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FULL PAPER

Mild C–F Activation in Perfluorinated Arenes through Photosensitized Insertion of Isonitriles at 350 nm

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Dedicated to Prof. Eric Jacobsen on the occasion of his 60th birthday.

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Abstract. Fluorinated compounds have become important in the fields of agrochemical industry, pharmaceutical chemistry and materials sciences. Accordingly, various methods for their preparation have been developed in the past. Fluorinated compounds can be accessed via conjugation with fluorinated building blocks, via C–H fluorination or via selective activation of perfluorinated compounds to give the partially fluorinated congeners. Especially the direct activation of C–F bonds, one of the strongest σ-bonds, still remains challenging and new strategies for C–F activation are desirable. Herein a method for the photochemical activation of aromatic C–F bonds is presented.

It is shown that isonitriles selectively insert into aromatic C–F bonds while aliphatic C–F bonds remain unaffected. Mechanistic studies reveal the reaction to proceed via the indirect excitation of the isonitrile to its triplet state by photoexcited acetophenone at 350 nm. Due to the relatively mild light used, the process shows high functional group tolerance and various compounds of the class of benzimidoyl fluorides are accessible from aryl isonitriles and commercially available perfluorinated arenes.
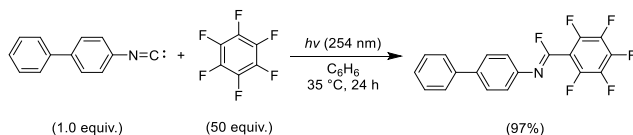
Keywords: C–F activation; fluorine; insertion; photochemistry; sensitizers; transition-metal free

Introduction

Over the past decades, fluorinated compounds have gained great importance in agrochemical industry and medicinal chemistry.[1–7] Around one quarter of drugs in use in 2014 contain fluorine atoms as their incorporation improves both the pharmacokinetics and membrane permeability compared to their non-fluorinated congeners.[2] The fluorine atom is about the size of the hydrogen atom[8] giving fluorinated and non-fluorinated molecules similar structural characteristics while they differ strongly in most other physical and electronic properties. Along with the conjugation of organic compounds with fluorinated building blocks, an obvious synthetic route to defined fluorinated compounds is the fluorination of their non-fluorinated derivatives, an approach that has been investigated extensively in the past.[2,6,9,10] An alternative and less exploited strategy is the selective defluorination of highly fluorinated and readily accessible compounds, and various methods have been developed along those lines.[11–14] However, the key step C–F activation is not trivial as this σ-bond is one of the strongest σ-C–X bonds (e.g. 154 kcal mol⁻¹ in hexafluorobenzene[13]), and hence the development of new and broadly applicable methods for C–F modification is challenging and remains important. Moreover, a deeper understanding of the mechanisms of such defluorination reactions is desirable and necessary for further improving existing methodology. In previous work, we introduced a method for the photochemical insertion of isonitriles into aromatic C–F bonds.[12] Upon irradiation with a high pressure mercury lamp (λ_{exc} = 254 nm) and using a large excess of a perfluorinated arene (mostly acting as a co-solvent) various benzimidoyl fluorides were successfully prepared, as exemplified in Scheme 1 for

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the insertion of isocyanobiphenyl into perfluorobenzene. Mechanistic studies revealed that the reaction proceeds from an isonitrile in its excited triplet state.[12,15] Unfortunately, high energy light was required for the excitation of the substrate isonitriles, resulting in a limited functional group tolerance.

Scheme 1. UV-light mediated insertion of isocyanobiphenyl into perfluorobenzene.[12]

We therefore decided to generate the active excited triplet state of an aryl isonitrile via photosensitization with an external photosensitizer. This alternative strategy should permit the isonitrile insertion into C–F bonds to be conducted upon irradiation with light of longer wavelengths. Photosensitization describes the indirect excitation of a substrate via an excited photosensitizer. This photosensitizer can either interact with the substrate via singlet electron transfer, in what is typically known as photoredox catalysis, or via energy transfer. There are three primary energy tranfer mechanisms: radiative, Förster and Dexter. In the former two, overlap between the emission of the photosensitizer and the absorption of the substrate is required while in Dexter energy transfer, orbital overlap is necessary to permit the double electron transfer to occur.[16–18] This orbital overlap can occur transiently through collisions between the photosensitizer and the substrate in solution. Through this triplet-triplet energy transfer[18] the substrate can be indirectly excited (sensitized) to its triplet state at a wavelength that would not be suitable to directly excite it. Herein we disclose our first results on the photosensitization of isonitriles at 350 nm, a wavelength where direct excitation of isocyanobiphenyl is not possible, and the use of these photoexcited intermediates in C–F insertion reactions.

