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Montmorillonite clay-catalyzed cyclotrimerization and oxidation of aliphatic aldehydes

Matthew R. Dintzner *, Yawo A. Mondjinou, Dominic J. Pileggi

Department of Chemistry, DePaul University, 1110 West Belden Ave., Chicago, IL 60614, United States

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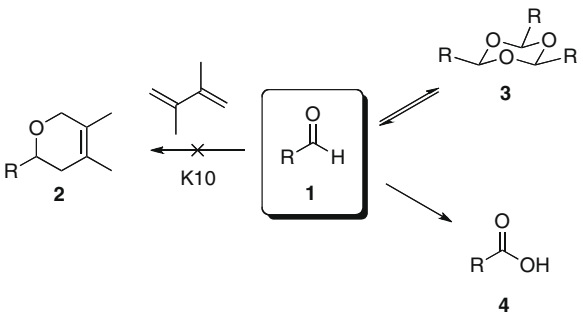
ABSTRACT

A temperature-dependent equilibrium is observed for the cyclotrimerization of aliphatic aldehydes in the presence of Montmorillonite K10 clay, while aerobic oxidation of aliphatic aldehydes to the corresponding carboxylic acids is favored at room temperature in the presence of Montmorillonite KSF clay.

1. Introduction

As concern for the environment continues to shape the way chemists think about the construction of physiologically active compounds, the development of synthetic methodologies that promote greener reactions is essential. Environmentally benign clays are ideally suited for the 'greening' of modern synthetic chemistry—they are naturally abundant, inexpensive, nontoxic, chemically versatile, and recyclable. We have shown that Montmorillonite K10 clay is an effective catalyst for a variety of reactions,[1] including the hetero-Diels–Alder reaction of aromatic aldehydes with 2,3-dimethyl-1,3-butadiene.[1b] Our efforts to effect the hetero-Diels–Alder reaction of *aliphatic* aldehydes with 2,3-dimethyl-1,3-butadiene (**1**–**2**, Scheme 1), however, were unsuccessful, primarily due to a competing side reaction: cyclotrimerization (**1**–**3**, Scheme 1).[1b] Because 1,3,5-trioxanes (**3**) have been implicated in a host of practical applications,[2] and because their synthesis[3] in the presence of untreated Montmorillonite clay had not been reported, we were encouraged to further pursue this reaction. In the course of our investigation of the clay-catalyzed cyclotrimerization of aliphatic aldehydes, we observed another competing reaction: oxidation to the corresponding carboxylic acids (**1**–**4**, Scheme 1). Herein we report our findings.

Under the conditions that were optimal for the hetero-Diels–Alder reaction (heat-activated Montmorillonite K10 clay, 1 h, 23 °C, neat) we observed only minimal formation of trioxane (**3**).[1b] Thus, we set out to optimize conditions for the cyclotrimerization reaction, with propanal as a model system, by varying the following experimental parameters: solvent, stoichiometry, temperature, time, and type of clay. In keeping with the tenets of green chemistry, we were delighted to find that solvent was completely unnecessary for cyclotrimerization. Similarly, varying the amount of clay (10–100% by mass relative to aldehyde) had minimal impact on the conversion of propanal to **3**. Further, the use of unactivated ('wet') clay was observed to be much more effective in promoting cyclotrimerization than the heat-activated clay. The effects of temperature and time were investigated simultaneously, using neat, wet



Scheme 1. Cyclotrimerization and oxidation of aliphatic aldehydes.

* Corresponding author. Tel.: +1 773 325 4726; fax: +1 773 3257421.
E-mail address: mdintzne@depaul.edu (M.R. Dintzner).

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clay. The relative ratio of trioxane-to-propanal (**3:1a**) was assessed over a range of temperatures (−80 to 50 °C) by ^{1}H NMR analysis of the reaction mixtures at 24-h increments over the course of 10 days, specifically by comparison of the relative integration values for the ketal protons of **3** with the aldehydic proton of **1a**. Interestingly, the K10 clay-mediated equilibrium appeared to favor the trioxane product at low temperature, with the highest ratio of trioxane-to-propanal (**3**:**1a**, Table 1) observed at −20 °C after 192 h (8 days). We rationalized this temperature dependence as an entropy effect.[4] Small amounts of by products, presumably from aldol condensations, were also observed at −20 °C.[5] In a typical procedure, propanal was thoroughly mixed using a metal spatula with untreated Montmorillonite K10 clay in a glass scintillation vial. The vial was capped and allowed to stand at specified temperatures for extended periods of time. Aliquots were periodically removed, and the reaction mixture filtered with $CDCl_3$ directly into an NMR tube for analysis. The ratio of trioxane-to-propanal (**3:1a**) was determined by comparison of the relative integration values for the ketal protons of **3** with the aldehydic proton of **1a** (Table 1).

