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INDAZOLES IN ORGANIC SYNTHESIS

FORMATION OF SOME FUSED HETEROCYCLES[1]

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Abstract—Derivatives of pyrimido(1,2-b)indazole and of s-triazino(1,2-b)indazole were prepared by several different routes and some transformations are described.

Recently we have described the synthetic utility of 3-diazo-3H-indazoles in formation of indazolo(3,2-c)-1,2,4-triazines.[2] Further experiments towards the formation of heterocyclic systems based on indazoles are described here.

3-Aminoindazole (**1**) reacted with 1,3-keto esters in the presence of triethylamine at 150° or, advantageously, in the presence of polyphosphoric acid at moderate temperature to give derivatives of pyrimido (1,2-b)indazol-4-one (**2**). In another synthetic route diethyl ethoxymethylenemalonate was used and the condensation product **3** underwent thermal cyclization to the corresponding tricyclic compound (**2**). Furthermore, **1** reacted with N,N-dimethylformamide dimethyl acetal to give the corresponding dimethylaminomethyleneamino derivative (**4**) which subsequently formed the hydroxyiminomethyleneamino compound (**5**). Attempts to convert the later compound into triazoloindazole failed, although these reactions were successful in the formation of fused triazoles to several other heterocycles.[3]

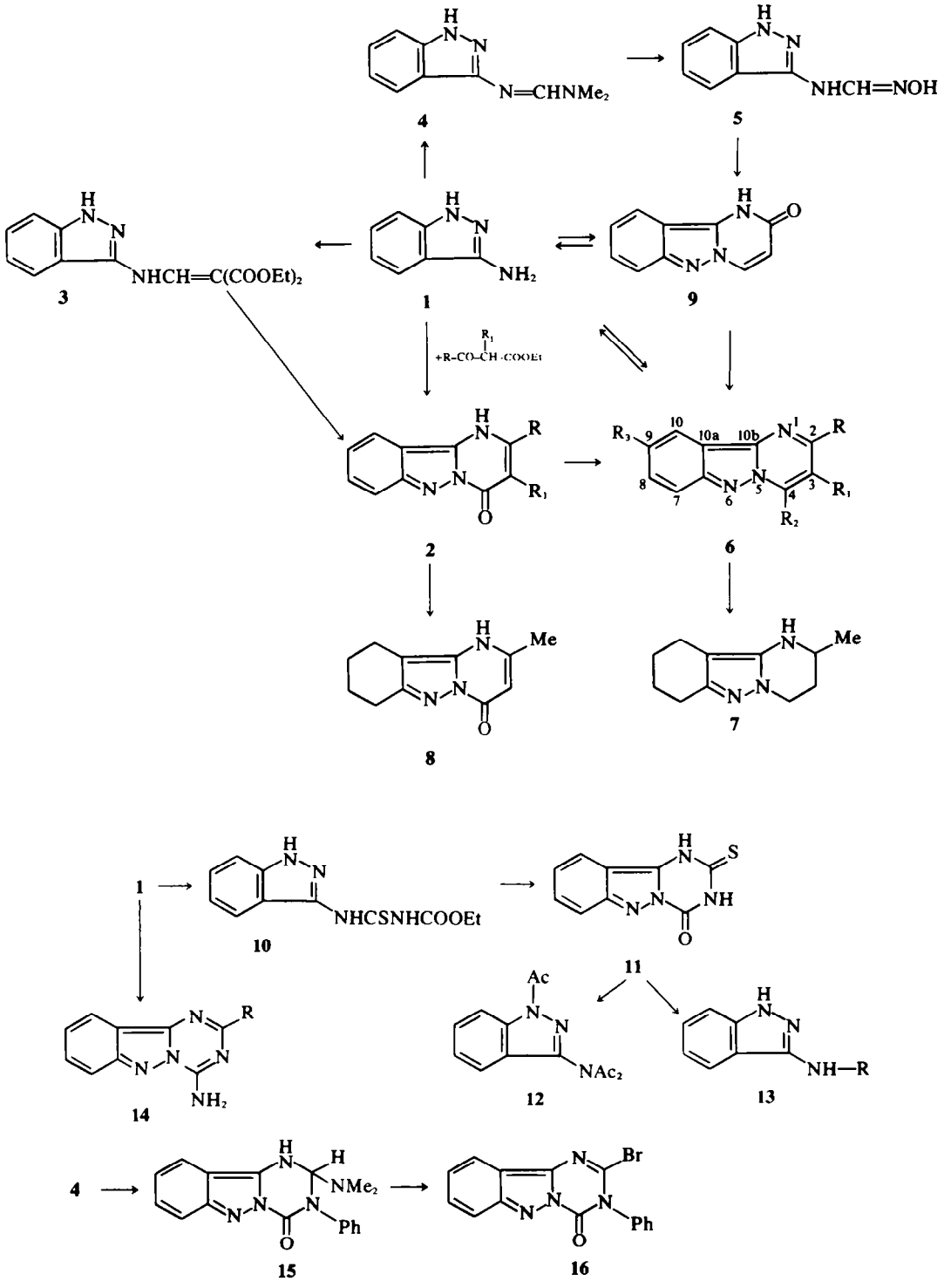
Pyrimido(1,2-b)indazol-4-ones (**2**) when treated with phosphorus oxychloride in the presence of N,N-dimethylaniline were converted into the corresponding 4-chloro compounds (**6**, $R_2 = Cl$) and subsequent dehalogenation afforded the corresponding pyrimido (1,2-b)-indazoles (**6**, $R_2 = H$). The parent compound is otherwise obtainable from pyrimido(1,2-b)indazol-2-one (**9**) via the 2-chloro derivative (**6**, $R = Cl$, $R_1 = R_2 = R_3 = H$). Moreover, pyrimido(1,2-b)indazole and its 2-Me analog may be obtained directly from 3-aminoindazole and 1,1,3,3-tetraethoxypropane or 1,1-diethoxy-3-butanone, respectively.

