371. *Volume Effects of Alkyl Groups in Aromatic Compounds. Part VI. The Constitution of the Iodo-*p*-cymene formed by Direct Iodination of the Hydrocarbon.*

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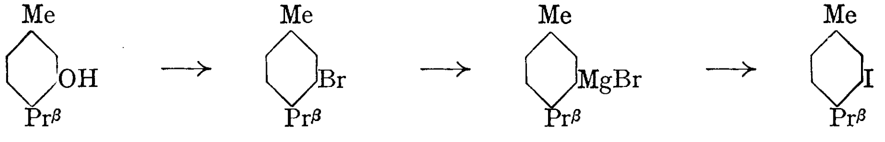
In Part II (J., 1933, 980) it was shown *inter alia* that during the chlorination and bromination of *p*-cymene the methyl apparently exerted a greater *o*-directive power than did the *iso*propyl group and it was suggested that this unexpected order was due to the relative insignificance in this hydrocarbon of the " inductive effects " of the two alkyl radicals concerned compared with their more widely different space-filling capacities (compare *Chem. and Ind.*, 1933, **52**, 505).

On such a view the volumes of the effective parts of chemically similar attacking reagents would not greatly alter the *ratio* of 2- to 3-substitution from one case to another—only the *rates* of total substitution should be considerably affected. It therefore followed that during the iodination of cymene the iodo-group should enter the 2-position almost exclusively, the orientation thus resembling that of the two other halogenations mentioned.

Nevertheless, this process has been stated (Klages and Storp, *J. pr. Chem.*, 1902, **65**, 572) to give 3-iodocymene as the only isolable product. Now, such a result is only consistent with the actual initial substitution having paralleled that by chlorine or bromine if 2-iodocymene is more rapidly reduced by hydrogen iodide than is its isomeride. Rough comparative experiments indicate that this is not the case and that cymene is re-formed from both iodohydrocarbons with equal readiness; for this reason, therefore, and because the formation of a 3-substituted derivative seemed unlikely by analogy, we have made a comparison between the direct iodination product and synthetically prepared 2- and 3-iodo-*p*-cymenes.

Care was taken to prevent the latter being mixtures *inter se*: the cymidine hydrochloride from which the 2-iodo-compound was obtained by diazotisation was recrystallised several times from dilute hydrochloric acid to ensure freedom from 3-aminocymene hydrochloride. Authentic 3-*iodocymene*, not having been previously described, was procured in low yields by the following sequence, the last stage of which was based on the work of Datta and Mitter (*J. Amer. Chem. Soc.*, 1919, **41**, 287):



The direct iodination of cymene has been carried out essentially as prescribed by Klages and Storp (*loc. cit.*); other methods (Töhl, *Ber.*, 1892, **25**, 1522; Thyssen, *J. pr. Chem.*, 1902, **65**, 5; Elbs and Zaroslawzew, *ibid.*, 1913, **88**, 92) were also tried but did not give improved yields, which were small in all cases.

The constitution of the product from the last group of experiments was established by mixed m. p. determinations made on freshly prepared specimens of the iodo-dichlorides of this and the two synthetic iodocymenes. The appropriate data are collected in Table I (approximately equal-part mixtures being used in each determination):

TABLE I.

M. p.'s and Mixed M. p.'s of the Iodocymene Dichlorides.

2-Iodocymene dichloride	97°	Mixture of 2- and 3- derivatives	*ca.* 75°
3-Iodocymene dichloride	85—87	,, 2- and ?- derivatives	90—91
?-Iodocymene dichloride	85—86	,, 3- and ?- derivatives	78—79

(All m. p.'s are with decomp.)

It thus appears that direct iodination of cymene produces mainly 2-iodocymene. Other isomeric substances (? side-chain substituted derivatives) with b. p.'s close to that of the main product are evidently also formed in small amounts and, under the above treatment, lead to dichlorides the presence of which reduces the m. p. of 2-iodocymene dichloride from 97° to 85—86°.

