CCXCVI.—*Optical Activity and the Polarity of Substituent Groups. Part XI.* sec.-β-*Octyl Esters of Benzoic Acids containing Basic and Acidic Substituents.*

By H. Gordon Rule, John Bramwell Miles, and (in part) W. Eoghan MacGillivray.

During the investigation of a number of *l*-menthyl esters of amino- and dimethylamino-benzoic acids (this vol., p. 401), great difficulty was experienced in isolating the pure compounds in good yield either by way of the acid chloride or by esterification in the presence of hydrogen chloride. Their preparation was ultimately achieved only by the sacrifice of an unduly large amount of menthol, and before undertaking the examination of similar esters of *sec.*-β-octyl alcohol, the optically active forms of which are much less accessible than menthol, it was considered advisable to discover a better means of approaching these compounds.

Experiment showed that the alternative method previously employed for the preparation of *l*-menthyl *o*-dimethylaminobenzoate (*loc. cit.*) gave satisfactory results. The majority of the esters now described were therefore obtained from the methyl esters (purchased as such, or readily prepared from the free acids), which were added to *d*- or *l*-octyl alcohol (1 mol.) in which had been dissolved a small amount (0·05 atom) of metallic sodium. The mixture was maintained at 130—140° in a small distilling flask, and a slow current of dry air was drawn through it for 3—4 hours. A distillate consisting chiefly of methyl and octyl alcohols was carried over, and the residue in the flask, after being washed, dried, and fractionated, gave the optically pure octyl esters in yields varying from 20 to 40%, calculated on the methyl ester. The process is rapidly carried out, requires little attention, and the bulk of unused octyl alcohol is recoverable. The absence of racemisation during the reaction has been proved by hydrolysis, whereby the pure optically active alcohol was regenerated, and also in the case of *l*-menthyl esters by preparing the compounds by other methods.

The rotatory powers $[M]_{5461}$ observed for the various esters at about 16—17°, in the un-ionised state and also in the form of their hydrochlorides or alkali salts, are given below. Values for other wave-lengths of light will be found in the experimental section.

d-sec.-β-*Octyl* o-*substituted benzoates.*

Subst.	Solvent.	*c*.	$[M]_{5461}$.	Subst.	Solvent.	*c*.	$[M]_{5461}$.
o-NH_2	EtOH	6	+ 21·0°	*o*-CO_2H	Homog. (90°)*	—	+110·8°
	,, + 1HCl	6	+ 63·7		EtOH *	5	+163
o-NMe_2	Homog.	—	+ 32·1		,, Na salt	1	+112·6
	EtOH	5	+ 31·7		,, ,,	5	+ 88·3
	MeOH	5	+ 27·1		,, ,,	15	+ 44·7
	EtOH + 1HCl	5	+ 68·5		,, ,,	25	+ 57·6
	,, + 2HCl	5	+ 70·0		H_2O, Na salt	1	+133·0
	,, + 4HCl	5	+ 70·9		,, ,,	5	+ 45·2
o-OH	Homog.	—	+ 90·9		,, ,,	15	− 10·0
	EtOH	5	+105		,, ,,	30	− 37·2
	,, + NaOEt	5	− 21·5				
	,, + KOEt	5	− 24·4				

d-sec.-β-*Octyl* m- *and* p-*substituted benzoates.*

m-NH_2	EtOH	6	+121	*p*-NMe_2	Homog.	—	+191
	,, + 1HCl	6	+119		EtOH	5	+213
p-NH_2	EtOH	4	+163		,, + 1HCl	5	+147
	,, + 1HCl	4	+109	*p*-CO_2H	EtOH *	5	+145
					,, Na salt	1	+148
					H_2O, Na salt	1	+169
					,, ,,	5	+172
					,, ,,	15	+168

* See J., 1928, 178.

In the above tables rotations are given as for *d*-octyl esters in order to facilitate comparison, although in some cases the measurements were actually carried out on the *l*-isomeride. For *d*-octyl benzoate (homog.) Pickard and Kenyon record $[M]^{20^\circ}_{5461}$ + 91·9° (J., 1915, **107**, 115).