Interesting is the behaviour of **2** and **6** towards reduction. Hydrogenation of **6** ($R = Me$, $R_1 = R_2 = R_3 = H$) gave the octahydro derivative **7**, whereas the corresponding 4-one (**2**, $R = Me$, $R_1 = H$) afforded under the same conditions the 7,8,9,10-tetrahydro derivative **8**.

Pyrimido(1,2-b)indazolo-2-one (**9**) was obtained earlier,[4] but it was stated that it was not possible to differentiate between the alternative structure of a 2-one or a 4-one. Later, some further investigations on this system,[5] based on UV spectral correlations and dehydrogenation of the 7,8,9,10-tetrahydro derivative, favoured the 2-one structure for the compound obtained from **1** and ethyl propiolate. However, one can easily differentiate between the alternative 2- and 4-one structures by means of the NMR data, similar to the case of pyrimido (1,2-b)pyridazines.[6] The coupling constant, $J_{3,4}$, of **6** ($R = Me$, $R_1 = R_2 = R_3 = H$), prepared from the corresponding 4-one (**2**, $R = Me$, $R_1 = H$) via the 4-chloro compound, is of the same magnitude as that of **9**. This is consistent with the observation of bond localization which consequently influences the magnitude of $J_{2,3}$ and $J_{3,4}$ ($J_{3,4} > J_{2,3}$)[6] and this is observed also in the case of pyrimido(1,2-b)indazole, i.e. $J_{2,3} = 5{\cdot}0$ and $J_{3,4} = 7{\cdot}5$ Hz. Moreover, $J_{3,4}$ in **6** ($R = R_1 = R_2 = R_3 = H$) is of the same magnitude as in the 2-one (**9**) from which it was prepared via the 2-chloro compound **6** ($R = Cl$, $R_1 = R_2 = R_3 = H$) after dehalogenation.

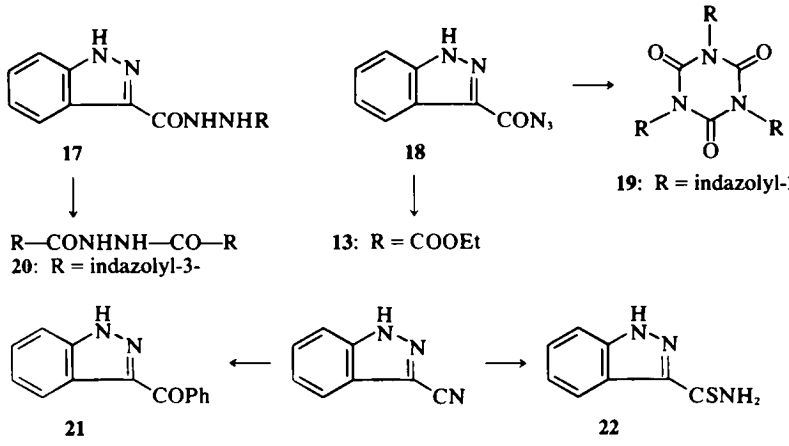
It is of interest to note that either pyrimido(1,2-b)indazole or its 2-one (**9**) when heated with hydrazine hydrate were reconverted into **1**. On the other hand, bromination of 2-chloropyrimido-(1,2-b)indazole or the 2-methyl-4-chloro analog afforded the corresponding 9-bromo derivatives (**6**, $R_3 = Br$). This is of interest when compared with the bromination of the related bicyclic analog, pyrazolo(1,5-a)pyrimidine. In this case bromine enters the pyrazole ring at position 3 and further electrophilic substitution gives the 3,6-dibromo derivative, the second bromine entering the pyrimidine ring at position *meta* to both nitrogens.[7] The observed reaction path revealed that the benzene ring of the tricyclic system underwent easier electrophilic substitution in comparison with position 3 at the pyrimidine ring of **6**, otherwise also susceptible for electrophilic substitutions.

Derivatives of different triazinoindazoles have been described in the literature and our interest was focused on the synthesis of the s-triazino(1,2-b)-indazole system. Such compounds have been obtained from s-triazinobenzotriazines or by cyclodeamination or thermolysis of certain s-triazine derivatives.[8] In all these transformations the pyrazole ring of the tricycle was formed in the last step. We have developed some syntheses based on 3-aminoindazole as starting material. Reaction of **1** with ethoxycarbonyl isothiocyanate afforded the corresponding thiourea derivative (**10**) and subsequent cyclization in the presence of sodium ethylate gave the s-triazino-(1,2-b)indazole derivative (**11**). This compound, when treated with acetic anhydride gave **12**, whereas in the presence of alkali indazolylthiourea (**13**, $R = CSNH_2$) was formed. The later gave then **13** ($R = CN$). Furthermore, **1** reacted with dicyandiamide to form the 2,4-diaminotriazine derivative (**14**, $R = NH_2$), obtained previously from 2,4-diamino-6-(2-hydrazinophenyl)-s-triazine.[8] By another method, the tricyclic compound **15** was obtained in a 2 + 4 cycloaddition reaction from **4** and phenyl isocyanate. The alternative structures of 1- or 2-phenylaminocarbonyl derivatives of **4** are eliminated since no hydrolytic cleavage with alkali, characteristic for di-



