Metal Ions and Complexes in Organic Reactions. Part XX.[1] Copper-catalysed Reactions of Aromatic Bromo-carboxylates with Carbanions, giving Oxo-acids, Isocoumarins, and Related Products

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Depending upon choice of solvent and other conditions, copper-catalysed reactions of sodium *o*-bromobenzoate with sodium acetylacetonate gave *o*-(diacetylmethyl)benzoic acid (1), *o*-acetonylbenzoic acid (2), or 3-methylisocoumarin (3), whereas reactions with ethyl sodioacetoacetate gave compound (2) or (3) or *o*-(ethoxycarbonylmethyl)benzoic acid (5); analogously, the products *o*-$CO_2H{\cdot}C_6H_4{\cdot}CH(CO_2Et)_2$ [or (5)], *o*-$CO_2H{\cdot}C_6H_4{\cdot}CH(CN){\cdot}CO_2H$, and *o*-$CO_2H{\cdot}C_6H_4{\cdot}CH(CN)_2$ were obtained with the corresponding nucleophiles. Sodium 1-bromo-2-, 3-bromo-2-, and 8-bromo-1-naphthoate gave similar substitution products, including, in the first two cases, naphthopyranones. Nucleophilic substitution by the carbanions was ineffective with substrates not containing a carboxylate-salt group adjacent to the halogen. Reductive substitution of halogen competed to a varying extent. Copper could be introduced as metal, or Cu^{I} or Cu^{II} species, but the effective reaction intermediates are considered to be copper(II) complexes incorporating the halogeno-carboxylate substrate and the carbanionic nucleophile.

SOME previous papers in this series concerned copper-catalysed nucleophilic substitutions in organic solvents between aryl halides and anionic species, X^-, contributed by alkali-metal salts of thiols,[2] phenols,[3] alcohols,[4] imides,[5] or sulphonamides.[5] These replacements, ArHal ⟶ ArX, showed sensitivity to steric effects of nuclear substituents in the halides, responded relatively feebly to their polar effects, and were often in competition with copper-catalysed reductive substitution, ArHal ⟶ ArH, by various hydrogen donors. Elsewhere, conditions for substitution of aryl halides by copper(I) carboxylates [6] and copper(I) acetylides [7] have been described.

The present investigation was prompted by a description [8] of a related copper-catalysed halogen replacement, performed in boiling ethanol with sodium *o*-bromobenzoate and sodium salts of β-dicarbonyl compounds in

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[1] Part XIX, R. G. R. Bacon and S. D. Hamilton, *J.C.S. Perkin I*, 1974, 1975.

[2] R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, 1964, 1097, 1108.

[3] R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc.*, 1965, 4953.

[4] R. G. R. Bacon and S. C. Rennison, *J. Chem. Soc.* (*C*), 1969, 312; R. G. R. Bacon and J. R. Wright, *ibid.*, p. 1978.

[5] R. G. R. Bacon and A. Karim, *J.C.S. Perkin I*, 1973, 272, 278.

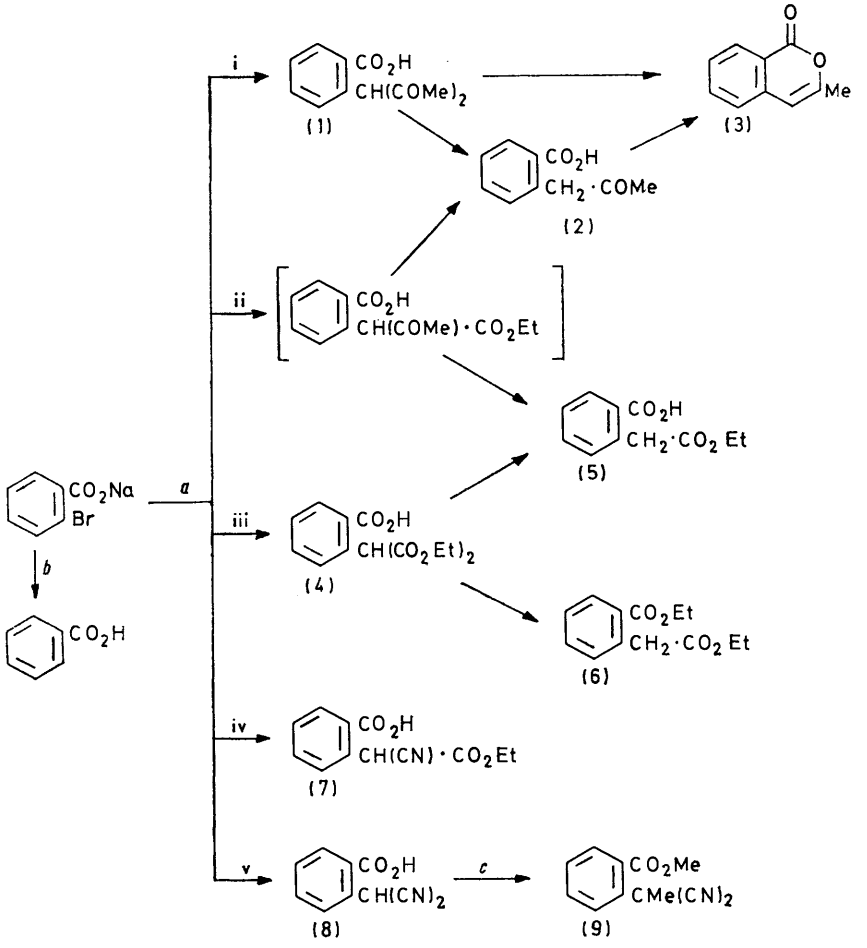
[6] T. Cohen and A. H. Lewin, *J. Amer. Chem. Soc.*, 1966, **88**, 4521.

