1124. *Triazinoindazoles.*

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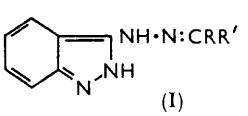
1,2,4-Triazino[4,3-*b*]indazoles have been prepared by interaction of 3-hydrazinoindazole and α-dicarbonyl compounds, and also from the product of a Japp–Klingemann reaction on an indazole-3-diazonium salt or diazoanhydride. Their properties include, in certain cases, the formation of an acyl derivative (V). A 1,2,4-triazino[4,5-*b*]indazole has been obtained from 3-hydrazinocarbonylindazole.

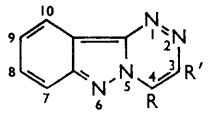
Triazinoindazoles were required for examination as potential schistosomicides. Observations of chemical interest on this hitherto unknown group are now reported.

3-Hydrazinoindazole, prepared by reduction of indazole-3-diazonium chloride, readily decomposed below its melting point into indazole and 3-aminoindazole, and was characterised as its salts and simple functional derivatives, *e.g.*, (I; R = H, R′ = Ph). It reacted with α-dicarbonyl compounds to give 1,2,4-triazino[4,3-*b*]indazoles (II; R = R′ = H, Me, or Ph) and (III). In the analogous reaction with pyruvaldehyde diethyl acetal, the 3-methyltriazine (II; R = H, R′ = Me) was formed, whereas with pyruvaldoxime, the

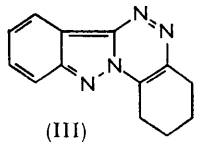
product was the 4-methyl derivative (II; R = Me, R′ = H). The intermediate in the formation of the dimethyl derivative (II; R = R′ = Me) was undoubtedly the hydrazone (I; R = Me, R′ = Ac) which cyclised during attempted recrystallisation and was accordingly identified as its acetyl derivative. This acetyl derivative, with hot mineral acid, readily afforded the cyclic compound (II; R = R′ = Me).



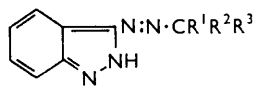
(I)



(II)



(III)



(IV)

The hydrazone (I; R = Me, R′ = Ac) also resulted from a Japp–Klingemann reaction between indazole-3-diazoanhydride and methylacetoacetic acid. Ethyl methylacetoacetate and indazole-3-diazoanhydride afforded the expected azo-compound (IV; R^1 = Me, R^2 = Ac, R^3 = CO_2Et), which with hot acid gave the hydroxytriazine (II; R = OH, R′ = Me). The coupling product (I; R = CN, R′ = CO_2Et) from indazole-3-diazonium chloride and ethyl cyanoacetate was sufficiently stable to be purified before cyclisation to the triazine (II; R = NH_2, R′ = CO_2Et). In contrast, diethyl α-methyl-α′-oxosuccinate underwent cleavage during the coupling, to form the hydrazone of ethyl pyruvate (I; R = Me, R′ = CO_2Et), which at 210° yielded the hydroxytriazine (II; R = OH, R′ = Me). The 4-methyltriazinoindazole (II; R = Me, R′ = H) was formed directly from indazole-3-diazonium chloride and acetoacetic acid, and by hydrolysis and decarboxylation of the 3-ethoxycarbonyl analogue (II; R = Me, R′ = CO_2Et) produced from indazole-3-diazoanhydride and ethyl acetoacetate.

The ultraviolet absorption spectra of triazinoindazoles (Table 1) resemble those of pyrido[1,2-*b*]indazole [1] and of β-carboline [2] with the addition of a band at 380—420 mμ which, analogously to the band at 390 mμ in cinnolines,[3] may be associated with an n–π^* transition in the –N=N– chromophore.

Prolonged boiling of the dimethyltriazine (II; R = R′ = Me), but not of its diphenyl analogue (II; R = R′ = Ph) with 10N-sodium hydroxide caused partial decomposition to 3-aminoindazole. The triazine ring was readily degraded by ketonic reagents and by vigorous reduction. In reactivity, methyl at the 3- and 4-positions resembled methyl in the corresponding cinnoline derivatives,[4] but differed from methyl in pyridazines;[5] partial bond fixation would result in poor transmission of the activating influence of the heteroatom to the 3-position. Thus the 4-methyltriazine (II; R = Me, R′ = H), in contrast with the isomeric 3-methyl derivative (II; R = H, R′ = Me), yielded a styryl derivative (II; R = CH:CHPh, R′ = H). The monostyryl derivative of the 3,4-dimethyltriazine was accordingly assigned the structure (II; R = CH:CHPh, R′ = Me). Phosphoryl chloride converted the hydroxytriazine (II; R = OH, R′ = Me) into a reactive chlorotriazine (II; R = Cl, R′ = Me).

Unexpectedly the 3,4-dimethyltriazine (II; R = R′ = Me) afforded an acetyl and a benzoyl derivative. An acetyl derivative was similarly obtained from the tetrahydrobenzotriazine (III), but not from the triazines (II; R = R′ = H or Ph; R = Cl or CH:CHPh, R′ = Me; R = Me, R′ = H; R = H, R′ = Me). Structure (V) for the acetyl derivative of (II; R = R′ = Me) appeared to be most consistent with the evidence summarised below.

