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Trimethylsilyl-1,3,4-oxadiazoles—new useful synthons for the synthesis of various 2,5-disubstituted-1,3,4-oxadiazoles

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ABSTRACT

The reactivity of 2-aryl-5-trimethylsilyl-1,3,4-oxadiazoles toward different types of electrophiles was investigated. These silanes readily react with chlorine, bromine, aliphatic acyl chlorides, 2-nitrobenzenesulfenyl chloride, and some reactive isocyanates affording the corresponding substituted 1,3,4-oxadiazoles. The reactions with carbonyl compounds proceed only in the presence of F^- anions.

1. Introduction

1,3,4-Oxadiazoles[1] have attracted an interest in medicinal chemistry as ester and amide bioisoesters for a number of biological targets.[2] Moreover, these compounds have also demonstrated a broad spectrum of biological properties in both pharmaceutical and agrochemical fields such as antibacterial, anti-inflammatory, antimitotic, antiarrhythmic, and insecticidal activities.[3] Also, 1,3,4-oxadiazole derivatives are among the most widely employed electron-transporting and hole-blocking materials in the development of organic light-emitting diodes (OLEDs) used in energy efficient, full-color, flat-panel displays.[4]

The classical synthetic routes to substituted 1,3,4-oxadiazoles involve ring-forming reactions. Widely used methods are cyclodehydratation of 1,2-diacylhydrazines with various reagents such as thionyl chloride, phosphorus oxychloride, PPA or sulfuric acid;[5] oxidation of *N*-acylhydrazones with different oxidizing agents;[6] and direct reaction of acyl chlorides or carboxylic acids with hydrazine or acid hydrazides.[7] Another convenient method of 1,3,4-oxadiazole synthesis is the thermal recyclization of *N*-acyltetrazoles, which are commonly generated in situ from appropriate *N*-unsubstituted tetrazoles and acyl chlorides.[8] Preparative methods via ring-metalated 1,3,4-oxadiazoles are much less common because of the opening of the heterocycle. Thus, the synthesis of the substituted 1,3,4-oxadiazoles via lithium derivatives was described for the first time only several years ago.[9] Only a few examples of direct electrophilic substitution reactions in 1,3,4-oxadiazole ring is known—acylation,[10] phosphorylation,[11] and silylation.[12] Therefore, the elaboration of new methods for 1,3,4-oxadiazoles functionalization is of interest.

Over the last years, *C*-silyl azoles have gained an increasing importance in heterocyclic chemistry. They provide a convenient alternative to organometallic compounds as they easily enter into electrophilic substitution with a wide range of electrophiles.[13] Thus, commercially available 2-(trimethylsilyl)thiazole is widely used in asymmetric syntheses with chiral aldehydes affording amino hydroxy aldehydes and *C*-glycosyl amino acids—precursors to modified peptides.[14]

Recently, we have developed a new synthetic approach to 2-aryl-5-trimethylsilyl-1,3,4-oxadiazoles via direct silylation of 2-aryl-1,3,4-oxadiazoles with bromotrimethylsilane in the presence of triethylamine.[12] With a ready source of these compounds at hand, their reactivity toward electrophiles was explored and the results are presented in this paper.

2. Results and discussion

2-Phenyl-5-trimethylsilyl-1,3,4-oxadiazole (**1a**) reacted with Cl_2 or Br_2 in hexane at 0 °C for 0.25–1.5 h affording the corresponding 2-halogen-5-phenyl-1,3,4-oxadiazoles **2** and **3**, which precipitated

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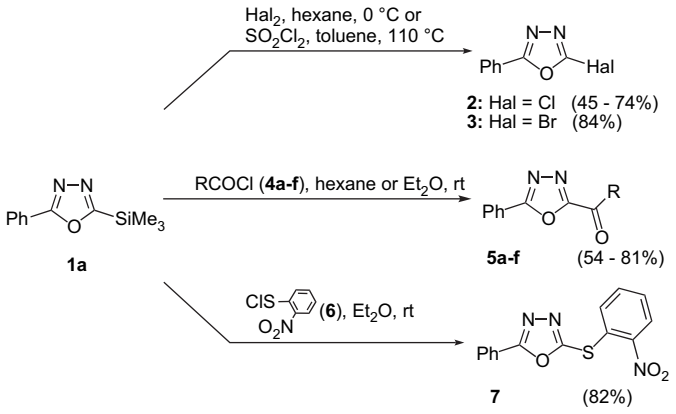
from the reaction mixture and were isolated in good yields (74% and 84%, respectively) (Scheme 1). A simple synthetic procedure makes this method complementary to known synthetic pathways to chloro- and bromosubstituted 1,3,4-oxadiazoles.[15] Sulfuryl chloride could also be employed in the reaction with **1a** but in this case the yield of **2** was lower (45%). Unfortunately, our attempts to use I_2 or ICl in this reaction failed.



Scheme 1.

Treatment of **1a** with acyl chlorides (**4a**–**f**) at ambient temperature gave the corresponding ketones **5a**–**f** in moderate to good yields (Scheme 1, Table 1). Hexane and diethyl ether were found to be the best solvents for running the reaction as ketones **5a**–**f** precipitated from the reaction mixture and byproducts remained in solution. While aliphatic acyl chlorides reacted with **1a** at room temperature, their aromatic counterparts remained intact under these conditions. The reaction of **1a** with cyclopropanecarbonyl chloride (**4b**) was carried out in toluene under reflux to give compound **5b** in moderate yield. When we tried to conduct the reactions of **1a** with aromatic acyl chlorides under such drastic conditions inseparable mixture of products were formed.

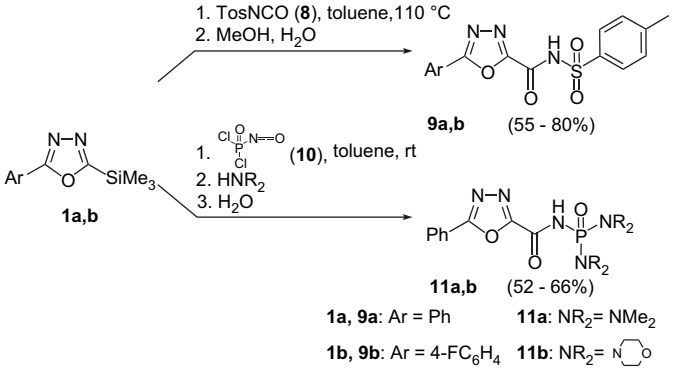
Table 1
Yields of products of the reaction of silane **1a** with acyl chlorides

Entry	Acyl chloride	Product	Solvent	Reaction time (h)	Yield[a] (%)
1	**4a**	**5a**	Hexane	96	61
2	**4b**	**5b**	Toluene[b]	2	57
3	**4c**	**5c**	Et_2O	24	54
4	**4d**	**5d**	Et_2O	96	56
5	**4e**	**5e**	Hexane	18	81
6	**4f**	**5f**	Et_2O	18	67

[a] Isolated yield of analytically pure product.
[b] The reaction was run under reflux.

The reaction of **1a** with 2-nitrobenzenesulfenyl chloride (**6**) in diethyl ether at room temperature for 9 days afforded **7** in 82% yield (Scheme 1). Less reactive tosyl chloride even under drastic conditions (6 h in toluene under reflux) does not enter into the reaction with **1a**.

Then, we tried to introduce heterocumulenes to the reaction with 2-aryl-5-trimethylsilyl-1,3,4-oxadiazoles. Unfortunately, none of the desired products was obtained when acyl and aryl isocyanates or isothiocyanates were employed, even under F^- catalysis. Only such activated isocyanates as tosyl isocyanate (**8**) and isocyanatophosphoryl dichloride (**10**) were found to react with 2-aryl-5-trimethylsilyl-1,3,4-oxadiazoles **1a**,**b**. Thus, tosyl isocyanate (**8**) was cleanly converted into the corresponding sulfonamides **9a**,**b**. These reactions were carried out in toluene under reflux. More reactive isocyanatophosphoryl dichloride (**10**) readily reacted with **1a** at room temperature followed by treatment with dimethylamine or morpholine affording phosphoric triamides **11a**,**b** (Scheme 2).

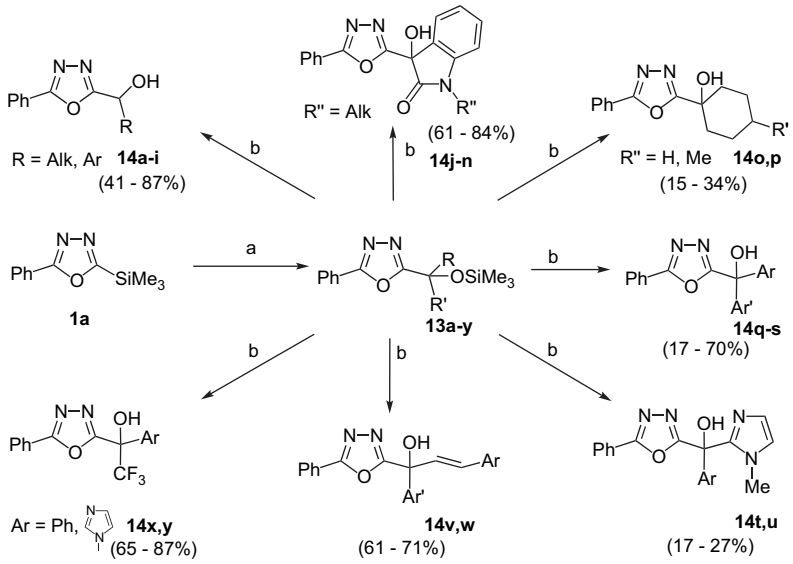


Scheme 2.

In contrast to such silylazoles as 2-trimethylsilylthiazole,[16] 1-alkyl-2-trimethylsilylimidazoles[17] and 2-trimethylsilyl substituted oxazoles,[18] 2-phenyl-5-trimethylsilyl-1,3,4-oxadiazole (**1a**) did not react with carbonyl compounds in the absence of a catalyst, even with an active ones (such as trifluoromethylketones). However, alkyl and aryl aldehydes (**12a**–**i**), isatins (**12j**–**n**), carbocyclic (**12o**,**p**) and diaryl (or aryl-hetaryl) ketones (**12q**–**u**), chalcones (**12v**,**w**), and trifluoromethylkethones (**12x**,**y**) react smoothly with **1a** in the presence of F^- anion to give trimethylsilyl ethers of 1,3,4-oxadiazolylcarbinoles **13a**–**y**, which in most cases were directly converted into the corresponding alcohols **14a**–**y** (Scheme 3, Table 2). KF/dibenzo-18-crown-6 system was used as the F^- anion source. The reaction was carried out in toluene or xylene under reflux. In almost all cases, excess amounts of silane **1a** were required to obtain **14a**–**y** in high yields. It is noteworthy that the treatment of **1a** with chalcones gave only the 1,2-addition products **14v** and **14w**. It was found that trimethylsilyl ethers **13a**–**y** are considerably stable in protic solvents and need F^- catalysis for solvolysis. In one case, the initial trimethylsilyl ether **13a** was isolated and characterized by ^1H and ^{13}C NMR spectroscopy.

3. Conclusion

The reactions of 2-aryl-5-trimethylsilyl-1,3,4-oxadiazoles with different electrophiles, such as chlorine, bromine, aliphatic acyl chlorides, 2-nitrobenzenesulfenyl chloride, isocyanates, and various carbonyl compounds were investigated. It has been found that



Scheme 3. (a) RCOR′ (**12a–y**), KF, DB-18-C-6, toluene or xylene, reflux; (b) MeOH, RbF (5% solution in water), rt.

in most cases the reactions proceed under mild conditions in average to good yields, while the reactions with carbonyl compounds need F^- catalysis. Readily available starting materials and simple synthetic procedures make these methods very attractive and convenient for the synthesis of various 2,5-disubstituted-1,3,4-oxadiazoles.

