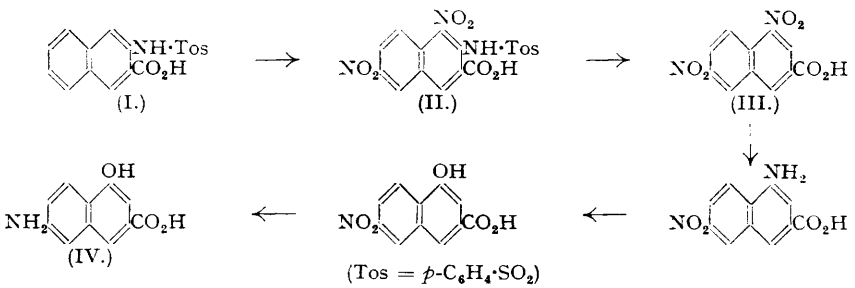
198. *Aminohydroxynaphthoic Acids. Part II. Attempted Synthesis of 7-Amino-4-hydroxy-2-naphthoic Acid ("Carboxy J-Acid") from 3-Amino-2-naphthoic Acid.*

By W. F. Beech and N. Legg.

A number of nitro- and bromo-derivatives of 3-amino-2-naphthoic acid have been prepared in an attempt to find a suitable route to 7-amino-4-hydroxy-2-naphthoic acid (IV). Poor yields of two suitable intermediates, 4 : 7-dinitro- and 4 : 7-dibromo-2-naphthoic acid, prevented their attempted conversion into the aminohydroxynaphthoic acid.

In Part I (*J.*, 1949, 1887), which described a synthesis of 6-amino-4-hydroxy-2-naphthoic acid ("carboxy γ-acid"), the reasons for undertaking this work were given, and as J-acid (7-amino-4-naphthol-2-sulphonic acid) is one of the most important dyestuffs intermediates of its class it was desirable to synthesise its carboxy-analogue.

Since toluene-*p*-sulphon-2-naphthalide can be nitrated to give the 1 : 6-dinitro-derivative (Morgan and Micklethwait, *J.*, 1912, **101**, 148), it was hoped that 3-toluene-*p*-sulphonamido-2-naphthoic acid (I) would similarly give a dinitro-derivative (II) which could be converted into "carboxy J-acid" by the following route :

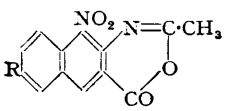


(Tos = *p*-C_6H_4·SO_2)

3-Amino-2-naphthoic acid reacted with toluene-*p*-sulphonyl chloride to give (I). This was nitrated in glacial acetic acid at 55° to give the 4-nitro-derivative, which on hydrolysis in concentrated sulphuric acid gave 4-nitro-3-amino-2-naphthoic acid, previously prepared by Cross and Drew (*J.*, 1949, 1532) by the nitration of 3-acetamido-2-naphthoic acid. 4-Nitro-3-toluene-*p*-sulphonamido-2-naphthoic acid on further nitration in acetic acid gave a small yield of 4 : 7-dinitro-3-toluene-*p*-sulphonamido-2-naphthoic acid (II), which after hydrolysis to 4 : 7-dinitro-3-amino-2-naphthoic acid was deaminated to give 4 : 7-dinitro-2-naphthoic acid (III). This was decarboxylated to 1 : 6-dinitronaphthalene thus orientating the nitro-groups.

As the yield of (II) was too low to permit a continuation of this synthesis of (IV) the nitration of 4-nitro-3-acetamido-2-naphthoic acid was investigated, but all attempts to obtain a dinitro-compound failed, the mononitro-derivative being recovered unchanged.

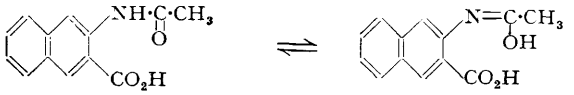
A sample of 4 : 7-dinitro-3-acetamido-2-naphthoic acid was prepared by acetylating 4 : 7-dinitro-3-amino-2-naphthoic acid with acetic anhydride and concentrated sulphuric acid. The use of acetic anhydride alone gave the anhydro-derivative (V) which was converted into the acetyl compound by hydrolysis with water.



(V; R = NO_2)
(VI; R = H)

4-Nitro-3-amino-2-naphthoic acid reacted similarly with acetic anhydride to give (VI), whilst the addition of concentrated sulphuric acid gave an inseparable mixture of the acetyl compound and the anhydro-derivative. Hydrolysis of this mixture with water gave 4-nitro-3-acetamido-2-naphthoic acid. 3-Amino-2-naphthoic acid, under similar conditions, gave 3-acetamido-2-naphthoic acid. From these results it is obvious that the nitro-group favours ring closure, by dehydration, of the acetyl compound when acetic anhydride is used. Addition

of concentrated sulphuric acid partially prevents this anhydro-formation in the 4-nitro-derivative, and completely prevents it in the 4 : 7-dinitro-derivative.