Results and Discussion

Xanthones are a class of heterocyclic natural products that show diverse biological activities and also useful photochemical characteristics. Antibacterial, antifungal and antiviral characteristics as well as cytotoxic activities towards cancer cells could be demonstrated.[19,20] Further, their photochemical characteristics, especially their triplet states and their use as photocatalysts, were studied intensively.[21–24] We therefore decided to choose the 2-isocyanoxanthone (**1a**) bearing an isonitrile

functionality. Initial reactions of xanthone **1a**, prepared in four steps from xanthone (see Supporting Information),[25–27] and hexafluorobenzene (**2**) (50-300 equiv.) were conducted under an argon atmosphere and irradiation (λ_{exc} = 350 nm) for up to 40 hours to give imidoyl fluoride **3a** (see Supporting Information). The reaction temperature in the experimental setup was around 40 °C. A large excess of the perfluoroarene **2** was required in order to obtain a high conversion. The solvent was varied and acetone was found to be the best solvent to run this reaction in. Progress of the isonitrile insertion was followed by GC-MS analysis and it was observed that the reaction rate decreases over time. All reactions were very clean and along with unreacted substrate **1a** only product **3a** was identified by GC-MS in the crude mixture.

Based on the hypothesis that the reaction likely involves a triplet state of the isonitrile,[12,15] the use of an external photosensitizer was considered next. To this end, four photosensitizers were tested (see Table 1). While the use of benzophenone, phenylacetone and 4'-(trifluoromethyl)acetophenone led to low yields between 7 and 29%, a much higher yield of 77% was achieved upon using acetophenone. Through further optimization of the reaction conditions and by conducting the reaction under air, a yield of 97% could be achieved. (Scheme 2).
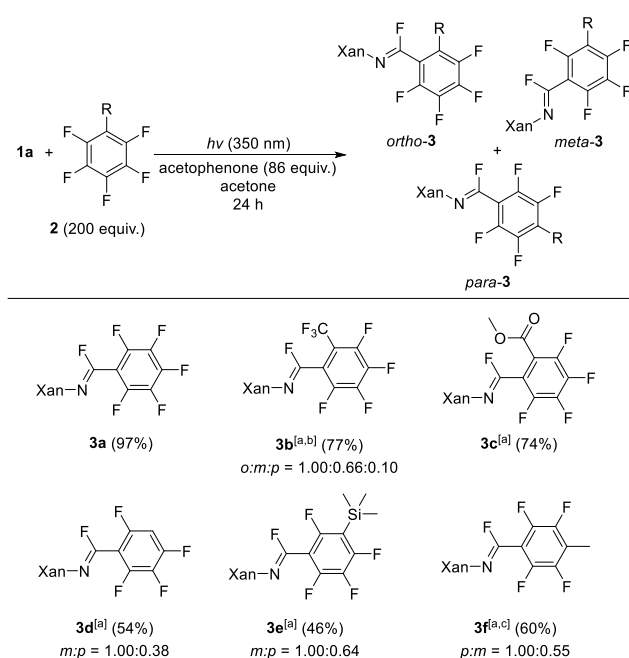
Table 1. Variation of the photosensitizer in the reaction of **1a** with **2**.

Entry	Acetone [mL]	Sensitizer	Time [h]	Yield [%][a]
1	1.9	Benzophenone	23	16
2	1.5	Phenylacetone	23	7
3	1.9	4'(Trifluoro methyl)aceto phenone	23	29
4	1.9	Acetophenone	24	77

[a] Yields were determined from ^{19}F-NMR spectra with Ph–CF$_3$ as the internal standard.

With optimized conditions in hand, the reaction scope was tested using isonitrile **1a** in combination with various perfluorinated arenes (Scheme 2). 200 equivalents of each perfluoroarene were used and the benzimidoyl fluorides **3a-f** were obtained in 46-97% isolated yields. In contrast to the parent perfluorobenzene, for all other fluoroarenes tested a regiochemistry problem arises. The reaction of isonitrile **1a** and perfluorotoluene provided the *ortho*- and *meta*-derivatives **3b** as major products with an

