NOTES.

Betulic Acid from Syncarpia laurifolia *Tenn.* By C. S. RALPH and D. E. WHITE.

THE bark of *Syncarpia laurifolia* Tenn. is interesting because of its resistance to the attack of marine borers. From an alcoholic extract of the bark a small amount of betulic acid has now been isolated, and identified by comparison with betulic acid prepared from betulin by the method of Ruzicka, Lamberton, and Christie (*Helv. Chim. Acta*, 1938, **21**, 1706). Meantime it has been reported that resistance to marine-borer attack is correlated with silica content (Amos and Dadswell, *J. Council Sci. Ind. Res.*, 1948, **21**, 190).

Betulic acid has also been reported in the barks of *Cornus florida* L. (Robertson, Soliman, and Owen, *J.*, 1939, 1267) and *Platanus acerifolia* (Brinckner, Kovacs, and Koczka, *J.*, 1948, 948), and in the seeds of *Zizyphus vulgaris* Lamark var. *spinosus* Bunge (Kawaguti and Kim, *J. Pharm. Soc. Japan*, 1940, **60**, 343; *Chem. Abstr.*, 1941, **35**, 1396). Purification of the acid from *S. laurifolia* bark was very difficult owing to contamination with a sulphur compound, which, however, was removed by the method outlined below.

Experimental.—(Melting points are corrected.) *Betulic acid.* The fibrous outer bark of *Syncarpia laurifolia* (15 kg.) was stripped from a tree growing near Cheltenham (N.S.W.), cut into short lengths in a chaff-cutter, and extracted twice by refluxing for 2 hours with alcohol (140 l. in all). The extracts were combined and the alcohol distilled off, the last traces, together with a minute amount of oil, being removed by steam-distillation. The solid residue (500 g.) obtained on cooling was filtered off, dried in air, powdered, and extracted in Soxhlet extractors, first with light petroleum (b. p. 40—60°) and then with ether. The ether extract was filtered from the solid which had separated (29 g.) and shaken with 10% sodium hydroxide solution. Insoluble sodium salts separated at the interface, and after separation of the alkaline solution and decantation of the clear ether solution, the remaining emulsion was filtered. The solid (20 g.) was dissolved in 70% alcohol and, after treatment with charcoal, filtered, and the acid precipitated with dilute hydrochloric acid, filtered off and crystallised thrice from alcohol. (Yield, 2·25 g.; m. p. ca. 295°.) A further crystallisation from alcohol, and filtration from a little amorphous material which separated after the solution had been cooled to 5°, followed by cooling the solution to 0° gave a product (0·9 g.), m. p. 310—312°, still containing sulphur (Found: S, 1·0%). When this acid was dissolved in 5% potassium hydroxide in 70% alcohol, treated with charcoal, filtered, and recovered by acidification and crystallisation from alcohol it was sulphur-free. Three further crystallisations from alcohol gave pure betulic acid (4 mg.), m. p. 319—320°, and on concentration of the mother liquors from the last three crystallisations a further 50 mg. (m. p. 320—321°) were obtained [Found: C, 78·79; H, 10·47%; *M* (Rast), 432 (after drying at 120° in high vacuum). Calc. for $C_{30}H_{48}O_3$: C, 78·9; H, 10·6%; *M*, 456·4]. The melting point of this material was not depressed by admixture with betulic acid of identical m. p. prepared, by the method of Ruzicka, Lamberton, and Christie (*loc. cit.*) from betulin, which was obtained from birch bark (*Betula alba* L.).

Acetylbetulic Acid. Acetylation of betulic acid from *S. laurifolia* by the method of Robertson, Soliman, and Owen (*loc. cit.*) followed by four crystallisations from a solution in methyl alcohol containing a little acetic acid to which warm water was added (cf. Ruzicka, Lamberton, and Christie, *loc. cit.*) gave acetybetulic acid, m. p. 293—294° (Found: C, 77·06; H, 10·17. Calc. for $C_{32}H_{50}O_4$: C, 77·1; H, 9·9%). The melting point of this material was not depressed by admixture with acetylbetulic acid of

identical melting point obtained by oxidation of betulin monoacetate (Ruzicka, Lamberton, and Christie, *loc. cit.*).

