Oxidative Displacement of Halogen from Alkyl Halides by Phenyliodine(III) Dicarboxylates

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The reaction of alkyl iodides with aryliodine(III) dicarboxylates affords as the main product the ester derived through substitution of iodine by an acyloxy group; in some cases α-iodoalkyl esters are also formed along with other minor products. Certain reactive bromides and chlorides react along similar lines. The mechanism of these reactions is briefly discussed.
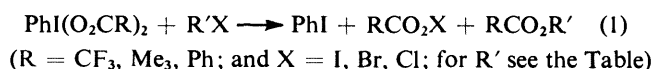
Aryliodine(III) dicarboxylates, abbreviated herein as AIDs, of the general type $ArI(O_2CR)_2$ are versatile reagents whose chemistry has recently been reviewed.[1] In continuation of our exploratory efforts[2] on the properties of phenyliodine(III) bistrifluoroacetate, $PhI(O_2CCF_3)_2$ (PIB), we were interested in examining its behaviour towards alkyl halides. Alkyl halides are normally inert to the more common oxidising agents, such as ozone, periodate, and hydrogen peroxide. However, alkyl iodides are oxidised easily by several oxidants, especially peracids and halogen compounds, and the last few years have witnessed a considerable activity in this field. Peracetic acid produces mixtures of acetates, *vic*-diacetates, and *vic*-iodo-acetates through the intermediacy of acetyl hypoiodite.[3,4] With *m*-chloroperbenzoic acid the products depend on the nature of the substrate and of the solvent, and they can be alcohols, ethers, esters, ketones, and oxiranes.[5-9] Oxidative elimination has also been observed in iodides bearing strongly electron-attracting substituents[5] and in some bicyclic iodides;[10] an iodosyl or iodyl intermediate has been postulated to be formed in these cases. Polyvalent iodine compounds are also effective in oxidising alkyl iodides. Thus, iodine(III) tristrifluoroacetate affords trifluoroacetoxylated products,[11-12] iodine penta-fluoride gives aldehydes,[13] while phenyliodine(III) dichloride leads to the formation of alkyl chlorides.[14] An analogous reaction which takes place between alkyl iodides and molecular chlorine or ICl has been studied in detail mechanistically.[15] Bromine reacts similarly,[16] while fluorine gives either alkyliodine(III) difluorides[17] or, in the case of 1-adamantyl iodide, ionic intermediates leading to 1-fluoroadamantane or 1-substituted adamantanes.[18] Other oxidations of iodides with dichlorine heptaoxide, chlorine oxide, and alkyl hypo-chlorites,[19] and also with t-butyl hypoiodite[20] and benzoyl hypoiodite[21] lead to mixtures of esters, ethers, and other products. It is of interest to note that lead tetra-acetate, which is similar in action[1] to an AID, oxidises alkyl iodides to tars, although it acetoxylates t-butyl chloride.[22]

Results and Discussion

We find that PIB as well as other AIDs react readily with alkyl iodides and also with some reactive bromides and chlorides, the trivalent iodine being reduced to the mono-valent ($+1$) state. The main products of these reactions, which are complete in a few hours at room temperature, are the trifluoroacetate or other carboxylic esters resulting from oxidative displacement of the alkyl halide halogen by the acyloxy group. Yields are usually fairly good, so that some of the reactions may be of preparative value in cases where conventional methods are unsatisfactory. No efforts to optimise yields were attempted and in most cases actual yields are considerably higher, especially in the trifluoro-

acetate esters which are partially hydrolysed inside the column during chromatographic separation.

