336. *Studies in Stereochemical Structure. Part VII. The Rotatory Powers and Racemisations of the Optically Active Benzoins.*

By Robert Roger and Alexander McGregor.

The optically active forms of benzoin are often used, but their rotatory powers are quoted only for acetone or ethyl-alcoholic solutions (McKenzie and Wren, J., 1908, **93**, 313; Wren, J., 1909, **95**, 1583, 1593; McKenzie, Roger, and Wills, J., 1926, 779; Hopper and Wilson, J., 1928, 2483; Smith, *Ber.*, 1931, **64**, 427; Weissberger, Dörker, and Schwarze, *Ber.*, 1931, **64**, 1202). It has now been found necessary to make a more elaborate study of the matter in connexion with other work.

The solvents used fall roughly into two classes : (1) acetone, ethyl alcohol, chloroform, carbon disulphide, carbon tetrachloride, and dioxan; and (2) basic nitrogen-containing solvents such as aniline, pyridine, piperidine, diethylamine, and triethylamine.

In the first group of solvents the rotatory powers of *D*-benzoin (obtained from lævorotatory mandelic acid) were lævorotatory for all wave-lengths between λ 6563 and 4358, and within the limited range of temperatures examined :

Solvent.	$[\alpha]_{5461}$.	Dipole moment of solvent, $\mu \times 10^{18}$.	Solvent.	$[\alpha]_{5461}$.	Dipole moment of solvent, $\mu \times 10^{18}$.
$COMe_2$	−144·7°	2·7	Dioxan	−200·5°	0·45
EtOH	−162	1·58	CCl_4	−241·7	0
$CHCl_3$	−253	1·1	CS_2	−494·5	0

The rotatory powers in chloroform and dioxan decreased with increasing temperature: in chloroform $[\alpha]^{0°}_{5461}$ — 269°, $[\alpha]^{20°}_{5461}$ — 253°; $[\alpha]^{35°}_{5461}$ — 240°; in dioxan, $[\alpha]^{20°}_{5461}$ — 200·5°, $[\alpha]^{45°}_{5461}$ — 180°, like mandelic acid and certain of its derivatives (Roger and McKay, J., 1931, 2229; Roger, J., 1932, 2168). The rotatory powers, however, are not in direct relationship to the dipole moment of the solvent (see Rule, Smith, and Harrower, J., 1933, 376; Rule, Barnett, and Cunningham, *ibid.*, p. 1217), for those in dioxan, carbon tetrachloride, and carbon disulphide are out of order. In the last two solvents the optically active benzoins are only sparingly soluble. The Rupe criteria for the various solutions were remarkably constant.

Solvent.	λ_α.	*P.R.D.*	*q*.	Solvent.	λ_α.	*P.R.D.*	*q*.
$COMe_2$	586	176	2·439	CCl_4	594	172	2·296
EtOH	588	176	2·339	CS_2	596	172	2·277
$CHCl_3$	594	174	2·284	Dioxan	589	175	2·323

There is, therefore, probably no change in the structure of benzoin in the various solvents.* Optically active benzoin was recovered unchanged.

The Lowry–Dickson criterion gave curves which departed only slightly from straight lines. The dispersions could all be expressed by modified equations of the type $[\alpha] = K_0/(\lambda^2 - \lambda_0^2) \pm K_1/\lambda^2$; *e.g.*, in chloroform solution :

$$[\alpha] = 38{\cdot}17/(\lambda^2 - 0{\cdot}1008) + 17{\cdot}88/\lambda^2$$

λ	6563	5893	5461	4358
[α] Obs.	157·2°	206·6°	253°	522·3°
[α] Calc.	157·2°	206·5°	253·3°	522·4°

The dispersion of benzoin in these solvents is, therefore, normal and complex.

Accurate determinations of the rotatory powers of the benzoins in aniline and pyridine were possible, but in piperidine, diethylamine, and triethylamine, the determinations were complicated in that the optically active benzoins racemised steadily, and no reliable dispersion figures could be obtained.

Solvent.	$[\alpha]_{5461}$.	$\mu \times 10^{18}$.	Solvent.	$[\alpha]_{5461}$.	$\mu \times 10^{18}$.
Aniline	−247·2°	1·51	Diethylamine *	+131°	0·96
Pyridine	−111	2·11	Triethylamine	+113	0·82
Piperidine *	+ 35·3	—			

* The determinations in piperidine and diethylamine were carried out with *L*-benzoin (obtained from dextrorotatory mandelic acid), and the figures quoted in this table are those values with the signs reversed.