Thanks are due to Dr. R. T. Patton and Mr. C. Venville for supplies of birch bark, to Dr. G. Burger for the micro-analyses and to St. Andrew's College, University of Sydney, for laboratory facilities.—UNIVERSITY OF SYDNEY, UNIVERSITY OF WESTERN AUSTRALIA. [*Received, August 3rd*, 1949.]

An Improved Method of Preparation of Two Aromatic Disulphides.

By L. BAUER and J. CYMERMAN.

THE preparation of di-*p*-cyanophenyl disulphide (I) in unstated yield is described by McClelland and Warren (*J.*, 1930, 1102) from di-*p*-carboxyphenyl disulphide which in turn is obtained in poor yield from toluene-*p*-sulphonyl chloride (Smiles and Harrison, *J.*, 1922, 2024), necessitating altogether seven separate stages. Challenger, Miller, and Gibson (*J.*, 1948, 770) mention the preparation of diphenyl disulphide (in unstated yield) by the action of concentrated hydriodic acid on benzenesulphonyl chloride and describe the preparation by this method of 2 : 2′-dithienyl disulphide from thiophen-2-sulphonyl chloride in 60—70% yield. Cleve (*Ber.*, 1887, **20**, 1534) prepared 2 : 2′- and 3 : 3′-dinitrodiphenyl disulphide, and also later (*Ber.*, 1888, **21**, 1099) diphenyl disulphide, by the same method, whilst Ekbom (*Ber.*, 1902, **35**, 651) obtained 4 : 4′-dinitrodiphenyl disulphide from *p*-nitrobenzenesulphonyl chloride only by boiling with an excess of hydriodic acid.

As (I) was required, the action of concentrated hydriodic acid on *p*-cyanobenzenesulphonyl chloride (Remsen, Hartman, and Muckenfuss, *Amer. Chem. J.*, 1896, **18**, 158), readily prepared from *p*-sulphamylbenzoic acid, a by-product from the manufacture of saccharin, was examined and a 66% yield of crude (I), and after one recrystallisation a 50% overall yield of pure (I), was readily achieved under mild conditions. Application of the same method to *p*-acetamidobenzenesulphonyl chloride (Smiles and Stewart, *Org. Synth.*, Coll. Vol. I, 1941, 8) afforded, after acid hydrolysis, a 77·5% yield of di-*p*-aminophenyl disulphide.

*Experimental.—Di-*p*-aminophenyl disulphide.* *p*-Acetamidobenzenesulphonyl chloride (7 g.), hydriodic acid (30 c.c.; *d* 1·72), and glacial acetic acid (90 c.c.) soon gave a homogeneous solution which was set aside at room temperature for 22 hours. The solution was then diluted with sodium thiosulphate solution (300 c.c.; 10%) and treated with anhydrous sodium carbonate (50 g.), followed by sodium hydroxide solution (350 c.c.; 10%) till alkaline (litmus). The light-brown acetyl derivative was filtered off, washed with water, and refluxed with concentrated hydrochloric acid (60 c.c.) in 95% alcohol (30 c.c.) for 1·5 hours. The hot solution was then treated with an additional 40 c.c. of concentrated hydrochloric acid and allowed to cool slowly, being finally cooled to 0°. The product was filtered off, washed with dilute hydrochloric acid (1 : 1) and ether, and recrystallised from dilute hydrochloric acid (1 : 1), giving 3·7 g. (77·5%) of di-*p*-aminophenyl disulphide dihydrochloride as white needles, m. p. 225° (Hodgson and Dix, *J.*, 1914, 955, give m. p. 225°). The base, liberated by addition of sodium hydroxide solution to an aqueous solution of the hydrochloride, crystallised from aqueous alcohol in pale cream-coloured needles, m. p. 75—76° (Price and Stacy, *Org. Synth.*, Vol. 28, p. 24, give m. p. 75—76°).

Di-p-cyanophenyl disulphide. A mixture of *p*-cyanobenzenesulphonyl chloride (6 g.), hydriodic acid (30 c.c.; *d* 1·72), and glacial acetic acid (90 c.c.) was kept at room temperature for 22 hours. The solution was then treated with sodium thiosulphate solution and basified as described above, giving 2·64 g. (66%) of the crude dinitrile, m. p. 168—169°. Recrystallisation from chloroform–light petroleum (b. p. 40—60°) afforded white needles, m. p. 172—173° (McClelland and Warren, *loc. cit.*, give m. p. 172—173°).