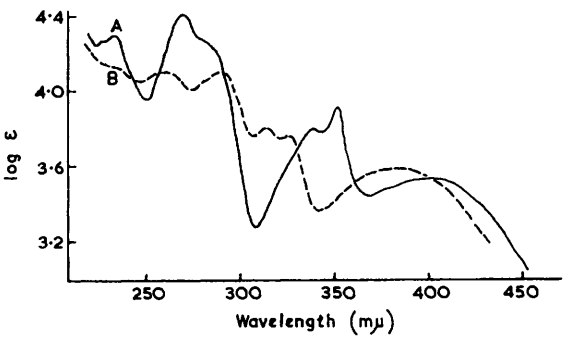
[1] Abramovitch, *Chem. and Ind.*, 1959, 422.
[2] Clemo and Felton, *J.*, 1952, 1658.
[3] Hearn, Morton, and Simpson, *J.*, 1951, 3318.
[4] Jacobs, Winstein, Henderson, and Spaeth, *J. Amer. Chem. Soc.*, 1946, **68**, 1310; Alford and Schofield, *J.*, 1953, 1811.
[5] Borsche and Klein, *Annalen*, 1941, **548**, 71; Poppenberg, *Ber.*, 1901, **34**, 3257.

Light absorption (λ in mμ) in ethanol.

Compound										
II; R = R′ = H	$\lambda_{max.}$	228	272		282 *		339	351		409
	log ε	4·31	4·42		4·22		3·73	3·78		3·44
II; R = Me, R′ = H	$\lambda_{max.}$	232	270				336	350		398
	log ε	4·24	4·39				3·77	3·85		3·50
II; R = H, R′ = Me	$\lambda_{max.}$	231	272		284		340	353		408
	log ε	4·30	4·44		4·25		3·67	3·71		3·41
III	$\lambda_{max.}$	236	270		280 *		338	352		398
	log ε	4·33	4·48		3·93		3·84	3·95		3·44
II; R = R′ = Ph	$\lambda_{max.}$	253			284			363		422
	log ε	4·27			4·55			3·98		3·61
V	$\lambda_{max.}$	242	255 *	274	285	296		350	360 *	
	log ε	4·30	4·24	4·14	4·30	4·42		4·00	3·95	
Dihydro II; R = R′ = Me	$\lambda_{max.}$	227	263	270 *		294		344		
	log ε	4·30	3·59	3·54		3·46		3·78		

* Inflexion.

The absence of an absorption band at 380—420 mμ (see Table 1) agreed with the loss of the –N=N– chromophore. *N*-Acetylation followed from its ready hydrolysis to the parent compound (II; R = R′ = Me), and from the absence of carbonyl reactions. Both the triazine (II; R = R′ = Me) and its *N*-acetyl derivative (V) with hydroxylamine and with 2,4-dinitrophenylhydrazine underwent ring fission to yield biacetyl dioxime and biacetyl bis-2,4-dinitrophenylhydrazone, respectively.



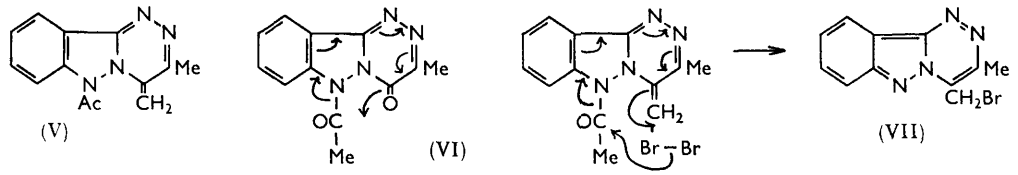
Absorption spectra of 3,4-dimethyl-1,2,4-triazino[4,3-*b*]indazole (A) and 4-acetoxy-3-methyl-1,2,4-triazino-[4,3-*b*]indazole (B) in ethanol.

Evidence for the methylene group was provided by its nuclear magnetic resonance spectrum. Two peaks assignable to methylene protons at τ 3·96 and 4·87, both split into doublets (J = 1·6 c./sec.), and two methyl peaks at τ 7·47 and 7·72 were observed. The large chemical shift between the two methylenic protons indicates a great difference in their chemical shielding; this is explained if the acetyl group is at position 6. Osmium tetroxide–periodate oxidation served to locate the methylene group; the product was identical with the 4-acetoxytriazine (II; R = OAc, R′ = Me), whose spectroscopic similarity to compound (II; R = R′ = Me) (see Figure) indicated the presence of similar chromophores and therefore of *O*-acetylation. Evidently migration of the acetyl occurred subsequently to oxidation (cf. VI).

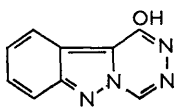
Bromination of the acetyl derivative (V) caused loss of the acetyl group and gave a readily hydrolysable monobromo-derivative (VII). In contrast, compound (II; R = R′ = Me) gave an isomeric, non-hydrolysable bromo-derivative.