Thus, *D*-benzoin becomes dextrorotatory in the last three solvents, piperidine ranking with the aliphatic amines in this respect.† This reversal of sign is no small one, the extremes of rotatory power being $[\alpha]_{5461} = -494{\cdot}5°$ in carbon disulphide and + 131° in diethylamine for the optically active benzoin derived from (—)mandelic acid. The dispersion of the pyridine solution was expressed by the equation

$$[\alpha] = 29{\cdot}93/(\lambda^2 - 0{\cdot}067) - 5{\cdot}48/\lambda^2.$$

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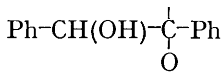
* As an example of how the Rupe criteria may be employed to detect change in chemical structure, see Rupe (*Annalen*, 1922, **428**, 188), where it is shown that camphorcarboxylic acid and certain of its derivatives may have a " bornylene " structure (see also Roger, J., 1932, 2168; Roger and McKay, J., 1931, 2229; Roger and Ritchie, *Biochem. Z.*, 1932, **253**, 239). Pope and Whitworth (*Proc. Roy. Soc.*, 1931, *A*, **134**, 357) used dispersion methods in their study of the isomerisation of the optically active *spiro*-5 : 5-dihydantoins.

† This change of sign causes difficulty in the designation of the optically active benzoins. Thus (—)benzoin in acetone becomes (+)benzoin in diethylamine. Roger (*Helv. Chim. Acta*, 1929, **12**, 1060) used *D*(—)mandelic acid to designate the lævo-acid obtained from amygdalin.

Benzoin contains both a carbonyl and a hydroxyl group, groups of relatively high polarity. Rotatory powers in the various solvents may be complicated by the formation of molecular complexes (see Patterson, J., 1902, **81**, 1111; Patterson and Thomson, *Ber.*, 1907, **40**, 1243; Rule, Barnett, and Cunningham, *loc. cit.*). Another factor enters into the question, however, *viz.*, that of asymmetric induction (cf. McKenzie and Mitchell, *Biochem. Z.*, 1929, **208**, 456, 471; 1930, **221**, 1; 1930, **224**, 242; McKenzie and Ritchie, *ibid.*, 1931, **231**, 412; 1931, **237**, 1; 1932, **250**, 276). Roger (*loc. cit.*) and Roger and Ritchie (*loc. cit.*) have already suggested that this phenomenon plays a part in the building up of the rotatory powers of the isomeric (—)menthyl mandelates, and of the (—)menthyl esters of α-ketonic acids. Roger and Gow (this vol., p. 130) suggested that the rotatory powers of the isomeric (—)menthyl α-naphthylglycollates were controlled in part by the extent to which induction of the induced centres of asymmetry (the carbonyl groups) had taken place. Hudson, Wolfram, and Lowry (J., 1933, 1179) later showed that derivatives of the μ-sugars (the true aldehydic sugars) have a characteristic "carbonyl" absorption band which is optically active, and gives rise to a lævorotation in the visible spectrum, the observed rotation being the algebraic sum of this contribution and the contributions of the centres of fixed asymmetry. Preiswerk and Erlenmeyer (*Helv. Chim. Acta*, 1934, **17**, 329) have studied the dispersion of (—)benzoin and determined the contribution of the carbonyl group to the activity. The observed rotatory powers of the optically active benzoins thus consist of two parts, the contribution of the centre of fixed asymmetry (the mandelyl complex), and that of the centre of induced asymmetry (the benzoyl group) (see inset), and change of solvent will probably markedly change the relative contributions (Kuhn, Freudenberg, and Seidler, *Z. physikal. Chem.*, 1931, **13**, 379). It has been shown that the position of the absorption bands may be affected by change of solvent (Tschugaev, *Ber.*, 1909, **42**, 2244; Schiebe, *Ber.*, 1926, **59**, 2619), and it might be expected that optical activities might be affected as a result of these changes. Kuhn ("Hand- und Jahrbuch der chemischen Physik," 1932, **8**, III, 123) does not support this conclusion. The case of benzoin is complicated by the fact that there is a phenyl group attached to both centres of asymmetry, and the exact nature of the radical R of the CO·R group in ketols derived from mandelic acid may play a considerable part in causing variation of the rotatory powers with solvent. This point is at present under examination.



