

Triphenylphosphine: An efficient catalyst for transesterification of β -ketoesters

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Abstract

An efficient transesterification of β -ketoesters using triphenylphosphine (10 mol%) has been described here with various alcohols. All the reactions were carried out in toluene at reflux conditions to obtain the desired products in very good yields.

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1. Introduction

The electrophilic and nucleophilic sites of β -ketoesters represent an important class of organic building blocks for the synthesis of a number of complex biologically active natural products of pharmaceuticals, agrochemicals and polymers [1]. The esterifications and transesterifications are very important reactions in synthetic organic chemistry laboratories as well as academic laboratories for the preparation of polyesters from alcohols and acids or esters. The use of these synthons in organic synthesis is more advantageous than ester synthesis due to the availability of several β -ketoesters in the market [2]. The transesterification reaction of β -ketoesters has been recognized as one of the most significant processes in producing other β -ketoesters (Scheme 1).

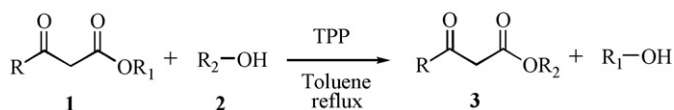
These reactions can be made spontaneous by using Dean-Stark apparatus or high temperature conditions. However, they are very often catalyzed for a high efficiency, faster reaction rates and milder conditions. Thus, a number of procedures catalyzed by a variety of protic acids [3], Lewis acids [4], solid catalysts [5], organic or inorganic basic catalysts [6] and enzymes [7] have been reported in the literature. But many of these catalysts have drawbacks such as expensive or difficult to prepare, toxic, require longer reaction time, unsuitable for acid sensitive functional groups, low selectivity and large amounts of solid supports

that would eventually result in the generation of a large amount of toxic waste. Depres and co-workers [8] has been reported transesterification without a catalyst with propargyl alcohols but the reaction time was 1–12 days at high temperature. Due to the environmental demand, there has been considerable interest in developing a new catalyst for organic reactions that would be mild, easily available at low-cost, high performance in transformation and wide applicability is desirable. In this regard, triphenylphosphine have received increasing attention as versatile and mild reagent in many occasions for various organic transformations under neutral conditions in recent years [9].

2. Results and discussions

With an ever-increasing quest for the exploration of newer catalysts and as part of our ongoing program in developing various new synthetic transformations [10], in this communication, we wish to explore the triphenylphosphine (TPP) as an efficient catalyst for transesterification of β -ketoesters with various alcohols. In a typical experimental procedure, the methyl acetoacetate (2 mmol), propargyl alcohol (2 mmol) and triphenylphosphine (10 mol%) were refluxed in toluene to obtain the corresponding transesterification product in excellent yield (entry **a**). The reaction was completed within 6.0 h. However, no transesterification was observed when the reaction was carried out in the absence of a catalyst over 10 h. The scope and generality of this process is illustrated with respect to various alcohols and β -ketoesters in presence of TPP. In a similar man-

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ner, a variety of β -ketoesters such as methyl, cycloalkyl and phenyl acetoacetates underwent transesterification with a wide range of alcohols like propargyl, butyl, prenyl, benzyl, heptyl, 2-chloroethyl, phenylethyl, allyl, menthyl and decenyl. In all the cases, the reactions were completed within 6–8 h of reaction time with high efficiency. It is important to note that the propargyl alcohol (entry **a**), sterically hindered menthol (entry **e**), phenyl ethanol (entry **h**) and prenyl (entry **g**) have been effectively catalyzed by triphenylphosphine, giving products in excellent yields. In case of heptyl alcohol, transesterification of aromatic ester is comparatively faster than aliphatic ester (entries **c** and **n**). The similar type of observation was found in the reaction of decenyl alcohol with aliphatic ester and aromatic ester (entries **d** and **o**). Among aliphatic and cyclic esters (entries **j** and **k**), the reaction of benzyl alcohol with cyclic system is comparatively slower than aliphatic system. In a similar manner, the reaction of allyl alcohol with aromatic ester is superior over cyclic ester (entries **l** and **m**) in terms of conversion and yields. The above observation clearly shows that the aromatic ester reacts faster than aliphatic ester and the aliphatic esters reacts faster than cyclic esters. In all the cases, the catalyst triphenylphosphine was used in catalytic amount (10 mol%) to carry out the reactions, which makes it simple and convenient process. Furthermore, the catalyst triphenylphosphine was recovered after the reaction. The probable reaction mechanism is shown in Scheme 2.

