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Ultrasound-promoted synthesis of α-hydroxyphosphonates catalyzed by 1-hexanesulphonic acid sodium salts in aqueous medium

KEYWORDS: α-Hydroxyphosphonates; 1-hexanesulphonic acid sodium salt; aqueous medium; ultrasonication; diethylphosphite

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ABSTRACT *Herein, α-hydroxyphosphonates were synthesized via ultrasound-assisted process. The influence of ultrasonic irradiation on the yield, time and catalyst concentrations were investigated and compared with the conventional method. The results showed that sonochemistry-assisted method significantly increased the synthetic efficiency. This method is an effective approach to synthesize α-hydroxyphosphonates via reaction of aldehydes and diethylphosphite by using 1-hexanesulphonic acid sodium salts in an aqueous medium.*

1. Introduction

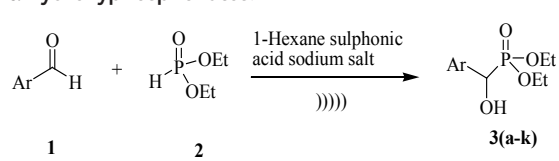
Phosphonates functionalized with hydroxy and amino groups have attracted considerable attention for their role in biologically relevant processes, and wide range of applications.[2] α-Hydroxyphosphonates act as an inhibitor of a diverse group of enzymes including Renin,[3a] FPTase,[3b] HIV protease [3c] and EPSP synthase.[3d] The cyclic and acyclic phosphate esters are normally considered as important pharmacological compounds.[4-8] In recent the synthesis of-hydroxy phosphonates, which are acyclic phosphorus esters, have received an increasing amount of attention due to significant biological interests.[9-12] Because of their potential bioactivity against wide spectrum of disease manifestations several methods are reported for their synthesis.A number of synthetic methods for the preparation of α-hydroxyhosphonates have been carried out in various catalysts, such as, Lewis acids,[13] alumina,[14] alumina/potassium fluoride,[15] NH_4VO_3,[16] and polymer/solid supported base,[17] enzymatics,[18] alkaloids,[19] phosphoric acids,[20] SALEN,[21] BINOL,[22] were tried for this reaction to improve the yields. But most of these procedures are not satisfactory from the points of view of simplicity, efficiency, cost and eco-friendliness. All these disadvantages had diminished by adopting the green chemical synthetic procedures[23-25] involving potassium carbonate,[26] sodium carbonate,[27] triethylamine[28] as catalysts under conventional and solvent free conditions, potassium dihydrogenphosphate[29] catalyst under ultrasound-assisted solvent-free conditions and iodine as catalyst in water as solvent[30] were reported for the synthesis of α-hydroxyphosphonates. Ultrasonication has increasingly been used in organic synthesis in the last three decades. It has been demonstrated as an alternative energy source for organic reactions ordinarily accomplished by heating. A great number of organic reactions can be carried out in short reaction time, high yields and mild reaction condition under ultrasonication.[31] The use of ultrasound irradiation technique for activating various reactions is well documented in the literature such as Reformatsky reaction,[32] Pinacol-pinacolone reaction,[33] Ullmann condensation[34] and Suzuki cross-coupling.[35] In recent years, the development of new methodologies to produce products of greater structural complexity from readily available simple starting materials with fewer synthetic steps but ensuring high yield under mild reaction conditions is the main challenge for the synthetic organic chemists.[36] Again, because of global environmental legislation on chemical process industries, aqueous environment has been currently receiving considerable attention in organic chemistry[37] because water is abundant in nature, has virtually no cost, and is safest among all available solvents, thus leading to environmentally benign chemical processes.[38]

A search of the literature revealed that the 1-hexanesulphonic acid sodium salt[39] liberates corresponding acid with extreme wide applications such as sulphonation of alkanes,[40] synthesis of α-aminophosphonates,[41] various organic transformation[42] etc. However, there are very few reports using 1-hexanesulphonic acid sodium salt as a catalyst therefore, for the first time we herein report the use of 1-hexanesulphonic acid sodium salt for the synthesis of α-hydroxyphosphonates under ultrasound-irradiation in aqueous medium.

2. Experimental

Melting points were determined in open capillaries in a paraffin bath and are uncorrected. IR spectra were recorded on a Bruker spectrophotometer using KBr discs, and the absorption bands are expressed in cm^{-1}. 1H-NMR spectra were recorded on a Varian AS 400 MHz spectrometer in $CDCl_3$, chemical shifts (δ) are in ppm relative to TMS. Mass spectra were taken on a Macro mass spectrometer (Waters) by electro-spray method (ES). Bandelin Sonorex (with a frequency of 35 KHz and a nominal power 200 W) ultrasonic bath was used for ultrasonic irradiation. Built-in heating, 30-80°C thermostatically adjustable. The reaction vessel placed inside the ultrasonic bath containing water.

