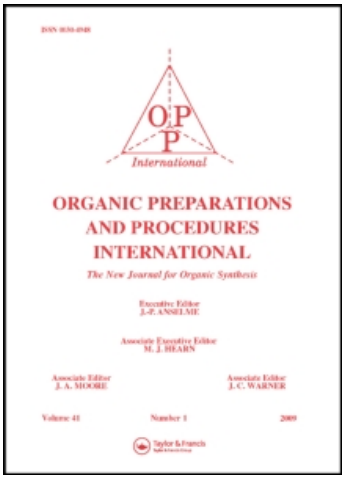

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AN IMPROVED SYNTHESIS OF 2-HETEROARYL-3-PHENYL-4(3H)-QUINAZOLINONES

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AN IMPROVED SYNTHESIS OF 2-HETEROARYL-3-PHENYL-4(3H)-QUINAZOLINONES

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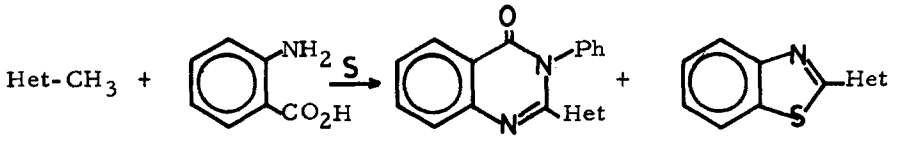
A modification of the Niementowski quinazolone synthesis[1] permits the obtention of 2-heteroaryl-3-aryl-4(3H)-quinazolinones by a one-step procedure in which the decarboxylation of a one molar excess of anthra-



I II III

a) 4-Picoline; b) 2-Picoline; c) 2,3-Lutidine; d) 2,5-Lutidine; e) Quinaldine

nilic acid under the high temperature conditions used, serves as the source of the aromatic amine in situ. Although the yields are poor to moderate, they are relatively good compared to those of previous preparations.[2] A by-product of this reaction is the 2-heteroaryl benzothiazoles (III),[2b,3] formed from the reaction of I with aniline and sulfur.

EXPERIMENTAL

Most of products are listed in Table I. IR spectra were recorded on Nippon Bunko IR-G spectrophotometer and nmr spectra were taken with JNM-C-60H spectrometer in ca 5% (w/v) $CHCl_3$ solution with tetramethylsilane as an internal standard and chemical shifts were expressed in τ value.

Typical Procedure.- A mixture of 0.10 mole of 4-picoline (Ia), 0.20 mole of anthranilic acid and 0.30 mole of sulfur was heated in an oil bath at 195-200° for 8 hrs. After removal of unchanged 4-picoline in vacuo, the brown residue was dissolved in 80 ml. of benzene and kept overnight below 15°. The crystals which separated were collected by suction and recrystallized from EtOH, give 0.7 g. (1.6%) of the anthranilic acid salt of IIa, mp. 249°, as colorless prisms. IR ν_{max}^{KBr} cm^{-1}: 3290 and 3340 (NH_2), 1686 (C=O), which was identical with 2-(4-pyridyl)-3-phenyl-4(3H)-quinazolinone anthranilate (mp. 249°)[4] by the mixed melting point test.

Anal. Calcd. for $C_{19}H_{13}ON_3 \cdot C_7H_7O_2N$: C, 71.56; H, 4.58; N, 12.84.
Found: C, 71.63; H, 4.51; N, 12.56.

The mothor liquor was concentrated to 40 ml. by distillation and then chromatographed over 180 g. of Al_2O_3 (200 mesh), benzene being used as eluent. From the first eluted fraction, a crude crystalline mass was obtained and recrystallized from pet. ether-benzene to give 11.9 g. (40%) of IIa, mp. 159°, as colorless prisms, which was identical with 2-(4-pyridyl)-3-phenyl-4(3H)-quinazolinone (mp. 159°)[4] by mixture melting point

test. IR ν_{max}^{KBr} cm^{-1}: 1680 (C=O); nmr (in $CDCl_3$) at 60 Mc: τ 1.62 (2H, d-d, J = 4.5 Hz, pyridine C_2- and C_6-H, 1.76 [1H, d (broad), J = 7.0, 4(3H)-quinazolinone ring C_5-H],[5,6] 2.10-3.10 (10H, m, remaining aromatic C-H).

Anal. Calcd. for $C_{19}H_{13}ON_3$: C, 76.25; H, 4.35; N, 14.05; MW, 299.
Found: C, 76.31; H, 4.25; N, 13.75; MW (mass spectrum 299.

From the second eluted fraction, a crude crystalline mass was obtained and recrystallized from pet. ether-benzene to give IIIa in 6% yield (1.2 g.), mp. 133-135°, as colorless plates, which was identical with 2-(4-pyridyl-benzthiazole (mp. 135°)[3] by mixture melting point and by ir spectral comparison.

Table I. 2-Heteroaryl-3-phenyl-4(3H)-quinazolones[a]

Cmpd	Appearance[b]	Heterocycle	mp. (°C)	Yield (%)	Analysis(%) Calcd. (Found) C	H	N
IVa	colorless (prisms)	4-pyridyl	159[4]	40	76.25 (76.31	4.35 4.25	14.05 13.75
IVb	colorless (amorphous)	2-pyridyl	162[2b]	25	76.25 (76.23	4.35 4.51	14.05 13.83)
IVc	colorless prisms	2-(3-methyl-pyridyl)	159-161	15	76.66 (76.91	4.83 4.57	13.41 13.36)
IVd	colorless prisms	2-(5-methyl-pyridyl	174	30	76.66 (76.47	4.83 4.60	13.41 13.48)
IVe	colorless needles[c]	2-quinolyl	186-187	30	79.08 (78.92	4.30 4.41	12.03 11.98)

a) All reactions were run using 1 equivalent of the heterocycle, 2 equivalents of anthranilic acid and 3 equivalents of sulfur. b) Recrystallized from pet ether/benzene except as otherwise noted c) From benzene.

Anal. Calcd. for $C_{12}H_8N_2S$: C, 67.88; H, 3.81; N, 13.21; MW, 212.

Found: C, 68.14; H, 3.93; N, 12.92; MW (mass spectrum), 212.

Other compounds (IIb-3) were synthesized as described for IIa (Table I).

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