3. Conclusion

In conclusion, we have demonstrated a novel and efficient protocol for the transesterification of β -ketoesters with various alcohols using triphenylphosphine as a novel catalyst. This method offers significant advantages such as mild reaction conditions faster reaction rates, high yields, readily availability of the catalyst and cleaner reaction profiles, which makes it an attractive and superiority over the existing methods for synthetically useful transesterification. The experimental procedure is also very simple, convenient and avoids tedious work-up procedure for the isolation of the products.

4. Experimental Section

4.1. General methods

Melting points were recorded on Buchi R-535 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer using KBr optics. ^1H NMR spectra were recorded on Gemini-200 spectrometer in CDCl_3 using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV.

4.2. General experimental procedure for transesterification

To a stirred mixture of β -ketoester (2 mmol) and alcohol (2 mmol) in toluene (10 mL) was added triphenylphosphine (0.2 mmol). The resulting reaction mixture was refluxed for appropriate time (Table 1). The progress of the reaction was monitored by TLC. After complete conversion of the substrate as indicated by TLC, the reaction mixture was directly adsorbed on silica gel (60–120 mesh) and eluted with ethyl acetate–hexane in 2:8 ratio to afford the corresponding pure products. The products were characterized by comparison of their ^1H NMR, IR and mass spectrometer with authentic samples. The spectral data of all the products were identical with those of authentic samples.

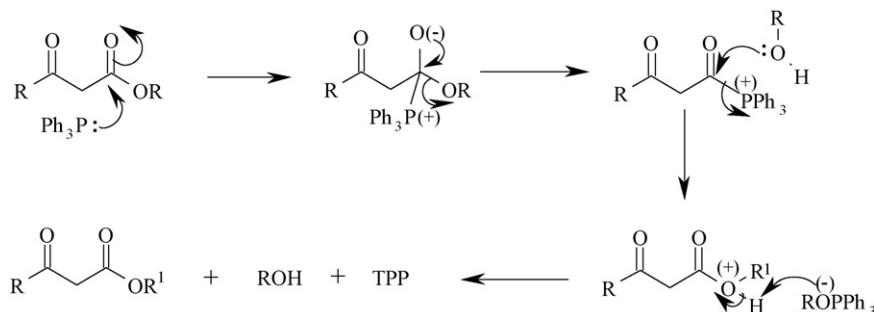
4.3. Spectral data for all the compounds

4.3.1. **3a**: Propargyl-3-oxo-butanoate

Colorless liquid. IR (neat): ν 2928, 2129, 1749, 1720, 1413, 1366, 1315, 1265, 1149, 1029, 767 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 2.30 (s, 3H), 2.42 (t, 1H, $J=2.4$ Hz), 3.40 (s, 2H), 4.70 (d, 2H, $J=2.4$ Hz). EIMS: m/z (%): 140 (M^+ 10), 123 (15), 98 (28), 85 (23), 70 (18), 55 (24), 39 (100).

