biphenyl, 16098-16-1; 4-methoxy-2-aminobiphenyl, 38088-00-5; 3-cyano-1(3*H*)-isobenzofuranone, 27613-27-0; *N*-[3-chloro-4-methoxyphenyl]benzamide, 125593-62-6; 3-chloro-*p*-anisidine, 5345-54-0; 1-bromo-2-(3-hydroxypropyl)-4,5-dimethoxybenzene, 125593-63-7; 1-bromo-2[3-(*tert*-butyldimethylsilyloxy)propyl]-4,5-dimethoxybenzene, 125593-64-8; 3-(2-bromo-4,5-dimethoxyphenyl)propionic acid, 52679-49-9.

Supplementary Material Available: Raney nickel reduction of **4d** and **5d** to **1a**, all nucleophilic substitution reactions of **2b**, zinc-copper reductions of **10a** and **10b**, all compounds dealing with the preparation of **14c** and its chemistry, the reaction of **2b** with *s*-BuLi, and ^{1}H NMR spectra of **3c**, **4d-f**, **5d,e**, and **12a** (15 pages). Ordering information is given on any current masthead page.

Descriptive Photochemistry of Polyfluorinated Azide Derivatives of Methyl Benzoate

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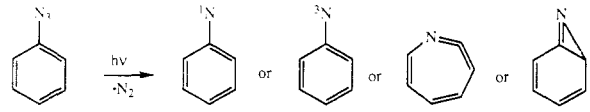
The photochemistry of several polyfluorinated azide derivatizes of methyl benzoate have been studied in a variety of solvents. We have photolyzed methyl 3-azido-6-fluorobenzoate, methyl 3-azido-4-fluorobenzoate, methyl 4-azido-2-fluorobenzoate, methyl 3-azido-2,4-difluorobenzoate, methyl 3-azido-2,6-difluorobenzoate, methyl 3-azido-2,4,6-trifluorobenzoate, and methyl 4-azido-2,3,5,6-tetrafluorobenzoate in toluene, cyclopentane, tetramethylethylene, diethylamine, dimethyl sulfide, dimethyl disulfide, and methanol in an attempt to capture the photogenerated reactive intermediates. Adducts were not formed in cyclopentane, dimethyl disulfide, and methanol solvents. Adducts were formed, however, but in modest yields, in the other solvents. In general the yield of adducts increases with the number of fluorine substituents present, and ortho and para fluorine substituents relative to the azide group are more effective in enhancing the yield of adducts relative to meta fluorine substitution.

Introduction

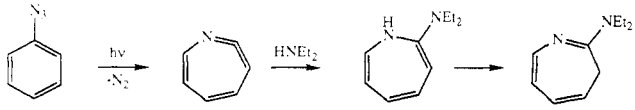
The photochemistry of aryl azides has been described as wonderfully complex.[1] Photolysis of parent phenyl azide (**1**) leads to fragmentation to produce molecular nitrogen and reactive intermediate C_6H_5N. The structure of C_6H_5N might in principle be either singlet phenylnitrene **2S**, triplet phenylnitrene **2T**, azacycloheptatetraene **3**, or benzazirine **4**.[2] To our knowledge singlet phenylnitrene



1 2S 2T 3 4

2S has never been chemically intercepted at ambient temperature. Braumann and Drzaic[3] have determined that the energy separation between singlet and triplet phenylnitrene is approximately 4.3 kcal/mol, with the triplet nitrene being the lower energy species.

Work performed in several laboratories is in agreement that the major, trappable, reactive species present in solution upon photolysis of **1** is the ketenimine **3**.[1,4] Doering an Odum[5] have trapped **3** with diethylamine to produce **5** in greater than 30% yield.



1 3 6 5

The absolute kinetics of this reaction were first studied by Sundberg[6] and subsequently by Schuster and Schrock[1] by flash photolysis with UV-vis detection of **6**. Very recently Schuster and Poliakof[1] have studied the dynamics of **3** directly by flash photolysis with IR detection.[1]

In the absence of amines, ketenimine **3** polymerizes; thus photolysis of **1** in nonnucleophilic solvents gives small amounts of aniline and azobenzene and mostly tar.[7]

These results do not automatically extrapolate to other aryl azides. It is now established that photolysis of various substituted aryl azides do indeed produce nitrenes and benzazirines as trappable intermediates in solution. Thus the nature of the reactive intermediate produced from a given azide is not readily predictable and as a consequence neither are the identities of the adducts that they might ultimately form in the presence of a particular trapping agent.

These considerations are of special importance in photoaffinity labeling,[8] a biochemical technique that frequently employs aromatic azides.[9] In a photoaffinity labeling (PAL) experiment one appends a light-sensitive moiety (e.g., an azide group) to a natural ligand of a biological receptor. The light-sensitive ligand is allowed to bind to a biological receptor. Upon photolysis of the complexed ligand a reactive intermediate is released that in a successful PAL experiment will react quickly and irreversibly with a nearby residue to produce a robust new covalent bond between the labeling reagent and the receptor. This results in "permanent" attachment of the label to the target biomolecule. An ideal reactive intermediate for PAL work will be one that reacts with the first bond it encounters, even an unactivated CH bond. Thus,

(1) (a) Schrock, A. K.; Schuster, G. B. *J. Am. Chem. Soc.* **1984**, *106*, 5229. (b) You-Zhuo, Li; Kirby, J. P.; George, M. V.; Poliakoff, M.; Schuster, G. B. *J. Am. Chem. Soc.* **1988**, *110*, 8092.

(2) Smith, P. A. S. *Azides and Nitrenes*; Scriven, E. F. V., Ed.; Academic Press: San Diego, 1984; p 95.

(3) Drzaic, P. S.; Braumann, J. I. *J. Am. Chem. Soc.* **1984**, *106*, 3443.

(4) (a) Leyva, E.; Platz, M. S.; Persy, G.; Wirz, *J. J. Am. Chem. Soc.* **1986**, *108*, 3783. (b) Li, Y.-Z.; Kirby, J. P.; George, M. W.; Poliakoff, M.; Schuster, G. B. *J. Am. Chem. Soc.* **1988**, *110*, 8092.

(5) Doering, W. von E.; Odum, R. A. *Tetrahedron* **1966**, *22*, 81.

(6) DeGraff, B. A.; Gillespi, D. W.; Sundberg, R. J. *J. Am. Chem. Soc.* **1973**, *95*, 7491.

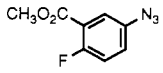
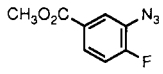
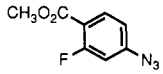
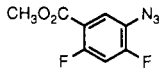
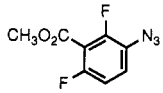
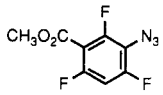
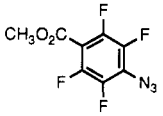
(7) Meijer, E. W.; Nijhuis, S.; von Vroonhaven, F. C. B. M. *J. Am. Chem. Soc.* **1988**, *110*, 7209.

(8) Bayley, H. *Photogenerated Reagents in Biochemistry and Molecular Biology*; Elsevier: New York, 1983.

(9) Bridges, A. J.; Knowles, J. R. *Biochem. J.* **1974**, *143*, 663.

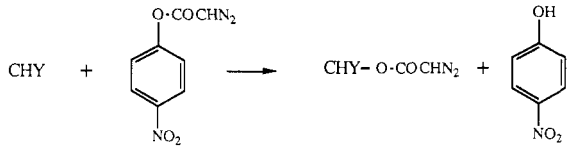
0022-3263/90/1955-2034$02.50/0

Table I. Photolysis of Azides 7a–13a in Toluene

azide 7a–13a	absolute % yield of products: aniline 7b–13b	insert. 7c–13c	subst. 7d–13d	azo 7e–13e	T (°C)
	15	2	Trace	27	15
	28	49	2	4	-196
	18	5	Trace	23	15
	11	42	5	3	-196
	13	Trace	Trace	18	15
	8	26	Trace	12	-196
	11	3	3	4	15
	9	45	8	0	-196
	10	2	2	8	15
	6	38	4	0	-196
	13	18	27	3	15
	5	68	7	Trace	-196
	Trace	28	12	Trace	15
	3	42	8	Trace	-196

the chances of achieving a successful PAL experiment depend critically upon the nature and absolute reactivity of the reactive intermediate produced from an aryl azide labeling reagent.

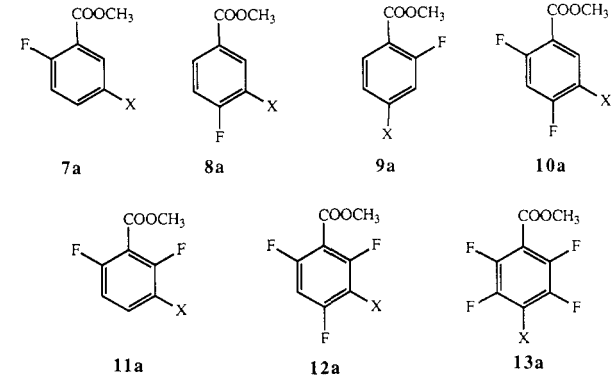
Photoaffinity labeling was introduced by Westheimer and co-workers.[10] α-Chymotrypsin (CHY) was covalently modified at serine-195 to produce a light-sensitive diazo ester that was subsequently photolyzed. In this historic



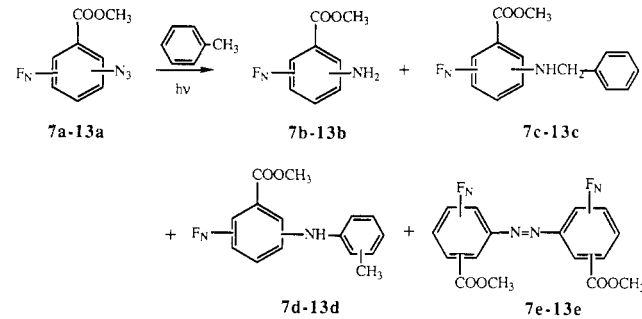
experiment Westheimer and co-workers were able to discover the presence of specific amino acid residues present in the binding site of the enzyme. In the ensuing 25 years the structure and mechanism of action of this enzyme have been studied in great detail.[11] For this and other reasons, including its ready accessibility and ease of covalent modification with labile esters, α-chymotrypsin is an ideal target enzyme around which one can design and test new azide labeling reagents.[12] Herein we are pleased to report that photolysis of polyfluorinated methyl benzoates produces reactive intermediates capable of reacting with a wider variety of functional groups than their nonfluorinated counterparts and that these reagents may have utility in the photoaffinity labeling of α-chymotrypsin and other enzymes. Fluorine appears to be a particularly beneficial substituent for PAL work because in addition to its enhancement of desirable reaction pathways,[13] it is a relatively small substituent[14] that should not interfere with substrate binding, and it also provides another analytical probe, ^{19}F NMR spectroscopy, with which to study the labeling process.[15]

Results and Discussion

The following fluorinated azides **7a–13a** have been synthesized, where X = N_3. The synthesis of these azides begins with the commercially available, fluorinated benzoic acids. The acids are esterified, nitrated, reduced to anilines, and converted to azides via standard procedures.



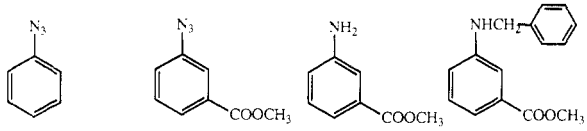
Photolysis in Toluene. There are scattered reports in the literature suggesting coupling reactions between electron-deficient nitrenes and electron-rich aromatics.[13,16] Azides **7a–13a** were separately photolyzed (320 < λ < 380 nm) in toluene solution (15 °C) and in frozen polycrystalline toluene (−196 °C). The products included anilines **7b–13b**, benzylic insertion adducts **7c–13c**, aromatic substitution products **7d–13d**, and azo compounds **7e–13e**.