According to Baker (" Tautomerism," 1934, p. 136) the amide grouping can exist in the tautomeric forms shown above. From the evidence obtained, it seems probable that 3-acetamido-2-naphthoic acid, in the presence of acetic anhydride, normally exists in the keto-form, but the presence of the 4-nitro-group favours the formation of the enol by withdrawing electrons from the side chain, the anhydro-compound being then formed by simple dehydration of the two hydroxyl groups. Addition of concentrated sulphuric acid represses the formation of the *aci*-nitro-form so that the amide remains in the keto-form and hence ring closure does not occur.

Since a route to " carboxy J-acid " using 4 : 7-dinitro-2-naphthoic acid (III) was impossible, practically, owing to the low yield at the second nitration stage, the bromination of 4-nitro-3-acetamido-2-naphthoic acid was investigated. The latter reacted with bromine in boiling glacial acetic acid to give 7-bromo-4-nitro-3-acetamido-2-naphthoic acid (VII), the orientation of which is discussed later.

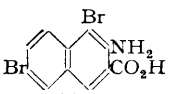
It was found that the yield of (VII) fell if the reaction mixture was heated under reflux after the addition of the bromine :

Time of heating under reflux after addition of bromine, hours	0	1	2½
Yield of (VII), %	63·5	53·7	45·5

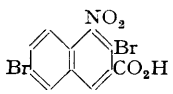
As the only other isolatable product of the reaction was 4-nitro-3-amino-2-naphthoic acid it would appear that (VII) was being reduced by the hydrogen bromide formed in the initial bromination reaction. Fries and Schimmelschmidt (*Annalen*, 1930, **484**, 245) found that the bromination of 2-naphthol is reversible in that 1-bromo- and 1 : 6-dibromo-2-naphthol on treatment with hydrogen bromide in acetic acid afforded 2-naphthol.

Attempts to convert 7-bromo-4-nitro-3-acetamido-2-naphthoic acid (VII) by hydrolysis and deamination into 7-bromo-4-nitro-2-naphthoic acid failed as no method could be found for removing the acetyl group without replacing either the nitro- or the bromo-group, the former by alkaline reagents and the latter by acids.

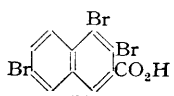
The acetamido-naphthoic acid (VII) reacted with aqueous sodium carbonate to give a compound of unknown structure containing bromine, and with diethylamine to give 7-bromo-3-amino-4-diethylamino-2-naphthoic acid. With ethanol and hydrochloric acid (VII) gave 4-nitro-3-amino-7-ethoxy-2-naphthoic acid and 4-nitro-3-amino-2-naphthoic acid. The formation of the latter compound is unusual and cannot readily be explained. Although (VII) had been reduced to 4-nitro-3-amino-2-naphthoic acid by the action of hydrogen bromide in acetic acid it was thought that aqueous hydrobromic acid would act solely as a deacetylating reagent. The use of 48% hydrobromic acid gave a mixture of 4 : 7-dibromo-3-amino-2-naphthoic acid (VIII) and 3 : 7-dibromo-4-nitro-2-naphthoic acid (IX).



(VIII.)



(IX.)



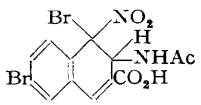
(X.)

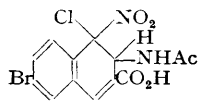
Prager (*Ber.*, 1885, **18**, 2164) found that 4-bromo-2-nitro-1-naphthylamine was converted by hydrobromic acid under pressure into 1 : 2 : 4-tribromonaphthalene. Presumably the milder conditions employed here prevented complete replacement of all the groups by bromine.

4 : 7-Dibromo-3-amino-2-naphthoic acid (VIII) was converted into 3 : 4 : 7-tribromo-2-naphthoic acid (X) by the Sandmeyer reaction. Attempts to decarboxylate this compound, for orientation purposes, by heating the acid with quinoline and copper powder or by direct distillation, failed, the acid being recovered unchanged. The acid (X) was therefore converted into the amide which would not undergo the Hofmann reaction in aqueous media; but in methanol (cf. Windaus, *Ber.*, 1924, **57**, 1731) 3 : 4 : 7-tribromo-2-naphthylamine was formed, and this was deaminated to give 1 : 2 : 6-tribromonaphthalene.

7-Bromo-4-nitro-3-acetamido-2-naphthoic acid (VII) reacted with 20% hydrobromic acid to give an addition compound which has been formulated as 4 : 7-dibromo-4-nitro-3-acetamido-

3 : 4-dihydro-2-naphthoic acid (XI). This compound reacted with 48% hydrobromic acid to give 3 : 7-dibromo-4-nitro-2-naphthoic acid (IX) and with 2N-sodium carbonate solution to give 4-nitro-3-hydroxy-2-naphthoic acid. (VII) reacted with constant-boiling hydrochloric acid to give 4-chloro-7-bromo-4-nitro-3-acetamido-3 : 4-dihydro-2-naphthoic acid (XII) which likewise gave 4-nitro-3-hydroxy-2-naphthoic acid on treatment with sodium carbonate solution.

(XI.) 



(XII.)

Although there are no references to the addition of halogens or halogeno-acids to nitronaphthols or nitronaphthylamines, Fries and Schimmelschmidt (*loc. cit.*) found that bromonaphthols gave addition compounds with hydrogen bromide.