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The Preparation of Some Aminonaphthol Derivatives. By FREDERICK KURZER.

IN the course of related work, it became necessary to prepare 1-*toluene*-p-*sulphonmethylamido*-2-*naphthol*. The synthesis, by general methods, of this compound involved the preparation of several new 1-amino-2-naphthol derivatives which are described below. Alkaline hydrolysis of 1-*toluene*-p-*sulphonamido*- and 1-*toluene*-p-*sulphonmethylamido*-2-*naphthyl toluene*-p-*sulphonate* gave the corresponding *naphthols*. The preparation of 1-methylamino-2-naphthol by hydrolytic removal, with almost concentrated sulphuric acid, of both toluene-*p*-sulphonyl groups from 1-toluene-*p*-sulphonmethylamido-2-naphthyl toluene-*p*-sulphonate was not possible, since far-reaching decomposition could not be avoided; alkali-soluble, black resinous materials, free from nitrogen, were obtained in some cases. Attempts to control the course of the hydrolysis by employing various mixtures of glacial acetic–sulphuric acid (cf. Usherwood and Whiteley, *J.*, 1923, 1084; Kuhn and Reinemund, *Ber.*, 1934, **67**, 1932) or ethanolic sulphuric acid (cf. Thorp and Walton, *J.*, 1948, 559) gave equally negative results. Under mild conditions the starting material was recovered, whilst vigorous treatment resulted in more complex reactions, and led to the partial destruction of the toluene-*p*-sulphonate. This preparation is readily accomplished with the corresponding aminophenols (Swiss P. 88,561; see also Hodgson and Birtwell, *J.*, 1943, 433); there is thus a marked difference in the behaviour of the corresponding toluene-*p*-sulphonyl esters in the aminophenol and the aminonaphthol series.

The preparation of Schiff's bases from aminonaphthols and furfuraldehyde is also described.

*Experimental.—*1-*Toluene*-p-*sulphonamido*-2-*naphthyl toluene*-p-*sulphonate.* A solution of 1-amino-2-naphthol hydrochloride (19·5 g., 0·1 mol.) in anhydrous pyridine was treated with excess of toluene-*p*-

sulphonyl chloride (58 g., 0·3 mol.), and heated on the steam-bath for 2 hours. The material was poured into water (500 ml.), and the separated oil solidified on stirring and was ground in a mortar with successive portions of hydrochloric acid, dilute sodium hydroxide solution, and water until it was nearly neutral. After two crystallisations fron acetone–ethanol–water (300, 600, and 50 ml., respectively) (charcoal), 1-*toluene*-p-*sulphonamido*-2-*naphthyl toluene*-p-*sulphonate*, m. p. 182—184°, was obtained in colourless compact prisms. Evaporation of the mother liquors to a small bulk gave further quantities of the product (total yield, 42—45 g., 90—96%) (Found : C, 61·5; H, 4·7; S, 13·5. $C_{24}H_{21}O_5NS_2$ requires C, 61·7; H, 4·5; S, 13·7%). The compound is insoluble in water, very sparingly soluble in warm sodium hydroxide solution, sparingly soluble in boiling ethanol, and soluble in acetone.

1-*Toluene*-p-*sulphonamido*-2-*naphthol*. A solution of 1-toluene-*p*-sulphonamido-2-naphthyl toluene-*p*-sulphonate (5 g.) in alcoholic potassium hydroxide (18 g. of potassium hydroxide in 150 ml. of ethanol) was boiled under reflux for 2 hours. After neutralisation of the alkali with hydrochloric acid, the solution was distilled to a small bulk (30 ml.), and diluted with hydrochloric acid (150 ml.; 2%). Crystallisation of the separated product from aqueous alcohol gave 1-*toluene*-p-*sulphonamido*-2-*naphthol*, m. p. 176—178°, in colourless short prisms (Found : S, 9·75. $C_{17}H_{15}O_3NS$ requires S, 10·2%). It is very soluble in ethanol and acetone.

