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Revision of the Structure of the Compound Obtained by the Reaction of 2-Hydrazino-4-methylquinoline and Acetylacetone

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Condensation of 2-hydrazino-4-methylquinoline (**1**) and acetylacetone gives a compound **A**, which has the structure of 3,5-dimethyl-1-(4-methylquinolino)-pyrazole (**2**) and not of 4-methylquinolino-(2,3—*c*)-3,5-dimethyl-1H-1,2-diazepine (**3**) assigned earlier. The structure **2** was confirmed on the basis of ^{1}H-NMR, ^{13}C-NMR, IR spectral data and its unambiguous synthesis.

(Keywords: Pyrazole; Benzodiazepine; Quinoline)

Revision der Struktur einer Verbindung aus der Reaktion von 2-Hydrazino-4-methylchinolin und Acetylaceton

Die Kondensation von 2-Hydrazino-4-methylchinolin (**1**) mit Acetylaceton ergibt eine Verbindung mit der Struktur eines 3,5-Dimethyl-1-(4-methylchinolin)pyrazols (**2**) und nicht eines 4-Methylchinolino-(2,3—*c*)-3,5-dimethyl-1H-1,2-diazepins (**3**) gemäß einer früheren Zuordnung. Die Struktur von **2** wurde auf Grund von ^{1}H-NMR, ^{13}C-NMR, IR und einer eindeutigen Synthese bewiesen.

Introduction

Benzodiazepines are well known for their various physiological activities. Some benzodiazepines[1] are being used as hypnotics and sedatives because of apparent safety and effectiveness as compared to other CNS active agents. Some benzodiazepines are also potent anti-convultants[2,3]. In a program for the syntheses of some benzodiazepine derivatives, it was of interest to prepare the known diazepines by using the method described in literature[4].

Results and Discussion

Condensation of 2-hydrazino-4-methylquinoline (**1**) and acetylacetone acetone in glycerol in the presence of fused sodium acetate gave a product **A** (m.p. 107°, as reported earlier[4]). However, the IR and ^{1}H-NMR spectra of compound **A** were more in accordance with a pyrazole structure **2** than with a diazepine structure **3**, reported earlier[4].

The IR spectrum showed no —NH— stretching. The ^{1}H-NMR spectrum indicated the presence of three methyl groups at δ2.33, 2.70 and 2.80 ppm respectively. Five aromatic protons resonated at 7.35–8.10. The presence of an olefinic proton at 6.00 ppm was characterised as —CH= of the pyrazole ring. No signal was observed between 6.0 to 10.0 ppm indicating the absence of —NH—, thus ruling out the possibility of a diazepine ring.

Further confirmation of the structure **2** was based on ^{13}C-NMR spectral studies of the compound **A**. Spin decoupled spectra showed the presence of 15 signals at 13.60, 14.90, 18.79, 109.39, 115.29, 123.65, 125.40, 126.53, 128.84, 129.46, 142.42, 146.49, 146.95, 150.14, and 152.24 ppm indicating altogether fifteen carbon atoms.

Off resonance spectra showed three quartets for three primary carbon atoms at 13.60, 14.90, and 18.79 ppm. Six doublets were obtained for six tertiary carbon atoms at 108.97 and 110.15, 114.75 and 116.08, 123.23 and 124.48, 125.08 and 126.30 and 130.04, 129.01, and 130.34 ppm respectively. Six singlets at 126.53, 142.42, 146.49, 146.95, 150.14 and 152.24 ppm were assigned to six quaternary carbon atoms.

The presence of six tertiary and six quaternary carbon atoms establishes a pyrazole structure **2** for compound **A**. Had it been a diazepine structure (**3**), then the number of tertiary and quaternary carbon atoms should be five and seven, respectively.

Further confirmation was gained by the synthesis of **2** by two different methods:

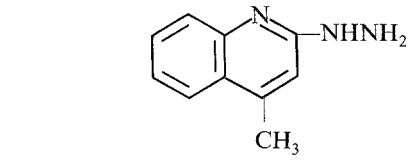
(1): 2-hydrazino-4-methylquinoline (**1**) was condensed with acetylacetone in alcohol in the presence of a few drops of acetic acid which gave a product identical with **A** in all respects (m.p., m.m.p., and IR).

(2): An unambiguous synthesis was performed by condensation of 3,5-dimethylpyrazole (**4**)[5] (obtained by the reaction of acetyl acetone with hydrazine hydrate) with 2-chloro-4-methylquinoline (**5**)[6] in the presence of pyridine. The compound obtained was also identical with compound **A** in all respects.

In summary, the diazepine structure **3** for the compound **A** has to be substituted by that of a 3,5-dimethyl-1-(4-methylquinolino)-pyrazole (**2**).

Experimental

Melting points are uncorrected. ^{1}H-NMR spectra ($CDCl_3$) were recorded on Perkin Elmer R-32 (90 MHz) spectrometer. ^{13}C-NMR spectra were recorded on FT NMR Jeol FX 200 spectrometer.



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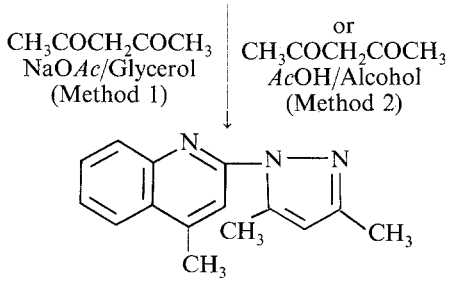

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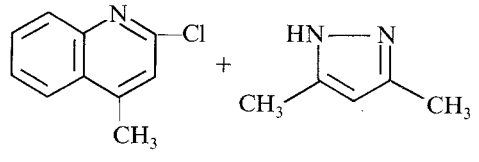

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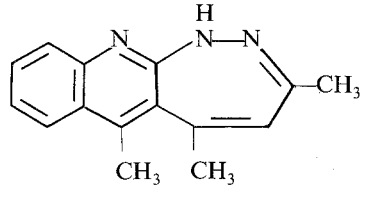

3

3,5-Dimethyl-1-(4-methylquinolino)-pyrazole (**2**)

Method 1

2-Hydrazino-4-methylquinoline (**1**) (1 g) and anhydrous sodium acetate (1 g) were stirred in glycerol (10 ml) for 10 min at 25–30°. Acetyl acetone (0.6 ml) was added dropwise over a period of 30 min and the reaction mixture was heated to 180–190° for 45 min; then the reaction mixture was poured over crushed ice. The crude product **2** was crystallised from ethyl alcohol; yield 1.1 g (73%); pale yellow needles; m.p. 106–107° (Lit.[4] m.p. 107°).

$C_{15}H_{15}N_3$ (237). Calc: C 75.9 H 6.3 N 17.7
Found: C 75.7 H 6.4 N 17.8

^{1}H-NMR and ^{13}C-NMR: see Results and Discussion.

Method 2

2-Hydrazino-4-methylquinoline (**1**, 1 g) and acetyl acetone (0.6 ml) in ethyl alcohol (100 ml) with a few drops of acetic acid were refluxed for 6 h. The reaction mixture was concentrated to obtain compound **2**; yield 1.2 g (80%); m.p. 106–107°.

Method 3

2-Chloro-4-methylquinoline (**5**, 1 g) and 3,5-dimethylpyrazole (**4**, 0.55 g) in absolute ethyl alcohol (60 ml) with a few drops of pyridine were refluxed for 6 h. The reaction mixture was concentrated to obtain **2**; yield 0.9 g (60%); m.p. 106–107°.

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