terial was prepared by sulfonation of *l*-camphor using the procedure of P. D. Bartlett and L. H. Knox, *Org. Syn.*, **45**, 12 (1965); the acid obtained showed $[\alpha]^{25}D$ −20.54° (*c* 2, H_2O).

(37) Efforts to confirm the intermediacy of this or alternative open-chain species either by spectroscopic means or trapping experiments were unsuccessful. It is also conceivable, although seemingly less likely, that ring opening could occur *via* cleavage of the C_6–N_1 bond.

(38) G. Saucy, R. Borer, and A. Fürst, *Helv. Chim. Acta*, **54**, 2034 (1971).

(39) Unless otherwise noted, reaction products were isolated by addition of NaCl or saturated brine and extraction with the specified solvent. Organic extract solutions were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered, and concentrated under water aspirator pressure at 40–50° on a rotary evaporator. The crude reaction products were then dried under high vacuum to constant weight. Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. All reactions except hydrogenations were carried out under an atmosphere of nitrogen. Unless otherwise noted, column chromatography was performed using Merck (Darmstadt) silica gel, 0.05–0.2 mm. Thin layer chromatography was performed using Brinkmann silica gel G plates with uv indicator. Plates were developed with one of the following systems: A, 9:1 benzene–triethylamine; B, 1:1 benzene–ethyl acetate; C, 1:1 hexane–ethyl acetate. Spots were detected with uv light, iodine vapor, or *p*-toluenesulfonic acid spray followed by heating. Varian A-60, HA-100, or Jeolco C-60H spectrometers were used to obtain the pmr spectra. Chemical shifts are reported relative to TMS as an internal standard. Infrared spectra were recorded on Beckman IR-9 or Perkin-Elmer 621 spectrophotometers. The ultraviolet spectra were recorded on a Cary Model 14M spectrophotometer. Low-resolution mass spectra were obtained on CEC 21-110 or JMS-01SG instruments. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter. Tetrahydrofuran (THF) and pyridine were dried by slurrying over Woelm grade I neutral alumina just prior to use.

(40) In naming the spiro compounds having an 8 substituent, we suggest that relative stereochemistry be designated by *c* and *t* to denote a cis or trans relationship to some reference (*r*) substituent. *Cf.* J. A. Marshall and P. C. Johnson, *J. Org. Chem.*, **35**, 192 (1970); Beilstein, "Handbuch der Organischen Chemie," E III, Vol. VI, Part 7, p x. Thus, for example, compound **15a** would be named (±)-2-amino-8*t*-methyl-(6*r*N^1)-7-oxa-3-thia-1-azaspiro[5.5]undec-1-ene and the epimer **16a**, (±)-2-amino-8*c*-methyl-(6*r*N^1)-7-oxa-3-thia-1-azaspiro[5.5]undec-1-ene. With regard to the acyl derivatives, compound **17a** (R′ = CH_3), for example would be named (±)-2-acetylimino-8*t*-methyl-(6*r*N^1)-7-oxa-3-thia-1-azaspiro[5.5]undecane.

(41) This preparation was carried out by Mrs. Angela Duggan.

(42) *Cf.* N. Cohen, B. L. Banner, J. F. Blount, M. Tsai, and G. Saucy, *J. Org. Chem.*, **38**, 3229 (1973), for a description of the preparation of the manganese dioxide used in this oxidation.

(43) G. M. Bennett and A. L. Hock, *J. Chem. Soc.*, 472 (1927).

(44) See paragraph at end of paper regarding supplementary material.

The Reaction of 3-Diazo-3*H*-indazole with Reactive Methylene Compounds and Formation of Indazolo[3,2-*c*]-1,2,4-triazines

