Synthesis of 3-Alkenyl-4-oxo-6,7-dihydro-1*H*-pyrano[4,3-*c*]pyrazole Derivatives

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A series of 1-substituted 3-alkenyl-4-oxo-6,7-dihydro-1*H*-pyrano[4,3-*c*]pyrazoles was prepared by reaction of arylhydrazines or benzylhydrazine with 4,5-dioxo-2,3,7,8-tetrahydro-4*H*,5*H*-pyrano[4,3-*b*]pyran derivatives.

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The accompanying paper describes the synthesis of 4,5-dioxo-2,3,7,8-tetrahydro-4*H*,5*H*-pyrano[4,3-*b*]pyrans (**1**) [1]. We now report on their conversion into 3-alkenyl-4-oxo-6,7-dihydropyrano[4,3-*c*]pyrazole derivatives **3**.

Treatment of compounds **1** with arylhydrazines (or their hydrochlorides) or with benzylhydrazine, in refluxing acetic acid, led to the pyranopyrazole derivatives **3**, in good yields. The reaction proceeds *via* the initial formation of the phenylhydrazones **2**. Heating **2** in acetic acid causes opening of the dihydro-4-pyrone ring and recyclization to give the substances **3** (Scheme 1). In fact, the phenylhydrazone **2h** was isolated under mild conditions. Thus, refluxing **2h** in acetic acid afforded the corresponding product **3h**.

The structure **3** was based upon mechanistic considerations, spectroscopic data cited in the experimental and the following chemical reactions. Chemical evidence for the structure **3a** was provided by preparing compound **5** according to the known route from 3-butyroyl-6-methyl-2,4-dioxo-3,4,5,6-tetrahydro-2*H*-pyran (**4**) and phenylhydraz-

Table 1

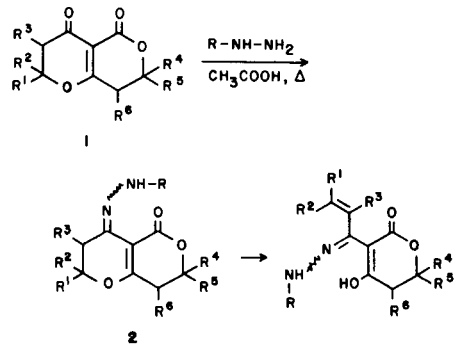
Physical Data for Compounds **3** and **5**

Compound No.	Yield % [a]	Mp °C	Molecular Formula	Analyses % (Calcd./Found) C	H	N	IR (Chloroform) νC=O cm^{-1}	UV (Ethanol) λ max nm (ϵ)
3a	73	131-132	$C_{16}H_{16}N_2O_2$	71.62	6.01	10.44	1730	259 (17500)
				71.31	5.97	10.21		
3b	67	124-125	$C_{16}H_{16}N_2O_2$	71.62	6.01	10.44	1730	248 (15500)
				71.75	5.89	10.26		
3c	74	162-163	$C_{17}H_{18}N_2O_2$	72.32	6.43	9.92	1730	260 (20300)
				71.95	6.38	9.94		
3d	56	146-147	$C_{17}H_{18}N_2O_2$	72.32	6.43	9.92	1730	250 (16400)
				72.20	6.39	9.84		
3e	45	100-101	$C_{16}H_{16}N_2O_2$	71.62	6.01	10.44	1730	256 (14800)
				71.70	6.10	10.30		
3f	40	77-78	$C_{16}H_{16}N_2O_2$	71.62	6.01	10.44	1730	252 (14500)
				71.64	6.06	10.67		
3g	60	153-154	$C_{17}H_{18}N_2O_2$	72.32	6.43	9.92	1730	259 (18200)
				72.19	6.47	9.63		
3h	70	139-140	$C_{18}H_{20}N_2O_2$	72.95	6.80	9.45	1730	259 (19400)
				72.83	6.80	9.35		
3i	50	114-115	$C_{17}H_{18}N_2O_2$	72.32	6.34	9.92	1730	248 (20800)
				72.16	6.37	9.86		
3j	65	194-195	$C_{16}H_{15}ClN_2O_2$	63.47	4.99	9.25 [b]	1730	256 (20300)
				63.54	4.98	9.06		
3k	67	240-241	$C_{16}H_5N_3O_4$	61.33	4.83	13.41	1730	250 (14200)
				60.96	4.83	13.46		
3l	68	105-106	$C_{17}H_{18}N_2O_2$	72.32	6.43	9.92	1730	250 (11400)
				72.05	6.36	10.20		
3m	70	130-131	$C_{19}H_{22}N_2O_2$	73.52	7.14	9.03	1730	248 (13300)
				73.60	7.24	9.03		
5	70 [c]	110-111	$C_{16}H_{18}N_2O_2$	71.09	6.71	10.36	1730	250 (14200)
				71.25	6.64	10.47		

[a] Isolated yields after recrystallization from ethanol, except **3k**, recrystallized from acetic acid. [b] Cl%, Calcd.: 11.70. Found: 11.62. [c] Yield from **3a**.

ine [2]. The physical properties of **5** obtained as shown in the Scheme 2 were identical with those furnished by catalytic hydrogenation of **3a**.

