Synthesis and Reactivity of 2-Oxidodiaryliodonium Zwitterions

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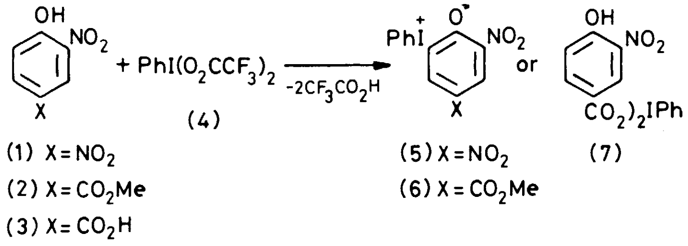
The direct synthesis of three new 2-oxidodiaryliodonium zwitterions from phenols and aryliodine(III) bistrifluoroacetate and their reaction with nucleophiles and electrophiles are reported. Especially noteworthy is the reactivity of 2-methoxy-3,5-dinitrophenyl(phenyl)iodonium tetrafluoroborate (15) which is hydrolysed by water and solvolysed by alcohols at room temperature.

The action of aryliodine(III) diacetates on phenols leads usually to acetoxylated phenols and/or quinones,[1] but with some oxidation-resistant phenols, bearing electron-withdrawing groups, iodonium salts are formed,[2] which may be converted by alkali into their zwitterions.[3,4] Similar compounds have been obtained from heterocyclic phenolic compounds, like 4-hydroxycoumarin, 4-hydroxy-2(1*H*)-quinolone, *etc.*[5,6] A different reactivity pathway has been observed with phenyliodine(III) dichloride and phenolate salts, where attack on trivalent iodine is by the phenolate O and the unstable phenyliodine(III) diphenolates initially formed undergo further transformation.[7]

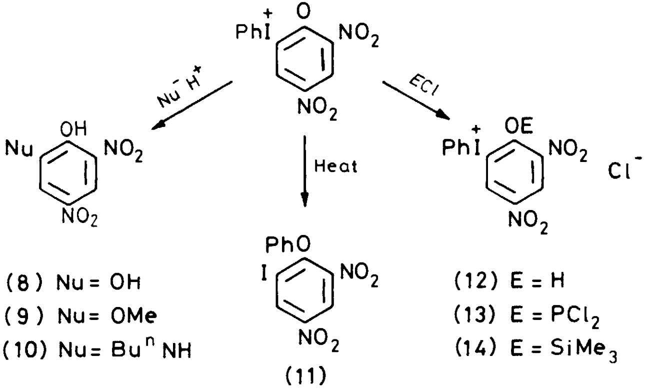
We find that among several acidic nitrophenols 2,4-dinitrophenol (1) and 2-nitro-4-methoxycarbonylphenol (2) react with phenyliodine(III) bistrifluoroacetate (4) at room temperature affording directly the zwitterions (5) and (6) in fair yields (Scheme 1).



Scheme 1.

Other 2-nitro-4-substituted phenols (with acetyl, formyl, cyano, and chloro groups) either do not react or are oxidised into a complex mixture of products. It is noted that 3-nitro-4-hydroxybenzoic acid (3) reacts with (4) from the carboxy group to form phenyliodine(III) bis(3-nitro-4-hydroxybenzoate) (7), despite the considerably less acidic character of the substituted benzoic acid in relation to trifluoroacetic acid, which is exchanged. This behaviour is attributed to the insolubility of (7), which shifts the equilibrium towards its formation.

The zwitterions (5) and (6) are insoluble in most solvents but they can be obtained analytically pure from dilute solutions of the reactants. Their characterisation was based on spectroscopic and chemical evidence. Thus, their u.v. spectrum shows a remarkable similarity to that of the corresponding phenolate ion, *e.g.* (5) has a small bathochromic shift, $\lambda_{max.}$ 372 nm (*cf.* 360 nm for the 2,4-dinitrophenolate and an almost identical ε value). The n.m.r. spectrum shows a characteristic paramagnetic shift for the *ortho* protons of the phenyl ring, which resonate in the range δ 8.37—8.48 because of the presence of I^+. Finally, the molecular ion as well as the expected fragments are present in the mass spectrum. Compounds (5) and (6) are characterised by an interesting reactivity pattern, since they are able to react with both strongly basic nucleophiles and strong electrophiles (Scheme 2).