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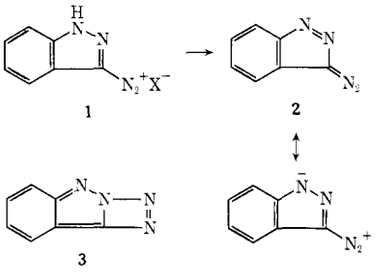
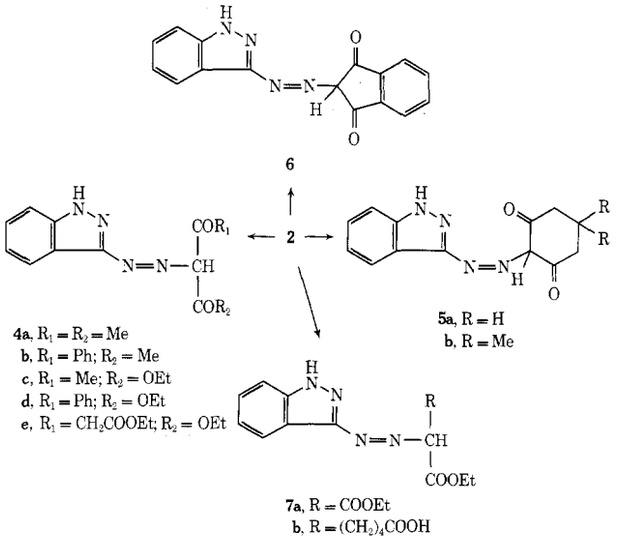
3-Diazo-3*H*-indazole reacts with 1,3-diketones, β-keto esters, or diethyl malonate and coupling occurs at the methylene group. The resulting products can be cyclized thermally or under the influence of acid into derivatives of indazolo[3,2-*c*]-1,2,4-triazine.

3-Aminoindazole, when diazotized, forms a diazonium salt (**1**) which can be converted upon treatment with alkali into the diazo compound. 3-Diazo-3*H*-indazole was the first heterocyclic diazo compound and was formulated by Bamberger[2] as indazolotriazolene (**3**), but later the diazo structure (**2**) was proposed.[3] 3-Diazo-3*H*-indazole exhibits



in solid state an ir absorption band at 2119 cm^{-1}, typical for diazo compounds,[4,5] and on the other hand it couples with phenols to give azo compounds or the diazo group can be replaced with halogens. So far, no other reactions of **2** have been investigated.

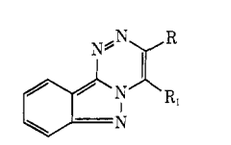
The reactivity of 3-diazo-3*H*-indazole was of interest in conjunction with our previous investigations on azido- and tetrazoloazines.[6-8] An ethanolic solution of **2**, when treated with a 1,3-dicarbonyl compound, a β-keto ester, or diethyl malonate, formed easily at room temperature the corresponding azo compound of the type **4**, **5**, **6**, or **7a**. Cyclic β-diketones, like cyclohexane-1,3-dione, its 5,5-dimethyl analog, or indan-1,3-dione, also reacted readily. For all compounds of this type several tautometric forms can be written. For example, compounds of the type **4** can be regarded as azo compounds or as hydrazones, and the carbonyl part can be written in the keto or enolized form. For compounds resulting from coupling of diazonium salts at a methyl or methylene carbon,[9] the hydrazone structure was postulated.[10] No attempt has been made to examine in detail the structures of our products.



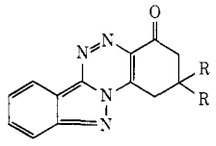
Compound **5a**, from 3-diazo-3*H*-indazole and 2-carbethoxycyclohexanone, reacted in ethanolic solution at room temperature to afford **7b** after 48 hr, indicating that ring opening of the cyclohexanone ring occurred during

the reaction. The reaction is comparable to the known Japp–Klingemann reaction[11] in which coupling of diazonium salts and cyclic β-keto esters gives ring-opened products.[12,13]

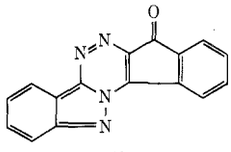
The azo compounds were transformed at widely differing rates into derivatives of indazolo[3,2-*c*]-1,2,4-triazine (**8, 9, 10**), a new heterocyclic system. In some cases cyclization occurred in hot ethanolic solution; with other compounds, temperatures around their melting point were required, whereas compound **6** was transformed into **10** only at 240°. These cyclic products are obtained rapidly at room temperature by acidification of an ethanolic solution of the azo compounds.