1-*Toluene*-p-*sulphonmethylamido*-2-*naphthyl toluene*-p-*sulphonate*. A solution of 1-toluene-*p*-sulphonamido-2-naphthyl toluene-*p*-sulphonate (9·35 g., 0·02 mol.) in acetone (150 ml.) was treated at 65—75° alternately with small portions of sodium hydroxide solution (40 ml.; 30% w/v) and dimethyl sulphate (25 g., 0·2 mol.) over a period of 20 minutes. Good contact between the acetone and the aqueous phase was maintained by vigorous shaking; each addition of dimethyl sulphate was accompanied by a transient colour change to deep-orange until methylation was complete. After ½ hour's refluxing, with continued addition of sodium hydroxide solution to keep the mixture alkaline, the acetone layer was separated from the aqueous phase while hot (separation being facilitated by the addition of ether if necessary), and the solvent removed in a vacuum. The residue gave, after two crystallisations from acetone–ethanol (80 and 100 ml., respectively), 1-*toluene*-p-*sulphonmethylamido*-2-*naphthyl toluene*-p-*sulphonate*, m. p. 168—171°, in colourless lustrous short needles (yield, 9·2—9·35 g., *i.e.*, nearly theoretical) (Found : C, 62·8; H, 5·2; S, 13·05. $C_{25}H_{23}O_5NS_2$ requires C, 62·4; H, 4·8; S, 13·3%). It is soluble in hot acetone and ether, and sparingly in ethanol. Crystallisation from aqueous ethanol (50 ml. of ethanol and 8 ml. of water per g.) gives minute prisms.

1-*Toluene*-p-*sulphonmethylamido*-2-*naphthol*. 1-Toluene-*p*-sulphonmethylamido-2-naphthyl toluene-*p*-sulphonate (9·6 g., 0·02 mol.), when boiled in alcoholic potassium hydroxide (150 ml.; 10% w/v) for two hours and worked up as described above, gave 1-*toluene*-p-*sulphonmethylamido*-2-*naphthol* (6·2 g., 94%) crystallising in lustrous platelets, m. p. 191—193°, from ethanol (Found : C, 66·3; H, 4·8; S, 9·2. $C_{18}H_{17}O_3NS$ requires C, 66·1; H, 5·2; S, 9·8%).

1-*Toluene*-p-*sulphonmethylamido*-2-*methoxynaphthalene*. A warm solution of 1-toluene-*p*-sulphonmethylamido-2-naphthol (13·0 g., 0·04 mol.) in acetone (100 ml.) was methylated at 30—40° by alternate additions, with shaking, of dimethyl sulphate (total, 25 g., 0·2 mol.) and sodium hydroxide solution (40 ml.; 35% w/v). After the solution had been shaken vigorously for a further 15 minutes, the acetone layer was removed, the aqueous phase again extracted with ether, and the combined, washed dark-red extracts evaporated in a vacuum. The residue, when taken up in acetone (30 ml.), filtered with carbon, and diluted with ethanol (50 ml.), deposited lustrous platelets of 1-*toluene*-p-*sulphonmethylamido*-2-*methoxynaphthalene*, m. p. 132—134° (yield, 11·3 g., 82%) (Found : C, 66·9; H, 5·2; S, 9·0. $C_{19}H_{19}O_3NS$ requires C, 66·9; H, 5·6; S, 9·4%).

1-*Furfurylideneamino*-2-*naphthol*. A suspension of 1-amino-2-naphthol [prepared by the addition at 60° of sodium acetate (10 g.) to a solution of 1-amino-2-naphthol hydrochloride (9·8 g., 0·05 mol.) in water (120 ml.), in the presence of a little sodium dithionite, cooling the solution to 0°, and filtering off the product] in benzene (300 ml.) was treated with excess of furfuraldehyde (5·4 g., 0·055 mol.), and heated on the steam-bath for 15 minutes, whereupon the naphthol dissolved rapidly. The deep-yellow liquid obtained was separated from small quantities of water while hot, and evaporated to a small bulk (100 ml.). On the addition of light petroleum (10—15 ml.; b. p. 60—80°), and cooling, the liquid deposited dark-yellow crystalline 1-*furfurylideneamino*-2-*naphthol*, m. p. 174—176° (decomp.) (yield, 9—10 g., 76—84%) (Found : N, 6·1. $C_{15}H_{11}O_2N$ requires N, 5·9%).

