

Neat Synthesis and Anti-oxidant Activity of α -Hydroxyphosphonates

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A simple efficient and neat synthesis of α -hydroxy phosphonates has been accomplished from aromatic/heterocyclic aldehydes and diethyl phosphite using KHSO_4 as a catalyst under solvent-free conditions at ambient temperature. These compounds are characterized by spectral and analytical data and tested for their anti-oxidant activity.

Key Words : α -Hydroxy phosphonates, KHSO_4 , Anti-oxidant activity

Introduction

Oxidation reactions can produce free radicals during metabolism, which start chain reactions and damage cells. Antioxidants terminate these chain reactions by removing free radical intermediates, and also inhibit other oxidation reactions.

In recent years, a detailed mechanism of the antioxidant action of organophosphorus compounds and their relationships between chemical structure and antioxidant activity has been comprehensively studied. Phosphites and phosphonates depending on their structure act as both primary and secondary antioxidants.^{1,2} Reactive oxygen species (ROS) produced by univalent reduction of dioxygen to superoxide anion which in turn disproportionate to H_2O_2 and O_2 spontaneously play a major role in the inflammatory process in rheumatoid arthritis (RA) and contribute to the destruction of cartilage and bone.^{3,4} The most important ROS implicated in inflammatory tissue injury are superoxide radical (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (HO^\cdot), and hypochlorous acid (HOCl). In the inflamed joint, these ROS are produced by macrophages, neutrophils, and chondrocytes.⁵ The inflamed rheumatoid joint also undergoes a hypoxia-reperfusion cycle, which results in ROS generation.⁶ The antioxidants may have a therapeutic role in rheumatoid arthritis by suppressing the inflammation.

The aim of this study was to investigate the *in vitro* antioxidant profile of different α -hydroxy phosphonates, which, the best of our knowledge has not yet been systematically studied. In recent times, α -hydroxyphosphonates are drawing increased attention due to their enzyme inhibitory bioactivity toward rennin,⁷ enolpyruvylshikimate-3-phosphate synthase,⁸ farnesyl protein transferase,⁹ human immunodeficiency virus protease and polymerase.¹⁰ They also have anti-virus¹¹ and anti-cancer activity.¹²

The available methods for the synthesis of α -hydroxyphosphonates involving the nucleophilic addition of di or trialkylphosphite to different carbonyl compounds in the presence of various catalysts, such as, enzymatics,¹³ alkaloids,¹⁴ phosphoric acids,¹⁵ Lewis acids,¹⁶ alumina,^{17a} SALALEN,^{17b} SALEN,^{18a} SALCYEN,^{18b} BINOL,¹⁹ alumina/potassium

fluoride,²⁰ NH_4VO_3 ²¹ and polymer/solid supported base²² were tried to improve the yields. But none of these is satisfactory. Hence, there is still a need to search for better catalysts with regards to their handling and economic viability.

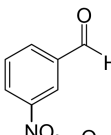
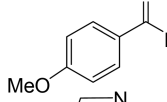
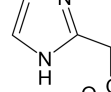
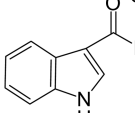
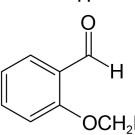
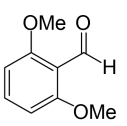
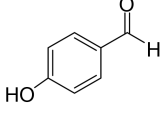
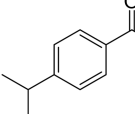
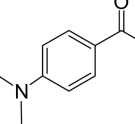
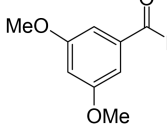
Recently the commonly available KHSO_4 is used as a catalyst instead of Lewis acids.²³ In continuation of our interest to develop efficient synthetic routes for biologically active organophosphorus compounds using green chemical techniques for organic synthesis,²⁴ we successfully used KHSO_4 as a catalyst instead of Lewis acids for the synthesis of α -hydroxyphosphonates under a neat condition. This catalyst is inexpensive, mild, and does not require the maintenance of anhydrous conditions. There have been no reports on the synthesis of α -hydroxyphosphonates using KHSO_4 as catalyst.

