Pergamon

Tetrahedron Letters 43 (2002) 1165–1168

TETRAHEDRON
LETTERS

Natural clays as efficient catalyst for transesterification of β-keto esters with carbohydrate derivatives

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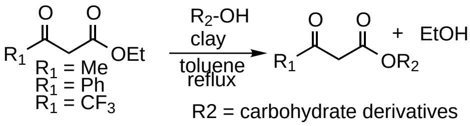
Received 15 October 2001; accepted 18 December 2001

Abstract—Smectite, atapulgite and vermiculite clays catalyzed efficiently transesterifications of β-keto esters and carbohydrate derivatives in good to high yields without decomposition of the carbohydrate moieties. © 2002 Elsevier Science Ltd. All rights reserved.

β-Keto esters have considerable application in academic and industrial fields. These compounds have been used as synthons in several syntheses of complex natural products.[1,2] The use of these synthons in organic synthesis is more advantageous than ester synthesis[3] due to the availability of several β-keto esters in the market. The transesterification reaction of β-keto esters (Scheme 1) has been recognized as one of the most important processes in producing other β-keto esters. However, it is worth mentioning that acid-catalyzed opening of diketene is another widely used method for preparing β-keto esters.[4]

Since the transesterification is an equilibrium process, it is accelerated by acidic and basic catalysts and also by removing ethanol[5] during the process. In this regard, various catalysts have been recently reported to effect this transesterification: distannoxanes,[6] indium triiodide,[7] DMAP,[8,9] diphenylammonium triflate,[10] amberlyst-**15**,[11] yttria-zirconia,[12] Mo-ZrO_2,[13] zinc dust,[14] lithium perchlorate,[15] titanium(IV) alkoxides[16] and, sulphated SnO_2.[17] Other processes such as polymer-supported lipase,[18] zeolites,[19] envirocat EPZG[20,21] have been also reported to catalyze efficiently the transesterification reaction. Some of these catalysts are difficult to prepare, toxic and unsuitable for acid sensitive functional groups.



Scheme 1. General transesterification reaction.

Due to environmental demands, there has been considerable interest in developing new catalysts for organic reactions based on inorganic solids. In this regard, layered clay catalysts have received increasing attention in many areas of organic chemistry, including organic synthesis, mainly due to their chemo- and regio-selectivity, availability, low cost raw materials, mild reaction conditions, noncorrosiveness, easy recovery and reuse.[22] These natural solids have been used successfully in many reactions.[23,24] Modified clays, such as, kaolinite (montmorillonite K-10)[25] and hydrotalcite,[26] were also used as catalyst in transesterification. Although few types of clay have been employed successfully in transesterification process, other abundant natural clays remain unexplored.

In a search for obtaining 2-diazo-β-keto esters of carbohydrate derivatives, such as acetonides **4a**–**e**, by direct transesterification, it was found that montmorillonite K-10 (commercially available) degraded extensively the carbohydrate moiety (entry 30, Table 1). Using DMAP as catalyst, the β-keto esters were obtained but in low yields (entries 31 and 32, Table 1).

Due to the low stability of these acetonides in the above-mentioned conditions, it was decided to investigate new catalysts, which could overcome this problem. We herein describe a very mild and efficient protocol for transesterification between β-keto esters (**1**–**3**) with methoxy-2,3-*O*-isopropylidene-α-D-ribofuranose (**4a**),

