The Chemistry of Azides derived from *N*-substituted Phthalamic and Tetrahalogenophthalamic Acids

By **Ting Keung Au, Ahmet E. Baydar,** and **Gerhard V. Boyd,*** Department of Chemistry, Chelsea College, London SW3 6LX

Treatment of eight phthalisoimidium perchlorates with sodium azide gave *N*-substituted *o*-carbamoylbenzoyl azides (2), which yielded *o*-carbamoylphenyl isocyanates (4) when heated. The isocyanates derived from tertiary phthalamic acids formed 4-dialkyl ammonio-1,4-dihydro-2*H*-3,1-benzoxazin-2-one perchlorates (8) by the action of perchloric acid and acetic anhydride; those containing secondary amide groups cyclised to 3-alkyl-quinazoline-2,4-(1*H*,3*H*)-diones (11) at rates depending on the size of the alkyl radicals. Tetrachloro- and tetrabromo-phthalic anhydride reacted with amines to yield the corresponding amic acids, their salts, or *N*-substituted 3-amino-4-hydroxyphthalides. Ring-chain isomerism was also observed in the case of the azides derived from two tertiary tetrachlorophthalamic acids.

We have extended our studies on the reaction of sodium azide with maleisoimidium perchlorates [1] to an investigation of the behaviour of the related phthalisoimidium salts (1a—i), many of which have been described previously.[2] These salts gave the corresponding acyl azides (2), with the exception of the phenyl-derivative (1i), which afforded *N*-phenylphthalimide. It appears that in this case the action of sodium azide caused deprotonation to yield *N*-phenylisoimide (3i), which is known [3] to rearrange readily to the normal imide under basic catalysis. In order to test whether the formation of the azides (2c—h) of secondary amic acids occurs by way of the respective isoimides (3c—h), we treated the exceptionally stable *N*-t-butylphthalisoimide (3f) [2] with sodium azide. We obtained solely *N*-t-butylphthalimide and therefore conclude that the acyl azides are produced directly by attack on the isoimidium cations.

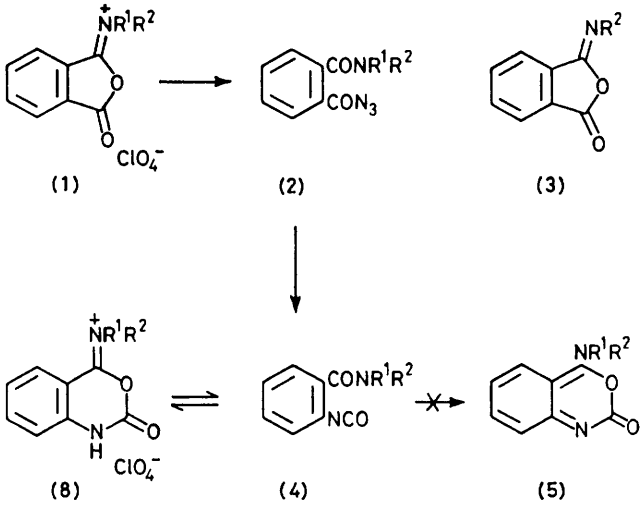
The azides (2a—h) were isolated as thermally unstable oils or solids; they were characterised by their i.r. spectra, which exhibited bands due to azide, azide carbonyl, and amide carbonyl groups at *ca.* 2 140, 1 700, and 1 650 cm^{-1}, respectively. The azides readily underwent a Curtius rearrangement to the corresponding isocyanates (4) ($\nu_{max.}$ at *ca.* 2 260 cm^{-1}) in boiling benzene. When the thermolysis of the azides (2a,b) derived from tertiary phthalamic acids was followed by i.r. spectroscopy, it was observed that the rearrangement was complete after about 1 h and that the resulting isocyanates (4a, b) were stable for at least 100 h in boiling benzene. Thus there was no evidence for electrocyclisation to the *ortho*-quinonoid benzoxazinones (5a,b), the benzologues of 1,3-oxazin-2-ones.[1] The isolated *o*-diethylcarbamoylphenyl isocyanate (4a) was very sensitive to moisture, being rapidly converted into the urea derivative (6a); attempted crystallisation of the latter from hot benzene resulted in a compound, whose mass spectrum and analysis showed that its formation involved the elimination of a molecule of diethylamine. Its ^1H n.m.r. and i.r. spectra accorded with the quinazolinedione structure (7).

The benzoxazinones (5a,b) were obtained in the form of their conjugate acids (8a, b) when the isocyanates (4a, b) were treated with acetic anhydride and perchloric acid. The products showed high-frequency carbonyl bands at *ca.* 1 815 cm^{-1}, typical of cyclic isoimidium salts,[2] as well as NH and $C{=}N^+$ absorptions. The diethyl compound (8a) afforded the urea derivatives (6a) and (9) when treated with water and t-butylamine, respectively. Both salts reverted to the original isocyanates on attempted deprotonation with triethylamine, and we failed to demonstrate the intermediate formation of the benzoxazinones (5) by trapping experiments, in which the deprotonation was carried out in the presence of *N*-phenylmaleimide or dimethyl acetylenedicarboxylate. These negative results were disappointing as we had considered that the benzoxazinone structure might be stabilised by resonance [*cf.* (5A)] and because a number of analogous *ortho*-quinonoid 2-benzopyran-3-ones have been generated and shown to function as dienes in Diels-Alder reactions.[4]

Decomposition of the azides (2c—h) derived from secondary phthalamic acids in boiling benzene gave transient isocyanates (10c—h), which reacted further to yield the corresponding 3-alkylquinazoline-2,4-diones (11c—h).† When the process was monitored by i.r. spectroscopy, it was seen that while the six azides underwent the Curtius rearrangement at about the same rate, the ease of the subsequent cyclisation depended on the bulk of the *N*-alkyl groups. The experiments were only qualitative because the two reactions proceeded side-by-side; transient isocyanate bands appeared and decayed the azides had completely decomposed. Isocyanates (10c,d) containing primary alkyl substituents underwent ring-closure so fast that they were barely detectable, bands due to the secondary butyl derivative (10e) persisted for *ca.* 1 min, those due to the t-butyl and cyclohexyl compounds (10f and g) for about 5 min, and the spectrum of the 1-adamantyl derivative (10h) was observable for *ca.* 15 min during the reaction.