Both triazines (II; R = R′ = Me or Ph), when hydrogenated in the presence of Adams catalyst or reduced with amalgamated zinc and aqueous acetic acid, furnished dihydro-derivatives. In these the absorption band at 380—420 mμ associated with the –N=N– chromophore had disappeared. Attempted syntheses of the dihydro-derivative of (II; R = R′ = Me) from 3-hydrazinoindazole and acetoin under various conditions gave low yields of the triazinoindazole (II; R = R′ = Me), owing presumably to disproportionation

of the intermediately formed hydrazone. The reduction product from the base (II; R = R′ = Me), which was readily dehydrogenated with mercuric oxide, was probably not the 1,2-dihydro-derivative, since it gave a readily hydrolysable monoacetyl derivative only. Since this acetyl dihydro-derivative was obtained both by acetylation of the reduction product of the triazine (II; R = R′ = Me) and by reduction of the 6-acetyl derivative



(V), one hydrogen atom was located at position 6. Nuclear magnetic resonance spectra of the dihydro- and dihydroacetyl derivatives indicated that a hydrogen atom was attached to the carbon at position 4 since the spectra showed quartets at τ 4·74 (J = 6·8 c./sec.), τ 4·83 (J = 7·0 c./sec.), and doublets at τ 8·42 (J = 6·8 c./sec.), τ 8·30 (J = 7·0 c./sec.), respectively. The dihydro-derivative also showed an NH peak at τ −1·0 and therefore appears to be a 4,6-dihydro-derivative.



(VIII)

Ethyl indazole-3-carboxylate readily furnished a hydrazide from which indazole-3-aldehyde was prepared by McFadyen and Stevens's method. The hydrazide evolved ammonia at 250° to yield *NN′*-di-indazol-3-ylcarbonylhydrazine which was the main product in the preparation of the triazino[4,5-*b*]indazole (VIII) from the hydrazide and ethyl orthoformate.

Biological tests carried out through the kindness of Dr. G. Woolfe of Boots Pure Drug Co. Ltd. failed to show any schistosomicidal activity in the foregoing triazinoindazoles.

Experimental

Nuclear magnetic resonance spectra were measured in 10% chloroform solution at 40 Mc. on a Perkin-Elmer spectrometer with tetramethylsilane as an internal standard.

3-*Hydrazinoindazole*.—3-Aminoindazole (18 g.), dissolved in 5N-hydrochloric acid (100 ml.), was diazotised at 5—10° with aqueous sodium nitrite (12 g. in 40 ml.). After being stirred for 30 min. and cooled to 0°, the solution was added during 30 min. to stannous chloride (60 g.) in concentrated hydrochloric acid (68 ml.), kept at 5° overnight, and filtered. The filtrate was covered with ether and made alkaline to Titan Yellow with aqueous sodium hydroxide; the crude hydrazine (10 g., 52%) was collected in ether. Crystallisation from toluene gave pale brown needles, m. p. 146—147° (decomp.), which could not be desolvated without decomposition. The *sulphate* (needles from ethanol), m. p. 152—154° (decomp.) (Found: C, 33·8; H, 4·1. $C_7H_8N_4,H_2SO_4$ requires C, 34·2; H, 4·1%), and *picrate* (needles from ethanol), m. p. 184—185° (Found: C, 41·8; H, 3·2. $C_{13}H_{11}N_7O_7$ requires C, 41·4; H, 2·9%), were used for characterisation.

With acetic anhydride on a steam-bath (1 hr.) it gave a *diacetyl derivative* (prisms from benzene), m. p. 182—183° (Found: C, 57·1; H, 5·1; N, 24·1. $C_{11}H_{12}N_4O_2$ requires C, 56·9; H, 5·2; N, 24·1%), whereas with boiling acetic anhydride it formed a *triacetyl derivative* (needles from light petroleum), m. p. 162—163·5° (Found: N, 20·6. $C_{13}H_{14}N_4O_3$ requires N, 20·4%). Interaction with benzaldehyde in boiling ethanol for 1 hr. gave a *benzylidene derivative* (needles from light petroleum), m. p. 184·5—185·5° (Found: C, 71·3; H, 5·1; N, 23·3. $C_{14}H_{12}N_4$ requires C, 71·2; H, 5·1; N, 23·7%). *p*-Anisaldehyde similarly furnished a 4-methoxybenzylidene derivative which was isolated as its *sulphate* [yellow needles, m. p. 218—220° (decomp.), from acetic acid] (Found: C, 49·0; H, 4·4. $C_{15}H_{14}N_4O,H_2SO_4$ requires C, 49·4; H, 4·4%).

At 90°, the hydrazine afforded ammonia, indazole (49%) as a sublimate, and 3-aminoindazole (39%).

