JOC Article

Photochemistry of Fluorinated Heterocyclic Compounds. An Expedient Route for the Synthesis of Fluorinated 1,3,4-Oxadiazoles and 1,2,4-Triazoles

Andrea Pace, Ivana Pibiri, Silvestre Buscemi, and Nicolò Vivona*

Dipartimento di Chimica Organica "E. Paternò", Università degli Studi di Palermo, Viale delle Scienze-Parco d'Orleans II, I-90128 Palermo, Italy

Luciana Malpezzi

Dipartimento di Chimica, Materiali e Ingegneria Chimica, Politecnico di Milano, Via Mancinelli 7, I-20131 Milano, Italy

nvivona@unipa.it

Received February 2, 2004

The photochemistry of some 3-*N*-alkylamino-5-perfluoroalkyl-1,2,4-oxadiazoles in the presence of nitrogen nucleophiles such as ammonia and primary and secondary aliphatic amines has been investigated. The primary photolytic intermediate from the cleavage of the ring O−N bond follows two distinct and competing pathways leading to (i) 5-perfluoroalkyl-1,3,4-oxadiazoles, through the *ring contraction−ring expansion* photoisomerization route favored by the presence of the base or (ii) 5-perfluoroalkyl-1,2,4-triazoles, through the intervention, as an internal nucleophile, of the exocyclic *N*-alkylamino moiety of the oxadiazole followed by the attack of the external nitrogen nucleophile and subsequent heterocyclization. Some comments on the photoreactivity of fluorinated oxadiazoles and on the applications of these photoprocesses in the synthesis of target fluorinated structures are emphasized. In this context, irradiations of 3-perfluoroalkanoylamino-4-phenylfurazan in the presence of primary aliphatic amines are reconsidered as feasible one-pot synthetic methodologies toward fluorinated heterocycles. X-ray analysis of two representative products 1-methyl-3-methylamino-5-perfluoroheptyl-1,2,4-triazole and 2-methylamino-5-trifluoromethyl-1,3,4-oxadiazole confirmed the proposed structures and furnished interesting information on the crystal packing of these fluorinated five-membered heterocycles.

Introduction

Fluorinated heterocycles represent an interesting class of fluorinated compounds that have found their wide application as agrochemicals, pharmaceuticals, and in the field of new materials science.[1] For this reason, an intriguing research area is looking at the development of new methodologies for the synthesis of these target structures.[2] Besides the direct fluorination or perfluoroalkylation reactions, a general and more convenient approach to fluorinated heterocyclic compounds considers the building-block strategy, which is the construction of the fluorinated heterocyclic structure by conventional heterocyclization reactions of acyclic fluorinated precursors.[2] Within the building-block strategy, an expedient route can be recognized in the ring-rearrangement reactions, which can be thermally or photochemically promoted.[3−5] This means that a readily available fluorinated

(1) See, among others: (a) Hudlicky, M. *Chemistry of Organic Fluorine Compounds*, 2nd ed.; Ellis Horwood: Chichester, 1976. (b) Filler, R.; *Organofluorine Chemicals and Their Industrial Applications*; Banks, R. E., Ed.; Ellis Horwood: Chichester, 1979. (c) Filler, R.; Kobayashi, Y. *Biomedical Aspects of Fluorine Chemistry*; Kodansha & Elsevier Biomedical: Tokyo, 1982. (d) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123−3197. (e) Reynolds, D. W.; Cassidy, P. E.; Johnson, C. G.; Cameron, M. L. *J. Org. Chem*. **1990**, *55*, 4448−4454. (f) Filler, R.; Kobayashi, Y.; Yagupolskii, L, M. *Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications*; Elsevier: Amsterdam, 1993. (g) *Chemistry of Organic Fluorine Compounds II. A Critical Review*; Hudlicky, M., Pavlath, A. E., Eds.; ACS Monograph 187; American Chemical Society: Washington, DC, 1995.

(2) (a) Chambers, R. D.; Sargent, C. R. *Adv. Heterocycl. Chem*. **1981**, *28*, 1−71. (b) Differding, E.; Frick, W.; Lang, R. W.; Martin, P.; Schmit, C.; Veenstra, S.; Greuter, H. *Bull. Soc. Chim. Belg*. **1990**, *99*, 647−671 (c) Silvester, M. J. *Adv. Heterocycl. Chem*. **1994**, *59*, 1−38. (c) Burger, K.; Wucherpfennig, U.; Brunner, E. *Adv. Heterocycl. Chem*. **1994**, *60*, 1−64. (d) Furin, G. G. *Targets in Heterocyclic Systems*; Attanasi, O. A., Spinelli, D., Eds.; Societa Chimica Italiana: Roma, 1998; Vol. 2, pp 355−441. (e) Zhu, S. Z.; Wang, Y. L.; Peng, W. M.; Song, L. P.; Jin, G. F. *Curr. Org. Chem*. **2002**, *6*, 1057−1096.

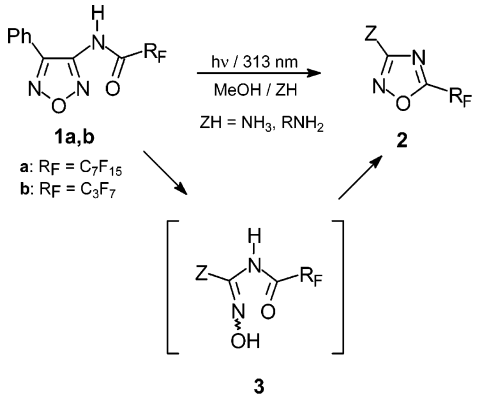
(3) For heterocyclic rearrangements, see: (a) Van der Plas, H. C. *Ring Transformations of Heterocycles*; Academic: New York, 1973; Vols. 1 and 2. (b) Boulton, A. J.; Katritzky, A. R.; Hamid, A. M. *J. Chem. Soc. C* **1967**, 2005−2007. (c) Afridi, A. S.; Katritzky, A. R.; Ramsden, C. A. *J. Chem. Soc., Perkin Trans. 1* **1976**, 315−320. (d) Ruccia, M.; Vivona, N.; Spinelli, D. *Adv. Heterocycl. Chem*. **1981**, *29*, 141−169. (e) L'abbé, G. *J. Heterocycl. Chem*. **1984**. *21*, 627−638. (f) Vivona, N.; Buscemi, S.; Frenna, V., Cusmano, G. *Adv. Heterocycl. Chem*. **1993**, *56*, 49−154.

(4) Van der Plas, H. C. *Adv. Heterocycl. Chem*. **1999**, *74*, 1−253.

(5) For photoinduced rearrangements of five-membered heterocycles, see: (a) Padwa, A. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. III, pp 501−547. (b) D'Auria, M. *Heterocycles* **1999**, *50*, 1115−1135. (c) D'Auria, M. In *Targets in Heterocyclic Systems*; Attanasi, O. A., Spinelli, D., Eds.; Società Chimica Italiana: Roma, 1999; Vol. 2, pp 233−279. (d) D'Auria, M. *Adv. Heterocycl. Chem*. **2001**, *79*, 41−88.

10.1021/jo049814e CCC: $27.50
Published on Web 05/08/2004

SCHEME 1



heterocycle could be used as a precursor to be rearranged into a new fluorinated structure that could be otherwise constructed with difficulty or by means of tedious procedures.

Examples of this approach come from our laboratories.[6−9] They regard photoinduced rearrangements of O−N bond-containing azoles,[6,7] as well as ANRORC-like rearrangements[4] of 5-perfluoroalkyl-1,2,4-oxadiazoles.[9,10] As an example of the photochemical approach, photolysis of 3-perfluoroalkanoylamino-furazans **1** in methanol and in the presence of ammonia or primary aliphatic amines allowed the synthesis of 3-amino- or 3-*N*-alkylamino-5-perfluoroalkyl-1,2,4-oxadiazoles **2** (Scheme 1).[6] This photoreaction follows the photofragmentation pattern[5a,11] of the furazan ring into benzonitrile and an acylamino-nitriloxide species that the nitrogen nucleophile will capture to give the *N*-acylamino-amidoxime intermediate **3** as a precursor of final oxadiazoles **2**. Yields of isolated oxadiazoles **2** were not excellent, and this is due to the photoreactivity of these compounds (unlike nonfluorinated analogues[12]) under the irradiation conditions. Besides the possibility of performing synthetic methodologies, these photochemical studies raised the issue of the photoreactivity of fluorinated heterocycles.

