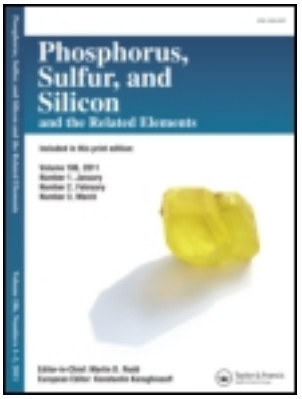

Phosphorus, Sulfur, and Silicon and the Related Elements

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(N-Isocyanimino)Triphenylphosphorane as an Efficient Reagent for the Preparation of N-Benzyl-1-Phenyl-1-(5-Phenyl-1,3,4-Oxadiazol- 2-yl)Methanamine Derivatives via in-Situ Generation of Densely Functionalized Iminophosphoranes

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(*N*-ISOCYANIMINO)TRIPHENYLPHOSPHORANE AS AN EFFICIENT REAGENT FOR THE PREPARATION OF *N*-BENZYL-1-PHENYL-1-(5-PHENYL-1,3,4-OXADIAZOL-2-YL)METHANAMINE DERIVATIVES VIA IN-SITU GENERATION OF DENSELY FUNCTIONALIZED IMINOPHOSPHORANES

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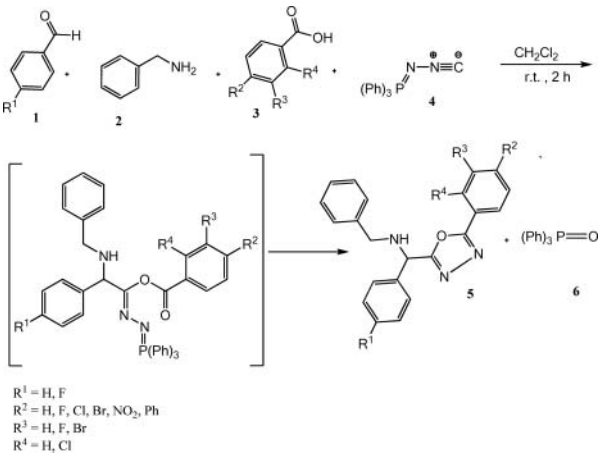
GRAPHICAL ABSTRACT



Abstract *A novel isocyanide-based four-component reaction between (*N*-isocyanimino) triphenylphosphorane, benzyl amine, benzaldehyde derivatives, and various carboxylic acids efficiently provides* N*-benzyl-1-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)methanamine derivatives in good yields without using any catalyst or activation. The reaction can be carried out as a simple one-pot protocol at room temperature.*

[Supplemental materials are available for this article. Go to the publisher's online edition of Phosphorus, Sulfur, and Silicon and the Related Elements *for the following free supplemental resource*: *NMR Spectra for 5i.]*

Keywords 1,3,4-Oxadiazole; four-component reaction; *aza*-wittig; iminophosphorane; heterocyclization

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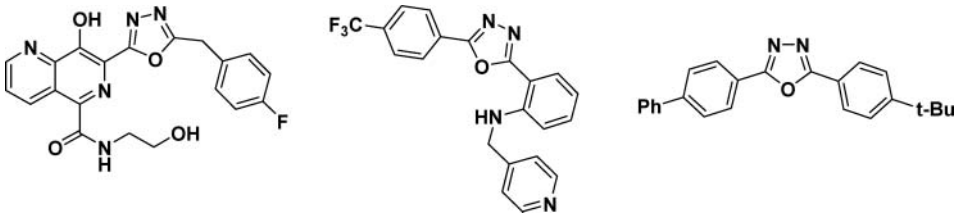


Figure 1 Examples of some biologically active 2,5-disubstituted-1,3,4-oxadiazole derivatives.

