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Solvent-free transesterification in a ball-mill over alumina surface

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ABSTRACT

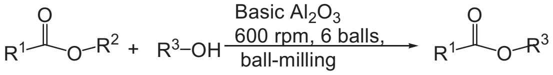
An efficient procedure for transesterification has been developed in a ball-mill in the absence of any solvent, acid/base or metal catalyst. A variety of methyl, ethyl, allyl esters have been transesterified to higher benzyl and other esters in high yields by this procedure.

Transesterification is a useful reaction which has wide applications in academic as well as industrial research. Usually, methyl and ethyl esters are readily available and thus they can be used in transesterification for an easy access to higher homologues which are of much importance for certain applications. Thus, a number of procedures have been developed for this useful reaction. Traditionally, a carboxylic ester was transesterified by reaction with an alcohol in the presence of a protic and Lewis base or acid.[1,2] However, these procedures have limited scope due to their incompatibility with sensitive functional groups and molecules. Several milder reactions using organometallic catalysts,[3] *N*-heterocyclic carbene[4] and indium triiodide[5] among others[6] have been developed in recent times. These methods also have drawbacks involving costly reagents and longer reaction times.

Recently, ball-milling (mechanical grinding) has emerged as a powerful tool for effecting a chemical reaction in a greener way.[7] A variety of reactions such as homocoupling of terminal alkynes,[8] Sonogashira,[9] Michael[10] and aldol reactions[11] among others[12] have been performed very efficiently by this technique. As a part of our continuing activities on green synthetic protocols, we report here an efficient transesterification over an alumina surface by ball milling without requirement of any solvent and conventional catalyst (Scheme 1).

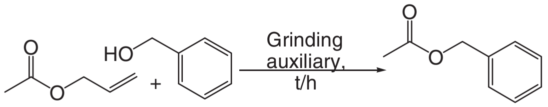
To standardize the reaction conditions several experiments for a representative reaction of allyl acetate and benzyl alcohol were carried out in a ball mill with the variation of grinding auxiliary and reaction time. The results are summarized in Table 1. The reaction over basic alumina gave best yield in 2 h (Table 1, entry 2). Reaction for a longer period than 2 h did not give a better result (Table 1, entry 3). Acidic alumina alone (Table 1, entry 4) failed to initiate any reaction although Al_2O_3–KF (Table 1, entry 5) improved the yield marginally (30%). Silica gel (60–120 mesh) (Table 1, entry 6) was also not effective for this reaction.

In a typical experimental procedure[13] a mixture of alcohol and ester (little excess) absorbed in basic alumina was subjected to ball-milling at 600 rpm for 2–3 h as required for maximum



Scheme 1. Transesterification in a ball-mill

Table 1
Standardization of reaction conditions in ball mill



Entry	Grinding auxiliary	t/h	Yield (%)
1	Basic Al_2O_3	1	61
2	Basic Al_2O_3	2	76
3	Basic Al_2O_3	3	76
4	Acidic Al_2O_3	2	0
5	KF–Al_2O_3	2	30
6	Silica	2	0

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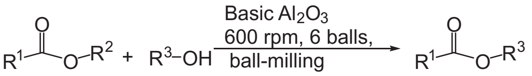
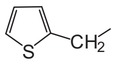
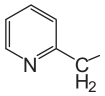
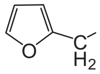
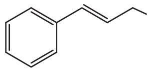
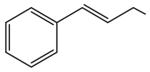
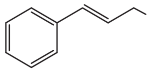
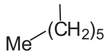
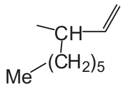
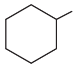
Table 2
Transesterification of esters with alcohols