As far as 1,2,4-oxadiazoles are concerned, this heterocycle presents photoreactivities that are strongly dependent on several factors such as the nature and position of the substituents or the presence of nucleophiles or bases in the photoreaction media.[11a,13−16] A particular case of photoreactivity is represented by the ring-photoisomerization into 1,3,4-oxadiazoles, which was found to be restricted to 1,2,4-oxadiazoles bearing an XH group at C(3) of the ring and favored by the presence of a base in the irradiation medium.[15,16] Tautomeric or acid−base equilibria in the starting oxadiazole or in the key intermediates have been claimed to occur during the transformation framed in the ring contraction−ring expansion pattern.[15] Moreover, depending on the nature of the substituent at C(5) of the oxadiazole ring, the occurrence of a competing photorearrangement through an internal cyclization−isomerization pathway[5] leading to the ring-degenerate isomers has been pointed out.[16]

Irradiations performed on the fluorinated analogues opened the way toward a more complete understanding of the general behavior of this quite interesting heterocycle. During our study on the photoreactivity of 3-amino-5-perfluoroalkyl-1,2,4-oxadiazoles **6**, we have recently reported[17] that these compounds show a marked photoreactivity that can be ascribed to a synergic effect of the amino group at C(3) and the perfluoroalkyl moiety at C(5) of the oxadiazole ring. In this context, we have observed that (i) irradiation of **6** (at $\lambda = 313$ nm) in methanol easily gave the solvolysis product **4** as a major component (by a reaction of the nucleophilic solvent with the electrophilic nitrogen of the photolytic species) and **5** (from an addition of the solvent to a nitrilimine species arising from an endocyclic diazirine intermediate (see after)) and (ii) similarly to what was observed for nonfluorinated analogues, irradiation of **6** (at $\lambda = 313$ nm) in methanol and in the presence of TEA gave competing phototransposition pathways leading to the ring-isomers 1,3,4-oxadiazoles **8** (through a ring contraction−ring expansion route) and the ring-degenerate oxadiazoles **7** (through an internal cyclization−isomerization route) (Scheme 2).[17]

Interestingly, the formation of the solvolytic compound **4** disclosed the electrophilic behavior of the nitrogen originally bound to the oxygen and opened the possibility to realize synthetic methodologies for different perfluoroalkyl-heterocycles or their open-chain precursors by irradiations of fluorinated 1,2,4-oxadiazoles in the presence of different nucleophiles. Actually, this approach has been utilized in the photochemistry of some nonfluorinated 1,2,4-oxadiazoles in the presence of nitrogen- or sulfur-containing nucleophiles.[13a,b] In this paper we report investigations on the photochemical behavior of the 3-*N*-alkylamino-1,2,4-oxadiazoles **9a,b** and **24** irradiated in the presence of nitrogen nucleophiles. Moreover, irradiations of the 3-perfluoroalkanoylamino-4-phenylfurazan **1a,b** and **28** in the presence of primary aliphatic amines will be reconsidered as feasible one-pot procedures for the synthesis of fluorinated 1,3,4-oxadiazoles and 1,2,4-triazoles.

(6) Buscemi, S.; Pace, A.; Vivona, N. *Tetrahedron Lett.* **2000**, *41*, 7977−7981.

(7) Buscemi, S.; Pace, A.; Calabrese, R.; Vivona, N.; Metrangolo, P. *Tetrahedron* **2001**, *57*, 5865−5871.

(8) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N. *Heterocycles* **2002**, *57*, 1891−1896.

(9) (a) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N.; Spinelli, D. *J. Org. Chem.* **2003**, *68*, 605−608. (b) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N.; Zaira Lanza, C.; Spinelli, D. *Eur. J. Org. Chem.* **2004**, 0000.

(10) These ANRORC-like rearrangements appear determined by the presence of the perfluoroalkyl group at C-5 of the oxadiazole.[9] The *A*ddition of the *N*ucleophile on the C-5 is followed by *R*ing *O*pening and then *R*ing *C*losure by attack of the β nucleophilic center of the bidentate reagent (hydrazine or hydroxylamine) at the C-3 of the initial oxadiazole ring, a molecule of hydroxylamine being displaced in the final step.

(11) (a) Vivona, N.; Buscemi, S. *Heterocycles* **1995**, *41*, 2095−2116 and references therein. (b) Buscemi, S.; Vivona, N.; Caronna, T. *J. Org. Chem.* **1995**, *60*, 4095−4101.

(12) Buscemi, S.; Vivona, N.; Caronna, T. *Synthesis* **1995**, 917−919.

(13) For photoinduced rearrangements involving the 1,2,4-oxadiazole heterocycle, see also: (a) Buscemi. S.; Vivona, N.; Caronna, T. *J. Org. Chem.* **1996**, *61*, 8397−8401. (b) Vivona, N.; Buscemi, S.; Asta, S.; Caronna, T. *Tetrahedron* **1997**, *53*, 12629−12636. (c) Buscemi, S.; Pace, A.; Vivona, N.; Caronna, T.; Galia, A. *J. Org. Chem.* **1999**, *64*, 7028−7033.

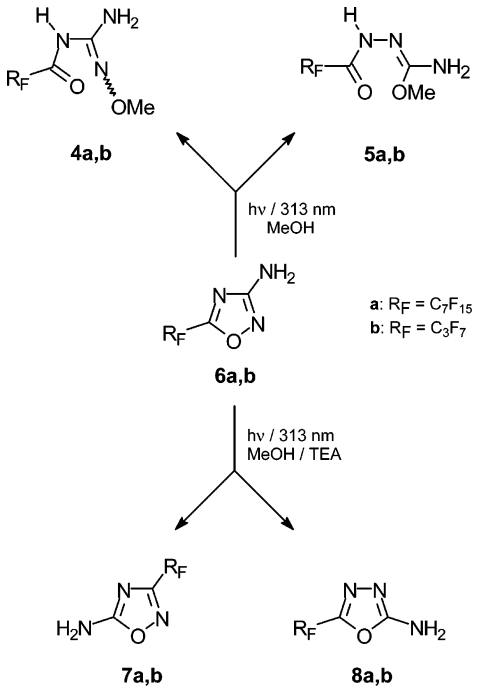
(14) (a) Newman, H. *Tetrahedron Lett.* **1968**, 2417−2420 (b) Newman, H. *Tetrahedron Lett.* **1968**, 2421−2424.

(15) (a) Buscemi. S.; Cicero, M. G.; Vivona, N.; Caronna, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1313−1315. (b) Buscemi. S.; Cicero, M. G.; Vivona, N.; Caronna, T. *J. Heterocycl. Chem.* **1988**, *25*, 931−935. (c) Buscemi, S.; Pace, A.; Vivona, N.; Caronna, T. *J. Heterocycl. Chem.* **2001**, *38*, 777−780.

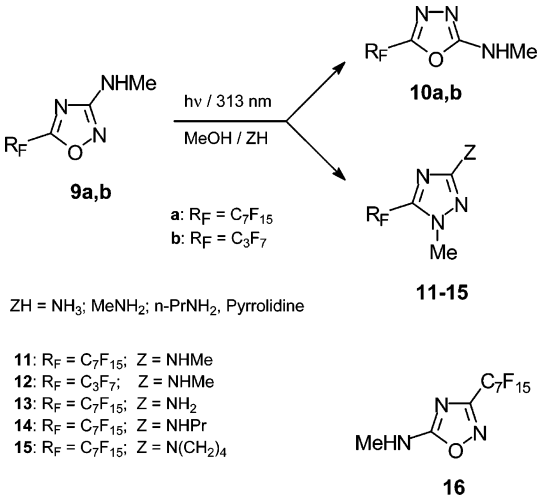
(16) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N. *J. Org. Chem.* **2002**, *67*, 6253−6255.