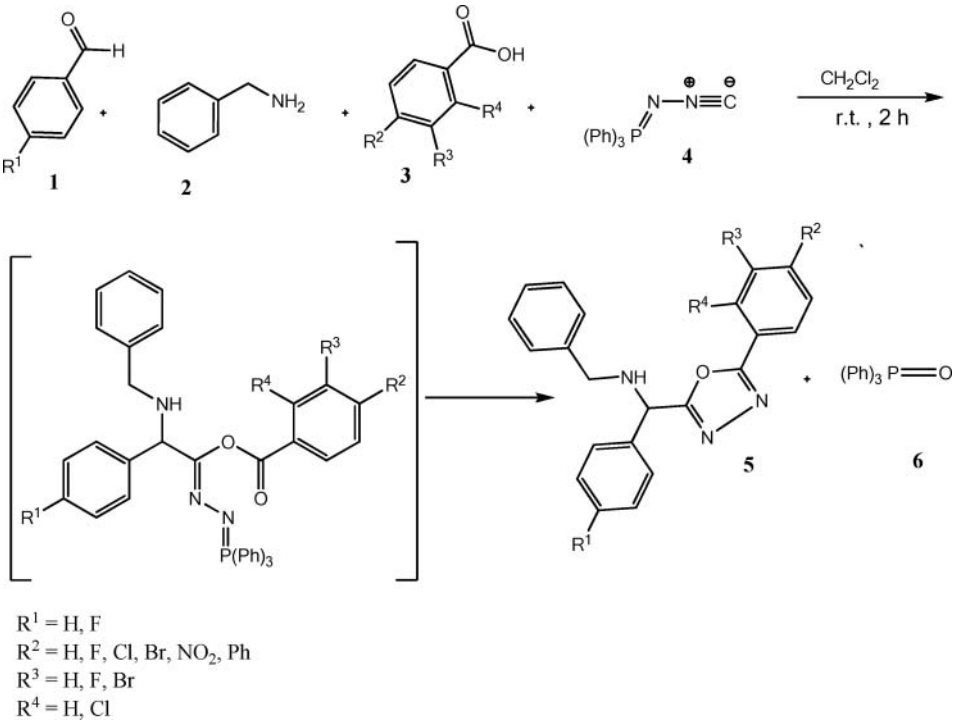
INTRODUCTION

1,3,4-Oxadiazoles have been an important pharmacophore in the pharmaceutical industry.[1] The therapeutic applications of 1,3,4-oxadizoles include HIV integrase inhibitor,[2] tyrosinase inhibitor,[3] anti-inflammatory,[4] antihypoglycemic,[5] anticancer,[6] antimalarial,[7] angiogenesis inhibitor,[8] anticonvulsive, antiemetic, diuretic,[9] and dopamine transporters.[10] Furthermore, 1,3,4-oxadiazole derivatives with an amine and an alkyl tail have been applied as electroluminescent materials.[11] In 1990, it was found that 2-(biphenyl-4-yl)-5-(4-*tert*-butylphenyl)-1,3,4-oxadiazole (PBD) functioned very well as an excellent electron transport material (ETM) in an organic multilayer EL diode.[12] 1,3,4-Oxadiazoles are also important starting materials for cycloaddition reactions[13] in the synthesis of furans and natural products (Figure 1).[14]

The *aza*-Wittig reactions of iminophosphoranes have attracted much attention in view of their usefulness in the synthesis of nitrogen-containing heterocyclic compounds since they were first prepared in 1919 by Staudinger and Meyer.[15] Several interesting heterocyclization reactions involving iminophosphoranes have been reviewed. These compounds can easily be altered through *aza*-Wittig reaction with carbon disulfide, isocyanates, or carbon dioxide into functionalized heterocumulenes which display a wealthy chemistry of of an uncommon synthetic covenant.[16] The nucleophilicity at nitrogen is a factor of necessary mechanistic importance in the use of these iminophosphoranes as *aza*-Wittig reagents. Iminophosphoranes are significant reagents in synthetic organic chemistry, specially in the synthesis of naturally occurring products, compounds with biological and pharmacological activity.[17] There are several reports for the utility of (*N*-isocyanimino)triphenylphosphorane **4** in the synthesis of metal complexes. Nevertheless, the organic chemistry of **4** remains relatively unexplored. The (*N*-isocyanimino)triphenylphosphorane **4** is presumed to have synthetic potential because it prepares a reaction system in which the iminophosphorane group can react with a reagent having a carbonyl functionality (Scheme 1).[18]

RESULTS AND DISCUSSION

Recently, 1,3,4-oxadiazoles have been the object of intense research in organic synthesis and medicinal chemistry, and several procedures have been reported for the synthesis of these heterocyclic compounds which are multistep in nature.[19] Accordingly, development of a synthetic procedure that could be used to prepare a diversity of these templates remains an significant task. In the last years, several synthetic approaches have been reported for the preparation of (*N*-isocyanimino)triphenylphosphorane ($CNNPPh_3$) **4**.[18] There are several reports on the use of (*N*-isocyanimino)triphenylphosphorane **4** in the synthesis of metal complexes.[18] Nevertheless, application of **4** in the synthesis of organic compounds



Scheme 1 Synthesis of *N*-benzyl-1-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)methanamine derivatives **5a–k**.

is scarce.[20] As part of our ongoing program to develop efficient and robust methods for the preparation of heteroatom-containing organic compounds,[21] we sought to develop a convenient preparation of sterically congested 2,5-disubstituted 1,3,4-oxadiazoles **5** by a multicomponent reaction between (*N*-isocyanimino)triphenylphosphorane (4), benzyl amine (2), benzaldehyde derivatives (1), and various carboxylic acids (3), followed by an aza-Wittig cyclization in CH_2Cl_2 at ambient temperature in excellent yields (Scheme 1 and Figure 2).