Scheme 1



	R1	R2	R3	R4	R5	R6	R
a	CH_3	H	H	CH_3	H	H	C_6H_5
b	H	H	CH_3	CH_3	H	H	C_6H_5
c	CH_3	CH_3	H	CH_3	H	H	C_6H_5
d	H	CH_3	CH_3	CH_3	H	H	C_6H_5
e	CH_3	H	H	H	H	CH_3	C_6H_5
f	H	H	CH_3	H	H	CH_3	C_6H_5
g	CH_3	CH_3	H	H	H	CH_3	C_6H_5
h	CH_3	CH_3	H	CH_3	CH_3	H	C_6H_5
i	CH_3	H	H	CH_3	H	H	p-CH_3-C_6H_4
j	CH_3	H	H	CH_3	H	H	p-Cl-C_6H_4
k	CH_3	H	H	CH_3	H	H	p-NO_2-C_6H_4
l	CH_3	H	H	CH_3	H	H	-CH_2-C_6H_5
m	CH_3	CH_3	H	CH_3	CH_3	H	-CH_2-C_6H_5

Scheme 2

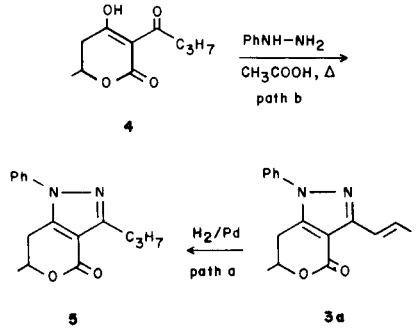


Table 2

Proton Magnetic Resonance Parameters

Compound No.	Chemical shift (deuteriochloroform)
3a	1.52 (d, 3H, J = 7 Hz), 1.92 (d, 3H, J = 6 Hz), 3.00 (d, 2H, J = 8 Hz), 4.63 (sex, 1H, J = 7 Hz), 6.75 (d, 1H, J = 16 Hz) and 7.08 (dq, 1H, J = 16 Hz, 6 Hz) [a], 7.52 (s, 5H)
3b	1.57 (d, 3H, J = 7 Hz), 2.31 (s, 3H), 3.06 (d, 2H, J = 8 Hz), 4.72 (m, 1H), 5.61 (m, 1H), 6.48 (s, 1H), 7.67 (s, 5H)
3c	1.53 (d, 3H, J = 7 Hz), 2.00 (s, 3H), 2.21 (s, 3H), 3.02 (d, 2H, J = 8 Hz), 4.65 (m, 1H), 6.75 (m, 1H), 7.52 (s, 5H)
3d	1.56 (d, 3H, J = 7 Hz), 1.90 (d, 3H, J = 7 Hz), 2.17 (s, 3H), 3.03 (d, 2H, J = 8 Hz), 4.70 (m, 1H), 6.80 (m, 1H), 7.63 (s, 5H)
3e	1.27 (d, 3H, J = 7 Hz), 1.97 (d, 3H, J = 5 Hz), 3.31 (m, 1H), 4.30 (dd, 1H, J = 11 Hz, 3 Hz) and 4.60 (dd, 1H, J = 11 Hz, 4 Hz) [b], 6.86 (d, 1H, J = 16 Hz) and 7.14 (dq, 1H, J = 16 Hz, 5 Hz) [a], 7.62 (s, 5H)
3f	1.28 (d, 3H, J = 7 Hz), 2.27 (s, 3H), 3.28 (m, 1H), 4.28 (dd, 1H, J = 12 Hz, 3 Hz) and 4.58 (dd, 1H, J = 12 Hz, 4 Hz) [b], 5.55 (m, 1H), 6.38 (s, 1H), 7.60 (s, 5H)
3g	1.27 (d, 3H, J = 7 Hz), 2.00 (s, 3H), 2.20 (s, 3H), 3.31 (m, 1H), 4.25 (dd, 1H, J = 11 Hz, 3.5 Hz) and 4.55 (dd, 1H, J = 11 Hz, 3.5 Hz) [b], 6.75 (m, 1H), 7.50 (s, 5H)
3h	1.50 (s, 6H), 2.00 (s, 3H), 2.23 (s, 3H), 3.10 (s, 2H), 6.75 (m, 1H), 7.50 (s, 5H)
3i	1.56 (d, 3H, J = 7 Hz), 1.96 (d, 3H, J = 6 Hz), 2.46 (s, 3H), 3.00 (d, 2H, J = 8 Hz), 4.71 (m, 1H), 6.87 (d, 1H, J = 16 Hz) and 7.20 (dq, 1H, J = 16 Hz, 6 Hz) [a,c], 7.47 (s, 4H)
3j	1.57 (d, 3H, J = 7 Hz), 1.97 (d, 3H, J = 6 Hz), 3.03 (d, 2H, J = 8 Hz), 4.75 (m, 1H), 6.87 (d, 1H, J = 16 Hz) and 7.17 (dq, 1H, J = 16 Hz, 6 Hz) [a], 7.63 (s, 5H)
3k	1.62 (d, 3H, J = 7 Hz), 2.00 (d, 3H, J = 6 Hz), 3.16 (d, 2H, J = 8 Hz), 4.77 (m, 1H), 6.87 (d, 1H, J = 16 Hz) and 7.20 (dq, 1H, J = 16 Hz, 6 Hz) [a], 7.90 and 8.55 (2d, 4H, J = 9 Hz)
3l	1.45 (d, 3H, J = 7 Hz), 1.91 (d, 3H, J = 6 Hz), 2.55 (dd, 1H, J = 16 Hz, 10 Hz) and 2.87 (dd, 1H, J = 16 Hz, 5 Hz) [b], 4.63 (m, 1H), 5.32 (s, 2H), 6.77 (d, 1H, J = 16 Hz) and 7.07 (dq, 1H, J = 16 Hz, 6 Hz) [a,c], 7.17-7.60 (m, 5H)
3m	1.43 (s, 6H), 1.98 (s, 3H), 2.17 (s, 3H), 2.79 (s, 2H), 5.33 (s, 2H), 6.73 (m, 1H), 7.12-7.47 (m, 5H)
5	1.02 (t, 3H, J = 7 Hz), 1.56 (d, 3H, J = 7 Hz), 1.85 (sex, 2H, J = 7 Hz), 2.98 (t, 2H, J = 7 Hz), 3.05 (d, 2H, J = 8 Hz), 4.75 (m, 1H), 7.62 (s, 5H)