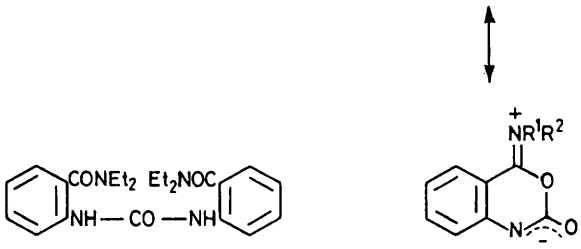
N-Substituted Tetrachloro- and Tetrabromo-phthalamic Acids.—A number of *N*-aryl-tetrachloro- and -tetrabromo-phthalamic acids are known,[5,6] but *N*-alkyl- and *NN*-dialkyl-derivatives have not been reported previously. Treatment of tetrachlorophthalic anhydride

† 3-Phenylquinazoline-2,4-dione (11i) results from the reaction of *N*-phenylphthalisoimide with hydrazoic acid (H. Behringer and H. J. Fischer, *Chem. Ber.*, 1961, **94**, 2662).

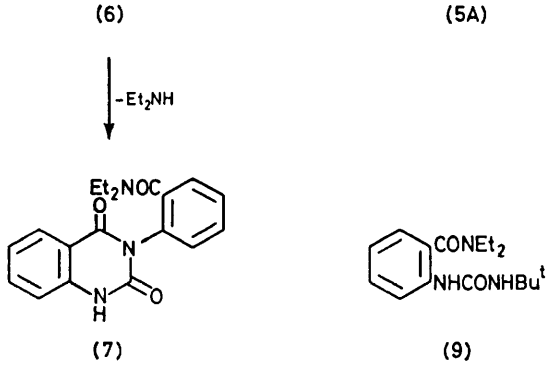


(1) (2) (3)

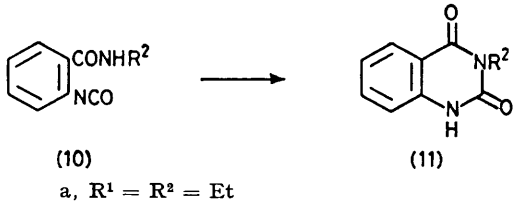
(8) (4) (5)



(6) (5A)



(7) (9)

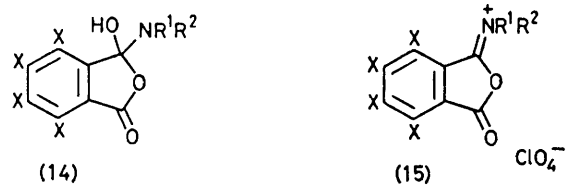


(10) (11)

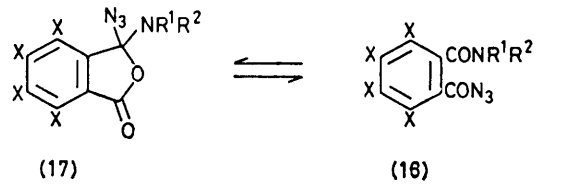
a, $R^1 = R^2 = Et$
b, NR^1R^2 = piperidino
c, $R^1 = H$, $R^2 = Bu^n$
d, $R^1 = H$, $R^2 = Bu^i$
e, $R^1 = H$, $R^2 = Bu^s$
f, $R^1 = H$, $R^2 = Bu^t$
g, $R^1 = H$, R^2 = cyclohexyl
h, $R^1 = H$, R^2 = 1-adamantyl
i, $R^1 = H$, $R^2 = Ph$

with diethylamine in refluxing benzene for 30 min gave a mixture of the expected amic acid (12a) and its diethylammonium salt (13a); extension of the time of heating to 1 h resulted in complete recovery of the anhydride. The use of boiling acetone or ethyl acetate gave a different product, which was shown by analysis and i.r. spectroscopy (ν_{CO} 1 733 cm^{-1}) to be the phthalide (14a), the cyclic tautomer of the amic acid. The phthalide was also formed when the amic acid (12a) was heated at 100 °C for 2 h; no conditions for reversing the process could be found. The unexpected formation of an aminohydroxyphthalide prompted a more detailed study of the action of primary and secondary amines on tetrachloro- and tetrabromo-phthalic anhydride. The experiments were conducted by heating equimolecular amounts of the components in various solvents; there usually was no reaction in the cold. The results are summarised in the Table. Three types of products were obtained, which were identified by their i.r. spectra.

