

SYNTHESIS AND SPECTRA OF 3-(3,5-DIMETHYL-2-FUROYL)-4-ARYL-5-CARBETHOXY- Δ^2 -PYRAZOLINES

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Abstract : 3-(3,5-Dimethyl-2-furoyl)-4-aryl-5-carbethoxy- Δ^2 -pyrazolines **2a-e** have been synthetized by the dipolar cycloaddition of 3,5-dimethyl-2-furoyl *para*-substituted-styryl ketones and ethyl diazoacetate. Their structure was determined by UV, IR, ¹H- and ¹³C-NMR spectroscopy ; only one racemic diastereomer (*cis* - H-8, H-9) was determined using homonuclear proton-proton n.O.e. experiments.

Introduction

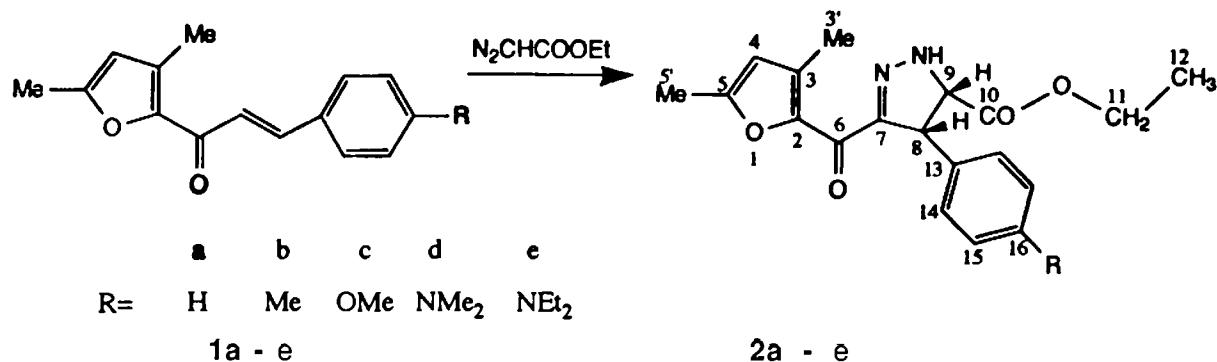
2,4,6-Trialkylpyrylium salts which are easily available from the diacylation of alkenes (1,2) undergo an oxidative ring contraction (3,4) under the action of hydrogen peroxide when 2-acyl-3,5-dialkylfurans are formed. the condensation of these furanic derivatives with substituted aromatic aldehydes leads to substituted 3,5-dialkyl-2-furyl styryl ketones **1** (5) which are interesting starting materials for the synthesis of other heterocyclic compounds. The above α,β -unsaturated ketones react with phenylhydrazine when 3-(3,5-dialkylfuryl)-1-phenyl-5-aryl- Δ^2 -pyrazolines are obtained (6) ; the condensation with ethyl cyanoacetate leads to 4-aryl-3-cyano-6-(2-furyl)-2-pyridones (7).

The present paper reports the preparation of 3-(3,5-dimethyl-2-furoyl)-4-aryl-5-carbethoxy- Δ^2 -pyrazolines **2** starting from the furyl styryl ketones **1** and ethyl diazoacetate. The structure of the title compounds **2a-e** was determined by UV, IR, ^1H - and ^{13}C -NMR spectroscopy and by mass spectra.

The synthesis and properties of pyrazolines were reviewed by Coispeau and Elguero (8), as well as by El-Rayyes et al. (9). An extensive stereochemical structural analysis was carried out by Tóth and Lévai (10) using ^1H - and ^{13}C -NMR spectroscopy. The use of pyrazolines as optical brightening agents was reviewed by Wagner et al. (11).

Synthesis and optical spectra

The furyl analogues of chalcone **1 a-e** were refluxed with the four-fold molar amount of ethyl diazoacetate in chloroform for various time periods depending on the nature of the R group. The unreacted ketone was separated from the product by preparative TLC chromatography using CHCl_3 (for **2a, d, e**) or $\text{CHCl}_3 + \text{iPrOH}$ (20 : 1) for **2e** (R_f for **2a** : 0.615, **2b** : 0.625, **2c** : 0.560, **2d** : 0.532, **2e** : 0.462). A further purification was carried out by recrystallization when yellow crystalline compounds were obtained. Yields varied from 45 to 95 % (Table 1). In the UV spectra recorded in ethanol a characteristic band at 290-295 nm was observed.