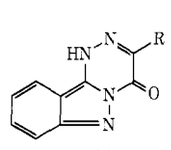
8a, R = COMe; R_1 = Me
b, R = COMe; R_1 = Ph
c, R = COOEt; R_1 = Me
d, R = COOEt; R_1 = Ph
e, R = COOEt; R_1 = CH_2COOEt



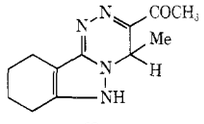
9a, R = H
b, R = Me



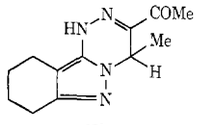
10



11a, R = COOEt
b, R = H



12a



12b

Thermal cyclization of compound **7a** was unsuccessful, but upon heating in polyphosphoric acid at 140° for 3 hr it was transformed into a cyclic product which was identified as **11b**. The reaction can be explained as the result of ring closure, hydrolysis of the carbethoxy group, and decarboxylation. However, acid-induced cyclization afforded the anticipated cyclic product **11a**. The reaction could be followed also in a nmr probe and progression of the elimination of ethanol was detected.

Compound **8a** could be easily reduced over palladized carbon at room temperature to give a hexahydro derivative which from its ir and nmr spectrum can be formulated as either **12a** or **12b**.

Finally, it should be mentioned that a solution of 3-diazo-3*H*-indazole in chloroform with dimethyl acetylenedicarboxylate gave a low yield of indazole after 10-hr reflux. Indazole was also obtained when a methanolic solution of **2** was irradiated; the reaction may be postulated to proceed through a carbene intermediate. On the other hand, treatment of either **8** or **4** with hydrazine hydrate or with a 5% aqueous solution of potassium hydroxide resulted in the formation of 3-aminoindazole. Under the influence of the base the heterocyclic ring of **8** is cleaved, as concluded from nmr evidence. Furthermore, as already mentioned, compounds of the type **4** can be regarded as hydrazones,[10] and therefore a base-induced N–N cleavage can be anticipated, which is consistent with previous observations of similar cases.[14,15]

Experimental Section

Melting points were taken on a Kofler micro hot stage and are corrected. Infrared spectra were recorded on a Perkin-Elmer 137 Infracord as KBr disks, nmr spectra were taken on a JEOL JNM-C-60HL spectrometer (TMS as internal standard), and mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6L mass spectrometer. 3-Diazo-3*H*-indazole was obtained from 3-aminoindazole[16] according to the procedure described in literature.[2]

General Procedure for the Preparation of Coupling Products from 3-Diazo-3*H*-indazole and 1,3-Dicarbonyl Compounds. A solution of 3-diazo-3*H*-indazole (0.01 mol) in ethanol (2 ml) was treated with the corresponding 1,3-diketone, β-keto ester, or diethyl malonate (0.001 mol) at room temperature. The separated product was filtered off and crystallized. In this manner the following compounds were prepared.

Compound **4a** in 86% yield: mp 173–173.5° (from ethanol-*N,N*-dimethylformamide, 4:1); mass spectrum M$^+$ *m/e* 244; nmr (DMSO-d_6) τ 2.60 (m, H_4, H_5, H_6, H_7), 7.66 and 7.57 (s, CH_3), 6.50 (broad, NH).

Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.01; H, 4.95; N, 22.94. Found: C, 59.29; H, 5.09; N, 23.28.

Compound **4b** in 82% yield: mp 153°; ir 1639 cm^{-1} (CO); mass spectrum M$^+$ *m/e* 306; nmr (DMSO-d_6) τ 7.43 (s, CH_3), 2.50 (m, C_6H_5 and H_4, H_5, H_6, H_7), 6.50 (broad, NH or OH).

Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.65; H, 4.61; N, 18.29. Found: C, 66.81; H, 5.10; N, 18.72.

Compound **5a** in 68% yield: mp 162°; ir 1695, 1664 cm^{-1} (CO); mass spectrum M$^+$ *m/e* 256; nmr (DMSO-d_6, 65°) τ 6.40 (m, 4′-CH_2), 7.95 (m, 5′-CH_2), 7.24 (m, 6′-CH_2), 2.0 (m, H_4, H_5, H_6, H_7).

Anal. Calcd for $C_{13}H_{12}N_4O_2$: C, 60.93; H, 4.72; N, 21,87. Found: C, 60.76; H, 4.56; N, 21.80.

