43. *Eight- and Higher-membered Ring Compounds. Part III. Di-, Tri-, and Tetra-cresotides.*

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The anhydro-derivatives of *o*-, *m*-, and *p*-cresotic acids have been re-investigated. The α- and β-" dicresotides " are shown to be the eight-membered *cis*-dicresotides and the twelve-membered tricresotides respectively. Both di- and tri-cresotides are formed by heating *O*-acetylcresotic acids. The preparation of the sixteen-membered, hitherto unknown, tetra-*m*-cresotide is described. The stereochemistry of these substances and its relationship to that of the salicylides is discussed.

ANHYDRO-DERIVATIVES of cresotic acids have been investigated by R. Anschütz (*Ber.*, 1892, **25**, 3509), Schöpff (*ibid.*, p. 3642), R. Anschütz (*Annalen*, 1893, **273**, 88, 94; D.R.-P. 70,158, " Friedländer," 1893, **3**, 825), R. Anschütz and Schroeter (*Annalen*, 1893, **273**, 97), Einhorn and Pfieiffer (*Ber.*, 1901, **34**, 2953), Einhorn and Mettler (*ibid.*, 1902, **35**, 3644), R. Anschütz (*Annalen*, 1924, **439**, 8), and by L. Anschütz and Gross (*Ber.*, 1944, **77**, 644). The last workers have described two dicresotides (α- and β-forms) derived from each of the *o*-, *m*-, and *p*-cresotic acids (2-hydroxy-3-methyl-, 2-hydroxy-4-methyl-, and 2-hydroxy-5-methylbenzoic acids). It was suggested that these pairs of cresotides were related to the α- and β-" disalicylides," but it has now been shown (see preceding paper) that the α- and β-disalicylides are, in fact, *cis*-disalicylide and trisalicylide respectively. We have, therefore, undertaken a re-investigation of the cresotides derived from *o*-, *m*-, and *p*-cresotic acids, and a preliminary announcement of the results has been made (Baker, Gilbert, Ollis, and Zealley, *Chem. and Ind.*, 1950, 333).

L. Anschütz and Gross prepared their α-dicresotides by distillation of the *O*-acetylcresotic acids under diminished pressure. We find that this procedure gives at least two compounds in each case, namely the *cis*-dicresotide and tricresotide, with, in the case of *O*-acetyl-*m*-cresotic acid, a small amount of tetra-*m*-cresotide. These results are analogous to those obtained by the distillation of *O*-acetylsalicylic acid (see Part II, where formulæ are given for the corresponding salicylides).

The fact that these products are di- and tri-cresotides was established by ebullioscopic determination of their molecular weights in chloroform and benzene (see the table); the slight difference between these results and those previously published by us are due to the fact that we now use the modified method described in Part II in calculating the molecular weights. The table also gives other relevant details (literature references are given in the text).

All the *cis*-dicresotides melt with some decomposition and the melting points depend upon the rate of heating. We have used the method of rapid heating described in Part II, and this undoubtedly accounts for some of the discrepancies between the melting points now recorded and those previously given by other workers. The variability of the melting points of the α-compounds was noticed by Anschütz and Gross (*loc. cit.*) and it is presumed that our *cis*-dicresotides are identical with the α-dicresotides described by them.

L. Anschütz and Gross prepared " β-di-cresotides " in low yield by dehydration of the cresotic acids with phosphorus oxychloride in pyridine. We have re-investigated this reaction with *o*- and *m*-cresotic acids and have isolated more than one crystalline compound in each case, but the main products were non-crystalline polymers, probably $H[O{\cdot}C_7H_6{\cdot}CO]_n{\cdot}OH$. From *o*-cresotic acid, *cis*-di-, tri-, and tetra-*o*-cresotide were obtained; *m*-cresotic acid gave small amounts of *cis*-di- and tri-*m*-cresotide.

