88. *The Skraup Reaction with* m-*Substituted Anilines.*

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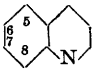
A number of 5- and 7-substituted quinoline derivatives have been unambiguously synthesised and used to identify the products of the Skraup reaction with *m*-substituted anilines. The modified Skraup reaction of B.P. 394,416 (I.G. Farbenindustrie A.-G.) has been applied to *m*-nitroaniline, *m*-toluidine, *m*-aminobenzoic acid, *m*-aminodimethylaniline, *m*-chloroaniline, *m*-bromoaniline, *m*-aminophenol, *m*-anisidine, and metanilic acid, and variations of the yield and of the ratio in which the isomers occur have been investigated. There is a relation between the nature of the *m*-substituent group in the aniline employed and the ratio of isomers obtained.

The Skraup reaction with *m*-substituted anilines in which both positions *o*- to the amino-group are free can give rise to either the 5- or the 7-substituted quinoline :



and, in general, the formation of a mixture of the two isomers would be anticipated. Information in the literature is often incomplete; in some cases only one isomer is recorded, whilst in others the relative proportions of the isomers have not been investigated. The modified Skraup reaction of B.P. 394,416 (I.G. Farbenindustrie A.-G.), using 60—80% aqueous sulphuric acid, is claimed to eliminate the normal violence of a Skraup reaction and to give products free

from tars in good yield, thus lending itself to more accurate investigation of the composition of the mixture obtained from a *m*-substituted aniline. The literature indicated that the orientation of 5- and 7-substituted quinolines in general was unsatisfactory, and we have now orientated the derivatives liable to be formed in the Skraup reaction from a number of *m*-substituted anilines.

4-Nitro-2-aminobenzoic acid was converted by a Skraup reaction into 5-nitroquinoline-8-carboxylic acid, which was then decarboxylated to give 5-nitroquinoline. This was reduced to 5-aminoquinoline which was converted *via* diazotisation into 5-chloroquinoline, identical in properties with the substance described as 7-chloroquinoline by Claus and Kayser (*J. pr. Chem.*, 1893, **48**, 270). The conclusion reached by Fourneau, Trefouel, and Wancolle (*Bull. Soc. chim.*, 1930, **47**, 738) that the substance so described is actually the 5-isomer is thus confirmed. 5-Bromo- and 5-cyano-quinoline were also obtained similarly. The existence of a so-called "*pseudo*-5-cyanoquinoline" in addition to 5-cyanoquinoline (Lellmann and Reusch, *Ber.*, 1888, **21**, 397) was disproved. Hydrolysis of 5-cyanoquinoline gave quinoline-5-carboxylic acid, identical in properties with the "*pseudo*quinoline-5-carboxylic acid" described by Lellmann and Alt (*Annalen*, 1887, **237**, 307). Consequently, the characteristics recorded by Schlosser and Skraup (*Monatsh.*, 1881, **2**, 518) for quinoline-5-carboxylic acid are incorrect. 5-Hydroxyquinoline was obtained from 5-aminoquinoline. Owing to the discrepancy in recorded b. p. of 5-methylquinoline, the synthesis of Jakubowski (*Ber.*, 1910, **43**, 3026) was repeated. 5-*Methoxyquinoline* also was synthesised in an analogous manner.

In an attempt to synthesise 7-chloroquinoline, 7-*chloro*-8-*methylquinoline* was obtained, but this could not be oxidised to 7-chloroquinoline-8-carboxylic acid. The synthesis of a 7-substituted quinoline derivative was finally achieved by preparing 7-methylquinoline from 2 : 3-diaminotoluene by converting it into 8-*amino*-7-*methylquinoline* and eliminating the amino-group from the latter. 7-Methylquinoline was oxidised to quinoline-7-carboxylic acid, and the latter formed a basis for the orientation of the second nitroquinoline obtained as a product of the Skraup reaction with *m*-nitroaniline. This nitroquinoline was converted, *via* an amino- and a cyano-quinoline, into a carboxylic acid identical with quinoline-7-carboxylic acid, thus confirming that these compounds are 7-nitro-, 7-amino-, and 7-*cyano-quinoline*, respectively. 7-Chloroquinoline was obtained from 7-aminoquinoline *via* the diazo-compound and possessed properties which agreed with those described by Claus and Junghanns (*J. pr. Chem.*, 1893, **48**, 253) for 5-chloroquinoline. Obviously these authors, together with Claus and Kayser (*loc. cit.*), confused the orientation of the two isomers. 7-Bromo- and 7-hydroxyquinoline were also obtained from 7-aminoquinoline. The halogen atom in both 7-chloro- and 7-bromo-quinoline proved to be sufficiently labile to be partially replaced by heating with aqueous dimethylamine under pressure to give 7-*dimethylaminoquinoline*. 7-Bromoquinoline was also converted into 7-methoxyquinoline by heating with sodium methoxide under pressure, but attempts to obtain amino- and hydroxy-compounds by analogous methods were unsuccessful.

The Skraup reaction with *m*-nitroaniline gave a mixture of 5- and 7-nitroquinolines in the ratio of 3·5 : 1. Experiments were carried out with 63% to 90% sulphuric acid, the reaction only becoming violent with concentrated acid. The isomers were separated by crystallising 5-nitroquinoline nitrate, followed by basifying and refluxing the residual mixture with ligroin. The use of sodium *m*-nitrobenzenesulphonate as oxidising agent in place of arsenic acid had little effect on the yield of 7-nitroquinoline, but considerably reduced the yield of 5-nitroquinoline.

The product of the Skraup reaction with *m*-toluidine was solely 7-methylquinoline identical with a synthetic specimen, and the reaction proceeded smoothly except with the highest concentration of sulphuric acid used.

The Skraup reaction with *m*-aminobenzoic acid gave a mixture of quinoline-5- and -7-carboxylic acids in the ratio of 5 : 1, whereas the formation of quinoline-5-carboxylic acid only has been recorded in the literature. The isomers were separated by means of their different acidities.

The Skraup reaction with *m*-aminodimethylaniline has only been previously described by Knüppel (*Ber.*, 1896, **29**, 703), who assumed the product to be 7-dimethylaminoquinoline, but recorded no characteristics. The yield obtained from *m*-aminodimethylaniline is low because it is easily oxidisable, but both 7- and 5-*dimethylaminoquinoline* were formed in the ratio of approximately 7 : 1.

The Skraup reaction with *m*-chloroaniline gave a mixture of 5- and 7-chloroquinolines (cf. La Coste, *Ber.*, 1885, **18**, 2940) which was separated by fractional crystallisation of the dichromates (Claus and Junghanns, *loc. cit.*); the perchlorates, oxalates, nitrates, or picrates

could not be utilised satisfactorily for this purpose. The ratio of the isomers obtained depended upon the concentration of sulphuric acid used in the Skraup reaction, but was independent of the time of reaction at any acid concentration examined. When 60% sulphuric acid was used, the ratio of 7- to 5-chloroquinoline was 1·4 : 1, rising gradually to 4·4 : 1 as the concentration of the sulphuric acid was increased to 85%.

