The Synthesis of 3*H*-Pyrazol-3-one Derivatives Containing a 9*H*-Xanthene Ring

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2,4-Dihydro-5-methyl-2-phenyl-4-(9*H*-xanthen-9-yl)-3*H*-pyrazol-3-one (**3**) was prepared by the condensation of phenylhydrazine and ethyl α-acetyl-9*H*-xanthene-9-acetate (**2**), or 9*H*-xanthen-9-ol (**1**) and 2,4-dihydro-5-methyl-2-phenyl-3*H*-pyrazol-3-one (**4**). 5-Amino-2,4-dihydro-2-phenyl-4-(9*H*-xanthen-9-yl)-3*H*-pyrazol-3-one (**6**) was obtained by the condensation of **1** and 5-amino-2,4-dihydro-2-phenyl-3*H*-pyrazol-3-one (**5**).

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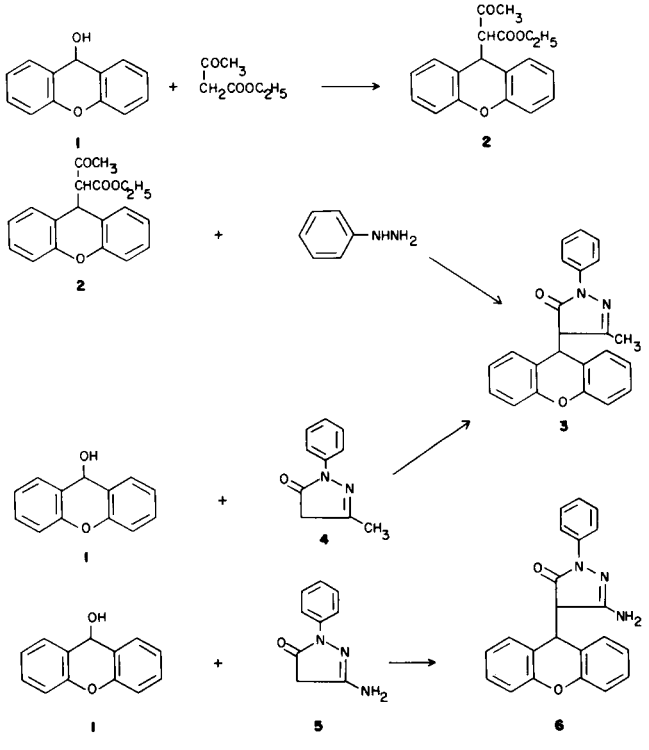
3*H*-Pyrazol-3-one derivatives containing a 9*H*-xanthene ring were synthesized for the purpose of studying the activity of the hydrogen atom contained in the 3*H*-pyrazol-3-one ring and the pharmacological activity of these 3*H*-pyrazol-3-one derivatives.

9*H*-Xanthen-9-ol (**1**) condenses with compounds containing an active hydrogen atom such as ethyl acetoacetate and ethyl cyanoacetate. Thus ethyl α-acetyl-9*H*-xanthene-9-acetate(**2**) (1) was obtained by heating a mixture of 9*H*-xanthen-9-ol (**1**) and ethyl acetoacetate in acetic acid. Compound **2** was then condensed with phenylhydrazine to give 2,4-dihydro-5-methyl-2-phenyl-4-(9*H*-xanthen-9-yl)-3*H*-pyrazol-3-one (**3**). The product obtained by condensing 9*H*-xanthen-9-ol (**1**) with 2,4-dihydro-5-methyl-2-phenyl-3*H*-pyrazol-3-one (**4**) (2) in acetic acid was identical in its physical properties with **3**.

Similarly, 5-amino-2,4-dihydro-2-phenyl-4-(9*H*-xanthen-9-yl)-3*H*-pyrazol-3-one (**6**) was prepared by the condensation of 9*H*-xanthen-9-ol (**1**) and 5-amino-2,4-dihydro-2-phenyl-3*H*-pyrazol-3-one (**5**) (3).



EXPERIMENTAL

Melting points were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Infrared absorption spectra were recorded in potassium bromide discs with a Hitachi model 215 spectrometer. Mass spectra were measured with a Hitachi RMU-7M double focusing spectrometer.

2,4-Dihydro-5-methyl-2-phenyl-4-(9*H*-xanthen-9-yl)-3*H*-pyrazol-3-one (**3**).

a) A mixture of ethyl α-acetyl-9*H*-xanthene-9-acetate (**2**) (3.10 g., 0.01 mole) and phenylhydrazine (1.08 g., 0.01 mole) was heated in an oil bath (120-130°) for 2 hours. Ether (20 ml.) was added to the cooled mixture, and the mixture was stirred. The separated solid (1.13 g., 32%) was collected, washed with ether, and recrystallized from aqueous ethanol as colorless pillars, m.p. 211-213° dec.; ms: m/e 354 (M^+); ir (potassium bromide): 3420, 3060, 1630, 1590, 1570, 1495, 1475, 1450 cm^{-1}.

Anal. Calcd. for $C_{23}H_{18}N_2O_2$: C, 77.95; H, 5.12; N, 7.90. Found: C, 78.23; H, 5.09; N, 7.87.

b) 9*H*-Xanthen-9-ol (**1**) (0.99 g., 0.005 mole) was added to a solution of 2,4-dihydro-5-methyl-2-phenyl-3*H*-pyrazol-3-one (**4**) (0.87 g., 0.005 mole) in glacial acetic acid (40 ml.). The mixture was heated in a boiling water bath for 3 hours, cooled, and poured into water (400 ml.). The mixture was warmed in a water bath. The separated solid (1.61 g., 91%) was collected and washed with water. Recrystallization from aqueous ethanol gave **3** as colorless pillars, m.p. 211.5-213° dec., alone and then admixed with a sample obtained by method a). The ir spectra were identical with that of a sample obtained by method a).

5-Amino-2,4-dihydro-2-phenyl-4-(9*H*-xanthen-9-yl)-3*H*-pyrazol-3-one (**6**).

9*H*-Xanthen-9-ol (**1**) (0.99 g., 0.005 mole) was added to a solution of 5-amino-2,4-dihydro-2-phenyl-3*H*-pyrazol-3-one (**5**) (0.88 g., 0.005 mole) in glacial acetic acid (40 ml.). The mixture was heated in a boiling water bath for 3 hours, cooled, and poured into water (400 ml.). The mixture was warmed in a water bath. The separated solid (1.50 g., 84%) was collected, washed with water, and recrystallized from ethanol as colorless needles, m.p. 206-207° dec.; ms: m/e 355(M^+); ir (potassium bromide): 3455, 3160, 1680, 1635, 1585, 1490, 1480, 1455 cm^{-1}.

Anal. Calcd. for $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found: C, 74.63; H, 4.85; N, 11.81.

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REFERENCES AND NOTES

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