The results of the reactions between three AIDs and several alkyl halides are listed in the Table where only the esters and other major products have been included. Formation of some other minor products is discussed below, while in all reactions phenyl iodide (85—100%) and iodine (15—100%) are normal by-products. Thus, whilst benzylic and primary, secondary, and tertiary alkyl iodides are reactive, only tertiary alkyl and benzylic bromides and chlorides react. We believe that two main consecutive reactions take place in all cases: the first involves formation of the ester and an acyl hypohalite according to equation (1). The second reaction takes place between

$$PhI(O_2CR)_2 + R'X \longrightarrow PhI + RCO_2X + RCO_2R' \quad (1)$$

(R $=$ CF$_3$, Me$_3$, Ph; and X $=$ I, Br, Cl; for R' see the Table)

RCO_2X and $R'X$ [equation (2)], a second quantity of ester being produced along with halogen. A related reaction has

$$RCO_2X + R'X \longrightarrow RCO_2R' + X_2 \quad (2)$$

been reported between alkyl chlorides or bromides and perfluoroalkanesulphonyl hypochlorites, R_FSO_2OCl, leading to their esters, R_FSO_2OR. Such reactions have been called ' substitutive electrophilic dehalogenations.'[23]

The overall stoicheiometry AID : alkyl halide is 1 : 2 and the amount of halogen produced is a measure of the contribution of equation (2) to the total production of ester. In those reactions where the amount of halogen was low, it was preferable to run them under a 1 : 1 stoicheiometry, the yield of the ester being then higher. This is possible because reaction (2), which has been previously reported,[3] occurs only to a certain extent. The reactive RCO_2X may decompose[24] into RX and CO$_2$ or it may react with phenyl iodide already formed from equation (1), affording p-phenylene di-iodide.[25] No attempts were made to isolate the latter because, in chromatographic separation, it is eluted with phenyl iodide, but its presence has been definitely demonstrated by its ^1H n.m.r. spectrum (a sharp singlet at δ 7.4 in CCl$_4$, increasing upon addition of authentic p-phenyl-ene di-iodide).

Therefore a 1 : 1 ratio of reactants is generally preferable for better yields of esters. Reaction (2) may be completely suppressed if the whole reaction is carried out in the presence of an activated arene. Thus, when ethyl iodide reacted with PIB in the presence of p-xylene, 2,5-dimethylphenyl iodide was isolated in 82% yield. In certain cases, even with a 1 : 1 ratio of reactants, some halide may remain unchanged because AIDs and halogens react to afford RCO_2X, and also because RCO_2I with phenyl iodide to give p-phenylene di-iodide.[25] Primary iodides with PIB give, as by-products, small amounts of α-iodoalkyl trifluoroacetates and α-trifluoroacetoxyalkyl
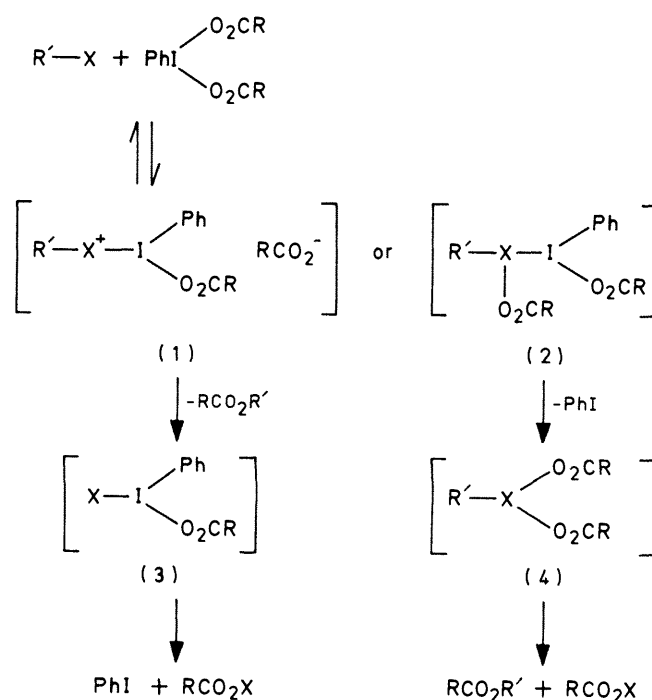
Table. Reaction products [a] of alkyl halides and AIDs

