752. *Synthesis of Plant-growth Regulators. Part I. Substituted β-Naphthyloxyacetic Acids.*

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A number of mono-, di-, and tri-chloro-, and mononitro-β-naphthyloxyacetic acids have been prepared for examination as parthenocarpic agents. New syntheses of 5-, 7-, and 8-chloro-2-naphthols are described, and a discrepancy in the m. p. of 5-chloro-2-naphthol is reported.

Substituted phenoxyacetic acids have a variety of biochemical roles, including rooting agents (Hitchcock and Zimmerman, *Contr. Boyce Thompson Inst.*, 1942, **12**, 497), herbicides (B.P. 573,929/1941; Hamner and Tukey, *Science*, 1944, **100**, 154; Templeman and Sexton, *Proc. Roy. Soc.*, *B*, 1946, **133**, 300; Slade, Templeman, and Sexton, *Nature*, 1945, **155**, 497; Nutman, Thornton, and Quastel, *ibid.*, p. 498; Blackman, *ibid.*, p. 500), and parthenocarpic agents (Zimmerman and Hitchcock, *Contr. Boyce Thompson Inst.*, 1942, **12**, 321). In several of these publications the effect of the number and the position of substituent halogen atoms and nitro-groups on physiological activity is described, and a wide variation noted.

The parthenocarpic activity shown by many of these acids is shared by β-naphthyloxyacetic acid (Gustafson, *Proc. Amer. Soc. Hort. Sci.*, 1943, **40**, 387), and it was decided to investigate the effect of nuclear chlorine substitution in this case. 1-Chloro-2-naphthyloxyacetic acid has already been described (Templeman and Sexton, *loc. cit.*) and we have prepared the remaining acids by condensing ethyl bromoacetate with the sodium salt of the appropriate naphthol. The 3-, 4-, 6-, and 7-chloro-2-naphthols were obtained by known methods, often with some improvement.

Dilthey, Quint, and Heinen (*J. pr. Chem.*, 1939, **152**, 73) recorded the preparation of 8-chloro-2-naphthol from the corresponding 8-amino-compound by diazotisation, followed by a Sandmeyer reaction using cuprous chloride. Attempts by us to prepare 5- or 8-chloro-2-naphthol using this procedure gave only tars. Similar treatment of 5-amino-2-methoxynaphthalene gave a red oil which on demethylation with hydriodic acid also resulted in the formation of tar. Finally 5- and 8-chloro-2-naphthols were prepared from the nitronaphthyl acetates by successive reduction, Sandmeyer reactions, and hydrolysis. The structure of our 5-chloro-2-naphthol is proved by the method of synthesis and confirmed by its oxidation to 3-chlorophthalic acid by alkaline potassium permanganate; it had m. p. 97—98°, although Claus (*J. pr. Chem.*, 1889, **39**, 317) gives m. p. 128°; his product may have been 7-chloro-2-naphthol, m. p. 126·5° (Franzen and Deibel, *ibid.*, 1908, **78**, 154).

The only dichloro-2-naphthyloxyacetic acid previously described is the 1 : 6-compound which is reported to have been obtained by direct chlorination of the unsubstituted acid at 60° (Haskelberg, *J. Org. Chem.*, 1947, **12**, 426). Repetition of this work gave 1 : 4-dichloro-2-naphthyloxyacetic acid, m. p. 188—189°, identical with that prepared from 1 : 4-dichloro-2-naphthol (James and Woodcock, *J.*, 1951, 1931). Attempts to obtain 1 : 6-dichloro-2-naphthol have already been described (James and Woodcock, *loc. cit.*) and there is no reliable evidence to support the view that it is formed in the direct chlorination of 1-chloro-2-naphthol. In addition to the 1 : 4-dichloro-acid, 1 : 3- and 3 : 4-dichloro- and 1 : 3 : 4-trichloro-2-naphthyloxyacetic acids were also obtained from the corresponding naphthols. The acids reported in this paper have been tested for parthenocarpic activity by Dr. L. C. Luckwill, using unpollinated tomato ovaries (Luckwill, *J. Hort. Sci.*, 1948, **24**, 19), and the results will be fully reported elsewhere.

EXPERIMENTAL.

M. p.s are uncorrected. Carbon and hydrogen analyses were by Drs. Weiler and Strauss, Oxford.

3-*Chloro*-2-*naphthol*.—In Marschalk's method of preparation (*Bull. Soc. chim.*, 1928, **43**, 1361), isolation is improved by steam-distillation at the final stage.

4-*Chloro*-2-*naphthol*.—This was obtained in 77% yield by the reduction of 1 : 4-dichloro-2-naphthol using stannous chloride and hydrochloric acid (cf. Burton, *J.*, 1945, 282).