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overall yield of 77% and the CF₃-group in **3b** remained unreacted. With methyl pentafluorobenzoate, the *ortho*-product **3c** was regioselectively formed in 74% yield while pentafluorobenzene delivered the *meta*- and *para*-products **3d** with the *meta*-derivative as the major compound in 54% overall yield. Light-mediated reaction of isonitrile **1a** with trimethyl (perfluorophenyl)silane afforded the *meta*- and *para*-products **3e** (46%) with moderate regioselectivity. Pentafluorotoluene led to an overall yield of 60% with the *para*-product **3f** being formed as the major isomer along with its *meta*-congener.
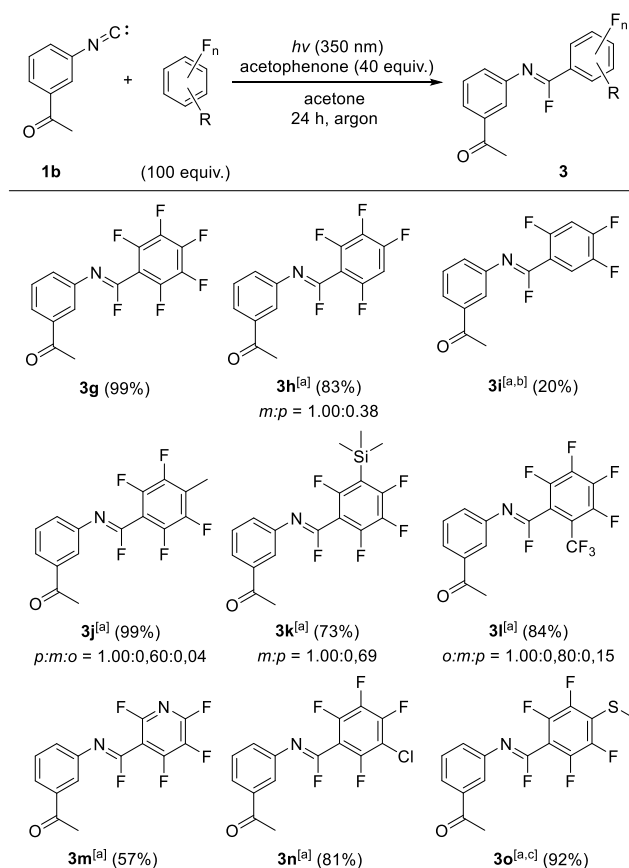

Scheme 2. Scope of C–F activation with 2-isocyanoxanthone (0.1 mmol) varying the perfluorinated arene ([a] reaction time is 48 h. [b] 224 equiv. of perfluorinated substrate were used. [c] 231 equiv. of perfluorinated substrate were used). Xan = xanthon-2-yl.

The overall yields in this series depend on the electronic nature of the substituents on the perfluorinated arenes with electron-poor systems generally showing higher yields. The yield significantly decreases upon replacement of a fluorine atom by a hydrogen atom, as documented by comparing yields obtained for **3a** and **3d**. Of note, upon replacing two fluorine atoms in the parent perfluorobenzene with hydrogen atoms using 1,2,4,5-tetrafluorobenzene as the substrate, only traces of the corresponding C–F insertion product were detected by GC-MS (not shown). The electronic character of the substituent is obviously controlling the efficiency and also the regioselectivity of the reaction. While electron-donating groups (EDG) lead to mixtures of

meta- and *para*-products (see **3d-f**), *ortho*-products were obtained as major regioisomers for compounds bearing an electron withdrawing group (EWG) along with the fluorine atoms (see **3b-c**).[12] The reasons behind the observed regioselectivity are currently not fully understood. As expected, due to the large excess of the perfluoroarene substrate used in these experiments, double C–F insertion leading to bisimidoyl fluorides was never observed.

To further underline the applicability of the reaction and to check whether the xanthone moiety is required for the C–F activation, the readily accessible isonitrile **1b**, prepared according to a literature protocol over two steps,[27] was tested in combination with various perfluoroarenes (Scheme 3). Pleasingly, reaction of isonitrile **1b** with hexafluorobenzene provided the benzimidoyl fluoride **3g** quantitatively and it was possible to lower the equivalents of substrate **2** to 100 without diminishing the yield. Notably, all reactions with **1b** had to be carried out under argon using dried acetone and acetophenone, since the product imidoyl fluorides readily hydrolyse. With pentafluorobenzene (100 equiv.) the *meta*-product **3h** was the major isomer formed and the regioselectivity was the same as that observed for the reaction with isonitrile **1a**. As compared to the analogous reaction with **1a**, the yield was significantly higher (83% versus 54%). Reaction of **1b** with 1,2,4,5-tetrafluorobenzene afforded 20% of **3i** using 200 equivalents of the perfluorinated arene. With pentafluorobenzenes bearing a methyl or a trimethylsilyl group (100 equiv.) the general reactivity trend was followed and isonitrile **1b** provided higher yields as compared with the yields obtained for the analogous reactions with isonitrile **1a**. Using 1,2,3,4,5-pentafluoro-6-methylbenzene, the *para*-product **3j** was obtained as the major product and the overall yield was 99%. Trimethyl(perfluorophenyl)silane provided the *meta*-product **3k** as the major product (73%). The reaction with perfluorotoluene (100 equiv.) proceeded in high yield (84%) delivering the *ortho*-product **3l** as the major isomer in analogy to the reaction with isonitrile **1a**. In general higher yields were achieved using **1b** instead of **1a** which might also be due to a better solubility of the resulting benzimidoyl fluorides. The reaction of isonitrile **1b** and perfluoropyridine (100 equiv.) afforded exclusively the *meta*-product **3m** with complete regioselectivity and moderate yield (57%).