Alkyl halide [b] (R'X)	AID [c]	Ester (%)	Halogen (%)	Other products [d]
X = iodine				
R' = n-Heptyl	PIB	$CF_3CO_2C_7H_{15}$ (43)	(84)	
Isopentyl	PIB	$CF_3CO_2C_5H_{11}$ (32)	(65)	
3-Phenylpropyl	PIB	$CF_3CO_2[CH_2]_3Ph$ (55)	(62)	
Benzyl	PIB	$CF_3CO_2CH_2Ph$ (54)	(100)	
Benzyl	PID	$CH_3CO_2CH_2Ph$ (85)	(99)	
Benzyl	PIBz	$PhCO_2CH_2Ph$ (70)	(92)	
Isopropyl	PIB	$CF_3CO_2C_3H_7$ (79) [e]	f	
Isopropyl	PIB (1 : 1)	$CF_3CO_2C_3H_7$ (100) [e]	f	
Cyclohexyl	PIB		(15)	Compounds (9) (17) and (10) (5)
Cyclohexyl	PIB (1 : 1)		(30)	Compounds (9) (26) and (10) (8)
1-Adamantyl	PIB	$CF_3CO_2C_{10}H_{13}$ (48)	(100)	
1-Adamantyl	PID	$CH_3CO_2C_{10}H_{13}$ (80)	(100)	
1-Adamantyl	PIBz	$PhCO_2C_{10}H_{13}$ (74)	(98)	
X = bromine				
Benzyl	PIB (1 : 1)	$CF_3CO_2CH_2Ph$ (28)	g	See text
1-Adamantyl	PIB (1 : 1)	$CF_3CO_2C_{10}H_{13}$ (79)	g	
1-Adamantyl	PIB	$CF_3CO_2C_{10}H_{13}$ (70)	(28)	
X = chlorine				
Benzyl	PIB (1 : 1)	$CF_3CO_2CH_2Ph$ (21)	g	See text
t-Butyl	PIB	$CF_3CO_2C_4H_9$ (20)	g	$PhICl_2$ (68)

[a] Yields in parentheses refer to isolated products and are based on the initial amount of R'X, even if some remained unchanged. [b] Molar ratio RX : AID 2 : 1 unless otherwise indicated. [c] Abbreviations: PIB is $PhI(O_2CCF_3)_2$, PID is $PhI(O_2CCH_3)_2$, PIBz is $PhI(O_2CPh)_2$. [d] Only major products are mentioned. Phenyl iodide and p-phenylene di-iodide, which are normal by-products, and some minor by-products are not mentioned here but in the text. [e] Estimated from the n.m.r. spectrum of the reaction mixture. [f] Not determined. [g] Not produced.

trifluoroacetates. These derivatives are the main products from the reaction of cyclohexyl iodide and PIB where no simple ester is produced. However, another secondary iodide, isopropyl iodide, gives in high yield only isopropyl trifluoroacetate.

Alkyl iodides are by far the most reactive halides. Both primary and secondary bromides as well as chlorides, with the exception of benzyl halides, are inert to oxidation but tertiary bromides are more reactive than tertiary chlorides. On the other hand PIB is considerably more reactive than the acetoxy (PID) and benzoyloxy (PIBz) analogues which are of a comparable reactivity and which react only with tertiary iodides. This reactivity pattern, as well as the insensitivity of the reactions when carried out in the presence of a radical inhibitor such as acrylonitrile, suggest that all reactions start with a nucleophilic attack from the halogen of the alkyl halides on the iodine of the AID. We favour this attack, rather than the alternative on the I—O oxygen, since then an unfavourable $PhI^-\!-\!O_2CR$ species would have resulted instead of the better leaving group RCO_2^-. Besides, iodine of RI and I^{3+} match each other better in soft–soft character than do RI and O. An analogous attack has been proposed [13] for the reaction between alkyl iodides and IF_5. In Scheme 1 it is shown that an unstable intermediate results, either as a halogenium ion (1) or as the covalent form (2); in both cases the sp^3 C bound to halogen is rendered very electrophilic and may be attacked by the weak nucleophile RCO_2^- to afford the ester and another intermediate (3), which collapses into PhI and RCO_2I. An alternative pathway might involve the transformation of (2) into PhI and the alkyliodine(III) dicarboxylate (4), the latter decomposing into the ester and RCO_2I. It should be noted that recently a stable tricyclyliodine(III) bis-(m-chlorobenzoate) has been isolated from the oxidation of the iodide with m-chloroperbenzoic acid.[26]

$$R'\!-\!X \;+\; PhI\!\!<^{O_2CR}_{O_2CR}$$

$$\left[R'\!-\!X^+\!-\!I\!\!<^{Ph}_{O_2CR} \quad RCO_2^- \right] \quad or \quad \left[R'\!-\!X\!-\!I\!\!<^{Ph}_{O_2CR} \atop O_2CR \right]$$

