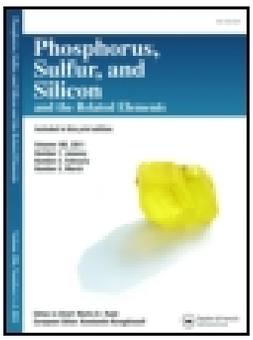

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SOLVENT-FREE SONOCHEMICAL KABACHNIC-FIELDS REACTION TO SYNTHESIZE SOME NEW α-AMINOPHOSPHONATES CATALYZED BY NANO-BF_3•SiO_2

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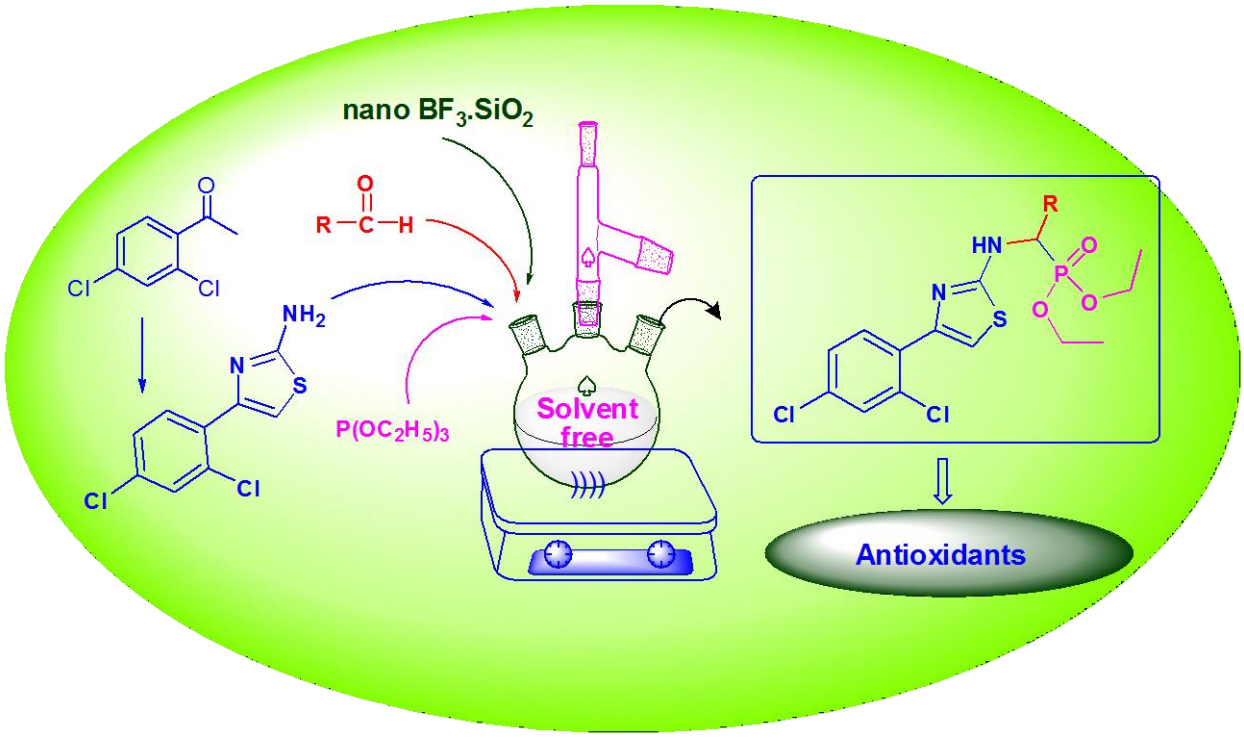
Running head**:** *Nano-BF_3•SiO_2 catalyzed synthesis of some novel α-aminophosphonates*

Abstract: To obtain a rapid, efficient synthesis of some new α-aminophosphonates, ultrasonic irradiation has been applied to the reaction mixtures containing amine, aromatic or heteroaromatic aldehydes and triethyl phosphite. The Kabachnik-Fields reaction was performed by using nano-BF_3•SiO_2 as a recyclable catalyst under solvent free conditions. Key advantages of this procedure consist in the eco-friendly and highly efficient reaction conditions, high yields, an easy work-up procedure, short reaction times and solvent free conditions. All title compounds were characterized by spectral and elemental analysis. They were further screened for their *in vitro* antioxidant activity by the DPPH, O^{2-} and NO methods. The majority of the title compounds showed good antioxidant activity when compared with the standard antioxidants.