1,2,4-*Triazino*[4,3-*b*]*indazole* (II; R = R′ = H).—3-Hydrazinoindazole (1 g.) in water (10 ml.) and ethanol (2 ml.), when treated with aqueous glyoxal (0·5 g. in 10 ml.) at 45° for 1 hr., gave a brown solid from which the *triazine* (0·2 g., 17%) was isolated as yellow needles (from light petroleum), m. p. 137—138° (Found: C, 63·7; H, 3·8. $C_9H_6N_4$ requires C, 63·5; H, 3·6%).

3,4-*Dimethyl*-1,2,4-*triazino*[4,3-*b*]*indazole* (II; R = R′ = Me).—(i) 3-Hydrazinoindazole (1·5 g.) and biacetyl (0·8 ml.) in boiling ethanol (10 ml.) yielded a pale brown solid (1·3 g.), m. p. 215—218° (effervescence), which when crystallised from acetic acid gave the *triazine* (0·8 g.) as yellow needles, m. p. 182—183·5° (Found: C, 66·8; H, 5·2; N, 28·2. $C_{11}H_{10}N_4$ requires C, 66·7; H, 5·1; N, 28·3%); its *picrate* (dark red needles from acetic acid) had m. p. 209—211° (Found: C, 47·9; H, 3·2; N, 22·7. $C_{17}H_{13}N_7O_7$ requires C, 47·8; H, 3·1; N, 23·0%) and the *sulphate* (brown needles from dilute sulphuric acid) had m. p. 233—234° (Found: N, 21·7. $2C_{11}H_{10}N_4,H_2SO_4,H_2O$ requires N, 21·8%). The *methiodide*, formed when the triazine was refluxed with methyl iodide in ethanol, gave red plates, m. p. 222—224°, from ethanol (Found: C, 42·0; H, 4·0; N, 16·1. $C_{12}H_{13}IN_4$ requires C, 42·3; H, 3·8; N, 16·5%).

Twenty minutes' heating of the above-mentioned solid of m. p. 215—218° (effervescence) with acetic anhydride at 80—90° gave x-*acetyl*-3-(N′-*indazol*-3-*ylhydrazono*)*butan*-2-*one* (83%), needles, m. p. 205—206° (from methanol) (Found: C, 60·8; H, 5·1; N, 21·9. $C_{13}H_{14}N_4O_2$ requires C, 60·5; H, 5·4; N, 21·7%). When crystallised from hot dilute hydrochloric acid and triturated with ammonia, the compound, m. p. 215—218° (effervescence), furnished the triazine (70%), m. p. and mixed m. p. 182—183·5°. The foregoing acetyl derivative (0·2 g.), when refluxed for 40 min. with 2N-sulphuric acid (8 ml.), deposited the triazinoindazole sulphate (0·18 g.), m. p. and mixed m. p. 233—234°.

(ii) Ethyl methylacetoacetate (1·4 ml.) was kept for 24 hr. in aqueous potassium hydroxide (0·6 g. in 25 ml.); concentrated hydrochloric acid (0·9 ml.) and indazole-3-diazoanhydride [6] (1·5 g.) in ethanol (20 ml.) were added at 5°. The solid product, m. p. 215—218° (effervescence), gave the same triazine (1·8 g., 80%) after being cyclised in hot dilute hydrochloric acid.

3,4-*Diphenyl*-1,2,4-*triazino*[4,3-*b*]*indazole* (II; R = R′ = Ph).—3-Hydrazinoindazole (1·5 g.) and benzil (2·1 g.) were refluxed together in acetic acid (15 ml.) for 45 min. The resulting *triazine* (2·1 g.) (yellow needles from butan-1-ol) had m. p. 272—274° (Found: N, 17·3. $C_{21}H_{14}N_4$ requires N, 17·4%). A mixture of this triazine (0·8 g.), amalgamated zinc (2 g.), concentrated hydrochloric acid (2 ml.), acetic acid (10 ml.), and water (1 ml.) was refluxed for 30 min. and filtered whilst hot. Stilbene (0·19 g.) separated from the filtrate; 3-aminoindazole (0·18 g.) was recovered by ether-extraction of the neutralised mother-liquor.

1,2,3,4-*Tetrahydrobenzo*-1,2,4-*triazino*[4,3-*b*]*indazole* (III).—3-Hydrazinoindazole (1·5 g.) and cyclohexane-1,2-dione (1·3 g.) were refluxed in ethanol; an orange solid rapidly separated and redissolved during 30 minutes' heating. The *benzotriazine* (1·8 g.) (golden prisms, m. p. 167—168°, from ethanol) separated from the cooled solution (Found: C, 69·9; H, 5·5; N, 25·2. $C_{13}H_{12}N_4$ requires C, 69·6; H, 5·4; N, 25·0%). With boiling acetic anhydride, it afforded an *acetyl derivative* (72%) (pale brown needles, m. p. 136—137°, from ethanol) (Found: C, 67·8; H, 5·2; N, 21·3. $C_{15}H_{14}N_4O$ requires C, 67·7; H, 5·3; N, 21·0%).