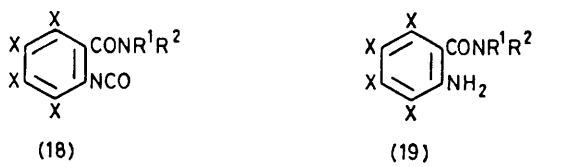
(12) (13)



(14) (15)



(17) (16)



(18) (19)

a, X = Cl, $R^1 = R^2 = Et$
b, X = Br, $R^1 = R^2 = Et$
c, X = Cl, NR^1R^2 = pyrrolidino
d, X = Br, NR^1R^2 = pyrrolidino
e, X = Cl, NR^1R^2 = piperidino
f, X = Br, NR^1R^2 = piperidino
g, X = Cl, $R^1 = H$, $R^2 = Bu^t$
h, X = Br, $R^1 = H$, $R^2 = Bu^t$
i, X = Cl, $R^1 = H$, $R^2 = Ph$
j, X = Br, $R^1 = H$, $R^2 = Ph$

Amic acids (12) showed acid and amide carbonyl bands at 1 720—1 695 and 1 660—1 600 cm^{-1}, respectively; the spectra of the salts (13) contained broad bands at 3 000—2 800 cm^{-1}, due to substituted ammonium ions, as well as carboxylate absorptions at 1 610—1 600 cm^{-1} and amide carbonyl bands in the 1 630 cm^{-1} region; while the phthalides (14) showed carbonyl bands at 1 749—1 733 cm^{-1}, typical of γ-lactones. It is seen that, in general, primary amines give amic acids, whereas secondary amines yield mainly phthalides and, less usually, salts of amic acids. We suggest that the phthalide forms are favoured over the open-chain isomers because in the latter the presence of the bulky halogen atoms causes congestion between the carboxyl and carbamoyl groups, which is relieved on cyclisation. Ring—chain tautomerism of esters [7] and halides [8] of phthalic acids has been studied extensively but has not been observed previously for phthalamic acids.

The phthalides (14a, c, e, and f) were converted into the corresponding isoimidium salts (15) by the action of acetic anhydride and perchloric acid. The reaction of the salts with sodium azide gave products which also exhibited the phenomenon of ring–chain tautomerism. The pyrrolidino–compound (15c) gave the expected acyl azide (16c), which showed azide, azide carbonyl, and amide carbonyl absorptions at 2 140, 1 715, and 1 647 cm^{-1}, respectively. The i.r. spectrum of a benzene solution of the compound gradually changed: bands at 2 120 and 1 770 cm^{-1} appeared, while those mentioned previously diminished. The new bands are assigned to the azidophthalide (17c). After 3 h at room temperature equilibrium had been established and the solution contained the open and cyclic tautomers in the approximate ratio 2 : 1, as estimated by i.r. spectroscopy. The action of sodium azide on the piperidinio perchlorates (15e and f) afforded the phthalides (17e and f) ($\nu_{max.}$ 1 780 cm^{-1}). When the former was dissolved in acetonitrile, it was gradually converted into the acyl azide (16e) ($\nu_{max.}$ 2 137, 1 700, and 1 640 cm^{-1}); the change was complete after 30 min.

Ring–chain tautomerism involving migration of an azide group is rare; the only other recorded case concerns *o*-azidosulphonylbenzophenones.[9]

Both the open-chain (16c) and cyclic azides (17e and f) rearranged to the corresponding isocyanates (18c, e, and f, respectively) in boiling benzene or toluene; further heating had no effect. The isolated isocyanates (18c and e) were readily hydrolysed when exposed to the atmosphere to yield the amines (19c and e).

TABLE

Reaction of amines with tetrachloro- and tetrabromophthalic anhydride [a]

Anhydride [b]	Amine	Solvent [c]	Products
TCP	Diethylamine	B	(12a) + (13a)
TCP	Diethylamine	A or EA	(14a)
TBP	Diethylamine	B [d]	(14b)
TBP	Diethylamine	B	(13b) + TBP
TBP	Diethylamine	A or EA [e]	(12b)
TBP	Diethylamine	A or EA	(14b)
TCP	Pyrrolidine	B, A, or EA	(14c)
TBP	Pyrrolidine	B	(13d)
TBP	Pyrrolidine	A or EA	(14d)
TCP	Piperidine	B [e]	(13e)
TCP	Piperidine	B, A, or EA	(14e)
TBP	Piperidine	B	(14f)
TBP	Piperidine	A or EA	(13f)
TCP	t-Butylamine	B, A, or EA	(12g)
TBP	t-Butylamine	B	(12h) + TBP
TBP	t-Butylamine	A or EA	(12h)
TCP	Aniline	B, A, or EA	(12i)
TBP	Aniline	B	(13j) + TBP
TBP	Aniline	A or EA	(12j)

[a] Equimolecular amounts (1 mmol) of amine and anhydride were added to the stated solvent (10 ml) and the mixture was refluxed for 30 min, unless stated otherwise. [b] TCP = Tetrachlorophthalic anhydride, TBP = tetrabromophthalic anhydride. [c] B = Benzene, A = acetone, EA = ethyl acetate. [d] Reflux for 15 min. [e] 24 h At room temperature.

EXPERIMENTAL

For general remarks, see ref. 1.