[7] C. E. Castro, R. Havlin, V. K. Honwad, A. Malte, and S. Mojé, *J. Amer. Chem. Soc.*, 1969, **91**, 6484, and references cited therein.

[8] W. R. H. Hurtley, *J. Chem. Soc.*, 1929, 1870.

which the nucleophile X^- was $CHAc_2^-$, $CHAc{\cdot}COPh^-$, $CHAc{\cdot}CO_2Et^-$, $CH(CO_2Et)_2^-$, or $CH(CO{\cdot}CH_2{\cdot}CO_2Et)_2^-$. The failure of some other aryl halides was mentioned,[8] and our own investigations show that the process has very restricted applicability. Thus, bromobenzene and 1-bromonaphthalene, which reacted readily with the methyl ester was used. It therefore appears that, for practical purposes, copper-catalysed replacement of nuclear halogen by carbanions of the β-dicarbonyl type requires the assistance of a suitably contiguous nuclear carboxylate-salt substituent.

Reaction between selected nucleophiles and sodium



SCHEME 1 [a] Acidification after heating in solution with CuBr and i, $NaCH(COMe)_2$; ii, $NaCH(COMe){\cdot}CO_2Et$; iii, $NaCH(CO_2Et)_2$; iv, $NaCH(CN){\cdot}CO_2Et$; or v, $NaCH(CN)_2$. [b] Competitive reduction by hydrogen donors. [c] CH_2N_2–Et_2O

other anions,[2-5] were unchanged under conditions suitable for sodium *o*-bromobenzoate, *e.g.* treatment with sodium acetylacetonate and copper(I) bromide in boiling ethanol. Sodium *o*-bromobenzenesulphonate likewise failed to react. *o*-Bromo- and *o*-iodo-nitrobenzene merely gave low yields of nitrobenzene and *o*-ethoxynitrobenzene; by contrast, both halogenonitrobenzenes and halogenobenzoic acids had shown high response to copper-catalysed substitution by phthalimide ion.[5]

Under conditions suitable for sodium *o*-bromobenzoate, there was no reaction with its *meta*- and *para*-isomers, or with sodium *o*-bromophenylacetate, but substitution was successful with sodium bromonaphthoates containing the substituents in *ortho*- or *peri*-relationship. Poor results were observed if bromobenzoic acid was used instead of its sodium salt, or (see below) if the *o*-bromobenzoate, carried out in dried organic solvents, are summarised in Scheme 1 and in Tables 1 and 2. Copper-catalysed substitution by sodium acetylacetonate gave *o*-(diacetylmethyl)benzoic acid (1),[8] but further reactions could occur, depending upon the time, temperature, and solvent employed, furnishing the retro-Claisen deacylation product, *o*-acetonylbenzoic acid (2), and the related cyclic product, 3-methylisocoumarin (3). Benzoic acid (up to *ca.* 25%) simultaneously resulted from copper-catalysed reductive substitution when the solvent was dimethylformamide, dimethylacetamide, or a heterocyclic base; other examples of such reductions in these solvents have been reported.[9]

[9] R. G. R. Bacon and H. A. O. Hill, *J. Chem. Soc.*, 1964, 1112; R. G. R. Bacon and O. J. Stewart, *J. Chem. Soc.* (C), 1969, 301; R. G. R. Bacon and S. C. Rennison, *ibid.*, 1969, 308; R. G. R. Bacon and S. G. Pande, *ibid.*, 1970, 1967; R. G. R. Bacon and D. J. Maitland, *ibid.*, 1970, 1973.