4. Experimental

4.1. General

All reagents were used as received unless otherwise noted. All reactions were conducted in flame-dried glassware under dry argon. Melting points (mp) were determined with electrothermal capillary melting point apparatus. ^{1}H, ^{19}F, and ^{13}C NMR spectra were recorded on a Varian VXR-300 (300 MHz for ^{1}H, 282 MHz for ^{19}F, and 75 MHz for ^{13}C) spectrometer. Chemical shifts are reported in parts per million (δ) downfield relative to internal standard (tetramethylsilane for ^{1}H and ^{13}C, C_6F_6 for ^{19}F NMR spectra). Abbreviations are as follows: s, singlet; d, doublet; t, triplet; m, multiplet; br s, broad singlet. *J* values are in hertz. IR spectra were recorded on a Nexus-470 spectrometer for samples in KBr disks. Mass spectra were obtained on a 'Hewlett-Packard' HP GS/MS 5890/5972 instrument (EI, 70 eV) by GS inlet, on VG 70–70EQ, VG Analytical (FAB) for substances **9a** and **9b** or a MX-1321 instrument (EI, 70 eV) by direct inlet for all other substances. Microanalyses were performed in the Microanalytical Laboratory of the Institute of Organic Chemistry, National Academy of Sciences of Ukraine. 2-Phenyl-5-trimethylsilyl-1,3,4-oxadiazole (**1a**) and 2-(4-fluorophenyl)-5-trimethylsilyl-1,3,4-oxadiazole (**1b**),[12] isocyanatophosphoryl dichloride.[19] 1-methyl-2-aroylimidazoles,[20] 2,2,2-trifluoro-1-(1-methyl-1*H*-imidazol-2-yl)ethanone,[20] *N*-alkylisatins[21] were prepared according to the literature. Hexane, toluene, xylene, diethyl ether were distilled from P_4O_{10}. KF was dried at 120 °C under high vacuum for 4 h. All acyl chlorides and all liquid aldehydes and ketones were freshly distilled. Yields refer to pure isolated products.

4.2. 2-Chloro-5-phenyl-1,3,4-oxadiazole (2)[15]

Method A. To a cold (0 °C) stirring solution of **1a** (2.18 g, 10 mmol) in hexane (20 mL) was bubbled dry Cl_2 over a period of 15 min. The precipitate formed was filtered and washed with hexane affording **2** (1.338 g, 74%) as colorless crystals.

Method B. To a solution of **1a** (0.980 g, 4.49 mmol) in toluene (5 mL) was added SO_2Cl_2 (0.606 g, 0.36 mL, 4.49 mmol) at room temperature. The reaction mixture warmed up and gas evolution was observed. The reaction mixture was left for 96 h at room temperature and then was heated to reflux for 2 h. The solvent was removed in vacuo and the residue crystallized from heptane and then from aqueous ethanol affording **2** (0.502 g, 45%) as colorless crystals. Mp 77–78 °C. ^{1}H NMR (C_6D_6): δ 7.67 (d, J=7.1 Hz, 2H), 7.03–6.91 (m, 3H). ^{13}C NMR (C_6D_6): δ 166.4, 152.3, 131.9, 129.1, 126.8, 123.6. IR ν_{max} (cm^{-1}): 3065, 1607, 1558, 1510, 1484, 1452, 1293, 1215, 1185, 1090, 1077, 1020, 978, 961, 780, 710, 698, 505. MS *m*/*z* (%): 182 (M^++2, 17), 180 (M^+, 56), 145 (45), 126 (12), 124 (39), 105 (15), 103 (25), 89 (30), 77 (100), 76 (10), 63 (25), 62 (7), 51 (27), 50 (16), 39 (16), 37 (9), 31 (25). Anal. Calcd for $C_8H_5ClN_2O$: C, 53.21; H, 2.79; Cl, 19.63; N, 15.51. Found: C, 53.18; H, 2.80; Cl, 19.58; N, 15.53.

4.3. 2-Bromo-5-phenyl-1,3,4-oxadiazole (3)[15]

A solution of anhydrous Br_2 (3.119 g, 19.5 mmol) in hexane (5 mL) was added dropwise to a stirred solution of **1a** (4.260 g, 19.5 mmol) in hexane (45 mL) at 0 °C. When the addition of Br_2 was complete the reaction mixture was allowed to warm to room temperature and stirred for 1.5 h. The precipitate formed was filtered and washed with hexane affording **3** (3.695 g, 84%) as yellowish solid. For further purification substance **3** could be crystallized from cyclohexane. Mp 104–105 °C. ^{1}H NMR (C_6D_6): δ 7.68 (d, J=6.6 Hz, 2H), 7.02–6.90 (m, 3H). ^{13}C NMR (C_6D_6): δ 167.8, 139.1, 131.9, 129.0, 126.8, 123.6. IR ν_{max} (cm^{-1}): 1610, 1555, 1487, 1449, 1178, 1077, 1038, 1003, 965, 890, 610, 594, 503, 485. MS *m*/*z* (%): 226 (M^++1, 31), 224 (M^+−1, 32), 162 (22), 145 (71), 105 (11), 103 (22), 89 (11), 77 (100), 63 (12), 51 (18). Anal. Calcd for $C_8H_5BrN_2O$: C, 42.70; H, 2.24; Br, 35.51; N, 12.45. Found: C, 42.74; H, 2.31; Br, 35.44; N, 12.48.

4.4. Typical experimental procedure for the reaction of 1a with acyl chlorides 4a–f

To a solution of 2-phenyl-5-trimethylsilyl-1,3,4-oxadiazole **1a** (2.5 mmol) in hexane or Et_2O (5 mL) the corresponding acyl chlorides (2.5 mmol) were added. The reaction mixture was left for the

Table 2
Yields of products of the reaction of silane **1a** with carbonyl compounds

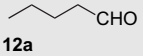
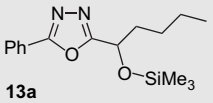
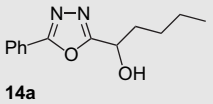
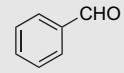
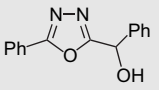
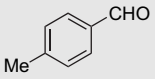
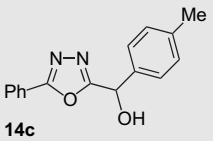
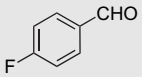
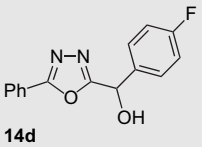
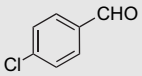
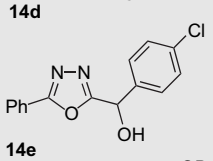
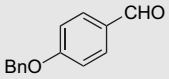
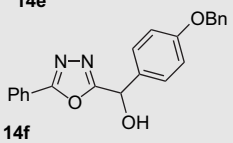
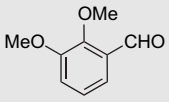
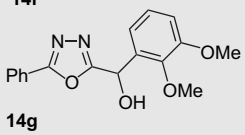
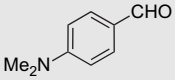
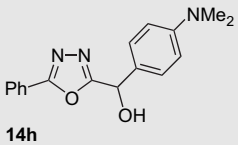
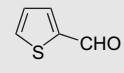
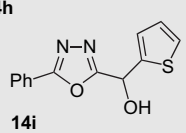
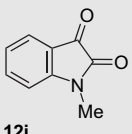
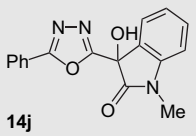
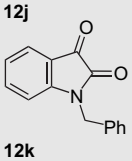
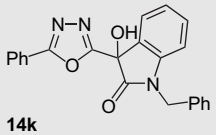
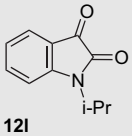
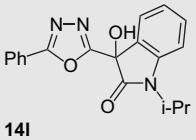
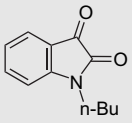
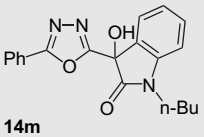
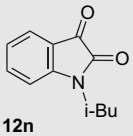
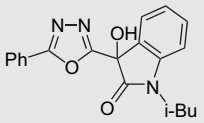
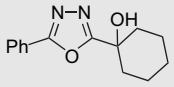
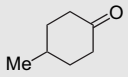
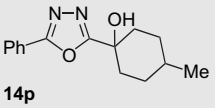
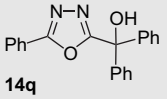
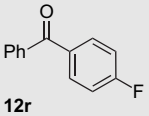
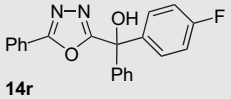
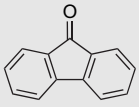
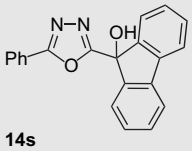
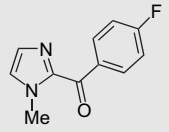
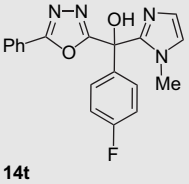
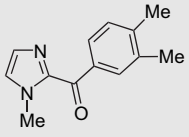
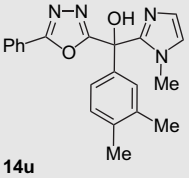
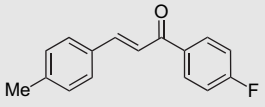
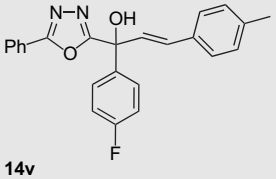
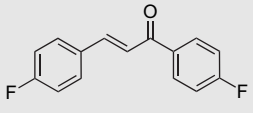
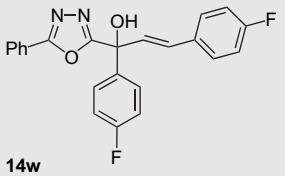
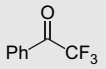
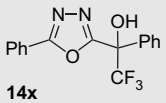
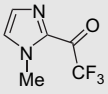
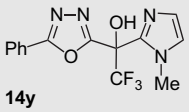
Entry	Carbonyl compound	Product	Mol ratio: **1a**/carbonyl compd/KF/DB-18-C-6	Solvent	Reaction time (h)	Yield[a] (%)
1	 **12a**	 **13a**	1/1/0.1/0.04	Benzene	1	50
		 **14a**		MeOH	5	90
2	 **12b**	 **14b**	1/1/0.1/0.04	Toluene	1.33	60
3	 **12c**	 **14c**	1.2/1/0.1/0.04	Toluene	1	76
4	 **12d**	 **14d**	1/1/0.1/0.02	Toluene	1	64
5	 **12e**	 **14e**	1.2/1/0.1/0.04	Toluene	1	87
6	 **12f**	 **14f**	1.2/1/0.1/0.03	Toluene	1	75
7	 **12g**	 **14g**	1.2/1/0.1/0.04	Toluene	1	71
8	 **12h**	 **14h**	1/1/0.1/0.04	Toluene	1.5	41
9	 **12i**	 **14i**	1.2/1/0.1/0.04	Toluene	1	68
10	 **12j**	 **14j**	1.2/1/0.1/0.04	Toluene	1	72
11	 **12k**	 **14k**	1/1/0.1/0.04	Toluene	3.5	61
12	 **12l**	 **14l**	1.2/1/0.1/0.04	Toluene	1	72

Table 2 (*continued*)

Entry	Carbonyl compound	Product	Mol ratio: **1a**/carbonyl compd/KF/DB-18-C-6	Solvent	Reaction time (h)	Yield[a] (%)
13	 **12m**	 **14m**	1.1/1/0.1/0.04	Toluene	3	84
14	 **12n**	 **14n**	1.2/1/0.1/0.04	Toluene	1	83
15	 **12o**	 **14o**	1/1/0.1/0.04	Toluene	4	34
16	 **12p**	 **14p**	1.1/1/0.1/0.04	Toluene	4.5	15
17	 **12q**	 **14q**	1.5/1/0.1/0.04	Toluene	4	50
18	 **12r**	 **14r**	1/1/0.2/0.04	Toluene	6	17
19	 **12s**	 **14s**	1/1/0.1/0.04	Toluene	5	70
20	 **12t**	 **14t**	1.2/1/0.1/0.04	Xylene	5.5	27
21	 **12u**	 **14u**	1.2/1/0.1/0.04	Xylene	8	17
22	 **12v**	 **14v**	2/1/0.1/0.04	Toluene	1	71
23	 **12w**	 **14w**	2/1/0.1/0.04	Toluene	1	61

(*continued on next page*)

Table 2 (*continued*)

Entry	Carbonyl compound	Product	Mol ratio: **1a**/carbonyl compd/KF/DB-18-C-6	Solvent	Reaction time (h)	Yield[a] (%)
24	 **12x**	 **14x**	1.2/1/0.1/0.04	Toluene	1	87
25	 **12y**	 **14y**	1/1/0.1/0.04	Toluene	1.75	65

[a] Isolated yield of analytically pure product.

time indicated in Table 1 (18–96 h) at room temperature. The precipitated ketone was filtered and washed with hexane.