Comparison of the melting points of our tri-*m*- and tri-*p*-cresotides suggests that they are identical with the " β-di-*m*-cresotide " and the " β-di-*p*-cresotide " described by L. Anschütz and Gross (*loc. cit.*). The melting point which they give for " β-di-*o*-cresotide " (231—231·5°) is much lower than the melting point of tri-*o*-cresotide (264—265°). The reason for this difference is not clear, since the melting points of these trimers do not depend upon the rate of heating and they do not decompose at the melting point. It may be significant that we have found that the only satisfactory method of isolating pure tri-*o*-cresotide is by first sorting the mixtures by hand.

The tetra-*o*- and -*p*-cresotides were prepared by R. Anschütz (*Ber.*, 1892, **25**, 3509; *Annalen*, 1893, **273**, 88) by dehydration of the cresotic acids with phosphorus oxychloride in toluene at 100°. R. Anschütz and Schroeter (*Annalen*, 1893, **273**, 97) determined their molecular weights cryoscopically in phenol, but since it is known that such substances will react with phenol we

Author(s)	Name	M. p.	*M*, average
	cis-*Di*-o-*cresotide* (*M*, 268).		
Schöpff (1892)	*o*-Cresotic acid anhydride	224—225°	260 *b*
R. Anschütz (1924)	α-Di-*o*-cresotide	224—225	—
L. Anschütz and Gross (1944) ...	α-*o*-Dicresotide	232—233 (235—236)	267 *d*
This paper	*cis*-Di-*o*-cresotide	240 (decomp.)	283 *b*, 278
	Tri-o-*cresotide* (*M*, 402).		
Einhorn and Pfeiffer (1901)	*o*-Dicresotide	231·5	—
Einhorn and Mettler (1902) ...	,,	231—231·5	298 *b*
L. Anschütz and Gross (1944) ...	β-Di-*o*-cresotide	231—231·5 (232·5)	273 *d*
This paper	Tri-*o*-cresotide	264—265	390 *b*, 390 *d*
	Tetra-o-*cresotide* (*M*, 536).		
R. Anschütz (1892; 1893)	*o*-Homosalicylide or β-Cresotide	293—295	—
R. Anschütz and Schroeter (1893)	*o*-Homosalicylide or tetra-*o*-homosalicylide	—	527 *a*
This paper	Tetra-*o*-cresotide	299—300	542 *b*, 548 *d*
	cis-*Di*-m-*cresotide* (*M*, 268).		
L. Anschütz and Gross (1944) *	α-*m*-Dicresotide	217—218 (221—222)	276 *d*
This paper	*cis*-Di-*m*-cresotide	255 (decomp.)	265 *b*, 271 *d*
	Tri-m-*cresotide* (*M*, 402).		
Einhorn and Pfeiffer (1901)	*m*-Dicresotide	207·5	—
Einhorn and Mettler (1902)	,,	207—207·5	262 *c*
L. Anschütz and Gross (1944) ...	β-*m*-Dicresotide	207—207·5 (209)	267 *d*
This paper	Tri-*m*-cresotide	207—207·5	405 *b*, 399 *d*
	Tetra-m-*cresotide* (*M*, 536).		
This paper	Tetra-*m*-cresotide	305 (decomp.)	542 *b*, 542 *d*
	Hexa(?)-m-*cresotide*.		
R. Anschütz (1892; 1893)	*m*-Homopolysalicylide or Poly-γ-cresotide	292—294	—
This paper	Hexa(?)-*m*-cresotide	Above 380 (decomp.)	—
	cis-*Di*-p-*cresotide* (*M*, 268).		
R. Anschütz (1924)	α-Di-*p*-cresotide	197—199	264 *d*
L. Anschütz and Gross (1944) ...	α-*p*-Dicresotide	223—224 (225—226)	259 *d*
This paper	*cis*-Di-*p*-cresotide	235—235·5 (decomp.)	274 *b*, 273 *d*
	Tri-p-*cresotide* (*M*, 402).		
Einhorn and Pfeiffer (1901)	*p*-Dicresotide	243·5	—
Einhorn and Mettler (1902)	,,	243	293 *c*
L. Anschütz and Gross (1944) ...	β-*p*-Dicresotide	243 (245)	265 *d*
This paper	Tri-*p*-cresotide	244·5—245	404 *b*, 393 *d*
	Tetra-p-*cresotide* (*M*, 536).		
R. Anschütz (1892; 1893)	*p*-Homosalicylide or α-cresotide	295—297	—
R. Anschütz and Schroeter (1893)	*p*-Homosalicylide or tetra-*p*-homosalicylide	—	537 *a*
This paper	Tetra-*p*-cresotide	347 (decomp.)	548 *d*