6-*Chloro*-2-*naphthol*.—6-Amino-2-naphthol-4-sulphonic acid (10 g.) (Ruggli *et al.*, *Helv. Chim. Acta*, 1929, **12**, 1051) was diazotised and the solution decomposed by dropwise addition to cuprous chloride (6·7 g.) in boiling concentrated hydrochloric acid (60 ml.). After removal of the copper with hydrogen sulphide, the solution was evaporated to half-bulk and stirred during the portionwise addition of sodium amalgam (400 g.; 4%) and concentrated hydrochloric acid (80 ml.). The crude dark product which separated was collected and purified by dissolving it in a minimum amount of 2N-sodium hydroxide, filtration, addition of 2N-hydrochloric acid to cloudiness, shaking with charcoal, filtration, and final acidification with acetic acid. The product crystallised from water in needles (3·2 g.), m. p. 114—115° (Found : Cl, 19·9. Calc. for $C_{10}H_7OCl$: 19·9%). Ruggli *et al.* give m. p. 115°. The *acetate*, prepared in the usual way crystallised from methyl alcohol in prisms, m. p. 100—101° (Found : C, 65·2; H, 4·2; Cl, 16·0. $C_{12}H_9O_2Cl$ requires C, 65·3; H, 4·1; Cl, 16·1%).

2 : 7-*Dinitronaphthalene*.—Clemo and Driver (*J.*, 1945, 829) reported poor yields from the decarboxylation of 3 : 6-dinitronaphthalic anhydride and abandoned the method. In our hands this route gave a 60% yield of 2 : 7-dinitronaphthalene, m. p. 229—230°, suitable for conversion without further purification into 7-nitro-2-naphthylamine.

2-*Chloro*-7-*nitronaphthalene*.—Diazotisation of 7-nitro-2-naphthylamine (Hodgson and Ward, *J.*, 1945, 590), followed by a Sandmeyer reaction using cuprous chloride, resulted in a 97% yield of the chloro-compound. This crystallised from ethyl alcohol in brownish prisms, m. p. 139—140° (Found : Cl, 17·3. Calc. for $C_{10}H_6O_2NCl$: 17·1%). Hodgson and Ward (*J.*, 1947, 330) give m. p. 136°.

7-*Chloro*-2-*naphthylamine*.—2-Chloro-7-nitronaphthalene (7·5 g.), suspended in ethyl alcohol (100 ml.) and shaken in hydrogen in the presence of Raney nickel, rapidly absorbed the theoretical amount of hydrogen. The filtered solution was concentrated to ⅓-bulk, water (5 ml.) added, and the solution chilled to 0°. The product (4·4 g.) crystallised from aqueous ethyl alcohol in prisms, m. p. 120—121° (Found : Cl, 19·8. Calc. for $C_{10}H_8NCl$: 20·0%). Hodgson and Ward (*loc. cit.*) give m. p. 118—119°. The *acetate*, prepared in the usual way, crystallised from aqueous methyl alcohol in plates, m. p. 101—102° (Found : C, 65·6; H, 4·6; Cl, 16·4. $C_{12}H_{10}ONCl$ requires C, 65·6; H, 4·6; Cl, 16·2%).

7-*Chloro*-2-*naphthol*.—The above chloro-amine (1·2 g.) was dissolved in a mixture of glacial acetic acid (7 ml.) and concentrated sulphuric acid (12 ml.) and stirred during the addition of water (60 ml.). The finely divided suspension of the amine sulphate was diazotised by dropwise addition of sodium nitrite (0·5 g.) in water (5 ml.) at 0—10°. After 3 hours' stirring excess of nitrous acid was destroyed by urea, and the diazonium solution was decomposed by dropwise addition to boiling 2N-sulphuric acid (80 ml.). The product was extracted from the cooled solution with ether, and the extract washed with sodium hydrogen carbonate solution, dried, and freed from solvent. Extraction of the residual dark red oil with boiling light petroleum (b. p. 60—80°) (charcoal) gave 7-chloro-2-naphthol (0·55 g., 46%), m. p. 124—126°, which crystallised from the same solvent in large rhombic prisms, m. p. 126—127° (Found : Cl, 19·7. Calc. for $C_{10}H_7OCl$: Cl, 19·9%). Franzel and Deibel (*loc. cit.*) give m. p. 126·5°. The *acetate*, crystallised from methyl alcohol in stout rhombs, m. p. 105—106° (Found : C, 65·3; H, 4·2; Cl, 16·0. $C_{12}H_9O_2Cl$ requires C, 65·3; H, 4·1; Cl, 16·1%).

