Synthesis of Plant-growth Regulators. Part III.* w-2-Naphthyloxyalkanecarboxylic Acids.

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The preparation of a number of chlorine-substituted and unsubstituted ω -2-naphthyloxyalkanecarboxylic acids is described.

An alternation in plant-growth regulating activity in homologous series of ω -substituted alkanecarboxylic acids has been reported by several workers (Thimann and Bonner, *Physiol. Reviews*, 1938, **18**, 524; Grace, *Canad. J. Res.*, *C*, 1939, **17**, 247; Synerholm and Zimmerman, *Contribn. Boyce Thompson Inst.*, 1947, **14**, 369; Fawcett, Ingram, and Wain, *Nature*, 1952, **170**, 887). The acids described in this paper belong to five homologous series of ω -2-naphthyloxyalkanecarboxylic acids. Their biological activity has been measured by the ability to induce parthenocarpic development of unpollinated tomato ovaries, and a full account will be published later (Luckwill and Woodcock, in preparation).

Two main synthetical routes were employed for the required acids :

(a)
$$C_{10}H_7ONa \longrightarrow C_{10}H_7O\cdot[CH_2]_n \cdot Br \longrightarrow C_{10}H_7O\cdot[CH_2]_n \cdot CN \longrightarrow C_{10}H_7O\cdot[CH_2]_n \cdot CO_2H$$

(b) $C_{10}H_7O\cdot[CH_2]_n \cdot CH(CO_2H)_2 \longrightarrow C_{10}H_7O\cdot[CH_2]_{n+1} \cdot CO_2H$

Where the appropriate polymethylene dibromide was readily available route (a) was used; in other cases a malonic ester synthesis (b), starting from the ω -2'-naphthyloxyalkyl bromide with two carbon atoms less than the final side-chain, led to the required acid. The β -substituted propionic acids were, however, more conveniently obtained by condensation of the sodium naphthoxide with β -propiolactone (cf. Byrde, Crowdy, and Woodcock, Ann. appl. Biol., 1953, 40, 152).

An interesting case of apparent dimorphism was observed with 6-2'-naphthyloxyhexanoic acid. Two forms, which do not mutually depress, have been obtained and all attempts at interconversion have so far failed. Both forms are equally active as agents for inducing parthenocarpy in the tomato-ovary test.

Some typical preparations are fully described in the experimental section; analytical details for all new compounds are given in the Tables.

* Part II, J., 1953, 2089.

EXPERIMENTAL

 β -2-Naphthyloxypropionic Acid.— β -Propiolactone (3.6 g.) was added dropwise during 10 min. to a boiling stirred solution of β -naphthol (7.2 g.) and sodium hydroxide (2 g.) in water (30 ml.). After being heated for a further 15 min., the solution was cooled, acidified, and extracted with ether. The acid, isolated from the ethereal solution by shaking it with sodium hydrogen carbonate solution and acidifying it, was washed with water and dried at 100°. It (1.8 g.) crystallised from methyl alcohol in rhombic prisms, m. p. 143—144° (Found : equiv., 216.8. Calc. for C₁₈H₁₂O₃ : equiv., 216). Chakravarti and Dutta, (J. Indian Chem. Soc., 1939, 16, 639) give m. p. 144—145°.

3-2'-Naphthyloxypropyl Chloride.— β -Naphthol (7·2 g.) was added to sodium ethoxide [from sodium (1·15 g.) and ethyl alcohol (40 ml.)], and the solution added dropwise during 1 hr. to a boiling mixture of 1-bromopropyl chloride (10 ml.) and ethyl alcohol (20 ml.). After being refluxed for 4 hr., the solution was cooled, diluted with water, and extracted with ether; an ether-insoluble solid (A) was filtered off. The ethereal solution after being washed with sodium hydroxide and water was dried, the solvent removed, and the residue distilled. The fraction, b. p. 138—142°/0·5 mm., solidified, and the *chloride* then crystallised from light petroleum (b. p. 40—60°) in small prisms (4·2 g.), m. p. 51—52° (Found : C, 70·9; H, 5·8; Cl, 15·8. C₁₃H₁₃OCl requires C, 70·8; H, 5·9; Cl, 16·1%). The solid (A) crystallised from benzene in nacreous plates, m. p. 146—147° (Found : C, 83·8; H, 6·0. C₂₃H₂₀O₂ requires C, 84·1; H, 6·1%).