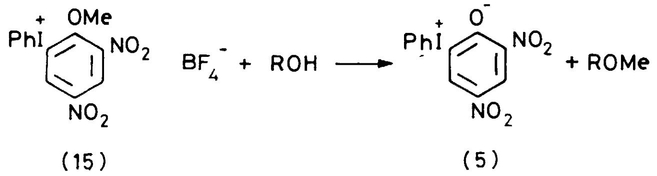


Scheme 2.

Thus, (5) reacts at room temperature with a large excess of sodium hydroxide, sodium alkoxides, and η-butylamine with displacement of iodobenzene and formation of 6-substituted 2,4-dinitrophenols (8)—(10). No other isomers could be detected, so that mechanisms involving benzyne or benzene oxide intermediates can be ruled out. Apparently an ordinary aromatic nucleophilic substitution takes place, favoured by the presence of the strong electron acceptors NO_2 and PhI^+. The good yields of the reaction products (up to 98% with methoxide and 85% with ethoxide) and the absence of simple by-products as well as the insensitivity of the reaction to inhibitors exclude the possibility that a trivalent iodine intermediate might have been formed, as in the reaction of iodonium salts with sodium ethoxide.[8] Non-basic nucleophiles like azide and cyanide and also non-charged soft nucleophiles, like sulphide, thiourea, and trivalent phosphorus do not react with (5) or (6) at room temperature, while on heating a rearrangement takes place into the corresponding iodoether, *e.g.* (11). This rearrangement is known to occur with other iodonium zwitterions and although not rigorously proven, it has been suggested [4] that it takes place through a spiro intermediate, analogously to another related rearrangement of a dimedonyl iodonium ylide.[9] The ease of this rearrangement, which represents a case of a thermally allowed 1,4-sigmatropic shift, is such that some phenols and phenyliodine(III) diacetate react to afford directly iodo ethers.[3] Similar rearrangements have been reported from an imidazolyl iodonium ylide [10] and also from 2-oxidoaryltrialkylammonium zwitterions.[11]

Strong electrophiles such as gaseous hydrogen chloride, phosphorus trichloride, and trimethylchlorosilane convert (5) into white compounds believed to be (12)—(14), respectively.

Compound (12) is water soluble, while (13) and (14) react with water. All three are insoluble in ordinary solvents (CH_3CN, $CHCl_3$ *etc.*). Apparently the formally charged oxygen of (5) is capable of attacking the electrophilic centres of the above reagents but the products are very labile and although reasonably stable when handled in the absence of moisture they revert to (5) on attempted recrystallisation. Although their insolubility also prevented their identification by n.m.r. spectroscopy, their mass spectra showed the presence of both moieties, *e.g.* of (5) and the trimethylsilyl group for (14). The water-soluble iodonium chloride (12) is also formed from (5) and concentrated hydrochloric acid; upon dilution of the acid solution with water (5) is precipitated. The reaction product between (5) and trimethyloxonium tetrafluoroborate is believed to be the iodonium salt (15). The possibility that methylation of the nitro oxygen atom occurs to give a nitronate ester is ruled out since analogous esters are red,[12] while (15) is white. This compound is exceptionally reactive for an ether, being hydrolysed by water at room temperature. It can also react with alcohols to afford methyl esters (Scheme 3); *e.g.* when dissolved in n-nonanol, methyl n-nonyl ether was obtained. This reaction is unique in that such a weak nucleophile can attack the sp³ C of an ether.

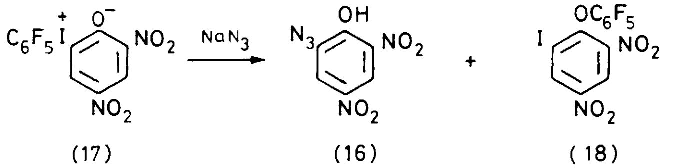


Scheme 3.

