CCCXXXIV.—*Optical Activity and the Polarity of Substituent Groups. Part XII. The Direct Space Effects of Meta and Ortho-para Directive Substituents. l-Menthyl Esters of Substituted Naphthoic Acids.*

By H. GORDON RULE, JOHN SPENCE, and EGON BRETSCHER.

THE examination of a number of isomeric *l*-menthyl methoxynaphthoates (Bretscher, Rule, and Spence, J., 1928, 1493) has shown that a methoxyl group in any position adjacent to the carbomenthoxy-complex leads to a diminished rotatory power, and that a similar depressive influence is exerted by a *peri*-methoxyl group in the 8 : 1-derivative. This provided further evidence in support of the view that the characteristic ortho-effect of groups in the *o*-substituted benzoic esters was not transmitted through the chain of atoms but operated directly through space, a conclusion which was also found to be in agreement with the properties of growing-chain compounds containing ω-carboxy- and ω-alkoxy-groups (Rule, Hay, and Paul, J., 1928, 1347).

Values of $[M]_{5461}$ *for* l-*Menthyl Esters of Substituted Naphthoic Acids.*

I. 1-*Naphthoates.*

Substituent.	Solvent.	$[M]_{5461}$.	Reference.
None	C_6H_6	−319°	This paper.
,,	$CHCl_3$	−266	,, ,,
2-Methoxy	C_6H_6	+ 45·3	Bretscher, Rule, and Spence.
,,	$CHCl_3$	− 76·2	,, ,, ,,
4-Methoxy	C_6H_6	−374	,, ,, ,,
,,	$CHCl_3$	−302	,, ,, ,,
5-Methoxy	C_6H_6	−325	,, ,, ,,
,,	$CHCl_3$	−287	,, ,, ,,
8-Methoxy	CS_2	−137	,, ,, ,,
,,	C_6H_6	−157	,, ,, ,,
,,	$CHCl_3$	−181	This paper.
,,	EtOH	−184·5	Bretscher, Rule, and Spence.
2-Methyl	C_6H_6	− 99·6	This paper.
,,	$CHCl_3$	−192	,, ,,
4-Nitro	C_6H_6	−273	,, ,,
5-Nitro	C_6H_6	−314	,, ,,
,,	$CHCl_3$	−284	,, ,,
8-Nitro*	CS_2	−644	,, ,,
,,	C_6H_6	−841	,, ,,
,,	$CHCl_3$	−389	,, ,,
,,	EtOH	−806	,, ,,
8-Chloro	C_6H_6	−172	,, ,,
,,	$CHCl_3$	−189	,, ,,

* The rotations for this compound are approximate only; see p. 2521.

II. 2-*Naphthoates.*

None	C_6H_6	−288°	Tschugaev, *C.*, 1902, II, 1238.
1-Methoxy	(Homog.)	−268	Bretscher, Rule, and Spence.
1-Hydroxy	C_6H_6	−384	This paper.
,,	$CHCl_3$	−342	,, ,,
,,	*EtOH	−316	,, ,,
,,	*EtOH + EtOK	−301	,, ,,
3-Methoxy	CS_2	−191	Kenyon and Pickard, J., 1915, **107**, 58.
,,	C_6H_6	−206	,, ,, ,,
,,	$CHCl_3$	−139	Bretscher, Rule, and Spence.
3-Hydroxy	C_6H_6	−407	This paper.
,,	$CHCl_3$	−299	,, ,,
3-Chloro	C_6H_6	−275	,, ,,
,,	$CHCl_3$	−218	,, ,,

* In alcohol and in alcohol containing an equivalent of potassium ethoxide it was necessary to work in 0·5% solution, owing to the low solubility of the ester.

The investigation has now been extended to various other substituted naphthoic esters of *l*-menthol, including nitro-compounds, with results which are summarised in Tables I and II. For the purpose of comparison, the rotatory powers recorded in the literature for other related esters are included. The figures refer to room temperature and a concentration approximating to 5%. Values for other wave-lengths of light will be found in the experimental section of this paper. In every case except that of the 2-methoxy-1-naphthoate, the dispersion is normal and complex, the graphs of $1/\alpha$ against λ^2 diverging only slightly from the linear.

Substituent Effect.

As may be seen by reference to Tables I and II, esters with a nitro- or a methoxyl group in position 5 do not differ appreciably from the parent compound in their optical properties. In the 4-position, a methoxyl group produces a small but definite increase in rotatory power, and a nitro-group leads to a slight decrease. The more interesting compounds, however, are those in which the substituent is either adjacent or in the peri-position to the asymmetric complex, producing large changes in rotatory power.