*4.4.1. 1-(5-Phenyl-1,3,4-oxadiazol-2-yl)ethanone (**5a**)*

Prepared according to Section 4.4. Reaction of **1a** (0.669 g, 3.06 mmol) and acetyl chloride **4a** (0.184 g, 3.06 mmol) in hexane (5 mL) gave 0.350 g (61%) of ketone **5a** as colorless crystals. Mp 81–82 °C. ^{1}H NMR (DMSO-d_6): δ 8.11–8.08 (m, 2H), 7.74–7.62 (m, 3H), 2.70 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 184.3, 165.1, 160.9, 132.8, 129.4, 127.1, 122.5, 27.0. IR ν_{max} (cm^{-1}): 3460 (br), 3412, 3068, 3008, 2924, 1716, 1606, 1541, 1524, 1479, 1450, 1406, 1354, 1296, 1271, 1132, 1097, 1072, 955, 785, 717, 694, 633, 550, 453. MS *m*/*z* (%): 188 (M$^+$, 75), 145 (100), 105 (19), 77 (74), 43 (80). Anal. Calcd for $C_{10}H_8N_2O_2$: C, 63.82; H, 4.28; N, 14.89. Found: C, 63.88; H, 4.35; N, 14.85.

*4.4.2. Cyclopropyl(5-phenyl-1,3,4-oxadiazol-2-yl)methanone (**5b**)*

To a solution of **1a** (1.000 g, 4.58 mmol) in toluene (5 mL) was added cyclopropanecarbonyl chloride **4b** (0.527 g, 5.04 mmol) and the mixture was heated to reflux for 2 h. The solvent was removed in vacuo and the residue was crystallized from MeOH. Yellowish crystals (0.558 g, 57%). Mp 99–100 °C. ^{1}H NMR ($CDCl_3$): δ 8.18 (d, *J*=8.1 Hz, 2H), 7.62–7.53 (m, 3H), 3.18 (m, 1H), 1.43 (m, 2H), 1.26 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 187.4, 166.4, 161.5, 132.9, 129.4, 127.9, 123.0, 19.4, 13.9. IR ν_{max} (cm^{-1}): 3460 (br), 3361, 3086, 3064, 3008, 1778, 1686, 1605, 1539, 1520, 1446, 1410, 1099, 1053, 1024, 991, 972, 958, 727, 714, 688. MS (FAB) *m*/*z* (%): 214 (M$^+$, 67), 186 (23), 185 (17), 145 (58), 105 (39), 104 (15), 103 (46), 77 (64), 69 (100), 55 (43), 51 (14), 41 (81), 39 (42). Anal. Calcd for $C_{12}H_{10}N_2O_2$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.30; H, 4.72; N, 13.03.

*4.4.3. 2-Phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethanone (**5c**)*

Prepared according to Section 4.4. Reaction of **1a** (0.662 g, 3.03 mmol) and phenylacetyl chloride **4c** (0.469 g, 3.03 mmol) in Et_2O (5 mL) gave 0.430 g (54%) of ketone **5c** as colorless crystals. Mp 107–108 °C. ^{1}H NMR ($CDCl_3$): δ 8.16 (d, *J*=8.4 Hz, 2H), 7.63–7.51 (m, 3H), 7.42–7.26 (m, 5H), 4.48 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 184.4, 166.6, 160.8, 132.9, 132.1, 130.0, 129.3, 128.9, 127.8, 127.6, 122.8, 46.3. IR ν_{max} (cm^{-1}): 3415, 3055, 3030, 2902, 1718, 1605, 1541, 1514, 1485, 1452, 1400, 1389, 1342, 1292, 1074, 1041, 1030, 997, 970, 779, 731, 714, 690, 580, 532, 517, 478, 449. MS *m*/*z* (%): 264 (M$^+$, 50), 118 (59), 91 (100), 77 (17), 65 (17). Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.72; H, 4.58; N, 10.60. Found: C, 72.81; H, 4.61; N, 10.52.

Note. In the ^{1}H NMR spectra recorded in DMSO-d_6, a mixture of keto and enolic forms of substance **4c** was observed.

*4.4.4. 3-Phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-1-one (**5d**)*

Prepared according to Section 4.4. Reaction of **1a** (0.546 g, 2.5 mmol) and 3-phenylpropanoyl chloride **4d** (0.423 g, 2.5 mmol) in Et_2O (5 mL) gave 0.388 g (56%) of ketone **5d** as colorless crystals. Mp 94–95 °C. ^{1}H NMR ($CDCl_3$): δ 8.17 (d, *J*=6.9 Hz, 2H), 7.65–7.52 (m, 3H), 7.35–7.19 (m, 5H), 3.56 (t, *J*=7.5 Hz, 2H), 3.14 (t, *J*=7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 186.4, 166.3, 160.8, 139.9, 132.9, 129.2, 128.6, 128.4, 127.7, 126.4, 122.8, 41.3, 29.4. IR ν_{max} (cm^{-1}): 3070, 3035, 2950, 1712, 1605, 1545, 1488, 1453, 1397, 1360, 1300, 1080, 1032, 998, 980, 798, 752, 722, 717, 696, 552, 547, 499, 460. MS *m*/*z* (%): 278 (M$^+$, 2), 251 (17), 250 (100), 249 (27), 173 (16), 131 (10), 105 (29), 104 (63), 103 (47), 91 (59), 77 (33), 65 (10), 51 (13). Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07. Found: C, 73.25; H, 5.03; N, 10.13.

*4.4.5. 2-Phenoxy-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethanone (**5e**)*

Prepared according to Section 4.4. Reaction of **1a** (0.546 g, 2.5 mmol) and phenoxyacetyl chloride **4e** (0.427 g, 2.5 mmol) in hexane (5 mL) gave 0.567 g (81%) of ketone **5e** as colorless crystals. Mp 146–147 °C. ^{1}H NMR ($CDCl_3$): δ 8.19 (d, *J*=7.5 Hz, 2H), 7.63 (distorted t, *J*=7.5 Hz, 1H), 7.56 (distorted t, *J*=7.5 Hz, 2H), 7.35–7.30 (m, 2H), 7.05–6.99 (m, 3H), 5.52 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 181.5, 166.7, 159.2, 157.6, 133.3, 129.8, 129.4, 128.0, 122.5, 122.2, 115.0, 70.4. IR ν_{max} (cm^{-1}): 3445, 3085, 2915, 1725, 1600, 1495, 1450, 1430, 1410, 1367, 1297, 1253, 1182, 1115, 1045, 998, 980, 878, 798, 766, 727, 694, 555, 515, 460. MS *m*/*z* (%): 280 (M$^+$, 37), 251 (10), 145 (14), 119 (17), 107 (26), 105 (37), 79 (11), 77 (100), 56 (27), 51 (16), 32 (31), 31 (39). Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99. Found: C, 68.57; H, 4.32; N, 10.04.

*4.4.6. 2-Chloro-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethanone (**5f**)*

Prepared according to Section 4.4. Reaction of **1a** (2.45 g, 11.2 mmol) and chloroacetyl chloride **4f** (1.27 g, 11.2 mmol) in Et_2O (20 mL) gave 1.678 g (67%) of ketone **5f** as colorless crystals. Mp 121–122 °C. ^{1}H NMR ($CDCl_3$): δ 8.18 (d, *J*=7 Hz, 2H), 7.64 (distorted t, *J*=7.5 Hz, 1H), 7.57 (distorted t, *J*=7 Hz, 2H), 4.95 (s, 2H). ^{13}C NMR ($CDCl_3$): δ 178.3, 166.9, 159.4, 133.3, 129.4, 127.9, 122.3, 46.0. IR ν_{max} (cm^{-1}): 3083, 3015, 2962, 1730, 1607, 1542, 1488, 1453, 1400, 1298, 1258, 1110, 1061, 1038, 982, 799, 755, 722, 695, 535, 458. MS (FAB) *m*/*z* (%): 224 (M$^+$+2, 6), 222 (M$^+$, 22), 145 (100), 105 (11), 103 (11), 77 (55). Anal. Calcd for $C_{10}H_7ClN_2O_2$: C, 53.95; H, 3.17; Cl, 15.92; N, 12.58. Found: C, 53.84; H, 3.14; Cl, 15.98; N, 12.49.

4.5. 2-[(2-Nitrophenyl)thio]-5-phenyl-1,3,4-oxadiazole (7)

To a solution of **1a** (0.658 g, 3.01 mmol) in Et_2O (5 mL) was added 2-nitrobenzenesulfenyl chloride **6** (0.476 g, 2.51 mmol). The reaction mixture was left for 9 days at room temperature. The precipitate formed was filtered affording **7** (0.616 g, 82%) as yellow crystals. Mp 112–113 °C. ^{1}H NMR ($CDCl_3$): δ 8.30 (dd, *J*=8.1, 1.3 Hz, 1H), 8.07 (dd, *J*=8.4, 1.5 Hz, 2H), 7.62–7.43 (m, 5H), 7.36 (d, *J*=8.1 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 167.8, 160.1, 146.2, 134.5, 132.5, 130.3, 129.8, 129.2, 128.0, 127.1, 126.1, 123.0. IR ν_{max} (cm^{-1}): 3454 (br), 3099, 1605, 1591, 1570, 1543, 1525, 1504, 1479, 1448, 1338, 1309, 1153, 1113, 1082, 1068, 1055, 1041, 962, 854, 783, 731, 719, 690, 526. MS *m*/*z* (%): 299 (M$^+$, 15), 146 (10), 145 (98), 105 (86), 103 (14), 77 (100). Anal. Calcd for $C_{14}H_9N_3O_3S$: C, 56.18; H, 3.03; N, 14.04; S, 10.71. Found: C, 56.25; H, 3.07; N, 13.93; S, 10.78.

4.6. 4-Methyl-*N*-[(5-phenyl-1,3,4-oxadiazol-2-yl)-carbonyl]benzenesulfonamide (9a)

To a solution of **1a** (0.630 g, 2.89 mmol) in toluene (5 mL) was added *p*-toluenesulfonyl isocyanate **8** (0.518 g, 2.63 mmol) and the mixture was heated to reflux for 2 h. The solvent was removed in vacuo and the residue was treated with MeOH. The precipitate formed was filtered affording **9a** (0.716 g, 80%) as colorless solid. Mp 214–216 °C. ^{1}H NMR ($CDCl_3$): δ 9.56 (br s, 1H), 8.10–8.06 (m, 4H), 7.63–7.50 (m, 3H), 7.38 (d, J=8.2 Hz, 2H), 2.45 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 165.4, 157.1, 152.0, 144.7, 136.0, 132.8, 129.6, 129.4, 127.9, 127.2, 122.5, 21.1. IR ν_{max} (cm^{-1}): 3442, 3043 (br), 2877, 2724, 1731, 1606, 1540, 1461 (br), 1386, 1348, 1189, 1172, 1130, 1087, 881, 808, 713, 690, 661, 570, 545, 545. MS (FAB) m/z (%): 344 (M^++H, 100), 307 (13), 289 (10), 154 (59), 136 (49), 107 (21), 105 (16), 92 (21), 90 (21), 75 (22). Anal. Calcd for $C_{16}H_{13}N_3O_4S$: C, 55.97; H, 3.82; N, 12.24; S, 9.34. Found: C, 56.11; H, 3.86; N, 12.17; S, 9.23.

4.7. *N*-{[5-(4-Fluorophenyl)-1,3,4-oxadiazol-2-yl]carbonyl}-4-methyl-benzenesulfonamide (9b)

To a solution of **1b** (0.466 g, 1.97 mmol) in toluene (5 mL) was added *p*-toluenesulfonyl isocyanate **8** (0.388 g, 1.97 mmol) and the mixture was heated to reflux for 1 h. The solvent was removed in vacuo and the residue was treated with MeOH. The precipitate formed was filtered and crystallized from MeCN affording **9b** (0.395 g, 55%) as colorless solid. Mp >245 °C. ^{1}H NMR ($CDCl_3$): δ 9.48 (br s, 1H), 8.12 (m, 2H), 8.06 (d, J=8 Hz, 2H), 7.39 (d, J=8 Hz, 2H), 7.24 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 164.6 (d, J_{CF}=251 Hz), 164.5, 157.3, 152.1, 144.6, 136.2, 130.0 (d, J_{CF}=9.4 Hz), 129.5, 127.9, 119.2 (d, J_{CF}=2.9 Hz), 116.8 (d, J_{CF}=22.8 Hz), 21.1. ^{19}F NMR (DMSO-d_6): δ −106.2. IR ν_{max} (cm^{-1}): 3550–3350 (br), 3250, 1736, 1606, 1537, 1493, 1446, 1419, 1383, 1350, 1240, 1227, 1192, 1176, 1161, 1126, 1088, 874, 850, 812, 739, 700, 669, 619, 571, 544, 523. Anal. Calcd for $C_{16}H_{12}FN_3O_4S$: C, 53.18; H, 3.35; N, 11.63; S, 8.87. Found: C, 53.14; H, 3.42; N, 11.71; S, 8.73.