With regard to the formation of 4-nitro-3-hydroxy-2-naphthoic acid from (XI) and (XII) by the action of alkali, Armstrong and Rossiter (*Proc. Chem. Soc.*, 1891, 87—89) found that the addition of nitric acid to 1-bromo-2-naphthol gave 1-bromo-1-nitro-2 : 2-dihydroxy-1 : 2-dihydronaphthalene which immediately decomposed to give 1-bromo-1-nitro-2-keto-1 : 2-dihydronaphthalene. This reacted with alkali to give 1-nitro-2-naphthol. 1 : 6-Dibromo-2-naphthol underwent a similar series of reactions but the final product was 6-bromo-1-nitro-2-naphthol. The loss of the 6-bromine atom in our case is therefore unusual. 4-Nitro-3-amino-2-naphthoic acid is probably a precursor of the 4-nitro-3-hydroxy-2-naphthoic acid since Cross and Drew (*loc. cit.*) found that 4-nitro-3-acetamido-2-naphthoic acid was hydrolysed by sodium hydroxide solution to 4-nitro-3-hydroxy-2-naphthoic acid. This reaction has been repeated by using sodium carbonate instead of sodium hydroxide, and a similar result was obtained.

4-Nitro-3-toluene-*p*-sulphonamido-2-naphthoic acid on treatment with bromine (1 mol.) in glacial acetic acid gave 3 : 4 : 7-tribromo-2-naphthoic acid (X), but in an experiment in which 97·5% acetic acid was accidentally used the product consisted of a mixture of unchanged material and 3 : 7-dibromo-4-nitro-2-naphthoic acid (IX). It was found that 1-nitro-2-acetamidonaphthalene on bromination (1 mol.) in glacial acetic acid gave 1 : 2 : 6-tribromonaphthalene (unpublished work). On these grounds 4-nitro-3-acetamido-2-naphthoic acid might have been expected to give 3 : 4 : 7-tribromo-2-naphthoic acid.

Attempts to brominate 4-nitro-3-toluene-*p*-sulphonamido-2-naphthoic acid in chloroform solution failed. In pyridine, however, 3-bromo-1-nitro-2-toluene-*p*-sulphon-naphthalide was formed. Consden and Kenyon (*J.*, 1935, 1591) prepared this substance by brominating 1-nitro-2-toluene-*p*-sulphon-naphthalide in pyridine. The introduction of a bromine atom in the 3-position of a naphthalene nucleus is not unusual, cf. Consden and Kenyon (*loc. cit.*) and Bell (*J.*, 1932, 2734) who likewise prepared 1 : 3-dibromo-2-toluene-*p*-sulphon-naphthalide.

4 : 7-Dibromo-2-naphthoic acid was prepared from 4 : 7-dibromo-3-amino-2-naphthoic acid (VIII) by deamination. Since it has been shown (unpublished work) that 10% sodium hydroxide at 150° will hydrolyse bromine atoms in a naphthalene ring [cf. Oehler (D.R.-P. 77,446)] 4 : 7-dibromo-2-naphthoic acid was expected to yield 4 : 7-dihydroxy-2-naphthoic acid which on treatment with ammonia and sodium bisulphite would probably yield " carboxy J-acid " (IV) (cf. Bucherer, *J. pr. Chem.*, 1904, **69**, 83). The yield of 4 : 7-dibromo-2-naphthoic acid by this method was too low to permit further work so the halogenation of the acetyl and toluene-*p*-sulphonyl derivatives of 3-amino-2-naphthoic acid itself was investigated.

4-Chloro-3-amino-2-naphthoic acid is the only halogenated 3-amino-2-naphthoic acid described in the literature; it has been prepared from 1-chloro-2 : 3-naphthisatin (F.P. 575, 314; *Chem. Zentr.*, 1925, I, 1021). 2-Acet- and 2-toluene-*p*-sulphon-naphthalide both give 1 : 6-dibromo-derivatives on bromination in acetic acid or chloroform (Bell, *loc. cit.*; Franzen and Stauble, *J. pr. Chem.*, 1921, **107**, 58). 3-Toluene-*p*-sulphonamido-2-naphthoic acid was brominated in pyridine to give 4-bromo-3-toluene-*p*-sulphonamido-2-naphthoic acid, which was hydrolysed and decarboxylated to give 1-bromo-2-naphthylamine. Attempts to brominate 4-bromo-3-toluene-*p*-sulphonamido-2-naphthoic acid in glacial acetic acid gave a tribromo-compound, presumably 4 : 5 : 7-tribromo-3-amino-2-naphthoic acid, which was also formed from 3-toluene-*p*-sulphonamido-2-naphthoic acid and bromine (1 mol.) in acetic acid. 3-Acetamido-2-naphthoic acid failed to brominate in glacial acetic acid and was only partly brominated in pyridine, giving an inseparable mixture.

Attempts to nitrate 4-bromo-3-toluene-*p*-sulphonamido-2-naphthoic acid, to give the 7-nitro-compound failed, even in the presence of a boron trifluoride catalyst.

Experimental.

(Analyses are by Mr. E. S. Morton. M. p.s are uncorrected.)