Especially challenging is the selective C–F activation in the presence of other C–halogen bonds, since 254 nm irradiation used in our previous study caused C–halogen bond homolysis. Along these lines, we reacted isonitrile **1b** with chloropentafluorobenzene (100 equiv.) and obtained the targeted product **3n** exclusively as the *meta*-isomer in 81% yield.
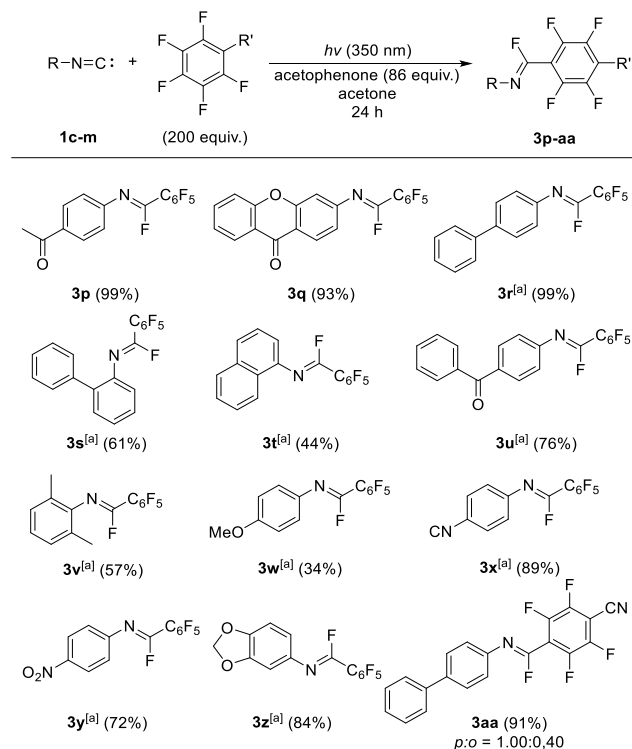
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Unfortunately, bromopentafluorobezene was not stable under the applied conditions. Isonitrile **1b** was also tested in the reaction with methyl(perfluorophenyl)sulfane and the *para*-isomer **3o** was selectively formed in excellent yield (92%). Notably, using our previously reported conditions (λ_{exc} = 254 nm),[12] the corresponding benzimidoyl fluoride could not be prepared, further underlining the advantage of using milder longer wavelength light in combination with a photosensitizer to conduct these C–F insertion reactions.

Scheme 3. Scope of C–F activation in perfluorinated arenes with **1b** (0.1 mmol) and 100 equiv. of perfluorinated substrate ([a] reaction time was 48 h. [b] 200 equiv. of perfluorinated substrate were used. [c] 89 equiv. of perfluorinated substrate were used).

The scope of the C–F activation was further tested with respect to the isonitrile component keeping hexafluorobenzene as the reaction partner (Scheme 4). The selected isonitriles were readily prepared from their aniline derivatives over two steps.[27,28] These reactions were carried out without careful exclusion of air and moisture, as hydrolysis of the product imidoyl fluorides turned out to be unproblematic in these cases. Isomers of 3-isocyanoacetophenone (**1b**) and 2-isocyanoxanthone (**1a**) were tested first and we found that both isonitriles **1c** and **1d** are eligible substrates in the reaction with C$_6$F$_6$, and **3p** and **3q**

were isolated in high yields (99% and 93%, respectively). Importantly, we found that a ketone moiety in the isonitrile component is not required as can be seen by the quantitative transformation of 4-isocyano-1,1'-biphenyl (**1e**) to the imidoyl fluoride **3r**. This fact significantly expands the isonitrile scope. Of note, irradiation of **1e** in the absence of acetophenone with C$_6$F$_6$ did not lead to the formation of the targeted **3r**. The isonitrile **1e** was also tested in the reaction with 2,3,4,5,6-pentafluoro benzonitrile. While this particular C–F insertion did not proceed under our previously disclosed conditions,[12] product **3aa** was obtained in excellent 91% yield with the *para*-isomer being formed as major compound.

Scheme 4. Scope of the C–F activation in hexafluorobenzene (200 equiv.) varying the isonitrile component ([a] reaction time was 48 h).

