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N-(1-Phenyl-3-methylpyrazol-5-yl)-*o*-aminobenzamide reacted with orthoesters to yield some new 3-pyrazolyl-substituted-4(3*H*)quinazolinones (VIIa,b,c,d). An alternative synthesis of VIIb was accomplished by reaction of acetylanthranyl with 1-phenyl-3-methyl-5-aminopyrazole.

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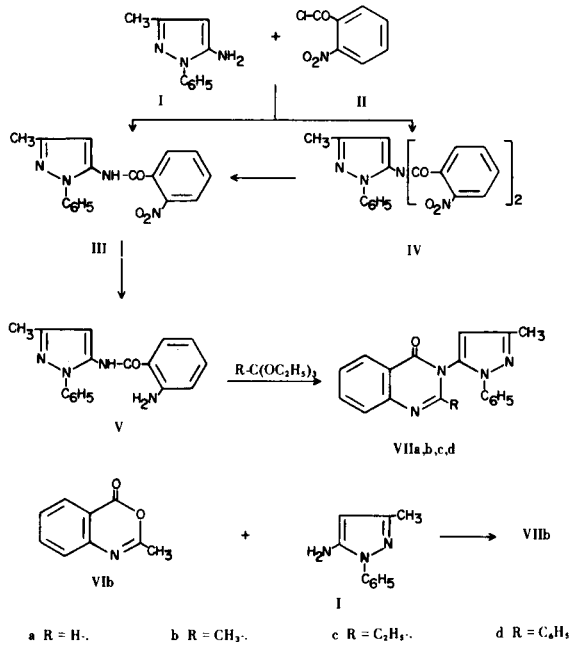
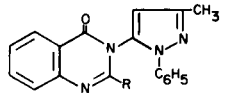
An examination of the current literature shows that 4-quinazolinones substituted in the 3-position with a heterocyclic system are attracting the attention of various types of chemists (1,2). Compounds of this type appear to be important because of their sedative, hypnotic and anticonvulsive effects (3). As part of a medicinal program it was desired to synthesize some 3-pyrazolyl-4(3*H*)quinazolinone derivatives, for pharmacological testing. We have now prepared the title compounds using *N*-(1-phenyl-3-methylpyrazol-5-yl)-*o*-nitrobenzamide (III) as the starting material. Thus, action of *o*-nitrobenzoyl chloride on aminopyrazole (I) in chloroform in the presence of triethylamine gave the expected III in 50% yield and a product formulated as *N,N'*-(1-phenyl-3-methylpyrazol-5-yl)-bis-*o*-nitrobenzamide (IV) in 15% yield. Hydrolysis of IV with ethanolic sodium hydroxide at room temperature gave III quantitatively. By catalytic reduction with palladium on charcoal III afforded V in 75-85% yield, which heated in refluxing orthoesters gave compounds VII in very good yield (*ca.* 90%). The structure of these new



Table

3-Pyrazolyl-4(3*H*)quinazolinones



	R	M.p. °C	Formula	Analyses Calcd. C	H	N	Found C	H	N
VIIa	H	120-122°	$C_{18}H_{14}N_4O$ (a)	71.51	4.67	18.53	71.66	4.71	18.42
VIIb	CH_3	162-164°	$C_{19}H_{16}N_4O$ (b)	72.13	5.10	17.71	72.11	5.15	17.70
VIIc	C_2H_5	125-127°	$C_{20}H_{18}N_4O$ (c)	72.70	5.49	16.96	72.68	5.50	16.92
VIId	C_6H_5	168-171°	$C_{24}H_{18}N_4O$ (d)	76.17	4.79	14.81	76.15	4.79	14.80

(a) Ir: 1700 cm^{-1} (CO); nmr: δ 2.30 (3H, s, CH_3), 6.54 (1H, s, pyrazole CH), 7.20-8.20 (9H, m, C_6H_5 and C_6H_4), 8.38 (1H, s, quinazoline CH); Mass: M^+ 302. (b) Ir: 1700 cm^{-1} (CO); nmr: δ 2.18 (3H, s, CH_3), 2.32 (3H, s, CH_3), 6.58 (1H, s, CH), 7.30-8.25 (9H, m, C_6H_5 and C_6H_4); mass: M^+ 316. (c) Ir: 1700 cm^{-1} (CO); nmr: δ 1.10 (3H, t, CH_3), 2.32 (3H, s, CH_3), 6.68 (1H, s, CH), 7.34-8.30 (9H, m, C_6H_5 and C_6H_4); Mass: M^+ 330. (d) Ir: 1700 cm^{-1} (CO); nmr: δ 2.20 (3H, s, CH_3), 6.58 (1H, s, CH), 6.80-8.50 (14H, m, 2 x C_6H_5 and C_6H_4); Mass: M^+ 378. For VIIa, ms: 302 (100), 301 (41), 285 (8), 274 (14), 273 (13), 261 (7), 232 (3), 151 (6, M^{++}), 130 (8), 129 (13), 104 (7), 103 (12), 102 (8), 89 (4), 77 (29), 76 (26), 51 (10), 50 (7), 39 (4). For VIIb, ms: 310 (20, M^+ +1), 316 (88, M^+), 315 (4), 302 (3), 301 (14), 275 (5), 274 (3), 273 (4), 260 (23), 158 (7, M^{++}), 144 (15), 143 (100), 118 (5), 117 (19), 116 (9), 104 (3), 102 (3), 90 (5), 89 (6), 77 (34), 76 (28), 75 (3), 51 (7), 50 (7), 39 (3). For VIIc, ms: 331 (23, M^+ +1), 330 (100, M^+), 329 (14), 315 (3), 301 (10), 289 (3), 288 (4), 274 (10), 260 (3), 253 (3), 239 (4), 238 (3), 197 (3), 186 (4), 185 (15), 184 (3), 183 (7), 171 (12), 165 (8, M^{++}), 157 (11), 156 (59), 147 (4), 131 (7), 130 (25), 129 (7), 118 (6), 104 (5), 103 (12), 102 (5), 91 (4), 90 (4), 89 (5), 77 (30), 76 (21), 51 (8), 50 (7), 39 (3). For VIId, ms: 379 (25, M^+ +1), 378 (85, M^+), 377 (7), 336 (3), 301 (5), 206 (18), 205 (100), 189 (8, M^{++}), 179 (21), 178 (14), 152 (6), 151 (4), 105 (6), 77 (28), 76 (21), 51 (5), 50 (8).