Nitro-derivatives of 3-*Amino*-2-*naphthoic acid.*

3-*Toluene*-p-*sulphonamido*-2-*naphthoic Acid.*—A solution of 3-amino-2-naphthoic acid (250 g.) in water (2·5 l.) and 10N-sodium hydroxide (135 c.c.) was filtered, the filtrate heated to 75° and toluene-*p*-sulphonyl chloride (275 g.) gradually added while the mixture was kept slightly alkaline to litmus by the addition of sodium carbonate. The boiling mixture was made alkaline to brilliant-yellow paper and filtered. The hot filtrate was added to water (300 c.c.) and concentrated hydrochloric acid (300 c.c.), and the solid was collected, washed with water, and dried. Crystallisation of this first from glacial acetic acid (1360 c.c.) then from methanol gave 3-*toluene*-p-*sulphonamido*-2-*naphthoic acid* as creamy white prisms (238 g.), m. p. 224° (Found : C, 63·5; H, 4·35; N, 4·0. $C_{18}H_{15}O_4NS$ requires C, 63·4; H, 4·4; N, 4·1%).

4-*Nitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic Acid.*—The sulphonamido-compound (51 g.) in glacial acetic acid (150 c.c.) was heated to 100°, then cooled to 54° with stirring. Sodium nitrite (0·1 g.) was added, followed by nitric acid (12·6 c.c.; *d* 1·4), the temperature being held at 54—57°. The solution was cooled to 10°, and the product was collected, washed with glacial acetic acid and carbon tetrachloride, and dried. Crystallisation of the solid from glacial acetic acid gave pale yellow prisms (39 g.), m. p. 188° (decomp.), of 4-*nitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic acid* (Found : C, 56·1; H, 3·8; N, 7·4. $C_{18}H_{14}O_6N_2S$ requires C, 56·0; H, 3·65; N, 7·25%).

4-*Nitro*-3-*amino*-2-*naphthoic Acid.*—The foregoing toluene-*p*-sulphonyl compound (30 g.) was dissolved in concentrated sulphuric acid (60 c.c.) at 30—40°, the solution poured on to ice, and the solid collected, washed with water, and dried. Crystallisation of the product from methanol gave orange needles (15 g.), m. p. 243—244° [Cross and Drew, *loc. cit.*, gave m. p. 240° (decomp.)] (Found : C, 57·3; H, 3·8; N, 12·1. Calc. for $C_{11}H_8O_4N_2$: C, 56·9; H, 3·45; N, 12·1%).

4 : 7-*Dinitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic Acid.*—4-Nitro-3-toluene-*p*-sulphonamido-2-naphthoic acid (19·3 g.) was boiled with glacial acetic acid (50 c.c.), cooled to 60°, and nitric acid (3·5 c.c.; *d* 1·5) added. The mixture was heated to 100° whereupon a reaction began. After 5 minutes the solution was cooled to 10°, and the solid collected, washed with glacial acetic acid then with carbon tetrachloride, and dried. Crystallisation of the solid from ethyl acetate gave pale yellow needles (3·7 g.), m. p. 177° (explosion), of 4 : 7-*dinitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic acid* (Found : C, 49·25; H, 2·15. $C_{18}H_{13}O_8N_3S$ requires C, 50·1; H, 3·0%).

4 : 7-*Dinitro*-3-*amino*-2-*naphthoic Acid.*—The toluene-*p*-sulphonyl derivative (3·6 g.) was dissolved in concentrated sulphuric acid (8 c.c.) at 35—40°, the solution poured on to ice, and the solid collected, washed with water, and dried. Crystallisation of the product from ethyl acetate gave orange micro-crystals (2·1 g.), m. p. 302°, of the *dinitroaminonaphthoic acid* (Found : C, 47·4; H, 2·6; N, 14·7. $C_{11}H_7O_6N_3$ requires C, 47·6; H, 2·55; N, 15·2%).

4 : 7-*Dinitro*-2-*naphthoic Acid.*—The 3-amino-compound (1 g.) was deaminated by the method of Hodgson and Walker (*J.*, 1933, 1620). Crystallisation of the *dinitronaphthoic acid* from glacial acetic acid gave yellowish brown micro-crystals (0·4 g.), m. p. 230—231° (Found : C, 50·7; H, 3·1; N, 10·3. $C_{11}H_6O_6N_2$ requires C, 50·4; H, 2·3; N, 10·7%).

Decarboxylation of 4 : 7-*Dinitro*-2-*naphthoic Acid.*—The dinitro-compound (0·2 g.) on being heated with copper bronze (0·2 g.) and quinoline (5 c.c.) for 10 minutes gave 1 : 6-dinitronaphthalene as pale yellow needles (from methanol), m. p. 163—164°, not depressed by admixture with an authentic sample.

3-*Acetamido*-2-*naphthoic Acid.*—3-Amino-2-naphthoic acid (100 g.), dissolved in water (800 c.c.) and 10N-sodium hydroxide (50 c.c.), was treated at 40° with acetic anhydride (80 c.c.). After the solution had been stirred for 1 hour excess of hydrochloric acid was added, and the solid was collected, washed with water, and dried. It was purified by treatment with boiling methanol, and dried. The product (90 g.) had m. p. 234—235°. An analytical specimen crystallised from ethanol in pale yellow needles, m. p. 237—238° (lit. gives m. p. 238°) (Found : C, 67·8; H, 4·95; N, 6·55. Calc. for $C_{13}H_{11}O_3N$: C, 68·1; H, 4·8; N, 6·1%).

