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Amberlyst-15 catalyzed synthesis of alkyl/aryl/heterocyclic phosphonates

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Abstract

A novel and efficient procedure for the synthesis of alkyl phosphonates through one pot condensation of alkyl halide and tri alkyl/aryl phosphite in the presence of amberlyst-15 as catalyst under solvent free conditions was applied. It demonstrated several advantages such as good yields of products, simple operation, convenient separation and inexpensive catalyst.

Keywords: Dialkyl/aryl alkyl phosphonates; Amberlyst-15

Alkyl phosphonates are one of the several pentavalent phosphorus compounds of considerable synthetic interest due to their utility as reagents in the Wadsworth–Emmons reaction [1] and their applications in bioorganic [2], pharmacoligical fields [3]. Although several synthetic methods exist for the preparation of phosphonates, Michaelis Arbuzov reaction [4] is largely used.

The Arbujov reaction has long been known and many catalysts such as iodine [5], ionic liquid [6], $BF_3{\cdot}OEt_2$ [7] catalysts and a few intramolecular rearrangements [8] have been described. However, these methods have some disadvantages such as long reaction times, high temperatures and pressures, low yields of desired products. Hence, there is a need to develop a convenient, environmentally benign and economically feasible method for the synthesis of alkyl phosphonates.

In the recent years, the use of solid acidic catalyst has attracted considerable attention [9]. In this regard, amberlyst-15 possesses unique properties to be used as a catalyst for the preparation of alkyl phosphonates from the trialkyl phosphite and alkyl halide. Amberlyst-15 is a strongly acidic, sulfonic acid, macroreticular polymeric resin based on crosslinked styrene divinylbenzene copolymers. Its continuous open pore structure and excellent physical, thermal and chemical stability makes it the resin of choice in many applications. It also possesses a greater resistance to oxidants such as chlorine, oxygen and chromates than most other polymeric resins. Its physical and chemical stability, non corrosive and non toxic nature, selectivity in reactions, reusability and environmental compatibility make this as a

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versatile catalyst for performing the various functional group transformations and in the general organic synthesis [10].

We now report a relatively simple synthesis of alkyl phosphonates in good yields using amberlyst-15 as an efficient and environmentally benign catalyst under solvent-free conditions.

1. Experimental

A mixture of propyl bromide **1a** (0.365 mL, 0.004 mol) and triethyl phosphite **2** (0.68 mL, 0.004 mol) and catalytic amount (0.1 g) of amberlyst-15 was taken in 25 mL round bottomed flask and stirred at room temperature for about one hour. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with acetone to separate the catalyst and reused for another reaction after 3 to 4 washings with acetone. The solvent was separated from the filtrate by rotaevaporator. The resulting product was purified by column chromatography on silica gel (100–200 mesh) using petroleum ether and ethyl acetate in 7:3 ratio as eluent to afford pure alkyl phosphonate **3a**. The other compounds **3b–j** were prepared by this procedure (Scheme 1).

Diethyl propyl phosphonate (**3a**): Semi solid, IR (KBr) cm^{-1}: 1243 (P=O, phosphonate), 735 (P–C aliphatic); ^1H NMR ($CDCl_3$): δ 3.29–3.41 (m, 4H, 2 × O–C$\underline{H}_2$), 1.69–1.78 (m, 2H, P–CH_2), 1.52–1.58 (m, 2H), 1.35 (t, 6H, J = 6.9 Hz, 2 × O–$CH_2C\underline{H}_3$), 1.05 (t, 3H, J = 7.7 Hz); ^{13}C NMR ($CDCl_3$): δ 65.2 (O$\underline{C}H_2CH_3$), 46.4 (P–$\underline{C}H_2$–), 23.8 (–$\underline{C}H_2$–), 19.6 ($OCH_2\underline{C}H_3$), 13.8(–$\underline{C}H_3$); ^{31}P NMR (DMSO-d_6): δ 1.54 (P=O); LC–MS m/z: 180($M^{\bullet+}$, 100%); anal. calcd. for $C_7H_{17}O_3P$:C, 46.66; H, 9.51; found C, 46.56; H, 9.49.