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PII: S0040-4039(01)02388-7

Table 1. Clays-catalyzed production of β-keto esters **5a**–**m** via Scheme 2

Entry	β-Keto ester	Alcohol (R_2-OH)	Product	Catalyst	Yield (%)
1	$R_1 = CH_3$	**4a**	**5a**	Smectite	73
2	$R_1 = Ph$	**4a**	**5b**	Smectite	72
3	$R_1 = CH_3$	**4b**	**5c**	Smectite	76
4	$R_1 = Ph$	**4b**	**5d**	Smectite	89
5	$R_1 = CH_3$	**4c**	**5e**	Smectite	50
6	$R_1 = Ph$	**4c**	**5f**	Smectite	78
7	$R_1 = CH_3$	**4d**	**5g**	Smectite	93 (>98, 95)[a]
8	$R_1 = Ph$	**4d**	**5h**	Smectite	91
9	$R_1 = CH_3$	**4a**	**5a**	Atapulgite	93
10	$R_1 = Ph$	**4a**	**5b**	Atapulgite	75
11	$R_1 = CH_3$	**4b**	**5c**	Atapulgite	86
12	$R_1 = Ph$	**4b**	**5d**	Atapulgite	82
13	$R_1 = CH_3$	**4c**	**5e**	Atapulgite	50
14	$R_1 = Ph$	**4c**	**5f**	Atapulgite	80
15	$R_1 = CH_3$	**4d**	**5g**	Atapulgite	>98 (98, 98)[a]
16	$R_1 = Ph$	**4d**	**5h**	Atapulgite	87
17	$R_1 = CH_3$	**4a**	**5a**	Vermiculite	93
18	$R_1 = Ph$	**4a**	**5b**	Vermiculite	76
19	$R_1 = CH_3$	**4b**	**5c**	Vermiculite	>98
20	$R_1 = Ph$	**4b**	**5d**	Vermiculite	82
21	$R_1 = CH_3$	**4c**	**5e**	Vermiculite	51
22	$R_1 = Ph$	**4c**	**5f**	Vermiculite	82
23	$R_1 = CH_3$	**4d**	**5g**	Vermiculite	93 (>98, 98)[a]
24	$R_1 = Ph$	**4d**	**5h**	Vermiculite	>98
25	$R_1 = CF_3$	**4a**	**5i**	Vermiculite	>98
26	$R_1 = CF_3$	**4b**	**5j**	Vermiculite	71
27	$R_1 = CF_3$	**4d**	**5k**	Vermiculite	>98
28	$R_1 = CH_3$	**4e**	**5l**	Vermiculite	84
29	$R_1 = CH_3$	**4f**	**5m**	Vermiculite	94
30	$R_1 = CH_3$	**4a**	**5a**	K-10[b]	36
31	$R_1 = CH_3$	**4a**	**5a**	DMAP	62
32	$R_1 = Ph$	**4a**	**5b**	DMAP	47
33	$R_1 = Me$	**4g**	**5n**	Vermiculite	0

[a] Catalyst was recovered and reused three time without loss of activity.

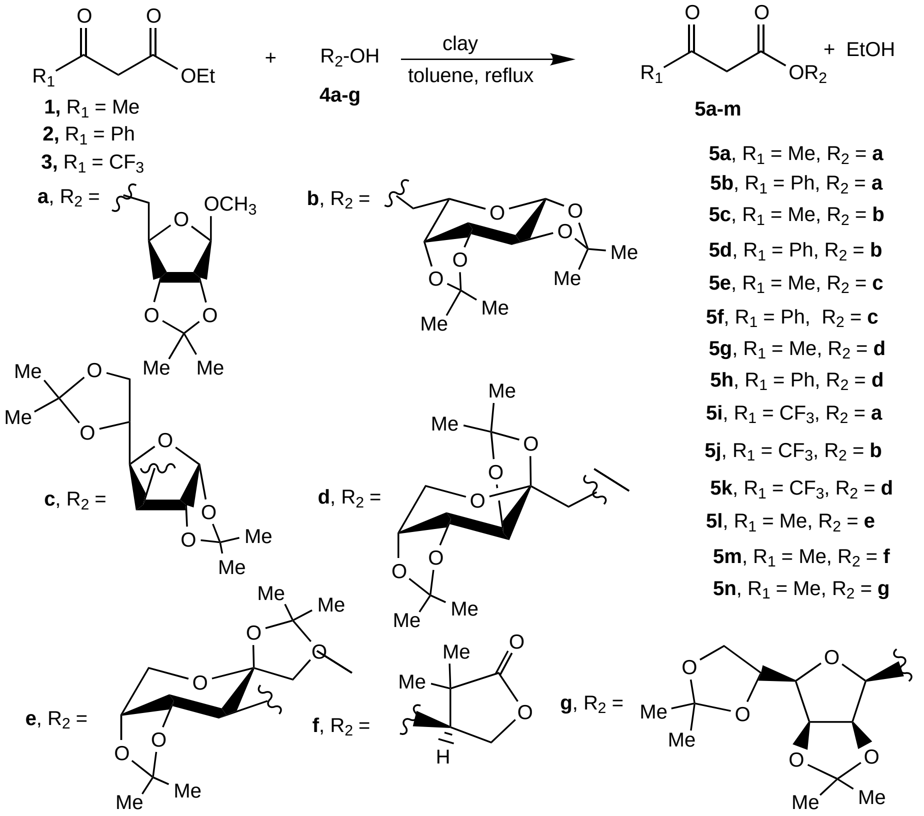
[b] Obtained from Aldrich Chemical Co.

