

CCI.—*Optical Activity and the Polarity of Substituent Groups. Part XVIII. 1-Menthyl and d- β -Octyl Esters of Picolinic, Quinaldinic, Nicotinic, and Cinchoninic Acids.*

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IN agreement with the theoretical considerations advanced in earlier communications (Rule, J., 1927, 54; *Trans. Faraday Soc.*, 1930, 328), it has been found that optically active menthyl and octyl

esters of acetic and ortho-substituted benzoic acids containing basic substituents have, in general, relatively low rotatory powers, which rise when the compounds are examined in the form of their hydrochlorides. Exceptional behaviour in this respect is shown by β -octyl *p*-dimethylamino- and *p*-amino-benzoates, both of which possess unusually high rotatory powers when compared with the remaining *p*-derivatives. These values fall in the presence of acid, although still remaining relatively high (J., 1929, 401, 2274).

In discussing the above optical changes it was noted that the exceptionally high rotations of the basic *p*-esters were accompanied by high boiling points, but the molecular weights in benzene solution proved to be normal and thus gave no support to the idea of intermolecular association. Substituents in the 1:4-position may, however, be brought into close spatial proximity, as has long been recognised in formulæ such as that advanced for diazobenzene-sulphonic acid. Hence it was concluded that the abnormal optical properties of the esters were possibly the result of interaction between the two groups in the 1:4-positions.

On stereochemical grounds such a relationship between the para-positions would appear to be much less probable in the case of esters of the corresponding pyridine- and quinoline-carboxylic acids. Accordingly, derivatives of this type have now been examined in order to determine the influence of salt formation upon the optical rotation. Quinoline- and pyridine-carboxylic acids are difficult to obtain and give very poor yields of their menthyl and octyl esters. For this reason the octyl compounds were made the chief subject of investigation. *l*-Menthyl esters of *m*- and *p*-substituted benzoic acids have been shown by Cohen to differ little from the unsubstituted ester in their optical properties; the menthyl esters examined in the present case were therefore limited to those derived from picolinic and quinaldinic acids.

The observed rotatory powers, $[M]_{5461}$, are summarised below; an analysis of these figures and others given in the experimental section shows that the dispersion of all the compounds under discussion is normal and complex.

	<i>l</i> -Menthyl.		<i>d</i> - β -Octyl.	
	In EtOH.	EtOH + HCl.	In EtOH.	EtOH + HCl.
Picolinate	-236°	-225°	+107°	+ 97°
Quinaldinate	-252	-292	+139	+113
Nicotinate	—	—	+103	+106
Cinchoninate	—	—	+ 69	+ 99

The rotatory powers of the above basic esters are low in comparison with those of the corresponding benzoates and naphthoates, the figures for which are appended below. For this purpose picolinates

and nicotines are to be compared with benzoates, quinaldines with 2-naphthoates, and cinchonines with 1-naphthoates.

Rotatory Powers, $[M]_{5461}$, in Alcohol ($c = 5$).

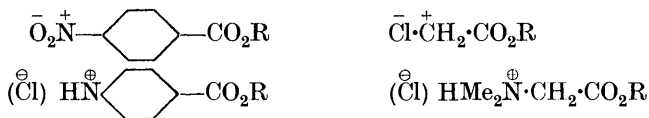
	Benzoate.	1-Naphthoate.	2-Naphthoate.
<i>l</i> -Menthyl	-275°	-302° (in MeOH) †	($[M]_D$ -288° in C_6H_6)
<i>d</i> - β -Octyl *	+111	+ 64.5	+157

* Kenyon and Pickard, J., 1915, **107**, 115.

† Rule and McLean, this vol., p. 674.

The only exception to the above statement is found in octyl cinchoninate, in which the presence of the N-atom brings about a slight rise as compared with the 1-naphthoate. This increase, however, is insignificant in comparison with that due to the basic groups in the *p*-dimethylaminobenzoate (+ 213°; hydrochloride + 147°) and the *p*-aminobenzoate (+ 163°; hydrochloride + 109°).

In *octyl nicotinate* and *cinchoninate*, having the nitrogen in the 3- and the 4-position respectively, the conversion of the basic ester into the hydrochloride is accompanied by a definite rise in rotation, which is of considerable magnitude in the case of the cinchoninic derivative. These compounds and their hydrochlorides therefore conform to the general rule covering the great majority of *l*-menthyl and β -octyl esters so far examined, namely, that the presence of an electron-attracting group situated so as to withdraw electrons from the active ester complex results in an increased rotatory power.



Among the picolinic and quinaldinic esters, in which the nitrogen atom is closer to the ester complex, no general conclusion can be drawn as to the influence of ionisation. *l*-Menthyl quinaldinate, the only solid ester in the group, possesses a much higher rotation in the form of its hydrochloride; but for *d*-octyl quinaldinate and the *menthyl* and *octyl picolinates* the change is in the reverse direction.

