

CYCLIZATION OF SOME 3-INDAZOLYLHYDRAZONES*

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Coupling of 3-indazoldiazonium chloride with malonodinitrile, ethyl cyanoacetylcarbamate, 2-cyanomethylbenzimidazole and methyl cyanoacetate has been used for preparation of the respective hydrazones *Ia* to *Id* which have been cyclized thermally to the corresponding 4-amino-1,2,4-triazino[4,3-*b*]indazole derivatives *IIa* to *IIc*. Both alkaline and thermal cyclization of the compound *Iib* gave 1,2,3,4-tetrahydropyrimido[4',5':5,6]1,2,4-triazino[4,3-*b*]indazole-2,4-dione (*III*). Alkaline cyclization of hydrazone *Ib* gave 2-(3-indazoly)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (*IV*).

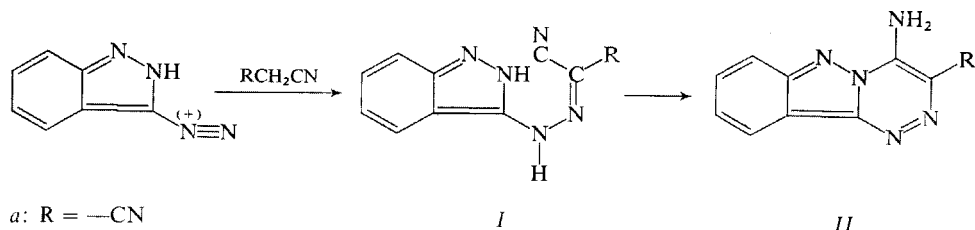
In contrast to cyclization of 3-indazolyhydrazones of α -dicarbonyl compounds¹⁻³, the analogous cyclization of 3-indazolyhydrazones of α -ketonitriles is much less investigated¹. In the present communication we have focused our attention to cyclizations of this type of compounds extending thus the analogous reactions of pyrazole series^{4,5}.

The hydrazones *Ia* to *Id* were obtained in good yields by coupling of indazole-3-diazonium chloride with malonodinitrile, ethyl cyanoacetylcarbamate, 2-cyanomethylbenzimidazole and methyl cyanoacetate. The compounds *Ia* to *Id* were transformed into the corresponding 3-substituted 4-amino-1,2,4-triazino[4,3-*b*]indazoles *IIa* to *IIc* by thermal cyclization. The cyclization was so easy with the hydrazones *Ia* to *Ic* that it was sufficient to heat them in ethanol or acetic acid for a short time. Therefore, these hydrazones could not be recrystallized without change. On the contrary, the cyclization of the hydrazone *Id* necessitated heating in acetic acid for several hours. The cyclization products *II* differ from the isomeric hydrazones *I* also by their absorption in the infra-red region. IR spectra of all the hydrazones *I* contain a marked band of CN group about 2225 cm^{-1} , those of triazinoindazoles (except for *IIa*) do not contain this band. Besides the both bands of CN groups the hydrazone *Ia* exhibits an intensive band at 2138 cm^{-1} indicating the presence of azoketeneimine form $\text{C}_7\text{H}_5\text{N}_2-\text{N}=\text{N}-\text{C}(\text{CN})=\text{C}=\text{NH}$. 3-Ethoxycarbonylamino-carbonyl-4-amino-1,2,4-triazino[4,3-*b*]indazole (*Iib*) was cyclized to 1,2,3,4-tetra-

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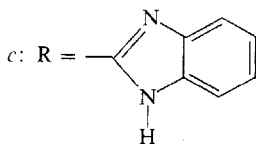
hydropyrimido[4',5' : 5,6]1,2,4-triazino[4,3-*b*]indazole-2,4-dione (*III*) by heating in aqueous sodium carbonate or by heating above the melting point.