The Skraup reaction with *m*-bromoaniline gave a mixture of 5- and 7-bromoquinolines (Claus and Tornier, *Ber.*, 1887, **20**, 2872) which was also separated by fractional crystallisation of the dichromates, but in this case the two isomers were formed in approximately equal proportion under all the conditions examined.

The Skraup reaction with *m*-aminophenol gave 7-hydroxyquinoline as sole product in moderate yield, although the m. p. of the picrate indicated that a little 5-hydroxyquinoline may be formed when low concentrations of sulphuric acid are used.

The Skraup reaction with *m*-anisidine using 65% to 75% sulphuric acid gave in low yield a product identical with synthetic 7-methoxyquinoline.

The Skraup reaction with metanilic acid using nitrobenzene as oxidising agent gave a mixture of quinoline-5- and -7-sulphonic acids (Lellmann and Lange, *Ber.*, 1887, **20**, 1446, referred to the presence of only the 5-sulphonic acid). Owing to difficulty in purifying the product, it was not found possible to use *m*-nitrobenzenesulphonic acid, its sodium salt, or arsenic acid as oxidising agent. The presence of both isomers was established by a cyanide fusion, followed by hydrolysis to the corresponding carboxylic acids, from which both quinoline-5- and -7-carboxylic acids were separated. In order to form a basis for the quantitative separation of the sulphonic acids many attempts were made to obtain suitable derivatives with m. ps. but none was successful; the chloride, ethyl ester, amide, anilide, methylanilide, arylamine salts, and *S*-benzylthiouronium salt could not be prepared. The following conclusions may be drawn from the results of examining the Skraup reaction under the conditions of B.P. 394,416 with nine *m*-substituted anilines :

(*a*) Strongly *o*-*p*-directing groups, *e.g.*, methyl, hydroxyl, and methoxyl groups, give only the 7-substituted quinoline.

(*b*) Relatively weaker *o*-*p*-directing groups, *e.g.*, chloro-, bromo-, and dimethylamino-groups, give a mixture of 5- and 7-substituted quinolines, in which the latter predominates.

(*c*) *m*-Directing groups, *e.g.*, nitro-, carboxyl, and sulphonic groups, give a mixture of 5- and 7-substituted quinolines, in which the former predominates.

(*d*) In only one case, *viz.*, *m*-chloroaniline, was the ratio of the isomers obtained found to be influenced by the concentration of the sulphuric acid used in the Skraup reaction.

Experimental.

Orientation of 5-Substituted Quinoline Derivatives.

5-Nitroquinoline.—4-Nitro-2-aminobenzoic acid (25 g.) (Wheeler and Johns, *Amer. Chem. J.*, 1910, **44**, 443), sulphuric acid (65%; 350 g.), glycerol (50 g.), and arsenic acid (80% w./w.; 125 g.) were refluxed with stirring for 4 hours; the temperature fell from 137° to 133°. The solution was diluted to 2 l., made alkaline with sodium hydroxide solution, and then acidified with acetic acid. The pale brown precipitate (21 g.), containing inorganic matter, was crystallised from alcohol to give colourless minute prisms, m. p. 215° (Howitz and Nöther, *Ber.*, 1906, **39**, 2705, give m. p. 212°) (Found : C, 55·3; H, 3·0; N, 12·2. Calc. for $C_{10}H_6O_4N_2$: C, 55·0; H, 2·75; N, 12·8%). 5-Nitroquinoline-8-carboxylic acid (4 g.) was converted into the silver salt and heated in a vacuum to give 5-nitroquinoline, which crystallised from aqueous alcohol (charcoal) in colourless plates, m. p. 70° (0·5 g.; 16%) (Found : C, 61·2; H, 3·5; N, 15·5. Calc. for $C_9H_6O_2N_2$: C, 62·1; H, 3·45; N, 16·1%). The nitrate crystallised from water in pale yellow minute prisms, m. p. 195°.

5-Aminoquinoline.—5-Nitroquinoline was reduced to 5-aminoquinoline by the method of Kochanska and Brobanski (*Ber.*, 1936, **69**, 1807). It crystallised from alcohol in yellow needles, m. p. 106° (Dikshoorn, *Rec. Trav. chim.*, 1929, **48**, 147, gives m. p. 110°) (Found : C, 74·6; H, 5·3; N, 20·2. Calc. for $C_9H_8N_2$: C, 75·0; H, 5·55; N, 19·5%); hydrochloride, colourless crystals, m. p. 259° (decomp.); the acetyl derivative crystallised from aqueous alcohol in colourless microscopic needles, m. p. 181° (Hamer, *J.*, 1921, **119**, 1436, gives m. p. 178°).

5-Cyanoquinoline.—5-Aminoquinoline was converted into 5-cyanoquinoline by the method of Freydl (*Monatsh.*, 1887, **8**, 580). After crystallising from ligroin in colourless minute plates and drying in a desiccator, it had m. p. 88° (Freydl gives m. p. 87°) (Found : C, 77·8; H, 4·0; N, 17·5. Calc. for $C_{10}H_6N_2$: C, 77·9; H, 3·9; N, 18·2%). After recrystallising from dilute alcohol and drying for 10 minutes on a porous plate, a hydrate, m. p. 70°, was obtained (cf. Lellmann and Reusch, *Ber.*, 1888, **21**, 397). It formed a yellow *picrate*, almost insoluble in alcohol, m. p. 241° (Found : C, 50·3; H, 2·5. $C_{10}H_6N_2,C_6H_3O_7N_3$ requires C, 50·1; H, 2·35%); a yellow *styphnate*, almost insoluble in alcohol, m. p. 241° (decomp.) (Found : C, 48·1; H, 2·6. $C_{10}H_6N_2,C_6H_3O_8N_3$ requires C, 48·1; H, 2·25%); a *nitrate*, which crystallised from water in colourless prisms, m. p. 219° (Found : C, 55·2; H, 3·2. $C_{10}H_6N_2,HNO_3$ requires C, 55·3; H, 3·2%); and a *hydrochloride*, colourless prisms, m. p. 248° (Found : Cl, 18·3. $C_{10}H_6N_2,HCl$ requires Cl, 18·6%).

Quinoline-5-carboxylic Acid.—5-Cyanoquinoline was refluxed with 60% sulphuric acid; the quinoline-5-carboxylic acid separated from glacial acetic acid–alcohol in colourless crystals, m. p. 342° (Lellmann and Alt, *Annalen*, 1887, **237**, 307, give m. p. 338°) (Found: C, 68·9; H, 4·15; N, 7·9. Calc. for $C_{10}H_7O_2N$: C, 69·3; H, 4·1; N, 8·1%). It was reduced by the method of Fischer and Körner (*Ber.*, 1884, **17**, 765) to 1 : 2 : 3 : 4-tetrahydroquinoline-5-carboxylic acid, colourless needles, m. p. 147°.