3-Amino-2-naphthoic acid (2 g.) was heated under reflux with acetic anhydride (4 c.c.) for 2 hours, the solution poured into water, and the product crystallised from ethanol to give 3-acetamido-2-naphthoic acid (1·7 g.), m. p. 237—238°.

4-*Nitro*-3-*acetamido*-2-*naphthoic Acid.*—The following method was found to be preferable to that reported by Cross and Drew (*loc. cit.*). 3-Acetamido-2-naphthoic acid (20 g.) and glacial acetic acid (140 c.c.) were heated to 80° and treated with sodium nitrite (0·1 g.) and nitric acid (8 c.c.; *d* 1·42). The temperature was cautiously raised to 95°, and as soon as a clear solution was obtained the reaction mixture was cooled. After 12 hours the solid (18 g.) was collected, washed with carbon tetrachloride, and dried. Crystallisation of the solid from glacial acetic acid gave rosettes of pale yellow needles, m. p. 199—200° (Found : C, 57·1; H, 3·45; N, 10·0. Calc. for $C_{13}H_{10}O_5N_2$: C, 56·9; H, 3·65; N, 10·2%).

Hydrolysis of the *acetyl* compound (4·4 g.) with a boiling mixture of ethanol (44 c.c.) and concentrated hydrochloric acid (22 c.c.) for 1½ hours gave 4-nitro-3-amino-2-naphthoic acid (2·2 g.), m. p. 243—244°.

Acetylation of 4-*Nitro*-3-*amino*-2-*naphthoic Acid.*—4-Nitro-3-amino-2-naphthoic acid (3 g.) and acetic anhydride (15 c.c.) were heated under reflux for 6 hours and cooled, and the crystalline solid collected. Crystallisation of this from glacial acetic acid gave yellow needles (2·7 g.) of *anhydro*-4-*nitro*-3-*acetamido*-2-*naphthoic acid*, m. p. 234—235°, insoluble in cold, dilute sodium carbonate solution (Found : C, 60·4; H, 3·1; N, 10·9. $C_{13}H_8O_4N_2$ requires C, 60·95; H, 3·1; N, 10·9%).

This compound (0·5 g.) was heated under reflux with water (40 c.c.) for 30 hours, sodium carbonate solution added, the mixture filtered, and the filtrate acidified. The product was collected and crystallised from glacial acetic acid to give pale yellow needles (0·4 g.) of 4-*nitro*-3-*acetamido*-2-*naphthoic acid*, m. p. 199—200°.

Acetylation of 4 : 7-*Dinitro*-3-*amino*-2-*naphthoic Acid.*—4 : 7-Dinitro-3-amino-2-naphthoic acid (1 g.) and acetic anhydride (5 c.c.) were heated under reflux for 1 hour, water was added, and the solid was

collected and crystallised from glacial acetic acid to give creamy white needles (0·8 g.) of *anhydro*-4 : 7-*dinitro*-3-*acetamido*-2-*naphthoic acid*, m. p. 202—203°, insoluble in cold, dilute sodium carbonate solution (Found : C, 51·4; H, 2·65; N, 13·7. $C_{13}H_7O_6N_3$ requires C, 51·8; H, 2·3; N, 14·0%).

This compound (0·1 g.) and water (40 c.c.) were heated under reflux for 18 hours, sodium carbonate was added, the mixture was filtered, and the filtrate was acidified. Crystallisation from glacial acetic acid of the solid so obtained gave yellow micro-crystals of 4 : 7-*dinitro*-3-*acetamido*-2-*naphthoic acid*, m. p. 262° (Found : C, 48·6; H, 3·25; N, 12·6. $C_{13}H_9O_7N_3$ requires C, 48·9; H, 2·8; N, 13·1%).

4 : 7-Dinitro-3-amino-2-naphthoic acid (0·5 g.), treated with acetic anhydride (3 c.c.) and concentrated sulphuric acid (0·2 c.c.), gave the acetyl derivative, m. p. 261—262°.

Halogenated Nitro-derivatives of 3-*Amino*-2-*naphthoic Acid*

7-*Bromo*-4-*nitro*-3-*acetamido*-2-*naphthoic Acid*.—(*a*) Bromine (18·6 c.c.) in glacial acetic acid (50 c.c.) was added to a boiling solution of 4-nitro-3-acetamido-2-naphthoic acid (100 g.) in glacial acetic acid (1220 c.c.). A vigorous reaction took place, and after 15 minutes the solution was cooled in ice and the solid collected. Crystallisation of this from glacial acetic acid gave pale yellow needles (82 g.; 63·5%), m. p. 228—229° (Found : C, 43·7; H, 2·75; N, 7·45; Br, 23·5. $C_{13}H_9O_5N_2Br$ requires C, 44·1; H, 2·55; N, 7·9; Br, 22·5%).

(*b*) The same quantities were used but the mixture was heated under reflux for 1 hour after the addition of the bromine. The yield was 53·7%.