Four other methods of comparison were also tried. (*a*) Dinitration and thence the isolation of one of the two known dinitropiperidinocymenes was not so successful as was the same sequence for the analogous chloro- and bromo-cymenes, because the iodohydrocarbons underwent loss of iodine in contact with nitric acid; nevertheless, the crude product of nitration remaining after removal of iodine, etc., yielded, by interaction with hot piperidine and several recrystallisations, ultimately a pure sample of 3 : 5-dinitro-2-piperidino-*p*-cymene identical with that obtained by the dinitration, etc., of 2-chlorocymene from carvacrol. (*b*) Oxidation in all three cases afforded iodoterephthalic acid (Abbes, *Ber.*, 1893, **26**, 2951) and could not be stopped at the keto-acid stage. (*c*) A series of direct observations of mixed m. p.'s of the iodocymenes themselves gave equivocal results, possibly owing to difficulties of manipulation. (*d*) An attempt has been made to apply the fact (Rule and McLean, J., 1931, 674) that the specific rotations for the same optically active solute dissolved in liquids related as aromatic position isomerides are not identical but vary from solvent to solvent. Solutions of *l*-menthol ([α] — 59·6° in alcohol) in the three monoiodocymenes were accordingly examined polarimetrically, analogous observations with the corresponding chloro- and bromo-derivatives being made as checks.

The results are tabulated below. With the chloro- and bromo-cymenes a slight increase in the value of the specific rotation ([α]) is observed when the 3- is replaced by the 2-isomeride. The difference occurs in the same direction between the two synthetic iodo-derivatives, and it will be noticed that the specific rotation of menthol in the direct iodination product is close to that for this substance in 2-iodocymene, implying essential identity of solvents, in agreement with the conclusion stated earlier.

TABLE II.

Specific Rotations of l-*Menthol in the Halogenocymenes.*

Solvent.	Temp.	*l* (dcm.).	G./100 c.c. of soln.	$\alpha^{t°}_{5893}$.	$[\alpha]^{t°}_{5893}$.
2-Chlorocymene	22°	1	12·082	— 5·72°	— 47·3°
,,	22	1	8·200	— 3·88	— 47·3
3-Chlorocymene	20	1	10·2248	— 4·78	— 46·7
,,	19·8	1	10·536	— 4·92	— 46·7
2-Bromocymene	19·9	1	10·162	— 4·76	— 46·8
,,	19·9	1	10·620	— 4·98	— 46·9
3-Bromocymene	19·9	2	10·1296	— 9·38	— 46·3
,,	19·9	2·2	6·227	— 6·34	— 46·3
2-Iodocymene	18	1	11·164	— 5·13	— 46·0
,,	18	1	10·735	— 4·94	— 46·0
3-Iodocymene	20	1	10·536	— 4·76	— 45·2
,,	20	1	12·498	— 5·65	— 45·2
?-Iodocymene	21	1	13·650	— 6·27	— 45·9

EXPERIMENTAL.

Preparation of 2-Iodocymene.—Recrystallised 2-aminocymene hydrochloride (40 g.) was suspended in dilute hydrochloric acid (conc. acid, 80 c.c.; water, 60 c.c.) and diazotised (sodium nitrite, 15 g., in water, 40 c.c.). The clear diazo-solution was treated with a solution of potassium iodide (95 g.) in water (150 c.c.), warmed under reflux for 2 hours, and then steam-distilled. The oil obtained was extracted with light petroleum and washed with aqueous sodium thiosulphate, caustic soda solution, and finally water. The dried (calcium chloride) solution was distilled; 21 g. were collected at 122°/11 mm. (Found : C, 46·9; H, 5·1; I, 48·1. Calc. for $C_{10}H_{13}I$: C, 46·2; H, 5·0; I, 48·8%).

Preparation of 3-*Iodocymene.*—To the ethereal solution obtained by admixture of 3-bromocymene (48 g.), dry ether (500 c.c.), and magnesium (6 g.), was added iodine (50 g.), dissolved in dry ether (200 c.c.), until the colour of the latter persisted. The product was decomposed by water, washed with aqueous sodium thiosulphate and with water, and dried over calcium chloride. Distillation afforded (1) *p*-cymene, b. p. 65—66°/11 mm.; (2) a little unchanged 3-bromocymene, b. p. 107—108°/11 mm.; (3) 3-*iodocymene,* b. p. 125—126°/11 mm. (yield, 7 g.), as a colourless mobile liquid (Found : C, 46·2; H, 5·0%).

