

CXLIV.—*The Relation of Position Isomerism to Optical Activity. VII. The Rotation of the Menthyl Esters of Three Isomeric Dinitrobenzoic Acids.*

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THE menthyl esters which were selected for investigation were those of the 2:4-, 2:6-, and 3:5-dinitrobenzoic acids, which were prepared from the corresponding acid chlorides by heating them with menthol in the manner described in former papers.

The following are the constants of the compounds in question :

	M. p. of acid chloride.	M. p. of ester.	In benzene solution.	
			$[\alpha]_D^{20^\circ}$ .	$[M]_D^{20^\circ}$ .
2 : 4.....	42—46°	69—71°	—134°	—470°
2 : 6.....	96—98	121—123	—183	—642
3 : 5.....	66—68	153—154	—70	—246

In a previous communication on this subject (Trans., 1905, 87, 1190), it was shown that, of the three mono-nitro-esters, the ortho-compound produced the greatest effect in increasing the laevorotation

and the para- the least, whilst the meta-compound occupied an intermediate position. The present experimental results fully confirm our former observations. The di-ortho-compound exhibits the highest and the di-meta- the lowest rotation of the three esters examined, whilst the compound which contains one nitro-group in the ortho- and one in the para-position has a constant which is nearly the mean of the other two. Attention should be drawn to the interesting fact that the rotation of the di-meta-compound is very little different from that of the unsubstituted benzoic ester.

Although similar observations have been made before, the large rotational effect of the nitro-group in the ortho-position renders the present result more striking. The results of the study of the seven isomeric series of substituted benzoic esters which have been laid before the Society furnish abundant evidence that it is only the substituent near the active group which materially influences its activity. The only apparent anomaly is presented by the three iodobenzoic esters. Unfortunately, the difficulty of preparing other isomeric series of substituted benzoic acids containing iodine renders the optical study of their esters very troublesome.

#### EXPERIMENTAL.

*Menthyl 2:4-Dinitrobenzoate*.—The 2:4-dinitrobenzoic acid which served for these experiments was obtained from Kahlbaum. It was converted into the acid chloride in the usual way by heating it with an equal weight of phosphorus pentachloride on the water-bath. After removal of the oxychloride by distillation under diminished pressure, the solid residue was crystallised from light petroleum. It forms colourless needles (m. p. 42—46°). The action of the acid chloride on menthol began at 140°, and when the process was completed the product was made alkaline and distilled in steam to remove any free menthol. The ester was crystallised from alcohol and melted at 69—71°. The following are the polarimetric observations in benzene solution at different concentrations:

Concentration, per cent.	Rotation.	$[\alpha]_D^{20^\circ}$ .	$[M]_D^{20^\circ}$ .
31·148	− 81·48°	− 130·79°	− 458·16°
15·57	− 42·00	− 134·84	− 472·34
7·78	− 21·37	− 137·21	− 480·65

Mean of  $[M]_D^{20^\circ}$  − 470°.

On analysis:

0·3104 gave 21·5 c.c. moist nitrogen at 15° and 750·5 mm.  $N = 8·05$ .

$C_{17}H_{22}O_6N_2$  requires  $N = 8·0$  per cent.

*Menthyl 2:6-Dinitrobenzoate*.—The preparation of 2:6-dinitro-

benzoic acid in any quantity is a very troublesome operation. After several trials, the method which was adopted was to heat 2 : 6-dinitrotoluene in sealed tubes for twelve hours at 125—130° with nitric acid, consisting of 2 volumes of strong acid of sp. gr. 1·4 and 1 volume of water. On account of the large quantity of gas liberated during oxidation, it is necessary to release the pressure occasionally by opening the tubes. The yield is always very poor and the crude acid very much discoloured. The product melted at 198—203°, and, after repeated crystallisation from water with the addition of charcoal, was obtained colourless and melted at 201—203°. Fourteen grams of dinitrotoluene gave about 3 grams of impure acid. The small yield necessitated frequent repetitions of the process in order to obtain the requisite quantity of material. The acid chloride was prepared by the usual method, and after crystallisation from light petroleum melted at 96—98°. On heating the latter with menthol in the oil-bath, the reaction began very slowly, and was completed in two and a half hours at 150—160°. The treatment of the product was the same as described in the case of the 2 : 4-ester. The crude ester was very dark-coloured and required frequent crystallisation from alcohol with the addition of charcoal to produce a pure substance. It crystallises in prisms, m. p. 121—123°.

The polarimetric readings in benzene solution were as follows :

Concentration, per cent.	Rotation.	$[\alpha]_D^{20^\circ}$ .	$[M]_D^{20^\circ}$ .
14·104	- 51·75°	- 183·4°	642·5°
7·052	- 25·76	- 182·7	640·0
3·526	- 12·96	- 183·9	644·2

Mean of  $[M]_D^{20^\circ}$  - 642°.

On analysis :

0·2557 gave 18·8 c.c. moist nitrogen at 18° and 751 mm.  $N = 8·45$

$C_{17}H_{22}O_6N_2$  requires  $N = 8·0$  per cent.

