Indazole Derivatives : The Synthesis of Various Amino- and Hydroxy-indazoles and Derived Sulphonic Acids.

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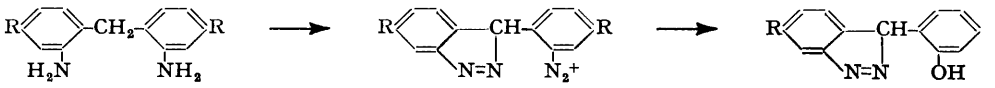
The preparation of a series of indazole derivatives from various substituted *o*-toluidines is described and evidence given that 3-nitro-2 : 6-xylidine affords a mixture of 6- (36%) and 4-nitro-7-methylindazole (64%). Chlorination of 6-nitroindazole affords 3-chloro-6-nitroindazole whereas sulphonation and nitration give the 5-substituted derivatives. Nitration and sulphonation of 5-nitroindazole give the 7-substituted derivatives.

The preparation and properties of several new amino- and hydroxy-indazolesulphonic acids * are described and tentative structures assigned to the products.

The preparation of nitroindazoles from the corresponding nitro-*o*-toluidines and related compounds *via* their diazo-derivatives is well known (see, *e.g.*, Grandmougin, Noelting, and Witt, *Ber.*, 1890, **23**, 3655; Grandmougin and Michel, *Ber.*, 1893, **26**, 2349; Noelting, *Ber.*, 1904, **37**, 2556). The method for the preparation of 5-nitroindazole (*Org. Synth.*, **20**, 72) by interaction of 4-nitro-*o*-toluidine ($NH_2 = 1$) with sodium nitrite in acetic acid was found of general easy applicability. With a series of *o*-toluidines indazoles are formed in good yield if a nitro-group is present and earlier work by Duval (*Compt. rend.*, 1908,

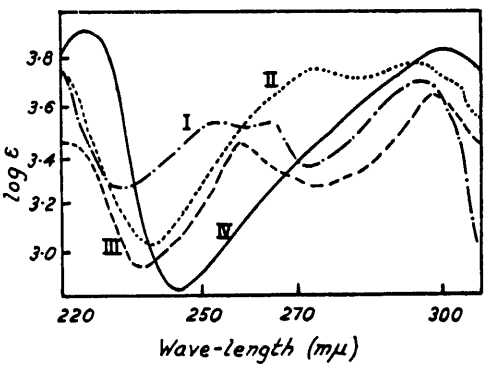
* Patent protection pending.

146, 1407; 1912, **154**, 780) on the ring closure of bis-*o*-aminophenylmethanes by tetrazotisation showed that electronegative groups in the *para*-position favoured ring closure. In the light of recent work and Duval's finding that his " bis-endo-azo compounds " gave a monohydroxy-compound on hydrolysis, it appears probable that his products were cyclised on one side.



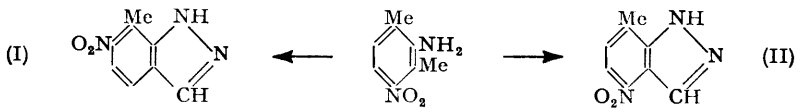
Although *o*-toluidine gives only 3—6% yields of indazole on reaction with nitrous acid (*Org. Synth.*, *loc. cit.*), Pschorr and Hope (*Ber.*, 1910, **43**, 2563) obtained a 75% yield of 3-cyanoindazole from 2-aminobenzyl cyanide. So, with electronegative substituents in the side chain and the nucleus, indazole formation might be expected to approach 100%. Conversely, chlorine or methyl in the 5-position depressed the yield.

Noelting (*Ber.*, 1904, **37**, 2556) stated that 3-nitro-2 : 6-xylidine gave two methylnitroindazoles, m. p. 175—176° and 222·5° respectively but did not assign structures. In our hands the reaction of 3-nitro-2 : 6-xylidine with nitrous acid in acetic acid gave 76% of mixed isomers, extraction of which with 50% alcohol afforded an insoluble isomer, m. p. 222° (64%), and a soluble isomer, m. p. 179° (36%). The former was 7-methyl-6- (I) and the latter 7-methyl-4-nitroindazole (II) since the amine derived from the latter coupled readily with diazo-compounds, as also did the derived hydroxyindazole, whereas the isomeric compounds did not. Further, the 2 : 3-hydroxynaphthoylamide derived from the



Absorption spectra for (I) 1-*methylindazole*, (II) 2-*methylindazole*, (III) 7-*hydroxy*-1-*methylindazole*, *and* (IV) 7-*hydroxy*-2-*methylindazole*. (I) and (II) after Rousseau and Lindwall, *loc. cit.* (III) and (IV) in MeOH.

soluble isomer gave shades with diazo-components corresponding to those from 4-(2-hydroxy-3-naphthoylamino)indazole whereas that from the insoluble isomer gave shades corresponding to those from 6-(2-hydroxy-3-naphthoylamino)indazole.



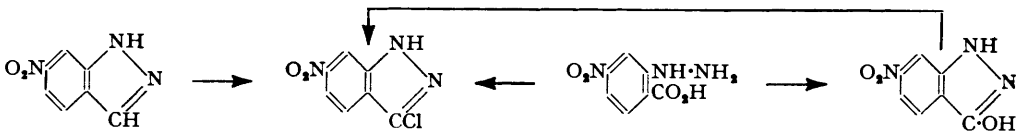
Methylation of 6-nitroindazole to about equal parts of 6-nitro-2- and 6-nitro-1-methylindazole was accomplished by the method of Barclay, Campbell, and Dodds (*J.*, 1941, 113). 7-Nitroindazole in water with methyl sulphate gave 82% of a mixture of isomers, m. p. 98° (53%) and 143° (47%) respectively. The two isomers were reduced and the amines converted into the corresponding hydroxyindazoles the ultraviolet absorption of which (see Figure) showed the hydroxyindazole derived from the isomer of m. p. 98° to correspond to the published curve for 1-methylindazole (Rousseau and Lindwall, *J. Amer. Chem. Soc.*, 1950, **72**, 3047) whereas that for the other hydroxy-indazole corresponded to that for 2-methylindazole.

Benzoylation of the various nitroindazoles likewise gave mixtures of two separable isomers. By analogy the less soluble were considered to be the 2-benzoyl isomers, which

received support from the finding that they were the more stable. The benzoylnitroindazoles were much less stable than the methylnitroindazoles (cf. earlier work on acetyl derivatives: Noelting, *Ber.*, 1904, **37**, 2556).

Ring-closure of diazotised 2-ethyl-5-nitroaniline to 3-methyl-6-nitroindazole was directly comparable with the ring-closure of diazotised 5-nitro-*o*-toluidine. The product was very similar to 6-nitroindazole.

It is stated in B.P. 518,987 without details or proof of orientation that 6-amino-3-chloroindazole (m. p. 185°) is obtained by the chlorination of 6-nitroindazole and reduction of the product. Chlorination of 6-nitroindazole in water at 90—95° afforded 98% of a chloroderivative, m. p. 154°, which gave an amine, m. p. 184°. The nitro-compound was not identical with 5-chloro-6-nitro- (m. p. 172°) or 4-chloro-6-nitro-indazole (m. p. 190°) and the shades obtained with azo-dyes prepared from the amine were similar to those from 6-aminoindazole and dissimilar from those from 4-, 5-, or 7-aminoindazole. Final evidence that the chlorine atom occupied the 3-position was obtained by the action of phosphorus oxychloride or phosphorus pentachloride on 2-hydrazino-4-nitrobenzoic acid or phosphorus trichloride on 6-nitroindazolone which gave the same chloronitroindazole.