3-2'-Naphthyloxypropyl Cyanide.—The chloride (8.7 g.) and sodium cyanide (2.5 g.) were heated in ethyl alcohol (40 ml.) under reflux for 18 hr. The alcohol was distilled off, water added, and the product extracted with ether. The residue, after removal of the ether, was distilled (b. p. 152—160°/0.5 mm.). The solid distillate of *cyanide* crystallised from ethyl alcohol-light petroleum (b. p. 40°) in nacreous plates, m. p. 41—42° (Found : C, 79.5; H, 6.2. $C_{14}H_{13}$ ON requires C, 79.6; H, 6.2%).

 γ -2-Naphthyloxybutyric Acid.—The cyanide (7.8 g.) was hydrolysed with a boiling solution of potassium hydroxide (2.5 g.) in water (5 ml.) and ethyl alcohol (20 ml.) for 18 hr. The solution was cooled, diluted with water, and extracted with ether. Extraction of the ethereal solution with aqueous sodium hydrogen carbonate, followed by acidification of the extract gave the required acid, which crystallised from benzene-light petroleum (b. p. 40°) in aggregates of small rhombs, m. p. 122—123° (Found : C, 73.3; H, 6.1. Calc. for C₁₄H₁₄O₃ : C, 73.0; H, 6.2%). This acid was prepared by Synerholm and Zimmerman (*loc. cit.*) who claimed it as a new compound, but it had been previously reported by Nair and Peacock (*J. Indian Chem. Soc.*, 1935, 12, 318) who gave m. p. 122°.

 δ -2-Naphthyloxyvaleric Acid.—A solution of the above chloride (13.6 g.) in ethyl alcohol (30 ml.) was refluxed for 6 hr. with sodiomalonic ester (from 8.4 g. of diethyl malonate and 1.2 g.