Dispersion.—The dispersion of the octyl esters under discussion is not only considerably more complex than that of the corresponding *l*-menthyl esters, but becomes definitely anomalous in the cases of the *o*-amino- and *o*-dimethylamino-derivatives in alcoholic solution. These basic esters exhibit a strong fluorescence and selective absorption in the violet region. For both compounds the dispersion of the hydrochloride is much less complex than that of the free base. *d*-Octyl salicylate, on the other hand, has a slightly complex dispersion in the homogeneous state or in alcohol, and this becomes highly complex in alcohol containing a molecular equivalent of potassium ethoxide, the rotations in the latter case being negative in sign. The *p*-amino- and *p*-dimethylamino-benzoic esters have abnormally high rotations, and whether in the free state or in the form of the hydrochlorides are normal and approximately simple in their dispersion. Dispersion ratios $\alpha_{4358}/\alpha_{5893}$ are given on p. 2280,

o-*Substituted Benzoic Esters.*

Among these compounds, as among other optically active esters of *o*-substituted benzoic acids, the presence of a substituent of *o,p*-directive type leads to a fall in rotatory power, which is very pronounced in the amino- and dimethylamino-derivatives. The effect of the hydroxyl group is small, probably owing to its existing largely in the form of a chelate ring. It has previously been observed (*loc. cit.*) that both *l*-menthyl salicylate and *l*-menthyl anthranilate have higher rotatory powers than the unsubstituted benzoate, and the abnormal influence of the *o,p*-directive grouping in these compounds has been ascribed to chelation. If this view is correct, the marked depression caused by the amino-group in the octyl series, coupled with the slight fall due to the hydroxyl, implies, first, that these octyl esters are less completely chelated than the corresponding menthyl compounds (a not improbable consequence of the greater intramolecular vibration due to the open octyl chain as compared with the rigid menthyl ring), and secondly, that the amino-group is less prone to enter into the chelate state than the hydroxyl group. The latter conclusion is in agreement with the chemical evidence. Sidgwick ("The Electronic Theory of Valency," p. 117) has expressed the opinion that "with hydrogen, co-ordination only occurs readily if it is in a hydroxyl group, . . . when the hydrogen is attached to nitrogen, as in the amines, it can occur, but much less readily."

The relative changes produced by substituents when introduced into the *o*-position in octyl benzoate (I) and menthyl benzoate (II) can now be written as follows ($^{\ominus}$ denotes in alcoholic solution) :

I. $NO_2 > CO_2H > H,OH > Me > Br > Cl > I > OMe > NMe_2 > NH_2^{\ominus}$
II. $NO_2 > CO_2H > NH_2^{\ominus} > OH > H > I > Me > Br > NMe_2 > Cl > OMe$

It is evident that the differences between the two series are mainly due to the different positions taken up by the basic groups.

Influence of Ionisation.—As in the case of the menthyl derivatives, the conversion of the basic esters into their hydrochlorides (formation of a positive pole) results in an increased rotatory power, although in the octyl compounds the values do not rise above that for the unsubstituted benzoate. The transformation of octyl salicylate into its potassium compound (formation of a negative pole) lowers the rotatory power to such an extent that the sign is inverted. This change is much greater than that undergone by menthyl salicylate under similar conditions.

An interesting case is that of *d*-octyl hydrogen phthalate, in which the substituent in the ortho-position is *m*-directive in type. This ester, in the homogeneous state or in alcoholic solution, has a considerably higher rotatory power than the benzoate. In the form of the sodium salt, however, the value is diminished and falls rapidly with increasing concentration, a minimum ($[M]^{20^\circ}_{5461} \doteqdot + 43^\circ$)

occurring in alcoholic solution at a concentration of $c = ca.\ 18$. In aqueous solution the rotatory power falls even more rapidly and becomes negative in sign at concentrations above $c = 13$.

All the foregoing changes on ionisation are in the direction anticipated from the known orientation effects of positive and negative poles in benzene substitution, and may be summarised in the statement that an ortho-substituent of *m*-directive type tends to raise the rotatory powers of menthyl and *sec.*-β-octyl benzoates, whereas one of *o,p*-directive type tends to diminish the values.

p- *and* m-*Substituted Esters.*

An amino- or a dimethylamino-group introduced into the *p*-position brings about an abnormal increase in the rotatory power of octyl benzoate. Whereas the values of $[M]_{5461}$ for the *p*-toluic and the *p*-chloro-, -bromo-, -methoxy-, -nitro-, and -carboxy-esters all lie within the range 123—145°, the *p*-amino- and *p*-dimethylamino-compounds possess the unexpectedly high rotations of 163° and 213°, respectively. The high rotatory powers are only a characteristic of the free basic esters, as the values for the hydrochlorides are of normal magnitude.