4-*Furfurylideneamino*-1-*naphthol*. Sodium acetate (4 g.) was added to a solution of 4-amino-1-naphthol hydrochloride (4·9 g., 0·025 mol) in water (60 ml.), and the aqueous suspension vigorously shaken with furfuraldehyde (2·7 g., 0·028 mol.) at 40° for 10 minutes. The dark oil obtained was extracted with benzene. The extracts, on partial evaporation, gave 4-*furfurylideneamino*-1-*naphthol* as a yellow powder, m. p. 156—157° (decomp.), which crystallised from a large volume of benzene in massive lustrous leaflets, disintegrating to a yellow powder on being dried (Found : N, 5·7. $C_{15}H_{11}O_2N$ requires N, 5·9%).

—KING'S COLLEGE OF HOUSEHOLD AND SOCIAL SCIENCE (UNIVERSITY OF LONDON), W.8. [*Received, August 16th*, 1949.]

2-*Chloro*-5-*nitroaniline*. By C. BUCHANAN and S. H. GRAHAM.

THE preparation of this compound by nitration of *o*-chloroaniline sulphate (Chattaway, Orton, and Evans, *Ber.*, 1900, **33**, 3062), or by reduction of 2 : 4-dinitrochlorobenzene (Claus and Stiebel, *Ber.*, 1887, **20**, 1379), not proving satisfactory, the following procedure was adopted (cf. Brady, *J.*, 1925, **127**, 2264). *N*-(*o*-Chlorophenyl)phthalimide (m. p. 141°) gave, on nitration, N-(2-*chloro*-5-*nitrophenyl*) *phthalimide* which was hydrolysed with 2N-sodium hydroxide to the required amine. Methylation of the toluene-*p*-sulphonyl derivative with methyl sulphate and sodium hydroxide, followed by hydrolysis with sulphuric acid, gave 2-chloro-5-nitro-*N*-methylaniline, the m. p. (110°) of which was substantially higher than that given by Phillips (*J.*, 1931, 1151), *viz.*, 99°.

Experimental.—N-(2-*Chloro*-5-*nitrophenyl*)*phthalimide*. To a suspension of *N*-(*o*-chlorophenyl)-phthalimide (30 g.) in 96% sulphuric acid (110 c.c.), 68% nitric acid (25 c.c.) was added gradually with

stirring. Heat was evolved and the temperature was kept at 30—40° by cooling in a stream of running water. The mixture was set aside for 30 minutes after addition of the acid was complete and poured into water; the precipitated *nitro*-product formed pale yellow prisms (33 g.), m. p. 197°, from acetic acid (Found: C, 55·6; H, 2·5. $C_{14}H_7O_4N_2Cl$ requires C, 55·6; H, 2·3%).

Hydrolysis. A solution of the nitration product (30 g.) in 2N-sodium hydroxide solution (250 c.c.) was boiled for 2 hours and cooled. The amine was filtered off, and crystallised from alcohol as bright yellow needles m. p. 120° (14 g.). The *N*-toluene-*p*-sulphonyl derivative formed diamond-shaped prisms, m. p. 159°, from acetic acid.

N-Toluene-*p*-sulphono-2-chloro-5-nitro-*N*-methylanilide, white prisms, m. p. 89°, from alcohol, was hydrolysed by 80% sulphuric acid at 140° to the free base, orange prisms, m. p. 110° (Found: C, 45·1; H, 3·7. Calc. for $C_7H_7O_2N_2Cl$: C, 45·1; H, 3·8%), from methanol.—THE UNIVERSITY, GLASGOW, W.2. [*Received, September 21st*, 1949.]

Some Diazoamino- and Aminoazo-naphthalenes. By HERBERT H. HODGSON and JOHN HABESHAW.

To obtain further evidence of isomeric changes of the diazoamino–aminoazo-type in the naphthalene series, 2-nitro-, 4-nitro-, and 4-chloro-1-naphthylamine were treated in ethanol solution, or suspension, with amyl nitrite in the presence of less sulphuric or hydrochloric acid than was necessary for the formation of the diazonium sulphate. The 4-substituted compounds gave their respective aminoazonaphthalenes *via* their unstable diazoamino-isomerides, but 2-nitro-1-naphthylamine gave 2 : 3′-*dinitro*-4′-*amino*-1 : 1′-*azonaphthalene* directly, no intermediate diazoamino-compound being observed. These reactions indicate that coupling in the *ortho*-position to an amino-group in the naphthalene series may be preceded by formation of the isomeric diazoamino-compound.