C. L				Found, %						Required, %		
Substi-		Douto	Solvent *	Ma	Fermula	6						
tuent	n	Route	Solvent .	м. р.	C	п	CI	Formula	C	п	CI	
н	4	b	C_6H_6-A	111—112°	74.1	6.6		$C_{15}H_{16}O_{3}$	73 ·8	6.6		
ч	к	aí	aq. MeOH	126 - 127	74 .5	7.0		$C_{16}H_{18}O_{3}$	74.4	7·0 ∖		
11	U	- " {	aq. MeOH	94—9 5	74 ·8	7.0		$C_{16}H_{18}O_{3}$	74.4	7·0 S		
н	6	b	Et_2O-B	9697	74 ·9	$7 \cdot 2$		$C_{17}H_{20}O_{3}$	75.0	7.4		
н	7	b	B^{-}	9192	75.2	7.7		$C_{18}H_{22}O_{3}$	75.5	7.7		
н	8	a	Et_2O-B	9899	76.4	8.0		$C_{19}H_{24}O_{3}$	76 ·0	8.0		
н	9	а	Benzene	114 - 115	76 ·0	8.3		$C_{20}H_{26}O_{3}$	76.4	8.3		
н	11	b	EtOH	9697	77.1	8.8		$C_{22}H_{30}O_{3}$	77.2	8.8		
3-Cl	2		MeOH	173 - 174	62.4	4 ·3	14.4	C ₁₃ H ₁₁ O ₃ Cl	62.3	4.4	14.2	
3-Cl	3	а	aq. AcOH	174 - 175	63.3	5.0	13.3	C ₁₄ H ₁₃ O ₃ Cl	63.5	4 ·9	13.4	
3-Cl	5	а	aq. MeOH	114—115	$65 \cdot 2$	5.8	12.0	$C_{16}H_{17}O_{3}Cl$	65.6	5.8	12.1	
3-Cl	7	b	aq. MeOH	74-75	67.8	6.6	11.0	C ₁₈ H ₂₁ O ₃ Cl	67.4	6.6	11.1	
3-C1	9	а	$E\bar{t}_{,0}O-B$	9091	68.8	6.9	10.5	C ₂₀ H ₂₅ O ₃ Cl	68.8	$7 \cdot 2$	10.2	
1-Cl	2		MeOH	170-171	62.3	4.4	14.6	C ₁₃ H ₁₁ O ₃ Cl	62.3	4.4	14.2	
1-Cl	3	а	MeOH	139 - 140	6 3·3	4 ·9	13.3	C ₁₄ H ₁₃ O ₃ Cl	63.5	4 ·9	13.4	
1-Cl	5	a	MeOH	144 - 145	65.9	$6 \cdot 2$	12.3	C ₁₆ H ₁₇ O ₃ Cl	65.7	5.8	12.1	
8-C1	3	а	AcOH	159 - 160	63 .5	4.9	$13 \cdot 2$	$C_{14}H_{13}O_{3}Cl$	63·5	4 ·9	13.4	
8-Cl	5	а	Et_2O-B	122 - 123	65.5	6 •0	$12 \cdot 2$	C ₁₆ H ₁₇ O ₃ Cl	65.7	5.8	12.1	
$3: 4-Cl_{2}$	2		MeOH	168 - 169	54.7	3.4	25.0	$C_{13}H_{10}O_{3}Cl_{2}$	$54 \cdot 8$	3.5	24.9	
3:4-Cl	3	a	Dioxan	175 - 177	56.5	4.0	23.7	C.H.O.CL	56.2	4.1	23.7	

Substituted ω -2-naphthyloxyalkanecarboxylic acids, $C_{10}H_7O\cdot[CH_2]\cdot_nCO_2H$ (substituents in the naphthalene system).

Substituted ω -2-naphthyloxyalkyl halides and cyanides, $C_{10}H_7O\cdot[CH_2]_n\cdot X$. (substituents									
in the naphthalene system).										

