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Reaction of 2-hydrazino-4-methyl-6-substituted quinolines with ethylacetoacetate: A structural reinvestigation

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Abstract. 1-(6′-substituted-4′-methyl-2′-quinolyl)-3-methyl-pyrazol-5-ols are obtained by the reaction of 2-hydrazino-4-methyl-6-substituted quinolines with ethylacetoacetate rather than the reported 6-substituted-4-methylquinolino(2,3-c)-3-methyl-4,5-dihydro-1H-1,2-diazepin-5-ones. Pyrazol-5-ol structure is assigned on the basis of IR, ^{1}H NMR, ^{13}C NMR (SFORD spectrum) and high resolution mass spectroscopy.

Keywords. Quinolylhydrazine; ethylacetoacetate; ^{13}C NMR spectra; mass spectra.

1. Introduction

In continuation of our studies on the electron-impact induced fragmentation of pyrazoles (Singh *et al* 1982, 1983, 1984), we needed 1-(6′-substituted-4′-methyl-2′-quinolyl)-3-methylpyrazol-5-ols (3). The most convenient route to synthesize (3) is the treatment of ethylacetoacetate with the corresponding hydrazines (Wiley and Wiley 1964; Kamal *et al* 1985), but a survey of literature (Surana *et al* 1972) revealed that the product of the reaction of 2-hydrazino-4-methylquinoline (1a) with ethylacetoacetate is 4-methylquinolino-(2,3-c)-3-methyl-4,5-dihydro-1H-1,2-diazepin-5-one (2) rather than 1-(4′-methyl-2′-quinolyl)-3-methylpyrazol-5-ol (3a). Considering the reaction conditions and the mechanistic grounds which require the formation of hydrazone by the reaction of (1) and ethylacetoacetate, followed by cyclization through an intramolecular Friedel-Crafts reaction for the formation of 2, we thought it worthwhile to reinvestigate the reaction.

2. Results and discussion

On performing the reaction under literature conditions (Surana *et al* 1972) using a standard procedure (Wiley and Wiley 1964; Kamal *et al* 1985) in ethanol-HCl, the product obtained was the same as reported (Surana *et al* 1972) (mixed m.p., superimposable IR and co-TLC: ethylacetate/$CHCl_3$) (scheme 1). The product obtained had a m.p. 168° while that reported for 2a was 150°. The evidence presented in support of structure (2a) included absorption at 1700 and 1600 cm^{-1} in the IR spectrum and 7·2–8·05 (4H, aromatic protons), 2·6 and 2·50 (two singlets,

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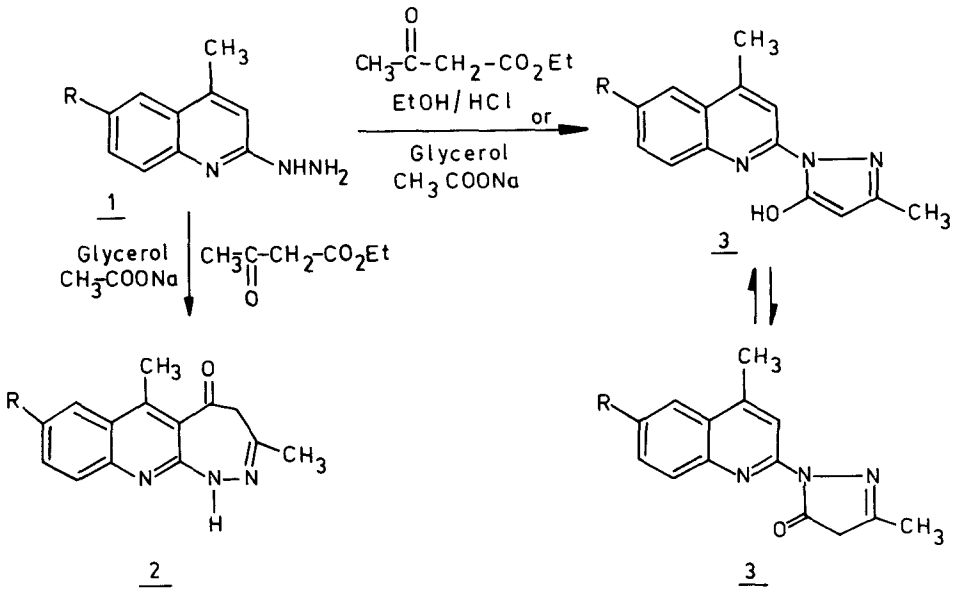