Compound **5b** in 90% yield: mp 175° (from EtOH); at the melting point the compound cyclized and melted again at 235°; mass spectrum M$^+$ *m/e* 284; nmr (DMSO-d_6) τ 7.40 (s, 4′-CH_2, 6′-CH_2), 8.92 (s, 5′-CH_3), 2.60 (m, H_4, H_5, H_6), 1.75 (m, H_7).

Anal. Calcd for $C_{15}H_{16}N_4O_2$: C, 63.36; H, 5.67; N, 19.71. Found: C, 62.97; H, 5.82; N, 19.23.

Compound **6** in 83% yield: mp 240–241° (from ethanol-*N,N*-dimethylformamide, 4:1); ir 1695, 1667 cm^{-1} (CO); mass spectrum M$^+$ *m/e* 290; nmr (DMF-d_7) τ 2.07 (s, $H_{4'}$, $H_{5'}$, $H_{6'}$, $H_{7'}$), 2.60 (m, $H_{4'}$, $H_{5'}$, H_6), 1.65 (m, H_7), 6.50 (broad, NH or OH).

Anal. Calcd for $C_{16}H_{10}N_4O_2$: C, 66.20; H, 3.47. Found: C, 66.67; H, 3.60.

Compound **4c** in 62% yield: mp 167–168° (from ethanol); mass spectrum M$^+$ *m/e* 274; ir 1639 cm^{-1} (CO); nmr (DMSO-d_6) τ 7.57 (s, CH_3), 8.62 (t, CH_2CH_3), 5.65 (q, CH_2CH_3) 2.55 (m, H_4, H_5, H_6), 1.87 (m, H_7), J_{Et} = 7.5 Hz.

Anal. Calcd for $C_{13}H_{14}N_4O_3$: C, 56.93; H, 5.15. Found: C, 57.03; H, 5.00.

Compound **4d** in 83% yield: mp 195–197° (from ethanol-*N,N*-dimethylformamide, 3:1); ir 1706, 1698 cm^{-1} (CO); mass spectrum M$^+$ *m/e* 336; nmr (DMSO-d_6) τ 8.23 (t, CH_2CH_3), 5.63 (q, CH_2CH_3), 2.50 (m, C_6H_5 and H_4, H_5, H_6, H_7), −2.5 (broad, NH or OH), J_{Et} = 7.5 Hz.

Anal. Calcd for $C_{18}H_{16}N_4O_3$: C, 64.27; H, 4.80; N, 16.66. Found: C, 64.14; H, 4.95; N, 16.35.

Compound **4e** in 61% yield: mp 138–139° (from ethanol); ir 1730, 1695 cm^{-1} (CO); mass spectrum M$^+$ *m/e* 346; nmr ($CDCl_3$) τ 8.54 (t, $CO_2CH_2CH_3$), 5.75 (q, $CO_2CH_2CH_3$), 8.67 (t, $CH_2COOCH_2CH_3$), 5.78 (q, $CH_2COOCH_2CH_3$), 5.95 (s, CH_2COOEt), 2.75 (m, H_4, H_5, H_6), 1.65 (m, H_7), −0.5 (broad, NH or OH), J_{Et} = 7.5 Hz.

Anal. Calcd for $C_{16}H_{18}N_4O_5$: C, 55.48; H, 5.25; N, 16.18. Found: C, 55.78; H, 5.19; N, 16.20.

Compound **7a** in 55% yield: mp 142–142,5° (from EtOH); mass spectrum M$^+$ *m/e* 304; ir 1701 cm^{-1} (COOEt); nmr ($CDCl_3$) τ 8.51 (t, CH_2CH_3), 5.58 (q, CH_2CH_3), 8.57 (t, CH_2CH_3), 2.70 (m, H_4, H_5, H_6), 1.60 (m, H_7), 0.0 and −3.1 (broad, two exchangeable protons), J_{Et} = 7.5 Hz.

Anal. Calcd for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.43; H, 5.36; N, 18.75.

Compound **7b** in 63% yield after 48 hr: mp 200–202° (from ethanol-*N,N*-dimethylformamide, 2:1); mass spectrum M$^+$ *m/e* 332; nmr (DMSO-d_6, 65°) τ 8.66 (t, OCH_2CH_3), 5.80 (q, OCH_2CH_3), 7.46 (t, CH), 8.35 (m, CH_2), 7.7 (t, CH_2), 2.6 and 1.7 (m, H_4, H_5, H_6, H_7), 5.8 (broad, OH), J_{OEt} = 7.0 Hz.