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Subeti		Found, %						Required, %			
tuent	n	x	Solvent *	М. р.	ć	Н	Halogen	Formula	ĉ	H	Halogen
ч	9	Br	B	0405°	57.5	4.5	31.8	C.H.OBr	57.4	4.4	31.8
ü	2	Br	4	56	50.2	5.0	29.9	$C_{H} OB_{r}$	58.9	â.ĝ	30.2
ü	2	Ĉ	<u>A</u>	51-52	70.9	5.8	15.8	$C_{13}H_{13}ODI$	70.8	5.9	16.1
ü	5	Br	liquid	1	61.5	6.2	27.5	C.H.OBr	61.4	5.8	27.3
н н	Ř	Br	A	40-41	62.5	6.3	26.2	C.H.OBr	62.5	6.2	26.1
H	8	Br	E+OH	47-48	64.6	7.1	23.6	C.H.OBr	64.5	6.9	23.9
ਜ	10	Br	FtOH	54-55	66.0	7.4	21.9	C.H.OBr	66.1	7.4	22.0
3-C1	3	ci	A	64-65	60.9	4.8	28.0	C ₁₀ H ₁₀ OCl	61.2	4.7	27.8
3-01	5	Br	Â	64-65	55.0	4.9	CL 10.6	C.H.OBrCl	55.0	4.9	Cl. 10.8
3-01	ĕ	Br	A	6768	56.1	5.6	C1 10.3	C.H.OBrCl	56.2	5.3	Cl. 10.4
1-01	š	ĉî	liquid	2	61.4	4.8	27.7	C.H.OCl.	61.2	4.7	27.8
î-CÎ	5	Br	A	48-49	55.1	4.8	Cl. 10.7	C.H.OBrCl	55.0	4.9	Cl. 10.8
8-C1	š	ĉî	liquid	3	61.5	4.5		C.H.OCl.	61.2	4.7	27.8
8-C1	5	Br	EtOH	58-60	54.8	5.1		C.H.OBrCl	55.0	4.9	Cl. 10.8
3:4-Cl.	3	ĈÎ	EtOH	92-93	53.9	3.6	36.6	C.H.OCL	53.9	3.8	36.8
3:4-Cl.	5	Br	EtOH	66-67	49.6	4.2	Cl. 19.4	C.H.OBrCl.	49.7	4.1	Cl. 19.6
H	3	ĊŇ	EtOH-A	4142	79.5	$6 \cdot 2$	·	C ₁₄ H ₁₃ ON	79.6	$6 \cdot 2$	·
H	5	CN	Et ₀ O-A	5960	80.2	$7 \cdot 1$		C ₁₆ H ₁₇ ON	80·3	$7 \cdot 1$	
н	8	ĊN	aq. MeOH	51 - 52	80.7	8.0		C ₁₉ H ₂₃ ON	81 ·1	$8 \cdot 2$	
н	9	CN	liquid	4	81.5	8.7		C ₂₀ H ₂₅ ON	81.4	8.5	
3-C1	3	CN	EŧOH	9697	67.9	$5 \cdot 1$	14.6	C ₁₄ H ₁₂ ONCl	68·4	4 ·9	14.4
3-C1	5	CN	EtOH	109-110	69.9	6.1	13.0	C ₁₆ H ₁₆ ONCl	70.2	5.9	13.0
1-Cl	3	CN	Et_O-B	82 - 83	68.4	4.6	14.6	C ₁₄ H ₁₂ ONCl	68·4	4 ·9	14.5
1-Cl	5	CN	EtÖH	74.575	70.2	5.8	13.0	C ₁₆ H ₁₆ ONCl	70.2	5.9	13 ·0
8-C1	3	CN	EtOH	56 - 57	68.7	5.0	14.6	C ₁₄ H ₁₂ ONCl	68·4	4 ·9	14.5
8-C1	5	CN	EtOH	74-76	70.1	5.7		$C_{16}H_{16}ONCl$	70.2	5.9	13 ·0
3:4-Cl ₂	3	CN	MeOH	8586	59.6	3.9	$25 \cdot 6$	$C_{14}H_{11}ONCl_2$	60 .0	3.9	$25 \cdot 4$
$3: 4-Cl_{2}$	5	CN	MeOH	81 - 82	62.0	4 ·7	$23 \cdot 3$	C ₁₆ H ₁₅ ONCl ₂	$62 \cdot 4$	4 ·9	23.0

Substituted ω -2-naphthyloxyalkylmalonic acids, $C_{10}H_7O\cdot[CH_2]_n\cdot CH(CO_2H)_2$ (substituents in the naphthalene system).

		1			1					
н	3	 Et ₂ O-B	171 - 172	66.6	5.6		$\mathrm{C_{16}H_{16}O_5}$	66 ·7	$5 \cdot 6$	
н	5	 Et ₂ O–B	(dec.) 153154	68.2	6 ·2		$C_{18}H_{20}O_5$	68·3	6·3	
н	6	 AcOH	161 - 162	69 ·0	6.9		$C_{19}H_{22}O_5$	69·3	6·7	
н	10	 aq. AcOH	(dec.) 134—135	71.5	7.8		$C_{23}H_{30}O_{5}$	71.5	7.8	
3-Cl	6	 aq. AcOH	149—150 (dec.)	$62 \cdot 2$	$5 \cdot 8$	9.7	C ₁₉ H ₂₁ O ₅ Cl	62.5	5.8	9.7

1 : ω -Bis-2'-naphthyloxyalkanes, $C_{10}H_7 \cdot O \cdot [CH_2]_n \cdot O \cdot C_{10}H_7$ (substituents in naphthalene system).