1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**4b**) 1,2:5,6-di-*O*-isopropylidene-β-D-glucofuranose (**4c**), 2,3:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**4d**), 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose (**4e**), (*R*)-(−)-pantolactone (**4f**) and, 2,3:5,6-di-*O*-isopropylidene-β-D-mannofuranose (**4g**) employing three eco-friendly natural clays as catalyst: smectite, atapulgite and vermiculite (Scheme 2). To the best of our knowledge, there is no report on the use of these clays in transesterification reactions. The transesterification results obtained are presented in Table 1.

With these clay-catalysts, the carbohydrate derivatives (**4a**–**e** and **4g**) and (*R*)-(−)-pantolactone (**4f**) underwent transesterifications with ethyl acetoacetate (**1**), 1-ethyl benzoylacetate (**2**) or ethyl trifluoro-acetoacetate (**3**), to afford synthetically useful esters **5a**–**n** in moderate to excellent yields. The degradations of the carbohydrates, which were observed using Montmorillonite K10, were reduced dramatically with these clays and, in some experiments the products were obtained in high degrees of purity (entries 14, 23–25) by simply removing excess starting materials. In general, atapulgite and vermiculite clays had better performance than smectite and produced the esters in higher yields. It was observed that the reactions were more selective for primary alcohols rather than secondary alcohols, but it also depended on the structure of the carbohydrate. While **5e** (entries 5, 13 and 21 were obtained in moderate yields, the esters **5l** (entry 28) and **5m** (entry 29) were obtained in much higher yields. The reaction fails in the case of anomeric alcohol **4g** (entry 33) possibly due to the lability of the product. The variation of R_1 groups on the β-keto esters **1**–**3** had very little effects on the chemical yields.

The clays were recovered and reused at least three times without appreciable loss of the activity as indicated in the entries 7, 15 and 23. We believe that the present procedure is quite general, since it was tested successfully with other non-carbohydrate primary and secondary alcohols.

Clays origin: The clays were obtained from Bravo farm,[27] Boa Vista district, Paraíba, Brazil. They were ground to 0.150 mm and used in the reactions without any pretreatment or activation. Their specific surface areas were measured by the BET-method:[28] smectite 68.88 m^2/g, atapulgite 49.30 m^2/g and vermiculite 119.67 m^2/g. Percentual composition of clays determined by X-ray powder diffraction (Table 2).



Scheme 2. Transesterification reaction calalyzed by clays.

Table 2.

Clay	MgO (%)	Al_2O_3 (%)	SiO_2 (%)	TiO_2 (%)	Fe_2O_3 (%)	K_2O (%)	CaO (%)
Smectite	2.2	12.1	60.9	0.68	7.4	–	0.79
Vermiculite	20.7	12.7	44.3	1.1	8.6	3.4	1.6
Atapulgite	6.6	13.5	66.6	0.64	8.6	1.41	0.10

The acetonides **4a**, **4b**–**e** and **4g** were prepared by standard methods described in the literature[29] from the appropriate carbohydrates. (*R*)-(−)-Pantolactone (**4f**) was purchased from Aldrich Chemical Company and used without further purification.