Anal. Calcd for $C_{16}H_{20}N_4O_4$: C, 57.82; H, 6.07; N, 16.86. Found: C, 58.16; H, 6.06; N, 16.33.

3-Acetyl-4-methylindazolo[3,2-*c*]-1,2,4-triazine (8a). Compound **4a** (0.21 g) was heated in a sublimation tube at 170° until the evolution of water had ceased (about 15 min). The residue was crystallized from ethanol-*N,N*-dimethylformamide (3:1), yield 0.18 g (93%), mp 187°. The same compound could be pre-

pared from **4a** after an ethanolic solution (2 ml) was acidified with hydrochloric acid: ir 1692 cm^{-1} (CO); mass spectrum M^+ m/e 226; nmr ($CDCl_3$) τ 7.02 (s, 3-CH_3), 6.78 (s, 4-CH_3), 2.40 (m, H_7, H_8, H_9), 1.55 (m, H_{10}).

Anal. Calcd for $C_{12}H_{10}N_4O$: C, 63.70; H, 4.46; N, 24.77. Found: C, 63.48; H, 4.69; N, 24.95.

3-Acetyl-4-phenylindazolo[3,2-c]-1,2,4-triazine (8b). The product was obtained after a solution of **4b** (0.25 g) in ethanol was heated under reflux for a few minutes. The same reaction took place if compound **4b** was dissolved in 2 ml of ethanol and the solution was acidified with hydrochloric acid at room temperature. The product was crystallized from ethanol: yield 0.21 g (90%); mp 198.5–199°; ir 1664 cm^{-1} (CO); mass spectrum M^+ m/e 288; nmr (DMSO-d_6) τ 7.0 (s, 3-CH_3), 2.60 (m, 4-C_6H_5), 2.70 (m, H_7, H_8, H_9), 1.45 (m, H_{10}).

Anal. Calcd for $C_{17}H_{12}N_4O$: C, 70.82; H, 4.20; N, 19.44. Found: C, 70.70; H, 4.30; N, 19.55.

8,9,10,11-Tetrahydroindazolo[3,2-c]-1,2,4-benzotriazin-8-one (9a). Compound **5a** (0.175 g) was dissolved in ethanol (2 ml) and the solution was heated under reflux for 5 min. The same conversion took place if the above solution was acidified with HCl at room temperature. The separated product was filtered off and crystallized from ethanol–*N,N*-dimethylformamide (2:1): yield 0.15 g (92%); mp 215–216°; ir 1689 cm^{-1} (CO); mass spectrum M^+ m/e 238; nmr (DMF-d_7, 75°) τ 6.45 (m, 9-CH_2), 6.87 (m, 10- and 11-CH_2), 2.40 (m, H_2, H_3, H_4), 1.60 (m, H_5).

Anal. Calcd for $C_{13}H_{10}N_4O$: C, 65.53; H, 4.23; N, 23.52. Found: C, 65.74; H, 4.36; N, 23.75.

10,10-Dimethyl-8,9,10,11-tetrahydroindazolo[3,2-c]-1,2,4-benzotriazin-8-one (9b). Compound **5b** (0.215 g) was heated in a sublimation tube at 220° for about 15 min until all water was evolved. Alternatively, a solution of the same amount in ethanol (2 ml) was acidified with hydrochloric acid. The product was crystallized from ethanol: yield 0.19 g (95%); mp 235°; ir 1695 cm^{-1} (CO); mass spectrum M^+ m/e 266; nmr ($CDCl_3$) τ 6.42 (s, 9-CH_2), 7.16 (s, 11-CH_2), 8.67 (s, 10,10-CH_3), 2.35 (m, H_2, H_3, H_4), 1.53 (m, H_5).

Anal. Calcd for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.83; H, 5.39; N, 20.75.