*Menthyl 3 : 5-Dinitrobenzoate*.—The acid was obtained from Kahlbaum, and was converted into the acid chloride in the usual way. After crystallisation from light petroleum it melted at 66—68°. The interaction of the acid chloride and menthol began at 100°, and became very vigorous at 110°. The process was completed in ten minutes, when the contents of the flask solidified. The ester crystallised from alcohol in colourless needles, m. p. 153—154°.

The polarimetric readings in benzene solution were as follows :

Concentration, per cent.	Rotation.	$[\alpha]_D^{20^\circ}$ .	$[M]_D^{20^\circ}$ .
9·612	- 13·47°	- 70·08°	- 245·6°
4·806	- 6·74	- 70·15	- 245·8
2·403	- 3·40	- 70·76	- 247·9

Mean of  $[M]_D^{20^\circ}$  - 246°.

On analysis :

0.3038 gave 21.9 c.c. moist nitrogen at 16° and 744.5 mm.  $N = 8.28$ .

$C_{17}H_{22}O_6N_2$  requires  $N = 8.0$  per cent.

#### APPENDIX.—By JULIUS BEREND COHEN.

##### *Steric Hindrance in the Interaction of Menthol with Diortho-substituted Benzoyl Chlorides.*

The following observations have been made incidentally during the preparation of a series of isomeric disubstituted benzoic esters of menthol by my co-workers and myself, and are now collected together with the object of furnishing a contribution to the theory of "steric hindrance." Sudborough (Trans., 1895, 67, 587) has shown that diortho-substituted benzoyl chlorides are more slowly hydrolysed than the corresponding isomerides. In reference to the action of alcohols, he points out that "in order to obtain the (ethereal) salts of the diortho-substituted acids it is necessary to boil the acid chlorides for some time with the alcohol, as the action seems to proceed more gradually."

No actual examples are quoted, but the methyl esters of 2:4-, 3:5-, and 2:6-dibromobenzoic acids and 2:6-dinitrobenzoic acid are described as being readily obtained from the acid chlorides and methyl alcohol.

A more definite indication of steric hindrance was apparently derived from the behaviour of 2:4:6-tribromobenzoyl chloride and 2:4:6-trinitrobenzoyl chloride, the methyl ester of the first being obtained by boiling the chloride "for some time" with methyl alcohol, and that of the second by boiling the chloride "with a very large excess of methyl alcohol for some time," whilst methyl alcohol appeared to leave 2:3:4:6-tetrabromobenzoyl chloride to a great extent unaltered. On the other hand, the methyl ester of 3:4:5-tribromobenzoic acid was prepared by boiling the chloride with methyl alcohol "for a few minutes." It will be seen that the examples are not very numerous, and that the indications of steric hindrance are not always of a very pronounced character.

During the last few years, six separate series of isomeric disubstituted benzoic esters of menthol have been prepared for optical examination by the interaction of the acid chlorides and menthol (Trans., 1903, 83, 1214; 1904, 85, 1265; 1906, 89, 49, 460). The series comprise 6 isomeric dichloro- and dibromo-benzoic esters, 10 chlorobromobenzoic esters, 8 chloronitrobenzoic esters, and 3 dinitrobenzoic esters. In all, 33 disubstituted benzoyl chlorides have been transformed into corresponding menthyl esters.

It is impossible to determine with accuracy the temperature at which the reaction between the acid chloride and alcohol commences, but by carefully watching the surface of the liquid and the outlet tube of the flask in which the process is going forward there is no difficulty in ascertaining within a very few degrees the visible indication of its commencement. Bubbles begin to rise in rapid succession from the body of the liquid, and fumes of hydrogen chloride escape.

As a rule the reaction, when once a definite temperature is reached, proceeds vigorously; but in the case of the diortho-substituted acid chloride it is invariably retarded. Briggs and the author (*Trans.*, 1903, 83, 1214) noticed that "evidence of steric hindrance is very clearly indicated in the case of the 2:6-dichlorobenzoic acid, for whereas the acid chlorides, as a rule, react vigorously with menthol at 135—140°, no reaction occurs with 2:6-dichlorobenzoyl chloride until the temperature reaches 180°, and even then it proceeds very slowly." A similar observation was made by Zortman and the author (*Trans.*, 1906, 89, 49), who found that "as in former examples of diortho-acid chlorides the 2:6-dibromobenzoyl chloride required a much higher temperature for esterification (175—180°) than the isomeric acid chlorides, all of which react rapidly below 130° with menthol." In another paper by Raper and the author (*Trans.*, 1904, 85, 1265) it is stated "that the 2:6-chlorobromobenzoyl chloride, like the corresponding dichlorobenzoyl chloride, does not react with menthol until a temperature of 180° is reached." In other cases the reaction was completed at 130—140° or below. In preparing the chloronitrobenzoic esters described by Armes and the author (*Trans.*, 1906, 89, 460) it was found that "the reaction (of the 2:6-acid chloride) with menthol does not begin until the temperature reaches 150°, and then proceeds very slowly at 150—160°." In other cases the reaction was completed at 120°; in that of the 3-chloro-5-nitro-compound at 95—100°. Armes and the author also find in the case of the dinitrobenzoic esters that whereas interaction with 2:6-dinitrobenzoyl chloride and menthol begins at 150° and proceeds very slowly, that with the 2:4-compounds begins at 140° and is rapidly completed, whilst with the 3:5-compound the reaction set in at 100° and was completed in a few minutes at 110°.

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