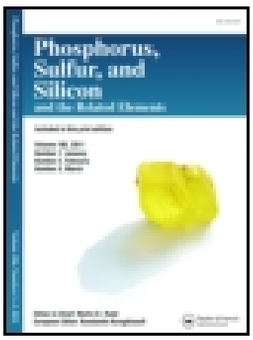

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PHOSPHORUS, SULFUR, AND SILICON AND THE RELATED ELEMENTS
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Ultrasound-promoted, rapid and green synthesis of phosphonamide derivatives under catalyst and solvent-free conditions

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ABSTRACT

We report a rapid, efficient, economic, environmentally benign, and easy to scale-up method for the synthesis of phosphonamide derivatives using ultrasound irradiation, under catalyst and solvent-free conditions starting from the corresponding amine and phenyl phosphonic dichloride. The reaction was achieved in excellent isolated yield in a short reaction time at room temperature. The structures of the synthesized compounds are confirmed by elemental analysis as well as by IR and ^{1}H, ^{13}C, ^{31}P NMR spectroscopic data and mass spectrometry.

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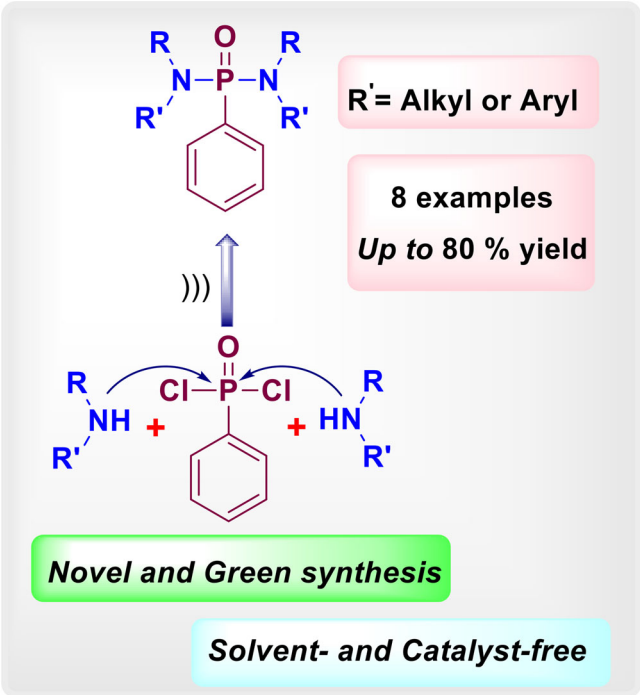
KEYWORDS
Green chemistry; phenylphosphonic dichloride; phosphonamide; ultrasound irradiation

GRAPHICAL ABSTRACT



Introduction

The phosphonamide functional group is a key structural feature present in a number of biologically active natural products such as phosmidosine,[1] agrocin 84,[2] and microcin.[3] Compounds containing the phosphonamide moiety are important in biochemistry because a very large number of the compounds of biological interest belong to this family: DNA, RNA, and nucleotides.[4] Many applications have been described and some clinical trials are under development from a chemotherapy perspective as inhibitors of matrix metalloproteinases MMP-1, MMP-3, and MMP-9 **1**, **2**,[5–8] inhibitors of tumor necrosis factor-α converting enzyme (TACE) **3**[9] (Figure 1).

Phosphonamides are important for the synthesis of various bioactive compounds serving as natural products, phosphates, phosphonopeptides, amino acids analogues,

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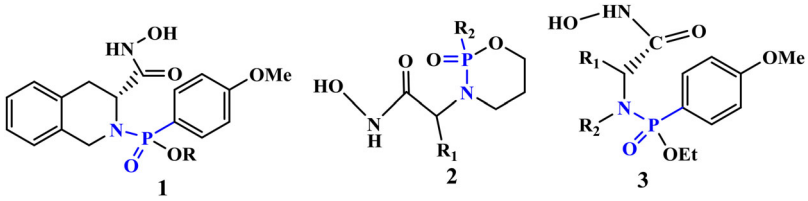


Figure 1. Examples of bioactive molecules containing phosphonamide moiety.

