



Scholars Research Library

Der Pharmacia Lettre, 2013, 5 (3):341-349
(<http://scholarsresearchlibrary.com/archive.html>)



CeCl₃.7H₂O-SiO₂: A heterogeneous catalyst for Michaelis-Arbuzov reaction: High yield synthesis of arylmethyl/heteroaryl phosphonates

D. Subba Rao, S. K. Thaslim Basha and C. Naga Raju *

Department of Chemistry, Sri Venkateswara University, Tirupati, Andhra Pradesh, India

ABSTRACT

A simplistic green and neat procedure was developed for the synthesis of arylmethyl and heteroaryl phosphonates or phosphinates by silica gel supported Lewis acid catalyst, CeCl₃.7H₂O-SiO₂ through Michaelis-Arbuzov reaction under conventional as well as microwave irradiation methods. Herein, tetraalkyl 1,4-phenylenebis(methylene)diphosphonates 5(a-d)/dimethyl 1,4-phenylenebis(methylene)bis (phenylphosphinate) 5(e) and tetraalkyl pyridine-2,6-diylidiphosphonates 7(a-d)/ dimethyl pyridine-2,6-diylbis(phenylphosphinate) 7(e) were accomplished in high yields (85-94%) with simple work-up procedure in the presence of CeCl₃.7H₂O-SiO₂ catalyst by the reaction of alkyl/aryl bromides with trialkyl phosphites. The present synthetic protocol demonstrated that silica supported Ce(III) is a easily prepared catalyst and recyclable, which catalyzed C-P bond formation in high yields in less time.

Keywords: Michaelis-Arbuzov reaction, Silica supported CeCl₃.7H₂O catalyst, Solvent-free conditions, Microwave conditions, Conventional conditions.

INTRODUCTION

Organophosphorus compounds particularly phosphonates have been played a key role in biologically active compounds [1]. Phosphonic acid [-P(O)(OH)₂] derivatives in which the phosphorus atom directly attached to a carbon atom of acyclic/arylmethyl/heteroaryl compounds have been wide range of biologically active molecules for example glyphosate (**1**) has attained a remarkable importance and marked as the world's largest sold herbicide [2], and two mono functionalized tiludronate (**2**) was developed as anti-inflammatory, and anti-rheumatismal agent (**Fig-1**). The replacement of the phosphonic acid by the phosphonates is modifying the physical and chemical properties of the substrates, and these modifications could improve the bio-availability of the compounds. Predominantly, the phosphonates of arylmethyl and heteroarylmethyl compounds have been widely utilized as prominent precursor for the synthesis of stilbene dendrimers [3] and optical materials like alkyl(phenylvinylenes) [4], trialkylamine tethered vinylenes [5], and thienylvinylenes [6]. The broad applications of phosphonates in medicinal chemistry and synthetic chemistry, the growing interest have been made the researchers for the development of new methodologies as well as the synthesis of various active phosphonate molecules.

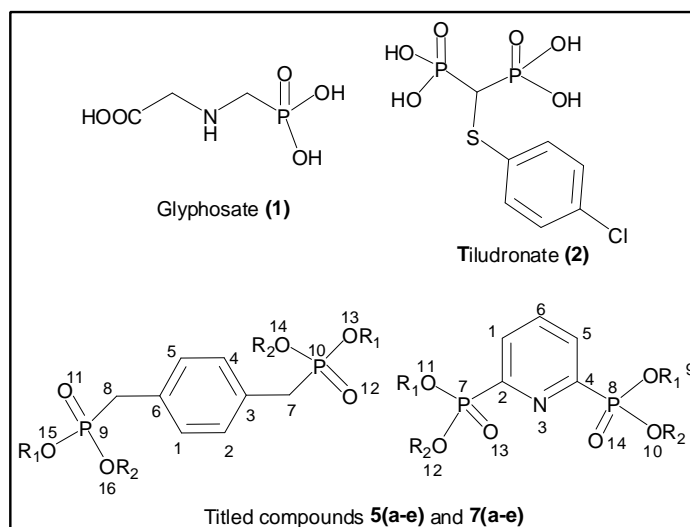


Fig-1 Some biologically active phosphonate derivatives.

Michaelis-Arbuzov reaction is a fundamental reaction in the conversion of tri-coordinate phosphate ester to tetra-coordinate phosphonate ester and has been used traditionally from a long time to synthesize required phosphonates [7] including simple and complex alkyl groups functionalized compounds have been substituted on the phosphorus [8]. However, the reaction has some drawbacks like elevated temperature required for the activation of the reaction, removal of the trialkyl phosphites used in excess and weaker electrophiles aryl/heteroaryl halides or vinyl halides give lower yields. To overcome the above problems, the researchers have been increased their attention for the development of new methodologies. Recently, an efficient method was developed for the preparation of benzyl phosphonates using Pd(OAc)₂ mediated cross-coupling reaction [9] and different Lewis acid catalyzed reactions are documented [10-11].

