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ARTICLE

Ethyl acrylate conjugated polystyryl-diphenylphosphine — An extremely efficient catalyst for Henry reaction under solvent-free conditions (SolFC)

Lalthazuala Rokhum and Ghanashyam Bez

Abstract: Over the last few decades, the fast-growing development of polymer supported reagents has led to the synthesis of a variety of reagents on solid support. Some of the major advantages of using such reagents are that they are less hygroscopic, easy to recover, and can be recycled. Here, we have demonstrated that in situ generated ethyl acrylate conjugated polystyryl-diphenylphosphine (PDPP–EA) derived from the reaction of a mixture of polystyryl-diphenylphosphine and ethyl acrylate in a stoichiometric ratio can efficiently catalyze the synthesis of β-nitroalcohols from the reaction of aldehydes and nitroalkanes under solvent-free conditions (SolFC).

Key words: Henry reaction, polystyryl-diphenylphosphine, ethyl acrylate, solvent-free conditions (SolFC).

Résumé : Le développement rapide qui a été observé au cours des dernières décades pour des réactifs supportés par des polymères a conduit à la synthèse d'une variété de réactifs sur des supports solides. Parmi les avantages majeurs qui découlent de l'utilisation de tels réactifs, on peut noter le fait qu'ils sont moins hygroscopiques, plus faciles à récupérer et particulièrement qu'on peut généralement les recycler. Dans le présent travail, on démontre que la polystyryl-diphénylphosphine conjuguée à de l'acrylate d'éthyle (PDPHP–AE), générée in situ par réaction d'un mélange de polystyryl-diphénylphosphine et d'acrylate d'éthyle dans un rapport stoechiométrique, permet de catalyser d'une façon efficace la synthèse de β-nitroalcools par réaction d'aldéhydes avec des nitroalcanes, dans des conditions sans solvant (CSSol). [Traduit par la Rédaction]

Mots-clés : réaction de Henry, polystyryl-diphénylphosphine, acrylate d'éthyle, conditions sans solvant (CSSol).

Introduction

The artificial production of chemical compounds for industrially and pharmaceutically important targets in the realm of academic and industrial pursuits has distinct pathways. In academia, exploration of science is the major objective, while industrial research is driven by cost-effectiveness of the product within the domain of stringent environmental regulations. Cost-cutting measures depend on a lot of engineering parameters such as the layout complexity of the necessary mechanical devices, control of large exotherms and endotherms, and safe mechanical transportation of chemicals. Although the solvent plays a vital role in controlling the kinetic and thermodynamic parameters in most of the synthetic protocols, the use of a solvent brings about many undesired elements in industrial reaction design. Their cost, ease of recoverability and recyclability, ease of separation from reagents and desired products, stability, flammability, autoignition temperature, acute and chronic exposure effects, etc. are mentionable. To avoid these problems, the application of organic reactions under solvent-free conditions[1] has been getting immense attention in recent years. Nevertheless, the environmental factor (E factor)[2] can be reduced in synthetic reaction design by minimizing the use of a solvent, which is the highest contributor to the E factor.

The synthesis of a new carbon–carbon bond is considered to be one of the most important aspects in organic synthesis because it generates greater molecular complexity. The synthesis of β-nitroalcohol[3–10] by Henry reaction is one of the best known examples of a C–C bond formation reaction, which can lead to numerous pharmaceutically important compounds[11–12] by manipulating the nitro and hydroxy groups. Classical methods[13–22] to synthesize β-nitroalcohols involve various base catalyzed additions of nitroalkane to aldehyde. Major drawbacks with base catalyzed synthesis of β-nitroalcohol from aromatic aldehydes lies in the easy dehydration driven by the formation of a more delocalized nitroalkene byproduct. Many other side reactions, such as aldol, Michael, and Knoevenagel reactions, take place under basic conditions. To avoid those unwanted side products, Ballini et al.[23] reported a NaOH catalyzed nitroaldol reaction with both aliphatic and aromatic aldehydes. Other than the use of the strong base NaOH, which may not be compatible to base-sensitive functionalities in multistep synthesis, the reaction works very well and is found to be highly useful. Additionally, the use of enzymes[24–26] and metal complexes[27] has been reported in recent years to facilitate mild reaction conditions for the said transformation. Recently, Tian and co-workers[28] reported the use of triphenylphosphine and electron deficient alkene complexes for Henry reaction. But the requirement of moisture-free reaction conditions, nonreusability of the catalyst, environmental concerns with triphenylphosphine based reagents, and a tedious purification process generally encountered in triphenylphosphine containing reactions, may affect the application of this catalyst system in spite of being effective and mild in nature.

