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The Preparation of 6-Chloro-*ortho*cresol and 4,6-Dichloro-*ortho*cresol and the Corresponding *Ortho*toloxyacetic acids

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From a mixture of the closeboiling *o*-cresol and 6-chloro-*o*-creso pure 6-chloro-*o*-cresol has been prepared over the corresponding acetates. From the 6-chloro-*o*-cresol pure 4,6-dichloro-*o*-cresol was obtained by chlorination. 6-Chloro-*o*-toloxyacetic acid and 4,6-dichloro-*o*-toloxyacetic acid have been synthesized and the infrared spectra of these compounds and *o*-toloxyacetic acid have been recorded.

In an earlier paper [1] describing the determination of chloro-2-methylphenoxyacetic acid by infrared spectrophotometry the preparation of 6-chloro-*o*-cresol (2-methyl-6-chlorophenol) and 4,6-dichloro-*o*-cresol (2-methyl-4,6-dichlorophenol) and the corresponding *o*-toloxyacetic acids was briefly mentioned. As an answer to many inquiries we now give the details about the preparation and further physical data.

By the chlorination of *ortho*cresol with an equivalent amount of chlorine the reaction product usually has the following composition: 5—10 % *ortho*-cresol, 57—60 % 4-chloro-*ortho*cresol, 22—26 % 6-chloro-*ortho*cresol and 3—7 % 4,6-dichloro*ortho*cresol. The boiling points of these compounds given in the literature are shown in Table 1.

Table 1. The boiling points of *o*-cresol and chlorinated *o*-cresols.

Compound	Boiling point, °C at 760 mm Hg
o-Cresol	191
6-Chloro-*o*-cresol [2]	189
4-Chloro-*o*-cresol [3]	220—225
4,6-Dichloro-*o*-cresol [4]	226.5

At the distillation of the crude chlorination product the first run will contain the low-boiling *o*-cresol and 6-chloro-*o*-cresol. These two compounds can hardly be separated by further distillation on account of their close boiling points. Neither can in the higher boiling fraction 4-chloro-*o*-cresol and 4,6-dichloro-*o*-cresol conveniently be separated by distillation.

In order to obtain better separation we transformed the mixture of *o*-cresol and 6-chloro-*o*-cresol from the distillation of the crude chlorination product into the corresponding acetates. *o*-Cresylacetate has previously been prepared by v. Auwers, Lechner and Bundesmann [5], who found a boiling point of 87°C at 12 mm Hg and by Raschig [6], who reports a boiling point of 212.5°C at 760 mm Hg. 6-Chloro-*o*-cresylacetate does not seem to have been prepared before. In the present investigation we found that 6-chloro-*o*-cresylacetate had an about 30°C higher boiling point than *o*-cresylacetate and that the two acetates could effectively be separated by fractional distillation. During the distillation we checked the purity of the fractions by means of infrared spectrographic analysis. The physical data of the carefully purified acetates are given in Table 2.

The pure 6-chloro-*o*-cresylacetate was hydrolyzed with dilute sodium hydroxide solution and from the alkaline solution 6-chloro-*o*-cresol was liberated with sulfuric acid. The cresol was distilled in vacuum and further purified by fractional freezing. In the pure 6-chloro-*o*-cresol no traces of other cresols could be found by vapor chromatography.

By chlorination of the pure 6-chloro-*o*-cresol with less than the equivalent amount of chlorine we obtained a 4,6-dichloro-*o*-cresol that could be purified by distillation and recrystallization. The physical data for 6-chloro-*o*-cresol and 4,6-dichloro-*o*-cresol are given in Table 2.