The results are given in Table I. Several trends are apparent. First a small amount of aniline and azo dimer is present in nearly all of the samples examined. Some intractable tar is also formed in these photolyses. At 15 °C the yields of benzylic insertion and aromatic substitution adducts, the desired products in a PAL experiment, are quite variable. Painfully low total yields of adducts

(10) Singh, A.; Thornton, E. R.; Westheimer, F. H. *J. Biol. Chem.* **1962**, *237*, 3006.
(11) Walsh, C. *Enzymatic Reaction Mechanisms*; W. H. Freeman: San Francisco, 1979; Chapter 3, p 53.
(12) Kanakarajan, K.; Goodrich, R.; Young, M. J. T.; Soundararajan, S.; Platz, M. S. *J. Am. Chem. Soc.* **1988**, *110*, 6536.
(13) (a) Abramovitch, R. A.; Challand, S. R.; Scriven, E. F. V. *J. Am. Chem. Soc.* **1972**, *94*, 1374. (b) Abramovitch, R. A.; Scriven, E. F. V. *Chem. Commun.* **1970**, 787. (c) Abramovitch, R. A.; Challand, S. R.; Scriven, E. F. V. *J. Org. Chem.* **1972**, *37*, 2705. (d) Banks, R. E.; Madany, I. M. *J. Fluorine Chem.* **1985**, *30*, 211. (e) Banks, R. E.; Prakash, A. *Tetrahedron Lett.* **1973**, *14*, 99; *J. Chem. Soc., Perkin Trans. I* **1974**, 1365. (f) Banks, R. E.; Sparkes, G. E. *J. Chem. Soc., Perkin Trans. I* **1972**, 2964. (g) Young, M. J. T.; Platz, M. *Tetrahedron Lett.* **1989**, *30*, 2199.
(14) The atomic radii in covalent bonds for H and F are 0.37 and 0.72 Å, respectively: Gordon, A. J.; Ford, R. A. *Chemists Companion*; Wiley: New York, 1972; pp 82–85.
(15) (a) Berliner, L. J.; Landis, B. H. *Nuclear Magnetic Resonance Spectroscopy in Molecular Biology*; Pullman, B., Ed.; D. Reidel Publishing: Dordrecht, Holland, 1978, p 311. (b) Landis, B. H.; Berliner, L. J. *J. Am. Chem. Soc.* **1980**, *102*, 5350, 5354.
(16) (a) Leyva, E.; Young, M. J. T.; Platz, M. S. *J. Am. Chem. Soc.* **1986**, *108*, 8307. (b) Torres, M. J.; Zayas, J.; Platz, M. S. *Tetrahedron Lett.* **1986**, *27*, 791. (c) Young, M. J. T.; Ph.D. The Ohio State University, 1988.

(trace–6%) are formed from the monofluorinated and difluorinated azido esters. However, moderate total yields of toluene adducts are observed in the trifluorinated (45%) and tetrafluorinated (40%) azido ester systems. An increase in fluorine content leads to an increase in the yields of adducts realized in toluene solution. This suggests that azides **12a** and **13a** might be useful in photoaffinity labeling of enzyme active sites containing tyrosine, tryptophan, phenylalanine, and perhaps histidine residues. For the sake of comparison photolysis of phenyl azide (**1**) and methyl *m*-azidobenzoate (**14a**) in toluene solution produces



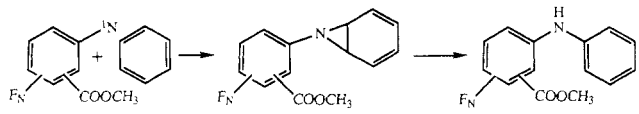
1 **14a** **14b** **14c**

no detectible yields of benzylic insertion product (e.g. **14c**). In the case of **14a** the only detectible product formed in toluene is **14b** and the total material balance is only 0.2%. Young[16] has observed a 52% yield of adducts with toluene upon photolysis of pentafluorophenyl azide.

Strikingly different results are obtained upon photolysis of azides **7a–13a** in frozen polycrystalline toluene at −196 °C. Under these conditions photolysis leads to rather clean yields of benzylic insertion products **7c–13c** and in yields as high as 68%! This suggests that very low temperature photolysis of aryl azides will lead to an increased efficiency of PAL in those cases where the target biomolecule can withstand a freeze–thaw cycle.[12]

The data of Table I can be understood within the context of Scheme I. Photolyses of **7a–13a** lead to extrusion of nitrogen and a singlet nitrene (^{1}**7f–^{1}13f**). The singlet nitrene can either formally insert into a benzylic or aromatic C–H bond or ring expand to a ketenimine. The evidence for ketenimines **7g–13g** will be presented later in connection with the discussion of the photochemistry of these azides in diethylamine. It is not clear whether the ketenimines can revert to single nitrenes (^{1}**7f–^{1}13f**). It is assumed that these substituted ketenimines polymerize to form tars in the absence of a nucleophile as per parent ketenimine **3**.

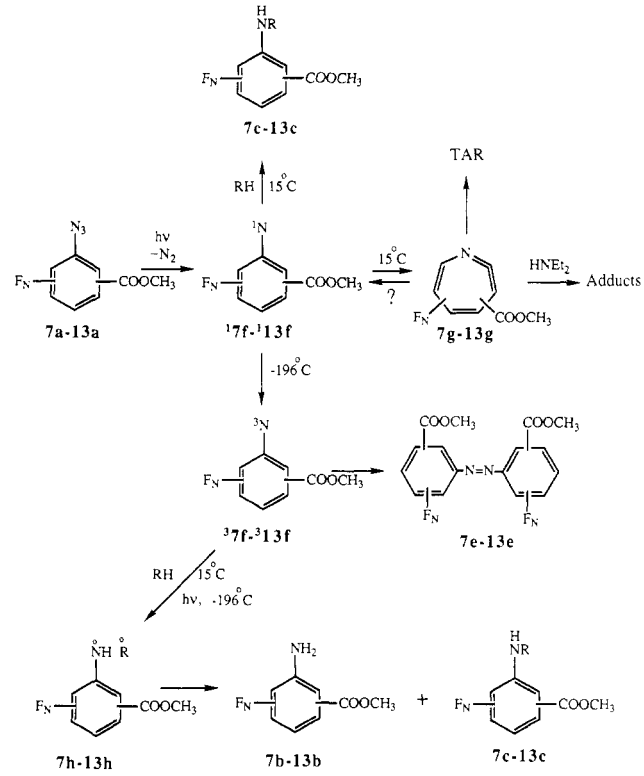
The net insertion of the fluorinated singlet nitrene esters into an aromatic CH bond is assumed to be a multistep process as shown below.[2,15]



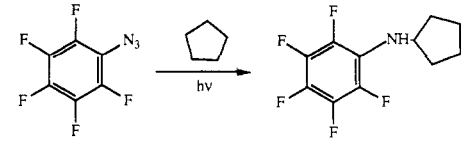
The simplest explanation of the fluorine effect on the product distribution is to associate it with a change in the partitioning of the singlet nitrene between intramolecular ring expansion and intermolecular capture. The effect of increasing fluorine substitution is consistent with an increase in the rate of adduct formation relative to ring expansion. However, it is not clear whether fluorine accelerates external trapping of the nitrene or whether it retards the rate of ring expansion, although the latter explanation is implied by the lack of ring expansion in the chemistry of singlet (pentafluorophenyl)nitrene.[16,17]

The low temperature effect on the photochemistry of aryl azides has been observed previously.[11,15] Photolysis of the azides at −196 °C again leads to fragmentation to molecular nitrogen and a singlet nitrene, but at this temperature the major decay channel of the singlet nitrene is intersystem crossing to form the triplet nitrene. In a frozen toluene polycrystal diffusion is limited and the triplet nitrene may be indefinitely stable. Under these conditions the triplet nitrene (^{3}**7f–^{3}13f**) may accumulate and as a consequence undergo photochemistry. Photolysis of triplet nitrenes (^{3}**7f–^{3}13f**) promotes hydrogen atom abstraction from the matrix to produce an anilino–benzyl type of radical pair **7h–13h**. Collapse of the radical pair accounts for prevalence of benzylic insertion products formed upon low temperature photolysis of the azides.[12,16]

Scheme I



Photolysis in Cyclopentane. Photolysis of azides **7a–13a** in cyclopentane was uniformly disappointing. Intractable tars were formed to the exclusion of volatile products in every case in a manner reminiscent of parent phenyl azide. By contrast photolysis of pentafluorophenyl azide (**15**) in cyclopentane produces the CH insertion adduct **16** in nearly 30% yield.[16]



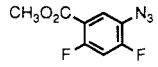
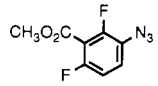
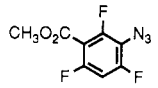
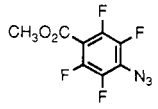
15 **16**

Even the expedient of photolyzing **7a–13a** in frozen cyclopentane at −196 °C failed to produce the hoped-for CH insertion adducts. This is probably a consequence of the opaque nature of frozen cyclopentane that prevents the light from penetrating the sample and exciting the azides and triplet nitrenes. This conclusion was reached in our previous study of **15**, which gives negligible yields of **16** upon photolysis in cyclopentane at −196 °C but high yields of C–H insertion adducts when the photochemistry is performed in 3-methylpentane, which forms a transparent glass at −196 °C.[16]

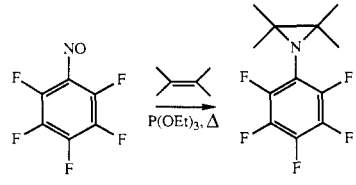
Photolysis in Tetramethylethylene. The addition of a carbene to an olefin to form a cyclopropane is widely utilized.[18] The corresponding reaction of a nitrene and

(17) Personal communiation from Professor G. B. Schuster.

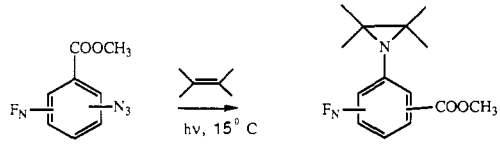
Table II. Photolysis of Azides 10a–13a in TME at 15 °C

azide 10a–13a	absolute % yield of products: aniline 10b–13b	aziridine 10i–13i	azo 10e–13e
	19	38	27
	12	39	32
	9	43	Trace
	7	47	Trace

an olefin to form an aziridine is very much less well documented. The only report of this reaction for an arylnitrene that we are aware of is due to Abramovitch[19] and co-workers, who deoxygenated pentafluoronitrosobenzene in the presence of olefins.

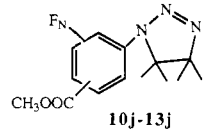


The distribution of products formed on photolysis of azides **10a–13a** in TME is given in Table II. Photolysis of the monofluorinated azido esters gave intractable product mixtures. However, photolysis of the di-, tri-, and tetrafluorinated azido esters in TME results in moderate yields of the corresponding aziridines (**10i–13i**) in addition to anilines (**10b–13b**) and azo dimers (**10e–13e**).



10a-13a **10i-13i**

We believe that these reactions proceed through nitrene species rather than through the intermediacy of 1,2,3-triazolines **7j–13j**. as the azides and TME can be stirred



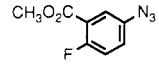
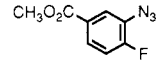
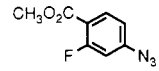
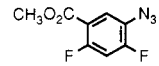
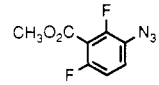
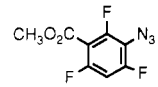
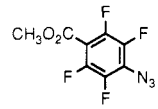
10j-13j

for prolonged periods at 15 °C without any evidence of reaction.

(18) For a review, see: Moss, R. A. In *Carbenes*, Vol. 1; Moss, R. A., Jones, M. Jr., Eds.; Wiley: New York, 1973; p 153.

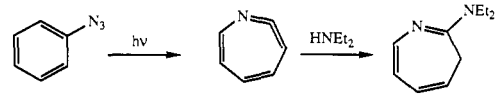
(19) (a) Abramovitch, R. A.; Azogu, C. I.; Sutherland, R. G. *Chem. Commun.* **1971**, 134. (b) Abramovitch, R. A.; Bailey, T. D.; Uma, V. *J. Org. Chem.* **1975**, *40*, 1541. (c) Abramovitch, R. A.; Challand, S. R.; Scriven, E. F. V. *J. Org. Chem.* **1974**, *39*, 340.