In the case of octyl hydrogen terephthalate the ionisation of the carboxyl group is almost without effect, resulting only in a rise of 2—3°. Sodium octyl terephthalate also differs from the ortho-isomeride in having a rotatory power which is practically independent of the concentration.

Octyl *m*-aminobenzoate was the only meta-derivative prepared, and the properties of this compound lie between those of the ortho- and para-isomerides. Attempts to isolate octyl hydrogen *iso*phthalate and the *m*- and *p*-hydroxybenzoic esters were unsuccessful.

The influence of substituents in the para-position does not appear to conform rigidly to any simple generalisation, although the suggestion made in an earlier communication (J., 1928, 181) that it is of the *general polar* type covers the majority of cases. A comparison of the rotatory powers of various *p*-substituted octyl benzoates gives the following sequence :

	$\overset{+}{N}Me_2H$.	$\overset{+}{N}\overset{-}{O}_2$.*	CO_2H.	Br.†	OMe.	Cl.	Me.	H.
$[M]^{20°}_{5461}$	147	145·2	145	140	136	124	123·5	92

* By interpolation (J., 1926, 2116). † Rule and Paul, unpublished result.

It will be observed that the esters having the highest rotations are those in which a positive pole or other group with a powerful attraction for electrons is directly attached to the para carbon atom : the lowest values are for the esters of the less acidic toluic and benzoic acids. The order of these groups agrees approximately with the series, NO_2, CO_2H, Cl, Br, OMe, H, Me, deduced from the rate of hydrolysis of *p*-substituted benzyl chlorides (Olivier) and the esterification of substituted benzoic anhydrides (Rule and Paterson, J., 1924, **125**, 2155). The direction of the change in rotation also corresponds with the influence of these groups in the monosubstituted acetic esters (J., 1925, **127**, 2188; 1926, 3202). There is thus some evidence in support of the view that the *general polar influence* is the main effect operating among the *p*-substituted benzoic esters of octyl alcohol.

On this supposition, however, exceptional values of $[M]_{5461}$ are given by the *p*-dimethylamino- (213°) and the *p*-amino-ester (unionised, 163°; ionised, 102°). The abnormally high rotations of the basic esters are accompanied by high boiling points (*p*-NH_2, 200°/8 mm.; *p*-NMe_2, 180°/1·8 mm.) as compared with a normal ester (*e.g.*, *p*-OMe, 189°/13 mm.), and were thought to indicate molecular association. Molecular-weight determinations in benzene solution gave normal values (272, 276; calc., 278), and hence negative the idea of intermolecular association, although there remains the possibility that the optical properties are a result of interaction between the two groups in the para-position. The unusual physical properties of isomeric benzene derivatives containing an amino- or a dimethylamino-group and an ester group have been commented upon by Sidgwick (J., 1920, **117**, 392).

Another rotatory power which is not in agreement with the *general polar* hypothesis is that of sodium octyl terephthalate, which tends to be higher than for the free acid ester. In this connexion it is well known that carboxylic acids form definite complexes with esters (Kendall and Booge, *J. Amer. Chem. Soc.*, 1916, **38**, 1712), hence the molecular rotation calculated for the acid ester (containing both carboxyl and ester groups) may not represent that of the simple *p*-carboxy-compound. In addition, the influence of the negative pole in the salt would be expected to be considerably diminished owing to the intervention of a carbon atom between it and the benzene nucleus.

EXPERIMENTAL.