1-Isocyanobiphenyl (**1f**) worked well leading to **3s** in 61% yield while 1-isocyanonaphthalene (**1g**) afforded **3t** with slightly lower efficiency (44%) and (4-isocyanophenyl)(phenyl)ketone (**1h**) gave **3u** in a good yield (76%). 2-Isocyano-1,3-dimethyl benzene (**1i**) and 1-isocyano-4-methoxybenzene (**1j**) were converted to their corresponding benzimidoyl fluorides **3v** and **3w** in 57% and 34% yield, respectively. Further, isonitrile and nitro functionalities in the isonitrile component are tolerated, as documented by the successful preparation of the benzimidoyl fluorides **3x** (89%) and **3y** (72%). 5-Isocyanobenzo[d][1,3]dioxole (**1m**)

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was also successfully used in the reaction with C_6F_6 to give the targeted product **3z** in high yield (84%). These studies show that the scope with respect to the isonitrile component is broad and different functional groups are tolerated.

In order to examine the reaction pathway and to account for the reactivity difference of the tested photosensitizers in the reaction (Table 1), we calculated the structures and energies of the singlet and triplet excited states of **1a** along with acetophenone and benzophenone (Figure 1). The computations show that acetophenone has an energetical higher S_1 state (3.84 eV) compared to **1a** (3.71 eV), but that the S_1 state of benzophenone is slightly lower at 3.67 eV. The T_1 states of **1a** and acetophenone are similar at 3.33 and 3.28 eV, respectively, while that of benzophenone is stabilized at 3.06 eV. The small energy difference between the excited triplet states of acetophenone and **1a**[29] seems to enable Dexter energy transfer between the two.
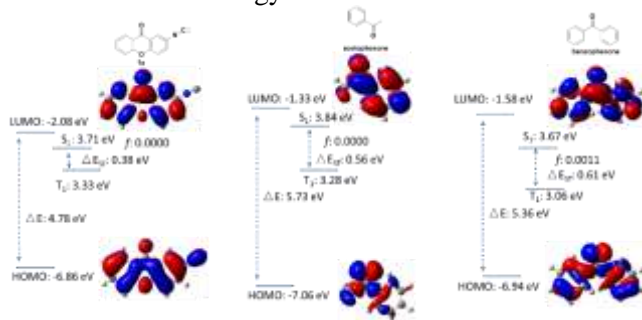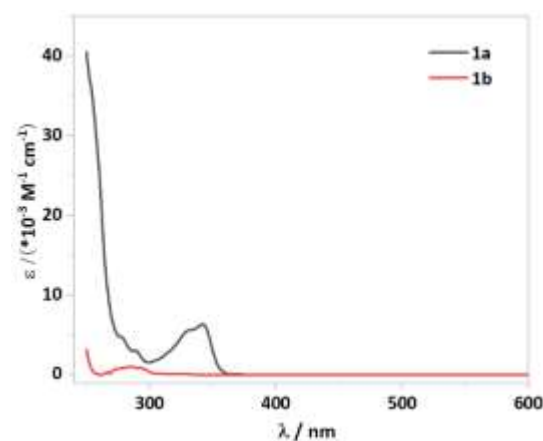

Figure 1. DFT and TDA modelling of the energies of the HOMO/LUMO orbitals and the S_1 and T_1 states of **1a,** acetophenone, and benzophenone and the electron density distribution of the frontier molecular orbitals at the PBE0/6-31G(d,p) level.[30,31]

In order to corroborate a Dexter mechanism experimentally, we first measured the absorption spectra of **1a** and **1b** in acetonitrile. Near the 350 nm excitation wavelength used for the photoreaction, **1a** possesses a much more absorptive band at 320 nm compared to the weak absorption detected for **1b** (Figure 2). We next investigated the spectral overlap between the emission spectra of acetophenone or benzophenone and the absorption spectra of **1a** or **1b** (Figure 3). Both acetophenone and benzophenone exhibited sharp emission at 366 nm in acetonitrile

solution. There is a small overlap of these emission spectra and the absorption spectra of **1a** and **1b**. In acetone as the solvent, the emission spectra of acetophenone and benzophenone are red-shifted, showing a shoulder peak at 368 nm and a broad peak at 402 nm. In this solvent, the spectral overlap is negligible. Thus, Förster energy transfer can be excluded as the sensitization mechanism due to poor spectral overlap between the donor acetophenone/ benzophenone and the acceptor isonitrile.

