JOC*Note*

Fluorinated Heterocyclic Compounds. An Effective Strategy for the Synthesis of Fluorinated *Z*-Oximes of 3-Perfluoroalkyl-6-phenyl-2*H*-1,2,4-triazin-5-ones via a Ring-Enlargement Reaction of 3-Benzoyl-5-perfluoroalkyl-1,2,4-oxadiazoles and Hydrazine

Silvestre Buscemi,* Andrea Pace, Antonio Palumbo Piccionello, Gabriella Macaluso, 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

Domenico Spinelli

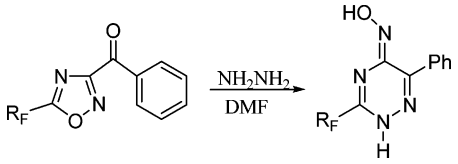
Dipartimento di Chimica Organica "A. Mangini", Università degli Studi di Bologna, Via S. Donato 15, I-40127 Bologna, Italy

Gianluca Giorgi

Dipartimento di Chimica, Università degli Studi di Siena, Via Aldo Moro, I-53100 Siena, Italy

sbuscemi@unipa.it

Received December 21, 2004



The reaction of 3-benzoyl-5-perfluoroalkyl-1,2,4-oxadiazoles with hydrazine has been investigated, evidencing the possibility of competitive reaction paths. Nucleophilic addition of the hydrazine to the electrophilic C(5) of the 1,2,4-oxadiazole ring, followed by ring opening and ring closure with enlargement, leads with high yield and in very mild experimental conditions to the formation of *Z*-oximes of 3-perfluoroalkyl-6-phenyl-2*H*-1,2,4-triazin-5-ones (**11a**−**c**) as major products of the reaction. In turn, the hydrazine can attack the electrophilic carbonyl carbon giving 4-perfluoroacylamino-5-phenyl-2*H*-1,2,3-triazoles (**13a**−**c**) through the well-known Boulton−Katritzky rearrangement of the intermediate hydrazones.

Fluorinated heterocycles represent a class of interesting compounds that find their applications as pharmaceuticals, agrochemicals, and biologically active molecules, and their syntheses represent a research area of growing interest.[1,2] As a general approach, they can be obtained either by direct introduction of fluorine or fluorinated groups or by using a *building block strategy* through heterocyclizations or ring transformations of fluorinated precursors.[1,2]

Among ring-to-ring interconversions, it appears noteworthy to consider processes which can occur *via* addition of a bidentate nucleophile, followed by ring-opening and ring-closure steps (an ANRORC-like pattern).[3] These reactions, which are well documented in the azine series[3,4] due to their large π-deficiency, appear to be less exploited in the case of five-membered ring derivatives.[3,5]

We recently used 5-perfluoroalkyl-1,2,4-oxadiazoles **1** as versatile synthons to realize heterocyclic rearrangements through an ANRORC-pattern exploiting the reaction with some 1,2-dinucleophilic (bidentate) reagents (see Scheme 1).[6,7] The highly electrophilic center C(5) of **1** undergoes the nucleophilic attack, giving **3** and then the open-chain intermediates **4**, whose subsequent heterocyclization involving oximic carbon furnishes **5** which collapses into **2**. The formation of compounds **2** is strictly linked to their high stability that represents the driving-force of the process. In such a way, by using NH_2-NH_2 we pointed out (Scheme 1) an efficient synthesis of the highly aromatic 1,2,4-triazoles **2a**,[6] and in turn, by using NH_2OH, we realized the first example of an irreversible ring-degenerate rearrangement by the attack of an external nucleophile which allowed to transform the same **1** into the thermodynamically more stable 3-perfluoroalkyl-regioisomers **2b**.[7] In these reactions, which appeared of some significance in the synthetic heterocyclic chemistry, the weakly aromatic 1,2,4-oxadiazoles[8,9] containing at C(5) the strongly electron-withdrawing perfluoroalkyl group behave as 1,3-dielectrophilic sub-

