

Furan Derivatives. XXI.
Furfurylidene Derivatives of
Alkyl-4-amino-5-acetamido-2-furoates

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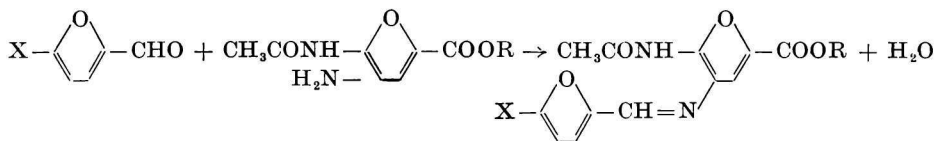
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By condensation of alkyl (methyl, ethyl, *n*-propyl, isopropyl, *n*-hexyl and *n*-octyl) 4-amino-5-acetamido-2-furoates with 5-*X*-2-furaldehydes in alcohol a series of alkyl-4-(5-*X*-furfurylideneamino)-5-acetamido-2-furoates was prepared (*X* = H, CH₃, Cl, Br, I, CH₃OOC, O₂N). A new route to reduce alkyl-4-nitro-5-acetamido-2-furoates with aluminium, activated with mercury(II) chloride, in a dioxan-ether mixture is presented.

In our previous papers, the preparation of 5-*X*-fural azomethines with α -amino derivatives of furan was discussed, where the conductive conjugation of the furan rings was discontinued by the methylene group [1], and also the preparation of azomethines in which two furan rings have conductive conjugation in the α, α' -positions [2]. Some of the above substances with the 1–10 μ g/ml concentration have been found to show strong antibacterial effects against gram-positive bacteria [3].

To make further study of the physicochemical and biological properties of furan compounds possible, a new series of azomethines of the furan- β -aminoderivatives was synthesized according to the scheme



X = H, CH₃, Cl, Br, I, CH₃OOC, O₂N;

R = CH₃, C₂H₅, CH(CH₃)₂, (CH₂)₂CH₃, (CH₂)₅CH₃, (CH₂)₇CH₃.

Azomethines of this kind have not been reported, analogous azomethines were prepared by condensation of benzaldehyde with 3-amino-2,5-dimethylfuran [4].

Experimental

Melting points have been determined by the method of Kofler. Infrared spectra of the compounds under investigation were measured in chloroform with the double-beam spectrophotometer UR-10 (Zeiss, Jena) in the 3600–700 cm⁻¹ range in KBr cells of 0.427 mm thickness. The concentration was 0.025 M. Due to its low solubility, the spectrum of the nitro derivative was measured in a KBr pellet (1.5 mg/1 g KBr) (Table 3).

The electron absorption spectra of the studied azomethines in the near ultraviolet region were measured with the spectrophotometer ORD/UV-5 (Jasco, Tokyo) in 1 cm cells. 96% ethanol was used as solvent. The concentration of compounds was $2.34 - 7.9 \times 10^{-5}$ M.

The 5-X-substituted 2-furaldehyde derivatives (methyl, bromo, iodo, carbomethoxy and nitro substituted) have been synthesized as reported in the papers [5–10]. The alkyl (methyl, ethyl, *n*-propyl, isopropyl, *n*-hexyl and *n*-octyl) 5-amino-2-furoates were prepared as reported in [11, 12]. Alkyl-5-acetamido-2-furoates were prepared by acetylation of amines with acetic anhydride according to [13], and alkyl-4-nitro-5-acetamido-2-furoates by nitration of alkyl-5-acetamido-2-furoates applying the method of *Rinkes* [14].

Preparation of 4-amino-5-acetamido-2-furoates

To the solution of 0.01 mole of alkyl-4-nitro-5-acetamido-2-furoates in 100 ml of a dioxan-ether mixture, 2 g of aluminium turnings activated with mercury(II) chloride were added. The mixture was allowed to stand for 24 hours while cooled with cold water. The solids were filtered off and washed with dioxan; the filtrate was evaporated *in vacuo* to small volume, and the precipitate filtered off and purified by crystallization of the dioxan-ether mixture. (Isopropyl-4-amino-5-acetamido-2-furoate in pure state has not been separated.) Table 1 lists the data of the derivatives prepared.

Preparation of furfurylidene derivatives of the 4-amino-5-acetamido-2-furoates

To the solution of 0.011 mole of the appropriate aldehyde in 20 ml ethanol, the solution of 0.010 mole of alkyl-4-amino-5-acetamido-2-furoate in 20 ml ethanol was added under stirring; the mixture was heated, the precipitated azomethines were filtered off and recrystallized from ethanol. The data of the prepared derivatives are listed in Table 2.

Results and Discussion

From the amines (Table 1) only ethyl-4-amino-5-acetamido-2-furoate was reported; it was prepared by catalytic reduction of the appropriate nitro derivative with hydrogen over PtO_2 in a 10.6% yield [15]. By reduction of alkyl-4-nitro-5-acetamido-2-furoates with mercury(II) chloride activated aluminium in dioxan-ether essentially higher yields of amines (44–70% of the theoretical amount) have been achieved.