Table 2. Physical data

	Boiling point °C/mm Hg	Melting point °C	d_4^{20}	n_D^{20}	MR_D Calc.[10]	MR_D Found
o-Cresylacetate	63.5/1.5 210.7—210.9/774		1.0482	1.4998	41.82	42.12
6-Chloro-*o*-cresyl acetate	78/1.2 238.4—239.0/753		1.1778	1.5134	46.68	47.14
6-Chloro-*o*-cresol	191.0—192.3/757	1.5—2.0	1.1966	1.5452	37.32	37.68
4,6-Dichloro-*o*-cresol	231.6—231.9/739	52.5—52.7				
6-Chloro-*o*-toloxy-acetic acid		109.5—109.8				
4,6-Dichloro-*o*-toloxy-acetic acid		187.9—188.2				
o-Toloxyacetic acid		154.8—154.9				

From the cresols we prepared 6-chloro-*o*-toloxyacetic acid and 4,6-dichloro-*o*-toloxyacetic acid [7, 8] by reaction with monochloro-acetic acid in an alkaline solution as has been described earlier [1, 9]. The acids were carefully purified by recrystallization from benzene (physical data in Table 2). The infrared spectra of the acids were recorded (Figs. 1 and 2). As a comparison we also recorded the infrared spectrum of *o*-toloxyacetic acid (Fig. 3).

From the comparison of the spectra it is obvious that the acids are not contaminated with each other.

EXPERIMENTAL

Preparation of o-cresylacetate and 6-chloro-o-cresylacetate. 900 g of a mixture of about 22 % cresol and 78 % 6-chloro-*o*-cresol, obtained from the distillation of chlorinated

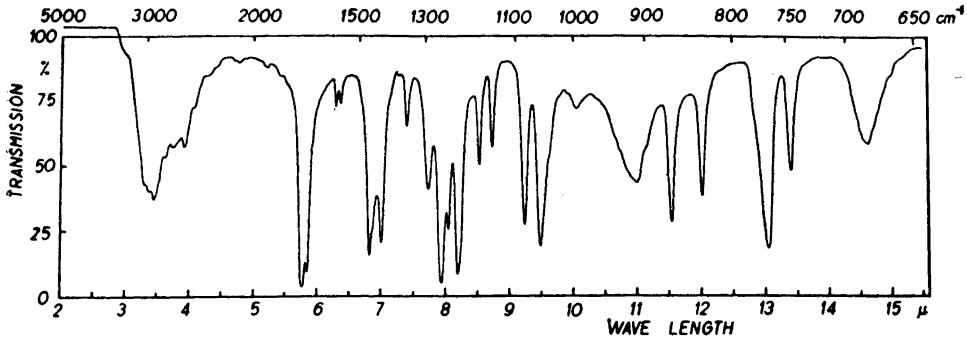

Fig. 1. The infrared spectrum of 6-chloro-*o*-toloxyacetic acid in KBr.

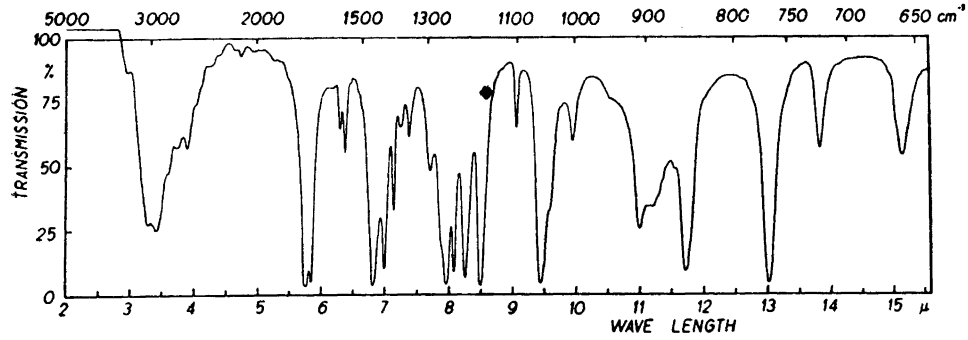

Fig. 2. The infrared spectrum of 4,6-dichloro-*o*-toloxyacetic acid in KBr.