This route permits us to introduce great molecular diversity under mild reaction conditions, including substitution and scaffold diversity. A large number of derivatives can be rapidly synthesized in excellent purity and high yield by using this method. The structures of the products were deduced from their IR, mass, H NMR, and ^{3}C NMR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate *m*/*z* values. The H NMR spectrum of **5a** consisted of an AB-quartet for CH_2 of benzyl group at 3.87 and 3.93 ($^2J_{HH} = 13.25$ Hz), a singlet at $\delta = 5.26$ for CH, and a multiplet at 7.30–7.77 and 8.01–8.18 for aromatic hydrogens. The ^{1}H-decoupled ^{13}C NMR spectrum of **5a** is in agreement with the proposed structure. In view of the success of the above-mentioned reaction, we explored the scope of this promising reaction by varying the structure of the benzaldehyde and carboxylic acid component (Table 1). As an example, the ^{1}H and ^{13}C NMR spectra for 5i are given in the Supplemental Materials (Figures S1 and S2). As indicated in Figure 2 and Scheme 1, the reaction proceeds very cleanly under mild reaction conditions at room temperature and no undesirable by-products were observed. Owing to the great diversity of substitution patterns, this reaction may be used in the production of combinatorial libraries.

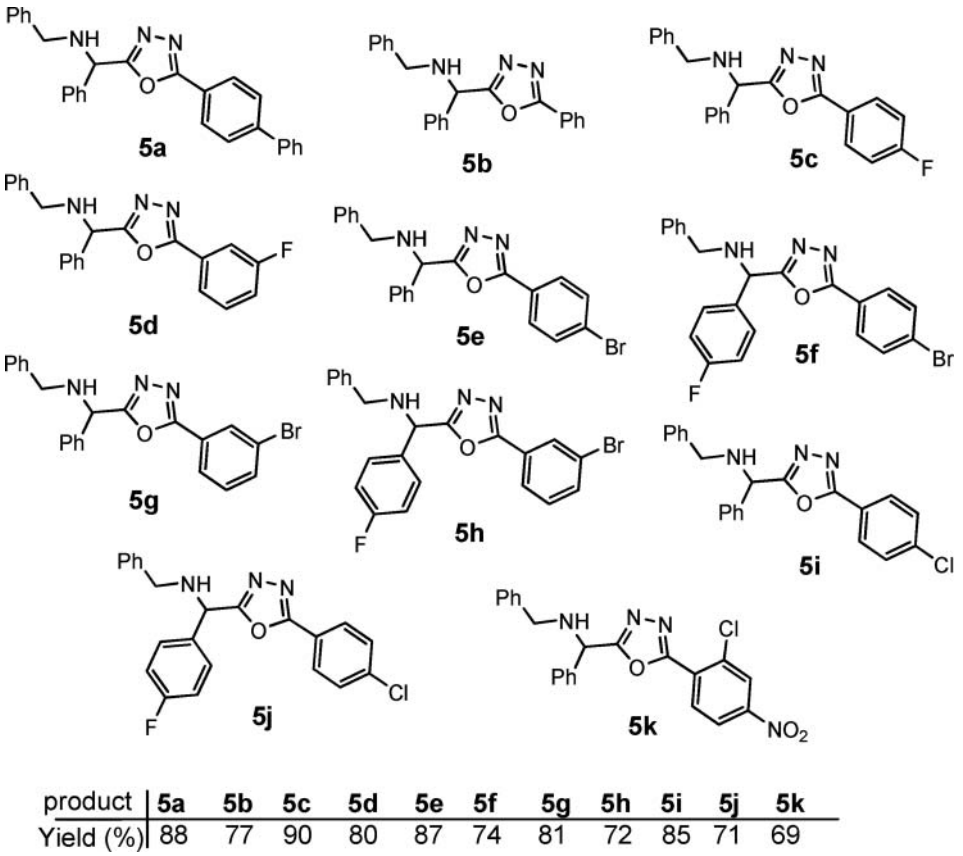
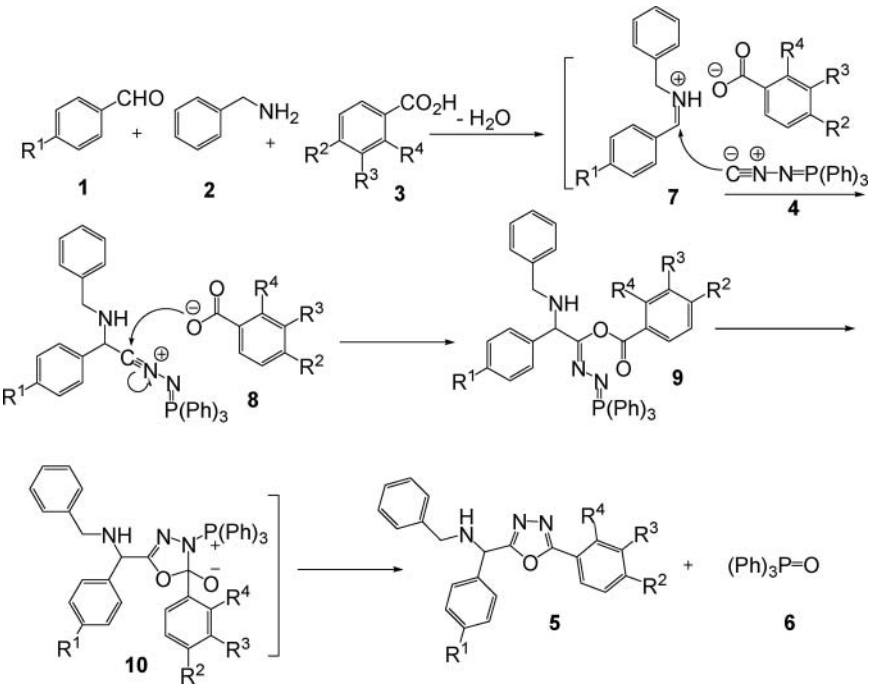


