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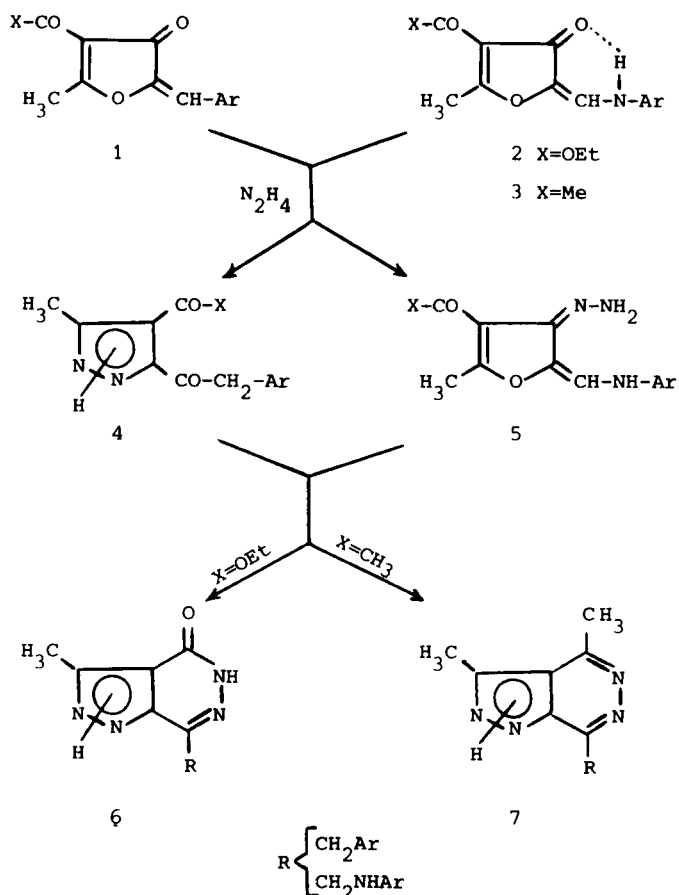
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The acetylation of 2-*N*-arylaminoacetyl-4-ethoxycarbonyl(or acetyl)-5-methyl-3(2*H*)furanones produces *N*-acetylated compounds which react with hydrazine to yield substituted pyrazoles.

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In a preceding paper (1), we showed that compounds **1** react with an equimolecular amount of hydrazine to afford the pyrazoles **4** while compounds **2** or **3** gave no pyrazole but hydrazones **5**. Compounds **4** and **5** lead to pyrazolo[3,4-*d*]pyridazines **6** or **7** with hydrazine (Scheme 1).

SCHEME 1



We now wish to report that compounds **8** or **9** can be converted to the pyrazoles **10** or **11**. The reaction proceeds with ring opening followed by cyclization. This result indicates that the reactivity of C-3 and C-5 was modified by the presence of an intramolecular hydrogen bond (2) (Scheme 2).

The structure of compounds **10** or **11** are consistent with the <sup>1</sup>H nmr spectra, ir data and elemental analysis (see Table II). The pyrazoles **10a** or **11a** were readily

converted into pyrazolo[3,4-*d*]pyridazines **6a** or **7a** R = CH<sub>2</sub>N(COCH<sub>3</sub>)C<sub>6</sub>H<sub>5</sub>. The same compounds were obtained by acetylation of **6a** or **7a** with R = CH<sub>2</sub>-NH-C<sub>6</sub>H<sub>5</sub> (Scheme 2).

The catalytic hydrogenation of **8a** gave **12a** (Scheme 3). The structure of **12a** was unambiguously established on the basis of <sup>1</sup>H nmr data, ir and ultraviolet spectra which closely resembled those of the corresponding 3-(2*H*)furanones (3). One proton appears at 4.92 δ as a triplet and two protons at 4.16 δ as a doublet, respectively, assigned to methine and methylene protons.

These results showed clearly that compounds **2** and **3** react with acetic anhydride to afford *N*-acetylated compounds **8** or **9** and no *O*-acetylated compounds as previously reported (2).

## EXPERIMENTAL

All melting points were taken on a Kofler block. The ir and uv spectra were obtained with a Beckman Model Acculab 2 and DB spectrophotometers. The nmr spectra were measured using tetramethylsilane as the internal standard, with a Varian A-60 spectrometer. Microanalyses were performed by Microanalytical Laboratory, Centre National de la Recherche Scientifique, Villeurbanne, France.

Compounds **2** and **3** were prepared as previously described (2).

