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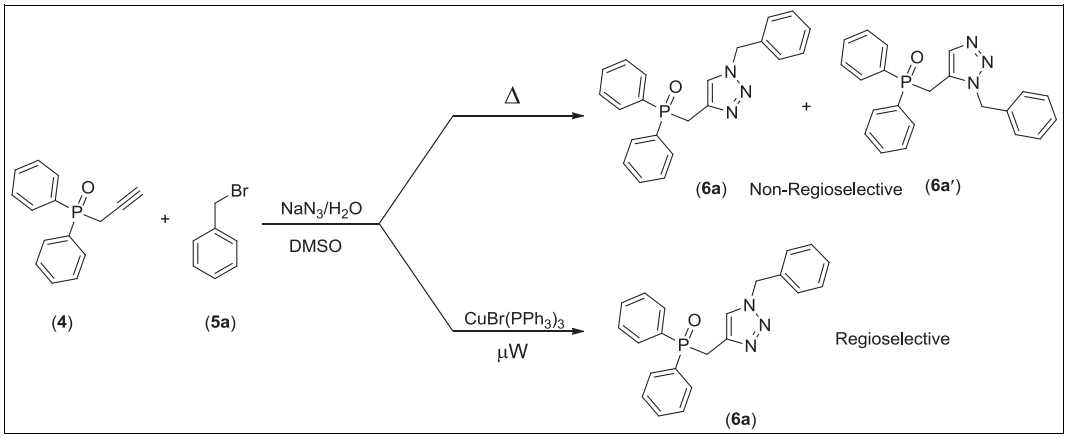

A simple and efficient one-pot microwave-assisted click formation of 1-(substituted)-1*H*-1,2,3-triazol-4-yl)methyl)diphenylphosphineoxide derivatives via Huisgen regioselective [3+2]-cycloaddition of an *in situ* generated organic azides and diphenyl(prop-2-yn-1-yl)phosphine oxide in highly polar DMSO-H_2O medium. This synthetic protocol is mild, requires shorter reaction time, and afforded products in excellent yields with high regioselectivity.

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INTRODUCTION

In the recent years, researchers focused more attention on the drug design with 1,2,3-triazole ring [1–5]. Several methodologies have been developed for their synthesis [6,7]. The Cu(I) catalyzed click [3+2]-cycloaddition reaction [8,9] of terminal alkynes and azides gained merit for the 1,2,3-triazole synthesis because of its remarkable efficiency and selectivity [10–12]. Organophosphorus compounds (OPCs) possess wide spectrum of biological properties particularly for their action on neuro transmission system and inhibition of the functioning of acetyl cholinesterase [13–17].

A logical connection of 1,2,3-triazole moiety with an already bioactive organophosphorus compounds through the click synthesis may further enhance the medicinal activity of the resulting molecules, which possess good polar hosting cites for effective chelation with the metal/metal complexes in the bio-fluids in the living system [18].

In continuation of our work on green synthetic methodologies of organophosphorus heterocycles [13,19–21], synthesis of title compounds was accomplished in a single step one-pot multicomponent by microwave irradiation (MWI) reaction at enhanced rate with high product yields [22,23].

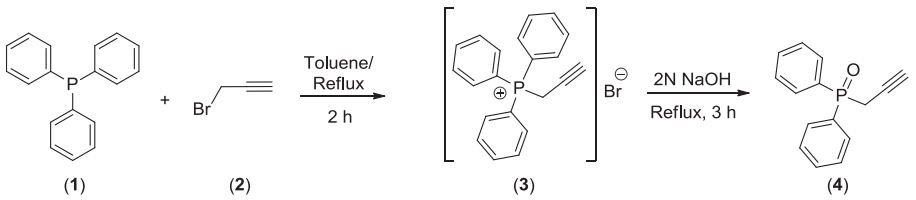
RESULTS AND DISCUSSION

The diphenyl(prop-2-yn-1-yl)phosphine oxide (**4**) precursor was prepared by nucleophilic addition of triphenylphosphine (**1**) and propargylbromide (**2**) in refluxing toluene. The stable triphenyl(prop-2yn-1-yl)phosphonium bromide salt (**3**) on base hydrolysis afforded phosphine oxide (**4**) in excellent yield (97.6%), (Scheme 1) [24,25].

Synthesis of the titled compounds (**6a–o**) was accomplished by Huisgen's click reaction after optimizing its reaction conditions. Several experimental conditions were tried. 1,3-Cycloaddition under thermal condition was performed between **4** and benzyl azide (**5a′**) generated *in situ* from NaN_3 and benzyl bromide (**5a**) in the presence of $CuBr(PPh_3)_3$ as catalyst in DMSO at room temperature for 30 min (Scheme 2). We observed only 61.1% of product yield (**6a**). When the reaction was performed at varying temperatures from 60 to 180°C, product yields increased from moderate to higher percentage. But the maximum yield (93.3%) was obtained at 180°C for 150 min reaction time (Table 1, entry 8).