In recent years, solid-phase organic syntheses (SPOS) are finding enormous applications in the synthesis of large libraries of compounds via combinatorial chemistry.[29–32] The solid-phase synthesis carries many advantages over classical solution-phase

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synthetic methods: (*i*) the compound of interest (starting material or catalyst) can be anchored to a solid matrix, which can be filtered, (*ii*) easy handling, (*iii*) low moisture susceptibility, (*iv*) minimum side reaction, (*v*) the ability to be recycled for repeated use, and (*vi*) the final product can released from the matrix and can be obtained in an almost pure form. Therefore, polymer-bound reagents have drawn huge attention from industry and academia for their easy handling, separation, and reusability.[33–36] The fact that the polymer can be recovered and the reagent or catalyst can be regenerated in many cases, they can be used in an excess amount to drive the reaction faster. Although triphenylphosphine is considered one of the worst atom-economic reagents due to its high carbon content, polysyryl-diphenylphosphine (PDPP) is getting a lot of use in recent years.[37–44] The fact that polymer-bound triphenylphosphine can be recycled by treatment with trichlorosilane in dry benezene,[45] commonly encountered problems in solution-phase chemistry involving triphenylphosphine, such as the removal of excess triphenylphosphine, triphenylphosphine complexes, and the byproduct triphenylphosphine oxide, can be easily overcome with polymer-bound triphenylphosphine.

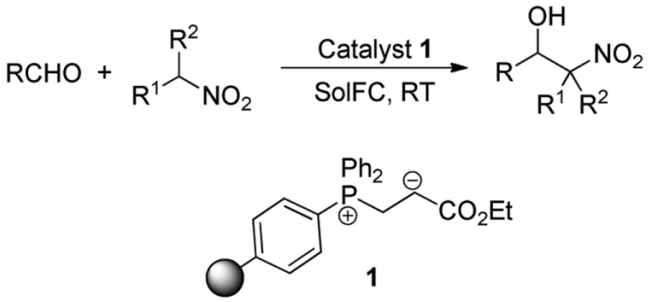
In solid-phase organic synthesis (SPOS), the access of the reactants to the active site is governed by the swelling of the resin by the reaction medium.[46–48] Many polymeric modifications involving linear soluble supports have been proposed to create a solution like microenvironment around the catalyst active site. It is usually achieved by either increasing the distance of the catalyst active site from that of the polymeric matrix by introducing polyethylene glycol (PEG) as a spacer or replacing 1,4-divinylbenzene with an alternative cross-linker having a wider distance between polymeric chains. Although solid-supported organic synthesis is generally believed to be carried out in solvents that can efficiently swell polystyrene, there are a number of instances where the efficiency of the catalysts anchored to a solid support[49–58] was found to be better under solvent-free conditions (SolFC) than in the presence of a reaction medium. But, polystyrene-bound catalysts were found to be less effective under SolFC for their applications. Since polystyrene cross-linked with divinylbenzene is readily available and can be functionalized with ease to introduce reactive sites, we wanted to explore its utility for reactions under SolFC. Although polystyryl-diphenylphosphine (PDPP) has been established as an effective alternative to triphenylphosphine in many synthetic applications[59–66] because of its reusability, we have not found any report on the application of PDPP under solvent-free conditions. Given the recent emphasis on the development of green methodologies, herein we wish to report our findings on the catalytic application of the commercially available polystyryl-diphenylphosphine (PDPP) and ethyl acrylate (EA) complex (PDPP–EA) for the synthesis of β-nitroalcohols by Henry reaction under SolFC (Scheme 1).

Experimental

General remarks

IR spectra were recorded on a PerkinElmer Spectrum One FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker (400 MHz) spectrometer using tetramethylsilane (TMS) as an internal reference. Chemical shifts for ^{1}H NMR spectra are reported (in parts per million (ppm)) relative to internal tetramethylsilane (Me_4Si = 0.0 ppm) with $CDCl_3$ as the solvent. ^{13}C NMR spectra were recorded at 100 MHz. Chemical shifts for ^{13}C NMR spectra are reported (in ppm) relative to internal tetramethylsilane (Me_4Si = 0.0 ppm) with $CDCl_3$ as the solvent. ^{1}H NMR data are reported in the order of chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublet, and m = multiplet), number of protons, and coupling constants in hertz (Hz). Mass spectra were obtained from a Waters ZQ 4000 mass spectrometer by the electrospray ionization (ESI) method, while the elemental analyses of the complexes were performed on a PerkinElmer 2400 CHN/S analyzer. Thin-layer chromatography (TLC) plates were visualized by exposing in an iodine chamber, UV lamp, or spraying with $KMnO_4$ and heating.