a = phenol (cryoscopic); *b* = benzene (ebullioscopic); *c* = nitrobenzene (cryoscopic); *d* = chloroform (ebullioscopic).

M. p.s given in parentheses are micro-m. p.s given by L. Anschütz and Gross, using the Kŏfler method.

* There is some doubt about the nature of the product, m. p. 208—209° (molecular weight undetermined), prepared by R. Anschütz (*Annalen*, 1924, **439**, 12) by distillation of *O*-acetyl-*m*-cresotic acid and described as α-di-*m*-cresotide. On account of its m. p., L. Anschütz and Gross (*loc. cit.*) have suggested that it may be identical with their β-*m*-dicresotide (now known to be tri-*m*-cresotide), but its chemical properties described by R. Anschütz lead us to believe that it was more probably *cis*-di-*m*-cresotide.

have determined their molecular weights ebullioscopically in chloroform and, if sufficiently soluble, in benzene. *o*-Cresotic acid and phosphorus oxychloride in hot toluene gave only tetra-*o*-cresotide. Similarly, *p*-cresotic acid gave only tetra-*p*-cresotide. *m*-Cresotic acid similarly treated gave a mixture from which a very high-melting *m*-cresotide (m. p. >380°) and the hitherto unknown tetra-*m*-cresotide were isolated. This tetra-*m*-cresotide was identical with the very small amount of the tetra-*m*-cresotide formed during the distillation of *O*-acetyl-*m*-cresotic acid. This reaction of *m*-cresotic acid with phosphorus oxychloride in toluene is to be compared with the corresponding reaction of salicylic acid with phosphorus oxychloride in which it is known that tetrasalicylide and the high-melting hexasalicylide are formed (see Part II). The physical properties of the high-melting *m*-cresotide are very similar to those of hexasalicylide and, since the formation of pentamers and heptamers is unlikely (see Part II), it is very probable that this compound is hexa-*m*-cresotide.

It is of interest that the reaction of phosphorus oxychloride with *o*- and *p*-cresotic acids gives only tetracresotides; hexacresotides are not formed in these cases.

It may be noted that several of these large-ring compounds crystallise with solvent of crystallisation. Tetrasalicylide crystallises with two molecules of chloroform (R. Anschütz, *Ber.*, 1892, **25**, 3512; *Annalen*, 1893, **273**, 94; see also preceding paper), as does also tetra-*o*-cresotide (*idem*, D.R.-P. 70,158, *Friedl.*, 1893, **3**, 825); tetra-*m*-cresotide crystallises with one molecule of benzene; tri-*p*-cresotide also separates with benzene of crystallisation.

The Constellation of the Cresotides.—Dipole-moment determination (Edgerley and Sutton, forthcoming publication, "The stereochemistry of the salicylides and some related compounds," *J.*, in the press) show that the dicresotides all have the *cis*-configuration, as has *cis*-disalicylide. Like *cis*-disalicylide, they are chemically reactive, undergoing hydrolysis with hot, slightly diluted acetic acid, and reaction with methanolic hydrogen chloride at 100° to give the methyl esters of the cresotoylcresotic acids.

The three tricresotides probably possess structures very similar to the structure of trisalicylide, but that of tri-*o*-cresotide may be slightly modified to reduce steric interaction involving the methyl groups. The three tetracresotides and hexa-*m*-cresotide presumably have structures analogous to those of the corresponding salicylides.

EXPERIMENTAL.

