

Crotonolactone — Precursor for Synthesis of β -Furans

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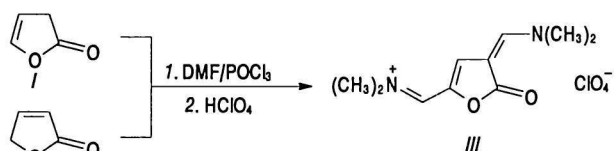
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4-(Dimethylaminomethylene)-5-oxo-2-furfurylidenedimethyliminium perchlorate (a new vinamidinium system with incorporated 2(3*H*)-furanone ring) was prepared by reaction of 2(5*H*)- resp. 2(3*H*)-furanone with the Vilsmeier type reagent; its reactions with C-nucleophiles were studied. Some spectral properties of the prepared compounds are discussed.

In connection with our previous works [1—4] concerning the possibilities of the synthesis of β -substituted furan derivatives based on the available 2-furaldehyde as starting compound, we have investigated some reactions of crotonolactone — a new possible precursor of β -furans. Recent works have shown that the vinamidinium system [5] with a built-in furan ring as in 5-dimethylamino-2-furfurylidenedimethyliminium salt V [1], has the electron density at the furan ring, reshuffled such as to allow introduction of substituents to the β -positions of furan by direct electrophilic displacement reactions [1—4].

We therefore examined the use of 2(5*H*)- resp. 2(3*H*)-furanone as a precursor to β -substituted furan compounds, we were also inspired by the aromatization of isoxazolone [6], pyrazolone [7], resp. pyrrolidione [8] ring by the action of dimethylamino-ketovinyl system with phosphorus oxychloride.

With the aim to investigate analogous reaction in the furan series 2(5*H*)-furanone I and 2(3*H*)-furanone II were prepared in the ratio 4 : 1 by oxidation of 2-furaldehyde [9]. Both isomers of 2-furanone I, II with dimethyliminiummethylene chloride give under the conditions of Vilsmeier—Haack reaction always only one product incorporating 2 mol of the reagent irrespective of the reagent used (1 mol, 2 mol, 10 mol) (Scheme 1).

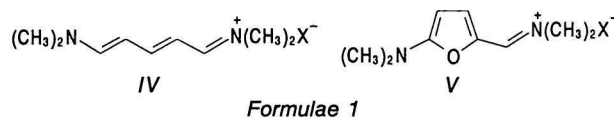


Scheme 1

The best results were obtained when we used 2.2 mol of Vilsmeier reagent, prepared from dimethylaminoformamide and phosphorus oxychloride without any solvent, and precipitated III in the form of perchlorate in a good yield (84 %). The fact that

perchlorate III was formed from both isomers of 2-furanone I and II allows the use of mixtures of isomers obtained by oxidation of 2-furaldehyde without first separating them.

The structure of 4-(dimethylaminomethylene)-5-oxo-2-furfurylidenedimethyliminium perchlorate III was established by means of ¹H and ¹³C NMR, IR, and UV VIS spectra. Chemical shifts of the carbon atoms of III in ¹³C NMR spectra (see Experimental) agree very well with those in the analogous derivative 4-(1-phenyl-1-dimethylaminomethyl)-5-dimethylamino-2-furfurylidenedimethyliminium perchlorate [4] (143.75 (s, C-2), 123.99 (d, C-3), 107.81 (s, C-5), 141.25 (d, CH=N⁺), 40.49 (q, CH₃), 43.79 (q, CH₃), 46.78 (q, N⁺(CH₃)₂)). Similarly, absorption bands of the vibration C=O ($\tilde{\nu}$ = 1736 cm⁻¹) and C=N⁺ ($\tilde{\nu}$ = 1672 cm⁻¹) correspond with C=O ($\tilde{\nu}$ = 1747 cm⁻¹) in the analogous I, respectively C=N⁺ ($\tilde{\nu}$ = 1658 cm⁻¹) in iminium salts [1, 4]. Generally, vinamidinium salts are characterized by considerable delocalization of π -electrons [5] and consequently, exhibit high wavelength UV maxima (λ_{max} = 416 nm) [10] for pentamethinium salts IV, (λ_{max} = 396 nm) for V [1]. In favour of the high delocalization of π -electrons in compound III is relatively high wavelength value (λ_{max} = 424 nm) (Formulae 1).