Scheme 1. Henry reaction under SolFC.



Synthesis of the catalyst

An equimolar mixture of PDPP (0.5 mmol) and ethyl acrylate (0.5 mmol) was stirred in a small vial for 10 min to get the polystyryl-diphenylphosphine–ethyl acrylate (PDPP–EA) complex. The catalyst so obtained was used for Henry reaction without any purification.

Typical procedure for Henry reaction – Synthesis of 1-(4-chlorophenyl)-2-nitroethanol (h)

To a mixture of polystyryl-diphenylphosphine (3 mmol/g; 0.085 g, 0.25 mmol, 10 mol%) and ethyl acrylate (0.025 g, 0.25 mmol, 10 mol%), nitromethane (0.305 g, 5 mmol) and *p*-chlorobenzaldehyde (0.355 g, 2.5 mmol) was added. After stirring at room temperature for 2 h, the reaction was found to be completed (as indicated by TLC). The reaction mixture was then diluted with dichloromethane (10 mL) and the resulting suspension was filtered through a sintered funnel. The resin was washed successively with dichloromethane (10 mL) and ethyl acetate (10 mL) thrice to confirm complete isolation of the product. The combined filtrate was concentrated in vacuum to get an almost pure crude product, which was passed through a small silica gel pad to obtain the pure product in a 92% (0.464 g, 2.3 mmol) yield. Solid, mp 34–36 °C (lit. value[67] mp 35–37 °C). IR (KBr, cm^{-1}) ν: 3509, 3297, 3032, 2934, 1560. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.17 (s, 1H), 4.38–4.51 (m, 2H), 3.35 (m, 1H), 7.26 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 7.29, 81.03, 127.35, 129.21, 134.78, 136.61. ESI-MS (*m*/*z*): 202.1 (M + 1$^+$). Anal. calcd. for $C_8H_8ClNO_3$: C 47.66, H 4.00, N 6.95; found: C 47.37, H 3.93, N 6.98.

1-Nitrotridecan-2-ol (k)

Solid, semisolid. IR (KBr, cm^{-1}) ν: 3402, 3018, 2932, 2866, 1527, 1434, 1222. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, J = 6.0 Hz, 3H), 1.04–1.64 (m, 20H), 2.58 (s, 1H), 4.31–4.46 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 22.6, 25.1, 29.31, 29.33, 29.4, 29.5, 29.6, 31.9, 33.7, 68.6, 80.6. ESI-MS (*m*/*z*): 245.03 (M$^+$). Anal. calcd. for $C_{13}H_{27}NO_3$: C 63.64, H 11.09, N 5.71; found: C 63.27, H 10.91, N 5.89.

4,8-Dimethyl-1-nitronon-7-en-2-ol (l)

Racemic mixture, colourless liquid. IR (KBr, cm^{-1}) ν: 3588, 3025, 2925, 1620, 1553, 1433, 1387, 1221. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 (d, J = 8.0 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H), 1.12–1.20 (m, 4H), 1.37–1.47 (m, 4H), 1.60 (s, 6H), 1.68 (s, 6H), 1.55–1.73 (m, 2H), 1.91–2.06 (m, 4H), 2.68 (d, J = 4.4 Hz, 1H), 2.71 (d, J = 4.8 Hz, 1H), 4.31–4.45 (m, 6H), 5.08 (t, J = 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 17.68, 18.81, 19.97, 25.19, 25.31, 25.73, 28.43, 28.87, 36.27, 37.53, 40.57, 40.89, 66.6, 66.98, 80.80, 81.14, 124.22, 124.27, 131.61, 131.71. ESI-MS (*m*/*z*): 214.93 (M$^+$), 217.01 (M + 2). Anal. calcd. for $C_{11}H_{21}NO_3$: C 61.37, H 9.83, N 6.51; found: C 61.10, H 9.68, N 6.72.

