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Hetarylpyrazoles III[1]. Synthesis of Some 5-Azolylpyrazoles[2]

Short Communication

Misbahul A. Khan* and **Antonio C. C. Freitas**

Seção de Quimica, Instituto Militar de Engenharia, Praia Vermelha, 22290 Rio de Janeiro, RJ, Brasil

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Some 5-azolylpyrazoles were obtained by the nucleophilic displacement of 5-chloropyrazoles.

(Keywords: Chloropyrazole; Nucleophilic reactions)

Hetarylpyrazole III[1]. Synthese einiger 5-Azolylpyrazole (Kurze Mitteilung)

Es wurden einige 5-Azolylpyrazole über nucleophile Substitution am 5-Chloropyrazol synthetisiert.

Introduction

Some derivatives of pyrazole in which a pyrazole ring is linked to another pyrazole ring or to another five membered ring are known in the literature[3–5] and some of these are reported to have antibacterial and antimicrobial activity[5]. During the course of our work on the nucleophilic substitution of 5-halopyrazoles[2] we obtained some pyrazoles linked to other azoles and would like to report the synthesis of these compounds.

Results and Discussion

5-Chloropyrazole can undergo nucleophilic substitution but we have found that unless activated by other groups the replacement needs vigorous conditions. However, the presence of an electron-withdrawing group in position 4 facilitates the substitution by appropriate nucleophiles, and in dimethyl sulfoxide solvent this substitution may take

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place even at room temperature[2]. Thus using azoles such as pyrazole and methylimidazole having a free NH in dimethyl sulfoxide in the presence of sodium hydride, 5-chloro-3-methyl-4-nitro-1-phenylpyrazole (**1**) gave the corresponding 5-hetarylpyrazoles (**2**) and (**4**) respectively in good yields. Using 4-nitroimidazole and 1,2,4-triazole the corresponding compounds (**3**) and (**5**) were obtained. The structures of these azolylpyrazoles were confirmed by elemental analysis, infrared and proton magnetic resonance spectra (Table 1).

The 5-chloro group of **1** can also be replaced by nitrile[6] and the 5-cyanopyrazole thus obtained on further reaction with sodium azide gave 5-(3′-methyl-4′-nitro-1′-phenylpyrazol-5′-yl)-tetrazole (**6**). The replacement of the chloro by the azido group and subsequent treatment with cyanacetamide has earlier been reported to give 1,2,3-triazole-substituted pyrazole or the condensed ring system pyrazolo[3,4-e]-1,2,3-triazolo[1,5-a]pyrimidine[8].

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Experimental

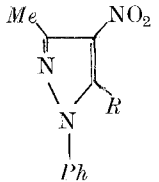
The proton magnetic resonance spectra (PMR) were obtained on a Hitachi Perkin-Elmer model R-20B spectrometer operating at 60 Mc/s (tetramethylsilane as internal standard). The infrared (IR) absorption spectra were taken by the Perkin-Elmer model 727 spectrophotometer and were measured in potassium bromide disks. Melting points (mp) were determined with a Fisher-Johns apparatus and are uncorrected. Elemental analyses were determined on a Perkin-Elmer model 240.

4-Nitroimidazole[9] and 5-cyano-3-methyl-4-nitro-1-phenylpyrazole[6] were obtained according to the reported methods.

Arylation: An equimolar mixture (0.005 mol) of an azole and 5-chloro-3-methyl-4-nitro-1-phenylpyrazole and sodium hydride (0.02 mol) in 15 ml of dimethyl sulfoxide was stirred for 24 h at room temperature. The reaction mixture was diluted with ice-cold water and extracted with chloroform. The residue obtained on evaporating the solvent was crystallized from an appropriate solvent to give the compounds **2**-**5** (Table 1).

5-(3′-Methyl-4′-nitro-1′-phenylpyrazol-5′-yl)tetrazole (**6**)

A mixture of 0.5 g of 5-cyano-3-methyl-4-nitro-1-phenylpyrazole[6], 0.13 g of sodium azide and 0.12 g of ammonium chloride in 7 ml of *N*,*N*-dimethylformamide was heated in an oil bath (120–130°) with stirring for a period of 10 h and then at room temperature for further 24 h. The reaction mixture was diluted with ice-cold water, and acidified with 5% hydrochloric acid. The precipitate was filtered off, washed, dried and crystallized from a mixture of acetone and light petroleum (bp 40–60°) to give **6**.