2-*N*-Acetyl-*N*-arylaminoacetyl-4-ethoxycarbonyl(or acetyl)-5-methyl-3(2*H*)furanones (**8** or **9**).

General Method.

Compound **2** or **3** (0.02 mole) was refluxed with 50 ml. of acetic anhydride for 5 minutes or 20 minutes. After cooling the reaction mixture was poured into 500 ml. of cold water. The crude product, which precipitated as a yellow-brown product, was removed by filtration, washed with water and recrystallized from ethanol (Tables I and III).

3-*N*-Acetyl-*N*-arylaminoacetyl-4-ethoxycarbonyl-5-methylpyrazoles (**10** or **11**).

General Method.

A suspension of **8** or **9** (0.01 mole) in 50 ml. of acetonitrile was cooled to 0° with stirring and 0.5 g. (0.01 mole) of hydrazine hydrate was added dropwise. The mixture was allowed to stand at room temperature for 1 hour, then poured into 200 ml. of cold water. The resulting solid product was collected by filtration and recrystallized from the proper solvent (Tables II and III).

Compounds **6** and **7** (R = CH<sub>2</sub>-N(COCH<sub>3</sub>)C<sub>6</sub>H<sub>5</sub>).

A mixture of **8a** or **9a** (0.01 mole), 20 ml. of ethanol and 1.5 g. (0.03 mole) of hydrazine hydrate was refluxed for 1 hour. After removal the solvent under reduced pressure, the residue was trit-

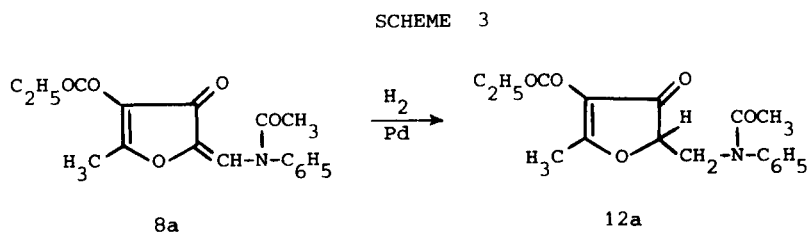
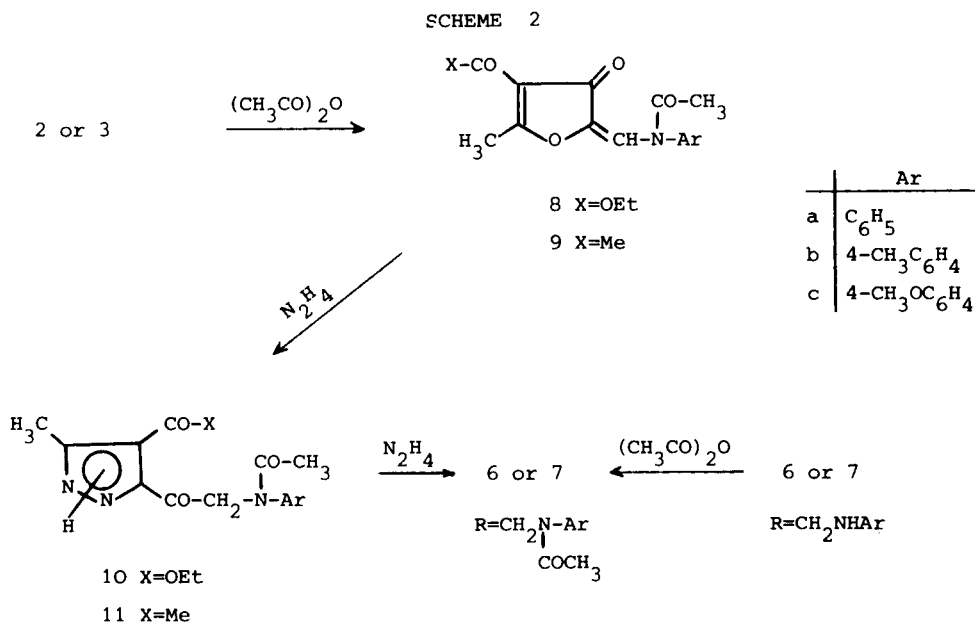