Scheme 1. 1, 2, 3. a. R = H, b. R = OCH_3, c. R = Cl, d. R = F

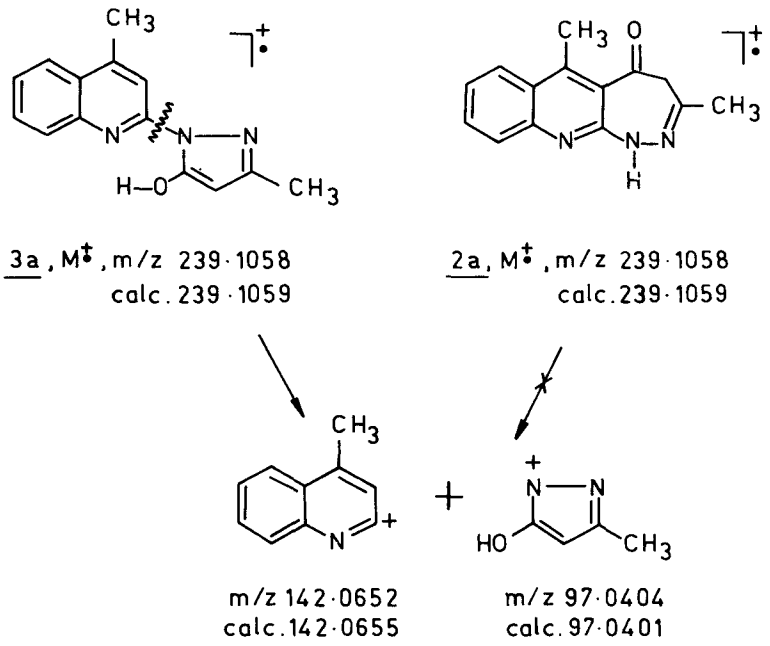
2-CH_3), 3·10 (singlet methylene protons), a proton at 8·85 (NH) and the absence of quinolin-3H appearing at 6·4 in hydrazine (1a) in ^{1}H NMR spectrum. However, no N-H stretching in IR and deuterium exchange for the NH proton in ^{1}H NMR spectra were observed for 2 by the earlier worker (Surana *et al* 1972).

The spectra, IR and ^{1}H NMR, recorded in our case, however, showed some vital differences. In the IR spectrum, a broad band around 3100–2600 cm^{-1}, due to O–H bonded vibrations, was observed. There was no band at 1700 cm^{-1}, but a sharp band at 1640 cm^{-1} due to ring carbonyl stretching was observed. ^{1}H NMR of 3a in $CDCl_3$ showed signals at 2·3 (s, 3H, pyrazol-3-CH_3), 2·7 (s, 3H, quinolin-4-CH_3), 5·4 (s, 1H, pyrazol-4-H), 7·2–7·9 (m, 5H, aromatic protons), 14·8 (s, 1H, O–H) exchanged with H_2O. It may be argued that the integration of the aromatic region might be in error but it is difficult to explain the position of the other signals. The absence of quinolin-3H presented to support the structure (2) was, in fact, the deshielding of the aromatic proton due to the formation of the pyrazol-5-ol nucleus, as it is observed that protons ortho to the hydrazine or the amino group are always shielded (Silverstein *et al* 1981). As no solvent was mentioned for ^{1}H NMR spectra, the spectrum was taken in a protic solvent to observe the keto form. The spectrum of 3a was scanned in TFA, where the compound exists in keto and enol forms (60 : 40), and exhibits signals at 2·3 and 2·5 (two singlets totally integrating for 3H of pyrazol-3-CH_3 of the keto-enol form respectively), 2·7 (s, 3H, quinolin-4-CH_3), 3·95 and 5·45 (two singlets integrating for 2H of methylene of keto and 1H of 4-H of enolic form), 7·5–8·25 (m, 5H, aromatic protons).

The diazepinone structure (2) was ruled out by comparing the carbon resonances of the pyrazol-5-ol nucleus of 3b in ^{13}C NMR spectra. C-3, C-4 and C-5 resonated at 151·115, 88·266 and 157·572, respectively, which are in complete agreement with

literature values (Feeny *et al* 1970; Kodali 1980). Further, by counting the number of tertiary and quaternary carbons in single frequency off-resonance decoupled spectrum of 3b, which appeared as doublet and singlet respectively, the pyrazol-5-ol structure for 3b was confirmed. The SFORD spectrum of 3b showed five tertiary carbons and seven quaternary carbons. Had it been a diazepin-5-one structure (2b), we should have observed one secondary, three tertiary and eight quaternary carbons.