Trivalent rare earth compounds, Ce(III) salts exhibited characteristic acidic properties [12]. Commonly employed Ce(III) salt is CeCl₃·7H₂O and it is a relative commercial available, non-toxic, water tolerant and easy to handle [13]. Therefore, it has been attained increasing interest in the usage of this catalyst in various organic transformations [14-15]. Silica supported inorganic catalysts, SiO₂ was originally introduced as only a support and kinetic studies have revealed that it not only acts as a carrier to increase the surface area as intended but also enhances the rate of the reaction [16]. This is possibly due to the interaction between the cerium(III) sites of the catalyst with the silanol group of the uncapped silica surface changing the environment of the catalyst active sight. This shows that SiO₂ functions as an activator for CeCl₃·7H₂O Lewis acid system as well as support.

Further, in recent years microwave irradiation was playing a prominent role to promote wide variety of the reactions in organic synthesis [17-18] and provide a number of advantages over the standard heating techniques such as improved reaction yield, shorten the reaction time and easy work-up procedure. Recently, the Michaelis-Arbuzov reaction is used for the preparation of heterocycles or alkyl phosphonates and this approach has recently improved by the use of microwave irradiation [19-20]. For the most part, microwave assisted solvent-free reaction provides an opportunity to work with open vessels thus avoiding the development of high pressure and provide a possibility of up scaling the reaction on a preparative scale and helps the induction of the reaction under dry conditions. Overview of literature and to overcome the former drawbacks, we familiarized to explore the use of CeCl₃·7H₂O-SiO₂ catalyst to promote the Michaelis-Arbuzov reaction for the preparation of arylmethyl phosphonates and heteroaryl phosphonates under conventional as well as microwave assisted methods using solvent-free conditions.

MATERIALS AND METHODS

Glassware was dried in oven at 150 °C prior to use and all the reactions were conducted under nitrogen atmosphere. Alkyl phosphites (P(OR)₃), dimethyl phenylphosphonite (P(OMe)₂Ph) and alkyl halides were purchased from Sigma-Aldrich. Solvents were distilled from the appropriate drying agents and stored under nitrogen atmosphere.

Melting points were determined in open capillaries on Guna melting point apparatus and are uncorrected. IR spectra were recorded on Bruker FT-IR 5300 using KBr discs. ^1H NMR, ^{31}P NMR and ^{13}C NMR spectra were recorded on Bruker AV-500 spectrometer. TMS was used as the internal standard for ^1H and ^{13}C NMR spectra and H_3PO_4 as the external standard for ^{31}P NMR spectra. LC-MS were recorded on a Jeol SX 102 DA/600. Elemental analysis was performed on Thermo Finnigan Flash 1112 instrument. Results are presented as chemical shifts δ in ppm and J values in Hertz (Hz). Multiplicities are shown as the abbreviations: s (singlet), brs (broad singlet), d (doublet), t (triplet), m (multiplet). The numbering was given to the title compound for assigning the proper spectral characterization (**Figure-1**).

General procedure for conventional method:

The mixture of triethyl phosphite (**4b**) (4 mmol) and 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O} \cdot \text{SiO}_2$ (20 mol%) were taken in flat-bottomed flask and stirred the reaction mixture vigorously at 40 °C. After completion of the reaction as indicated by TLC, the reaction mixture was cooled to room temperature and 10 mL of DCM was added followed by filtered-off the content to remove the catalyst. The catalyst was recovered by washing it with DCM properly to remove the stains on the catalyst. The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography using 30% ethyl acetate and hexane as eluent to obtain pure tetraethyl 1,4-phenylenebis(methylene)diphosphonate (**5b**). The same procedure was adopted for the preparation of the remaining titled compounds.

General procedure for microwave irradiation method:

The mixture of triethyl phosphite (**4b**) (3 mmol) and 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and $\text{CeCl}_3 \cdot 7\text{H}_2\text{O} \cdot \text{SiO}_2$ (20 mol%) were taken in flat-bottomed flask and irradiated with microwave radiations using catalyst systems (CATA-4R,) at 490 Watts. The progress of the reaction was checked for each 1 min interval by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature and then added 10 mL of DCM followed by filtered-off the content to remove the catalyst as residue. The residue catalyst was washed with DCM properly to remove the stains on the catalyst. The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography using 30% ethyl acetate and hexane as eluent to obtain pure tetraethyl 1,4-phenylenebis(methylene)diphosphonate (**5b**). The same procedure was employed for the preparation of the remaining titled compounds.

SPECTRA DATA

Tetramethyl 1,4-phenylenebis(methylene)diphosphonate (5a).

White solid, Mol. Wt: 322.07. Yield 91.51%, mp: 91-92 °C. IR (KBr, ν_{max} cm^{-1}): 3028 (=C-H, str), 2962 (-C-H, str), 1259 (-P=O, str), 1090 (-P-O-C, str); ^1H -NMR (400 MHz, DMSO- d_6): δ 3.19 (s, 4H, Ph- CH_2 -), 3.83 (s, 12H, -OCH₃), 7.27 (s, 4H, Ar-H); ^{13}C -NMR (100.16 MHz, DMSO- d_6): δ 36.3 (C_{7,8}), 62.9 (-OC), 130.6 (C_{3,6}), 135.9 (C_{1,2,4,5}); ^{31}P -NMR (DMSO- d_6 , 125.01 MHz): δ 25.27. LC-MS (+ mode): 323 (M^+H). Anal. Calcd. for $\text{C}_{12}\text{H}_{20}\text{O}_6\text{P}_2$: C, 44.73; H, 6.26; found: C, 44.51; H, 6.12%.