methylaminomethyleneamino compounds, could be observed. Compound **15** is stable and with alkali the anticipated 2,4-dione could not be obtained. However, with bromine in acetic acid the compound is dehydrogenated to give **16**. Finally, compound **14** (R = H) could be prepared from **1** and ethyl N-cyanoimidate. After a shorter reaction time, however, the intermediate N-cyano-N'-(indazolyl-3)-formamidine (**13**, R = CH=NCN) was obtained and it was thermally cyclized to the triazine derivative. It should be noted that the 4-amino group could not be diazotized.

From the hydrazide of indazole-3-carboxylic acid (**17**, R = H) the corresponding azide (**18**) could be prepared in the conventional manner. In attempted Curtius rearrangement to indazolyl isocyanate this compound could not be isolated and instead tris-indazolyl-3-s-triazinetrione (**19**) was obtained. The mass spectrum of **19** exhibited a strong peak at $m/e = 159$ corresponding to the indazolyl-3-isocyanate. However, the compound does not react with ethanol and its IR spectrum shows no absorption at about 2100 cm^{-1} which would be expected for an isocyanate. The formation of **19**, although under relatively mild condi-



tions, is consistent with the known formation of triazines from isocyanates.[9] The Curtius rearrangement of **18** occured also in ethanol and the corresponding urethane (**13**, R = COOEt) was obtained.

Attempts have been made to condense **17** (R = H) with β-keto esters in order to obtain new cyclic systems. Whereas the reaction with ethyl acetoacetate afforded only the corresponding acrylate (**17**, R = –C(Me)=CHCOOEt), with the analogous ethyl benzoylacetate a completely different reaction course was observed. Here, N,N'-bis-indazolyl-3'-hydrazine (**20**) was formed. The ready formation of this compound could be observed also from an attempt to cyclise the above acrylate or 1-(indazolyl-3')-4-phenylsemicarbazide (**17**, R = CONHPh). Apparently, the formation of **20** is the preferential transformation, although it is known that acylhydrazides are usually transformed into dihydrazides after prolonged heating above their m.ps.[10]

EXPERIMENTAL

M.ps were determined on a Kofler apparatus. Spectral data were obtained from a Jeol-C-60HL NMR spectrometer and Hitachi-Perkin-Elmer RMU-6L mass spectrometer.

General procedure for the preparation of pyrimido(1,2-b)*indazol-4*(1*H*)*-ones* (**2**). (a) A mixture of **1**,[11,12] (0·5 g), the corresponding β-keto ester (3–4 ml) and polyphosphoric acid (85% P_2O_5); 10 g) was heated on an oil bath at 60–80° for 4 hr until a clear soln was obtained. The cooled mixture was treated with 20–50 ml water and neutralized with solid $NaHCO_3$ until pH 4. The product was filtered off and crystallized from EtOH.

(b) Alternatively, the same amount of aminoindazole and the β-keto ester as above, and 1 ml of triethylamine were heated on an oil bath at 150° for 7–15 hr. The product was filtered off or, alternatively, excess β-keto ester and triethylamine were distilled off *in vacuo* and after addition of EtOH the product separated. The products were crystallized from EtOH.

In this manner the following compounds were prepared:

Compound **2** (R = Me, R_1 = H) in 35% yield (13% for procedure (b) and the product was accompanied with a small amount of the uncyclized product as evidenced from spectroscopic data), m.p. 325° (dec.). Mass spectrum: M⁺ = 199; NMR (DMSO-d_6): τ = 4·12 (s, H_1), 2·05 (m, H_7), 2·80 (m, $H_{8,9,10}$), 7·59 (s, Me), 3·40 (broad, NH). (Found: C, 66·64; H, 4·93; N, 21·30. Calc. for $C_{11}H_9N_3O$: C, 66·32; H, 4·55; N, 21·30%).

Compound **2** (R = Ph, R_1 = H) in 38% yield, m.p. 319° (dec). Mass spectrum: M⁺ = 261; NMR (DMSO-d_6, 85°): τ = 3·27 (s, H_3), 1·80 and 2·50 (m, Ph and $H_{7,8,9,10}$). (Found: C, 73·50; H, 4·34; N, 16·30. Calc. for $C_{16}H_{11}N_3O$: C, 73·55; H, 4·24; N, 16·08%).

Compound **2** (R = CH_2COOEt) in 39% yield, m.p. 235–239°. Mass spectrum: M⁺ = 271; NMR (DMSO-d_6, 180°): τ = 3·83 (s, H_3), 2·0 (m, H_7), 2·70 (m, $H_{8,9,10}$), 5·82 (q, CH_2CH_3), 8·70 (t, CH_2CH_3), 6·17 (s, $-CH_2CO-$), J_{Et} = 7·3 Hz.

Compound **2** (R = R_1 = $-(CH_2)_3-$) in 12% yield, m.p. 318° (dec). Mass spectrum: M⁺ = 225; NMR (DMSO-d_6, 150°): τ = 2·10 (m, H_8), 2·75 (m, $H_{9,10,11}$), 7·90 (m, 3-CH_2), 7·10 (m, 2-CH_2, 4-CH_2). (Found: C, 69·67; H, 4·92; N, 18·75. Calc. for $C_{13}H_{11}N_3O$: C, 69·32; H, 4·92; N, 18·66%).