8*H*-Indazolo[3,2-c[indeno[1,2-e]-1,2,4-triazin-8-one (10). Compound **6** (0.24 g) was heated in a tube at 240° for about 30 min. The residue was sublimed at 239° (1 mm): yield 0.21 g (93%); mp >300°; ir 1730 cm^{-1} (CO); mass spectrum M^+ m/e 272; nmr ($CDCl_3$) τ 2.25 (m, H_2, H_3, H_4, H_5, H_9, H_{10}, H_{11}, H_{12}).

Anal. Calcd for $C_{16}H_8N_4O$; C, 70.58; H, 2.96; N, 20.58. Found: C, 70.52; H, 3.08; N, 20.75.

3-Carbethoxy-4-methylindazolo[3,2-c]1,2,4-triazine (8c). Compound **4c** (0.170 g) was heated in a tube at 167° for about 15 min. Alternatively, an ethanolic solution was treated with hydrochloric acid. The product was crystallized from ethanol: yield 0.15 g (94%); mp 150°; ir 1721 cm^{-1} (CO); mass spectrum M^+ m/e 256; nmr ($CDCl_3$) τ 6.78 (s, 4-CH_3), 8.50 (t, CH_2CH_3), 5.45 (q, CH_2CH_3), 2.4 (m, H_7, H_8, H_9), 1.5 (m, H_{10}), J_{Et} = 7.2 Hz.

Anal. Calcd for $C_{13}H_{12}N_4O_2$: C, 60.93; H, 4.72; N, 21.87. Found: C, 60.70; H, 4.90; N, 22.35.

3-Carbethoxy-4-phenylindazolo[3,2-c]-1,2,4-triazine (8d). Compound **4d** (0.28 g) was heated in a tube at 200° for 15 min. The same conversion took place after addition of HCl to an ethanolic solution. The product was crystallized from ethanol: yield 0.24 g (91%); mp 148°; ir 1721 cm^{-1} (COOEt); mass spectrum M^+ m/e 318; nmr ($CDCl_3$) τ 8.82 (t, CH_2CH_3), 5.65 (q, CH_2CH_3), 2.4 (m, 4-C_6H_5), 2.4 (m, H_7, H_8, H_9), 1.40 (m, H_{10}).

Anal. Calcd for $C_{18}H_{14}N_4O_2$: C, 67.91; H, 4.43; N, 17.60. Found: C, 67.55; H, 4.65; N, 17.62.

3-Carbethoxy-4-carbethoxymethylindazolo[3,2-c]-1,2,4-triazine (8e). Compound **4e** (0.21 g) was heated in a tube at 140° for about 15 min. Alternatively, an ethanolic solution was acidified with hydrochloric acid and heated under reflux for 5 min. The product was crystallized from ethanol–water (3:1): yield 0.18 g (90%); mp 114–115°; ir 1745, 1727 cm^{-1} (CO); mass specfrum M^+ m/e 328; nmr ($CDCl_3$) τ 8.48 (t, $COOCH_2CH_3$), 5.40 (q, $COOCH_2CH_3$), 8.75 (t, $CH_2COOCH_2CH_3$), 5.77 (q, $CH_2COOCH_2CH_3$), 5.02 (CH_2COOEt), 1.35 (m, H_{10}), 2.25 (m, H_7, H_8, H_9), J_{Et} = 7.2 Hz.

Anal. Calcd for $C_{16}H_{16}N_4O_4$: C, 58.53; H, 4.91; N, 17.07. Found: C, 58.29; H, 5.00; N, 17.50.

3-Carbethoxyindazolo[3,2-c]-1,2,4-triazin-4(1*H*)-one (11a). Compound **7a** (0.17 g) was dissolved in ethanol (2 ml), acidified with hydrochloric acid, and heated under reflux for 30 min. The separated product was filtered off and crystallized from ethanol–*N,N*-dimethylformamide (3:1); yield 0.12 g (83%); mp 165°; ir 1739 cm^{-1} (COOEt); mass spectrum M^+ m/e 258; nmr (DMSO-d_6, 88°) τ 2.58 (t, CH_2CH_3), 5.55 (q, CH_2CH_3), 2.50 (m, H_7, H_8, H_9), 1.55 (m, H_{10}), J_{Et} = 7.2 Hz.

Anal. Calcd for $C_{12}H_{10}N_4O_3$: C, 55.81; H, 3.90; N, 21.70. Found: C, 55.98; H, 4.08; N, 21.95.