In studying ethyl-4-amino-5-acetamido-2-furoate *Gilman* and *Wright* [15] have found that this compound shows to a considerable degree the properties of aromatic amines. It reacts for example, with sodium nitrite to give diazonium salt which undergoes coupling with β -naphthol, but the diazonium salt behaves in the Gattermann reaction differently and does not give the substitution products expected. The condensation reactions of β -amino derivatives of furan with carbonyl compounds have not yet been studied in detail. The condensation of 5-X-2-furaldehydes with α -amino derivatives of furan [2] leads to considerable resinification — due to the instability of amines. The yields of azomethines are within 28–58% of the theoretical amount. The studied system of β -amino derivatives of furan appeared to be more stable as the preparation under similar conditions does not lead to resinification and the yields are over 90% of the theoretical amount (Table 2).

Table 1

Alkyl-4-(5-X-acetamido)-2-furoates

No.	X	Alkyl	Molecular formula	M	Calculated/found			Yield [%]	M.p. [°C]
					% C	% H	% N		
1	H	CH ₃	C ₈ H ₉ NO ₄	182.15	52.45 51.92	4.95 4.80	7.64 7.61	96	198
2	H	C ₂ H ₅	C ₉ H ₁₁ NO ₄	197.18				94	173–175 ^a
3	H	(CH ₂) ₂ CH ₃	C ₁₀ H ₁₃ NO ₄	211.21	56.86 56.21	6.20 5.95	6.63 6.45	93	128–129
4	H	CH(CH ₃) ₂	C ₁₀ H ₁₃ NO ₄	211.21	56.86 56.15	6.20 6.31	6.63 6.60	37	91–94
5	H	(CH ₂) ₅ CH ₃	C ₁₃ H ₁₉ NO ₄	235.29	61.64 61.06	7.56 7.37	5.53 5.90	57	108–109
6	H	(CH ₂) ₇ CH ₃	C ₁₅ H ₂₃ NO ₄	281.34	64.03 64.15	8.23 8.03	4.97 4.67	46	84–86
7	NO ₂	CH ₃	C ₈ H ₈ N ₂ O ₆	228.16	42.11 41.65	3.53 3.42	12.27 12.06	69	189–191
8	NO ₂	C ₂ H ₅	C ₉ H ₁₀ N ₂ O ₆	242.18				56	138 ^b
9	NO ₂	(CH ₂) ₂ CH ₃	C ₁₀ H ₁₂ N ₂ O ₆	256.21	46.87 46.15	4.72 4.55	10.93 10.66	59	102–103
10	NO ₂	CH(CH ₃) ₂	C ₁₀ H ₁₂ N ₂ O ₆	256.21	46.87 46.24	4.72 4.62	10.93 10.67	50	84–85

Table 1 (Continued)

No.	X	Alkyl	Molecular formula	M	Calculated/found			Yield [%]	M.p. [°C]
					% C	% H	% N		
11	NO ₂	(CH ₂) ₅ CH ₃	C ₁₃ H ₁₈ N ₂ O ₆	298.29	52.34	6.08	9.39	73	66–68
					51.65	5.75	9.02		
12	NO ₂	(CH ₂) ₇ CH ₃	C ₁₅ H ₂₂ N ₂ O ₆	326.34	55.20	6.79	8.58	73	60–62
					54.71	6.63	8.42		
13	NH ₂	CH ₃	C ₈ H ₁₀ N ₂ O ₄	198.17	48.48	5.08	14.13	65	148–151
					47.87	5.11	13.98		
14	NH ₂	C ₂ H ₅	C ₉ H ₁₂ N ₂ O ₄	212.20				51	162 ^c
15	NH ₂	(CH ₂) ₂ CH ₃	C ₁₀ H ₁₄ N ₂ O ₄	226.22	53.08	6.23	12.38	70	118–130 darkens
					52.90	6.32	11.72		
16	NH ₂	(CH ₂) ₅ CH ₃	C ₁₃ H ₂₀ N ₂ O ₄	260.30	58.19	7.51	10.44	47	120–130
					57.24	7.36	10.28		
17	NH ₂	(CH ₂) ₇ CH ₃	C ₁₅ H ₂₄ N ₂ O ₄	296.35	60.78	8.16	9.45	44	135–137
					60.92	8.40	9.25		

^aAccording to [13] m.p. 173–175°C.

^bAccording to [15] m.p. 138°C.


^cAccording to [15] m.p. 160.5°C.