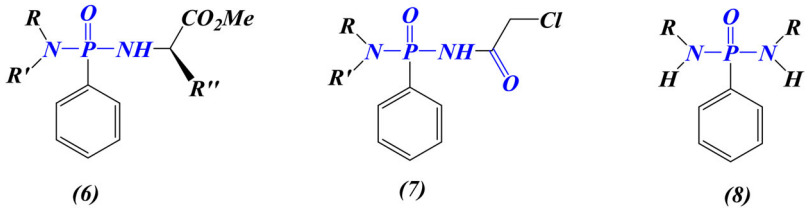
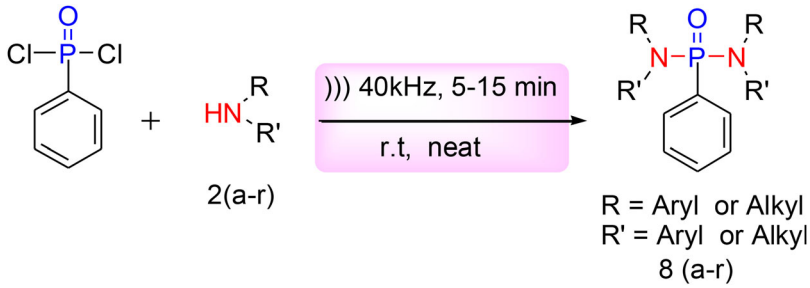


Figure 2. Structures of phosphonamides prepared by the conventional method.



Scheme 1. Synthesis of phosphonamides under ultrasound irradiation.

prodrugs, pharmacological agents, and as important synthetic precursors.[10–13] Despite the importance of phosphonamides, their synthesis requires harsh conditions and/or the use of halides or precious transition metals.[14] The quest for green procedures has become of paramount importance for organic chemists in the last decade.[15] Discovery of benign, green and atom economic processes is one of the current corner stones for chemists.[16] One of the most promising ecofriendly processes is the use ultrasound irradiation to catalyze organic reactions.

One of the main objectives of our research group is the synthesis a new series of organophosphorus compound,[17–25] including phosphonamides.

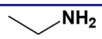
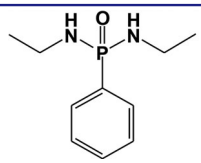
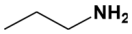
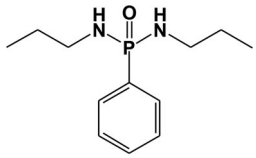
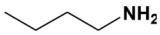
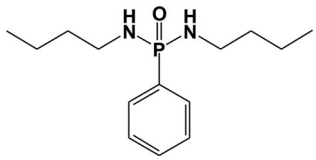
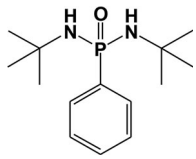
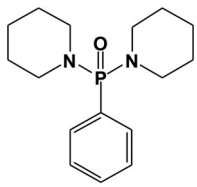
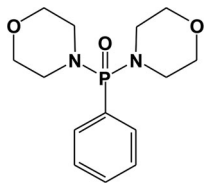
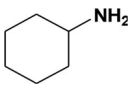
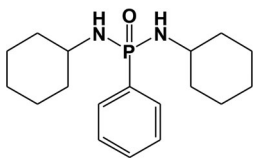
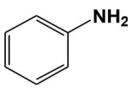
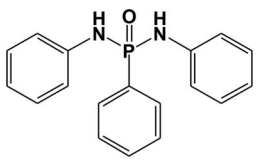
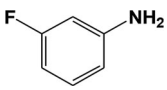
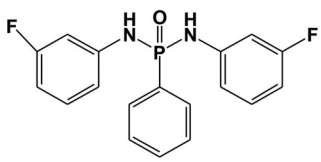
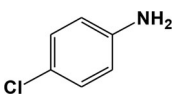
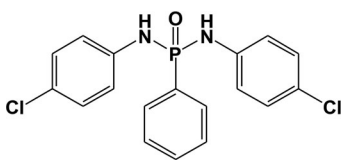
In previous work, we have prepared a series of bisphosphonamides (**8**) (Figure 2) in good isolated yield by conventional method *via* a one-pot synthetic route, starting from corresponding primary amines with phenyl phosphonic dichloride in dry acetonitrile at −5 °C.[26] We also have synthesized another derivative (**6, 7**) (Figure 2) from amines and aminoester or chloroacetamide with phenyl phosphonic dichloride in dry THF at 0 °C in tow steps.[27] Different process parameters such as temperature, solvent, catalyst type, and other factors are utilized by other researchers to prepare these compounds in excellent isolated yield.[28–35] But the traditional notion of yield is no longer sufficient to assess the efficiency of chemical processes.