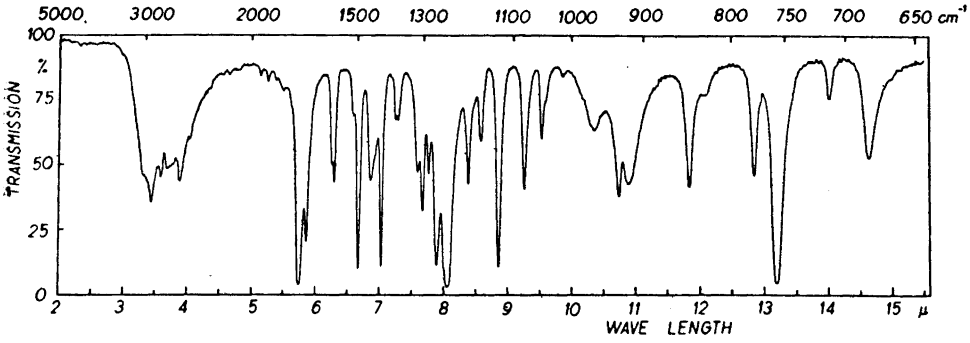

Fig. 3. The infrared spectrum of *o*-toloxyacetic acid in KBr.

o-cresol, was heated with reflux with 900 g acetic acid anhydride and 2 ml konc. sulfuric acid for about 2 h. From the reaction product most of the remaining anhydride and the acetic acid formed was distilled off at 100 mm Hg. The rest was fractionated in vacuum with an 1.5 m highly effective column. At about 90°C and 10 mm Hg we obtained 236 g *o*-cresylacetate and at about 105°C and 10 mm Hg 813 g 6-chloro-*o*-cresylacetate. The acetates were carefully purified by further distillation and the purity checked by infra-

red spectrometry. o-*Cresylacetate* (Found: C 71.4; H 6.74. Calc. for $C_9H_{10}O_2$: C 72.0; H 6.71). *6-Chloro*-o-*cresylacetate* (Found: C 58.3; H 4.79; Cl 19.26. Calc. for $C_9H_9ClO_2$: C 58.6; H 4.91; Cl 19.21).

Preparation of 6-chloro-o-*cresol:* 200 g sodium hydroxide dissolved in 500 ml water was heated to 110°. With good agitation 386 g 6-chloro-*o*-cresylacetate was added in about half an hour. After cooling to room temperature the reaction product was acidified with 300 ml sulfuric acid (50 %). The separated oil was washed with a saturated solution of sodium bicarbonate and distilled in vacuum. To prevent oxidation carbon dioxide was led through the capillary in the distillation pot. At 76°C and 10 mm Hg we obtained 285 g 6-chloro-*o*-cresol (yield 95 %). The cresol was redistilled and purified by fractional freezing. The purity of the 6-chloro-*o*-cresol was checked with vapor chromatography. We used a Perkin Elmer chromatograph, model 154 B with column C at a temperature of 190°C. No traces of other cresols could be found in the purified 6-chloro-*o*-cresol. *6-Chloro*-o-*cresol* (Found: C 58.4; H 4.87; Cl 24.99. Calc. for C_7H_7ClO: C 59.0; H 4.95; Cl 24.87).

Preparation of 4,6-dichloro-o-*cresol.* 150 g 6-chloro-*o*-cresol (1.05 mole) was heated to 50—60°C in a round bottom flask equipped with agitator and reflux condenser. At this temperature the cresol was reacted with 71 g chlorine which was slowly introduced during about 5 h. The reaction product was distilled in vacuum. After a forerun of 37 g, mainly containing unchlorinated 6-chloro-*o*-cresol we obtained 111 g 4,6-dichloro-*o*-cresol boiling between 111 and 113°C at 16 mm Hg (yield 60 %). The cresol was further purified by recrystallization from petroleum ether. *4,6-Dichloro*-o-*cresol* (Found: C 47.6; H 3.46; Cl 40.25. Calc. for $C_7H_6Cl_2O$: C 47.5; H 3.42; Cl 40.06).