Tetraethyl 1,4-phenylenebis(methylene)diphosphonate (5b).

White crystalline solid, Mol. Wt: 378.14. Yield 91.07%, mp: 76-78 °C. IR (KBr, ν_{max} cm^{-1}): 3027 (=C-H, str), 2962 (-C-H, str), 1262 (-P=O, str), 1070 (-P-O-C, str); ^1H -NMR (400 MHz, DMSO- d_6): δ 1.15 (t, J = 6.8 Hz, 12H, -OCH₂-CH₃), 2.85 (s, 4H, Ph- CH_2 -), 4.03 (q, J = 6.4 Hz, 8H, -O-CH₂-CH₃), 7.21 (s, 4H, Ar-H); ^{13}C -NMR (100.16 MHz, DMSO- d_6): δ 22.0 (-O-C-C), 31.2 (C_{7,8}), 69.0 (d, $J_{\text{P-O-C}}$ = 37.3 Hz, -O-C), 130.8 (C_{3,6}), 137.4 (C_{1,2,4,5}); ^{31}P -NMR (DMSO- d_6 , 125.01 MHz): δ 25.68. LC-MS (+ mode): 379 (M^+H). Anal. Calcd. for $\text{C}_{16}\text{H}_{28}\text{O}_6\text{P}_2$: C, 50.79; H, 7.46; found: C, 50.60; H, 7.35%.

Diisopropyl 1,4-phenylenebis(methylene)diphosphonate (5c).

White solid, Mol. Wt: 434.20. Yield 89.92%, mp: 132-134 °C. IR (KBr, ν_{max} cm^{-1}): 3028 (=C-H, str), 2980 (-C-H, str), 1218 (-P=O, str), 1065 (-P-O-C, str); ^1H -NMR (400 MHz, DMSO- d_6): δ 1.08 (d, J = 6.4 Hz, 12H, -OCH-(CH₃)₂), 1.16 (d, J = 6.4 Hz, 12H, -OCH-(CH₃)₂), 2.91 (s, 4H, Ph- CH_2 -), 4.54 (m, 4H, -O-CH-(CH₃)₂), 7.08 (s, 4H, Ar-H); ^{13}C -NMR (100.16 MHz, DMSO- d_6): δ 26.2 (-O-C-(C)₂), 26.3 (-O-C-(C)₂), 36.7 (C_{7,8}), 73.4 (d, $J_{\text{P-O-C}}$ = 23.2 Hz, -O-C), 130.2 (C_{3,6}), 133.9 (C_{1,2,4,5}); ^{31}P -NMR (DMSO- d_6 , 125.01 MHz): δ 20.73. LC-MS (+ mode): 435 (M^+H).

Tetraethyl 1,4-phenylenebis(methylene)diphosphonate (5d).

Light brown solid, Mol. Wt: 490.26. Yield 90.74%, mp: 84-86 °C. IR (KBr, ν_{max} cm^{-1}): 3091 (=C-H, str), 2960 (-C-H, str), 1243 (-P=O, str), 1092 (-P-O-C, str); ^1H -NMR (400 MHz, DMSO- d_6): δ 0.98 (t, J = 6.4 Hz, 12H, -O-CH₂-

CH₂-CH₂-CH₃), 1.42-1.51 (m, 10H, -O-CH₂-CH₂-CH₂-CH₃), 1.58-1.69 (m, 6H, -O-CH₂-CH₂-CH₂-CH₃), 3.01 (m, 4H, Ph-CH₂-), 3.97-4.04 (m, 8H, -O-CH₂-), 7.36 (s, 4H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 16.4 (-O-CH₂-CH₂-CH₂-CH₃), 20.4 (-O-CH₂-CH₂-CH₂-CH₃), 31.7 (-O-CH₂-CH₂-CH₂-CH₃), 34.5 (C_{7,8}), 68.4 (-O-C₂J_{P-O-C} = 24.5 Hz), 130.2 (C_{3,6}), 134.4 (C_{1,2,4,5}); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 24.64. LC-MS (+ mode): 491 (M⁺H).

Dimethyl 1,4-phenylenebis(methylene)bis(phenylphosphinate) (5e).

White amorphous solid, Mol. Wt: 414.11. Yield 93.21%, mp: 81-83 °C. IR (KBr, ν_{\max} cm⁻¹): 3032 (=C-H, str), 2974 (-C-H, str), 1263 (-P=O, str), 1078 (-P-O-C, str); ¹H-NMR (400 MHz, DMSO-*d*₆): δ 3.31 (s, 4H, Ph-CH₂-), 3.88 (s, 6H, -O-CH₃), 7.23 (s, 4H, Ar-H), 7.24-7.48 (m, 10H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 36.1 (C_{7,8}), 63.2 (-O-C₂J_{P-O-C} = 38.0 Hz), 128.5 (C_{3,5}',C_{3,5}''), 129.3 (C₁',C₁''), 129.4 (C_{3,6}), 132.7 (C_{1,2,4,5}), 134.7 (C_{2,4}',C_{2,4}''), 140.2 (C₄',C₄''); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 18.29. LC-MS (+ mode): 415 (M⁺H).