Sustainable chemistry requires introducing new concepts that aim to reduce or eliminate the source of hazardous substances, the use of renewable raw materials, and greater energy efficiency of products. With the awareness of the environmental impact of human activities and the emergence of the concept of sustainable development, chemists strive to put principles into practice by developing methods aimed at minimizing chance during synthesis, and have control over reactivity in order to avoid the production of undesirable compounds and thus limit the quantities of waste the concepts of "Green Chemistry".[36]

The objective of this work is to carry out the reactions under ultrasonic irradiation, without solvent. This powerful technique became extremely efficient and attractive in synthetic organic chemistry, and is able to activate many reactions due to cavitational collapse. it greatly contributes to the development of sustainable green chemistry, by responding to scientific challenges and current economic and environmental problems. Indeed, it is capable of inducing a myriad of chemical transformations.[37]

In continuation with our research on the synthesis of organophosphorus compounds, we report herein a simple, green, and efficient method for the preparation of these compounds under ultrasound irradiation techniques, solvent and catalyst-free conditions. This technique provides higher yields, shorter reaction times, and milder reaction conditions, nontoxic, environmentally friendly solvent, in a one-step reaction, without isolation of any intermediate thus reducing time, saving money, energy, and raw materials.[38–47]

Table 1. Synthesis of phosphonamides under ultrasound irradiation.

Entry	Substrate	Product	Time (min)	Yield (%)
a			5	95
*b**			5	98
c			5	97
d			10	98
e			10	91
f			5	90
*g**			5	97
h			5	94
i			5	90
j			5	92

(*continued*)

Table 1. Continued.

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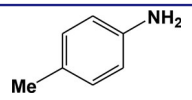
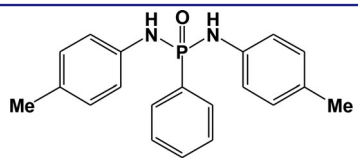
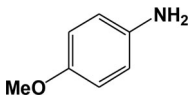
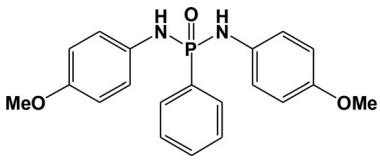
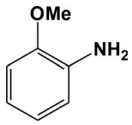
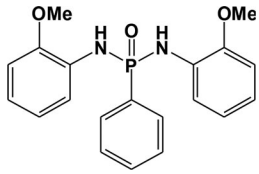
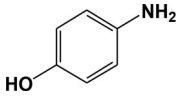
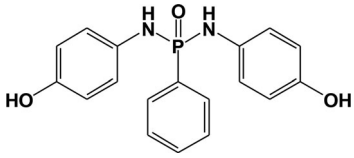
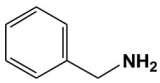
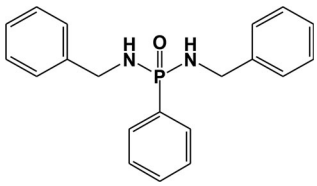
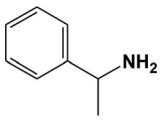
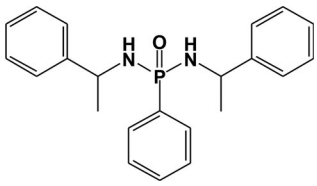
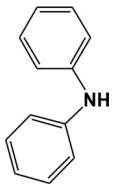
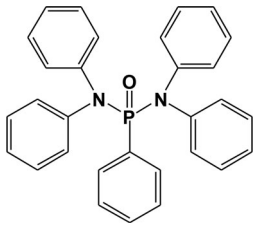
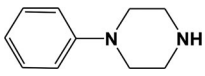
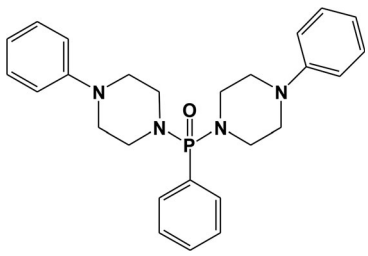
k			5	90
l			5	95
m			10	92
n			5	93
*o**			5	95
*p**			10	94
q			15	97
r			10	89

*[26].