The composition of reaction products was monitored by g.l.c. analysis after conversion of carboxylic acids into methyl esters.

The initial product (1) was best obtained by brief reaction in boiling ethanol, and the mono-oxo-acid (2) by a longer reaction time in the same solvent (Tables 1 and 2). The isocoumarin (3) was the dominant product (50—60%) at higher temperatures, *e.g.* when the amides were used as solvents (Table 1). A good deal of unchanged bromobenzoate was recovered from these media, though not from ethanol, in spite of the lower b.p. of the latter solvent. When methyl *o*-bromobenzoate was examined as substrate, the only significant products were a small amount of the isocoumarin (3) in dimethylacetamide, and dimethyl biphenyl-2,2′-dicarboxylate, resulting from Ullmann coupling, in collidine (Table 1; footnotes).

Copper catalysis was necessary to achieve substitution by acetylacetonate in ethanol, but a minor amount of unassisted reaction occurred at 120—170° in the higher boiling solvents. The ratio of copper to substrate was not critical and was arbitrarily fixed at *ca.* 1 : 15 for most of the experiments and at 1 : 2 when less reactive combinations of halide and nucleophile were employed (Tables 1—3). Copper could be introduced as a Cu^{I} or Cu^{II} species, or as the metal (Table 2). As reactions proceeded, initially insoluble copper species dissolved, at least partially, with development of a blue-green colour, indicative of copper(II).

Under comparable conditions, with sodium salts of the acids (1) and (2), the following facts were ascertained. (*a*) In ethanol there was >90% conversion of the dioxo-acid (1) into the mono-oxo-acid (2), either in the presence or absence of copper(I) bromide. (*b*) In dimethylformamide the isocoumarin (3) was formed in low yield (<10%) from the acid (2), but in fairly high yield (60%) from the acid (1), either in the presence or in the absence of copper(I) bromide. It thus appears that the reactions subsequent to substitution (Scheme 1) do not involve copper catalysis and that, under the conditions employed, formation of the isocoumarin direct from the dioxo-acid (1) occurs more readily than its stepwise formation *via* the mono-oxo-acid (2). This direct transformation may be envisaged as involving cyclisation between the carboxylate group and an

TABLE 1

Sodium *o*-bromobenzoate (10 mmol) + NaCHXY (10 mmol), with or without CuBr, in solvent (15 ml), heated under nitrogen

Nucleophile NaCHXY	Solvent	CuBr (mmol)	Temp.[a] (°C)	Time (h)	Recovered bromo-acid (%)	$PhCO_2H$	Substitution products (%) (1)	(2)	(3)	Others
$NaCHAc_2$	EtOH	0·7	78	3				70		
$NaCHAc_2$	EtOH	Nil	78	3	94					
$NaCHAc_2$	$(CH_2{\cdot}OMe)_2$	0·7	85	18	Trace	Trace	62		21	
$NaCHAc_2$	$(CH_2{\cdot}OMe)_2$	Nil	85	18	89					
$NaCHAc_2$	$MeCO{\cdot}NMe_2$	0·7	88	18	38		Trace	21	27	
$NaCHAc_2$	2,4,6-Collidine	0·7	88	18	30	Trace	24	17	9	
$NaCHAc_2$	Pyridine	0·7	114	18	20	21		7	42	
$NaCHAc_2$	$MeO{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	0·7	124	18					43	
$NaCHAc_2$	$MeO{\cdot}CH_2{\cdot}CH_2{\cdot}OH$	Nil	124	18	60			5	7	
$NaCHAc_2$	$HCO{\cdot}NMe_2$	0·7	153	18	28	4		9	55	
$NaCHAc_2$	$AcNMe_2$ [b]	0·7	165	18	30	9		4	53	
$NaCHAc_2$	$AcNMe_2$	Nil	165	18	78				7	
$NaCHAc_2$	2,4,6-Collidine [c]	0·7	170	18	3	23			50	
$NaCHAc_2$	2,4,6-Collidine	Nil	170	18	60	Trace			17	
$NaCHAc{\cdot}CO_2Et$	EtOH	0·7	78	3						(5) 90
$NaCHAc{\cdot}CO_2Et$	$HCO{\cdot}NMe_2$	5·0 [d]	153	3	47	17		19	11	(5) trace
$NaCH(CO_2Et)_2$	EtOH	0·7	78	8	*ca.* 45	Trace				(4) *ca.* 45, (5) trace
$NaCH(CO_2Et)_2$	$HCO{\cdot}NMe_2$	5·0 [d]	153	3		*ca.* 7				(4) *ca.* 7, (5) *ca.* 7, (6) 25
$NaCH(CN){\cdot}CO_2Et$	EtOH	0·7	78	3						(7) 67
$NaCH(CN)_2$	EtOH	5·0 [d]	78	3						(8) 22