Tetramethyl pyridine-2,6-diylldiphosphonate (7a).

White solid, Mol. Wt: 295.04. Yield 90.38%, mp: 137-139 °C. IR (KBr, ν_{\max} cm⁻¹): 2970 (=C-H, str), 2923 (-C-H, str), 1418 (-C=N, str), 1253 (-P=O, str), 1084 (-P-O-C, str); ¹H-NMR (400 MHz, DMSO-*d*₆): δ 3.70 (s, 12H, -OCH₃), 7.93 (t, J = 8.0 Hz, 1H, Ar-H), 8.12 (d, J = 8.8 Hz, 2H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 59.6 (-O-C₂J_{P-O-C} = 33.9 Hz), 130.0 (C_{1,5}), 139.9 (C₆), 161.5 (C_{2,4}); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 20.16. LC-MS (+ mode): 296 (M⁺H). Anal. Calcd. for C₉H₁₅NO₆P₂: C, 36.62; H, 5.12; N, 4.75; found: C, 36.54; H, 5.10; N, 4.71%.

Tetraethyl pyridine-2,6-diylldiphosphonate (7b).

White solid, Mol. Wt: 351.10. Yield 90.07%, mp: 133-134 °C. IR (KBr, ν_{\max} cm⁻¹): 2970 (=C-H, str), 2926 (-C-H, str), 1418 (-C=N, str), 1256 (-P=O, str), 1084 (-P-O-C, str); ¹H-NMR (400 MHz, DMSO-*d*₆): δ 1.28 (t, J = 6.4 Hz, 12H, -OCH₂-CH₃), 4.31 (q, J = 6.4 Hz, 8H, -O-CH₂-CH₃), 7.87 (t, J = 7.6 Hz, 1H, Ar-H), 8.11 (d, J = 8.4 Hz, 2H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 19.2 (-O-C-C), 62.9 (-O-C₂J_{P-O-C} = 31.8 Hz), 133.4 (C_{1,5}), 138.6 (C₆), 157.6 (C_{2,4}); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 19.67. LC-MS (+ mode): 352 (M⁺H). Anal. Calcd. for C₁₃H₂₃NO₆P₂: C, 44.45; H, 6.60; N, 3.99; found: C, 44.38; H, 6.54; N, 3.94%.

Diisopropyl pyridine-2,6-diylldiphosphonate (7c).

Light brown solid, Mol. Wt: 407.16. Yield 86.65%, mp: 110-112 °C. IR (KBr, ν_{\max} cm⁻¹): 2963 (=C-H, str), 2925 (-C-H, str), 1418 (-C=N, str), 1257 (-P=O, str), 1076 (-P-O-C, str); ¹H-NMR (400 MHz, DMSO-*d*₆): δ 1.14 (d, J = 6.8 Hz, 12H, -OCH-(CH₃)₂), 1.16 (d, J = 6.8 Hz, 12H, -OCH-(CH₃)₂), 4.63 (m, 4H, -O-CH-(CH₃)₂), 7.74 (t, J = 7.6 Hz, 1H, Ar-H), 8.18 (d, J = 8.4 Hz, 2H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 25.8 (-O-C-C₂), 74.1 (d, J_{P-O-C} = 31.6 Hz, -O-C), 132.6 (C_{1,5}), 139.1 (C₆), 157.2 (C_{2,4}); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 22.31. LC-MS (+ mode): 408 (M⁺H).

Tetrabutyl pyridine-2,6-diylldiphosphonate (7d).