Results and discussion

Herein we studied the synthesis of organophosphorus compounds under green chemical conditions using ultrasound irradiation. The phosphonamides **8**(**a**–**r**), were prepared in a one-pot synthetic route, starting from corresponding amine with phenyl phosphonic dichloride in the absence of any

solvent and any catalyst after 5–15 min (Table 1), the reaction was completed with an excellent yield.

Notably, no product was observed when the reaction was realized in the absence of ultrasound irradiation even after 48 h in the same conditions this shows the essential role of ultrasound irradiation. This excellent result encourages us to extend this study to various structurally primary and secondary amines (Scheme 1).

Spectrometric methods confirmed the structures of all synthesized phosphonamides; in the ^{1}H NMR, the formation of phosphonamide 8 g is confirmed by the appearance of a singlet at 2.40 ppm of the NH group, the phenyl bound to phosphorus atom appears between 7.90 and 7.50 ppm as multiplet. In infrared, we observed an absorption band toward 3155 cm^{-1} which corresponds to NH group. The bands of C = C and P = O groups appear, respectively, around 1461 and 1250 cm^{-1}. ^{31}P NMR signals of 8 g were observed at 16 ppm.

Experimental

Materials

The chemicals used in this work were obtained from Fluka and Merck Chemical Company and were used without purification.

Apparatus

Infrared (IR) spectra were recorded as KBr pellets on a Perkin-Elmer FT-600 spectrometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded in DMSO-d_6 or $CDCl_3$ solvents on a 250 or 300 MHz Bruker spectrometer with tetramethylsilane (TMS) as internal reference. Chemical shifts are reported in δ units (ppm). All coupling constants (J) are reported in Hertz. Multiplicity is indicated as s (singlet), d (doublet), t (triplet), m (multiplet), and combination of these signals. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded in DMSO-d_6 or $CDCl_3$ solvents at 60 or 100 MHz on a Bruker spectrometer with tetramethylsilane (TMS) as internal reference. Phosphorus nuclear magnetic resonance (^{31}P NMR) spectra were recorded on a Brucker instrument at 100 or 121.5 MHz. Chemical Shift (ppm) Relative to 85% H_3PO_4. Mass spectra were recorded on a Shimadzu QP 1100 Ex mass spectrometer operating at an ionization potential of 70 eV. All reactions were monitored by thin-layer chromatography TLC on silica Merck h60 F_{254} (Art. 5554) percolated aluminum plates and were developed by Spraying with ninhydrin solution. Ultrasound assisted reactions were carried out using a FUNGILAB ultrasonic bath with a frequency of 40 kHz and a nominal power of 250 W. The supplemental materials contain sample ^{1}H, ^{13}C and ^{31}P NMR and mass spectra for the products 8 (supplementary information, Figures S1–S46).

Typical experimental procedure for the synthesis of phosphoramidates

In a 10 mL round bottom flask taken a mixture of phenylphosphonic dichloride (1 mmol) with amine (2 mmol) was added. Then reaction mixture was subjected to the ultrasonication for an appropriate time. After completion of the reaction, as indicated by TLC, silica gel; dichloromethane: methanol (9:1). Recrystallization of the crude product in ether afforded pure expected bisphosphonamides **8(a–r)** as white solids.