[a] Under reflux except for the lower-temperature reactions in dimethylacetamide or 2,4,6-collidine. [b] In this solvent, with 15 mmol $NaCHAc_2$ and 5 mmol CuBr (3 h) Me *o*-bromobenzoate gave (3) (12%). [c] In this solvent, with 15 mmol $NaCHAc_2$ and 5 mmol CuBr (3 h), Me *o*-bromobenzoate gave dimethyl biphenyl-2,2′-dicarboxylate (19%). [d] Nucleophile, 15 mmol.

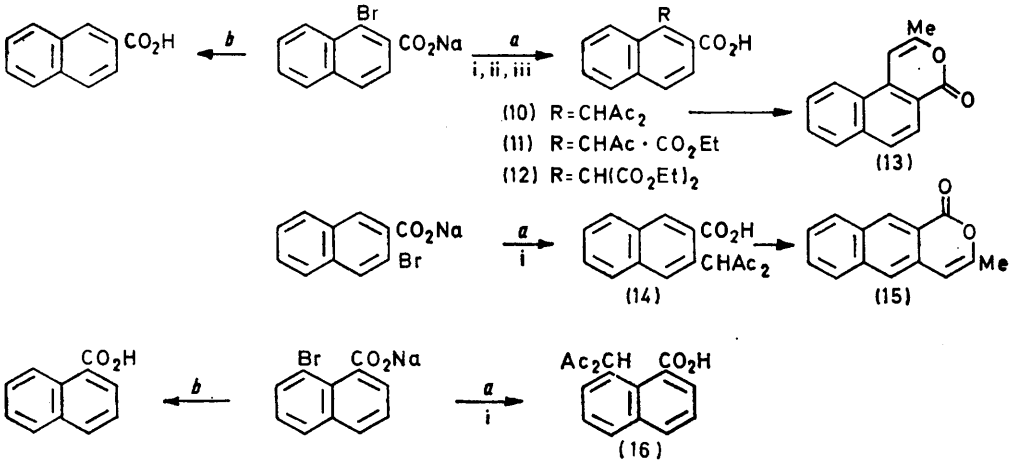
TABLE 2

Sodium *o*-bromobenzoate (10 mmol) + $NaCHAc_2$ (10 mmol) + copper species (0·7 mmol), under nitrogen, in refluxing ethanol (15 ml)

Catalyst	Time (h)	Recovered bromo-acid (%)	Product yields (%) (1)	(2)
None	3	94		
Cu bronze	3		73 [a]	
Cu bronze	24			67
CuBr	0·6		72	
CuBr	3			68
Cu_2O	3	21	4	66
$Cu(OAc)_2$ [a]	3		69	
$Cu(CHAc_2)_2$	3	46		47
$(o\text{-}C_6H_4Br{\cdot}CO_2)_2Cu$	3	27		66

[a] Lit.,[8] 64—73% with Cu; $Cu(OAc)_2$ was employed [8] with $NaCH(CO_2Et)_2$.

incipient enolate carbanion generated by fission of the acyl group. For isocoumarin syntheses,[10] *o*-carboxybenzyl ketones, such as (2), have been used as intermediates, but their cyclisation has commonly been carried out in acidic media. Conditions here found effective for producing isocoumarins (Tables 1 and 3) might also be applied, with use of appropriately constituted bromo-carboxylates and salts of β-diketones, malonate (4) [8] and a trace of the half ester (5), but in dimethylformamide the chief product was ethyl *o*-(ethoxycarbonyl)phenylacetate (6), presumably a consequence of transesterification between the $CH(CO_2Et)_2$ and CO_2H groups in (4), followed by decarboxylation. The sodium derivatives of ethyl cyanoacetate and malononitrile reacted with sodium *o*-bromobenzoate in ethanol to give the expected substitution products, (7)