Figure 2. UV-vis absorption spectra of **1a** and **1b** in acetonitrile.
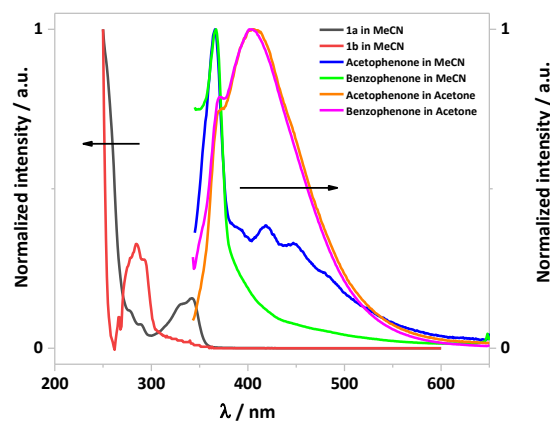

Figure 3. Normalized UV-vis absorption spectra of **1a** and **1b** and emission spectra of acetophenone and benzophenone in MeCN and acetone (λ_{exc} = 330 nm).
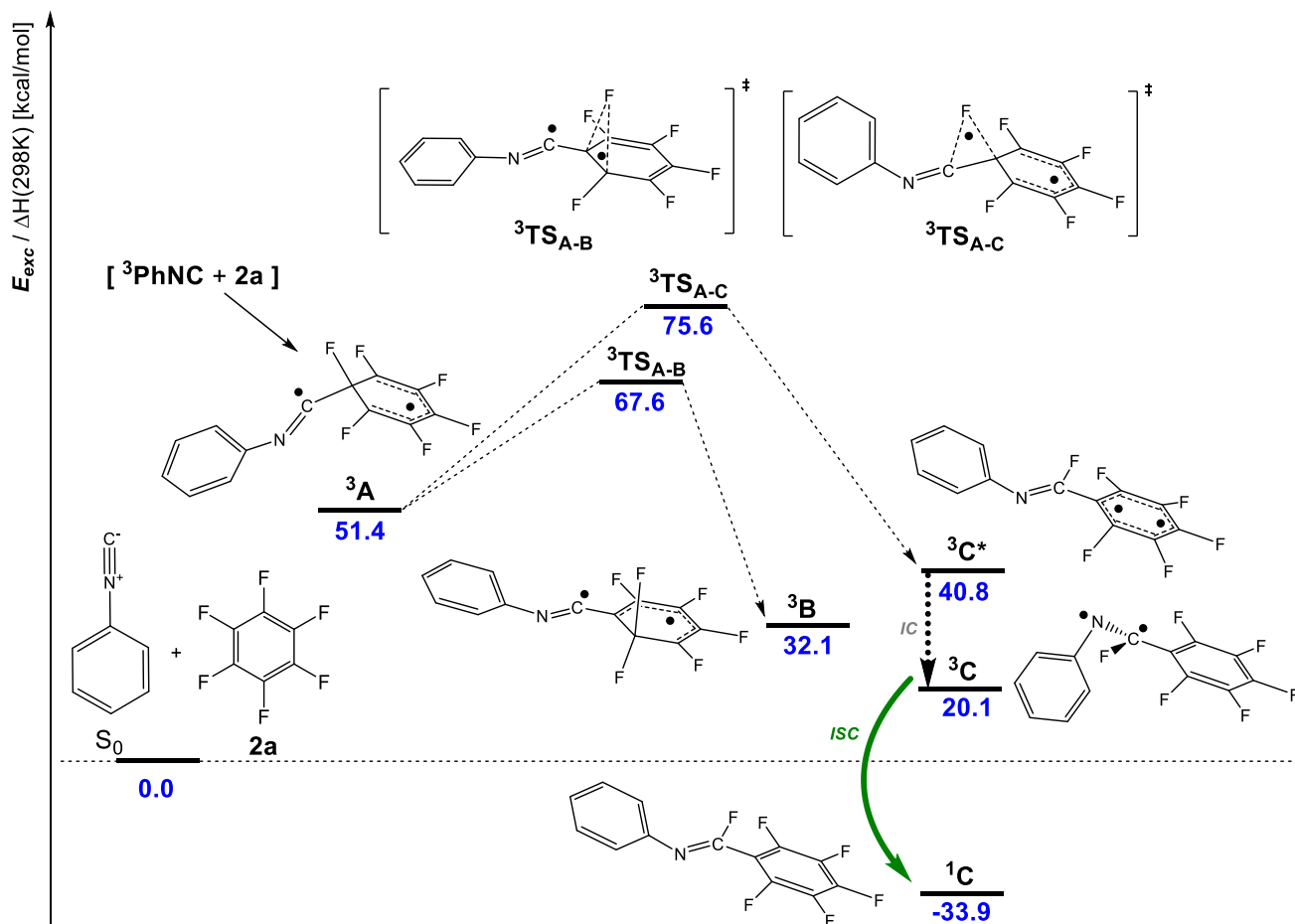
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Figure 4. DFT enthalpies of intermediates for the reaction of triplet phenyl isonitrile with C_6F_6 (**2a**). Geometries, enthalpic corrections and excitation energies: ωB97X/6-31G(d,p), electronic energies: PWPB95-D3/def2-TZVP (see Supporting Information).