Ortho-substituted Esters.—Among these compounds the usual depressive effect of an *o,p*-directive group is observed. For the 2-substituted 1-naphthoates the relative rotatory powers are given by $OMe \ll Me < H$, and for the 3-substituted 2-naphthoates by $OMe < Cl < H$. In both cases the order of the groups is the same as that found for the *l*-menthyl *o*-substituted benzoates by Cohen, and for the *sec.*-β-octyl benzoates (Rule, Hay, Numbers, and Paterson, J., 1928, 178). It is also in agreement with the orienting powers of the respective substituents in benzene substitution.

l-*Menthyl* 1-*hydroxy*-2-*naphthoate* and the corresponding 3-*hydroxy*-

ester, although containing an *o,p*-directive group in the adjacent position to the carboxyl group, nevertheless possess abnormally high rotatory powers and thus resemble *l*-menthyl salicylate (Rule and MacGillivray, this vol., p. 401). They also exhibit in an enhanced degree the unusual solubility relationships peculiar to this compound; although they dissolve readily in benzene and chloroform, the solubility of the hydroxynaphthoic esters in alcohol is so low that the rotatory power of the 1 : 2-derivative had to be measured in 0·5% solution, and the 3 : 2-compound proved too insoluble for its rotation to be determined in this solvent. These properties indicate that the esters probably exist in the chelated state (compare Sidgwick, J., 1920, **117**, 402; Sidgwick and Ewbank, J., 1921, **119**, 979) and that the high rotatory power is connected with this structural condition. The foregoing menthyl hydroxy-esters and the corresponding anthranilate are the only compounds of this type so far discovered in which an *o,p*-directive group in the ortho-position to the carboxyl results in an increased rotatory power.

Attempts were made to prepare menthyl naphthoates having a nitro-group in the ortho-position, but without success. These acids are known to be unstable and it was not found possible to convert them into the menthyl esters.

Peri-compounds.—Derivatives of this class include the methoxy-, chloro-, and nitro-1-naphthoic esters. The last-named *compound* could not be obtained by way of the 8-nitro-1-naphthoyl chloride, as the latter suffered drastic change during the treatment with thionyl chloride, apparently being converted in part into 8-chloro-1-naphthoyl chloride. It was eventually prepared in very small amount by prolonged esterification of the 8-nitro-acid in a slow current of hydrogen chloride at 140°. The acid is extraordinarily resistant to esterification. Only a small yield of highly impure ester was obtained after 120 hours' treatment, and after purification the total amount of comparatively pure ester available was no more than 0·3—0·4 g., hence the values recorded in Table I can only be regarded as approximate : they were determined in 1·8% solution, the solute being recovered each time by evaporation of the solvent. The 8-nitro-ester crystallises remarkably well and has an exceptionally high rotatory power.

l-*Menthyl* 8-*chloro*-1-*naphthoate* was isolated in crystalline form as the result of an attempt to prepare the nitro-ester by way of the acid chloride. It was highly resistant to hydrolysis with boiling alcoholic alkali, but was converted into the 8-chloro-acid by fusion with potassium hydroxide for two hours at 180°, thus confirming the supposition that treatment with thionyl chloride had resulted in the partial replacement of the nitro-group by chlorine. This unexpected reaction is evidently connected with the spatial proximity of the groups in the 8 : 1-positions.

The relative influence of substituents in the peri-position is given by $NO_2 \gg H > Cl > OMe$, in agreement with the orienting powers of the groups and identical with their influence in the menthyl and *sec.*-β-octyl ortho-substituted benzoates. This similarity between peri and ortho effects, coupled with the absence of any such influence in the *m*- or *p*-substituted esters, can only be explained on the assumption of a direct propagation through space. So far as can be judged from the cases now known, a substituent in the peri-position exerts a greater influence on the rotatory power than the same substituent in an ortho-position. This is not unexpected, considering the relative properties of the two types of derivatives. Attention may be directed to the great ease of formation of naphtholactone, naphthostyril, and naphthoic anhydride; to the greater steric hindrance observed in the esterification and hydrolysis of the peri-compounds; and to the existence of the benzenesulphonyl derivative of 8-nitronaphthylglycine in optically active forms (Mills and Elliott, J., 1928, 1291). All these properties indicate that the above substituents are in closer proximity in the peri-compounds than when in the ortho-position to one another. On the assumption of a direct effect operating through space, a rational explanation is thus provided for the greater influence on optical activity exerted by a peri-substituent.