Keywords

α-aminophosphonates; ultrasonic irradiation; nano-BF_3•SiO_2; antioxidant activity

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INTRODUCTION

The synthesis and applications of *α*-aminophosphonates has received the attention of organic chemists since these compounds represent structural analogues of the important *α*-

aminoacids. Various applications of α-aminophosphonates as antimicrobial [1-3], antioxidant [2], antitumor [4-6], antiviral [7], anti-inflammatory [8] and enzyme inhibitors [9-11] have been reported. These numerous applications have encouraged the development of a number of techniques for the synthesis of α-aminophosphonates.[12, 13] The Kabachnik-Fields reaction is one of the most direct and efficient routes for the synthesis of α-aminophosphonates. It consists in a one-pot-three-component reaction of aldehyde, amine and dialkyl phosphite[14] or trialkyl phosphite.[15]

Recently several reports have been published which described the synthesis of α-aminophosphonates *via* Kabachnik-Fields reaction using Lewis acids like $In(OT_f)_3$,[16a] $Yb(P_fO)_3$,[16b] $Fe_3O_4@ZrO_2/SO_4$,[2-16c] SmI_2,[16d] BF_3-Et_2O,[16e] CdI_2/benzene,[16f] CdI_2/microwave,[16g] Brønsted acids like o-benzenedisulfonimide,[17a] acetic acid,[17b] formic acid,[17c] sulfamic acid[17d] and oxalic acid,[17e] solid acids like $H_3PMo_{12}O_{40}$,[18a] silica sulfuric acid,[18b] bases such as NaOH,[19a] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),[19b] nano-catalysts like nano-TiO_2,[20a] $CuO@Fe_3O_4$,[20b] and other catalysts like quaternary ammonium salts,[21a] boric acid,[21b] Cu(I)/Cu(II),[21c] zirconocene-bis(perfluorobutanesulfonate).[21d] Microwave irradiation[22a,b,c] technique is also used for one-pot syntheses of α-aminophosphonates. However, some of the reported procedures are associated with disadvantages like the need to use solvents and additional reagents, long reaction times, costly and moisture sensitive catalyst, etc. As a result, there is still need to develop a more efficient, simple, milder and high yield protocol for the synthesis of α-aminophosphonates.

Ultrasonication has increasingly been used in organic synthesis in the last three decades. For many organic reactions which are ordinarily accomplished by heating, ultrasonication has been demonstrated as an alternative energy source. The use of ultrasound in organic transformations, particularly for the synthesis of α-aminophosphonates is well known to enhance

reaction rates, yields and selectivity.[23a,b] Ultrasound facilitates organic transformations at ambient temperatures, which otherwise require drastic conditions of high temperature and/or pressure.

$BF_3 \cdot Et_2O$ as a strong Lewis acid is corrosive, toxic, volatile and it also generates significant amounts of waste. Nano-BF_3•SiO_2[24a,b] is a bench-top catalyst that has many advantages such as simple preparation, reusability, large surface area, strong Lewis acid character, easy handling and being environmentally benign.

By considering the above facts and in continuation of our studies towards developing new methods for the synthesis of *α*-aminophosphonates,[3, 8] we decided to explore the possibility of implementing a one-pot three-component reaction for the preparation of *α*-aminophosphonates in the presence of nano-BF_3•SiO_2, using ultrasonication under solvent-free conditions. Both conventional and ultrasonicated conditions are used to optimize the method. The catalyst, nano-BF_3•SiO_2 has been described as an effective promoting catalyst in the preparation of *α*-aminophosphonates by the reaction of amine, various aldehydes and triethyl phospite *via* the Kabachnic-Fields reaction under two methods. High yield of the products in the range of 87-97% are reported under ultrasonication conditions.

The antioxidant activity was screened for the title compounds by the DPPH, O^{2-} and NO methods. The majority of the title compounds showed good antioxidant activity.

RESULTS AND DISCUSSION

In this letter, we report an efficient and environmentally benign protocol for the synthesis of *α*-aminophosphonates (**5a**-**k**) by condensation of 4-(2,4-dichlorophenyl)thiazol-2-amine (**2**)

which was previously prepared from 2,4-dichloroacetophenone (**1**), various aldehydes (**3a**-**k**) and triethyl phosphite (**3**) in the presence of 37% nano-BF_3•SiO_2 under solvent-free conditions using conventional and ultrasonic irradiation methods (**Scheme 1**).

[Insert Scheme 1]

At the beginning of our investigation, the reaction was tested with 4-(2,4-dichlorophenyl)thiazol-2-amine (**2**) (0.010 mol), benzaldehyde (**3a**) **(**0.010 mol) and triethyl phosphite (**4**) (0.020 mol) as model components (**Table 1**) in tetrahydrofuran (THF) at reflux temperature without using any catalyst. Under this condition, the model compounds were not able to undergo an effective reaction to produce the desired product, diethyl [4-(2,4-dichlorophenyl)thiazol-2-ylamino]phenylmethanephosphonate (**5a**) but gave a very poor product yield (20%) (**Table 1**, entry 1). Thus, a new method was developed to attain higher product yields by using a catalyst. In search for an efficient catalyst and the best operational conditions, the model reaction was carried out with different Lewis acid catalysts (10 mol%) such as $ZnCl_2$, $CuCl_2$, $AlCl_3$ and BF_3•Et_2O. The results are summarized in **Table 1** (entries 2-5).