The IR spectra recorded in KBr pellets showed for all compounds a strong sharp band at $3300-3340\text{ cm}^{-1}$ due to N-H stretching. Thus, a cyclic azo tautomer **3** is ruled out. The carbonyl frequency appeared at about 1650 cm^{-1} and the carbethoxy group gave rise to a strong band at $1722-1730\text{ cm}^{-1}$.

Table 1. Physical constants and spectral data of compounds 2a - e

Compound	R	Yield (%)	M.P.(°C)	Parent peak	IR (KBr, cm ⁻¹) ν_{co}	IR (KBr, cm ⁻¹) ν_{coo}
2a	H	94.2	122 ^a	340	1622	1700
2b	Me	73.2	120-2 ^b	354	1640	1730
2c	OMe	67.2	115-6 ^a	370	1650	1724
2d	NMe ₂	45.3	175-6 ^a	383	1640	1722
2e	NET ₂	51.4	151-2 ^a	c	1660	1722

^a Recrystallization from CCl₄; ^b Recrystallization from ethanol; ^c Not recorded.

¹H-NMR Spectra

All ¹H-NMR spectra were recorded in CDCl₃. The chemical shifts are presented in Table 2. The assignments agree with the data for the furyl styryl ketones published earlier (5). Thus, the H-4 furanic proton in the title compounds appears as a singlet at 6.08-6.12 ppm as in the furanic analogues of chalcone 1. The broad singlet at 6.86-6.96 ppm is assigned to the nitrogen-bonded proton which undergoes exchange with D₂O. The ¹H-NMR spectra show that only one tautomer 2 with two adjacent CH groups was obtained, another one (structure 3) is ruled out. The two protons connected with the two C(sp³) atoms of the pyrazoline ring (H-8 and H-9, respectively) appear as doublets having a coupling constant *J* of 3.7 - 4.3 Hz.

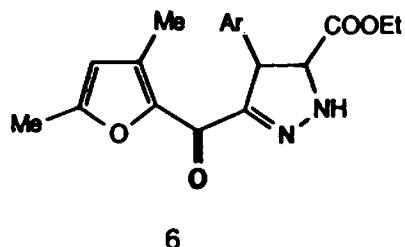
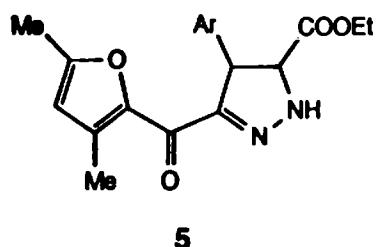
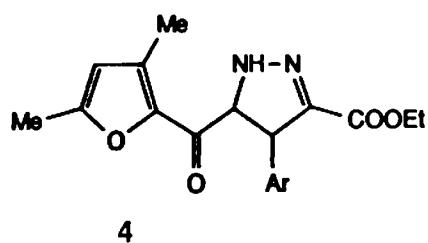
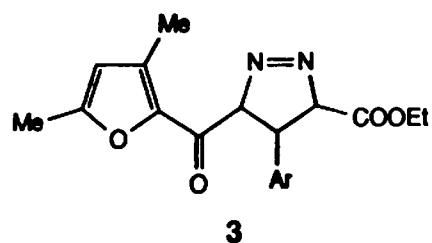


Table 2. ^1H -NMR chemical shifts ($\delta_{\text{TMS}} = 0.00$ ppm) and coupling constants J (Hz) of compounds **2a-e** in CDCl_3 .

δ and J	2 a R = H	2 b Me	2c OMe	2 d NMe ₂	2 e NEt ₂
H - 3'	2.30	2.31	2.32	2.32	2.33
H - 4	6.08	6.08	6.12	6.09	6.09
H - 5'	2.35	2.36	2.36	2.35	2.36
H - N	6.95	6.99	6.92	6.88	6.86
H - 8	4.59	4.55	4.60	4.55	4.54
H - 9	4.88	4.84	4.89	4.87	4.87
H - 11	4.10	4.10	4.00	4.12	a
H' -11	4.17	4.17	4.17	4.18	4.17
H - 12	1.21	1.24	1.24	1.24	1.23
H - 14	7.30	7.19	6.90	7.19	7.14
H - 15	7.30	7.13	7.25	6.69	6.62
H ^R	7.30	2.34	3.84	2.94	1.15
					3.34
$J_{8,9}$	4.26	4.05	3.90	3.70	3.70
$J_{11\text{ gem}}$	11.2	-	-	-	-
J_{11-12}	7.14	7.32	7.20	7.14	7.14
J_{14-15}	-	8.07	8.64	8.90	8.90

^a Unresolved multiplet.