Attempts to hydrolyse 3-chloro-6-nitroindazole to 3-hydroxy-6-nitroindazole failed. 2-Hydrazino-4-nitrobenzoic acid (cf. Pfannstiel and Janecke, *Ber.*, 1942, **75** 1096) was cyclised by dehydration in nitrobenzene.

2-*p*-Methoxyphenyl-6-nitroindazole was prepared by Chardonneus and Buch's route (*Helv. Chim. Acta*, 1943, **65**, 874) except that the 2-methylazobenzene was oxidised in 75% yield with hydrogen peroxide in presence of ferrous sulphate instead of nitrosobenzene, the latter giving only small yields.

Reduction of the various nitroindazoles and characterisation of the amines proceeded normally. Conversion into the hydroxyindazoles was readily accomplished by hydrolysis with 10% sulphuric acid at 170—180° (as described in B.P. 697,977), after several other methods for their preparation had failed. Alkali fusion of indazole-5-sulphonic acid, prepared by diazotisation and cyclisation of 3-methylsulphanilic acid, gave only a small amount of *m*-cresol and much alkali-insoluble material. A Bücherer reaction on 5-aminoindazole gave only negligible yields of 5-hydroxyindazole. All the monohydroxyindazoles except 6-hydroxy-7-methylindazole gave nitroso-derivatives which yielded intensely coloured iron complexes.

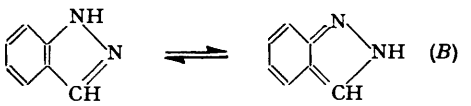
Fries, Fabel, and Echardt (*Annalen*, 1942, **550**, 31) found that nitration of 6-nitroindazole gave 5 : 6-dinitroindazole which could be reduced to the 5 : 6-diamine and then hydrolysed to 5 : 6-dihydroxyindazole. As evidence for this *ortho*-nitration, the authors stated that the diamine gave the usual *ortho*-condensation products, was not identical with 6 : 7-diaminoindazole, and formed a triazole with nitrous acid. This work has been confirmed. The 5 : 6-diaminoindazole was obtained as remarkably stable white crystals. It reacted with only one equivalent of nitrous acid, presumably giving a triazole since the product did not couple. With phenanthraquinone it gave a yellow product (m. p. 325°) which in concentrated sulphuric acid gave the carmine colour associated with such condensation products. The diamine gave intensely coloured bisazo-dyes and was hydrolysed to the dihydroxyindazole in 85% yield by 20% sulphuric acid at 150°.

Fries *et al.* (*loc. cit.*) state that the ultraviolet absorption spectra of 1-methylindazole and indazole correspond and are different from that of 2-methylindazole. 1-Methyl-6-nitroindazole paralleled 6-nitroindazole in giving exclusively 5-nitration. 2-Methyl-6-nitroindazole, on nitration and reduction, gave mainly an *o*-diamine, but also a *m*-diamine which, however, was not obtained pure. 5-Nitroindazole gave a dinitro-compound (not 5 : 6-dinitroindazole) and thence a *m*-diamine.

Sulphonation of 6-nitroindazole with 20% oleum at 120—130°, followed by reduction,

gave the presumed 6-aminoindazole-5 sulphonic acid obtained from 6-aminoindazole (see below). Identity was established by (*a*) hydrolysis with 10% sulphuric acid to 6-hydroxyindazole (total desulphonation) and (*b*) hydrolysis with water to 6-hydroxyindazole-5-sulphonic acid (see below). Similarly, it was proved that 5-nitroindazole undergoes *meta*-sulphonation, to give 5-nitroindazole-7-sulphonic acid.

The activity of the 5-position in 6-nitroindazole may be explicable in terms similar to those used by Efros (*J. Gen. Chem.*, *U.S.S.R.*, U.S. translation, 1952, **22**, 1063) for 5(6)nitrobenziminazoles which also undergo *ortho*-nitration. On this basis, the link between the 5- and the 6-carbon atom of the indazole nucleus is considered to be preponderantly of single-



bond character; the approximate proportion of 2 : 1 in the ratio of 2-methyl derivatives to 1-methyl derivatives suggests a preponderance of structure (*B*). The only other exception to the naphthalene character of indazole derivatives encountered in this work was the chlorination of 6-nitroindazole in the 3-position which may perhaps have analogy in the side-chain chlorination of the benzene series. Apart from such exceptions, which may be explicable by the directing influence of the heterocyclic nitrogen atoms, the naphthalene character of the indazole ring was generally supported. The resemblance of 5- and 6-hydroxyindazole to β-naphthol was exemplified by their carboxylation to 5-hydroxyindazole-6- and 6-hydroxyindazole-5-carboxylic acid respectively. These acids resembled 2 : 3-hydroxynaphthoic acid and coupled with diazonium compounds without loss of carbon dioxide. The shades of azo-dyes prepared from the various indazole derivatives were similar to those from the naphthalene analogues. The much stronger bathochromic effect of a hydroxy- or an amino-group in the 5- and the 7-position compared with the 4- and the 6-position was evident throughout the series.

Little has previously been recorded on indazolesulphonic acids. After our work on them was completed, Peticolas and Sureau (*Bull. Soc. chim. France*, 1950, 466) described the preparation of indazole-4-, -5-, -6-, and -7-sulphonic acid by diverse routes and characterised them as benzoylguanidinium salts and sulphonyl chlorides, and by alkali fusion to the hydroxyindazoles, the last being the main criterion for configuration. Our results differed in some respects; possibly the sulphonation conditions are critical (cf. naphthalene). It is surprising that the indazole nucleus is stable to caustic fusion. The main divergencies lie in the sulphonation products of 5- and 6-aminoindazole. Peticolas and Sureau concluded that oleum afforded 6-aminoindazole-7- and 5-aminoindazole-4-sulphonic acid. We, however, obtained acids which coupled readily, both before and after acid hydrolysis, to give soluble azo-dyes, and consider sulphonation to have given 6-aminoindazole-4- and 5-aminoindazole-7-sulphonic acid. In view of these apparent anomalies the configurations below are only tentative; they are based on three criteria, namely, coupling reactions of the products, configuration of the starting material, and the melting point of the *S*-*p*-chlorobenzylthiuronium hydroxyindazolesulphonates. It is pertinent that the compounds considered to be 6-hydroxyindazole-7- and 5-hydroxyindazole-4-sulphonic acid did not couple.

Sulphonation of 6-aminoindazole with 20% oleum at 120° gave a product which with diazotised *p*-chloroaniline in alkali readily gave a soluble red azo-dye. Coupling was assumed to take place in the 7-position and the constitution tentatively considered to be 6-aminoindazole-4-sulphonic acid. Heating this product at 180° with a molar equivalent of 10% sulphuric acid gave a hydroxyindazolesulphonic acid without detectable desulphonation. This compound gave a soluble orange azo-dye.