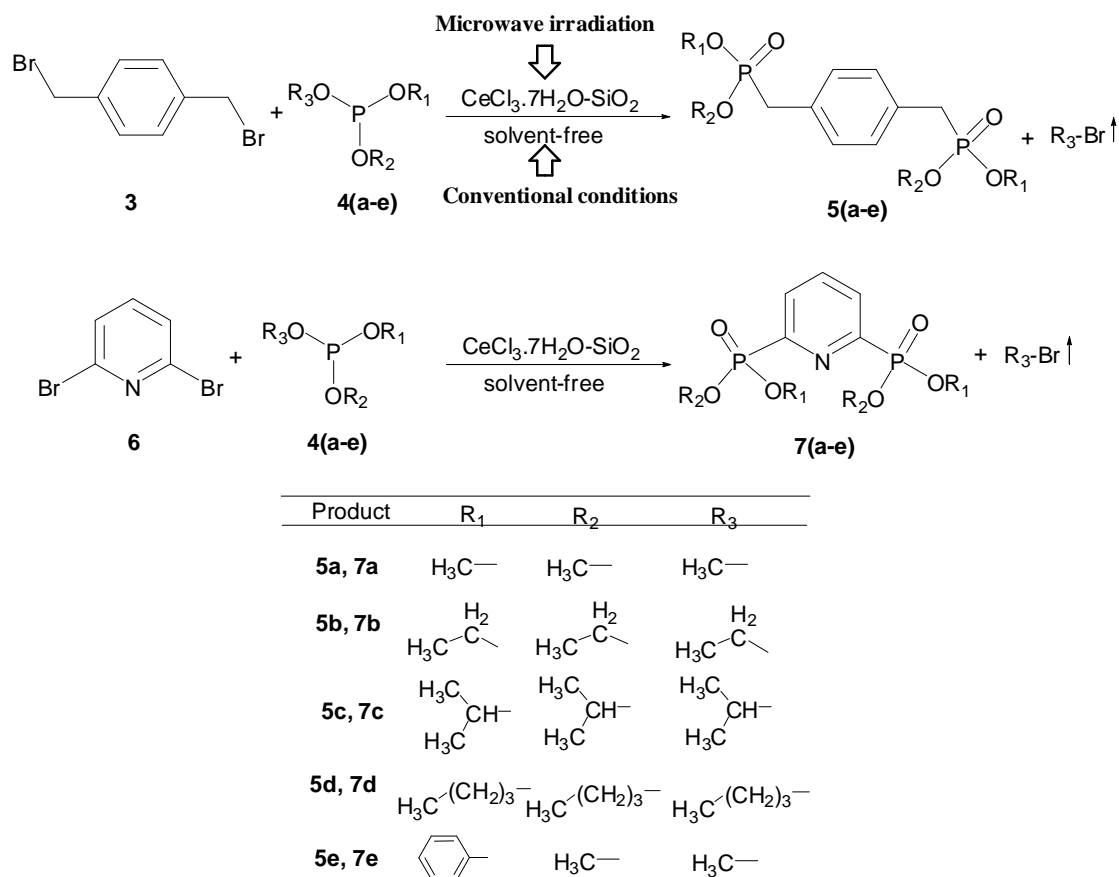
White solid, Mol. Wt: 463.23. Yield 89.62%, mp: 97-98 °C. IR (KBr, ν_{\max} cm⁻¹): 2968 (=C-H, str), 2932 (-C-H, str), 1421 (-C=N, str), 1259 (-P=O, str), 1081 (-P-O-C, str); ¹H-NMR (400 MHz, DMSO-*d*₆): δ 1.14-1.18 (m, 16H, -O-CH₂-CH₂-CH₂-CH₃), 1.23-1.29 (m, 8H, -O-CH₂-CH₂-CH₂-CH₃), 1.34-1.39 (m, 4H, -O-CH₂-CH₂-CH₂-CH₃), 4.51-4.55 (m, 8H, -O-CH₂-), 7.82 (t, J = 7.6 Hz, 1H, Ar-H), 8.04 (d, J = 8.4 Hz, 2H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 18.1 (-O-CH₂-CH₂-CH₂-CH₃), 20.2 (-O-CH₂-CH₂-CH₂-CH₃), 33.4 (-O-CH₂-CH₂-CH₂-CH₃), 34.5 (C_{7,8}), 69.6 (-O-C₂J_{P-O-C} = 28.4 Hz), 131.4 (C_{1,5}), 137.8 (C₆), 154.3 (C_{2,4}); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 21.19. LC-MS (+ mode): 464 (M⁺H).

Dimethyl pyridine-2,6-diylbis(phenylphosphinate) (7e).

White amorphous solid, Mol. Wt: 387.08. Yield 91.29%, mp: 85-86 °C. IR (KBr, ν_{\max} cm⁻¹): 3012 (=C-H, str), 2937 (-C-H, str), 1437 (-C=N, str), 1217 (-P=O, str), 1022 (-P-O-C, str); ¹H-NMR (400 MHz, DMSO-*d*₆): δ 3.81 (s, 6H, -O-CH₃), 7.35-7.39 (m, 10H, Ar-H), 7.76 (t, J = 7.6 Hz, 1H, Ar-H), 8.01 (d, J = 8.4 Hz, 2H, Ar-H); ¹³C-NMR (100.16 MHz, DMSO-*d*₆): δ 67.4 (-O-C₂J_{P-O-C} = 32.6 Hz), 127.2 (C_{3,5}',C_{3,5}''), 129.8 (C₁',C₁''), 133.2 (C_{1,5}), 134.1 (C_{2,4}',C_{2,4}''), 136.3 (C₆), 140.9 (C₄',C₄''), 156.7 (C_{2,4}); ³¹P-NMR (DMSO-*d*₆, 125.01 MHz): δ 23.48. LC-MS (+ mode): 388 (M⁺H).

RESULTS AND DISCUSSION

The outstanding catalytic properties of $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ in organic synthesis, we prepared silica supported $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ catalyst and investigated its catalytic nature for the synthesis of various arylmethyl and heteroaryl phosphonates or phosphinate derivatives through Michaelis-Arbuzov reaction under conventional and microwave irradiation methods using neat reaction conditions was depicted in **Scheme-1**.



Scheme-1 Synthesis of phosphonates/phosphinate derivatives using $\text{CeCl}_3 \cdot 7\text{H}_2\text{O} \cdot \text{SiO}_2$ catalyzed Michaelis-Arbuzov reaction.

To find out the optimum reaction conditions, 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and triethyl phosphite (**4b**) (2 mmol) are selected as substrates and stirred the reaction mixture in THF at 60 °C in the absence of the catalyst. The reaction was completed in 16 h with moderate yield (52.7%) (**Table-1** entry 1). The same reaction condition was carried out in different catalysts (**Table-1** entry 2-6), it was observed that $\text{CeCl}_3 \cdot 7\text{H}_2\text{O} \cdot \text{SiO}_2$ (10 mol%) detected high yield of the product, **5b** (70.6%) (**Table-1** entry 6). To our delight, the same model reaction was progressed in different solvents and solvent-free conditions (**Table-2** entry 1-7). Though, solvent-free conditions produced expected product in high yields (**Table-2** entry 6^d) at the reaction temperature of 40 °C.

