

Kurzmittelungen:

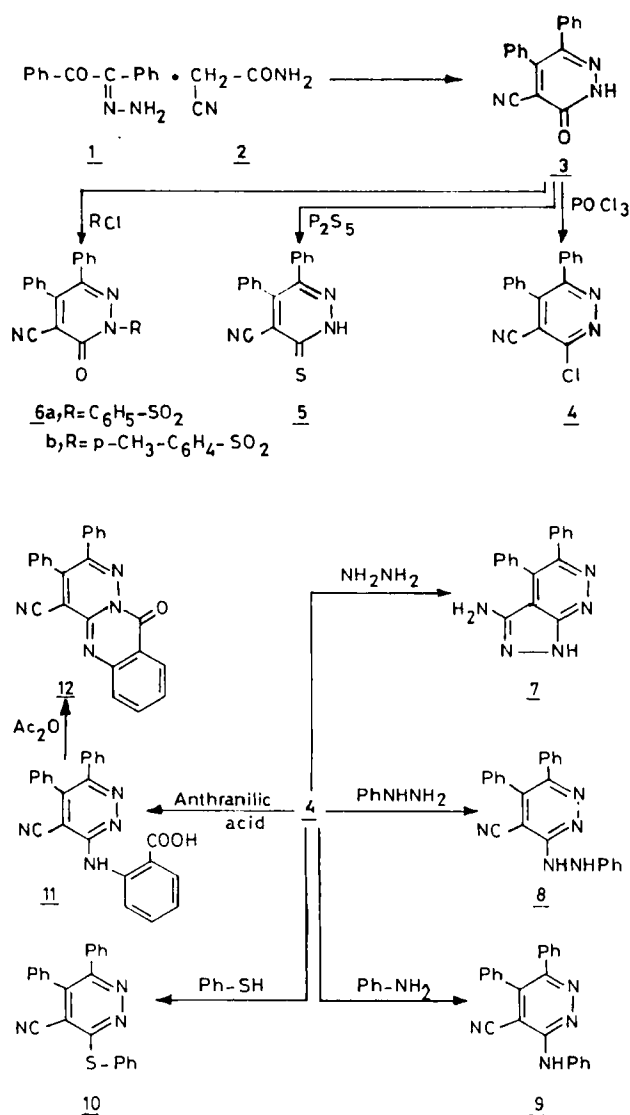
Synthesis and Reactions of Some Pyridazine Derivatives

Synthese und Reaktionen einiger Pyridazin-Derivate

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Biological and pharmacological activities of pyridazine derivatives stimulated considerable research in this field^{1,2}. As a part of a programme^{3,4} directed to the synthesis of some pyridazine derivatives as anticancer⁵, bactericidal⁶, and fungicidal compounds⁷, a novel synthesis of some pyridazine derivatives and their substitution reactions are reported here.

Benzilhydrazone (1) reacted with cyanoacetamide (2) to yield 3,4-diphenyl-5-cyanopyridazin-6-one (3). The struc-

ture of 3 was confirmed by elemental analysis, IR- and ¹H-NMR spectra (Tables 1 and 2). Treatment of 3 with P_2S_5 in pyridine afforded 3,4-diphenyl-5-cyanopyridazin-6-thione (5) identical with an authentic sample prepared by another route⁸. Treatment of 3 with benzenesulphonyl chloride or p-toluene sulphonyl chloride, respectively in basic medium afforded 6a, b. The structure of 5 and 6a, b were confirmed by elemental analyses, IR- and ¹H-NMR spectra (Tables 1 and 2). 3,4-Diphenyl-5-cyano-6-chloropyridazine (4) is obtained by the action of $POCl_3$ ⁹ on 3 in dioxane (Tables 1 and 2). The IR-spectrum of 4 displays no absorption in the carbonyl region. The reactivity of C-6-Cl in 4 is proved by its substitution with phenylhydrazine, aniline and thiophenol to yield the corresponding 6-substituted pyridazine derivatives 8, 9, and 10, respectively. The IR spectra of 8, 9, and 10 display the corresponding characteristic bands and the ¹H-NMR spectra of 8, 9, and 10 were in a good agreement with the proposed structures (Tables 1 and 2). In contrast to phenylhydrazine, hydrazine hydrate reacted with 4 under the same condition to afford the pyrazolopyridazine derivative 7. The assignment of structure 7 was based on analytical and spectral data. The IR-spectrum displays no CN group, and the ¹H-NMR spectrum shows the corresponding characteristic signals (Tables 1 and 2). Compound 4 reacted with anthranilic acid in glacial acetic acid to give 11. The structures of compounds 10, 11 were confirmed by elemental analyses, IR- and ¹H-NMR spectra (Tables 1, 2).

Experimental Part

M.P.: uncorr. - IR spectra (KBr): Pye unicam SO-1100 spectrophotometer. - ¹H-NMR spectra: Varian EM-360, 60 MHz, in DMSO. TMS int. stand. Chemical shifts (δ ppm). - Elementary analyses: Microanalytical Centre, Cairo University.

3,4-Diphenyl-5-cyano-6-chloropyridazine (4)

A mixture of 3 (0.01 mole), $POCl_3$ (30 ml) and dioxane (50 ml) was heated under reflux for 3 h. The solution was cooled and poured onto ice water. The solid was crystallised from ethanol to give 4 (Table 1).