Heating 6-aminoindazole sulphate with sulphuric acid in *o*-dichlorobenzene at 176° gave a different sulphonic acid. This also coupled readily with diazotised *p*-chloroaniline to give a soluble red azo-dye, indicating the 7-position to be unoccupied, and so was considered to be 6-aminoindazole-5-sulphonic acid which, as stated above, was also obtained from 6-nitroindazole by sulphonation and reduction. Heating this new acid at

180° with a molar equivalent of 10% sulphuric acid gave a quantitative yield of 6-hydroxyindazole. Desulphonation preponderated even with only traces of mineral acid or with neutral solutions in the presence of iron. Heating at 180° with water alone in glass, however, gave good yields of, presumably, 6-hydroxyindazole-5-sulphonic acid. This also coupled readily, to give a soluble orange azo-dye, and its *S*-*p*-chlorobenzylthiuronium salt differed from that of its isomer.

With 100% sulphuric acid at 100° 6-hydroxyindazole gave a monosulphonic acid which did not couple; its *S*-*p*-chlorobenzylthiuronium salt differed from that of the preceding acid. The product is considered to be 6-hydroxyindazole-7-sulphonic acid. Prolonged heating of this sulphonic acid or 6-hydroxyindazole with 95% sulphuric acid at 130° gave a mixture containing 20—30% of 6-hydroxyindazole-5-sulphonic acid. Treatment with ammonia in the presence of sodium hydrogen sulphite gave 6-aminoindazole-7-sulphonic acid which did not couple in acetic acid.

Nitrosation of 6-hydroxyindazole, followed by reaction with sodium hydrogen sulphite, as in the preparation of 4-amino-3-hydroxynaphthalene-1-sulphonic acid, gave a product considered to be 7-amino-6-hydroxyindazole-4-sulphonic acid. The product diazotised in the presence of copper sulphate to give a stable diazo-compound which coupled with α- or β-naphthol in 2-ethoxyethanol.

Application of the same series of reactions to 5-aminoindazole and 5-hydroxyindazole gave analogous products except that 5-aminoindazole-6-sulphonic acid was desulphonated even with water in glass, so that 5-hydroxyindazole-6-sulphonic acid was not prepared.

4-Methyl-5-nitrometanilic acid and nitrous acid gave 4-nitroindazole-6-sulphonic acid and thence the amino- and hydroxy-acid, the last giving a soluble orange azo-dye.

Experimental

Coupling was with diazotised *o*-chloroaniline unless otherwise stated.

Preparation of Nitroindazoles.—The method of *Org. Synth.*, **20**, 72, for the preparation of 5-nitroindazole was applied to a series of *o*-toluidines, the product being isolated by distillation of the glacial acetic acid under reduced pressure and recrystallised from 10% acetic acid or ethanol. Thus were obtained : 4- (79%), m. p. 202°, 5- (72%), m. p. 180°, 6- (88·5%), m. p. 209°, and 7-nitroindazole (71%), m. p. 180° (Noelting, *loc. cit.*, gives m. p. 203°, 181°, 208°, and 186·5—187·5°, respectively) ; 5-methyl-6-nitroindazole (53%), m. p. 173° (Noelting, *loc. cit.*, gives m. p. 173—174°) ; 4-*chloro*- (81%), pale yellow needles (from water), m. p. 190° (Found : C, 42·0; H, 1·9; N, 20·9; Cl, 18·1. $C_7H_4O_2N_3Cl$ requires C, 42·5; H, 2·0; N, 21·25; Cl, 17·95%), and 5-*chloro*-6-*nitroindazole* (34%), yellow needles (from water), m. p. 172° (Found : C, 42·1; H, 2·1; N, 21·3; Cl, 17·8%) ; 6-*methoxy*-5-*nitroindazole* (35%), fawn, m. p. 191° (Found : C, 49·3; H, 3·45; N, 21·2. $C_8H_7O_3N_3$ requires C, 49·7; H, 3·6; N, 21·75%) ; 6-*chloro*-5-*nitroindazole* (63·3%), pale brown, m. p. 213° (Found : N, 20·8; Cl, 18·2%) ; 6-*methyl*-4-*nitroindazole* (73·5%), buff, m. p. 204° yield (Found : N, 23·2. $C_8H_7O_2N_3$ requires N, 23·7%) ; 3-*methyl*-6-*nitroindazole* (73·5%), cream-coloured, m. p. 182° (Found : C, 54; H, 4·1; N, 23·4. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·95; N, 23·7%).

Ring-closure of 3-*Nitro*-2 : 6-*xylidine.*—The mixture (110 g.) of isomers produced, m. p. 209—210°, was extracted three times with boiling 50% v/v ethyl alcohol (1 l.) for ½ hr. The insoluble 7-methyl-6-nitroindazole (see below), dried at 100°, was fawn-coloured (64 g.) and had m. p. 222° (Noelting, *loc. cit.*, gives m. p. 222·5°). The ethanol liquors were evaporated to 500 c.c. and allowed to crystallise. 7-Methyl-4-nitroindazole (see below) was filtered off and dried (37 g. ; m. p. 179° ; Noelting, *loc. cit.*, gives m. p. 175—176°).

Methylation of 7-*Nitroindazole.*—To 7-nitroindazole (60 g.), dissolved in water (1·4 l.) and 32% sodium hydroxide solution (200 c.c.) at 80°, methyl sulphate (132 g.) was added while the temperature was allowed to fall to 65° during ½ hr. The mixture was stirred at 60—65° for 2 hr. After cooling to 30° the fawn precipitate was filtered off and recrystallised from butanol repeatedly to separate 2-*methyl*-7-*nitroindazole* (30·6 g.), m. p. 143° (Found : N, 23·8. $C_8H_7O_2N_3$ requires N, 23·7%), from 1-*methyl*-7-*nitroindazole* (34·6 g.), m. p. 98° (Found : N, 23·4%).

Methylation of 6-*Nitroindazole.*—Methylation of 6-nitroindazole by the same method followed by separation by Barclay, Campbell, and Dodds's method (*J.*, 1941, 113; fractionation from methyl alcohol) gave 1-methyl-, m. p. 122°, and 2-methyl-6-nitroindazole, m. p. 158° (Barclay *et al.* give m. p. 125° and 160° respectively).

Benzoylation of Nitroindazoles.—Benzoylation of 6-nitroindazole in dilute sodium hydroxide

solution at 50° gave a mixture, m. p. 138° (62% yield). Repeated recrystallisation from methanol separated the 2-*benzoyl isomer*, m. p. 165° (20%) (Found: N, 15·2. $C_{14}H_9O_3N_3$ requires N, 15·7%), from the more soluble 1-*benzoyl isomer*, m. p. 161° (42%) (Found: N, 14·9%).

5-Methyl-6-nitroindazole similarly afforded a mixture (73·5%; m. p. 122°) of the 1-*benzoyl compound*, m. p. 163° (37·5%) (Found: N, 14·7. $C_{15}H_{11}O_3N_3$ requires N, 14·9%), and the 2-*benzoyl isomer* (36%), m. p. 162° (Found: N, 15·2%), separated by crystallisation from butanol.