Table-1 Optimization of the reaction conditions for the Michaelis-Arbuzov reaction^a.

Entry	Catalyst	Time (h)	Yield (%)
1	No catalyst	14.0	52.7
2	CuCl_2 (5 mol%)	8.5	62.4
3	ZnCl_2 (5 mol%)	6.0	62.8
4	ZnBr_2 (5 mol%)	5.0	64.6
5	$\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (5 mol%)	5.0	65.7
6	$\text{CeCl}_3 \cdot 7\text{H}_2\text{O} \cdot \text{SiO}_2$ (10 mol%)	5.0	70.6

^aThe reaction was performed using 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and triethyl phosphite (**4b**) (2 mmol). Appropriate conditions are highlighted.

Table-2 The solvent effect on the Michaelis-Arbuzov reaction in CeCl₃.7H₂O-SiO₂ (10 mol%) catalyst under conventional conditions^a.

Entry	Solvent	Time (h)	Yield (%)
1	THF	7.0	70.65
2	Toluene	7.5	66.94
3	ACN	7.0	68.31
4	Solvent-free	6.5 ^b	71.5 ^b
5	Solvent-free	6.0 ^c	72.1 ^c
6	Solvent-free	5.5 ^d	74.0 ^d
7	Solvent-free	5.5 ^e	74.5 ^e

^aThe reaction was performed using 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and triethyl phosphite (**4b**) (2 mmol). ^bThe time and corresponding yield of the reaction was performed at room temperature. ^cThe time and corresponding yield of the reaction was performed at 35 °C. ^dThe time and corresponding yield of the reaction was performed at 40 °C. ^eThe time and corresponding yield of the reaction was performed at 45 °C. Appropriate conditions are highlighted.

Also, the amount of the catalyst effect on the reaction was examined by altered the loading of the catalyst (**Table-3** entry 1-5), the reaction effectively worked at 20 mol% of CeCl₃.7H₂O-SiO₂ catalyst (**Table-3** entry 3). Further, we have scrutinized this reaction by altering the amount of triethyl phosphite. It was found that excellent yield was observed by adding 4 equiv of phosphite in conventional method and no significant yield increase was observed by adding excess of phosphite (**Table-4, entry 1-7**). The reusability of the catalyst, CeCl₃.7H₂O-SiO₂ was also examined up to four cycles to synthesize compound **5b** and gave corresponding yields (86.5%, 86.3%, 84.7%, 83.2% and 82.5%). After each run, the product was filtered-off and washed with CHCl₃ to remove tars on the catalyst surface and dried at 50 °C to reuse.

Table-3 The effect of the amount of the catalyst, CeCl₃.7H₂O-SiO₂ to promote the Michaelis-Arbuzov reaction under conventional and solvent-free conditions^a.

Entry	Amount of the CeCl ₃ .7H ₂ O-SiO ₂	Time (h)	Yield (%)
1	10 mol%	5.5	74.08
2	15 mol%	4.0	75.54
3	20 mol%	4.0	79.9
4	25 mol%	4.0	80.2
5	30 mol%	4.0	80.2

^aThe reaction was performed using 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and triethyl phosphite (**4b**) (2 mmol).

Table-4 The effect of the amount of alkyl phosphite on Michaelis-Arbuzov reaction catalyzed by CeCl₃.7H₂O-SiO₂ (20 mol%) employing solvent-free conditions^a.

Entry	Amount of P(OEt) ₃	Time ^{b,c}	Yield ^{d,e}
1	2.0 equiv	6.0 ^b /11 ^c	80.2 ^d /88.5 ^e
2	2.5 equiv	5.5 ^b /10 ^c	81.6 ^d /89.7 ^e
3	3.0 equiv	4.5 ^b /9 ^c	83.3 ^d /91.0 ^e
4	3.5 equiv	4.0 ^b /9 ^c	83.9 ^d /91.2 ^e
5	4 equiv	4.0 ^b /9 ^c	86.5 ^d /91.2 ^e
6	4.5 equiv	4.0 ^b /9 ^c	86.5 ^d /91.9 ^e
7	5.0 equiv	4.0 ^b /9 ^c	86.9 ^d /92.7 ^e

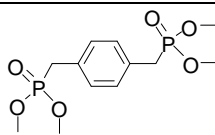
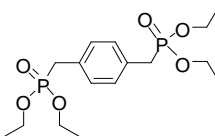
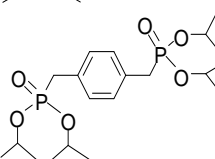
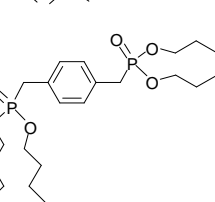
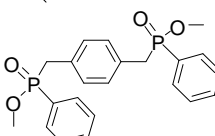
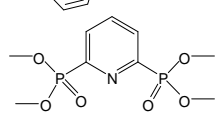
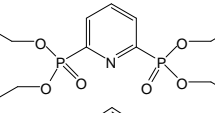
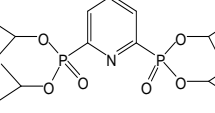
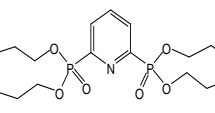
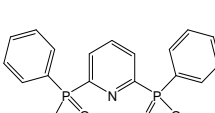
^aThe reaction was performed using 1,4-bis(bromomethyl)benzene (**3**) (1 mmol) and triethyl phosphite (**4b**) (alter mmol). ^bTime of the reaction under conventional conditions. ^cTime of the reaction under microwave method. ^dYield of the of the product, **5b** under convention conditions.

