Studies with Reissert Compounds; Part VII[1]. A Synthesis of the Pyrrolo[2,1-*a*]phthalazine System

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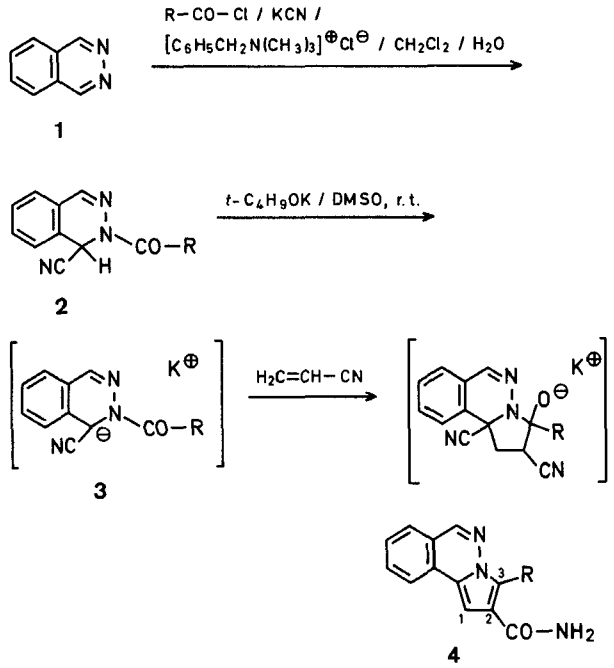
We report a straightforward synthesis of the little known[2] pyrrolo[2,1-*a*]phthalazine system, **4**, from a phthalazine Reissert compound **2**. The latter is readily prepared from phthalazine **1** by treatment with an acid chloride and potassium cyanide, in a two-phase system, in the presence of a phase transfer catalyst[1,3]. Generation of the carbanion **3** by use of potassium *t*-butoxide in dimethyl sulphoxide followed by addition of acrylonitrile leads to the 3-arylpyrrolo[2,1-*a*]phthalazine-2-carboxamide, **4**, (R = aryl) in good yields (54–65%).



The pyrrolo[2,1-*a*]phthalazines **4**, which are variously coloured from deep orange to brick red, are spectroscopically similar to pyrrolo[2,1-*a*]isoquinolines, which can be elaborated by a related procedure[4]. The ultraviolet spectrum of **4c** (R = 4-H_3C—C_6H_4), for example, compares with that of 3-(*p*-tolyl)-pyrrolo[2,1-*a*]isoquinoline-2-carboxamide[4a] with λ_{max} = 256 (log ε = 4.12), 294 (4.51), 369 (3.80), 428 (3.83) nm.

The cyclisation reaction was unsuccessful with 2-acetyl-1-cyano-1,2-dihydrophthalazine (**2**, R = CH_3) suggesting that resonance stabilisation, as provided by R = aryl, is needed at an intermediate stage between **3** and **4** to benefit favourably the equilibria involved.

3-Arylpyrrolo[2,1-*a*]phthalazine-2-carboxamides (4a–d); General Procedure:

The phthalazine Reissert compound[1] (**2**; 0.05 mol) dissolved in dry dimethyl sulphoxide is added dropwise to a stirred suspension of potassium *t*-butoxide (0.20 mol) in dry dimethyl sulphoxide under nitrogen at room temperature. After 15 min acrylonitrile (0.20 mol) is added and the mixture stirred for a further 0.5 h. Most of the dimethyl sulphoxide is removed by evaporation under reduced pressure. The residue is suspended in water and extracted with chloroform. The extracts are washed with dilute hydrochloric acid and water and dried (K_2CO_3). Evaporation of the chloroform gives the 3-arylpyrrolo[2,1-*a*]phthalazine-2-carboxamide (**4a–d**) which readily crystallises from ethanol.

3-Phenylpyrrolo[2,1-*a*]phthalazine-2-carboxamide (**4a**; R = C_6H_5); yield: 65%; m.p. 210–211°.

$C_{18}H_{13}N_3O$	calc.	C 75.24	H 4.56	N 14.63
(287.3)	found	75.15	4.60	14.30

I.R. (KBr): ν_{max} = 3430, 3320, 1632 cm^{-1} ($CONH_2$).

U.V. (C_2H_5OH): λ_{max} = 246 (log ε = 4.18), 284 (4.66), 366 (3.9), 446 nm (3.72).

^{1}H-N.M.R. ($CDCl_3$): δ = 8.2–6.8 (m, 11 H_{arom}); 5.80 ppm (br, 2H, NH_2).

3-(4-Methoxyphenyl)-pyrrolo[2,1-*a*]phthalazine-2-carboxamide (**4b**; R = 4-H_3CO—C_6H_4); yield: 60%; m.p. 177–178°.

$C_{19}H_{15}N_3O_2$	calc.	C 71.91	H 4.76	N 13.24
(317.3)	found	71.90	4.80	13.00

I.R. (KBr): ν_{max} = 3460, 3340, 1638 cm^{-1} ($CONH_2$).

U.V. (C_2H_5OH): λ_{max} = 282 (log ε = 4.58), 293 (4.59), 370 (3.85), 450 nm (3.63).

^{1}H-N.M.R. ($CDCl_3$): δ = 8.2–6.8 (m, 10 H_{arom}); 5.10 (br, 2H, NH_2); 3.92 ppm (s, 3H, CH_3).

3-(4-Methoxyphenyl)-pyrrolo[2,1-*a*]phthalazine-2-carboxamide (**4c**; R = 4-H_3C—C_6H_4); yield: 54%; m.p. 175–178°.

$C_{19}H_{15}N_3O$	calc.	C 75.73	H 5.02	N 13.95
(301.3)	found	75.20	5.00	14.15

I.R. (KBr): ν_{max} = 3442, 3327, 1630 cm^{-1} ($CONH_2$).

U.V. (C_2H_5OH): λ_{max} = 255 (log ε = 4.39), 293 (4.75), 372 (3.85), 450 nm (3.72).

^{1}H-N.M.R. ($CDCl_3$): δ = 8.2–6.8 (m, 10 H_{arom}); 6.34 (br, 2H, NH_2); 2.47 ppm (s, 3H, CH_3).

3-(4-Chlorophenyl)-pyrrolo[2,1-*a*]phthalazine-2-carboxamide (**4d**; R = 4-Cl—C_6H_4); yield: 65%; m.p. 200–202°.

$C_{18}H_{12}ClN_3O$	calc.	C 67.19	H 3.76	N 13.06
(321.8)	found	66.9	3.9	12.8

I.R. (KBr): ν_{max} = 3448, 3343, 1633 cm^{-1} ($CONH_2$).

U.V. (C_2H_5OH): λ_{max} = 257 (log ε = 4.39), 293 (4.91), 372 (4.13), 450 nm (391).

^{1}H-N.M.R. ($CDCl_3$): δ = 8.2–6.7 (m, 10 H_{arom}); 6.38 ppm (br, 2H, NH_2).

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