4-*Methyl*-1,2,4-*triazino*[4,3-*b*]*indazole* (II; R = Me, R′ = H).—(i) 3-Aminoindazole (5·3 g.) dissolved in 5N-hydrochloric acid (32 ml.) was diazotised at 0° with aqueous sodium nitrite (2·9 g. in 20 ml.). A solution of acetoacetic acid prepared from ethyl acetoacetate [7] (5·4 ml.) and cooled to 0° was added, followed immediately by sodium acetate (22 g.) in water (50 ml.). After being stirred for 3 hr., the suspension was kept at 60—70° for 10 min. The red precipitate was digested with cold 2N-hydrochloric acid (75 ml.) overnight, then neutralised with aqueous ammonia, and the insoluble *triazine* (4 g., m. p. 232—234°) was recrystallised, forming golden needles, m. p. 236—238° (decomp.), from methanol (Found: C, 65·0; H, 4·3; N, 30·3. $C_{10}H_8N_4$ requires C, 65·2; H, 4·4; N, 30·4%).

(ii) The ester (II; R = Me, R′ = CO_2Et) (1·1 g.), after being hydrolysed by 1 hour's boiling in 2N-hydrochloric acid, gave an acid which underwent decarboxylation on recrystallisation from butan-1-ol, to yield the triazine (0·6 g.), m. p. and mixed m. p. 236—238° (decomp.).

(iii) 3-Hydrazinoindazole (0·18 g.) and pyruvaldoxime (0·1 g.) were refluxed (30 min.) in acetic acid (2 ml.), hydrochloric acid (0·15 ml.) was added, and refluxing was continued for 30 min. The residue from vacuum-evaporation was treated with aqueous ammonia and

[6] Bamberger, *Ber.*, 1899, **32**, 1773.
[7] Reynolds and VanAllen, *Org. Synth.*, 1952, **32**, 84.

crystallised from light petroleum, to give the same triazine (0·07 g.), m. p. and mixed m. p. 235—236° (decomp.).

3-Methyl-1,2,4-triazino[4,3-b]indazole (II; R = H, R′ = Me).—3-Hydrazinoindazole sulphate (2·5 g.) was added during 30 min. at 20° to pyruvaldehyde diethyl acetal [8] (1·5 g.) in methanol (80 ml.) and water (30 ml.). After 2 hr., solvent (60 ml.) was removed and the *methyltriazine* (0·9 g.) (yellow plates, m. p. 188—189°, from benzene–light petroleum) was collected (Found: C, 64·8; H, 4·0; N, 30·1. $C_{10}H_8N_4$ requires C, 65·2; H, 4·4; N, 30·4%).

Ethyl 4-Methyl-1,2,4-triazino[4,3-b]indazole-3-carboxylate (II; R = Me; R′ = CO_2Et).—Indazole-3-diazoanhydride (2·5 g.) and ethyl acetoacetate (2·2 ml.), dissolved in ethanol (35 ml.), reacted exothermally. The solid, deposited during 24 hr., afforded this *triazine* (3·5 g.) as yellow needles (from light petroleum), m. p. 149—150° (Found: C, 61·1; H, 4·7; N, 21·9. $C_{13}H_{12}N_4O_2$ requires C, 60·9; H, 4·7; N, 21·9%). Its *hydrazide* (orange needles from acetic acid) had m. p. 291—293° (decomp.) (Found: C, 55·0; H, 4·4; N, 34·5. $C_{11}H_{10}N_6O$ requires C, 54·5; H, 4·2; N, 34·7%). The *hydroxamic acid* (golden plates, m. p. 220—221°, from acetic acid) separated immediately when the ester and hydroxylamine hydrochloride in ethanol and pyridine were heated (Found: C, 54·5; H, 3·7; N, 29·0. $C_{11}H_9N_5O_2$ requires C, 54·3; H, 3·7; N, 28·8%).

Ethyl 4-Amino-1,2,4-triazino[4,3-b]indazole-3-carboxylate (II; R = NH_2; R′ = CO_2Et).—3-Aminoindazole (5·3 g.), diazotised at 0—5° in 5N-hydrochloric acid (32 ml.) with sodium nitrite (2·9 g.) during 30 min., was stirred at 0° for 30 min. and added during 5 min. at 0° to ethyl cyanoacetate (5·0 g.) in ethanol (20 ml.). Sodium acetate trihydrate (21·8 g.) in water (50 ml.) was immediately added and stirring was continued for 2 hr. The precipitate [9·5 g.; m. p. 187—189° (with resolidification)] afforded pure *ethyl α-cyano-α-(N′-indazol-3-ylhydrazono)-glyoxylate*, which had m. p. 188—190° (with resolidification) when recrystallised from toluene, and $\lambda_{max.}$ 271, 380 mμ (log ε 3·79 and 4·25, respectively) (Found: C, 56·0; H, 4·4; N, 27·2. $C_{12}H_{11}N_5O_2$ requires C, 56·0; H, 4·3; N, 27·2%). A solution of the hydrazone (6 g.) in acetic acid (50 ml.), when refluxed for 2 hr., deposited the *triazinoindazole* [5·6 g.; m. p. 260—262° (decomp.)] which crystallised from toluene as yellow plates, m. p. 262—264° (decomp.), $\lambda_{max.}$ 257, 290 (infl.), 379 mμ (log ε 4·34, 3·94, and 4·18, respectively) (Found: C, 56·1; H, 4·6; N, 27·2. $C_{12}H_{11}N_5O_2$ requires C, 56·0; H, 4·3; N, 27·2%).