Finally, the C–F insertion reaction between a photoexcited aryl isonitrile and a fluoroarene was investigated computationally.[12] As a test reaction, the insertion of triplet phenyl isonitrile into C_6F_6 (**2a**) was addressed by using density functional theory (DFT) methods (Figure 4). We started the model calculation from the triplet adduct **³A** which has a lower energy than the T_1 energy of **1a** (76.8 kcal/mol). A transition structure ³TS$_{A-C}$ for 1,2-migration of F to the imidoyl carbon has been located, but the energetic barrier is rather high ($\Delta H^{\neq} = 24.2$ kcal/mol) and this path leads to an excited triplet state **³C*** of the product. The activation energy required for F-migration to the *ortho*-position of the fluorinated arene is lower (³TS$_{A-B}$, $\Delta H^{\neq} = 16$ kcal/mol) and intermediate **³B** is formed exothermically. Thus, **³B** is likely an intermediate. We could not locate a transition structure for the direct conversion of **³B** to one of the triplet states of the product, but it is reasonable to assume that a pathway involving the mixing of π,π and n,π states exists. The lowest triplet intermediate we could locate is **³C**, a π,π*-excited triplet state of the product imidoyl fluoride. It will revert to the singlet state (**¹C**) by intersystem crossing involving the rotation of the C-N bond.

Conclusion

In conclusion, we have introduced a mild method for the photosensitized insertion of various isonitriles into the C–F bond of perfluorinated arenes to afford benzimidoyl fluorides in moderate to good yields. Acetophenone was identified as a suitable sensitizer and C–F activation reactions could be achieved upon irradiation at 350 nm. The rather mild light used to mediate these reactions warrant high functional group tolerance. The transition-metal free reaction provides ready access to benzimidoyl fluorides with, in selected cases, high regioselectivity. Previous mechanistic studies showed that these C–F activation reactions proceed via the triplet state of the aryl isonitriles. While in previous work the triplet state was generated upon 250 nm excitation, the acetophenone-sensitized process proceeds likely via a Dexter energy transfer at 350 nm, as analyzed by excited state calculations and spectroscopic studies.

Experimental Section

General procedure I: Synthesis of isonitriles 1 from anilines:

Aromatic isonitriles **1a-m** were synthesized from their aniline derivatives according to a literature known procedure.[27] The aniline derivative (1.0 equiv.) was dissolved in dry THF (0.6 M) under argon. Acetic anhydride (2.3 equiv.) and formic acid (2.7 equiv.) were stirred under argon for 2 h at 55 °C and subsequently added dropwise to the aniline solution at 0 °C. The reaction mixture was stirred at rt for 2 h. The reaction was quenched by adding saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over $MgSO_4$ and the solvent was removed in vacuo. The product, used further without any purification, was dissolved in dry THF (0.6 M) under argon, Et_3N (6.7 equiv.) was added and the solution was cooled to 0 °C. $POCl_3$ (1.7 equiv.) was added dropwise and the mixture was stirred for 1 h at 0 °C. The reaction was quenched with saturated aqueous Na_2CO_3 solution and the resulting mixture was stirred for 1 h at rt. The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over $MgSO_4$. The solvent was removed in vacuo and the product was isolated via flash column chromatography with pentane and diethyl ether. The solvent was removed in vacuo until about 50 mL remained and the product **1** was finally freeze dried to prevent it from polymerization.[32]

General procedure II: Photoreaction

Isonitrile **1** (0.1 mmol, 1.0 equiv.) was added to a *Schlenk* tube under argon atmosphere. Acetophenone (40 to 86 equiv.), acetone (0.033 M, 3.0 mL) and the perfluorinated substrate **2** (100 to 200 equiv.) were added. The tube was irradiated with light of 350 nm wavelength in an UV reactor for 24 to 48 h while stirring. During the reaction the inside temperature of the reactor was constantly held at around 40 °C through circulating air. Subsequently, the mixture was transferred to a flask and volatile compounds were removed in vacuo. Acetophenone and some remaining perfluorinated arenes with very high boiling points were removed via bulb-to-bulb distillation. Product **3** was isolated after column chromatography on silica gel.
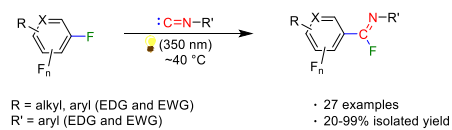
Acknowledgements

References

[1] J. Saadi, H. Wennemers, *Nat. Chem.* **2016**, *8*, 276–280.