(17) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N.; Caronna, T. *J. Fluorine Chem.* **2004**, *125*, 165−173.

SCHEME 2



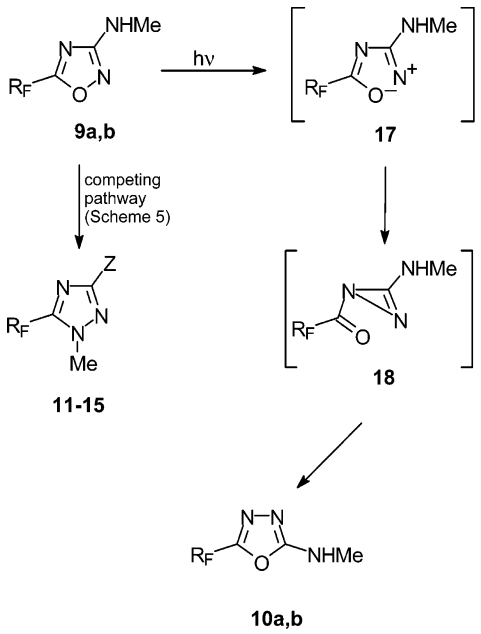
SCHEME 3



Results and Discussion

We initially observed that during the irradiation of 3-amino compound **6a** in the presence of an excess of methylamine, the amine was not incorporated in the final products; the exclusive formation of **8a** and **7a** indicated that the methylamine acted as a base (similarly to what was observed[17] in the TEA-assisted photoreactions) rather than as a nucleophile involved in the reaction. Quite different results were found in the case of 3-*N*-methylamino-oxadiazoles **9**. In fact, irradiation of oxadiazoles **9a,b** in the presence of an excess of methylamine essentially gave a mixture of the ring photoisomer 1,3,4-oxadiazoles **10a,b** and 1,2,4-triazoles **11** and **12**, respectively (Scheme 3). In a typical experiment, irradiation of **9a** gave **10a** and **11** in 27% and 25% yields, respectively. Unexpectedly, no ring-degenerate rearrangement to 5-*N*-methylamino-1,2,4-oxadiazole **16** (whose formation should have implied an internal cyclization−isomerization route)

SCHEME 4

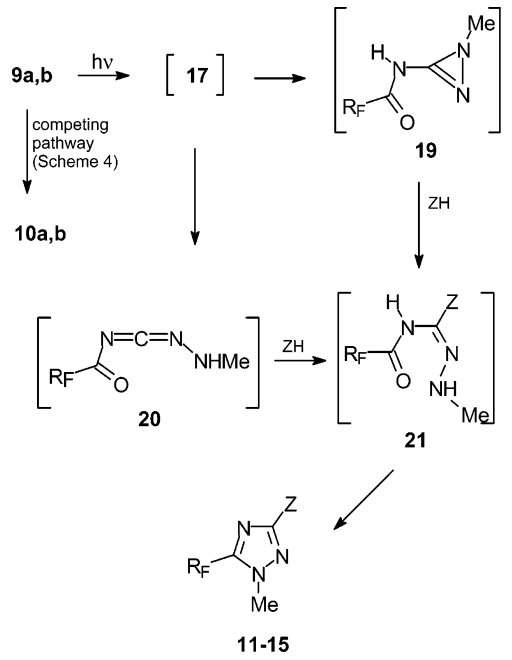


was detected. Oxadiazoles **10a,b** on one hand and triazoles **11** or **12** on the other must be considered primary photoproducts, as they do not interconvert each other under the used photoreaction conditions and their formation takes place even at low conversion of the starting substrate.

As previously documented[17] for 3-amino-5-perfluoroalkyl-1,2,4-oxadiazoles irradiated in the presence of TEA, the formation of the 1,3,4-oxadiazoles **10** clearly arises from the ring contraction−ring expansion photoisomerization route through the diazirine **18**, whose ring expansion into **10** could be favored by the presence of the base methylamine (Scheme 4).[18] On the other hand, the concomitant formation of the 1-methyl-1,2,4-triazoles **11** and **12** (structure of representative compound **11** was confirmed by X-ray analysis), as well as their analogues **13**−**15** (see after), is a surprising result. In fact, on the basis of the previously reported reactivity of 1,2,4-oxadiazoles,[13a] one could have explained the formation of 1-methyl-3-*N*-methylamino-triazole **11** during the reaction of **9a** with methylamine by assuming a direct reaction between the photolytic species **17** and methylamine in a N−N bond formation pattern, followed by cyclodehydration of the resulting intermediate **21** (Z = NHMe). However, this reaction pattern must be excluded because during the irradiations in the presence of nitrogen nucleophiles different than methylamine there is no evidence of such attack: irradiation of the representative oxadiazole **9a** in the presence of ammonia, propylamine, or pyrrolidine, besides the photoisomer 1,3,4-oxadiazole **10a** (as major component), produced the 3-amino- (or 3-*N*-alkyl-amino)-1-methyl-1,2,4-triazoles **13**, **14**, and **15**, respectively.

(18) As previously observed,[15c,16,17] the presence of an XH moiety at C-3 of the 1,2,4-oxadiazole heterocycle is needed for the ring photoisomerization to occurr, and this is valid for both fluorinated and nonfluorinated substrates. Therefore, in the presence of a base, the involvement of deprotonated species from 3-*N*-methylaminooxadiazoles **9** in the reaction pathway cannot be excluded. In this context, it is worthy to note that the NH moiety of the starting oxadiazole is expected to show a significant acidity in the excited state and could be efficiently deprotonated.

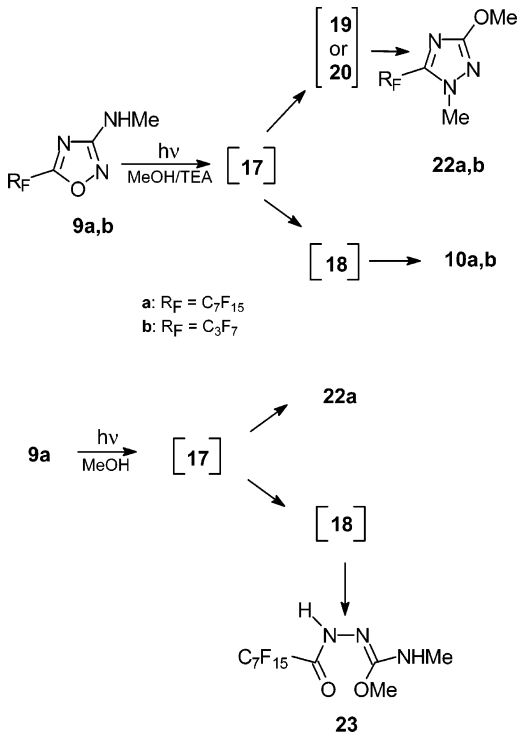
SCHEME 5



In these products, the nitrogen nucleophile is found attached at C(3) and the presence of the methyl moiety at N(1) suggests that the exocyclic nitrogen of the methylamino group in the original 1,2,4-oxadiazole has a primary role in the reaction pattern (Scheme 5). From the common photolytic intermediate **17**, the methylamino group can either form a diazirine **19** or directly transpose to the carbodiimide **20**. The nucleophilic attack of the external reagent at C(3) of the diazirine **19** or at the carbodiimidic species **20** and the subsequent heterocyclization of the resulting acylaminoamhydrazones **21** will lead to the final 1-methyl-1,2,4-triazoles **11**−**15** (Scheme 5). These findings constitute a peculiar photoreactivity of the 3-*N*-methylamino-substituted 1,2,4-oxadiazole system, not observed in the case of 3-amino-5-perfluoroalkyloxadiazoles nor in the case of nonfluorinated 3-aminooxadiazoles. Examples proceeding through a carbodiimidic intermediate arising from migration of the C(3) group to the electrophilic N(2) of the photolytic species in the photochemistry of 1,2,4-oxadiazoles have been reported.[13a,15b] Moreover, a 1,2,4-oxadiazole ring-opening reaction involving diazirines formed bethween exocyclic nitrogen at C(3) and N(2) of the oxadiazole ring has been suggested in the base-induced rearrangement of some 3-*N*-arylamino-5-methoxy-1,2,4-oxadiazoles[19] and of some *N*-(1,2,4-oxadiazol-3-yl)-*β*-enamino ketones.[20] In our case, the diazirine **19** formed with the exocyclic nitrogen must arise from a photochemical reaction, that is, through a preliminary formation of the photolytic species **17**; this is confimed by a separate experiment carried out in the dark on compound **9a** from which no base-induced thermal process was observed.