1.1 General procedure for the synthesis of α-hydroxyphosphonates:-



1 2 3(a-k)

A mixture of substituted aldehydes/ketone (1 mmol) and diiethyl phosphite (1.2 mmol) were placed in a round bottom flask. Further 1-hexanesulphonic acid (10 mol%) & water (1 ml) was added, this mixture was irradiated under ultrasonic irradiation at ambient temperature for the précised time After the completion of reaction as monitored by TLC; 20 mL ice cold water was added to the reaction mixture and product was extracted by chloroform (2 × 25 mL). The organic layer washed by brine (2 × 20 mL) and dried over anhydrous sodium sulphate. The solvent was distilled out on Rota-evaporator under reduced pressure to afford the pure products. The products 3(a-k) were confirmed by their spectral data after comparisons with authentic samples,[30] IR, ^{1}H NMR, mass spectra and melting point.

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2.2 Spectral data of representative compounds.
Diethyl (hydroxyl)(phenyl)methylphosphonate **(3a)**: Solid, Yield: 96 %, mp 74-75 °C.^{1}H NMR ($CDCl_3$, 400 MHz δ): _7.21-7.22 (m, 5H), 5.21 (s, 2H), 4.44 (d, 2H), 3.90-4.00(m, 4H), 1.26-1.17 (m, 6H); IR (KBr): 3270 (brs, OH), 1235 (P=O), 1035 (P-O-C) cm^{-1}; ESI-MS: *m/z* 244 (M+H)+;Anal. calcd. for $C1_1H_{17}O_4P$: C, 55.10; H, 7.04; Found: C, 54.01; H, 6.96.

3. Results and discussion
In continuation of our research devoted to phosphorus chemistry[41] and interest in the development of novel synthetic methodologies,[43] Here we have carried out the reaction of benzaldehyde (1a) and diethylphosphite (2) catalyzed by 1-hexanesulphonic acid sodium salt under ultrasonic irradiation, it has been considered as a standard model reaction. We also have studied the catalyst concentration on model reaction. We have varied the concentration of catalyst to 2, 4, 6, 8, 10 and 12 mol %. The result revealed that, when the reaction was carried out in the presence of 2, 4, 6 mol% of catalyst it gave lower yield of product even after prolonged reaction time. At the same time when the concentration of catalyst was 10 and 12 mol% we got the excellent yields of product in short span. Even after increasing the catalyst concentration the yields of the products were found to be constant. So, the use of 10 mol% of catalyst is sufficient to push the reaction forward. The obtained results summarized in (Table 1).

Table 1
Effect of catalyst concentration on model reaction[a]

Entry	Catalyst(mol%)	Yield[b](%)
1	2	43
2	4	55
3	6	62
4	8	79
5	10	96
6	12	96

[a]Reaction of benzaldehyde and diethyphosphite in presence of 1-hexanesulphonic acid sodium salt under ultra sonic waves for 5 min. [b]Isolated yield.

Further, we have also studied the effect of solvents on model reaction. Here, we have kept the concentration of catalyst constant on model reaction and varied the solvents condition like solvent-free, methanol, dichloromethane, toluene, ethanol and water. The observation revealed that in methanol, dichloromethane, toluene solvents the yields of the products were found to be low. At the same time we have carried out the same reaction under solvent-free condition but in such case we got moderate yield. We also tried same reaction in the presence of water then we got the excellent yield of product as compare to other solvents. The obtained results summarized in (Table 2).

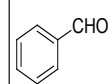
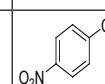
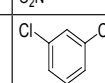
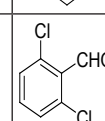
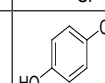
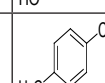
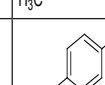
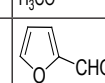
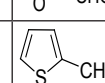
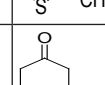
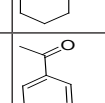
Table 2.
Optimization of solvent effect on the model reaction

Entry	Solvents	Time (min)	Yield[b] (%)
1	Solvent-free	5	60
2	Methanol	5	50
3	Dichloromethane	5	35
4	Toluene	5	54
5	Ethanol	5	75
6	Water	5	96

[a]Reaction of benzaldehyde and diethylphosphite catalyzed by 1-hexenesulphonic acid sodium salt (10 mol %) under ultrasonic waves for 5 min. [b]Isolated yield.