(1) *Inter alia*: (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) Hudlicky, M., Pavlath, A. E., Eds. *Chemistry of Organic Fluorine Compounds II. A Critical Review*; 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*, 647−0.671 (c) Silvester, M. J. *Adv. Heterocycl. Chem.* **1994**, *59*, 1−38. (d) Burger, K.; Wucherpfennig, U.; Brunner, E. *Adv. Heterocycl. Chem.* **1994**, *60*, 1−64. (e) Furin, G. G. In *Targets in Heterocyclic Systems*; Attanasi, O. A., Spinelli, D., Eds.; Societa Chimica Italiana: Roma, 1998; Vol. 2, pp 355−441. (f) Zhu, S. Z.; Wang, Y. L.; Peng, W. M.; Song, L. P.; Jin, G. F. *Curr. Org. Chem.* **2002**, *6*, 1057−1096.

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

(4) *Inter alia*, see: (a) Dickinson, R. G.; Jacobsen, N. W. *Aust. J. Chem.* **1975**, *28*, 2435−2446. (b) Rykowski, A.; Wolinska, E. *Tetrahedron Lett.* **1996**, *37*, 5795−5796. (c) Rykowski, A.; Branowska, D. *Heterocycles* **1996**, *43*, 2095−2098. (d) Chupakhin, O. N.; Kozhevnikov, V. N.; Kozhevnikov, D. N.; Rusinov, V. L. *Tetrahedron Lett.* **1999**, *40*, 6099−6100. (e) Chupakhin, O. N.; Kozhevnikov, V. N.; Prokhorov, A. M.; Kozhevnikov, D. N.; Rusinov, V. L. *Tetrahedron Lett.* **2000**, *41*, 7379−7382.

(5) See, for example: (a) Hetzheim, A.; Mockel, K. *Adv. Heterocycl. Chem.* **1966**, *7*, 183−224. (b) Reid, J. R.; Heindel, N. D. *J. Heterocycl. Chem.* **1976**, *13*, 925−926. (c) Sandstrom, J. *Adv. Heterocycl. Chem.* **1968**, *9*, 165−209. (d) Suwinski, J.; Pawlus, W.; Salwinska, E.; Swierczek, K. *Heterocycles* **1994**, *37*, 1511−1520. (e) Reitz, D. B.; Finkes, M. J. *J. Heterocycl. Chem.* **1989**, *26*, 225−230. (e) Reitz, D. B.; Finkes, M. J. *J. Org. Chem.* **1989**, *54*, 1760−1762. (g) Critchley, J. P.; Pippett, J. S. *J. Fluorine Chem.* **1973**, *2*, 137−156.

(6) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N.; Spinelli, D. *J. Org. Chem.* **2003**, *68*, 605−608.

(7) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N.; Lanza, C. Z.; Spinelli, D. *Eur. J. Org. Chem.* **2004**, 974−980.

(8) (a) Bird, C. W. *Tetrahedron* **1985**, *41*, 1409−1414. (b) Bird, C. W. *Tetrahedron* **1992**, *48*, 335−340.

10.1021/jo047766s CCC: $30.25
Published on Web 03/12/2005

SCHEME 1

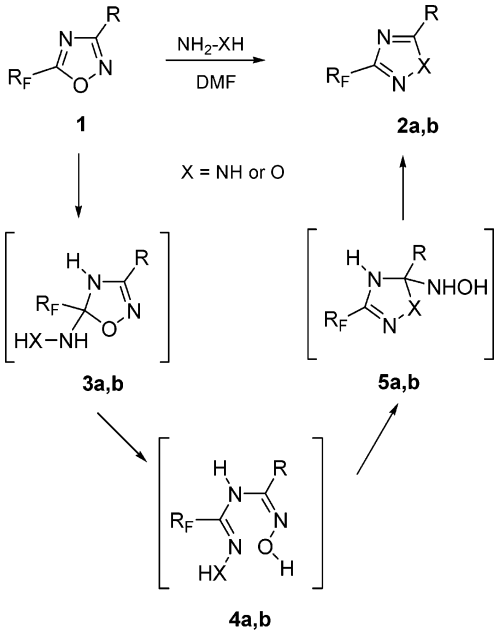
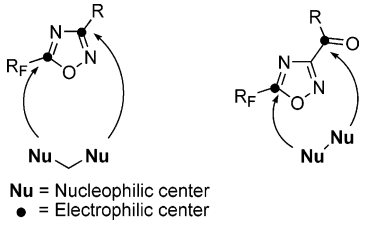


CHART 1



strates [the two electrophilic sites are at the C(5) and C(3) of the starting ring] which is then able to react with 1,2-dinucleophilic reagents (NH_2-NH_2, or NH_2OH) giving rise to new fluorinated five-membered heterocyclic compounds *via* a [3 + 2] heterocyclization process.