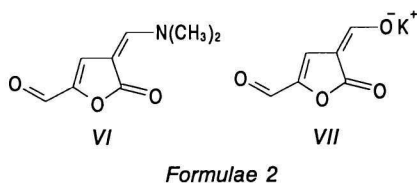


Formulae 1

Thus compound III, a new pentamethinium system with incorporated 2(3*H*)-furanone ring, opens up a new promising synthetic pathway to β -furans and lactones.

The hydrolysis of perchlorate III under mildly basic conditions (K₂CO₃, H₂O) led to the corresponding 2-furaldehyde VI; under more vigorous conditions (KOH, H₂O) the potassium salt of 4-(hydroxymethylene)-5-oxo-2-furaldehyde VII was obtained.

The structure of vinamidine *VI* and the position of the formyl group (C-2 vs. C-4) was established by the comparison of chemical shifts in ^1H and ^{13}C NMR spectra (9.06 (s, 1H, C₂HO) resp. 176.39 (d, C₂HO) for *VI*) with those of analogous derivatives (*i.e.* 9.22 (s, 1H, C₂HO) and 9.67 (s, 1H, C₄HO) resp. 172.28 (d, C₂HO) and 181.0 (d, C₄HO) in 5-dimethylamino-2,4-furandicarbaldehyde) [1, 4] (Formulae 2).



By the similarity of its NMR data and failure to liberate upon acidification of the potassium salt *VII* resembles the sodium salt of α -formyl- β -butyrolactone, an intermediate in the synthesis of natural tulipalins A and B [11, 12].

The enhanced reactivity at C $_{\alpha}$ -carbons in vinamidinium salts towards nucleophiles was utilized in condensation reactions. Due to electron density distribution in the vinamidinium system positions 6 and 7 (see Scheme 2 for numbering of the carbons) of *III* become eligible for a nucleophilic attack. With one mole of the methylene component compound *III* reacts selectively at its more reactive iminium group to give the derivative *VIII*. With two moles compounds *IX* were obtained, the products of the displacement of another dimethylamino group at C-2 were not observed (Scheme 2).

As in condensation of 5-X-2-furaldehydes [13] resp. 4,5-X-2-furaldehydes [14], the above reaction gives solely the isomer in which the more bulky groups are

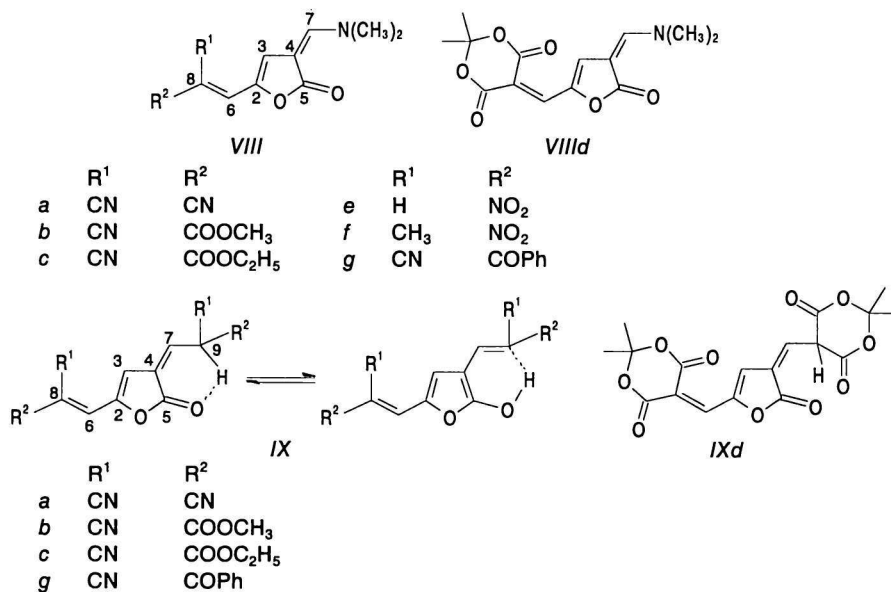
in the *trans* relation. The prepared compounds were identified by elemental analyses, ^1H NMR, ^{13}C NMR, UV, IR, and mass spectra (Tables 1—4).