5-*Nitro*-2-*naphthol*.—Prepared from 5-nitro-2-naphthylamine in quantitative yield (cf. Cook *et al.*, *J.*, 1934, 653) this gave an *acetate* which crystallised from ethyl alcohol in dark yellow, stout prisms, m. p. 98—99° (Found : C, 62·1; H, 4·0. $C_{12}H_9O_4N$ requires C, 62·3; H, 3·9%), and a methyl ether, golden yellow plates (from methyl alcohol), m. p. 76—77° (Found : C, 65·2; H, 4·4. Calc. for $C_{11}H_9O_3N$: C, 65·0; H, 4·4%) (Cook *et al.*, *loc. cit.*, give m. p. 74·5—75·5°).

5-*Amino*-2-*naphthol*.—The above nitronaphthol (4·0 g.), shaken in alcoholic solution with Raney nickel, rapidly absorbed the theoretical amount of hydrogen. The filtered solution was concentrated and gave the amino-naphthol (2·8 g.) in colourless prisms, m. p. 183—184° (Friedlander and Szymanski, *Ber.*, 1892, **25**, 2079, give m. p. 186°). The *monoacetate*, obtained by Raney nickel reduction of 5-nitro-2-naphthyl acetate and crystallised from methyl alcohol (charcoal), had m. p. 101—102° (Found : C, 71·6; H, 5·5. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5%). The methyl ether prepared by a similar reduction of methyl 5-nitro-2-naphthyl ether crystallised from aqueous ethyl alcohol in nacreous plates, m. p. 73—74° (Found : C, 76·0; H, 6·3. Calc. for $C_{11}H_{11}ON$: C, 76·3; H, 6·3%). Cook *et al.* (*loc. cit.*) give m. p. 73—74°.

5-*Chloro*-2-*naphthol*.—A solution of 5-amino-2-naphthyl acetate (2·0 g.) in concentrated hydrochloric acid (20 ml.) was stirred at 0—5° during the dropwise addition of sodium nitrite (0·8 g.) in water (3 ml.) and for a further 2 hours. The clear solution was then stirred for 1 hour at room temperature with a solution of cuprous chloride in concentrated hydrochloric acid. Extraction with ether gave an oily product containing some free chloronaphthol. Hydrolysis by boiling for 10 minutes with dilute aqueous sodium hydroxide, followed by acidification and isolation with ether, gave a solid which crystallised from light petroleum (b. p. 60—80°) (charcoal) in rectangular prisms, m. p. 97—98° (42%) (Found : C, 67·3; H, 4·0; Cl, 19·9. Calc. for $C_{10}H_7OCl$: C, 67·2; H, 3·9; Cl, 19·9%). The *acetate* crystallised from methyl alcohol in colourless prisms, m. p. 55—56° (Found : C, 65·2; H, 4·2; Cl, 16·4. $C_{12}H_9O_2Cl$ requires C, 65·3; H, 4·1; Cl, 16·1%). Oxidation of 5-chloro-2-naphthol with alkaline potassium permanganate gave a product, isolated with ether, which crystallised from ether–light petroleum (b. p. 40—60°) in prisms, m. p. 185—187°, undepressed on admixture with an authentic specimen of 3-chlorophthalic acid.

8-*Amino*-2-*naphthyl Acetate*.—8-Nitro-2-naphthyl acetate (5 g.) from 8-nitro-2-naphthol (Friedlander and Szymanski, *loc. cit.*), in dioxan (30 ml.), was reduced by hydrogen in the presence of Raney nickel. The *ester*, isolated by filtration and concentration of the solution, crystallised from aqueous methyl alcohol in prisms, m. p. 82—83° (Found : C, 71·6; H, 5·6. $C_{12}H_{11}O_2N$ requires C, 71·6; H, 5·5%).

8-*Chloro*-2-*naphthol*.—This was obtained from 8-amino-2-naphthyl acetate in 36% yield by the procedure used for 5-chloro-2-naphthol, the acetyl group being lost during the Sandmeyer reaction. It crystallised from light petroleum (b. p. 60—80°) in a matte of colourless needles, m. p. 101—102° (Found : C, 67·1; H, 3·7; Cl, 20·0. Calc. for $C_{10}H_7OCl$: C, 67·2; H, 3·9; Cl, 19·9%). Dilthey *et al.* (*loc. cit.*) and Claus and Volz (*Ber.*, 1885, **18**, 3157) give 101°. The *acetate* crystallised from aqueous methyl alcohol in prisms, m. p. 70—71° (Found : C, 65·4; H, 4·3. $C_{12}H_9O_2Cl$ requires C, 65·3; H, 4·1%).