products are supported by elemental analyses, nmr, ir and mass spectrometry. Moreover, the synthesis of this heterocyclic ring system, *i.e.*, VIIb, was achieved in high yield, by a facile one-step alternative route starting from the readily available acetylanthranyl (VIb), which was allowed to react with 5-aminopyrazole (I) in boiling xylene by eliminating water azeotropically.

EXPERIMENTAL

All melting points were taken on a Buchi-Tottoli capillary melting point apparatus and are uncorrected. Infrared spectra were determined in nujol mull with a Perkin Elmer 137 spectrophotometer; nmr spectra (DMSO-d_6, unless otherwise specified) were obtained with a jeol C-60H spectrometer (TMS as internal reference). A Jeol-JMS-01-SG-2 mass spectrometer was employed for determination of low resolution 75 eV mass spectra.

N-(1-Phenyl-3-methylpyrazol-5-yl)-*o*-nitrobenzamide (III) and *N*,*N'*-(1-Phenyl-3-methylpyrazol-5-yl)bis-*o*-nitrobenzamide (IV).

Compound I (10 mmoles) (4) was dissolved in 100 ml. of dry chloroform and 10 mmoles of *o*-nitrobenzoyl chloride (II) was added. Triethylamine (10 mmoles) was added in one portion and the mixture was refluxed for 3 hours. The solution was evaporated under vacuum and the resulting crude solid mixed with aqueous sodium hydroxide 20% (100 ml.) was shaken at room temperature for 3 hours. The solution was extracted with ether (3 x 100 ml.). The organic layer upon evaporation gave a residue (IV), which was recrystallized from ethanol (yield 15%), m.p. 208-210°; ir cm^{-1}: 1720-1740 (CO); nmr (deuteriochloroform): δ 2.20 (s, 3H, CH_3), 6.18 (s, 1H, pyrazole CH), 6.80-8.20 (m, 13H, 2 x C_6H_4 and C_6H_5).

Anal. Calcd. for $C_{24}H_{17}N_5O_6$: C, 61.14; H, 3.64; N, 14.86. Found: C, 61.28; H, 3.58; N, 14.71.

To the alkaline aqueous solution, ammonium chloride was added. The precipitate was filtered, washed thoroughly with water, air dried and recrystallized from benzene to give III (yield 50%), m.p. 150-152°; ir: cm^{-1} 3240 (NH), 1680 (CO); nmr: δ 24 (s, 3H, CH_3), 6.32 (s, 1H, pyrazole CH), 7.00-8.30 (m, 9H, C_6H_4 and C_6H_5), 10.70 (s, 1H, NH).

Anal. Calcd. for $C_{17}H_{14}N_4O_3$: C, 63.35; H, 4.38; N, 17.38. Found: C, 63.51; H, 4.44; N, 17.50.

Hydrolysis of IV.

A suspension of 10 mmoles of IV in ethanolic potassium hydroxide 10% (20 ml.) was stirred for 4 hours at room temperature. The resultant solution was evaporated under vacuum and the residue was dissolved in water (20 ml.), the addition of ammonium chloride gave a precipitate which was collected and recrystallized from benzene. The product was identical with *N*-(1-phenyl-3-methylpyrazol-5-yl)-*o*-nitrobenzamide (m.p. and mixed m.p., ir, nmr).

N-(1-Phenyl-3-methylpyrazol-5-yl)-*o*-aminobenzamide (V).

A mixture of 3 mmoles of III, 300 ml. of ethanol and 500 mg. of 10% palladium on charcoal was hydrogenated in a Parr apparatus at 45-50 psi for 8 hours. After removal of the catalyst, the solution was evaporated under vacuum to dryness and the residue was recrystallized from ethanol, yield 75-85%, m.p. 170-172°; ir: cm^{-1} 3200 (broad) 3300 and 3440 (NH, NH_2), 1650 (CO); nmr: δ 2.20 (s, 3H, CH_3), 6.22 (s, 1H, pyrazole CH), 6.30-7.70 (m, 11H, NH_2, C_6H_4 and C_6H_5), 10.00 (broad NH).

Anal. Calcd. for $C_{17}H_{16}N_4O$: C, 69.84; H, 5.52; N, 19.17. Found: C, 69.98; H, 5.63; N, 19.11.

General Procedure for 4(3*H*)Quinazolinonepyrazoles (VIIa,b,c,d).

Compound V (10 mmoles) and triethyl orthoester (20 ml.) was heated under reflux for 5 hours. The solution was evaporated under vacuum and the residue recrystallized from ethanol to yield 80-90% of the desired products VII which are listed in Table.

Reaction of Acetylanthranil with I to give VIIb.

Equimolar amounts (10 mmoles) of acetylanthranil (VIb) (5) and 1-phenyl-3-methyl-5-aminopyrazole (I) in xylene (30 ml.) were refluxed for 24 hours, by eliminating water azeotropically. The product separated in the form of a white powder and was identified by comparison (m.p. and mixed m.p., nmr, ir) with an authentic sample prepared by the above method.

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