We have also discussed the effect of ultrasonic irradiation. When the model reaction was carried out under conventional method it gave comparatively low yields of products, while at the same time the model reaction carried in the influence of ultrasonic irradiation it gives excellent yields of product in short reaction time (Table 3). After optimizing the conditions, the generality of this method was examined by the reaction of several substituted aryl/heteroaryl aldehydes/ketone and diethylphosphite using 1-hexanesulphonic acid as a catalyst under ultrasound irradiation in aqueous medium, the results are shown in Table 3. Here, we have found that the use of electron donating group on aldehyde results into excellent yield, while at the same time the electron withdrawing group affords corresponding lower yield of product. Further study of ketone revealed that it gives very low yields of products even after prolonged reaction time. All the synthesized compounds were characterized by spectral data and compared (MS, NMR and IR) with authentic sample. This comparison revealed that the compounds synthesized by this newly developed method were exactly similar in all aspects

Table 3.
Sonochemical effect on the synthesis of α hydroxyphosphonates.

Entry	Product	Aldehyde/ Ketone	With US[a]		Without US[b]	
			Time (min)	Yield[c,d] (%)	Time (min)	Yield[c,d] (%)
1	3a		5	96	60	75
2	3b		10	90	60	70
3	3c		10	86	60	72
4	3d		12	84	60	69
5	3e		12	80	60	65
6	3f		07	94	60	70
7	3g		05	95	60	71
8	3h		25	79	60	42
9	3i		30	83	60	39
10	3j		80	50	60	34
11	3k		120	38	60	30

[a]Reaction of aldehyde/ketone and diethylphosphite in presence of 1-hexanesulphonic acid sodium salt (10 mol%) in aqueous medium under ultrasonic waves. [b]Reaction of aldehyde/ketone, diethylphosphite in presence of 1-hexanesulphonic acid sodium salt (10 mol%) in aqueous medium under stirring at ambient temperature. [c]Isolated yield. [d]Compounds were characterized by ^{1}H NMR, MS spectral data and were

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compared with the reference compounds.

4. Conclusion

In conclusion, 1-hexanesulphonic acid sodium salt was found to be an efficient catalyst for the reaction of aldehydes and diethylphosphite to afford α-hydroxyphosphonates. The main advantages of this method are mild, clean, environmentally benign and good to excellent yields. The developed methodology is simple and will gives good contribution in the field of phosphorous chemistry.