Table I

Physical Data for Compounds 8 and 9

Compounds	Yield %	M.p. °C	Molecular Formula	Analyses			Uv		Ir (cm <sup>-1</sup> ) Potassium bromide $\nu$ C=O
				Calcd.	Found %		$\lambda$ max (nm)	$\epsilon$	
				C	H	N			
8a	66	185	C <sub>17</sub> H <sub>17</sub> O <sub>5</sub> N	64.75	5.43	4.44	211	14,900	1720
				64.37	5.63	4.38	283	11,400	1710
							337	15,200	1650
8b	61	156	C <sub>18</sub> H <sub>19</sub> O <sub>5</sub> N	65.64	5.82	4.25	213	15,800	1740
				65.70	5.99	4.20	281	11,000	1710
							338	15,400	1690
8c	67	132	C <sub>18</sub> H <sub>19</sub> O <sub>6</sub> N	62.60	5.55	4.06	214	14,900	1715
				62.86	5.40	4.23	278	11,600	1645
							340	16,000	
9a	77	163	C <sub>16</sub> H <sub>15</sub> O <sub>4</sub> N	67.36	5.30	4.91	228	12,000	1715
				67.02	5.32	5.07	285	10,300	1680
							339	15,800	1645
9b	72	134	C <sub>17</sub> H <sub>17</sub> O <sub>4</sub> N	68.21	5.73	4.68	226	15,500	1715
				68.19	5.70	4.80	284	10,300	1685
							340	15,900	1650

Table II

Physical Data for Compounds **10** and **11**

Compounds	Yield %	M.p. °C	Molecular Formula	Analyses			Uv		Ir (cm <sup>-1</sup> )	
				Calcd. %	Found %	N	in Ethanol		Potassium bromide	
				C	H	N	λ max (nm) ε		ν NH	ν C=O
<b>10a</b>	81	158 (a)	C <sub>17</sub> H <sub>19</sub> O <sub>4</sub> N <sub>3</sub>	61.99	5.82	12.76	213	13,600	3200	1725
				61.78	5.80	12.54	230	12,300	3125	1715
<b>10b</b>	82	164 (a)	C <sub>18</sub> H <sub>21</sub> O <sub>4</sub> N <sub>3</sub>	62.96	6.16	12.24	212	12,400	3220	1740
				62.91	6.15	12.17	231	10,600	3130	1720
<b>10c</b>	86	115 (b)	C <sub>18</sub> H <sub>21</sub> O <sub>5</sub> N <sub>3</sub>	60.16	5.89	11.69	213	11,100	3190	1740
				59.86	5.89	11.68	230	14,800	3120	1720
<b>11a</b>	67	105 (a)	C <sub>16</sub> H <sub>17</sub> O <sub>3</sub> N <sub>3</sub> ·H <sub>2</sub> O	60.55	6.04	13.24	219	11,900	3150	1715
				60.47	6.03	12.50	245	8,200	3080	1675
<b>11b</b>	63	162 (c)	C <sub>17</sub> H <sub>19</sub> O <sub>3</sub> N <sub>3</sub>	65.16	6.11	13.41	219	13,600	3190	1720
				65.15	6.11	13.65	243	8,800	3100	1680
										1640

Crystallization solvent: (a) ethyl acetate, (b) ethanol, (c) acetonitrile.

Table III

## Proton Magnetic Resonance Parameters (a)

## Compounds

<b>6(b)</b>	1.95 (s, 3H); 2.66 (s, 3H); 5.19 (s, 2H); 7.50 (s, 5H); 12.27 (1H)(c); 14.1 (1H)(c)(d)
<b>7(b)</b>	1.97 (s, 3H); 2.72 (s, 3H); 2.89 (s, 3H); 5.48 (s, 2H); 7.54 (s, 5H), (f) (d)
<b>8a</b>	1.30 (t, 3H); 2.03 (s, 3H); 2.15 (s, 3H); 4.27 (q, 2H); 7.2-7.7 (m, 5H) (e)
<b>8b</b>	1.35 (t, 3H); 2.07 (s, 3H); 2.22 (s, 3H); 2.52 (s, 3H); 4.38 (q, 2H); 7.27 (d, 2H); 7.47 (d, 2H); 8.13 (s, 1H) (e)
<b>8c</b>	1.33 (t, 3H); 2.07 (s, 3H); 2.26 (s, 3H); 3.98 (s, 3H); 4.35 (q, 2H); 7.15 (d, 2H); 7.42 (d, 2H); 8.10 (s, 1H) (e)
<b>9a</b>	2.10 (s, 3H); 2.22 (s, 3H); 2.52 (s, 3H); 7.2-7.9 (m, 5H); 8.20 (s, 1H) (e)
<b>9b</b>	2.10 (s, 3H); 2.24 (s, 3H); 2.50 (s, 3H); 7.32 (d, 2H); 7.51 (d, 2H); 8.18 (s, 1H) (e)
<b>10a</b>	1.35 (t, 3H); 2.02 (s, 3H); 2.43 (s, 3H); 4.36 (q, 2H); 5.25 (s, 2H); 7.52 (s, 5H); 12.8 (1H)(c)(e)
<b>10b</b>	1.33 (t, 3H); 2.02 (s, 3H); 2.38 (s, 3H); 2.43 (s, 3H); 4.36 (q, 2H); 5.24 (s, 2H); 7.1-7.6 (5H); 12.9 (1H)(c)(e)
<b>10c</b>	1.35 (t, 3H); 2.01 (s, 3H); 2.42 (s, 3H); 3.86 (s, 3H); 4.35 (q, 2H); 5.21 (s, 2H); 6.98 (d, 2H); 7.45 (d, 2H); 12.8 (1H)(c)(e)
<b>11a</b>	1.91 (s, 3H); 2.37 (s, 3H); 2.42 (s, 3H); 5.15 (s, 2H); 7.54 (s, 5H); 13.9 (1H)(c)(d)