Alkaline cyclization of the hydrazone *Ib* was investigated, too: in contrast to the thermal cyclization, this reaction gave 2-(3-indazoly)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (*IV*), which agrees fully with the results obtained in the

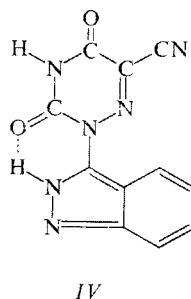
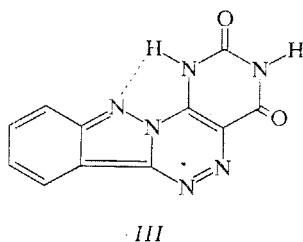


a: R = —CN

b: R = —CO—NH—COOC₂H₅



d: R = —COOCH₃



pyrazole series⁴ and with the earlier results⁶. ¹H-NMR spectroscopy proved the presence of an intramolecular hydrogen bond N—H...O in this triazine *IV*, which indicates the 2H-indazole tautomeric form. The triazine *IV* differs from the isomeric substance *III* also by the IR band of CN group at 2248 cm⁻¹.

EXPERIMENTAL

The melting points were determined with a Boetius apparatus and are not corrected. The IR and ¹H-NMR spectra were measured with a UR-20 (Zeiss, Jena) and a Varian A 60 spectrophotometers, respectively, the latter measurement being carried out in hexadeuteriodimethyl sulphoxide with tetramethylsilane as internal standard.

3-Indazolyhydrazones *Ia* to *Id*

Solution of 140 mg (2.03 mmol) NaNO_2 in 5 ml cold water was added portionwise to solution of 270 mg (2.03 mmol) 3-aminoindazole in 8 ml 5% HCl at 0°C with stirring. After 15 min the solution was added portionwise to the cold solution of the respective coupling component and sodium acetate with stirring and cooling. The following proportions were used for the individual hydrazones: *Ia*, 400 mg (5.77 mmol) malonodinitrile and 5.0 g sodium acetate in 20 ml water; *Ib*, 400 mg (2.56 mmol) ethyl cyanoacetylcarbamate and 6.0 g sodium acetate in 100 ml water; *Ic*, 350 mg (2.23 mmol) 2-cyanomethylbenzimidazole and 6.0 g sodium acetate in 100 ml water; *Id*, emulsion of 0.30 ml (3.40 mmol) methyl cyanoacetate in solution of 5.0 g sodium acetate in 15 ml water. The mixture was left to stand 4 to 24 h at 0 to 5°C, the precipitated yellow crystalline solid of the respective hydrazone *I* was collected by suction, thoroughly washed with water, and dried *in vacuo* over P_2O_5 at the room temperature. For analysis the hydrazone *Id* was recrystallized from ethanol, the other hydrazones were not crystallized. For further data see Table I.

3-Substituted 4-Amino-1,2,4-triazino[4,3-*b*]indazoles *Ila* to *Ild*

Mixture of 1.0 mmol of the respective hydrazone *Ia* to *Ic* and 120 ml ethanol was boiled under reflux for 2 h, concentrated to a small volume, and cooled. Then the crystalline solid was col-

TABLE I

3-Indazolyhydrazones *I* and 3-Substituted 4-Amino-1,2,4-triazino[4,3-*b*]indazoles *II*

Compound (yield, %)	Formula (m.w.)	Calculated/Found			M.p., °C (solvent)	$\nu(\text{C}\equiv\text{N})$ (Nujol, cm^{-1})	
		% C	% H	% N			
<i>Ia</i> (97.5)	$\text{C}_{10}\text{H}_6\text{N}_6$ (210.2)	57.14	2.88	39.99	over 350	2228	2138
		57.20	3.01	39.70	—	2220	
<i>Ib</i> (90.8)	$\text{C}_{13}\text{H}_{12}\text{N}_6\text{O}_3$ (300.3)	52.00	4.03	27.99	222—224	2227	
		51.80	4.12	28.15	—		
<i>Ic</i> (92.0)	$\text{C}_{16}\text{H}_{11}\text{N}_7$ (301.3)	63.78	3.68	32.54	over 350	2225	
		63.96	3.79	32.66	—		
<i>Id</i> (92.6)	$\text{C}_{11}\text{H}_9\text{N}_5\text{O}_2$ (243.2)	54.32	3.73	28.80	196—198	2220	
		54.30	3.81	29.01	(ethanol)		
<i>Ila</i> (89.5)	$\text{C}_{10}\text{H}_6\text{N}_6$ (210.2)	57.14	2.88	39.99	over 350	2232	
		57.05	2.82	40.10	(ethanol)		
<i>Ilb</i> (92.0)	$\text{C}_{13}\text{H}_{12}\text{N}_6\text{O}_3$ (300.3)	52.00	4.03	27.99	242—244	—	
		52.03	4.10	27.81	(ethanol)		
<i>Ilc</i> (98.7)	$\text{C}_{16}\text{H}_{11}\text{N}_7$ (301.3)	63.78	3.68	32.54	over 350	—	
		64.06	3.76	32.76	(nitrobenzene)		
<i>Ild</i> (78.3)	$\text{C}_{11}\text{H}_9\text{N}_5\text{O}_2$ (243.2)	54.32	3.73	28.80	240—242	—	
		54.42	3.84	28.52	(acetic acid)		