5-*Chloroquinoline.*—5-Aminoquinoline (6 g.) was dissolved in concentrated hydrochloric acid (25 c.c.) and water (25 c.c.) and the solution diazotised at 0° by adding sodium nitrite (5 g.) in water. The diazo-solution was poured into a cooled solution of cuprous chloride (4 g.) in hydrochloric acid (30%; 30 c.c.) and, after 5 minutes, the mixture was heated on the steam-bath for 30 minutes. After the mixture had been made alkaline with sodium hydroxide, the 5-chloroquinoline was distilled with steam and extracted from the distillate with ether. It crystallised from ether in colourless needles, m. p. 43°, b. p. 256—257°/756 mm. (4 g.; 59%) (Found: C, 65·9; H, 3·9; N, 8·1. Calc. for C_9H_6NCl: C, 66·1; H, 3·7; N, 8·6%); the dichromate formed orange microscopic needles, m. p. 121° (decomp.); the *nitrate*, colourless prismatic needles from water, m. p. 159—161° (Found: N, 12·0. C_9H_6NCl,HNO_3 requires N, 12·4%); the oxalate, colourless needles, m. p. 145°; the *perchlorate*, colourless microscopic needles from aqueous alcohol, m. p. 198° (Found: C, 41·3; H, 2·8. $C_9H_6NCl,HClO_4$ requires C, 40·9; H, 2·65%).

5-*Bromoquinoline.*—5-Aminoquinoline (10 g.) was dissolved in hydrobromic acid (40%; 25 c.c.) and water (250 c.c.), and diazotised at 0° with sodium nitrite (5 g.) in water. Cuprous bromide (12 g.) was dissolved in hydrobromic acid (40%; 40 c.c.) and water, and the diazo-solution was added to this solution. The mixture was heated on the steam-bath for 30 minutes, made alkaline with sodium hydroxide, and distilled with steam, and the 5-bromoquinoline was extracted from the distillate with ether. It crystallised from ether in colourless needles, m. p. 46—48°, b. p. 280°/756 mm. (7 g.; 48%); the *dichromate* formed deep-yellow needles from water, m. p. 134° (decomp.) (Found: C, 33·8; H, 2·7. $(C_9H_6NBr)_2,H_2Cr_2O_7$ requires C, 34·1; H, 3·1%); the nitrate, colourless needles, m. p. 193° (decomp.) (Claus and Vis, *J. pr. Chem.*, 1888, **38**, 387, give m. p. 185°); the oxalate, colourless needles, m. p. 152°; the *picrate*, insoluble in alcohol, m. p. 235° (Found: N, 12·4. $C_9H_6NBr,C_6H_3O_7N_3$ requires N, 12·8%).

5-*Hydroxyquinoline.*—5-Aminoquinoline (5 g.) was converted into 5-hydroxyquinoline (cf. Kochanska and Brobanski, *loc. cit.*), buff-coloured leaflets, m. p. 224° (1 g.; 20%). It formed a hydrochloride, dark-coloured prisms, m. p. 242°; a *picrate*, which crystallised from alcohol in long orange-yellow needles, m. p. 187° (Found: N, 14·7. $C_9H_7ON,C_6H_3O_7N_3$ requires N, 14·95%); and an *oxalate*, buff-coloured microscopic needles from alcohol, m. p. 193° [Found: C, 64·3; H, 3·9. $(C_9H_7ON)_2,(CO_2H)_2$ requires C, 64·6; H, 4·2%].

5-*Methylquinoline.*—*m*-Amino-*p*-tolyl cyanide (20 g.) (von Niementowski, *J. pr. Chem.*, 1889, **40**, 4), sulphuric acid (70%; 150 g.), glycerol (35 g.), and sodium *m*-nitrobenzenesulphonate (40 g.) were refluxed with stirring for 5 hours; the temperature fell from 148° to 137°. The solution was diluted with water (200 c.c.), made alkaline with ammonia, and acidified with acetic acid. On concentration, 5-methylquinoline-8-carboxylic acid was obtained in colourless minute needles, m. p. 174° (Jakubowski, *Ber.*, 1910, **43**, 3026, gives m. p. 173—174°) (Found: C, 69·8; H, 4·8; N, 7·8. Calc. for $C_{11}H_9O_2N$: C, 70·0; H, 4·8; N, 7·5%). The silver salt was heated in a vacuum to give 5-methylquinoline, yellow oil, b. p. 262°/755 mm. (0·3 g.; 10%) (Jakubowski, *loc. cit.*, gives b. p. 253—255°/735 mm., and Gabriel and Thieme, *Ber.*, 1919, **52**, 1088, give b. p. 263—264°/753 mm.). It formed a styphnate, which crystallised from alcohol in greenish-yellow needles, m. p. 216° (Manske, Marion, and Leger, *Canadian J. Res.*, 1942, **20** *B*, 133, give m. p. 218°); and a picrate, yellow microscopic needles, m. p. 221° (Manske, Marion, and Leger, *loc. cit.*, give m. p. 223°).

5-*Methoxyquinoline.*—3-Nitro-*p*-anisidine (50 g.) was stirred with water (300 c.c.) and concentrated hydrochloric acid (90 c.c.) for 2 hours and the suspension diazotised by adding sodium nitrite (30 g.) in water (150 c.c.) during 30 minutes with external cooling. A little undiazotised amine was filtered off and the orange diazo-solution added gradually to a solution of cuprous cyanide (from 150 g. copper sulphate and 160 g. potassium cyanide in 1 l. of water) at 70—80°; after vigorous effervescence, an orange solid separated and was filtered off when cold. 3-*Nitro*-4-*cyanoanisole* crystallised from alcohol in dark red needles, m. p. 138° (42 g.; 79·3%) (Found: C, 53·2; H, 3·95; N, 15·6. $C_8H_6O_3N_2$ requires C, 53·9; H, 3·35; N, 15·7%). This (50 g.) was reduced on the steam-bath with hydrochloric acid (15%; 600 c.c.) and granulated tin (150 g.). The pale yellow solution was filtered and made alkaline with sodium hydroxide, and the product was extracted with chloroform. 4-*Cyano*-m-*anisidine* crystallised from aqueous alcohol in pale yellow prismatic needles, m. p. 92° (26·5 g.; 64%) (Found: C, 64·5; H, 5·5; N, 18·5. $C_8H_8O_2N_2$ requires C, 64·9; H, 5·4; N, 18·9%). 4-Cyano-*m*-anisidine (20 g.), sulphuric acid (70%; 110 c.c.), glycerol (35 g.), and sodium *m*-nitrobenzenesulphonate (40 g.) were refluxed with stirring for 3 hours (b. p. 145—137·5°). The solution was made alkaline with ammonia, cooled, filtered, acidified with acetic acid, and concentrated (300 c.c.). 5-*Methoxyquinoline*-8-*carboxylic acid* crystallised from alcohol in very fine, colourless needles, m. p. 210° (5·5 g.; 20%) (Found: C, 65·1; H, 4·5; N, 6·0. $C_{11}H_9O_3N$ requires C, 65·5; H, 4·45; N, 6·9%). This acid (5 g.) was decarboxylated by heating its silver salt in a vacuum and gave 5-*methoxyquinoline*, colourless oil, b. p. 282°/758 mm. (0·5 g.; 14%); the *picrate*, almost insoluble in alcohol, had m. p. 230° (Found: C, 49·8; H, 3·4; N, 14·1. $C_{10}H_9ON,C_6H_3O_7N_3$ requires C, 49·5; H, 3·1; N, 14·4%); the *oxalate*, pale yellow prismatic needles from alcohol, m. p. 156° [Found: C, 57·2; H, 4·5; N, 5·2; OMe, 11·5. $C_{10}H_9ON,(CO_2H)_2$ requires C, 57·8; H, 4·4; N, 5·6; OMe, 12·45%].