5-Nitroindazole afforded a mixture, m. p. 172° (77%), separated by methanol into 1- (50·5%), m. p. 190° (Found: N, 15·4%), and 2-*benzoyl-5-nitroindazole* (Found: N, 15·8%). Similar benzoylation of 6-chloro-5-nitroindazole and crystallisation from butanol gave 1- (24%), m. p. 203° (Found: N, 13·3. $C_{14}H_8O_3N_3Cl$ requires N, 13·9%), and 2-*benzoyl-6-chloro-5-nitroindazole* (46·5%), m. p. 192° (Found: N, 13·5%). Benzoylation of 6-methoxy-5-nitroindazole and crystallisation from methanol gave 1- (20%), m. p. 192° (Found: N, 13·8. $C_{15}H_{11}O_4N_3$ requires N, 14·1%), and 2-*benzoyl-6-methoxy-5-nitroindazole* (40%), m. p. 186° (Found: N, 14·3%).

Chlorination of 6-Nitroindazole.—B.P. 518,987 states without experimental details that 3-chloro-6-nitroindazole is obtained by chlorination of 6-nitroindazole. Chlorine was passed for 3 hr. into a suspension of 6-nitro-indazole (0·1 mole) in water (100 c.c.) at 95° ± 2°. The precipitate, recrystallised from ethanol, gave yellow needles (18 g.), m. p. 154° (3-*chloro-6-nitroindazole*) (Found: Cl, 18·2. $C_7H_4O_2N_3Cl$ requires Cl, 17·95%). The mixed m. p. with 5-chloro-6-nitroindazole (m. p. 185°) was 111—113° and with 4-chloro-6-nitroindazole (m. p. 184°) was 136°. Attempts to convert it into 3-amino-6-nitroindazole failed.

6-*Nitroindazolone* (3-*Hydroxy-6-nitroindazole*) (cf. Pfannstiel and Janecke, *Ber.*, 1942, **75**, 1096).—4-Nitroanthranilic acid (113 g.; m. p. 271°) was dissolved in water (1·7 l.) and 32% sodium hydroxide solution (60 c.c.). 40% Sodium nitrite solution was added (120 c.c.) and the resulting dark orange solution added during 20 min. to 36% hydrochloric acid (214 c.c.) and the minimum amount of ice to hold the temperature below 5°. The resulting solution was added at 0—5° to a mixture of 32% sodium hydroxide solution (260 c.c.) and 40% sodium hydrogen sulphite solution (427 c.c.), and stirring at 0—10° continued for 1 hr. 36% Hydrochloric acid (820 c.c.) was added and the temperature raised to 60° during ½ hr. After being stirred at room temperature overnight, sodium chloride was added to 20% concentration, the mixture cooled to 10°, and the hydrazine hydrochloride filtered off. The hydrazine hydrochloride paste (220 g., 60% yield) was added portionwise during 2 hr. to nitrobenzene (350 g.) during gradual distillation to remove water, the volume being held constant by addition of nitrobenzene. Then distillation was continued for a further ½ hr. The mixture was cooled in ice, diluted with benzene (200 c.c.), and filtered. The filter cake was suspended in water (500 c.c.) and steam distilled to remove benzene and nitrobenzene. The solution was treated with carbon and filtered, and the filtrate cooled. The orange-red needles of 3-hydroxy-6-nitroindazole were filtered off and dried at 60° (60 g.; m. p. 237·5°). A single recrystallisation from water raised the m. p. to 243° (Pfannstiel and Janecke, *loc. cit.*, give m. p. 244°) (Found: N, 23·2. Calc. for $C_7H_5O_3N_3$: N, 23·45%). No success attended attempts to aminate 3-hydroxy-6-nitroindazole.

Conversion of 3-Hydroxy-6-nitroindazole into 3-Chloro-6-nitroindazole.—Various methods for the ring-closure of 2-hydrazinobenzoic acid gave unsatisfactory results with 2-hydrazino-4-nitrobenzoic acid; use of phosphorus trichloride or phosphorus oxychloride giving 3-chloro-6-nitroindazole. 3-Hydroxy-6-nitroindazole was converted into 3-chloro-6-nitroindazole by an excess of boiling phosphorus trichloride: the product, recrystallised from ethanol, had m. p. and mixed m. p. 154°.

2-p-*Methoxyphenyl-6-nitroindazole* (cf. Chardonneus and Buch, *loc. cit.*).—The preparation of 4′-methoxy-2-methyl-3-nitroazobenzene offered no difficulty but ring-closure by nitrosobenzene gave only a negligible yield of material of the correct m. p. A suspension (80 g.) in glacial acetic acid (450 c.c.) was heated with hydrogen peroxide (100-vol.; 49 c.c.) in the presence of ferrous sulphate (3 g.) at 80—85°; the product (75%), purified by extraction with ethanol, had m. p. 150° (Chardonneus and Buch give m. p. 152°).

Preparation of Aminoindazoles.—Since reduction of nitroindazoles with iron in water (method A) sometimes caused decomposition, it was often accomplished in alcohol (method B) or by hydrogenation in presence of Raney nickel (method C) (cf. Kwurther and Lucas, *J. Amer. Chem. Soc.*, 1943, **65**, 1804). *Products* (see Table) were recrystallised from alcohol or water, and converted into the 3-hydroxy-2-naphthoyl derivatives (cf. B.P. 707,897), which were coupled with diazotised *o*-chloroaniline.

Preparation of the Hydroxyindazoles.—Aminoindazoles gave the corresponding hydroxyindazoles readily on acid hydrolysis (cf. B.P. 697,977). This method was also applicable to

the preparation of several hydroxyindazolesulphonic acids. Alternative methods gave very poor results, negligible amounts being formed by caustic fusion of the sulphonic acid and diazotisation of the amino-compound followed by boiling with sulphuric acid afforded low yields of impure products.

Aminoindazoles.

Substituent at position							Method of prep.	Yield (%)	M. p.	Found N (%)	Reqd. N (%)	2 : 3-HO·$C_{10}H_7$·CO deriv. M. p.	2 : 3-HO·$C_{10}H_7$·CO deriv. coupling, shade of orange
1	2	3	4	5	6	7							
			NH_2				C	92·5	150° [a]	31·3	31·6	296°	Yellow
				NH_2			C	82	183 [b]	31·25		245	Red
					NH_2		A	86	209 [c]	31·4		274	
						NH_2	C	86	162	31·6		218	Red
				Me	NH_2		B	71·5	165	28·3	28·6	258	
				Cl	NH_2		C	88	194	25·2 [d]	25·05	248	Dull
			Cl		NH_2		C	88	198	24·8 [e]	25·05	294	
			NH_2	Cl			A	88	178	—[f]		252	Red
			NH_2	OMe			B	90	165	25·3	25·75	263	Red
					NH_2	Me	C	84	182	28·5	28·6	299	
			NH_2			Me	C	87·5	124	28·2		279	Yellow
			NH_2		Me		C	79	126	28·2		279	Yellow
		Me			NH_2		C	91	205	28·2		284	
	Me				NH_2		B	81	165	28·4		212	Dull
Me					NH_2		C	75·3	130	28·3		180	Dull
Me						NH_2	B	72	135	28·4		—	
	Me					NH_2	B	(90) [g]	73	28·2		—	
Bz					NH_2		C	80	194	17·2	17·7	257	
	Bz				NH_2		C	70	179	17·4	17·7	266	
	Bz			Me	NH_2		C	74	185	16·3	16·7	249	Dull
Bz				NH_2			—[h]	90	178	16·9	17·7	249	Red
	Bz			NH_2			—[h]	60	170	17·5	17·7	276	Red
		Cl			NH_2		C	76	184	25·2 [i]	25·05	269	
	Ar [j]				NH_2		—	32	174	17·1	17·6	211	Dull
		OH			NH_2		C	80·5	285	28·2	28·2	—	

[a] Plates. [b] Prisms. [c] Needles. [d] Found: Cl, 20·8. Reqd.: Cl, 21·2%. [e] Found: Cl, 20·6%. [f] Found: Cl, 21·0%. [g] Partly oily. [h] Prep. by Zn in EtOH. [i] Found: Cl, 20·6. Reqd.: Cl, 21·2%. [j] Ar = *p*-MeO·C_6H_4; prep. by aq. Na_2S.