It should also be noted that 2,4,6-trinitroanisole has been reported to react with tertiary amines[13] to give tetra-alkylammonium picrates, but it is stable in ethanol from which it can be recrystallised.[14] Apparently the electron-withdrawing capability of the phenyliodonio group (PhI^+) is much more pronounced than that of the nitro group, at an *ortho* position, despite their comparable σ values.[15]

In the salts (12)—(15) no phenyl rearrangement can take place, since oxygen is blocked. Therefore heating is permitted and reactions with non-basic nucleophiles are possible, *e.g.* (12) and sodium azide when heated in dimethylformamide (DMF) afford a mixture of 6-azido-2,4-dinitrophenol (16) and the ether (11).

In order to enhance the reactivity of the zwitterions towards nucleophiles, the pentafluorophenyl analogue of (5), *i.e.* (17), was prepared from (1) and $C_6F_5I(O_2CCF_3)_2$.[16] This zwitterion has a much better leaving group than (5) and it is indeed more reactive, since it reacts with sodium azide in hot MeCN to give the azidophenol (16), along with traces of the rearranged ether (18). The latter is obtained quantitatively when (17) is heated in MeCN (Scheme 4).



Scheme 4.

Experimental

I.r. spectra were recorded with a Perkin-Elmer 257 spectrometer (Nujol mulls). Mass spectra were obtained from a Hitachi-Perkin-Elmer RMU-6L (single focusing) spectrometer at 70 eV. ¹H N.m.r. spectra were recorded on a Varian A-60A spectrometer.

2,4-*Dinitro*-6-*phenyliodoniophenolate* (5).—A solution of 2,4-dinitrophenol (1) (1.84 g) in acetonitrile (10 ml) was added to a solution of phenyliodine(III) bistrifluoroacetate (4) (4.3 g) in acetonitrile (10 ml). After 72 h at room temperature fine yellow crystals of (5) were deposited (1.35 g) from the mixture and had m.p. 195—196 °C (without further purification) $\lambda_{max.}$ (Me_2SO) 372 nm (log ε 4.15); $\bar{\nu}_{max.}$ 3 086, 1 585, 1 560, 1 555, 1 260, 1 090, and 715 cm^{-1}; δ [$(CD_3)_2SO$] 8.98 (2 H, s), 8.37—8.48 (2 H, m), 7.78 (3 H, m); *m/z* 386 ($M^{+\cdot}$, 93), 204(30), 139*(95), and 93(100) (Found: C, 37.5; H, 1.64; N, 6.99. $C_{12}H_7IN_2O_5$ requires C, 37.32; H, 1.83; N, 7.25%).

The filtrate from the above procedure was concentrated under reduced pressure without heating and fresh solvent (10 ml) added. After 24 h a second crop of (5) was collected (0.58 g) and upon repetition of the procedure the total yield of (5) amounted to 65—70%.

4-*Methoxycarbonyl*-2-*nitro*-6-*phenyliodoniophenolate* (6).—Using a similar procedure as for (5), the phenol (2) (1.97 g) and (4) (4.3 g) gave (6) as yellow crystals (1.2 g, 30%), m.p. 203—205 °C; $\lambda_{max.}$ (Me_2SO) 412 nm (log ε 3.87); $\bar{\nu}_{max.}$ 1 693, 1 600, 1 545, 1 532, 1 270, 1 215, and 770 cm^{-1}; δ [$(CD_3)_2SO$] 8.63 (1 H, d, *J* 2 Hz), 8.38 (2 H, m), 8.14 (1 H, d, *J* 2 Hz), 7.74 (3 H, m), and 3.95 (3 H, s); *m/z* 399 ($M^{+\cdot}$, trace), 384(49), 368(12), 339(12), 292(20), 204(18), 183(22), 139(58), 127(30), and 94(100) (Found: C, 41.9; H, 2.1; N, 3.45. $C_{14}H_{10}INO_5$ requires C, 42.14; H, 2.50; N, 3.51%).