Table III. Product Distribution in the Photolysis of Azides 7a–13a in Diethylamine at 15 °C

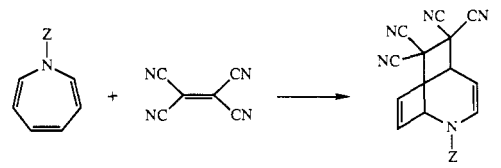
azide 7a–13a	aniline 7b–13b	azepine 7l–13l	azepine 7m–13m	hydrazine 7n–13n
	18.0	6.0	6.0	7.0
	11.0	---	---	8.0
	3.0	2.7	6.3	---
	10.0	12.0	---	Trace
	9.0	4.0	3.0	---
	18.0	---	---	58.0
	17.0	---	---	62.0

Photolysis in Diethylamine. Photolysis of azides **7a–13a** in neat diethylamine leads to complex results (Table III). Four types of reaction products are generally detected in addition to tar. Typically, one of the reaction products is diethylammonium fluoride, which precipitates out of the reaction mixture during the course of photolysis. A second type of product formed in 4.3–35.0% yield was the anilines **7b–13b**. By gas chromatography–mass spectroscopy it was possible to detect additional products formed in the photolysis of azides **7a–13a** in neat diethylamine. These products had masses corresponding to the appropriate nitrene (or ketenimine) plus diethylamine, or a mass of the nitrene plus 2 equiv of diethylamine minus a fluorine atom. The second product would appear to be derived from reaction of diethylamine with an adduct between nitrene **7f–13f** (or ketenimine **7g–13g**) with diethylamine. Unfortunately the adducts formed in neat diethylamine defied all our attempts at their isolation.

Doering and Odum discovered that photolysis of phenyl azide in diethylamine leads to ring expansion and the formation of a 3*H*-azepine. This is a reasonable possibility



for the photochemistry of fluorinated azides **7a–13a.** Previous workers[20] have found that 1*H*-azepines react with tetracycloethylene in Diels–Alder fashion. Thus tetra-

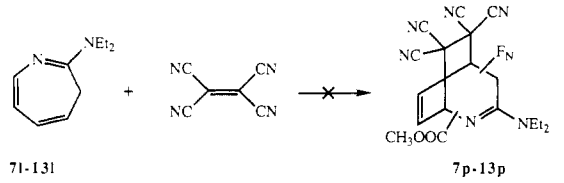


Z= $COOCH_2CH_3$, C_6F_5, CH_3SO_2

cyanoethylene was added to solutions of previously pho-

(20) (a) Baldwin, J. E.; Smith, R. A. *J. Am. Chem. Soc.* **1965**, *87*, 4819. (b) Abramovitch, R. A.; Challand, S. R.; Scriven, E. F. V. *J. Am. Chem. Soc.* **1972**, *94*, 1347.

tolyzed azides **7a–13a** in an attempt to trap and isolate the putative 3*H*-azepines **7l–13l** as stable Diels–Alder adducts **7p–13p**. Unfortunately, no such adducts were produced.

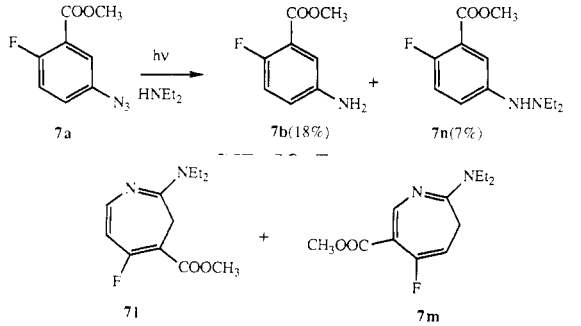


7l-13l **7p-13p**

All the successful examples cited earlier involve 1*H*-azepines with an electron-withdrawing group on nitrogen, which are quite unlike the 3*H*-azepines of this work (vide infra).

Better results were obtained upon photolysis (3200 < λ > 3700 Å) of azides **7a–13a** in 9:1 hexane/tetrahydrofuran containing 0.1 M diethylamine. This solvent combination was employed as some of the azides were not completely soluble in *n*-hexane. Under these conditions it was possible to isolate and characterize the azepine products. The yields were rather low, perhaps due to the relatively low concentration of the amine, but these conditions minimized secondary reactions of the adducts with the nucleophilic trapping agent.

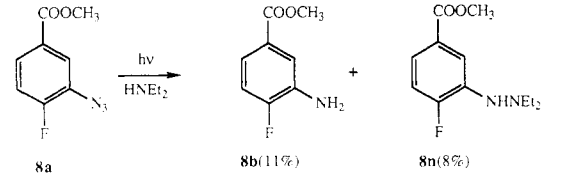
Photolysis of **7a** in 9:1 hexane/tetrahydrofuran containing 0.1 M diethylamine produces four products. The two azepine adducts **7l** and **7m** were formed as a 1:1 mixture in a total yield of 12%.



7a **7b(18%)** **7n(7%)**

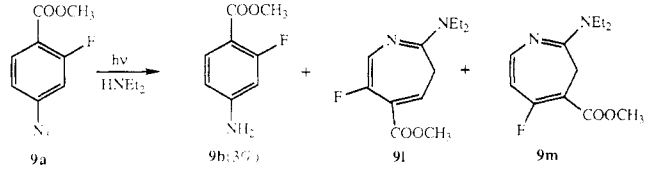
7l **7m**

Photolysis of **8a** produced only two isolable products, one of which is the hydrazide **8n**.



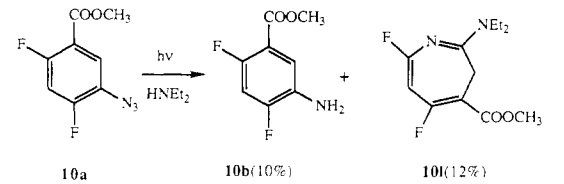
8a **8b(11%)** **8n(8%)**

By way of contrast, photolysis of isomeric monofluorinated azide **9a** leads to azepine rather than the hydrazide. The azepines **9l** and **9m** were formed in a total yield of 9% in a 5:12 mixture.



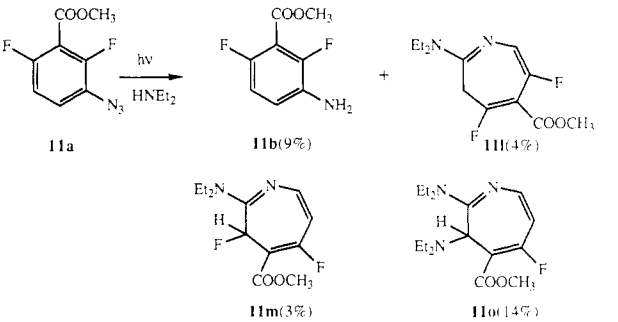
9a **9b(3%)** **9l** **9m**

Photolysis of difluorinated azide **10a** produces traces of hydrazide **10n** and a 12% yield of azepine **10l**.



10a **10b(10%)** **10l(12%)**

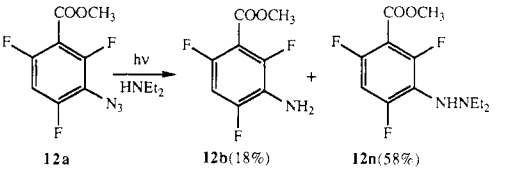
Similar results were obtained with difluorinated azide **11a**, although in this system an allylic fluorine in the azepine adduct has been displaced by diethylamine.



11a **11b(9%)** **11l(4%)**

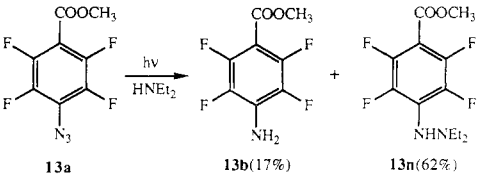
11m(3%) **11o(14%)**

Azepine products are not observed upon photolysis of trifluorinated azide **12a**, although a substantial yield of hydrazide has now been realized.



12a **12b(18%)** **12n(58%)**

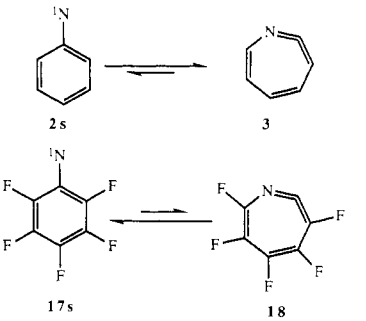
A very good yield of hydrazide was obtained upon photolysis of the tetrafluorinated azide **13a**.



13a **13b(17%)** **13n(62%)**

Two trends are apparent from this series. With mono- and difluorinated azido esters the azepine adducts are produced whereas with tri- and tetrafluorinated azides only hydrazides are formed. It is also clear that the yields of the adducts formed with diethylamine increases with the number of fluorine substituents.

These results can be interpreted with the aid of Scheme II and the assumption that singlet arylnitrenes and ketenimines can equilibrate. The literature suggests that in

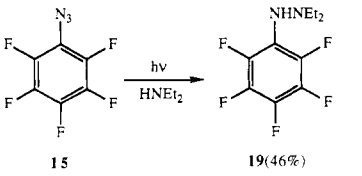


2s **3**

17s **18**

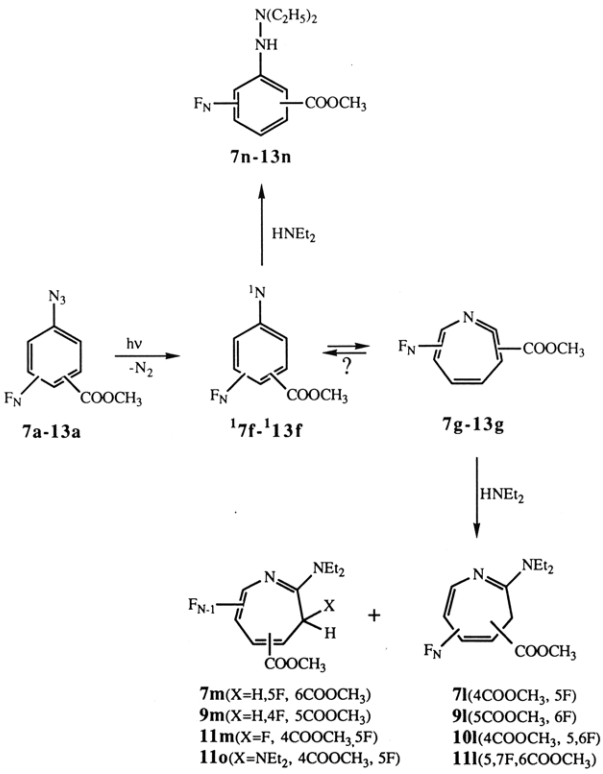
the parent system the equilibrium lies completely on the side of **3** at 20 °C as singlet phenylnitrene has never been intercepted at this temperature.

Young has found that photolysis of **15** in neat diethylamine produces hydrazine **19** in 46% yield. Similar results were obtained in dilute solutions of the amine.



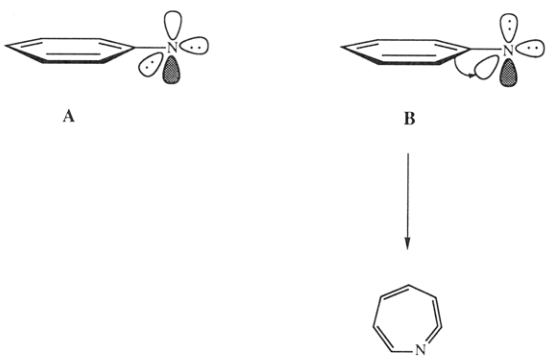
15 **19(46%)**

Scheme II



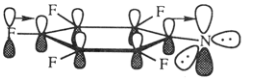
Thus in this system it appears that **17s** is greatly preferred to **18** at equilibrium. The photochemistry of the trifluorinated azide **12a** and the tetrafluorinated azide **13a** clearly resemble the pentafluorinated azide **15**, whereas the mono- and difluorinated azides in diethylamine more closely approximate that of phenyl azide itself.