Ethyl 2-indazol-3′-ylazo-2-methylacetoacetate (IV; R^1 = Me, R^2 = Ac, R^3 = CO_2Et) (colourless prisms, m. p. 197—198°, from ethanol) crystallised when indazole-3-diazoanhydride (1·5 g.) and ethyl methylacetoacetate (1·4 ml.) were kept in ethanol (30 ml.) for 24 hr. (yield, 1·7 g.) (Found: C, 58·2; H, 5·7; N, 19·4. $C_{14}H_{16}N_4O_3$ requires C, 58·3; H, 5·6; N, 19·4%).

Ethyl α-Indazol-3-ylazopropionate (IV; R^1 = H, R^2 = Me, R^3 = CO_2Et).—Indazole-3-diazoanhydride (1·5 g.) and diethyl α-methyl-α′-oxosuccinate (2 ml.), when kept overnight in ethanol (20 ml.), gave the *azopropionate* (colourless needles from light petroleum), m. p. 182—183° (Found: C, 58·3; H, 5·7; N, 23·0. $C_{12}H_{14}N_4O_2$ requires C, 58·5; H, 5·7; N, 22·8%).

4-Hydroxy-3-methyl-1,2,4-triazino[4,3-b]indazole (II; R = OH, R′ = Me).—(i) Ethyl α-indazol-3-ylazopropionate (1 g.) was heated at 210° until completely resolidified (30 min.) and crystallised from dimethylformamide to give the *hydroxytriazine* (0·6 g.) as yellow cubes, m. p. 348—350° (Found: C, 60·3; H, 4·1; N, 27·6. $C_{10}H_8N_4O$ requires C, 60·0; H, 4·0; N, 28·0%). Its *acetyl derivative* (yellow needles from ethanol) had m. p. 221—223°, $\lambda_{max.}$ 258, 290, 314, 325, and 383 mμ (log ε 4·11, 4·10, 3·81, 3·77, and 3·59, respectively) (Found: C, 59·5; H, 4·2; N, 23·2. $C_{12}H_{10}N_4O_2$ requires C, 59·5; H, 4·2; N, 23·1%).

(ii) Ethyl 2-indazol-3′-ylazo-2-methylacetoacetate (1 g.), when refluxed in 20% hydrochloric acid (60 ml.) for 1 hr., yielded a precipitate from which the same hydroxytriazine (0·55 g.) was isolated by crystallisation from acetic acid.

4-Chloro-3-methyl-1,2,4-triazino[4,3-b]indazole.—The foregoing hydroxy-compound (1 g.) was refluxed in phosphoryl chloride (8 ml.) and dimethylaniline (0·8 ml.) for 6 hr. When quenched in ice, the mixture gave a black solid from which the *chlorotriazine* (0·42 g.) was isolated by extraction with cold chloroform, filtration through charcoal, removal of the solvent, and crystallisation from light petroleum; it had m. p. 177—178·5° (Found: C, 54·7; H, 3·2; N, 25·2; Cl, 16·1. $C_{10}H_7ClN_4$ requires C, 54·9; H, 3·2; N, 25·6; Cl, 16·2%). With piperidine in dry acetone, this afforded a *1-piperidyl derivative* (II; R = NC_5H_{10}, R′ = Me) (yellow needles from light petroleum), m. p. 167—168° (Found: C, 67·3; H, 6·6. $C_{15}H_{17}N_5$ requires C, 67·4; H, 6·4%).

[8] Braude and Evans, *J.*, 1955, 3324.

Reactions of the Dimethyltriazine (II; R = R′ = Me).—(i) When this triazine was kept for 1 hr. in ethanol with 2,4-dinitrophenylhydrazine, biacetyl bis-2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 314—315°, separated.

(ii) One hour's boiling with hydroxylamine hydrochloride in ethanol and pyridine yielded biacetyl dioxime, m. p. and mixed m. p. 234°.

(iii) The triazine (0·4 g.) was boiled with 10N-sodium hydroxide (20 ml.) for 5 hr. Unattacked triazine (0·14 g.) was removed by filtration; the soluble products, collected in ether, furnished 3-aminoindazole (0·12 g.).

(iv) Reduction with amalgamated zinc as described for the 3,4-diphenyl analogue gave 3-aminoindazole (66%).

(v) Addition of an excess of bromine water to a solution in dilute hydrochloric acid at 40° gave a red solid which, after trituration with aqueous sodium hydrogen carbonate and crystallisation from light petroleum, afforded a yellow *bromo-derivative*, m. p. 193—194° (Found: C, 47·9; H, 3·2; Br, 28·5; N, 19·9. $C_{11}H_9BrN_4$ requires C, 47·7; H, 3·3; Br, 28·9; N, 20·2%).