2,4-*Dinitro*-6-*pentafluorophenyliodoniophenolate* (17).—Pentafluorophenyliodine(III) bistrifluoroacetate[16] (2.6 g) in acetonitrile (7 ml) was mixed with 2,4-dinitrophenol (1) (0.92 g) in acetonitrile (7 ml). After 1 week at room temperature the solution deposited yellow crystals (0.48 g, 10%), m.p. 184—186 °C; $\lambda_{max.}$ (Me_2SO) 472 nm (log ε 4.26); $\bar{\nu}_{max.}$ 3 100, 1 590, 1 550, 1 530, 1 345, 1 235, 995, 740, and 718 cm^{-1}; δ [$(CD_3)_2SO$)] 9.23 (1 H, d, *J* 2 Hz), 8.95 (1 H, d, *J* 2 Hz); *m/z* 476 ($M^{+\cdot}$, 54), 294(100), 238(26), 229(68), 205(49), 183(35), 167(13), and 155(27) (Found: C, 30.6; H, 0.55; N, 5.95. $C_{12}H_2F_5IN_2O_5$ requires C, 30.27; H, 0.42; N, 5.88)

Phenyliodine(III) *Bis*(4-*hydroxy*-3-*nitrobenzoate*) (7).—A solution of 4-hydroxy-3-nitrobenzoic acid (1.83 g) in acetonitrile (10 ml) was added to a solution of (4) (4.3 g) in acetonitrile (10 ml). Immediately a white precipitate was formed. Recrystallisation from acetonitrile gave white crystals (2.1 g, 74%), m.p. 169—172 °C; $\bar{\nu}_{max.}$ 3 295, 3095, 1 650, 1 635, 1 535, 1 330, 1 295, 1 170, and 710 cm^{-1}; δ [$(CD_3)_2SO$] 7.20—8.74 (m, ArH); *m/z* (no $M^{+\cdot}$), 204(100) and 183(45) (Found: C, 42.1; H, 1.9; N, 4.75. $C_{20}H_{13}IN_2O_{10}$ requires C, 42.34; H, 2.13; N, 4.94).

Rearrangement of Zwitterions.—(*a*) (5) *to* (11). A solution of (5) (100 mg) in dimethyl sulphoxide (5 ml) was refluxed for 2 min. Upon dilution with water (11) was precipitated (83 mg); it recrystallised from ethanol as off-white crystals, m.p. 115—116 °C; $\bar{\nu}_{max.}$ 3 100, 1 590, 1 550, 1 530, 1 343, and 1 250; δ($CDCl_3$) 9.22 (1 H, d, *J* 2 Hz), 9.01 (1 H, d, *J* 2 Hz), and 7.18 (5 H, m); *m/z* 386 ($M^{+\cdot}$, 85), 360(5), 339(8), 239(89),

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* This fragment is present also in (6) and (11) and may be due either to *o*-nitrophenol or to dibenzofuran.

165(11), 139(86), and 93(100) (Found: C, 36.9; H, 1.85; N, 7.05. $C_{12}H_7IN_2O_5$ requires C, 37.32; H, 1.83; N, 7.25).

(*b*) (17) *to* (18). A similar procedure as above gave off-white crystals (90%), m.p. 114—116 °C (from ethanol–water); $\tilde{\nu}_{max.}$ 3 097, 1 600, 1 568, 1 520, 1 500, 1 345, 1 328, 1 275, 1 128, 978, 740, and 720 cm^{-1}; δ [$(CD_3)_2SO$] 9.30 (1 H, d, *J* 2 Hz), 9.12 (1 H, d, *J* 2 Hz); *m/z* 476 ($M^{+\cdot}$, 100), 293(78), 229(42), and 183(23) (Found: C, 29.6; H, 0.55; N, 5.25. $C_{12}H_2F_5IN_2O_5$ requires C, 30.27; H, 0.42; N, 5.88).