Orientation of 7-Substituted Quinoline Derivatives.

7-*Methylquinoline.*—3-Nitro-*o*-toluidine (15 g.) (Gabriel and Thieme, *Ber.*, 1919, **52**, 1079) was reduced with concentrated hydrochloric acid (50 c.c.) and granulated tin (20 g.) (Lellmann, *Annalen*, 1885, **228**, 243). 2 : 3-Diaminotoluene was extracted with ether and distilled as a red oil, b. p. 256°/750 mm., m. p. 60° (7 g.; 60%). The base reacted with phenanthraquinone in aqueous sodium hydrogen sulphite in presence of sodium acetate to give 6-*methyl*-1 : 2 : 3 : 4-*dibenzphenazine*, which crystallised from alcohol in pale yellow, very fine needles, m. p. 223° (Found: C, 84·0; H, 4·8; N, 9·6. $C_{21}H_{14}N_2$ requires

C, 85·7; H, 4·75; N, 9·5%). 2 : 3-Diaminotoluene (7 g.), sulphuric acid (65%; 80 g.), glycerol (15 g.), and sodium *m*-nitrobenzenesulphonate (15 g.) were refluxed with stirring for 2·25 hours (b. p. 139—135°). The solution was made alkaline with sodium hydroxide and distilled with steam, and the 8-*amino*-7-*methylquinoline* was filtered off and dried in a desiccator (2·2 g.; 22%). It formed pale yellow microscopic needles, m. p. 38—40°, b. p. 306°/753 mm., containing water of crystallisation (Found : C, 69·2; H, 6·7; N, 15·5. $C_{10}H_{10}N_2,H_2O$ requires C, 68·2; H, 6·8; N, 15·9%); the *acetyl* derivative separated from aqueous alcohol (charcoal) in colourless crystals, m. p. 155° (Found : C, 71·3; H, 6·1; N, 14·3. $C_{12}H_{12}ON_2$ requires C, 72·0; H, 6·0; N, 14·0%). 8-Amino-7-methylquinoline (1·5 g.) was dissolved in water (100 c.c.) and hydrochloric acid (5 c.c.) and the orange solution diazotised at 0°. The diazo-solution was poured into boiling alcohol (95%; 150 c.c.) containing zinc dust (1 g.). Nitrogen was steadily evolved. After filtration, the solution was made strongly acid, alcohol evaporated, and the residual solution made alkaline with ammonia and distilled with steam. 7-Methylquinoline was extracted from the distillate with ether and distilled at 257°/756 mm. (0·3 g.; 22%); the picrate formed yellow microscopic needles almost insoluble in alcohol, m. p. 242°; the styphnate, yellow microscopic needles almost insoluble in alcohol, m. p. 242° (cf. Manske, Marion, and Leger, *loc. cit.*).

Quinoline-7-carboxylic Acid.—7-Methylquinoline was oxidised to quinoline-7-carboxylic acid (Skraup and Brünner, *Monatsh.*, 1886, **7**, 139), colourless crystals, m. p. 251° (Skraup and Brünner give m. p. 247°) (Found : C, 68·6; H, 4·3; N, 7·6. Calc. for $C_{10}H_7O_2N$: C, 69·3; H, 4·1; N, 8·1%), which was reduced to 1 : 2 : 3 : 4-tetrahydroquinoline-7-carboxylic acid (Fischer and Endres, *Ber.*, 1902, **35**, 2612), straw-coloured leaflets, m. p. 190°.

7-*Nitro-*, *-Amino-*, *and -Cyano-quinolines.*—7-Nitroquinoline, colourless needles, m. p. 136°, was reduced to 7-aminoquinoline (Kochanska and Brobanski, *loc. cit.*), long pale yellow needles, m. p. 94° (Found : C, 74·7; H, 5·6; N, 19·1. Calc. for $C_9H_8N_2$: C, 75·0; H, 5·5; N, 19·5%); the acetyl derivative had m. p. 168·5° (Hamer, *loc. cit.*, gives m. p. 167·5°). 7-Aminoquinoline (6 g.) was converted into 7-*cyanoquinoline* (cf. Freydl, *loc. cit.*), which crystallised from aqueous alcohol (charcoal) in pale brown microscopic needles, m. p. 104° (Found : C, 77·7; H, 3·5; N, 17·0. $C_{10}H_6N_2$ requires C, 77·9; H, 3·9; N, 17·8%); the *picrate* had m. p. 249° (darkens at 200°) (Found : C, 49·7; H, 2·3; N, 17·8. $C_{10}H_6N_2,C_6H_3O_7N_3$ requires C, 50·2; H, 2·35; N, 18·3%); a *nitrate*, which crystallised from water in minute colourless needles, had m. p. 200° (Found : N, 18·7. $C_{10}H_6N_2,HNO_3$ requires N, 19·2%). 7-Cyanoquinoline was hydrolysed by refluxing with 60% sulphuric acid and gave quinoline-7-carboxylic acid, m. p. 251°, not depressed on admixture with the above quinoline-7-carboxylic acid obtained by oxidising 7-methylquinoline.

7-*Chloroquinoline.*—7-Aminoquinoline (6 g.) was dissolved in concentrated hydrochloric acid (25 c.c.) and water (25 c.c.) and the solution diazotised at 0° by adding sodium nitrite (5 g.) in water. The diazo-solution was poured into a cooled solution of cuprous chloride (4 g.) in hydrochloric acid (30%; 30 c.c.), and, after 5 minutes, the mixture was heated on the steam-bath for 30 minutes. The resulting mixture was made alkaline with sodium hydroxide and distilled with steam, and the 7-chloroquinoline was extracted from the distillate with ether. It crystallised from ether in colourless needles, m. p. 30°, b. p. 267—268° (3·8 g.; 59%) (Found : C, 65·6; H, 3·2; N, 8·05. Calc. for C_9H_6NCl : C, 66·1; H, 3·6; N, 8·6%); the dichromate formed yellow needles from hot water, m. p. 178° (decomp.); the *nitrate*, colourless, prismatic needles from water, m. p. 199° (Found : N, 11·9. C_9H_6NCl,HNO_3 requires N, 12·4%); the *oxalate*, colourless microscopic leaflets from alcohol, m. p. 155° [Found : C, 57·6; H, 3·3; N, 6·7. $(C_9H_6NCl)_2,(CO_2H)_2$ requires C, 57·7; H, 3·35; N, 6·7%].