Experimental

General. NMR spectra were recorded on a Bruker instrument at 400 MHz for ^1H NMR, 100 MHz for ^{13}C NMR, and 161.3 MHz for ^{31}P NMR in CDCl_3 solution, using TMS as internal and 85% H_3PO_4 as external standard, respectively. Positive chemical shifts downfield from that of external 85% H_3PO_4 for ^{31}P NMR spectra. Chemical shifts (δ) are indicated in ppm and coupling constants (J) in Hz. Mass spectra were recorded on ESI-MS mass spectrometer and IR spectra were measured on Perkin-Elmer FT-IR 240-c spectrophotometer using KBr optics. Elemental analyses were performed on a Thermo Finnigan Instrument. mp were determined in open capillaries and are uncorrected. All reagents were purchased from Sigma Aldrich and were used without further purification.

General Procedure for the Synthesis of α -Hydroxyphosphonate Derivatives. A mixture of aldehyde (1 mmol), diethyl phosphite (1.5 mmol), and KHSO_4 (20 mol %) under a neat condition was stirred at rt. After completion of the reaction as indicated by TLC, the contents were poured into H_2O and extracted with EtOAc. The extract was dried with *anh.* Na_2SO_4 and evaporated under vacuum. The crude residue was chromatographed and the products are isolated.

Table 1. Synthesis of α -hydroxyphosphonate derivatives (**3a-j**)

Entry	Compounds	Substrate	Time (h)	Yield (%) ^a
1	3a		2	91
2	3b		3.5	82
3	3c		2.5	89
4	3d		2.5	85
5	3e		3	90
6	3f		4	82
7	3g		3	87
8	3h		2	90
9	3i		2.5	85
10	3j		4	84

Diethyl hydroxy (3-nitrophenyl)methylphosphonate

(3a): Semisolid. IR (KBr): 3265 (brs, OH), 1221 (P=O, Phosphonate), 1009 (P-O-C). ¹H-NMR (CDCl₃): 7.63-7.79 (m, 4Ar-H); 5.23 (d, ²J_{P-H} = 10.2 Hz, P-C-H); 3.93-4.08 (m, 4H, P(O)CH₂CH₃); 1.185 (t, ³J_{H-H} = 7.2 Hz, 6H, P(O)CH₂CH₃). ¹³C-NMR (CDCl₃): 147.47 (C-3); 141.13 (C-1); 133.86 (C-6); 129.37 (C-5); 122.36 (C-2); 121.72 (C-4); 69.05 (P-C); 52.59 (d, ²J_{P-C} = 7.6 Hz, P-OCH₂CH₃); 18.53 (d, ³J_{P-C} = 5.8 Hz, P-OCH₂-CH₃). ³¹P-NMR (CDCl₃): 21.61 (P=O). ESI-MS *m/z* 289 (100, M⁺). Anal. calcd. for C₁₁H₁₆NO₆P: C, 45.68; H, 5.58. found: C, 45.65; H, 5.54.

Diethyl hydroxy (4-methoxyphenyl)methylphosphonate
(3b): Solid. mp 121-123. IR (KBr): 3281 (brs, OH), 1225 (P=O, Phosphonate), 1052 (P-O-C). ¹H-NMR (CDCl₃):

7.05-7.13 (m, 4Ar-H); 4.52 (d, ²J_{P-H} = 10.2 Hz, P-C-H); 3.96-4.25 (m, 4H, P(O)CH₂CH₃); 3.48 (s, 3H); 1.189 (t, ³J_{H-H} = 7.0 Hz, 6H, P(O)CH₂CH₃). ¹³C-NMR (CDCl₃): 148.5 (C-4); 139.23 (C-1); 129.36 (C-2); 128.42 (C-6); 121.73 (C-3); 121.54 (C-5); 73.4 (P-C); 56.9 (d, ²J_{P-C} = 7.5 Hz, P-OCH₂CH₃); 55.9 (Ar-OCH₃); 17.8 (d, ³J_{P-C} = 5.8 Hz, P-OCH₂-CH₃). ³¹P-NMR (CDCl₃): 20.24 (P=O). ESI-MS *m/z* 274 (76, M⁺), 137 (100). Anal. calcd. for C₁₂H₁₉O₅P: C, 52.55; H, 6.98. found: C, 52.51; H, 6.95.

