PHOTOCYCLIZATIONS OF ARYLTHIOFLUOROAROMATIC COMPOUNDS: SYNTHESIS OF BENZOTHIOPHENES

Ziqi Jiang and Jorge Marquet*

Department of Chemistry, Universitat Autònoma de Barcelona, 08193 Bellaterra,
Barcelona, Spain

Abstract - Intramolecular defluoro-photocyclizations of *o*-arylthiofluoroaromatic compounds in aqueous solution afforded benzothiophene derivatives. Similar photoreactions in acetonitrile led, when possible, to arene thiolate displacement. A mechanistic rationale is discussed.

The photoreactions of halogenoaromatic compounds, usually, involve loss of halogen from the ring giving rise to aryl radicals which may be exploited in synthesis. In this sense the broad outlines of the photochemical reactions of halogenoaromatic compounds are related to the relative strength of the bonds involved: Ph-F > Ph-H > Ph-Cl > Ph-Br > Ph-I.[1] Thus, the C-F bond in fluoroaromatic compounds has been commonly considered as photochemically inactive, those compounds showing a variety of fascinating photoisomerization and photoaddition reactions without the loss of fluorine.[2] However, several exceptions are known to this photochemical inertia of the C-F bond. For instance, halogenonitroaromatic compounds undergo nucleophilic aromatic photosubstitutions with different nucleophiles.[3] This process can be considered the photochemical version (S_NAr^*) of the thermal addition-elimination mechanism. In addition, halogenoanisoles photoreact in aqueous solution with nucleophiles *via* the formation of a radical cation from the triplet excited state of the aromatic compound, the so called $S_{R+N}1\,{}^3Ar^*$ type mechanism.[4] This process can be considered the photochemical version of the more general $S_{ON}2$ mechanism.[5] Finally, polyfluoronitroaromatic compounds have been recently shown to react in a photostimulated process *via* direct nucleophilic substitution on the corresponding radical anion ($S_{RN}2$ mechanism).[6] Common features to these three processes are the relative

---

Dedicated to Prof. Alan R. Katritzky on the occasion of his 65th birthday.

reactivity of the substrates, that decrease in the order Ar-F > Ar-Cl > Ar-Br > Ar-I, just the opposite to the relative strength of the bond involved, and that the reactions are normally carried out in aqueous solutions.

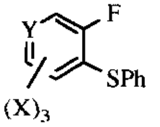
Intramolecular dehalogeno-photocyclization of aromatic compounds has been used in the synthesis of a variety of heterocyclic compounds, examples of dechlorination,[7] debromination,[8] and deiodination[9] processes being common. However, as far as we know, only one example of photocyclization with loss of fluorine has been reported,[10] other attempts being unsuccesfull.[11]

Analysis of the commented precedents led us to consider that a new entry to some heterocyclic systems could be achieved through intramolecular photoarylation of fluoroaromatic compounds using the appropriate substrates and conditions (aqueous solution). Here we report our preliminary studies on the synthesis of benzothiophene derivatives through defluoro-photocyclizations of *o*-arylthiofluoroaromatic compounds.

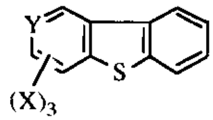
The experiments 1, 3-8 (Table) were carried out in aqueous solution using potassium carbonate as a base (to trap the produced HF) and in the presence of benzophenone as a photosensitizer. As a standard procedure, a solution of the substrate (5 mmol), K_2CO_3 (0.60 g, 5 mmol), and benzophenone (0.055 g, 0.3 mmol) in water/acetonitrile (1 : 4, 500 ml) was irradiated for the time given. Isolation of the products was carried out by column chromatography (silica gel, hexane/$CHCl_3$). Moderate to fair yields of the cyclized benzothiophene derivatives (**2a**), (**2b**), (**2c**), (**2f**), and (**6**) were obtained. Experiments 5 and 6, using phenylthiofluoronitrobenzenes (**1d**) and (**1e**) as a substrates failed.