lected by suction, washed with little ethanol, dried at 100°C, weighed, and recrystallized. Cyclization of the hydrazone *Id* was carried out analogously by boiling in acetic acid for 4 h. For further data see Table I.

1,2,3,4-Tetrahydro-pyrimido[4',5' : 5,6]1,2,4-triazino[4,3-*b*]indazole-2,4-dione (*III*)

a) *Alkaline cyclization*: Mixture of 150 mg (0.50 mmol) *Iib*, 80 mg Na₂CO₃, and 25 ml water was heated on water bath until dissolution and then further 20 min. The solution was acidified with concentrated hydrochloric acid to pH 0. After cooling the precipitated yellow crystalline solid was collected by suction, washed with water, and dried at 160°C. Yield 115 mg (91.8%), m.p. above 350°C (nitrobenzene).

b) *Thermal cyclization*: *Iib* (60 mg; 0.20 mmol) was heated at 240 to 250°C until complete decomposition and solidification of the originally formed melt. The product was recrystallized from nitrobenzene. Yield 45 mg (88.5%), m.p. above 350°C (nitrobenzene). For analysis the sample was dried *in vacuo* at 160°C. For C₁₁H₆N₆O₂ (254.2) calculated: 51.97% C, 2.38% H, 33.06% N; found: 52.09% C, 2.35% H, 32.93% N. IR spectrum (KBr): 427 m, 443 w, 463 m, 533 w, 552 w, 585 m, 607 w, 635 w, 662 m, 672 m, 712 m, 745 sh, 754 s, 765 w, 802 m, 870 w, 930 w, 980 w, 1045 sh, 1055 m, 1120 m, 1169 s, 1196 m, 1257 s, 1287 w, 1306 m, 1327 m, 1355 m, 1365 m, 1390 m, 1410 m, 1440 s, 1540 s, 1570 s, 1602 m, 1633 s, 1680 sh, 1700 s, 1743 s, 2865 m, 2933 m, 3085 m, 3200 m cm⁻¹.

2-(3-Indazolyl)-3,5-dioxo-2,3,4,5-tetrahydro-1,2,4-triazine-6-carbonitrile (*IV*)

Mixture of 300 mg (1.00 mmol) fresh hydrazone *Ib*, 160 mg Na₂CO₃, and 60 ml water was stirred at the room temperature 3 days, filtered, the filtrate was heated on water bath 10 min and acidified to pH 1. After cooling the crystalline solid was collected by suction, washed with water, and dried at 150°C. Yield 185 mg (72.3%). After reprecipitation from aqueous sodium hydrogen-carbonate and recrystallization from water the substance melted at 314 to 316°C with decomposition. IR spectrum (KBr, cm⁻¹): 460 m, 500 w, 543 w, 553 w, 583 w, 593 m, 593 m, 650 m, 690 m, 710 w, 752 m, 768 w, 975 w, 834 m, 907 m, 981 m, 1011 m, 1098 w, 1110 m, 1164 m, 1187 m, 1228 m, 1259 w, 1276 w, 1298 m, 1330 w, 1353 w, 1371 w, 1387 w, 1415 w, 1443 m, 1505 m, 1620 m, 1727 s, 1763 s, 2248 w, 3365 m, 3410 m. ¹H-NMR spectrum (δ, p.p.m.): 13.42, 7.1 to 7.8. For C₁₁H₆N₆O₂ (254.2) calculated: 51.97% C, 2.38% H, 33.06% N; found: 51.79% C, 2.52% H, 33.29% N.

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