On the basis of these considerations, we were induced to exploit this approach for the synthesis of new fluorinated heterocycles containing a six-membered ring. Generally speaking, two strategies may be envisaged (Chart 1): the first (still under investigation) involves a reaction between a 1,3-dinucleophilic reagent and a 1,3-dielectrophilic 1,2,4-oxadiazole (a 3 + 3 heterocyclization); the second envisages a 1,2-dinucleophilic reagent and an oxadiazole containing a 1,4-dielectrophilic moiety (a 2 + 4 heterocyclization). For this purpose we have addressed our attention to a new class of polydentate electrophilic substrates: the 3-acyl-5-perfluoroalkyl-1,2,4-oxadiazoles containing three strong electrophilic centers, that is the C(5) and C(3) carbons of the 1,2,4-oxadiazoles, whose reactivity with bidentate nucleophiles has been already examined, and the carbon of 3-acyl group, whose ability to react with nucleophiles is well documented.[10]

Following this line, one can expect that the reaction of 3-acyl-5-perfluoroalkyl-1,2,4-oxadiazoles with nucleophiles creates the possibility of competition between *different* initial nucleophilic attacks and then toward *different* cyclization patterns.

SCHEME 2

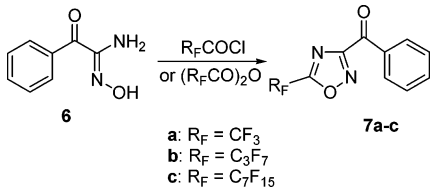


TABLE 1. Product Distribution of the Reaction of 7a-c with Hydrazine

substrate	products (yield, %)	
7a	**11a** (92)	**13a** (5)
7b	**11b** (70)	**13b** (24)
7c	**11c** (65)	**13c** (29)

In this report, we looked at the reaction of 3-benzoyl-5-perfluoroalkyl-1,2,4-oxadiazoles **7a**−**c** with hydrazine investigating the effect of the 5-perfluoroalkyl moiety size in determining the competition between different reaction patterns, presumably furnishing products distribution structure-affected.

Oxadiazoles **7a**−**c** selected for this study have been obtained by the reaction of the amidoxime **6** with corresponding perfluoroalkanoyl chloride or anhydride (Scheme 2), following conventional procedures.[6,7,11] The reaction of compounds **7a**−**c** with hydrazine in DMF at room temperature allowed us to directly isolate two main products, the triazines **11a**−**c** and the triazoles **13a**−**c**[12] (Table 1). The possible triazoles **8a**−**c** deriving from an ANRORC-like process similar to those previously observed in 5-perfluoroalkyl-3-aryl-1,2,4-oxadiazoles[6] (see Schemes 1 and 3) were not obtained.

The structures supposed for **11a**−**c** and **13a**−**c** have been confirmed from analytical and spectroscopic (IR, ^{1}H NMR, GC/MS, and HRMS) data. In the instance of **11a**, the triazine structure has been also confirmed by crystallographic analysis carried out on the O-*p*-bromobenzoyl derivative **15** (Chart 2). X-ray analysis also confirmed the *Z* configuration of the oxime which was expected on the basis of a preservation along the reaction process of the

(9) For aromaticity criteria of five-membered heterocycles, see also: (a) Katritzky, A. R.; Barczynski, P.; Musumarra, G.; Pisano, D.; Szafran, M. *J. Am. Chem. Soc.* **1989**, *111*, 7−15. (b) Katritzky, A. R.; Jug, K.; Oniciu, D. C. *Chem. Rev.* **2001**, *101*, 1421−1449. (c) Bean, P. G. *J. Org. Chem.* **1998**, *63*, 2497−2506. (d) Valavan, A. T.; Oniciu, T. D.; Katritzky, A. R. *Chem. Rev.* **2004**, *104*, 2777−2812.

