Synthesis of Some 3 (or 5)-Substituted 5(or 3)-(2-Hydroxyalkyl)-pyrazoles from 2,3-Dihydro-4-pyrones

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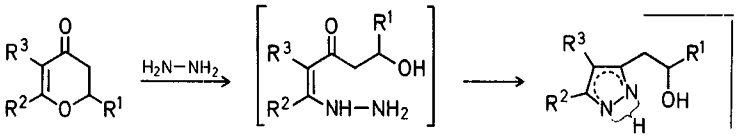
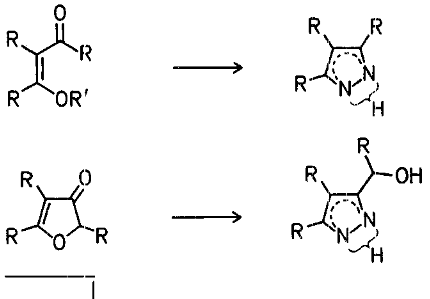
We have previously described the preparation of 2,3-dihydro-4-pyrones **1** and some reactions of them under basic conditions[1,2]. We have now reacted the dihydro-pyrones **1** with hydrazine hydrate and obtained the functionalised 3 (or 5)-(2-hydroxyalkyl)-pyrazoles **2**. Compounds **2** were not conveniently available and reported syntheses involved reactions of β-diketones[3,4] or acetylenic compounds[5-8] with hydrazine hydrate.



1 **2**

It is known that reactions of γ-pyrones with hydrazine hydrate lead to 3-pyrazoleacetaldehydes via ring opening and subsequent cyclisation[9,10]. A similar reaction occurs with the dihydropyrones **1** through initial nucleophilic attack of the hydrazino group at C-6. The initially formed open-chain intermediate subsequently cyclises to give the various pyrazoles **2**. Analogous reactions have been reported with hydrazine and the corresponding open chain[11] and five-membered ring[12] compounds as shown below.



The structures of compounds **2** are in accord with the ^{1}H-N.M.R., I.R., and U.V. spectra and microanalytical data. Reactions of pyrones **1** with other nitrogen nucleophiles are in progress.

Table. 3(or 5)-Substituted 5(or 3)-(2-Hydroxyalkyl)-pyrazoles **2**

Product No.	R^1	R^2	R^3	Yield [%]	m.p. or b.p./torr	Molecular formula[a]	I.R. ($CHCl_3$)[b] ν [cm^{-1}]	U.V. (C_2H_5OH)[c] λ [nm] (ε)	^{1}H-N.M.R. (DMSO-d_6)[d] δ [ppm]
2a	H	CH_3	H	80	124°	$C_6H_{10}N_2O$ (126.2)	3695, 3600, 3470, 1580	221 (2800)	2.16 (s, 3H); 2.68 (t, 2H, J=7 Hz); 3.63 (t, 2H, J=7 Hz); 4.0–5.45 (1H, exchangeable with CF_3COOH); 5.82 (s, 1H)[e]
2b	H	CH_3	$COOC_2H_5$	85	154°	$C_9H_{14}N_2O_3$ (198.2)	3680, 3600, 3450, 1705, 1575	227 (8600)	1.33 (t, 3H, J=7 Hz); 2.40 (s, 3H); 3.07 (t, 2H, J=7 Hz); 3.78 (t, 2H, J=7 Hz); 4.25 (q, 2H, J=7 Hz); 4.65 (br, 1H, exchangeable with CF_3COOH); 12.9 (broad, 1H)
2c	CH_3	CH_3	H	75	70°; 148°/0.7	$C_7H_{12}N_2O$ (140.2)	3675, 3600, 3470, 3260, 1580	221 (3000)	1.07 (d, 3H, J=6 Hz); 2.15 (s, 3H); 2.63 (d, 2H, J=6 Hz); 3.93 (sext, 1H, J=6 Hz); 4.25–5.75 (br, 1H, exchangeable with CF_3COOH); 5.83 (s, 1H)[e].
2d	CH_3	CH_3	$COOC_2H_5$	68	94°	$C_{10}H_{16}N_2O_3$ (212.2)	3675, 3600, 3455, 3200, 1710, 1580	227 (8500)	1.08 (d, 3H, J=6 Hz); 1.30 (t, 3H, J=7 Hz); 2.38 (s, 3H); 2.93 (d, 2H, J=6 Hz); 3.70–4.52 (m, 3H); 4.60 (br, 1H, exchangeable with CF_3COOH); 12.9 (broad, 1H).
2e	CH_3	C_6H_5	$COOC_2H_5$	75	82°	$C_{15}H_{18}N_2O_3$ (274.3)	3680, 3600, 3450, 3200, 1705, 1560	216 (12600) 242 (9300)	1.12 (d, 3H, J=6 Hz); 1.17 (t, 3H, J=7 Hz); 2.98 (d, 2H, J=6.5 Hz); 3.78–4.42 (m, 3H); 4.77 (br, 1H, exchangeable with CF_3COOH); 7.22–7.82 (m, 5H); 12.9 (br, 1H).