2-Nitro-1-(4-nitrophenyl)-3-[(tetrahydro-2H-pyran-2-yl)oxy] propan-1-ol (p)

Diastereomeric mixture, colourless semisolid. IR (KBr, cm^{-1}) ν: 3456, 3018, 2932, 1533, 1440, 1361, 1215, 1036. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.52–1.75 (m, 6H), 3.45–3.56 (m, 3H), 3.95–4.11 (m, 2H), 4.53–4.57 (m, 1H), 4.87–4.92 (m, 1H), 5.40–5.45 (m, 1H), 7.60–7.63 (m, 2H), 8.25–8.28 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.76, 19.06, 19.15, 19.38, 25.03, 29.72, 29.96, 30.18, 30.23, 62.16, 62.62, 62.70, 63.17, 64.19, 64.38, 64.80, 65.17, 71.32, 71.35, 71.62, 72.33, 90.52, 90.89, 91.26, 91.33, 98.68, 99.42, 99.92, 124.04, 124.15, 127.11, 127.41, 127.55, 127.71, 145.12, 145.34, 148.23. ESI-MS (*m*/*z*): 326.0 (M^+). Anal. calcd. for $C_{14}H_{18}N_2O_7$: C 51.53, H 5.56, N 8.59; found: C 51.66, H 5.62, N 8.41.

2-Nitro-tetradecan-3-ol (u)

Diastereomeric mixture, colourless liquid. IR (KBr, cm^{-1}) ν: 3431, 3018, 2925, 2866, 1553, 1440, 1215. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 6.4 Hz, 6H), 1.25 (bs, 32H), 1.35–1.52 (m, 4H), 1.56 (dd, *J* = 6.8, 3.2 Hz, 6H), 2.28 (s, 1H), 2.37 (s, 1H), 3.90 (m, 1H), 4.18 (m, 1H), 4.51 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.3, 14.1, 16.2, 22.69, 25.14, 25.73, 29.3, 29.4, 29.5, 29.6, 31.9, 33.0, 72.0, 72.8, 86.3, 87.7. ESI-MS (*m*/*z*): 259.10 (M^+). Anal. calcd. for $C_{14}H_{29}NO_3$: C 64.83, H 11.27, N 5.40; found: C 64.49, H 11.00, N 5.55.

2-Methyl-2-nitrotetradecan-3-ol (v)

Racemic mixture, colourless liquid. IR (KBr, cm^{-1}) ν: 3343, 3018, 2932, 2859, 1540, 1460. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, *J* = 6.4 Hz, 3H), 1.28–1.69 (m, 16H), 1.55 (s, 3H), 1.56 (s, 3H), 1.85–1.89 (m, 1H), 2.01–2.07 (m, 1H), 2.25–2.30 (m, 1H), 3.89 (m, 1H), 4.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.22, 14.15, 20.19, 22.70, 23.79, 23.90, 25.26, 26.40, 29.36, 29.46, 29.54, 29.61, 31.44, 31.91, 33.54, 71.82, 92.22, 94.32. ESI-MS (*m*/*z*): 274.2 ($M^+ + 1$). Anal. calcd. for $C_{15}H_{31}NO_3$: C 65.89, H 11.43, N 5.12; found: C 65.65, H 11.09, N 5.32.

5,9-Dimethyl-2-nitrodec-8-en-3-ol (w)

Diastereomeric mixture, colourless liquid. IR (KBr, cm^{-1}) ν: 3540, 3025, 2925, 1620, 1553, 1454, 1381, 1215. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.93 (d, *J* = 6.8 Hz, 3H), 0.96 (dd, *J* = 6.4, 3.2 Hz, 3H), 1.06–1.49 (m, 8H), 1.54 (t, *J* = 6.4, 6H), 1.60 (s, 6H), 1.68 (s, 6H), 1.55–1.73 (m, 2H), 1.95–2.02 (m, 4H), 2.35–2.39 (m, 1H), 2.40–2.46 (m, 1H), 3.94–4.03 (m, 1H), 4.25–4.34 (m, 1H), 4.45–4.55 (m, 2H), 5.06–5.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 10.1, 10.2, 17.6, 18.6, 18.7, 20.0, 20.3, 25.14, 25.19, 25.3, 25.7, 28.4, 28.6, 28.8, 29.1, 35.7, 36.1, 37.6, 37.8, 40.0, 40.1, 40.4, 69.8, 70.1, 70.8, 71.1, 86.3, 86.8, 87.9, 88.4, 124.3, 131.5, 131.6. ESI-MS (*m*/*z*): 219 (M^+). Anal. calcd. for $C_{12}H_{23}NO_3$: C 62.85, H 10.11, N 6.11; found: C 62.71, H 9.98, N 6.23.