(10) See, for example: (a) Ruccia, M.; Spinelli, D. *Gazz. Chim. Ital.* **1959**, *89*, 1654−1669. (b) Vivona, N.; Frenna, V.; Buscemi, S.; Ruccia, M. *J. Heterocycl. Chem.* **1985**, *22*, 97−99. (c) Vivona, N.; Buscemi, S.; Frenna, V.; Ruccia, M *J. Chem. Res., Synop.* **1985**, 190; *J. Chem. Res., Miniprint* **1985**, 2184−2197. (d) Vivona, N.; Ruccia, M.; Frenna, V.; Spinelli, D. *J. Heterocycl. Chem.* **1980**, *17*, 401−402. (e) Vivona, N.; Macaluso, G.; Cusmano, G.; Frenna, V. *J. Chem. Soc., Perkin Trans. 1* **1982**, 165−167.

(11) For recent methodologies for synthesizing 1,2,4-oxadiazoles by the amidoxime route, see also: (a) Young, J. R. De Vita, R. J. *Tetrahedron Lett.* **1998**, *39*, 3931−3934. (b) Hébert, N.; Hannah, A. L.; C. Sutton, S. *Tetrahedron Lett.* **1999**, *40*, 8547−8550. (c) Gangloff, A. R.; Litvak, J.; Shelton, E. J.; Sperandio, D.; Wang, V. R.; Rice, K. D. *Tetrahedron Lett.* **2001**, *42*, 1441−1443. (d) Hamzé, A.; Hernandez, J. F.; Fulcrand, P.; Martinez, J. *J. Org. Chem.* **2003**, *68*, 7316−7321. (e) Hamzé, A.; Hernandez, J. F.; Martinez, J. *Tetrahedron Lett.* **2003**, *44*, 6079−6082.

(12) 2*H*-1,2,3-Triazoles are much more stable (that is, aromatic) than 1*H*-1,2,3-triazoles as confirmed by the aromatic index (I_A).[8b] For annular prototropic tautomerism of 1,2,3-triazoles unsubstituted on nitrogen, see: (a) Elguero, J.; Marzin, C.; Katritzky, A. R.; Linda P. *Adv. Heterocycl. Chem. Suppl.* **1976**, 295. (b) Wamhoff, H. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Exeter, 1984; Vol.4, Chapter 11, pp 669ff.

SCHEME 3

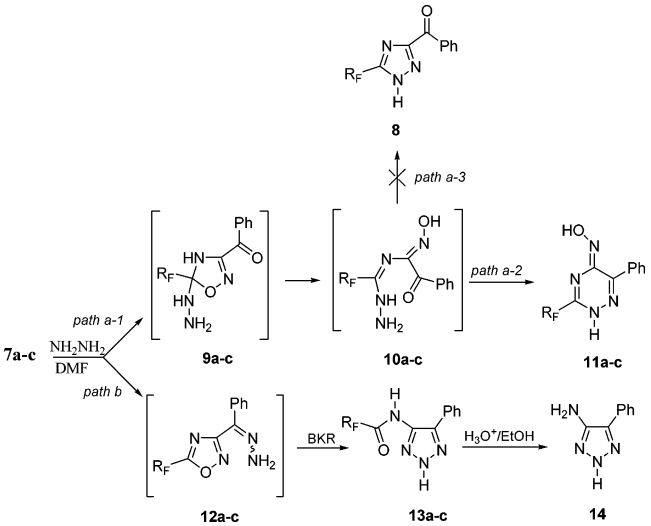
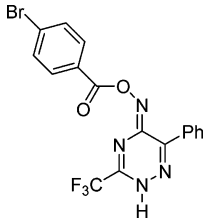


CHART 2



initial configuration present in the oxadiazole ring. Instead, the structure of **13a**−**c** has been confirmed carrying out their acidic hydrolysis which gives the same known triazole **14**.[10a]