[a] Microanalyses were in satisfactory agreement with the calculated values (C ±0.29, H ±0.10, N ±0.24).
[b] Measured on a Beckman Acculab 2 spectrometer.
[c] Measured on a Beckman DB spectrometer.
[d] Measured on a Varian A-60 spectrometer.
[e] NH proton is not observed.

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3 (or 5)-Substituted 5(or 3)-(2-Hydroxyalkyl)-pyrazoles 2; General Procedure:

To a solution of the 2,3-dihydro-4-pyrone **1** (10 mmol) in ethanol (10 ml) at room temperature is added hydrazine hydrate (0.7 g, 14 mmol) in one portion. The mixture is allowed to stand at room temperature for 3 h and is then evaporated under reduced pressure to leave a residue. Compounds **2a** and **b** are recrystallised from ethyl acetate or water, respectively; compound **2c** is distilled under reduced pressure. In the case of compound **2d**, the residue is dissolved in water (5 ml), the aqueous solution is extracted with dichloromethane and the extracts dried and evaporated. The residue is recrystallised from hexane/ethyl acetate (4:1). In the case of **2e**, the viscous residue crystallises after standing at room temperature for several days. The solid is purified by chromatography through a column (25 cm × 17 mm) of silica gel (35 g) using hexane/ethyl acetate (3:7) as eluent, the product being obtained in the fraction 100 to 250 ml; yield: 2.05 g.

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[1] S. Gelin, R. Gelin, *Bull. Soc. Chim. Fr.* **1968**, 288.

[2] S. Gelin, R. Gelin, *Bull. Soc. Chim. Fr.* **1969**, 1383.

[3] R. J. Light, T. M. Harris, C. R. Hauser, *J. Org. Chem.* **26**, 1344 (1961).

[4] R. J. Light, C. R. Hauser, *J. Org. Chem.* **26**, 1716 (1961).

[5] F. Bardone-Gaudemar, *Ann. Chim.* **3**, 52 (1958).

[6] W. W. Paudler, A. G. Zeiger, *J. Org. Chem.* **34**, 999 (1969).

[7] E. G. Darbinyan, Yu. B. Mitardzhyan, S. G. Matsoyan, *Arm. Khim. Zh.* **23**, 640 (1970); *C. A.* **74**, 76362 (1971).
E. G. Darbinyan, S. G. Mitardzhyan, G. A. Vliazyan, S. G. Matsoyan, *Dokl. Vses. Konf. Khim. Atsetilena 4th* **1**, 305 (1972); *C. A.* **79**, 92140 (1973).

[8] E. P. Levanova, A. N. Volkov, A. N. Nikol'skaya, K. A. Volkova, E. O. Tsetlina, *Zh. Org. Khim.* **10**, 1835 (1974); *C. A.* **81**, 169474 (1974).

[9] R. G. Jones, M. J. Mann, *J. Am. Chem. Soc.* **75**, 4048 (1953).

[10] C. Ainsworth, R. G. Jones, *J. Am. Chem. Soc.* **76**, 3172 (1954).

[11] A. N. Kost, I. I. Grandberg, *Adv. Heterocyclic Chem.* **6**, 358 (1966).

[12] S. Gelin, M. Chabannet, *Synthesis* **1978**, 448.