Phthalisoimidium Perchlorates (1).—A suspension of a *N*-substituted phthalamic acid (50 mmol) in acetic anhydride (50 ml) was treated dropwise with perchloric acid (7 ml) with occasional cooling. The product was filtered off and washed with ether. *N*-n-Butylphthalamic acid [10] gave N-*n-butylphthalisoimidium perchlorate* (1c) (9.1 g, 60%), m.p. 142—144 °C (decomp.), $\nu_{max.}$ 3 220, 1 860, 1 720, and 1 110 cm^{-1} (Found: C, 46.7; H, 4.7; N, 4.5. $C_{12}H_{14}ClNO_6 \cdot \frac{1}{4}H_2O$ requires C, 46.7; H, 4.7; N, 4.5%); *N*-isobutylphthalamic acid [11] gave N-*isobutylphthalisoimidium perchlorate* (1d) (11.8 g, 78%), m.p. 165—167 °C (decomp.), $\nu_{max.}$ 3 220, 1 860, 1 720, and 1 100 cm^{-1}; δ 8.2—7.4 (m, 4 H, Ar), 3.2 (br t, CH_2), 2.1—1.7 (m, CH), and 1.01 (d, 2 × Me) (Found: C, 46.3; H, 4.6; N, 4.4. $C_{12}H_{14}ClNO_6 \cdot \frac{1}{2}H_2O$ requires C, 46.1; H, 4.5; N, 4.5%); *N*-cyclohexylphthalamic acid [12] gave N-*cyclohexylphthalisoimidium perchlorate* (1g) (14.2 g, 86%), m.p. 179—181 °C (decomp.), $\nu_{max.}$ 3 220, 1 870, 1 710, and 1 100 cm^{-1}; δ 8.0—7.3 (m, 4 H, Ar), 3.9—3.6 (m, CH), and 2.2—1.0 (m, 10 H) (cyclohexyl) (Found: C, 50.6; H, 5.0; N, 4.15. $C_{14}H_{16}ClNO_6$ requires C, 51.0; H, 4.9; N, 4.25%); and *N*-1-adamantylphthalamic acid [13] gave N-1-*adamantylphthalisoimidium perchlorate* (1h) (18.3 g, 96%), m.p. 193—195 °C (decomp.), $\nu_{max.}$ 3 220, 1 870, 1 700, and 1 100 cm^{-1}; δ 8.1—7.3 (m, 4 H, Ar) and 2.3—1.6 (m, 15 H, adamantyl) (Found: C, 55.9; H, 5.45; N, 3.75. $C_{18}H_{20}ClNO_6 \cdot \frac{1}{4}H_2O$ requires C, 55.8; H, 5.4; N, 3.6%).

Phthalamoyl Azides (2).—A phthalisoimidium perchlorate (20 mmol) was added in small portions to a stirred solution of sodium azide (1.95 g, 1.5 mol equiv.) in a mixture of water (8 ml) and acetone (15 ml), and the acetone was removed *in vacuo* at room temperature. The resulting azide, if solid, was filtered off and dried over P_2O_5. If the azide was an oil, it was extracted three times with ether; the combined extracts were dried ($MgSO_4$) and the ether was removed *in vacuo* at room temperature. The products were characterised by their i.r. spectra, as they were too unstable to be purified for analysis. The following benzoyl azides were obtained: *o*-diethylcarbamoyl-(2a) (4.4 g, 89%), unstable oil, $\nu_{max.}$ (C_6H_6) 2 140, 1 700, and 1 648 cm^{-1}; *o*-piperidinocarbonyl- (2b) (3.2 g, 62%), oil, $\nu_{max.}$ (neat) 2 135, 1 690, and 1 630 cm^{-1}; *o*-n-butylcarbamoyl- (2c) (1.48 g, 30%), unstable oil, $\nu_{max.}$ (C_6H_6) 3 200, 2 140, 1 700, and 1 630 cm^{-1}; *o*-isobutylcarbamoyl- (2d) (3.44 g, 70%), m.p. 71—73 °C (decomp.), $\nu_{max.}$ 3 280, 2 140, 1 720, and 1 650 cm^{-1}; *o*-s-butylcarbamoyl- (2e) (1.72 g, 35%),

oil, $\nu_{max.}$ (C_6H_6) 3 250, 2 140, 1 700, and 1 642 cm^{-1}; *o*-t-butylcarbamoyl- (2f) (3.84 g, 78%), m.p. 76—77 °C (decomp.), $\nu_{max.}$ 3 200, 2 140, 1 700, and 1 642 cm^{-1}; *o*-cyclohexylcarbamoyl- (2g) (3.81 g, 70%), m.p. 78—80 °C (decomp.), $\nu_{max.}$ 3 300, 2 140, 1 700, and 1 638 cm^{-1}; and *o*-1-adamantylcarbamoyl- (2h) (4.67 g, 72%), m.p. 116—117 °C (decomp.), $\nu_{max.}$ 3 280, 2 140, 1 700, and 1 630 cm^{-1}.