To increase the product yield further and decrease the reaction time, we applied the microwave energy instead of the thermal energy for this reaction at 40°C for 5 min and obtained 68.7% product yield (Table 1, entry 2). To

Scheme 1. Synthesis of diphenyl(prop-2-yn-1-yl)phosphine oxide (**4**).



Scheme 2. Regioselective preparation of ((1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl)diphenylphosphine oxide (**6a**).

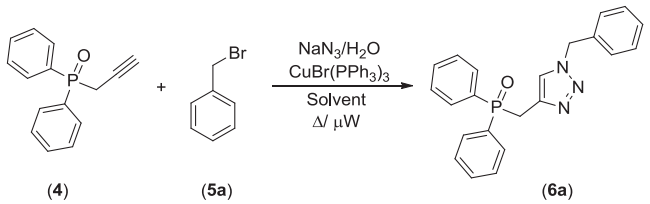


Table 1

Huisgen 1,3-dipolar cycloaddition of CuAAC of the model click ingredients[a].

	Conventional heating			Microwave heating			
Entry	Temp. (°C)	Time (min)	Yield[b] (%)	Power (W)	Temp. (°C)	Time (min)	Yield[b] (%)
1	r.t.	30	61.1	---	---	---	---
2	60	60	65.0	140	40	5	68.7
3	80	60	74.5	210	50	5	74.8
4	100	60	78.2	210	50	6	77.7
5	100	90	86.9	280	70	6	90.1
6	100	120	89.7	280	80	7	97.4
7	140	120	91.4	280	80	8	97.6
8	180	150	93.3	280	100	10	97.9

[a]Reaction conditions of CuAAC of the model click ingredients are **4,** NaN_3 and **5a** using 0.5 mol% of $CuBr(PPh_3)_3$ as catalyst in 1**:**1.2**:**1 mol ratio, [b]Isolated yield.

Table 2

Effect of the solvent on Huisgen 1,3-dipolar cycloaddition of CuAAC of the model click ingredients (**6a**)[a].

		Yield[b] (%)	
Entry	Solvent	Thermal condition	Microwave condition
1	Carbon tetrachloride	55.3	58.3
2	Toluene	58.4	63.7
3	Dichloromethane	56.2	65.8
4	Tetrahydrofuran	59.8	69.3
5	Chloroform	60.5	72.1
6	Methanol	72.7	81.7
7	Ethanol	72.9	82.2
8	Acetonitrile	80.7	86.3
9	Dimethyl formamide	88.8	92.8
10	Dimethyl sulfoxide	90.2	95.9
11	Water	93.1	97.6
12	Water–DMSO	95.2	98.7
13	Solvent-free	81.2	89.5

[a]Reaction conditions: **4**, NaN_3 and **5a** using 0.5 mol% of $CuBr(PPh_3)_3$ as catalyst in 1:1.2:1 mol ratio. All the reactions in conventional and microwave (at 280 W) conditions are made at 180 and 100°C for 150 and 10-min reaction time, respectively, [b]Isolated yield.

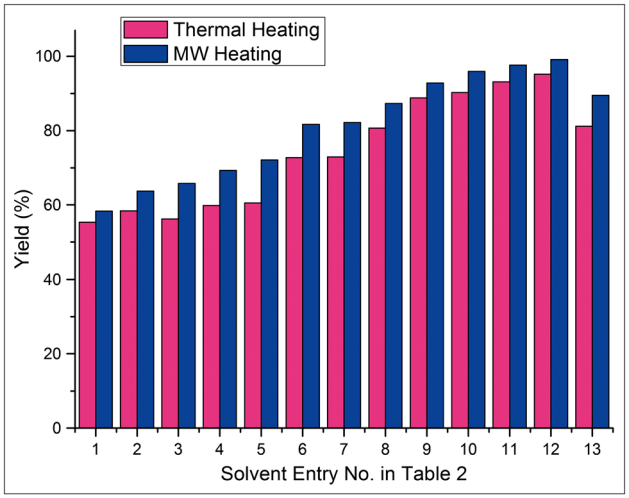


Figure 1. Optimization of various solvents for the model reaction in thermal and microwave conditions. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table 3

Microwave assisted CuAAC synthesis of **6a–o** via Scheme 3.