Interestingly, the above concomitant pathways involving both *endo*- and *exocyclic* nitrogen in the formation of the intermediates take also place during the irradiation

SCHEME 6



of compounds **9a,b** in methanol and in the presence of TEA. In this case, besides the expected ring-photoisomer 1,3,4-oxadiazoles **10a,b** (major component), the 3-methoxy-1,2,4-triazoles **22** were isolated[21] (Scheme 6), while the ring-degenerate 5-*N*-methylamino-1,2,4-oxadiazoles such as **16** were not detected. Obviously, formation of 3-methoxy-triazoles **22** agrees with our hypothesis of an involvement of the exocyclic diazirine **19** (or the open-chain carbodiimide **20**) subsequently attacked by the nucleophilic solvent.

Overall, the experimental results show that both 3-*N*-methylamino-1,2,4-oxadiazoles **9** and 3-amino analogues **6** photorearrange into the corresponding 1,3,4-oxadiazoles through the ring contraction−ring expansion route involving an exocyclic diazirine intermediate. As pointed out in the Introduction, besides this common route, the 3-amino compounds presented an additional reaction involving an internal cyclization-isomerization route. However, in the case of our 3-*N*-methylamino derivatives, a different competing reaction is observed, involving the exocyclic diazirine (or carbodiimide) route leading to 1,2,4-triazoles. A speculative hypothesis to explain this different behavior considers that the methylamino group could play a significant role both in stabilizing the photolytic intermediate and in assisting either the exocyclic diazirine formation or its transposition to the electrophilic N-2, thus favoring photoreactions involving these species.

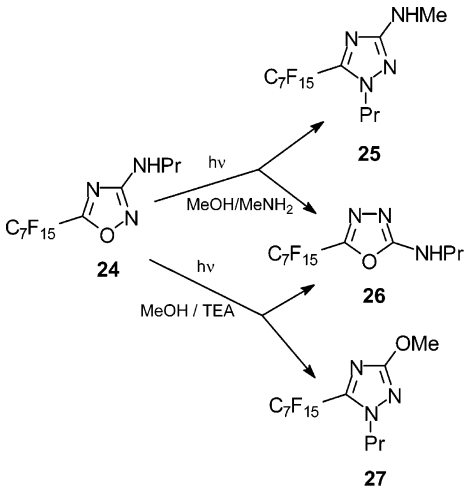
The peculiar photoreactivity of 3-*N*-methylamino oxadiazoles is also observed when photolysis was carried out in methanol only; irradiation of representative **9a** gave

(19) Jones, S. S.; Staiger, D: B.; Chodosh, D. F. *J. Org. Chem*. **1982**, *47*, 1969−1971.

(20) Braun, M.; Buchi, G.; Bushey, D. F. *J. Am. Chem. Soc*. **1978**, *100*, 4209−4213.

(21) In an independent experiment, aminolysis on representative 3-methoxy-triazole **22a** in the presence of methylamine left the starting material unchanged, thus excluding that compounds **11**−**15** could be formed by an aminolysis reaction of the first formed compounds **22** with the employed amines.

SCHEME 7

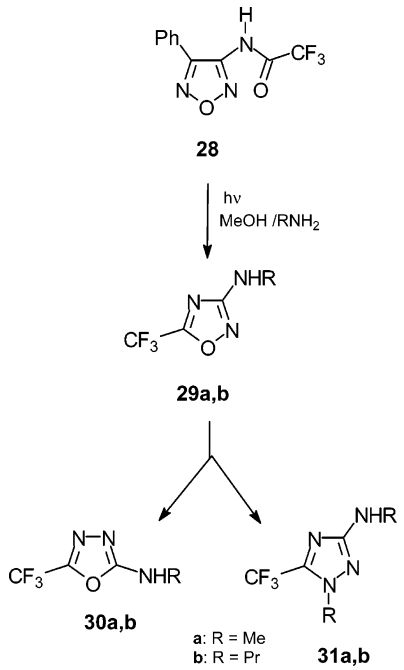


the open-chain product **23** on one hand (as a result of solvolysis of the *endo* diazirine **18**) and 3-methoxy-triazole **22a** on the other (Scheme 6). Treatment of **23** with hydrochloric acid in methanol gave the ring-photoisomer **10a**, confirming the assigned structure.[22] In contrast with what observed in the case of 3-amino compounds **6** (Scheme 2; formation of open-chain products **4**), insertion of methanol into the electrophilic nitrene-like nitrogen of the photolytic species **17** in a O−N bond formation pattern has not been observed. In this case, besides the lower electrophilic character of the N-2 site due to the *N*-methylamino group, one can simply consider that the pathways that allow the species **17** to develop into **18** and **23** on one hand and into triazole **22** on the other are kinetically more favored than the bimolecular nucleophilic attack at N-2 by the nucleophilic solvent.

Besides the quite interesting insight that these photoreactions gave on the reactivity of the 1,2,4-oxadiazole ring, we also wanted to evaluate the applications of this photochemical approach in synthesis. In view of this, we at first considered extension of the above reactivity to the 3-*N*-propylamino-oxadiazole **24** (Scheme 7). As expected, irradiation of **24** in the presence of methylamine allowed us to obtain the 1,3,4-oxadiazole **26** on one hand and the 1,2,4-triazole **25** on the other. Moreover, irradiation of **24** in methanol and TEA produced **26** and **27**. Furthermore, taking into account the synthetic procedure leading to 3-*N*-alkylamino-5-perfluoroalkyl-1,2,4-oxadiazoles (that is, irradiation of 3-perfluoroalkanoylamino-furazans in the presence of primary aliphatic amines; see Scheme 1),[6] we reconsidered irradiation of perfluoroalkanoylamino-furazans **1a,b** in the presence of an excess of methylamine, aiming to realize one-pot phototransformations. In a typical experiment, irradiation of compound **1a** in the presence of an excess of methylamine, besides the 3-*N*-methylamino oxadiazole **9a** (42%), allowed us to obtain the 2-*N*-methylamino-1,3,4-oxadiazole **10a** (25%) and the 3-*N*-methylamino-1,2,4-triazole **11** (17%). Similarly, prolonged irradiation of **1b** in the presence of an excess of methylamine gave compounds **9b** (9%), **10b** (49%), and **12** (10%).[23]

(22) For the open-chain compound **23**, one could anticipate different tautomeric hydrogen-bonded structure or ring-chain equilibria. However, this structural aspect has not been developed in this study.

SCHEME 8



This one-pot methodology appears of some interest, particularly when 1,2,4-oxadiazole intermediates, such as trifluoromethylated compounds **29**, are difficult to be isolated. As expected, one-pot irradiation of compound **28** in the presence of an excess of methylamine or propylamine allowed us to isolate the 2-*N*-alkylamino-5-trifluoromethyl-1,3,4-oxadiazoles **30a** (32%) (structure confirmed by X-ray analysis) or **30b** (32%) and 1-alkyl-3-*N*-alkylamino-1,2,4-triazoles **31a** (15%) or **31b** (27%) (Scheme 8). The involvement of the 1,2,4-oxadiazoles **29** as intermediates has been proved by isolating compound **29a** (in low yields, indeed) that irradiated in the same conditions gave **30a** and **31a**.

