LXIII.—*The Action of Substituted Aromatic Amines on Camphoric Anhydride. The Rotatory Powers of some Disubstituted Camphoranilic Acids.*

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IN support of Rule's statement (J., 1924, **125**, 1127) that "groups of like polarity reinforce each other in the ortho-position, whilst the introduction of a positive and a negative group, both of marked polarity, leaves the rotation of the unsubstituted ester comparatively unaltered," the case of the menthyl esters of *o*-disubstituted benzoic acid prepared by Cohen (J., 1914, **105**, 1892) may be cited. Very little work, however, has been done in this direction and the present investigation was undertaken to test the validity of the statement.

The condensation products of camphoric anhydride and the following disubstituted anilines are described: *o*-, *m*-, and *p*-xylidine, 4- and 5-nitro-*o*-anisidine, 4- and 5-nitro-*o*-toluidine, and 2- and 3-nitro-*p*-toluidine. The *mononitro*-derivatives of 4′-methyl-, 4′-chloro-, and 4′-bromo-camphoranilic acid and the *dinitro*-derivatives of 4′-methoxy- and 4′-ethoxy-camphoranilic acid have also been prepared.

The nitro-derivative of 4′-bromocamphoranilic acid prepared by Wootton (J., 1910, **97**, 405) and displaying lævorotation in alcoholic solution is described by him as 4′-bromo-3′-nitrocamphoranilic acid. It may be 4′-bromo-2′-nitrocamphoranilic acid for the following reasons : (1) 2′-Nitro-4′-methylcamphoranilic acid, the condensation product of 3-nitro-*p*-toluidine and camphoric anhydride, is identical with the nitration product of 4′-methylcamphoranilic acid : the nitro-group therefore enters the ortho-position with respect to the substituted amino-group during nitration. (2) 3′-Nitrocamphoranilic acid (Wootton, *loc. cit.*) and derivatives of camphoranilic acid with the nitro-group in the 3′-position all show positive rotations, whereas the nitro-derivatives of the 4′-substituted acid give negative rotations in all solvents.

Effect of Substituents on the Rotatory Power.—Table I records the molecular rotatory powers, $[M]_D$, of 2′-methylcamphoranilic acid and some dimethylcamphoranilic acids in various solvents. The introduction of the second methyl group increases the rotation in every case, and most when the two methyl groups are in the para-position with respect to each other. The increase due to two methyls in the ortho-positions with respect to the optically active group is much less than was expected.

TABLE I.

Substituent.	MeOH.	EtOH.	Me$_2$CO.	MeEtCO.
2′-Methyl	+151°	+144° *	+ 98°	+ 91°
2′ : 3′-Dimethyl	168	148	120	109
2′ : 5′-Dimethyl	203	165	147	127
2′ : 6′-Dimethyl	174	168	109	102

* Singh and Puri, J., 1926, 504.

In Table II are the molecular rotatory powers, $[M]_D$, of 2′- and 4′-methoxy- and 4′-ethoxy-camphoranilic acids and their nitro-derivatives. The nitro- and the methoxy-group have marked polarities and stand at the ends of the polar series. The rotatory power of 5′-nitro-2′-methoxycamphoranilic acid is almost the same as that of the unsubstituted compound. (The values of the rotatory power of the latter are shown in parentheses in Table II.) When the nitro-group is in the 4′-position the compound shows a feeble rotation, $[\alpha]_D = + 5{\cdot}0°$ in methyl ethyl ketone. On nitration of 4′-methoxy- and 4′-ethoxy-camphoranilic acids, dinitro-derivatives are produced. Both nitro-groups enter the ortho-positions with respect to the optically active group and, as was expected, there is a considerable rise in the rotatory power, accompanied by a reversal of sign.

TABLE II.

Substituent.	MeOH.	EtOH.	Me$_2$CO.	MeEtCO.
2′-Methoxy	+ 30°	+ 28°	− 16°	− 10°
4′-Methoxy	+163	+153	+123	+100
4′-Ethoxy	+179	+154	+116	+104
5′-Nitro-2′-methoxy	+144 (150)	+128 (131)	+109 (101)	+104 (—)
4′-Nitro-2′-methoxy		Feeble rotation		
2′ : 6′-Dinitro-4′-methoxy	−306	−412	−270	−255
2′ : 5′-Dinitro-4′-ethoxy ...	−263	−353	−211	−192

Table III records the rotatory powers, $[M]_D$, of 2′- and 4′-methylcamphoranilic acids and their nitro-derivatives. The nitro- and the methyl group (both of similar polarity) enhance the rotation

TABLE III.