The structures of known compounds, viz., **a**,[6] **b**,[6] **c**,[6] **d**,[7] **e**,[8] **f**,[6] **g**,[6] **i**,[6] **j**,[6] **m**,[6] **n**,[10] **o**,[69] **q**,[70] **r**,[6] **s**,[71] and **t**[10] (for IR, NMR, and MS data, see the Supplementary data) were confirmed by comparing their analytical data with the literature values.

Results and discussion

Synthesis of the catalyst

The polystyryl-diphenylphosphine–ethyl acrylate (PDPP–EA) complex prepared by mixing an equimolar ratio of PDPP (0.5 mmol) and ethyl acrylate (0.5 mmol) was analyzed by IR spectroscopy. In the PDPP–EA complex, **1** (Fig. 1), it was observed that the IR peak at 1719 cm^{-1} for C=O stretching (str.) of the ester moiety in ethyl acrylate was absent. This might be due to the fact that the anion formed in complex **1** as a result of the addition of triphenylphosphine to ethyl acrylate might be predominant as oxygen centered rather than carbon centered and hence the peak for C=O str. was absent after complexation.

Optimization of reaction conditions

We chose the reaction of *p*-chlorobenzaldehyde with nitromethane as the pilot reaction to optimize the reaction conditions. As our stated aim was to accomplish the reaction under SolFC, a mixture of preformed PDPP–EA complex (0.05 mmol), *p*-chlorobenzaldehyde (0.5 mmol), and nitromethane (1.0 mmol) was stirred without solvent with continuous monitoring by thin-layer chromatography (TLC) after every 0.5 h. The reaction was found to be complete within 2 h and the formation of only one polar product was observed, which was confirmed to be the desired product after characterization by spectroscopic methods. Additionally, we observed that the reaction behaved exactly the same way, even after mixing 10 mol% of both the catalysts with reactants in no particular order, to give the desired β-nitroalcohol exclusively under similar reaction conditions. Since swelling of the resin often governs the activity of polymer-bound catalysts, we wanted to study the effect of the solvent on the overall efficiency of the protocol. It was observed that the reaction works well in ethanol, chloroform, and dichloromethane and takes almost 4 h for completion. But the reactions in dimethyl sulfoxide (DMSO), dimethylformamide (DMF), and tetrahydrofuran (THF) did not lead to completion even after 12 h (Table 1). These observations led us to conclude that the reaction indeed works better under SolFC than in solvent media.

Fig. 1. Probable structure of the catalyst.

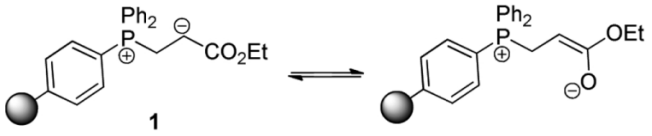
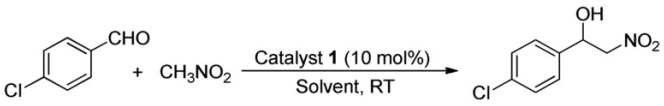


Table 1. Study of the solvent effect.



Entry	Solvent[a]	Time (h)	Yield (%)[b]
1	DMSO	12	38
2	DMF	12	56
3	$CHCl_3$	4	93
4	CH_2Cl_2	4	89
5	THF	12	62
6	EtOH	4	90
7	No solvent	2	92

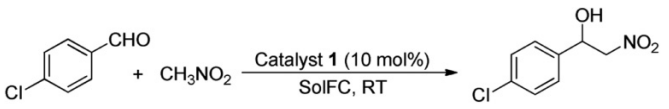
Note: Aldehyde (1 mmol)/nitromethane/PDPP/ethyl acrylate = 1:2:0.1:0.1.
[a]0.5 mL of solvent.
[b]Isolated yields.