The obtained results can be explained on the basis of the occurring competitive reactions shown in Scheme 3. In the first route (path *a*), the initial attack of hydrazine at the electrophilic C(5) followed by the ring-opening (*a-1*) and then by the intramolecular cyclization of the intermediates **10a**−**c** (*a-2*) leads to **11a**−**c** by the involvement of the second nitrogen atom of hydrazine and the carbonyl group. The alternative intramolecular cyclization of **10** involving the second nitrogen atom of the hydrazine and the carbon of the oxime group to give the 1,2,4-triazoles **8** (Scheme 3; path *a-3*) does not occur, indicating that in the competition between the two electrophilic centers in **10** (the carbonyl carbon and the carbon of the oxime group), the nucleophilic heterocyclization concerns only the carbonyl carbon. It should be remarked that the selectivity of the heterocyclization could be affected by the nature (that is, stability) of the reaction products.

The second route (Scheme 3; path *b*) implies the initial nucleophilic attack of the hydrazine to the carbonyl carbon of the side chain giving the hydrazones **12a**−**c** which in turn easily undergo the Boulton−Katritzky rearrangement[13,14] (BKR) to give the 1,2,3-triazoles **14a**−**c**. In the considered case, the use of a dipolar aprotic solvent and the presence of a highly electron-withdrawing group at C(5) strongly accelerate the rearrangement reaction and do not allow the isolation of the hydrazones **12a**−**c**.

The hypothesis that the competition between the two routes *a* and *b* depends on the ease of the initial nucleophilic attack is well supported by the analysis of the results reported in Table 1. The nucleophilic attack of hydrazine to the C(5) is preferred: as a matter of fact, the strong electron-withdrawing 5-perfluoroalkyl group (e.g., for CF_3 σ_I +0.40)[15] makes it a good electrophilic center, but clearly its size affects the reactivity and a long perfluoroalkyl chain slows down such attack and makes significantly competitive the route *b*. In fact, because of a primary steric effect[16] the **11/13** ratios go down from 19.4:1 to 2.9:1 and 2.2:1 as the bulkiness of the perfluoroalkyl group goes up from C_1 to C_3 and C_7, respectively. An analogous primary steric effect was previously observed by examining the reactivity of a series of 5-perfluoroalkyl-3-phenyl-1,2,4-oxadiazoles with hydroxylamine.[7]

On the whole, the obtained results confirm our hypothesis that functionalyzed 5-perfluoroalkyl-1,2,4-oxadiazoles can behave as polydentate electrophiles opening the way to a 2+4 heterocyclization that occurs in very mild experimental conditions with yields from good to excellent of the *Z*-oximes of 3-perfluoroalkyl-6-phenyl-2*H*-1,2,4-triazin-5-ones **11a**−**c**. These compounds could have biological activity[17] and the use of this ANRORC-enlargement approach to obtain similar heterocycles is currently in progress.

Experimental Section

X-ray Crystal Structure Determination of 15. Single crystals of **15** were obtained by dissolving a few milligrams of powder in EtOAc and allowing the solution to concentrate at room temperature. A Siemens P4 four-circle diffractometer with graphite-monochromated MoKα radiation (λ = 0.71073 Å) and the ω scan technique were used for data collections. The structure was solved by direct methods implemented in the SHELXS-97 program.[18] The refinement was carried out by full-matrix anisotropic least-squares methods on F^2 for all reflections for non-H atoms by using the SHELXL-97 program.[19] The final refinement converged to R_1 = 0.067, wR_2 = 0.093 for $I > 2\sigma I$, goodness-of-fit = 1.01. Min max height in last $\Delta\rho$ map of −0.33 and 0.31 e Å^{-3}.

General Methods and Materials. Melting points were determined with a hot-stage apparatus and are uncorrected. IR spectra were recorded from Nujol mulls. ^{1}H NMR spectra (250

(13) (a) Boulton, A. J.; Katritzky, A. R.; Hamid, A. M. *J. Chem. Soc. C* **1967**, 2005−2007. (b) Afridi, A. S.; Katritzky, A. R.; Ramsden, C. A. *J. Chem. Soc., Perkin Trans. 1* **1976**, 315−320. (c) Ruccia, M.; Vivona, N.; Spinelli, D. *Adv. Heterocycl. Chem.* **1981**, *29*, 141−169. (d) L'abbé, G. *J. Heterocycl. Chem.* **1984**, *21*, 627−638. (e) Vivona, N.; Buscemi, S.; Frenna, V.; Cusmano, G. *Adv. Heterocycl. Chem.* **1993**, *56*, 49−154.