Substituent.	MeOH.	EtOH.	Me_2CO.	MeEtCO.
2′-Methyl	+146°	+144°	+ 98°	+ 90°
4′-Methyl	+170	+146	+122	—
5′-Nitro-2′-methyl	+214	+219	+154	+144
4′-Nitro-2′-methyl	+ 96	+ 80	+ 77	—
5′-Nitro-4′-methyl	+141	+123	+111	+101
2′-Nitro-4′-methyl	−167	−202	−161	−138

considerably when they are in the para-position with respect to each other, but there is a fall when they are in the meta-position. Again, there is a slight fall in the rotation of 4′-methylcamphoranilic acid when a nitro-group is introduced in the 5′-position. But there is a considerable rise when the nitro-group is in the 2′-position and in every solvent the sign of the rotation is changed.

EXPERIMENTAL.

Condensation of Camphoric Anhydride with Substituted Amines.—Camphoric anhydride and the amine (equal mols.) were heated together with fused sodium acetate at 145—150° for 3—4 hours. The product was dissolved in 90% alcohol, precipitated, extracted with a dilute solution of alkali, and crystallised from alcohol. In no case was there any residue of imide.

The following acids were prepared. 2′ : 3′-*Dimethylcamphoranilic acid*, light prisms, m. p. 190—192° (Found: N, 5·0; equiv., 298. $C_{18}H_{25}O_3N$ requires N, 4·6%; equiv., 303). 2′ : 6′-*Dimethylcamphoranilic acid*, silky needles, m. p. 236—238° (Found: N, 5·1%; equiv., 306). 2′ : 5′-*Dimethylcamphoranilic acid*, needles, m. p. 203—204° (Found: N, 5·2%; equiv., 301). 5′-*Nitro*-2′-*methoxycamphoranilic acid*, needles, m. p. 162—163° (Found: N, 8·35. $C_{17}H_{22}O_6N_2$ requires N, 8·0%). 4′-*Nitro*-2′-*methoxycamphoranilic acid*, light brown, powdery mass, m. p. 185—186° (Found: N, 8·4%). 5′-*Nitro*-2′-*methylcamphoranilic acid*, straw-coloured needles, m. p. 220—221° (Found: N, 8·6. $C_{17}H_{22}O_5N_2$ requires N, 8·4%). 3′-*Nitro*-4′-*methylcamphoranilic acid*, light brown, prismatic crystals, m. p. 204—205° (Found: N, 8·5%). 2′-*Nitro*-4′-*methylcamphoranilic acid*, deep yellow plates, m. p. 187° (Found: N, 8·6%). 4′-*Nitro*-2′-*methylcamphoranilic acid*, needles, m. p. 229—230° (Found: N, 8·7%).

Nitration of 4′-*Chloro*, 4′-*Bromo*-, 4′-*Methoxy*-, 4′-*Ethoxy*-, *and* 4′-*Methyl-camphoranilic Acids.*—To a mixture of 10 c.c. of fuming nitric acid and 8 c.c. of glacial acetic acid, 3 g. of the acid were gradually added. The clear solution obtained after 5—10 minutes was kept for 30—45 minutes and then poured on ice. The deep yellow or orange precipitate produced was crystallised from alcohol.

The following acids were prepared. *4′-Chloro-2′-nitrocamphoranilic acid*, deep yellow needles, m. p. 204—205° (Found: N, 8·25. $C_{16}H_{19}O_5N_2Cl$ requires N, 7·9%). 4′-Bromo-2′-nitrocamphoranilic acid, deep yellow needles, m. p. 212° (Wootton, *loc. cit.*, 204—206°) (Found: N, 7·3. Calc.: N, 7·0%). 2′ : 6′-*Dinitro*-4′-

TABLE IV.

Rotatory Powers of Disubstituted Camphoranilic Acids.