Entry	Product	Temp. (°C)	Time (min)	Yield[a] (%)
1	**6a**	80	10	99.2
2	**6b**	80	10	99.2
3	**6c**	80	10	99.3
4	**6d**	90	11	97.0
5	**6e**	100	11	96.0
6	**6f**	110	11	95.2
7	**6g**	110	11	95.0
8	**6h**	110	11	95.1
9	**6i**	110	12	95.0
10	**6j**	110	12	95.0
11	**6k**	110	12	97.4
12	**6l**	110	12	98.3
13	**6m**	110	13	95.0
14	**6n**	120	14	91.0
15	**6o**	120	14	90.0

[a]Isolated yield.

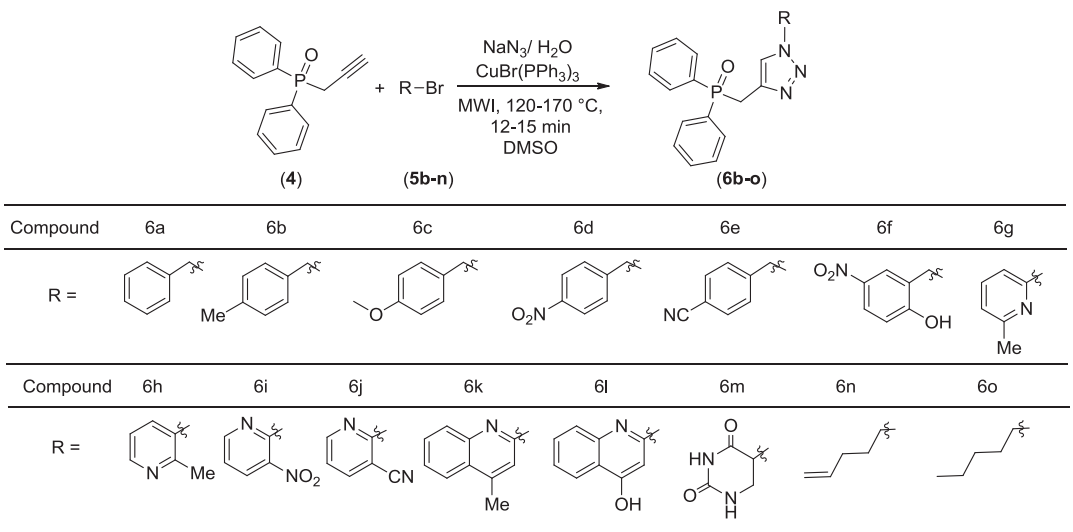
identify the best microwave irradiation reaction conditions, we performed this reaction with 0.5 mol% of the catalyst at various temperatures, different microwave power and reaction times (Table 1, entries 3–8). It is observed that, increase of temperature, MW power and reaction time has significant effect on the rate of the reaction and product yield (Table 1, entry 8).

The effect of the solvent on this reaction also studied with 0.5 mol% of $CuBr(PPh_3)_3$ catalyst at 180°C for 150 min and 100°C for 10 min in conventional and MWI conditions respectively using different solvents (Table 2, entries 1–12). The results showed (Fig. 1) that lower product yields are observed in non-polar/less polar solvents (Table 2, entries 1–5), whereas the product yield increased with the increase of solvent polarity (Table 2, entries 6–11). This might be because that polar solvents undergo higher dipole rotation under microwave irradiation and generates abnormal heat energy that effectively converted the reactants to the products in higher yields at fast rate (Table 2, entry 12). But the same reaction under solvent-free conditions afforded only lower product yield (Table 2, entry 13).

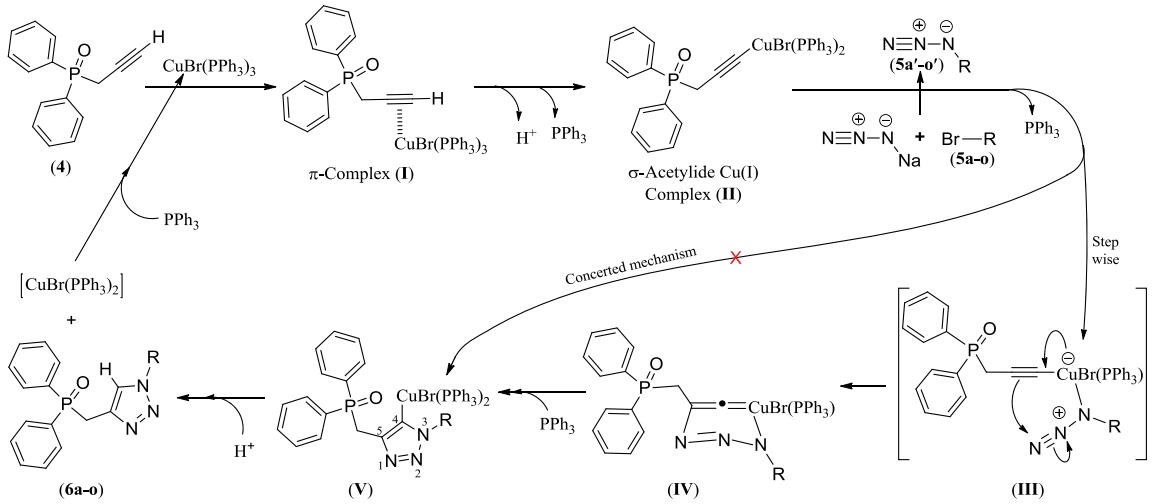
Finally, the established optimum experimental conditions for this reaction are high polar solvent medium of DMSO/H_2O (1:1) and 280 W of microwave irradiation at 100°C for 10 min (Table 2, entry 12) using 0.5 mol% of $CuBr(PPh_3)_3$ as catalyst. Synthesis of all the other titled 1,2,3-triazole diphenylphosphine oxides (**6b–o**) containing different functionalised alkyl/aryl moieties were accomplished by following this procedure (Scheme 3) and achieved excellent yields (Table 3).