Compound **2** (R = R_1 = $-(CH_2)_4-$) in 25% yield, m.p. 317° (dec). Mass spectrum: M⁺ = 239; NMR (DMSO-d_6, 150°): τ = 2·05 (m, H_9), 2·80 (m, $H_{10,11,12}$), 8·20 (m, 3-CH_2, 4-CH_2), 7·30 (m, 2-CH_2, 5-CH_2). (Found: N, 17·22. Calc. for $C_{14}H_{13}N_3O$: N, 17·56%).

Diethyl N-(*indazolyl-3*)*aminomethylenemalonate* (**3**). A mixture of 3-aminoindazole (1·36 g) and diethyl ethoxymethylenemalonate (2·2 g) was heated under reflux. After about 30 min a ppt separated, it was crystallized from EtOH, m.p. 153–156° (yield 45%). Mass spectrum: M⁺ = 303; NMR (DMSO-d_6): τ = 2·25 (n, H_7), 2·75 (m, $H_{4,5,6}$), 1·25 (d, CH), 8·74 and 8·69 (t, CH_2CH_3), 5·86 and 5·73 (q, CH_2CH_3), −0·9 (broad s, NH–CH), −2·65 (broad s, NH), J_{Et} = 7·2, J_{CHNH} = 8 Hz. (Found: C, 59·66; H, 5·62; N, 13·76; Calc. for $C_{15}H_{17}N_3O_4$: C, 59·39; H, 5·65; N, 13·86%).

3 - *Carbethoxy-pyrimido*(1,2-b)*indazol-4*(1H)*-one* (**2**, R = H, R_1 = COOEt). Compound **3** (0·5 g) and diphenylether (1 g) were heated on an oil bath at 160° for 1 hr. The product was filtered off. It was insoluble in water, MeOH or EtOH, m.p. 315° (yield 73%). Mass spectrum: M⁺ = 257; NMR (DMSO-d_6, 115°): τ = 1·25 (s, H_2), 2·80 (m, $H_{7,8,9,10}$), 5·85 (q, CH_2CH_3), 8·66 (t, CH_2CH_3), J_{Et} = 7 Hz. (Found: C, 60·46; H, 4·63; N, 16·36. Calc. for $C_{13}H_{11}N_3O_3$: C, 60·69; H, 4·31; N, 16·34%).

3-N,N-*dimethylaminomethyleneaminoindazole* (**4**). A mixture of **1** (1·33 g), N,N-dimethylformamide dimethyl acetal (1·5 ml) and toluene (2 ml) was heated under reflux for 3 hr. The solvent was distilled off *in vacuo*, the residue was dissolved in chloroform, charcoaled, filtered hot and the cold filtrate was treated with n-hexane (10 ml). The product was filtered off, m.p. 111–112° (yield 83%). Mass spectrum: M⁺ = 188; NMR (DMSO-d_6): τ = 1·86 (s, CH), 2·45 (m, H_4), 3·00 (m, $H_{5,6,7}$), 7·02 (s, NMe_2), 1·9 (broad, NH). (Found: C, 63·76; H, 6·60. Calc. for $C_{10}H_{12}N_4$: C, 63·81; H, 6·43%).

3-*Hydroxyiminomethylenaminoindazole* (**5**). Compound **4** (1·4 g) was dissolved in MeOH (10 ml), treated with hydroxylamine hydrochloride (1 g) and the mixture left at room temp. for 2 hr. The solvent was evaporated *in vacuo* and the residual oil crystallized after standing on ice. The product was crystallized from MeOH, m.p. 168° (yield 0·21 g). Mass spectrum: M⁺ = 176; NMR (DMSO-d_6): τ = 2·54 (d, CH), 2·05 (m, H_4), 2·95 (m, $H_{5,6,7}$), 1·00 (d, NH–CH), 0·16 and 2·01 (broad, OH, NH), J_{CHNH} = 10 Hz. (Found: C, 54·45; H, 4·76; N, 31·76. Calc. for $C_8H_8N_4O$: C, 54·54; H, 4·58; N, 31·80%).

2 - *Methyl* - 4 - *chloropyrimido*(1,2-b)*indazole* (**6**, R = Me, R_1 = R_3 = H, R_2 = Cl). The corresponding **2**, (R = Me, R_1 = H; 1 g), $POCl_3$ (6 ml) and N,N-dimethylaniline (1 ml) were heated on an oil bath at 100° for 4 hr. The cooled mixture was poured onto a mixture of ice (150 g) and conc ammonia (50 ml) in such a manner that the temp. did not exceed 4°. The product was crystallized

from EtOH, m.p. 146–148° (yield 18%). Mass spectrum: $M^+ = 217$; NMR ($CDCl_3$): τ = 2·93 (s, H_3), 1·78 (m, H_7), 2·41 (m, $H_{8,9,10}$), 7·33 (s, Me). (Found: C, 61·08; H, 3·77; N, 19·78. Calc. for $C_{11}H_8ClN_3$: C, 60·72; H, 3·69; N, 19·35%).

