410. *Reactivity of* peri-*Substituted Naphthalenes. Part II. The Replacement of Halogen in* 8-Halogeno-1-*naphthoic Acids and in* o-*Halogenobenzoic Acids.*

By H. GORDON RULE and A. JOHN G. BARNETT.

THE influence of other substituent groups upon the reactivity of halogen atoms attached to aromatic nuclei has already been the subject of numerous investigations. According to earlier views (cf. Schöpf and co-workers, *Ber.*, 1891, **24**, 3784), at least two other *m*-directive groups situated preferably in the *o*- or *p*-position to the halogen atom are required to render it labile. No appreciable mobility was believed to be conferred by the presence of only one other substituent unless this were a nitro-group. More recently, Rosenmund and Harms (*Ber.*, 1920, **53**, 2226) have directed attention to the reactivity of chlorine and bromine in *o*-chloro- and *o*-bromo-benzoic acids in the presence of catalysts : they converted the former into salicylic acid in 85% yield by heating it with aqueous sodium acetate and copper-bronze for 9—10 hours at 140—150°; the bromo-acid underwent a similar change in the presence of sodium β-naphthalenesulphonate. Hurtley (*J.*, 1929, 1870) effected the transformation of the bromo-acid into salicylic acid by heating the salt with a mixture of copper-bronze and copper acetate for 30 minutes at 100°, and also found that in the presence of either of these catalysts sodium *o*-bromobenzoate could be readily condensed with sodiomalonic ester, sodioacetoacetic ester, and other keto-enolic compounds at moderate temperatures. This author noted that ethyl *o*-bromobenzoate, free *p*-bromobenzoic acid, and *o*-bromo-nitrobenzene all failed to react appreciably under these conditions.

In view of the useful double decompositions thus undergone by *o*-bromobenzoic acid under the influence of copper-bronze, it was considered of interest to investigate the behaviour of the 8-halo-geno-1-naphthoic acids, two of which are now relatively easily prepared from the 8-nitro-acid by treatment with thionyl halide (Rule and Barnett, this vol., p. 175), or, better, by the mercuration of naphthalic acid (Whitmore and co-workers, *J. Amer. Chem. Soc.*, 1929, **51**, 1831, 3363 ; Rule and Barnett, *loc. cit.*). Before examining the naphthalene derivatives, however, we carried out some further experiments with the benzoic acids in order to determine whether the halogen atom could be exchanged for radicals other than those mentioned above. Ullmann and Zlokasoff (*Ber.*, 1905, **38**, 2112) have, for example, described the conversion of potassium *o*-chloro-benzoate into the phenoxy-benzoate by heating it with sodium

phenoxide and copper powder at 180—190°, but no reference is made in Beilstein's " Handbuch " to the formation of alkoxy-acids at moderate temperatures by this means. Since the usual methods of obtaining the ethers of hydroxy-acids are often both tedious and wasteful, the direct exchange of halogen for an alkoxy-group might well provide a valuable alternative process.

It was found that sodium *o*-bromobenzoate does not react perceptibly at moderate temperatures with sodium methoxide in the presence of copper-bronze. The iodobenzoate, however, reacted rapidly at the b. p. of methyl alcohol to form the *o*-methoxybenzoate. Various other displacements have been effected, which are summarised in the table below. Owing to the small scale of the experiments and the disproportionate losses on purification of the products, the yields quoted are not strictly comparable.

Reactions of Sodium o-*Halogenobenzoates in Presence of Copper-bronze.*

Activating group.	Change effected.	Temp.	Time (hrs.).	Yield, %.
o-CO_2Na	I $\longrightarrow$ OH	100°	1	77
,,	I $\longrightarrow$ OMe	70	4	33
,,	I $\longrightarrow$ OPh	110	2	30
,,	I $\longrightarrow$ *m*-OC_6H_4Me	120	2	41
,,	I $\longrightarrow$ $OC_{10}H_{19}$*	100	2	33
,,	I $\longrightarrow$ NO_2	100	12	54
,,	Br $\longrightarrow$ I	80	12	75
o-CO_2Me	I $\longrightarrow$ OMe	70	3½	62
,,	I $\longrightarrow$ $OC_{10}H_{19}$*	120	2	30

* *l*-Menthoxy-group.