The polarimetric studies of optically active esters described in this series of communications therefore lead to the conclusion that when, as in peri- and ortho-compounds, a substituent is in close proximity to the carboxylic group, the latter is subject to a direct influence propagated through space. The space influence of a positive pole or other *m*-directive substituent modifies the rotatory power in the same sense as the general polar (or inductive; compare Ingold) influence of the substituent, which is transmitted through the chain of atoms and leads to an enhanced rotation. On the other hand, the direct effect due to a negative pole or *o,p*-directive substituent is in the opposite sense to that of a *m*-directive one and results in diminished rotatory power. This effect is probably the most definite and powerful substituent influence yet established in optical activity. In the following communication it is shown that the same effect may possibly be traced in aliphatic compounds, not necessarily of the ester class, in which the substituent is sufficiently close to the asymmetric atom.

Influence of Solvents.

Owing to the comparatively high melting points of most of the esters it was necessary to examine them in solution, and as the compounds were freely soluble in benzene and chloroform these solvents were used throughout. In some cases other solvents were also employed. On account of the various ways in which the presence of the solvent may affect the physical and chemical condition of the solute, it is notoriously difficult to correlate changes in optical activity with the properties of the liquid medium. It is worthy of note, however, that the substituent influence exhibited in the various 8 : 1-, 2 : 1-, and 1 : 2-naphthoates listed in Tables I and II tends to be exerted to the maximum extent in solvents of low dielectric constant, whether it is the depressive effect due to OMe, Cl, or CH_3, or the exaltation caused by OH or NO_2. For the 8-methoxy-ester the magnitude of the effect in the four solvents used is in the inverse order of their dielectric constants, and the same regularity holds for the 1-hydroxy-2-naphthoate, in which chelation should be assisted by an increased electrostatic attraction between the hydroxyl and the keto-group. Similarly, the highest rotation for the 8-nitro-ester is given in benzene solution, although alcohol also gives a comparatively high value. These relationships suggest the possibility that the direct effect in question is electrostatic in nature and that a change of medium, in addition to producing other and more specific changes, may influence the rotation by increasing or decreasing the electrostatic forces between the side chains.

EXPERIMENTAL.

l-*Menthyl* 4-*Nitro*-1-*naphthoate*.—4-Nitro-1-methylnaphthalene, prepared by Lesser's method (*Annalen*, 1913, **402**, 16), was oxidised in small quantities (5 g.) at a time by heating with 8% nitric acid (60 c.c.) for 10 hours at 150°. After five recrystallisations from alcohol, the acid melted at 226°. It was converted into the acid chloride by treatment with thionyl chloride and thence into the menthyl ester (yield of crude ester, 90% of the theoretical). The l-*menthyl* 4-*nitro*-1-*naphthoate* melted at 63—63·5° and was recrystallised from alcohol until of constant rotatory power (Found : N, 4·1. $C_{21}H_{25}O_4N$ requires N, 3·9%).

l-*Menthyl* 5- *and* 8-*Nitro*-1-*naphthoates*.—Technical sodium α-naphthalenesulphonate was converted by successive stages into α-naphthonitrile, α-naphthoic acid, and the mixed 5- and 8-nitro-acids (Eckstrand, *J. pr. Chem.*, 1888, **38**, 160). These were separated in the usual manner by crystallisation from absolute alcohol, and the 8-acid was treated with methyl alcohol and hydrogen chloride in order to remove any 5-acid still present. The 5- and 8-nitro-acids employed melted at 239° and 217° (corr.), respectively (Eckstrand, *loc. cit.*, records 239° and 215°).

Crude l-*menthyl* 5-*nitro*-1-*naphthoate*, obtained in the usual way, was purified by repeated crystallisation from light petroleum. The ester melts at 102·5° and is triboluminescent. It dissolves readily in benzene or chloroform and to a moderate extent in alcohol (Found, micro-estimation by ter Meulen's method of catalytic reduction : N, 4·1. $C_{21}H_{25}O_4N$ requires N, 3·9%).