We have previously commented that fluorine could presumably act as a leaving group in three different photochemical mechanisms, all of them taking place predominantly in aqueous solution. Of those three mechanisms, the S_NAr^* and the $S_{RN}2$ are favored in the presence of a nitro group in the aromatic ring. Therefore, the results of the experiments 5 and 6 suggest that for experiments 1, 3, 4, 7, and 8 (Table), the mechanism is probably oxidatively initiated (mechanism through a radical-cation intermediate).

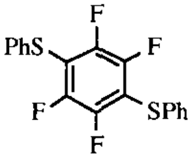
The strong dependence of our photoreactions on the used medium is demonstrated by the results of the experiments 2, 9, and 10 (Table). The substrates (**4**) and (**5**) were irradiated in acetonitrile due to their very poor solubility in aqueous solutions. Arylthiolate displacement was observed[12]. In addition, when **1a** was irradiated in acetonitrile solution (experiment 2, Table) only trace of dibenzothiophene (**2a**) was obtained. The observed leaving group order (SAr > F), and the used solvent (ACN) and base (Et_3N has good photoreductive properties) suggest that experiments 9 and 10 could be examples of $S_{RN}1$ type processes.[13] This mechanism has been already proposed for a very related process.[14]



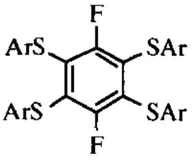
(1)



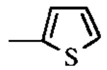
(2)



(3)



(4) : Ar = C_6H_5

(5) : Ar = 

(a) : Y = C-H , X = H

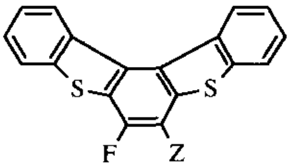
(b) : Y = C-NH_2 , X = H

(c) : Y = C-$NHCOCH_3$, X = H

(d) : Y = C-NO_2 , X = H

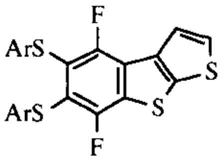
(e) : Y = C-NO_2 , X = F

(f) : Y = N , X = F



(6) : Z = F

(7) : Z = SPh



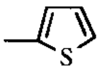
(8) : Ar = 

Table. Photolysis of arylthiofluoroaromatic compounds.

Exp.	Substrate[a]	Conditions[b]	Additives[c]	Product (mp)[a]	Yield (%)[d]
1	**1a**	ACN / H_2O (4:1), 1 h	K_2CO_3/Ph_2CO	**2a** (99-102°C)	60
2	**1a**	ACN, 1 h	K_2CO_3/Ph_2CO	**2a**	traces
3	**1b**	ACN / H_2O (4:1), 2 h	K_2CO_3/Ph_2CO	**2b** (266-268°C)	15
4	**1c**	ACN / H_2O (4:1), 3 h	K_2CO_3/Ph_2CO	**2c**[e]	10
5	**1d**	ACN / H_2O (4:1), 8 h	K_2CO_3/Ph_2CO	---	---
6	**1e**	ACN / H_2O (4:1), 8 h	K_2CO_3/Ph_2CO	---	---
7	**1f**	ACN / H_2O (4:1), 24 h	K_2CO_3/Ph_2CO	**2f** (151-153°C)	23
8	**3**	ACN / H_2O (5:1), 2 h	K_2CO_3/Ph_2CO	**6** (165-167°C)	41
9	**4**	ACN, 2 h	Et_3N	**7** (157-159°C)	66
10	**5**	ACN, 6 h	Et_3N	**8** (127-130°C)	23

a) Starting materials were prepared following standard procedures. All the new products showed the expected spectroscopic behavior and gave correct elemental analyses. Their full characterization will be reported elsewhere (see however reference 12). b) ACN = acetonitrile. The irradiation was carried out with a medium pressure lamp with Pyrex filter. c) 0.15 eq. of benzophenone were introduced as photosensitizer when indicated. The bases were used in excess. d) Isolated yields based on non recovered starting material. e) Product (**2c**) was not isolated, the crude material was directly hydrolyzed, to **2b**. The given yield corresponds to the whole process.

ACNOWLEDGEMENTS

Financial support from DGICYT ("Ministerio de Educación y Ciencia" of Spain) through project No. PB90-0693 is gratefully acknowledged.