The following esters were prepared by the method already described from methyl esters which had been purified by recrystallisation or fractional distillation. For further experimental details, see previous communications.

l-sec.-β-*Octyl anthranilate* was obtained as an odourless, pale yellow oil, b. p. 183°/10 mm., having a pronounced violet fluorescence (Found : N, 5·8. $C_{15}H_{23}O_2N$ requires N, 5·6%). After determination of the rotatory power, the remaining ester was hydrolysed;

the liberated alcohol after a single distillation had $\alpha_D^{16^\circ} = -8{\cdot}08^\circ$ ($l = 1$) (for original alcohol, $\alpha_D^{16^\circ} = -8{\cdot}12^\circ$). Owing to the small amount available, further fractionation was not attempted, but it is evident that the optical activity had not been affected appreciably (see also Pickard and Kenyon, on the action of alkalis on esters of optically active secondary alcohols, J., 1911, **99**, 62).

l-β-*Octyl* p-*aminobenzoate*, b. p. 200°/10 mm., formed a white solid on cooling. After recrystallisation from light petroleum it melted at 69—70°. Gentle warming with excess of aqueous hydrochloric acid, followed by evaporation in a vacuum, gave the solid hydrochloride, m. p. 131—133°; yield of optically pure ester, 21% of the theoretical (Found, by ter Meulen's catalytic method: N, 5·6. $C_{15}H_{23}O_2N$ requires N, 5·6%).

d-β-*Octyl* o-*dimethylaminobenzoate*, b. p. 126°/0·2 mm., was obtained (yield, 22%) as an odourless and almost colourless liquid. It has a violet fluorescence and is soluble in dilute acids (Found: N, 5·2. $C_{17}H_{27}O_2N$ requires N, 5·1%).

d-β-*Octyl* p-*dimethylaminobenzoate*, b. p. 180°/1·8 mm. (yield 40%), is a colourless oil with a violet fluorescence. Unlike the menthyl ester, it is soluble in dilute acids. Considerable difficulty was encountered in attempting to analyse this ester for nitrogen by the Dumas method, variable amounts of an inflammable gas (probably methane or ethane) escaping oxidation and being collected with the nitrogen. Analysis was readily effected by ter Meulen's hydrogenation method, nickel being used as catalyst (Found: N, 5·0. $C_{17}H_{27}O_2N$ requires N, 5·05%).

d-β-*Octyl salicylate*, b. p. 170°/10 mm., distilled as a colourless oil (yield, 39%), miscible with organic liquids (Found: C, 71·9; H, 9·0. $C_{15}H_{22}O_2$ requires C, 71·9; H, 8·8%).

The alkyloxide method gave unsatisfactory results in the case of the *m*-aminobenzoate, of which only a 10% yield of crude ester was obtained. This compound was therefore prepared by reducing the optically pure *l*-octyl *m*-nitrobenzoate (Rule and Numbers, J., 1926, 2116) with aluminium amalgam as recommended by Auwers and Rohrig (*Ber.*, 1897, **30**, 989), double the amount of amalgam employed by these authors being used. The pale yellow l-*octyl* m-*aminobenzoate* was collected at 195—198°/18 mm., but as slight decomposition appeared to occur it was not further fractionated (yield, 20%). Attempts were made to discover a solid derivative by which purification could be effected, but without success, and the ester was then analysed and examined in the crude state (Found, by ter Meulen's method: N, 5·3. $C_{15}H_{23}O_2N$ requires N, 5·6%).

No yield of octyl ester was obtained by the alkyloxide method from methyl *m*- or *p*-hydroxybenzoate, probably owing to the insolubility of the sodium derivative under the conditions of experiment; nor was it practicable to convert the free *m*- or *p*-hydroxy-acid into the octyl ester, either by direct esterification or by the use of thionyl chloride (compare menthyl esters, this vol., p. 403).

The rotatory powers of sodium *d*-octyl phthalate and terephthalate were determined in 5% aqueous and alcoholic solutions. As the rotatory power of the phthalate was found to vary markedly with the concentration, the determinations with both isomerides were extended up to the neighbourhood of the saturation points. The terephthalate required for this purpose was prepared by the half hydrolysis of di-*d*-octyl terephthalate dissolved in pure *d*-octyl alcohol (J., 1928, 178). Di-*d*-octyl *iso*phthalate was also prepared as an oil which could not be distilled without decomposition, but an attempt to convert this into the octyl hydrogen *iso*phthalate by the same method led only to the isolation of potassium phthalate and unchanged ester.

Measurements of Rotatory Power.

The following measurements were made at room temperature (15—17°) in a 2-dcm. tube, except in cases marked * for which $l = 1$. References to hydrogen chloride and sodium or potassium ethoxide denote molecular equivalents. Rotations for λ 5461 have already been given (p. 2275).