6-*Hydroxyindazole*. 6-Aminoindazole (66·5 g.), 96% sulphuric acid (50 g.), and water (500 c.c.) were heated in an enamel-lined autoclave (750-c.c. capacity) to 170° in 1 hr. and then at 170—175° for 10 hr. (pressure 200—220 lb. per sq. in.). The pale brown solution was filtered, neutralised to Congo-red with sodium hydroxide solution, and cooled to 30°. The 6-hydroxyindazole was filtered off, washed with water, and dried at 60° (65 g., 95·5%; m. p. 216°). Recrystallisation from water gave pale fawn crystals, m. p. 217° (Found: N, 19·7. Calc. for $C_7H_6ON_2,\frac{1}{2}H_2O$: N, 19·6%). 6-Hydroxyindazole gave an orange colour on coupling and a red-brown colour with ferric chloride.

5-*Hydroxyindazole*. 5-Aminoindazole (66·5 g.), 100% sulphuric acid (50 g.), and water (500 c.c.) were heated at 175—180° as above (150 lb. per sq. in.). The mixture was made alkaline to Clayton Yellow by addition of 32% sodium hydroxide solution, acidified to Clayton Yellow with acetic acid, filtered, acidified to Brilliant Yellow with acetic acid, and treated with salt to 20% concentration. After 3 hr. the white crystals were filtered off and dried (62·5 g., 93%; m. p. 181—183°). Recrystallised from water, the product had m. p. 186° (Found: N, 18·7. Calc. for $C_7H_6ON_2,H_2O$: N, 18·4%). On coupling it gave a reddish-orange colour, and with ferric chloride a brown one.

4-*Hydroxyindazole*. The procedure described for 6-hydroxyindazole gave 4-hydroxyindazole in 72% yield, as needles, m. p. 163° (Found: N, 21·2. Calc. for $C_7H_6ON_2$: N, 20·9%); with ferric chloride it gave a yellow-brown, and on coupling a yellowish-orange colour.

7-*Hydroxyindazole*. The procedure described for 5-hydroxyindazole gave 64% of 7-hydroxyindazole, as pale pink needles (from water), m. p. 174° (Found: N, 21·0%), giving a brown precipitate with ferric chloride and a yellow-brown colour on coupling.

7-*Hydroxy*-1-*methylindazole*. The procedure described for 6-hydroxyindazole gave 79% of this *compound* as pale grey needles (from water), m. p. 163° (Found: N, 18·8. $C_8H_8ON_2$ requires N, 18·9%) (see Figure).

7-*Hydroxy*-2-*methylindazole*. Similarly, 7-*hydroxy*-2-*methylindazole* (71%) was obtained as pale pink needles, m. p. 179°, from water (Found: N, 19·3%) (see Figure).

4-Hydroxy-6-methylindazole (64·2%), pale orange needles, m. p. 176° (Found: N, 19·2%) (orange colour on coupling; pale brown with ferric chloride), and *4-hydroxy-7-methylindazole* (68%), yellow needles, m. p. 179° (Found: N, 19·1%) (orange colour on coupling; red-brown with ferric chloride), *6-hydroxy-7-methylindazole* (62%), cream needles, m. p. 164° (Found: N, 18·5%) (does not couple; brown colour with ferric chloride), and *6-hydroxy-3-methylindazole* (57·5%), m. p. 221° (Found: N, 19·2%) (bright orange on coupling; a red colour with ferric chloride), were similarly prepared.

Carboxylation of 5- and 6-Hydroxyindazole.—*6-Hydroxyindazole-5-carboxylic acid.* A solution of 6-hydroxyindazole (75 g.) in water (500 c.c.), with 50% w/v potassium hydroxide (60 c.c.) to alkalinity to Clayton Yellow, was evaporated to dryness under reduced pressure. The resulting powder was passed through a 60-mesh sieve, and heated in a rotating autoclave at 130°/20 mm. for ½ hr. The autoclave was charged with carbon dioxide to 200 lb. and heated to 210° during 3 hr. Heating at 210° ± 2° and 300 lb./sq. in. was continued for 12 hr. The mixture was dissolved in boiling water (300 c.c.), neutralised to faint alkalinity to Brilliant Yellow with 36% hydrochloric acid, cooled to 10°, and filtered. The filtrate was acidified to Congo-red with 36% hydrochloric acid. The white precipitate was filtered off, washed free from mineral acid with water, and dried at 60° (70 g.). Recrystallisation from butanol gave the *acid* as cream prisms, m. p. 202° (decomp.) (Found: N, 15·6. $C_8H_6O_3N_2$ requires N, 15·7%). The product dissolved in dilute sodium carbonate solution, coupled readily to give an orange colour, and gave a reddish-brown colour with ferric chloride.

5-Hydroxyindazole-6-carboxylic acid. 5-Hydroxyindazole (27 g.) was ground with potassium hydrogen carbonate (50 g.), the mixture passed through a 60-mesh sieve, and heated in a rotating autoclave at 210°/20 mm. during 1½ hr. Carbon dioxide was then passed in, to 420 lb./sq. in. Heating at 210° ± 2° was continued for 15 hr. during which the pressure dropped to 365 lb./sq. in. The autoclave was cooled and the solid product dissolved in water (500 c.c.) at 60°. The solution was filtered from insoluble material (7 g.), and the filtrate acidified to Congo-red with 36% hydrochloric acid. The white precipitate was filtered off, washed with water, and dried (24 g.). The *acid* crystallised from butanol as white needles, m. p. 205° (Found: N, 15·5%). The product was readily soluble in dilute sodium carbonate solution, coupled readily to give a reddish-orange solution, and gave a bluish-brown colour with ferric chloride.

Products from the Nitration and Sulphonation of Nitroindazoles.—*Nitration of 6-nitroindazole* (cf. Fries *et al.*, *loc. cit.*). To a solution of 6-nitroindazole (250 g.) in 96% sulphuric acid (2·5 l.) mixed 96% sulphuric (500 c.c.) and 96% nitric acid (500 c.c.) were added at 8—10° during 1 hr. Stirring at 8—10° was continued for 3 hr. and the solution poured on ice (8 kg.). The canary-yellow suspension was filtered, and the 5 : 6-dinitroindazole was washed, dried at 100° (290 g., 91%), and recrystallised from 10% acetic acid as yellow needles, m. p. 225° (Fries *et al.*, *loc. cit.*, give m. p. 224°, 70% yield).