X-ray Crystallographic Analysis. The X-ray diffraction analysis of the two representative products 1-methyl-3-*N*-methylamino-5-perfluoroheptyl-1,2,4-triazole (**11**) and 2-*N*-methylamino-5-trifluoromethyl-1,3,4-oxadiazole (**30a**) was carried out to assess the conformation of the two compounds and to have information on the crystal packing of these target fluorinated five-membered heterocycles.

Compound **11** may be regarded as consisting of two moieties: the 1-methyl-3-*N*-methylamino-1,2,4-triazole and the perfluoroalkyl chain. The perfluorinated chain displays a "pony-tail" behavior, exhibiting thermal motion or disorder that increases toward the tail end. This disorder is typically found in crystal structures having a perfluoroalkyl chain;[24] however, it is unambiguously found that the alkyl chain adopts a nearly fully extended conformation, with the chain C−C−C−C torsion angles ranging between 163° and 175°.

(23) This observation explains low yields of 3-amino- (or 3-*N*-alkylamino-)1,2,4-oxadiazoles obtained in the irradiation of 3-perfluoroalkanoylamino furazans in the presence of ammonia or aliphatic primary amines (see Scheme 1).[6]

(24) (a) Kromm, P.; Bideau, J. P.; Cotrait, M.; Destrade, C.; Nguyen, H. *Acta Crystallogr.* **1994**, *C50*, 112−115. (b) Jessop, P. G.; Olmstead, M. M.; Ablan, C. D.; Grabenauer, D. S.; Eckert, C. A.; Liotta, C. L. *Inorg. Chem.* **2002**, *41*, 3463−3468. (c) Croxtall, B.; Fawcett, J.; Hope, E. G.; Stuart, A. M. *J. Fluorine Chem.* **2003**, *119*, 65−73.

A systematic search on the crystallographic Cambridge Structural Database (CSD)[25] revealed only two entries with the same moiety [refcodes FECQAF[26a] and LERKEY[26b]]. The hetero-substituted rings of compound **11** and of compound LERKEY are fully planar, whereas the structure FECQAF shows an angle of ca. 24° between the ring plane and the plane defined by the methylamino group. In all the three molecules the N(2) of the triazol ring and the methyl of the methylamino moiety are *syn* with respect to the C(3)−NHMe exocyclic bond. In **11** the plane defined by the nearly all-*anti* alkyl chain is rotated ca. 90° out of the triazole plane. In the crystal, the perfluoroalkyl chains are aligned in a distinct fluorous domain in a packing arrangement observed also for the other fluorinated structures above cited.[24]

The crystal structure of compound **30a** contains two independent molecules in the unit cell. An inspection on the CSD with respect to the molecular moiety of **30a** revealed 3 entries [refcodes QACLAH,[27a] XIHSEM,[27b] and ZAMKUT[27c]]. Molecules of compounds **30a** and XIHSEM are completely planar, with a *syn* conformation of the N(3) of the oxadiazole ring and the methyl of the methylamino moiety with respect to the C(2)−NHMe exocyclic bond. In compound QACLAH, the methylamino plane is rotated of ca. 30° out of the oxadiazole plane. Structure ZAMKUT is nearly planar. The crystal packing of **30a** is characterized by infinite and parallel ribbons of hydrogen-bonded molecules.

Conclusions

As a result of to their peculiar properties, fluorinated 1,3,4-oxadiazoles have recently found their application in several fields.[28] Taking into account our previous work[17] and present results, our photochemical approach offers a way to synthesize 1,3,4-oxadiazoles where the fluorinated group at C(5) can be varied to tune the physicochemical properties of the compound, and the amino group at C(2) can represent an ideal linking group for the functionalization of different structures. The same considerations can be made for fluorinated 1,2,4-triazoles, for which some applications as ionic liquids are recently reported.[29] Interestingly, our representative compound **11** showed in its crystal packing the formation of an oriented fluorous domain whose dimension could potentially be varied by changing the length of the perfluoroalkyl chain. Over all, from a synthetic point of view, this photochemical approach could represent an alterative way to obtain the above fluorinated compounds when nonphotochemical methodologies present some difficulties.

This study has also a significant mechanistic importance as the information gained in this work allows more insight in the photoreactivity of the 1,2,4-oxadiazole heterocycle. We have already described previous reactions as strongly dependent on substituents and experimental conditions; under the light of these new results we can indicate that a 5-perfluoroalkyl group, as well as a 3-amino on one hand and a 3-*N*-alkylamino group on the other, play a decisive role in the different primary photochemical pattern that will subsequently develop, by means of intra- or intermolecular processes, into the final products.

Experimental Section

General Methods and Materials. Melting points were determined with a hot-stage apparatus and are uncorrected. IR spectra were recorded from Nujol mulls or in $CHCl_3$, when indicated. ^{1}H NMR spectra (250 MHz) were taken with TMS as internal standard. Flash chromatography was performed by using mixtures of ethyl acetate and light petroleum (fraction boiling in the range of 40−60 °C) in varying ratios. Freshly prepared saturated methanolic ammonia, ethanolic (33%) methylamine, propylamine, freshly distilled pyrrolidine, and triethylamine (TEA) (99.9%) were used as reagents. Photochemical reactions were carried out in anhydrous methanol in Pyrex vessels, by using a photoreactor, equipped with 16 Hg lamps irradiating at 313 nm (RPR-3000 Å) and a merry-go-round apparatus set up for nine tubes. Pyrex tubes either of 20 or 50 mL capacity were employed. X-ray data were collected on an automatic diffractometer.

Compounds **1a,b**,[6,12] **6a**,[6] **9a,b**,[6] and **24**[6] were obtained as reported. Compound **28** was prepared by a similar procedure, as reported below.

3-Trifluoroacethylamino-4-phenylfurazan (28). To a solution of 3-amino-4-phenylfurazan (2.3 g; 0.014 mol) in anhydrous benzene (400 mL) was added trifluoroacetic anhydride (8 mL; 0.056 mol) diluted in anhydrous benzene (100 mL) dropwise, and then the reaction mixture was stirred at room temperature for 3 h. After removal of the solvent, workup with water and filtration gave 3-trifluoroacetylamino-4-phenylfurazan (**28**) (3.2 g; 93%) mp 80−81 °C (from benzene/light petroleum). IR: 3258, 1726 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.58 (m, 5H), 8.46 (br s, 1H). MS: *m*/*z* 257 (28) (M^+), 188 (10), 161 (100), 104 (70), 69 (50). Anal. Calcd for $C_{10}H_6F_3N_3O_2$: C, 46.70; H, 2.35; N, 16.34. Found: C, 46.80; H, 2.40; N, 16.40.

Irradiation of Oxadiazole 6a in the Presence of Methylamine. To a solution of compound **6a** (10 mg) in methanol (10 mL) purged by nitrogen bubbling was added a 10-fold excess of methylamine, and the mixture was irradiated for 1 h. GC/MS analysis of photolyzate gave starting material and compounds **7a** and **8a**.[17] No evidence indicating incorporation of the methylamine was detected.