Table 2

Alkyl-4-(5-X-furfurylideneamino)-5-acetamido-2-furoates

No.	X	R	Molecular formula	M	Calculated/found			Yield [%]	M.p. [°C]
					% C	% H	% N		
1	H	C ₂ H ₅	C ₁₄ H ₁₄ N ₂ O ₅	290.26	57.92 57.91	4.86 4.88	9.64 10.08	92	167
2	CH ₃	C ₂ H ₅	C ₁₅ H ₁₆ N ₂ O ₅	304.28	59.20 59.32	5.30 5.42	9.20 9.11	92	130
3	Cl	C ₂ H ₅	C ₁₄ H ₁₃ ClN ₂ O ₅	324.70	51.78 52.12	4.03 4.14	8.62 9.01	94	196
4	Br	C ₂ H ₅	C ₁₄ H ₁₃ BrN ₂ O ₅	369.17	43.54 43.93	3.54 3.43	7.58 7.49	95	179
5	I	C ₂ H ₅	C ₁₄ H ₁₃ IN ₂ O ₅	416.17	40.40 40.71	3.14 3.04	6.73 6.60	94	175
6	CH ₃ OOC	C ₂ H ₅	C ₁₆ H ₁₆ N ₂ O ₇	348.30	55.17 55.87	4.63 4.89	8.04 8.11	92	233
7	NO ₂	C ₂ H ₅	C ₁₄ H ₁₃ N ₃ O ₇	335.26	50.15 50.24	3.90 4.09	12.53 12.63	96	243
8	NO ₂	CH ₃	C ₁₃ H ₁₁ N ₃ O ₇	321.24	48.60 48.13	3.45 3.56	13.08 12.82	96	237–239
9	NO ₂	(CH ₂) ₂ CH ₃	C ₁₅ H ₁₅ N ₃ O ₇	349.29	51.57 50.85	4.32 4.42	12.03 11.88	94	217–219
10	NO ₂	CH(CH ₃) ₂	C ₁₅ H ₁₅ N ₃ O ₇	349.29	51.57 51.65	4.32 4.18	12.03 11.94	92	210–211
11	NO ₂	(CH ₂) ₅ CH ₃	C ₁₈ H ₂₁ N ₃ O ₇	391.37	55.23 54.67	5.40 5.58	10.73 10.61	93	184–186
12	NO ₂	(CH ₂) ₇ CH ₃	C ₂₀ H ₂₅ N ₃ O ₇	419.42	57.27 57.60	6.00 5.88	10.01 9.78	87	153–154

Table 3
 Values of infrared and ultraviolet spectra
 of ethyl-4-(5-X-furfurylideneamino)-5-acetamido-2-furoates

No.	X	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$		$[\text{cm}^{-1}]$	λ_{max} [nm] (log ϵ)		
1	H	1720 vs	1633 s	1022 m	887 w	231 (4.05)	280 (4.22)	322 (4.21)
2	CH ₃	1720 vs	1630 s	1026 s	881 w	231 (3.98)	293 (4.22)	330 (4.21)
3	Cl	1720 vs	1632 s	1022 s	878 w	225 (4.03)	283 (4.24)	332 (4.30)
4	Br	1720 vs	1631 s	1021 m	880 w	228 (4.01)	295 (4.24)	335 (4.30)
5	I	1720 vs	1630 s	1020 m	880 w	230 (4.05)	305 (4.20)	341 (4.26)
6	COOCH ₃	1720 vs	1630 vs	1023 m	880 w	208, 224 (4.04)(4.09)	288 (4.20)	348 (4.22)
7	NO ₂	1710 vs 1680 vs	1628 s	1018 m	876 w	233 (4.05)	297 (4.20)	385 (4.16)

vs = very strong, s = strong, m = medium, w = weak.

In connection with our previous studies [1, 2] the characteristic frequencies of the infrared spectra of azomethines have been recorded and are listed in Table 3.

The absorption band $\nu(\text{C}=\text{N})$ in the 1639–1628 cm^{-1} region is of great intensity and is located between the bands of 5-X-furfurylideneaminomethyl derivatives of furan (1654–1650 cm^{-1}) [1] and of alkyl-5-X-furfurylideneamino-2-furoates (1627–1610 cm^{-1}) [2]. This lets suggest a more restricted conjugation of the azomethine group in the β -position when compared with that in the α -position. The location of the other bands shows a good agreement with [16].

In the near ultraviolet region the absorption curve of azomethines shows three bands (Table 3). The absorption bands in the 233–224 nm region are due to electron transfers localized in the furan ring; the bands in the 305–280 nm region probably belong to the molecule part grouping the ethyl-5-acetamido-2-furoate. This furoate itself has its band at 289 nm [17]. The absorption bands within the 385–322 nm region are due to π -electron transitions of the whole conjugated system. The position of the bands considerably depends on the nature of the substituent of the 5-X-furfurylidene group, the bathochromic shift increasing in the order $\text{X} = \text{H}, \text{CH}_3, \text{Cl}, \text{Br}, \text{I}, \text{CH}_3\text{OOC}, \text{O}_2\text{N}$. Comparison of the spectra under investigation with those of the analogous 5-X-furfurylidene derivatives of ethyl-5-amino-2-furoate [2], having their π -electron transition band of the whole conjugated system at 410–316 nm, shows that replacing of the 5-X-furfurylidene group to the β -position of the furan ring is to be seen in the hypsochromic shift, indicating also the more restricted conjugation in the β -position.

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