M. p.s are uncorrected.

Action of Heat on O-*Acetyl*-o-*cresotic acid* (cis-*Di- and Tri*-o-*cresotide*).—*O*-Acetyl-*o*-cresotic acid (50 g.) was heated in the apparatus previously described (Part II). At *ca.* 170°/17 mm. acetic acid (*ca.* 10 g.) first distilled, followed at *ca.* 200° by a sublimate consisting mainly of *o*-cresotic acid. The temperature was gradually raised to 300°, and during 2 hours a sublimate was obtained, leaving finally a pitch-like residue. The sublimate (16 g.) was crystallised from chloroform (*ca.* 200 c.c.), giving *cis*-di-*o*-cresotide (3·8 g.), colourless needles, m. p. 240° (decomp.) (Found: C, 71·6; H, 4·4. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%).

Concentration of the chloroform mother-liquors gave successive crops, each consisting of a mixture of needles and rhombs which were separated by hand. The needles on recrystallisation gave more *cis*-di-*o*-cresotide, m. p. and mixed m. p. 240°. The rhombic crystals after recrystallisation from benzene gave *tri*-o-*cresotide* (2·3 g.), m. p. 264—265° (Found: C, 71·9; H, 4·4. $C_{24}H_{18}O_6$ requires C, 71·6; H, 4·5%).

Reaction of o-*Cresotic Acid with Phosphorus Oxychloride in Pyridine.*—Satisfactory results were not obtained using the conditions given by L. Anschütz and Gross (*loc. cit.*), and a more concentrated solution in pyridine was used.

Redistilled phosphorus oxychloride (11·2 g.) was added dropwise to a stirred solution of *o*-cresotic acid (20 g.) in dry pyridine (100 c.c.). After being stirred for 7 hours and left overnight, the mixture was poured on ice, and the precipitate (16 g.) collected, washed, triturated with 2N-hydrochloric acid, then with 2N-sodium hydroxide, and water. The dried product (13·5 g.) was dissolved in a small quantity of hot chloroform, and the pure tetra-*o*-cresotide–dichloroform complex (0·7 g.; m. p. and mixed m. p. 299—300°) (see below) separated on cooling. The mother-liquors yielded *cis*-di-*o*-cresotide (0·6 g.), m. p. and mixed m. p. 240° (decomp.), and rhombic crystals of tri-*o*-cresotide, m. p. and mixed m. p. 264—265°, which were separated by hand and recrystallised from benzene.

Reaction of o-*Cresotic Acid with Phosphorus Oxychloride in Toluene* (*Tetra*-o-*cresotide*).—*o*-Cresotic acid (55 g.), redistilled phosphorus oxychloride (50 g.), and toluene (100 c.c.) were heated on a steam-bath for 11 hours, and then poured on ice (100 g.), and the solid (18·6 g.) was collected, washed, and dried. After trituration with 2N-sodium hydroxide and water, the solid (18·0 g.; m. p. 296—298°) was recrystallised from benzene, giving *tetra*-o-*cresotide* as colourless needles, m. p. 299—300° (Found: C, 71·4; H, 4·5. $C_{32}H_{24}O_8$ requires C, 71·6; H, 4·5%).

Tetra-o-cresotide, when crystallised from chloroform, gave the *dichloroform* complex as large, colourless rhombs (Found: loss on heating to constant weight at 100°/1 mm., 31·5. Calc. for $C_{32}H_{24}O_8,2CHCl_3$: loss, 30·8%).

Reaction of the Three o-*Cresotides with Benzylamine* (N-*Benzyl*-o-*cresotamide*).—*cis*-Di-*o*-cresotide (0·5 g.) was refluxed with benzylamine (1·5 c.c.) and a trace of ammonium chloride for 4 hours, and then poured into 2N-hydrochloric acid. The solid was collected and dissolved in 2N-sodium hydroxide, and the solution filtered and acidified. The precipitated *benzylamide* (0·8 g., 90%; m. p. 72—73°) separated from aqueous ethanol in colourless needles, m. p. 73° (Found : C, 74·7; H, 6·5; N, 5·6. $C_{15}H_{15}O_2N$ requires C, 74·6; H, 6·3; N, 5·8%).

