

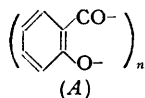
236. *The Stereochemistry of the Salicylides and Some Related Compounds.*

By P. G. EDGERLEY and L. E. SUTTON.

Following the discovery that " α - and β -disalicylides" are not stereoisomers but are the only known forms of di- and tri-salicylides respectively (Baker, Ollis, and Zealley, *Nature*, 1949, **164**, 1049; Edgerley and Sutton, *ibid.*, p. 1050; Baker, Ollis, and Zealley, *J.*, 1951, 201), a systematic study of the electric dipole moments of these compounds, the tetrasalicylide, and of the corresponding cresotides has been made. From the results it is possible to give a consistent account of the stereochemistry of these systems. It has also been shown that there is likely to be steric hindrance between certain atoms in phenyl acetate and some related esters.

CERTAIN anhydro-derivatives of salicylic acid are known, *viz.*, (A) where n is 2, 3, 4, or more (see R. Anschütz, *Ber.*, 1919, **52**, 1880, and later works by L. Anschütz *et al.*; and, especially,

Baker, Ollis, and Zealley, *Nature*, 1949, **164**, 1049; *idem* with Gilbert, *Chem. and Ind.*, 1950, 333; *J.*, 1951, 201, 208). Such compounds raise interesting stereochemical problems since, in theory, it is possible to obtain several different stereoisomeric modifications of each polymer. At the request of Professor W. Baker, we undertook the investigation of what were then thought to be the two



stereoisomers of disalicylide, by measuring their dipole moments in benzene solution.

The *trans*-form Fig. 1a, should have a dipole moment of approximately zero (one might expect a small apparent moment due to atom polarisation) and the *cis*-form Fig. 1b, ought to have one of about 6.0—6.2 D. (see "Discussion" below). In actuality, while the compound known as α -disalicylide, to which the *cis*-configuration had been tentatively ascribed, has the predicted

dipole moment (actually 6.26 D.), the other "isomer" has a moment of 2.41 D. This high value is unlikely to arise from atom polarisation. Professor Baker and his co-workers therefore

FIG. 1a.

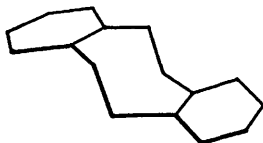
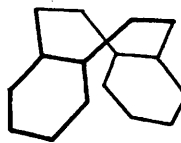


FIG. 1b.



remeasured the molecular weight of " β -disalicylide" and showed that it is not a dimer but is a trimer, so that its dipole moment is really 2.95 D. Following this discovery, a systematic study of the salicylides and the corresponding *o*-, *m*-, and *p*-cresotides has been made in the hope of finding out more about the stereochemistry of such systems.

RESULTS.

The preparative and molecular-weight determination work which is reported elsewhere (Baker *et al.*, *loc. cit.*) has indicated that each polymer is ordinarily obtainable in only one form, contrary to earlier results for the dimers. The dipole moments, in benzene solution, of di-, tri-, and tetra-salicylides and of most of the corresponding derivatives from three of the cresotic acids are shown in the annexed Table. The compounds were all sparingly soluble in benzene

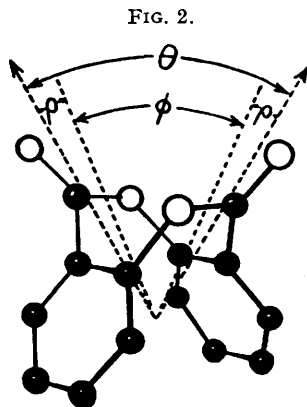
	Di-	Tri-	Tetra-		Di-	Tri-	Tetra-
Salicylide	6.26	2.95	2.07	<i>m</i> -Cresotide	6.74	3.08	—
<i>o</i> -Cresotide	6.34	4.28	1.25	<i>p</i> -Cresotide	6.67	3.18	—

All dipole moments were measured in benzene solution at 25° and are quoted in Debye units (see Experimental section).

so it was necessary to warm the mixture to about 70° to ensure complete dissolution. There was no indication, such as the change of polarisation with time, that such treatment caused any change within the molecules.