UV VIS, IR, ^1H NMR, and ^{13}C NMR spectra of condensation products *IX* show that an equilibrium exists between both tautomeric structures (oxo, enol). The strong bathochromic shift into visible part of the spectrum ($\lambda_{\text{max}} = 534\text{--}576\text{ nm}$) comparable with absorption maxima of 5-dimethylamino-2,4-furyl-ethylenes ($\lambda_{\text{max}} = 466\text{--}520\text{ nm}$) [15], and characteristics of compounds with two "push-pull" systems, makes the existence of the enol form of *IX* improbable. In IR spectra both bands, that of furanone C=O vibration ($\tilde{\nu} = 1697\text{--}1740\text{ cm}^{-1}$) and also that of hydroxy group ($\tilde{\nu} = 3421\text{--}3528\text{ cm}^{-1}$) were observed. The broad singlet ($\delta = 8.13\text{--}9.42$) in ^1H NMR spectra of the compounds *IXa*, *IXd*, *IXe* corresponds to a hydroxy group. In ^{13}C NMR spectra of *IX* the resonance signal of carbonyl group in position 5 ($\delta = 167.7\text{--}168.9$) for the oxo form and signal ($\delta = 33.9\text{--}36.4$) characteristic of C₉H in the enol form were observed, analogically to *N*-substituted 3-aryl-4-cyano-2,5-dihydro-5-oxo-furan-2-carboxamides [16].

Thus, a new vinamidinium system with incorporated furanone ring was prepared by a very simple approach, which due to large reaction variability and capability to aromatize the 2-furanone ring, predestines it for the role of a precursor for the synthesis of β -substituted furan derivatives and furocondensed compounds.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage. Ultraviolet spectra of methanolic solutions ($c = 3\text{--}5.5 \times 10^{-5}\text{ mol dm}^{-3}$) in 1 cm cells were recorded



Scheme 2

Table 1. Physicochemical Characteristics of the Compounds VIII

Compound	Formula ^{a, b} M _r	Yield/% M.p./°C	Reaction conditions	λ _{max} /nm		ν̃/cm ⁻¹		
				log {ε}		v(C=O)	v(CN)	v(C=C)
VIIIa	C ₁₁ H ₉ N ₃ O ₂	41	1 h, r.t.	218	449	1716 s	2218 s	1647 s
	215.23	269—272		2.87	3.39			
VIIIb	C ₁₂ H ₁₂ N ₂ O ₄	91	2 h, reflux.	218	449	1720 s	2206 s	1637 s
	248.24	276—279		3.14	3.63	1707 s		
VIIIc	C ₁₃ H ₁₄ N ₂ O ₄	85	4 h, reflux.	218	449	1734 s	2210 s	1635 s
	262.26	221—223		3.13	3.63	1703 s		
VIId	C ₁₄ H ₁₅ NO ₆	40	1 h, reflux.	205	486	1741 s		1653 s
	293.20	233—236		2.89	3.30			
VIIf	C ₉ H ₁₀ N ₂ O ₄	55	1 h, r.t.	223	454	1728 s		1639 s
	210.19	220—223		2.99	3.49			
VIIf	C ₁₀ H ₁₂ N ₂ O ₄	65	4 h, reflux.	230	341	1720 s		1624 s
	224.22	216—219		3.16	3.29			
VIIfg	C ₁₇ H ₁₄ N ₂ O ₃	68	2 h, r.t.	200	475	1724 s	2199 s	1624 s
	294.31	217—220		3.43	3.42			

a) All compounds gave satisfactory microanalyses for C, H, and N (within ± 0.3 %). b) Molecular peaks M⁺ in mass spectrum are in accord with calculated values.