It was observed that, upon addition of Lewis acid catalysts, the yield of the product **5a** was improved from 20% to the range of 58-63%, indicating that the Lewis acid catalyst plays a promising role in the process. BF_3•SiO_2 was found to be an excellent proton source in terms of convenience, ease of production, cheapness and insolubility in all organic solvents. Hence it was used for the synthesis of many organic compounds.[25-28] On the other hand, nano-BF_3•SiO_2 exhibits a high surface to volume ratio in addition to the above mentioned properties that makes use of this catalyst in many chemical reactions.[24b, 29] Hence 37% nano-BF_3•SiO_2 (0.25g) was used as catalyst in the model reaction to synthesize compound **5a**. We obtained a good product

yield (70%, **Table 1**, entry 6) when THF was used as solvent. Further, we studied the effect of solvents on the model reaction. The concentration of catalyst (0.25g) was kept constant for the model reaction, and the solvent like methanol, dichloromethane, toluene, ethanol and solvent-free condition was varied. The scrutiny revealed that in all solvents the product yields were found to be 71-76% (**Table 1**, entry 7-10) after 2h. But in case of solvent-free conditions, we obtained a good product yield (80%) after 1h (**Table 1**, entry 11). The use of ultrasound in organic transformations is well known to enhance reaction rates, yields and selectivity. Hence, ultrasonic irradiation under solvent free condition was used to synthesize compound **5a**. We got an excellent yield of the product (90%) in a very short period of time (10min) at room temperature (**Table 1**, entry 12). The obtained results are summarized in **Table 1**.

Keeping in mind the above results and to achieve better results, we carried out the model reaction with the catalysts $ZnCl_2$, $CuCl_2$, $AlCl_3$ and BF_3•Et_2O under solvent free condition with and without ultrasonic irradiation (**Table 1**, entry 13-20). We got better results with ultrasonic irradiation under solvent free condition (**Table 1**, entry 14, 16, 18, 20). However, the time and yield of the product **5a** obtained with 37% nano-BF_3•SiO_2 (0.25g) as catalyst under solvent free condition was found to be better than the other catalysts used in the model reaction. Hence, 37% nano-BF_3•SiO_2 was selected as catalyst for further optimization of the reaction conditions.

[Insert Table 1]

The effect of the amount of the catalyst (37% nano-BF_3•SiO_2) was also scrutinized by varying the amount of the catalyst with ultrasonic irradiation under solvent free condition (**Table 2**, entry 1-7). We have varied the concentration of catalyst to 0.05, 0.1, 0.15, 0.2, 0.25, 0.30 and 0.35g. The result revealed that, when the reaction was carried out in the presence of 0.05, 0.1,

0.15, 0.2g of catalyst, it gave lower yield of product (**Table 2**, entry 1-4). It was observed that almost same yield (96%) of the product **5a** was obtained with the catalyst amount in the range of 0.30-0.40g (**Table 2**, entry 6-8) and a lower yield (90%) for 0.25g (**Table 2**, entry 5). Hence, the optimum amount of the catalyst, 0.30g was confirmed under ultrasound irradiation. The obtained results are summarized in **Table 2**.

[Insert Table 2]

The reusability of the nano-BF_3•SiO_2 catalyst was also examined. After each run, the product was filtered and the residue of catalyst was washed with $CHCl_3$ to remove stains from the catalyst surface and reuse it up to five cycles for the synthesis of compound **5a**. (**Table 3**, entry 1-5). It was found that 37% nano-BF_3•SiO_2 could effectively catalyze this reaction under solvent-free conditions to afford the desired products in high yields.

[Insert Table 3]

After optimizing the conditions, the generality of this method for the synthesis of *α*-aminophosphonates (**5a-k**) (**Scheme 1**) was examined by the reaction of several substituted aldehydes (**3b-k**), amine (**2**) and triethyl phosphite (**4**) using 37% nano BF_3•SiO_2 as a catalyst under solvent free conditions by conventional and ultrasound irradiation methods. The results are summarized in **Table 4**. A plausible reaction mechanism for the formation of *α*-aminophosphonates in the presence of 37% nano-BF_3•SiO_2 as a catalyst is shown in Fig. 1 [see Supplementary Material files]. Initially the carbonyl group of the aldehyde reacts with the amine to form an intermediate imine A. The activated intermediate imine then reacts with triethyl phosphite to produce the corresponding *α*-aminophosphonates.

[Insert Table 4]

The chemical structure of the title compounds **5a-k** were supported by spectral data (^{31}P, ^{1}H and ^{13}C NMR, IR and LC-MS), elemental analysis. The results are presented in the experimental section. ^{31}P NMR signals were observed in the region 19.3-16.7 ppm for all the compounds **5a-k**. The ^{1}H NMR spectra gave signals as multiplets due to Ar-H in the range of δ 8.39-6.67 ppm. The proton signals in the range of 5.42-5.21 and 4.74-4.42 ppm are due to C-NH and P-CH, respectively. The methylene protons of P-O-C**H**$_2$CH$_3$ gave a multiplet and methyl protons of P-O-CH$_2$C**H**$_3$ resonated as a triplet in the region δ 4.09-3.88 and δ 1.30-1.19, respectively for **5a-k**. ^{13}C NMR signals for P-CH, methylene and methyl carbons were observed in the region 57.4-56.4, 64.3-63.7 and 16.9-16.7 ppm, respectively, for **5a-k**. IR absorptions in the regions 3399-3380, 1502-1485 and 1248-1225 cm^{-1} were assigned to indazole-NH, NH and P=O stretching vibrations respectively for **5a-k**. The expected *m/z* values of M^+ ions were observed in the corresponding mass spectra. Representative ^{1}H, ^{13}C and ^{31}P NMR spectra for the new compounds **5a**, **5d**, **5g, 5i** and **5k** are presented in the Supplemental Materials (Figures S 2 - S 15).