Diethyl hydroxy (1H-imidazol-2-yl)methylphosphonate
(3c): Semisolid. IR (KBr): 3323 (NH), 3245 (brs, OH), 1219 (P=O, Phosphonate), 1026 (P-O-C). ¹H-NMR (CDCl₃): 9.38 (s, 1H, imidazole NH); 7.32-7.39 (m, 2Ar-H); 5.12 (d, ²J_{P-H} = 10.3 Hz, P-C-H); 3.52-3.78 (m, 4H, P(O)CH₂CH₃); 1.23 (t, ³J_{H-H} = 7.3 Hz, 6H, P(O)CH₂CH₃). ¹³C-NMR (CDCl₃): 149.3 (C-1); 125.2 (C-3); 124.6 (C-4); 72.8 (P-C); 60.1 (d, ²J_{P-C} = 7.6 Hz, P-OCH₂CH₃); 15.6 (d, ³J_{P-C} = 5.7 Hz, P-OCH₂-CH₃). ³¹P-NMR (CDCl₃): 21.72 (P=O). ESI-MS *m/z* 235 (100, M⁺). Anal. calcd. for C₈H₁₆N₂O₄P: C, 40.85; H, 6.86. found: C, 40.82; H, 6.81.

Diethyl hydroxy (1H-indol-3-yl)methylphosphonate
(3d): Semisolid. IR (KBr): 3356 (NH), 3259 (brs, OH), 1119 (P=O, Phosphonate), 1005 (P-O-C). ¹H-NMR (CDCl₃): 9.94 (s, 1H, indole NH); 7.02-8.66 (m, 5Ar-H); 4.76 (d, ²J_{P-H} = 10.2 Hz, P-C-H); 3.61-3.77 (m, 4H, P(O)CH₂CH₃); 1.18 (t, ³J_{H-H} = 7.3 Hz, 6H, P(O)CH₂CH₃). ¹³C-NMR (CDCl₃): 138.36 (C-4); 135.52 (C-9); 121.06 (C-2); 120.64 (C-6); 119.04 (C-7); 117.35 (C-8); 116.38 (C-1); 115.15 (C-5); 76.26 (P-C); 59.96 (d, ²J_{P-C} = 7.6 Hz, P-OCH₂CH₃); 16.12 (d, ³J_{P-C} = 5.8 Hz, P-OCH₂-CH₃). ³¹P-NMR (CDCl₃): 20.69 (P=O). ESI-MS *m/z* 283 (M⁺), 146 (100). Anal. calcd. for C₁₃H₁₈NO₄P: C, 55.12; H, 6.41. found: C, 55.09; H, 6.38.

Diethyl [(2-benzyloxy)phenyl]Hydroxymethylphosphonate

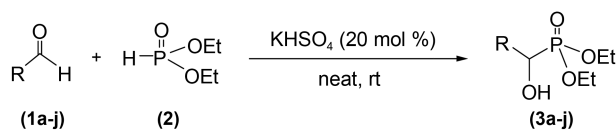
(3e): Semisolid. IR (KBr): 3257 (brs, OH), 1218 (P=O, Phosphonate), 1011 (P-O-C). ¹H-NMR (CDCl₃): 7.32-8.43 (m, 9Ar-H); 5.06 (s, 2H); 4.94 (d, ²J_{P-H} = 10.0 Hz, P-C-H); 3.92-4.09 (m, 4H, P(O)CH₂CH₃); 1.27 (t, ³J_{H-H} = 7.2 Hz, 6H, P(O)CH₂CH₃). ¹³C-NMR (CDCl₃): 158.8 (C-6); 136.9 (C-1'); 128.7 (C-2); 128.6 (C-4); 128.4 (C-3'&C-5'); 128.0 (C-1); 127.4 (C-4'); 126.9 (C-2'&C-6'); 125.3 (C-3); 124.1 (C-5); 78.6 (O-CH₂-Ph); 76.1 (P-C); 63.0 (d, ²J_{P-C} = 7.5 Hz, P-OCH₂CH₃); 16.3 (d, ³J_{P-C} = 5.7 Hz, P-OCH₂-CH₃). ³¹P-NMR (CDCl₃): 22.70 (P=O). ESI-MS *m/z* 350 (85, M⁺), 213 (100). Anal. calcd. for C₁₈H₂₃O₅P: C, 61.71; H, 6.62. found: C, 61.68; H, 6.58.