(14) For mechanistic studies on azole-to-azole interconversion reactions of the Boulton−Katritzky type, see: Cosimelli, B.; Guernelli, S.; Spinelli, D.; Buscemi, S.; Frenna, V.; Macaluso, G. *J. Org. Chem.* **2001**, *66*, 6124−6129 and references therein for several papers on this series from Spinelli's research group.

(15) Exner, O. *Correlation Analysis of Chemical Data*; Plenum Press: New York and London, 1988.

(16) (a) Shorter, J. In *Advances in Linear Free Energy Relationships*; Chapman, N. B., Shorter, J., Eds.; Plenum Press: London, 1972; Chapter 2. (b) Ingold, C. K. *Structure and Mechanism inOrganic Chemistry*, 2nd ed.; Cornell University Press: Ithaca, 1969; pp 69, 544ff.

(17) Abdel-Rahman, R. M. *Pharmazie* **1999**, *54*, 791−803.

(18) Sheldrick, G. *SHELXS-97, A program for automatic solution of crystal structures*; University of Göttingen: Germany, 1997; Release 97-2.

(19) Sheldrick, G. *SHELXL-97, A program for crystal structure refinement*; University of Göttingen: Germany, 1997; Release 97-2.

MHz) were taken with TMS as internal standard. Flash chromatography (silica gel 0.040−0.063 mesh) was performed by using mixtures of ethyl acetate and light petroleum (fraction boiling in the range of 40−60 °C) in varying ratios.

General Procedure for the Synthesis of 3-Benzoyl-5-perfluoroalkyl-1,2,4-oxadiazoles 7a−c. A mixture of the benzoylamidoxime **6**[20] (1,76 g; 10 mmol), pyridine (0.9 mL; 11 mmol), and the appropriate perfluoroalkanoyl chloride (for compoud **7c**) (4.75 g, 11 mmol) or anhydride (for compounds **7a**,**b**) (11 mmol) in anhydrous toluene (100 mL) was refluxed for 8 h. After removal of the solvent, the residue was treated with water and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography of the residue gave the 1,2,4-oxadiazoles **7a**−**c**.

3-Benzoyl-5-trifluoromethyl-1,2,4-oxadiazole 7a: yield 77%; colorless oil; IR 1685, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52−7.59 (m, 2H), 7.71 (tt, 1H, $J_1 = 7.4$ Hz, $J_2 = 1.3$ Hz), 8.22−8.27 (m, 2H); GC/MS *m/z* 242 (M^+, 15), 145 (25), 105 (100), 77 (41), 69 (11), 51 (23). Anal. Calcd for $C_{10}H_5F_3N_2O_2$: C, 49.60; H, 2.08; N, 11.57. Found: C, 49.50; H, 2.00; N, 11.40.

3-Benzoyl-5-perfluoropropyl-1,2,4-oxadiazole 7b: yield 70%; colorless oil; IR 1685, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.56−7.62 (m, 2H), 7.75 (tt, 1H, $J_1 = 7.4$ Hz, $J_2 = 1.3$ Hz), 8.26−8.29 (m, 2H); GC/MS *m/z* 342 (M^+, 4), 145 (34), 105 (100), 77 (42), 69 (17), 51 (24). Anal. Calcd for $C_{12}H_5F_7N_2O_2$: C, 42.12; H, 1.47; N, 8.19. Found: C, 42.10; H, 1.50; N, 8.20.

3-Benzoyl-5-perfluorohepthyl-1,2,4-oxadiazole 7c: yield 64%; mp 49−50 °C (white crystals, from light petroleum); IR 1675, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61−7.68 (m, 2H), 7.81 (tt, 1H, $J_1 = 7.4$ Hz, $J_2 = 1,3$ Hz), 8.31−8.35 (m, 2H); GC/MS *m/z* 542 (M^+, 2), 145 (30), 105 (100), 77 (43), 69 (22), 51 (21). Anal. Calcd for $C_{15}H_5F_{15}N_2O_2$: C, 33.98; H, 0.95; N, 5.28. Found: C, 33.80; H, 0.90; N, 5.10.