Antioxidant activity

The antioxidant activity was examined using DPPH,[30] O^{2-} [31, 32] and NO[33] methods in the concentration range 25-100μg/mL. The results are shown in **Fig. 1**, **Fig. 2** and **Fig. 3**, respectively.

[Insert Fig. 1], [Insert Fig. 2], [Insert Fig. 3]

All tested samples showed good to moderate antioxidant activity. Among **5a-k**, compound **5b** bearing a 4-fluorophenyl moiety and **5i** bearing a 3-chloro-4-fluorophenyl moiety exhibited a slightly higher activity compared with the standard antioxidant ascorbic acid in superoxide and

NO methods. The compounds **5k** bearing a 6-methoxypyridin-2-yl moiety, **5c** bearing a 4-nitrophenyl moiety, **5f** with an allylphenyl moiety, **5g** bearing a 3-nitrophenyl moiety and **5h** with a 3-chlorophenyl moiety exhibited good activities compared with standard antioxidant in all three methods. Their high antioxidant activity is due to the presence of the electronegative heteroatom group which renders their N–H bond weaker. Consequently, the N–H bond easily cleaves homolytically with the formation of the corresponding free radicals. The functionalities like NH, NO_2, F, Cl and allyl in the title compounds might be the cause of the significantly enhanced antioxidant activity. Overall, significant antioxidant activities were observed in *α*-aminophosphonates **5a-k** when compared with standard antioxidants.

CONCLUSION

In conclusion, we demonstrated here an efficient, inexpensive, environmentally benign protocol for the formation of *α*-aminophosphonates through an intermediate imine by the Kabachnik-Fields reaction under solvent free condition in the presence of an efficient solid acid, nano-BF_3•SiO_2 at room temperature by conventional and ultrasonication methods. The advantages of this attractive method are good yield of the products, less reaction time, easy workup procedure and reusability of the heterogeneous catalyst, nano-BF_3•SiO_2. Promisingly, high product yields (69-83%) were obtained under conventional conditions, and 87-97% under ultrasonication. Moreover, the reaction time in ultrasonication method (10 min) is much shorter as compared with conventional (1h) conditions. The antioxidant activity *α*-aminophosphonates was evaluated by the DPPH, O^{2-} and NO methods. Compound **5b** bearing a 4-fluorophenyl motif and **5i** bearing a 3-chloro-4-fluorophenyl ring exhibited potent antioxidant activity when

compared with the standard antioxidants. The remaining compounds showed moderate to good antioxidant activity. These remarkable results of this study can provide a foundation for the design and development of some more structurally diversified α-aminophosphonates as potential antioxidants.

EXPERIMENTAL DETAILS

Chemicals and analytical-grade reagents used for the synthesis are commercially available and were procured from Sigma-Aldrich/Merck, and Sd Fine-Chem Limited. Glassware was dried in an oven at 150 °C prior to use. All solvents are reagent grade and were further purified and stored under a nitrogen atmosphere. IR spectra were recorded on Bruker Alpha FT-IR spectrophotometer. NMR spectra were recorded on a Bruker 400-MHz spectrometer operating at 400MHz for ^{1}H NMR, 100.25MHz for ^{13}C NMR, and 161.9MHz for ^{31}P NMR in DMSO-d_6. Tetramethylsilane and 85% H_3PO_4 were used as internal standards for ^{1}H and ^{13}C NMR spectra and external standard for ^{31}P NMR spectra, respectively. L.C. mass spectra were recorded on a SHIMADZU 2010A mass spectrometer. Elemental analyses were performed on a Thermo Finnigan Flash 1112 instrument at the University of Hyderabad, Hyderabad. Chemical shift values δ and coupling constants J are reported in ppm and Hz, respectively. The reaction progress was monitored by pre-coated thin-layer chromatography (TLC) plates (Merck) and spots were visualized with ultraviolet (UV) light. Sonication was performed using BANDELIN SONOREXR (Germany) with a frequency of 35 kHz and a nominal power of 200 W ultrasonic bath for ultrasonic irradiation with inbuilt heating 30-80 °C, which is thermostatically changeable. The reaction vessel was placed inside the ultrasonic bath containing water.