How does fluorine effect the rate of interconversion between singlet nitrene and ketenimine? A simple view of the MO structure of singlet phenylnitrene is shown below. There will be filled orbital on nitrogen that is



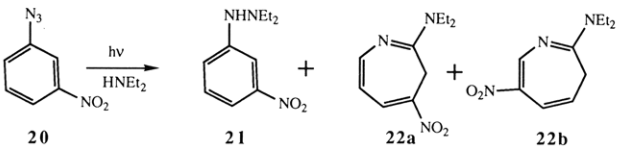
colinear with the C–N bond and two orbitals on nitrogen that are orthogonal to the C–N bond. One orthogonal orbital can interact with the π-system of the benzene ring, one orbital cannot. There are two closed shell singlet configurations corresponding to whether or not the orbital that can conjugate with the ring is populated (forms A and B). We speculate that it is form B in which the unoccupied orbital is in the plane of the phenyl ring that is prone to ring expansion. Undoubtedly forms A and B will mix; thus the rate of the singlet nitrene to ketenimine rearrangement will depend upon the extent of form B character in the singlet nitrene as well as the thermodynamics of the rearrangement.

Placement of five fluorine substituents on the ring introduces five π-donating, σ-withdrawing groups. π-donation of the fluorine substituent will greatly stabilize form A, the configuration less likely to rearrange. This will slow



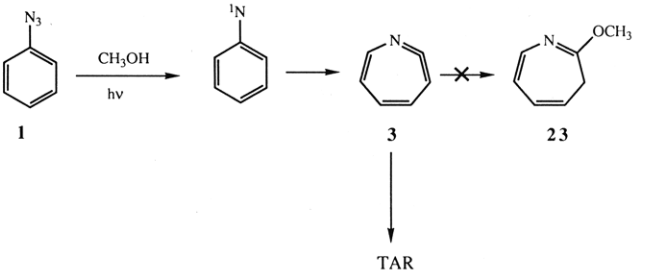
down the rate of singlet nitrene rearrangement regardless of the thermodynamic effect of fluorine on this process.

The production of two distinct reactive intermediates from a single aryl azide is rather common. In fact Schuster and Liang[21] have found that both azepine and hydrazine types of adducts are formed upon photolysis of 3-nitrophenyl azide in diethylamine. The ratio of nitrene-derived

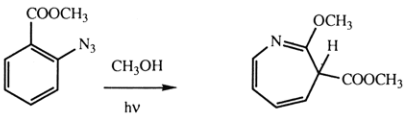


adduct **21** to ketenimine-derived adducts **22a,b** was a function of the concentration of diethylamine. Schuster and Liang[21] have concluded that the *m*-nitro-substituted singlet phenylnitrene and ketenimines are interconverting species. The most relevant conclusion for photoaffinity labeling of this work is that the presence of two or less fluorine substituents on the aromatic ring does not prevent ring expansion and subsequent nucleophilic addition of amines to form 3*H*-azepines.

Photolysis in Methanol. Upon photolysis of phenyl azide (**1**) in methanol the major product obtained is polymeric tar.[2] A 2-methoxy-3*H*-azepine compound (e.g. **23**) is not formed. Apparently methanol is not sufficiently nucleophilic to intercept ketenimine **3**.



However, Suschitzky has found that several ortho-substituted phenyl azide derivatives do indeed yield adducts upon photolysis in methanol.[22] Accordingly azides **7a–13a**



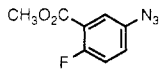
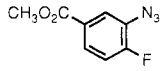
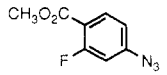
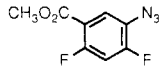
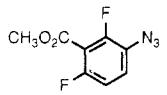
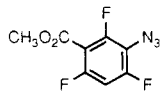
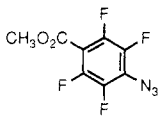
were photolyzed in neat methanol in an attempt to prepare the corresponding azepines. However, as shown in Table IV there was no trace of a 2-methoxy-3*H*-azepine formed in the photolysis of the fluorinated azidobenzoates. The material balances in these reactions ranged from 30% to 67% and consisted of the corresponding anilines and azo compounds. The implication for photoaffinity labeling is

(21) (a) Schuster, G. B.; Liang, T.-y. *Tetrahedron Lett.* **1986**, *27*, 3325. (b) Liang, T.-Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1987**, *105*, 7803.

(22) Purvis, R.; Smalley, R. K.; Strachan, W. A.; Suschitzky, H. *J. Chem. Soc., Perkin Trans. 1* **1978**, 191.

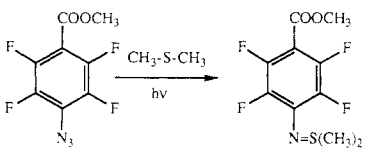
(23) (a) Benati, L.; Montevecchi, P. C.; Spagnola, P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 625. (b) Benati, L.; Montevecchi, P. C.; Spagnola, P. *J. Chem. Soc., Perkin Trans. 1* **1983**, 771.

Table IV. Photolysis of Azides 7a–13a in Methanol at 15 °C

azide 7a–13a	absolute % yield of products: aniline 7b–13b	azo 7e–13e
	38.0	6.0
	5.0	47.0
	30.0	--
	4.0	63.0
	Traces	57.0
	5.0	43.0 (Two isomers)
	23.0	29.0 (Two isomers)

that these azides will not generate species which will rapidly be consumed by aqueous solvent. This may increase the likelihood of reaction of the photogenerated intermediates with a nearby amino acid residue. These results also demonstrate that there is little likelihood that these azides will generate intermediates capable of labeling hydroxylic amino acids such as serine.

Photolysis in Dimethyl Sulfide and Dimethyl Disulfide. Dimethyl sulfide and dimethyl sulfoxide have been reported to scavenge nitrenes to produce sulfenamines and sulfoximines.[24] However, of the seven azides of this study, only tetrafluoroazidobenzoate **13a** produces isolable sulfenamine derivative **13o** upon photolysis in dimethyl sulfide. This implies that derivatives of **13a**

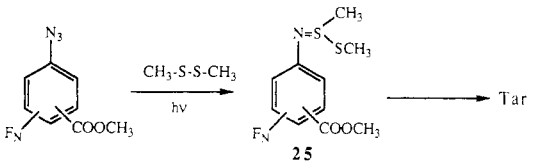


13a **13o**

might be useful in labeling methionine residues in a photoaffinity labeling experiment. The other azides produce mainly tar and traces of anilines and azo compounds upon photolysis in dimethyl sulfide.

Photolysis of azides **7a–13a** in dimethyl disulfide does not lead to the formation of adducts. The major products are tars, although trace amounts of anilines can be detected. Similar results are obtained with pentafluorophenyl azide (**15**). We speculate that photolysis of azides **7a–13a** leads to singlet nitrene formation and subsequent capture to form an ylide (**26**), which is unstable to further reaction. Thus these reagents will not be useful in labeling cystine residues.

(24) Valkanas, G.; Hopff, H. *J. Chem. Soc.* **1963**, 1925.



25

Conclusions

Seven fluorinated azide derivatives of methyl benzoate have been synthesized and evaluated as potential photoaffinity labeling reagents. Photolysis of the fluorinated azides produces intermediates that form adducts with a wider variety of functional groups than in the case of phenyl azide. Photolysis of these azides produces both nitrene- and ketenimine-reactive intermediates. The nitrene intermediates gave stable adducts with toluene, diethylamine, and tetramethylethylene and in one case with dimethyl sulfide. The ketenimine intermediates could be trapped with diethylamine to form azepines. Adduct formation was not observed in cyclopentane, methanol, or dimethyl disulfide.

Experimental Section

General. Melting points are uncorrected and were recorded on an Electrothermal apparatus; infrared spectra were obtained on a Beckman IR 4250 spectrophotometer and UV spectra on a Perkin-Elmer Lambda 3B UV/VIS spectrophotometer; high resolution mass spectra were obtained with a VG, 70-250 S (or Kratos MS-30) mass spectrometer and gas chromatograph/mass spectra on a Finigan 4021 GC/MS instrument. Elemental analyses were performed by M-H-W Laboratories. Gas chromatographic (GC) analyses were performed on a Perkin-Elmer 8500 gas chromatograph fitted with 5% DB1701 column (30 m × 0.254 mm). ^1H NMR ($CDCl_3$) and ^{19}F NMR ($CDCl_3$) spectra were recorded on a Bruker AM-250 spectrometer. ^1H NMR spectra are reported in ppm from internal standard tetramethylsilane (TMS) on the δ scale with splitting patterns, coupling constants, and relative integrated areas. The letter designates the multiplicity of the signal: s, singlet; bs, broad singlet; d, doublet; dd, doublet of doublet; t, triplet, q, quartet; m, multiplet. ^{19}F NMR chemical shifts are from the proton-decoupled spectra and are reported in ppm relative to internal hexafluorobenzene (-162.9 relative to $CFCl_3$ = 0).

The solvents and reagents used were dried and purified prior to use. Benzene, toluene, and tetrahydrofuran were distilled from sodium metal and benzophenone; methanol and ethanol were distilled from their corresponding magnesium alkoxides. Column chromatography was performed, depending on the nature of the compound to be purified, over either Brockman activity 1 basic or neutral (80–200 mesh) alumina. Preparative thin layer chromatography was performed on EM Laboratories 0.5-mm thick precoated silica gel 60 F-254 plates. All photolyses were performed with a Rayonet RPR reactor 3500 lamp source. This lamp has emission between 3200 and 3700 Å with maximum intensity at 3650 Å. The samples were irradiated through Pyrex tubes.

Methyl Fluoronitrobenzoates. 2-Fluoro-, 4-fluoro-, 2,4-difluoro-, and 2,6-difluorobenzoic acids were commercially available (Aldrich). 2-Fluoro-4-nitrobenzoic acid was prepared by the oxidation of 2-fluoro-4-nitrotoluene using dilute nitric acid following the literature procedure.[24] 2,4,6-Trifluorobenzoic acid was synthesized from 1,3,5-trifluorobenzene by lithiation with *n*-butyllithium followed by carbonation using CO_2. The fluorobenzoic acids were converted into the corresponding methyl esters by treatment with thionyl chloride followed by methanolysis of the acid chlorides. The methyl esters were nitrated by using a mixture of concentrated sulfuric and fuming nitric acid mixtures at appropriate temperatures specified under each compound.

Methyl 6-fluoro-3-nitrobenzoate: colorless crystalline solid; mp 48–49 °C; yield 78% (from 2-fluorobenzoic acid by nitration of the methyl ester at 25–30 °C); ^1H NMR δ 3.99 (s, 3 H, ester CH_3), 7.29–7.36 (m, 1 H, aromatic H), 8.36–8.44 (m, 1 H, aromatic H), 8.82–8.86 (m, 1 H, aromatic H); ^{19}F NMR -99.58 (s, 1 F); IR ($CHCl_3$) 1720, 1630, 1585, 1350, and 1120 cm^{-1}; exact mass calcd

for $C_8H_6FNO_4$ *m/e* 199.0281, found 199.0290, major fragments 199 (M^+), 168, 152, 138, 122, 110, 94, and 69. Anal. Calcd for $C_8H_6FNO_4$: C, 48.23; H, 3.04; N, 7.04; F, 9.55. Found: C, 48.27; H, 3.24; N, 6.91.

Methyl 4-fluoro-3-nitrobenzoate: colorless crystalline solid; mp 58–59 °C; yield 69% (from 4-fluorobenzoic acid by nitration of the methyl ester at 0 °C); ^1H NMR δ 3.92 (s, 3 H, ester CH_3), 7.35–7.43 (m, 1 H, aromatic H), 8.71–8.75 (m, 1 H, aromatic H); ^{19}F NMR −111.78 (s, 1 F); IR ($CHCl_3$) 1710, 1595, 1340, 1100, 960, and 840 cm^{-1}; exact mass calcd for $C_8H_6FNO_4$ *m/e* 199.0281, found 199.0280, major fragments 199 (M^+), 168, 153, 138, 122, 94, and 50. Anal. Calcd for $C_8H_6FNO_4$: C, 48.23; H, 3.04; N, 7.04. Found: C, 48.28; H, 3.18; N, 7.08.