7-*Bromoquinoline.*—7-Aminoquinoline (10 g.) was converted into 7-bromoquinoline, colourless needles, m. p. 35°, b. p. 288°/753 mm. (6·4 g.; 45%), in a similar manner to that already described for 5-bromoquinoline; the dichromate formed pale yellow needles from water, m. p. 202° (Claus and Tornier, *Ber.*, 1887, **20**, 2872, give m. p. 190°); the nitrate, colourless microscopic needles from water, m. p. 205—206° (decomp.) (Claus and Vis, *J. pr. Chem.*, 1888, **38**, 387, give m. p. 199°); the *oxalate*, colourless prisms from alcohol, m. p. 168° [Found : C, 47·1; H, 3·0; N, 4·7. $(C_9H_6NBr)_2,(CO_2H)_2$ requires C, 47·4; H, 2·75; N, 5·5%]; the *picrate*, almost insoluble in alcohol, yellow crystals, m. p. 238° (Found : N, 12·0. $C_9H_6NBr,C_6H_3O_7N_3$ requires N, 12·8%).

7-*Hydroxyquinoline.*—7-Aminoquinoline (5 g.) was converted into 7-hydroxyquinoline (Kochanska and Brobanski, *loc. cit.*), m. p. 238° (1 g.; 20%); the picrate formed yellow microscopic needles from alcohol, m. p. 245° (cf. Skraup, *Monatsh.*, 1882, **3**, 559); the *oxalate*, buff-coloured prisms from alcohol, m. p. 164° [Found : C, 64·3; H, 4·0; N, 7·0. $(C_9H_7ON)_2,(CO_2H)_2$ requires C, 64·6; H, 4·2; N, 7·5%]; the *nitrate*, pale brown needles from water, m. p. 151° (decomp.) (Found : N, 12·8. C_9H_7ON,HNO_3 requires N, 13·4%).

7-*Dimethylaminoquinoline.*—7-Bromoquinoline (4 g.) was heated with aqueous dimethylamin (33%; 20 c.c.) in a sealed tube at 250° for 8 hours. The resulting mixture was extracted with ether. The oil, b. p. 295—325°, contained unchanged 7-bromoquinoline. Purification was effected by fractional crystallisation of the perchlorate from alcohol. The perchlorate was made alkaline with sodium hydroxide and the mixture extracted with ether. 7-*Dimethylaminoquinoline* formed a yellow oil, b. p. 326°/751 mm. (Found : C, 75·9; H, 7·5; N, 16·6. $C_{11}H_{12}N_2$ requires C, 76·8; H, 7·0; N, 16·3%); the *perchlorate* formed minute orange needles from alcohol, m. p. 240° (Found : C, 48·8; H, 4·8; N, 10·4; Cl, 13·0. $C_{11}H_{12}N_2,HClO_4$ requires C, 48·4; H, 4·8; N, 10·3; Cl, 13·0%); the *oxalate*, minute orange needles from alcohol, m. p. 195° [Found : C, 59·7; H, 5·5; N, 9·9. $C_{11}H_{12}N_2,(CO_2H)_2$ requires C, 59·5; H, 5·35; N, 10·7%]; the *picrate*, almost insoluble in alcohol, orange-yellow crystals, m. p. 242° (Found : C, 51·1; H, 4·0. $C_{11}H_{12}N_2,C_6H_3O_7N_3$ requires C, 50·9; H, 3·8%). 7-Dimethylaminoquinoline was also obtained by heating 7-chloroquinoline with aqueous dimethylamine at 290° for 7 hours.

7-*Methoxyquinoline.*—7-Bromoquinoline (5 g.) was heated with a solution of sodium (2 g) in methyl alcohol (25 c.c.) at 250° for 7 hours. The resulting solution was acidified, alcohol evaporated, and the residue basified with sodium hydroxide and distilled with steam. The oil, extracted from the distillate with ether, contained no halogen and formed a *dichromate*, which crystallised from hot water in long, pale yellow needles, m. p. 210° [Found : C, 44·5; H, 3·85; N, 5·7; Cr_2O_3, 27·1. $(C_{10}H_9ON)_2,H_2Cr_2O_7$ requires C, 44·8; H, 3·7; N, 5·2; Cr_2O_3, 28·3%].

7-Chloro-8-methylquinoline.—6-Chloroacet-*o*-toluidide (20 g.), sulphuric acid (70%; 100 c.c.), glycerol (30 g.), and sodium *m*-nitrobenzenesulphonate (50 g.) were refluxed with stirring for 1·25 hours (b. p. 150—142°). The solution was diluted, diazotised, boiled to decompose any diazo-compounds, then made alkaline with sodium hydroxide and distilled with steam, and the distillate extracted with ether. *7-Chloro-8-methylquinoline* crystallised from aqueous alcohol in microscopic colourless needles, m. p. 45—48°, b. p. 278°/759 mm. (15 g.; 74%) (Found: C, 67·2; H, 4·25; N, 7·2. $C_{10}H_8NCl$ requires C, 67·6; H, 4·5; N, 7·9%); the *nitrate* formed colourless needles from water, m. p. 149° (Found: C, 49·9; H, 3·7. $C_{10}H_8NCl,HNO_3$ requires C, 49·9; H, 3·7%); the *oxalate*, colourless prisms from alcohol, m. p. 146° [Found: C, 58·6; H, 3·6; N, 5·7. $(C_{10}H_8NCl)_2(CO_2H)_2$ requires C, 59·3; H, 4·0; N, 6·3%); the *perchlorate*, long colourless needles from alcohol, m. p. 171° (Found: C, 43·3; H, 3·9. $C_{10}H_8NCl,HClO_4$ requires C, 43·2; H, 3·2%); the *dichromate*, yellow prismatic needles from hot water, m. p. 148° [Found: C, 41·6; H, 3·2. $(C_{10}H_8NCl)_2,H_2Cr_2O_7$ requires C, 41·9; H, 3·1%].