Bis (ethylamino) phenylphosphine oxide (8a)

Yield: 95%. R_f=0.65 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3435, 1512, 1200. ^{1}H NMR (DMSO, 300 MHz): 7.60 (m, 2H, H–Ar); 7.30 (m, 3H, H–Ar); 3.60 (s, 2H, NH); 2.75 (q, J = 7.16 Hz, 4H, CH_2); 1.15 (t, J = 7.30 Hz, 6H, CH_3). ^{31}P NMR (DMSO, 100 MHz) δ = 16.3 ppm. ^{13}C NMR (DMSO, 100 MHz): 131.0; 130.9; 129.9; 128.2; 127.9; 127.8; 34.4; 12.9. MS ESI+ 30 eV m/z: 213.1 $[M+H]^+$ 100% calcd for $[C_{10}H_{17}N_2OP]$ 212. Anal. Calcd for $C_{10}H_{17}N_2OP$: C 56.59, H 8.07, N 13.20. Found: C 56.50, H 8.00, N 13.25%.

Bis (propylamino) phenylphosphine oxide (8b)

Yield: 98%. R_f=0.61 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3193, 1465, 1200. ^{1}H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 2.90 (m, 4H, CH_2–NH); 2.50 (m, 2H, NH); 1.50 (m, 4H, CH_2–CH_3); 0.90 (t, J_1=7.31 Hz, J_2 =7.46 Hz, 6H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) δ = 16.3 ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 135.2; 131.5; 128.3; 128.3; 42.5; 25.3; 11.3. MS ESI+ 30 eV m/z: 241.1 $[M+H]^+$ 100% calcd for $[C_{12}H_{21}N_2OP]$ 240. Anal. Calcd for $C_{12}H_{21}N_2OP$: C 59.98, H 8.81, N 11.66. Found: C 59.90, H 8.75, N 11.70%.

Bis (butylamino) phenylphosphine oxide (8c)

Yield: 97%. R_f=0.60 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3428, 1506, 1467, 1269. ^{1}H NMR ($CDCl_3$, 250 MHz): 7.60 (m, 2H, H–Ar); 7.45 (m, 3H, H-Ar); 4.75 (m, 2H, NH); 3.20 (m, 4H, CH_2–NH); 1.55 (m, 4H, CH_2) ; 1.33 (m, 4H, CH_2–CH_3); 0.90 (t, J = 8.0 Hz, 6H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) δ = 16.3 ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 135.0; 131.5; 129.6; 128.6; 47.4; 32.1; 20.0; 13.9. MS ESI$^+$ 30 eV m/z: 269.2 $[M+H]^+$ 100% calcd for $[C_{14}H_{25}N_2OP]$ 268. Anal. Calcd for $C_{14}H_{25}N_2OP$: C 62.66, H 9.39, N 10.44. Found: C 62.62, H 9.30, N 10.50%.

Bis (tert-butylamino) phenylphosphine oxide (8d)

Yield: 98%. R_f=0.61 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3228, 1436, 1221. ^{1}H NMR ($CDCl_3$, 250 MHz): 7.80 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 2.00 (m, 2H, NH) 1.27 (s, 18H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) δ = 16.3 ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 135.0; 131.5; 129.6; 128.6; 47.6; 29.1. MS ESI+ 30 eV m/z: 269.2 $[M+H]^+$ 100% calcd for

$[C_{14}H_{25}N_2OP]$ 268. Anal. Calcd for $C_{14}H_{25}N_2OP$: C 62.66, H 9.39, N 10.44. Found: C 62.62, H 9.30, N 10.50%.

Bis (piperidine) phenylphosphine oxide (8e)

Yield: 91%. R_f=0.62 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 1591, 1456, 1211. ^1H NMR (DMSO, 300 MHz): 7.60 (m, 2H, H–Ar); 7.30 (m, 3H, H–Ar); 2.95 (t, $J = 10.05$ Hz, 8H, CH_2); 1.65 (m, 8H, CH_2) 1.55 (m, 4H, CH_2). ^{31}P NMR (DMSO, 100 MHz) $\delta = 16.2$ ppm. ^{13}C NMR (DMSO, 100 MHz): 131.0; 130.7; 129.9; 128.1; 127.9; 127.8; 43.9; 22.5; 22.1. MS ESI+ 30 eV *m/z*: 293.1 $[M+H]^+$ 100% calcd for $[C_{16}H_{25}N_2OP]$ 292. Anal. Calcd for $C_{16}H_{25}N_2OP$: C 65.73, H 8.62, N 9.58. Found: C 65.70, H 8.59, N 9.60%.