Indazolo[3,2-c]-1,2,4-triazin-4(1*H*)-one (11b). A mixture of compound **7a** (0.17 g) and polyphosphoric acid (1 g) was heated at 140° for 3 hr. The cooled mixture was treated with water and the separated product was filtered off and sublimed at 270° (1 mm): yield 0.09 g (90%); mp 315°; ir 1712 cm^{-1} (CO); mass spectrum M^+ m/e 186; nmr (DMSO-d_6) τ 2.65 (m, H_7, H_8, H_9), 2.0 (m, H_{10}), 3.85 (broad, NH), H_3 was exchanged.

Anal. Calcd for $C_9H_6N_4O$: C, 58.06; H, 3.25. Found: C, 58.28; H, 3.55.

Hydrogenation of Compound 8a into 12. A mixture of **8a** (0.5 g), methanol (50 ml), and palladized carbon (0.2 g of 10%) was stirred in an atmosphere of hydrogen at room temperature for about 50 hr. Upon filtration the solution was evaporated to dryness and the residue was crystallized from ethanol: yield 0.45 g (90%); mp 260°; mass spectrum M^+ m/e 232; ir 1658 cm^{-1} (CO); nmr (DMSO-d_6) τ 8.69 (d, $CHCH_3$), 4.87 (q, CH), 7.68 (s, $COCH_3$), 7.65 (m, 7,10-CH_2), 8.36 (m, 8,9-CH_2), 6.70 (broad, NH), J_{CHMe} = 7.0 Hz.

Anal. Calcd for $C_{12}H_{16}N_4O$: C, 62.05; H, 6.94; N, 24.12. Found: C, 62.18; H, 7.08; N, 24.45.

Reaction between 3-Diazo-3*H*-indazole and Dimethyl Acetylenedicarboxylate. A solution of **2** (0.144 g) in chloroform (5 ml) was treated with dimethyl acetylenedicarboxylate (0.108 g) and the reaction mixture was heated under reflux for 10 hr. The solvent was evaporated to one-third of its original volume, and after addition of petroleum ether and cooling the product separated. It was identified as indazole. The same compound could be obtained when a methanolic solution of **2** was irradiated with a wavelength of 300 nm: yield 0.02 g (17%); mp 145–148° (lit.[17-19] mp *ca.* 145–148°); nmr ($CDCl_3$) τ 2.85 (s, H_3), 2.6 (m, H_4, H_5, H_6, H_7).

Reaction between Indazolo[3,2-c]-1,2,4-triazines and a Base. A suspension of the corresponding indazolo[3,2-c]-1,2,4-triazine (0.001 mol) in ethanol (5 ml) was treated with hydrazine hydrate (0.5 ml of 80%) (or 0.5 ml of a 5% aqueous solution of potassium hydroxide can be used) and the mixture was heated under reflux until no more of the starting compound was present. The latter was slowly dissolved and the progression of the reaction can be followed by tlc; 1–2 hr are necessary for a complete conversion. The reaction mixture was evaporated to dryness (if KOH is used, the solution is first neutralized) and the residue was treated with water (15 ml) and extracted with chloroform (3 × 10 ml). The combined extracts were dried over anhydrous sodium sulfate and upon evaporation of the solvent the product was identified as 3-aminoindazole, identical with an authentic specimen[16,20] (yields were 80–90%).

3-Aminoindazole was obtained similarly if compounds of the type **4, 5, 6,** or **7a** were treated with a base.[21]