<b>11b</b>	1.92 (s, 3H); 2.38 (s, 3H); 2.42 (s, 3H); 2.47 (s, 3H); 5.13 (s, 2H); 7.37 (s, 4H); 13.8 (1H)(c) (d)
<b>12a</b>	1.33 (t, 3H); 1.92 (s, 3H); 2.62 (s, 3H); 4.16 (d, 2H); 4.37 (q, 2H); 4.92 (t, 1H); 7.2-7.8 (m, 5H) (e)

(a) Coupling constants carboxy group CH<sub>3</sub>-CH<sub>2</sub>: J = 7 Hz. Coupling constants *ortho*-aromatic ring protons: J = 8.5 Hz. (b) With R = CH<sub>2</sub>-N(COCH<sub>3</sub>)C<sub>6</sub>H<sub>5</sub>. (c) Broad. (d) In DMSO-d<sub>6</sub>. (e) In deuteriochloroform. (f) N-H proton: none observed.

urated with ether, filtered and recrystallized from ethanol.

Compound **6**.

This compound was obtained in a yield of 79%, m.p. 250°; ir (potassium bromide): 3200 (NH); 1680, 1660 (>C=O amide); uv (95% ethanol): λ max (ε), 216 (14,400), 270 (5,500); nmr: see Table III.

*Anal.* Calcd. for C<sub>15</sub>H<sub>15</sub>N<sub>5</sub>O<sub>2</sub>: C, 60.59; H, 5.09; N, 23.56. Found: C, 60.41; H, 5.20; N, 23.40.

Compound **7**.

This compound was obtained in a yield of 73%, m.p. 98-100°; ir (potassium bromide): 3320, 3120 (NH); 1650 (>C=O amide); uv (95% ethanol): λ max (ε), 216 (16,200), 280 (4,000); nmr: see Table III.

*Anal.* Calcd. for C<sub>16</sub>H<sub>17</sub>N<sub>5</sub>O·H<sub>2</sub>O: C, 61.32; H, 6.11; N, 22.35. Found: C, 61.06; H, 6.13; N, 22.25.

The same products were also obtained by heating of **6** or **7** (R = CH<sub>2</sub>-NH-C<sub>6</sub>H<sub>5</sub>), previously described (1), with acetic anhydride.

2-*N*-Acetylanilinomethyl-4-ethoxycarbonyl-5-methyl-3(2*H*)furanone (**12a**).

A suspension of **8a** (0.01 mole) in dioxane (120 ml.) was hydrogenated with 5% palladium on carbon (1.5 g.) at room temperature using a low pressure (ca 1 atmosphere) hydrogenation apparatus with magnetic stirring. Uptake of the calculated amount of hydrogen required 30 minutes, the catalyst was filtered off and the solvent was evaporated under reduced pressure. The crude product was recrystallized from ethyl acetate, yield 73%, m.p. 139°; ir (potassium bromide): 1720, 1705 (sh), 1660 (>C=O); uv (95% ethanol):  $\lambda$  max ( $\epsilon$ ), 214 (13,100), 261 (9,600); nmr:

see Table III.

*Anal.* Calcd. for C<sub>17</sub>H<sub>19</sub>NO<sub>5</sub>: C, 64.34; H, 6.04; N, 4.41. Found: C, 64.29; H, 6.11; N, 4.48.

#### REFERENCES AND NOTES

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- (3) R. Gelin, A. Galliaud, B. Chantegrel and S. Gelin, *Bull. Soc. Chim. France*, 1043 (1974).