To explore the role of nitroalkane as a solvent, we stirred an equimolar mixture of *p*-chlorobenzaldehyde and nitromethane in the presence of 1 equiv. of ethyl acrylate conjugated polystyryl-diphenylphosphine without adding any additional solvent (Table 2, entry 1). Here, the reaction took a significantly longer time (7 h) for complete conversion. As the reaction was comparatively much slower under this reaction condition, the role of nitromethane was subjected to further investigations. It was observed that the addition of 3 and 4 equiv. nitromethane to that of *p*-chlorobenzaldehyde did not help under our reaction conditions (Table 2, entries 3 and 4) and gave similar yields. These observations suggested that nitromethane did not play the same role as that of other solvents, which is the swelling of the polystyryl resin. Therefore, it was concluded that the better reaction rate in pure nitromethane (2 equiv.) may be the result of a concentration effect under SolFC rather than a solvent effect.

Correlation of catalyst loading and reaction time

The catalyst requirement for optimum efficiency of the protocol was also studied to find that 10 mol% of the catalyst (in situ

Table 2. Study of the solvent effect of nitromethane.



Entry	Nitromethane (equiv.)	Time (h)	Yield (%)[a]
1	1	7	89
2	2	2	92
3	3	2	91
4	4	2	93

Note: Aldehyde (1 mmol)/PDPP/ethyl acrylate = 1:0.1:0.1.
[a]Isolated yields.

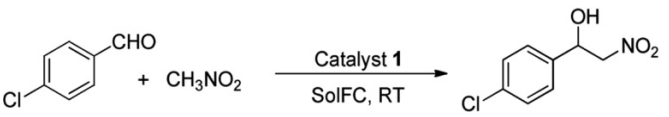
formed PDPP–EA complex) is sufficient to yield the maximum yield at optimum time. The reduction of catalyst loading to 5 mol% tripled the reaction time for complete conversion, while enhancing the catalyst loading to 15 mol% and 20 mol% did not help in the reduction of the reaction time in spite of giving similar yields (Table 3).

Regeneration of the catalyst

To study the reusability of the catalyst, we washed the catalyst successively with dichloromethane and ethyl acetate thrice, allowed it to dry in an oven at 100 °C overnight, and cooled it to room temperature before use. The reaction of the recovered catalyst with *p*-chlorobenzaldehyde (0.5 mmol) and nitromethane (1.0 mmol) resulted in no product even after 5 h at room temperature. We chose to record an IR spectrum of the properly rinsed and dried (in an oven at 100 °C) recovered catalyst to compare the spectra with the initial catalyst. Interestingly, the IR spectrum of the recovered catalyst was exactly the same as that of the starting polystyryl-diphenylphosphine (PDPP). This particular observation led us to explore the possibility of reversible complexation of PDPP with ethyl acrylate, which might have broken upon heating to eliminate ethyl acrylate and left behind polystyryl-diphenylphosphine only. To test our assumption, the recovered polystyryl-diphenylphosphine was again mixed with 1 equiv. of ethyl acrylate and allowed to react with *p*-chlorobenzaldehyde (0.5 mmol) and nitromethane (1.0 mmol) under similar reaction conditions. Interestingly, the reaction showed the reactivity at par with the fresh polystyryl-diphenylphosphine to generate corresponding β-nitroalcohol in a 90% yield. The recovered resin-bound triphenylphosphine was used five times without appreciable loss of activity to synthesize β-nitroalcohol from the said reaction (Table 4), albeit the sixth batch took a little longer (Table 4, entry 7) for complete conversion.

In an attempt to recover the PDPP–EA complex **1** rather than regenerating it, the recovered resin was rinsed successively with dichloromethane (10 mL) and ether (10 mL) thrice and allowed to dry in the open air overnight without subjecting it to drying at an elevated temperature (100 °C). The recovered resin was found to have similar IR spectra to that of the PDPP–EA complex **1**, but showed no catalytic activity indicating that the majority of acrylate in the PDPP–EA complex **1** might have leaked away. The leakage of acrylate on solvent-wash was also confirmed by rinsing the resin successively with dichloromethane (10 mL) and ether (10 mL) six times to get the starting polystyryl-diphenylphosphine in a pure form. When the combined filtrate was concentrated under reduced pressure and IR spectra was taken, a weak band at 1719 cm^{-1} responsible for C=O str. of the acrylate carbonyl was detected. These observations confirmed gradual leakage of the acrylate from PDPP–EA complex **1** upon washing with solvents to generate polystyryl-diphenylphosphine.

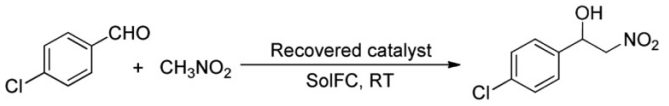
Table 3. Optimization of catalyst loading.



