The Acid Decomposition of 1-Aryl-3,3-dialkyltriazenes. Mechanistic Changes as a Function of Aromatic Substitution, Nucleophile Strength, and Solvent

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Solvent, nucleophile strength, and substituents on the phenyl ring modified the yield of aromatic halogenation using 1-aryl-3,3-dialkyltriazenes (**2a**—**f**) and halide ion in anhydrous acidic media.

We report herein the first observation that the yields of aromatic halogenation using 1-aryl-3,3-dialkyltriazenes (**2a**—**f**) and halide ion in anhydrous acidic media depend strongly upon the competing homolytic cleavage of the aryl–nitrogen bond.

In an effort to analyse the influence of the strength of the nucleophile in the reaction, we caused the model triazenes (**2a**—**e**) (0.1 mmol) to react with well dried samples of NaI, LiBr, Bu^n_4NF, or CsF (0.2 mmol) in the presence of acid

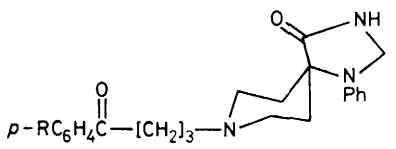
$$p\text{-R-C}_6\text{H}_4\text{-N=N-NEt}_2 \xrightarrow[H^+]{X^-} p\text{-R-C}_6\text{H}_4\text{X} + \text{R-Ph} \quad [\text{or } p\text{-R-C}_6\text{H}_4\text{Cl}]$$

(2) (1) (3) (4a) R = COMe

a, R = COMe
b, R = CN
c, R = H
d, R = Me
e, R = OMe

a, R = COMe, X = F
b, R = COMe, X = Br
c, R = COMe, X = I
d, R = CN, X = F
e, R = CN, X = Br
f, R = CN, X = I
g, R = H, X = I
h, R = Me, X = I
i, R = OMe, X = I

a, R = COMe
b, R = CN
c, R = OMe



(1j) R = ^{18}F

(2f) R = -N=N-NEt_2

($MeSO_3H$, CF_3CO_2H, or cation exchange resin, BioRad AG 50W-X12) (5 mol. equiv.) in dry acetonitrile (3 ml) at 75 °C.†

The thermally induced acid decomposition of the aromatic dialkyltriazenes (**2a**—**e**) in the presence of iodide and bromide ions and cation exchange resin provides an unusually simple procedure for aromatic iodination and bromination, respectively. With yields ranging from 75 to 99% this method is readily applicable to the preparation of aromatic radiohalide compounds. In all cases with 1-(*p*-acetylphenyl)-3,3-diethyltriazene (**2a**),[1] a mixture of the corresponding *p*-halogenoacetophenone and acetophenone (**3a**) was obtained, suggesting the possible competition of the heterolytic dediazoniation with a radical pathway.[2] As expected, nucleophile strength modified the reaction course with only 6% of acetophenone being formed with iodide ion in comparison with 46% in the case of fluoride ion [yield ratio (**1a**):(**3a**) = 0.09].[3] In wanting to avoid the formation of acetophenone during the acid decomposition of (**2a**) in the presence of Bu^n_4NF in acetonitrile we studied the same reaction in trichloroacetonitrile and found that the yield of *p*-fluoroacetophenone was increased, indicative of a shift in the balance between homolytic and heterolytic pathways [yield ratio (**1a**):(**4a**) = 0.28].

Table 1

Starting triazene	Reacting halide	Medium	Yield[a] (%) ArX	ArH	ArCl
(**2a**)	Bu^n_4NF or CsF[b,c,d]	MeCN	(**1a**) (4)	(**3a**) (46)	—
(**2a**)	Bu^n_4NF or CsF[b,c,d]	CCl_3CN	(**1a**) (10)	—	(**4a**) (36)
(**2a**)	LiBr[b]	MeCN	(**1b**) (75)	(**3a**) (25)	—
(**2a**)	LiBr[b]	CCl_3CN	(**1b**) (80)	—	(**4a**) (20)
(**2a**)	NaI[b]	MeCN	(**1c**) (94)	(**3a**) (6)	—
(**2b**)	Bu^n_4NF or CsF[b,c,d]	MeCN	(**1d**) (9)	(**3b**) (38)	—
(**2b**)	LiBr[b]	MeCN	(**1e**) (>99)	(0)	—
(**2b**)	NaI[b]	MeCN	(**1f**) (>99)	(0)	—
(**2c**)	NaI[b]	MeCN	(**1g**) (>99)	(0)	—
(**2d**)	NaI[b]	MeCN	(**1h**) (>99)	(0)	—
(**2e**)	NaI[b]	MeCN	(**1i**) (96)	(**3c**) (4)	—
(**2f**)	$Cs^{18}F$[d]	CCl_3CN	(**1j**) (4)[e]	—	—

[a] Yields were measured by h.p.l.c. Acid used: [b] cation exchange resin, BioRad AG 50W-X12 (hydrogen form); [c] CF_3CO_2H; [d] methanesulphonic acid. For aromatic fluorination methanesulphonic acid furnished the best yields and these are the values reported in Table 1. [e] Radiochemical yield.

† Reactions were also carried out in tetrahydrofuran (THF), dimethylformamide (DMF), and dimethyl sulphoxide (DMSO). The optimum reaction temperature for aromatic triazene decomposition in most solvents is 70—80 °C.

The delicate balance that exists between both pathways in this system can also be shifted by the substituents on the phenyl ring.[4] In the decomposition of the *para*-substituted 1-aryl-3,3-dialkyltriazenes (**2a**) and (**2b**) in acetonitrile the relative stabilities of the aryl radical Ar· and the aryl cation Ar^+ (where Ar = *p*-$MeCOC_6H_4$ and *p*-CNC_6H_4, respectively) certainly play a major role in the product distribution [yield ratio (**1a**):(**3a**) = 0.09 from (**2a**) *vs.* the yield ratio (**1d**):(**3b**) = 0.24 from (**2b**)].

These observations have implications in the synthesis of ^{18}F labelled spiperone[5] from its corresponding triazene (**2f**).[6] The acid decomposition of (**2f**) in the presence of non-carrier-added (N.C.A.) ^{18}F-fluoride ion in solvents like acetonitrile, bromobenzene, or chloroform follows mainly the protodediazoniation path and gives only trace amounts of the product of fluorodediazoniation (**1j**) (radiochemical yield <0.5%). The same reaction using trichloroacetonitrile as a solvent, as expected from previous observations with triazene (**2a**), permitted the preparation of N.C.A. ^{18}F labelled spiperone (**1j**) with higher radiochemical yields (up to 4%). The work reported here demonstrates for the first time the conditions for controlling the competitive paths of the reaction.

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