Tri-*o*-cresotide and tetra-*o*-cresotide similarly gave the benzylamide, in 87 and 81% yields respectively.

Action of Heat on O-*Acetyl*-m-*cresotic Acid* (cis-*Di*-m-*cresotide*, *Tri*-m-*cresotide*, *and Tetra*-m-*cresotide*).—*O*-Acetyl-*m*-cresotic acid (50 g.; L. Anschütz and Gross, *loc. cit.*) was heated as previously described at 150°/18 mm., giving first acetic acid, and then at 250°/18 mm. a product (24·75 g.) which became semi-solid on cooling. It was collected, and washed first with cold and then hot light petroleum (b. p. 60—80°; 100 c.c. portions) [the washings gave a viscous oil (6·0 g.) from which no crystalline product could be isolated]. The insoluble material (17·4 g.) was washed with cold chloroform (40 c.c.); one of the components, which was present as large crystals, did not dissolve rapidly and was collected. This substance (5·2 g.), after four recrystallisations from benzene (40 c.c.), gave *cis*-di-*m*-cresotide (2·66 g.) as colourless prisms, m. p. 255° (decomp.). This m. p. was markedly dependent upon the rate of heating and reproducible results were only obtained by using a preheated oil-bath (Found : C, 71·9; H, 4·4. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%).

The chloroform filtrate was washed with 2N-sodium hydroxide (20 c.c.) and then with water, dried ($MgSO_4$), and distilled, leaving a solid (10·5 g.) which was triturated with hot benzene (50 c.c.). The insoluble material (4·0 g.) was crystallised from carbon tetrachloride (75 c.c.), and the resultant mixture was freed from *cis*-di-*m*-cresotide by three crystallisations from hot, slightly dilute acetic acid, giving a product (2·6 g.), m. p. 196—197°. Two further recrystallisations from acetic acid (150 c.c.) gave tri-*m*-cresotide (1·3 g.) as colourless needles, m. p. 207—207·5° (Found : C, 71·5; H, 4·4. Calc. for $C_{24}H_{18}O_6$: C, 71·6; H, 4·5%). The benzene filtrate gave a residue (3·7 g.) which was crystallised from ethanol (25 c.c.), then from acetic acid (5 c.c.), yielding colourless needles (0·18 g.), m. p. and mixed m. p. with tri-*m*-cresotide, 207°. Concentration of the acetic acid mother-liquors (to 2 c.c.) gave a fraction (0·20 g.), m. p. 210—284°, which, after recrystallisation 6 times from benzene (2 c.c.)–light petroleum (b. p. 60—80°; 1 c.c.) gave tetra-*m*-cresotide as the *benzene* complex (30 mg.) in colourless prisms, m. p. 305° (decomp.) (Found : C, 74·5; H, 4·5. $C_{32}H_{24}O_8,C_6H_6$ requires C, 74·4; H, 4·9%). This material was identical with that obtained by dehydration of *m*-cresotic acid with phosphorus oxychloride in toluene (see below).

Small amounts of 3 : 6-dimethylxanthone (m. p. 170—172°) were also isolated (L. Anschütz and Gross, *loc. cit.*, give m. p. 166°).

Reaction of m-*Cresotic Acid with Phosphorus Oxychloride in Pyridine.*—The method of L. Anschütz and Gross (*loc. cit.*) did not yield a solid product and the method was modified as follows. Re-distilled phosphorus oxychloride (2·8 g.) was added with stirring to *m*-cresotic acid (5 g.) in dry pyridine (25 c.c.). After 15 hours at room temperature, the mixture was poured on ice and water (250 g.) and centrifuged. The solid (2·2 g.; m. p. 124—200°) was collected, dissolved in chloroform (50 c.c.), washed with 5% sodium hydroxide (10 c.c.) and then water, and dried ($MgSO_4$), and the solvent removed, giving a solid (1·1 g.), m. p. 190—200°. Recrystallisation from benzene (20 c.c.) gave *cis*-di-*m*-cresotide (30 mg.), m. p. and mixed m. p. 250° (decomp.). The benzene mother-liquors yielded a product which was recrystallised from slightly diluted acetic acid and eventually gave tri-*m*-cresotide (30 mg.; m. p. and mixed m. p. 207—208°).