2-*Methylpyrimido*(1,2-b)*indazole* (**6**, R = Me, $R_1 = R_2 = R_3$ = H). (a) The above chloro compound (0·5 g) was dissolved in EtOH (150 ml) and the soln treated with PdC (50 mg of 5%) and conc. ammonia (2 ml). The mixture was shaken in an atmosphere of H_2 at room temp. till about 50 ml of H_2 were consumed. Upon filtration and evaporation of the solvent the residue was extracted with chloroform. The product was crystallized from MeOH, m.p. 157–159° (yield 49%). Mass spectrum: $M^+ = 183$; NMR ($CDCl_3$): τ = 3·04 (d, H_3), 1·16 (d, H_4), 1·71 (m, H_7), 2·50 (m, $H_{8,9,10}$), 7·27 (s, Me), $J_{3,4} = 8$ Hz. (Found: C, 71·97; H, 4·88; N, 23·15. Calc. for $C_{11}H_9N_3$: C, 72·11; H, 4·95; N, 22·94%).

(b) Alternatively, the compound was prepared as described for pyrimido(1,2-b)indazole under (b), but using 1,1-diethoxy-3-butanone (47% yield). The compound was identical in all respects with the product obtained as described under (a).

2-*Methyl*-1,2,3,4,7,8,9,10-*octahydropyrimido*-(1,2-b)*indazole* (**7**). A soln of **6** (R = Me, $R_1 = R_2 = R_3$ = H) (0·47 g) in MeOH (150 ml) was treated with PdC (0·3 g of 10%) and hydrogenated under 3 atm for 2 days at room temp. Upon filtration and evaporation of the solvent, the crude product was sublimed at 160°/10 mm, m.p. 166–167° yield 15%). Mass spectrum: $M^+ = 191$; NMR ($CDCl_3$): τ = 8·70 (d, Me), 6·57 (m, H_2), 8·0 (m, 3-CH_2), 6·0 (m, 4-CH_2), 7·74 (m, 7-CH_2), 7·47 (m, 10-CH_2), 8·27 (m, 8- and 9-CH_2), 6·17 (broad, NH), $J_{CHCH_3} = 6·5$ Hz. (Found: C, 68·92; H, 9·11; N, 21·72. Calc. for $C_{11}H_{17}N_3$: C, 69·07; H, 8·96; N, 21·97%).

2-*Methyl*-7,8,9,10-*tetrahydropyrimido*(1,2-b)*indazol*-4(1H)-*one* (**8**) was prepared as above, except that the reaction time was 3 days. The crude product was crystallized from MeOH, m.p. 312° (dec) (yield 18%). Mass spectrum: $M^+ = 203$. NMR (DMSO-d_6, 125°): τ = 4·67 (s, H_3), 7·75 (s, Me), 7·46 (m, 7- and 10-CH_2), 8·25 (m, 8- and 9-CH_2). (Found: C, 65·30; H, 6·51; N, 20·39. Calc. for $C_{11}H_{13}N_3O$: C, 65·00; H, 6·45; N, 20·68%).

Pyrimido(1,2-b)*indazol*-2(1H)-*one* (**9**). A mixture of **1** (1·0 g) and ethyl propiolate (15 ml) was heated under reflux for 1 hr. The product was crystallized from EtOH (yield 35%), m.p. 323–325°. (Lit. 4 gives m.p. 335–339°, dec); NMR (DMSO-d_6, 136°): τ = 3·71 (d, H_3), 1·45 (d, H_4), 2·66 (m, H_7), 3·06 (m, $H_{8,9}$), 2·14 (m, H_{10}), $J_{3,4} = 8$ Hz. The compound, when heated with 80% hydrazine hydrate under reflux for 18 hr was transformed into 3-aminoindazole in 31% yield.

2-*Chloropyrimino*(1,2-b)*indazole* (**6**, R = Cl, $R_1 = R_2 = R_3$ = H). The indazolone **9** (1·7 g) was dissolved in $POCl_3$ (7 ml) and N,N-dimethylaniline (2 ml). The mixture was heated on oil bath for 30 min and the product was crystallized from EtOH (yield 45%), m.p. 212–213°. Mass spectrum: $M^+ = 203$; NMR (DMSO-d_6, 125°): τ = 2·64 (d, H_3), 0·79 (d, H_4), 1·92 (m, H_{10}), 2·55 (m, $H_{7,8,9}$), $J_{3,4} = 7·5$ Hz. (Found: C, 58·86; H, 3·00; N, 20·80. Calc. for $C_{10}H_6ClN_3$: C, 59·00; H, 2·94; N, 20·63%).

Pyrimido(1,2-b)*indazole* (**6**, R = $R_1 = R_2 = R_3$ = H). (a) A mixture of the above chloro compound (0·27 g), MeOH (30 ml), conc. ammonia (1 ml) and PdC (30 mg of 5%) was stirred in an atmosphere of H_2 at room temp. for 24 hr. Upon filtration, the filtrate was evaporated to dryness and the residue extracted with hot chloroform. The crude product obtained after evaporation of chloroform, was crystallized from EtOH (yield 36%), m.p. 119–121°. Mass spectrum: $M^+ = 169$; NMR (DMSO-d_6): τ = 1·30 (dd, H_2), 2·54 (dd, H_3), 0·63 (dd, H_4), 2·30 (m, H_7), 2·63 (m, $H_{8,9}$), 1·77 (m, H_{10}), $J_{2,3} = 5·0$, $J_{3,4} = 7·5$ Hz. (Found: C, 70·87; H, 3·86; N, 24·77. Calc. for $C_{10}H_7N_3$: C, 70·99; H, 4·17; N, 24·84%).

