



Montmorillonite K10 clay-catalyzed synthesis of homoallylic silyl ethers: an efficient and environmentally friendly Hosomi–Sakurai reaction

Matthew R. Dintzner*, Yawo A. Mondjinou, Barrett Unger

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

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ABSTRACT

Aromatic aldehydes react with allyltrimethylsilane in the presence of activated Montmorillonite K10 clay to give homoallylic silyl ethers in good to excellent yields.

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The Hosomi–Sakurai¹ reaction of allylsilanes with aldehydes is among the most widely utilized carbon–carbon bond-forming reactions in natural products synthesis.² The resulting homoallylic alcohol products are useful platforms for further synthetic elaboration, especially in the event that the allylation reaction proceeds stereoselectively.³ Although powerful Lewis acids, such as SnCl₄, TiCl₄, BF₃·OEt₂, AlCl₃, and Sc(OTf)₃, have been shown to successfully catalyze the Hosomi–Sakurai reaction, the negative impact of these reagents on the environment has urged the development of alternative, greener methodologies for effecting this and related synthetic transformations.⁴ We have developed a number of applications for naturally benign Montmorillonite clay, all of which involve the catalysis of carbon–carbon bond-forming reactions.⁵ In the course of these ongoing investigations, we have observed that activated Montmorillonite K10 clay is an extremely efficient catalyst for the addition of allyltrimethylsilane to electron-deficient benzaldehydes (**1**) to give homoallylic silyl ethers (**2**) in good to excellent yields (Fig. 1).⁶ In the best-case scenarios, the reaction proceeds rapidly at room temperature or below in the presence of minimal solvent, and in quantitative yield with near perfect atom economy.

Previous work in our laboratories has shown that Montmorillonite K10 clay is effective in activating aromatic aldehydes toward nucleophilic attack, particularly when the clay is first activated by heating (200 °C, 1 h).⁵ Heating results in the collapse of the clay's

interlayer structure and marked increase in its Lewis acidity, as water is extruded.⁷ We set out to investigate the clay-catalyzed addition of allyltrimethylsilane to aromatic aldehydes and observed that the treatment of 3-nitrobenzaldehyde with allyltrimethylsilane in the presence of activated Montmorillonite K10 (neat) led to a highly exothermic reaction.⁶ Extraction of the product mixture with dichloromethane and analysis by ¹H NMR and GC–MS showed evidence of the desired homoallylic silyl ether product, along with some unreacted starting materials and a mixture of other unidentified products. We proceeded to effect better control of the reaction by taking up a mixture of the clay and aldehyde in a minimal amount of dichloromethane and cooling the mixture to 0 °C prior to careful addition of the allyltrimethylsilane. The reaction mixture was stirred at 0 °C for 5 min, and then allowed to warm to ambient temperature over the course of 1 h. Filtration of the reaction solution and concentration under vacuum gave a near quantitative yield of the desired product, with no further purification necessary. Next, we assayed a variety of aromatic aldehydes and observed similar results with other electron-deficient

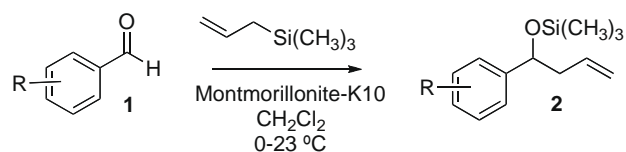


Figure 1. Clay-catalyzed Hosomi–Sakurai reaction.

* Corresponding author. Tel.: +1 773 325 4726; fax: +1 773 325 7421.

E-mail address: mdintzne@depaul.edu (M.R. Dintzner).