It is interesting to find decrease in the yields with increase in the alkyl chain of the halide (Table 3, entries 14, 15). This

Scheme 3. Microwave-assisted CuAAC synthesis of 1-(substituted)-1*H*-1,2,3-triazol-4-yl)methyl)diphenylphosphine oxides (**6b–o**).



Scheme 4. Mechanism of microwave-assisted CuAAC synthesis of **6a–o**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]



might be due to the hydrophobicity of longer hydrocarbon chain in the halide (**5b–o**). Aromatic halides afforded higher product yields irrespective of the electronic nature of substituents. Steric repulsion of the bulky groups closer to azide functionality resulted in lesser product yields (Table 3, entries 6 and 8–10).

This reaction proceeds with the initial formation of a $CuBr(PPh_3)_3$ acetylide π-complex (**I**) [26–28]. Substitution of its terminal alkyne hydrogen with copper leads to corresponding σ-acetylide Cu(I) complex (**II**). Addition of **5a′–o′**, which are formed *in situ* from **5a–o** and sodium azide to **II** leads to Cu(0) complex **IV** through the intermediate **III** in stepwise mechanism according to the density functional theory calculations [29]. Cleavage of allene double bond and rearrangement of **IV** leads to compound **V,** which on acidification leads to formation of **6a–o** (Scheme 4). In this process, the $CuBr(PPh_3)_3$ gets eliminated in pure form and as such it could continue to play its role in the process again and again.

CONCLUSIONS

We have successfully developed a simple and effective method for the preparation of 1-(substituted)-1*H*-1,2,3-Triazol-4-yl)methyl)diphenylphosphineoxides (**6a–o**) by regioselective [3+2]-cycloaddition of organic azides to terminal alkynes with click chemistry using 280-W microwave power at 100°C for 10 min in 1:1 DMSO/H_2O medium in the presence of 0.5 mol% of $CuBr(PPh_3)_3$ catalyst. The simplicity and efficiency of this procedure allows it for a one-pot three-component commercial preparation of a wide variety of bio-active 1,2,3-triazole diphenylphosphine oxides.

EXPERIMENTAL

Materials and methods. All the chemicals/reagents, $CuBr(PPh_3)_3$ catalyst and analytical grade solvents procured from Merck (Mumbai, India), Lancaster Chemical (Mumbai, India), and Sigma–Aldrich (Hyderabad, India) were used as received. Melting points were determined in the Guna Digital melting point apparatus (Guna Enterprises, Chennai, India) using a calibrated thermometer. All the reactions were carried out in air in technical solvents without excluding moisture or oxygen. Column/TLC chromatography was performed on silica gel using UV light and iodine to visualize the products. IR spectra were recorded on FTIR spectrophotometer (IR-Prestige 21, Shimadzu Corporation, Japan) using KBr optics. ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded at room temperature in $CDCl_3$ on a Varian 400-MHz NMR spectrometer operating at 400, 100, and 161.89 MHz, respectively, at the Pusan National University, Pusan, Republic of Korea. The ^{1}H and ^{13}C chemical shifts (δ) are reported in ppm with respect to TMS and those of ^{31}P in 85% H_3PO_4. Mass spectra were recorded on a Jeol JMS-700 mass spectrometer at Pukyong National University, Busan, Republic of Korea. Elemental analyses were performed on a Thermo Finnigan instrument at the University of Hyderabad, India. All reported yields are isolated product yields, and in the catalytic studies, the average yield of at least two runs is taken.