4.8. *N,N,N′,N′*-Tetramethyl-*N″*-[(5-phenyl-1,3,4-oxadiazol-2-yl)carbonyl]-phosphoric triamide (11a)

To a solution of **1a** (0.675 g, 3.09 mmol) in toluene (5 mL) was added isocyanatophosphoryl dichloride **10** (0.495 g, 3.09 mmol) at room temperature. After 1 h the reaction mixture was cooled down to −30 °C and dimethylamine (0.697 g, 15.47 mmol) was added. The resulting mixture was left for 16 h at room temperature. The solvent was removed in vacuo and the residue was treated with water. The precipitate formed was filtered and crystallized from ethyl acetate affording **11a** (0.665 g, 66%) as colorless crystals. Mp 165–167 °C. ^{1}H NMR (DMSO-d_6): δ 9.94 (br s, 1H), 8.14 (d, J=6.6 Hz, 2H), 7.73–7.62 (m, 3H), 2.67 (s, 6H), 2.63 (s, 6H). ^{13}C NMR (DMSO-d_6): δ 165.2, 158.1 (d, J_{CP}=11.7 Hz), 154.4, 132.7, 129.4, 127.2, 122.7, 36.1 (d, J_{CP}=4.3 Hz). ^{31}P NMR (DMSO-d_6): δ 14.3. IR ν_{max} (cm^{-1}): 3473 (br), 3398, 3070, 3059, 2999, 2947, 2885, 2827, 2814, 1705, 1608, 1547, 1481, 1450, 1365, 1304, 1257, 1207, 1173, 1093, 1074, 1028, 997, 964, 858, 816, 783, 769, 715, 694, 661, 634, 546, 511, 476, 426. MS m/z (%): 323 (M^+, 18), 295 (26), 280 (15), 279 (28), 278 (55), 250 (5), 147 (9), 133 (9), 77 (7), 44 (100). Anal. Calcd for $C_{13}H_{18}N_5O_3P$: C, 48.30; H, 5.61; N, 21.66; P, 9.58. Found: C, 48.42; H, 5.63; N, 21.60; P, 9.54.

4.9. *N*-(Dimorpholin-4-ylphosphoryl)-5-phenyl-1,3,4-oxadiazole-2-carboxamide (11b)

To a solution of **1a** (0.675 g, 3.09 mmol) in toluene (5 mL) was added isocyanatophosphoryl dichloride **10** (0.495 g, 3.09 mmol) at room temperature. After 5.5 h the reaction mixture was cooled down to −30 °C and morpholine (1.348 g, 15.47 mmol) was added. The resulting mixture was left for 72 h at room temperature. The solvent was removed in vacuo and the residue was treated with water. The precipitate formed was filtered and crystallized from ethanol affording **11b** (0.658 g, 52%) as colorless crystals. Mp 206–207 °C. ^{1}H NMR (DMSO-d_6): δ 9.99 (br s, 1H), 8.14 (d, J=8.1 Hz, 2H), 7.72–7.61 (m, 3H), 3.57 (t, J=4.5 Hz, 8H), 3.13 (m, 8H). ^{13}C NMR (DMSO-d_6): δ 165.1, 157.9 (d, J_{CP}=12.4 Hz), 154.3, 132.6, 129.3, 127.1, 122.5, 66.2 (d, J_{CP}=5.5 Hz), 44.2. ^{31}P NMR (DMSO-d_6): δ 8.7. IR, ν_{max} (cm^{-1}): 3463 (br), 3396, 3112 (br), 2975, 2958, 2910, 2856, 1704, 1546, 1488, 1436 (br), 1369, 1259, 1207, 1174, 1132, 1112, 1081, 977 (br), 912, 860, 811, 707, 684, 636, 499. MS m/z (%): 407 (M^+, 16), 362 (14), 322 (13), 321 (18), 230 (10), 218 (10), 204 (25), 147 (12), 146 (27), 105 (15), 87 (27), 86 (100), 85 (12), 77 (13), 57 (16), 56 (19), 42 (11). Anal. Calcd for $C_{17}H_{22}N_5O_5P$: C, 50.12; H, 5.44; N, 17.19; P, 7.60. Found: C, 49.93; H, 5.51; N, 17.08; P, 7.72.

4.10. Typical experimental procedures for the reaction of 1a with carbonyl compounds 12a–y

Method A. To a stirred solution of the corresponding carbonyl compound (3.00 mmol) and **1a** (3.00 mmol) in toluene (5 mL) were added KF (0.016 g, 0.30 mmol) and dibenzo-18-crown-6 (0.12 mmol). The mixture was heated to reflux for the time indicated in Table 2 (1–4 h) and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 24 h. In some cases pure product was precipitated. In other cases, solvent was removed in vacuo and the residue was crystallized from an appropriate solvent.

Method B. To a stirred solution of the corresponding carbonyl compound (3.00 mmol) and **1a** (3.60 mmol) in toluene or xylene (5 mL) were added KF (0.016 g, 0.30 mmol) and dibenzo-18-crown-6 (0.12 mmol). The mixture was heated to reflux for the time indicated in Table 2 (1–8 h) and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 24 h. In some cases pure product was precipitated. In other cases, solvent was removed in vacuo and the residue was crystallized from an appropriate solvent.

*4.10.1. 2-Phenyl-5-{1-[(trimethylsilyl)oxy]pentyl}-1,3,4-oxadiazole (**13a**)*

To a stirred solution of valeraldehyde **12a** (0.86 g, 10 mmol) and **1a** (2.18 g, 10 mmol) in benzene (10 mL) were added KF (0.058 g, 1 mmol) and dibenzo-18-crown-6 (0.144 g, 0.4 mmol). The mixture was heated to reflux for 1 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated under reduced pressure. The residue was distilled in vacuo to give **13a** (1.536 g, 50%) as colorless oil. Bp 122–124 °C/0.05 Torr. ^{1}H NMR (C_6D_6): δ 8.03 (d, J=6.6 Hz, 2H), 7.01 (m, 3H), 4.93 (m, 1H), 2.03–1.85 (m, 2H), 1.46–1.19 (m, 4H), 0.81 (t, J=7 Hz, 3H), 0.09 (s, 9H). ^{13}C NMR (C_6D_6): δ 167.5, 165.1, 131.5, 129.2, 127.1, 124.8, 66.8, 35.8, 27.7, 22.7, 14.1, −0.1. ^{29}Si NMR (C_6D_6): δ 20.0. IR ν_{max} (film, cm^{-1}): 3077, 2970 (br), 2881, 1612, 1560, 1489, 1456, 1375, 1262, 1100 (br), 1034, 970, 949, 870 (br), 778, 757, 716, 697, 508. MS (FAB) m/z (%): 304 (M^+, 8), 290 (20), 289 (100), 248 (10), 247 (41), 100 (34), 77 (14), 75 (20), 73 (78). Anal. Calcd for $C_{16}H_{24}N_2O_2Si$: C, 63.12; H, 7.95; N, 9.20. Found: C, 63.31; H, 7.88; N, 9.28.

*4.10.2. 1-(5-Phenyl-1,3,4-oxadiazol-2-yl)pentan-1-ol (**14a**)*

To a solution of **13a** (0.680 g, 2.23 mmol) in methanol (10 mL) was added 5% water solution of RbF (0.5 mL). The reaction mixture

was left for 5 h at room temperature. Solvent was evaporated in vacuo and the residue oil was treated with water. The precipitate formed was filtered affording **14a** (0.466 g, 90%) as colorless solid. Mp 59–60 °C. ^{1}H NMR ($CDCl_3$): δ 8.05 (d, J=6.8 Hz, 2H), 7.56–7.48 (m, 3H), 5.02 (t, J=6.8 Hz, 1H), 3.08 (br s, 1H), 2.02 (m, 2H), 1.55–1.36 (m, 4H), 0.93 (t, J=7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 168.1, 165.1, 131.9, 129.1, 127.1, 123.7, 65.9, 34.9, 27.2, 22.4, 14.0. IR ν_{max} (cm^{-1}): 3500–3000 (br), 2970, 2880, 1565, 1495, 1455, 1395, 1325, 1085, 1040, 1020, 985, 915, 835, 795, 715, 695, 555. MS m/z (%): 232 (M^+, 28), 189 (17), 188 (36), 187 (100), 176 (80), 175 (30), 173 (39), 147 (16), 105 (44), 104 (53), 103 (19), 77 (62), 41 (22), 32 (19), 31 (32). Anal. Calcd for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.13; H, 6.98; N, 12.09.

4.10.3. Phenyl(5-phenyl-1,3,4-oxadiazol-2-yl)methanol (**14b**)

Prepared according to Section 4.10, *Method A*. Reaction of **1a** (0.618 g, 2.83 mmol), benzaldehyde **12b** (0.300 g, 2.83 mmol), KF (0.016 g, 0.28 mmol), and dibenzo-18-crown-6 (0.041 g, 0.11 mmol) in toluene (5 mL) gave 0.428 g (60%) of **14b** as colorless crystals (crystallized from ethyl acetate/cyclohexane). Mp 151–152 °C. ^{1}H NMR (DMSO-d_6): δ 7.96 (d, J=6.5 Hz, 2H), 7.65–7.51 (m, 5H), 7.43–7.31 (m, 3H), 6.81 (d, J=4.6 Hz, 1H), 6.09 (d, J=4.6 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 167.4, 164.2, 139.4, 131.9, 129.3, 128.4, 128.1, 126.5, 126.4, 123.2, 66.6. IR ν_{max} (cm^{-1}): 3442 (br), 1610, 1570, 1552, 1491, 1452, 1213, 1194, 1092, 1065, 1018, 957, 775, 742, 702, 685, 627. MS m/z (%): 253 (M^++H, 14), 252 (M^+, 95), 147 (22), 145 (29), 107 (53), 106 (14), 105 (100), 104 (17), 103 (13), 79 (32), 78 (10), 77 (70), 51 (19). Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.42; H, 4.79; N, 11.10.

4.10.4. (4-Methylphenyl)(5-phenyl-1,3,4-oxadiazol-2-yl)-methanol (**14c**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (3.745 g, 17.15 mmol), *p*-tolualdehyde **12c** (1.717 g, 14.29 mmol), KF (0.083 g, 1.43 mmol), and dibenzo-18-crown-6 (0.206 g, 0.57 mmol) in toluene (20 mL) gave 2.910 g (76%) of **14c** as colorless crystals (crystallized from ethyl acetate/cyclohexane). Mp 125–126 °C. ^{1}H NMR (DMSO-d_6): δ 7.96 (d, J=8.1 Hz, 2H), 7.64–7.56 (m, 3H), 7.42 (d, J=8 Hz, 2H), 7.21 (d, J=8 Hz, 2H), 6.73 (d, J=5 Hz, 1H), 6.05 (d, J=5 Hz, 1H), 2.30 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 167.6, 164.2, 137.4, 136.5, 132.0, 129.4, 129.0, 126.5, 126.4, 123.2, 66.4, 20.7. IR ν_{max} (cm^{-1}): 3435 (br), 3066, 2922, 1608, 1574, 1556, 1514, 1489, 1450, 1267, 1217, 1180, 1084, 1070, 1018, 957, 924, 847, 789, 771, 708, 687, 584, 530, 509. MS m/z (%): 266 (M^+, 100), 147 (14), 121 (54), 119 (57), 105 (40), 93 (22), 91 (32), 77 (57), 65 (10). Anal. Calcd for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.30; H, 5.24; N, 10.38.