^eYield of the product, **5b** under microwave method.

To our interest, again the model reaction using 20 mol% of CeCl₃.7H₂O-SiO₂ was monitored in microwave oven (CATA-4R, 70% of power, 490 Watts). Interestingly, high yield (91.0%) of the product, **5b** was observed in very short time 9 min as compared with conventional condition and 3.0 equiv of phosphite was sufficient to get maximum yield of product **5b** (**Table-4**, entry 3). After optimization of the reaction conditions, a variety of the alkyl phosphites/phosphinates and alkyl/heteroaryl halides were altered for the generality of the reaction (**Table-5**). Structures of the title compounds **5(a-e)** and **7(a-e)** were confirmed by spectral and analytical data. IR stretching absorption bands were observed in the regions of 3150-3000, 2998-2850, 1210-1285 and 1070-1030 cm⁻¹ for -C=H, -C-H, -P=O and -C-P-O- respectively. ³¹P NMR signals appeared in the region of δ_p = 19.01-28.00 ppm. In addition, ¹H NMR, ¹³C NMR and mass spectra are regarded as positive evidence for the formation of title compounds.

Based on overview and literature survey, we proposed the plausible mechanism for $\text{CeCl}_3 \cdot 7\text{H}_2\text{O} \cdot \text{SiO}_2$ mediated Michaelis-Arbuzov reaction (**Fig-2**). The alkyl halide and Lewis acid catalyst form a complex, which enhances the electrophilic nature of the alkyl halide and make feasibility to $\text{S}_{\text{N}}2$ attack of lone pair electrons of the phosphorus of trialkyl phosphite and determine the reaction pathway.

Table-5 Physical data of the synthesized phosphonates, 5(a-e) and 7(a-e).

Compd	Product	Conventional conditions		Microwave conditions		M. P (°C)
		Time (h)	Yield (%)	Time (min)	Yield (%)	
5a		3	87.2	8	91.5	91-92
5b		4	86.5	9	91.0	76-78
5c		6	81.6	11	89.9	132-134
5d		5	85.0	7	90.7	84-86
5e		3.5	89.3	5	93.2	81-83
7a		5.5	83.5	13	90.3	137-139
7b		6	82.0	13	90.0	133-134
7c		8	79.8	15	86.6	110-112
7d		5	81.4	13	88.6	97-98
7e		4	84.6	9	91.2	85-86

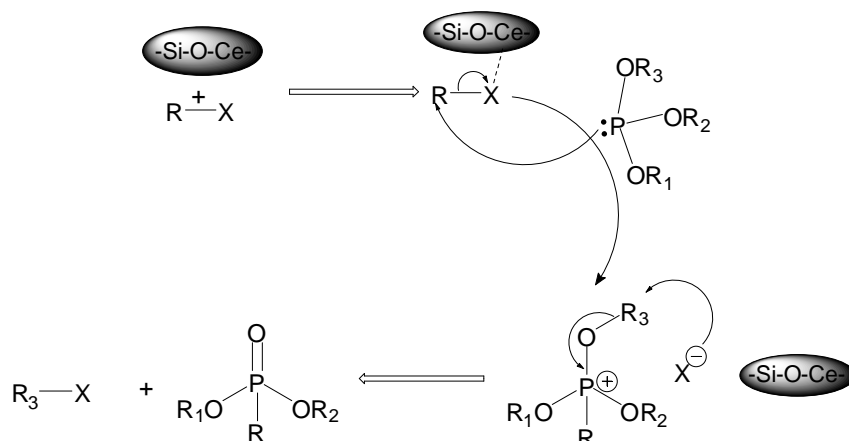


Fig-2 The plausible proposed mechanism for CeCl₃·7H₂O-SiO₂ mediated Michaelis-Arbuzov reaction.

CONCLUSION

Keeping in view the numerous applications of the phosphonates in various fields, we reported a green and an efficient solvent-free procedure for the synthesis of arylmethyl and heteroaryl phosphonates/phosphinates in high yields using CeCl₃·7H₂O-SiO₂ catalyzed Michaelis-Arbuzov reaction under conventional and microwave irradiation methods. The excellent yields of phosphonates were obtained in microwave irradiation method in short reaction times. The synthetic protocol and synthesized derivatives may be considered as intermediates and can be used for beneficial applications in the field of phosphorus chemistry.

Acknowledgement

One of the authors (DSR) (JRF) is grateful to acknowledge financial support from University Grant Commissions under the Basic Scientific Research Programme (UGC-BSR) and SK. Thaslim Basha wish to thank to UGC for financial support.