Finally, the pyrazol-5-ol structure was confirmed by a study of electron-impact induced fragmentation of 2a. Linked scan data on 2a showed that the parent ion at *m/z* 239·1058 (100%; calculated for $C_{14}H_{13}N_3O$ 239·1059), which undergoes homolytic fission of two moieties to generate ions at *m/z* 142·0652 (8%; calculated for $C_{10}H_8N$ 142·0655) and *m/z* 97·0404 (3%; calculated for $C_4H_5N_2O$ 97·0401) (scheme 2). Had it been a diazepin-5-one structure, such type of cleavage would have been absent.



Scheme 2.

3. Experimental

Melting points were taken in open capillary tubes in a liquid bath and are uncorrected. Infrared spectra were recorded on a Beckman IR-20 spectrophotometer. PMR spectra were taken on a R-32 Perkin-Elmer (90 MHz) instrument, ^{13}C NMR spectra were obtained on JEOL FX-60 FT NMR spectrometer operating at 15·03 MHz with 8K data points. Samples taken as 10% v/v solutions in $CDCl_3$ with 2% TMS as reference. The deuterium of the solvent provided the lock signal and the probe temperature was kept at 298 ± 1 K. Mass spectra were scanned on an Hitachi

Table 1. Physical data of 1-(6′-substituted-4′-methyl-2′-quinolyl)-3-methylpyrazol-5-ols (3)*.

Compound	R	m.p. °C	Yield %	Molecular formula	Found (Required %) C	H	N
3a	H	168	53	$C_{14}H_{13}N_3O$	70·29 (70·24)	5·40 (5·43)	17·60 (17·57)
3b	OCH_3	184	54	$C_{15}H_{15}N_3O_2$	66·88 (66·91)	5·54 (5·57)	15·65 (15·61)
3c	Cl	212	60	$C_{14}H_{12}N_3ClO$	61·58 (61·53)	4·36 (4·39)	15·43 (15·38)
3d	F	196	56	$C_{14}H_{12}N_3FO$	65·33 (65·36)	4·69 (4·66)	16·29 (16·34)

All compounds (3) were recrystallized from ethanol

RMU-60 mass spectrometer. High resolution mass spectral data and *B/E* linked scan measurements were obtained through JEOL JMS-D-X 300 mass spectrometer linked to a JEOL, JMA 3100 data system at 70 eV, ionizing current 300 μA accelerating voltage 3·0 kV, and ion source temperature 150°C.

3·1 *2-Hydrazino-4-methyl-6-substituted quinolines*

2-Hydrazino-4-methyl-6-substituted quinolines (1) were prepared following the literature procedure (Potts *et al* 1972; Mehrotra *et al* 1980; Vaid 1984).

3·2 *1-(6′-Methoxy-4′-methyl-2′-quinolyl)-3-methylpyrazol-5-ol*

2-Hydrazino-4-methyl-6-methoxyquinoline (0·203 g, 0·001 mol) and ethyl acetoacetate (0·130 g, 0·001 mol) were taken in ethanol (60 ml) containing two drops of concentrated HCl and the mixture was heated under reflux for 4–5 hr. Half of the solvent was removed and the reaction mixture kept at room temperature overnight. The product 1-(6′-methoxy-4′-methyl-2′-quinolyl)-3-methylpyrazol-5-d (2a) obtained after filtration was washed with ethanol and recrystallized from ethanol (54%), m.p. 184°; IR: 3100–2800 (OH-bonding vibration), 1640 cm^{-1} (ring carbonyl stretching), ^1H NMR ($CDCl_3$) : 2·3 (s, 3H, pyrazol-3-CH_3), 2·7 (s, 3H, quinolin-4-CH_3), 4·0 (s, 3H, OCH_3), 5·45 (s, 1H, pyrazol-4-H), 7·1–7·9 (m, 4H, aromatic protons), 14·8 (b, 1H, OH exchanged with D_2O on shaking), M^+ , *m/z* 269·1155. $C_{15}H_{13}N_3O_2$ (calculated 269·1164).

Other compounds (3) thus prepared are listed in table 1.

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