4.10.5. (4-Fluorophenyl)(5-phenyl-1,3,4-oxadiazol-2-yl)-methanol (**14d**)

To a stirred solution of 4-fluorobenzaldehyde **12d** (0.618 g, 4.98 mmol) and **1a** (1.088 g, 4.98 mmol) in toluene (5 mL) were added KF (0.029 g, 0.50 mmol) and dibenzo-18-crown-6 (0.036 g, 0.10 mmol). The mixture was heated to reflux for 1 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, ethanol (10 mL) and KF (5% solution in water, 1 mL) were added to the residual oil, and the mixture was allowed to stand for 2 h. The solvent was removed in vacuo and the residue was crystallized from ethanol/cyclohexane affording **14d** (0.864 g, 64%) as colorless crystals. Mp 133–134 °C. ^{1}H NMR (DMSO-d_6): δ 7.97 (d, J=7.6 Hz, 2H), 7.65–7.58 (m, 5H), 7.26–7.22 (m, 2H), 6.84 (d, J=4 Hz, 1H), 6.11 (d, J=4 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 167.3, 164.2, 161.9 (d, J_{CF}=244.1 Hz), 135.6 (d, J_{CF}=2.7 Hz), 132.1, 129.4, 128.7 (d, J_{CF}=8.4 Hz), 126.5, 123.1, 115.2 (d, J_{CF}=21.7 Hz), 65.8. ^{19}F NMR (DMSO-d_6): δ −114.4. IR ν_{max} (cm^{-1}): 3230 (br), 3074, 2895, 1892, 1608, 1552, 1508, 1485, 1450, 1414, 1298, 1255, 1219, 1190, 1157, 1109, 1068, 1011, 976, 860, 849, 783, 734, 708, 690, 579, 525, 496, 469. MS m/z (%): 271 (M^++H, 18), 270 (M^+, 100), 147 (17), 145 (48), 125 (71), 124 (11), 123 (48), 105 (56), 104 (27), 103 (15), 97 (34), 95 (38), 77 (69), 51 (14). Anal. Calcd for $C_{15}H_{11}FN_2O_2$: C, 66.66; H, 4.10; N, 10.37. Found: C, 66.48; H, 3.98; N, 10.25.

4.10.6. (4-Chlorophenyl)(5-phenyl-1,3,4-oxadiazol-2-yl)-methanol (**14e**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.712 g, 3.26 mmol), 4-chlorobenzaldehyde **12e** (0.381 g, 2.72 mmol), KF (0.016 g, 0.27 mmol), and dibenzo-18-crown-6 (0.039 g, 0.11 mmol) in toluene (5 mL) gave 0.680 g (87%) of **14e** as colorless crystals. Mp 167–168 °C. ^{1}H NMR (DMSO-d_6): δ 7.98 (d, J=7.8 Hz, 2H), 7.66–7.56 (m, 5H), 7.49 (d, J=8.4 Hz, 2H), 6.92 (d, J=5.1 Hz, 1H), 6.14 (d, J=5.1 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 167.1, 164.3, 138.3, 132.8, 132.1, 129.4, 128.5, 128.4, 126.5, 123.1, 65.7. IR ν_{max} (cm^{-1}): 3250 (br), 3068, 2906, 1610, 1568, 1552, 1483, 1446, 1406, 1375, 1296, 1254, 1238, 1194, 1169, 1088, 1063, 1012, 976, 849, 783, 748, 710, 687, 540, 499. MS m/z (%): 288 (M^++2, 19), 287 (M^++H, 10), 286 (M^+, 55), 147 (13), 145 (46), 143 (13), 141 (56), 139 (34), 113 (10), 105 (12), 104 (27), 103 (16), 77 (100), 51 (16). Anal. Calcd for $C_{15}H_{11}ClN_2O_2$: C, 62.84; H, 3.87; Cl, 12.37; N, 9.77. Found: C, 62.98; H, 3.95; Cl, 12.24; N, 9.61.

4.10.7. [4-(Benzyloxy)phenyl](5-phenyl-1,3,4-oxadiazol-2-yl)-methanol (**14f**)

To a stirred solution of 4-benzyloxybenzaldehyde **12f** (0.730 g, 3.44 mmol) and **1a** (0.902 g, 4.13 mmol) in toluene (5 mL) were added KF (0.020 g, 0.34 mmol) and dibenzo-18-crown-6 (0.036 g, 0.10 mmol). The mixture was heated to reflux for 1 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, hot methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 2.5 h. The precipitate formed was filtered affording **14f** (0.930 g, 75%) as colorless crystals. Mp 193–194 °C. ^{1}H NMR (DMSO-d_6): δ 7.96 (d, J=8 Hz, 2H), 7.66–7.55 (m, 3H), 7.47–7.29 (m, 7H), 7.04 (d, J=8.7 Hz, 2H), 6.68 (d, J=5 Hz, 1H), 6.02 (d, J=5 Hz, 1H), 5.10 (s, 2H). ^{13}C NMR (DMSO-d_6): δ 167.6, 164.1, 158.2, 137.0, 132.0, 131.7, 129.4, 128.4, 128.0, 127.8, 127.6, 126.5, 123.2, 114.7, 69.2, 66.2. IR ν_{max} (cm^{-1}): 3500–3100 (br), 3061, 3030, 2947, 2891, 1610, 1585, 1568, 1554, 1510, 1485, 1450, 1323, 1304, 1259, 1225, 1204, 1174, 1082, 1011, 957, 849, 796, 775, 741, 708, 696, 687, 638, 615, 588, 544, 517, 438. MS m/z (%): 358 (M^+, 8), 92 (7), 91 (100). Anal. Calcd for $C_{22}H_{18}N_2O_3$: C, 73.73; H, 5.06; N, 7.82. Found: C, 73.92; H, 5.17; N, 7.69.

4.10.8. (2,3-Dimethoxyphenyl)(5-phenyl-1,3,4-oxadiazol-2-yl)-methanol (**14g**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.889 g, 4.07 mmol), 2,3-dimethoxybenzaldehyde **12g** (0.564 g, 3.39 mmol), KF (0.020 g, 0.34 mmol), and dibenzo-18-crown-6 (0.049 g, 0.14 mmol) in toluene (5 mL) gave 0.752 g (71%) of **14g** as colorless crystals (crystallized from 2-propanol). Mp 129–130 °C. ^{1}H NMR (DMSO-d_6): δ 7.97 (d, J=8.1 Hz, 2H), 7.64–7.56 (m, 3H), 7.26 (d, J=8.1 Hz, 1H), 7.16 (t, J=8.1 Hz, 1H), 7.07 (d, J=8.1 Hz, 1H), 6.72 (d, J=5.3 Hz, 1H), 6.25 (d, J=5.3 Hz, 1H), 3.81 (s, 3H), 3.66 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 167.4, 163.9, 152.0, 145.5, 132.8, 131.9, 129.4, 126.4, 124.0, 123.2, 119.0, 112.9, 61.3, 60.1, 55.7. IR ν_{max} (cm^{-1}): 3213 (br), 2995, 2960, 2933, 2831, 1608, 1591, 1560, 1552, 1485, 1450, 1431, 1279, 1261, 1221, 1088, 1051, 1005, 962, 831, 773, 754, 714, 692. MS m/z (%): 312 (M^+, 16), 160 (100), 151 (10), 77 (19). Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.14; H, 5.25; N, 8.81.

4.10.9. [4-(Dimethylamino)phenyl](5-phenyl-1,3,4-oxadiazol-2-yl)-methanol (**14h**)

Prepared according to Section 4.10, *Method A*. Reaction of **1a** (0.564 g, 2.58 mmol), 4-(dimethylamino)benzaldehyde **12h** (0.385 g,

2.58 mmol), KF (0.015 g, 0.26 mmol), and dibenzo-18-crown-6 (0.037 g, 0.10 mmol) in toluene (5 mL) gave 0.310 g (41%) of **14h** as colorless crystals (crystallized from ethyl acetate). Mp 155–157 °C. ^{1}H NMR ($CDCl_3$): δ 7.99 (d, J=7.3 Hz, 2H), 7.51–7.43 (m, 3H), 7.37 (d, J=8.6 Hz, 2H), 6.70 (d, J=8.6 Hz, 2H), 6.02 (s, 1H), 3.62 (s, 1H), 2.94 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 167.2, 165.2, 150.9, 131.7, 128.9, 127.8, 127.0, 125.6, 123.7, 112.4, 68.5, 40.4. IR ν_{max} (cm^{-1}): 3439 (br), 3066, 2920, 2883, 2850, 2800, 1616, 1570, 1556, 1525, 1483, 1450, 1354, 1207, 1186, 1165, 1080, 1070, 1018, 957, 947, 924, 793, 737, 706, 688, 577, 534. MS m/z (%): 296 (M^++H, 15), 295 (M^+, 74), 278 (12), 150 (77), 149 (100), 148 (41), 122 (11), 120 (10), 105 (13), 77 (23). Anal. Calcd for $C_{17}H_{17}N_3O_2$: C, 69.14; H, 5.80; N, 14.23. Found: C, 68.97; H, 5.89; N, 14.13.

4.10.10. (5-Phenyl-1,3,4-oxadiazol-2-yl)(thien-2-yl)methanol (**14i**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.887 g, 4.06 mmol), 2-thiophenecarboxaldehyde **12i** (0.380 g, 3.39 mmol), KF (0.020 g, 0.34 mmol), and dibenzo-18-crown-6 (0.049 g, 0.14 mmol) in toluene (5 mL) gave 0.598 g (68%) of **14i** as yellowish crystals. Mp 152–153 °C. ^{1}H NMR (DMSO-d_6): δ 7.98 (d, J=7 Hz, 2H), 7.66–7.56 (m, 4H), 7.17 (d, J=3.5 Hz, 1H), 7.08 (s, 1H), 7.03 (t, J=3.5 Hz, 1H), 6.37 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 166.7, 164.3, 142.7, 132.2, 129.5, 126.8, 126.6, 126.5, 125.8, 123.1, 62.9. IR ν_{max} (cm^{-1}): 3425 (br), 3105, 3066, 2920, 1606, 1572, 1554, 1481, 1450, 1433, 1346, 1225, 1173, 1086, 1070, 1016, 957, 858, 802, 773, 704, 687, 644. MS m/z (%): 260 (M^++2, 5), 259 (M^++H, 17), 258 (M^+, 97), 145 (34), 113 (100), 112 (17), 111 (44), 104 (20), 103 (20), 85 (33), 51 (12), 45 (21). Anal. Calcd for $C_{13}H_{10}N_2O_2S$: C, 60.45; H, 3.90; N, 10.85; S, 12.41. Found: C, 60.59; H, 3.94; N, 10.71; S, 12.24.

4.10.11. 3-Hydroxy-1-methyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-1,3-dihydro-2H-indol-2-one (**14j**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.655 g, 3.00 mmol), 1-methylisatin **12j** (0.403 g, 2.50 mmol), KF (0.015 g, 0.25 mmol), and dibenzo-18-crown-6 (0.036 g, 0.10 mmol) in toluene (5 mL) gave 0.555 g (72%) of **14j** as colorless crystals (crystallized from 2-propanol). Mp 178–179 °C. ^{1}H NMR (DMSO-d_6): δ 8.01 (d, J=7.5 Hz, 2H), 7.75 (s, 1H), 7.68–7.61 (m, 3H), 7.54 (d, J=7.5 Hz, 1H), 7.45 (t, J=7.5 Hz, 1H), 7.15–7.12 (m, 2H), 3.22 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 172.1, 164.9, 164.5, 143.4, 132.2, 130.8, 129.4, 127.7, 126.7, 125.1, 123.1, 122.9, 109.4, 72.3, 26.4. IR ν_{max} (cm^{-1}): 3448 (br), 3217 (br), 3070, 2931, 1736, 1614, 1556, 1491, 1470, 1373, 1350, 1209, 1119, 1086, 1061, 1016, 922, 764, 756, 692. MS m/z (%): 308 (M^++H, 19), 307 (M^+, 100), 251 (11), 250 (14), 162 (40), 146 (17), 145 (74), 134 (11), 133 (21), 105 (49), 104 (19), 103 (13), 90 (11), 78 (14), 77 (85), 51 (13). Anal. Calcd for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.26; N, 13.67. Found: C, 66.62; H, 4.35; N, 13.53.