5 : 6-Diaminoindazole. 5 : 6-Dinitroindazole (290 g.) was added during ¾ hr. to a solution of stannous chloride (2·9 kg.) in 36% hydrochloric acid (2·9 l.) with stirring at 5°. The first portion added (100 g.) raised the temperature to 50° and thereafter the temperature was held at 50—52° by cooling. The suspension of the double *salt* was stirred at 50—52° for 3 hr., cooled to 5°, and filtered off. A sample was recrystallised from water (Found: N, 13·6; Cl, 34·25. $C_7H_{10}N_4,2HCl,SnCl_2$ requires N, 13·6; Cl, 34·3%). The double salt paste was dissolved in water (3 l.) at 90°, carbon (10 g.) added, and, after 10 minutes' stirring at 90°. the solution was filtered and poured into water (1·3 l.) and 32% sodium hydroxide solution (1·3 l.) with stirring. The resulting white suspension was boiled for 10 min., cooled to 35°, and filtered. The solid was again boiled with dilute sodium hydroxide solution (2 l.), cooled to 35°, filtered, and washed free from alkali with water. The precipitated diamine was dried at 60° (85%; m. p. 280·5°) and recrystallised from water as white needles, m. p. 286° (Found: C, 56·6; H, 5·2; N, 37·2. Calc. for $C_7H_8N_4$: C, 56·7; H, 5·4; N, 37·8%). The product did not deteriorate in colour or nitrite strength in 4 years. It coupled readily with two equivalents of a diazo-compound to give deeply coloured products and absorbed only on equivalent of nitrous acid to give a triazole. Condensation in alcohol with a molar proportion of phenanthraquinone gave an orange derivative, m. p. 325° (decomp.), which dissolved in concentrated sulphuric acid to a carmine solution.

5 : 6-Dihydroxyindazole. The conditions given by Fries *et al.* (*loc. cit.*) gave a product difficult to purify. The following gave the best results: 5 : 6-Diaminoindazole (41·3 g.) and 20% w/w sulphuric acid (560 c.c.) were heated in an enamel-lined autoclave for 5 hr. at 145—150°, then cooled to 10° for ½ hr. and the 5 : 6-dihydroxyindazole sulphate was filtered off. The solid was stirred at 98—100° with water (500 c.c.) and sodium acetate crystals (43 g.) for 5 min.,

the solution filtered hot, and the residue extracted twice with hot water (200, 150 c.c.). The combined filtrates were boiled with carbon (5 g.) for 5 min., then filtered, and the filtrate acidified to Congo-red (faint purple) with 36% hydrochloric acid. The resulting white suspension was cooled in ice for 2 hr., then filtered and the product washed with water (100 c.c.), dried at 60°, (35·7 g.; m. p. 232·5°) and recrystallised from water (m. p. 234°; Fries *et al.*, *loc. cit.*, give m. p. 235°) (Found : N, 18·6. Calc. for $C_7H_6O_2N_2$: N, 18·7%).

Nitration of 1-*methyl*-6-*nitroindazole*. This indazole was nitrated as described for 6-nitroindazole. The product (m. p. of sample recrystallised from 10% acetic acid, 171°) was reduced similarly to a *diamine* which crystallised from water as white prisms, m. p. 263° (Found : C, 59·4; H, 6·7; N, 34·5. $C_8H_{10}N_4$ requires C, 59·2; H, 6·2; N, 34·55%). This absorbed one equiv. of nitrous acid and gave a phenanthraquinone derivative, m. p. 291° (carmine in sulphuric acid).

Nitration of 2-*methyl*-6-*nitroindazole*. Similar nitration of 2-methyl-6-nitroindazole gave a *product*, m. p. 213° (Found : N, 24·4. $C_8H_6O_4N_4$ requires N, 25·2%), reduced to a product which behaved as a *m*-diamine in that it gave a brown precipitate with nitrous acid and was very susceptible to air-oxidation. When purified by recrystallisation from water, 5 : 6-*diamino*-2-*methylindazole* crystallised in white needles, m. p. 226° (Found : C, 59·6; H, 7·1; N, 34·8%). The phenanthraquinone derivative, m. p. 291°, gave a mixed m. p. of 256° with the 1-methyl isomer and in concentrated sulphuric acid gave a red solution. Attempts to characterise the compound remaining in the liquors gave intractable tars. Catalytic hydrogenation of the dinitro-compound gave a larger amount of this impurity.

Nitration of 5-*nitroindazole*. 5-Nitroindazole (20 g.) in 98% sulphuric acid (200 g.) at 10° was treated with 95% nitric acid (40 c.c.) and 98% sulphuric acid (40 c.c.) dropwise during 3 hr. at 8—12°, and stirring at 8—12° continued for 3½ hr. The mixture was poured on ice (750 g.), then filtered, and the residue washed with water (400 c.c.) and with dilute ammonia solution (500 c.c.), dried at 70° (19 g.), and recrystallised from butanol as yellow prismatic needles, m. p. 222·5° (Zincke, *Annalen*, 1905, **339**, 224, gives m. p. 215° for 5 : 7-dinitroindazole prepared from 4 : 6-dinitro-*o*-toluidine). Reduction of the dinitro-derivative with stannous chloride was unsatisfactory owing to the high solubility and instability of the diamine. It was satisfactory as follows : the dinitro-compound (5 g.) in ethanol (90 c.c.) was hydrogenated at 20—25°/400 lb. per sq. in. in the presence of 50% Raney nickel (5 g.). Filtration and evaporation to dryness in nitrogen gave a pale fawn product (2·5 g.) which darkened rapidly in air and gave no condensation products typical of *o*-diamines. Attempted hydrolysis by the method used for 5 : 6-diaminoindazole resulted in de-amination, a 23% yield of 5-hydroxyindazole (m. p. and mixed m. p. 183°) being isolated by recrystallisation of the heterogeneous product from water.

Sulphonation of 6-*nitroindazole*. 6-Nitroindazole (49 g.) was added below 50° to 20% oleum (200 g.). The mixture was heated to 120° in ½ hr. and stirred at 120—130° for 5 hr., then poured on ice (100 g.) and water (100 c.c.), the resulting solution was diluted to 1 l. with water, and the sulphate was removed by addition of calcium oxide at 95°. The precipitate was extracted with hot water and the combined filtrates treated with sodium carbonate (16 g.). After filtration from calcium carbonate the liquid (5 l.) was evaporated to dryness. The product (59 g.) was dissolved in water (300 c.c.) and added during 3 hr. to iron filings (100 g.), ferrous sulphate (10 g.), and water (300 c.c.) with stirring at 90—95°. After a further hour's stirring at 95°, soluble iron was removed by the addition of 15% sodium carbonate solution (10 c.c.), the iron residue was filtered off and extracted with hot water, and the combined filtrates (2 l.) were acidified with hydrochloric acid and evaporated to dryness (50 g.). The crude product was purified as described below, yielding 6-*aminoindazole*-5-*sulphonic acid* (Found : N, 18·7. $C_7H_7O_3NS,\frac{1}{2}H_2O$ requires N, 18·9%). Hydrolysis with water as described for 6-hydroxyindazole-5-sulphonic acid (see below) gave a product, the *S*-*p*-chlorobenzylthiuronium salt of which had m. p. and mixed m. p. 226° with that from 6-hydroxyindazole-5-sulphonic acid.