Although interesting theoretically, we found this reversible reaction to be rather capricious in the presence of Montmorillonite K10, minimizing its potential usefulness in synthesis. Thus, we next investigated the use of Montmorillonite KSF clay in place of the K10, anticipating that the smaller surface area of KSF compared to K10 might afford better control of the cyclotrimerization reaction. Remarkably, in the presence of Montmorillonite KSF we observed a different reaction all together: oxidation of propanal to propanoic acid (**1a**–**4a**, Scheme 1). Oxidation proceeded slowly at ambient temperature or above, but was irreversible, giving near quantitative yield of the acid in approximately 168 h (7 days).In order to confirm that atmospheric oxygen was acting as the oxidizing agent for this reaction, a control experiment was conducted at room temperature under a nitrogen environment. Indeed, in the absence of atmospheric oxygen, no reaction was observed after 168 h. The oxidation reaction appears to be fairly general with aliphatic aldehydes (Table 2, entries 1–6), but no reaction was observed for aromatic or a,b-unsaturated systems (Table 2, entries 7–10). The Montmorillonite KSF-catalyzed air oxidation of aliphatic aldehydes constitutes a much milder and environmentally friendlier alternative to traditional methodology for the synthesis of aliphatic carboxylic acids.[6]

Table 1
Trioxane (**3**) formation after 192 h at various temperatures

Entry	*T* (°C)	3:1a[a]
1	50	0.1:1
2	23	1.3:1
3	8	1.0:1
4	−20	3.9:1
5	−80	0.2:1

[a] Determined by ^{1}H NMR integration.

Table 2
KSF-catalyzed oxidation reaction

Entry	Aldehyde	Carboxylic acid	% Yield
1	Propanal (**1a**)	Propanoic acid (**4a**)	59
2	Butanal (**1b**)	Butanoic acid (**4b**)	81
3	Isobutyraldehyde (**1c**)	Isobutyric acid (**4c**)	58
4	Pentanal (**1d**)	Pentanoic acid (**4d**)	95
5	Hexanal (**1e**)	Hexanoic acid (**4e**)	90
6	Cyclohexanecarboxaldehyde (**1f**)	Cyclohexanecarboxylic acid (**4f**)	57
7	Benzaldehyde (**1g**)	Benzoic acid (**4g**)	0
8	2-Butenal (**1h**)	2-Butenoic acid (**4h**)	0
9	3-Methyl-2-butenal (**1i**)	3-Methyl-2-butenoic acid (**4i**)	0
10	Cinnamaldehyde (**1j**)	Cinnamic acid (**4j**)	0

A typical procedure for the KSF clay-catalyzed air oxidation of aliphatic aldehydes follows. Propanal (200 mg, 3.44 mmol) was thoroughly mixed with Montmorillonite KSF clay (200 mg) in a scintillation vial. The mixture was allowed to stand at room temperature for 168 h, and then taken up in 3 mL CH_2Cl_2 and the mixture filtered and washed with 3–5 mL methanol. The filtrate was concentrated under vacuum to give propanoic acid (149 mg, 59%).[7]

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7. *Analytical data for compounds* **4a**–**4f**: Proton nuclear magnetic resonance (^{1}H) spectra and carbon-13 (^{13}C) spectra were recorded at 300 MHz and 75 MHz, respectively. The proton signal of residual, non-deuterated solvent (δ 7.26 ppm for $CHCl_3$) was used as an internal reference for ^{1}H spectra. For ^{13}C spectra, chemical shifts are reported relative to the δ 77.23 ppm resonance of $CDCl_3$. Coupling constants are reported in Hz. Infrared spectra were recorded as thin films on a Nicolet Avatar 360 spectrometer. *Propanoic acid* (**4a**):IR ($CDCl_3$) 2968, 2940, 2880, 1734, 1653, 1463, 1412, 1381, 1340, 1154, 1095, 950, 668 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.73 (s, 1H), 2.40 (m, 2H), 1.17 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 27.2, 8.9. *Butanoic acid* (**4b**): IR ($CDCl_3$) 2963, 2936, 2875, 1711, 1465, 1412, 1381, 1150, 1105, 966, 775 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.70 (s, 1H), 2.35 (t, *J* = 7.4 Hz, 2H), 1.68 (m, 2H), 1.00 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 36.0, 18.7, 13.3.*Isobutyric acid* (**4c**): IR 2966, 2876, 1703, 1682, 1471, 1390, 1368, 1253, 1221, 1120, 1025, 994, 752, 739, 702, 665 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.76 (s, 1H), 2.6 (m, 1H), 1.22 (d, *J* = 7.0, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.4, 32.8, 18.8. *Pentanoic acid* (**4d**):IR ($CDCl_3$) 2960, 2935, 2874, 1711, 1467, 1413, 1381, 1279, 1216, 1108, 940, 751 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.77 (s, 1H), 2.36 (t, *J* = 7.4 Hz, 2H), 1.62 (m, 2H), 1.37 (m, 2H), 0.9 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.0, 34.0, 27.8, 22.6, 14.0. *Hexanoic acid* (**4e**):IR ($CDCl_3$) 2957, 2933, 2870, 2861, 2700, 1711, 1467, 1450, 1414, 1379, 1292, 1245, 1213, 1146, 1111, 934 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.80 (s, 1H), 2.35 (m, 2H), 1.65 (m, 2H), 1.30 (m, 4H), 0.9 (t, *J* = 6.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.3, 34.0, 31.7, 24.6, 22.0, 14.0. *Cyclohexanecaboxylic acid* (**4f**): IR ($CDCl_3$) 2934, 2856, 1701, 1452, 1420, 1312, 1256, 1213, 1182, 1136, 922, 895 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.81 (s, 1H), 2.35 (m, 1H), 1.92 (m, 1H), 1.76 (m, 1H), 1.65 (m, 1H), 1.46 (m,1H), 1.3 (m, 1H), 1.2 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.3, 43.0, 28.8, 25.7, 25.45.