Figure 2 Synthesis of *N*-benzyl-1-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)methanamine derivatives **5a–k**.

Table 1 Synthesis of *N*-benzyl-1-phenyl-1-(5-phenyl-1,3,4-oxaddiazol-2-yl)methanamine derivatives **5a–k** from benzaldehyde **1**, amine **2**, and carboxylic acid **3** in the presence of (*N*-isocyanimino)triphenylphosphorane **4**

	Aldehyde 1	Amine 2	Carboxylic acid 3	Product
1	benzaldehyde	benzyl amine	biphenyl-4-carboxylic acid	**5a**
2	benzaldehyde	benzyl amine	benzoic acid	**5b**
3	benzaldehyde	benzyl amine	4-fluorobenzoic acid	**5c**
4	benzaldehyde	benzyl amine	3-fluorobenzoic acid	**5d**
5	benzaldehyde	benzyl amine	4-bromobenzoic acid	**5e**
6	4-fluoro benzaldehyde	benzyl amine	4-bromobenzoic acid	**5f**
7	benzaldehyde	benzyl amine	3-bromobenzoic acid	**5g**
8	4-fluoro benzaldehyde	benzyl amine	3-bromobenzoic acid	**5h**
9	benzaldehyde	benzyl amine	4-chlorobenzoic acid	**5i**
10	4-fluoro benzaldehyde	benzyl amine	4-chlorobenzoic acid	**5g**
11	benzaldehyde	benzyl amine	2-chloro-4-nitrobenzoic acid	**5k**



Scheme 2 A possible mechanism for the formation of products **5a–k**.

A mechanistic rationalization for this reaction is provided in Scheme 2. It is conceivable that, the initial event is the condensation of the benzaldehyde **1**, benzyl amine **2**, and carboxylic acid **3** entities to an intermediate imine **7**. Nucleophilic addition of the (*N*-isocyanimino)triphenylphosphorane **4** to the imine intermediate **7**, leads to nitrilium intermediate **8**. This intermediate may be attacked by the conjugate base of acid **3** to form 1:1:1 adduct **9**. This adduct may undergo intramolecular *aza*-Wittig reaction of iminophosphorane moiety with the ester carbonyl group to afford the isolated 2,5-disubstituted 1,3,4-oxadiazole **5** by removal of triphenylphosphine oxide **6** from intermediate **10**.[20e]

To the best of our knowledge, this is the first report in which (*N*-isocyanimino) triphenylphosphorane is used in a four-component condensation in the presence of benzyl amine followed by an intramolecular *aza*-Wittig[22,23] ring closure of the iminophosphorane moiety with the ester carbonyl. In conclusion, we are reporting a new IMCR,[24] yielding 2,5-disubstituted 1,3,4-oxadiazole derivatives, by a sequence of a multicomponent reaction, and an intramolecular aza-Wittig closure. Due to the easy availability of the synthetic approach and the neutral ring closure conditions, this new synthetic approach discussed here has the potential to synthesize various 2,5-disubstituted 1,3,4-oxadiazoles, which are of considerable interest as potential biological active compounds or pharmaceuticals. Other aspects of this process are under investigation.