Entry	R^1	R^2	R^3	Time (h)	Yield[a] (%)	Ref.
1	Me	Allyl	Ph-CH_2–	2	76	4a
2	Me	Allyl	(3-Cl)C_6H_4-CH_2–	2	75	14
3	Et	Et	(3-Cl)C_6H_4-CH_2–	2	71	
4	Me	Allyl	(4-F)C_6H_4-CH_2–	2	70	15
5	n-pr	Me	(4-OCH_3)C_6H_4-CH_2–	2	81	16
6	Ph	Benzyl	(4-OCH_3)C_6H_4-CH_2–	3	80	17
7	Vinyl	Me	(4-OCH_3)C_6H_4-CH_2–	2.5	78	
8	n-pr	Me	(4-NO_2)C_6H_4-CH_2–	2	72	18
9	Vinyl	Me	(4-NO_2)C_6H_4-CH_2–	2.5	70	19
10	Me	Allyl	Ph-$(CH_2)_2$–	2	76	3b
11	n-pr	Me	Ph-$(CH_2)_2$–	2	71	20
12	Me	Allyl	Ph-$(CH_2)_3$–	2	73	4b
13	Et	Et	Ph-$(CH_2)_3$–	2	76	21
14	Me	Allyl	Ph-$(CH_2)_4$–	2	75	4b
15	n-pr	Me	Ph-$(CH_2)_4$–	2	70	22
16	Et	Et	Ph-$(CH_2)_5$–	2	72	
17	n-pr	Me	Ph-$(CH_2)_5$–	2	75	
18	Me	Allyl	$CH_3CH(Ph)(CH_2)_2$–	2	72	23
19	n-pr	Me	$CH_3CH(Ph)(CH_2)_2$–	2	70	
20	n-pr	Me		3	66	
21	Et	Et		2.5	71	24
22	n-pr	Me		2.5	65	
23	Et	Et		2	76	3c
24	n-pr	Me		2	69	3c
25	Ph	Benzyl		3	68	3c
26	Et	Et		2	74	25
27	Me	Allyl		2.5	67	26
28	Et	Et		2.5	66	27
29	Et	Et		3	0	

[a] Yields refer to those of purified isolated products characterized by spectroscopic data (IR, ^1H NMR and ^{13}C NMR).

conversion (TLC/NMR). A quick column chromatography of the crude reaction mass over alumina (hexane/ether = 95:5) provided pure product.

A wide range of carboxylic esters underwent transesterification with several structurally diverse alcohols by this procedure. The results are reported in Table 2. A variety of alcohols including substituted benzyl, cinnamyl, heterocyclic, open chain and cyclic secondary underwent exchange with methyl, ethyl, allyl and benzyl esters to produce the corresponding transesters. The tertiary alcohols did not participate in this transesterification process. In general, the reactions are very clean and the products are obtained in high purity. The yields of transesterified products are reasonably good considering the reversible nature of the reaction. The reaction conditions are mild and thus several functional groups and sensitive heterocyclic units like thiophene, pyridine and furan remained unaffected in this procedure. No solvent was used in the reaction and the work-up procedure was skipped. Thus, use of organic solvent was considerably reduced. Ball-milling accelerated the process substantially and the reactions are complete by 2–3 h.

In conclusion, we have developed a simple and efficient procedure for transesterification over alumina surface in ball-milling. The notable advantages offered by this procedure are use of no solvent and no acid or base catalyst in the reaction, considerably fast reaction, tolerance to sensitive functionalities and molecules, applicability to varied esters and alcohols and greener aspects using less organic solvents and recyclability of grinding auxiliary. To the best of our knowledge we are not aware of any earlier report of transesterification under ball-milling using only a grinding auxiliary (alumina). We believe, this will make an important addition to the existing procedures of transesterification and will find useful applications in organic synthesis.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.05.127.

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13. Representative experimental procedure for transesterification of allyl acetate and benzyl alcohol (Table 2, entry 1). A mixture of allyl acetate (120 mg, 1.2 mmol) and benzyl alcohol (108 mg, 1 mmol) adsorbed on basic Al_2O_3 (3.5 g) was ball-milled in a 25 mL stainless steel vessel at 600 rpm using six balls (d = 10 mm) for 2 h (PM 100, Retsch GmbH, Germany). The crude reaction mixture was filtered through a short column of neutral alumina (hexane/ether = 95:5) to provide benzyl acetate as a colourless liquid (114 mg, 76%), IR 3066, 3034, 2954, 1740, 1488, 1026 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36 (s, 5H), 5.12 (s, 2H), 2.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171, 136.0, 128.6 (2C), 128.3 (3C), 66.3, 21.0. These data are in good agreement with those of an authentic sample.
    This procedure is followed for all the reactions listed in Table 2. The known products were identified by comparison of their spectroscopic (IR, ^1H NMR and ^{13}C NMR) data with those reported (See references in Table 2). The unknown products (Table 2, entries 3, 7, 16, 17, 19, 20 and 22) were properly characterized by their spectroscopic (IR, ^1H NMR and ^{13}C NMR) data which are provided below.

3-Chlorobenzyl propionate (Table 2, entry 3): Colourless liquid; IR 3470, 3066, 2982, 2943, 2831, 1741, 1600, 1577, 1462, 1431, 1377, 1346, 1273, 1176, 1080, 871, 783 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34–7.21 (m, 4H), 5.08 (s, 2H), 2.43–2.35 (m, 2H) 1.17 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 140.3, 134.5, 129.9, 128.2, 128.1, 126.2, 65.3, 27.6, 9.2; Anal. calcd for $C_{10}H_{11}ClO_2$: C 60.46, H 5.58%; Found: C 60.32, H 5.66%.