Dipheyl propyl phosphonate (**3b**): Semi solid, IR (KBr) cm^{-1}: 1240 (P=O, phosphonate), 755 (P–C aliphatic); ^1H NMR ($CDCl_3$): δ 6.77–7.35 (m, 10H, Ar–H), 1.76–1.83 (m, 2H, P–CH_2), 1.67–1.69 (m, 2H), 1.01 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 149.22 (C-1 and 1′), 120.36 (C-2 and 2′), 129.17 (C-3 and 3′), 119.6 (C-4 and 4′), 129.87 (C-5 and 5′), 125.62 (C-6 and 6′), 34.2 (P–$\underline{C}H_2$–), 25.81(–$\underline{C}H_2$), 11.94 (–$\underline{C}H_3$); ^{31}P NMR (DMSO-d_6): δ 1.98 (P=O); anal. calcd. for $C_{15}H_{17}O_3P$:C, 65.21; H, 6.20; found C, 65.14; H, 6.12.

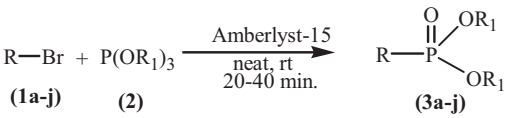
Diethyl sec. butyl phosphonate (**3c**): Semi solid, IR (KBr) cm^{-1}: 1232 (P=O, phosphonate), 729 (P–C aliphatic); ^1H NMR ($CDCl_3$): δ 4.06–4.19 (m, 4H, 2 × O–C$\underline{H}_2$), 1.79–1.88 (m, 1H, P–CH), 1.68 (d, 3H, J = 4.0 Hz), 1.33–1.41 (m, 2H), 1.33 (t, 6H, J = 6.8 Hz, 2 × O–$CH_2C\underline{H}_3$), 1.04 (t, 3H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$): δ 61.8 (O$\underline{C}H_2CH_3$), 44.0 (P–$\underline{C}H_2$–), 25.8 (–$\underline{C}H_2$–), 17.8 (–$\underline{C}H_2$–), 19.1 ($OCH_2\underline{C}H_3$), 11.9(–$\underline{C}H_3$); ^{31}P NMR (DMSO-d_6): δ 1.64 (P=O); LC–MS m/z: 194($M^{\bullet+}$, 100%); anal. calcd. for $C_8H_{19}O_3P$:C, 49.48; H, 9.86; found C, 49.42; H, 9.81.

Dipheyl sec. butyl phosphonate (**3d**): Semi solid, IR (KBr) cm^{-1}: 1244 (P=O, phosphonate), 757 (P–C aliphatic); ^1H NMR ($CDCl_3$): δ 6.79–7.36 (m, 10H, Ar–H), 1.81–1.90 (m, 2H, P–CH_2), 1.54–1.62 (m, 2H), 1.41–1.50 (m, 2H), 1.19 (t, 3H, J = 7.5 Hz); ^{31}P NMR (DMSO-d_6): δ 2.04 (P=O); LC–MS m/z: 290 ($M^{\bullet+}$, 100%); anal. calcd. for $C_{16}H_{19}O_3P$:C, 66.20; H, 6.60; found C, 65.97; H, 6.56.

2. Results and discussion

The conventional method of this two component one pot reaction requires high temperatures and long reaction times to afford the corresponding phosphonates. A new method is developed for the preparation of alkyl phosphonates from a mixture of alkyl halide and trialkyl/aryl phosphonates in the presence of amberlyst-15 as catalyst at room temperature under solvent free conditions.

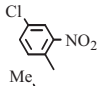
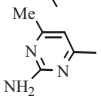
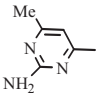
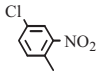
Reaction of a mixture of alkyl halide and triethyl phosphite, triphenyl phosphite in the presence amberlyst-15 under solvent free condition at room temperature afforded the desired phosphonates in high yields after a reaction time of about 20–40 min. The progress of the reaction was followed by analysis of the reaction mixture by TLC on silica gel using hexane and ethyl acetate (3:1 v/v) at different time intervals. After completion of the reaction the catalyst can be separated simply by filtration and reused for another 4 to 5 times without losing its activity [11].



