Synthesis of Some Substituted 6-Oxo-6,7-dihydro-4*H*-pyrazolo[5,1-*c*][1,4]oxazines from 3-Oxo-2,3-dihydrofurans

Suzanne GELIN, Michel CHABANNET

Laboratoire de Chimie Organique, Institut National des Sciences Appliquées, F-69621 Villeurbanne Cedex, France

We have previously[1,2] described a simple preparation of 3(or 5)-(1-hydroxyalkyl)-pyrazole derivatives from 3-oxo-2,3-dihydrofurans **1**. We now report the application of this approach to the synthesis of some pyrazolo[5,1-*c*][1,4]oxazines **5**, a class of compound of which very few examples have been reported in the chemical literature[3,4].

Treatment of 3-oxo-2,3-dihydrofurans **1** with ethyl hydrazinoacetate **(2)** affords the *N*-ethoxycarbonylmethylpyrazole derivatives **3** in good yields. In all cases the condensation takes the indicated course, there being no evidence for the formation of an isomeric *N*-alkylpyrazole.

1-Aminocarbonylmethyl compounds **4** are produced in quantitative yield by the action of aqueous ammonia. On heating, compounds **3** (path *a*) or compounds **4** (path *b*) at 200 °C, ring closure occurs to afford the 6-oxo-6,7-dihydro-4*H*-pyrazolo[5,1-*c*][1,4]oxazines **5**. However, better yields are obtained from compounds **4** (Table).

The structure of compounds **3** and **5** were confirmed by I.R., U.V., and ^{1}H-N.M.R. spectral data.

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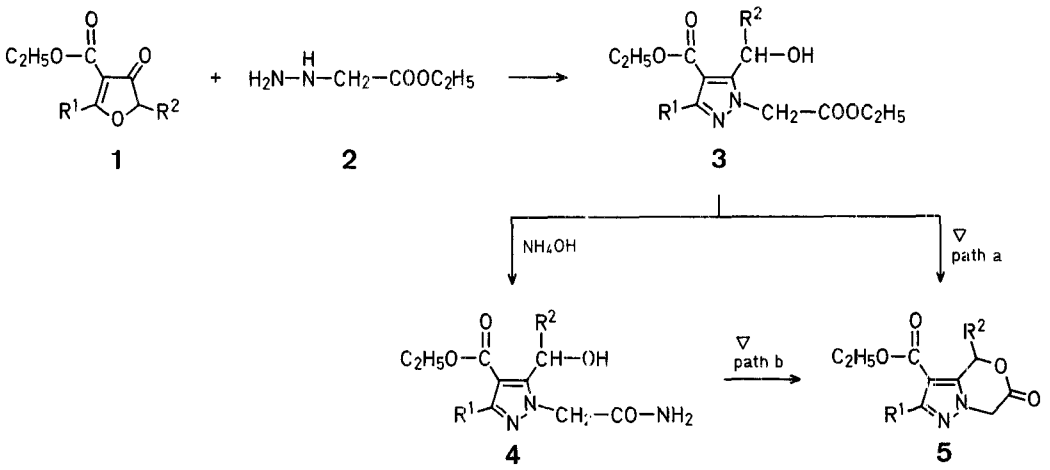

1 2 3 4 5

4-Ethoxycarbonyl-1-ethoxycarbonylmethyl-5-(1-hydroxyalkyl)-3-methyl(or -phenyl)-pyrazoles 3; General Procedure:

To a stirred suspension of ethyl hydrazinoacetate hydrochloride (2; 3.1 g, 0.02 mol) in ethanol (20 ml) is added a 2 molar solution of sodium ethoxide in ethanol (10 ml) and then, in one portion, the dihydrofuran **1**[1] (0.02 mol) in ethanol (20 ml). The mixture is heated under reflux for 2 h. After cooling to room temperature, the precipitated sodium chloride is filtered off. Evaporation of the filtrate in vacuo furnishes the almost pure compounds **3**; yields: **3a**, 5.4 g; **3b**, 5.6 g; **3c**, 6.6 g; **3d**, 6.8 g. Analytical samples are obtained by chro-