Diazotisation of 4-Nitro-1-naphthylamine with Insufficient Mineral Acid.—A solution of 4-nitro-1-naphthylamine (10 g.) in ethanol (150 c.c.) and sulphuric acid (2 c.c.; *d* 1·84) was treated with amyl nitrite (15 c.c.) at 5—10°, and the mixture kept for an hour, whereafter the brown solid (7 g.) which separated was filtered off and washed with ether. The separation of the solid from the mixture was assisted by the addition of ether (100 c.c.); the product exploded in a flame, melted with explosive decomposition at *ca.* 113°, and, when boiled (2 g.) with ethanol (50 c.c.) containing hydrochloric acid (35 c.c.; *d* 1·16) for 30 minutes and then steam-distilled, afforded 1-nitronaphthalene (0·6 g.), while the residual 4-nitro-1-naphthylamine in the steam-flask when crystallised from ethanol had m. p. 194°. When the brown solid (2 g.) was boiled with hydrochloric acid (35 c.c.; *d* 1·16) and water (100 c.c.) for 30 minutes, the solution became yellow and, when filtered hot, deposited 4-nitro-1-naphthol, while the residue contained 4-nitro-1-naphthylamine. These reactions indicate the brown solid to be the 4 : 4′-dinitro-1 : 1′-diazoaminonaphthalene.

When the reaction mixture as above was kept for 48 hours (cf. also Hodgson, Nicholson, and Turner, *J.*, 1944, 15), bright red 4 : 4′-dinitro-1-amino-1′ : 2-azonaphthalene was formed, and was then filtered off, washed with ethanol, and crystallised from nitrobenzene in bright needles, m. p. 279—280° alone or mixed with a specimen prepared by coupling 4-nitronaphthalene-1-diazonium chloride with 4-nitro-1-naphthylamine (Hodgson, Nicholson, and Turner, *loc. cit.*, give m. p. 274°) (Found: N, 17·9. Calc. for $C_{20}H_{13}O_4N_5$: N, 18·1%). It gave an initial deep-blue colour with concentrated sulphuric acid. When hydrogen chloride was passed into a nitrobenzene solution of the aminoazo-compound, the *hydrochloride* separated in small metallic-looking plates which did not melt, and lost hydrogen chloride in the air too rapidly for analysis.

1′-*Chloro*-4 : 4′-*dinitro*-1 : 2′-*azonaphthalene* was formed when a suspension of the above aminoazo-compound (3 g.) in glacial acetic acid (40 c.c.) was stirred at 20—25° into a solution of sodium nitrite (1 g.) in sulphuric acid (9 c.c.; *d* 1·84), and the stirring continued for 1 hour; a red solution was obtained which was then added to one of cuprous chloride (5 g.) in hydrochloric acid (50 c.c.; *d* 1·16). There was a vigorous evolution of nitrogen, and, after being stirred for 2 hours, the mixture was heated for 15 minutes on the water-bath, cooled, and diluted with water (100 c.c.). The crude 1′-*chloro*-4 : 4′-*dinitro*-1 : 2′-*azonaphthalene* (1·6 g.) was filtered off, washed with water, dilute aqueous ammonia, and water, and dried; after crystallisation 3 times from glacial acetic acid, it was obtained in light-red needles (much paler than the parent aminoazo-compound), m. p. 206—207° (Found: Cl, 8·4. $C_{20}H_{11}O_4N_4Cl$ requires Cl, 8·7%), which gave a deep-blue solution in concentrated sulphuric acid.

2 : 3′-*Dinitro*-4′-*amino*-1 : 1′-*azonaphthalene* was obtained when 2-nitro-1-naphthylamine (10 g.) was diazotised as was the above 4-nitro-isomeride. On addition of ether, however, to the diazo-solution, some 2-nitronaphthalene-1-diazonium sulphate was precipitated. This was filtered off. The filtrate was kept overnight, whereupon the red aminoazo-compound was deposited and crystallised from nitrobenzene in bright scarlet needles, m. p. 272—273° (Found: N, 18·3. $C_{20}H_{13}O_4N_5$ requires N, 18·1%), which gave a very deep-blue solution in concentrated sulphuric acid and remained unchanged in the Sandmeyer reaction.