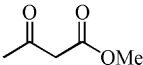
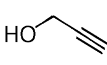
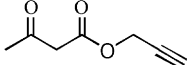
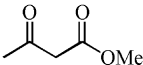
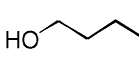
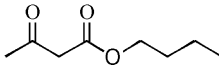
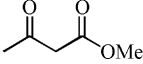
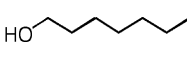
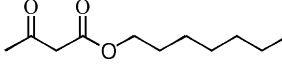
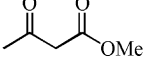
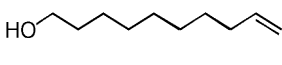
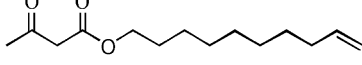
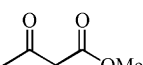
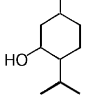
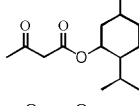
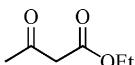
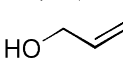
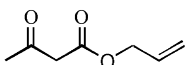
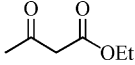
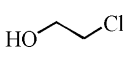
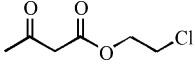
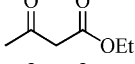
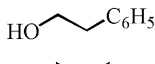
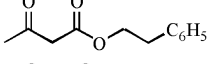
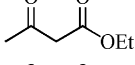
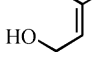
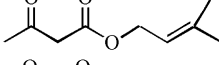
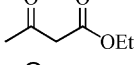
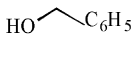
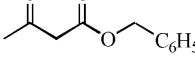
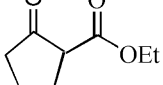
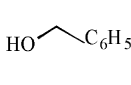
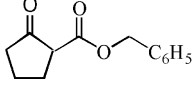
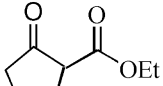
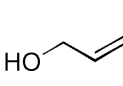
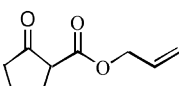
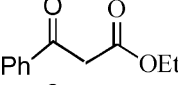
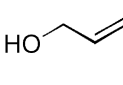
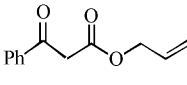
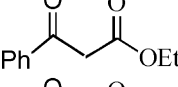
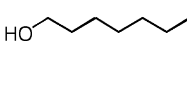
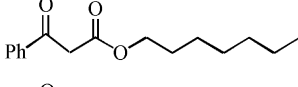
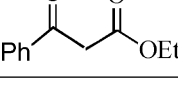
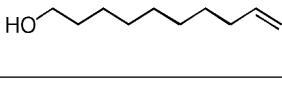
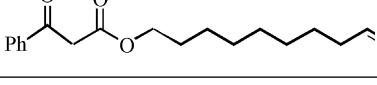
4.3.2. **3b**: Butyl-3-oxo-butanoate

Colorless liquid. IR (neat): ν 2961, 2871, 1749, 1723, 1648, 1460, 1414, 1316, 1246, 1153, 1032, 836, 742 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 0.91 (t, 3H, $J=6.8$ Hz), 1.39 (tt, 2H, $J=6.8, 7.3$ Hz), 1.60 (q, 2H, $J=6.8$ Hz), 2.30 (s, 3H), 3.40 (s, 2H), 4.10 (t, 2H, $J=6.8$ Hz). EIMS: m/z (%): 158 (M^+ 18), 129 (11), 101 (43), 85 (15), 69 (21), 57 (100), 43 (69).



Scheme 2.

Table 1
TPP-catalysed transesterification of β -ketoesters

Entry	β -Ketoester (1)	Alcohol (2)	Product ^a (3)	Time (h)	Yields ^b (%)
a				6.0	90
b				6.5	87
c				7.0	79
d				6.5	84
e				6.5	90
f				8.0	78
g				7.0	84
h				6.0	90
i				6.5	90
j				6.0	78
k				8.0	73
l				7.0	84
m				6.0	87
n				6.5	88
o				6.0	86

^a All the products were characterized by IR, ¹H NMR and mass spectroscopy and compared with literature reports.

^b Isolated and unoptimized yields.

4.3.3. 3c: Heptyl-3-oxo-butanoate

Colorless liquid. IR (neat): ν 2957, 2929, 1743, 1718, 1649, 1465, 1414, 1368, 1315, 1238, 1151, 1034, 841, 736 cm^{-1} . ¹H NMR (200 MHz, CDCl_3): δ 0.90 (t, 3H, $J=6.8$ Hz), 1.25–1.40 (m, 8H), 1.65 (q, 2H, $J=6.8$ Hz), 2.25 (s, 3H), 3.38 (s, 2H), 4.12 (t, 2H, $J=6.8$ Hz). EIMS: m/z (%): 200 (M^+ 10), 157 (15), 103 (45), 85 (25), 70 (20), 57 (35), 43 (100).

4.3.4. 3d: 9-Decene-3-oxo-butanoate

Colorless syrup. IR (neat): ν 2928, 2856, 2345, 1745, 1721, 1640, 1414, 1316, 1305, 1232, 1152, 1029, 958, 839, 746 cm^{-1} .