EXPERIMENTAL

General

Starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The methods used to follow

the reactions are TLC and NMR. TLC and NMR indicated that there is no side product. Melting points were measured on an Electrothermal 9100 apparatus and were uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ solution) with a BRUKER DRX-250 AVANCE spectrometer at 250.0 and 62.5 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 eV. Flash chromatography columns were prepared from Merck silica gel powder.

General Procedure for the Preparation of Compounds 5a–k; General Procedure Exemplified for 5a

To a magnetically stirred solution of benzylamine (1 mmol), benzaldehyde (1mmol), and (*N*-isocyanimino)triphenylphosphorane (1 mmol) in CH_2Cl_2 (5 mL) was added dropwise of a solution of biphenyl-4-carboxylic acid (1 mmol) in CH_2Cl_2 (5 mL) at room temperature over 15 min. The mixture was stirred for 2 h. The solvent was removed under reduced pressure, and the viscous residue was purified by flash column chromatography (silica gel powder; petroleum ether-ethyl acetate (2:1)) to afford **5a** (93%) as a yellow oil. The characterization data of the compounds are given below:

***N*-Benzyl-1-(5-(Biphenyl-4-yl)-1,3,4-Oxadiazol-2-yl)-*N*-Methyl-1-Phenyl methanamine (5a).** Yellow Oil (yield 88%), IR (KBr) (ν_{max}/cm^{-1}): 3030, 2924, 2374, 2345, 1547, 1451, 1051, 845. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br, s, NH, exchanged by D_2O addition), 3.87 and 3.93 (AB quartet, 2H, $^2J_{HH}$ = 13.25 Hz, CH_2 of Benzyl), 5.26 (s, 1H, CH), 7.30–7.77 and 8.01–8.18 (m, 19 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.37 (CH_2 of Benzyl), 57.84 (CH), 127.1, 127.4, 127.6, 127.7, 128.2, 128.5, 128.6, 128.7, 129.0, 139.8, and 144.5 (19 CH of arom), 122.5, 137.5, and 138.4 (5 $C_{ipso(C=C)}$ of 3 C_6H_5 and C_6H_4), 165.2 and 166.5 (2 C=N). MS *m/z*: 418 (M^+, 2), 312 (100), 269 (6), 194 (21), 178 (18), 151 (23), 106 (33), 90 (67), 76 (15), 65 (7). Anal. Calcd for $C_{28}H_{23}N_3O$: C, 80.55; H, 5.55; N, 10.06; Found: C, 80.57; H, 5.53; N, 10.03.

***N*-Benzyl-1-Phenyl-1-(5-Phenyl-1,3,4-Oxadiazol-2-yl)Methanamine (5b).** Orange Powder (yield 77%), mp: 106.1 °C–107.8 °C. IR (KBr) (ν_{max}/cm^{-1}): 3304, 2924, 2375, 2345, 1558, 1482, 1452, 1121, 834. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.37 (1H, br, s, NH, exchanged by D_2O addition), 3.83–3.94 (m, 2H, CH_2 of Benzyl), 5.24 (s, 1H, CH), 7.16–7.53, and 8.01–8.02 (m, 15 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.4 (CH_2 of Benzyl), 57.9 (CH), 127.0, 127.4, 127.7, 128.4, 128.6, 128.6, 129.0, and 131.7 (15 CH of arom), 123.7, 137.6, and 138.7 (3 $C_{ipso(C=C)}$ of 3 C_6H_5), 165.2 and 166.6 (2 C=N). MS *m/z*: 342 (M^+, 1), 249 (1), 236 (100), 193 (23), 179 (16), 132 (12), 105 (93), 76 (36), 65 (12), 51 (14). Anal. Calcd for $C_{22}H_{19}N_3O$: C, 77.40; H, 5.61; N, 12.31; Found: C, 77.46; H, 5.59; N, 12.33.