Preparation and Reactions of o-*Diethylcarbamoylphenyl Isocyanate* (4a).—A solution of the azide (2a) (2.46 g) in benzene (20 ml) was refluxed for 51 min, when i.r. spectroscopy indicated that decomposition was complete. Removal of the solvent *in vacuo* left the isocyanate (2.18 g, 100%) as an unstable oil, $\nu_{max.}$ (C_6H_6) 2 265 and 1 632 cm^{-1}. When the azide (2a) or the isocyanate were left in an open container they gradually changed to *NN'*-bis(o-diethylcarbamoylphenyl)urea (6) (100%), m.p. 180—183 °C (decomp.), $\nu_{max.}$ 3 300, 1 710, and 1 620 cm^{-1}; δ 8.42 (br s, slowly disappears on adding D_2O, NH), 8.0—6.9 (m, 4 H, Ar), 3.35 (q, 4 × CH_2), and 1.09 (t, 4 × Me). Attempted crystallisation of the urea from hot benzene gave 3-(o-*diethylcarbamoylphenyl*)*quinazoline*-2,4(1H,3H)-*dione* (7) (100%), m.p. 257—259 °C (from benzene), $\nu_{max.}$ 3 220, 1 728, 1 672, and 1 618 cm^{-1}; δ[$(CD_3)_2SO$] 8.1—7.0 (m, 8 H, Ar), 3.22 (br q, 2 × CH_2), 2.88 (s, exchanges with deuterium, NH), 1.11 (t, Me), and 0.89 (t, Me); *m/e* 337 (M^+) and 265 ($M - NEt_2$)$^+$ (Found: C, 67.7; H, 5.75; N, 12.3. $C_{19}H_{19}N_3O_3$ requires C, 67.65; H, 5.7; N, 12.45%). A suspension of the isocyanate (4a) (1.06 g) in acetic anhydride (6 ml) was treated with perchloric acid (1.2 ml), whereupon 4-*diethylammonio*-1,4-*dihydro*-2H-3,1-*benzoxazin*-2-*one perchlorate* (8a) (1.24 g, 78%) crystallised; it had m.p. 188—190 °C (decomp.), $\nu_{max.}$ 3 230, 1 810, 1 632, 1 593, and 1 100 cm^{-1}; δ 9.85 (br s, NH), 8.08—7.3 (m, 4 H, Ar), 4.12 (sextet, 2 × CH_2), 1.68 (t, Me), and 1.49 (t, Me) (Found: C, 44.9; H, 4.85; Cl, 11.3; N, 8.6. $C_{12}H_{15}ClN_2O_6$ requires C, 45.2; H, 4.7; Cl, 11.4; N, 8.8%). The perchlorate (0.318 g, 1 mmol) was suspended in dry benzene (10 ml) and freshly distilled triethylamine (0.09 g, 0.9 mol equiv.) was added. The benzene solution was decanted from unchanged salt and triethylammonium perchlorate; i.r. spectroscopy showed that the solution contained only the isocyanate (4a). A solution of t-butylamine (2.19 g, 3 mol equiv.) in tetrahydrofuran (30 ml) was treated with the perchlorate (8a) (3.185 g, 10 mmol); addition of water to the resulting solution precipitated N-*t-butyl*-N'-(o-*diethylcarbamoylphenyl*)*urea* (9) (2.3 g, 79%), m.p. 155—157 °C (from aqueous ethanol), $\nu_{max.}$ 3 372, 3 340, 1 702, 1 600, and 1 590 cm^{-1}; δ 7.7 (br s, exchangeable for deuterium, NH), 7.9—6.88 (m, 4 H, Ar), 5.55 (br s, exchangeable for deuterium, NH), 3.41 (br q, 2 × CH_2), 1.27 (s, Bu^t), and 1.15 (t, 2 × Me) (Found: C, 65.6; H, 8.7; N, 14.5. $C_{16}H_{25}N_3O_2$ requires C, 65.9; H, 8.65; N, 14.4%).

o-*Piperidineocarbonylphenyl Isocyanate* (4b).—A solution of the azide (2b) (2.58 g) in toluene (25 ml) was refluxed until i.r. spectroscopy showed that decomposition was complete (1.5 h); evaporation of the solution under reduced pressure left the oily isocyanate (2.3 g, 100%), $\nu_{max.}$ 2 258, 1 620, and 1 600 cm^{-1}. A suspension of it (1.15 g, 5 mmol) in acetic anhydride (6 ml) was slowly treated with perchloric acid (0.75 ml); ether was added to the resulting solution to incipient turbidity, whereupon 1,4-*dihydro*-4-*piperidinio*-2H-3,1-*benzoxazin*-2-*one perchlorate* (8b) (1.27 g, 76%) crystallised; it had m.p. 234—235 °C (decomp.), $\nu_{max.}$ 3 210, 1 818, 1 679, 1 600, and 1 120 cm^{-1}; δ 9.9 (br s, NH), 8.25—7.45 (m, 4 H, Ar), and 4.1—3.7 (m, 4 H) and 2.1—1.8 (m, 6 H) (piperidino) (Found: C, 47.2; H, 4.6; Cl, 10.7; N, 8.5. $C_{13}H_{15}ClN_2O_6$ requires C, 47.2; H, 4.6; Cl, 10.7; N, 8.45%). A suspension of the salt (0.33 g) in dry benzene (10 ml) was treated with triethylamine (0.09 g, 0.9 mol equiv.). The i.r. spectrum of the benzene layer showed that it contained only the isocyanate (4b).

Thermolysis of o-*Carbamoylbenzoyl Azides* (2) *to yield Quinazolinediones* (11).—A solution of an azide (10 mmol) in benzene (40 ml) was heated under reflux. Small portions were withdrawn at intervals and their i.r. spectra determined; the time required for the disappearance of the azide absorption band (*t*) was noted. The resulting solution was evaporated under reduced pressure and the product isolated.

