

SYNTHESIS OF 1,2-DIPHENYLPYRROLO[1,2-a]QUINAZOLINES

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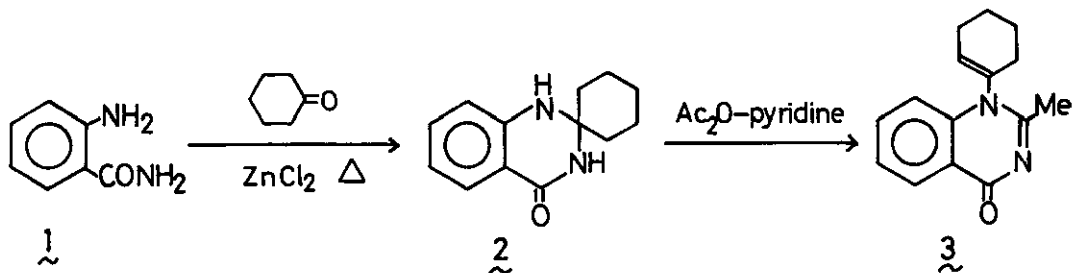
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Abstract — Heating of 2-aminobenzamide (1) with benzoin (4) in the presence of anhydrous zinc chloride gave 2-(1-benzoylbenzylamino)benzamide (5a) which, on treatment with acetic anhydride, was transformed to 1,2-diphenyl-4,5-dihydropyrrolo-[1,2-a]quinazolin-5-one (6).

Previously, we have reported the reaction of 2-aminobenzamide (1) with ketones to give 2,2-disubstituted 1,2,3,4-tetrahydroquinazolin-4-one.^{1,2} For instance, heating of compound 1 with cyclohexanone in the presence of anhydrous zinc chloride afforded the 2-spiro compound (2), which, on treatment with acetic anhydride in pyridine, was transformed to 1-cyclohexenyl-2-methyl-1,4-dihydroquinazolin-4-one (3).



As a continuation of this study, we investigated similar reaction of 2-aminobenzamide (1) with benzoin (4). Though the objective 2,2-disubstituted tetrahydroquinazoline corresponding to compound 2 could not be detected, the reaction gave the product (5a), which subsequently underwent cyclization, on treatment with acetic anhydride, to give the pyrrolo[1,2-a]quinazoline (6).

When a mixture of benzoin (4) and an equimolar amount of 2-aminobenzamide (1) was heated at 120 °C in the presence of anhydrous zinc chloride, 2-(1-benzoylbenzylamino)benzamide (5a)³ was obtained, in 38% yield, colorless plates (from MeOH), m.p. 188 - 191 °C; ν_{\max} . (KBr) 3 450 - 3 300, 1 680, and 1 640 cm^{-1} ; ¹³C-nmr δ (DMSO-d₆) 60.88 (d, -CH<), 171.79 (s, -CONH₂), and 196.80 (s, C₆Ph); *m/e* 330 (*M*⁺) and 225 (*M*⁺-C₆Ph).

Heating of 5a in acetic anhydride at 110 °C for 5 h gave 2-(1-benzoylbenzylamino)benzimidazole (5b), colorless prisms (from MeOH), m.p. 134 - 135 °C, and yellow needles (6) (from MeOH) of m.p. >300 °C in 34% and 64% yields, respectively. 5b: ν_{\max} . (KBr) 3 350, 3 050, 2 210, and 1 675 cm^{-1} ; ¹³C-nmr δ (CDCl₃) 62.24 (d, -CH<), 117.47 (s, -CN), and 195.31 (s, C₆Ph); *m/e* 312 (*M*⁺).

Compound 6 was assigned to be 1,2-diphenyl-4,5-dihydropyrrolo[1,2-a]quinazolin-5-one on the basis of elemental analyses and spectroscopic data. 6: Found: C, 82.26; H, 4.76; N, 8.23. C₂₃H₁₆N₂O requires C, 82.12; H, 4.79; N, 8.33; ν_{\max} . (KBr) 1 670 cm^{-1} (CO); ¹H-nmr δ (DMSO-d₆) 5.87 (s, pyrrole ring proton); ¹³C-nmr δ (DMSO-d₆) 88.51 (d, pyrrole-C₃) and 157.04 (s, CO); *m/e* 336 (*M*⁺).