Methyl 2-fluoro-4-nitrobenzoate: colorless crystalline solid; mp 69–70 °C; yield 92% (from 2-fluoro-4-nitrotoluene, by oxidation with dilute nitric acid followed by esterification using methanol); ^1H NMR δ 3.99 (s, 3 H, ester CH_3), 8.00–8.17 (m, 3 H, aromatic protons); ^{19}F NMR −105.58 (s, 1 F); IR ($CDCl_3$) 1680, 1570, 1470, 1310, 1230, 1070, and 940 cm^{-1}; exact mass calcd for $C_8H_6FNO_4$ *m/e* 199.0281, found 199.0350, major fragments 199 (M^+), 182, 168, 152, 138, 122, 110, 94, 74, and 69. Anal. Calcd for $C_8H_6FNO_4$: C, 48.23; H, 3.04; N, 7.04. Found: C, 48.28; H, 3.18; N, 7.08.

Methyl 4,6-difluoro-3-nitrobenzoate: colorless crystalline solid; mp 74–75 °C; yield 82% (from 2,4-difluorobenzoic acid by the nitration of the methyl ester at 0–5 °C); ^1H NMR δ 3.98 (s, 3 H, ester CH_3), 7.15 (t, J = 5.0 Hz, 1 H, aromatic C-5 H), 8.77 (dd, J = 7.3, 7.2 Hz, 1 H, aromatic C-2 H); ^{19}F NMR −94.34 (d, J = 20.75 Hz, 1 F), −105.48 (d, J = 20.75 Hz, 1 F); IR ($CHCl_3$) 1720, 1625, 1595, 1350, 1130, and 860 cm^{-1}; exact mass calcd for $C_8H_5F_2NO_4$ *m/e* 217.0186, found 217.0184, major fragments 217 (M^+), 186, 171, 156, 140, 128, 112, 100, 81, and 62. Anal. Calcd for $C_8H_5F_2NO_4$: C, 44.24; H, 2.32; N, 6.45. Found: C, 44.21; H, 2.26; N, 6.44.

Methyl 2,6-difluoro-3-nitrobenzoate: colorless crystalline solid; mp 56–57 °C (lit.[24] mp 55–56 °C); yield 82% (from 2,6-difluorobenzoic acid by nitration of the methyl ester at 0–5 °C); ^1H NMR δ 4.01 (s, 3 H, ester CH_3), 7.10–7.18 (m, 1 H, aromatic H), 8.19–8.28 (m, 1 H, aromatic H); ^{19}F NMR −99.44 (d, J = 10.5 Hz, 1 F), −113.91 (d, J = 10.5 Hz, 1 F); IR ($CHCl_3$) 1740, 1620, 1600, 1350, 1130, and 960 cm^{-1}; exact mass calcd for $C_8H_5F_2NO_4$ *m/e* 217.0186, found 217.0193, major fragments 217 (M^+), 198, 186, 172, 156, 140, 128, 112, 81, and 62.

Methyl 2,4,6-trifluoro-3-nitrobenzoate: colorless crystalline solid; mp 57–59 °C; yield 77% (from 2,4,6-trifluorobenzoic acid by nitration of the methyl ester at 0–5 °C); ^1H NMR δ 3.99 (s, 3 H, ester CH_3), 6.93–7.01 (m, 1 H, aromatic C-5 H); ^{19}F NMR −99.2 (dd, J = 5.50, 5.75 Hz, 1 F), −111.33 (d, J = 11.5 Hz, 1 F), −115.09 (d, J = 6.5 Hz, 1 F); IR ($CHCl_3$) 1740, 1630, 1600, 1540, 1430, 1350, 1275, 1140, 1065, and 970 cm^{-1}; exact mass calcd for $C_8H_4F_3NO_4$ *m/e* 235.0092, found 235.0097, major fragments at 235 (M^+), 219, 201, 190, 174, 158, 146, 170, 118, 80, and 69. Anal. Calcd for $C_8H_4F_3NO_4$: C, 40.85; H, 1.72; N, 5.96. Found: C, 40.69; H, 1.65; N, 5.92.

Methyl Aminofluorobenzoates. General Procedure. The methyl fluoronitrobenzoates were reduced to the corresponding methyl aminobenzoates by catalytic hydrogenation in methanol over 10% Pd/C using a Parr-hydrogenation apparatus operating at an outlet pressure of 20–30 psi. The amines were recovered after filtering off the catalyst through Celite followed by purification by column chromatography over basic alumina in benzene.

Methyl 3-amino-6-fluorobenzoate (7b): colorless crystalline solid; mp 87–88 °C (lit.[25] mp 85–87 °C, lig.[26] mp 86 °C); yield 97%; ^1H NMR δ 3.67 (bs, 2 H, amine H), 3.89 (s, 3 H, ester CH_3), 6.75–6.78 (m, 1 H, aromatic H), 6.79–6.88 (m, 1 H, aromatic H), 6.91–6.95 (m, 1 H, aromatic H); ^{19}F NMR −124.81 (s, 1 F); IR ($CHCl_3$) 3360, 1695, 1620, 1070, and 980 cm^{-1}; exact mass calcd for $C_8H_8FNO_2$ *m/e* 169.0539, found 169.0520, major fragments 169 (M^+), 138, 110, 83, 63, and 57.

Methyl 3-amino-4-fluorobenzoate (8b): colorless crystalline solid; mp 69–70 °C; yield 89%; ^1H NMR δ 3.82 (bs, 2 H, amine H), 3.87 (s, 3 H, ester CH_3), 6.97–7.03 (m, 1 H, aromatic H), 7.37–7.43 (m, 1 H, aromatic H), 7.45–7.50 (m, 1 H, aromatic H); IR ($CHCl_3$) 3430, 3350, 1690, 1605, 1580, 1400, 1090, and 970 cm^{-1}; exact mass calcd for $C_8H_8FNO_2$ *m/e* 169.0539 found 169.0537, major fragments 169 (M^+), 138, 110, 90, 83, 69, and 57. Anal. Calcd for $C_8H_6FNO_2$: C, 56.79; H, 4.77; N, 8.28. Found: C, 56.71; H, 4.79; N, 8.40.

Methyl 4-amino-2-fluorobenzoate (9b): colorless crystalline solid; mp 108–110 °C; yield 86%; ^1H NMR δ 3.75 (s, 3 H, ester CH_3), 4.73 (bs, 2 H, amine H), 6.37–6.49 (m, 2 H, aromatic H), 7.61–7.68 (m, 1 H, aromatic H); ^{19}F NMR −109.20 (s, 1 F); IR ($CHCl_3$) 3500, 3420, 1710, 1620, 1425, 1200, 1110, and 955 cm^{-1}; exact mass calcd for $C_8H_8FNO_2$ *m/e* 169.0539, found 169.0551, major fragments 169 (M^+), 138, 110, 83, and 57. Anal. Calcd for $C_8H_6FNO_2$: C, 56.79; H, 4.77; N, 8.28. Found: C, 56.80; H, 4.80; N, 8.37.

Methyl 3-amino-4,6-difluorobenzoate (10b): colorless crystalline solid: mp 111–113 °C; yield 92%; ^1H NMR δ 3.71 (bs, 2 H, amine H), 3.89 (s, 3 H, ester CH_3), 6.82 (t, J = 10.39 Hz, 1 H, aromatic C-5 H), 7.35 (dd, J = 6.96, 6.95 Hz, 1 H, aromatic C-2 H); ^{19}F NMR −119.72 (d, J = 6.75 Hz, 1 F), −124.34 (d, J = 6.75 Hz, 1 F); IR ($CHCl_3$) 3480, 3400, 1720, 1600, 1420, 1310, and 1140 cm^{-1}; exact mass calcd for $C_8H_7F_2NO_2$ *m/e* 187.04488 found 187.0448, major fragments 187 (M^+), 156, 128, 101, 81, and 57. Anal. Calcd for $C_8H_7F_2NO_2$: C, 51.32; H, 3.77; N, 7.49. Found: C, 51.09; H, 3.86; N, 7.29.

Methyl 3-amino-2,6-difluorobenzoate (11b): dark brown oil; yield 92%; ^1H NMR δ 3.74 (bs, 2 H, amine H), 3.93 (s, 3 H, ester CH_3), 6.70–6.86 (m, 2 H, aromatic H); ^{19}F NMR −126.34 (d, J = 3.25 Hz, 1 F), −133.23 (d, J = 3.25 Hz, 1 F); IR (neat) 3480, 3400, 1735, 1630, 1500, 1470, and 1450 cm^{-1}; exact mass calcd for $C_8H_7F_2NO_2$ *m/e* 187.0448, found 187.0457, major fragments 187 (M^+), 156, 128, 108, 78, and 51.

Methyl 3-amino-2,4,6-trifluorobenzoate (12b): colorless crystalline solid; mp 40–41 °C; yield 87%; ^1H NMR δ 3.67 (bs, 2 H, amine H), 3.93 (s, 3 H, ester CH_3), 6.66–6.75 (m, 1 H, aromatic H); ^{19}F NMR −124.62 (m, 1 F), −125.65 (m, 1 F), −130.70 (m, 1 F); IR ($CHCl_3$) 3480, 3400, 1720, 1600, 1440, 1370, and 960 cm^{-1}; exact mass calcd for $C_8H_6F_3NO_2$ *m/e* 205.0350, found 205.0376, major fragments 205 (M^+), 186, 174, 168, 158, 146, 114, 86, and 55. Anal. Calcd for $C_8H_6F_3NO_2$: C, 46.82; H, 2.95; N, 6.83. Found: C, 46.66; H, 2.92; N, 6.88.

Methyl 4-Amino-2,3,5,6-tetrafluorobenzoate (13b). This compound was prepared from commercially available 4-amino-2,3,5,6-tetrafluorobenzoic acid by esterification according to a literature procedure.[27]

Methyl Azidofluorobenzoates 7a–13a. The methyl aminofluorobenzoates were converted into the corresponding azidofluorobenzoates **7a–13a** by using the following typical procedure. The purified aminofluorobenzoate (0.05 mol) was stirred in 25–50 mL of 50% hydrochloric acid. (In the case of the azides **12a** and **13a**, trifluoroacetic acid was used as solvent). The solution/suspension was cooled to 0 °C and a solution of sodium nitrite (0.065 mol) in 10 mL of water was added in drops over a period of 15 min with stirring. After 10 min of further stirring at 0–5 °C, a solution of sodium azide (0.075 mol) in 10 mL of water was added at such a rate that the temperature of the reaction mixture did not exceed 15 °C toward the end of addition. The azides that are solids precipitated after 10–15 min of stirring. The solid was filtered, washed with ice water, and purified by chromatography over neutral alumina. In case of azides that are oils, the reaction mixture was extracted into methylene chloride three times (3 × 25 mL) and the combined extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure. The residue was purified by chromatography over neutral alumina in benzene.

Methyl 3-azido-6-fluorobenzoate (7a): pale yellow colored oil; yield 87%; ^1H NMR δ 3.93 (s, 3 H, ester CH_3), 7.10–7.18 (m, 2 H, aromatic H), 7.54–7.58 (m, 1 H, aromatic H); ^{19}F NMR −118.48 (s, 1 F); IR (neat) 2130, 1740, 1610, 1510, 1440, 1420, and 1330 cm^{-1}; UV (methanol) λ_{max} (ϵ) 206 (1.15×10^6), 222 (1.02×10^6), 247 (6.05×10^5); exact mass calcd for $C_8H_6FN_3O_2$ *m/e*

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195.0440, found 195.0423, major fragments 195 (M^+), 167, 152, 138, 124, 108, 96, 81, 69, and 59.