SCHEME 2 [a] Acidification after heating in solution with CuBr and i, $NaCHAc_2$; ii, $NaCHAc{\cdot}CO_2Et$; or iii, $NaCH(CO_2Et)_2$. [b] Competitive reduction by hydrogen donors

TABLE 3

Na bromonaphthalenecarboxylates (10 mmol) + NaCHXY (15 mmol) + CuBr, in solvent (15 ml), refluxing under nitrogen

Na bromonaphthalene-carboxylate	Nucleophile NaCHXY	CuBr (mmol)	Solvent	Temp. (°C)	Time (h)	Recovered bromo-acid (%)	Naphthoic acid (%)	Substitution products (%)	
1-Br-2-CO_2Na	$NaCHAc_2$	Nil	EtOH	78	3	70			
1-Br-2-CO_2Na	$NaCHAc_2$	0·7	EtOH	78	18		Trace	(10) 81	(13) 1
1-Br-2-CO_2Na	$NaCHAc_2$	5	EtOH	78	3		Trace	(10) 83	(13) 1
1-Br-2-CO_2Na	$NaCHAc_2$	5	$HCO{\cdot}NMe_2$	153	3	25			(13) 20
1-Br-2-CO_2Na	$NaCHAc_2$	5	2,4,6-Collidine	170	3		55		(13) 4
1-Br-2-CO_2Na	$NaCHAc{\cdot}CO_2Et$	5	EtOH	78	3			(11) 62	
1-Br-2-CO_2Na	$NaCH(CO_2Et)_2$	5	EtOH	78	3			(12) 45	
3-Br-2-CO_2Na	$NaCHAc_2$	5	EtOH	78	3	4		(14) 40	
3-Br-2-CO_2Na	$NaCHAc_2$	5	$HCO{\cdot}NMe_2$	153	3				(15) 9
8-Br-1-CO_2Na	$NaCHAc_2$	5	EtOH	78	3		42	(16) 21	

with the aim of synthesising naturally occurring members of the series,[10] which are commonly substituted in the 3-position and carry methoxy- or hydroxy-groups on the benzene ring.

Reactions of sodium *o*-bromobenzoate with four other nucleophiles were briefly examined (Scheme 1 and Table 1). Substitution in ethanol by ethyl sodioacetoacetate was followed by deacylation, furnishing exclusively *o*-(ethoxycarbonylmethyl)benzoic acid (5) [8] in high yield. In dimethylformamide, as with acetylacetonate, reductive substitution competed; also, the nucleophilic substitution was less extensive than in ethanol and led to different products, *i.e.* the oxo-acid (2) and the isocoumarin (3), resulting from de-esterification, decarboxylation, and cyclisation. Reaction in ethanol with diethyl sodiomalonate gave the expected and (8), respectively. The dicyano-compound (8) underwent both *O*- and *C*-methylation by diazomethane, giving methyl *o*-(1,1-dicyanoethyl)benzoate (9).

To test reactivity in the naphthalene series, 1-bromo-2-, 3-bromo-2-, and 8-bromo-1-naphthoic acids were synthesised. Their sodium salts underwent nucleophilic substitution (Scheme 2 and Table 3) but this occurred less readily than with sodium *o*-bromobenzoate and there were indications of increased susceptibility to reductive substitution (*cf.* competitive effects in reactions of aryl halides with alkoxides [4]). Sodium 1-bromo-2-naphthoate was the most responsive of the three and, analogously to sodium *o*-bromobenzoate, gave a high yield of the dioxo-acid (10) in ethanol and the naphthopyranone (13) in dimethylformamide, whilst reaction in collidine gave

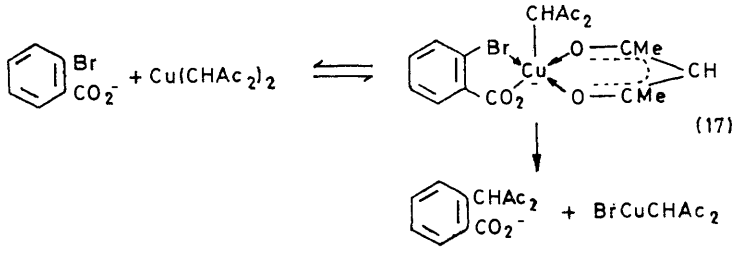
[10] R. D. Barry, *Chem. Rev.*, 1966, **66**, 229.