The preparation of l-*menthyl* 8-*nitro*-1-*naphthoate* proved to be a matter of some difficulty. In a preliminary experiment the addition of thionyl chloride to the acid was followed by a violent reaction which resulted in charring and considerable decomposition. An attempt to dry the moist sodium salt at about 90° led to sudden and explosive decomposition. Treatment of the acid in well-cooled benzene solution with thionyl chloride, followed by removal of the solvent and the excess of the reagent at 60—70°, also brought about darkening and some decomposition. In this case further treatment with menthol led to the isolation of *l*-menthyl 8-chloro-1-naphthoate in 25% yield.

Esterification of the crude 8-nitro-acid (containing about 20% of the 5-isomeride) with menthol and hydrogen chloride for 60 hours at 120° gave a syrupy ester which in the unpurified state had $[M]_{5461} = -355°$ in benzene ($c = 5$). As the 5-nitro-ester has a much lower rotation (—314°), this indicated that the *peri*-acid undergoes slow esterification. The pure 8-nitro-acid (10 g.) was therefore heated with menthol (30 g.) for 120 hours at 140°, a slow current of hydrogen chloride being passed through the flask; a mixture of water, menthol, menthene, and menthyl chloride slowly distilled over. The dark carbonaceous residue was freed from acid and blown through with steam, and the remaining crude ester (1 g.) was dissolved in alcohol and decolorised with animal charcoal. The clear yellowish-brown ester was precipitated with water, separated, and dried in ethereal solution. The viscous product obtained after removal of the ether became solid on being stirred with a little light petroleum, and was recrystallised from this solvent. The yield of pale yellow ester, which crystallised in magnificent pyramids, m. p. 115—118°, was only 0·2 g. A repetition of the preparation gave similar results, and the rotations recorded in Table I refer to the compound in this somewhat impure state. A smaller amount of pure ester was obtained of m. p. 122—123° (Found : N, 3·8. $C_{21}H_{25}O_4N$ requires N, 3·9%). The bulk of the acid was recovered unchanged from each preparation.

l-*Menthyl* 8-*chloro*-1-*naphthoate* was isolated as stated above from the 8-nitro-acid. The product obtained by treating the acid (10 g.) with thionyl chloride in benzene solution was heated with menthol for 4 days at 60°. A slow evolution of hydrogen chloride occurred and the mixture was worked up in the usual way. The ester (4 g.)

was recrystallised from alcohol until of constant rotatory power and was obtained as a colourless crystalline solid, m. p. 131·5°, readily soluble in benzene, chloroform, or warm alcohol (Found : Cl, 10·6. $C_{21}H_{25}O_2Cl$ requires Cl, 10·3%). No perceptible change occurred when the ester was boiled for 7 days with alcoholic potash. Hydrolysis was effected by fusion with solid potassium hydroxide at 180° for 2 hours. The chloro-acid obtained melted at 155—162°, and after one recrystallisation from alcohol at 168° (Eckstrand, *loc. cit.*, records 167°). No trace of naphtholactone appeared to be formed during the fusion.

l-*Menthyl* 3-*hydroxy*-2-*naphthoate* was obtained in 80% yield from the acid by way of the acid chloride. It was also prepared in 30% yield from a mixture of methyl hydroxynaphthoate, menthol, and a trace of sodium (compare Rule and MacGillivray, this vol., p. 407). The colourless crystalline ester was recrystallised from hot alcohol until pure; it then melted at 119·5° (corr.). Although readily soluble in cold benzene or chloroform, the compound only dissolves very sparingly in cold alcohol (approximately 0·5 g. in 100 c.c.). It is strongly triboluminescent (Found : C, 77·0; H, 8·0. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·0%).

l-*Menthyl* 1-*hydroxy*-2-*naphthoate*, prepared from the acid chloride (80% yield) and purified by recrystallisation from alcohol, was a colourless crystalline solid, m. p. 106·5—107° (corr.), having similar solubility relationships to those of the 3-hydroxy-ester, and possessing even more marked triboluminescence (Found : C, 77·3; H, 8·0%).

l-*Menthyl* 3-*chloro*-2-*naphthoate* was prepared from the 3-hydroxy-acid, which was converted into the chloro-acid and the corresponding acid chloride (Strobach, *Ber.*, 1901, **34**, 4159). Esterification in the presence of pyridine gave the ester in 93% yield. The ester, purified from alcohol, is a colourless, crystalline, triboluminescent solid, m. p. 96·5° (corr.). It is freely soluble in light petroleum, benzene, and chloroform, and moderately easily soluble in methyl and ethyl alcohols (Found : Cl, 10·7. $C_{21}H_{25}O_2Cl$ requires Cl, 10·3%).