Diethyl (2,6-dimethoxyphenyl)Hydroxymethylphosphonate

(3f): Semisolid. IR (KBr): 3278 (brs, OH), 1208 (P=O, Phosphonate), 1028 (P-O-C). ¹H-NMR (CDCl₃): 6.81-7.02 (m, 3Ar-H); 4.72 (d, ²J_{P-H} = 10.2 Hz, P-C-H); 3.87-4.16 (m, 4H, P(O)CH₂CH₃); 3.78 (s, 3H); 3.62 (s, 3H); 1.33 (t, ³J_{H-H} = 7.0 Hz, 6H, P(O)CH₂CH₃). ³¹P-NMR (CDCl₃): 23.71 (P=O). ESI-MS *m/z* 304 (76, M⁺), 167 (100). Anal. calcd. for C₁₃H₂₁O₆P: C, 51.31; H, 6.96. found: C, 51.28; H, 6.92.

Diethyl (4-hydroxyphenyl)Hydroxymethylphosphonate

(3g): Solid. mp 110-112. IR (KBr): 3291 (brs, OH), 3249 (brs, OH), 1205 (P=O, Phosphonate), 1025 (P-O-C). ¹H-NMR (CDCl₃): 6.56-6.94 (m, 4Ar-H); 4.80 (d, ²J_{P-H} = 10.4



Scheme 1. Synthesis of α -hydroxyphosphonates (**3a-j**).

Hz, P-C-H); 3.65-3.84 (m, 4H, P(O)CH₂CH₃); 1.13 (t, ³J_{H-H} = 7.2 Hz, 6H, P(O)CH₂CH₃). ³¹P-NMR (CDCl₃): 22.63 (P=O). ESI-MS *m/z* 260 (100, M⁺). Anal. calcd. for C₁₁H₁₇O₅P: C, 50.77; H, 6.58. found: C, 50.72; H, 6.51.

Diethyl hydroxy (4-isopropylphenyl)methylphosphonate (3h): Semisolid. IR (KBr): 3273 (brs, OH), 1240 (P=O, Phosphonate), 1042 (P-O-C). ¹H NMR (CDCl₃): 7.19-7.38 (m, 4Ar-H); 4.94 (d, ²J_{P-H} = 10.4 Hz, 1H); 3.92-4.08 (m, 4H, P(O)CH₂CH₃); 2.85-2.92 (m, 1H); 1.17-1.26 (m, 6H); 1.165 (t, ³J_{H-H} = 7.2 Hz, 6H, P(O)CH₂CH₃). ³¹P NMR (CDCl₃): 22.83 (P=O). ESI-MS *m/z* 286 (100, M⁺). Anal. calcd. for C₁₄H₂₃O₄P: C, 58.73; H, 8.10. found: C, 58.69; H, 8.07.

Diethyl (4-(dimethylamino)phenyl)Hydroxymethylphosphonate (3i): Semisolid. IR (KBr): 3246 (brs, OH), 1237 (P=O, Phosphonate), 1061 (P-O-C). ¹H-NMR (CDCl₃): 6.87-7.01 (m, 4Ar-H); 5.18 (d, ²J_{P-H} = 10.3 Hz, P-C-H); 4.02-4.29 (m, 4H, P(O)CH₂CH₃); 1.19 (t, ³J = 7.3 Hz, 6H, P(O)CH₂CH₃); 2.82 (s, 6H). ³¹P-NMR (CDCl₃): 21.40 (P=O). ESI-MS *m/z* 287 (89, M⁺), 150 (100). Anal. calcd. for C₁₃H₂₂NO₄P: C, 54.35; H, 7.72. found: C, 54.31; H, 7.69.