Solvent.	Conc., g./25 c.c.	α_D.	$[\alpha]_D$.	Conc., g./25 c.c.	α_D.	$[\alpha]_D$.
	2′ : 3′-Dimethylcamphoranilic acid.			2′ : 6′-Dimethylcamphoranilic acid.		
MeOH	0·1842	0·82°	55·6°	0·1850	0·85°	57·4°
EtOH	0·1998	0·78	48·8	0·1986	0·88	55·4
Me_2CO	0·1961	0·62	39·5	0·2006	0·58	36·1
MeEtCO	0·1982	0·57	35·9	0·1994	0·54	33·8
	2′ : 5′-Dimethylcamphoranilic acid.			5′-Nitro-2′-methoxycamphoranilic acid.		
MeOH	0·2016	1·08	67·0	0·1859	0·61	41·0
EtOH	0·1978	0·86	54·4	0·1907	0·56	36·7
Me_2CO	0·2014	0·78	48·4	0·2166	0·54	31·1
MeEtCO	0·2000	0·65	40·6	0·1893	0·45	29·7
	4′-Nitro-2′-methoxycamphoranilic acid.			5′-Nitro-2′-methylcamphoranilic acid.		
MeOH	Shows very feeble rotatory power.			0·1894	0·96	64·0
EtOH				0·1985	1·04	65·5
Me_2CO	0·1278	0·09	8·8	0·2000	0·74	46·2
MeEtCO	0·1991	0·08	5·0	0·2064	0·71	43·0
	5′-Nitro-4′-methylcamphoranilic acid.			2′-Nitro-4′-methylcamphoranilic acid.		
MeOH	0·1897	0·64	42·2	0·1900	−0·76	−50·0
EtOH	0·1975	0·58	36·7	0·2004	−0·97	−60·5
Me_2CO	0·2000	0·53	33·1	0·1195	−0·46	−48·1
MeEtCO	0·1986	0·48	30·2	0·1668	−0·55	−41·2
	4′-Nitro-2′-methyl camphoranilic acid.			4′-Chloro-2′-nitrocamphoranilic acid.		
MeOH	0·1886	0·44	29·1	0·1840	−0·60	−40·76
EtOH	0·1868	0·36	24·0	0·1979	−0·82	−51·8
Me_2CO	—	—	—	0·1933	−0·73	−47·2
MeEtCO	0·1947	0·36	23·1	0·1990	−0·56	−35·2
	4′-Bromo-2′-nitrocamphoranilic acid.			2′ : 6′-Dinitro-4′-methoxycamphoranilic acid.		
MeOH	0·1880	−0·59	−39·2	0·1813	−1·22	− 84·1
EtOH	0·1958	−0·71	−45·3	0·1811	−1·64	−113·2
Me_2CO	0·1950	−0·56	−35·9	0·1955	−1·16	− 74·2
MeEtCO	0·1985	−0·50	−31·5	0·1950	−1·09	− 70·0

2′ : 6′-Dinitro-4′-ethoxycamphoranilic acid.

Solvent.	Conc., g./25 c.c.	α_D.	$[\alpha]_D$.
MeOH	0·1523	−0·85°	−69·7°
EtOH	0·1579	−1·18	−93·4
Me_2CO	0·1966	−0·88	−55·9
MeEtCO	0·1566	−0·73	−50·8

methoxycamphoranilic acid, light orange needles, m. p. 228—229° (Found: N, 10·6. $C_{17}H_{21}O_8N_3$ requires N, 10·6%). 2′ : 6′-*Dinitro-4′-ethoxycamphoranilic acid*, orange plates, m. p. 189—190° (Found: N, 10·2. $C_{18}H_{23}O_8N_3$ requires N, 10·3%). 2′-Nitro-4′-methylcamphoranilic acid, deep yellow plates, m. p. 187°, alone or mixed with the same acid prepared as described on p. 480.

Summary.

The rotatory powers of some disubstituted camphoranilic acids have been determined. Two groups of the same polarity reinforce each other when they are in the para-position with respect to each other; for instance, 2′ : 5′-dimethylcamphoranilic acid and 5′-nitro-2′-methylcamphoranilic acid exceed any of their respective isomerides in rotatory power. Groups of opposite polarity neutralise each other's effect. The rotatory power of 5′-nitro-2′-methoxycamphoranilic acid is practically the same as that of the unsubstituted compound. The nitro-group in the 4′-position has a depressing effect on the rotatory power of the original compound; *e.g.*, 4′-nitro-2′-methoxycamphoranilic acid has a lower rotatory power than 2′-methoxycamphoranilic acid. Similarly, 4′-nitro-2′-methylcamphoranilic acid has a lower rotatory power than 2′-methylcamphoranilic acid.

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