(1)   (2)

$\downarrow -RCO_2R'$ $\downarrow -PhI$

$$\left[X\!-\!I\!\!<^{Ph}_{O_2CR} \right] \qquad \left[R'\!-\!X\!\!<^{O_2CR}_{O_2CR} \right]$$

(3)   (4)

$PhI + RCO_2X$ $RCO_2R' + RCO_2X$

Scheme 1.

The limited reactivity of PID and PIBz is due to the less electrophilic character of their trivalent iodine, since both acetoxy and benzoyloxy groups are not strong electron acceptors. Nevertheless, in their reactions with the most
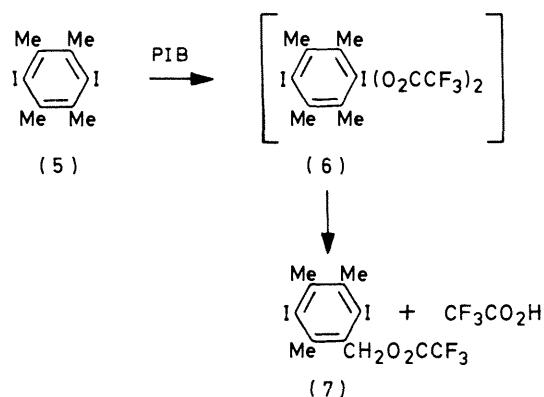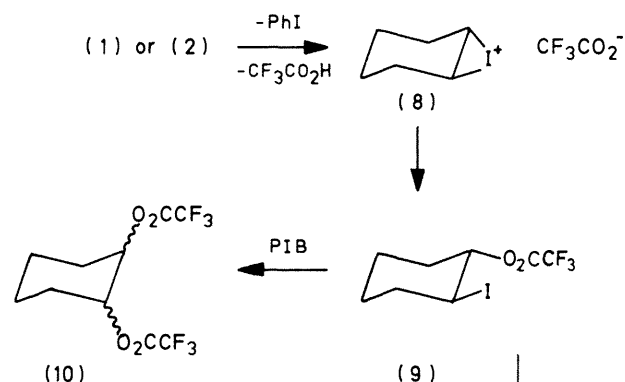
Scheme 2.

Scheme 3.

reactive iodides, *i.e.* those with increased nucleophilic character on the iodine, the yields of esters are considerably higher than with PIB because CH_3CO_2I and $C_6H_5CO_2I$ are less reactive (they have a less electrophilic iodine) and they do not decompose as easily as CF_3CO_2I; they are also incapable of reacting with phenyl iodide to give *p*-phenylene di-iodide.[25]

Further corroboration of the proposed mechanism was provided by an experiment where the reaction between PIB and benzyl iodide was carried out in the presence of tetramethylammonium chloride; benzyl chloride was then isolated in 18% yield, no doubt as the result of nucleophilic attack by chloride ion on intermediate (1) or (2). These considerations led us to examine the possibility of a reaction between an aryl iodide and PIB. We chose durylene di-iodide * (5) as a suitable substrate because of its lack of aromatic H which, if present, would lead to iodonium salts,[1] and also because of the enhanced nucleophilicity of its iodine. Indeed, after 20 d PIB was completely consumed to PhI, while the major product isolated was the trifluoroacetoxy derivative (7) in 26% yield (Scheme 2).