4 : 4′-Dichloro-1 : 1′-diazoaminonaphthalene was formed when a solution of 4-chloro-1-naphthylamine (10 g.) in ethanol (200 c.c.) was treated with amyl nitrite (10 c.c.) and hydrochloric acid (7 c.c.; *d* 1·16). The intense red solution, when treated with ether (100 c.c.), deposited the diazoamino-compound as a red solid (4 g.) after *ca.* an hour; this was filtered off, washed with a little cold ethanol, and dried; it exploded in a flame, decomposed very rapidly when heated to 90°, and, when boiled (2 g.) with ethanol (50 c.c.) and hydrochloric acid (35 c.c.; *d* 1·16) for 30 minutes and then steam-distilled, afforded 4-chloronaphthalene (0·5 g.). The residue in the flask was washed free from acid and steam-distilled in the presence of alkali, whereupon 4-chloro-1-naphthylamine (0·6 g.) was obtained. When the diazoamino-compound (2 g.) was boiled for 30 minutes with hydrochloric acid (50 c.c.; *d* 1·16) and the mixture steam-distilled, 4-chloro-1-naphthol (0·6 g.) passed over, the flask residue when distilled with alkali affording 4-chloro-1-naphthylamine. The stable red 4 : 4′-*dichloro*-1′-*amino*-1 : 2′-*azonaphthalene* was formed slowly when the above reaction mixture was kept for several days; it crystallised from benzene

in very small red crystals, m. p. 231—232° (Found : Cl, 19·1. $C_{20}H_{13}N_3Cl_2$ requires Cl, 19·4%), its solution being intensely coloured.

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The Monochlorination of 3-Fluoro-6-nitrophenol in the 4-Position.
By HERBERT H. HODGSON and JOSEPH NIXON.

ONLY monochlorination occurs when 3-fluoro-6-nitrophenol (10 g.) is stirred at room temperature into 1·45N-sodium hypochlorite (200 c.c.). The mixture was kept overnight, then heated on the water-bath for 15 minutes, cooled, and acidified with dilute sulphuric acid; the separated oil was removed and steam-distilled, the distillate frozen, the solid dissolved in ethanol, and the solution allowed to evaporate, whereupon *4-chloro-5-fluoro-2-nitrophenol* separated. This crystallised from light petroleum in yellow needles, m. p. 98° (Found : Cl, 18·4. $C_6H_3O_3NClF$ requires Cl, 18·5%). The constitution of the chlorinated product follows from its synthesis as follows : 4-chloro-3-fluoroanisole was demethylated by hydriodic acid (Hodgson and Nixon, *J.*, 1931, 981); the resultant phenol, isolated by distillation in steam, was treated with sodium nitrite solution and then with hydrochloric acid. 4-Chloro-5-fluoro-2-nitrophenol thus formed was isolated by distillation in steam; it crystallised from light petroleum in yellow needles (Found : Cl, 18·3%), m. p. 98° alone or mixed with the above products.

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Formylation of Bile Acids. By I. W. HUGHES, F. SMITH, and M. WEBB.

FORMYLATION offers a valuable means for protecting the hydroxyl groups of bile acids in certain synthetic reactions and we have therefore explored various methods for increasing the efficiency of the formylation process. The preparation of formyl derivatives of bile acids by the method of Cortese and Bauman (*J. Amer. Chem. Soc.*, 1935, **57**, 1393; *J. Biol. Chem.*, 1936, **113**, 779) frequently results in the formation of mixtures of partly substituted derivatives which fail to crystallise, and it is only by re-treatment with formic acid at 60—70° that complete formylation is attained.

Previous experiments have indicated that improved formylation can be achieved by use of a mixture of formic acid and sodium formate (Stacey and Webb, *Proc. Roy. Soc.*, 1947, *B*, **134**, 522). The profound catalytic effect of small amounts of perchloric acid in the acetylation of phenols (Conant and Bramann, *J. Amer. Chem. Soc.*, 1928, **50**, 2305) and bile acids (Whitman and Schwenk, *ibid.*, 1946, **68**, 1865) has been noted and extended to sugars (Nicholas and Smith, *Nature*, 1948, **161**, 349) and sugar alcohols (Nicholas and Smith, unpublished work; cf. Krüger and Roman, *Ber.*, 1936, **69**, 1830). We now find that this acid is also an excellent catalyst in formylation reactions. For example, it was found that in the presence of perchloric acid the formylation of bile acids and their derivatives was brought about by one treatment with formic acid at 50—55° with the production of good yields of the fully formylated products. Experiments in which the formylation of cholic acid was carried out with formic acid purified by distillation first from phosphoric oxide (Schlesinger and Martin, *J. Amer. Chem. Soc.*, 1914, **36**, 1589) and then from anhydrous oxalic acid, or by distillation over boric anhydride (Schierz, *ibid.*, 1923, **45**, 477), showed that the yield of *O*-triformylcholic acid obtained in the presence of perchloric acid increased with increasing purity of the formic acid.