Registry No.—2, 2596-89-6; **4a,** 51271-52-4; **4b,** 51271-53-5; **4c,** 51271-54-6; **4d,** 51271-55-7; **4e,** 51271-56-8; **5a,** 51271-57-9; **5b,** 51271-58-0; **6,** 51271-59-1; **7a,** 51271-60-4; **7b,** 51271-61-5; **8a,** 51293-26-6; **8b,** 51271-62-6; **8c,** 51271-63-7; **8d,** 51271-64-8; **8e,** 51271-65-9; **9a,** 51271-66-0; **9b,** 51271-67-1; **10,** 51271-68-2; **11a,** 51271-69-3; **11b,** 51271-70-6; **12,** 51271-72-8; 2,4-pentanedione, 123-54-6; 1-phenyl-1,3-butanedione, 93-91-4; 1,3-cyclohexanedione, 504-02-9; 5,5-dimethyl-1,3-cyclohexanedione, 126-81-8; 1,3-indandione, 606-23-5; ethyl 3-oxobutyric acid, 141-97-9; ethyl 3-oxobenzenepropanoic acid, 94-02-0; diethyl 3-oxopentanedioic acid, 105-50-0; diethyl malonate, 105-53-3; diethyl heptanedioate, 2050-20-6; dimethyl acetylenedicarboxylate, 762-42-5; indazole, 271-44-3.

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Studies on Organic Fluorine Compounds. XIV.[1] Syntheses and Reactions of (Trifluoromethyl)indoles[2]

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To compare the reactivity of (trifluoromethyl)indoles with that of (trifluoromethyl)quinolines, 2- and 3-(trifluoromethyl)indoles (**12** and **13**) were synthesized from 3- and 4-(trifluoromethyl)quinoline in four steps: N-oxidation, oxidative cyanation using potassium cyanide and potassium ferricyanide, photomigration reaction to benzoxazepine derivatives, and recyclization with hydrogen chloride to indoles. Reactions of **12** and **13** with nucleophiles (sodium ethoxide, lithium aluminum hydride, sodium borohydride, and sodium amide) were examined, and **12** and **13** were found to undergo SN1-type reaction and the trifluoromethyl group in **13** was more reactive than that in **12**. These results were discussed.

A trifluoromethyl group on an aromatic ring is generally a very stable substituent,[3] and there has been little study of the reactions of the trifluoromethyl group on the heterocyclic ring. In previous papers[4] we have reported a study of the reactivity of the trifluoromethyl group on the quinoline ring with nucleophilic reagents and found three types of reactions: SN2 substitution of fluoride, elimination of fluoride, and displacement of the trifluoromethyl carbanion. Typical examples are shown in Scheme I.

Since the trifluoromethyl group on the π-deficient quinoline ring shows unusual reactivity to nucleophilic reagents, it was of interest to examine the reactivity of this group on the π-electron excess indole ring. Indoles with a trifluoromethyl group on the pyrrole ring have not been reported to date. We have devised a synthetic route to such indoles from (trifluoromethyl)quinoline by the series of reactions shown in Scheme II.

In this method, 3- or 4-(trifluoromethyl)quinoline (**4** or **5**), obtained with sulfur tetrafluoride[5] or copper powder–trifluoromethyl iodide,[6] was converted into its *N*-oxide (**6** or **7**) by acetic acid–hydrogen peroxide.[7] A cyano group was introduced into the 2 position of **6** or **7** with retention of the *N*-oxide group by oxidative cyanation with potassium ferricyanide and potassium cyanide.[8] The resultant compound (**8** or **9**) was photoirradiated in an aprotic solvent to produce a benzoxazepine derivative (**10** or **11**), and the corresponding 2- or 3-(trifluoromethyl)indole (**12** or **13**) was successfully synthesized by ring opening and then closure with dry hydrogen chloride gas in methanol. When photoirradiation was carried out in methanol, the *N*-methoxycarbonylindole derivative (**14** or **15**) was obtained as a by-product. However, hydrolysis of **14** (or **15**) to **12** (or **13**) was unsuccessful; this may be due to the carbamate group of **14** (or **15**), which was stabilized by the electronic effect of the indole ring, and to the fact that indole itself is unstable to acids.

Next, we examined the reaction of **12** or **13** with nucleophilic reagents. We used sodium ethoxide and sodium amide; we also used metal hydrides to examine the reduction, since they attack as the hydride anion. These results are shown in Scheme III.

The fact that benzotrifluoride was recovered in these reaction conditions shows that susceptibility of the trifluoromethyl group to nucleophilic attack is increased by the electronic effect of the indole ring. This suggests that the carbon–fluorine bond in the trifluoromethyl group is cleaved in SN1-like manner. Further investigation of the results from **12** and **13** shows a considerable difference in their reactivity. Both compounds undergo alcoholysis when refluxed with sodium ethoxide in ethanol. With the

Scheme I