Synthesis of diphenyl(prop-2-yn-1-yl)phosphine oxide (4). Diphenyl(prop-2-yn-1-yl)phosphine oxide was prepared [24,30] by Michaelis–Arbuzov reaction between triphenyl phosphine (6.82 g, 0.026 mol) and propargyl bromide (3.77 g, 0.032 mol) in 10 mL of dry toluene, charged in to 250-mL round-bottom flask (Scheme 1). The reaction mixture was then heated to reflux at 110°C for 2 h and then cooled at room temperature. The phosphonium salt (**3**) was obtained as white powdered. It was filtered and washed several times with diethyl ether. The product was taken in 100 mL of water and then refluxed half an hour. After this, 60 mL of 2.77 M NaOH aqueous solution was added into the dense suspension and gently refluxed for an additional 2 h. After cooling, the mixture was extracted with dichloromethane and the extractant was evaporated under vacuum after drying with anhydrous sodium sulfate. The crud product was recrystallized from hexane–diethyl ether to obtain the product as a white crystalline solid, 6. About 10 g (97.6%); mp: 152–154°C, ^{31}P-NMR (162 MHz, $CDCl_3$) $\delta = 22.22$ ppm; ^{1}H-NMR (400 MHz, $CDCl_3$)

δ = 7.67–7.41 (m, 10H, Ar–H), 2.21–2.17 (dd, 2H, $^2J_{PH}$ = 12, 4 Hz, P–CH_2), 2.88 (s, 1H, C–H_{Alkyne}) ppm; ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ = 53.5, 128.4, 128.5, 131.9, 132.0, 132.9, 133.5 ppm. MS (70 eV): *m/z* = 240 ($M^{+\bullet}$). IR (KBR) ν_{max} = 2299 (C–H_{Alkyne}), 2933 and 2865 (C–H), 2217 (C–C_{Alkyne}), 1264 (P=O) cm^{-1}. *Anal*. Calcd. for $C_{15}H_{13}OP$: C, 74.99; H, 5.45. Found: C, 74.90; H, 5.37.

Synthesis of ((1-benzyl-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6a). ***MWI method.*** In a two-necked round-bottom flask, fitted with air condenser and thermo probe a mixture of **4** (0.5 mmol), **5a** (0.5 mmol), $CuBr(PPh_3)_3$, (2.3 mg, 0.5 mol%), and NaN_3 (42 mg, 0.65 mmol) in water (5 mL) and in DMSO (5 mL) were taken (Scheme 3). All the contents were mixed thoroughly and exposed to MWI in CATA-4R—Scientific Microwave oven at 40–100°C with 140–280 W at ambient pressure. The reaction mixture was stirred continually during microwave radiation to maintain the temperature homogeneously. After the total consumption of the starting benzyl bromide in 5–10 min as indicated by TLC, the solvents were removed in the rotary evaporator, and the crud product obtained was washed thoroughly with water to remove any azide residue. This crude product was purified by column chromatography on 60–120 mesh silica gel using ethyl acetate/hexane (1:3) as eluent, and the solvent was evaporated in a rotary evaporator. This compound was further recrystallized from ethyl acetate to afford pure **6a** (Table 1).

Conventional method. The reactants were heated in an oil-bath up to 180°C from room temperature (r.t.) for 30–150 min and the workup and purification of products were carried out as described in the MWI procedure.

Microwave synthesis of 1-(substituted)-1H-1,2,3-triazol-4-yl) methyl)diphenylphosphine oxides (6b–o). As described in the model reaction, **4** (0.5 mmol) and **5b–o** (0.5 mmol), DMSO (5 mL), NaN_3 (42 mg, 0.65 mmol) in water (5 mL) and 0.5 mol% CuBr $(PPh_3)_3$, (2.3 mg) were mixed thoroughly in a two-necked round-bottom flask and exposed to MWI at 280 W with 80–120°C in ambient pressure (Scheme 2). The reaction was completed (TLC) in 10–14 min. The compounds were purified as per the procedure described in the model reaction. All the newly synthesized titled compounds (**6b–r**) were characterized by IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR, mass spectral, and elemental analysis.

Physical and spectral characterization of the titled compounds (6a–o). ***((1-Benzyl-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6a).*** Yellow solid, mp: 166–168°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.82. ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.68–6.88 (15H, m, Ar–H), 8.21 (1H, s, N–CH=), 5.48 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 3.42 (2H, s, N–CH_2); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 136.2, 135.3, 133.3, 131.2, 130.3, 129.5, 129.1, 127.9, 126.3, 123.4, 59.3, 39.6. MS ($M^{+\bullet}$; m/z): 373. IR (KBR), (ν_{max} cm^{-1}): 2932 and 2854 (C–H), 1621 (C=N), 1443 (C–N), 1381, 1229 (P=O), 1021, 975 (P–O), 735 (P–C). *Anal*. Calcd. for $C_{22}H_{20}N_3OP$: C, 70.77; H, 5.40, N, 11.25. Found: C, 70.61; H, 5.32; N, 11.17.