¹H NMR (200 MHz, CDCl_3): δ 1.22–1.40 (m, 10H), 1.60–1.66 (m, 2H), 2.05 (q, 2H, $J=6.8$ Hz), 2.25 (s, 3H), 3.38 (s, 2H), 4.12 (t, 2H, $J=6.0$ Hz), 4.92 (dd, 2H, $J=11.0, 18.0$ Hz), 5.68–5.82 (m, 1H). EIMS: m/z (%): 240 (M^+ 21), 199 (12), 157 (26), 101 (17), 85 (10), 57 (100), 43 (21).

4.3.5. 3e: Menthyl-3-oxo-butanoate

Syrup. IR (KBr): ν 2978, 2820, 1729, 1701, 1653, 1527, 1453, 1405, 1321, 1247, 1152, 1082, 1021, 981, 902, 849, 734 cm^{-1} . ¹H NMR (200 MHz, CDCl_3): δ 0.79 (d, 3H, $J=6.8$ Hz), 0.88 (d, 3H, $J=6.8$ Hz), 0.91 (d, 3H, $J=6.5$ Hz), 0.97–1.20 (m, 1H),

1.35–1.45 (m, 1H), 1.60–1.70 (m, 2H), 1.92–2.02 (m, 2H), 2.30 (s, 3H), 3.40 (s, 2H), 4.72 (dt, 1H, $J=4.2, 10.5$ Hz), 4.92 (dd, 2H, $J=11.0, 18.0$ Hz), 5.68–5.82 (m, 1H). EIMS: m/z (%): 240 (M^+ 21), 199 (12), 157 (26), 138 (100), 123 (45), 101 (17), 95 (71), 80 (60), 68 (25), 57 (79), 43 (21).

4.3.6. **3f**: Allyl-3-oxo-butanoate

Free-floating liquid. IR (neat): ν 2951, 2863, 2289, 1748, 1723, 1647, 1428, 1406, 1379, 1281, 1143, 1022, 1008, 951, 841, 735 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 2.20 (s, 3H), 3.40 (s, 2H), 4.61 (d, 2H, $J=6.0$ Hz), 5.18–5.28 (m, 2H), 5.75–5.85 (m, 1H). EIMS: m/z (%): 142 (M^+ 15), 129 (11), 101 (68), 85 (26), 69 (21), 57 (100), 43 (39).

4.3.7. **3g**: 2-Chloro ethyl-3-oxo-butanoate

Light colored liquid. IR (neat): ν 3018, 2906, 1751, 1722, 1649, 1600, 1508, 1456, 1361, 1263, 1037, 927, 839, 741 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 2.30 (s, 3H), 3.45 (s, 2H), 3.72 (t, 2H, $J=6.5$ Hz), 4.41 (t, 2H, $J=6.5$ Hz). EIMS: m/z (%): 166 (M^+ 10), 164 (M^+ 57), 129 (28), 115 (10), 101 (16), 85 (12), 57 (100), 43 (21).

4.3.8. **3h**: 2-Chloro ethyl-3-oxo-butanoate

Colorless syrup. IR (neat): ν 3029, 2959, 2847, 1741, 1717, 1646, 1608, 1521, 1496, 1315, 1257, 1146, 1032, 943, 856, 738 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 2.18 (s, 3H), 2.95 (t, 2H, $J=6.8$ Hz), 3.37 (s, 2H), 4.30 (t, 2H, $J=6.8$ Hz), 7.12–7.30 (m, 5H). EIMS: m/z (%): 206 (M^+ 20), 129 (51), 104 (100), 101 (11), 91 (24), 85 (10), 77 (12), 57 (17), 43 (85).

4.3.9. **3i**: Prenyl-3-oxo-butanoate

Liquid. IR (neat): ν 2927, 2861, 1749, 1723, 1529, 1446, 1237, 1152, 958, 826, 741 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 1.80 (s, 3H), 1.92 (s, 3H), 2.33 (s, 3H), 3.40 (s, 2H), 4.70 (d, 2H, $J=7.0$ Hz), 5.43 (t, 1H, $J=7.0$ Hz). EIMS: m/z (%): 170 (M^+ 26), 149 (16), 101 (10), 91 (29), 85 (43), 69 (100), 55 (18), 41 (60).