Table 2. Physicochemical Characteristics of the Compounds IX

Compound	Formula ^{a, b} M _r	Yield/% M.p./°C	λ _{max} /nm		ν̃/cm ⁻¹		
			log {ε}		v(C=O)	v(CN)	v(C=C)
IXa	C ₁₂ H ₄ N ₄ O ₂	94	223	534	1714 s	2210 s	1603 s
	236.19	172—175	2.40	3.27			
IXb	C ₁₄ H ₁₀ N ₂ O ₆	93	227	534	1711 s	2214 s	1630 s
	306.24	176—180	2.53	3.15			
IXc	C ₁₆ H ₁₄ N ₂ O ₆	85	201	534	1697 s	2212 s	1631 s
	330.29	158—164	2.83	3.37			
IXd	C ₁₈ H ₁₆ O ₁₀	81	249	572	1734 s		1591 s
	392.32	162—165	2.91	3.74			
IXe	C ₂₄ H ₁₃ N ₂ O ₄	82	383	576	1740 s	2202 s	1653 s
	393.38	177—180	3.19	3.28			

a) All compounds gave satisfactory microanalyses for C, H, and N (within ± 0.3 %).

Table 3. ¹H NMR Data of Compounds VIII and IX

Compound	δ						Other
	H-7	H-3	H-6	H-9	NMe ₂		
VIIIa	7.39	7.70	7.95	—	3.49	3.36	
VIIIb	7.53	7.85	7.88	—	3.59	3.48	3.72 (s, 3H, OCH ₃)
VIIIc	7.56	7.88	7.91	—	3.45	3.32	4.25 (q, 2H, CH ₂), 1.26 (t, 3H, CH ₃)
VIIId	8.00	8.02	8.72	—	3.52	3.42	1.64 (s, 6H, CH ₃)
VIIIe	7.59	7.71	7.29	—	3.39	3.29	7.61 (d, 1H, H-8, J = 12.6 Hz)
VIIIf	8.35	7.20	6.31	—	3.35	3.14	2.13 (s, 3H, CH ₃)
VIIIfg	7.37—7.91	7.09	6.46	—	3.45	3.32	7.37—7.91 (m, 5H, Ph)
IXa	7.36	7.45	7.73	8.13	—	—	
IXb	7.46	7.75	7.87	—	—	—	3.72, 3.73 (all s, 3H, OCH ₃)
IXc	7.47	7.74	7.86	—	—	—	4.17 (q, 4H, CH ₂), 1.17 (t, 6H, CH ₃)
IXd	7.55	7.55	8.02	9.42	—	—	1.65 (s, 12H, CH ₃)
IXe	6.46	7.10	7.47—8.08	9.10	—	—	7.47—8.08 (m, 1H, 2 × Ph)

on a Specord M-40 spectrophotometer (Zeiss, Jena), ε values are given in m² mol⁻¹. Infrared spectra were taken of KBr discs (1 mg/300 mg of KBr) or chloroform solutions (c = 3 × 10⁻² mol dm⁻³) on the

spectrometer PU 9800 FTIR (Philips Analytical). ¹H NMR spectra were obtained on the Tesla BS 487 C (80 MHz) and Varian model VXR 300 (300.3 MHz) spectrometers, respectively. ¹³C NMR spectra were

Table 4. ^{13}C NMR Data of Compounds *VIIIa*—*VIIIc* and *IXa*, *IXb*

Compound	δ										
	C-5	C-7	C-2	C-6	C-3	C-4	C-8	C-9	NMe ₂	Other	
<i>VIIIa</i>	168.57	154.13	139.30	139.30	129.51	96.99	65.78	—	47.98	42.06	117.23 (s, CN), 115.29 (s, CN)
<i>VIIIb</i>	169.50	153.40	139.23	136.44	128.52	96.47	89.43	—	47.76	41.12	164.15 (s, CO), 116.43 (s, CN)
<i>VIIIc</i>	169.23	151.69	137.59	130.49	125.68	96.06	123.38	—	47.31	40.45	—
<i>IXa</i>	167.69	146.76	138.88	137.94	127.63	103.61	63.21	62.28	—	—	117.28, 117.17, 116.53, 115.56 (s, CN), 36.39 (d, C ₉ H)
<i>IXb</i>	168.87	143.08	137.88	134.51	127.90	101.88	85.24	84.38	—	—	164.72, 164.61 (all s, CO), 118.41, 117.19 (all s, CN), 51.92, 51.65 (all q, OCH ₃), 33.97 (d, C ₉ H)