Diethyl (3,5-dimethoxyphenyl)Hydroxymethylphosphonate (3j): Solid. mp 101-103. IR (KBr): 3272 (brs, OH), 1212 (P=O, Phosphonate), 1032 (P-O-C). ¹H-NMR (CDCl₃): 6.78-7.07 (m, 4Ar-H); 4.87 (d, ²J_{P-H} = 10.2 Hz, P-C-H); 3.90-4.19 (m, 4H, P(O)CH₂CH₃); 3.86 (s, 3H); 3.57 (s, 3H); 1.28 (t, ³J = 7.2 Hz, 6H, P(O)CH₂CH₃). ³¹P-NMR (CDCl₃): 22.20 (P=O). ESI-MS: 304 (100, M⁺). Anal. calcd. for C₁₃H₂₁O₆P: C 51.31, H 6.96; found: C 51.29, H 6.92.

Results and Discussions

In an initial study to optimize the experimental conditions, we carried out the reaction of 3-nitrobenzaldehyde (**1**), and diethyl phosphite (**2**) in the presence of KHSO₄ with various catalytic amounts (Table 2, 10-40 mol %) in various solvents (Table 3) at ambient temperatures. Excellent results were obtained, when the reaction was performed with 20 mol % of KHSO₄ under a neat condition. It was found that the amount of KHSO₄ affects the yield of the product. The

Table 2. Influence of the catalyst on the synthesis of α -hydroxyphosphonate^a

Entry	Catalyst (mol %)	Time (h)	Yield ^b (%)
1	KHSO ₄ (10)	3.5	85
2	KHSO ₄ (20)	2	91
3	KHSO ₄ (30)	2.5	80
4	KHSO ₄ (40)	2.5	80

^aReaction of 3-nitrobenzaldehyde (1 mmol), diethyl phosphite (1.5 mmol) under neat condition at rt. ^bIsolated yield.

Table 3. Influence of the solvent on the synthesis of α -hydroxyphosphonate^a

Entry	Solvent	Time (h)	Yield ^b (%)
1	Ethanol	7	40
2	dioxane	6	65
3	THF	6	84
4	Acetonitrile	6	50
5	Dichloromethane	6	60
6	Toluene	6	80
7	neat	2	91

^aReaction of 3-nitrobenzaldehyde (1 mmol), diethyl phosphite (1.5 mmol) using 20 mol % KHSO₄ at rt. ^bIsolated yield.

reaction was carried out with a wide variety of aromatic and heterocyclic aldehydes bearing various substituents under optimized conditions. The prepared α -hydroxyphosphonates (**3a-j**) were thoroughly characterized with spectral and elemental analysis.

IR absorptions for hydroxyl group for **3a-j** appeared as broad signal in the region 3245-3281 cm⁻¹ and for P=O group absorption appeared in the region 1205-1240 cm⁻¹.²⁵ The PCH group exhibited doublet at δ 4.52-5.23 due to its coupling with phosphorus.²⁵ The carbon chemical shifts in the title compounds were observed in their expected regions.²⁶ Their ³¹P NMR chemical shifts were observed at δ 20.24-22.71. ESI-MS spectra gave molecular ions and diagnostic daughter ion peaks at their respective expected *m/z* values.

Antioxidant Activity. As predicted, the α -hydroxy phosphonates **3a-j** have the ability to scavenge the DPPH radical by donating one electron. Since phosphorus has affinity towards oxygen, it can easily bind and scavenge ROS effectively. The compounds **3a-j**, containing phosphorus and oxygen atoms are more active due to the presence of non-bonded electron pairs containing hetero atoms that serve as binding sites in the bio-matrix. **3a**, **3c** and **3d** displayed appreciable antioxidant activity. **3a** showed the highest activity because of -NO₂ substituent which affects the electron and hydrogen donating capacities. Since -NO₂ group is highly electron withdrawing moiety, the electron density around P=O moiety decreases and increases affinity towards oxygen derived free radicals and mobilizes ROS to be scavenged out of the living system.

DPPH Radical Scavenging Activity. The free radical scavenging activity of α -hydroxyphosphonates against DPPH radical was performed in accordance with Choi *et al.*²⁷ 85 μ M of DPPH was added to a medium containing different α -hydroxyphosphonates. The medium was incubated for 30 min at room temperature. The decrease in absorbance was measured at 518 nm. Ascorbic acid was used as standard reference to record maximal decrease in DPPH radical absorbance. The values are expressed in percentage of inhibition of DPPH radical absorbance with those of the standard control values without the title compounds (Figure 1) (ascorbic acid maximal inhibition was considered 100% of inhibition).