3-Methyl-4-styryl-1,2,4-triazino[4,3-b]indazole (II; R = CH:CHPh, R′ = Me). Dry hydrogen chloride was passed into the 3,4-dimethyltriazine (II; R = R′ = Me) (1 g.) in benzaldehyde (6 ml.) at 155° for 90 min. The precipitated *styryl derivative* (1·3 g.) (red needles, m. p. 216—218°, from light petroleum) was triturated with benzene and aqueous ammonia (Found: C, 75·3; H, 4·9; N, 19·9. $C_{18}H_{14}N_4$ requires C, 75·5; H, 4·9; N, 19·6%).

4-Styryl-1,2,4-triazino[4,3-b]indazole (II; R = CH:CHPh, R′ = H) was analogously prepared (96%) from the 4-methyltriazine (II; R = Me, R′ = H) and crystallised from methanol as red needles, m. p. 194—196° (Found: C, 75·4; H, 4·4; N, 20·4. $C_{17}H_{12}N_4$ requires C, 75·0; H, 4·4; N, 20·6%).

6-Acetyl-3-methyl-4-methylene-1,2,4-triazino[4,3-b]indazole (V) (1·7 g., 70%) (pale green needles, m. p. 156—157°, from light petroleum) separated when the triazine (II; R = R′ = Me) (2 g.) was refluxed with acetic anhydride (15 ml.) for 1 hr. and cooled [Found: C, 64·7; H, 4·9; N, 23·1%; *M* (Rast), 216. $C_{13}H_{12}N_4O$ requires C, 65·0; H, 5·0; N, 23·3%; *M*, 240]. The same compound (1·6 g.) was produced when acetyl chloride (0·4 ml.) and pyridine were used for the acetylation.

Hydrolysis of this product (V) with aqueous-ethanolic sodium hydroxide or 10% sulphuric acid yielded the 3,4-dimethyltriazine (II; R = R′ = Me), m. p. and mixed m. p. 182—183·5°, or its sulphate, m. p. and mixed m. p. 233—234°.

To a solution of product (V) (0·72 g.) in ether (100 ml.), water (40 ml.) and osmium tetroxide (0·1 g.) were added and the mixture was stirred for 20 min. Sodium metaperiodate (2·5 g.) was added during 40 min. After 4 days' stirring, a dark green material was recovered by ether-extraction and fractionally crystallised from ethanol to give starting material (0·33 g.) and the acetoxytriazine (II; R = OAc, R′ = Me) (0·09 g.), m. p. and mixed m. p. 221—223°, $\lambda_{max.}$ 258, 290, 314, 326, and 384 mμ (log ε 4·12, 4·10, 3·79, 3·76, and 3·60, respectively).

A solution of product (V) in carbon tetrachloride, when shaken with an excess of bromine water, afforded a red solid, which became yellow when triturated with sodium hydrogen carbonate, giving a *bromomethyl derivative* (VII) [brown plates, m. p. 162—165° (decomp.), from light petroleum] (Found: C, 47·8; H, 3·4; Br, 28·5; N, 20·1. $C_{11}H_9BrN_4$ requires C, 47·7; H, 3·3; Br, 28·9; N, 20·2%). With boiling aqueous sodium hydroxide, this compound gave bromide and, with piperidine in acetone, piperidine hydrobromide, m. p. and mixed m. p. 235°.

4,6-Dihydro-3,4-dimethyl-1,2,4-triazino[4,3-b]indazole.—(i) Hydrogenation of the triazine (II; R = R′ = Me) (0·5 g.) in ethanol (100 ml.) with Adams catalyst (25 mg.) led to the uptake of 1 mol. of hydrogen and afforded the *dihydro-derivative* (0·4 g.) (colourless needles, m. p. 231—233°, from benzene) on removal of the solvent (Found: C, 66·1; H, 6·3; N, 27·6. $C_{11}H_{12}N_4$ requires C, 66·0; H, 6·0; N, 28·0%). The nuclear magnetic resonance spectrum of this compound was determined in dimethyl sulphoxide (see above).

(ii) A suspension of amalgamated zinc wool (2 g.) in 40% acetic acid (7 ml.) containing the triazine (0·5 g.), when refluxed until pale green, gave the same dihydro-derivative (0·33 g.), m. p. and mixed m. p. 231—233°.

The dihydro-derivative (0·2 g.) in dry toluene (50 ml.) was refluxed for 12 hr. with mercuric oxide (4·3 g.). Removal of the solvent from the filtrate and crystallisation of the residue from light petroleum gave the triazinoindazole (II; R = R′ = Me) (0·12 g.), m. p. and mixed m. p. 181—183°.

Dihydro-3,4-diphenyl-1,2,4-triazino[4,3-b]indazole (colourless needles, m. p. 266—268°, from benzene) was prepared by analogous catalytic and chemical reductions (Found: C, 77·6; H, 5·3. $C_{21}H_{16}N_4$ requires C, 77·8; H, 5·0%). Its *acetyl derivative* (needles from methanol) had m. p. 168—169° (Found: C, 75·0; H, 4·8; N, 15·5. $C_{23}H_{18}N_4O$ requires C, 75·4; H, 4·9; N, 15·3%).