DISCUSSION.

cis-Disalicylide is represented on Fig. 2. The geometry of ring systems of this sort is variable (see Baker, Banks, Lyon, and Mann, *J.*, 1945, 27), but, in the configuration shown, the resonance energy should be a maximum (see below) for in it the lactone groups are coplanar. The moment of the compound should then be approximately the resultant of two lactone-group moments (each of 4.1 D.; Marsden and Sutton, *J.*, 1936, 1383) at an angle θ , which can be calculated if the angles ϕ and ρ are known (see Fig. 2). The angles Ph-C-O and Ph-O-C (where O is the bridge-oxygen atom) may be assumed to lie between the limits 109.5° and 120°. Since the rest of the geometry of the molecule is determined by the benzene rings, $\phi = 64.5-70.5^\circ$. The value of ρ , which is controlled by the direction of the *cis*-ester-group moment, has been estimated by Mr. L. E. Orgel (private communication) from a molecular-orbital calculation to be about 27°. θ is therefore 82-86°, and the calculated moment is 6.2-6.0 D.



Plates Ia and Ib show a scale model of di-*o*-cresotide. It can be seen (Plate Ia) that there is no interference between the methyl groups and any other atom or group of atoms in the molecule; also the two groups are in such positions (Plate Ib) as to produce a resultant moment of zero. The small difference between the dipole moments of disalicylide and di-*o*-cresotide is not

significant. It may be due to a small inductive effect or to the theoretical and practical limitations of the method. The other two isomers have their methyl groups in such positions as to increase the total moment by the same amount. It will be seen (Fig. 2) that the planes of the two benzene rings are set at an angle of 49.5-60° (for Ph-C-O and Ph-O-C = 109.5-120°) which means that the additional moment caused by the presence of the methyl groups in both di-*m*- and di-*p*-cresotides should be 0.7-0.5 D. (the dipole moment of toluene is 0.35-0.40 D). Thus the moments of the two cresotides should be 6.95-6.75 D. For both compounds, the agreement with experiment is as good as can be expected and serves further to verify the *cis*-configuration ascribed.

PLATE Ia.

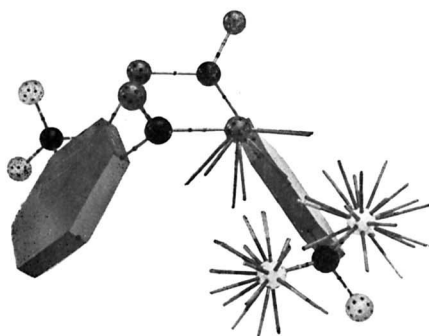


PLATE Ib.

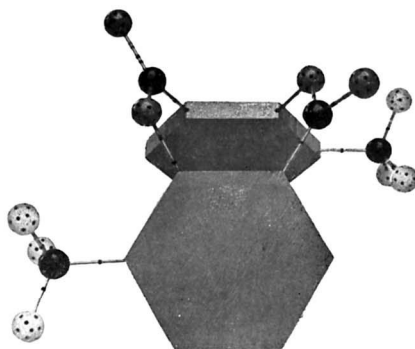
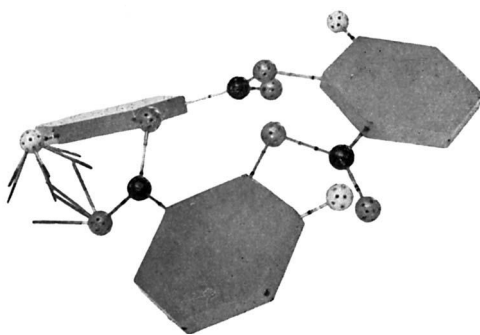


PLATE II.