We interpret this reaction by assuming that probably the bistrifluoroacetate (6) is initially formed, as in Scheme 1. This AID is expected to be an unstable and strong oxidising agent and to undergo a self-redox reaction into (7) and CF_3CO_2H. A similar transformation was observed during an attempted preparation of duryliodine(III) bistrifluoroacetate † from duryliodine(III) diacetate and CF_3CO_2H; the former derivative was unstable and with time, decomposed into a mixture of 2,3,6-trimethyl-5- and 2,3,5-trimethyl-6-trifluoroacetoxymethylphenyl iodide.[27] It must be mentioned that durylene dichloride does not react with PIB under similar conditions.

Concerning the formation of minor products, which in the case of cyclohexyl iodide become the main ones, it is possible that from intermediate (1) or (2) an iodiranium cation (8) is formed, which is then transformed into (9). The existence of compound (8) is very probable, because (9) is exclusively the *trans* isomer, as shown by its ^1H n.m.r. spectrum which was identical with that mentioned in the literature.[12] Some of the product (9) reacts further to give, in the normal way, compound (10) (Scheme 3) which is probably a mixture of *cis* and *trans* isomers. The low yields of (9) and (10) (Table) are due to unchanged cyclohexyl iodide, even though PIB was completely consumed.

The mechanism of reaction (2) is formally a double nucleo-

philic substitution, although a concerted mechanism may operate as well;[23] first the halogen from the alkyl halide attacks the halogen of the acyl hypohalite, and then RCO_2^- attacks the halogenium ion, according to equation (3).

$$R-X + RCO_2-X \longrightarrow R-X^+-X + RCO_2^- \longrightarrow$$
$$RCO_2R + X_2 \quad (3)$$
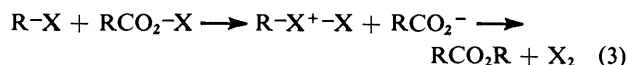
In the reaction of benzyl bromide with PIB, ring-brominated compounds were also isolated such as *o*- and *p*-BrC_6H_4I, $BrC_6H_4CH_2Br$, and $BrC_6H_4CH_2O_2CCF_3$. These derivatives resulted from an electrophilic substitution of the substrates with CF_3CO_2Br which has been shown to be an effective brominating agent.[25]

Small amounts of benzaldehyde isolated from the above reaction came from the hydrolysis of the acylal [equation (4)] which is formed by oxidation of benzyl trifluoroacetate by intermediate (3) or (4) rather than by PIB since the latter, in an independent reaction, did not react with benzyl trifluoroacetate under the same conditions.

$$(3) \text{ or } (4) + PhCH_2O_2CCF_3 \longrightarrow$$
$$(X = Br) \quad\quad PhCH(O_2CCF_3)_2 + HBr + PhI \quad (4)$$
$$(11)$$
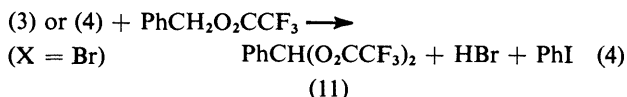
The reaction of PIB and (5) similarly afforded a small amount of 2,5-di-iodo-3,4,6-trimethylbenzaldehyde.

Among chlorides, t-butyl and benzyl chlorides react with PIB. In the first case $PhICl_2$ is mainly formed along with the ester, probably directly from (3) and t-butyl chloride [equation (5)]. It is of interest to note that, with time, $PhICl_2$ reacts slowly with the ester to give unidentified products.

$$PhI(Cl)O_2CCF_3 + t\text{-}BuCl \longrightarrow PhICl_2 + t\text{-}BuO_2CCF_3 \quad (5)$$
$$(3; R = CF_3, X = Cl)$$
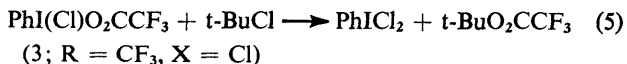
With benzyl chloride, ring-chlorinated products similar to those with benzyl bromide were also obtained.

The lack of formation of $PhICl_2$ is attributed to the weak nucleophilic character of Cl in benzyl chloride, compared with its enhanced nucleophilicity in Bu^tCl. In both these cases free chlorine is not formed because it would then combine with PhI in the reaction of benzyl chloride as well.