[a] AB part of ABX_3 system, in first order treatment. [b] AB part of ABX system, in first order treatment. [c] Partially masked by the aromatic protons.

EXPERIMENTAL

Melting points were determined on a Kofler hot place. Infrared and ultraviolet spectra were obtained with a Beckman Model Acculab 2 and DB spectrometers. The ^{1}H-nmr spectra were taken on a Brucker WP 80 spectrometer with respect to TMS. Elemental analyses were performed by Microanalytical laboratory, Centre National de la recherche scientifique, 69390 Vernaison, France.

1-Aryl- or -Benzyl-3-alkenyl-4-oxo-6,7-dihydro-1*H*-pyrano[4,3-*c*]pyrazoles (**3**).

General Procedure.

A mixture of **1** [1] (0.01 mole), acetic acid (50 ml) and the appropriate hydrazine or its chlorhydrate (0.01 mole), was refluxed for 1 hour. The reaction mixture was evaporated *in vacuo* and the residue was dissolved in methylene chloride (50 ml). The organic phase was washed with 10% hydrochloric acid, then with 5% sodium hydrogen carbonate solution, then water. After drying and evaporation of the solvent, the residue was recrystallized.

6-Methyl-4-oxo-1-phenyl-3-propyl-6,7-dihydropyrano[4,3-*c*]pyrazole (**5**).

Method a.

A mixture of 6-methyl-4-oxo-1-phenyl-3-propenyl-6,7-dihydro-1*H*-pyrano[4,3-*c*]pyrazole (**3a**) (2.68 g, 0.01 mole) in ethyl acetate (60 ml) and 1 g of a 5% Pd-C catalyst was hydrogenated at room temperature using low pressure (*ca.* 1 atmosphere). After uptake of the calculated amount of

hydrogen (30 minutes), the catalyst was filtered off and the solvent was evaporated under reduced pressure. The residue was recrystallized from ethanol to give 1.89 g (70%) of the title compound.

Method b.

This compound was obtained in a 41% yield according to the literature procedure [2] from 3-butyroyl-6-methyl-2,4-dioxo-3,4,5,6-tetrahydro-2*H*-pyrane (**4**) [3] and phenylhydrazine, in refluxing acetic acid.

REFERENCES AND NOTES

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[3] L. Cattel, G. Nobili, O. Caputo and G. Biglino, *Farmaco, Ed. Sci.*, **26**, 247 (1971).