Compound 6 was heated in phosphoryl chloride at 100 °C for 1 h. Purification of the product by silica gel column chromatography afforded a 75% yield of 5-chloro-1,2-diphenylpyrrolo[1,2-a]quinazoline (7a), m.p. 193 °C (dec.) (from AcOEt), and a 20% yield of the bis-derivative (8), yellow powder (from benzene) of m.p. 300 °C. 7a: ¹H-nmr δ (CDCl₃) 6.92 (1H, s, 3-H) and 8.15 (1H, m, 6-H); ¹³C-nmr δ (DMSO-d₆) 102.79 (d, 3-C) and 136.32 (s, 5-C); *m/e* 354 (*M*⁺) and 356 (*M*⁺+2). 8: ¹³C-nmr δ (DMSO-d₆) 102.11 (d, 3'-C) and 103.96 (s, 3-C); *m/e* 672 (*M*⁺) and 674 (*M*⁺+2).

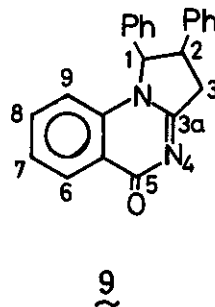
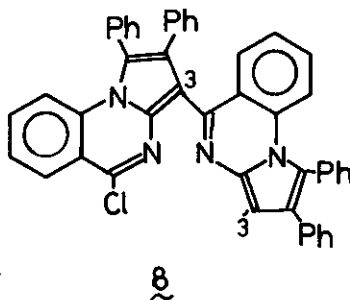
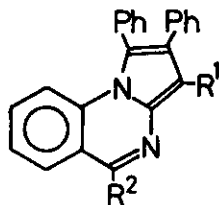
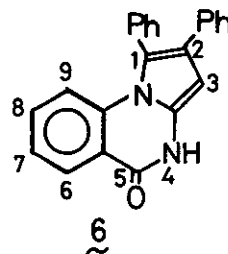
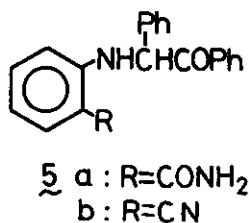
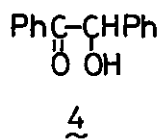
Similar treatment of compound 6 with an equimolar amount of phosphorus pentachloride afforded 3,5-dichloro-1,2-diphenylpyrrolo[1,2-a]quinazoline (7b), yellow needles (from MeOH) of m.p. 276 - 280 °C; ¹H-nmr δ (DMSO-d₆) 8.12 (1H, m, 6-H); ¹³C-nmr δ (DMSO-d₆) 103.50 (s, 3-C) and 139.30 (s, 5-C); *m/e*

388 (M^+), 390 (M^++2), and 392 (M^++4).

In the ^1H -nmr spectrum of 7b, the signal due to the proton at C_3 -position was not detected. Upon catalytic reduction with Pd-C in methanol, compound 7a was transformed to 1,2-diphenyl-1,2,3,5-tetrahydropyrrolo[1,2-a]quinazolin-5-one (9) in 67% yield, pale yellow needles (from EtOH) of m.p. 280 °C (dec.); ν_{max} . (CHCl_3) 1645 cm^{-1} (C=O); ^1H -nmr δ (CDCl_3) 3.0 - 4.9 (3H, m, 2,3-Hs) and 5.84 (1H, d, $J = 8$ Hz, 1-H); ^{13}C -nmr δ (DMSO-d_6) 38.83 (t, 3-C), 44.31 (d, 2-C), 67.18 (d, 1-C), 166.20 (s, 3a-C), and 168.20 (s, 5-C); m/e 338 (M^+).

The configuration of 9 was not determined.

Catalytic reduction of compound 7a with Pd-C in methanol in the presence of magnesium oxide gave 1,2-diphenylpyrrolo[1,2-a]quinazoline (7c) in a quantitative yield, yellow needles (from MeOH) of m.p. 203 °C; ^1H -nmr δ (CDCl_3) 7.02 (1H, s, 3-H) and 8.48 (1H, s, 5-H); ^{13}C -nmr δ (DMSO-d_6) 102.40 (d, 3-C), 122.93 (s, 2-C), 127.48 (s, 1-C), 138.14 (s, 3a-C), and 146.32 (d, 5-C); m/e 320 (M^+).



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References and Notes

1. M. Yamato, J. Horiuchi, and Y. Takeuchi, *Chem. Pharm. Bull.*, 1980, 28, 2623.
2. M. Yamato, J. Horiuchi, and Y. Takeuchi, *Chem. Pharm. Bull.*, 1981, 29, 3055.
3. Satisfactory analytical data were obtained for all new compounds herein reported.

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