Table 1
Results with aromatic aldehydes

Entry	Aldehyde	Product	Yield ^a (%)
1	2-Nitrobenzaldehyde (1a)	2a	84
2	3-Nitrobenzaldehyde (1b)	2b	99
3	4-Nitrobenzaldehyde (1c)	2c	99
4	3-Fluorobenzaldehyde (1d)	2d	97
5	4-Chlorobenzaldehyde (1e)	2e	99
6	2,6-Dichlorobenzaldehyde (1f)	2f	99
7	3-Cyanobenzaldehyde (1g)	2g	99
8	Benzaldehyde (1h)	2h	75 ^b
9	4-Anisaldehyde (1i)	2i	0 ^c
10	2-Anisaldehyde ^c (1j)	2j	70 ^b

^a Isolated yield.

^b GC yield.

^c Based on recovered starting materials.

compounds (Table 1, entries 1–8). No reaction was observed with the more electron-rich 4-anisaldehyde, presumably due to its decreased electrophilicity. The reaction with 2-anisaldehyde, however, proceeded to some extent but did not go to completion. As we reported in a previous study, apparently favorable chelation of the clay's metal ions with the oxygen atoms of 2-anisaldehyde may compensate for its diminished electrophilicity.^{5a}

Control experiments with 3-nitrobenzaldehyde showed that varying the amount of clay, from 100% to 25% by mass relative to the mass of the aldehyde, had minimal effect on the yield of the product. However, no reaction between 3-nitrobenzaldehyde and allyltrimethylsilane was observed in the absence of clay or in the presence of unactivated clay.

Although the reaction proceeded fairly with some aliphatic aldehydes (Table 2, entries 1–4), it was neither as clean nor as high yielding as with the aromatic systems, presumably due to competitive cyclotrimerization.^{5a} No reaction was observed with α,β -unsaturated aldehydes (Table 2, entries 5–7). While treatment of some aliphatic ketones (Table 2, entries 8 and 9) with allyltrimethylsilane in the presence of activated K10 gave good yields of the corresponding 3° homoallylic silyl ethers, no reaction was observed with cyclopentanone or with aromatic ketones (Table 2, entries 10–12).

In contrast to the computational and experimental evidence reported for the mechanism of the homogeneous Lewis acid-catalyzed Hosomi–Sakurai reaction, our results suggest a closed transition state model, concerted mechanism for the clay-mediated process (Fig. 2).⁸ Thus, not only does the reaction generate a new C–C bond, but it also has the advantage of providing the products in their protected form, as the trimethylsilyl ethers. Deprotection, if desired, can be effected quantitatively by adding a slight excess of methanol to the reaction mixture and stirring for 20 min prior to filtering.

Table 2
Results with aliphatic and α,β -unsaturated aldehydes, and ketones

Entry	Carbonyl compound	Yield ^a (%)
1	Propionaldehyde	16
2	Butyraldehyde	47
3	Isobutyraldehyde	61
4	Cyclohexanecarboxaldehyde	25
5	3-Methyl-2-butenal	0 ^b
6	Crotonaldehyde	0 ^b
7	<i>trans</i> -Cinnamaldehyde	0 ^b
8	Acetone	70
9	2-Butanone	90
10	Cyclopentanone	0 ^b
11	Acetophenone	0 ^b
12	Benzophenone	0 ^b

^a GC yield.

^b Based on recovered starting material.

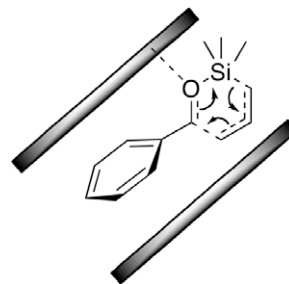


Figure 2. Suggested mechanism for the clay-catalyzed Hosomi–Sakurai reaction.

In summary, we have found that activated Montmorillonite K10 clay efficiently catalyzes the addition of allyltrimethylsilane to electron-deficient aromatic aldehydes as well as some aliphatic aldehydes and ketones at room temperature or below in dichloromethane to give homoallylic silyl ethers in good to excellent yields. This methodology constitutes a milder, environmentally friendlier, and more cost effective alternative to the use of transition metal halides or oxides for the catalysis of the Hosomi–Sakurai reaction.