***N*-Benzyl-1-(5-(4-Fluorophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethana mine (5c).** White Powder (yield 90%), mp: 111.0 °C–113.3 °C. IR (KBr) (ν_{max}/cm^{-1}): 3287, 2925, 2372, 2345, 1610, 1499, 1454, 1235, 1078, 856. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.33 (1H, br s, NH, exchanged by D_2O addition), 3.81–3.92 (m, 2H, CH_2 of Benzyl), 5.22 (s, 1H, CH), 7.13–7.53 and 7.97–8.13 (m, 14 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.4 (CH_2 of Benzyl), 57.9 (CH), 116.3 (d, $^2J_{CF}$ = 22.0 Hz), 120.1 (d, $^4J_{CF}$ = 3.6 Hz), 129.2 (d, $^3J_{CF}$ = 8.8 Hz), 164.7 (d, $^1J_{CF}$ = 252.1 Hz), 127.4, 127.6, 128.4, 128.5, 128.6, and 129.0 (10 CH of arom), 137.7 and 138.9 (2 $C_{ipso(C=C)}$ of 2 C_6H_5), 164.4 and 165.6 (2 C=N). MS *m/z*: 360 (M^+, 1), 254 (99), 211 (17), 196 (20), 122 (35),

106 (100), 95 (17), 65 (13), 50 (8). Anal. Calcd for $C_{22}H_{18}FN_3O$: C, 73.52; H, 5.05; N, 11.69; Found: C, 73.55; H, 5.06; N, 11.66.

***N*-Benzyl-1-(5-(3-Fluorophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethanamine (5d).** Yellow Powder (yield 80%), mp: 103.8 °C–105.4 °C. IR (KBr) (ν_{max}/cm^{-1}): 3309, 2922, 2374, 2345, 1561, 1488, 1453, 1120, 870. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br s, NH, exchanged by D_2O addition), 3.81–3.92 (m, 2H, CH_2 of Benzyl), 5.23 (s, 1H, CH), 7.04–8.01 (m, 14 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.5 (CH_2 of Benzyl), 58.0 (CH), 114.0 (d, $^2J_{CF} = 24.5$ Hz), 118.8 (d, $^2J_{CF} = 21.3$ Hz), 122.7 (d, $^4J_{CF} = 3.1$ Hz), 125.6 (d, $^3J_{CF} = 9.1$ Hz), 130.8 (d, $^3J_{CF} = 8.2$ Hz), 164.9 (d, $^1J_{CF} = 269.8$ Hz), 127.4, 127.6, 127.8, 128.3, 128.6, 128.7, and 129.0 (10 CH of arom), 137.7 and 138.9 (2 $C_{ipso(C=C)}$ of C_6H_5), 164.7 and 165.7 (2 C=N). MS *m*/z: 360 (M^+, 1), 254 (88), 211 (13), 132 (14), 123 (27), 106 (95), 90 (100), 76 (20), 65 (13), 50 (11). Anal. Calcd for $C_{22}H_{18}FN_3O$: C, 73.52; H, 5.05; N, 11.69; Found: C, 73.53; H, 5.07; N, 11.72.

***N*-Benzyl-1-(5-(4-Bromophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethanamine (5e).** White powder (yield 87%), mp: 123.1 °C–125.2 °C. IR (KBr) (ν_{max}/cm^{-1}): 3285, 2924, 2376, 2345, 1604, 1482, 1452, 1078, 1006, 830. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.39 (1H, br, s, NH, exchanged by D_2O addition), 3.81–3.93 (m, 2H, CH_2 of Benzyl), 5.22 (s, 1H, CH), 7.16–7.65 and 7.83–7.97 (m, 14 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.4 (CH_2 of Benzyl), 57.8 (CH), 122.6 (C_{Ar}–Br of C_6H_4Br), 126.4 ($C_{ipso(C=C)}$ of C_6H_4Br), 127.4, 127.7, 128.3, 128.4, 128.6, 128.7, 129.0, and 132.3 (14 CH of arom), 137.4 and 138.6 (2 $C_{ipso(C=C)}$ of 2 C_6H_5), 164.5 and 166.8 (2 C=N). MS *m*/z: 422 (M^++2, 1), 316 (31), 236 (9), 183 (14), 132 (13), 106 (88), 90 (100), 76 (33), 65 (17), 50 (15). Anal. Calcd for $C_{22}H_{18}BrN_3O$: C, 62.87; H, 4.32; N, 10.00; Found: C, 62.84; H, 4.36; N, 9.97.