Methyl 3-azido-4-fluorobenzoate (8a): yellowish brown oil; yield 82%; ^1H NMR δ 3.90 (s, 3 H, ester CH_3), 7.07–7.17 (m, 1 H, aromatic H), 7.73–7.78 (m, 2 H, aromatic H); ^{19}F NMR −123.55 (s, 1 F); IR (neat) 2140, 1730, 1610, 1510, 1440, 1420, and 1380 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 207 (1.21×10^6), 223 (9.48×10^5), 249 (1.34×10^5); exact mass calcd for $C_8H_6FN_3O_2$ m/e 195.0443, found 195.0464, major fragments 195 (M^+), 167, 152, 138, 124. 108, 96, 81, 59, and 50.

Methyl 4-azido-2-fluorobenzoate (9a): colorless crystalline solid; mp 56–58 °C; yield 92%; ^1H NMR δ 3.92 (s, 3 H, ester CH_3), 6.75–6.88 (m, 2 H, aromatic H), 7.91–7.98 (m, 1 H, aromatic H); ^{19}F NMR −110.44 (δ, 1 F); IR ($CHCl_3$) 2120, 1610, 1570, 1420, 1280, 1125, 1110, 1075, 960, and 855 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 208 (1.02×10^6), 267 (1.57×10^6); exact mass calcd for $C_8H_6FN_3O_2$ m/e 195.04431, found 195.0459, major fragments 195 (M^+), 167, 135, 124, 108, 96, 81, 69, 58, and 50. Anal. Calcd for $C_8H_6FN_3O_2$: C, 49.22; H, 3.30; N, 21.54. Found: C, 49.46; H, 3.30; N, 21.76.

Methyl 3-azido-4,6-difluorobenzoate (10a): colorless crystalline solid; mp 48–50 °C; yield 87% ^1H NMR δ 3.93 (s, 3 H, ester CH_3), 6.96 (t, J = 10.22 Hz, 1 H, aromatic H), 7.68 (dd, J = 6.97, 6.99 Hz, 1 H, aromatic H); ^{19}F NMR −109.66 (d, J = 10.75 Hz, 1 F), −115.49 (d, J = 10.75 Hz, 1 F); IR ($CHCl_3$) 2140, 1720, 1600, 1410, 1330, 1190, and 960 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 208 (1.49×10^6), 222 (1.26×10^6), 247 (7.32×10^5); exact mass calcd for $C_8H_5F_2N_3O_2$ m/e 213.0349, found 213.0377, major fragments 213 (M^+), 185, 170, 156, 142, 126, 114, 100, 91, 75, and 59. Anal. Calcd for $C_8H_5F_2N_3O_2$: C, 45.06; H, 2.37; N, 19.72. Found: C, 45.07; H, 2.21; N, 19.97.

Methyl 3-azido-2,6-difluorobenzoate (11a): colorless crystalline solid; mp 62–64 °C; yield 80%; ^1H NMR δ 3.96 (s, 3 H, ester CH_3), 6.90–7.09 (m, 1 H, aromatic C-5 H), 7.10–7.27 (m, 1 H, aromatic C-4 H); ^{19}F NMR −118.71 (s, 1 F), −126.63 (s, 1 F); IR ($CHCl_3$) 2130, 1740, 1630, 1600, and 1340 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 204 (1.78×10^5), 243 (1.03×10^6), 290 (1.94×10^4); exact mass calcd for $C_8H_5F_2N_3O_2$ m/e 213.0350, found 213.0355, major fragments 213 (M^+), 1851, 170, 154, 142, 137, 126, 114, 102, 99, 75, 59, and 51. Anal. Calcd for $C_8H_5F_2N_3O_2$: C, 45.06; H, 2.37; N, 19.72. Found: C, 45.07; H, 2.21; N, 19.82.

Methyl 3-azido-2,4,6-trifluorobenzoate (12a): colorless crystalline solid; mp 42–43 °C; ^1H NMR δ 3.95 (s, 3 H ester CH_3), 6.75–6.84 (m, 1 H, aromatic H); ^{19}F NMR −115.99 (d, J = 6.5 Hz, 1 F), −118.99 (dd, J = 5.95, 5.95 Hz, 1 F), −123.26 (d, J = 10.02 Hz, 1 F); IR ($CHCl_3$) 21401, 1740, 1640, 1610, 1450, and 1320 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 206 (2.8×10^6), 243 (1.96×10^6); exact mass calcd for $C_8H_4F_3N_3O_2$ m/e 231.0256, found 231.0232, major fragments 231 (M^+) 203, 172, 160, 144, 132, 120, 100, 91, 82, 75, 68, 59. Anal. Calcd for $C_8H_4F_3N_3O_2$: C, 41.55; H, 1.74; N, 18.18. Found: C, 41.70; H, 1.81; N, 18.46.

Methyl 4-azido-2,3,5,6-tetrafluorobenzoate (13a): creamy white crystalline solid; mp 51–52 °C; yield 46%; ^1H NMR δ 3.96 (s, 3 H, ester CH_3); ^{19}F NMR −143.05 (m, 2 F), −155.32 (m, 2 F); IR ($CHCl_3$) 2120, 1740, 1410, 1330, 1000, 950, and 875 cm^{-1}; UV (MeOH) λ_{max} (ϵ) 199 (2.06×10^6), 261 (4.88×10^5); exact mass calcd for $C_8H_3F_4N_3O_2$ m/e 249.0161, found 249.0165, major fragments 249 (M^+), 221, 192, 163, 138, 124, 100, 81, and 59. Anal. Calcd for $C_8H_3F_4N_3O_2$: C, 38.55; H, 1.21; N, 16.87. Found: C, 38.49; H, 1.43; N, 16.82.

Product Analyses: Photolysis of the Azides 7a–13a in the Presence of Toluene, Cyclopentane, Tetramethylethylene, Methanol, and Dimethyl Sulfide. A solution of the azide ($(4.00–5.10) \times 10^{-5}$ mol) in 1.00 mL of the dry reagent (toluene, cyclopentane, tetramethylethylene, diethylamine, methanol or dimethyl sulfide) was sealed in a Pyrex tube (6 mm diameter) after 3 freeze–thaw cycles in a liquid nitrogen bath. Photolyses were performed in a thermostated bath maintained at 15 °C for 4 h and in a separate experiment, at liquid nitrogen temperature for 10 h using a battery of 350-nm bulbs in a Rayonet photochemical reactor. The photolysates from the 15 °C photolyses were analyzed immediately after photolysis and the ones from the liquid nitrogen temperature photolysis were kept in dark for 48 h and allowed to warm up to room temperature before analysis. Analyses of the products were performed by GC and peak identities were established by retention time and GC/MS comparisons with authentic samples.

General Method for the Preparation of Authentic Samples of the Methyl *N*-Benzylaminofluorobenzoates 7c–13c. A solution of a purified methyl aminofluorobenzoate (5.0×10^{-3} mol) in anhydrous alcohol (50 mL) and freshly distilled benzaldehyde (5.25×10^{-3} mol) was treated with 10 drops of glacial acetic acid and refluxed under a cover of nitrogen for 4 h. Thereafter, the solvent was distilled off under reduced pressure and the residue was taken up in benzene (30 mL) and evaporated to near dryness under reduced pressure. The gluey solid thus obtained was dissolved in 25 mL of dry methanol, cooled, and treated with sodium borohydride (1×10^{-2} mol) added in small quantities with stirring. After addition, the resulting reaction mixture was warmed in a steam bath for 10 min and the solvent evaporated under reduced pressure. The residue obtained was partitioned between chloroform (25 mL) and water (25 mL). The chloroform layer was washed with water, dried (anhydrous magnesium sulfate), and filtered and the solvent was evaporated under reduced pressure. The residue obtained was either recrystallized or purified by column chromatography over basic alumina. In some cases, reduction of the initially formed imine was carried out by using catalytic hydrogenation over Pd/C in a Parr hydrogenator.

Methyl *N*-benzyl-3-amino-6-fluorobenzoate (7c): colorless crystalline needles; mp 84–85 °C; yield 81%; ^1H NMR δ 3.90 (s, 3 H, ester CH_3), 4.31 (s, 2 H, benzylic H), 6.69–6.75 (m, 1 H, aromatic H), 6.90–6.98 (m, 1 H, aromatic H), 7.14–7.17 (m, 1 H, aromatic H), 7.25–7.40 (m, 6 H, aromatic and NH protons); ^{19}F NMR −125.84 (s, 1 F); IR ($CHCl_3$) 3400, 2820, 1700, 1590, 1400, and 1070 cm^{-1}; exact mass calcd for $C_{15}H_{14}FNO_2$ m/e 259.1008, found 259.0987, major fragments 2591 (M^+), 228, 198, 182, 169, 153, 138, 122, 109, 91, and 65. Anal. Calcd for $C_{15}H_{14}FNO_2$: C, 69.47; H, 5.45; N, 5.40. Found: C, 69.49; H, 5.35; N, 5.48.

Methyl *N*-benzyl-3-amino-4-fluorobenzoate (8c): colorless crystalline needles; mp 71–72 °C; yield 78%; ^1H NMR δ 3.86 (s, 3 H, ester CH_3), 4.34 (bs, 1 H, NH), 4.39 (s, 2 H, benzylic H), 6.96–7.05 (m, 1 H, aromatic H), 7.28–7.43 (m, 7 H, aromatic H); ^{19}F NMR −130.58 (s, 1 F); IR ($CHCl_3$) 3400, 1700, 1600, 1420, 1320, 1280, and 1080 cm^{-1}; exact mass calcd for $C_{15}H_{14}FNO_2$ m/e 259.1008, found 259.1010, major fragments 259 (M^+), 228, 20, 182, 160, 118, 91, and 69. Anal. Calcd for $C_{15}H_{14}FNO_2$: C, 69.47; H, 5.45; N, 5.40. Found: C, 69.49; H, 5.33; N, 5.46.

Methyl *N*-benzyl-4-amino-2-fluorobenzoate (9c): colorless crystalline powder; mp 118–120 °C; yield 87% (catalytic reduction); ^1H NMR δ 3.85 (s, 3 H, ester CH_3), 4.35 (d, J = 5.35, 2 H, benzylic H), 4.61 (bs, 1 H, NH), 6.24–6.40 (m, 2 H, aromatic H), 7.34 (s, 5 H, NH), 7.76 (t, J = 8.56 H_2, 1 H, aromatic H); ^{19}F NMR −108.483 (s, 1 F); IR ($CHCl_3$) 3400, 1690, 1610, 1420, 1340, 1270, and 1125 cm^{-1}; exact mass calcd for $C_{15}H_{14}FNO_2$ m/e 259.1008, found 259.1007, major fragments 259 (M^+), 228, 198, 182, 91, and 69. Anal. Calcd for $C_{15}H_{14}FNO_2$: C, 69.47; H, 5.45; N, 5.40. Found: C, 69.60; H, 5.44; N, 5.36.

Methyl *N*-benzyl-3-amino-4,6-difluorobenzoate (10c): colorless crystalline needles; mp 94–96 °C; yield 86%; ^1H NMR δ 3.88 (s, 3 H, ester CH_3), 4.17 (bs, 1 H, NH), 4.36 (s, 2 H, benzylic H), 6.79–6.87 (m, 1 H, aromatic H), 7.20–7.37 (m, 6 H, aromatic H); IR ($CHCl_3$) 3420, 2980, 2800, 1720, 1600, 1440, 1130, and 950 cm^{-1}; exact mass calcd for $C_{15}H_{13}F_2NO_2$ m/e 277.0914, found 277.0910, major fragments 277 (M^+), 246, 218, 200, 91, and 65. Anal. Calcd for $C_{15}H_{13}F_2NO_2$: C, 64.96; H, 4.73; N, 5.05. Found: C, 65.09; H, 4.85; N, 5.12.