(b) A mixture of **1** (1·0 g), 1,1,3,3-tetraethoxypropane (1·8 g), AcOH (2 ml), water (2 ml) and conc. HCl (0·5 ml) was heated under reflux for 3 hr. The mixture was evaporated to dryness and the residue crystallized from EtOH (yield 41%). The compound was found to be identical in all respects with the compound obtained as described under (a).

Pyrimido(1,2-b)-indazole when heated under reflux with 80% hydrazine hydrate for 12 hr was transformed in 38% yield into 3-aminoindazole.

9-*Bromo*-2-*chloropyrimido*(1,2-b)*indazole* (**6**, R = Cl, $R_1 = R_2$ = H, R_3 = Br). To a cold soln of 2-chloropyrimido(1,2-b)indazole (0·2 g) in glacial AcOH (3 ml) a soln of Br_2 (0·16 g) in glacial AcOH (2 ml) was added dropwise. The mixture was poured into ice cold water (30 ml) and neutralized with ammonia until pH 5–6. The product was crystallized from EtOH (yield 36%), m.p. 206–211°. Mass spectrum: $M^+ = 283$. NMR (DMSO-d_6, 75°): τ = 2·48 (d, H_3), 0·41 (d, H_4), 2·33 (m, $H_{7,8}$), 1·23 (m, H_{10}), $J_{3,4} = 7·5$ Hz. (Found: C, 41·97; H, 1·75; N, 14·53. Calc. for $C_{10}H_5BrClN_3$: C, 42·33; H, 1·76; N, 14·84%).

9-*Bromo*-4-*chloro*-2-*methylpyrimido*(1,2-b)*indazole* (**6**, R = Me, R_1 = H, R_2 = Cl, R_3 = Br) was prepared in a similar manner from 4-chloro-2-methylpyrimido(1,2-b)-indazole in 30% yield, m.p. 170°. Mass spectrum: $M^+ = 295$. NMR (DMSO-d_6, 96°): τ = 2·34 (m, $H_{3,7,8}$), 1·74 (m, H_{10}), 7·31 (s, Me). (Found: C, 44·43; H, 2·58; N, 14·46. Calc. for $C_{11}H_7BrClN_3$: C, 44·67; H, 2·36; N, 14·21%).

N-(*Indazolyl*-3-)-N'-*carbethoxythiourea* (**10**). A mixture of **1** (0·266 g), chloroform (5 ml) and ethoxycarbonylisothiocyanate (0·262 g)[13] was heated under reflux for 15 min. The solvent was evaporated *in vacuo* and the residue was crystallized from EtOH (yield 0·403 g, 76%), m.p. 186–188°. Mass spectrum: $M^+ = 264$; NMR (DMSO-d_6): τ = 2·55 (m, $H_{4,5,6,7}$), 5·75 (q, CH_2), 8·70 (t, CH_3), −1·5 (broad NH), $J_{CH_2,CH_3} = 7·2$ Hz. (Found: C, 50·43; H, 4·81; N, 21·39. Calc. for $C_{11}H_{12}N_4O_2S$: C, 50·00; H, 4·85; N, 21·20%).

Further treatment with carbethoxy isothiocyanate afforded the 1-carbethoxyaminothiocarbonyl derivative, m.p. 151–154°.

4(3H)-*Oxo*-2(1H)-*thioxo*-s-*triazino*(1,2-b)*indazole* (**11**). A mixture of **10** (0·528 g) and an ethanolic soln of NaOEt (prepared from 0·1 g of Na in 14 ml of EtOH) was heated under reflux for 30 min. The solvent was evaporated and the residue was dissolved in water and acidified with HCl (1:1) until pH 4. The product was crystallized from EtOH (yield 0·368 g, 84%), m.p. 249–251°. Mass spectrum: $M^+ = 218$; NMR (DMSO-d_6, 100°): τ = 2·05 (m, H_{10}), 2·75 (m, $H_{7,8,9}$), 2·5 (broad, NH). (Found: C, 49·40; H, 3·08; N, 25·54. Calc. for $C_9H_6N_4OS$: C, 49·54; H, 2·77; N, 25·68%).

If the product was treated with boiling Ac_2O for 3 hr compound **12**, m.p. 127–128°, was obtained in 37% yield.

An authentic specimen could be prepared as follows:

A mixture of **1** (0·5 g) and Ac_2O (5 ml) was heated under reflux for 25 hr. The solvent was evaporated to dryness and the product was purified by sublimation at 100°/100 mm (yield 20%), m.p. 124°. Mass spectrum: $M^+ = 259$; NMR ($CDCl_3$): τ = 1·56 (m, H_4), 2·54 (m, $H_{5,6,7}$), 7·26 (s, N-$COCH_3$), 7·61 (s, N($COCH_3$)$_2$). (Found: C, 60·02; H, 5·18; N, 15·75. Calc. for $C_{13}H_{13}N_3O_3$: C, 60·22; H, 5·05; N, 16·21%).

N-(*Indazolyl*-3)*thiourea* (**13**, R = $CSNH_2$). Compound **11** (0·218 g) was heated under reflux in an aqueous soln of 2 N KOH (5 ml) for 2 hr. Upon neutralization, the product was crystallized from EtOH (yield 57%, 0·11 g), m.p. 230–231°. Mass spectrum: $M^+ = 192$. NMR (DMSO-d_6): τ = 1·76 (m, H_4), 2·75 (m, $H_{5,6,7}$), −2·6, −1·0, 0·75 and 1·25 (broad, NH groups). (Found: C, 49·99; H, 4·53; N, 28·91. Calc. for $C_8H_8N_4S$: C, 49·99; H, 4·20; N, 29·16%).