The results in the case of the picolinic and quinaldinic esters are unexpectedly irregular, and appear to show that in these compounds the observed changes depend to a considerable degree upon the molecular constitution of the ester radical present, and also upon small modifications in the structure of the acid. Similar variations may be observed in other series and in the rotatory powers of the benzoates and naphthoates recorded above, among which the value for *d*-octyl 1-naphthoate is very low compared with that of the menthyl ester. The normal optical properties of *d*- β -octyl cinchoninate afford support for the earlier suggestion that the ex-

ceptionally high rotations of the *p*-dimethylamino- and *p*-amino-benzoates are the result of chemical interaction between the basic group and the ester complex.

EXPERIMENTAL.

l-Menthyl quinaldinate was prepared by heating *l*-menthol (12 g.) with purified quinaldiny chloride (12 g., m. p. 175—177°). The latter was obtained by treating the acid with thionyl chloride at 60° for 5 hours, dissolving the yellowish solid in fresh thionyl chloride, and precipitating the quinaldiny chloride by the addition of benzene. The esterification is extremely slow, even at 150—170°, and the yield poor, 5 g. being the best obtained from the above quantities. *l*-Menthyl quinaldinate, m. p. 141—142°, separates from light petroleum in colourless crystals, which may be needles or cubical in form, according to conditions. It is sparingly soluble in light petroleum and comparatively insoluble in alcohol (Found: C, 76.9; H, 8.4. $C_{20}H_{25}O_2N$ requires C, 77.1; H, 8.1%).

d- β -Octyl quinaldinate was obtained in very small yield by the above method. It was therefore prepared from the crystalline acid chloride (the lower-melting variety, m. p. 97°; compare Ham-mick and Dickinson, J., 1929, 214), which was converted into the methyl ester by the method of Besthorn and Ibele (*Ber.*, 1906, **39**, 2332). The solid methyl ester (6 g.) was heated with *d*- β -octyl alcohol containing a trace of sodium octyloxide, giving 4 g. of crude octyl ester, $\alpha_{5461} - 1.28^\circ$ ($l = 1$). On fractionation this boiled at 168°/0.6 mm. and gave an oil having $\alpha_{5461} - 1.32^\circ$, the rotation of which remained constant on further fractionation [Found: N, 4.9 (ter Meulen's method). $C_{18}H_{23}O_2N$ requires N, 4.9%].

The optical data for this and the above menthyl ester were confirmed by second preparations.

The following esters were all prepared from the corresponding methyl esters (obtained from the acid by way of the purified acid chloride).

l-Menthyl picolinate was obtained from methyl picolinate, m. p. 14° (Engler, *Ber.*, 1894, **27**, 1785, records m. p. 14°), as a colourless odourless viscous oil, b. p. 170°/1 mm. (yield, 65% of the theoretical) (Found: N, 5.4. $C_{16}H_{23}O_2N$ requires N, 5.4%).

d- β -Octyl picolinate (25% yield) formed an odourless oil, b. p. 170—173°/12 mm., which had a faint yellow colour (Found: N, 5.8. $C_{14}H_{21}O_2N$ requires N, 5.95%).

d- β -Octyl nicotinate, b. p. 142—145°/0.02 mm., was obtained as a colourless liquid in 35% yield (Found: N, 5.9. $C_{14}H_{21}O_2N$ requires N, 5.95%).

d- β -Octyl cinchoninate was obtained from cinchoninic acid (m. p.

240°), prepared by the oxidation of cinchonine. The methyl ester melted at 20° (Meyer, *Monatsh.*, 1901, **22**, 115, records m. p. 24°). Octyl cinchoninate formed a green-tinted viscous oil, b. p. 154—156°/0.3 mm. (yield, 22%) (Found: N, 4.9. $C_{18}H_{23}O_2N$ requires N, 4.9%).

Determinations of Rotatory Power.—The following determinations were made in a 1 dm. tube, except in cases marked with an asterisk, for which $l = 2$. Solvent alcohol was dried over calcium.

Solvent.	c.	$[M]_{6708}^{18^\circ}$.	$[M]_{5895}^{18^\circ}$.	$[M]_{4358}^{18^\circ}$.
<i>l-Menthyl quinaldinate.</i>				
Alcohol *	0.9856	-182°	-216°	-418°
EtOH + 4HCl	0.8696	-192	-252	-540
<i>d-β-Octyl quinaldinate.</i>				
Alcohol	3.808	+81.6	+112	+253
EtOH + 1HCl	3.370	+76.2	+99.0	+232
<i>l-Menthyl picolinate.</i>				
EtOH	4.368	-162	-199	-399
EtOH + 1HCl	4.363	-152	-192	-376
<i>d-β-Octyl picolinate.</i>				
EtOH	5.240	+70.0	+89.3	+191
EtOH + 1HCl	6.810	+62.5	+80.8	+176
<i>d-β-Octyl nicotinate.</i>				
Homogeneous	$(d_4^{18^\circ} 0.9887)$	+61.0	+81.0	+163
EtOH	5.016	+65.7	+86.8	+179
EtOH + 1HCl	5.132	+67.4	+87.5	+184
<i>d-β-Octyl cinchoninate.</i>				
Homogeneous	$(d_4^{18^\circ} 1.0430)$	+17.7	+21.8	—
EtOH	5.048	+46.0	+59.0	+121
EtOH + 1HCl	5.000	+58.2	+86.1	+193

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