For the *s*-tribenzcyclo-dodecatriene ring system, which is similar to that of the trisalicylides, Baker, Banks, Lyon, and Mann (*loc. cit.*) showed that there is a continuous series of strainless configurations: there are two configurations of relatively high symmetry, one planar (Photograph 2A) and one trigonal (2D). From our point of view, these are especially interesting. The former contains all three ester groupings in the *trans*-configuration: * and because it is planar it is non-polar. The latter contains all three groupings in the *cis*-configuration, and it is highly polar. The other configurations may be regarded as lying between these two extremes, because they can all be shown to involve a gradual change in the relative degrees of *cis*- and *trans*-character in the ester groupings. We can distinguish an intermediate configuration with two *trans*-ester groupings and one *cis*- (2C), and another with one *trans*- and two *cis*-. From these considerations, it can be seen that the dipole moment of any configuration must lie between that for the planar, triply-*trans*-form, and that for the crown, triply-*cis*-form. The moment of the *trans*-ester grouping may be taken as that of phenyl benzoate—1.9 (Warren, *J.*, 1937, 1858)—and that of the *cis*-form as that of γ -butyrolactone—4.1 (Marsden and Sutton, *loc. cit.*). The calculated moments of the various forms are:

	Moment, D.		Moment, D.
3 <i>trans</i> -, 0 <i>cis</i> -linkages	0.0	1 <i>trans</i> -, 2 <i>cis</i> -linkages	6.5
2 <i>trans</i> -, 1 <i>cis</i> - ,,	4.5	0 <i>trans</i> -, 3 <i>cis</i> - ,,	10.0



From the observed moment (2.95 D.), we may conclude that the actual configuration approaches the planar, non-polar one.

Considering now the effects of steric hindrance which hitherto have been completely ignored, we see (Plate II) that, because of steric hindrance between the carbonyl oxygen atoms and the hydrogen atoms *ortho* to the ring-oxygen atoms, it would be impossible for a planar configuration to be assumed. There is another "planar" configuration of trisalicylide with the three carbonyl groups directed towards the centre: this is also stereochemically impossible, even in a somewhat distorted form. The actual configuration can, therefore, be explained by supposing that each ester group tends to take up the *trans*-configuration, so far as steric hindrance allows; it could be such that the planes of the benzene rings would intersect at the apex of a trigonal pyramid, giving a propeller-like structure. Plate II shows the twisting effect on one of the ester linkages of the overlapping of the van der Waals radii of the hydrogen atom and of the carbonyl oxygen atom † (see below): it also shows the arrangement of the whole molecule.

It is clear that tri-*m*-cresotide and tri-*p*-cresotide adopt the same configuration, for their dipole moments differ only by small amounts from that of trisalicylide. This is in agreement with the above explanation: for the additional methyl groups would not cause further steric hindrance. The *o*-isomer is interesting, in that the hydrogen atom, which in trisalicylide interferes with the carbonyl oxygen atom, is now replaced by the larger methyl group; this gives rise to a stronger repulsion of the carbonyl oxygen atom, which forces the system still further out of a plane and so causes a higher moment (4.28 instead of 2.95).

Rough calculations show that if it is assumed that the distance between the centres of the sterically interfering hydrogen and carbonyl oxygen atoms is the sum of Pauling's van der Waals radii, then the C=O bond is deflected out of the plane of the benzene ring attached to the ring oxygen atom by about 50°, which means that trisalicylide should have a dipole moment of 3.7 D. If the distances are taken as 0.2—0.3 Å. less than these sums, the calculated moment agrees with that observed. A similar calculation for tri-*o*-cresotide shows that there is an out-of-plane deflection of the carbonyl bond of about 90°, which corresponds to a dipole moment of 4.8 D. If an overlap of 0.5 Å. is permissible, then the moment approximates to the value observed. Rough though these calculations are, they serve further to confirm the postulate of steric hindrance in the trimers. The overlap or "contraction" of the van der Waals radii is to be expected. It has been observed before that the use of van der Waals radii in investigating steric hindrance tends to exaggerate the actual interference. Stanley and Adams (*J. Amer. Chem. Soc.*, 1930, 52, 1200) find that a difference of 0.39 Å. or more between the actual and the calculated van der Waals distances is normally necessary and sufficient for optical isomers to be obtainable in the diphenyls with *o*-substituents.