4.10.12. 1-Benzyl-3-hydroxy-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-1,3-dihydro-2H-indol-2-one (**14k**)

Prepared according to Section 4.10, *Method A*. Reaction of **1a** (0.782 g, 3.58 mmol), 1-benzylisatin **12k** (0.850 g, 3.58 mmol), KF (0.021 g, 0.36 mmol), and dibenzo-18-crown-6 (0.052 g, 0.14 mmol) in toluene (5 mL) gave 0.840 g (61%) of **14k** as colorless crystals (crystallized from acetonitrile). Mp 184–185 °C. ^{1}H NMR (DMSO-d_6): δ 8.00 (d, J=6.9 Hz, 2H), 7.91 (s, 1H), 7.69–7.62 (m, 3H), 7.55 (d, J=7.1 Hz, 1H), 7.42–7.29 (m, 6H), 7.11 (distorted t, J=7.1 Hz, 1H), 7.02 (d, J=8.1 Hz, 1H), 5.00 (m, 2H). ^{13}C NMR (DMSO-d_6): δ 172.3, 164.7, 164.4, 142.2, 135.7, 132.3, 130.7, 129.4, 128.6, 127.7, 127.5, 127.1, 126.6, 125.1, 123.2, 122.8, 110.0, 72.4, 42.9. IR ν_{max} (cm^{-1}): 3288 (br), 3062, 2926, 1726 (br), 1610, 1552, 1487, 1468, 1450, 1369, 1221, 1178, 1124, 1080, 1057, 920, 758, 694. MS m/z (%): 384 (M^++H, 10), 383 (M^+, 37), 293 (9), 292 (55), 264 (13), 147 (8), 146 (100), 145 (5), 105 (9), 92 (5), 91 (52), 90 (9), 77 (16), 65 (6). Anal. Calcd for $C_{23}H_{17}N_3O_3$: C, 72.05; H, 4.47; N, 10.96. Found: C, 72.31; H, 4.62; N, 10.84.

4.10.13. 3-Hydroxy-1-isopropyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-1,3-dihydro-2H-indol-2-one (**14l**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.815 g, 3.73 mmol), 1-isopropylisatin **12l** (0.588 g, 3.11 mmol), KF (0.018 g, 0.31 mmol), and dibenzo-18-crown-6 (0.045 g, 0.12 mmol) in toluene (5 mL) gave 0.755 g (72%) of **14l** as colorless crystals (crystallized from aqueous ethanol). Mp 185–186 °C. ^{1}H NMR (DMSO-d_6): δ 8.01 (d, J=7.8 Hz, 2H), 7.73 (s, 1H), 7.70–7.59 (m, 3H), 7.54 (d, J=7.5 Hz, 1H), 7.42 (t, J=7.8 Hz, 1H), 7.30 (d, J=7.8 Hz, 1H), 7.12 (t, J=7.5 Hz, 1H), 4.55 (septet, J=7 Hz, 1H), 1.49–1.45 (m, 6H). ^{13}C NMR (DMSO-d_6): δ 171.8, 164.7, 164.5, 142.0, 132.2, 130.6, 129.4, 128.0, 126.6, 125.3, 122.8, 122.6, 110.5, 72.2, 44.0, 18.9, 18.7. IR ν_{max} (cm^{-1}): 3286 (br), 3049, 2966, 2933, 1703 (br), 1610, 1554, 1543, 1489, 1470, 1448, 1383, 1367, 1354, 1325, 1300, 1194, 1115, 1080, 1026, 970, 922, 827, 764, 725, 687, 658, 505. MS m/z (%): 336 (M^++H, 11), 335 (M^+, 53), 293 (15), 292 (28), 264 (15), 147 (10), 146 (100), 145 (12), 119 (12), 105 (35), 90 (12), 77 (27). Anal. Calcd for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53. Found: C, 68.22; H, 5.18; N, 12.31.

4.10.14. 1-Butyl-3-hydroxy-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-1,3-dihydro-2H-indol-2-one (**14m**)

To a stirred solution of 1-butylisatin **12m** (0.525 g, 2.58 mmol) and **1a** (0.620 g, 2.84 mmol) in toluene (5 mL) were added KF (0.015 g, 0.26 mmol) and dibenzo-18-crown-6 (0.037 g, 0.10 mmol). The mixture was heated to reflux for 3 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 24 h. The solvent was removed in vacuo and the residue was crystallized from ethyl acetate/cyclohexane affording **14m** (0.757 g, 84%) as colorless crystals. Mp 155–156 °C. ^{1}H NMR ($CDCl_3$): δ 7.96 (d, J=7.3 Hz, 2H), 7.59 (d, J=7.3 Hz, 1H), 7.49 (distorted t, J=7.3 Hz, 1H), 7.43–7.39 (m, 3H), 7.14 (distorted t, J=7.5 Hz, 1H), 6.93 (d, J=7.9 Hz, 1H), 5.55 (s, 1H), 3.85–3.67 (m, 2H), 1.71 (m, 2H), 1.42 (m, 2H), 0.95 (t, J=7.3 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 172.9, 165.9, 164.1, 143.2, 132.0, 131.2, 128.9, 127.2, 126.7, 125.8, 123.7, 123.4, 109.5, 73.0, 40.4, 29.3, 20.0, 13.7. IR ν_{max} (cm^{-1}): 3396 (br), 3300 (br), 2958, 2931, 2972, 1709 (br), 1612, 1564, 1551, 1487, 1468, 1448, 1383, 1352, 1223, 1188, 1128, 1066, 918, 766, 756, 710, 688. MS m/z (%): 350 (M^++H, 23), 349 (M^+, 100), 292 (16), 148 (21), 146 (71), 145 (61), 132 (39), 119 (16), 105 (64), 104 (12), 90 (14), 77 (71), 41 (16). Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.51; H, 5.59; N, 11.94.

4.10.15. 3-Hydroxy-1-isobutyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)-1,3-dihydro-2H-indol-2-one (**14n**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.784 g, 3.59 mmol), 1-isobutylisatin **12n** (0.608 g, 2.99 mmol), KF (0.017 g, 0.30 mmol), and dibenzo-18-crown-6 (0.043 g, 0.12 mmol) in toluene (5 mL) gave 0.863 g (83%) of **14n** as colorless crystals. Mp 177–178 °C. ^{1}H NMR (DMSO-d_6): δ 8.00 (d, J=7.5 Hz, 2H), 7.81 (s, 1H), 7.69–7.59 (m, 3H), 7.54 (d, J=7.5 Hz, 1H), 7.43 (t, J=7.8 Hz, 1H), 7.20 (d, J=7.8 Hz, 1H), 7.13 (t, J=7.5 Hz, 1H), 3.65–3.49 (m, 2H), 2.16–2.05 (m, 1H), 0.95 (m, 6H). ^{13}C NMR (DMSO-d_6): δ 172.4, 164.7, 164.6, 142.9, 132.2, 130.7, 129.4, 127.6, 126.6, 125.0, 122.9, 122.8, 109.8, 72.3, 46.8, 26.5, 19.8, 19.7. IR ν_{max} (cm^{-1}): 3356 (br), 3298 (br), 3059, 2962, 2937, 2873, 1707 (br), 1612, 1547, 1489, 1468, 1448, 1385, 1356, 1196, 1122, 1059, 1026, 1012, 922, 760, 706, 687, 656, 571, 507, 494. MS m/z (%): 350 (M^++H, 27), 349 (M^+, 83), 293 (18), 250 (30), 148 (23), 147 (18), 146 (68), 145 (55), 133 (14), 132 (93), 105 (89), 104 (20), 103 (17), 90 (18), 78 (11), 77 (100), 57 (16), 51 (12), 41 (28), 39 (13). Anal. Calcd for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03. Found: C, 68.63; H, 5.41; N, 11.91.

4.10.16. 1-(5-Phenyl-1,3,4-oxadiazol-2-yl)cyclohexanol (**14o**)

Prepared according to Section 4.10, *Method A*. Reaction of **1a** (0.930 g, 4.26 mmol), cyclohexanone **12o** (0.418 g, 4.26 mmol), KF

(0.025 g, 0.43 mmol), and dibenzo-18-crown-6 (0.061 g, 0.17 mmol) in toluene (5 mL) gave 0.352 g (34%) of **14o** as colorless crystals (crystallized from ethyl acetate). Mp 137–138 °C. ^{1}H NMR (DMSO-d_6): δ 8.01 (d, J=7.5 Hz, 2H), 7.67–7.57 (m, 3H), 5.74 (s, 1H), 2.11–1.99 (m, 2H), 1.95–1.84 (m, 2H), 1.78–1.65 (m, 2H), 1.53–1.32 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 170.5, 164.7, 131.7, 128.9, 127.0, 123.8, 69.7, 36.1, 25.1, 21.6. IR ν_{max} (cm^{-1}): 3263 (br), 2953, 2935, 2854, 1608, 1562, 1551, 1485, 1452, 1419, 1371, 1354, 1267, 1244, 1159, 1142, 1074, 1043, 982, 974, 926, 852, 785, 741, 710, 690. MS m/z (%): 244 (M^+, 32), 202 (12), 201 (15), 187 (14), 174 (15), 173 (100), 160 (66), 147 (19), 105 (26), 104 (10), 103 (12), 77 (38), 55 (22), 41 (21). Anal. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.71; H, 6.72; N, 11.29.

4.10.17. 4-Methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)-cyclohexanol (**14p**)

To a stirred solution of 4-methylcyclohexanone **12p** (0.390 g, 3.47 mmol) and **1a** (0.834 g, 3.82 mmol) in toluene (5 mL) were added KF (0.020 g, 0.35 mmol) and dibenzo-18-crown-6 (0.050 g, 0.14 mmol). The mixture was heated to reflux for 4.5 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 24 h. The solvent was removed in vacuo and the residue was crystallized from ethyl acetate/cyclohexane affording **14p** (0.132 g, 15%) as colorless crystals. Mp 149–150 °C. ^{1}H NMR (DMSO-d_6): δ 8.00 (d, J=7.5 Hz, 2H), 7.64–7.58 (m, 3H), 5.90 (s, 1H), 2.41 (m, 2H), 1.67 (m, 4H), 1.46 (m, 1H), 0.99 (m, 2H), 0.81 (d, J=6 Hz, 3H). ^{13}C NMR (DMSO-d_6): δ 169.0, 163.7, 131.9, 129.4, 126.4, 123.4, 68.8, 35.9, 31.1, 30.6, 21.2. IR ν_{max} (cm^{-1}): 3294 (br), 2951, 2933, 2862, 1560, 1487, 1450, 1400, 1365, 1342, 1103, 1059, 1018, 1012, 966, 783, 748, 706, 696. MS m/z (%): 258 (M^+, 17), 201 (30), 189 (16), 188 (17), 187 (100), 173 (30), 161 (10), 160 (78), 147 (24), 105 (25), 104 (11), 103 (12), 77 (30), 55 (29), 43 (10), 41 (17). Anal. Calcd for $C_{15}H_{18}N_2O_2$: C, 69.74; H, 7.02; N, 10.84. Found: C, 69.52; H, 7.15; N, 10.63.

4.10.18. Diphenyl(5-phenyl-1,3,4-oxadiazol-2-yl)methanol (**14q**)[22]

To a stirred solution of benzophenone **12q** (0.396 g, 2.17 mmol) and **1a** (0.711 g, 3.26 mmol) in toluene (5 mL) were added KF (0.013 g, 0.22 mmol) and dibenzo-18-crown-6 (0.031 g, 0.09 mmol). The mixture was heated to reflux for 4 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 24 h. The solvent was removed in vacuo and the residue was treated with water affording the crude product as colorless solidified oil. Flash chromatography using ethyl acetate/hexane (1:3) as the eluant afforded the title compound **14q** (0.360 g, 50%) as colorless solid. Mp 153–154 °C. ^{1}H NMR (DMSO-d_6): δ 7.96 (d, J=7.5 Hz, 2H), 7.65–7.58 (m, 3H), 7.43–7.30 (m, 11H). ^{13}C NMR (DMSO-d_6): δ 169.1, 164.3, 143.4, 131.9, 129.3, 127.8, 127.6, 126.5, 126.4, 123.1, 76.1. IR ν_{max} (cm^{-1}): 3433 (br), 3062, 1610, 1560, 1547, 1493, 1448, 1362, 1344, 1234, 1169, 1053, 1009, 891, 779, 760, 750, 741, 698, 690, 634, 530, 472. MS m/z (%): 328 (M^+, 16), 251 (16), 223 (44), 105 (100), 77 (43). Anal. Calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.88; H, 4.85; N, 8.44.