Reactions with Nucleophiles.—(*a*) *Sodium alkoxides with* (5). To a solution of methanolic sodium methoxide (115 mg of sodium in 10 ml of methanol) compound (5) (100 mg) was added. After 5 min an orange precipitate was formed; upon acidification and dilution with water yellow crystals of the ether (9) were collected and recrystallised from ethanol (54 mg, 98%), m.p. 121—123 °C (lit.,[17] 123—124 °C). Similarly, (5) and sodium ethoxide afforded 2-ethoxy-4,6-dinitrophenol (85%), m.p. 155 °C (lit.,[18] 155 °C).

(*b*) *n-Butylamine with* (5). A quantity (125 mg) of (5) was dissolved in n-butylamine (10 ml). The red solution was concentrated to a small volume, diluted with water, and acidified with acetic acid. The resulting suspension was extracted with ether, and the ether extracts dried; the residue after removal of ether was chromatographed on silica gel (with light petroleum–chloroform as eluant) to give (10) (40 mg, 48%), m.p. 81—82 °C; $\tilde{\nu}_{max.}$ 3 395, 1 630, 1 580, and 1 273 cm^{-1}; δ (CCl_4) 11.41 (1 H, s, OH), 9.36 (1 H, s), 8.97 (1 H, br s, NH), 6.42 (1 H, s), 3.44 (2 H, q, CH_2), and 0.85—1.95 (7 H, m, $CH_2CH_2CH_3$); *m/z* 255 ($M^{+\cdot}$, 63), 239(10), and 212(100) (Found: C, 46.85; H, 4.95; N, 16.1. $C_{10}H_{13}N_2O_5$ requires C, 47.06; H, 5.10; N, 16.47).

(*c*) *Sodium hydroxide with* (5) *or* (17). A quantity of (5) (200 mg) was added to a solution of 25% sodium hydroxide (5 ml) and methanol (15 ml) and the mixture was stirred for 2 h. The resulting clear solution was acidified with concentrated hydrochloric acid and the precipitate recrystallised from ethanol to give (8) (34 mg, 35%), m.p. 162—164 °C (lit.,[19] 164 °C). Under the same conditions (17) gave (8) in 95% yield.

(*d*) *Sodium azide with* (17). The zwitterion (17) (100 mg) was added to a solution of sodium azide (130 mg) in acetonitrile (5 ml) and the suspension heated at 60 °C for 5 min. Water was added, followed by ether extraction. The residue after drying and removal of solvent was chromatographed on silica gel (chloroform–methanol as eluant) to give after pentafluoroiodobenzene and some (18) the 6-azido-2,4-dinitrophenol (16) (27 mg, 58%), m.p. 78 °C (lit.,[20] 78—79 °C). Under the same conditions the iodonium salt (12) gave (11) and (16) in 35 and 30% yields, respectively.

Reactions with Electrophiles.—(*a*) *Trimethylchlorosilane with* (5). Compound (5) (100 mg) was stirred with trimethylchlorosilane (3 ml) for 10 min, after which its yellow colour disappeared and a white precipitate was formed; this was believed to be (13). All attempts to purify it failed, because of its rapid reaction with atmospheric or residual moisture. Further, rapid thermal decomposition prevented even a rough m.p. being recorded. Similar behaviour was observed with gaseous hydrogen chloride and phosphorus trichloride.

(*b*) *Trimethyloxonium tetrafluoroborate and then nonan-*1-*ol with* (5). Trimethyloxonium tetrafluoroborate (148 mg) was added to a stirred suspension of (5) (350 mg) in acetonitrile (7 ml). After a few minutes a clear colourless solution resulted. Removal of solvents under reduced pressure left an oil which crystallised after storage over P_2O_5 in a desiccator. White crystals were obtained quantitatively, m.p. 148—153 °C, believed to be (14). Because of its lability neither purification nor recording of any spectra were possible. The product was therefore treated with a solution of nonan-1-ol (150 mg) in acetonitrile (3 ml). Immediately the characteristic yellow crystals of (5) appeared and were filtered off. From the filtrate after concentration and column chromatography (silica gel, chloroform) methyl n-nonyl ether was isolated (91 mg, 62%), identical in all respects with an authentic sample prepared from sodium n-nonanolate and iodomethane.

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