General Procedure for the Hydrazinolysis of 3-Benzoyl-5-perfluoroalkyl-1,2,4-oxadiazoles 7a−c in DMF. To a mixture of the oxadiazole **7** (1 mmol) in dry DMF (2 mL) was slowly added an excess of 99% hydrazine monohydrate (0.15 g, 3 mmol), and the mixture was left at room temperature for 1 h. After dilution with water, the mixture was extracted with EtOAc which was dried over Na_2SO_4 and evaporated and the residue chromatographed.

Hydrazinolysis of the 3-Benzoyl-5-trifluoromethyl-1,2,4-oxadiazole 7a. Chromatography of the residue gave the *Z*-oxime of 3-trifluoromethyl-6-phenyl-2*H*-1,2,4-triazin-5-one **11a** (92%) and the 4-trifluoroacetylamino-5-phenyl-2*H*-1,2,3-triazole **13a** (5%). **11a:** mp 162−163 °C (yellow crystals, from $CHCl_3$); IR 3215, 3120, 3060, 1625 cm^{-1}; ^1H NMR (DMSO) δ 7.42−7.59 (m, 3H), 7.81−7.84 (m, 2H), 10.47 (s, 1H, exch D_2O), 13.25 (s, 1H, exch D_2O); GC/MS *m/z* 256 (M^+, 100), 239 (72), 117 (39), 104 (77), 89 (53), 77 (58), 69 (51); HRMS calcd for $C_{10}H_7F_3N_4O$ 256.05720, found 256.05695. Anal. Calcd for $C_{10}H_7F_3N_4O$: C, 48.68; H, 2.75; N, 21.87. Found: C, 48.50; H, 2.60; N, 21.70. **13a:** mp 164−166 °C (white crystals, from $CHCl_3$); IR 3260, 1720 cm^{-1}; ^1H NMR (DMSO) δ 7.47−7.59 (m, 3H), 7.69−7.72 (m, 2H), 11.76 (s, 1H, exch D_2O), 15.34 (s, 1H, exch D_2O); GC/MS *m/z* 256 (M^+, 100), 187 (78), 177 (22), 132 (23), 104 (41), 77 (50), 69 (53), 50 (29). Anal. Calcd for $C_{10}H_7F_3N_4O$: C, 48.68; H, 2.75; N, 21.87. Found: C, 48.50; H, 2.60; N, 21.70.

Hydrazinolysis of the 3-Benzoyl-5-perfluoropropyl-1,2,4-oxadiazole 7b. Chromatography of the residue gave the *Z*-oxime of 3-perfluoropropyl-6-phenyl-2*H*-1,2,4-triazin-5-one **11b** (70%) and the 4-perfluorobutanoylamino-5-phenyl-2*H*-1,2,3-triazole **13b** (24%). **11b:** mp 140−142 °C (yellow crystals, from $CHCl_3$); IR 3230, 1600 cm^{-1};^1H NMR (DMSO) δ 7.53−7.59 (m, 3H), 7.83−7.86 (m, 2H), 10.45 (s, 1H, exch D_2O), 13.11 (s, 1H, exch D_2O); GC/MS *m/z* 356 (M^+, 100), 340 (56), 117 (69), 104 (69), 89 (58), 77 (46), 69 (76). Anal. Calcd for $C_{12}H_7F_7N_4O$: C, 40.46; H, 1.98; N, 15.73. Found: C, 40.50; H, 1.90; N, 15.60. **13b:** mp 180−181 °C (white crystals, from $CHCl_3$); IR 3260, 1720 cm^{-1}; ^1H NMR (DMSO) δ 7.51−7.68 (m, 5H), 11.80 (s, 1H, exch D_2O), 15.36 (s, 1H, exch D_2O); GC/MS *m/z* 356 (M^+, 100), 187 (57), 169 (12), 132 (30), 104 (45), 83 (89), 77 (46), 69 (40). Anal. Calcd for $C_{12}H_7F_7N_4O$: C, 40.46; H, 1.98; N, 15.73. Found: C, 40.40; H, 1.90; N, 15.60.