General Procedure for Photochemical Reactions. A solution of the 3-alkylamino-5-perfluoroalkyl-1,2,4-oxadiazoles **9a,b** or **24** or the 3-perfluoroalkanoylamino-4-phenyl-furazans **1a,b** or **28** in anhydrous methanol was apportioned into a series of Pyrex tubes and then purged by nitrogen bubbling. Then, a 10-fold excess (unless otherwise indicated) of ethanolic methylamine, methanolic ammonia, pyrrolidine, propylamine, or TEA was added to each tube, and all tubes were irradiated for the time indicated. Concentrations of the substrate and irradiation times were chosen in order to minimize the formation of secondary photoproducts (monitoring the reaction by TLC and GC/MS). After removal of the solvent under reduced pressure, the residue was chromatographed. As neces-

(25) Allen, F. H. *Acta Crystallogr*. **2002**, *B58*, 380−388.
(26) (a) Gyorgydeak, Z.; Holzer, W.; Kunz, R. W.; Linden, A. *Monatsh. Chem*. **1995**, *126*, 733−746. (b) Pohl, M.; Bechstein, U.; Paetzel, M.; Liebscher, J.; Jones, P. G. *J. Prakt. Chem.-Chem.-Zeitung* **1992**, *334*, 630−636.
(27) (a) Zhong, L.; Zhixiang, Z.; Gonghua, S.; Xuhong, Q.; Jie, S. *J. Chem Res*. **1999**, 66. (b) Gomez-Saiz, P.; Garcia-Tojal, J.; Maestro, M. A.; Arnaiz, F. J.; Rojo, T. *Inorg. Chem*. **2002**, *41*, 1345−1347. (c) Wang, X.; Wang, W.; Liu, H. *Acta Crystallogr*. **1995**, *C51*, 1585−1587.
(28) See, for example: (a) Lavrenko, P.; Okatova, O.; Strelina, I.; Bruma, M.; Schulz, B. *Polymer* **2003**, *44*, 2919−2925. (b) Hamciuc, E.; Hamciuc, C.; Sava, I.; Bruma, M. *Eur. Polym. J*. **2001**, *37*, 287−293. (c) Sitzmann, M. E. *J. Fluorine Chem*. **1995**, *70*, 31−38. (d) Cao, S.; Qian, X.; Song, G.; Huang, Q. *J. Fluorine Chem*. **2002**, *117*, 63−66. (e) Zheng, X.; Li, Z.; Wang, Y.; Chen, W.; Huang, Q.; Liu, C.; Song, G. *J. Fluorine Chem*. **2003**, *123*, 163−169.
(29) (a) Mirzaei, Y. R.; Twamley, B.; Shreeve, J. M. *J. Org. Chem*. **2002**, *67*, 9340−9345. (b) Mirzaei, Y. R.; Shreeve, J. M. *Synthesis* **2003**, 24−26. (c) Xue, H.; Twamley, B.; Shreeve, J. M. *J. Org. Chem*. **2004**, *69*, 1397−1400.

sary, elution was carefully monitored by GC/MS. When otherwise not specified, yields reported refer to the isolated products.

Irradiation of Oxadiazole 9a in the Presence of Methylamine. A sample of compound **9a** (0.15 g; 0.3 mmol) in methanol (150 mL) was apportioned into nine Pyrex tubes. An excess of methylamine was added, and the solution was irradiated for 30 min. Chromatography of the residue returned starting material (0.027 g; 20%) and gave 1-methyl-3-*N*-methylamino-5-pentadecafluoroheptyl-1,2,4-triazole (**11**) (0.037 g; 25%) and 2-*N*-methylamino-5-pentadecafluoroheptyl-1,3,4-oxadiazole (**10a**) (0.04 g; 27%). Compound **11** had mp 115−117 °C (from benzene). IR: 3300 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.75 (d, 3H, J = 5.0 Hz), 3.89 (s, 3H), 6.38 (q, 1H, J = 5.0 Hz). MS: m/z 480 (100) (M^+), 452 (25), 410 (19), 161 (73), 119 (28), 69 (30). Anal. Calcd for $C_{11}H_7F_{15}N_4$: C, 27.51; H, 1.47; N, 11.67. Found: C, 27.60; H, 1.60; N, 11.80. Compound **10a** had mp 90−91 °C (from light petroleum). IR: 3240 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.92 (s, 3H), 8.44 (br s, 1H). MS: m/z 468 (40) (M + 1), 448 (10), 100 (3), 91(28), 69 (33), 58 (100). Anal. Calcd for $C_{10}H_4F_{15}N_3O$: C, 25.71; H, 0.86; N, 9.00. Found: C, 25.90; H, 0.90; N, 9.20.

Irradiation of Oxadiazole 9b in the Presence of Methylamine. Irradiation of compound **9b** (0.15 g; 0.6 mmol) in the presence of methylamine as before and chromatography returned starting material (0.023 g; 15%) and gave 1-methyl-3-*N*-methylamino-5-heptafluoropropyl-1,2,4-triazole (**12**) (0.045 g; 27%) and 2-*N*-methylamino-5-heptafluoropropyl-1,3,4-oxadiazole (**10b**) (0.045 g; 28%). Compound **12** had mp 89−91 °C (from light petroleum). IR: 3310 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.69 (d, 3H, J = 5.1 Hz,), 3.82 (t, 3H, J = 1.7 Hz), 6.30 (q, 1H, J = 5.1 Hz). MS: m/z 280 (100) (M^+), 252 (24), 210 (33), 161 (28), 119 (24), 69 (26), 42 (37). Anal. Calcd for $C_7H_7F_7N_4$: C, 30.01; H, 2.52; N, 20.00. Found: C, 30.10; H, 2.60; N, 20.10. Compound **10b** had mp 74−75 °C (from light petroleum). IR: 3220, 3160, 1684 cm^{-1}. IR ($CHCl_3$): 3450, 1640 cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.13 (s, 3H), 5.61 (br s, 1H). MS: m/z 267 (51) (M^+), 169 (9), 148 (38), 119 (12), 69 (42), 58 (100), 42 (45). Anal. Calcd for $C_6H_4F_7N_3O$: C, 26.98; H, 1.51; N, 15.73. Found: C, 27.10; H, 1.60; N, 15.90.

Irradiation of Oxadiazole 9a in the Presence of Ammonia. A sample of compound **9a** (0.25 g; 0.5 mmol) in methanol (250 mL) was apportioned into two series of nine Pyrex tubes. An excess of methanolic ammonia was added, and the solution was irradiated for 1 h. Chromatography of the residue returned starting material (0.025 g; 10%) and gave 3-amino-1-methyl-5-pentadecafluoroheptyl-1,2,4-triazole (**13**) (0.05 g; 24%) and **10a** (0.07 g; 28%). Compound **13** had mp 156 °C (from benzene/light petroleum). IR: 3377, 1647 cm^{-1}. ^1H NMR (DMSO-d_6): δ 3.79 (t, 3H, J_{H-F} = 1.7 Hz), 5.64 (s, 2H). MS: m/z 466 (100) (M^+), 447 (14), 148 (41), 104 (10), 69 (20), 43 (18). Anal. Calcd for $C_{10}H_5F_{15}N_4$: C, 25.77; H, 1.08; N, 12.02. Found: C, 25.90; H, 1.20; N, 12.10.

Irradiation of Oxadiazole 9a in the Presence of Propylamine. A sample of compound **9a** (0.25 g; 0.5 mmol) in methanol (250 mL) was irradiated as described above in the presence of an excess of propylamine. Chromatography of the residue returned starting material (0.048 g; 19%) and gave 1-methyl-3-*N*-propylamino-5-pentadecafluoroheptyl-1,2,4-triazole (**14**) (0.053 g; 21%) and **10a** (0.110 g; 44%). Compound **14** had mp 82−85 °C (from light petroleum). IR: 3315 cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.86 (t, 3H, J = 7.5 Hz), 1.50 (m, 2H), 3.03 (m, 2H), 3.81 (s, 3H), 6.43 (t, 1H, J = 5.8 Hz). MS: m/z 508 (27) (M^+), 480 (100), 162 (10), 70 (29), 43 (18). Anal. Calcd for $C_{13}H_{11}F_{15}N_4$: C, 30.72; H, 2.18; N, 11.02. Found: C, 30.80; H, 2.30; N, 11.10.

Irradiation of Oxadiazole 9a in the Presence of Pyrrolidine. Irradiation of compound **9a** (0.25 g; 0.5 mmol) was performed as described above in the presence of an excess of pyrrolidine, and chromatography returned starting material (0.010 g; 4%) and gave 1-methyl-3-*N*-pyrrolidyl-5-pentadecafluoroheptyl-1,2,4-triazole (**15**) (0.062 g; 23%) and **10a** (0.133 g; 53%). Compound **15** had mp 62−65 °C (from light petroleum). ^1H NMR ($CDCl_3$): δ 1.96 (m, 4H), 3.43 (m, 4H), 3.88 (t, 3H; J_{H-F} = 1.5 Hz). MS: m/z 520 (100) (M^+), 491 (4), 70 (5), 42 (3). Anal. Calcd for $C_{14}H_{11}F_{15}N_4$: C, 32.32; H, 2.13; N, 10.77. Found: C, 32.40; H, 2.20; N, 10.90.