1-Benzenesulphonyl-3,4-diphenyl-5-cyanopyridazin-6-one (6a) and 1-p-Toluene sulphonyl-3,4-diphenyl-5-cyanopyridazin-6-one (6b)

A mixture of 3 (0.01 mole), arylsulphonyl halide (0.01 mole) and anhydrous K_2CO_3 was refluxed for 5 h in dry acetone (40 ml). Compounds 6a, b were crystallized from the proper solvent (Table 1).

Table 1: List of pyridazine derivatives 3-12

Compound	Solvent of Crystallization	Colour	M.p. (°C)	Yield (%)	Mol. Formula	Analysis, % Calcd./Found				
						C	H	N	S	Cl
3	Ethanol	Colourless	260-1	70	C ₁₇ H ₁₁ N ₃ O	74.7	4.1	15.4		
						74.2	4.0	15.4		
4	Ethanol	Colourless	201	63	C ₁₇ H ₁₀ N ₃ Cl	70.0	3.5	14.4	-	12.2
						69.6	4.0	13.9	-	12.2
5	Acetic acid	Brown	290-2	55	C ₁₇ H ₁₁ N ₃ S	70.6	3.8	14.5	11.1	-
						71.0	4.0	14.6	11.1	-
6a	Petroleum ether	Yellow	131	60	C ₂₃ H ₁₅ N ₃ O ₃ S	66.8	3.1	10.2	7.8	-
						66.6	3.5	10.3	7.8	-
6b	Ethanol	Brown	142	60	C ₂₄ H ₁₇ N ₃ O ₃ S	67.4	4.0	9.8	7.5	-
						67.5	4.6	9.6	7.4	-
7	Ethanol	Yellow	273-4	65	C ₁₈ H ₁₃ N ₅	72.2	4.1	23.4	-	-
						72.5	4.3	23.1	-	-
8	Ethanol	Brown	230-1	70	C ₂₃ H ₁₇ N ₅	76.0	4.7	19.2	-	-
						76.0	4.7	19.3	-	-
9	Ethanol	Brown	222	65	C ₂₃ H ₁₆ N ₄	79.3	4.6	16.1	-	-
						79.3	4.5	16.2	-	-
10	Petroleum ether	Yellow	220	70	C ₂₃ H ₁₅ N ₃ S	75.6	4.1	11.5	8.8	-
						75.4	4.1	11.7	8.7	-
11	Dioxane	Brown	>300	65	C ₂₄ H ₁₆ N ₄ O ₂	73.5	4.1	14.	-	-
						73.5	4.0	14.2	-	-
12	Ethyl acetate	Brown	271-3	55	C ₂₄ H ₁₄ N ₄ O	77.0	3.8	15.0	-	-
						76.8	3.8	15.0	-	-

Table 2: IR- and ¹H-NMR data of compounds 3-12

Compound	IR (KBr), cm ⁻¹	¹ H-NMR (δ ppm)
3	3400, 3300, 3120 (NH); 2220 (CN) and 1690 (ring C=O)	8.8 (s, 1H, NH); 7.62-7.9 (m, 10 H, aromat.).
4	2220 (CN)	
5	3400, 3300, 3100 (NH); 2220 (CN)	8.7 (s, 1H, NH); 7.63-7.90 (m, 10 H, aromat.).
6a	2220 (CN), 1690 (ring C=O), 1390 1195 (N-SO ₂).	
6b	2100 (CN), 1690 (ring C=O); 1380, 1195 (N-SO ₂)	1.75 (s, 3H, CH ₃); 6.9-7.80 (m, 14 H aromat.).
7	3350, 3250, 3180 (NH ₂ , and NH).	8.8 (s, 1H, NH), 7.61-7.91 (m, 10 H aromat.); 10.1 (s, 2H, NH ₂).
8	3400, 3300, 3120 (NH); 2220 (CN).	
9	3500, 3250, 3120 (NH), 2220 (CN)	7.60-7.92 (m, 15 H aromat.); 9.58 (s, 1H, NH).
10	2220 (CN).	
11	3150 (broad), NH, OH, 2220 (CN), 1650 (CO).	7.63-7.97 (m, 14 H aromat.); 8.64 (s, 1H, NH); 11.93 (s, 1H, COOH).
12	2220 (CN), 1680 (CO)	7.78, 8.20 (m, 14 H aromat.).

3,4-Diphenyl-5-aminopyrazolo[3,4-c]pyridazine (7), *3,4-Diphenyl-5-cyano-6-phenylbarazinopyridazine (8)*, *3,4-Diphenyl-5-cyano-6-anilinopyridazine (9)*, *3,4-Diphenyl-5-cyano-6-phenylmercapto pyridazine (10)*, and *3,4-Diphenyl-5-cyano-6-(o-carboxyanilino)pyridazine (11)*

A mixture of **4** (0.01 mole) and aniline, phenylhydrazine, hydrazine, thiophenol or anthranilic acid, respectively, (0.01 mole) in glacial acetic acid (60 ml) was refluxed for 5 h. The mixture was poured onto water after cooling. The solid was collected and crystallized from the proper solvent (Table 1).

3,4-Diphenyl-5-cyanopyridazino[2,1-b]quinazolin-11-one (12)

A solution of **11** (1.5 g) in acetic anhydride (20 ml) was refluxed for 3 h. The solid separating while boiling was crystallized from ethyl acetate to give **12** (Table 1).

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