taken on Varian VXR 300 (75.12 MHz) spectrometer. In NMR experiments hexadeuterodimethyl sulfoxide solutions with tetramethylsilane as internal standard were measured. Mass spectra were taken with an MS 902 S spectrometer (AEI Manchester), direct inlet, ionization energy 70 eV, electron current 100 μA , ionization chamber temperature according to the sample volatility.

4-(Dimethylaminomethylene)-5-oxo-2-furfurylidenedimethyliminium Perchlorate (*III*)

To a stirred dimethylformamide (19.13 g; 0.26 mol), kept at 0— -5°C , phosphorus oxychloride (40.12 g; 0.26 mol) was added dropwise over 20 min, then the mixture was left to stand at room temperature for another 20 min. The Vilsmeier—Haack reagent was cooled (ice bath) again and 2(5*H*)-furanone *I* (10 g; 0.12 mol) was added during 30 min, and the content of the flask was heated to 60—70 $^\circ\text{C}$ for 3 h. When cooled to room temperature, the residue was dissolved in ethanol (50 cm^3) and treated with perchloric acid (11.95 g; 0.12 mol). The precipitated solid was filtered off and recrystallized from glacial acetic acid to give *III* in the form of yellow needles, yield 29.5 g (84 %), m.p. = 243—244 $^\circ\text{C}$.

For $\text{C}_{10}\text{H}_{15}\text{ClN}_2\text{O}_6$ ($M_r = 294.69$) $w_i(\text{calc.})$: 40.76 % C, 5.13 % H, 9.51 % N; $w_i(\text{found})$: 41.03 % C, 5.27 % H, 9.73 % N. UV spectrum (methanol), $\lambda_{\text{max}}/\text{nm}$ (log $\{\epsilon\}$): 297 (2.47), 424 (3.45). IR spectrum (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 2999 w, 2939 w, 1736 s (CO), 1658 s, 1628 s, 1400 s, 1086 s. ^1H NMR spectrum (DMSO- d_6), δ : 8.11 (s, 1H, H-6), 8.10 (s, 1H, H-7), 7.82 (s, 1H, H-3), 3.54 (s, 6H, NMe₂), 3.48, 3.43 (all s, 3H, =NMe₂). ^{13}C NMR spectrum (DMSO- d_6), δ : 168.04 (s, C-5), 155.47 (d, C-7), 146.44 (d, C-6), 137.96 (d, C-3), 132.63 (s, C-2), 96.11 (s, C-4), 48.18, 48.07, 41.37, 41.05 (all q, NMe₂).

The reaction was carried out also with the isomeric 2(3*H*)-furanone *II* under the same reaction conditions. The identical compound *III* was obtained in 80 % yield. Starting from the mixture of both isomers *I* and

II (ratio 4 : 1), prepared by oxidation of 2-furaldehyde [9], 83 % of *III* could be obtained.

4-(Dimethylaminomethylene)-5-oxo-2-furancarbaldehyde (*VI*)

Potassium carbonate (2.35 g; 0.017 mol) was added to a suspension of *III* (5 g; 0.017 mol) in 125 cm^3 of water at room temperature, and the reaction mixture was stirred for 2 h. The precipitated solid was filtered off and washed several times with water. Yield 2.22 g (78 %), m.p. = 246—248 $^\circ\text{C}$.