In conclusion the reaction between AIDs and alkyl iodides is suitable in most cases for substitution of iodine by an acyloxy group. Compared with similar reactions with peracids[3-8] and iodine(III) tristrifluoroacetate,[10-12] AIDs appear to give cleaner products in better yields.

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* Durylene is 2,3,5,6-tetramethyl-*p*-phenylene.
† Duryl is 2,3,5,6-tetramethylphenyl.

Experimental

PIB, PID, and PIBz were prepared by standard methods.[1] Most alkyl halides were commercially available, except benzyl iodide and 3-phenylpropyl iodide, which were prepared from the corresponding chlorides and sodium iodide [28,29] and also 1-adamantyl iodide, which was prepared from adamantan-1-ol and 47% HI.[30] Durylene di-iodide and durylene dichloride were prepared by halogenation of durene.[31,25]

Most of the reaction products were known compounds and their identification was based on comparison of their physical and spectroscopic properties with those of authentic samples or from the literature.

N.m.r. and mass spectra were recorded on Varian A-60A and Hitachi-Perkin-Elmer RMU-6L spectrometers, respectively. I.r. spectra were recorded on a Perkin-Elmer 297 spectrophotometer.

Reaction of AIDs with Alkyl Halides.—Normally the alkyl halide (4 mmol) and an AID (2 or 4 mmol, for ratios 2 : 1 or 1 : 1) were dissolved in ethanol-free chloroform (20 ml). The solution was allowed to stand at room temperature in the dark for 2—8 h, until all AID was consumed. The amount of iodine produced was determined volumetrically with $Na_2S_2O_3$. The chloroform layer after iodine determination was washed with water and dried with Na_2SO_4. Chloroform was removed carefully in a rotary evaporator and the residue was separated into its components by column chromatography (silica gel; hexane–chloroform). The order of elution was phenyl iodide together with *p*-phenylene di-iodide sometimes a little unchanged alkyl halide, and then the ester; 2-iodoalkyl and 2-trifluoroacetoxyalkyl trifluoroacetates, when formed, were subsequently eluted.

Reaction of p-*Xylene with PIB and Ethyl Iodide.*—Ethyl iodide (5 mmol), *p*-xylene (10 mmol), and PIB (5 mmol) were dissolved in chloroform (20 ml). After 2 h the solvent and ethyl trifluoroacetate were removed in a rotary evaporator and *p*-xylene, together with phenyl iodide, were fractionally distilled under reduced pressure. The oily residue was shown to consist entirely of pure 2,5-xylyl iodide in 82% yield.

Reaction of Benzyl Iodide with PIB and Tetramethyl-ammonium Chloride.—Tetramethylammonium chloride (5 mmol), benzyl iodide (5 mmol), and PIB (5 mmol) were added to chloroform. After the usual work-up, column chromatography gave first, phenyl iodide, then benzyl chloride in 18% yield. Under the same conditions benzyl iodide did not react with tetramethylammonium chloride.

Reaction of Durylene Di-iodide with PIB.—Durylene di-iodide (5 mmol) and PIB (5 mmol) in chloroform (30 ml) were kept in the dark for 20 d. The reaction mixture, after removal of volatiles, was chromatographed on a silica-gel column

and the main product, eluted after phenyl iodide and durylene di-iodide, was 2,3,6-trimethyl-5-trifluoroacetoxymethyl-*p*-phenylene di-iodide (7) in 26% yield, m.p. 59—61 °C (from ethanol); $\nu_{max.}$ 1 787 cm^{-1}; δ (in CCl_4 with $SiMe_4$ as internal standard) 5.82 (2 H, s) and 2.63 (9 H, s); m/z M^+ absent; fragment ions, *inter alia*, 385 ($M - CF_3CO_2$, 42%), 384 $M - CF_3CO_2H$, 38), and 371($M - I$, 100) (Found: C, 29.15, H, 2.25. $C_{12}H_{11}F_3I_2O_2$ requires C, 28.95; H, 2.25%). Under the same conditions durylene dichloride did not react with PIB.

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