Reaction of m-*Cresotic Acid with Phosphorus Oxychloride* [*Tetra*-m-*cresotide and Hexa*(?)-m-*cresotide*].—*m*-Cresotic acid (50 g.), phosphorus oxychloride (50·5 g.), and dry toluene (100 c.c.) were heated on a steam-bath for 10 hours, and after 36 hours poured into ice-water (150 g.). The precipitate (15 g.) was collected, washed with 2N-sodium hydroxide and then water, dried, and recrystallised three times from boiling nitrobenzene (1·2 l.), from which it separated on cooling and very long standing. This *hexa*(?)-m-*cresotide* (4·3 g.) formed colourless, microcrystalline, rhombic plates which decomposed at 380° without melting (Found : C, 71·8; H, 4·5. $C_{48}H_{36}O_{12}$ requires C, 71·6; H, 4·5%).

The toluene layer (above) was washed with 2N-sodium hydroxide (2 × 25 c.c.) and then water, dried ($MgSO_4$), and distilled. The residue (5·1 g.) was recrystallised 6 times from benzene (30 c.c.)–light petroleum (b. p. 60—80°; 30 c.c.), giving tetra-*m*-cresotide as the *benzene* complex (1·3 g.) in colourless prisms, m. p. and mixed m. p. 305° (decomp.). The benzene was detected by the micro-modification of Ramsden's test for aromatic hydrocarbons (see Baker and Leeds, *J.*, 1948, 979) (Found : loss on heating to constant weight at 125°, 13·1. $C_{32}H_{24}O_8,C_6H_6$ requires loss, 12·7%). The resulting pseudomorphic *tetra*-m-*cresotide*, m. p. 305° (decomp.), was analysed (Found : C, 71·7; H, 4·2. $C_{32}H_{24}O_8$ requires C, 71·6; H, 4·5%).

p-*Cresotic Acid.*—The Kolbe–Schmitt synthesis of this acid described by Cameron, Jeskey, and Baine (*J. Org. Chem.*, 1950, **15**, 233) gives a maximum yield of 87% and requires high-pressure apparatus. The method given below gives a 48% yield and is carried out at atmospheric pressure.

p-Cresol (100 g.) was slowly added to sodium hydroxide (37 g.) in water (50 c.c.), and the paste was heated with stirring until dry enough to powder. The powder was heated and stirred at 170° for 4 hours in a stream of dry nitrogen, and then dry carbon dioxide was passed over the powder for 6 hours, the temperature being raised from 150° to 200° during the first 3 hours. The product was dissolved in water (1 l.) and shaken with ether, and the precipitate obtained by acidification was collected and recrystallised from water (5 l.), giving *p*-cresotic acid (77·6 g.), m. p. 150° (lit., m. p. 152°).

Action of Heat on O-*Acetyl*-p-*cresotic Acid* (cis-*Di*-p-*cresotide and Tri*-p-*cresotide*).—The thermal decomposition of *O*-acetyl-*p*-cresotic acid (25 g.) was carried out as in previous cases. The crude sublimate (14·5 g.), which was a mixture, was washed with cold chloroform (50 c.c.), and the compound which was present as large crystals was collected before complete dissolution occurred. This crude material (2·95 g.; m. p. 231—233°) was crystallised 3 times from benzene (60 c.c.) and gave *cis*-di-*p*-cresotide (2·0 g.) as colourless plates, m. p. 235—235·5° (decomp.) (Found : C, 71·8; H, 4·7. Calc. for $C_{16}H_{12}O_4$: C, 71·6; H, 4·5%).