An interesting change of another type is the conversion of the bromo-acid into the iodo-acid in 75% yield by boiling the salt with a concentrated solution of sodium iodide in propyl alcohol. A previous experiment in acetone solution showed little change, presumably on account of the lower b. p. of the solvent. The iodo-acid was also transformed into the nitro-acid by boiling the sodium salt in propyl-alcoholic solution over an excess of solid silver nitrite. Copper-bronze was used in both of these cases, and owing to the slower speed of the reactions, heating was continued for 12 hours.

Although the halogen in *o*-bromobenzoic acid cannot be exchanged for alkoxy- or aryloxy-groups under the above conditions, it will be seen from the times given in the table that the reactions proceed readily with the more active iodo-compound. The superior reactivity of the iodine atom is also brought out in the conversion of *p*-iodobenzoic acid into the hydroxy-acid and in the preparation of alkoxy-benzoic esters from methyl *o*-iodobenzoate. In the latter case the activating group is CO_2Me. Neither of these two reactions

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proceeds with the corresponding bromo-derivatives (Hurtley, *loc. cit.*).

When the two recently discovered 8-halogeno-1-naphthoic acids were examined in the same manner, the chloro-compound proved to be chemically inactive, but the halogen atom in the bromo-acid was readily exchanged for a variety of ethereal radicals as indicated in tabular form below. The conditions employed were the same as those described for the benzene derivatives, except that a somewhat higher proportion of catalyst was used (see also p. 2732).

Reactions of Sodium 8-Bromo-1-naphthoate in Presence of Copper-bronze.

Br ex-changed for	Temp.	Time (hrs.).	Yield, %.	Br ex-changed for	Temp.	Time (hrs.).	Yield, %.
OH*	100°	0·5	47	OBu	120°	2	50
OMe	70	4	69	*l*-Menthoxy	120	16	30
OEt	80	2	50	OCH₂Ph	120	2	40
OPr	100	1	50	OPh	120	4	38

* Hydroxy-acid isolated in the form of naptholactone.

All attempts to make the bromonaphthoate react with sodio-malonic or sodioacetoacetic ester in ethyl-alcoholic solution failed, the only isolable product being the 8-ethoxy-acid. In the absence of alcohol no interaction occurred even after prolonged heating, and the starting materials were recovered unchanged. Similarly, the methods adopted for converting *o*-bromobenzoic acid into the iodo-acid, and *o*-iodobenzoic acid into the nitro-compound were ineffective when applied to 8-bromo-1-naphthoic acid.

Discussion of Results.—From the data given above it is seen that in the presence of copper-bronze *o*-iodobenzoic acid and 8-bromo-1-naphthoic acid react readily with a number of sodium derivatives, the speed of reaction being comparable with that of an ordinary alkyl halide double decomposition. In general, a substituent in the *peri*-position to carboxyl in the naphthalene nucleus appears to be more easily replaced than one in an ortho-substituted benzoic acid, since reactions (*e.g.*, halogen ⟶ OMe) which only proceed readily with the iodo-compound of the benzene group may be completed without difficulty by using the bromo-compound of the naphthalene series. Another case in point is the conversion of 8-nitro-1-naphthoic acid into the 8-chloro- or 8-bromo-compound in the presence of thionyl halide, an exchange which does not occur in the benzoic series. One reason for a differentiation in this sense is no doubt the more labile nature of substituents linked to the naphthalene nucleus, but probably a further contributory factor is the greater proximity of the groups in the *peri*- as compared with the ortho-position.

In view of the very similar behaviour of iodobenzoic and bromo-naphthoic acids towards alkoxides and aryloxides, the marked differences exhibited towards sodiomalonic ester, sodium iodide, and silver nitrite are noteworthy. The inability of these last reagents to attack bromonaphthoic acid under mild experimental conditions may be traced in part to steric hindrance, which would retard the entry of a more bulky substituent into the *peri*-position. This factor may also explain the difficulty encountered in introducing the *l*-menthoxy-radical, a change which required 16 hours' heating, although it occurred rapidly in the case of *o*-iodobenzoic acid. Presumably the halogen in 8-iodo-1-naphthoic acid would exist in a very highly reactive condition, but unfortunately all attempts to prepare this compound, whether from the 8-amino-acid or by iodination of the mercury compound of naphthalic acid, were unsuccessful, the latter process leading only to the isolation of some α-naphthoic acid. A similar partial dehalogenation was also observed in an attempt to replace bromine by iodine in the *peri*-substituted acid by heating it with copper powder and sodium iodide in propyl alcohol.