These conclusions are supported by the infra-red spectra of the substances (Short, to be

* *trans* is used to mean  and *cis* to mean , these being the structures with the lower and the higher moment respectively.

† Values for the van der Waals radii are taken from L. Pauling, "The Nature of the Chemical Bond," Cornell, 1940.

published). In the trimers and tetramers the carbonyl-bond frequency is close to where it is normally observed in esters with the exception of tri-*o*-cresotide, where it is somewhat higher. This is in good agreement with the above explanation of the high dipole moment of this compound. The still higher carbonyl-bond frequencies in the dimers is likely to be a result of the presence of *cis*-linkages as opposed to *trans*- or distorted *trans*-linkages.

It seems that tetrasalicylide ($\mu = 2.07$) does not take up a propeller-like structure analogous to that of trisalicylide for the moment of tetra-*o*-cresotide ($\mu = 1.25$) is less and not greater than that of the parent salicylide. From the carbonyl-bond frequencies of the two compounds, it appears that the configuration of the ester linkages is likely to be of the *trans*-type (see above); furthermore as the frequencies are about the same it is unlikely that any steric hindrance in the former is aggravated in the latter. Baker, Ollis, and Zealley (*J.*, 1951, 201) have suggested a configuration for the tetrasalicylide in which planar $\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{CO}$ units are arranged alternately up and down round a central ring of four oxygen atoms. This would normally have an axis of alternating symmetry and be non-planar; but from a model it seems likely that it could lose symmetry by movements of the units parallel to the axis of rotation, and that this could result in considerable change in configuration with relatively little change in the ether-oxygen valency angles. They therefore suggested further that the appreciable dipole moment of the tetrasalicylide is apparent rather than real, and arises from an abnormally large atom polarisation (cf. Coop and Sutton, *J.*, 1938, 1269).

Some support is given to this hypothesis by the moment of the tetra-*o*-cresotide being less than that of the tetrasalicylide. The vibrating moments effective in giving rise to atom polarisation in the latter would be those of the four $\text{O}\cdot\text{C}_6\text{H}_4\cdot\text{CO}$ units perpendicular to the respective $\text{O}\dots\dots\text{O}$ lines, *i.e.*, the moments of two C-O bonds less $\mu(\text{C}=\text{O}) \sin 30^\circ$; and our estimate of this is between 0.68 and 0.40. The effective component of the nuclear *o*-methyl group is $0.4 \sin 30^\circ = 0.2$ and it would reduce the vibrating component. The ratio of the apparent moments for the salicylide and cresotide should therefore be between 0.68 : 0.48 and 0.40 : 0.20, *i.e.*, between 1.3 and 2.0. The actual value is 1.65. It must be emphasised, however, that the vibrating components are individually small, and that therefore, although there are four of them, for this hypothesis to be correct the force constant controlling the vibration must be very small indeed, *i.e.*, there must be very little change in the valency angles as the distortion occurs.

It remains to attempt to explain why each polymer can ordinarily be obtained in only one form, so far as is known, and why it takes up the particular form that it does. In a previous paper by Marsden and Sutton (*loc. cit.*), it was shown that the ester linkage always takes up the *trans*-configuration when there is a free choice. In lactones, however, owing to the restriction imposed by the ring, the *cis*-form is assumed; and, since this appears true even in the ϵ -lactone where the restriction is less complete, it seems that the ester grouping takes up either the *trans*- or the *cis*-configuration but no intermediate one. The fixation in planar configurations

was explained by resonance involving the structure $\begin{array}{c} \text{O}^+ \\ \diagup \\ \text{C} \\ \diagdown \\ \text{O}^- \end{array}$ or $\begin{array}{c} \text{O}^- \\ \diagdown \\ \text{C} \\ \diagup \\ \text{O}^+ \end{array}$, which has double-bond character in the O-C link. Rough calculations indicated that it is necessary to surmount an energy barrier of 5.5—7.5 k.cals./mole in order to pass from one configuration to the other. Thus it can be readily seen why it is not easy to pass from one polysalicylide configuration to another; furthermore, in the dimer the molecule would have to pass through a highly strained intermediate state for the change to happen. The preference for the *trans*-configuration when apparently there is free choice was not explained: but, for the present, we may take it as an empiricism that this preference exists.