The azide (2c) decomposed with $t = 2$ h (no isocyanate band was observed) to yield 3-n-butylquinazoline-2,4-(1*H*,4*H*)-dione (11c) (1.31 g, 60%), m.p. 155—157 °C (from ethyl acetate) (lit.,[14] m.p. 155—157 °C), $\nu_{max.}$ 3 200, 1 720, and 1 650 cm^{-1}; azide (2d) decomposed with $t = 1$ h (a weak isocyanate band was detected in only one of the spectra, which was determined after 35 min) to yield 3-*isobutyl*-*quinazoline*-2,4-(1H,3H)-*dione* (11d) (1.44 g, 66%), m.p. 206—208 °C (from ethyl acetate), $\nu_{max.}$ 3 200, 1 720, and 1 640 cm^{-1}; δ[$(CD_3)_2SO$] 11—10 (br s, NH), 7.98 (d, 1 H), 7.75—7.62 (m, 1 H), and 7.3—7.2 (m, 2 H) (Ar), 3.82 (d, CH_2), 2.3—2.0 (m, CH), and 0.95 (d, 2 × Me) (Found: C, 66.3; H, 6.5; N, 12.8. $C_{12}H_{14}N_2O_2$ requires C, 66.0; H, 6.5; N, 12.85%); the azide (2e) decomposed with $t = 1.5$ h to yield 3-s-butylquinazoline-2,4(1*H*,3*H*)-dione (11e) (1.42 g, 65%), m.p. 131—132 °C (from benzene) (lit.,[15] m.p. 131—132.5 °C), $\nu_{max.}$ 3 200, 1 715, and 1 670 cm^{-1}; azide (2f) decomposed with $t = 1.5$ h to yield 3-t-butylquinazoline-2,4-(1*H*,3*H*)-dione (11f) (1.31 g, 60%), m.p. 198—199 °C (from benzene) (lit.,[16] m.p. 200 °C), $\nu_{max.}$ 3 200, 1 715, and 1 660; azide (2g) decomposed with $t = 2$ h to give 3-cyclohexylquinazoline-2,4-(1H,3H)-dione (11g) (1.71 g, 70%), m.p. 269—271 °C (from ethyl acetate) (lit.,[14] m.p. 270—271 °C), $\nu_{max.}$ 3 200, 1 720, and 1 650 cm^{-1}; and azide (2h) decomposed with $t = 1.5$ h to give 3-(1-*adamantyl*)*quinazoline*-2,4-(1H,3H)-*dione* (11h) (1.98 g, 67%), m.p. 239—241 °C (from ethyl acetate), $\nu_{max.}$ 3 200, 1 720, and 1 650 cm^{-1} (Found: C, 72.8; H, 6.75; N, 9.5. $C_{18}H_{20}N_2O_2$ requires C, 72.95; H, 6.8; N, 9.45%).

The Action of Amines on Tetrachloro- and Tetrabromophthalic Anhydride.—(*a*) *Diethylamine.* (i) Diethylamine (0.73 g, 10 mmol) was added to a stirred suspension of tetrachlorophthalic anhydride (2.86 g, 1 mol equiv.) in benzene (20 ml); the mixture was refluxed for 1 h and then cooled, when *tetrachloro*-NN-*diethylphthalamic acid* (12a) (2.1 g, 58%) crystallised; it had m.p. 169—171 °C (decomp.), $\nu_{max.}$ 1 710 and 1 630 cm^{-1}; δ 8.4 (br s, disappears on adding D_2O, OH), 3.5 (q, CH_2), 3.2 (q, CH_2), 1.22 (t, Me), and 1.15 (t, Me); *m/e* 363, 361, 359, and 357 (M^+). Attempts to recrystallise the acid for analysis resulted in the formation of a mixture of tetrachlorophthalic anhydride and the phthalide (14a).

(ii) A mixture of diethylamine (1.81 g, 2.5 mol equiv.), tetrachlorophthalic anhydride (2.86 g, 10 mmol), and benzene was refluxed for 20 min. The solvent was removed and the residue was triturated with ether, leaving semi-solid diethylammonium tetrachloro-*NN*-diethylphthalamate (13a) (2.8 g, 64%), $\nu_{max.}$ 2 800—2 500 and 1 620br cm^{-1}; δ 8.5 (br s, NH_2), 3.52 (q, CH_2), 3.25 (q, CH_2), 2.94 (q, 2 × CH_2), 1.27 (t, 2 × Me), 1.23 (t, Me), and 1.15 (t, Me).

(iii) A mixture of diethylamine (0.73 g), tetrachloro-

phthalic anhydride (2.86 g), and ethyl acetate (50 ml) was refluxed for 2 h. The solvent was removed and the residual gum was triturated with ether until solid. 4,5,6,7-*Tetrachloro*-3-*diethylamino*-3-*hydroxyphthalide* (14a) (2.4 g, 67%) had m.p. 141 °C (from ethyl acetate), $\nu_{max.}$ 1 733 and 1 600 cm^{-1}; δ[$(CD_3)_2SO$] 3.3—2.9 (m, 2 × CH_2), 1.21 (t, Me), and 1.15 (t, Me) (Found: C, 40.0; H, 2.95; N, 3.8. $C_{12}H_{11}Cl_4NO_3$ requires C, 40.15; H, 3.1; N, 3.9%).

(iv) A mixture of diethylamine (0.073 g, 1 mmol), tetrabromophthalic anhydride (0.464 g, 1 mol equiv.), and benzene (10 ml) was heated for 1 h after which the solvent was removed to give crude 3,4,5,6-*tetrabromo*-NN-*diethylphthalamic acid* (12b) (0.324 g, 60%), which could not be purified. It had m.p. 189—193 °C (decomp.), $\nu_{max.}$ 1 720 and 1 610 cm^{-1} (Found: C, 27.4; H, 2.2; N, 2.45. $C_{12}H_{11}Br_4NO_3$ requires C, 26.85; H, 2.1; N, 2.6%).

(*b*) *Pyrrolidine*. When pyrrolidine (0.71 g, 10 mmol) was added dropwise to a stirred solution of tetrachlorophthalic anhydride (2.86 g, 1 mol equiv.) in acetone (20 ml) there formed a precipitate of 4,5,6,7-*tetrachloro*-3-*hydroxy*-3-*pyrrolidinophthalide* (14c) (2.5 g, 70%), m.p. 178 °C (from ethyl acetate), $\nu_{max.}$ 1 749 and 1 608 cm^{-1}; δ 8.37 (br s, disappears on adding D_2O, OH), 3.7—3.0 (m, 4 H) and 2.1—1.7 (m, 4 H) (pyrrolidino) (Found: C, 40.3; H, 2.55; Cl, 39.8; N, 3.75. $C_{12}H_9Cl_4NO_3$ requires C, 40.35; H, 2.55; Cl, 39.75; N, 3.9%).