4.10.19. (4-Fluorophenyl)(phenyl)(5-phenyl-1,3,4-oxadiazol-2-yl)methanol (**14r**)

To a stirred solution of 4-fluorobenzophenone **12r** (0.527 g, 2.63 mmol) and **1a** (0.575 g, 2.63 mmol) in toluene (7 mL) were added KF (0.030 g, 0.52 mmol) and dibenzo-18-crown-6 (0.038 g, 0.11 mmol). The mixture was heated to reflux for 6 h and then the solvent was removed in vacuo. Methanol (20 mL) and NaF (5% solution in water, 0.5 mL) were added to the residual oil and the mixture was allowed to stand for 24 h. The solvent was removed in vacuo and the residue was treated with water. Resulted solidified oil was crystallized from ethanol affording **14r** (0.155 g, 17%) as colorless crystals. Mp 143–144 °C. ^{1}H NMR (DMSO-d_6): δ 7.97 (d, J=7.2 Hz, 2H), 7.65–7.58 (m, 4H), 7.49–7.32 (m, 7H), 7.21 (t, J=8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ 168.9, 165.7, 162.7 (d, J_{CF}=248 Hz), 142.3, 138.2 (d, J_{CF}=3.2 Hz), 132.1, 129.3, 129.2, 129.1, 128.7, 128.6, 127.1 (d, J_{CF}=4.9 Hz), 123.4, 115.3 (d, J_{CF}=22 Hz), 77.2. ^{19}F NMR (DMSO-d_6): δ −115.1. IR ν_{max} (cm^{-1}): 3236 (br), 3061, 1605, 1556, 1508, 1491, 1450, 1363, 1227, 1223, 1180, 1159, 1086, 1065, 1016, 895, 825, 812, 779, 754, 708, 688, 663, 582, 534, 496. MS m/z (%): 346 (M^+, 22), 269 (11), 241 (20), 223 (23), 213 (8), 200 (19), 146 (10), 123 (97), 105 (100), 95 (32), 77 (60), 51 (16). Anal. Calcd for $C_{21}H_{15}FN_2O_2$: C, 72.82; H, 4.37; N, 8.09. Found: C, 72.69; H, 4.43; N, 8.18.

4.10.20. 9-(5-Phenyl-1,3,4-oxadiazol-2-yl)-9H-fluoren-9-ol (**14s**)

Prepared according to Section 4.10, *Method A*. Reaction of **1a** (0.923 g, 4.23 mmol), 9-fluorenone **12s** (0.762 g, 4.23 mmol), KF (0.025 g, 0.42 mmol), and dibenzo-18-crown-6 (0.061 g, 0.17 mmol) in toluene (5 mL) gave 0.970 g (70%) of **14s** as colorless crystals. Mp 217–218 °C. ^{1}H NMR (DMSO-d_6): δ 8.03 (d, J=8.1 Hz, 2H), 7.87 (d, J=7.5 Hz, 2H), 7.81 (d, J=7.2 Hz, 2H), 7.68–7.59 (m, 3H), 7.50 (t, J=7.5 Hz, 2H), 7.41 (t, J=7.2 Hz, 2H), 7.27 (s, 1H). ^{13}C NMR (DMSO-d_6): δ 167.3, 164.5, 145.0, 139.2, 131.9, 129.7, 129.3, 128.0, 126.4, 125.5, 123.0, 120.2, 77.3. IR ν_{max} (cm^{-1}): 3247 (br), 3054, 2811, 1606, 1556, 1540, 1483, 1450, 1415, 1191, 1103, 1062, 1016, 960, 921, 771, 736, 725, 707, 696, 690, 588, 424. MS m/z (%): 326 (M^+, 73), 195 (9), 181 (100), 152 (42), 145 (27), 105 (26), 77 (35), 51 (6). Anal. Calcd for $C_{21}H_{14}N_2O_2$: C, 77.29; H, 4.32; N, 8.58. Found: C, 77.21; H, 4.38; N, 8.45.

4.10.21. (4-Fluorophenyl)(1-methyl-1H-imidazol-2-yl)(5-phenyl-1,3,4-oxadiazol-2-yl)methanol (**14t**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.689 g, 3.16 mmol), (4-fluorophenyl)(1-methyl-1*H*-imidazol-2-yl)methanone **12t** (0.537 g, 2.63 mmol), KF (0.015 g, 0.26 mmol), and dibenzo-18-crown-6 (0.038 g, 0.11 mmol) in xylene (5 mL) gave 0.303 g (27%) of **14t** as colorless crystals (crystallized from acetonitrile). Mp 212–213 °C. ^{1}H NMR (DMSO-d_6): δ 8.03–7.96 (m, 3H), 7.65–7.60 (m, 3H), 7.39 (m, 2H), 7.27–7.20 (m, 3H), 6.80 (s, 1H), 3.39 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 168.0, 164.5, 161.8 (d, J_{CF}=244.7 Hz), 146.3, 136.0 (d, J_{CF}=3.2 Hz), 132.0, 129.4, 128.5 (d, J_{CF}=8.3 Hz), 126.4, 125.8, 123.9, 123.2, 114.8 (d, J_{CF}=21.5 Hz), 73.2, 33.6 (d, J=1.8 Hz). ^{19}F NMR (DMSO-d_6): δ −114.6. IR ν_{max} (cm^{-1}): 3442 (br), 2920 (br), 2698 (br), 1605, 1549, 1508, 1487, 1448, 1410, 1356, 1286, 1225, 1178, 1161, 1080, 1020, 914, 904, 835, 781, 764, 733, 712, 704, 696, 687, 596, 559, 526, 478. MS m/z (%): 351 (M^++H, 11), 350 (M^+, 54), 255 (13), 205 (25), 204 (34), 203 (80), 189 (10), 188 (88), 187 (100), 176 (32), 175 (72), 146 (52), 124 (19), 123 (92), 109 (49), 105 (41), 103 (15), 95 (68), 90 (15), 82 (15), 77 (40), 75 (15), 51 (11), 42 (9). Anal. Calcd for $C_{19}H_{15}FN_4O_2$: C, 65.14; H, 4.32; N, 15.99. Found: C, 64.89; H, 4.18; N, 16.11.

4.10.22. (3,4-Dimethylphenyl)(1-methyl-1H-imidazol-2-yl)-(5-phenyl-1,3,4-oxadiazol-2-yl)methanol (**14u**)

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (0.737 g, 3.38 mmol), (3,4-dimethylphenyl)(1-methyl-1*H*-imidazol-2-yl)methanone **12u** (0.602 g, 2.81 mmol), KF (0.016 g, 0.28 mmol), and dibenzo-18-crown-6 (0.041 g, 0.11 mmol) in xylene (5 mL) gave 0.171 g (17%) of **14u** as colorless crystals (crystallized from ethyl acetate). Mp 193–194 °C. ^{1}H NMR (DMSO-d_6): δ 7.95 (d, J=6.5 Hz, 2H), 7.76 (s, 1H), 7.66–7.57 (m, 3H), 7.16 (m, 3H), 7.01 (d, J=7.8 Hz, 1H), 6.77 (s, 1H), 3.36 (s, 3H), 2.23 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 168.4, 164.3, 146.7, 137.3, 136.1, 135.7, 131.9, 129.4, 129.1, 127.2, 126.4, 125.6, 123.7, 123.6, 123.3, 73.4, 33.6, 19.6, 19.0. IR ν_{max} (cm^{-1}): 3439 (br), 3059 (br), 2760 (br), 1558, 1549,

1487, 1450, 1389, 1362, 1284, 1201, 1144, 1124, 1068, 1020, 908, 876, 841, 818, 769, 706, 692. MS *m*/*z* (%): 361 (M^++H, 18), 360 (M^+, 75), 255 (37), 215 (15), 214 (24), 213 (43), 199 (11), 198 (45), 197 (12), 186 (23), 185 (36), 184 (14), 183 (100), 146 (20), 133 (39), 124 (12), 109 (38), 105 (50), 103 (16), 79 (14), 77 (35). Anal. Calcd for $C_{21}H_{20}N_4O_2$: C, 69.98; H, 5.59; N, 15.54. Found: C, 70.11; H, 5.51; N, 15.38.

*4.10.23. (2E)-1-(4-Fluorophenyl)-3-(4-methylphenyl)-1-(5-phenyl-1,3,4-oxadiazol-2-yl)prop-2-en-1-ol (**14v**)*

To a stirred solution of (2*E*)-1-(4-fluorophenyl)-3-(4-methylphenyl)prop-2-en-1-one **12v** (0.462 g, 1.92 mmol) and **1a** (0.840 g, 3.85 mmol) in toluene (5 mL) were added KF (0.011 g, 0.19 mmol) and dibenzo-18-crown-6 (0.028 g, 0.08 mmol). The mixture was heated to reflux for 1 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 72 h. The precipitate formed was filtered affording **14v** (0.530 g, 71%) as colorless crystals. Mp 161–162 °C. ^{1}H NMR (DMSO-d_6): δ 7.97 (d, J=8.3 Hz, 2H), 7.64–7.56 (m, 5H), 7.42 (d, J=7.8 Hz, 2H), 7.27–7.21 (m, 3H), 7.16 (d, J=7.8 Hz, 2H), 6.99 (d, J=16 Hz, 1H), 6.71 (d, J=16 Hz, 1H), 2.29 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 168.7, 164.5, 161.7 (d, J_{CF}=244.3 Hz), 138.5 (d, J_{CF}=3.1 Hz), 137.5, 133.0, 132.1, 130.5, 129.4, 129.3, 129.0, 128.1 (d, J_{CF}=8.3 Hz), 126.8, 126.6, 123.2, 115.1 (d, J_{CF}=21.4 Hz), 73.5, 20.8. ^{19}F NMR (DMSO-d_6): δ −115.2. IR ν_{max} (cm^{-1}): 3282 (br), 1605, 1545, 1508, 1485, 1450, 1227, 1161, 1082, 1038, 1009, 976, 918, 841, 816, 748, 708, 685, 548, 530, 505. MS *m*/*z* (%): 387 (M^++H, 10), 386 (M^+, 41), 358 (12), 263 (10), 241 (11), 240 (32), 239 (37), 225 (57), 213 (11), 212 (48), 197 (14), 145 (41), 136 (21), 132 (20), 120 (20), 119 (14), 117 (24), 115 (28), 105 (100), 104 (12), 103 (37), 95 (52), 92 (22), 91 (26), 90 (12), 89 (11), 77 (43), 76 (12), 75 (10), 51 (14), 39 (14). Anal. Calcd for $C_{24}H_{19}FN_2O_2$: C, 74.60; H, 4.96; N, 7.25. Found: C, 74.44; H, 5.08; N, 7.13.

*4.10.24. (2E)-1,3-Bis(4-fluorophenyl)-1-(5-phenyl-1,3,4-oxadiazol-2-yl)prop-2-en-1-ol (**14w**)*

To a stirred solution of (2*E*)-1,3-bis(4-fluorophenyl)prop-2-en-1-one **12w** (0.425 g, 1.74 mmol) and **1a** (0.760 g, 3.48 mmol) in toluene (5 mL) were added KF (0.010 g, 0.17 mmol) and dibenzo-18-crown-6 (0.025 g, 0.07 mmol). The mixture was heated to reflux for 1 h and then placed into a freezer. The precipitate was filtered off and washed with toluene. The combined filtrate and washings were evaporated in vacuo, methanol (10 mL) and RbF (5% solution in water, 0.5 mL) were added to the residual oil, and the mixture was allowed to stand for 72 h. The solvent was removed in vacuo and the residue was treated with water. The precipitate formed was crystallized from 2-propanol and then subjected to column chromatography over silica gel affording **14w** (0.414 g, 61%) as colorless solid. Mp 148–149 °C. ^{1}H NMR (DMSO-d_6): δ 7.98 (d, J=7.5 Hz, 2H), 7.66–7.57 (m, 7H), 7.30 (s, 1H), 7.26–7.17 (m, 4H), 7.03 (d, J=16 Hz, 1H), 6.78 (d, J=16 Hz, 1H). ^{13}C NMR (DMSO-d_6): δ 168.5, 164.5, 161.9 (d, J_{CF}=245.2 Hz), 161.6 (d, J_{CF}=244.7 Hz), 138.3 (d, J_{CF}=3.2 Hz), 132.4 (d, J_{CF}=3.2 Hz), 132.1, 131.4 (d, J_{CF}=1.8 Hz), 129.4, 128.8 (d, J_{CF}=8.2 Hz), 128.1 (d, J_{CF}=8.2 Hz), 127.9, 126.6, 123.1, 115.5 (d, J_{CF}=21.5 Hz), 115.1 (d, J_{CF}=21.5 Hz), 73.4. ^{19}F NMR (DMSO-d_6): δ −114.2, −115.1. IR ν_{max} (cm^{-1}): 3321 (br), 3066, 1603, 1558, 1508, 1483, 1448, 1414, 1365, 1346, 1306, 1230, 1159, 1093, 1068, 1045, 1011, 972, 924, 866, 843, 822, 783, 750, 708, 694, 667, 596, 530, 505, 492. MS *m*/*z* (%): 391 (M^++H, 11), 390 (M^+, 44), 362 (24), 267 (21), 244 (42), 243 (28), 217 (15), 216 (76), 215 (15), 150 (11), 149 (52), 148 (14), 146 (26), 136 (74), 124 (19), 123 (100), 122 (14), 121 (36), 109 (48), 105 (37), 104 (14), 103 (30), 101 (31), 95 (55), 77 (52), 75 (17), 51 (15). Anal. Calcd for $C_{23}H_{16}F_2N_2O_2$: C, 70.76; H, 4.13; N, 7.18. Found: C, 70.85; H, 4.12; N, 7.01.