A typical procedure for the clay-catalyzed Hosomi–Sakurai reaction follows: Montmorillonite K10 clay (200 mg) was added to a glass scintillation vial and heated in an oven at 200 °C for 1 h. The clay was cooled to ambient temperature in a desiccator, and then treated with 3-nitrobenzaldehyde (200 mg, 1.32 mmol) and 2 mL dichloromethane. The mixture was cooled to 0 °C in an ice water bath and stirred gently with a magnetic stir bar. To the cooled mixture was added allyltrimethylsilane (1.98 mmol) and the resulting mixture was stirred at 0 °C for 5 min. The ice water bath was removed and the reaction mixture was allowed to warm to ambient temperature over the course of 1 h. The reaction mixture was vacuum filtered, washed with an additional 1 mL of dichloromethane, and concentrated under vacuum to give the desired product (**2b**) as a pale yellow oil (345 mg, 99%).⁹

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9. *Analytical data for compounds 2a–g*: Proton nuclear magnetic resonance (^1H) spectra and carbon-13 (^{13}C) spectra were recorded at 400 and 100 MHz, respectively. The proton signal of residual, non-deuterated solvent (δ 7.26 ppm for CHCl_3) was used as an internal reference for ^1H 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. Gas chromatographic analysis was performed on a Hewlett–Packard 5890 Series II gas chromatograph with a 5971 Series mass selective detector. *1-Nitro-2-[1-[(trimethylsilyloxy)-3-buten-1-yl]benzene (2a)*: IR (CDCl_3) 3077, 2958, 1701, 1641, 1610, 1577, 1527, 1445, 1346, 1298, 1252 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.89 (m, 2H), 7.63 (m, 1H), 7.40 (m, 1H), 5.86 (m, 1H), 5.38 (dd, $J = 4.05, 7.63$ Hz), 5.07 (m, 2H), 2.52 (m, 1H), 2.41 (m, 1H), 0.05 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.17, 140.64, 139.31, 134.46, 133.12, 128.63, 127.72, 123.98, 117.59, 69.63, 44.24, 0.27; GC–MS (70 eV), $t_{\text{R}} = 11.843$ min, m/z 265 M^+ (<1%); 224 $[\text{M}-41]^+$ (60%); 73 $[\text{M}-192]^+$ (100%). *1-Nitro-3-[1-[(trimethylsilyloxy)-3-buten-1-yl]benzene (2b)*: IR (CDCl_3) 3077, 2958, 2902, 1641, 1432, 1479, 1437, 1351, 1310, 1252 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.19 (s, 1H), 8.10 (ddd, $J = 1.13, 2.26, 8.1$ Hz, 1H), 7.66 (d, $J = 7.72$ Hz, 1H), 7.49 (t, $J = 7.91$ Hz, 1H), 5.75 (m, 1H), 5.02 (m, 2H), 4.81 (dd, $J = 5.56, 6.88$ Hz, 1H), 2.45 (m, 2H), 0.07 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 148.21, 147.12, 133.96, 131.99, 129.06, 122.12, 120.89, 117.88, 73.75, 44.88, 0.05; GC–MS (70 eV), $t_{\text{R}} = 18.158$ min, m/z 265 (<1%); 250 $[\text{M}-15]^+$ (2%); 224 $[\text{M}-41]^+$ (50%); 73 $[\text{M}-192]^+$ (100%). *1-Nitro-4-[1-[(trimethylsilyloxy)-3-buten-1-yl]benzene (2c)*: IR (CDCl_3) 3079, 2958, 2903, 1641, 1607, 1522, 1492, 1432, 1416, 1350, 1316, 