***N*-Benzyl-1-(5-(4-Bromophenyl)-1,3,4-Oxadiazol-2-yl)-1-(4-Fluorophenyl) Methanamine (5f).** White Oil (yield 74%). IR (KBr) (ν_{max}/cm^{-1}): 3288, 2925, 2376, 2345, 1603, 1490, 1452, 1236, 835. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br s, NH, exchanged by D_2O addition), 3.82 and 3.89 (AB quartet, 2H, $^2J_{HH} = 13.25$ Hz, CH_2 of Benzyl), 5.21 (s, 1H, CH), 7.04–7.97 (m, 13 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.3 (CH_2 of Benzyl), 57.1 (CH), 116.0 (d, $^2J_{CF} = 22.0$ Hz), 119.4 (d, $^4J_{CF} = 3.4$ Hz), 129.5 (d, $^3J_{CF} = 8.8$ Hz), 163.7 (d, $^1J_{CF} = 251.8$ Hz), 122.5 (C_{Ar}–Br of C_6H_4Br), 126.5 ($C_{ipso(C=C)}$ of C_6H_4Br), 127.5, 128.3, 128.4, 128.5, 128.6, 132.4, and 132.5 (9 CH of arom), 138.5 ($C_{ipso(C=C)}$ of C_6H_5), 164.1 and 164.6 (2 C=N). MS *m*/z: 438 (M^+, 1), 334 (24), 272 (12), 198 (5), 183 (16), 122 (21), 106 (100), 90 (89), 75 (19), 65 (10), 50 (7). Anal. Calcd for $C_{22}H_{17}BrFN_3O$: C, 60.29; H, 3.91; N, 9.59; Found: C, 60.33; H, 3.93; N, 9.61.

***N*-Benzyl-1-(5-(3-Bromophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethanamine (5g).** Colorless Oil (yield 81%). IR (KBr) (ν_{max}/cm^{-1}): 3286, 2925, 2376, 2345, 1604, 1488, 1451, 1073, 830. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br s, NH, exchanged by D_2O addition), 3.81–3.93 (m, 2H, CH_2 of Benzyl), 5.23 (s, 1H, CH), 7.11–7.70 and 7.93–8.12 (m, 14 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.4 (CH_2 of Benzyl), 57.9 (CH), 123.0 (C_{Ar}–Br of C_6H_4Br), 125.6 ($C_{ipso(C=C)}$ of C_6H_4Br), 125.5, 127.4, 127.6, 128.4, 128.6, 128.7, 129.0, 129.8, 130.5, and 134.7 (14 CH of arom), 135.0 and 137.5 (2 $C_{ipso(C=C)}$ of 2 C_6H_5), 163.9 and 167.1 (2 C=N). MS *m*/z: 316 (4), 224 (3), 183 (8), 157 (7), 105 (35), 91 (86), 76 (100), 62 (35), 50 (52), 41 (17). Anal. Calcd for $C_{22}H_{18}BrN_3O$: C, 62.87; H, 4.32; N, 10.00; Found: C, 62.84; H, 4.28; N, 10.04.

***N*-Benzyl-1-(5-(3-Bromophenyl)-1,3,4-Oxadiazol-2-yl)-1-(4-Fluorophenyl) Methanamine (5h).** Orange Oil (yield 72%). IR (KBr) (ν_{max}/cm^{-1}): 3321, 3066, 2927,

2383, 2346, 1605, 1550, 1512, 1230, 1107, 833. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br, s, NH, exchanged by D_2O addition), 3.82 and 3.90 (m, 2H, CH_2 of Benzyl), 5.22 (s, 1H, CH), 7.05–7.71 and 7.92–8.50 (m, 13 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.3 (CH_2 of Benzyl), 57.1 (CH), 116.0 (d, $^2J_{CF} = 21.7$ Hz), 119.2 (d, $^4J_{CF} = 3.7$ Hz), 129.6 (d, $^3J_{CF} = 8.7$ Hz), 163.4 (d, $^1J_{CF} = 251.9$ Hz), 123.0 (C_{Ar}–Br of C_6H_4Br), 125.4 ($C_{ipso(C=C)}$ of C_6H_4Br), 125.5, 127.6, 128.4, 128.6, 129.8, 130.6, and 134.8 (9 CH of arom), 138.5 and 139.9 (2 $C_{ipso(C=C)}$ of 2 C_6H_5), 164.0 and 166.7 (2 C=N). MS *m/*z: 224 (45), 183 (42), 168 (12), 155 (17), 88 (100), 75 (51), 62 (38), 50 (28), 41 (7). Anal. Calcd for $C_{22}H_{17}BrFN_3O$: C, 60.29; H, 3.91; N, 9.59; Found: C, 60.32; H, 3.93; N, 9.57.