4-Methoxybenzyl acrylate (Table 2, entry 7): Colourless liquid; IR 2956, 2837, 1722, 1614, 1516, 1464, 1406, 1296, 1249, 1172, 1035, 985, 966, 810 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 6.42 (d, J = 17.4 Hz, 1H), 6.19–6.09 (m, 1H), 5.82 (d, J = 10.2 Hz, 1H), 5.13 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 159.7, 130.9, 130.1 (2C), 128.5, 128.0, 114.0 (2C), 66.2, 55.2; Anal. calcd for $C_{11}H_{12}O_3$: C 68.74, H 6.29%; Found: C 68.88, H 6.19%.

5-Phenylpentyl propionate (Table 2, entry 16): Colourless liquid; IR 2937, 2858, 1737, 1602, 1496, 1454, 1350, 1190, 1084, 746, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.24 (m, 2H), 7.18–7.15 (m, 3H), 4.05 (t, J = 7 Hz, 2H), 2.61 (t, J = 7.5 Hz, 2H), 2.32–2.28 (m, 2H), 1.67–1.61 (m, 4H), 1.42–1.35 (m, 2H), 1.12 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.7, 142.5, 128.5 (2C), 128.4 (2C), 125.8, 64.4, 35.9, 31.1, 28.6, 27.7, 25.7, 9.3; HRMS calcd for $C_{14}H_{20}O_2Na$ $[M+Na]^+$: 243.1361; Found: 243.1362.

5-Phenylpentyl butyrate (Table 2, entry 17): Colourless liquid; IR 2935, 2858, 1732, 1602, 1494, 1454, 1257, 1184, 1091, 910, 758, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 7 Hz, 2H), 7.18–7.14 (m, 3H), 4.05 (t, J = 7 Hz, 2H), 2.61 (t, J = 7.5 Hz, 2H), 2.25 (t, J = 7.5 Hz, 2H), 1.71–1.59 (m, 6H), 1.43–1.35 (m, 2H), 0.93 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.8, 142.4, 128.4 (2C), 128.3 (2C), 125.7, 64.2, 36.3, 35.8, 31.1, 28.6, 25.6, 18.5, 13.7; HRMS calcd for $C_{15}H_{22}O_2Na$ $[M+Na]^+$: 257.1517; Found: 257.1518.

3-Phenylbutyl butyrate (Table 2, entry 19): Colourless liquid; IR 2962, 2875, 1735, 1602, 1492, 1454, 1359, 1305, 1253, 1178, 1091, 761, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (t, J = 7 Hz, 2H), 7.20–7.17 (m, 3H), 4.04–3.92 (m, 2H), 2.86–2.81 (m, 1H), 2.24 (t, J = 7.5 Hz, 2H), 1.93–1.89 (m, 2H), 1.67–1.60 (m, 2H), 1.28 (d, J = 7 Hz, 3H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 146.4, 128.6 (2C), 127.0 (2C), 126.3, 62.8, 37.0, 36.8, 36.3, 22.3, 18.6, 13.8; HRMS calcd for $C_{15}H_{20}O_2Na$ $[M+Na]^+$: 243.1361; Found: 243.1361.

(Thiophen-2-yl) methyl butyrate (Table 2, entry 20): Colourless liquid; IR 2962, 2856, 1735, 1440, 1365, 1226, 1168, 1070, 966, 854, 831, 702 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99–6.97 (m, 3H), 5.27 (s, 2H), 2.32 (t, J = 7.5 Hz, 2H), 1.70–1.64 (m, 2H), 0.94 (t, J = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5, 140.7, 128.1, 126.8, 126.1, 65.9, 36.2, 18.5, 13.7; anal calcd for $C_9H_{12}O_2S$: C 58.67, H 6.56%; Found: C 58.74, H 6.62%.

(Furan-2-yl) methyl butyrate (Table 2, entry 22): Colourless liquid; IR 2964, 2931, 2875, 1735, 1512, 1458, 1381, 1249, 1170, 1080, 970, 744 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 (s, 1H), 6.33–6.28 (m, 2H), 4.99 (s, 2H), 2.24 (t, J = 7 Hz, 2H), 1.62–1.55 (m, 2H), 0.863 (t, J = 7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4, 149.8, 143.8, 110.7, 110.6, 58.0, 36.1, 18.5, 13.7; Anal. calcd for $C_9H_{12}O_3$: C 64.27, H 7.19%; Found: C 64.34, H 7.11%.

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