(*c*) The time of heating under reflux was increased to 2½ hours, and the yield obtained was 45·5%.

The acetic acid mother liquors were diluted with water, and the resulting sticky solid was crystallised from methanol giving 4-nitro-3-amino-2-naphthoic acid (26·5%). The methanol mother liquors were concentrated, and the residue heated under reflux with ethanol (200 c.c.) and concentrated hydrochloric acid (100 c.c.) for 2 hours. Water was added, and the solid was collected and crystallised from glacial acetic acid to give 4-nitro-3-amino-2-naphthoic acid (16%).

Bromination of 4-*Nitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic Acid in Glacial Acetic Acid*.—4-Nitro-3-toluene-*p*-sulphonamido-2-naphthoic acid (38·6 g.) was dissolved in boiling glacial acetic acid (250 c.c.) and bromine (5·4 c.c.; 1 mol.) added. After the solution had been heated under reflux for 6 hours it was cooled and the solid (12 g.) collected. Crystallisation of this from glacial acetic acid gave pale cream needles of 3 : 4 : 7-*tribromo*-2-*naphthoic acid*, m. p. 244—245° (Found : C, 33·0; H, 1·4; Br, 58·7. $C_{11}H_5O_2Br_3$ requires C, 32·3; H, 1·2; Br, 58·6%).

Orientation of 3 : 4 : 7-*Tribromo*-2-*naphthoic Acid*.—(a) 3 : 4 : 7-*Tribromo*-2-*naphthoamide*. The acid (14 g.) in benzene (40 c.c.) was heated under reflux with thionyl chloride (4 c.c.) for 7 hours, the solution cooled, and excess of ammonium carbonate added. After 2 hours the benzene was removed by steam, and the solid was collected and washed with hot water. Crystallisation of this from β-ethoxyethanol gave white micro-crystals of the *amide* (10 g.), m. p. >280° (Found : C, 32·2; H, 1·75; N, 3·7. $C_{11}H_6ONBr_3$ requires C, 32·3; H, 1·5; N, 3·4%).

(b) 3 : 4 : 7-*Tribromo*-2-*naphthylamine*. The amide (9·3 g.) was suspended in methanol (100 c.c.) and sodium hypochlorite solution (17 c.c.; 15%) added, the temperature rising to 45°. After 15 minutes, 10N-sodium hydroxide (25 c.c.) and methanol (40 c.c.) were added. The methanol was removed by distillation and the residue extracted with water. Crystallisation of the *amine* from ethanol gave white needles (4·2 g.), m. p. 157—159° (Found : C, 31·4; H, 1·65; N, 3·65. $C_{10}H_6NBr_3$ requires C, 31·6; H, 1·6; N, 3·7%).

The *acetyl* derivative, prepared from the amine and acetic anhydride, crystallised from acetic acid in white needles, m. p. 205—206° (Found : C, 34·2; H, 1·85. $C_{12}H_8ONBr_3$ requires C, 34·1; H, 1·9%).

(c) 3 : 4 : 7-*Tribromonaphthalene*. The amine (1·2 g.) was deaminated by the method used for 4 : 7-dinitro-3-amino-2-naphthoic acid. Crystallisation from acetic acid gave white needles of 3 : 4 : 7-tribromonaphthalene, m. p. 113—114° not depressed by admixture with an authentic sample.

Bromination of 4-*Nitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic Acid in* 97·5% *Acetic Acid*.—The compound (19·3 g.) was dissolved in boiling acetic acid (125 c.c.), and bromine (2·7 c.c.) added. After the solution had been heated under reflux for 6 hours, and cooled, water (450 c.c.) was added. The solid obtained (11 g.) was dissolved in ethanol and chromatographed on alumina. The upper band was separated, extracted with sodium carbonate, the extract filtered, and the filtrate acidified. The solid (4 g.), m. p. 186—188°, obtained was shown to be unchanged. The lower band was similarly separated. Crystallisation from acetic acid of the solid obtained gave 3 : 7-*dibromo*-4-*nitro*-2-*naphthoic acid* (3·2 g.), m. p. and mixed m. p. (see below) 234—236°.

Bromination of 1-*Nitro*-3-*toluene*-p-*sulphonamido*-2-*naphthoic Acid in Pyridine*.—A solution of the compound (7·7 g.) in pyridine (30 c.c.) was cooled to 5° and treated with a cold solution of bromine (1·2 c.c.) in pyridine (10 c.c.). After 15 minutes the solution was run into a mixture of ice and concentrated hydrochloric acid, and the solid was collected and washed with water. Crystallisation of it from dioxan gave orange micro-crystals (3·5 g.) of 3-bromo-1-nitro-2-toluene-*p*-sulphon-naphthalide, m. p. 229—231° (Consden and Kenyon, *loc. cit.*, give m. p. 237°) (Found : C, 48·5; H, 2·85; N, 6·4; Br, 18·4. Calc. for $C_{17}H_{13}O_4N_2BrS$: C, 48·5; H, 3·1; N, 6·65; Br, 19·0%).