(*c*) *Piperidine*. (i) A mixture of tetrachlorophthalic anhydride (2.86 g), piperidine (0.85 g, 1 mol equiv.), and ethyl acetate (50 ml) was refluxed for 1 h; the resulting 4,5,6,7-*tetrachloro*-3-*hydroxy*-3-*piperidinophthalide* (14e) (3.12 g, 84%) had m.p. 178—179 °C (from acetone), $\nu_{max.}$ 1 740 cm^{-1}; δ 4.1—3.2 (m, 4 H) and 2.1—1.6 (m, 6 H) (piperidino) (Found: C, 42.3; H, 3.0; Cl, 38.1; N, 3.6. $C_{13}H_{11}Cl_4NO_3$ requires C, 42.1; H, 3.0; Cl, 38.2; N, 3.75%).

(ii) Treatment of a suspension of tetrabromophthalic anhydride (0.464 g, 1 mmol) in benzene (10 ml) with piperidine (0.213 g, 2.5 mol equiv.) gave *piperidinium* 3,4,5,6-*tetrabromo*-2-*piperidinocarbonylbenzoate* (13f) (0.583 g, 92%), m.p. 101—102 °C (from benzene), $\nu_{max.}$ 2 700—2 500 and 1 640br cm^{-1}; δ 3.9—2.9 (m, 8 H) and 1.8—1.4 (m, 12 H) (2 × piperidino) (Found: C, 34.2; H, 3.6; N, 4.4. $C_{18}H_{22}Br_4N_2O_3$ requires C, 34.1; H, 3.5; N, 4.4%).

(iii) A mixture of tetrabromophthalic anhydride (4.64 g), piperidine (0.85 g, 1 mol equiv.), and ethyl acetate (50 ml) was refluxed for 1 h. 4,5,6,7-*Tetrabromo*-3-*hydroxy*-3-*piperidinophthalide* (14f) (5.43 g, 99%) separated on cooling; it had m.p. 185 °C (from acetonitrile–ethyl acetate), $\nu_{max.}$ 1 742 cm^{-1}; δ 3.45—3.1 (m, 4 H) and 2.0—1.8 (m, 6 H) (piperidino) (Found: C, 28.5; H, 2.0; N, 2.55. $C_{13}H_{11}Br_4NO_3$ requires C, 28.45; H, 2.0; N, 2.55%).

(*d*) *t-Butylamine*. (i) A mixture of tetrachlorophthalic anhydride (0.572 g), t-butylamine (0.146 g, 1 mol equiv.), and ethyl acetate (10 ml) was refluxed for 1 h; N-*t-butyltetrachlorophthalamic acid* (12g) (0.62 g, 86%) separated on cooling. It had m.p. 188—190 °C, $\nu_{max.}$ 1 725 and 1 660 cm^{-1} (Found: C, 40.0; H, 3.4; N, 3.8. $C_{12}H_{11}Cl_4NO_3$ requires C, 40.15; H, 3.1; N, 3.9%).

(ii) A similar reaction, using tetrabromophthalic anhydride (0.464 g), gave *tetrabromo*-N-*t-butylphthalamic acid* (12h) (0.349 g, 65%), m.p. 203—205 °C, $\nu_{max.}$ 1 695 and 1 600 cm^{-1} (Found: C, 26.3; H, 2.45; N, 2.45. $C_{12}H_{11}Br_4NO_3$ requires C, 26.85; H, 2.1; N, 2.6%).

(*e*) *Aniline*. (i) A mixture of tetrachlorophthalic anhydride (0.572 g), aniline (0.186 g, 1 mol equiv.), and acetone (10 ml) was refluxed for 10 min. The solvent was removed and the residual gum was triturated with ether, whereupon it solidified to give tetrachloro-*N*-phenylphthalamic acid (12i) (0.424 g, 56%), m.p. 275 °C (lit.,[5] m.p. 266 °C), $\nu_{max.}$ 1 718, 1 653, and 1 600 cm^{-1}.

(ii) A similar reaction, using tetrabromophthalic anhydride (0.464 g), gave tetrabromo-*N*-phenylphthalamic acid (12j) (0.376 g, 68%), m.p. 274—276 °C (lit.,[6] m.p. 279—280 °C), $\nu_{max.}$ 3 430, 1 700, and 1 600 cm^{-1}.