Irradiation of Oxadiazole 9a in the Presence of Triethylamine (TEA). A sample of compound **9a** (0.5 g; 1.0 mmol) in methanol (500 mL) was apportioned into three series of nine Pyrex tubes. An excess of TEA was added, and all of the samples were irradiated for 1 h. Chromatography of the residue returned starting material (0.012 g, 2%) and gave 1-methyl-3-methoxy-5-pentadecafluoroheptyl-1,2,4-triazole (**22a**) (0.165 g 32%) and **10a** (0.175 g; 36%). Compound **22a** had mp 35 °C (from light petroleum). ^1H NMR ($CDCl_3$): δ 3.93 (t, 3H, J_{H-F} = 1.5 Hz), 3.99 (s, 3H). MS: m/z 481 (97) (M^+), 410 (14), 162(100), 105(21), 69(22). Anal. Calcd for $C_{11}H_6F_{15}N_3O$: C, 27.46; H, 1.26; N, 8.73. Found: C, 27.60; H, 1.40; N, 8.80.

Irradiation of Oxadiazole 9b in the Presence of Triethylamine (TEA). A solution of **9b** (0.2 g; 0.8 mmol) in methanol (160 mL) apportioned into nine tubes was irradiated in the presence of an excess of TEA for 1 h; chromatography returned starting material (0.035 g; 17%) and gave 1-methyl-3-methoxy-5-heptafluoropropyl-1,2,4-triazole (**22b**) (0.035 g; 17%) and **10b** (0.075 g; 38%). Compound **22b**, isolated as viscous oil: ^1H NMR ($CDCl_3$) δ 3.93 (t, 3H; J = 1.5 Hz), 3.99 (s, 3H). MS: m/z 281 (100) (M^+), 210 (4), 161 (20), 105 (7), 70 (19), 43 (13). Anal. Calcd for $C_7H_6F_7N_3O$: C, 29.91; H, 2.15; N, 14.95. Found: C, 29.80; H, 2.30; N, 15.10.

Irradiation of Oxadiazole 9a in Methanol. A sample of **9a** (0.2 g; 0.4 mmol) in methanol (160 mL) was apportioned into nine Pyrex tubes and irradiated for 1 h. Chromatography of the residue gave **22a** (0.075 g; 39%) and compound **23** (0.100 g; 50%), mp 49 °C (from light petroleum). IR: 3325, 3200, 1620 cm^{-1}. IR ($CHCl_3$): 3420, 3240, 1730 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.81 (d, 3H, J = 5.3 Hz), 3.72 (s, 3H), 8.20 (br s, 1H), 11.4 (s, 1H). MS: m/z 499 (100) (M^+), 453 (15), 169 (8), 130 (20), 100 (10), 69 (28). Anal. Calcd for $C_{11}H_8F_{15}N_3O_2$: C, 26.47; H, 1.62; N, 8.42. Found: C, 26.60; H, 1.70; N, 8.50.

After refluxing compound **23** in methanol containing hydrochloric acid, GC/MS analysis showed an almost complete conversion of **23** into **10a**.

Irradiation of Oxadiazole 24 in the Presence of Methylamine. A sample of compound **24** (0.20 g; 0.40 mmol) in methanol (160 mL) was irradiated as described above in the presence of an excess of methylamine. Chromatography of the residue returned starting material (0.01 g; 5%) and gave 1-propyl-3-*N*-methylamino-5-pentadecafluoroheptyl-1,2,4-triazole (**25**) (0.044 g; 22%) and the 2-*N*-propylamino-5-pentadecafluoroheptyl-1,3,4-oxadiazole (**26**) (0.10 g; 50%). Compound **25** had mp 70−72 °C (from light petroleum). IR: 3302 cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.85 (t, 3H, J = 7.4 Hz), 1.79 (m, 2H), 2.69 (d, 3H, J = 5.0 Hz), 4.05 (t, 2H, J = 7.0 Hz), 6.34 (q, 1H, J = 5.0 Hz). MS: m/z 509 (100) (M + 1), 466 (16), 141 (15), 58 (13). Anal. Calcd for $C_{13}H_{11}F_{15}N_4$: C, 30.72; H, 2.18; N, 11.02. Found: C, 30.60; H, 2.10; N, 11.10. Compound **26** had mp 73−76 °C (from light petroleum). IR: 3246 cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.92 (t, 3H, J = 7.4 Hz), 1.58 (m, 2H), 3.24 (m, 2H), 8.55 (t, 1H, J = 5.5 Hz). MS: m/z 496 (100) (M + 1), 454 (29), 411 (7), 128 (48), 100 (14), 69 (52), 44(55). Anal. Calcd for $C_{12}H_8F_{15}N_3O$: C, 29.11; H, 1.63; N, 8.49. Found: C, 29.20; H, 1.70; N, 8.60.

Irradiation of Oxadiazole 24 in the Presence of Triethylamine (TEA). Irradiation of compound **24** (0.20 g; 0.40 mmol) in methanol (160 mL) was performed as above in the presence of an excess of TEA and chromatography gave 1-propyl-3-methoxy-5-pentadecafluoroheptyl-1,2,4-triazole (**27**) (0.075 g; 37%), and compound **26** (0.075 g; 36%). Compound **27** was isolated as an oil. ^1H NMR ($CDCl_3$): δ 0.95 (t, 3H, J = 7.4 Hz), 1.93 (m, 2H), 3.99 (s, 3H), 4.11 (t, 2H J = 7.3 Hz). MS: m/z 510 (100) (M + 1), 480 (6), 448 (12), 410 (7), 141 (63), 70 (14), 42 (15). Anal. Calcd for $C_{13}H_{10}F_{15}N_3O$: C, 30.66; H, 1.98; N, 8.25. Found: C, 30.80; H, 1.90; N, 8.40.

Irradiation of Furazan 1a in the Presence of Methylamine. A sample of compound **1a** (0.75 g; 1, 35 mmol) in methanol (450 mL) was apportioned into nine Pyrex tubes. An excess of methylamine was added, and the solution was irradiated for 2 h. The photolyzate was left to stand in the dark for 24 h, and the solvent was removed. Chromatography returned starting material (0.030 g; 4%) and gave 3-*N*-methylamino-5-pentadecafluoroheptyl-1,2,4-oxadiazole **9a** (0.265 g; 42%), mp 59−60 °C (from light petroleum), lit.[6] mp 59−60 °C, and compounds **11** (0.11 g; 17%), and **10a** (0.16 g; 25%).

Irradiation of Furazan 1b in the Presence of Methylamine. A sample of compound **1b** (0.5 g; 1.4 mmol) in methanol (300 mL) was apportioned into seven Pyrex tubes. An excess of methylamine was added, and the solution was irradiated for 3 h. Chromatography gave 3-*N*-methylamino-5-heptafluoropropyl-1,2,4-oxadiazole **9b** (0.032 g; 9%), mp 50−52 °C, lit[6] mp 50−52 °C, and compounds **12** (0.04 g; 10%) and **10b** (0.18 g; 49%).

Irradiation of Furazan 28 in the Presence of Methylamine. A sample of compound **28** (0.5 g; 1.9 mmol) in methanol (400 mL) was apportioned into nine Pyrex tubes. An excess of methylamine was added, and the solution was irradiated for 3 h. Chromatography gave 1-methyl-3-*N*-methylamino-5-trifluoromethyl-1,2,4-triazole **31a** (0.05 g; 15%) and 2-*N*-methylamino-5-trifluoromethyl-1,3,4-oxadiazole **30a** (0.100 g; 32%). Compound **31a** had mp 68−70 °C (from light petroleum). IR: 3304 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.69 (d, 3H, J = 4.9 Hz), 3.81 (s, 3H), 6.22 (q, 1H, J = 4.9 Hz). MS: *m*/*z* 180 (55) (M^+), 161(10), 152 (15), 110 (20), 69 (18), 59 (20), 43 (100). Anal. Calcd for $C_5H_7F_3N_4$: C, 33.34; H, 3.92; N, 31.10. Found: C, 33.40; H, 3.80; N, 31.20. Compound **30a** had mp 102−104 °C (from light petroleum). IR: 3235, 3170, 1680, cm^{-1}; IR ($CHCl_3$): 3450, 1640 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.92 (s, 3H), 8.35 (br s, 1H). MS: *m*/*z* 167 (100) (M^+), 137 (8), 110 (13), 69 (77), 58 (96). Anal. Calcd for $C_4H_4F_3N_3O$: C, 28.75; H, 2.41; N, 25.15. Found: C, 28.90; H, 2.50; N, 25.30.