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REFERENCE

1. Kukhar V P and Hudson H. R. Chemistry and Biological Activity Eds John Wiley New York 2000. | 2. Engel R. In Handbook of Organophsosphorus Chemistry, Marcel Dekker New York 1992. | 3. (a) Patel D V, Rielly-Gauvin K and Ryono D E 1990, Tetrahedron Lett. 31 5587; (b) Pompliano D L, Rands E, Schaber M D, Mosser S D, Anthony N J and Gibbs J B 1992 Biochem. 31 3800; (c) Stowasser B, Budt K H, Li J Q, Peyman A and Ruppert D 1992 Tetrahedron Lett. 33 6625; (d) Sikorski J A, Miller M J, Braccolino D S, Cleary D G, Corey S D, Font J L, Gruys K J, Han C Y, Lin K C, Pansegrau P D, Ream J E, Schnur D, Shah A and Walker M C 1993 Phosphorus, Sulfur, Silicon Relat. Elem. 76 115. | 4. Krishna B S, Rao A J, Naidu K R M, Rao V K and Raju C N 2010 Org.Commun. 3 98. | 5. Mohan C, Rao A J, Raju C N and Nagalakshmi R U 2009 Org. Commun. 2 120. | 6. Reddy K R, Reddy C B, Kumar K S, Raju C N and Reddy C S 2009 Org. Commun. 2 28. | 7. Reddy M V N, Annar S, Krishna A B, Reddy G C S and Reddy C S 2010 Org. Commun. 3 39. | 8. Babu Y H, Sankar A U R, Kumar B S and Reddy C S 2010 Org. Commun. 3 15. | 9. Kim D Y and Wiemer D F 2003 Tetrahedron Lett. 44 2003. | 10. Neyts J, De Clercq E 1997 Antimicrob. Agents Chemother. 41 2754. | 11. Lee M V, Fong E M, Singere F R, Guenette R S 2001 Cancer Res. 61 2602. | 12. Patel D V, Rielly-Gauvin K, Ryono D E, Free C A, Rogers W L, Smith S A, DeForrest J M, Oehl R S, Petrillo J E W 1995 J. Med. Chem. 38 4557. | 13. Groaning M D, Rowe B J, Spilling C D 1998 Tetrahedron Lett. 39 5485. | 14. Zhou X, Liu X, Yang X, Shang D, Xin J and Feng X 2007 Angew. Chem. Int. Ed. 120 398. | 15. Texier-Boullet F and Lequitte M 1986 Tetrahedron Lett. 27 3515. | 16. Sonar S S, Kategaonkar A H, Ware M N, Gill C H, Shingate B B and Shingare M S 2009 Arkivoc II 138. | 17. Simoni D, Rondanin R, Morini M, Baruchello R and Invidiata F P 2000 Tetrahedron Lett. 41 1607. | 18. Kafarski P and Lecjzak B 2004 J. Mol. Catal. B. 29 99. | 19. Wynberg H and Smaardijk A A 1983 Tetrahedron Lett. 24 5899. | 20. Akiyamam T, Morita H, Itoh J and Fuchibe K 2005 Org. Lett. 7 2583. | 21. Duxbury J P, Cawley A, Pett-Thornton M, Wantz L, Warne J N D, Greatrex R, Brown D and Kee T P 1999 Tetrahedron Lett. 40 4403. | 22. Arai T, Bougauchi M, Sasai H and Shibaski M, 1996 J. Org. Chem. 61 2926. | 23. Shinde P V, Kategaonkar A H, Shingate B B and Shingare, M. S. 2011 Tetrahedron Lett. 52 2889. | 24. Shen L, Liu R, Liao X and Ye Y Green 2010 Huaxue Yanjiu. 21 40. | 25. Sadaphal S A, Sonar S S, Pokalwar R, Shitole N V and Shingare M S 2009 J. Korean Chem. Soc. 53 536. | 26. Shen L, Liu R, Liao X and Ye Y 2010 Huaxue Yanjiu Yu Yingyong. 21 40. | 27. Keglevich G, Toth V R and Drahos L 2011 Heteroatom Chem. 22 15. | 28. Sun J Y, Wang J X, Pei Q, Jin C X and Zhang X N 2009 Xinyang Shifan Xueyuan Xuebao. 22 588. | 29. Mandhane P G, Joshi R S, Nagargoje D and Gill C H 2010 Tetrahedron Lett. 51 1490. | 30. Wang H S and Zeng J E 2010 Phosphorus, Sulfur Silicon Relat. Elem. 185 1425. | 31. (a) Song B A, Zhang G P, Yang S, Hu D Y and Jin L H 2001 Ultra. Chem. 13 1544; (b) Gaplovsky A, Goplosky M, Toma S and Luche J L 2000 J. Org. Chem. 65 8444. | 32. Singh V, Sapehiyia V and Kad G L 2003 Synthesis 198. | 33. Li J T, Bian Y J, Zang H J and Li T S 2002 Synth. Commun. 32 547. | 34. Robin M, Pique V, Faure R and Glay J P 2002 J. Hetero. Chem. 39 1083. | 35. Rajagopal R, Jarikote D V and Srinivasan K V 2002 Chem. Commun. 616. | 36. (a) Parenty A D C, Smith L V, Pickering A L, Long D L and Cronin L 2004 J. Org. Chem. 69 5934; (b) Tietze L F 1996 Chem. Rev. 96 115. | 37. (a) Bai L, Wang J X and Zhang Y 2003 Green Chem. 5 615; (b) Pironti V and Colonna S 2005 Green Chem. 7 43; (c) Nu chter M, Ondruschka B, Bonrath W and Gum A 2004 Green Chem. 6 128. | 38. Herrerias C I, Xiaoquan Y, Li Z and Li C 2007 J. Chem. Rev. 107 2546. | 39. (a) Weiss J, Verlags V C H, gesellschaft mbH, IInd ed., VCH Publisher, Inc. New York, Weinheim, Germany 1995; (b) Small H Ion Chromatography, Plenum Press, New York and London 1989. | 40. Boyer J L, Gilot B and Canselierm J P 1984 Phosphorus, Sulphur and Silicon Relat. Elem. 20 259. | 41. Niralwad K S, Shingate B B and Shingare M S 2010 Ultrasonics Sonochem. 17 760. | 42. (a) Joshi R S, Mandhane P G, Diwakar S D and Gill C H 2010 Ultrason. Sonochem. 17 298; (b) Jadhav G R, Shaikh M U, Kale R P and Gill C H 2009 Chin. Chem. Lett. 20 292. | 43. (a) Niralwad K S, Shingate B B and Shingare M S 2010 Tetrahedron Lett. 51 3616; (b) Niralwad K S Shingate B B and Shingare M S 2010 J. Chin. Chem. Soc. 57 89; (c) Niralwad K S, Shingate B B and Shingare M S 2011 Chin. Chem. Lett. 22 551; (d) Niralwad K S, Shingate B B and Shingare M S 2011 J. Heterocyclic Chem. 48 742; (e) Niralwad K S, Shingate B B and Shingare M S 2010 Bull. Korean Chem. Soc. 31 981.