Tetrahalogenophthalisoimidium Salts (15).—Perchloric acid (1.5 ml) was added to a suspension of the appropriate phthalide (14) (10 mmol) in acetic anhydride (15 ml), and the product was collected and washed with ether. The following *perchlorates* were obtained: *tetrachloro*-NN-*diethylphthalisoimidium* (15a) (2.92 g, 70%), m.p. 164—165 °C (decomp.), $\nu_{max.}$ 1 860, 1 680, and 1 100 cm^{-1}; δ 4.39 (q, CH_2), 4.14 (q, CH_2), 1.67 (t, Me), and 1.55 (t, Me) (Found: C, 32.2; H, 2.45; Cl, 39.8; N, 3.1. $C_{12}H_{10}Cl_5NO_6$ requires C, 32.6; H, 2.3; Cl, 40.15; N, 3.15%); 4,5,6,7-*tetrachloro*-3-*pyrrolidiniophthalide* (15c) (4.22 g, 96%), hygroscopic, m.p. 196 °C (decomp.), $\nu_{max.}$ 1 858, 1 690, and 1 090 cm^{-1}; δ 3.9—3.3 (m, 4 H) and 2.2—1.9 (m, 4 H) (pyrrolidino) (Found: C, 32.5; H, 1.8; Cl, 40.1; N, 3.0. $C_{12}H_8Cl_5NO_6$ requires C, 32.8; H, 1.85; Cl, 40.35; N, 3.2%); 4,5,6,7-*tetrachloro*-3-*piperidiniophthalide* (15e) (4.08 g, 90%), hygroscopic, m.p. 218 °C (decomp.), $\nu_{max.}$ 1 850, 1 685, and 1 100 cm^{-1}; δ 4.6—3.2 (m, 4 H) and 2.7—1.8 (m, 6 H) (piperidino) (Found: C, 34.0; H, 2.2; Cl, 39.2; N, 2.95. $C_{13}H_{10}Cl_5NO_6$ requires C, 34.45; H, 2.25; Cl, 39.1; N, 3.1%); and 4,5,6,7-*tetrabromo*-3-*piperidiniophthalide* (15f) (4.29 g, 68%), m.p. 240 °C (decomp.), $\nu_{max.}$ 1 862, 1 682, and 1 100 cm^{-1}; δ 4.5—3.15 (m, 4 H) and 2.0—1.8 (m, 6 H) (piperidino) (Found: C, 24.7; H, 1.85; Br, 50.6; N, 2.25. $C_{13}H_{10}Br_4ClNO_6$ requires C, 24.7; H, 1.6; Br, 50.65; N, 2.2%).

The Action of Sodium Azide on the Salts (15).—(*a*) The pyrrolidinio perchlorate (15c) (2.2 g, 5 mmol) was added to a stirred solution of sodium azide (0.65 g, 2 mol equiv.) in a mixture of water (5 ml) and acetone (5 ml), and the resulting 3,4,5,6-tetrachloro-2-pyrrolidinocarbonylbenzoyl azide (16c) (1.39 g, 73%) was collected; it had m.p. 74—76 °C (decomp.), $\nu_{max.}$ 2 140, 1 715, and 1 647 cm^{-1}; δ 3.8—3.0 (m, 4 H) and 2.15—1.5 (m, 4 H) (pyrrolidino).

(*b*) A similar reaction of the piperidinio perchlorate (15e) (0.453 g) with sodium azide (0.13 g) in water (3 ml) and acetone (3 ml) gave 3-azido-4,5,6,7-tetrachloro-3-piperidinophthalide (17e) (0.306 g, 80%), m.p. 82—83 °C (decomp.), $\nu_{max.}$ 2 120 and 1 780 cm^{-1}.

(*c*) The tetrabromo-compound (15f) (0.631 g) with sodium azide (0.13 g) in aqueous acetone gave 3-azido-4,5,6,7-tetrabromo-3-piperidinophthalide (17f) (0.31 g, 54%), m.p. 105—106 °C (decomp.), $\nu_{max.}$ 2 130 and 1 780 cm^{-1}. When the azidophthalide was boiled in toluene for 20 min it was completely converted into the isocyanate (18f) [$\nu_{max.}$ (C_6H_6) 2 270 and 1 675 cm^{-1}].

NN-*Disubstituted* 2-*Carbamoyl*-3,4,5,6-*tetrachlorophenyl Isocyanates* (18).—(*a*) A solution of the azide (16c) (0.382 g) in benzene (20 ml) was refluxed for 20 min, after which time the i.r. spectrum of the solution (2 250 and 1 640 cm^{-1}) no longer changed. Evaporation of the solvent left the semi-solid isocyanate (18c) (0.354 g, 100%), which, when left in air, gradually changed to 3,4,5,6-*tetrachloro*-2-*pyrrolidinocarbonylaniline* (19c) (0.328 g, 100%), m.p. 295—297 °C (from benzene), $\nu_{max.}$ 3 476, 3 320, and 1 625 cm^{-1}; δ[$(CD_3)_2SO$] 5.31 (br s, exchanges for deuterium, NH_2), 3.7—3.1 (m, 4 H), and 2.05—1.8 (m, 4 H) (pyrrolidino), *m/e* 332, 330, 328, and 326 (M^+) (Found: C, 39.9; H, 3.1; Cl, 43.2;

N, 8.4. $C_{11}H_{10}Cl_4N_2O$ requires C, 40.25; H, 3.1; Cl, 43.25; N, 8.55%).

(*b*) The conversion of the azidophthalide (17e) (0.396 g) in refluxing benzene (20 ml) into 3,4,5,6-tetrachloro-2-piperidinocarbonylphenyl isocyanate (18e) [$\nu_{max.}$ (C_6H_6) 2 260 and 1 650 cm^{-1}] required 2 h. The isolated gummy isocyanate (0.368 g, 100%) was gradually converted into *3,4,5,6-tetrachloro-2-piperidinocarbonylaniline* (19e) (0.342 g, 100%), m.p. 174—175 °C (from ethanol), $\nu_{max.}$ 3 485, 3 360, 1 632, and 1 610 cm^{-1}; δ 4.5 (br s, exchangeable for deuterium, NH_2), 4.1—3.2 (m, 4 H) and 1.7—1.5 (m, 6 H) (piperidino), *m/e* 346, 344, 342, and 340 (M^+) (Found: C, 42.0; H, 3.65; N, 8.2. $C_{12}H_{12}Cl_4N_2O$ requires C, 42.1; H, 3.5; N, 8.2%).

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