largely the reduction product, 2-naphthoic acid. The cyclisation (10) ⟶ (13) did not require copper catalysis and appeared to be a direct transformation, as with the benzoate analogue. Formation of the acetoacetate derivative (11) and the malonate derivative (12) proceeded normally in ethanol. Similarly, sodium 3-bromo-2-naphthoate and sodium acetylacetonate gave the dioxo-acid (14) in ethanol and the naphthopyranone (15) in dimethylformamide. Sodium 8-bromo-1-naphthoate in ethanol likewise gave the dioxo-acid (16), but the major effect was reductive substitution to 1-naphthoic acid. Copper-catalysed reactions of alkoxides with this bromo-acid have been reported.[11] These replacements are in accord with the reactivity of *peri*-substituted naphthalenes.[12]

Possible Intermediate Complexes.—Acetylacetonate anions stabilise the Cu^{II} state at the expense of Cu^{I}, causing disproportionation: [13]

$$2Cu^{+} + 2CHAc_2^{-} \longrightarrow Cu(CHAc_2)_2 + Cu$$

Hence, irrespective of the initial oxidation state of the copper employed, intermediates in the substitutions may be copper(II) complexes. If reaction is considered to involve complexes containing both an acetylacetonate ligand and an *ortho*- or *peri*-chelated bromocarboxylate ligand, as *e.g.* in (17), the substitution may be depicted as in Scheme 3. A similar concept has been advanced [14] in the case of assisted ester exchange involving ethyl 2-pyridylacetate and a copper(II) methoxyacetylacetonate complex.



SCHEME 3

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were obtained with a Varian HR-100 instrument (tetramethylsilane as internal standard). Chromatographic alumina was Spence type H; when 'deactivated,' it had been treated with 5% of aqueous 10% acetic acid. Solvents were dried by standard procedures and redistilled. In the case of ethanol the method was to add sodium, reflux with diethyl succinate, and redistil. Copper species were vacuum-dried.

Acetylacetone was converted into the sodium salt with sodium hydroxide in aqueous methanol.[15] If not generated *in situ*, sodium salts of carboxylic acids were pre-prepared by mixing the acid in methanol with an equivalent amount of sodium methoxide in methanol, followed by precipitation with ether.

Products from 2-Bromobenzoic Acid.—(a) *With acetylacetone as nucleophile.* The reactions summarised in Tables 1 and 2 were carried out in an atmosphere of dried nitrogen. Either the reagents were employed as sodium salts, or the carboxylic acid, the nucleophile, and sodium were introduced in the molar ratio 1 : 1 : 2. Sodium bromide separated as reaction proceeded and a green-blue colour developed, but was masked in the higher-boiling solvents, particularly collidine, as tar formation occurred. Products were isolated by addition to dilute hydrochloric acid and extraction with ether. A portion of the extract was treated with diazomethane in ether and the mixture of methyl esters was subjected to g.l.c. analysis [Versamid 930 column in a Perkin-Elmer F11 instrument; retention times Me benzoate, 1·5; *o*-bromobenzoate, 4; *o*-acetonylbenzoate, 8; *o*-(diacetylmethyl)benzoate, 10 min]. Under appropriate preparative conditions (see Tables 1 and 2) the following products were isolated.

o-(Diacetylmethyl)benzoic acid (1) formed needles, m.p. 142—143° (from ether–light petroleum) (lit.,[8] 142°) (Found: C, 65·3; H, 5·5. Calc. for $C_{12}H_{12}O_4$: C, 65·5; H, 5·5%), τ −0·4br (s, CO_2H), 1·76—2·74 (m, aromatic + 3-CH), and 8·14 (s, 2 Me). This was converted by diazomethane into the *methyl ester*, m.p. 80° (from light petroleum) (Found: C, 66·6; H, 6·2. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%), τ 1·96—2·85 (m, aromatic + 3-CH), 6·17 (s, CO_2Me), and 8·21 (s, 2 COMe). *o*-Acetonylbenzoic acid (2) was obtained as crystals, m.p. 120—121° (lit.,[16] 119—120°), τ 1·8—2·9 (m, aromatic), 6·05br (s, CH_2), and 7·85 (s, Me), identical with a sample prepared [17] by alkaline hydrolysis of 3-methylisocoumarin. The *methyl ester* was an oil, b.p. 103—104° at 0·2 mmHg (Found: C, 68·9; H, 6·5. $C_{11}H_{12}O_3$ requires C, 68·7; H, 6·3%), τ 2·0—3·0 (m, aromatic), 6·02 (s, CH_2), 6·20 (s, CO_2Me), and 7·85 (s, COMe). 3-Methylisocoumarin (3), purified by sublimation, formed needles, m.p. 73—74° (lit.,[17] 73—74°) (Found: C, 74·8; H, 5·0. Calc. for $C_{10}H_8O_2$: C, 75·0; H, 5·0%), τ 1·7—2·7 (m, aromatic), 3·72 (s, 4-H), and 7·72 (s, Me).