4.3.10. **3j**: Benzyl-3-oxo-butanoate

Liquid. IR (neat): ν 3079, 2958, 2847, 2362, 1740, 1714, 1628, 1509, 1438, 1217, 1153, 1027, 943, 816, 739 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 2.30 (s, 3H), 3.42 (s, 2H), 5.25 (s, 2H), 7.30 (s, 5H). EIMS: m/z (%): 192 (M^+ 16), 188 (18), 174 (25), 158 (20), 141 (30), 129 (18), 107 (37), 105 (25), 91 (100), 77 (20), 63 (18), 55 (18), 43 (30).

4.3.11. **3k**: Benzyl-oxo-cyclopentane carboxylate

Syrup. IR (neat): ν 3083, 2967, 2853, 1757, 1728, 1618, 1527, 1453, 1337, 1255, 1218, 1182, 1007, 913, 846, 741 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 1.95–2.05 (m, 2H), 2.20–2.30 (m, 4H), 3.10 (t, 1H, $J=8.8$ Hz), 5.14 (s, 2H), 7.32 (s, 5H). EIMS: m/z (%): 218 (M^+ 20), 190 (23), 127 (18), 111 (13), 107 (17), 99 (12), 91 (100), 84 (90), 65 (28), 55 (43), 39 (20).

4.3.12. **3l**: Allyl-2-oxo-cyclopentane carboxylate

Colorless liquid. IR (neat): ν 2970, 2886, 1745, 1729, 1649, 1517, 1453, 1297, 1251, 1184, 1027, 993, 934, 835, 748 cm^{-1} .

^1H NMR (200 MHz, CDCl_3): δ 1.90–2.10 (m, 2H), 2.24–2.35 (m, 4H), 3.10 (t, 1H, $J=8.8$ Hz), 4.63 (d, 2H, $J=6.0$ Hz), 5.24–5.35 (m, 2H), 5.75–5.85 (m, 1H). EIMS: m/z (%): 168 (M^+ 16), 140 (24), 111 (50), 99 (25), 83 (30), 68 (18), 55 (100), 41 (98).

4.3.13. **3m**: Allyl-3-oxo-3-phenyl propanoate

Syrup. IR (neat): ν 3072, 2957, 2836, 2139, 1749, 1720, 1689, 1645, 1598, 1450, 1401, 1327, 1269, 1201, 1134, 1047, 963, 869, 734 cm^{-1} . ^1H NMR (200 MHz, CDCl_3): δ 3.98 (s, 2H), 4.66 (d, 2H, $J=6.8$ Hz), 5.18–5.39 (m, 2H), 5.81–5.99 (m, 1H), 7.32–7.95 (m, 5H). EIMS: m/z (%): 204 (M^+ 12), 192 (13), 147 (18), 120 (37), 105 (100), 77 (87), 41 (36).

4.3.14. **3n**: Heptyl-3-oxo-3-phenyl propanoate

Syrup. IR (neat): ν 3083, 2929, 2859, 1742, 1689, 1630, 1455, 1413, 1267, 1208, 1194, 1148, 1078, 932, 739 cm^{-1} . ^1H NMR (CDCl_3): δ 0.90 (t, 3H, $J=6.80$ Hz), 1.25–1.40 (m, 8H), 1.65 (q, 2H, $J=6.0$ Hz), 3.95 (s, 2H), 4.12 (t, 2H, $J=6.8$ Hz), 7.32–7.95 (m, 5H). EIMS: m/z (%): 262 (M^+ 20), 165 (43), 147 (28), 120 (37), 105 (100), 77 (47), 41 (30).

4.3.15. **3o**: 9-Decenyl-3-oxo-3-phenyl propanoate

Colorless syrup. IR (neat): ν 3071, 2927, 2855, 1743, 1699, 1636, 1578, 1453, 1328, 1266, 1196, 1079, 996, 749 cm^{-1} . ^1H NMR (CDCl_3): δ 1.22–1.40 (m, 10H), 1.60–1.70 (m, 2H), 2.05 (q, 2H, $J=6.80$ Hz), 3.96 (s, 2H), 4.12 (t, 2H, $J=6.0$ Hz), 4.95 (t, 2H, $J=18.0$ Hz), 5.62–5.82 (m, 1H), 7.32–7.95 (m, 5H). EIMS: m/z (%): 262 (M^+ 20), 165 (43), 147 (28), 120 (37), 105 (100), 77 (47), 41 (30).

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