REFERENCES AND NOTES

1. G. Lodder, "The Chemistry of Functional Groups. Suplement D: Recent Advances in the Photochemistry of the Carbon-halogen Bond", ed. by S. Patai and Z. Rappoport, J. Wiley, 1983 pp. 1605-1683.
2. B. Sket and M. Zupan, *J. Am. Chem. Soc.*, 1977, **99**, 3504; M. G. Barlow, D. E. Brown, and R. N. Haszeldine, *J. Chem. Soc., Perkin Trans. 1*, 1978, 363; R. D. Chambers, J. A. H. MacBride, J. R. Maslakiewicz, and K. C. Srivastava, *J. Chem. Soc., Perkin Trans. 1*, 1975, 396; R. D. Chambers, J. A. H. MacBride, J. R. Maslakiewicz, and K. C. Srivastava, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1130.
3. J. Cornelisse and E. Havinga, *Chem. Rev.*, 1975, **75**, 353; R. Pleixats, M. Figueredo, J. Marquet, M. Moreno-Mañas, and A. Cantos, *Tetrahedron*, 1989, **45**, 7817.
4. J. den Heyer, O. B. Shadid, J. Cornelisse, and E. Havinga, *Tetrahedron*, 1977, **33**, 779.
5. R. W. Alder, *J. Chem. Soc., Chem. Commun.*, 1980, 1184; L. Eberson, L. Jönsson, and L. G. Wistrand, *Tetrahedron* ,1982, **38**, 1087.
6. J. Marquet, Z. Jiang, I. Gallardo, A. Batlle, and E. Cayón, *Tetrahedron Lett.*, 1993, **34**, 2801.
7. S. Pakray and R. N. Castle, *J. Heterocyc. Chem.*, 1987, **24**, 231; J. K. Luo and R. N. Castle, *J. Heterocyc. Chem.*, 1990, **27**, 1031; L. Jayabalan and P. Shanmugan, *Synthesis*, 1990, 789; L. Jayabalan and P. Shanmugan, *Synthesis*, 1991, 217; S. Zekter and R. N. Castle, *J. Heterocyc. Chem.*, 1991, **28**, 737.
8. S. Gupta and D. S. Bhakuni, *Synth. Commun.*, 1989, **19**, 393; N. S. Narasimhan and I. S. Aidhen, *Tetrahedron Lett.*, 1988, **29**, 2987; M. R. Devi, J. M. Rao, and V. R. Srinivasan, *Synth. Commun.*, 1989 , **19**, 2345.
9. C. J. Chandler, D. J. Craik, and K. J. Waterman, *Aust. J. Chem.*, 1989, **42**, 1407; C. J. Moody, C. W. Rees, and R. Thomas, *Tetrahedron Lett.*, 1990, **31**, 4375.
10. E. P. Fokin, T. N. Gerasimova, T. V. Fomenko, and N. V. Semikolenova, *Zh. Org. Khim.*, 1978, **14**, 834.
11. J. Bratt, B. Iddon, A. G. Mack, H. Suschitzky, J. A. Taylor, and B. J. Wakefield, *J. Chem. Soc., Perkin Trans. 1*, 1980, 648.
12. Discrimination between structure (**7**) and the other possible isomer (resulting from the alternative arylthiolate displacement) was achieved by ^{13}Cnmr spectroscopy. Thus, two carbons showing fluorine long distance coupling (δ 127.28 and 125.54, J = 20 Hz, C-C-F) are present in the spectrum. The chemical shift values indicate a very similar environement. This agrees with the structure (**7**) in which both carbons are linked to sulfur. The alternative isomeric structure should show a larger chemical shift difference, in the order of what it is observed (132.88 and 124.10, J = 19 Hz) for the product (**8**) in which one of the carbons is linked to sulfur but the other not.
13. J. F. Bunnett, *Acc. Chem. Res.*, 1978, **11**, 413.
14. C. J. Gilmore, D. D. MacNicol, A. Murphy, and M. A. Russell, *Tetrahedron Lett.*, 1984, **25**, 4303.

Received, 16th September, 1993