Bis (morpholine) phenylphosphine oxide (8f)

Yield: 90%. R_f=0.68 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 1457, 1200. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.65 (m, 3H, H–Ar); 3.67 (t, $J = 8.45$ Hz, 8H, **CH_2**–O); 2.90 (t, $J = 7.30$ Hz, 8H, **CH_2**–N). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.3$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 135.0; 131.5; 129.6; 128.6; 72.8; 46.2. MS ESI+ 30 eV *m/z*: 297.2 $[M+H]^+$ 100% calcd for $[C_{14}H_{21}N_2O_3P]$ 296. Anal. Calcs for $C_{14}H_{21}N_2O_3P$: C 56.75, H 7.14, N 9.45. Found: C 56.70, H 7.10, N 9.50%.

Bis (cyclohexylamino) phenylphosphine oxide (8g)

Yield: 97%. R_f=0.62 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3155, 1461, 1250. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 3.15 (m, 2H, CH-cyc); 2.40 (m, 2H, NH); 1.90 (m, 4H, CH_2-cyc); 1.65 (m, 4H, CH_2-cyc); 1.15 (m, 12H, CH_2-cyc). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.5$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 134.1; 132.4; 129.3; 55.2; 35.1; 25.2; 24.8. MS ESI+ 30 eV *m/z*: 321.1 $[M+H]^+$ 100% calcd for $[C_{18}H_{29}N_2OP]$ 320. Anal. Calcd for $C_{18}H_{29}N_2OP$: C 67.47, H 9.12, N 8.74. Found: C 67.50, H 9.20, N 8.70%.

Bis (phenylamino) phenylphosphine oxide (8h)

Yield: 94%. R_f=0.67 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3223, 1599, 1499, 1293. ^1H NMR (DMSO, 300 MHz): 7.95 (m, 2H, H–Ar); 7.85 (m, 3H, H–Ar); 7.50 (m, 4H, H–Ar); 7.20 (m, 2H, H–Ar); 6.80 (m, 4H, H–Ar). ^{31}P NMR (DMSO, 100 MHz) $\delta = 17.8$ ppm. ^{13}C NMR (DMSO, 100 MHz): 142.6; 132.1; 132.0; 129.2; 128.9; 128.8; 120.7; 118.2; 118.1. MS ESI+ 30 eV *m/z*: 309.1 $[M+H]^+$ 100% calcd for $[C_{18}H_{17}N_2OP]$ 308. Anal. Calcd for $C_{18}H_{17}N_2OP$: C 70.12, H 5.56, N 9.09. Found: C 70.10, H 5.51, N 9.19%.

Bis (3-fluorophenylamino) phenylphosphine oxide (8i)

Yield: 90%. R_f=0.67 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3415, 1529, 1494, 1279. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 6.99 (m, 2H, H–Ar); 6.33 (m, 2H, H–Ar); 6.23 (m, 2H, H–Ar); 6.17 (m, 2H, H–Ar); 4.00 (m, 2H, NH). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.1$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 162.9; 148.3;135.0; 131.5; 130.9; 129.6; 128.6; 110.7; 105.5. MS ESI+ 30 eV *m/z*: 345.1 $[M+H]^+$ 100% calcd for $[C_{18}H_{15}\ F_2\ N_2OP]$ 344. Anal. Calcd for $C_{18}H_{15}F_2N_2OP$: C 62.79, H 4.39, N 8.14. Found: C 62.75, H 4.35, N 8.24%.

Bis (4-chlorophenylamino) phenylphosphine oxide (8j)

Yield: 92%. R_f=0.68 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3264, 1597, 1492, 1275. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 7.02 (m, 4H, H–Ar); 6.40 (m, 4H, H–Ar); 4.00 (m, 2H, NH). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.4$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 144.8; 135.0; 131.5; 129.7; 129.6; 128.6; 123.8; 116.5. MS ESI+ 30 eV *m/z*: 377.1 $[M+H]^+$ 100% calcd for $[C_{18}H_{15}Cl_2N_2OP]$ 376. Anal. Calcd for $C_{18}H_{15}Cl_2N_2OP$: C 57.32, H 4.01, N 7.43. Found: C 57.39, H 4.10, N 7.40%.