In the dimer the ester groupings cannot be planar if the molecule as a whole is *trans*, so much of the resonance energy is lost because the ester groups are twisted out of planarity. In this case, therefore, the *cis*-configuration of the molecule is the more stable for in it, though the ester groups are *cis*, they are planar. In the trimers and tetramers, the configurations with triply- or quadruply-*cis*-ester groups could have these planar, though, as we have seen, because of steric hindrance, co-planarity is not possible if the ester groups are all *trans*. It must, therefore, be supposed that the "*trans* preference" postulated above overweighs the loss of resonance energy when the groups are imperfectly *trans* to this degree. While it is still not possible to give a convincing explanation of this preference in the case of the aliphatic esters, there is a factor in the aromatic compounds discussed in this paper which could cause it or augment it.

In the salicylides and cresotides, there could be conjugation of each ester group with the two phenyl groups attached to it, if the whole system were co-planar. For the dimers, this is impossible for either the *cis*- or the *trans*-configuration: so it need not be taken into account. For the trimers and tetramers, it is not, in fact, completely possible in any configuration: but whereas in the triply-*cis*-configuration, *neither* ring can resonate with an ester grouping, in the distorted triply-*trans*-configuration, one ring can do it with each ester grouping. Therefore, there may be resonance in the latter (involving benzene rings) which is absent in the former and this may compensate for the loss of stabilisation in the latter caused by the ester groups themselves being imperfectly planar (see above). The balance of energy, when steric repulsion is taken into account, may well favour a distorted triply-*trans*-configuration.

It is relevant to remark here that there can only be limited resonance between the ester grouping and the benzene ring in phenyl acetate ($\mu = 1.6$), because there is interference between the carbonyl-oxygen and the hydrogen atom in the *ortho*-position, which inhibits the co-planar configuration, just as in trisalicylide. The moment, therefore, far from being anomalous, as was previously thought (Donle, *Z. physikal. Chem.*, 1931, *B*, **14**, 326; Marsden and Sutton, *loc. cit.*) because it is not greater than that of methyl acetate ($\mu = 1.7$), should be no different apart from a small induced moment. Correspondingly the moments of phenyl benzoate and methyl benzoate should be equal as, in fact, they are.

In the tetramer there is, besides resonance (*a*) in the ester group and (*b*) with benzene rings, and steric repulsion, a fourth factor, *viz.*, bond strain energy. It is hardly possible to predict what the result of their interplay should be.

EXPERIMENTAL.

All the compounds were supplied by Professor W. Baker, Dr. W. D. Ollis, and their co-workers of the University of Bristol. Their methods of preparation and purification have been described (*Nature*, 1949, **164**, 1049; *Chem. and Ind.*, 1950, 333; *J.*, 1951, 201, 208).

Solvent purification and polarisation measurements were carried out in the manner described by Everard and Sutton (*J.*, 1949, 2312). The refractive indices of the solutions were determined on a Pulfrich refractometer. The calculations of the polarisations were performed by the methods advocated by Everard, Hill, and Sutton (*Trans. Faraday Soc.*, 1950, **46**, 417). The symbol convention is the same as in the last-mentioned paper, *viz.*, ω , ϵ , v , and n refer respectively to the weight fraction of solute and the dielectric constant, the specific volume, and the refractive index of the solution, and α , β , and γ are defined by the least square plots of the equations, $\epsilon = \epsilon_1 + \alpha\omega$, $v = v_1 + \beta\omega$, and $n = n_1 + \gamma\omega$.