Compd. No.	*R*	yield (%)	mp° (from)	Molecular formula[a]	IR (cm^{-1})	PMR δ (*J* in Hz) in $CDCl_3$
2	pyrazol-5-yl	77	81–82 (50% *Et*OH)	$C_{13}H_{11}N_5O_2$	3160, 3130, 1605, 1600, 1580, 1500 (NO_2), 1480, 1460, 1430, 1355 (NO_2), 1305, 1140, 930, 860, 770	2.68 (3H, s, *Me*); 6.49 (1H, t, $J_{3,4}=J_{4,5}=2.5$, H-4); 7.0–7.50 (5H, m, *Ph*); 7.68 (1H, d, $J_{3,4}=2.5$, H-3); 7.71 (1H, d, $J_{4,5}=2.5$, H-5)
3	4-nitroimid-azol-1-yl	53	159–160 (*Et*OH)	$C_{13}H_{10}N_6O_4$	3120, 3100, 1595, 1580, 1550 (NO_2), 1510, 1500 (NO_2), 1460, 1440, 1380, 1368, 1348 (NO_2), 1285, 1045, 825, 775, 701	2.69 (3H, s, *Me*); 7.00–7.50 (5H, m, *Ph*); 7.53 (1H, d, $J_{2,5}=2$, H-2); 7.88 (1H, d, $J_{2,5}=2$, H-5)
4	2-methylimid-azol-1-yl	52	122–123 ($CHCl_3$/ light pet.)	$C_{14}H_{13}N_5O_2$	3160, 3130, 1600, 1585, 1500 (NO_2), 1440, 1380, 1350 (NO_2), 1300, 1280, 860, 770	2.10 (3H, s, *Me imidazole*); 2.70 (3H, s, *Me pyrazole*); 6.89 (1H, d, $J_{4,5}=1.5$, H-4); 7.04 (1H, d, $J_{4,5}=1.5$, H-5); 7.00–7.50 (5H, m, *Ph*)
5	1,2,4-triazol-1-yl	64	104–105 ($CHCl_3$/ light pet.)	$C_{12}H_{10}N_6O_2$	3125, 3120, 1605, 1585, 1500 (NO_2), 1435, 1400, 1360, 1325 (NO_2), 1140, 1120, 1005, 955, 860, 770, 660	2.70 (3H, s, *Me*); 7.10 7.50 (5H, m, *Ph*); 8.10 (1H, s, H-3); 8.39 (1H, s, H-5)
6	tetrazol-5-yl	79	190–191 (acetone/ light pet.)	$C_{11}H_9N_7O_2$	3200–2700 (br., NH), 1625, 1590, 1540 (NO_2), 1505, 1470, 1435, 1380, 1370, 1320 (NO_2), 1220, 1078, 980, 860, 780, 700	2.64 (3H, s, *Me*); 7.39 (5H, s, *Ph*)[b]

[a] Elemental analyses are in full agreement with the calculated values.

[b] In acetone-d_6.

References

[1] Part II. *Khan, M. A., Pinto, A. A. A.*, J. Heterocycl. Chem., in print.

[2] Taken in part from the Master's Thesis of *Freitas, A. C. C.*, Instituto Militar de Engenharia, Rio de Janeiro, 1978.

[3] *Behr, L. C., Fusco, R., Jarboe, C. H.*, The Chemistry of Heterocyclic Compounds, Vol. 22, Pyrazoles, Pyrazolines, Pyrazolidines, Indazoles and Condensed Rings. New York: Wiley. 1967.

[4] *Alonso, G., Madronero, R., Nebreda, L.*, Ann. Quim **72**, 897 (1976), C.A. **87**, 167969 (1977); *Scot, F. L., O'Donovan, D. G., Reilly, J.*, J. Appl. Chem. **2**, 368 (1952), C.A. **48**, 3354 (1954); *Pollak, A., Polanc, S., Stanovnik, B., Fisher, M.*, Mh. Chem. **103**, 1591 (1972); *Finar, I. L., Manning, M.*, J. Chem. Soc. **1961**, 2733; *Ainsworth, C.*, J. Amer. Chem. Soc. **78**, 4475 (1956); *Fedetova, A. P., Kazymov, A. V., Shchelkina, E. P.*, U.S.S.R. Patent, **1969**, 245, 554, C.A. **72**, 3491 (1970); *Polanc, S., Verbek, B., Sek, B., Stanovnik, B., Tisler, M.*, J. Org. Chem. **39**, 2143 (1974).

[5] *Verge, J. P., Neville, C., Friedman, H.*, Ger. Offen. **1975**, 2, 431, 775, C.A. **83**, 10079 (1975); *Rufer, C., Schwarz, K., Kessler, H. J.*, Ger. Offen. **1975**, 2, 412, 656, C.A. **84**, 4960 (1976); *Rufer, C., Schwarz, K., Winterfeldt, E.*, Justus Liebigs Ann. Chem. **1975**, 1465.

[6] *Khan, M. A., Freitas, A. C. C.*, Rev. Latinoamer. Quim., in print.

[7] *Finnegan, W. G., Henry, R. A., Lofquist, R.*, J. Amer. Chem. Soc. **80**, 3908 (1958).

[8] *Khan, M. A., Freitas, A. C. C.*, J. Heterocycl. Chem. **17**, 1603 (1980).

[9] *Farghar, R. G., Pyman, F. L.*, J. Chem. Soc. **1919**, 217.