Methyl *N*-benzyl-3-amino-2,6-difluorobenzoate (11c): colorless oil; yield 82%; ^1H NMR δ 3.92 (s, 3 H, ester CH_3), 4.32 (bs, 3 H, NH and benzylic H), 6.59–6.68 (m, 1 H, aromatic C-4 H), 6.69–6.78 (m, 1 H, aromatic C-5 H), 7.32 (s, 5 H, aromatic H); ^{19}F NMR −128.73 (d, J = 3.25 Hz, 1 F), −134.45 (d, J = 3.25 Hz, 1 F); IR (neat) 3400, 3010, 2900, 1730, 1630, 1590, 1500, 1430, 1350, 1290, and 1100; exact mass calcd for $C_{15}H_{13}F_2NO_2$ m/e 277.0914, found 277.0910, major fragments 277 (M^+), 246, 218, 200, 185, 140, 112, 91, 65.

Methyl *N*-benzyl-3-amino-2,4,6-trifluorobenzoate (12c): colorless oil; yield 76% (catalytic reduction); ^1H NMR δ 3.83 (bs, 1 H, NH), 3.92 (s, 3 H, ester CH_3), 4.43 (s, 2 H, benzylic H), 6.62–6.72 (m, 1 H, aromatic H), 7.33 (s, 5 H, aromatic H); ^{19}F NMR −120.80 (m, 1 F), −122.62 (m, 1 F), −12265 (m, 1 F); IR (neat) 3400, 1735, 1610, 1500, 1450, 1430, 1290, 1230, and 1150; exact mass calcd for $C_{15}H_{12}F_3NO_2$ m/e 295, found 295.0844, major fragments

295 (M^+), 264, 218, 174, 121, 105, 91, and 65.

Methyl *N*-benzyl-4-amino-2,3,5,6-tetrafluorobenzoate (13): colorless crystalline powder; mp 90–91 °C; yield 68% (catalytic reduction); ^{1}H NMR δ 3.90 (s, 3 H, ester CH_3), 4.51 (bs, 1 H, NH), 4.63 (d, J = 6.0 Hz, 2 H benzylic H), 7.25–7.40 (m, 5 H, aromatic H); IR ($CHCl_3$) 3420, 2960, 2800, 1740, 1650, 1450, 1370, 1310, and 1000 cm^{-1}; exact mass calcd for $C_{15}H_{11}F_4NO_2$ m/e 313.0725, found 313.0720, major fragments 313 (M^+), 282, 191, 91, 65, and 55. Anal. Calcd for $C_{15}H_{11}F_4NO_2$: C, 57.49; H, 3.54; N, 4.47. Found: C, 57.47; H, 3.59; N, 4.45.

General Procedure for the Photolysis of the Azides 10a–13a in Tetramethylethylene. The purified azides **10a–13a** (1.0×10^{-3} mol) were dissolved in 3 mL of tetramethylethylene, degassed, and sealed in 8-mm diameter Pyrex tubes and photolyzed at 15 °C using a battery of 350-nm UV lamps in a Rayonet photochemical reactor for 18 h. The solvent was then evaporated at reduced pressure and the residue was purified by preparative thin layer chromatography.

2,2,3,3-Tetramethyl-1-(2,4-difluoro-5-carbomethoxyphenyl)aziridine (10i): colorless crystalline solid; mp 83–84 °C; yield 62%; ^{1}H NMR δ 1.27 (s, 12 H, aziridine H), 3.91 (s, 3 H, ester CH_3), 6.84 (t, J = 10.5 Hz, 1 H, aromatic C-3 H), 7.34 (dd, J = 7.37, 7.36 Hz, 1 H, aromatic C-6 H); ^{19}F NMR −118.29 (m, 1 F), −119.79 (m, 1 F); IR ($CHCl_3$) 2940, 1720, 1610, 1600, 1490, 1440, 1380, 1330, 1260, 1140, and 1080 cm^{-1}; exact mass calcd for $C_{14}H_{17}F_2NO_2$ m/e 269.1227, found 269.1223, major fragments 289 (M^+), 254, 239, 227, 213, 185, 153, 112, 98, 84, and 43. Anal. Calcd for $C_{14}H_{17}F_2NO_2$: C, 62.43; H, 6.37; N, 5.20. Found: C, 62.48; H, 6.69; N, 5.18.

2,2,3,3-Tetramethyl-1-(4,6-difluoro-5-carbomethoxyphenyl)aziridine (11i): colorless oil; yield 59%; ^{1}H NMR δ 1.25 (s, 12 H, aziridine protons), 3.93 (s, 3 H, ester CH_3), 6.74–6.86 (m, 2 H, aromatic H); ^{19}F NMR −151.36 (m, 1 F), −152.26 (m, 1 F); IR (neat) 2935, 1715, 1600, 1480, 1375, 1255, 1130, and 1075 cm^{-1}; exact mass calcd for $C_{14}H_{17}F_2NO_2$ m/e 269.1227, found 269.1218, major fragments 269 (M^+), 254, 238, 227, 213, 185, 112, 84, 59, and 42.

2,2,3,3-Tetramethyl-1-(2,4,6-trifluoro-5-carbomethoxyphenyl)aziridine (12i): colorless oil; yield 48%; ^{1}H NMR δ 1.27 (s, 12 H, aziridine H), 3.93 (s, 3 H, ester CH_3), 6.65–6.73 (m, 1 H, aromatic CH); ^{19}F NMR −112.76 (m, 1 F), −120.07 (m, 1 F), −124.74 (m, 1 F); IR (neat) 2990, 1740, 1600, 1500, 1490, 1440, 1370, 1295, 1140, and 1040; exact mass calcd for $C_{14}H_{16}F_3NO_2$ m/e 287.1133, found 287.1068, major fragments 287 (M^+), 277, 252, 231, 208, 193, 172, 146, 99, 69, and 59.

2,2,3,4-Tetramethyl-1-(2,3,5,6-tetrafluoro-4-carbomethoxyphenyl)aziridine (13i): colorless oil; yield 59%; ^{1}H NMR δ 1.32 (δ, 12 H, aziridine protons), 3.93 (s, 3 H, ester CH_3); ^{19}F NMR −141.97 (m, 2 F), −154.15 (m, 2 F); IR (neat) 3000, 1730, 1645, 1500, 1480, 1430, 1410, 1320, 1230, and 1110 cm^{-1}; exact mass calcd for $C_{14}H_{15}F_4NO_2$ m/e 305.0518, found 305.0500, major fragments 305 (M^+), 264, 223, 192, 148, 83, and 55.

***N*-(2,3,5,6-Tetrafluoro-5-carbomethoxyphenyl)dimethylsulfimide (13o).** Methyl 4-azido-2,3,5,6-tetrafluorobenzoate (**13a**) (2.0×10^{-4} mol) was dissolved in 2 mL of freshly distilled dimethyl sulfide, sealed in a 8-mm diameter Pyrex tube after being degassed and photolyzed at 15 °C for 18 h. After photolysis, the crystalline solid that precipitated was filtered, washed with hexane, and recrystallized from hexane–ethyl acetate to yield an almost colorless crystalline powder: mp 141–143 °C; yield 68%; ^{1}H NMR δ 2.81 (s, 6 H, S-CH_3 protons), 3.89 (s, 3 H, ester CH_3); ^{19}F NMR −143.54 (m, 2 F), −160.13 (m, 2 F); IR ($CHCl_3$) 1710, 1630, 1455, 1390, 1300, 1120, 970, and 890 cm^{-1}; exact mass calcd for $C_{10}H_9F_4NO_2S$ m/e 283.0290, found 283.0281, major fragments 283 (M^+), 268, 252, 236, 223, 206, 192, 164, 137, 69, and 61. Anal. Calcd for $C_{10}H_9F_4NO_2S$: C, 51.88; H, 2.72; N, 7.57. Found: C, 51.97; H, 2.70; N, 7.62.

General Procedure for Preparing the Authentic Samples of the Dicarbomethoxyfluoroazobenzenes 7e–13e. Degassed solutions of the azides **7a–13a** ($(1.0–1.5) \times 10^{-3}$ mol) and benzophenone ($(1.0–1.5) \times 10^{-2}$ mol) in dry dichloromethane (40 mL) were photolyzed at 15 °C using a battery of 350-nm UV lamps in a Rayonet photochemical reactor continuously for a period of 18 h. The solvent was evaporated under reduced pressure and the residue was filtered through a small column of basic alumina in methylene chloride. Purification of the residue obtained after distilling off the solvent under reduced pressure by preparative TLC using precoated silica gel plates gave the dicarbomethoxyfluoroazobenzenes **7e–13e** as crystalline solids.

3,3′-Dicarbomethoxy-4,4′-difluoroazobenzene (7e): yellowish orange crystals; mp 126–128 °C; yield 38%; ^{1}H NMR δ 4.08 (s, 6 H, ester CH_3), 7.26–7.33 (m, 2 H, aromatic H), 8.07–8.13 (m, 2 H, aromatic H), 8.43–8.59 (m, 2 H, aromatic H); ^{19}F NMR −106.24 (s, 2 F); IR ($CHCl_3$) 1720, 1610, 1600, 1570, 1480, 1425, 1270, 1115, 1070, 980, 900, and 820 cm^{-1}; exact mass calcd for $C_{16}H_{12}F_2N_2O_4$ m/e 334.0765, found 334.0764, major fragments 334 (M^+), 303, 181, 153, 138, 121, 94, and 69. Anal. Calcd for $C_{16}H_{12}F_2NO_2$: C, 57.47; H, 3.62; N, 8.38. Found: C, 57.61; H, 3.82; N, 8.43.

3,3′-Dicarbomethoxy-6,6′-difluoroazobenzene (8e): red-orange crystals; mp 178–179 °C; yield 42%; ^{1}H NMR δ 3.95 (s, 6 H, ester CH_3), 7.29–7.40 (m, 2 H, aromatic H), 8.18–8.26 (m, 2 H, aromatic H), 8.42–8.46 (m, 2 H, aromatic H); ^{19}F NMR −117.29 (s, 2 F); IR ($CHCl_3$) 1720, 1625, 1600, 1350, 1290, 1110, 1030, and 900 cm^{-1}; exact mass calcd for $C_{16}H_{12}F_2N_2O_4$ m/e 334.0765, found 334.0759, major fragments 334 (M^+), 303, 203, 186, 173, 153, 125, 112, 93, 75, 63, and 45. Anal. Calcd for $C_{16}H_{12}F_2NO_2$: C, 57.47; H, 3.62; N, 8.38. Found: C, 57.61; H, 3.82; N, 8.43.

4,4′-Dicarbomethoxy-3,3′-difluoroazobenzene (9e): red-orange needles; mp 185–187 °C; yield 32%; ^{1}H NMR δ 3.98 (s, 6 H, ester CH_3), 7.65–7.70 (m, 2 H, aromatic H), 7.79–7.83 (m, 2 H, aromatic H), 8.09–8.16 (m, 2 H, aromatic H), ^{19}F NMR −108.24 (s, 2 F); IR ($CHCl_3$) 1720, 1610, 1580, 1410, 1290, 1120, 1080, 950, and 880 cm^{-1}; exact mass calcd for $C_{16}H_{12}F_2N_2O_4$ m/e 334.0765, found 334.0743, major fragments 334 (M^+), 303, 181, 153, 121, 94, and 59. Anal. Calcd for $C_{16}H_{12}F_2NO_2$: C, 57.47; H, 3.62; N, 8.38. Found: C, 57.61; H, 3.69; N, 8.48.

3,3′-Dicarbomethoxy-4,4′,6,6′-tetrafluoroazobenzene (10e): crystalline yellow solid; mp 219–221 °C; yield 43%; ^{1}H NMR δ 3.92 (s, 3 H, ester CH_3), 6.82 (t, J = 9.7 Hz, 1 H, aromatic H), 7.12 (t, J = 9.7 Hz, 1 H), 7.69 (t, J = 9.7 Hz, 1 H, aromatic H), 8.41 (t, J = 9.7 Hz, 1 H, aromatic H); ^{19}F NMR −100.13 (d, J = 16.5 Hz, 1 F), −103.82 (d, J = 16.5 Hz, 1 F), −110.06 (d, J = 16.5 Hz, 1 F), −112.72 (d, J = 16.5 Hz, 1 F). It appears from the NMR data that the azo compound is a mixture of two forms, the *Z* and *E*, in the ratio 3:2. However GC analysis showed only a single trace: IR ($CHCl_3$) 1730, 1610, 1590, 1480, 1430, 1300, 1140, 960, and 850 cm^{-1}; exact mass calcd for $C_{16}H_{10}F_4N_2O_4$ m/e 370.0576, found 370.0581, major fragments 370 (M^+), 339, 316, 199, 171, 156, 139, 112, and 69. Anal. Calcd for $C_{16}H_{10}F_4N_2O_4$: C, 57.47; H, 3.62; N, 8.38. Found: C, 57.61; H, 3.82; N, 8.43.