((1-(4-Methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6b). Yellow solid, mp: 167–169°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.90; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.46–6.96 (14H, m, Ar–H), 8.27 (1H, s, N–CH=), 5.50 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 3.41 (2H, s, N–CH_2), 1.58 (3H, s, Ar–CH_3); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 136.1, 135.8, 134.2, 132.8, 131.3, 130.6, 129.4, 129.2, 127.7, 123.7, 59.5, 39.4, 23.5. MS ($M^{+\bullet}$; m/z): 387. IR (KBR) (ν_{max} cm^{-1}): 2933 and 2854 (C–H), 1619 (C=N), 1444 (C–N), 1380, 1228 (P=O), 1024, 974 (P–O), 734 (P–C). *Anal*. Calcd. for $C_{23}H_{22}N_3OP$: C, 71.31; H, 5.72, N, 10.85. Found: C, 71.22; H, 5.65; N, 10.77.

((1-(4-Methoxybenzyl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6c). Yellow solid, mp: 165–167°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.59; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.48–6.98 (14H, m, Ar–H), 8.27 (1H, s, N–CH=), 5.43 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 2.42 (3H, s, OCH_3); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 136.3, 135.6, 134.3, 132.7, 131.5, 130.7, 129.5, 129.5, 127.4, 123.5, 59.5, 39.5, 56.6. MS ($M^{+\bullet}$; m/z): 403. IR (KBR) (ν_{max} cm^{-1}): 2938 and 2856 (C–H), 1620 (C=N), 1446 (C–N), 1386, 1223 (P=O), 1020, 971 (P–O), 731 (P–C). *Anal*. Calcd. for $C_{23}H_{22}N_3O_2P$: C, 68.48; H, 5.50, N, 10.42. Found: C, 68.40; H, 5.42; N, 10.35.

((1-(4-Nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl)diphenylphosphine oxide (6d). Dark yellow solid, mp: 159–161°C, ^{31}P-NMR ($CDCl_3$) δ [ppm]: 24.23; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.69–7.18 (14H, m, Ar–H), 8.22 (1H, s, N–CH=), 5.46 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 3.52 (2H, s, N–CH_2); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 145.8, 143.7, 136.1, 133.2, 132.3, 131.4, 131.4, 130.5, 129.8, 124.7, 124.1, 58.7. MS ($M^{+\bullet}$; m/z): 418. IR (KBR) (ν_{max} cm^{-1}): 2930 and 2853 (C-H), 1542 (N=O), 1626 (C=N), 1441 (C–N), 1384, 1231 (P=O), 1020, 971 (P–O), 732 (P–C). *Anal*. Calcd. for $C_{22}H_{19}N_4O_3P$: C, 63.16; H, 4.58, N, 13.39. Found: C, 63.03; H, 4.49; N, 13.30.

4-((4-((Diphenylphosphoryl)methyl)-1H-1,2,3-triazol-1-yl) methyl)benzonitrile (6e). Yellow solid, mp: 169–171°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 24.39; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.92–6.88 (14H, m, Ar–H), 8.27 (1H, s, N–CH=), 5.57 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 3.49 (2H, s, N–CH_2); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 141.3, 136.4, 133.7, 133.2, 132.4, 131.3, 131.3, 130.7, 130.1, 124.1, 110.8, 119.8, 58.7. MS ($M^{+\bullet}$; m/z): 398. IR (KBR) (ν_{max} cm^{-1}): 2936 and 2852 (C–H), 2230 (C≡N), 1624 (C=N), 1445 (C–N), 1383, 1232 (P=O), 1024, 975 (P–O), 733 (P–C). *Anal*. Calcd. for $C_{23}H_{19}N_4OP$: C, 69.34; H, 4.81, N, 14.06. Found: C, 69.25; H, 4.74; N, 13.92.

((1-(2-Hydroxy-5-nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6f). Yellow solid, mp: 174–176°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 22.98, ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 10.87 (1H, s, Ar–OH), 7.88–7.18 (13H, m, Ar–H), 8.25 (1H, s, N–CH=), 5.56 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 3.56 (2H, s, N–CH_2); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 163.7, 141.5, 136.3, 133.5, 132.4, 131.9, 131.7, 130.6, 129.8, 128.4, 126.3, 124.6, 116.5, 49.8. MS ($M^{+\bullet}$; m/z): 434. IR (KBR) (ν_{max} cm^{-1}): 3420 (O–H), 2932 and 2853 (C–H), 1623 (C=N), 1548 (N=O), 1446 (C–N), 1380, 1234 (P=O), 1020, 976 (P–O), 730 (P–C). *Anal*. Calcd. for $C_{22}H_{19}N_4O_4P$: C, 60.83; H, 4.41, N, 12.90. Found: C, 60.74; H, 4.32; N, 12.84.