l-*Menthyl* 2-*methyl*-1-*naphthoate* was prepared in 90% yield from the corresponding acid chloride, pyridine being used as catalyst. The acid was obtained by the method of Mayer and Sieglitz (*Ber.*, 1922, **55**, 1839), but in the final stage the organo-magnesium derivative from 1-bromo-2-methylnaphthalene was treated with solid carbon dioxide in place of the gas used by the above authors, the yield of acid thus being raised to 72% of the theoretical. The ester, purified from alcohol, melted at 139·5° (corr.) (Found : C, 81·4; H, 8·7. $C_{22}H_{28}O_2$ requires C, 81·5; H, 8·6%).

Menthyl 1-naphthoate was also prepared in order to determine its rotatory power in certain solvents at $c = 5$, these values not being available in the literature.

Molecular Rotatory Powers.

The following rotatory powers were determined at approximately 20° in a 1 dcm. tube, except in a few cases marked *, in which $l = 2$. Densities were measured in a pyknometer holding 2—3 c.c. For values of $[M]_{5461}$ see Tables I and II.

Solvent.	c.	$[M]_{6708}$.	$[M]_{5893}$.	$[M]_{4358}$.
		l-*Menthyl* 1-*naphthoate*.		
Alcohol	8·991	—	−247°	—
Benzene	4·938	−201°	273	−560°
Chloroform	4·990	172	222	461
		l-*Menthyl* 4-*nitro*-1-*naphthoate*.		
Benzene	1·690	212	246	—
		l-*Menthyl* 5-*nitro*-1-*naphthoate*.		
*Benzene	4·920	197	259	—
*Chloroform	5·038	183	240	—
		l-*Menthyl* 8-*nitro*-1-*naphthoate*.†		
Carbon disulphide	1·618	356	504	—
Benzene	1·688	—	672	—
Chloroform	1·662	244	333	—
		l-*Menthyl* 8-*chloro*-1-*naphthoate*.		
Benzene	5·047	98·2	140·5	—
Chloroform	4·411	105	152	—
		l-*Menthyl* 2-*methyl*-1-*naphthoate*.		
*Benzene	4·977	60·9	81·4	189
*Chloroform	5·053	114·5	160	359
		l-*Menthyl* 3-*hydroxy*-2-*naphthoate*.		
Benzene	5·060	257	351	734
Chloroform	5·054	197	250	537
		l-*Menthyl* 1-*hydroxy*-2-*naphthoate*.‡		
Benzene	5·029	235	318	—
Chloroform	4·979	215	282	—
*Alcohol	0·495	198	270	553
*Alcohol + KOEt	0·636	—	250	—
		l-*Menthyl* 3-*chloro*-2-*naphthoate*.		
Benzene	3·781	182	237	483
Chloroform	3·956	148	191	373

† Figures for this ester are approximate only; see p. 2521.
‡ This ester is only very sparingly soluble in alcohol.

In certain of the above cases it was not possible to read values for λ_{4358} owing to selective absorption in the violet region.

Summary.

1. The rotatory power of *l*-menthyl 1-naphthoate is diminished in the sense $\mathrm{OMe} < \mathrm{CH_3} < \mathrm{H}$, and of the 2-naphthoate in the sense

$OMe < Cl < H$, when one of these substituents is introduced into a position adjacent to the carboxylic complex. The relative effects are in the same order as those observed among the *o*-substituted benzoic esters and are in agreement with the *o,p*-directive powers of the groups in benzene substitution.

2. Similarly among the 8-substituted 1-naphthoates the relative influence is given by $OMe < Cl < H < NO_2$, the *m*-directive nitro-group raising the rotation. The parallelism thus established between substituent effects in the peri- and ortho-positions is regarded as proof that the influence is propagated directly through space.

3. In the 4- and 5-positions, methoxyl and the nitro-group have very little influence on the rotatory power.

4. The 1 : 2- and 3 : 2-hydroxynaphthoic esters resemble *l*-menthyl salicylate in having abnormally high rotatory powers, high solubility in benzene, and very low solubility in alcohol. They are probably of chelate type. The potassium salt of the former ester has a diminished rotation in alcohol.

5. Values obtained in different solvents suggest the possibility that the characteristic influence may be electrostatic in nature. The effect of a given group, whether in diminishing or increasing the rotation of the parent compound, tends to be exerted to its maximum extent in solvents of low dielectric constant.

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