The formyl derivatives of bile acids were found to be much more sensitive to acid and alkaline hydrolysis than the corresponding acetyl derivatives, and it was not possible to effect partial deformylation of triformylcholic acid with those reagents examined. Thus, the compound was completely deformylated by methyl-alcoholic hydrogen chloride, sodium ethoxide in ethanol, and by sodium hydroxide equivalent to one formyl group, whereas it was recovered unchanged after prolonged boiling in aqueous-alcoholic solution.

Experimental.—*O-Triformylcholic acid.* A solution of cholic acid (1 g.) in freshly distilled formic acid (70%, 10 c.c.) containing perchloric acid (6N.; 0·1 c.c.) was heated for 2 hours at 55° and then concentrated to half its volume *in vacuo* at 40°. The solution was then poured with stirring into water (400 c.c.), and the resulting precipitate collected after 3 hours. The solid was repeatedly washed with water until free from formic acid and then crystallised and recrystallised from ethyl alcohol–water (2 : 3) to give *O*-triformylcholic acid (0·95 g.). With 76, 82, and 92% formic acid the yield of triformylcholic acid was, respectively. 71·3, 79·6, and 85·5%. The product has m. p. 208—210° and $[\alpha]_D^{19}$ +83° (*c*, 0·6 in ethyl alcohol) (Found : C, 66·0; H, 7·9; ·CHO, 17·3. Calc. for $C_{27}H_{40}O_8$: C, 65·85; H, 8·1; ·CHO, 17·6%).

Methyl O-triformylcholate. A solution of methyl cholate (1 g.) in freshly distilled formic acid (70%, 8 c.c.) containing perchloric acid (6N; 0·1 c.c.) was treated as above. Recrystallisation of the crude product from methyl alcohol gave fine needles of methyl triformylcholate (0·98 g.), m. p. 150—152°, $[\alpha]_D^{19}$ +75·9° (*c*, 0·9 in methyl alcohol) (Found : C, 66·1; H, 8·1; ·CHO, 17·8. Calc. for $C_{28}H_{42}O_8$: C, 66·4; H, 8·3; ·CHO, 17·2%).

Triformylcholamide. The product obtained from the formylation of cholamide (0·5 g., m. p. 104—105°) under the above conditions was recrystallised from a mixture of dioxan and light petroleum (1 : 1) to give triformylcholamide (0·53 g.), m. p. 186—187°, $[\alpha]_D^{20}$ +79·3° (*c*, 0·8 in ethyl alcohol) (Found : ·CHO, 17·7. Calc. for $C_{27}H_{41}O_7N$: ·CHO, 17·7%), identical with the authentic specimen (m. p. 187°) previously prepared (James, Smith, Stacey, and Webb, *J.*, 1946, 665).

O-Diformyldeoxycholic acid. A solution of deoxycholic acid (1 g.) in redistilled formic acid (70%,

15 c.c.) containing perchloric acid (6N.; 0·1 c.c.) was heated for 2·5 hours at 60° and then concentrated *in vacuo* at 40° to small bulk. The residual solution was poured with stirring into water (300 c.c.), and the resulting precipitate collected after 12 hours, washed with water, and dried *in vacuo*. The solid was crystallised with some difficulty from ethyl alcohol to yield *O*-diformyldeoxycholic acid (0·74 g.), m. p. 193—196°, $[\alpha]_D^{21}$ +103° (*c*, 0·6 in dioxan) (Found: C, 68·9; H, 8·7; ·CHO, 12·2. Calc. for $C_{26}H_{40}O_6$: C, 69·6; H, 8·9; ·CHO, 12·9%). It was identical with a specimen prepared by the method of Hoehn and Moffett (*J. Amer. Chem. Soc.*, 1945, **67**, 740).—CHEMISTRY DEPARTMENT, THE UNIVERSITY, EDGBASTON, BIRMINGHAM 15. [*Received, September 23rd*, 1949.]