1292, 1253 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 8.19 (d, $J = 8.29$ Hz, 2H), 7.49 (d, $J = 8.29$ Hz, 2H), 5.74 (m, 1H), 5.03 (m, 2H), 4.80 (dd, $J = 5.65, 6.78$ Hz, 1H), 2.45 (m, 2H), 0.08 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 152.37, 147.06, 133.93, 126.63, 123.43, 117.85, 73.85, 44.79, 0.02; GC–MS (70 eV), $t_{\text{R}} = 20.424$ min, m/z 265 M^+ (<1%); 224 $[\text{M}-41]^+$ (70%); 73 $[\text{M}-192]^+$ (100%). *1-Fluoro-3-[1-[(trimethylsilyloxy)-3-buten-1-yl]benzene (2d)*: IR (CDCl_3) 3078, 2957, 2903, 1704, 1642, 1616, 1593, 1489, 1450, 1359, 1252 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.30 (m, 1H), 7.10 (m, 2H), 6.95 (m, 1H), 5.80 (m, 1H), 5.06 (m, 2H), 4.72 (dd, $J = 5.46, 7.16$ Hz, 1H), 2.48 (m, 2H), 0.11 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 147.73, 146.57, 134.77, 130.20, 121.4, 118.94, 113.97, 112.61, 72.56, 43.82, 0.06; GC–MS (70 eV), $t_{\text{R}} = 8.711$ min, m/z 238 M^+ (<1%); 223 $[\text{M}-15]^+$ (5%); 197 $[\text{M}-41]^+$ (100%); 73 $[\text{M}-165]^+$ (95%). *1-Chloro-4-[1-[(trimethylsilyloxy)-3-buten-1-yl]benzene (2e)*: IR (CDCl_3) 3078, 2958, 2903, 1641, 1598, 1491, 1432, 1409, 1360, 1295, 1262, 1252 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.30 (m, 4H), 5.77 (m, 1H), 5.05 (m, 2H), 4.68 (dd, $J = 5.46, 7.35$ Hz, 1H), 2.43 (m, 2H), 0.07 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 143.41, 134.77, 132.62, 128.06, 127.28, 117.20, 74.17, 45.04, 0.10; GC–MS (70 eV), $t_{\text{R}} = 11.263$ min, m/z 254/256 $\text{M}^+/\text{M}+2$ (<1%); 213/215 $[\text{M}-41]^+$ (98%); 73 $[\text{M}-181]^+$ (100%). *1,3-Dichloro-2-[1-[(trimethylsilyloxy)-3-buten-1-yl]benzene (2f)*: IR (CDCl_3) 3078, 2958, 1642, 1581, 1562, 1437, 1251 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.29 (m, 2H), 7.11 (m, 1H), 5.81 (m, 1H), 5.50 (m, 1H), 5.05 (dd, $J = 6.40, 8.10$ Hz, 1H), 2.86 (m, 1H), 2.68 (m, 1H), 0.04 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 137.92, 134.73, 129.38, 128.93, 128.60, 117.16, 71.45, 40.00, 0.12; GC–MS (70 eV), $t_{\text{R}} = 13.209$ min, m/z 288/290/292 $\text{M}^+/\text{M}+2/\text{M}+4$ (<1%); 247/249/251 $[\text{M}-41]^+$ (93%); 73 $[\text{M}-215]^+$ (100%). *3-[1-[(Trimethylsilyloxy)-3-buten-1-yl]benzonitrile (2g)*: IR (CDCl_3) 3078, 2958, 2902, 2230, 1641, 1602, 1584, 1482, 1434, 1359, 1285, 1252 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.62 (m, 1H), 7.53 (m, 2H), 7.42 (m, 1H), 5.73 (m, 1H), 5.01 (m, 2H), 4.72 (dd, $J = 5.65, 6.78$ Hz, 1H), 2.41 (m, 2H), 0.06 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 146.41, 134.01, 130.76, 130.33, 129.55, 119.00, 117.79, 112.16, 73.73, 44.89, 0.04; GC–MS (70 eV), $t_{\text{R}} = 14.267$, m/z 245 M^+ (<1%); 230 $[\text{M}-15]^+$ (10%); 204 $[\text{M}-41]^+$ (98%); 73 $[\text{M}-172]^+$ (100%).