From a comparative study of aromatic halogen derivatives, Davies and Wood (J., 1928, 1123) concluded that a nitro-group activates a halogen atom approximately 200,000 times more strongly than does a carboxyl group in the same position. In the presence of copper catalyst, however, the position is apparently reversed, since the bromine in *o*-bromonitrobenzene is not reactive under conditions which permit its displacement from *o*-bromobenzoic acid (Hurtley, *loc. cit.*). Naphthalene derivatives have been less completely examined in this connexion, and although Salkind (*Ber.*, 1931, **64**, 289) has concluded that the nitro-group in bromonitro-naphthalenes has little influence upon the reactivity of halogen situated in the adjoining ring, these experiments did not include an investigation of the 1 : 8-bromonitro-compound and were conducted without the use of copper catalyst. From the present work, however, it is clear that *in the presence of copper-bronze a carboxyl group in position 8 powerfully activates a bromine atom in position 1 in the adjacent ring.*

EXPERIMENTAL.

Experiments with hydroxylic reagents were carried out as follows. The *o*-halogenated acid (1—3 g.) was treated with 2 at. propns. of Na dissolved n excess of the desired hydroxy-compound (15—20 c.c.), containing a small amount of Naturkupfer C in suspension (0·1—0·3 g.). The mixture was then heated at its b. p. or on an oil-bath for the time specified.

The following naphthalene derivatives were prepared from 8-bromo-1-naphthoic acid (see this vol., p. 175). Yields are given in the table on p. 2730.

Naphtholactone. The bromo-acid (0·5 g.) dissolved in excess of aq. NaOH was boiled in the presence of a trace of Cu-bronze for 30 mins. The filtered and acidified product was heated at 100° for 1½ hrs., and the yellow ppt. dried and recryst. from ligroin; m. p. 106—108°.

8-Alkoxy- and 8-aryloxy-naphthoic acids were obtained from the bromo-acid (1 g.), Cu-bronze (0·2 g.) and the requisite alcohol (15 c.c.) in which Na (0·2 g.) had been dissolved. All the compounds examined were moderately sol. in warm EtOH or C_6H_6, but only very sparingly in light petroleum.

8-Methoxy-1-naphthoic acid, recryst. from C_6H_6, had m. p. 159—160°, unchanged on admixture with a specimen prepared by methylation of the 8-hydroxy-acid (Bretscher, Rule, and Spence, J., 1928, 1500). *8-Ethoxy-1-naphthoic acid* separated from C_6H_6 in needles, m. p. 210—211° (Found : C, 72·1; H, 5·6. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·5%).

8-Propoxy-1-naphthoic acid, from C_6H_6, melted at 176—177° [mixed m. p. with 8-bromo-acid (m. p. 178°), 130—145°] (Found : C, 72·8; H, 6·2. $C_{14}H_{14}O_3$ requires C, 73·0; H, 6·1%). 8-n-*Butoxy-1-naphthoic acid* separated from C_6H_6 in needles, m. p. 154—155° (Found : C, 73·7; H, 6·7. $C_{15}H_{16}O_3$ requires C, 73·8; H, 6·5%). 8-l-*Menthoxy-1-naphthoic acid* separated from ligroin in prisms, m. p. 206—207° (Found : C, 77·3; H, 7·9. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·0%). Owing to the prolonged heating required (16 hrs.) considerable darkening occurred during this prepn., which probably adversely affected the yield. 8-*Phenoxy-1-naphthoic acid* was deposited in short lustrous needles, m. p. 139—140°, from a mixture (1 : 1) of ligroin and light petroleum (Found : C, 77·1; H, 4·6. $C_{17}H_{12}O_3$ requires C, 77·3; H, 4·5%). 8-*Benzyloxy-1-naphthoic acid*, recryst. from ligroin, melted at 125—126° (Found : C, 77·5; H, 5·1. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%).

EDINBURGH UNIVERSITY.   [*Received, October 3rd*, 1932.]