Skraup Reaction with m-*Nitroaniline.*—A mixture of *m*-nitroaniline (30 g.), arsenic acid (80%; 125 g.), sulphuric acid (of concentration and amount as indicated in the table), and glycerol (in amount as indicated in the table) was refluxed with stirring until no unaltered *m*-nitroaniline could be detected. Boiling began at temperatures between 130° and 180° (depending on acid concentration), and the b. p. fell during the course of the reaction. The reaction mixture was diluted to 2 l. and filtered, then made alkaline with sodium hydroxide solution with the addition of ice to prevent the low-melting product from forming a tar. The greenish precipitate of nitroquinolines was filtered off and freed from inorganic matter by boiling with chloroform (300 c.c.; charcoal). After filtration, the chloroform layer was separated and the chloroform evaporated. The mixture of 5- and 7-nitroquinolines was dissolved in boiling water (300 c.c.) and concentrated nitric acid (25 c.c.) and cooled to 20°, and the precipitate of pure 5-nitroquinoline nitrate was filtered off. The filtrate was made alkaline with sodium hydroxide, and the precipitate collected, dried in a desiccator, refluxed with ligroin (b. p. 40—60°; 200 c.c.), and filtered through a hot funnel to separate the insoluble 7- from the 5-nitroquinoline. 5-Nitroquinoline crystallised in colourless plates, m. p. 71°, and formed a nitrate, pale yellow minute prisms, m. p. 195°, both of which were identical with the synthetic products already described. It formed an *oxalate* which crystallised from alcohol in colourless needles, m. p. 175° [Found: C, 54·8; H, 3·35. $(C_9H_6O_2N_2)_2,(CO_2H)_2$ requires C, 54·8; H, 3·2%]; a *perchlorate* which crystallised from aqueous alcohol in colourless needles, m. p. 167° [Found: Cl, 7·7. $(C_9H_6O_2N_2)_2,HClO_4$ requires Cl, 7·9%]; a *picrate*, insoluble in alcohol, m. p. 214° (Found: C, 45·1; H, 2·3. $C_9H_6O_2N_2,C_6H_3O_7N_3$ requires C, 44·7; H, 2·2%); a *dichromate*, yellow prisms, m. p. 129° [Found: C, 38·8; H, 3·0; Cr, 19·8. $(C_9H_6O_2N_2)_2,H_2Cr_2O_7$ requires C, 38·2; H, 2·5; Cr, 18·4%]; and a hydrochloride, straw-coloured needles, m. p. 224°. 7-Nitroquinoline crystallised in colourless needles, m. p. 136°, and formed an *oxalate*, colourless needles, m. p. 200° [Found: C, 54·9; H, 3·25. $(C_9H_6O_2N_2)_2,(CO_2H)_2$ requires C, 54·8; H, 3·2%]; a *picrate*, insoluble in alcohol, m. p. 217° (Found: C, 45·6; H, 2·35. $C_9H_6O_2N_2,C_6H_3O_7N_3$ requires C, 44·7; H, 2·2%); and a hydrochloride, straw-coloured needles, m. p. 234°.

Yield (%) *of* 5- *and* 7-*nitroquinoline, and times of reaction.*

Weight of glycerol (g.).	Concentration and quantity of sulphuric acid.					
	65%; 350 g.	70%; 350 g.	75%; 300 g.	80%; 300 g.	85%; 250 g.	90%; 250 g.
30	—	65 (5 hr.)	61 (1·5 hr.)	58 (0·5 hr.)	52 (0·25 hr.)	—
40	—	—	65 (1·25 hr.)	63·5 (0·5 hr.)	55 (0·25 hr.)	45 (5 min.)
50	—	77·3 (2·75 hr.)	64 (1 hr.)	—	53 (0·25 hr.)	—
60	75 (6·75 hr.)	74 (2·25 hr.)	—	60 (0·5 hr.)	—	—
70	74 (4·75 hr.)	—	57 (1 hr.)	—	—	—
80	—	62·7 (2·25 hr.)	—	—	—	—
90	62 (5·75 hr.)	—	—	—	—	—

The ratio of 5- to 7-nitroquinoline was determined from the weights of the pure compounds isolated and was 3·5 : 1, being independent of the concentration of sulphuric acid used.

Skraup Reaction with m-*Toluidine.*—A mixture of *m*-toluidine (30 g.), glycerol (50 g.), sodium *m*-nitrobenzenesulphonate (80 g.), and sulphuric acid (of concentration and amount as indicated in the table) was refluxed with stirring for various times (b. p. between 139° and 162°). The mixture was diluted with water (200 c.c.), cooled, treated with excess of sodium nitrite (25 g.), and the solution boiled to decompose any unchanged *m*-toluidine, then made alkaline with sodium hydroxide and distilled with steam. The sole product was 7-methylquinoline, which was extracted with ether and distilled, b. p. 257°/754 mm. It formed a picrate, yellow microscopic needles, m. p. 242°, and a styphnate, yellow microscopic needles, m. p. 242°, both of which were identical with the synthetic products already described.

Yield (%) *of* 7-*methylquinoline.*

Time (hrs.).	Concentration and quantity of sulphuric acid.			
	65%; 250 g.	70%; 250 g.	75%; 200 g.	80%; 200 g.
0·5	—	42	59	—
0·75	—	—	—	73
1	—	53	64	73
2	36	61	71	—
2·5	—	—	—	73
3	40	70	74	—
4	43	69	74	—
5	43	—	—	—

Skraup Reaction with m-*Aminobenzoic Acid.*—A mixture of *m*-aminobenzoic acid (30 g.), glycerol (50 g.), sodium *m*-nitrobenzenesulphonate (60 g.), and sulphuric acid (of concentration and amount as indicated in the table) was refluxed with stirring for various times. The mixture was diluted with water (250 c.c.), made weakly alkaline with ammonia (*d* 0·880), then stirred well with charcoal (10 g.). The coagulated tar was filtered off, and the filtrate (800 c.c.) boiled (charcoal; 5 g.) and filtered. The clear red-brown solution was cooled to 50° and acidified with glacial acetic acid (15 c.c.), and the precipitate filtered off. The filtrate was concentrated to 400 c.c. and cooled; a second precipitate so obtained was washed free from ammonium sulphate. The first precipitate was boiled with water (600 c.c.) and glacial acetic acid (10 c.c.), and the insoluble quinoline-5-carboxylic acid filtered off hot. The filtrate was concentrated to 100 c.c. and cooled, and a precipitate of quinoline-7-carboxylic acid was obtained. The second precipitate, which consisted of quinoline-7-carboxylic acid containing inorganic matter, was dissolved in water (75 c.c.) and ammonia, and on acidification with acetic acid gave a precipitate of pure quinoline-7-carboxylic acid. In no case was any unaltered *m*-aminobenzoic acid detected. Quinoline-5-carboxylic acid formed colourless crystals, m. p. 342°, and formed a tetrahydro-derivative, colourless needles, m. p. 147°, both identical with the synthetic products already described. Quinoline-7-carboxylic acid formed colourless crystals, m. p. 251°, and formed a tetrahydro-derivative, straw-coloured leaflets, m. p. 190°, both identical with the synthetic products already described.

Yield (%) *of quinoline-5- and -7-carboxylic acids.*

	Concentration and quantity of sulphuric acid.		
Time (hrs.).	65%; 250 g.	70%; 250 g.	75%; 200 g.
1	—	54	56
2	38	61	35
3	—	70	—
4	—	66	—
4·5	60	—	—
6	63	—	—

The ratio of quinoline-5- to -7-carboxylic acid was 5 : 1 and was independent of the concentration of sulphuric acid used.