Bis (4-methylphenylamino) phenylphosphine oxide (8k)

Yield: 90%. R_f=0.66 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3418, 1513,1436, 1279. ^1H NMR ($CDCl_3$, 250 MHz): 7.95 (m, 2H, H–Ar); 7.55 (m, 3H, H–Ar); 6.81 (m, 4H, H–Ar); 6.34 (m, 4H, H–Ar); 4.00 (m, 2H, NH); 2.35 (s, 6H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.4$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 143.7; 135.0; 131.5; 130.0; 129.6; 128.6; 127.7; 115.0; 20.9. MS ESI+ 30 eV *m/z*: 337.2 $[M+H]^+$ 100% calcd for $[C_{20}H_{21}N_2OP]$ 336. Anal. Calcd for $C_{20}H_{21}N_2OP$: C 71.41, H 6.29, N 8.33. Found: C 71.35, H 6.20, N 8.39%.

Bis (4-methoxyphenylamino) phenylphosphine oxide (8l)

Yield: 95%. R_f=0.67 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3427, 1598, 1442, 1258. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 6.52 (m, 4H, H–Ar); 6.35 (m, 4H, H–Ar); 4.00 (m, 2H, NH) 3.73 (s, 6H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.4$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 152.0; 139.0; 135.0; 131.5; 129.6; 128.6; 116.1; 114.9; 56.0. MS ESI+ 30 eV *m/z*: 369.2 $[M+H]^+$ 100% calcd for $[C_{20}H_{21}N_2O_3P]$ 368. Anal. Calcd for $C_{20}H_{21}N_2O_3P$: C 65.21, H 5.75, N 7.60. Found: C 65.25, H 5.80, N 7.57%.

Bis (2-methoxyphenylamino) phenylphosphine oxide (8m)

Yield: 92%. R_f=0.66 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3414, 1599, 1498, 1256. ^1H NMR ($CDCl_3$, 250 MHz): 7.95 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 6.57 (m, 2H, H–Ar); 6.52 (m, 2H, H–Ar); 6.51 (m, 2H, H–Ar); 6.35 (m, 2H, H–Ar); 4.00 (m, 2H, NH) 3.73 (s, 6H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.4$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 148.6; 135.0; 132.3; 131.5; 129.6; 128.6; 121.6; 119.5; 116.1; 114.9; 56.0. MS ESI+ 30 eV *m/z*: 369.2 $[M+H]^+$ 100% calcd for $[C_{20}H_{21}N_2O_3P]$368. Anal. Calcd for $C_{20}H_{21}N_2O_3P$: C 65.21, H 5.75, N 7.60. Found: C 65.25, H 5.80, N 7.57%.

Bis (4-hydroxyphenylamino) phenylphosphine oxide (8n)

Yield: 93%. R_f=0.65 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3175, 1511, 1468, 1247. ^1H NMR ($CDCl_3$, 250 MHz): 7.85 (m, 2H, H–Ar); 7.45 (m, 3H, H–Ar); 6.48 (m, 4H, H–Ar); 6.29 (m, 4H, H–Ar); 5.10 (s, 1H, OH); 4.00 (m, 2H, NH). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.3$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 147.3; 139.3; 135.0; 131.5; 129.6; 128.6; 116.5. MS ESI+ 30 eV *m/z*: 341.1 $[M+H]^+$ 100% calcd for $[C_{18}H_{17}N_2O_3P]$ 340. Anal. Calcd for $C_{18}H_{17}N_2O_3P$: C 63.53, H 5.04, N 8.23. Found: C 63.50, H 5.00, N 8.27%.