Hydrazinolysis of the 3-Benzoyl-5-perfluorohepthyl-1,2,4-oxadiazole 7c. Chromatography of the residue gave the *Z*-oxime of 3-perfluorohephtyl-6-phenyl-2*H*-1,2,4-triazin-5-one (65%) and the 4-perfluorooctanoylamino-5-phenyl-2*H*-1,2,3-triazole (29%). **11c:** mp 155−157 °C (yellow crystals, from $CHCl_3$); IR 3230, 1620 cm^{-1}; ^1H NMR (DMSO) δ 7.50−7.59 (m, 3H), 7.82−7.85 (m, 2H), 10.42 (s, 1H, exch D_2O), 13.01 (s, 1H, exch D_2O); GC/MS *m/z* 540 ($M^+ - 16$, 56), 117 (100), 104 (12), 89 (35), 77 (7), 69 (31). Anal. Calcd for $C_{15}H_7F_{15}N_4O$: C, 33.11; H, 1.30; N, 10.29. Found: C, 33.00; H, 1.20; N, 10.10. **13c:** mp 158−160 °C (white crystals, from $CHCl_3$); IR 3300, 1720 cm^{-1}; ^1H NMR (DMSO) δ 7.50−7.67 (m, 5H), 11.79 (s, 1H, exch D_2O), 15.34 (s, 1H, exch D_2O); GC/MS *m/z* 556 (M^+, 100), 187 (46), 132 (47), 119 (14), 104 (45), 77 (36), 69 (38), 50 (16). Anal. Calcd for $C_{15}H_7F_{15}N_4O$: C, 33.11; H, 1.30; N, 10.29. Found: C, 33.00; H, 1.20; N, 10.20.

Synthesis of the p-Bromobenzoate of the *Z*-Oxime of 3-Trifluoromethyl-6-phenyl-2*H*-1,2,4-triazin-5-one 15. 4-Bromobenzoyl chloride (0.25 g; 1.1 mmol) was slowly added to a mixture of **11a** (0.25 g; 1 mmol) and pyridine (0.09 mL; 1.1 mmol) in anhydrous benzene (20 mL). The solution was stirred for 8 h at rt. After removal of the solvent, the residue was treated with water and then extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and evaporated, giving compound **15** (0.33 g; 76%): mp 212−215 °C (yellow crystals, from $CHCl_3$); ^1H NMR (DMSO) δ 7.62−7.57 (m, 3H), 7.86 (d, 2H, $J = 6.4$ Hz), 7.96 (d, 2H, $J = 6.4$ Hz), 8.12−8.09 (m, 2H); GC/MS *m/z* 441 ($M^+ + 2$, 10), 439 (M^+, 11), 239 (20), 183 (100); IR 3210, 1740 cm^{-1}. Anal. Calcd for $C_{17}H_{10}BrF_3N_4O_2$: C, 46.49; H, 2.29; N, 12.76. Found: C, 46.30; H, 2.10; N, 12.60.

Hydrolysis of 4-Perfluoroacylamino-5-phenyl-2*H*-1,2,3-triazoles 13a−c. To a mixture of 4-perfluoroacylamino-5-phenyl-2*H*-1,2,3-triazoles (1.0 mmol) in ethanol (10 mL) was added hydrochloric acid (0.5 mL). The solution was refluxed for 36 h. After removal of the solvent, the residue was treated with water, neutralized with solid $NaHCO_3$, and extracted with EtOAc. The combined organic layers were dried over Na_2SO_4 and evaporated. Crystallization of the residue from chloroform gave 4-amino-5-phenyl-2*H*-1,2,3-triazole **14** (65−90%): mp 125 °C (lit.[10a] mp 125 °C).

Acknowledgment. Financial support through the Italian MIUR and University of Palermo within the National Research Projects "Fluorinated Compounds: New Materials for Advanced Applications" (PRIN 2001) and "Fluorinated Nanoreactors with Designed Structures and Optimized Functions" (PRIN 2003) is gratefully acknowledged.

Supporting Information Available: Crystallographic data and the ORTEP drawing of compound **15**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO047766S

(20) Daroszewski, J.; Serafin, B.; Borkowska, G.; Rump, S. *Pharmazie* **1986**, *41*, 699−702.