Preparation of 6-chloro-o-*toloxyacetic acid.* 71 g 6-chloro-*o*-cresol (0.5 mole) and 27 ml sodium hydroxide solution (35 %) were charged in a round bottom flask equipped with agitator, two separating funnels as charging means, a reflux condenser, an antimony electrode with a calomel reference electrode and a heating device. The solution was heated to about 100°C. Then 57 g monochloroacetic acid (0.6 mole) dissolved in 15 ml water was added from one of the separating funnels in the course of about one hour. Through the other separating funnel sodium hydroxide solution of 35 % strength was simultaneously added to keep the solution during the whole reaction at a pH value of 10.5 as measured by means of the antimony electrode. Altogether 80 ml sodium hydroxide solution was added. After 3 h at 100°C the reaction mixture was cooled to room temperature and adjusted with acid to pH 7.0. Nonreacted 6-chloro-*o*-cresol was extracted with ether. The solution was then acidified to complete precipitation of the acid, which was filtered, washed and dried. Yield 92 g or 92 %. The acid was purified by recrystallization from benzene. *6-Chloro*-o-*toloxyacetic acid* (Found: C 53.8; H 4.46; Cl 17.69. Calc. for $C_9H_9ClO_3$: C 53.9; H 4.52; Cl 17.68).

Preparation of 4,6-dichloro-o-*toloxyacetic acid.* 80 g 4,6-dichloro-*o*-cresol (0.45 mole) was reacted with 52 g monochloroacetic acid (0.55 mole) in alkaline solution in the same way as described for 6-chloro-*o*-toloxyacetic acid. We obtained 89 g 4,6-dichloro-*o*-toxyacetic acid (yield 84 %) which was purified by recrystallization from benzene. *4,6-Dichloro*-o-*toloxyacetic acid* (Found: C 45.9; H 3.36; Cl 30.30. Calc. for $C_9H_8Cl_2O_3$: C 46.0; H 3.43; Cl 30.17).

The infrared spectra. The infrared spectra were recorded with a Perkin-Elmer spectrometer, Model 21a, with a rock-salt prism. Slit schedule 927, corresponding to program 4. Speed: 3 min/μ. The frequencies of the absorption bands are given below in cm^{-1}.

6-Chloro-toloxyacetic acid (Fig. 1). 1.4 mg/0.35 g KBr. At 2 500—3 100 broad band with peaks at 2 920, 2 774, 2 685 and 2 561, 1 741(s), 1 717 (m), 1 594(w), 1 576(w), 1 470(s), 1 432(s), 1 354(w), 1 296(w), 1 262(s), 1 245(w), 1 223(s), 1 174(w), 1 146(w), 1 084(m), 1 057(s), 996(w), 910(m), 868(m), 833(m), 767(s), 747(m) and 685(m).

4,6-Dichloro-o-*toloxyacetic acid* (Fig. 2). 1.8 mg/0.35 g KBr. At 2 500—3 100 broad band with peaks at 3 044, 2 920, 2 677 and 2 574, 2 107(w), 1 738(s), 1 714(m), 1 589(w), 1 569(m), 1 470(s), 1 430(m), 1 400(m), 1 378(w), 1 356(w), 1 296(w), 1 257(s), 1 237(m), 1 210(s), 1 177(s), 1 103(w), 1 060(s), 1 006(w), 910(m) 854(s) 768(s), 723(m) and 661 (m).

o-*Toloxyacetic acid* (Fig. 3). 1.6 mg/0.35 g KBr. At 2 500—3 100 broad band with peaks at 2 928, 2 805, 2 714 and 2 587, 1 744(s), 1 711(m), 1 601(w), 1 592(m), 1 503(s), 1 461(m), 1 426(s), 1 380(w), 1 373(w), 1 320(w), 1 306(m), 1 289(w), 1 268(s), 1 243(vs), 1 194(m), 1 166(w), 1 130(s), 1 082(m), 1 051(w), 1 017(vw), 965(w), 932(m), 918(m), 845(m), 825(vw), 779(m), 758(s), 713(w) and 684(m).

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