Preparation of the catalyst [24a, 29]

0.37g of BF_3 (0.7 mL of BF_3•Et_2O) was added drop-wise to a mixture of 0.63g of silica gel or nano-silica gel and 5 mL of $CHCl_3$. The mixture was stirred for 1 h at room temperature. The resulting suspension was filtered. The obtained solid was washed with $CHCl_3$ and dried at room temperature.

Synthesis of 4-(2,4-dichlorophenyl)thiazol-2-amine (2)

Bromine **(**0.010 mol**)** was added drop wise to a mixture of 2,4-dichloroacetophenone (1.4 mL, 0.010 mol) and thiourea (1.52g, 0.020 mol). After the complete addition of bromine, the reaction mixture was heated on a water bath overnight. Then, water was added and again heated until most of the solid had dissolved. The hot reaction mixture was filtered and the filtrate was cooled, made alkaline with ammonium hydroxide to obtain compound **2**. It was filtered, washed with alcohol and dried over P_2O_5. It was finally crystallized from ethanol to obtain pure compound 4-(2,4-dichlorophenyl)thiazol-2-amine (**2**). M.p. 156-158 °C.

Conventional procedure for the synthesis of *α*-aminophosphonates (5a-k)

The mixture of benzaldehyde (**3a**) (1 mL, 0.010 mol), 4-(2,4-dichlorophenyl)thiazol-2-amine (**2**) (2.45g, 0.010 mol) and triethyl phosphite (**4**) (3.4 mL, 0.020 mol) was placed in a round bottomed flask. To this mixture, 37% nano-BF_3•SiO_2 (0.30g) was added and the mixture was heated to 70 °C and agitated for 1h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. CH_2Cl_2 (15 mL) was added to the reaction mixture and stirred for 10 min. The catalyst, nano-BF_3•SiO_2 was separated by filtration, washed with CH_2Cl_2 (2×10 mL) and the residue was dried under vacuum at 100 °C to be utilized in further studies. The organic layer was washed with water

(15mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum at 50 °C to obtain crude products. The pure diethyl [4-(2,4-dichlorophenyl)thiazol-2-ylamino]phenylmethanephosphonate (**5a**) was obtained by column chromatography using EtOAc/*n*-hexane 7:3 as eluent. The same procedure was used for the preparation of the remaining compounds **5b**-**k**.

Ultrasonication procedure for the synthesis of *α*-aminophosphonates (5a-k):

The mixture of benzaldehyde (**3a**) (1 mL, 0.010 mol), **2** (2.45g, 0.010 mol) and triethyl phosphite (**4**) (3.4 mL, 0.020 mol) was placed in a round bottomed flask. To this mixture, 37% nano-BF_3•SiO_2 (0.30g) was added and the mixture was irradiated in the ultrasonicator at ambient temperature for about 10 minutes. The progress of the reaction was monitored by TLC (EtOAc/*n*-hexane 7:3). After completion of the reaction as checked by TLC, the reaction mixture was cooled to room temperature. CH_2Cl_2 (15 mL) was added to the reaction content and stirred for 10 min. The catalyst nano-BF_3•SiO_2 was separated by filtration as residue, washed with CH_2Cl_2 (2×10 mL) and the residue was dried under vacuum at 100 °C to be utilized in further studies. The combined organic layer was washed with water (15 mL), dried over anhydrous Na_2SO_4 and concentrated under vacuum at 50 °C to obtain crude **5a**. Pure **5a** was obtained by column chromatography (EtOAc/*n*-hexane 7:3). The same procedure was used for the preparation of the remaining compounds **5b**-**k**.

*Diethyl [4-(2,4-dichlorophenyl)thiazol-2-ylamino]phenylmethanephosphonate (**5a**)*. Yield: 96%; semi-solid. ^{31}P NMR: δ 17.4 ppm; ^{1}H NMR**:** δ 8.16-6.90 (m, 9H, Ar-H), 5.28 (s, 1H, C-NH), 4.48 (d, J = 9.2 Hz, 1H, PCH), 4.02 (m, 4H, O$\underline{CH_2}CH_3$), 1.21 (t, J = 7.2 Hz, 6H, $OCH_2\underline{CH_3}$); ^{13}C NMR: δ 166.3 (C-12), 149.2 (C-9), 138.3 (C-17), 136.9 (C-2), 132.4 (C-4), 129.8 (C-3), 128.5 (C-6), 127.6 (C-26, C-28), 126.8 (C-25, C-29), 125.5 (C-5), 123.6 (C-1), 123.1 (C-27), 108.4 (C-

10), 63.4 (C-21, C-23), 57.0 (C-15), 16.7 (C-22, C-24); IR (KBr) (ν_{max}/cm^{-1}): 3380 (NH), 1485 (C=N), 1228 (P=O); LCMS (*m/z*, %): 471 ($M+H^+$, 100), 473 (M+2, 64); Anal. Calcd. for $C_{20}H_{21}Cl_2N_2O_3PS$: C, 50.96; H, 4.49; N, 5.94%; found: C, 50.88; H, 4.55; N, 5.90%.

Spectroscopic data of **5b-5k** are given in the Supplemental Material files.