Skraup Reaction with m-*Aminodimethylaniline.*—A mixture of *m*-acetamidodimethylaniline (39 g.), glycerol (50 g.), sodium *m*-nitrobenzenesulphonate (60 g.), and sulphuric acid (70%; 250 g.) was refluxed with stirring for 5 hours. The mixture was diluted with water (100 c.c.) and basified with ammonia (*d* 0·880) which precipitated a considerable amount of tar. The mixture was extracted with ether, the ether removed, and the residue distilled as a yellow oil, b. p. 290—326° (10 g.; 27%). It was dissolved in boiling alcohol (75 c.c.) and to the solution was added an aqueous solution of perchloric acid (20%; 30 c.c.). On cooling, pure 7-dimethylaminoquinoline perchlorate (11 g.), m. p. 240°, was precipitated. The filtrate was basified with sodium hydroxide and extracted with ether, and the ether removed. The residual brown oil was dissolved in boiling alcohol (20 c.c.) and a solution of picric acid (2·5 g.) in boiling alcohol (10 c.c.) was added. The orange-yellow precipitate, m. p. *ca.* 175°, was boiled with alcohol (250 c.c.) and the insoluble residue (1 g.), m. p. 220°, was filtered off. After crystallisation from alcohol, it had m. p. 242° and was identical with 7-dimethylaminoquinoline picrate. The alcoholic filtrate after removal of the above residue, m. p. 220°, was concentrated to 100 c.c. and cooled, and gave an orange-yellow crystalline precipitate (2·5 g.), m. p. 184°. This picrate was basified with sodium hydroxide and extracted with ether, the ether removed, and the residue of *5-dimethylaminoquinoline* distilled as a yellow oil, b. p. 292°/741 mm. (1 g.) (Found: C, 76·0; H, 7·4; N, 16·3. $C_{11}H_{12}N_2$ requires C, 76·8; H, 7·0; N, 16·3%). It formed a *picrate*, orange-yellow microscopic needles, m. p. 184° (Found: C, 50·6; H, 3·6; N, 17·8. $C_{11}H_{12}N_2,C_6H_3O_7N_3$ requires C, 50·9; H, 3·7; N, 17·5%); and a *styphnate*, orange-yellow minute prisms, m. p. 215° (Found: C, 48·6; H, 3·6; N, 16·2. $C_{11}H_{12}N_2,C_6H_3O_8N_3$ requires C, 48·9; H, 3·6; N, 16·8%). When 65% sulphuric acid was used, the reaction was incomplete in 7 hours, and with 75% sulphuric acid the yield was the same as with 70% acid, but the reaction was complete in 5 hours. The ratio of 7- to 5-dimethylaminoquinoline was about 7 : 1, but this is probably only an approximation owing to the difficulty in separating the isomers.

7-Dimethylaminoquinoline formed a *styphnate*, orange-yellow microscopic needles, m. p. 225° (Found: C, 48·8; H, 3·9. $C_{11}H_{12}N_2,C_6H_3O_8N_3$ requires C, 48·9; H, 3·6%); a *dichromate*, orange microscopic needles, m. p. 152° (decomp.) [Found: C, 46·6; H, 3·9; N, 10·35; Cr, 19·1. $(C_{11}H_{12}N_2)_2,H_2Cr_2O_7$ requires C, 47·0; H, 4·6; N, 9·95; Cr, 18·5%]; and a *methiodide*, prepared by adding methyl iodide without warming, orange minute prisms, m. p. 257° (Found: I, 41·8. $C_{12}H_{15}N_2I$ requires I, 40·4%).

Skraup Reaction with m-*Chloroaniline.*—*m*-Chloroaniline (30 g.), sulphuric acid (of concentration and amount as indicated in the table), glycerol (45 g.), and sodium *m*-nitrobenzenesulphonate (70 g.) were refluxed with stirring for the time indicated. Boiling began at temperatures between 130° and 170°, and the b. p. fell during the course of the reaction. The cooled reaction mixture was treated with excess of sodium nitrite (up to 30 g.), and the solution boiled to decompose any unaltered *m*-chloroaniline, then made alkaline with sodium hydroxide and distilled with steam. The resulting mixture of 5- and 7-chloroquinolines was extracted with ether and distilled (yields given are weights of the distillate). This mixture was separated into the isomers by fractional crystallisation of the mixture of dichromates obtained by adding the theoretical amount of potassium (or sodium) dichromate to a very dilute solution of the bases in sulphuric acid (just acid to Congo-red). 7-Chloroquinoline, obtained from the dichromate fraction, m. p. 178°, after basification and distillation with steam, crystallised in colourless needles, m. p. 30°, b. p. 267—268°, and formed a nitrate, colourless, prismatic needles, m. p. 199°, and an oxalate, colourless microscopical leaflets, m. p. 155° (all identical with the synthetic products already described). It also formed a *perchlorate*, small colourless needles from ethyl acetate, m. p. 126° (Found: C, 40·1; H, 2·5. $C_9H_6NCl,HClO_4$ requires C, 40·9; H, 2·65%); and a *picrate*, almost insoluble in alcohol, m. p. 225° (Found: N, 14·9. $C_9H_6NCl,C_6H_3O_7N_3$ requires N, 14·25%).

5-Chloroquinoline, colourless needles, m. p. 43°, b. p. 256—257°, was obtained from the dichromate fraction, m. p. 110—120°, and filtrates after purification through the sparingly alcohol-soluble oxalate, colourless needles, m. p. 145°; it formed a nitrate; colourless prismatic needles, m. p. 159—161°, a perchlorate, colourless microscopic needles, m. p. 198° (all being identical with the synthetic products already described), and a lemon-yellow *picrate*, almost insoluble in alcohol, m. p. 220° (Found : N, 13·6. $C_9H_6NCl,C_6H_3O_7N_3$ requires N, 14·25%).

The ratio of 7- to 5-chloroquinoline was determined from the weights of the pure compounds isolated, losses during separation amounting to about 10%.

Yield (%) *of* 5- *and* 7-*chloroquinolines.*

	Concentration and quantity of sulphuric acid.				
Time (hrs.).	60%; 170 c.c.	65%; 155 c.c.	70%; 140 c.c.	75%; 125 c.c.	80%; 115 c.c.
0·5	—	—	40	83	70
1·25	—	36	70	82	—
2	30	52	83	80	62
2·75	—	65	88	78	—
3·5	38	66	91	—	—
4·25	40	—	—	—	—
5	43	—	—	—	—
Ratio of 7- to 5-chloroquinoline	1·4 : 1	1·6 : 1	2·7 : 1	3·4 : 1	3·9 : 1

The use of 85% sulphuric acid (105 c.c.), glycerol being added gradually in order to control the violence of the reaction, gave 7- and 5-chloroquinoline in 40% yield in the ratio of 4·4 : 1.