***N*-Benzyl-1-(5-(4-Chlorophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethanamine (5i).** Yellow Powder (yield 85%), mp: 118.4–120.0 °C. IR (KBr) (ν_{max}/cm^{-1}): 3283, 2925, 2373, 2345, 1606, 1484, 1452, 1094, 861. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.34 (1H, br s, NH, exchanged by D_2O addition), 3.81–3.86 (m, 2H, CH_2 of Benzyl), 5.22 (s, 1H, CH), 7.34–7.51 and 7.91–8.04 (m, 14 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.5 (CH_2 of Benzyl), 57.9 (CH), 122.2 ($C_{ipso(C=C)}$ of C_6H_4Cl), 127.4, 127.6, 128.2, 128.4, 128.6, 128.7, 129.0, and 129.4 (19 CH of arom), 137.6, 138.0, and 138.9 (2 $C_{ipso(C=C)}$ of 2 C_6H_5 and C_{Ar}–Cl of C_6H_4Cl), 164.4 and 166.9 (2 C=N). MS *m/*z: 376 (M^+, 1), 270 (50), 236 (6), 179 (15), 149 (22), 139 (28), 106 (98), 91 (100), 77 (34), 65 (20), 50 (22), 41 (12). Anal. Calcd for $C_{22}H_{18}ClN_3O$: C, 70.30; H, 4.83; N, 11.18; Found: C, 70.33; H, 4.85; N, 11.20.

***N*-Benzyl-1-(5-(4-Chlorophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethanamine (5j).** Yellow Powder (yield 71%), mp: 110 °C–113 °C. IR (KBr) (ν_{max}/cm^{-1}): 3283, 2927, 2376, 2345, 1609, 1482, 14.45, 1093, 857. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br s, NH, exchanged by D_2O addition), 3.82 and 3.90 (AB quartet, 2H, $^2J_{HH} = 13.25$ Hz, CH_2 of Benzyl), 5.21 (s, 1H, CH), 7.04–7.52 and 7.90–8.05 (m, 13 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.3 (CH_2 of Benzyl), 57.1 (CH), 116.0 (d, $^2J_{CF} = 21.4$ Hz), 119.2 (d, $^4J_{CF} = 3.1$ Hz), 129.5 (d, $^3J_{CF} = 8.8$ Hz), 164.7 (d, $^1J_{CF} = 252.1$ Hz), 122.1 ($C_{ipso(C=C)}$ of C_6H_4Cl), 127.6, 128.2, 128.4, and 128.6 (19 CH of arom), 133.1, 138.2, and 139.3 (2 $C_{ipso(C=C)}$ of 2 C_6H_5 and C_{Ar}–Cl of C_6H_4Cl), 164.4 and 165.6 (2 C=N). MS *m/*z: 394 (M^+, 1), 288 (30), 272 (12), 180 (27), 139 (49), 122 (29), 106 (100), 91 (70), 74 (23), 62 (12), 50 (17), 41 (6). Anal. Calcd for $C_{22}H_{17}ClFN_3O$: C, 67.09; H, 4.35; N, 10.67; Found: C, 67.05; H, 4.37; N, 10.68.

***N*-Benzyl-1-(5-(2-Chloro-4-Nitrophenyl)-1,3,4-Oxadiazol-2-yl)-1-Phenylmethanamine (5k).** Colorless Oil (yield 69%). IR (KBr) (ν_{max}/cm^{-1}): 3288, 2927, 2374, 2344, 1609, 1482, 14.45, 1093, 836. ^{1}H NMR ($CDCl_3$, 250 MHz): δ_H (ppm) 2.17 (1H, br s, NH, exchanged by D_2O addition), 3.85 and 3.93 (AB quartet, 2H, $^2J_{HH} = 13.25$ Hz, CH_2 of Benzyl), 5.29 (s, 1H, CH), 7.24–7.66 and 8.16–8.40 (m, 13 H, arom). ^{13}C NMR ($CDCl_3$, 62.5 MHz): δ_C (ppm) 51.4 (CH_2 of Benzyl), 57.9 (CH), 121.8 ($C_{ipso(C=C)}$ of C_6H_4Cl), 126.4, 127.5, 127.7, 128.4, 128.6, 128.9, 129.1, and 132.0 (13 CH of arom), 133.6, 134.3, and 138.1 (3 $C_{ipso(C=C)}$ of 2 C_6H_5 and C_{Ar}–Cl), 149.3 ($C(NO_2)$), 165.2 and 166.5 (2 C=N). MS *m/*z: 421 (M^+, 1), 270 (50), 236 (6), 179 (15), 149 (22), 139 (28), 106 (98), 91 (100), 77 (34), 65 (20), 50 (22), 41 (12). Anal. Calcd for $C_{22}H_{17}ClN_4O_3$: C, 62.79; H, 4.07; N, 13.31; Found: C, 62.80; H, 4.09; N, 13.33.

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