1 : 3-*Dichloro*-2-*naphthol*.—This was prepared in 90% yield by refluxing a solution of 1 : 1 : 3 : 3 : 4-pentachloro-1 : 2 : 3 : 4-tetrahydro-2-ketonaphthalene (Fries and Schimmelschmidt, *Annalen*, 1930, **484**, 297) (6·0 g.) in glacial acetic acid (30 ml.) with zinc dust (6 g.) for 0·5 hour. When the mixture was poured into water a white solid (3·8 g.) was obtained which crystallised from light petroleum (b. p. 40—60°) in aggregates of hexagonal prisms, m. p. 72—74° (Found : Cl, 33·3. Calc. for $C_{10}H_6OCl_2$: Cl, 33·3%). Fries and Schimmelschmidt (*loc. cit.*) give m. p. 78°.

1 : 3 : 4-*Trichloro*-2-*naphthol*.—A solution of 1 : 1 : 3 : 3 : 4-pentachloro-1 : 2 : 3 : 4-tetrahydro-2-ketonaphthalene (10 g.) in ethyl alcohol (35 ml.) was refluxed for 0·5 hour during the dropwise addition of a solution of stannous chloride (8 g.) in concentrated hydrochloric acid (24 ml.). Addition of water to the cooled solution gave a solid (6·8 g.) which crystallised from aqueous methyl alcohol in prisms, m. p. 160—161° (Found : Cl, 42·4. Calc. for $C_{10}H_5OCl_3$: Cl, 43·0%). Fries and Schimmelschmidt (*loc. cit.*) give m. p. 162°. The *acetate*, crystallised from methyl alcohol, had m. p. 130—131° (Found : Cl, 36·1. $C_{12}H_7O_2Cl_3$ requires Cl, 36·7%).

3 : 4-*Dichloro*-2-*naphthol*.—Attempts to prepare this naphthol by reduction of the above trichloronaphthol with a zinc–copper couple (cf. G.P. 431,165) were unsuccessful. The required product was obtained in 90% yield, however, by the following method : 1 : 3 : 4-Trichloro-2-naphthol (2 g.) was dissolved in a solution of sodium hydroxide (2·8 g., 1 mol.) in water (10 ml.) and heated with a solution of ferrous sulphate (10 g.) in water (10 ml.) at 145° for 15—17 hours. On cooling, the contents of the tube were made alkaline with a little dilute sodium hydroxide solution and filtered, and the product was isolated by extracting the acidified filtrate with ether. It crystallised from light petroleum (b. p. 60—80°) in colourless slender rectangular prisms (1·5 g.), m. p. 106—108° (Found : Cl, 33·2. Calc. for $C_{10}H_6OCl_2$: Cl, 33·3%). G.P. 431,165 gives m. p. 108°. The *acetate* crystallised from methyl alcohol in feathery prisms, m. p. 72—73° (Found : C, 56·7; H, 3·2. $C_{12}H_8O_2Cl_2$ requires C, 56·5; H, 3·1%).

2-*Naphthyloxyacetic Acids*.—These were prepared by the following general procedure, analytical details being given in the Table. An ethyl-alcoholic solution of the naphthol was treated with sodium ethoxide (1 mol.), and the whole heated for 2 hours under reflux with ethyl bromoacetate (1 mol.). After the addition of excess of 10% sodium hydroxide solution the whole was heated for a further 1 hour, cooled, and acidified with concentrated hydrochloric acid. The product was isolated with ether and obtained free from naphthol by extraction with sodium hydrogen carbonate solution.

Substituted 2-naphthyloxyacetic acids.

			Found :				Required :		
Substituent	M. p.	Solvent	C, %	H, %	Cl, %	Formula	C, %	H, %	Cl, %
3-Chloro	182—183°	AcOH	60·5	4·0	15·4	$C_{12}H_9O_3Cl$	60·9	3·8	15·0
4- ,, ...	168—169	,,	60·6	4·2	14·4				
5- ,, ...	202—203	MeOH	61·0	3·6	14·5				
6- ,, ...	208—209	MeOH	61·1	3·6	15·5				
7- ,, ...	168—169	MeOH	60·8	3·8	14·7				
8- ,, ...	131—132	Et_2O–light petroleum	60·7	3·6	14·8				
1 : 3-Dichloro	179—180	aq. MeOH	53·5	3·2	25·8	$C_{12}H_8O_3Cl_2$	53·1	3·0	26·2
1 : 4- ,,	188—189	,,	53·3	3·0	25·9				
3 : 4- ,,	182—184	MeOH	53·0	3·3	25·7				
1 : 3 : 4-Trichloro	207—208	AcOH	47·3	2·4	34·7	$C_{12}H_7O_3Cl_3$	47·15	2·3	34·8
5-Nitro	211—212	EtOH	58·5	3·5	—	$C_{12}H_9O_5N$	58·3	3·6	—
8- ,, ...	179—180	aq. MeOH	58·0	3·7	—				

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