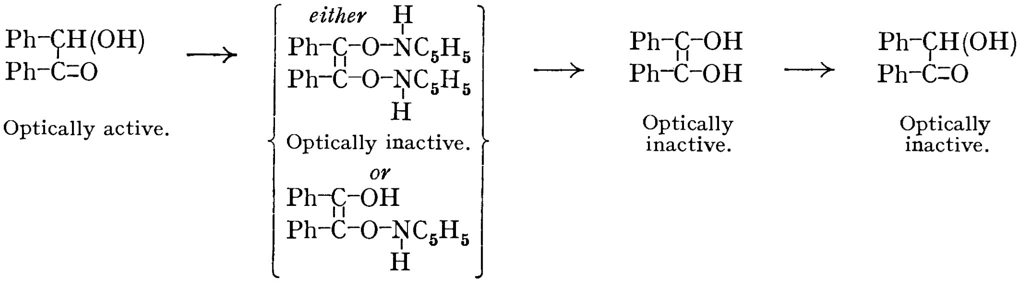
$$\mathrm{Ph{-}CH(OH){-}\underset{\underset{\displaystyle O}{|}}{\overset{|}{C}}{-}Ph}$$

The racemisation of *D*(—)benzoin with alcoholic potash has already been studied by McKenzie and Wren (*loc. cit.*), who found that it was complete after short boiling with alcoholic potash. McKenzie, Roger, and Wills (*loc. cit.*) showed that catalytic racemisation of the compound was effected by adding a trace of alcoholic potash to its ethyl-alcoholic solution. Weissberger, Dörken, and Schwarze (*loc. cit.*) measured the rate of racemisation under conditions which precluded loss of optical activity by oxidation.

We found that the conditions under which the optically active benzoins were racemised can be considerably extended. (1) If *D*(—)benzoin was melted in a glass vessel and cooled, the product was *r*-benzoin. (2) When the experiment was carried out in a quartz vessel, loss of activity was much slower; the product was not solely *r*-benzoin, but a mixture, m. p. 65—85°, and possibly contained deoxybenzoin and benzil (cf. Engler and Grimm, *Ber.*, 1897, **30**, 2923). (3) When *D*(—)benzoin was kept in anisole solution in a quartz flask at 152° for 1½ hours, the observed angle of the solution fell only slightly. On prolonged heating the activity slowly disappeared, but it was found that much of the benzoin had also disappeared, considerable decomposition having taken place. Solutions of the optically active benzoins in (4) diethylamine and (5) triethylamine lost their activities steadily, following a course similar to that of a catalytic racemisation. In the triethylamine solutions, considerable decomposition took place, only a very small amount of the benzoin being recovered. Raising the temperature of the diethylamine and triethylamine solutions accelerated the rate of racemisation. (6) Racemisation of solutions in piperidine was rapid, being complete within an hour. (7) If the benzoin was dissolved in ethyl alcohol, however, and small amounts of piperidine added, the rate of racemisation was much reduced (cf. Rupe and Lenzinger, *Annalen*, 1913, **398**, 372). Smith (*loc. cit.*) has definitely shown that the concentration of catalyst in the racemisation of (+)mandelonitrile controls the rate of racemisation (cf. Ingold and Wilson, this vol., p. 93; Wilson, *ibid.*, p. 98). Hopper and Wilson (*loc. cit.*) found that solutions of the benzoins in pyridine were quite stable in quartz containers, and we found them also to be stable in glass, but observed that pyridine solutions of impure *D*(—)benzoin were steadily racemised in glass tubes. (8) *D*(—)Benzoin was stable in aniline solution at ordinary temperature.

(9) When the pyridine-*D*(—)benzoin complex (cf. Ward, J., 1929, 1544) was formed by heating *D*(—)benzoin with the calculated amount of pyridine to 115° in glass vessels, it was found to be optically inactive; so also was the benzoin recovered. (10) A similar observation was made with piperidine.

The loss of activity in the experiments (1), (4), (6), (7), (9), and (10) is probably due to catalytic racemisation. In other cases, the loss is due to decomposition of the benzoin into products containing no centres of asymmetry. In the case of pyridine and piperidine, complexes are formed, and these possibly are derivatives of the still unknown, isomeric, ω-dihydroxystilbene. This dienol formation (*i.e.*, isomeric change), in these circumstances, takes place very rapidly, and would be depicted thus :



(cf. McKenzie and Smith, J., 1922, **121**, 1348), addition of the catalyst preceding formation of the optically inactive, symmetrical systems.