Solvent.	c.	$[M]_{6708}$.	$[M]_{5893}$.	$[M]_{4358}$.	$\alpha_{4358}/\alpha_{5893}$.
1-β-*Octyl anthranilate.*					
*EtOH	6·033	− 25°	− 23°	+ 67°	—
EtOH + HCl	5·517	− 41·8	− 54·7	− 97·9	1·79
1-β-*Octyl* m-*aminobenzoate.*					
*EtOH	6·391	− 92·8	−108	−226	2·09
*EtOH + HCl	6·160	− 77·3	−102	[−204] [1]	[1·99] [1]
1-β-*Octyl* p-*aminobenzoate.*					
*EtOH	4·317	−107	−134	−319	2·37
*EtOH + HCl	4·051	− 84·3	− 96·0	−212	2·21
d-β-*Octyl* o-*dimethylaminobenzoate.*					
Homog.	($d_{4°}^{17°}$ 0·9772)	+ 23·2	+ 28·1	—	—
EtOH	5·112	+ 24·1	+ 29·6	+ 12·2	0·41
*MeOH	4·714	—	—	+ 4·7	—
*EtOH + 1HCl	4·975	+ 47·9	+ 57·9	+119	2·06
d-β-*Octyl* p-*dimethylaminobenzoate.*					
Homog.	($d_{4°}^{16°}$ 0·9897)	+114·1	+156·4	[+372] [1]	2·38
EtOH	5·069	+131	+174	+431	2·48
EtOH + HCl	5·009	+ 89·7	+123·0	+271	2·21

---

[1] These figures are approximate only; owing to the strong absorption of violet light they were determined in a 0·5-dcm. tube.

Solvent.	c.	$[M]_{6708}$.	$[M]_{5893}$.	$[M]_{4358}$.	$\alpha_{4358}/\alpha_{5893}$.
	d-β-Octyl salicylate.				
*Homog.	($d_{4^\circ}^{18^\circ}$ 1·009)	+ 59·2	+ 78·2	+141·5	1·81
EtOH	5·023	+ 67·0	+ 93·1	+155	1·67
EtOH + KOEt	5·546	− 4·5	− 13·3	−139	10·42
	(With W. E. MacGillivray.)				
	Sodium d-β-octyl phthalate.				
EtOH	0·9948 [1]	—	—	+205	—
	5·158	+ 53·1	+ 71·6	+162	2·26
	15·56	+ 27·2	+ 36·8	+ 81·8	2·22
	25·03	+ 37·0	+ 48·3	+100·5	2·08
H_2O	0·9876 [1]	—	—	+238	—
	5·229	+ 31·2	+ 39·3	+ 68·3	1·74
	15·29	− 1·73	− 5·46	− 41·5	7·62
	29·93	− 17·7	− 26·6	− 98·4	3·71
	Sodium d-β-octyl terephthalate.				
EtOH	0·9932 [2]	—	—	+256	—
H_2O	1·015 [2]	+104	+137	+318	2·32
	5·009	+104	+143	+318	2·22
	14·54	+103	+140	+305	2·18

[1] In a 4-dcm. tube.

[2] In a 4-dcm. tube. The salt is very sparingly soluble in alcohol.

Summary.

The examination of optically active *sec.*-β-octyl esters of benzoic acids containing ionisable substituents shows that the relative changes in rotatory power due to different *ortho*-substituents are as follows :

$$NO_2 > CO_2H > H,OH > Me > Br > Cl > I > OMe > NMe_2 > NH_2.$$

Ionisation of the carboxyl or hydroxyl group strongly depresses the rotatory power, and in both cases the sign of the rotation may be inverted. Ionisation of the basic groupings leads to a considerable increase in rotatory power. The free basic esters exhibit anomalous dispersion.

Among the para-compounds, the dimethylamino- and amino-esters have abnormally high rotations, which fall to a normal level on ionisation. The ionisation of a *p*-carboxyl group produces no appreciable change.

The *o*- and *p*-amino- and -dimethylamino-esters and octyl salicylate are readily prepared in the optically pure state by heating the corresponding methyl esters with octyl alcohol in which a small amount of metallic sodium has been dissolved.

UNIVERSITY OF EDINBURGH. [*Received, September 2nd,* 1929.]