((1-(6-Methylpyridin-2-yl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6g). Brown solid, mp: 168–170°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.63; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.80–7.23 (13H, m, Ar–H), 8.24 (1H, s, N–CH=), 5.54 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 1.68 (3H, s, Ar–CH_3); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 154.2, 141.3, 136.5, 133.5, 132.4, 131.5, 131.6, 130.6, 129.9, 125.1, 124.2, 120.7, 25.3. MS ($M^{+\bullet}$; m/z): 374. IR (KBR) (ν_{max} cm^{-1}): 2935 and 2855 (C–H), 1625 (C=N), 1447 (C–N), 1384, 1230 (P=O), 1023, 977 (P–O), 733 (P–C). *Anal*. Calcd. for $C_{21}H_{19}N_4OP$: C, 67.37; H, 5.12, N, 14.97. Found: C, 67.30; H, 5.03; N, 14.89.

((1-(2-Methylpyridin-3-yl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6h). Brown solid, mp: 161–163°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.29; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.88–7.25 (13H, m, Ar–H), 8.20 (1H, s, N–CH=), 5.50 (2H, d, $^2J_{H-P}$ = 6.54 Hz, P–CH_2), 1.66 (3H, s, Ar–CH_3);

^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 149.8, 142.8, 139.1, 136.7, 133.5, 132.5, 131.9, 131.5, 130.9, 130.3, 124.1, 121.6, 21.5. MS ($M^{+\bullet}$; m/z): 374. IR (KBR) (ν_{max} cm^{-1}): 2932 and 2853 (C–H), 1634 (C=N), 1443 (C–N), 1381, 1233 (P=O), 1020, 976 (P–O), 735 (P–C). *Anal*. Calcd. for $C_{21}H_{19}N_4OP$: C, 67.37; H, 5.12, N, 14.97. Found: C, 67.29; H, 5.04; N, 14.88.

((1-(3-Nitropyridin-2-yl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6i). Yellow solid, mp: 166–168°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.67; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.98–7.28 (13H, m, Ar–H), 8.36 (1H, s, N–CH=), 5.53 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 155.4, 150.2, 144.9 136.0, 133.6, 133.2, 132.3, 131.7, 131.3, 130.3, 125.6, 124.4. MS ($M^{+\bullet}$; m/z): 405. IR (KBR) (ν_{max} cm^{-1}): 2932 and 2853 (C–H), 1630 (C=N), 1547 (N=O), 1443 (C–N), 1381, 1228 (P=O), 1021, 971 (P–O), 732 (P–C). *Anal*. Calcd. for $C_{20}H_{16}N_5O_3P$: C, 59.26; H, 3.98, N, 17.28. Found: C, 59.19; H, 3.89; N, 17.20.

2-(4-((Diphenylphosphoryl)methyl)-1H-1,2,3-triazol-1-yl) nicotinonitrile (6j). Brown solid, mp: 171–173°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 23.11; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.98–7.28 (13H, m, Ar–H), 8.37 (1H, s, N–CH=), 5.55 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 158.2, 153.6, 141.3, 135.9, 133.9, 133.1, 132.3, 131.7, 131.1, 130.5, 124.2, 117.8, 108.2. MS ($M^{+\bullet}$; m/z): 385. IR (KBR) (ν_{max} cm^{-1}): 2937 and 2856 (C–H), 2235 (C≡N), 1629 (C=N), 1448 (C–N), 1385, 1235 (P=O), 1020, 973 (P–O), 737 (P–C). *Anal*. Calcd. for $C_{21}H_{16}N_5OP$: C, 65.45; H, 4.18, N, 18.17. Found: C, 65.37; H, 4.07; N, 18.09.

((1-(4-Methylquinolin-2-yl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6k). Brown solid, mp: 176–178°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 24.36; ^{1}H-NMR ($CDCl_3$) δ [ppm]: 7.83–7.28 (15H, m, Ar–H), 8.26 (1H, s, N–CH=), 5.55 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2), 1.96 (3H, s, Ar–CH_3); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 147.9, 146.8, 146.1, 135.5, 133.2, 132.3, 131.9, 131.5, 130.9, 130.4, 130.1, 127.1, 125.9, 125.5, 124.3, 113.5, 21.0. MS ($M^{+\bullet}$; m/z): 424. IR (KBR) (ν_{max} cm^{-1}): 2937 and 2855 (C–H), 1628 (C=N), 1449 (C–N), 1378, 1236 (P=O), 1027, 975 (P–O), 738 (P–C). *Anal*. Calcd. for $C_{25}H_{21}N_4OP$: C, 70.75; H, 4.99, N, 13.20. Found: C, 70.66; H, 4.90; N, 13.12.