The thiourea, when dissolved in EtOH and heated under reflux in the presence of yellow HgO, gave **13** (R = CN), m.p. 235–240° in 12% yield.

2,4-*Diamino*-s-*triazino*(1,2-b)*indazole* (**14**, R = NH_2). A mixture of **1** (1·33 g), conc. HCl (1·14 g), dicyandiamide (1·45 g) and water (6 ml) was heated under reflux for 1 hr. The product was crystallized from EtOH (yield 1·33 g, 67%), m.p. 310–312° (lit.[8] gives m.p. 313°). Mass spectrum: $M^+ = 200$. NMR (DMSO-d_6): τ = 2·2 (m, H_{10}), 2·55 and 3·1 (m, $H_{7,8,9}$), 1·8 and 6·2 (broad, NH_2). (Found: C, 53·56; H, 4·25; N, 42·11. Calc. for $C_9H_8N_6$: C, 53·99; H, 4·03; N, 41·98%).

The compound is acetylated with Ac_2O to the derivative **14** (R = NHCOMe), m.p. 242–245°. Mass spectrum: $M^+ = 242$.

4-*Amino*-s-*triazino*(1,2-b)*indazole* (**14**, R = H). A soln of **1** (2·128 g) in dimethoxyethane (10 ml) was treated with ethyl N-cyanoimidate (1·568 g)[14] and the mixture was heated under reflux for 6 hr. The solvent was evaporated and the residue was crystallized from a mixture of EtOH and N,N-dimethylformamide (yield 0·82 g, 28%), m.p. 266–268°. Mass spectrum: $M^+ = 185$. NMR (DMSO-d_6, 72°): τ = 1·53 (s, H_7), 1·84 (m, H_{10}), 2·5 (m, $H_{7,8,9}$), 1·28 (broad, NH_2). (Found: C, 58·49; H, 4·02; N, 37·81. Calc. for $C_9H_7N_5$: C, 58·37; H, 3·81; N, 37·82%).

The compound formed an acetyl derivative, m.p. 135°.

If the same mixture was heated under reflux for 0·5 hr the corresponding **13** (R = CH=NCN) could be isolated, m.p. 220–221°. Mass spectrum: $M^+ = 185$; NMR (DMSO-d_6): $\tau = 0{\cdot}6$ (s, CH), 2·1 (m, $H_{4,5,6,7}$), 3·3 (broad, NH). (Found: C, 58·34; H, 3·86; N, 37·89. Calc. for $C_9H_7N_5$: C, 58·37; H, 3·81; N, 37·82%).

2 - *Dimethylamino* - 3 - *phenyl* - 1,2 - *dihydro* - s - *triazolo*(1,2-b)*indazol* - 4(3H) - *on* (**15**). Compound **4** (0·188 g) was dissolved in toluene (5 ml) and after phenyl isocyanate (0·119 g) was added the mixture was heated under reflux for 1·5 hr. The solvent was evaporated and the product crystallized from EtOH (yield 0·145 g, 47%), m.p. 120–121°. Mass spectrum: $M^- = 307$; NMR (DMSO-d_6): $\tau = 6{\cdot}90$ (d, NMe_2), 1·45 (s, H_2), 1·67 (m, H_{10}), 2·5 (m, $H_{7,8,9}$, Ph), 0·15 (broad, NH). (Found: C, 66·78; H, 5·72; N, 22·41. Calc. for $C_{17}H_{17}N_5O$: C, 66·43; H, 5·58; N, 22·79%).

2 - *Bromo* - 3 - *phenyl* - s - *triazino*(1,2-b)*indazol* - 4(3H)*one* (**16**). The above compound (0·094 g) was dissolved in AcOH (4 ml) and AcONa (0·082 g) was added. Then, a soln of Br_2 (0·079 g) in AcOH (1 ml) was added dropwise. The product crystallized from a mixture of EtOH and cyclohexane (yield 16 mg, 9%), m.p. 179–182°. Mass spectrum: $M^- = 341$. (Found: N, 16·60. Calc. for $C_{15}H_9BrN_4O$: N, 16·43%).

3-*Indazoloyl azide* (**18**). A suspension of **17** (R = H)[15] (0·88 g) in water (2 ml) was treated with HCl (1 : 1, 10 ml) and cooled to 0°. An ice cold soln of $NaNO_2$ (0·37 g) in a minimum of water was added portionwise in such a manner that the temp. remained between 0 and 5°. The product was suspended in water and filtered off. The compound was crystallized from water, m.p. 138°. NMR (DMSO-d_6): $\tau = 1{\cdot}95$ (m, H_4), 2·5 (m, $H_{5,6,7}$), −0·1 (broad, NH). (Found: C, 51·54; H, 2·95; N, 37·47. Calc. for $C_8H_5N_5O$: C, 51·34; H, 2·69; N, 37·42%).