The amine, prepared from the toluene-*p*-sulphonyl derivative by hydrolysis with concentrated sulphuric acid, crystallised from ethanol in red needles, m. p. 100—101° (Consden and Kenyon, *loc. cit.*, give m. p. 105°) (Found : C, 45·0; H, 2·7; N, 10·4. Calc. for $C_{10}H_7O_2N_2Br$: C, 45·0; H, 2·6; N, 10·5%).

Reactions of 7-*Bromo*-4-*nitro*-3-*acetamido*-2-*naphthoic Acid*.—(a) *With sodium carbonate solution*. The compound (2 g.) was heated under reflux with 2N-sodium carbonate solution (30 c.c.) for 20 hours, cooled, and acidified with hydrochloric acid. The solid was collected and crystallised from glacial acetic acid to give yellow micro-crystals (1 g.), m. p. >300° (Found : C, 50·95, 51·2; H, 2·95, 3·0; N, 7·95, 7·65; Br, 21·3%). No structural formula can be ascribed to these figures which agree best with $C_{15}H_{11}O_4N_2Br$ (C, 49·6; H, 3·0; N, 7·7; Br, 22·0%) or $C_{16}H_{11}O_4N_2Br$ (C, 51·0; H, 2·95; N, 7·5; Br, 21·4%).

(b) *With diethylamine*. The compound (3 g.) and diethylamine (35 c.c.) were heated under reflux for 24 hours, the excess of diethylamine removed by distillation, and excess of 2N-sodium hydroxide added. After being heated on a steam-bath for 1 hour the solution was filtered and acidified (litmus)

with acetic acid; the solid was collected and crystallised from glacial acetic acid to give 7-*bromo*-3-*amino*-4-*diethylamino*-2-*naphthoic acid* as a pale brown powder (2 g.), m. p. >310° (Found: C, 53·8, 53·6; H, 4·65, 4·7; N, 8·3, 8·0; Br, 23·1. $C_{15}H_{17}O_2N_2Br$ requires C, 53·4; H, 5·0; N, 8·3; Br, 23·7%).

(c) *With 48% hydrobromic acid.* The compound (10 g.) and hydrobromic acid (90 c.c.; 48%) were heated under reflux for 24 hours and poured into water (500 c.c.). The solid which was collected was fractionally crystallised from glacial acetic acid; it gave a sparingly soluble product, 4 : 7-*dibromo*-3-*amino*-2-*naphthoic acid* (bright yellow needles) (2·0 g.), m. p. 256—257° (Found: C, 37·8; H, 1·95; N, 3·8; Br, 46·7. $C_{11}H_7O_2NBr_2$ requires C, 38·3; H, 2·0; N, 4·1; Br, 46·4%), and an easily soluble portion which crystallised from ethanol to give orange needles (1·5 g.) of 3 : 7-*dibromo*-4-*nitro*-2-*naphthoic acid*, m. p. 236—238° (Found: C, 35·4; H, 1·6; N, 3·45; Br, 43·0. $C_{11}H_5O_4NBr_2$ requires C, 35·2; H, 1·3; N, 3·7; Br, 42·7%).

4 : 7-Dibromo-3-amino-2-naphthoic acid (1·0 g.) in glacial acetic acid (8·0 c.c.) was added to a solution of sodium nitrite (0·35 g.) in concentrated sulphuric acid (3·5 c.c.) at 20—25°. The diazo-compound was then added to cuprous bromide (1 g.) in hydrobromic acid (10 c.c.; 48%), the mixture was stirred for 1 hour, water added, and the solid collected. Crystallisation of this from acetic acid gave 3 : 4 : 7-tribromo-2-naphthoic acid, m. p. and mixed m. p. 244—245°.

By a similar reaction 4 : 7-dibromo-3-amino-2-naphthoic acid (0·6 g.) gave 3-*chloro*-4 : 7-*dibromo*-2-*naphthoic acid* as pale yellow needles (0·3 g.), m. p. 234—236°, from acetic acid (Found: C, 36·0; H, 1·5. $C_{11}H_5O_2ClBr_2$ requires C, 36·2; H, 1·4%).

4 : 7-Dibromo-3-amino-2-naphthoic acid (1 g.) was deaminated by Hodgson and Walker's method (*loc. cit.*) giving 4 : 7-*dibromo*-2-*naphthoic acid* (0·6 g.), m. p. 258—259° (Found: C, 39·9; H, 2·15. $C_{11}H_6O_2Br_2$ requires C, 40·0; H, 1·8%).

(d) *With dilute hydrobromic acid.* The compound (7 g.) was heated under reflux with hydrobromic acid (19 c.c.; 48%) and water (38 c.c.) for 24 hours, water (150 c.c.) was added, and the solid (6·5 g.) was collected. Crystallisation of this from glacial acetic acid gave pale yellow micro-needles (3·8 g.) of 4 : 7-*dibromo*-4-*nitro*-3-*acetamido*-3 : 4-*dihydro*-2-*naphthoic acid*, m. p. 240—242° (Found: C, 35·6; H, 2·5; N, 6·2; Br, 36·3. $C_{13}H_{10}O_5N_2Br_2$ requires C, 35·9; H, 2·3; N, 6·45; Br, 36·8%).