General experimental procedure: A mixture of the appropriate β-keto ester (5 mmol), carbohydrate–acetonides (4 mmol) and the clay (20 mol%) in toluene (20 mL) was refluxed for 48 h. The mixture was filtered to remove the clay and the filtrated evaporated under reduced pressure. The residue was chromatographed on silica gel column (Merck 70–230 mesh) and eluted with a mixture of *n*-hexane: ethyl acetate (98:2).

The yields are indicated on Table 1. The esters **5c,e,g**[30] and **4f**[31] were analyzed by NMR, IR and mass spectra and were in accordance with those described in the literature.

Spectral data of some new ester: **5a**, $[\alpha]_D$ −30.8 (*c* 0.3, $CHCl_3$), IR (film) $\nu_{max.}$ 1750 and 1730 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (3H, s, Me); 1.49 (3H, s, Me); 2.28 (3H, s, Me); 3.32 (3H, s, OCH_3); 3.51 (2H, s); 4.19–4.16 (2H, m, H5 and H5'); 4.38–4.36 (2H, m, H4); 4.60 (1H, d, *J* 5.7 Hz, H2); 4.67 (1H, d, *J* 6.0 Hz, H3), 4.98 (1H, s, H1); HRMS found for $[M-15]^{+\bullet}$: 273.0913, calcd for $C_{12}H_{17}O_7$); **5b**, $[\alpha]_D$ −22.7 (*c* 0.3, $CHCl_3$); HRMS found for $[M-15]^{+\bullet}$: 335.1168, calcd for $C_{17}H_{19}O_7$: 335.1131; **5c**, $[\alpha]_D$−30.6 (*c* 0.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (3H, s, Me), 1.34 (3H, s, Me), 1.46 (3H, s, Me), 1.52 (3H, s, Me), 2.29 (3H, s, Me), 3.49 (1H, t, *J* 6.6 Hz, H4), 3.50 (2H, d, *J* 0.9 Hz, H14), 4.05 (1H, ddd, *J* 7.4, 4.9 and 2.4 Hz, H2), 4.35–4.23 (3H, m, H5 or H6 or H6'), 4.63 (1H, dd, *J* 7.9 and 2.5 Hz, H3), 5.54 (1H, d, *J* 4.8 Hz, H1); **5d**, $[\alpha]_D$ −23.1 (*c* 0.2, $CHCl_3$), **5f**, $[\alpha]_D$ −9.5 (*c* 0.2, $CHCl_3$; **5h,** $[\alpha]_D$ −14.88 (*c* 0.2, $CHCl_3$), HRMS found for $[M-15]^{+\bullet}$: 391.1231, calcd for $C_{20}H_{23}O_8$: 391.1293; **5i**, $[\alpha]_D$ −29.1 (*c* 0.2, $CHCl_3$); **5j**, $[\alpha]_D$ −20.1 (*c* 0.2, $CHCl_3$); **5k**, $[\alpha]_D$ −18.0 (*c* 0.2, $CHCl_3$).

In summary, considering the environmental issues as well as process optimization that requires the substitution of toxic catalysts by more friendly solid catalysts, we have shown for the first time that three types of naturally occurring clays can efficiently catalyze transesterification of β-keto esters with carbohydrate derivatives in good to high yields without decomposition of the carbohydrate moieties.

Acknowledgements

A fellowship granted to F.C.S and R.S.R. from CNPq (Brazil) is gratefully acknowledged. V.F.F. is grateful to CNPq for an individual research fellowship. This work was partially supported by CNPq (National Council of Research of Brazil), FAPERJ, CETEM and Universidade Federal Fluminense.

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