*4.10.25. 2,2,2-Trifluoro-1-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethanol (**14x**)*

Prepared according to Section 4.10, *Method B*. Reaction of **1a** (1.050 g, 4.81 mmol), 2,2,2-trifluoroacetophenone **12x** (0.698 g, 4.01 mmol), KF (0.023 g, 0.40 mmol), and dibenzo-18-crown-6 (0.058 g, 0.16 mmol) in toluene (5 mL) gave 1.118 g (87%) of **14x** as colorless solid (crystallized from cyclohexane). Mp 106–108 °C. ^{1}H NMR (DMSO-d_6): δ 8.59 (br s, 1H), 7.97 (d, J=7.5 Hz, 2H), 7.68–7.55 (m, 5H), 7.49 (m, 3H). ^{13}C NMR (DMSO-d_6): δ 164.9, 163.2, 134.2, 132.5, 129.7, 129.5, 128.5, 126.8, 126.7, 123.6 (q, J_{CF}=287 Hz), 122.6, 74.7 (q, J_{CF}=30.6 Hz). ^{19}F NMR (DMSO-d_6): δ −76.6. IR ν_{max} (cm^{-1}): 3300–2950 (br), 2810 (br), 2640 (br), 1608, 1557, 1490, 1458, 1417, 1373, 1280, 1197, 1183, 1130, 1104, 1080, 1037, 1001, 959, 929, 732, 717, 702, 671, 608, 525. MS *m*/*z* (%): 321 (M^++H, 6), 320 (M^+, 11), 252 (6), 251 (38), 145 (13), 106 (8), 105 (100), 103 (8), 77 (39), 51 (6). Anal. Calcd for $C_{16}H_{11}F_3N_2O_2$: C, 60.00; H, 3.46; N, 8.75. Found: C, 59.89; H, 3.55; N, 8.63.

*4.10.26. 2,2,2-Trifluoro-1-(1-methyl-1H-imidazol-2-yl)-1-(5-phenyl-1,3,4-oxadiazol-2-yl)ethanol (**14y**)*

Prepared according to Section 4.10, *Method A*. Reaction of **1a** (0.740 g, 3.39 mmol), 2,2,2-trifluoro-1-(1-methyl-1*H*-imidazol-2-yl)ethanone **12y** (0.603 g, 3.39 mmol), KF (0.020 g, 0.34 mmol), and dibenzo-18-crown-6 (0.049 g, 0.14 mmol) in toluene (5 mL) gave 0.717 g (65%) of **14y** as colorless crystals (crystallized from ethyl acetate/cyclohexane). Mp 170 °C (dec). ^{1}H NMR (DMSO-d_6): δ 8.97 (br s, 1H), 8.00 (d, J=6.9 Hz, 2H), 7.71–7.60 (m, 3H), 7.32 (s, 1H), 6.88 (s, 1H), 3.79 (s, 3H). ^{13}C NMR (DMSO-d_6): δ 165.0, 162.3, 138.8, 132.5, 129.5, 127.0, 126.8, 125.3, 123.2 (q, J_{CF}=285.5 Hz), 122.7, 74.0 (q, J_{CF}=32 Hz), 34.5. ^{19}F NMR (DMSO-d_6): δ −75.2. IR ν_{max} (cm^{-1}): 3425 (br), 3118, 1610, 1560, 1552, 1489, 1448, 1396, 1362, 1279, 1244, 1196, 1182, 1165, 1117, 1088, 1018, 955, 931, 906, 768, 712, 685, 523. MS *m*/*z* (%): 324 (M^+, 4), 255 (62), 179 (58), 145 (16), 109 (100), 103 (14), 81 (13), 77 (49), 54 (18), 42 (18). Anal. Calcd for $C_{14}H_{11}F_3N_4O_2$: C, 51.86; H, 3.42; N, 17.28. Found: C, 51.74; H, 3.48; N, 17.19.

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References and notes

1. The chemistry of 1,3,4-oxadiazoles has been reviewed: (a) Hetzheim, A.; Moeckel, K. *Adv. Heterocycl. Chem.* **1966**, *7*, 183; (b) Hill, J. In *Comprehensive Heterocyclic Chemistry*; Potts, K. T., Ed.; Pergamon: Oxford, 1984; Vol. 6, pp 427–446.
2. (a) Leung, D.; Du, W.; Hardouin, C.; Cheng, H.; Hwang, I.; Cravatt, B. F.; Boger, D. L. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1423; (b) Omar, F. A.; Mahfouz, N. M.; Rahman, M. A. *Eur. J. Med. Chem.* **1996**, *31*, 819.
3. (a) Holla, B. S.; Gonsalves, R.; Shenoy, S. *Eur. J. Med. Chem.* **2000**, *35*, 267; (b) Brown, P.; Best, D. J.; Broom, N. J. P.; Cassels, R.; O'Hanlon, P. J.; Mitchell, T. J.; Osborne, N. F.; Wilson, J. M. *J. Med. Chem.* **1997**, *40*, 2563; (c) Palaska, E.; Sahin, G.; Kelicen, P.; Durlu, N. T.; Altintok, G. *Il Farmaco* **2002**, *57*, 101; (d) Lokanatha Rai, K. M.; Linganna, N. *Il Farmaco* **2000**, *55*, 389; (e) Adelstein, G. W. *J. Med. Chem.* **1973**, *16*, 309; (f) Zheng, X.; Li, Z.; Wang, Y.; Chen, W.; Huang, Q.; Liu, C.; Song, G. *J. Fluorine Chem.* **2003**, *123*, 163.
4. (a) Chan, L.-H.; Lee, R.-H.; Hsieh, C.-F.; Yeh, H.-C.; Chen, C.-T. *J. Am. Chem. Soc.* **2002**, *124*, 6469; (b) Lee, Y.-Z.; Chen, X.; Chen, S.-A.; Wei, P.-K.; Fann, W.-S. *J. Am. Chem. Soc.* **2001**, *123*, 2296; (c) Guan, M.; Bian, Z. Q.; Zhou, Y. F.; Li, F. Y.; Li, Z. J.; Huang, C. H. *Chem. Commun.* **2003**, 2708; (d) Wang, J.; Wang, R.; Yang, J.; Zheng, Z.; Carducci, M. D.; Cayou, T.; Peyghambarian, N.; Jabbour, G. E. *J. Am. Chem. Soc.* **2001**, *123*, 6179.
5. (a) Al-Talib, M.; Tashtoush, H.; Odeh, N. *Synth. Commun.* **1990**, *20*, 1811; (b) Kerr, V. N.; Ott, D. G.; Hayes, F. N. *J. Am. Chem. Soc.* **1960**, *82*, 186; (c) Short, F. W.; Long, L. M. *J. Heterocycl. Chem.* **1969**, *6*, 707; (d) Klingsberg, E. *J. Am. Chem. Soc.* **1958**, *80*, 5786; (e) Reddy, C. K.; Reddy, P. S. N.; Ratnam, C. V. *Synthesis* **1983**, 842.
6. (a) Balachandran, K. S.; George, M. V. *Tetrahedron* **1973**, *29*, 2119; (b) Yang, R.-Y.; Dai, L.-X. *J. Org. Chem.* **1993**, *58*, 3381; (c) Chiba, T.; Okimoto, M. *J. Org. Chem.* **1992**, *57*, 1375.
7. (a) Tandon, V. K.; Chhor, R. B. *Synth. Commun.* **2001**, *31*, 1727; (b) Mashraqui, S. H.; Ghadigaonkar, S. G.; Kenny, R. S. *Synth. Commun.* **2003**, *33*, 2541; (c) Bentiss, F.; Lagrenee, M.; Barbry, D. *Synth. Commun.* **2001**, *31*, 935; (d) Kangani, C. O.; Kelley, D. E.; Day, B. W. *Tetrahedron Lett.* **2006**, *47*, 6497.

8. (a) Fürmeier, S.; Metzger, J. O. *Eur. J. Org. Chem.* **2003**, 885; (b) Semenov, B. B.; Smushkevich, Yu. I. *Izv. Akad. Nauk, Ser. Khim.* **2002**, 334; *Russ. Chem. Bull. (Engl. Transl.)* **2002**, *51*, 357; (c) Huisgen, R.; Sauer, J.; Sturm, H. J. *Angew. Chem.* **1958**, *70*, 272.
9. (a) Ohmoto, K.; Yamamoto, T.; Okuma, M.; Horiuchi, T.; Imanishi, H.; Odagaki, Y.; Kawabata, K.; Sekioka, T.; Hirota, Y.; Matsuoka, S.; Nakai, H.; Toda, M.; Cheronis, J. C.; Spruce, L. W.; Gyorkos, A.; Wieczorek, M. *J. Med. Chem.* **2001**, *44*, 1268; (b) Ohmoto, K.; Yamamoto, T.; Horiuchi, T.; Kojima, T.; Hachiya, K.; Hashimoto, S.; Kawamura, M.; Nakai, H.; Toda, M. *Synlett* **2001**, 299; (c) Rydzewski, R. M.; Burrill, L.; Mendonca, R.; Palmer, J. T.; Rice, M.; Tahilramani, R.; Bass, K. E.; Leung, L.; Gjerstad, E.; Janc, J. W.; Pan, L. *J. Med. Chem.* **2006**, *49*, 2953.
10. Regel, E.; Büchel, K.-H. *Liebigs Ann. Chem.* **1977**, 159.
11. Tolmachev, A. A.; Zarudnitskii, E. V.; Yurchenko, A. A.; Pinchuk, A. M. *Khim. Geterotsikl. Soedin.* **1999**, *35*, 1261; *Chem. Heterocycl. Compd. (Engl. Transl.)* **1999**, *35*, 1117.
12. Zarudnitskii, E. V.; Pervak, I. I.; Merkulov, A. S.; Yurchenko, A. A.; Tolmachev, A. A.; Pinchuk, A. M. *Synthesis* **2006**, 1279.
13. Lopyrev, V. A.; Larina, L. I.; Voronkov, M. G. *Zh. Org. Khim.* **2001**, *37*, 165; *Russ. J. Org. Chem. (Engl. Transl.)* **2001**, *37*, 149.
14. Dondoni, A. *Synthesis* **1998**, 1681.
15. (a) Seyferth, D.; Shih, H.-M. *J. Org. Chem.* **1974**, *39*, 2336; (b) Madhavan, R.; Srinivasan, V. R. *Indian J. Chem.* **1969**, *7*, 760; (c) Deshpande, D. S.; Surendra Nath, T. G.; Srinivasan, V. R. *Indian J. Chem.* **1975**, *13*, 851; (d) Vachal, P.; Toth, L. M. *Tetrahedron Lett.* **2004**, *45*, 7157.
16. Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *J. Org. Chem.* **1988**, *53*, 1748.
17. Pinkerton, F. H.; Thames, S. F. *J. Heterocycl. Chem.* **1972**, *9*, 67.
18. Dondoni, A.; Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P. *J. Org. Chem.* **1987**, *52*, 3413.
19. Kirsanov, A. V. *Zh. Obshch. Khim.* **1954**, *24*, 1033; *Chem. Abstr.* **1955**, *49*, 8787a.
20. Regel, E.; Büchel, K.-H. *Liebigs Ann. Chem.* **1977**, 145.
21. Tacconi, G.; Righetti, P. P.; Desimoni, G. *J. Prakt. Chem.* **1973**, *315*, 339.
22. Aspelund, H. *Chem. Ber.* **1930**, *63*, 1191.