Antioxidant activity

The evaluation of antioxidant activity of newly synthesized compounds was performed by the DPPH radical scavenging activity assay, following the method of Cotelle *et.al*., the Superoxide radical scavenging activity following the method of Robak and Gryglewski and the Nitric oxide scavenging activity using the modified protocol of Green *et al*. and Marcocci *et al* [see Supplemental Materials].

The experiment was carried out in triplicate. The results are presented in **Fig. 1**, **Fig. 2** and **Fig. 3**, respectively, for the three methods. The results revealed that the majority of the title compounds showed good antioxidant activity when compared with standard antioxidants.

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Scheme 1. Synthesis of some novel α-aminophosphonates (**5a-k**)

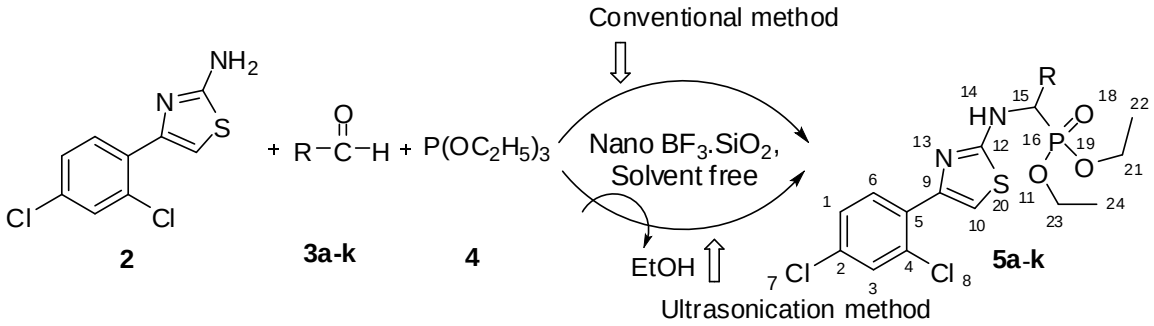


Fig. 1: Antioxidant activity of novel *α*-aminophosphonates **5a-k** by DPPH radical Scavenging method**.**

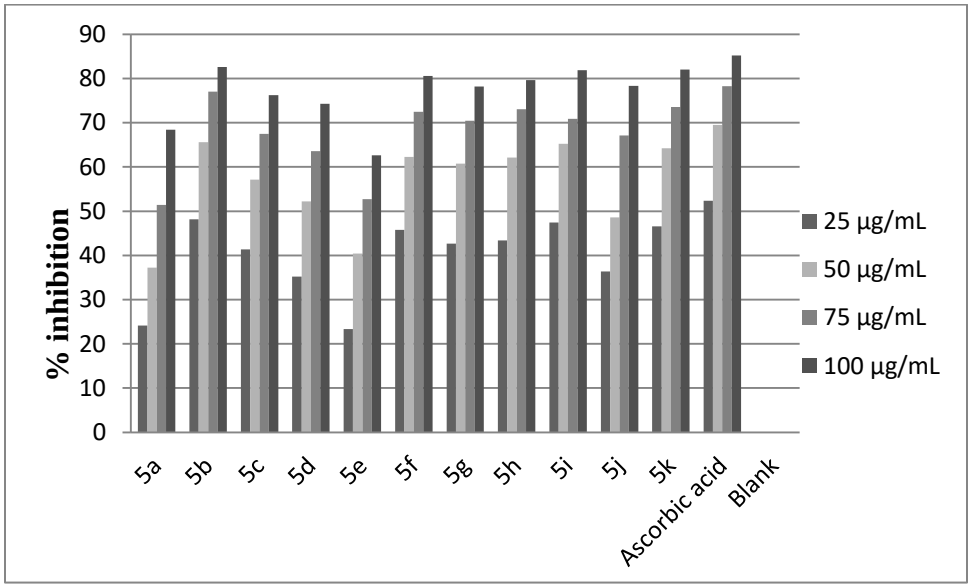


Fig. 2: Antioxidant activity of novel *α*-aminophosphonates **5a-k** by Superoxide radical scavenging method.