1,3,5 - *Tris*(*indazolyl* - 3') - s - *triazine* - 2,4,6 - *trione* (**19**). The above azide (0·2 g) in benzene (3 ml) was heated under reflux for 3 hr. Upon cooling the product was suspended in boiling N,N-dimethylformamide, filtered and washed with EtOH, m.p. over 300°. Mass spectrum: $M^+ = 159$ (M/3); IR: no azide band. (Found: C, 60·68; H, 3·48; N, 26·25. Calc. for $C_{24}H_{15}N_9O_3$: C, 60·37; H, 3·17; N, 26·41%)

3-*Carbethoxyaminoindazole* (**13**, R = COOEt). This azide **18** (0·15 g), when heated under reflux in abs EtOH (3 ml) for 4 hr, afforded the urethane in 30% yield, m.p. 185–187° (from EtOAc). (Found: C, 58·77; H, 5·60; N, 20·74. Calc. for $C_{10}H_{11}N_3O_2$: C, 58·53; H, 5·40; N, 20·48%).

Ethyl N - (*indazolyl* - 3 - *hydrazino*) - N' - β - *methyl acrylate* (**17**, R = –C(CH₃)=CH–COOEt. A soln of **17** (R = H) (0·88 g) in n-propanol (10 ml) and ethyl acetoacetate (0·65 g) was heated under reflux for 2 hr. After cooling the product was crystallized from N,N-dimethylformamide and EtOH, m.p. 213–217°; from the melt new crystals separated and did not melt until 280°. Mass spectrum: $M^+ = 288$. (Found: C, 58·66; H, 5·93; Calc. for $C_{14}H_{16}N_4O_3$: C, 58·32; H, 5·59%).

1 - (*Indazolyl* - 3') - 4 - *phenylsemicarbazide* (**17**, R = CONHPh). A mixture of **17** (R = H) (0·88 g), diethyleneglycol dimethylether (10 ml) and phenyl isocyanate (0·595 g) was heated under reflux for 2 hr. Upon cooling the product was crystallized from EtOH and N,N-dimethylformamide (yield 0·61 g, 41%), m.p. over 290°. Mass spectrum: $M^+ = 202$ (M–$PhNH_2$); NMR (DMSO-d_6): $\tau = 1{\cdot}67$ (m, H_4), 2·67 (m, $H_{5,6,7}$ and Ph), 1·19 and −0·1 (broad, NH). (Found: C, 60·94; H, 4·66; N, 23·43. Calc. For $C_{15}H_{13}N_5O_2$: C, 61·01; H, 4·44; N, 23·72%).

N,N' - *Bis-indazoloyl* - 3 - *hydrazine* (**20**). (a) Compound **17** (R = H) (0·88 g) and ethyl benzoylacetate (0·96 g) were dissolved in a n-propanol (10 ml) and the soln was heated under reflux for 16 hr. The product was crystallized from N,N-dimethylformamide and some water, m.p. over 300°. Mass spectrum: $m/e = 176$ and 145 (indazolyl-CO); NMR (DMSO-d_6): $\tau = 2{\cdot}5$ (m, $H_{5,6,7,5',6',7'}$), 1·75 (m, $H_{4,4'}$), −0·3 and −3·5 (broad, NH). (Found: C, 60·26; H, 4·16; N, 26·20. Calc. for $C_{16}H_{12}N_6O_2$: C, 59·99; H, 3·78; N, 26·24%).

(b) The acrylate **17** (R = –C(CH₃)=CHCOOEt (0·253 g) was suspended in diphenyl ether (3 ml) and the mixture was heated under reflux for 0·5 hr. The product was washed with a little EtOH and crystallized from N,N-dimethylformamide with addition of water. The product was found to be identical in all respects with compound prepared as described under (a).

(c) Compound **17** (R = CONHPh; 0·88 g) was suspended in diphenyl ether (4 ml) and the mixture heated under reflux for 2 hr. The product was identical in all respects with the compound prepared as described under (a) or (b).

Indazol - 3 - *yl phenylketone* (**21**). To a stirred Grignard reagent soln, prepared from 0·4 Mg turnings and bromobenzene (1·57 g) in dry diethyl ether (9 ml), a soln of 3-cyanoindazole[16] (0·715 g) in diethyl ether (15 ml) was added dropwise. After addition was complete, stirring was continued for 10 min the solvent was evaporated and the residue was treated with a mixture of water (25 ml) and HCl (25 ml of 3 N). The mixture was then heated under reflux for 20 min, filtered and the residue crystallized from chloroform (0·47 g, 43%), m.p. 188°. Mass spectrum: $M^+ = 222$; NMR (DNSO-d_6): $\tau = 1{\cdot}67$ (m, H_4), 2·36 (m, $H_{5,6,7}$ and Ph), −5·0 (broad, NH). (Found: C, 75·50; H, 4·62; N, 12·38. Calc. for $C_{14}H_{10}N_2O$: C, 75·65; H, 4·54; N, 12·61%).

Indazole - 3 - *carboxylic acid thioamide* (**22**). 3-Cyanoindazole (0·715 g) was dissolved in pyridine (0·715 g) and triethylamine (0·505 g) and H_2S was introduced at room temp. for 4·5 hr. The mixture was evaporated *in vacuo* to dryness and the residue was crystallized from EtOH and washed with diethyl ether (0·365 g, 41%), m.p. 216–217°. Mass spectrum: $M^+ = 177$; NMR (DMSO-d_6): $\tau = 1{\cdot}34$ (m, H_4), 2·6 (m, $H_{5,6,7}$), 0·75 (broad, NH_2), −3·4 (broad, NH). (Found: C, 54·02; H, 4·16; N, 23·49. Calc. for $C_8H_7N_3S$: C, 54·23; H, 3·98; N, 23·72%).

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