The intermediate formation of ω-dihydroxystilbene would apply particularly in the case of loss of activity on the melting of the optically active benzoins in glass vessels, since benzoin, in the molten state, may consist largely of ω-dihydroxystilbene. The catalyst in this case was probably alkali from the glass. A similar series of changes may also take place in diethylamine, in which case these solutions apparently afford further examples of catalytic racemisation, although the " catalyst " is not present in traces. In triethylamine solutions, decomposition occurs to such an extent as to preclude our forming any definite opinion as to the course of the action.

The mechanism of these racemisations can also be considered on ionic or prototropic bases (cf. Ingold and Wilson, *loc. cit.*; Lowry, J., 1923, **123**, 828; Weissberger, Dörken, and Schwarze, *loc. cit.*).

EXPERIMENTAL.

(*D*-Benzoin is the benzoin derived from the lævorotatory mandelic acid.)

D(—)Benzoin.

	λ 6563.	λ 6162.	λ 5893.	λ 5461.	λ 5106.	λ 4861.	λ 4358.
(1) In acetone ($c = 4·416$, $l = 1$, $t = 20°$) :							
[α]	—85·1°	102·6°	116·7°	144·7°	178°	210°	306·8°
(2) In ethyl alcohol ($c = 1·685$, $l = 2$, $t = 20·5°$) :							
[α]	—98·9	116·3	132·4	162	197·4	231·3	—
(3) In chloroform ($c = 1·537$, $l = 2$, $t = 0°$) :							
[α]	—167·9	—	220·3	268·8	—	382·6	—
Ditto ($t = 20·6°$) :							
[α]	—157·2	183·2	206·6	253	308·8	359	522·3
Ditto ($t = 35°$) :							
[α]	—150	—	194	239·8	—	347·2	—

D(−)Benzoin.

	λ 6563.	λ 6162.	λ 5893.	λ 5461.	λ 5106.	λ 4861.	λ 4358.
(4) In carbon disulphide (*c* = 1·0315, *l* = 2, *t* = 20·8°) :							
[α]	−309·7	362·8	408	500·8	605	705	1029
(5) In dioxan (*c* = 1·5225, *l* = 2, *t* = 20·8°) :							
[α]	−123	145·2	161·9	200·5	260·7	285·6	423·4
Ditto (*t* = 45°) :							
[α]	−111·5	—	147·2	179·9	—	254·7	—
(6) In carbon tetrachloride (*c* = 1·171, *l* = 1, *t* = 20°) :							
[α]	−182·7	214·3	241·7	294·6	—	419·3	608·1

L(+)Benzoin.

	λ 6563.	λ 6162.	λ 5893.	λ 5461.	λ 5106.	λ 4861.	λ 4358.
(7) In pyridine (*c* = 2·252, *l* = 1, *t* = 20°) :							
[α]	+ 69·7	79·9	91	111	—	157·6	215·8

D(−)Benzoin.

	λ 6563.	λ 6162.	λ 5893.	λ 5461.	λ 5106.	λ 4861.	λ 4358.
(8) In aniline (*c* = 2·367, *l* = 1, *t* = 21·2°) :							
[α] Obs.	−150·4	174·9	199·8	209·5	247·2	302·1	354·5
[α] Calc.	−149·7	176·1	199	208·7	246·8	302·5	354·5

There was no alteration of the rotatory power after this solution had stood for 24 hours at ordinary temperature.

Hopper and Wilson (*loc. cit.*) record that solutions of *D*(−)benzoin in pyridine are not racemised in quartz vessels. We also found that *L*(+)benzoin was not racemised in either quartz * or glass rotation tubes :

Rotation (in pyridine) in quartz polarimeter tube :

$$c = 2{\cdot}252,\ l = 1,\ \alpha_{5461} = +\ 2{\cdot}53°,\ [\alpha]_{5461} = +\ 112{\cdot}2°.$$

The solution was kept for 24 hours without alteration. Some of the above solution was placed in an ordinary glass polarimeter tube, and showed no change in rotatory power after 24 hours, but it became very brown. The temperature was raised to 38°, and on re-cooling to 20°, no change in rotation was detected; 2 drops of alcoholic potash (0·841*N*) were then added, and the rotatory power fell to $[\alpha]_{5461}$ + 96·8°. The addition of more alcoholic potash gave a solution on which readings could not be taken. The benzoin recovered had no rotatory power for the wave-lengths 5893, 5461, and 4358 in acetone solution (*c* = 1·518, *l* = 1).