ω .	ϵ .	v .	Δn .	ω .	ϵ .	v .	Δn .
<i>Disalicylide (formerly α-disalicylide) (I).</i>				<i>Trisalicylide (formerly β-disalicylide) (II).</i>			
0.00066	2.2850	1.14464	—	0.00150 ₅	2.2759	1.14448	—
0.00149	2.2993	1.14435	—	0.00292	2.2796	1.14393	—
0.00290	2.3241	1.14385 *	—	0.00333	—	—	0.00033
0.00360	—	—	0.00027	0.00353	2.2818	1.14360	—
0.00395 ₅	2.3442	1.14355 *	—	0.00463	2.2849	1.14306	—
<i>Tetrasalicylide (III).</i>				<i>Di-o-cresotide (IV).</i>			
0.00089	2.2738	1.14383	—	0.00	—	1.14453	—
0.00158	2.2746	1.14362	—	0.00097	2.2892	1.14425	—
0.00344	2.2771	1.14293	0.00043	0.00163	2.2993	1.14386	—
				0.00203	2.3062	1.14368	—
				0.00390	2.3372	1.14314	0.00029
<i>Tri-o-cresotide (V).</i>				<i>Tetra-o-cresotide (VI).</i>			
0.00	—	1.14583	—	0.00	—	1.14438	—
0.00104	2.2769	1.14537	—	0.00145	2.2740	1.14380	—
0.00338	2.2888	1.14441	0.00023	0.00272 ₅	2.2749	1.14341	—
0.00584	2.3015	1.14338	0.00040	0.00387	2.2752	1.14296	0.00021
<i>Di-m-cresotide (VII).</i>				<i>Tri-m-cresotide (VIII).</i>			
0.00	—	1.14453	—	0.00	—	1.14483	—
0.00166	2.3049	1.14395	—	0.00119	2.2759	1.14422	—
0.00248	2.3190	1.14359	—	0.00227	2.2791	1.14374	—
0.00390	2.3453	1.14308	0.00026	0.00399	2.2840	1.14302	0.00038
<i>Di-p-cresotide (IX).</i>				<i>Tri-p-cresotide (X).</i>			
0.00129	2.2961	1.14428	—	0.00	—	1.14478	—
0.00239	2.3164	1.14389	—	0.00117	2.2760	1.14419	—
0.00383	2.3427	1.14335	0.00028	0.00269	2.2803	1.14370	—
				0.00407	2.2845	1.14314	0.00033

* Values obtained by extrapolation.

Dipole moments of the salicylides and related compounds.

	α .	ϵ_1 .	$-\beta$.	ν_1 .	γ .	πP_1 .	πP_2 .	μ .
(I) ...	17.914	2.2728	0.34	1.14495	0.074	866.5	66.3	6.26 \pm 0.02
(II) ...	2.909	2.2714	0.45	1.14520	0.100	271.4	93.6	2.95 \pm 0.03
(III) ...	1.239	2.2727	0.35	1.14415	0.102	225.7	139.9	2.07 \pm 0.05
(IV) ...	16.458	2.2729	0.36	1.14450	0.073	893.3	72.9	6.34 \pm 0.02
(V) ...	5.124	2.2715	0.41	1.14579	0.068	475.8	101.9	4.28 \pm 0.04
(VI) ...	0.499	2.2733	0.35	1.14432	0.061	172.9	140.1	1.25 \pm 0.10
(VII) ...	18.572	2.2727	0.38	1.14455	0.071	998.8	71.2	6.74 \pm 0.02
(VIII) ...	2.834	2.2727	0.45	1.14479	0.093	297.7	103.7	3.08 \pm 0.03
(IX) ...	18.306	2.2727	0.38	1.14480	0.074	984.9	71.4	6.67 \pm 0.02
(X) ...	2.897	2.2726	0.39	1.14473	0.080	309.8	107.4	3.18 \pm 0.04

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