(b) *With other nucleophiles* (*Table* 1). Salts were generated *in situ* by using sodium metal in the reaction mixtures. Reaction with ethyl acetoacetate in ethanol gave *o*-(ethoxycarbonylmethyl)benzoic acid (5), m.p. 107—108° (lit.,[8] 109°), τ −0·8br (s, CO_2H), 0·8—1·8 (m, aromatic), 5·8 (q, CH_2), 5·92 (s, CH_2), and 8·72 (t, CH_3). The mixture of products obtained in dimethylformamide was treated with

[11] H. G. Rule and A. J. G. Barnett, *J. Chem. Soc.*, 1932, 2728.
[12] V. Balasubramaniyan, *Chem. Rev.*, 1966, **66**, 567.
[13] R. Nast, R. Mohr, and C. Schultze, *Chem. Ber.*, 1963, **96**, 2127.
[14] R. P. Houghton and C. S. Williams, *Tetrahedron Letters*, 1967, 5091.
[15] R. G. Charles, *Org. Synth.*, Coll. Vol. IV, 1963, p. 869.
[16] A. H. Salway and F. S. Kipping, *J. Chem. Soc.*, 1909, **95**, 166.
[17] J. Gottlieb, *Ber.*, 1899, **32**, 958.

alkali, leaving 3-methylisocoumarin. Reaction with diethyl malonate in ethanol gave diethyl *o*-carboxyphenylmalonate (4), m.p. 102° (lit.,[8] 102°). Reaction in dimethylformamide, followed by treatment with alkali, and chromatography of the neutral fraction on deactivated alumina yielded ethyl *o*-(ethoxycarbonyl)phenylacetate (6), identical with a sample prepared by treating the monoethyl ester (5) with ethanol saturated with hydrogen chloride; τ 2·0—2·9 (m, aromatic), 5·6—6·05 (2 q, 2 CH_2), 6·1 (s, CH_2), and 8·6—8·85 (2 t, 2 Me). Reaction with ethyl cyanoacetate in ethanol gave o-[*cyano*(*ethoxycarbonyl*)*methyl*]*benzoic acid* (7), obtained as a pale yellow solid, m.p. 208—209°, after sublimation (Found: C, 61·8; H, 4·9; N, 5·9. $C_{12}H_{11}NO_4$ requires C, 61·8; H, 4·7; N, 6·0%), *m/e* 233 (M^+), τ 1·4—2·7 (aromatic), 5·5 (q, CH_2), and 8·6 (t, Me). Reaction with malononitrile in ethanol left a yellow solution which on acidification gave a yellow precipitate, not dissolved by ether or chloroform, but going into solution when stirred for some hours with diazomethane in ether. The resulting ester solution showed two constituents in a t.l.c. test; the major component was isolated by elution with light petroleum on a column of deactivated alumina and identified as *methyl* o-(1,1-*dicyanoethyl*)*benzoate* (9), forming needles, m.p. 130—131° (Found: M^+, 214·0737. $C_{12}H_{10}N_2O_2$ requires *M*, 214·0742), τ 1·8—2·7 (m, aromatic), 5·84 (s, Me), and 5·90 (s, Me). A yellow minor component, m.p. 209—210°, was eluted with dichloromethane–light petroleum.