			-		•	•				
н	2	 Dioxan	215 - 216	84·1	5.8		$C_{22}H_{18}O_{2}$	84·1	5.7	
н	3	 Benzene	146 - 147	83.8	6.3		$C_{23}H_{29}O_{2}$	84·1	6.1	
н	5	 A	74-76	8 4 ·0	7.0		$C_{25}H_{24}O_{2}$	8 4 ·3	6.7	
н	6	 Benzene	152 - 153	8 4·3	$7 \cdot 1$		$C_{26}H_{26}O_{2}$	8 4 ·3	7.0	
н	8	 Benzene	129-130	$84 \cdot 2$	7.5		$C_{28}H_{30}O_{2}$	84·4	7.5	
н	9	 $C_{6}H_{6}-A$	128 - 129	84.5	7.6		$C_{29}H_{32}O_{2}$	84 ·5	7.8	
н	10	 Benzene	126 - 127	84.5	7.9		$C_{30}H_{34}O_{2}$	84.5	8.0	
3-Cl	3	 C_6H_6-A	192 - 193	69.3	4.7	18.0	$C_{23}H_{18}O_2Cl_2$	6 9·5	4 ·5	17.9
3 Cl	5	 $C_{6}H_{6}-A$	144 - 145	71·1	5.5	16 ·0	$C_{26}H_{24}O_2Cl_2$	71·1	5.5	16.2

* Solvents, other than those named are : A light petroleum (b. p. $40-60^{\circ}$); B, light petroleum (b. p. 60-80°). ¹ B. p. 180-184°/0·2 mm. ² B. p. 170-172°/ 0·5 mm. ³ B. p. 162-164°/0·5 mm. ⁴ B. p. 180-184°/0·5 mm.

of sodium). 40% Sodium hydroxide (50 ml.) was then added, and after a further hour's refluxing the solution was cooled, diluted with water, and extracted with ether. Acidification of the alkaline layer gave the 2'-naphthyloxypropylmalonic acid, m. p. 167° (decomp.), which crystallised from acetone-benzene in monoclinic prisms, m. p. 171-172° (decomp.) (Found : C, 66.6; H, 5.6. C₁₆H₁₆O₅ requires C, 66.7; H, 5.6%). Decarboxylation was carried out at 185° for 1 hr. The valeric acid crystallised from benzene-light petroleum (b. p. 40°) in rhombic plates, m. p. 111–112° (Found : C, 74·1; H, 6·6. $C_{15}H_{16}O_3$ requires C, 73·8; H, 6·6%).

6-2'-Naphthyloxyhexanoic Acid.—5-2'-Naphthyloxypentyl cyanide was hydrolysed with ethyl alcoholic potassium hydroxide as described above. When the ethereal extract was shaken with sodium hydrogen carbonate solution an insoluble sodium salt was formed which was washed with ether and decomposed with concentrated hydrochloric acid. The acid, isolated by ether, crystallised from aqueous methyl alcohol in wedge-shaped prisms, m. p. 94—95° (Found : C, 74.8; H, 7.0. C₁₆H₁₈O₃ requires C, 74.4; H, 7.0%). In another experiment, under apparently identical conditions, the product crystallised from aqueous methyl alcohol in acreous plates, m. p. 126—127° (Found : C, 74.5; H, 7.0%). This product did not depress the m. p. of the isomeric acid, but we have so far failed to demonstrate dimorphism by the mutual seeding of solutions in aqueous methyl alcohol. The S-benzylthiuronium salt from the low-m. p. form only crystallised from aqueous ethyl alcohol in rectangular prisms, m. p. 156—157° (Found : C, 68.0; H, 6.6; S, 7.5. C₂₄H₂₈O₃N₂S requires C, 67.9; H, 6.6; S, 7.5%).

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