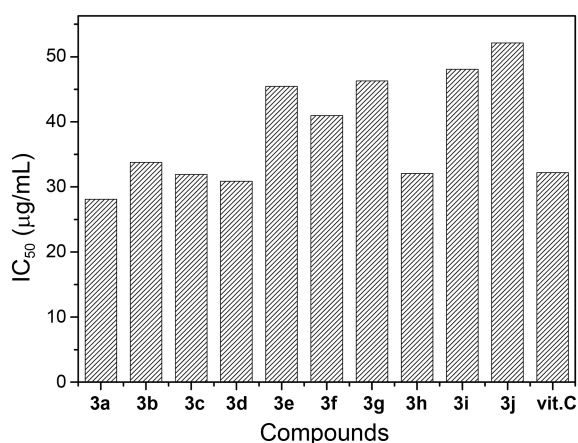


Figure 1. DPPH Radical Scavenging Activity.

$$\text{DPPH Scavenged (\%)} = \frac{(A_{cont} - A_{test})}{A_{cont}} \times 100$$

Where A_{cont} is the absorbance of the control reaction and A_{test} is the absorbance in the presence of the sample.

In the case of α -hydroxyphosphonates **3a-j**, nitro substituted compound **3a** showed the highest DPPH radical scavenging activity with IC₅₀ at 28.08 $\mu\text{g/mL}$ when compared with others. The remaining compounds exhibited DPPH radical scavenging activity in the following order: **3d** (IC₅₀ 30.86 $\mu\text{g/mL}$), **3c** (IC₅₀ 31.91 $\mu\text{g/mL}$), **3h** (IC₅₀ 32.05 $\mu\text{g/mL}$), **3b** (IC₅₀ 33.78 $\mu\text{g/mL}$), **3f** (IC₅₀ 40.98 $\mu\text{g/mL}$), **3e** (IC₅₀ 45.45 $\mu\text{g/mL}$), **3g** (IC₅₀ 46.29 $\mu\text{g/mL}$), **3i** (IC₅₀ 48.06 $\mu\text{g/mL}$), **3j** (IC₅₀ 52.12 $\mu\text{g/mL}$) and when compared with ascorbic acid (IC₅₀ 32.2 $\mu\text{g/mL}$).

Reducing Power Assay. The reducing power of **3a-j** was determined according to the method of Oyaizu *et al.*²⁸ The compounds having 50-100 μM were mixed with 2.5 mL of phosphate buffer (0.2 M, pH 6.6) and 2.5 mL of 1% potassium ferricyanide and incubated at 50 °C for 20 min. To this mixture 2.5 mL of 10% trichloroacetic acid (TCA) was added and the mixture was centrifuged at 3000 rpm for 20 min. The upper layer (2.5 mL) was mixed with 2.5 mL of deionised water and 0.5 mL of 0.1% Ferric chloride and the UV absorbance was measured at 700 nm using a spectro-

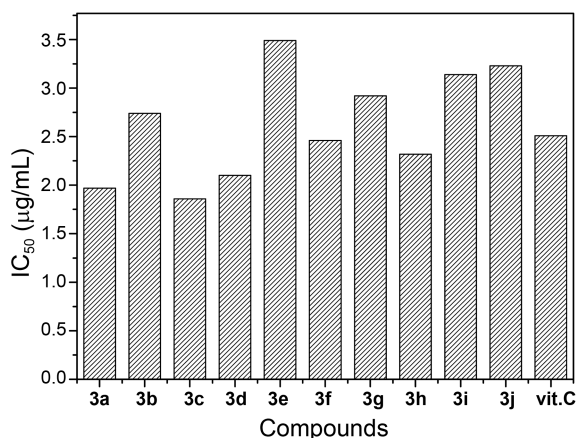


Figure 2. Reducing power assay.