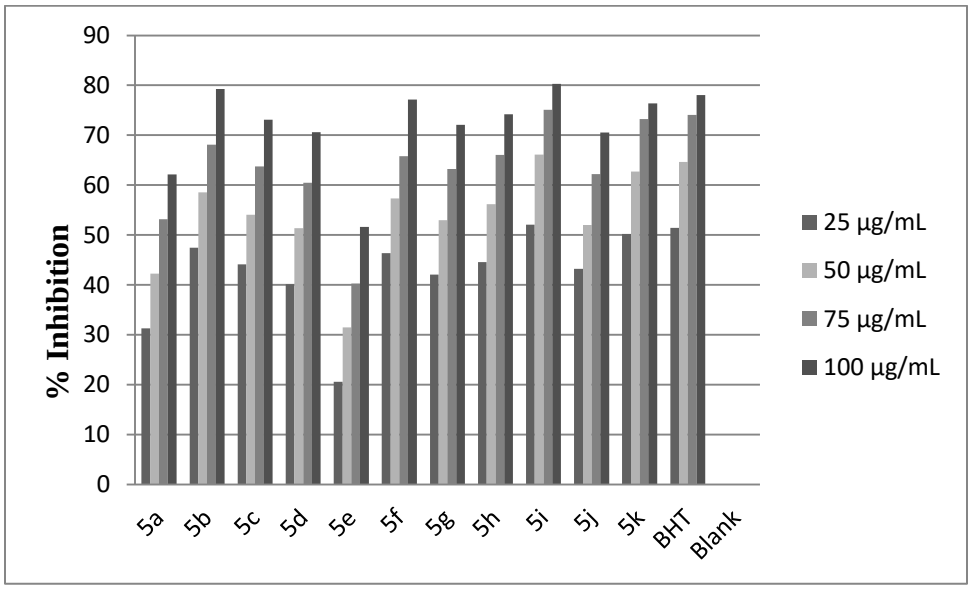


Fig. 3: Antioxidant activity of novel *α*-aminophosphonates **5a-k** by Nitric Oxide method.

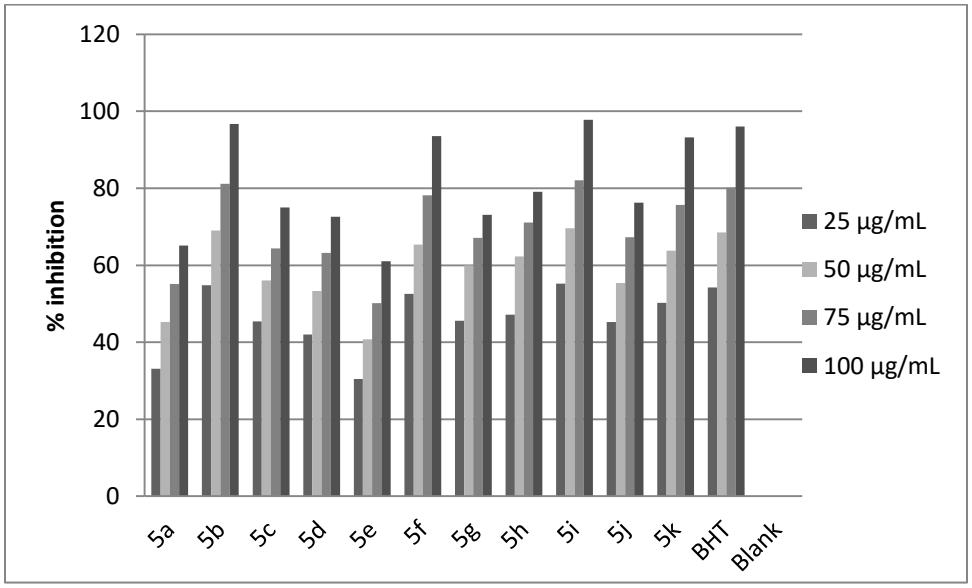
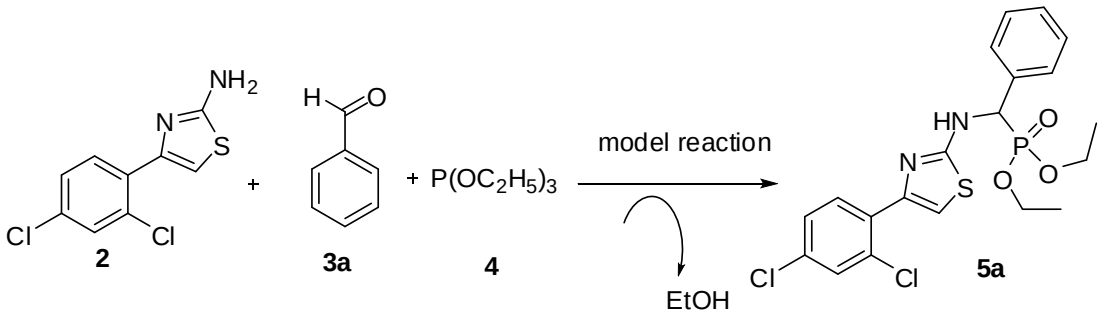


Table 1. Synthesis of compound **5a** under various conditions[a]



Entry	Catalyst	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1	-----	THF	r.t	8	20
2	$ZnCl_2$ (10mol%)	THF	r.t	4.5	58
3	$CuCl_2$ (10mol%)	THF	r.t	5.0	56
4	$AlCl_3$ (10mol%)	THF	r.t	3.0	60
5	$BF_3.Et_2O$ (10mol%)	THF	r.t	2.5h	63
6	37% nano $BF_3.Et_2O$ (0.25g)	THF	r.t	2.0	70
7	37% nano $BF_3.Et_2O$ (0.25g)	Methanol	r.t	2.0	73
8	37% nano $BF_3.Et_2O$ (0.25g)	DCM	r.t	2.0	71
9	37% nano $BF_3.Et_2O$ (0.25g)	Toluene	r.t	2.0	74
10	37% nano $BF_3.Et_2O$ (0.25g)	Ethanol	r.t	2.0	76
11	37% nano $BF_3.Et_2O$ (0.25g)	Solvent-free	70 °C	1h	82
12	37% nano $BF_3.Et_2O$ (0.25g)	Solvent-free (Ultrasonication)	room temp.	10min	90
13	$ZnCl_2$ (10mol%)	Solvent-free	70 °C	3h	66