Products from Reactions of Bromonaphthoic Acids.—(a) *From* 1-*bromo*-2-*naphthoic acid*. 1-Bromo-2-methylnaphthalene [18] was converted [19] into the bromo-acid. The following products were obtained under conditions shown in Table 3. 1-(*Diacetylmethyl*)-2-*naphthoic acid* (10) formed sublimable crystals, m.p. (sealed tube) 187° (from ether–light petroleum) (Found: C, 71·0; H, 5·4. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%), τ 0·4br (CO_2H), 1·8—2·45 (m, aromatic and CO·CH·CO), and 8·26 (s, 2 Me). 2-Naphthoic acid, from the reaction in collidine, was identical with an authentic sample. The neutral fraction from the reaction in dimethylformamide yielded 2-*methylnaphtho*[2,1-c]*pyran*-4-*one* (13) as needles, m.p. 169—170° (from benzene) (Found: C, 80·0; H, 4·7. $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%), τ 1·7—2·5 (m, aromatic), 3·03 (s, 1-H), and 7·63 (s, Me), $\nu_{max.}$ 1715 cm^{-1} [CO, as in (3)]. The reaction with ethyl acetoacetate gave 1-(1-*ethoxycarbonylacetonyl*)-2-*naphthoic acid* (11) as yellow crystals, m.p. 137° (from chloroform–light petroleum) (Found: C, 68·1; H, 5·4. $C_{17}H_{16}O_5$ requires C, 68·0; H, 5·4%), *m/e* 300 (M^+). The n.m.r. spectrum included two sets of peaks for protons in the CHAc·CO_2Et substituent, attributed to different conformers: τ 1·7—2·5 (m, aromatic), 5·20 and 5·25 (s, CH), 5·85 and 5·90 (q, CH_2), 8·08 and 8·42 (s, COMe), and 8·83 and 8·97 (t, Me). The reaction with diethyl malonate gave *diethyl* (2-*carboxy*-1-*naphthyl*)*malonate* (12) as yellow crystals, m.p. 163—164° (from methanol) (Found: C, 65·2; H, 5·6. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·5%), *m/e* 330 (M^+), τ 1·8—2·5 (m, aromatic), 3·56 (s, CH), 5·87 (q, 2 CH_2), and 8·87 (t, 2 Me).

(b) *From* 3-*bromo*-2-*naphthoic acid*. 3-Hydroxy-2-naphthoic acid was converted into 3-amino-2-naphthoic acid [20] and the latter into the corresponding bromo-acid,[21] which gave the substitution products shown in Table 3. The reaction in ethanol yielded a gummy sample of 3-(diacetylmethyl)-2-naphthoic acid (14), which was treated with diazomethane; the *methyl ester* was isolated by elution with dichloromethane–light petroleum (4 : 1) from a silica gel column and was purified by repeated crystallisation from methanol, which gave crystals, m.p. 94—95° (Found: M^+, 248·1048. $C_{17}H_{16}O_4$ requires *M*, 248·1048), τ 1·45 (s, *ortho* to CO_2Me), 2·0—2·5 (m, other aromatic), 6·12 (s, CO_2Me), and 8·18 (s, 2 COMe). The reaction in dimethylformamide gave 3-*methylnaphtho*[2,3-c]*pyran*-1-*one* (15) as yellow plates, m.p. 195—196° (from benzene) (Found: C, 79·9; H, 4·8 $C_{14}H_{10}O_2$ requires C, 80·0; H, 4·8%), *m/e* 210 (M^+), τ 1·19 (s, 10-H), 2·0—2·65 (m, other aromatic H), 3·71 (s, 4-H), and 7·74 (s, Me)

(c) *From* 8-*bromo*-2-*naphthoic acid* This was prepared from benz[*cd*]indol-1(2*H*)-one (naphthastyril).[22] The product from the reaction with acetylacetone (Table 3) was chromatographed on a silica gel column, which gave 1-naphthoic acid, followed by an impure sample of the desired dioxo-acid. The latter was treated with diazomethane and the product similarly chromatographed with dichloromethane–light petroleum; this gave methyl 1-naphthoate followed by *methyl* 8-(*diacetylmethyl*)-1-*naphthoate* (16), isolated as large prisms (from methanol–light petroleum), m.p. 130—131° (Found: C, 72·0; H, 5·9. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·7%), *m/e* 284 (M^+), τ 2·0—2·2 and 2·35—2·7 (m, aromatic), 6·18 (s, CO_2Me), and 8·20 (s, 2 COMe).

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[18] D. M. Hall and R. K. Mitchell, *J. Chem. Soc.*, 1951, 1375.
[19] E. D. Bergmann and J. Szmuszkovicz, *J. Amer. Chem. Soc.*, 1951, **73**, 5153.
[20] P. C. Dutta, *Ber.*, 1934, **67**, 1319.
[21] J. Kenner, W. H. Ritchie, and R. L. Wain, *J. Chem. Soc.*, 1937, 1526.
[22] H. Goldstein and P. Francey, *Helv. Chim. Acta*, 1932, **15**, 1362.