The chloroform filtrate was washed with 5% sodium hydroxide and dried ($MgSO_4$), and then gave a residue (7·8 g.) which was crystallised from benzene (70 c.c.). The crystals (4·8 g.; m. p. 196—200°) were dissolved in hot benzene (150 c.c.), and two main fractions separated (*A*, 2·1 g., m. p. 208—229°; *B*, 1·5 g., m. p. 200—220°). Fraction *A* was washed with cold chloroform, the more slowly dissolving *cis*-di-*p*-cresotide (0·3 g.) collected, and the chloroform removed from the filtrate, giving a residue (1·6 g.) which was combined with fraction *B*. These combined fractions were freed from *cis*-di-*p*-cresotide by refluxing them twice with 95% aqueous acetic acid (50 c.c.), and the crystalline product (1·1 g.; m. p. 244—244·5°) which separated on cooling was recrystallised 3 times from benzene (20 c.c.), giving tri-*p*-cresotide (0·8 g.) as colourless rhombs, m. p. 244·5—245°, containing benzene of crystallisation. This material gave a positive Ramsden's test for benzene, and when heated at 100°/1 mm. gave white pseudomorphic *tri-*p*-cresotide*, m. p. 244·5—245° (Found : C, 71·4; H, 4·4. $C_{24}H_{18}O_6$ requires C, 71·6; H, 4·5%).

Reaction of p-*Cresotic Acid with Phosphorus Oxychloride in Toluene* (*Tetra*-p-*cresotide*).—A mixture of *p*-cresotic acid (50 g.), re-distilled phosphorus oxychloride (50·5 g.), and dry toluene (100 c.c.) was heated on a steam-bath for 11 hours, and after 30 hours was poured on ice-water (200 c.c.). The precipitate was collected, washed with 5% sodium hydroxide, then with water, and dried, yielding a white crystalline solid (38·7 g.; m. p. 285—295°). This was washed with cold chloroform (100 c.c.) and recrystallised twice from chloroform (1 l.)–light petroleum (b. p. 60—80°; 400 c.c.), giving *tetra*-p-*cresotide* (21·3 g.) as colourless hexagonal prisms, m. p. 347° (decomp.) (Found : C, 71·4; H, 4·6. $C_{32}H_{24}O_8$ requires C, 71·6; H, 4·5%).

Alkaline Hydrolysis of the Cresotides.—Method (a). The cresotide (50 mg.) was heated on the steam-bath with 5% aqueous sodium hydroxide solution (4 c.c.) till complete dissolution occurred. Acidificaton gave the corresponding cresotic acid (*o*-cresotic acid, m. p. 163—164°; *m*-cresotic acid, m. p. 176—177°; *p*-cresotic acid, m. p. 150°), identified by mixed m. p.s. The times required for complete dissolution were : *cis*-di-*o*-cresotide, 1 hour (94%); *cis*-di-*m*-cresotide, ½ hour (92%); tri-*m*-cresotide, 5½ hours (91%); *cis*-di-*p*-cresotide, 1½ hours (94%); tri-*p*-cresotide, 96 hours (65%). The percentages given in parentheses are the yields of the cresotic acids.

Method (b). The cresotide (100 mg.) was heated under reflux with 5% *n*-amyl-alcoholic sodium hydroxide (7 c.c.) for the times given below. The amyl alcohol was removed under reduced pressure, water (5 c.c.) added to the residue, and the solution again evaporated under reduced pressure. The residue was dissolved in water, the solution filtered and acidified, and the precipitate collected and recrystallised from water. The reaction times were : tetra-*m*-cresotide, 3 days (80%); hexa(?)-*m*-cresotide, 5 days (80%); tetra-*p*-cresotide, 5 days (95%).

Where the hydrolysis required long heating, the use of glass apparatus caused difficulties in the isolation of the cresotic acids. In the following cases hydrolysis was carried out at 100° in nickel vessels with, initially 70%, sodium hydroxide. The times used were : tri-*o*-cresotide, 7 days (79%); tetra-*o*-cresotide, 6 days (86%).

Molecular Weights of the Cresotides.—These determinations were carried out as described in Part II, and after each determination the solute was recovered unchanged.

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