14	$ZnCl_2$ (10mol%)	Solvent-free (Ultrasonication)	room temp.	1.5h	70
15	$CuCl_2$ (10mol%)	Solvent-free	70 °C	3.5h	62
16	$CuCl_2$ (10mol%)	Solvent-free (Ultrasonication)	room temp.	1h	69
17	$AlCl_3$ (10mol%)	Solvent-free	70 °C	2.5h	67
18	$AlCl_3$ (10mol%)	Solvent-free (Ultrasonication)	room temp.	50min	73
19	$BF_3.Et_2O$ (10mol%)	Solvent-free	70 °C	1.5h	71
20	$BF_3.Et_2O$ (10mol%)	Solvent-free (Ultrasonication)	room temp.	40min	77

[a] *Reaction of benzaldehyde, 4-(2,4-dichlorophenyl)thiazol-2-amine and triethyl phosphite were* selected as models for the optimization of reaction conditions

[b] *Isolated yield.*

Table 2. The effect of the amount of the catalyst, 37% nano-BF_3-SiO_2 to promote the Kabachnik-Fields reaction[a]

Entry	Amount of Catalyst (gm)	Time (min)	Yield[b] (%)
1	0.05	10	60
2	0.1	10	64
3	0.15	10	69
4	0.2	10	75
5	0.25	10	90
6	0.3	10	96
7	0.35	10	96
8	0.40	10	96

[a] *Reaction of benzaldehyde, 4-(2,4-dichlorophenyl)thiazol-2-amine and triethyl phosphite in presence of 37% nano-BF_3-SiO_2 under ultrasonic waves in solvent-free condition for 10 min. at room temperature.*

[b] *Isolated yield.*

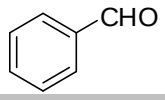
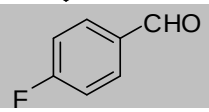
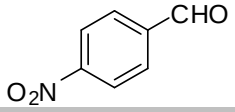
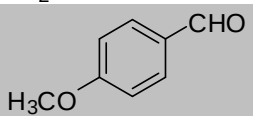
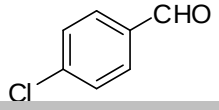
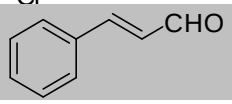
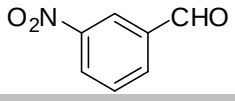
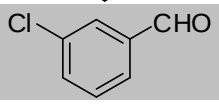
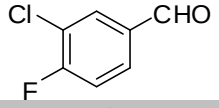
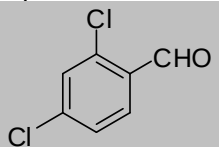
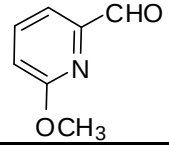
Table 3. Reusability of the catalyst, 37% nano-BF_3-SiO_2 for the synthesis of compound 5a[a]

Entry	37% nano $BF_3.SiO_2$ (0.30g)	Time (min.)	Yield[b] (%)
1	1st run	10	96
2	2nd run	10	93
3	3rd run	10	91
4	4th run	10	89
5	5th run	10	81

[a]*Reaction of benzaldehyde, 4-(2,4-dichlorophenyl)thiazol-2-amine and triethyl phosphite in presence of 37% nano-$BF_3.SiO_2$ under ultrasonic waves in solvent-free condition for 10 min. at room temperature.*

[b] *Isolated yield.*

Table 4. Sonochemical effect on the synthesis of α-aminophosphonates **(5a-k)**

Entry	Aldehyde (R-CHO)	Without Ultrasonication[a]		With Ultrasonication[b]	
		Time (min)	Yield[c] (%)	Time (min)	Yield[c] (%)
5a		60	82	10	96
5b		60	81	13	92
5c		60	83	12	97
5d		60	77	15	91
5e		60	79	11	93
5f		60	69	17	87
5g		60	70	20	89
5h		60	72	15	90
5i		60	71	14	92
5j		60	68	18	90
5k		60	70	19	94

[a]*Reaction of 4-(2,4-dichlorophenyl)thiazol-2-amine, aldehyde and triethyl phosphite in presence of 37% nano-BF_3-SiO_2 (0.30g) under solvent-free condition at 70 °C by conventional method.*

[b]*Reaction of 4-(2,4-dichlorophenyl)thiazol-2-amine, aldehyde and triethyl phosphite in presence of 37% nano-BF_3-SiO_2 (0.30g) under solvent-free condition at room temperature by ultrasonic irradiation[b] method .*

[c] *Isolated yield.*