Table. Compounds **3** and **5** prepared

Compound	R^1	R^2	Yield[a] [%]	m.p. [°C] (solvent)	Molecular Formula[b]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]	I.R. ($CHCl_3$) ν [cm^{-1}]	U.V. (ethanol) λ_{max} (nm) (ε)
3a	CH_3	H	76	66° (*c*-C_6H_{12})	$C_{12}H_{18}N_2O_5$ (270.3)	1.30 (t, 3H, J=7 Hz); 1.40 (t, 3H, J=7 Hz); 2.45 (s, 3H); 4.07 (s, 1H, exchangeable); 4.34 (q, 2H, J=7 Hz); 4.42 (q, 2H, J=7 Hz); 4.92 (s, 2H); 5.08 (s, 2H)	3400–2980; 1750–1680	236 (9250)
3b	CH_3	CH_3	78	oil	$C_{13}H_{20}N_2O_5$ (284.3)	1.31 (t, 3H, J=7 Hz); 1.41 (t, 3H, J=7 Hz); 1.57 (d, 3H, J=7 Hz); 2.46 (s, 3H); 4.35 (q, 2H, J=7 Hz); 4.48 (q, 2H, J=7 Hz); 4.17–4.65 (1H, masked, exchangeable); 5.08 (s, 2H); 5.26 (q, 1H, J=7 Hz)	3400–2980; 1750–1680	235 (7650)
3c	C_6H_5	H	90	75° (*c*-C_6H_{12})	$C_{17}H_{20}N_2O_5$ (332.4)	1.12 (t, 3H, J=7 Hz); 1.25 (t, 3H, J=7 Hz); 4.30 (q, 2H, J=7 Hz); 4.32 (q, 2H, J=7 Hz); 4.96 (s, 2H); 5.18 (s, 2H); 7.5–7.7 (m, 3H); 7.7–7.9 (m, 2H)	3400–2980; 1750–1680	234 (11600)
3d	C_6H_5	CH_3	92	oil	$C_{18}H_{22}N_2O_5$ (346.4)	1.11 (t, 3H, J=7 Hz); 1.30 (t, 3H, J=7 Hz); 1.61 (d, 3H, J=7 Hz); 4.30 (q, 2H, J=7 Hz); 4.36 (q, 2H, J=7 Hz); 5.26 (s, 2H); 5.46 (q, 1H, J=7 Hz); 7.5–7.9 (m, 5H)	3380–2980; 1760–1730; 1700	228 (10300)
5a	CH_3	H	*b:* 89 *a:* 40	109° (7:3 C_6H_{14}/C_2H_5OAc)	$C_{10}H_{12}N_2O_4$ (224.2)	1.40 (t, 3H, J=7 Hz); 2.52 (s, 3H); 4.44 (q, 2H, J=7 Hz); 5.05 (s, 2H); 5.85 (s, 2H)	3420; 2980; 1765; 1715; 1690	237 (7700)
5b	CH_3	CH_3	*b:* 84 *a:* 43	90° (7:3 C_6H_{14}/C_2H_5OAc)	$C_{11}H_{14}N_2O_4$ (238.2)	1.40 (t, 3H, J=7 Hz); 1.75 (d, 3H, J=7 Hz); 2.50 (s, 3H); 4.41 (q, 2H, J=7 Hz); 4.75 and 4.97 (2H, 2d, J_{AB}=18.5 Hz); 6.25 (q, 1H, J=7 Hz)	3360; 2980; 1760; 1720; 1700	233 (7800)
5c	C_6H_5	H	*b:* 84 *a:* 40	104° (1:1 C_6H_{14}/C_2H_5OAc)	$C_{15}H_{14}N_2O_4$ (286.3)	1.26 (t, 3H, J=7 Hz); 4.22 (q, 2H, J=7 Hz); 4.98 (s, 2H); 5.72 (s, 2H); 7.3–7.5 (m, 3H); 7.6–7.7 (m, 2H)	3500; 2980; 1770; 1730; 1695	238 (10000); 212 (6900)
5d	C_6H_5	CH_3	*b:* 79 *a:* 27	107° (4:1 C_6H_{14}/C_2H_5OAc)	$C_{16}H_{16}N_2O_4$ (300.3)	1.27 (t, 3H, J=7 Hz); 1.82 (d, 3H, J=7 Hz); 4.37 (q, 2H, J=7 Hz); 4.89 and 5.13 (2H, 2d, J_{AB}=19 Hz); 6.34 (q, 1H, J=7 Hz); 7.5–7.7 (m, 3H); 7.8–8.0 (m, 2H)	3400; 2980; 1765; 1730; 1700	234 (9200); 212 (6800)

[a] Yields of purified products, yield of **5** based on **3**.

[b] All products gave satisfactory microanalyses (C ±0.24, H ±0.42, N ±0.43).

matographing 1.5 g portions of these materials [silica gel 30 g, column: 18 mm × 30 cm; eluent, ether], the product being obtained in the fraction 50 to 110 ml (Table).

1-Aminocarbonylmethylpyrazoles 4; General Procedure:
A mixture of the 1-ethoxycarbonylmethylpyrazole **3** (0.01 mol) and 28% aqueous ammonium hydroxide (10 ml, 0.29 mol) is heated under reflux for 2 h. Elimination of the excess of ammonium hydroxide under reduced pressure, affords either a solid **(4a–c)** or an oil **(4d)**, yield: quantitative; pratically pure material, as evidenced by ^{1}H-N.M.R., which is not purified further; m.p. (solvent): **4a**, 130 °C (ethanol); **4b**, 95 °C (ethanol/ethyl acetate 3:7); **4c**, 138 °C (ethanol); **4d**, viscous oil.

6-Oxo-6,7-dihydro-4*H*-pyrazolo[5,1-*c*][1,4]oxazines 5; General Procedure:
Compounds **3** (path *a*) or compounds **4** (path *b*) are heated on an oil bath at 180–200 °C. After the evolution of gas has ceased (10 to 15 min), the residue is cooled to room temperature. Compounds **5** are separated by vacuum sublimation at 140 °C/20 torr (Table).

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