Bis (benzylamino) phenylphosphine oxide (8o)

Yield: 95%. R_f=0.60 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 3163,1461, 1253. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.50 (m, 3H, H–Ar); 7.25 (m, 10H, H–Ar); 4.15 (m, 4H, CH_2–N); 3.0 (m, 2H, NH). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.3$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 140.0; 139.9; 133.4; 131.9; 131.8; 131.7; 131.4; 128.7; 128.5; 127.7; 127.5; 127.3; 44.8. MS ESI+ 30 eV *m/z*: 337.2 $[M+H]^+$ 100% calcd for $[C_{20}H_{21}N_2OP]$ 336. Anal. Calcd for $C_{20}H_{21}N_2OP$: C 71.41, H 6.29, N 8.33. Found: C 71.47, H 6.33, N 8.30%.

Bis (phenylethylamino) phenylphosphine oxide (8p)

Yield: 94%. R_f=0.63 (CH_2Cl_2/MeOH). IR (KBr, cm^1): 3209, 1450, 1191. ^1H NMR ($CDCl_3$, 250 MHz): 7.75 (m, 2H, H–Ar); 7.40 (m, 3H, H-Ar); 7.35–7.00 (m, 10H, H–Ar); 4.60 (m, 1H,*CH); 4.35 (m, 1H,*CH); 2.75 (s, 2H, NH); 1.5 (d, $J = 6.25$ Hz, 3H, CH_3); 1.30 (d, $J = 6.77$ Hz, 3H, CH_3). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.3$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 145.2; 134.2; 132.1; 130.1; 128.8; 128.5; 126.9; 126.7; 55.4; 24.1. MS ESI+ 30 eV *m/z*: 365.1 $[M+H]^+$ 100% calcd for $[C_{22}H_{25}N_2OP]$ 364. Anal. Calcd for $C_{22}H_{25}N_2OP$: C 72.51, H 6.91, N 7.69. Found: C 72.50, H 6.90, N 7.70%.

Bis (diphenylamino) phenylphosphine oxide (8q)

Yield: 97%. R_f=0.69 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 1594, 1494, 1199. ^1H NMR ($CDCl_3$, 250 MHz): 7.98 (m, 2H, H–Ar); 7.80 (m, 3H, H–Ar); 7.50 (m, 8H, H–Ar); 7.20 (m, 4H, H–Ar); 6.80 (m, 8H, H–Ar).^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.3$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 142.6; 132.1; 132.0; 129.2; 128.9; 128.8; 120.7; 118.2; 118.1. MS ESI+ 30 eV *m/z*: 461.1 $[M+H]^+$ 100% calcd for $[C_{30}H_{25}N_2OP]$ 460. Anal. Calcd for $C_{30}H_{25}N_2OP$: C 78.24, H 5.47, N 6.08. Found: C 78.20, H 5.40, N 6.10%.

Bis (phenylpiperazine) phenylphosphine oxide (8r)

Yield: 89%. R_f=0.67 (CH_2Cl_2/MeOH). IR (KBr, cm^{-1}): 1512, 1405, 1222. ^1H NMR ($CDCl_3$, 250 MHz): 7.90 (m, 2H, H–Ar); 7.60 (m, 3H, H–Ar); 7.08 (m, 4H, H–Ar); 6.60 (m, 2H, H–Ar); 6.59 (m, 4H, H–Ar); 3.47 (t, $J = 6.85$, 8H, CH_2); 2.78 (t, $J = 6.95$, 8H, CH_2). ^{31}P NMR ($CDCl_3$, 100 MHz) $\delta = 16.3$ ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): 144.5; 135.0; 131.5; 129.6; 129.4; 128.6; 118.0; 113.1; 58.9; 44.8. MS ESI+ 30 eV *m/z*: 447.1 $[M+H]+100\%$ calcd for $[C_{26}H_{31}N_4OP]$ 446. Anal. Calcd for $C_{26}H_{31}N_4OP$: C 69.94, H 7.00, N 12.55. Found: C 69.99, H 7.09, N 12.50%.

Conclusion

We have successfully developed a simple, efficient, and environmentally benign methodology toward the synthesis of phosphonamides under ultrasonic techniques, but solvent and catalyst-free conditions at room temperature. We achieved the synthesis of phenyl phosphonamides derived from amines with phenyl phosphonic dichloride in one step. This methodology was established with many advantages, including mild reaction conditions, short reaction times, excellent yields, simple work-up procedures.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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