REFERENCES

- [1] R. Engel, *Handbook of Organophosphorus Chemistry*, Marcel Dekker: New York, NY, **1992**.
- [2] J. E. Franz, Ger. Offen, 2 152 826, **1972**, *Chem. Abstr.*, **1972**, 77, 165079k.
- [3] J. L. Segura, R. Gomez, N. Martin, D. M. Guldi, *Org. Lett.*, **2001**, 3, 2645.
- [4] (a) L. Zhen, R. C. Urian, Y. Liu, A. K. Y. Jen, L. Pu, *Chem. Mater.*, **2000**, 12, 13 (b) Y. J. Pu, M. Soma, J. Kido, H. Nishide, *Chem. Mater.*, **2001**, 13, 3817; (c) L. Liao, Y. Pang, L. Ding, F. E. Karasz, *Macromolecules*, **2002**, 35, 3819.
- [5] (a) G. Bordeau, R. Larita, G. Metge, C. Fiorini-Debuisschert, F. Charra, M. P. Teulade-Fichou, *J. Am. Chem. Soc.*, **2008**, 130, 16836; (b) P. Shen, G. Sang, J. Lu, B. Zhao, M. Wan, Y. Zou, Y. Li, S. Tan, *Macromolecules*, **2008**, 41, 5716.
- [6] (a) E. H. Elandaloussi, P. Frere, P. Richomme, J. Orduna, J. Grain, J. Roncali, *J. Am. Chem. Soc.*, **1997**, 119, 10774; (b) P. Frere, J. M. Raimundo, P. Blanchard, J. Delaunay, P. Richomme, J. L. Sauvajol, J. Orduna, J. Grain, J. Roncali, *J. Org. Chem.*, **2003**, 68, 7254.
- [7] (a) A. Michaelis, R. Kaehne, *Chem. Ber.*, **1898**, 31, 1048; (b) B. A. Arbuzov, *Pure Appl. Chem.*, **1964**, 9, 315; (c) A. K. Bhattacharya, G. Thyagarajan, *Chem. Rev.*, **1981**, 81, 415.
- [8] L. D. A. Quin, *Guide to Organophosphorus Chemistry*; John Wiley & Sons, **2000**.
- [9] (a) G. Laven, J. Stawinski, *Synlett*, **2009**, 2, 225; (b) G. Laven, M. Kalek, M. Jezowska, J. Stawinski, *New. J. Chem.*, **2010**, 34, 967.
- [10] T. M. Balthazor, R. C. Grabiak, *J. Org. Chem.*, **1980**, 45, 5425.
- [11] (a) A. K. Bhattacharya, G. Thyagarajan, *Chem. Rev.*, **1981**, 81, 415; (b) P. Y. Renard, P. Vayron, E. Leclerc, A. Valleix, C. Mioskowski, *Angew. Chem. Int. Ed.*, **2003**, 42, 2389.
- [12] S. Kobayashi, *Lanthanide: Chemistry and Use inorganic Synthesis*; Springer-Verlag: Heidelberg, Germany, **1999**.

- [13] D. S. Bose, L. Fatima, H. B. Mereyala, *J. Org. Chem.* **2003**, 68, 587; (b) C. C. K. Keh, V. V. Namboodiri, R. S. Varma, C. J. Li, *Tetrahedron Lett.* **2002**, 43, 4993; (c) G. Martelli, S. Morri, D. Savoia, *Synlett*, **2002**, 158; (d) S. Warren, J. Clayden, *Angew. Chem., Int. Ed.* **1996**, 35, 241.
- [14] (a) G. Sabitha, G.S. Kirankumar Reddy, K.B. Reddy, J. S. Yadav, *Adv. Synth. Catal.*, **2004**, 346, 921; (b) G. Sabitha, N. M. Reddy, K. Sudhakar, J. S. Yadav, *Lett. Org. Chem.*, **2005**, 2(8), 763; (c) G. Sabitha, J. S. Yadav, *Electronic Encyclopedia of Reagents for Organic Synthesis*, **2006**.
- [15] S. Alessandrini, G. Bartoli, M. C. Bellucci, R. Dalpozzo, M. Malavolta, E. Marcantoni, L. Sambri, *Eur. J. Org. Chem.*, **1999**, 21, 617.
- [16] M. A. Ciufolini, M. V. Deaton, S. Zhu, M. Chen, *Tetrahedron.*, **1997**, 53, 16299.
- [17] (a) R. A. Abramovitch, *Org. Prep. Proced. Int.*, **1991**, 23, 685; (b) S. Caddick, *Tetrahedron*, 1995, 51, 10403.
- [18] (a) A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacquault, D. Mathe, *Synthesis*, **1998**, 9, 1213; (b) R. S. Varma, *Green Chem.*, **1999**, 1, 43; (c) K. Tanaka, F. Toda, *Chem. Rev.*, **2000**, 100, 1025.
- [19] (a) D. Villemin, F. Simeon, H. Decreus, P. A. Jaffres, *Phosphorus, Sulfur and Silicon and the Relat. Elem.* **1998**, 133, 209; (b) J. J. Kiddle, *Synth. Commun.*, **2001**, 31, 3377.
- [20] G. G. Rajeshwaran, M. Nandakumar, R. Sureshababu, A. K. Mohankrishnan, *Org. Lett.*, **2011**, 13, 1270.