Skraup Reaction with m-*Bromoaniline.*—*m*-Bromoaniline (30 g.), sulphuric acid (of concentration and amount as indicated in the table), glycerol (45 g.), and sodium *m*-nitrobenzenesulphonate (70 g.) were refluxed with stirring for the time indicated (b. p. between 130° and 160°). The 5- and 7-bromoquinolines were isolated as described above for the chloro-analogues by fractional crystallisation of the dichromates. 5-Bromoquinoline, obtained by basification and steam distillation of the dichromate fraction, m. p. 133°, crystallised in colourless needles, m. p. 46—48°, b. p. 280°/759 mm.; and 7-bromoquinoline, obtained from the dichromate fraction, m. p. 202°, crystallised in colourless needles, m. p. 35°, b. p. 289°/759 mm.; they were identical with the synthetic products already described.

Yield (%) *of* 5- *and* 7-*bromoquinolines.*

	Concentration and quantity of sulphuric acid.			
Time (hrs.).	60%; 170 c.c.	65%; 155 c.c.	70%; 140 c.c.	75%; 125 c.c.
0·5	—	—	66·2	71·7
1·25	—	49·6	—	60·6
2	33·1	—	66·2	46·9
2·75	—	66·2	—	—
3·5	49·6	71·7	60·6	—
4·25	51·9	—	—	—
Ratio of 7- to 5-bromoquinoline	1·014 : 1	1·018 : 1	1·017 : 1	0·991 : 1

Skraup Reaction with m-*Aminophenol.*—*m*-Aminophenol (10 g.), sulphuric acid (65%; 100 g.), glycerol (20 g.), and sodium *m*-nitrobenzenesulphonate (20 g.) were refluxed with stirring for 4·5 hours (b. p. 139—134°). Sodium hydroxide was then added until the mixture was just acid to Congo-red, the mixture filtered, and excess of sodium carbonate added to the filtrate to precipitate 7-hydroxyquinoline (5·9 g.; 46%). This crystallised from chlorobenzene in pale yellow needles, m. p. 238°; the picrate formed yellow microscopic needles, m. p. 245°, and the nitrate, pale brown needles, m. p. 151° (decomp.) (all being identical with the synthetic products already described). The use of 70% sulphuric acid (95 g.) in a parallel experiment (b. p. 148—138°) for 3·5 hours gave solely 7-hydroxyquinoline (3·8 g.; 30%). The use of 60% sulphuric acid (80 c.c.), however, in a similar experiment (b. p. 135—131°) for 7·5 hours gave a product (7·6 g.; 60%), m. p. 210—234°, which formed an oxalate, m. p. 154°, and a picrate, m. p. 140—240°, the latter being separated into a fraction, m. p. 245°, identical with 7-hydroxyquinoline picrate, and a residue, m. p. 140—150°, indicating the possible presence of a little 5-hydroxyquinoline picrate.

Skraup Reaction with m-*Anisidine.*—A mixture of *m*-anisidine (20 g.), sulphuric acid (70%; 110 c.c.), glycerol (35 g.), and sodium *m*-nitrobenzenesulphonate (50 g.) was refluxed with stirring for 3 hours. The mixture was diluted with water and cooled, and excess of sodium nitrite added. The solution was boiled to decompose unaltered *m*-anisidine, then made alkaline with sodium hydroxide and distilled with steam. The product, consisting solely of 7-methoxyquinoline, was extracted with ether and distilled as a yellow oil, b. p. 287°/758 mm. (7 g.; 27%) (Found : C, 75·3; H, 5·4; N, 9·2; OMe, 19·0. Calc. for $C_{10}H_9ON$: C, 75·5; H, 5·65; N, 8·8; OMe, 19·5%); the dichromate, pale yellow needles, m. p. 210°, was identical with the synthetic product already described. It also formed a picrate, m. p. 229° (Robinson and Lempert, *J.*, 1934, 1419, give m. p. 216°) (Found : C, 49·4; H, 3·2; N, 15·2. Calc. for $C_{10}H_9ON,C_6H_3O_7N_3$: C, 49·5; H, 3·1; N, 14·4%); an *oxalate*, colourless needles, m. p. 126° [Found : C, 57·3; H, 4·1; N, 5·65. $C_{10}H_9ON,(CO_2H)_2$ requires C, 57·8; H, 4·4; N, 5·6%]; and a methiodide, yellow prismatic needles, m. p. 210° (Robinson and Lempert, *loc. cit.*, give m. p. 204°). The use of 65% and 75% sulphuric acid did not alter the yield.

Skraup Reaction with Metanilic Acid.—Metanilic acid (30 g.), sulphuric acid (70%; 130 c.c.), glycerol (40 g.), and nitrobenzene (35 g.) were refluxed with stirring for 3 hours (b. p. 148—137°). Water (200 c.c.) was then added, nitrobenzene removed by steam distillation, and the solution basified with excess of an aqueous suspension of calcium hydroxide. After filtration, the filtrate was boiled (charcoal), neutralised with dilute sulphuric acid, filtered, boiled (charcoal), filtered, and concentrated. Fractions were filtered off at intervals and a final fraction obtained by adding alcohol to the viscous residue (total, 18·7 g.; 51·5%). The first fraction crystallised from water in colourless, well-formed plates, decomposing above 350°. After drying for several hours at 100°, the crystals still contained water and were hygroscopic (Found : C, 49·6; H, 3·85; N, 7·3; S, 15·4. Calc. for $C_9H_7O_3NS$: C, 51·7; H, 3·35; N, 6·7; S, 15·3%).

The sulphonic acid (20 g.) was dissolved in water (200 c.c.) and the solution evaporated until 9·5 g. had crystallised. The remaining sulphonic acid (10·5 g.) was converted into a mixture of cyanoquinolines (cf. Lellmann and Lange, *Ber.*, 1887, **20**, 1446), but the conversion was far from complete (1·5 g.; 20%). The mixture of cyanoquinolines was hydrolysed with 50% sulphuric acid to a mixture of quinoline carboxylic acids (1·1 g.) which was separated by the method already described under the Skraup reaction with *m*-aminobenzoic acid. Quinoline-5-carboxylic acid (0·2 g.), colourless crystals, m. p. 342°, and quinoline-7-carboxylic acid (0·6 g.), colourless crystals, m. p. 251°, were obtained, identical with the synthetic products already described. When the sulphonic acid was used without separating the more insoluble fraction, only quinoline-5-carboxylic acid could be isolated after hydrolysis of the cyanoquinoline, indicating that quinoline-5-sulphonic acid preponderated in the mixture.

When 60% sulphuric acid was used, the reaction was incomplete after 8 hours, but with 65% sulphuric acid the yield was 75% after 3 hours, and with 70% sulphuric acid the yield was 77% after 0·5 hour, this product containing no unaltered metanilic acid.

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