Irradiation of **28** (0.5 g; 1.9 mmol) in methanol (400 mL) in the presence of an excess of methylamine (molar ratio 3/1) for 1.5 h, followed by a careful workup procedure including standing the photolyzate for 24 h in the dark, careful removal of the solvent, and chromatography allowed to isolate 3-*N*-methylamino-5-trifluoromethyl-1,2,4-oxadiazole **29a** (0.032 g; 10%), together with amounts of starting material and compounds **30a** and **31a**. Analytical determinations of the photolyzate (GC/MS) gave: starting material 20%, **29a** (50%), **30a** (15%), **31a** (15%). Analytical irradiations of **29a** in the presence of methylamine gave **30a** and **31a** (GC/MS). Compound **29a** had mp 37 °C (from light petroleum). IR: 3290, 3120 cm^{-1}. ^1H NMR (DMSO-d_6): δ 2.81 (d, 3H, J = 5 Hz), 7.49 (br s, 1H). MS: *m*/*z* 167 (100) (M^+), 147 (18), 139(20), 95 (22), 69 (95), 55 (48), 42 (85). Anal. Calcd for $C_4H_4F_3N_3O$: C, 28.75; H, 2.41; N, 25.15. Found: C, 28.80; H, 2.30; N, 25.20.

Irradiation of Furazan 28 in the Presence of Propylamine. A sample of compound **28** (0.5 g; 1.9 mmol) in methanol (400 mL) was apportioned into nine Pyrex tubes. An excess of propylamine was added, and the solution was irradiated for 3 h. Chromatography of the residue returned starting material (0.05 g; 10%) and gave 1-propyl-3-*N*-propylamino-5-trifluoromethyl-1,2,4-triazole (**31b**) (0.12 g; 27%) and 2-*N*-propylamino-5-trifluoromethyl-1,3,4-oxadiazole (**30b**) (0.12 g; 32%). Compound **31b** was isolated as an oil. IR: 3320 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.94 (m, 6H), 1.60 (m, 2H), 1.86 (m, 2H), 3.20 (m, 2H), 4.02 (t, 2H, J = 7.3 Hz), 4.35 (br s, 1H). MS: *m*/*z* 236 (21) (M^+), 207 (100), 165 (94), 145 (19), 69 (3), 41 (27). Anal. Calcd for $C_9H_{15}F_3N_4$: C, 45.76; H, 6.40; N, 23.72. Found: C, 45.90; H, 6.50; N, 23.80. Compound **30b** had mp 52 °C (from light petroleum). IR: 3215, 3160, 1670 cm^{-1}. IR-($CHCl_3$) 3440, 1635 cm^{-1}. ^1H NMR ($CDCl_3$): δ 0.99 (t, 3H, J = 7.4 Hz), 1.70 (m, 2H), 3.38 (m, 2H), 6.37 (br s, 1H). MS: *m*/*z* 195 (42) (M^+), 166(71), 153 (100), 137 (68), 126 (79), 118 (51), 69 (92), 41 (89). Anal. Calcd for $C_6H_8F_3N_3O$: C, 36.93; H, 4.13; N, 21.53. Found: C, 36.80; H, 4.20; N, 21.40.

Crystallography. Crystal data for compound **11**: $C_{11}H_7N_4F_{15}$, M_r = 480.2; orthorhombic, space group *Pbca*, a = 11.212(5), b = 10.022(5), c = 30.647(5) Å, V = 3444(2) $Å^3$, Z = 8, D_c = 1.852 g cm^{-3}, F(000) = 1888, μ (Cu Kα) = 2.127 mm^{-1}; colorless crystal (0.5 × 0.6 × 0.7 mm^3). Diffraction data were collected on a diffractometer with graphite monochromated (Cu Kα) radiation (λ = 1.54179 Å), using $\theta/2\theta$ scan technique. Unit cell parameters were determined using 58 reflections in the range 4.9° ≤ θ ≤ 25.3°. A total of 3676 reflections (2840 unique, R_{int} = 0.044) were collected at room temperature in the range 2.88° < θ < 68°. No intensity decay was observed during the data collection. The structure was solved by direct methods (SIR97)[30] and refined by full-matrix least-squares on F2 (SHELXL97)[31] with anisotropic temperature factors for non-H atoms, for 274 parameters. The perfluoroalkyl chain exhibits disorder that increases toward the end of the tail, such that any attempt to split the involved carbon and fluorine atoms into well-defined positions failed. The final stage converged to R = 0.1192 for 1975 observed reflections, with $I \geq 2\sigma(I)$, and R = 0.144 for all unique reflections after merging. The final difference map showed a maximum and a minimum residual peaks of 0.933 and −0.553 e $Å^{-3}$, respectively, near the disordered chain atoms.

Crystal data for compound **30a**: $C_4H_4F_3N_3O$, M_r = 167.1; monoclinic, space group $P2_1/c$, a = 8.703(5), b = 19.702(5), and c = 8.968(4) Å, β = 115.33(5)°, V = 1390(1) $Å^3$, Z = 8, D_c = 1.597 g cm^{-3}, F(000) = 672, μ (Cu Kα) = 1.542 mm^{-1}, colorless crystal (0.4 × 0.5 × 0.8 mm^3). Diffraction data were collected on a diffractometer with graphite monochromated (Cu Kα) radiation (λ = 1.54179 Å), using $\theta/2\theta$ scan technique. Unit cell parameters were determined using 52 reflections in the range 5.8° ≤ θ ≤ 30.1°. Two independent molecules are contained in the unit cell. Under the X-ray beam, the crystal showed considerable degradation and an intensity decay up to 60% was observed in the standard reflections. Therefore, data collection was interrupted at a completeness of 66.8%. and a linear decay correction was applied during data reduction (Siemens, 1994). A total of 2264 reflections (1689 unique, R_{int} = 0.0579) were collected at room temperature in the range 4.48° < θ < 67.9°. Despite the incomplete data collection, the structure was well solved by direct methods (SIR97)[30] and refined by full-matrix least-squares on F2 (SHELXL97).[31] Due to the presence of the two independent molecules in the unit cell and to the uncompleted data collection, the last refinement, with anisotropic temperature factors for non-H atoms, was separately carried out on each molecule. The final stage, for 193 parameters, converged to R = 0.0634 for 1449 observed reflections, with $I \geq 2\sigma(I)$, and R = 0.0695 for all unique reflections after merging. The final difference map showed a maximum and a minimum residual peaks of 0.3431 and −0.296 e $Å^{-3}$, respectively.

Acknowledgment. Financial support from Italian MIUR and University of Palermo within the National Research Project "Fluorinated Compounds: New Materials for Advanced Applications" is gratefully acknowledged.

Supporting Information Available: Full details of the X-ray structures of compounds **11** and **30a**, including ORTEP drawings of the molecules, packing diagrams, complete tables of crystal data, atomic coordinates, bond lengths and angles, torsion angles and anisotropic displacement parameters. This material is available free of charge via the Internet at http://pubs.acs.org.

JO049814E

(30) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G. L.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *SIR97*: A New Tool for Crystal Structure Determination and Refinement. *J. Appl. Cryst.* **1999**, *32*, 115−119.

(31) Sheldrick, G. M. *SHELXL-97*, Release 97-2; University of Göttingen: Germany, 1997.