The fact that these are the *cis* isomers can be determined only tentatively from the magnitude of this coupling constant ; hence homonuclear proton-proton n.O.e. difference spectroscopy for neighboring protons H-8 and H-9 was carried out. The irradiation of H-8 in **2c** causes a large enhancement in the intensity of H-9, a small enhancement of the pair of equivalent H-14 protons in the aromatic ring, and a sizeable enhancement of the two furanic methyl peaks. It can be concluded unambiguously that the H-8 and H-9 protons are *cis* to each other, and that structure **4** is ruled out. From the four possible rotamers of the racemic *cis*-configuration only structures **5** and **6** exist in the ground state.

The methylene group in the ethyl substituent appears as an ABX_3 multiplet with 18 lines because its hydrogens are diastereotopic since the molecule has chiral centers ; its coupling constants are 7 Hz for the ethyl coupling and about 11 Hz for the geminal coupling.

^{13}C -NMR Spectra

^{13}C -NMR Spectra were recorded in CDCl_3 . The assignments for the chemical shifts (Table 3) were made using 2D ^1H - ^{13}C correlation maps and a.p.t. spectra. Results are in good agreement with literature data (5, 10a).

Table 3. ^{13}C -NMR chemical shifts ($\delta_{\text{TMS}} = 0.00$ ppm) of compounds **2a-e** in CDCl_3 .

Comp.	2a	2b	2c	2d	2e
R =	H	Me	OMe	NMe ₂	NEt ₂
C- 2	156.30	156.22	156.80	156.67	156.67
C- 3	135.36	135.33	135.86	135.62	135.59
C- 3'	11.65	11.67	11.83	11.79	11.84
C- 4	113.12	113.09	113.33	113.20	113.24
C- 5	145.55	a	a	145.50	146.33
C- 5	13.81	13.81	14.11	13.99	14.04
C- 6	184.64	184.83	185.15	185.52	185.66
C- 7	145.10	145.95	146.28	146.67	146.84
C- 8	53.80	53.54	53.24	53.24	53.26
C- 9	73.86	73.89	73.97	74.04	74.17
C-10	161.26	161.23	161.70	161.46	161.89
C-11	60.70	60.77	61.12	61.02	61.04
C-12	14.01	14.61	14.01	14.10	14.15
C-13	140.03	a	132.06	a	135.59
C-14	127.38	129.45	128.55	128.16	128.39
C-15	128.72	127.27	114.27	112.82	112.02
C-16	127.38	136.89	159.03	149.98	147.30
C- R	-	21.07	55.26	40.55	44.35
					12.64

^a Not detected.

Mass spectra

In the electron-impact mass spectra of compounds **2a** and **2d**, the parent peak has low intensity (5.3 and 19.4 %, respectively). The base peak is the 4-aryl-5-ethoxypyrazolyl radical-ion resulted from the loss of carbon dioxide from the ester group and of a 3,5-dimethyl-2-furoyl radical ; the later radical-ion appears at $m/z = 123$ with an intensity of 68.2 and 52.5 %, respectively. The direct fragmentation affording the latter radical leaves a 4-aryl-5-carboxethylpyrazolyl radical-ion whose intensity is 62.3 and 39.0 %, respectively.

Experimental Part

Melting points were determined on a Boetius hot plate and are uncorrected. IR spectra were recorded with a FT-IR 5300 JASCO apparatus ; ^1H - and ^{13}C -NMR spectra were recorded with 300 MHz Varian spectrometer.

Ethyl diazoacetate was prepared according to literature data (11).

Preparation of Pyrazolines **2a-e**.

General Procedure

Furyl styryl ketones **1** (5 mmoles) were refluxed with 20 mmoles ethyl diazoacetate in chloroform for 24 hours (compounds **2a** and **2b**) and three weeks (compounds **2c-e**). The reaction mixture was analyzed by TLC. After the removal of the solvent the oily mixture was separated by preparative TLC using either CHCl_3 (for **2a**, **b**, **d**, **e**) or $\text{CHCl}_3 + \text{iPrOH}$ (20 : 1) for **2c**.

R_f values are : **2a** : 0.615, **2b** : 0.625, **2c** : 0.560, **2d** : 0.532, **2e** : 0.463.

Physical constants, analytical, IR and mass spectroscopic data are presented in Table 1.

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