(1a-j) (2) (3a-j)

Scheme 1. Neat synthetic rout of alkyl/aryl/heterocyclic phosphonates.

Table 1
Preparation of alkyl/aryl/heterocyclic phosphonates catalyzed by amberlyst-15.

Compound	R	R_1	Time (min)	Yield(%)	Compound	R	R_1	Time (min)	Yield(%)
3a	CH_3-CH_2-CH_2-	Et	20	90 (89,90,87,89)[a]	**3h**		Ph	38	82
3b	CH_3-CH_2-CH_2-	Ph	35	85					
3c	CH_3-CH_2-$\underset{\backslash}{\overset{\backslash}{CH}}$-$CH_3$	Et	20	91	**3i**		Et	25	89
3d	CH_3-CH_2-$\underset{\backslash}{\overset{\backslash}{CH}}$-$CH_3$	Ph	35	86					
3e	CH_3-CH=CH-	Et	23	88	**3j**		Ph	40	85
3f	CH_3-CH=CH-	Ph	40	83					
3g		Et	22	90					

[a]Isolated yields after recycling of catalyst.

To optimize the reaction conditions, the reaction of 2-bromo butane and triethyl phosphite was selected as a model. This reaction has been performed in different organic solvents such as toluene, methanol, dioxane, tetrahydrofuran, acrylonitrile, chloroform, dichloromethane, diethyl ether in the presence of amberlyst-15 at room temperature and a low yield (<60%) of the alkyl phosphonates was obtained in all these experiments. Use of higher amount of catalyst also did not lead to significant change in the reaction yields. The best result was obtained when the same reaction was done under solvent free conditions with small amount of (0.1 g) catalyst.

Based on the optimized reaction conditions, a group of alkyl/aryl/heterocyclic phosphonates were synthesized by the reaction of alkyl/aryl/heterocyclic halides and trialkyl/aryl phosphonates in the presence of amberlyst-15. The reaction proceeded at room temperature within 20–40 min in good to excellent yields. In these experiments, the catalyst was isolated by filtration and could be reloaded with fresh reagents for further runs, thus, recyclization of the catalyst is possible without significant loss of activity (Table 1, entry **3a**). The products were obtained as semi solids and purified by column chromatography using silica gel as adsorbent and petroleum ether–ethyl acetate (3:1) as eluent. The chemical structures of **3a–j** were confirmed by elemental analysis, IR, ^{1}H, ^{13}C, ^{31}P NMR and mass spectral data.

Compounds (**3a–j**) exhibited characteristic IR stretching frequencies in the regions 1240–1289 and 746–1018 cm^{-1} for P=O (phosphonates) and $P–C_{(aliphatic)}$, respectively [12]. The P–C–H proton signal appeared as multiplet [13] at δ 1.69–2.49 due to its coupling with phosphorus. The methylene protons of $P(O)C\underline{H}_2CH_3$ group showed as a multiplet at δ 3.29–4.19. The methyl protons of $P(O)CH_2C\underline{H}_3$ group protons showed a triplet signal at δ 1.32–1.39 [14]. The carbon chemical shifts for methylenoxy carbons resonated as doublet at δ 61.8–67.2 (d, J = 6.8 Hz) [15], ^{31}P NMR and mass spectral data are given in experimental section. LCMS were recorded for **3a**, **3c**, **3d**, **3f**, **3h**, **3j** and they gave $M^{\bullet+}$ ions at their respective m/z values.

3. Conclusions

We have developed a simple, efficient and green protocol for the sythesis of dialkyl/aryl alkyl phosphonates using amberlyst-15 under solvent-free conditions. The short reaction times, room temperature, simple work-up in isolation of products in good yields with high purity are features of this new procedure.

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