Direct Iodination of p-*Cymene.*—A mixture of cymene (67·5 g.), iodine (62·5 g.), alcohol (250 c.c.), and iodic acid (20 g., in water, 60 c.c.) was boiled under reflux for 8 hours. The liquid product was washed successively with sodium thiosulphate solution, water, a hot solution of sodium hydroxide in methyl alcohol, and finally with water. Extraction with light petroleum, drying over calcium chloride, and careful fractionation under reduced pressure afforded about 12 g. of liquid product, b. p. 120—130°/14 mm. During redistillation of several samples together a b. p. of 118—122°/12 mm. was observed (Found: C, 46·3; H, 5·3%).

Formation of the Iodo-dichlorides of the Preceding Compounds.—The iodohydrocarbons were dissolved in 4—5 vols. of dry carbon tetrachloride, cooled to 0°, and a slow current of dry chlorine passed through in each case. The dichlorides separated rapidly as yellow needles; these were washed with the solvent and rapidly dried in the air for analysis. The m. p.'s are given above. These derivatives decomposed spontaneously at room temperature into red liquids, but could be preserved for several days in the dark at 0°. The analytical data are as follow :

	Found.		Calc. for $C_{10}H_{13}Cl_2I$.	
	C.	H.	C.	H.
2-Iodocymene dichloride	36·5	3·9	36·2	3·9
3-Iodocymene dichloride	36·2	3·9		
?-Iodocymene dichloride	36·4	4·1		

Oxidation of the Iodocymenes.—The substance (10 g.) was added to 10% sodium hydroxide solution (80 c.c.) diluted with water (400 c.c.), and the mixture was treated with 5% potassium permanganate to excess and, after being heated for various times, worked up by the usual procedure. A whitish solid was always obtained which, on crystallisation from much benzene, water, or aqueous alcohol, had m. p. above 300°. Its appearance and analysis suggest that it is iodoterephthalic acid (Found : C, 33·0; H, 1·9. Calc. for $C_8H_5O_4I$: C, 32·8; H, 1·7%).

Nitration of the Direct Iodination Product.—The iodocymene (2 g.) was dropped slowly into nitric acid (*d* 1·5, 20 c.c.), diluted with acetic acid (equal volume), below 0°. After ½ hour the deep red solution was poured on ice, and the semi-solid oil was extracted with benzene, washed successively with dilute sodium hydroxide solution, aqueous sodium thiosulphate, water, and dried over sodium sulphate. The solid obtained by evaporation of the solvent was heated for 1 hour on the steam-bath with an excess of piperidine, the resulting solution diluted with water, etc.; three recrystallisations from dilute alcohol then gave yellow needles, m. p. 123—124°, identified as 3 : 5-dinitro-2-piperidino-*p*-cymene by mixed m. p. with an authentic specimen (J., 1933, 980).

Polarimetric Observations.—The *l*-menthol was once recrystallised from low-boiling light petroleum; it had m. p. 42° and its rotatory power (in alcohol) was — 59·6°.

The 2-chloro- and 2-bromo-cymene were prepared by direct halogenation of cymene (J., 1933, 981); the 3-isomerides were obtained from thymol by interaction with the appropriate phosphorus pentahalide. They were purified by redistillation and showed the following constants; certain data for the three iodo-derivatives are also tabulated :

	B. p.	$d^{17°}_{4°}$.	$n^{17°}_{5461}$.
2-Chloro-*p*-cymene	216—218°/762 mm.	1·152	1·51776
3-Chloro-*p*-cymene	120—122/20 mm.	—	—
2-Bromo-*p*-cymene	130/35 mm.	—	—
3-Bromo-*p*-cymene	130/35 mm.	—	—
2-Iodo-*p*-cymene	122/11 mm.	1·4205	1·57998
3-Iodo-*p*-cymene	125—126/11 mm.	1·4113	1·56899
?-Iodo-*p*-cymene	118—122/12 mm.	1·4231	1·57595

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