6-Acetyl-4,6-dihydro-3,4-dimethyl-1,2,4-triazino[4,3-b]indazole.—(i) Hydrogenation of the acetyl derivative (V) with Adams catalyst in ethanol resulted in the uptake of 1 mol. of hydrogen. The *dihydro-derivative* (needles, m. p. 129—130·5°, from light petroleum) separated on evaporation of most of the ethanol and had $\lambda_{max.}$ 243 (infl.) 271, 282, 308, and 318 mμ (log ε 3·96, 3·82, 3·79, 3·94, and 4·02, respectively) (Found: C, 64·6; H, 5·5; N, 23·1. $C_{13}H_{14}N_4O$ requires C, 64·4; H, 5·8; N, 23·1%).

(ii) One hour's boiling of the dihydrodimethyltriazine with acetic anhydride furnished the same compound, m. p. and mixed m. p. 129—130·5°, $\lambda_{max.}$ 243 (infl.), 271, 282, 308, and 318 mμ (log ε 3·96, 3·81, 3·78, 3·94, and 4·02, respectively).

On hydrolysis with aqueous-ethanolic alkali, this compound gave the dihydrodimethyltriazine (80%), m. p. and mixed m. p. 231—233°.

6-Benzoyl-3-methyl-4-methylene-1,2,4-triazino[4,3-b]indazole (0·5 g.) separated from a cooled and concentrated mixture of the triazine (II; R = R′ = Me) (0·5 g.), pyridine (8 ml.), and benzoyl chloride (0·25 ml.) which had been refluxed for 1 hr.; after crystallisation from ethanol it had m. p. 192·5—194° (Found: C, 71·5; H, 5·0; N, 18·4. $C_{18}H_{14}N_4O$ requires C, 71·5; H, 4·7; N, 18·5%).

Indazole-3-aldehyde.—Ethyl indazole-3-carboxylate [9] (5 g.) was heated on a steam-bath with 99% hydrazine hydrate (7·5 ml.) for 4 hr. *3-Hydrazinocarbonylindazole* (4·1 g.) (needles from water) which separated had m. p. 220—222° (Found: C, 54·9; H, 4·7; N, 31·5. $C_8H_8N_4O$ requires C, 54·5; H, 4·6; N, 31·8%). Its *benzenesulphonyl derivative* (orange needles from aqueous ethanol) had m. p. 238—241° (Found: C, 53·1; H, 4·2; N, 17·6. $C_{14}H_{12}N_4O_3S$ requires C, 53·2; H, 3·8; N, 17·7%). This derivative (1·4 g.) in ethylene glycol (15 ml.) was heated with sodium carbonate (2·5 g.) at 150° for 90 sec. and hot water (70 ml.) was added. *Indazole-3-aldehyde* (0·36 g.), isolated by ether-extraction and crystallisation from benzene–light petroleum, had m. p. 125—127° (Found: C, 66·2; H, 4·0. $C_8H_6N_2O$ requires C, 65·8; H, 4·1%). When heated at 250° for 1 hr., the foregoing hydrazide melted, resolidified, and yielded *NN′-di-indazol-3-ylcarbonylhydrazine* (colourless needles from dimethylformamide), m. p. 367—370° (decomp.) (C, 59·9; H, 3·6; N, 26·3. $C_{16}H_{12}N_6O_2$ requires C, 60·0; H, 3·8; N, 26·2%).

1-Hydroxy-1,2,4-triazino[4,5-b]indazole (VIII).—3-Hydrazinocarbonylindazole (1 g.) was boiled with ethyl orthoformate (20 ml.) for 6 hr., whilst products volatile below 100° were removed. Ethyl orthoformate (15 ml.) was distilled off, the residue was stirred with dilute hydrochloric acid (15 ml.), and the resulting solid (0·6 g.) then furnished as an ethanol-soluble fraction (0·15 g., 17%), the *hydroxytriazine* (needles from ethanol), m. p. 240—242° (Found: C, 57·8; H, 3·0; N, 30·2. $C_9H_6N_4O$ requires C, 58·1; H, 3·3; N, 30·1%). The ethanol-insoluble fraction (0·39 g.) was *NN′*-di-indazol-3-ylcarbonylhydrazine, m. p. and mixed m. p. 367—370° (decomp.).

Interaction of the hydrazide with ethyl orthoformate (2 mol.) at 130° for 4 hr. gave material, m. p. 125—127°, for which consistent analytical results could not be obtained. Crystallisation of this material from aqueous acetone afforded *N-indazol-3-ylcarbonyl-N′-isopropylidenehydrazine* (needles, m. p. 296—300°, from ethanol) (Found: C, 61·3; H, 5·9; N, 25·9. $C_{11}H_{12}N_4O$ requires C, 61·1; H, 5·6; N, 25·9%).

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[9] von Auwers and Dereser, *Ber.*, 1919, **52**, 1340.