Entry	Catalyst (mol%)	Time (h)	Yield (%)[a]
1	5	2	46
2	5	6	87
3	10	2	92
4	15	2	91
5	20	2	93

Note: Aldehyde/nitromethane/PDPP/ethyl acrylate = 1:2:0.1:0.1.
[a]Isolated yields.

Table 4. Study of the reusability of the catalyst.



Entry	Batch	Catalyst	Time (h)	Yield (%)[a]
1	1	PDPP–EA, **1** (10 mol%)	2	92
2	—	Recovered PDPP (R-PDPP)	5	NR[b]
3	2	R-PDPP + EA (10 mol%)	2	90
4	3	R-PDPP + EA (10 mol%)	2	87
5	4	R-PDPP + EA (10 mol%)	2	89
6	5	R-PDPP + EA (10 mol%)	2	86
7	6	R-PDPP + EA (10 mol%)	3	87

Note: Aldehyde/nitromethane = 1:2.
[a]Isolated yields.
[b]NR = no reaction.

Generalization of the method

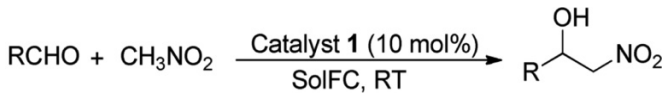
Having optimized the parameters, we set out to study the general application of the protocol in the case of aromatic aldehydes. As we stated earlier, aromatic aldehyde derived β-nitroalcohols often lead to nitroalkene byproducts, and they have been our primary targets. Interestingly, all of them resulted in very good isolated yields (Table 5) under our reaction conditions without any trace of nitroalkene byproduct. The less electrophilic aldehydes (Table 5 entries 3–5) required longer reaction times for complete conversion. The reaction of aliphatic aldehydes with nitromethane were comparatively slower than aromatic aldehydes, but gave very good yields.

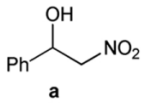
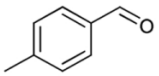
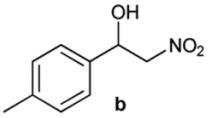
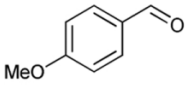
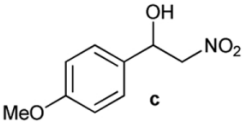
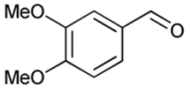
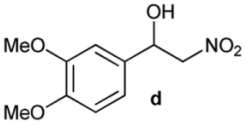
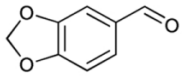
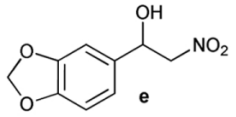
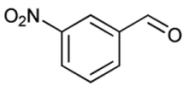
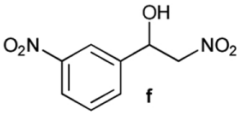
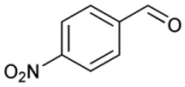
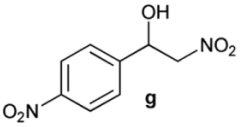
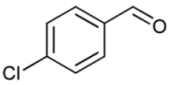
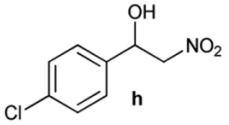
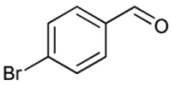
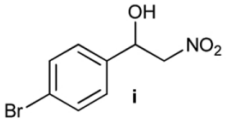
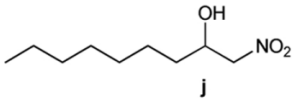
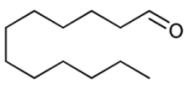
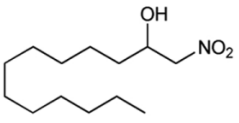
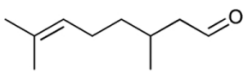
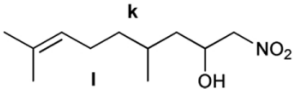
When our reaction protocol was applied for the reaction of *p*-nitrobenzaldehyde with other nitroalkanes (Table 6, entries 1–4), it was observed that the reaction works well to generate corresponding β-nitroalcohols irrespective of the nature of nitroalkane; be it nitroethane, 1-nitropropane, 2-nitropropane, or 2-tetrahydropyranyl-1-nitroethane. Since triphenylphosphine can bind with both nitro and hydroxy groups, we explored the possibility of diastereoselectivity in those β-nitroalcohols by high-performance liquid chromatography (HPLC) using Chiralcel OD-H and Chiralpak AD-H columns, but both the diastereomers formed in equal proportions in all cases. Upon extending the reaction protocol to other aldehydes, we observed that both the aromatic (Table 6, entries 4 and 5) and aliphatic aldehydes[6–10] gave excellent yields of corresponding β-nitroalcohols under SolFC. In all cases, the formation of alkenes was not detected at all.