[2] J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432–2506.

[3] T. Fujiwara, D. O'Hagan, *J. Fluor. Chem.* **2014**, *167*, 16–29.

[4] K. Müller, C. Faeh, F. Diederich, *Science (80-.).* **2007**, *317*, 1881–1886.

[5] D. O'Hagan, *Chem. Soc. Rev.* **2008**, *37*, 308–319.

[6] D. E. Yerien, S. Bonesi, A. Postigo, *Org. Biomol. Chem.* **2016**, *14*, 8398–8427.

[7] R. Berger, G. Resnati, P. Metrangolo, E. Weber, J. Hulliger, *Chem. Soc. Rev.* **2011**, *40*, 3496–3508.

[8] B. Cordero, V. Gómez, A. E. Platero-Prats, M. Revés, J. Echeverría, E. Cremades, F. Barragán, S. Alvarez, *Dalt. Trans.* **2008**, 2832–2838.

[9] K. L. Hull, W. Q. Anani, M. S. Sanford, *J. Am. Chem. Soc.* **2006**, *128*, 7134–7135.

[10] T. Liang, C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed.* **2013**, 8214–8264.

[11] M. F. Kuehnel, D. Lentz, T. Braun, *Angew. Chem. Int. Ed.* **2013**, 3328–3348.

[12] A. Dewanji, C. Mück-Lichtenfeld, K. Bergander, C. G. Daniliuc, A. Studer, *Chem. Eur. J.* **2015**, *21*, 12295–12298.

[13] H. Amii, K. Uneyama, *Chem. Rev.* **2009**, *109*, 2119–2183.

[14] J. L. Kiplinger, T. G. Richmond, C. E. Osterberg, *Chem. Rev.* **1994**, *94*, 373–431.

[15] M.-D. Su, *ChemistrySelect* **2016**, *1*, 1588–1592.

[16] M. D. Ward, *Coord. Chem. Rev.* **2010**, *254*, 2634–2642.

[17] J. F. Specht, A. Knorr, M. Richter, *Phys. Rev. B* **2015**, *91*, 155313-1-155313–11.

[18] D. L. Dexter, *J. Chem. Phys.* **1953**, *21*, 836–850.

[19] M. M. M. Pinto, M. E. Sousa, M. S. J. Nascimento, *Curr. Med. Chem.* **2005**, *12*, 2517–2538.

[20] L. M. M. Vieira, A. Kijjoa, *Curr. Med. Chem.* **2005**, *12*, 2413–2446.

[21] J. Lalevée, N. Blanchard, M. A. Tehfe, C. Fries, F. Morlet-Savary, D. Gigmes, J. P. Fouassier, *Polym. Chem.* **2011**, *2*, 1077.

[22] D. Weir, J. C. Scaiano, *Tetrahedron* **1987**, *43*, 1617–1623.

[23] J. C. Scaiano, *J. Am. Chem. Soc.* **1980**, *102*, 7747–7753.

[24] A. Garner, F. Wilkinson, *J. Chem. Soc., Faraday Trans. 2* **1976**, *72*, 1010–1020.

[25] T. C. S. Pace, S. L. Monahan, A. I. MacRae, M. Kaila, C. Bohne, *Photochem. Photobiol.* **2006**, *82*, 78–87.

[26] H. Adams, R. A. Bawa, K. G. McMillan, S. Jones, *Tetrahedron Asymmetry* **2007**, *18*, 1003–1012.

[27] M. Tobisu, K. Koh, T. Furukawa, N. Chatani, *Angew. Chem. Int. Ed.* **2012**, *51*, 11363–11366.

[28] D. Leifert, D. G. Artiukhin, J. Neugebauer, A. Galstyan, C. A. Strassert, A. Studer, *Chem. Commun.* **2016**, *52*, 5997–6000.

[29] W. G. Herkstroeter, A. A. Lamola, G. S. Hammond, *J. Am. Chem. Soc.* **1964**, *86*, 4537–4540.

[30] C. Adamo, V. Barone, *J. Chem. Phys.* **1999**, *110*, 6158–6170.

[31] J. A. Pople, J. S. Binkley, R. Seeger, *Int. J. Quantum Chem.* **1976**, *10*, 1–19.

[32] C. Grundmann, *Chem. Ber.* **1958**, *91*.

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FULL PAPER

Mild C–F Activation in Perfluorinated Arenes through Photosensitized Insertion of Isonitriles at 350 nm

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R = alkyl, aryl (EDG and EWG)
R' = aryl (EDG and EWG)

· 27 examples
· 20-99% isolated yield

✔ Direct C−F insertion
✔ Atom economic
✔ Mild conditions
✔ Transition-metal free