Sulphonation of 5-*nitroindazole*. Sulphonation of 5-nitroindazole (49 g.) and reduction of the product as described above for 6-nitroindazole gave an *aminoindazolesulphonic acid* (36 g.), which was purified by reprecipitation from alkaline solution with sulphuric acid (Found : N, 19·5. $C_7H_7O_3N_3S$ requires N, 19·7%). Hydrolysis with dilute sulphuric acid as described below for 5-aminoindazole-7-sulphonic acid gave 5-hydroxyindazole-7-sulphonic acid (*S*-*p*-chlorobenzylthiuronium salt, m. p. 204°).

6-*Aminoindazole*-4-*sulphonic acid*. 6-Aminoindazole (53·2 g.) was added during ½ hr. to 20% oleum (200 g.) with stirring at $<50°$. After further stirring for 1 hr. the mixture was heated and stirred at 120—125° for 2 hr. The mixture was poured on ice (100 g.) and water

(200 c.c.), and treated with calcium oxide at 95°; the precipitate was converted into the sodium salt and its solution evaporated to dryness (78 g.). Purified by solution in dilute sodium carbonate (carbon), acidification with sulphuric acid, and crystallisation, the *acid* was colourless (Found : C, 36·4; H, 4·2; N, 18·6; S, 13·8. $C_7H_7O_3N_3S,H_2O$ requires C, 36·4; H, 3·9; N, 18·2; S, 13·8%). It absorbed one equiv. of nitrous acid and coupled in acetic acid solution with one equiv. of diazo-compounds.

6-Hydroxyindazole-4-sulphonic acid. 6-Aminoindazole-4-sulphonic acid (0·4 mole), water (500 c.c.), and 96% sulphuric acid (50 g.) were heated in an enamel-lined autoclave at 175—180° for 10 hr., then treated as above. The crude product (118 g.) was boiled in water (600 c.c.) with carbon (5 g.) and filtered at 100°. The filtrate was acidified to Congo-red (purple), and cooled to 30°. The white crystals, washed with water and dried at 100° (35 g.) (Found : N, 13·7. $C_7H_6O_4N_2S$ requires N, 13·1%), were soluble in water and coupled with one equiv. of *p*-chlorodiazobenzene to a soluble yellowish-orange dye and with ferric chloride gave a brown precipitate. The *S-p*-chlorobenzylthiuronium salt had m. p. 212·5—213·5°.

5-Aminoindazole-7-sulphonic acid. 5-Aminoindazole (39·9 g.) was added below 50° to 20% oleum (150 g.) and the mixture stirred at 120—125° for 2 hr. and poured on ice (300 g.). After 1 hr. the precipitated *acid* (63 g.) was purified as was 6-aminoindazole-4-sulphonic acid (Found : C, 39·2; H, 3·4; N, 19·3; S, 15·0. $C_7H_7O_3N_3S$ requires C, 39·4; H, 3·3; N, 19·7; S, 15·0%).

5-Hydroxyindazole-7-sulphonic acid. The foregoing acid (0·15 mole), 96% sulphuric acid (30 g.), and water (300 c.c.) were heated in an enamel-lined autoclave at 175—180° for 12 hr. The solution was boiled with carbon (5 g.) and filtered. The filtrate was neutralised with sodium acetate, treated with sodium chloride to 10% concentration, and cooled in ice for 3 hr. The white precipitate (27 g.) recrystallised from dilute acetic acid (Found : C, 38·8; H, 2·9; N, 13·0; S, 15·1. $C_7H_6O_4N_2S$ requires C, 39·2; H, 2·8; N, 13·1; S, 14·9%). The *acid* coupled with one equiv. of *p*-chlorodiazobenzene to give a reddish-orange and gave a red precipitate with ferric chloride. The *S-p*-chlorobenzylthiuronium salts had m. p. 205°.

6-Aminoindazole-5-sulphonic acid (cf. Adams *et al.*, B.I.O.S. report 1153). In a 2-l. 3-necked flask, equipped with ¼" diam. delivery tube approx. 7" long to the top of a 500 c.c. capacity calcium chloride trap, agitator with rubber gland and thermometer. The calcium chloride trap had two arms with taps, one to return to the flask and the other, at a lower level, to draw off. The top of the trap was connected to a vacuum line through a water reflux condenser. This apparatus was designed to ensure easy separation of water and return of *o*-dichlorobenzene to the flask. Heating was applied by an electric oil bath. 6-Aminoindazole sulphate (109 g.), mixed with 100% sulphuric acid (53·5 g.), was heated with *o*-dichlorobenzene (980 c.c.) to 160° with decreasing vacuum during 3 hr. and held at 100° under partial vacuum to maintain reflux through the calcium chloride trap for 1 hr. The temperature was raised to reflux (176°) without vacuum and stirring and refluxing were continued overnight. The *o*-dichlorobenzene was decanted and the residual solid dissolved in water (1 l.) and 32% sodium hydroxide solution (135 g.). The solution was boiled with charcoal (10 g.) and filtered and the filtrate acidified to Congo-red with sulphuric acid and cooled. The *acid* (80 g.) was recrystallised from dilute sulphuric acid (Found : C, 38·4; H, 4·0; N, 18·5; S, 14·5. $C_7H_7O_3N_3S,\frac{1}{2}H_2O$ requires C, 37·8; H, 3·6; N, 18·9; S, 14·4%). It absorbed one equiv. of nitrous acid and, when coupled in dilute acetic acid with diazotised *p*-chloroaniline, gave a soluble azo-derivative.

6-Hydroxyindazole-5-sulphonic acid. 6-Aminoindazole-5-sulphonic acid and dilute sulphuric acid gave 6-hydroxyindazole (desulphonation). The acid (21·3 g.) was heated in a glass-lined autoclave with water (150 c.c.) at 155—160° for 10 hr. The solution was made alkaline to Brilliant Yellow with sodium carbonate solution, cooled to 15°, and filtered from a trace of 6-hydroxyindazole. The filtrate was evaporated to dryness *in vacuo* (24 g.). Recrystallisation from dilute sulphuric acid resulted in desulphonation. The unpurified product was of 82% strength by coupling and gave an orange dye with diazotised *p*-chloroaniline and a blue colour with ferric chloride. The *S-p*-chlorobenzylthiuronium salt had m. p. 227·5°.

5-Aminoindazole-6-sulphonic acid. Treatment of 5-aminoindazole sulphate as for 6-aminoindazole-5-sulphonic acid gave *5-aminoindazole-6-sulphonic acid*, pale grey needles from dilute sulphuric acid (Found : C, 39·2; H, 3·4; N, 19; S, 15·0%), which absorbed one equiv. of nitrous acid and with diazotised *p*-chloroaniline in acetic acid gave a red water-soluble azo-dye. Attempts to hydrolyse the presumed 5-aminoindazole-6-sulphonic acid gave only 5-hydroxyindazole.