When impure, crude *D*(−)benzoin ($[\alpha]_{5893}$ = − 83° in acetone, *c* = 1·273, *l* = 2) was dissolved in pyridine (*c* = 1·39, *l* = 1), the rotatory power of the solution diminished steadily from $[\alpha]_{5461}$ = − 89·9° to − 67·6° after 189 hours. *D*(−)Benzoin (0·5 g.) was heated with pyridine (0·25 g.) to 155° for 30 minutes. The complex had no rotatory power in pyridine solution (*c* = 1·397, *l* = 2) for λ 5461. The benzoin recovered from this complex had also no rotatory power in pyridine solution (*c* = 0·6845, *l* = 2).

A solution of *L*(−)benzoin in piperidine (*c* = 2·011, *l* = 1), in a quartz rotation tube with glass ends, was found to be completely racemised in a short time; moreover, the initial solution was lævorotatory.

t, mins.	5	10	15	30	60
$[\alpha]_{5461}$	−35·3°	−4·5°	−0·7°	−0·5°	−0·0°

The recovered benzoin had m. p. 129—132°, and had no rotatory power in acetone (*c* = 1·563, *l* = 1).

It was also found that *D*-benzoin (0·5 g.) was immediately racemised when heated with piperidine (0·25 g.) to 110° in a glass flask.

The rate of racemisation of *L*(+)benzoin was markedly reduced when dissolved in alcohol and a small amount of piperidine added. *L*(+)Benzoin in alcohol (*c* = 1·483, *l* = 1) had $[\alpha]_{5461}$ = + 158·4°. To this solution 2 drops of piperidine were added, and the rotatory power fell to $[\alpha]_{5461}$ = + 152·4° after 70 minutes; 2 more drops of piperidine were then added, and the rotation fell to $[\alpha]_{5461}$ = + 19·6° after 3 days. The addition of another 2 drops of piperidine caused a fall in rotatory power to $[\alpha]_{5461}$ = + 8·1° after 2 days. The benzoin recovered from

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* The quartz polarimeter tube had glass ends which had been boiled in concentrated hydrochloric acid to remove alkali.

this solution had m. p. 124—130°, and had a very small dextrorotation ($[\alpha]_{5461}$ = + 2·32°) in acetone (c = 1·294, l = 1).

L(−)*Benzoin in Diethylamine.*—*L*(−)Benzoin racemised steadily in diethylamine solution (c = 2·151, l = 1) contained in a quartz rotation tube with glass ends :

t, mins.	0	20	65	125	210	1200
$[\alpha]_{5461}$	−131°	93·5°	52·5°	26·5°	8·8°	0·0°

The original sample of *L*(+)benzoin had $[\alpha]_{5893}$ = + 117·2° (c = 1·834, l = 1, in acetone), so the sign of rotation had changed in this solvent. The benzoin was recovered from the diethylamine solution and had m. p. 133—135°, and no rotatory power in acetone solution (c = 1·605, l = 1).

D(+)*Benzoin in Triethylamine.*—This experiment was carried out in a glass polarimeter tube. Values for various wave-lengths were determined as quickly as possible, but racemisation was proceeding all the time (c = 1·342, l = 2, t = 21°) :

	λ 6563.	λ 6162.	λ 5893.	λ 5461.	λ 5106.	λ 4861.	λ 4358.
$[\alpha]^{21°}$	+ 66·3	79	89·4	112·5	142·4	173·2	294·4
t, hours	0	2	26	50	122	146	218
$[\alpha]^{21°}_{5461}$	+113°	100°	84°	57°	18·3°	13°	3°

The solution finally had become very dark, and the material recovered was largely decomposed.

A solution of *D*(−)benzoin (0·2455 g.) was made in pure anisole (23·4861 g.). It had α_{5893} = − 2·52° (l = 1, t = 20°). It was boiled gently for 1½ hours, and then had α_{5893} = − 2·47° (l = 1, t = 20°). After 22 hours' heating, the rotatory power had fallen to α_{5893} = − 0·51°. The solid recovered from the solution had m. p. 70—110°, and could not be separated further.

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