((1-(8-Hydroxyquinolin-5-yl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6l). Brown solid, mp: 174–176°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: δ 23.93; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.89–7.18 (15H, m, Ar–H), 8.21 (1H, s, N–CH=), 5.51 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2), 10.26 (1H, s, Ar–OH); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 156.5, 152.1, 139.6, 135.8, 133.8, 133.3, 132.5, 131.6, 131.2, 130.1, 127.6, 127.1, 124.5, 123.1, 118.9, 114.8. MS ($M^{+\bullet}$; m/z): 426. IR (KBR), (ν_{max} cm^{-1}): 3430 (OH), 2936 and 2859 (C–H), 1645 (C=N), 1449 (C–N), 1385, 1226 (P=O), 1021, 972 (P–O), 730 (P–C). *Anal*. Calcd. for $C_{24}H_{19}N_4O_2P$: C, 67.60; H, 4.49, N, 13.14. Found: C, 67.52; H, 4.41; N, 13.08.

5-(4-((Diphenylphosphoryl)methyl)-1H-1,2,3-triazol-1-yl) dihydropyrimidine-2,4(1H,3H)-dione (6m). Brown solid, mp: 148–150°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: 24.59; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 9.92 (1H, s, CO–NH–CO), 8.22 (1H, s, C–NH–CO), 8.20 (1H, s, N–CH=), 7.48–7.18 (10H, m, Ar–H), 5.50 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2), 3.44–3.37 (1H, m, N–CH), 2.70–2.55 (2H, m, N–CH_2), ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 178.5, 165.1, 135.7, 133.7, 132.6, 131.2, 131.5, 130.9, 124.2, 77.3, 42.3. MS ($M^{+\bullet}$; m/z): 395. IR (KBR) (ν_{max} cm^{-1}): 3341–3354 (NH), 2982 and 2863 (C–H), 1695–1710 (C=O) 1644 (C=N), 1436 (C–N), 1228 (P=O), 932 (P–O), 739 (P–C). *Anal*. Calcd. for $C_{19}H_{18}N_5O_3P$: C, 57.72; H, 4.59, N, 17.71. Found: C, 57.64 H, 4.50; N, 17.64.

((1-(Pent-4-en-1-yl)-1H-1,2,3-triazol-4-yl)methyl) diphenylphosphine oxide (6n). Pale yellow solid, mp: 147–149°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: δ 24.13; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.46–7.18 (10H, m, Ar–H), 8.12 (1H, s, N–CH=), 6.13 (1H, m, C–CH=), 5.45 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2), 5.35–5.27 (2H, m, =CH_2), 2.63–2.51 (2H, t, N–CH_2), 1.50–1.44 (4H, m, –(CH_2–)$_2$); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 138.1, 136.4, 133.7, 132.5, 131.1, 131.1, 130.3, 124.1, 118.2, 54.2, 33.5, 27.2; MS ($M^{+\bullet}$; m/z): 351. IR IR (KBR) (ν_{max} cm^{-1}): 2931 and 2853 (C–H), 1635 (C=N), 1441 (C–N), 1382, 1228 (P=O), 1631 (C=C), 1022, 974 (P–O), 733 (P–C). *Anal*. Calcd. for $C_{20}H_{22}N_3OP$: C, 68.36; H, 6.31, N, 11.96. Found: C, 68.27; H, 6.24; N, 11.88.

((1-Pentyl-1H-1,2,3-triazol-4-yl)methyl)diphenylphosphine oxide (6o). Pale yellow solid, mp: 142–144°C. ^{31}P-NMR ($CDCl_3$) δ [ppm]: δ 24.33; ^{1}H-NMR (400 MHz, $CDCl_3$) δ [ppm]: 7.41–7.16 (10H, m, Ar–H), 8.22 (1H, s, N–CH=), 5.42 (2H, d, $^2J_{H\text{-}P}$ = 6.54 Hz, P–CH_2), 2.58 (2H, t, $^3J_{H\text{-}H}$ = 2.20 Hz, N–CH_2), 1.50–1.41 (4H, m, –(CH_2–)$_3$), 1.79 (2H, t, $^3J_{H\text{-}H}$ = 6.51 Hz, CH_3); ^{13}C-NMR (100.56 MHz, $CDCl_3$) δ [ppm]: 135.9, 133.3, 132.3, 131.1, 131.1, 130.4, 124.9, 53.2, 30.8, 29.8, 23.5, 15.3. MS ($M^{+\bullet}$; m/z): 353. IR (KBR) (ν_{max} cm^{-1}): 2933 and 2854 (C–H), 1637 (C=N), 1444 (C–N), 1383, 1230 (P=O), 1024, 972 (P–O), 735 (P–C). *Anal*. Calcd. for $C_{20}H_{24}N_3OP$: C, 67.97; H, 6.85, N, 11.89. Found: C, 67.90; H, 6.76; N, 11.80.

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