6-Hydroxyindazole-7-sulphonic acid. 6-Hydroxyindazole (27 g.) was added during ½ hr. to 100% sulphuric acid (100 g.) with stirring at 20—30°. The reaction was slightly exothermic and, when the addition was 70% complete, crystallisation began. The mixture was then stirred at 100° for 1 hr., poured on ice (200 g.) and water (200 c.c.), and kept for 1 hr. The white

precipitate was recrystallised from water (yield 93·3%) (Found : C, 39·2; H, 2·7; N, 13·3; S, 14·85. $C_7H_6O_4N_2S$ requires C, 39·2; H, 2·8; N, 13·1; S, 14·9%). The *product* did not couple but gave a mauve precipitate with ferric chloride. The *S*-*p*-chlorobenzylthiuronium salt had m. p. 204·5°. Heating this product with 95% sulphuric acid (10 parts) to 130° for 5 hr., or 6-hydroxy-indazole (27 g.) with 95% sulphuric acid (100 g.) at 130° for 5 hr., gave a product which had a coupling strength of 32·5—34% and gave an orange soluble dye with diazotised *p*-chloroaniline. Crystallising the *S*-*p*-chlorobenzylthiuronium salt from 60% ethanol gave approx. equal proportions of a fraction, m. p. and mixed m. p. with above derivative 202—204·5° (hydrolysis with dilute sodium hydroxide solution regenerated the same hydroxyindazolesulphonic acid) and a fraction of m. p. 224° and mixed m. p. with the salt from 6-hydroxyindazole-5-sulphonic acid 226° (regenerated a hydroxyindazolesulphonic acid similar to 6-hydroxyindazole-5-sulphonic acid).

5-Hydroxyindazole-4-sulphonic acid. 5-Hydroxyindazole (13·5 g.) was added to 100% sulphuric acid (50 g.) with stirring at 20—30° during ½ hr., then stirred at 95—100° for 1 hr., poured on ice (50 g.) and water (100 c.c.) and kept for ½ hr. The pale grey crystals (17·5 g.) were recrystallised from water (Found : C, 38·8; H, 2·9; N, 13·0; S, 15·1%). The *product* did not couple and gave a reddish-mauve colour with ferric chloride. The *S*-*p*-chlorobenzylthiuronium salt had m. p. 215°.

6-Aminoindazole-7-sulphonic acid. 6-Hydroxyindazole (32 g.) was heated in a stainless-steel autoclave with 40% sodium hydrogen sulphite solution (45 g.) and ammonia (*d* 0·88; 300 c.c.) at 150—160° with stirring for 6 hr., then filtered at 75°, and the filtrate was evaporated to dryness under reduced pressure. The solid residue was dissolved in water (300 c.c.) and acidified with hydrochloric acid, and sulphur dioxide was boiled off. The solution was filtered and the filtrate neutralised to litmus with sodium hydroxide solution and cooled. The *product* (45%) was dissolved in dilute sodium carbonate solution, treated with carbon, and recovered by sulphuric acid as grey crystals (Found : N, 19·5%). It absorbed one equiv. of nitrous acid and did not couple in dilute acetic acid.

5-Aminoindazole-4-sulphonic acid. Amination of 5-hydroxyindazole-4-sulphonic acid as for 6-hydroxyindazole-7-sulphonic acid and purification of the product by carbon in alkaline solution, acidification, and crystallisation gave an *acid* (40·5%) (Found : C, 39·4; H, 3·2; N, 19·7; S, 14·7%), which absorbed 1 equiv. of nitrous acid and did not couple in dilute acetic acid.

7-Amino-6-hydroxyindazole-4-sulphonic acid (cf. Fieser, *J. Amer. Chem. Soc.*, 1926, **48**, 1103). 6-Hydroxyindazole (67 g.), dissolved in water (320 c.c.) and 32% sodium hydroxide solution (66 g.), was added with good stirring to 10% sulphuric acid (250 g.) and ice (250 g.). To the resulting fine suspension (alkaline to Brilliant Yellow) was added sodium nitrite (35 g.). After 5 minutes' stirring half of a solution of sulphuric acid (30 g.) in water (320 g.) was added during ½ hr. and the remainder during 2 hr., the temperature being held below 7° by addition of ice. After being stirred in an ice-bath overnight the nitroso-suspension was neutralised to Congo-red by sodium acetate crystals (20 g.), and 40% sodium hydrogen sulphite solution (312 g.) was added at 8°. Stirring was continued for ½ hr., the temperature being allowed to rise to 20°. After filtration, the solution (3 l.) was stirred at 40° while copper sulphate (5 g.) and concentrated sulphuric acid (120 g.) in water (300 c.c.) were added, the temperature rising 50°. After 10 minutes' stirring the mixture was kept for 24 hr., cooled to 10°, and filtered. The *acid* (crude, 80 g.) was purified by carbon, etc., forming cream needles (Found : N, 18·1. $C_7H_7O_4N_3S$ requires N, 18·3%).

A neutral suspension of this product (32 g.) was stirred with a solution of hydrated copper sulphate (0·3 g.) in water (50 c.c.) at 17°. Sodium nitrite (11·6 g.) was added. The temperature rose to 40°, and ice was added to reduce it to 18°; green prisms of the diazo-compound then began to separate. After ½ hour's stirring 10% sodium chloride solution (100 c.c.) was added, and the diazo-compound was filtered off, washed with 10% sodium chloride solution (50 c.c.), suspended in water (200 c.c.), and acidified with hydrochloric acid. The precipitate was washed with water (100 c.c.) and dried at 40—50° under reduced pressure (28 g.). The diazo-compound coupled in a similar manner to 1-diazo-2-naphthol-4-sulphonic acid.

4-Amino-5-hydroxyindazole-7-sulphonic acid. In the manner last described, 5-hydroxyindazole gave *4-amino-5-hydroxyindazole-7-sulphonic acid* (47%) as fawn needles (Found : N, 17·9%), which was very readily oxidised in air. Diazotisation as just described required working in nitrogen and total darkness.

4-Aminoindazole-6-sulphonic acid. 4-Methyl-5-nitrometanilic acid (116 g.; supplied by Mr. F. Hall) was suspended in glacial acetic acid (2·5 l.) and stirred at 15°. 40% Sodium nitrite solution (88 c.c.) was added all at once and stirring at 18—20° continued overnight.

The acetic acid was distilled off below 100° under reduced pressure. The residual solid (148 g.) was dissolved in hot water (400 c.c.) and added during 2 hr. to iron borings (40—60 mesh; 200 g.), ferrous chloride (14 g.), and water (800 c.c.) with stirring at 90—95° in an iron vessel. After a further 2 hours' stirring at 90—95° in presence of soluble iron, reduction was complete. Soluble iron was removed by the addition of sodium carbonate, and the iron sludge filtered off and repeatedly extracted with hot water. The combined filtrates (1·7 l.) were acidified with sulphuric acid and cooled. The crystalline *amino-acid* (73·5%) was purified by treatment with carbon in alkaline solution and precipitation with sulphuric acid as fawn plates (Found : N, 19·2%). The product reacted with one equiv. of nitrous acid and coupled in acetic acid solution with diazo-compounds.

4-*Hydroxyindazole*-6-*sulphonic acid.* 4-Aminoindazole-6-sulphonic acid (72·4 g.) was heated in an enamel-lined autoclave with 4% sulphuric acid (420 c.c.) at 175—180° for 10 hr. The dry sodium salt (108 g.), obtained as above *via* the calcium salt, was stirred with 36% hydrochloric acid (110 c.c.) and water (1 l.) for 10 min. The resulting *acid* (45 g.), purified as in the preceding case, formed pale brown needles (Found : N, 12·7. $C_7H_6O_4N_2S$ requires N, 13·1%), was soluble in water, coupled with one equiv. of diazotised *p*-chloroaniline (orange dye), and gave a brown precipitate with ferric chloride.

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