

A NEW TETRACYCLIC SYSTEM-3*H*,10*H*- PYRAZOLO[4', 3': 5, 6] PYRIDO[4, 3- *B*]INDOLE

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ABSTRACT :- A 6, 7, 8, 9- tetrahydro derivative of a new heteroaromatic tetracyclic ring system – 3*H*,10*H*-pyrazolo[4',3': 5,6]pyrido[4,3-*b*]indole has been obtained from a Fisher-indolization of cyclohexanone hydrazone of IIb in excellent yield .

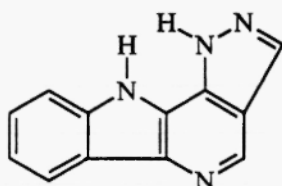
INTRODUCTION

Among various possible isomeric pyrazolopyridoindoles, only one pyrazolo[3', 4': 4, 5]pyrido[3, 2-*b*]indole (I) has been reported in the literature and its various derivatives are claimed to have anticonvulsant, anxiolytic and sedative activities¹. Now we would like to describe the synthesis of another isomer of (I) - 3*H*,10*H*-pyrazolo[4',3': 5,6]pyrido[4, 3-*b*]indole (III).

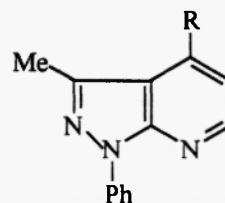
During the course of our work on the chemistry of pyrazolo[3, 4-*b*]pyridine system, we had prepared its 4-chloro derivative which undergoes facile nucleophilic substitution^{2,3}. In one of these reactions 4-hydrazino-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine, (IIb) was obtained in 77% yield from hydrazine hydrate and 4-chloro-3-methyl-1-phenyl-1*H*-pyrazolo[3,4-*b*]pyridine(IIa). When cyclohexanone hydrazone of IIb was heated in diethylene glycol, it underwent a smooth fisher-indolization to afford the title ring system III in 70% yield. This was duly characterized through its elemental analysis, mass(*m/z*:302,52% *M*⁺) and ¹H NMR spectra.

The ¹H NMR spectra displayed methylene signals between δ 1.60 and 2.96, appearance of a singlet at δ 8.62 with the disappearance of the H-5 proton signal at δ 6.58.

The Fisher- indolization of IIb was carried out under thermal conditions⁴ to avoid protonation of pyridine nitrogen in the usual acid-catalyzed cyclization.

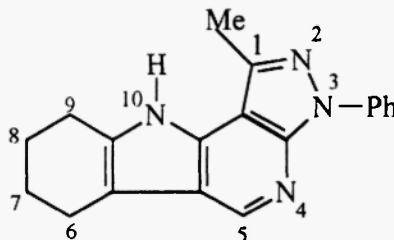


I



II a R=Cl

b R=NHNH₂



III

EXPERIMENTAL

4-Hydrazino-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine (IIb)

A mixture of IIa (4g), 85% hydrazine hydrate (15 mL) and ethanol (30mL) was heated under reflux for 10 hrs. The reaction mixture was inverted over ice-water and the precipitate filtered, dried and crystallized from a mixture of benzene/ pet. ether (40-60°C) to give IIb, 3g (77%); m.p. 174-175°C.

Anal. Calcd. for $C_{17}H_{13}N_5$: C, 65.25; H, 5.47; N, 29.27. Found: C, 65.09; H, 5.57; N, 29.00.

1H NMR($CDCl_3$): δ 2.68 (s, 3H, CH_3); 3.6-3.88 to 6.18-6.40 (br., 3H, $NHNH_2$); 6.58 (d, 1H, $J_{5,6}=4.5$ Hz, H-5); 7.10-7.60 and 8.10-8.24 (m, 5H, Ph); 8.28 (d, 1H, $J_{5,6}=4.5$ Hz, H-6).

IR (KBr) cm^{-1} : 3340 ($NHNH_2$ str.), 1590, 1500, 1490, 1285, 870, 790, 760.

MS, $M^+ = 239$.

1-Methyl-3-phenyl-6,7,8,9-tetrahydro-3H,10H-pyrazolo[4',3':5,6]pyrido[4,3-b]indole (III)

A mixture of 0.6g of IIb, 0.25g of cyclohexanone, 0.6g of sodium acetate in 12mL of 30% ethanol was heated for an hour and the resulting hydrazone was extracted with 3 x 15mL of chloroform. The solvent was removed and the residue was taken up in 5mL of diethylene glycol, heated under reflux for one hour and diluted with 10mL of water. The precipitate was filtered, dried and crystallized from ethanol to yield III, 0.54g; 70% m.p. 258-260°C.

Anal. Calcd. For $C_{19}H_{18}N_4$: C, 75.46; H, 6.00; N, 18.55. Found: 75.20; H, 5.92; N, 18.44.

1H NMR($CDCl_3$): δ 1.60-2.40 and 2.54-2.96 (m, 8H, $4CH_2$); 2.78 (s, 3H, CH_3); 7.04-7.60 and 8.04-8.34 (m, 5H, Ph); 8.62 (s, 1H, H-5).

IR (KBr) cm^{-1} : 3620, 3200 (NH str.); 2930, 1640.

MS, $M^+ = 302$.

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