Conclusion

We report an efficient protocol for the synthesis of β-nitroalcohols by Henry reaction using a catalytic amount of the polysyryl-diphenylphosphine–ethyl acrylate complex (PDPP–EA)

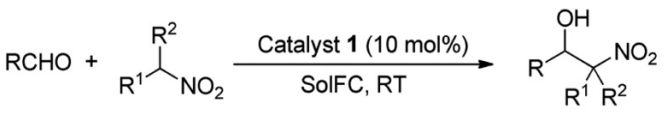
Table 5. Henry reaction with nitromethane.

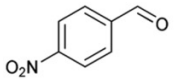
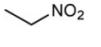
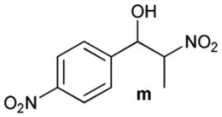
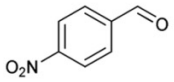
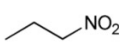
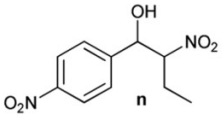
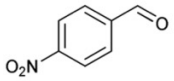
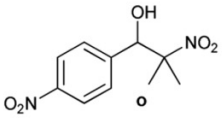
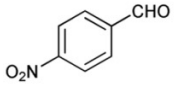
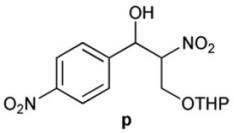
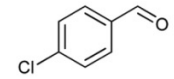
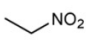
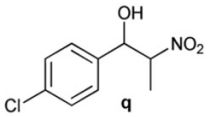
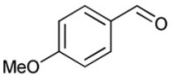
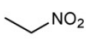
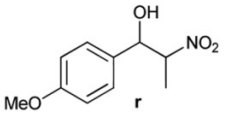
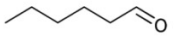
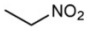
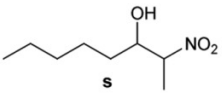
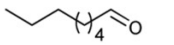
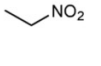
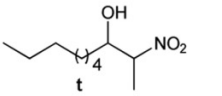
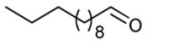
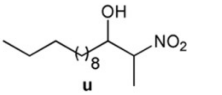
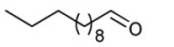
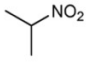
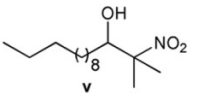
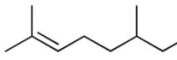
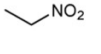
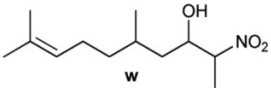


Entry	Substrate	Product	Time (h)	Yield (%)[a]
1		 **a**	2	86
2		 **b**	2	83
3		 **c**	2	88
4		 **d**	6	80
5		 **e**	4	88
6		 **f**	2	94
7		 **g**	2	90
8		 **h**	2	92
9		 **i**	2	89
10		 **j**	2	78
11		 **k**	2	86
12		 **l**	2	82

Note: Aldehyde/nitromethane/PDPP/ethyl acrylate = 1:2:0.1:0.1.
[a]Isolated yield of the pure product.

Table 6. Henry reaction with nitroalkane.



Entry	Substrate	Product	Time (h)	Time (h)	Yield (%)[a]
1				2	90
2				3	94
3				3	91
4				2	84
5				2	92
6				4	91
7				2	91
8				2	87
9				2	91
10				2	89
11				2	88

Note: Aldehyde/nitromethane/PDPP/ethyl acrylate = 1:2:0.1:0.1.
[a]Isolated yield of the pure product.

under solvent-free conditions (SolFC). The use of polystyryldiphenylphosphine has facilitated an efficient regeneration of the catalyst system, thereby removing the disposal issue commonly encountered for triphenylphosphines. The fact that the reaction works better under SolFC without the hazardous organic solvents and gives good to excellent yields in reasonably short reaction times may make the method useful for academic and industrial applications.

Supplementary data

Supplementary data are available with the article through the journal Web site at http://nrcresearchpress.com/doi/suppl/10.1139/cjc-2012-0164.

Acknowledgements

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