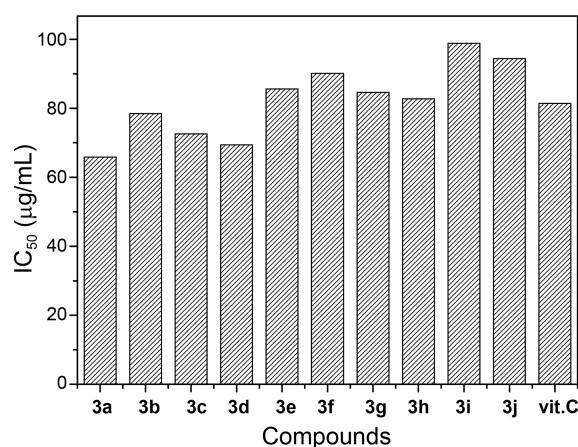


Figure 3. Lipid Peroxidation Assay.

photometer. Increase of absorbance of the reaction mixture indicate higher reducing power. Mean values from three independent samples were calculated for each compound and standard deviations were less than 5%.

In the case of α -hydroxyphosphonates **3a-j** (Figure 2), derivatives **3c** showed the highest reducing power with IC₅₀ of 1.86 $\mu\text{g/mL}$ when compared with other compounds. The remaining compounds exhibited reducing power activity in the following order: **3a** (IC₅₀ 1.97 $\mu\text{g/mL}$), **3d** (IC₅₀ 2.10 $\mu\text{g/mL}$), **3h** (IC₅₀ 2.32 $\mu\text{g/mL}$), **3f** (IC₅₀ 2.46 $\mu\text{g/mL}$), **3b** (IC₅₀ 2.74 $\mu\text{g/mL}$), **3g** (IC₅₀ 2.92 $\mu\text{g/mL}$), **3i** (IC₅₀ 3.14 $\mu\text{g/mL}$), **3j** (IC₅₀ 3.23 $\mu\text{g/mL}$), **3e** (IC₅₀ 3.49 $\mu\text{g/mL}$) and when compared with ascorbic acid (IC₅₀ 2.51 $\mu\text{g/mL}$).

Lipid Peroxidation Assay. Lipid peroxidation was induced by Fe^{2+} ascorbate complex system in rat liver cells and was estimated as thiobarbituric acid reacting substances (TBARS) by the method of Ohkawa *et al.*²⁹ Experiments *in vitro* lipid peroxidation were carried out to clarify the mode of the protective effect of the α -hydroxyphosphonates against oxidative stress-induced cell damage. The inhibition of lipid peroxidation has been used as a model to elucidate antioxidant activity.

According to the results obtained (Figure 3), **3a** (IC₅₀ 65.82 $\mu\text{g/mL}$) significantly inhibited the ferric ion plus ascorbic acid in rat liver cells. The remaining compounds exhibited hydroxyl radical scavenging activity in the following order: **3d** (IC₅₀ 69.41 $\mu\text{g/mL}$), **3c** (IC₅₀ 72.57 $\mu\text{g/mL}$), **3b** (IC₅₀ 78.49 $\mu\text{g/mL}$), **3h** (IC₅₀ 82.74 $\mu\text{g/mL}$), **3g** (IC₅₀ 84.62 $\mu\text{g/mL}$), **3e** (IC₅₀ 85.59 $\mu\text{g/mL}$), **3f** (IC₅₀ 90.12 $\mu\text{g/mL}$), **3j** (IC₅₀ 94.36 $\mu\text{g/mL}$), **3i** (IC₅₀ 98.79 $\mu\text{g/mL}$) and when compared with ascorbic acid (IC₅₀ 81.4 $\mu\text{g/mL}$).

Conclusion

In conclusion, KHSO_4 was found to be an efficient catalyst for the one-pot reaction of aldehyde and diethyl phosphite to afford the corresponding α -hydroxyphosphonates in moderate to good yields. The main advantages of the present synthetic protocol are mild, solvent-free, eco-friendly catalyst and easy reaction work-up procedure. It is

expected that the present methodology will find application in organic synthesis.

All the title compounds were screened for antioxidant properties by radical scavenging methods such as 1,1-diphenyl-2-picryl hydrazyl (DPPH), Reducing power and lipid peroxidation. They exhibited potent *in vitro* antioxidant activity dose dependently.

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