3,3′-Dicarbomethoxy-2,2′,4,4′-tetrafluoroazobenzene (11e): crystalline yellow solid; mp 163–165 °C; yield 28%; ^{1}H NMR δ 4.02 (s, 6 H, ester CH_3); ^{19}F NMR −104.89 (d, J = 6 Hz, 2 F), −120.79 (d, J = 6 Hz, 2 F); IR ($CHCl_3$) 1730, 1620, 1590, 1470, 1430, 1300, 1125, 1020, and 990 cm^{-1}; exact mass calcd for $C_{16}H_{10}F_4N_2O_4$ m/e 370.0576, found 370.0576, major fragments 370 (M^+), 339, 224, 199, 171, 156, 137, 112, 69, and 59. Anal. Calcd for $C_{16}H_{10}F_4N_2O_4$: C, 51.88; H, 2.72; N, 7.57. Found: C 52.03; H, 2.88; N, 7.59.

General Procedure for the Photolysis of the Azides 7a–13a with Diethylamine. A solution of the azide **7a–13a** ($(1.5–3.0) \times 10^{-2}$ M) in 40 mL of hexane/tetrahydrofuran (9:1) containing diethylamine (0.1 M) was placed in a Pyrex tube with a cold finger insert and purged with argon. The tube was placed inside a Rayonet photochemical reactor and photolyzed with 350-nm UV lamps at 20–21 °C for 2 h. The photolyzed solution was allowed to stand at room temperature until the tar settled down, decanted into a roung-bottomed flask, and concentrated under reduced pressure. The residue obtained was quickly filtered through a small column of activated neutral alumina in a 1:1 hexane/ethyl acetate mixture. The filtrate was concentrated and the products were separated by preparative thin layer chromatography on silica gel using a 2:3:1 hexane–chloroform–ethyl acetate mixture. The yields of the products reported are the isolated yields (Table III) and are based on the amount of azide consumed in the reaction.

Azepine 7l: pale brown oil; yield 12% (as 1:1 mixture of **7l** and **7m**); ^{1}H NMR ($CDCl_3$) δ 1.09 (t, J = 7 Hz, 6 H, CH_3 protons), 3.35 (q, J = 7 Hz, 4 H, CH_2 protons), 3.80 (s, 3 H, ester CH_3), 4.74–4.93 (m, 2 H, azepine CH_2), 7.10 (dd, J = 6, 9 Hz, 1 Hz, azepine H), 7.43 (dd, J = 6, 9 Hz, 1 H, azepine H); ^{19}F NMR

($CDCl_3$) −124.68 (s, 1 F); exact mass calcd for $C_{12}H_{17}FN_2O_2$ *m/e* 240.127, found 240.072, major fragments 240 (M^+) 211, 168, 153, 138, 109, 83, and 72.

Azepine 7m: ^1H NMR ($CDCl_3$) δ 1.16 (t, *J* = 7 Hz, 6 H, CH_3 protons), 3.49 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.80 (s, 3 H, ester CH_3), 4.74–4.93 (m, 2 H, azepine CH_2), 6.42 (d, *J* = 9 Hz, 1 Hz, azepine H), 6.68 (dt, *J* = 7, 9 Hz, 1 H, azepine H); ^{19}F NMR ($CDCl_3$) −124.68 (s, 1 F); exact mass calcd for $C_{12}H_{17}FN_2O_2$ *m/e* 240.127, found 240.120, major fragments 240 (M^+), 211, 168, 153, 138, 109, and 72.

Hydrazine 7n: brown oil; yield 7%; ^1H NMR ($CDCl_3$) δ 0.99 (t, *J* = 7 Hz, 6 H, CH_3 protons), 2.52–2.69 (m, 4 H, CH_2 protons), 3.69 (s, 3 H, ester CH_3), 4.31 (bs, 1 H, NH proton), 6.80–6.83 (m, 1 H, aromatic H), 7.18–7.22 (m, 1 H, aromatic H); ^{19}F NMR ($CDCl_3$) −124.68 (s, 1 F); exact mass calcd for $C_{12}H_{17}FN_2O_2$ *m/e* 240.127, found 240.110, major fragments 240 (M^+), 211, 173, 163, 151, 126, 111, 98, and 72.

Hydrazine 8n: light brown oil; yield 8%; ^1H NMR ($CDCl_3$) δ 1.08 (t, *J* = 7 Hz, 6 H, CH_3 protons), 2.73 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.88 (s, 3 H, ester CH_3), 4.57 (bs, 1 H, NH proton), 6.91–6.99 (m, 1 H, aromatic H), 7.32–7.38 (m, 1 H, aromatic H), and 7.89–7.93 (m, 1 H, aromatic H); ^{19}F NMR ($CDCl_3$) −131.52 (s, 1 F); exact mass calcd for $C_{12}H_{17}FN_2O_2$ *m/e* 240.127, found 240.120, major fragments 240 (M^+), 225, 211, 197, 168, 138, 109, 81, and 56.

Azepine 9l: pale brown oil; yield 9% (as 5:12 mixture of **9l** and **9m**); ^1H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7 Hz, 6 H, CH_3 protons), 3.44 (q, *J* = 7 Hz, 6 H, CH_2 protons), 3.89 (s, 3 H, ester CH_3), 3.44–3.75 (m, 2 H, azepine CH_2 protons), 7.79 (d, *J* = 8.5 Hz, 1 H, azepine H), 7.83 (dq, *J* = 7, 8 Hz, 1H, azepine H); ^{19}F NMR ($CDCl_3$) −110.24 (s, 1 F); exact mass calcd for $C_{12}H_{17}FN_2O_2$ *m/e* 240.127, found 240.100, major fragments 240 (M^+), 225, 211, 168, 153, 138, 109, 83, and 72.

Azepine 9m: ^1H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7 Hz, 6 H, CH_3 protons), 3.44 (q, *J* = 7 Hz, 6 H, CH_2 protons), 3.44–3.75 (m, 2 H, azepine CH_2 protons), 3.89 (s, 3 H, ester CH_3), 7.79 (d, *J* = 8.5 Hz, 1 Hz, azepine H), 7.83 (dq, *J* = 7, 8 Hz, 1 H, azepine H); ^{19}F NMR ($CDCl_3$) −110.24 (s, 1 F); exact mass calcd for $C_{12}H_{17}FN_2O_2$ *m/e* 240.127, found 240.110, major fragments 240 (M^+), 225, 168, 138, 109, 83, and 72.

Azepine 10l: light brown oil; yield 12%; ^1H NMR ($CDCl_3$) δ 1.09 (t, *J* = 7 Hz, 6 H, CH_3 protons), 2.70 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.91 (s, 3 H, ester CH_3), 6.95 (t, 1 H, aromatic H), 7.66–7.73 (m, 1 H, aromatic H); ^{19}F NMR ($CDCl_3$) −115.42 (m, 1 F); exact mass calcd for $C_{12}H_{16}F_2N_2O_2$ *m/E* 258.118, found 258.110, major fragments 258 (M^+), 229, 186, 152, 127, 100, and 58.

Hydrazine 10n: oil; yield traces (<1%); ^1H NMR ($CDCl_3$) δ 1.09 (t, *J* = 7 Hz, 6 H, CH_3 protons), 2.70 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.91 (s, 3 H, ester CH_3), 6.95 (m, 1 H, aromatic H), 7.66–7.73 (m, 1 H, aromatic H); ^{19}F NMR ($CDCl_3$) −109.65 (m, 1 F), −115.42 (m, 1 F); exact mass calcd for $C_{12}H_{16}F_2N_2O_2$ *m/e* 258.118, found 258.200, major fragments 258 (M^+), 243, 229, 215, 199, 155, 143, and 73.

Azepine 11l: pale brown oil; yield 4%; ^1H NMR ($CDCl_3$) δ 1.19 (t, *J* = 7 Hz, 6 H, CH_3 protons), 3.43 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.68–3.89 (m, 2 H, azepine CH_2), 6.78–6.88 (m, 1 H, azepine H); ^{19}F NMR ($CDCl_3$) −125.11 (m, 1 F), −122.53 (m, 1 F); exact mass calcd for $C_{12}H_{16}F_2N_2O_2$ *m/e* 258.118, found 258.110, major fragments 258 (M^+), 243, 229, 215, 186, 156, 127, 100, 87, and 56.

Azepine 11m: brown oil; yield 3%; ^1H NMR ($CDCl_3$) δ 1.22 (t, *J* = 7 Hz, 6 H, CH_3 protons), 3.46 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.52–3.78 (m, 1 H, azepine H), 6.95–7.01 (m, 2 H, azepine H), 7.66–7.73 (m, 1 H, aromatic H); ^{19}F NMR ($CDCl_3$) −127.31 (bs, 1 F); exact mass calcd for $C_{12}H_{16}F_2N_2O_2$ *m/e* 258.118, found 258.100, major fragments 258 (M^+), 243, 229, 215, 186, 156, 127, 100, 87, and 56.

Azepine 11o: pale yellow oil; yield 14%; ^1H NMR ($CDCl_3$) δ 0.99 (t, *J* = 7 Hz, 6 H, CH_3 protons), 1.04 (t, *J* = 7 Hz, 6 H, CH_3 protons), 2.67–2.84 (m, 4 H, CH_2 protons), 3.20–3.37 (m, 4 H, CH_2 protons), 3.69 (s, 3 H, ester CH_3), 5.04 (bs, 1 H, azepine H); ^{19}F NMR ($CDCl_3$) −100.290 (s, 1 F); exact mass calcd for $C_{16}H_{26}FN_3O_2$ *m/e* 311.201, found 311.10, major fragments 311 (M^+), 282, 252, 240, 223, 211, 181, 151, 137, 110, 96, 72, and 72.

Hydrazine 12n: dark brown oil; yield 58%; ^1H NMR ($CDCl_3$) δ 1.11 (t, *J* = 7 Hz, 6 H, CH_3 protons), 2.72 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.93 (s, 3 H, ester CH_3), 4.13 (bs, 1 H, NH proton); ^{19}F NMR ($CDCl_3$) −117.61 (m, 1 F), −120.01 (m, 1 F), −124.30 (m, 1 F), −120.01 (m, 1 F), −124.30 (m, 1 F); exact mass calcd for $C_{12}H_{15}F_3N_2O_2$ *m/e* 276.108, found 276.100, major fragments 276 (M^+), 261, 241, 233, 204, 170, 142, 115, 87, and 58.

Hydrazine 13n: colorless crystalline solid; mp 95–97 °C; yield 62%; ^1H NMR ($CDCl_3$) δ 1.11 (t, J = 7 Hz, 6 H, CH_3 protons), 2.75 (q, *J* = 7 Hz, 4 H, CH_2 protons), 3.92 (s, 3 H, ester CH_3), 4.60 (bs, 1 H, NH proton); ^{19}F NMR ($CDCl_3$) −117.61 (m, 1 F), −120.01 (m, 1 F), −124.30 (m, 1 F), −120.01 (m, 1 F), −124.30 (m, 1 F); exact mass calcd for $C_{12}H_{14}F_4N_2O_2$ *m/e* 294.099, found 294.099, major fragments 294 (M^+), 273, 263, 251, 236, 222, 194, 176, 164, 137, 131, 118, 56, and 42. Anal. Calcd for $C_{12}H_{14}F_4N_2O_2$: C, 48.96; H, 4.80; N, 9.52. Found: C, 48.92; H, 5.01; N, 9.31.

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