc</i>	2 190	1 716	1 640 1 568	258 (2·30)	370 (2·40)	472 (2·73)	— —
<i>Vd</i>	2 196	—	1 615 1 583	264 (3·03)	388 (2·88)	462 (3·27)	— —
<i>Ve</i>	2 200	1 713	1 654 1 588	262 (3·03)	381 (3·16)	468 (3·68)	— —
<i>Vf</i>	2 205	1 713	1 610 1 551	260 (3·03)	378 (3·04)	464 (3·67)	— —
<i>Vg</i>	2 198	1 712	1 642 1 578	270 (2·51)	392 (2·36)	524 (2·86)	676 (2·08)
<i>Vh</i>	—	1 721	1 631 1 587	249 (2·73)	365 (2·87)	454 (3·14)	— —
<i>Vi</i>	—	1 712	1 621 1 578	253 (3·06)	380 (2·82)	451 (3·21)	— —



III

VI a, R¹ = R² = CNVI b, R¹ = CN, R² = CO₂CH₃VI c, R¹ = CN, R² = CONH₂VI d, R¹ = CN, R² = C₆H₅

Similarly to condensations of 5-X-2-furaldehydes^{6,7}, the reaction gives solely the isomer in which the more bulky groups are in the *trans*-relation (Table IV). The prepared compounds were identified by elemental analyses, ¹H NMR, IR and UV spectra (Tables I–IX).

EXPERIMENTAL

Melting points were determined on a Kofler block. Infrared spectra were measured in chloroform (concentration 10⁻² mol l⁻¹, cell thickness 0.26 mm) on an IR-75 (Zeiss, Jena) spectrophotometer, UV spectra were taken on a UV-VIS spectrometer (Zeiss, Jena) in 10 mm cells in methanol (3 · 10⁻⁵–5 · 10⁻⁵ mol l⁻¹), ¹H NMR spectra were measured in deuteriochloroform on a BS 487 C (Tesla) 80 MHz spectrometer with tetramethylsilane as internal standard.

5-(N,N-Dimethylamino)-2-furylethylenes

Method A: Equivalent amounts of the methylene component and sodium methoxide were added at room temperature to a stirred solution of the carbonyl compound (0.002 mol) in ethanol (10 ml). The solid which had immediately precipitated was filtered, washed with ethanol and crystallized either from methanol or ethanol.

Method B: A solution of the methylene component (0.0021 mol or 0.0042 mol) in tetrahydrofuran (10 ml) was added dropwise at room temperature during 1 h to a stirred solution of the carbonyl component (0.002 mol) and sodium hydride (0.003 mol or 0.006 mol) in pyridine (10 ml). After stirring for 5–48 h, the solvents were evaporated under reduced pressure and the residue was mixed with water (30 ml) and extracted with chloroform. The chloroform extract was dried and the solvent evaporated. The product was purified by chromatography on silica gel in chloroform acetone (7 : 3).

Method C: A solution of the methylene component (0.0042 mol) and sodium hydride (0.006 mol) in anhydrous tetrahydrofuran (10 ml) was added at room temperature to a stirred solution of the carbonyl compound (0.002 mol) in dry pyridine (10 ml) in the course of 1 h. The reaction mixture was processed as described under *B*.

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Translated by M. Tichý.

Note added in proof: In formula *Ve* $R^4 = C_6H_5$.