For $\text{C}_8\text{H}_9\text{NO}_3$ ($M_r = 167.16$) $w_i(\text{calc.})$: 57.48 % C, 5.43 % H, 8.38 % N; $w_i(\text{found})$: 57.39 % C, 5.56 % H, 8.47 % N. UV spectrum (methanol), $\lambda_{\text{max}}/\text{nm}$ (log $\{\epsilon\}$): 290 (2.895), 377 (3.327). IR spectrum (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 3090 w, 2978 w, 2936 w, 1722 s (CO), 1655 s (C=C), 1606 s, 1554 s, 1022 m, 929 s, 779 m, 760 m. ^1H NMR spectrum (DMSO- d_6), δ : 9.06 (s, 1H, CHO), 7.78 (s, 1H, H-3), 7.74 (s, 1H, H-7), 3.40, 3.31 (all s, 3H, NMe₂). ^{13}C NMR spectrum (DMSO- d_6), δ : 176.39 (d, C-6), 170.46 (s, C-5), 154.02 (d, C-7), 143.03 (s, C-2), 126.64 (d, C-3), 94.02 (s, C-4), 47.90, 41.12 (all q, NMe₂). Mass spectrum, m/z ($I_r/\%$): 167 (45) (M^+), 139 (5), 138 (7), 111 (6), 83 (14), 82 (100), 66 (10), 57 (7), 55 (9), 44 (43), 42 (48), 39 (24).

Potassium Salt of 4-(Hydroxymethylene)-5-oxo-2-furancarbaldehyde (*VII*)

Potassium hydroxide (0.8 g; 0.033 mol) was added to a suspension of *III* (2 g; 0.0067 mol) in 150 cm^3 of water and the mixture was stirred at 70 $^\circ\text{C}$ for 4 h. After cooling the solvent was removed at reduced pressure (2 kPa) and the solid residue recrystallized from methanol. Yield 0.795 g (80 %), m.p. = 232—236 $^\circ\text{C}$.

IR spectrum (KBr), $\tilde{\nu}/\text{cm}^{-1}$: 1716 s (CO), 1653 s (C=C), 1518 s, 1397 s, 1315 m, 1122 s, 931 m, 758 m, 719 m, 503 m. ^1H NMR spectrum (DMSO- d_6), δ :

9.25 (s, 1H, CHO), 8.69 (s, 1H, CHOK), 7.28 (s, 1H, H-3). ^{13}C NMR spectrum (DMSO- d_6), δ : 182.92 (s, C-5), 180.92 (d, C-6), 71.85 (d, C-7), 138.88 (s, C-2), 128.58 (d, C-3), 104.76 (s, C-4).

4-(Dimethylaminomethylene)-5-oxo-2-furylethylenes (VIII)

To a solution of III (0.002 mol) in methanol (10 cm³) or ethanol (10 cm³, for VIIIe) a solution of compound with active methylene group (0.0022 mol) in methanol (10 cm³) or ethanol with catalytic amount of sodium methoxide or ethoxide was added. The reaction mixture was then stirred at room temperature or refluxed (see Table 1). After completion of the reaction (TLC-monitoring, SiO₂, MeOH), the separated solid portion was filtered off and washed with methanol or ethanol. Crude products were purified by crystallization from methanol or by passage through silica gel column (with chloroform—acetone, $\varphi_r = 8 : 2$). The characteristic data of compounds VIII are summarized in Tables 1, 3, and 4.

4-(2,2-R¹,R²-Ethylene)-5-oxo-2-furylethylenes (IX)

A solution of methylene component (0.0044 mol) in methanol (10 cm³) or ethanol (10 cm³, for IXe), containing a catalytic amount of sodium methoxide or ethoxide was added to a solution of III (0.002 mol) in methanol (10 cm³) or ethanol (10 cm³, for IXe). The mixture was stirred under reflux until a TLC control (SiO₂, MeOH) indicated the consumption of the educt III. The solid separated after cooling was filtered off and purified by crystallization from the mixture of ethyl acetate—toluene ($\varphi_r = 1 : 1$), or by

column chromatography (silica gel, with chloroform—acetone, $\varphi_r = 8 : 2$, then MeOH). The physical constants of compounds IX are summarized in Tables 2—4.

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