This compound (1·3 g.) was heated under reflux with hydrobromic acid (25 c.c.; 48%) for 20 hours and diluted with water. The solid (1 g.) was crystallised from acetic acid and gave orange needles, m. p. 234—236°, of 3 : 7-dibromo-4-nitro-2-naphthoic acid.

The compound (0·5 g.) was heated under reflux with 2N-sodium carbonate (20 c.c.) for 6 hours, hydrochloric acid was added, and the solid was collected; it crystallised from acetic acid in yellow needles (0·2 g.) of 4-*nitro*-3-*hydroxy*-2-*naphthoic acid*, m. p. 234—236° not depressed by admixture with an authentic sample (Found: C, 56·4; H, 3·2; N, 5·9. Calc. for $C_{11}H_7O_5N$: C, 56·5; H, 3·0; N, 6·0%).

(e) *With hydrochloric acid.* The compound (7 g.), concentrated hydrochloric acid (140 c.c.), and water (70 c.c.) were heated under reflux for 24 hours, water (150 c.c.) was added, and the solid was collected, boiled with ethanol (100 c.c.), and filtered off. 4-*Chloro*-7-*bromo*-4-*nitro*-3-*acetamido*-3 : 4-*dihydro*-2-*naphthoic acid* (3·5 g.) crystallised from acetic acid as creamy white needles, m. p. 239—240° (Found: C, 39·7, 40·0; H, 2·25, 2·4; N, 6·95, 7·3; Cl + Br, 28·6. $C_{13}H_{10}O_5N_2ClBr$ requires C, 40·05; H, 2·6; N, 7·2; Cl + Br, 29·7%).

This compound on hydrolysis with 2N-sodium carbonate gave 4-nitro-3-hydroxy-2-naphthoic acid.

(f) *With hydrochloric acid and ethanol.* The compound (10 g.), ethanol (200 c.c.), and concentrated hydrochloric acid (75 c.c.) were heated under reflux for 48 hours and water was added. The resultant solid was dissolved in methanol and chromatographed on alumina. A band, which remained at the top of the column, was extracted with sodium carbonate, acidified, and crystallised from ethanol giving 4-nitro-3-amino-2-naphthoic acid (2·0 g.), m. p. and mixed m. p. 238—240°. The remaining material was isolated by concentration of the eluate, and the solid crystallised from methanol to give orange needles (1 g.), m. p. 103—104°, of 4-*nitro*-3-*amino*-7-*ethoxy*-2-*naphthoic acid* (Found: C, 56·9; H, 4·1; N, 10·65. $C_{13}H_{12}O_5N_2$ requires C, 56·5; H, 4·35; N, 10·2%).

Bromo-derivatives of 3-Amino-2-naphthoic Acid.

4-*Bromo*-3-*toluene*-p-*sulphonamido*-2-*naphthoic Acid.*—3-Toluene-*p*-sulphonamido-2-naphthoic acid (8·5 g.) was dissolved in pyridine (40 c.c.), and an ice-cold solution of bromine (1·3 c.c.) in pyridine (10 c.c.) added. Next morning the solution was poured into excess of hydrochloric acid, and the solid was collected and crystallised from glacial acetic acid to give the 4-*bromo*-compound as pale yellow needles, m. p. 197—198° (5 g.) (Found: C, 51·7; H, 3·55; N, 3·75. $C_{18}H_{14}O_4NBrS$ requires C, 51·4; H, 3·3; N, 3·4%).

4-*Bromo*-3-*amino*-2-*naphthoic Acid.*—The toluene-*p*-sulphonyl compound (5 g.) was dissolved in concentrated sulphuric acid (10 c.c.) at 35—40°, the solution poured on to ice, and the solid collected. Crystallisation of this from glacial acetic acid gave bright yellow needles (2 g.), m. p. 220—222° (Found: C, 49·1; H, 3·05; N, 5·7. $C_{11}H_8O_2NBr$ requires C, 49·6; H, 3·0; N, 5·25%).

On decarboxylation in quinoline in the presence of copper bronze, 1-bromo-2-naphthylamine, m. p. and mixed m. p. with an authetic sample 61—63°, was obtained.

4 : 5 : 7(?)-*Tribromo*-3-*amino*-2-*naphthoic Acid.*—(*a*) 3-Toluene-*p*-sulphonamido-2-naphthoic acid (10·2 g.) in boiling glacial acetic acid (100 c.c.) was treated with bromine (4·6 c.c.; 3 mols.). After being heated under reflux for 1 hour the solution was cooled and the solid (8 g.) collected. Crystallised from glacial acetic acid it gave yellow micro-crystals, m. p. 254°, of a *tribromo*-compound (Found: C, 30·9; H, 1·9; N, 3·3; Br, 56·0. $C_{11}H_6O_2NBr_3$ requires C, 31·2; H, 1·4; N, 3·3; Br, 56·6%).

(*b*) 4-Bromo-3-toluene-*p*-sulphonamido-2-naphthoic acid (4·1 g.) in boiling glacial acetic acid (20 c.c.) was treated with bromine (0·5 c.c., 1 mol.). After being heated under reflux for 30 minutes the solution was cooled and the solid collected. Crystallisation of this from acetic acid gave 2 g. of a solid, m. p. 253—254°, identical with the previous compound.

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