CLAY CATALYZED REARRANGEMENT OF SUBSTITUTED ALLYL PHENYL ETHERS: SYNTHESIS OF ORTHO-ALLYL PHENOLS, CHROMANS AND COUMARANS

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Abstract: Montmorillonite clays catalyze the rearrangement of substituted allyl phenyl ethers to provide ortho-allyl phenols, chromans and coumarans under mild conditions.

The [3,3] signatropic shift (Claisen rearrangement) of allyl aryl ethers provides convenient access to *ortho*-allyl phenols, precursors to a variety of natural products, including chromans and coumarans. The difficulty in preparing 2,2-disubstituted ethers such as 1 often renders the Claisen rearrangement inconvenient for the preparation of terminally substituted *ortho*-allyl phenols such as 2. A mild and convenient method to carry out a [1,3] shift¹ of ethers such as 3 is, therefore, desired as a supplementary method to the Claisen rearrangement and the often difficult direct *ortho*-allylation of phenols for the synthesis of substituted *ortho*-allyl phenols. Isolated examples of related rearrangements under forcing acidic conditions have been reported.²



Acid catalysis of organic transformations by clay aluminosilicates is an area of considerable potential and interest due to ease of handling and workup, low corrosiveness and low cost of clays.³ Due to their Brønsted and Lewis acidities, clays, both in their natural and ion exchanged forms, function as efficient catalysts for a variety of important transformations,³ including [3,3] sigmatropic rearrangements^{4a} and aromatic alkylations.^{4b}

The general effectiveness of montmorillonite clay for acid catalysis led us to explore its use for the desired [1,3] shift. We have found that [1,3] and [3,3] rearrangements of substituted allyl phenyl ethers are efficiently catalyzed by montmorillonite clays under mild conditions (Table 1).



Short reaction times or low temperatures permit isolation of the ortho-allyl phenol, while longer reaction times or higher temperatures provide the corresponding chroman or coumaran in moderate yields (Table 1).

Entry	Ether	Temp.°C /Time	e Major Product	Yield
1	\sim	r.t. / 9.0 h ^a		(34%)
2	\sim	= r.t. / 5.3 h	OH 4	(53%)
3	$>\sim$	=< 50 / 4.3 h	5	(61%)
4		°−−< r.t. / 5.2 h		(53%)
5		°−−< 50/8.0 h		(50%)
6	\sim	r.t. / 72 h		(50%)
7		r.t. / 48 h	OH IO	(67%)
8	\sim	= 50 / 25 h		(60%)

Table 1. Summary of montmorillonite clay catalyzed ether rearrangements.

^a r.t. = room temperature

Reported yields are after purification by silica gel column chromatography. Product identification was based on 250 MHz ¹H NMR spectroscopy. In entries 1, 2, 4, 6 and 7 small amounts of starting material (5-15%), cyclized products (2-10%) and *para*-substituted isomers (5-15%, except entry 4) were isolated. Similarly, in entries 3 and 8 approximately 10% *para*-allylated phenol isomers were formed. In Table 1, only compounds isolated in greater than 15% are reported.

Several effects are evident from the results in Table 1. First, it is clear that transfer of the allyl group with retention (in a [1,3] fashion) is most selective when it has two terminal substituents (entries 1-5), presumably due to steric hindrance upon recombination of the prenyl cation with the phenol formed upon acid catalyzed cleavage of the ether. In addition, activating groups on the ring result in a more facile and more efficient rearrangement (entries 2-5, 7 and 8). With ethers containing less substituted allyl groups, such as crotyl (entries 6-8), the regiochemical outcome becomes less predictable, leading to a mixture of [1,3] and [3,3] products with crotyl phenyl ether (entry 6), and almost exclusive [3,3] rearrangement ([3,3]:[1,3] > 20:1) with crotyl dimethylphenyl ether (entry 7). The lack of selectivity for [1,3] rearrangement observed in entries 6 and 7 may be due to the involvement of the well studied charge-accelerated Claisen rearrangement,⁵ which does not occur in the prenyl ethers for steric reasons.

The clay catalyzed reaction does not occur in polar coordinating solvents such as THF and acetonitrile, most likely because of competition for acidic surface sites in these cases,⁶ while noncoordinating solvents such as methylene chloride, benzene and hexane work well. As to whether or not the catalysis is occurring on the outer surface of the clay or in the interlamellar regions, two observations point toward the former. (1) Although intercalation of even highly polar molecules typically takes several hours to occur,⁷ these ether rearrangements are often complete in about five hours, and no induction period is observed; (2) a quick filtration and rinse of the clay is sufficient to achieve nearly 100% mass recovery in these reactions, in contrast to the expected sluggish extractability expected if the products were formed in the interlamellar regions of the clay. Finally, it should be mentioned that preliminary experiments have found that these rearrangements are also catalyzed by 13X zeolites.

In a typical experiment, 0.30g of montmorillonite KSF clay (Aldrich, used as received; montmorillonite K 10 also works) was combined with 6 mL of benzene. Then 0.30 g of the desired allyl phenyl ether was added, the mixture was stirred under nitrogen at the indicated temperature, and the progress of the reaction was followed by thin layer chromatography (TLC). When isolation of the *ortho*-prenylated phenol is desired, the reaction must be carefully monitored by TLC, since formation of the chroman usually begins before all starting material is consumed.

The mixture was then filtered, and the clay was rinsed, in several portions, with 20 mL of ethyl acetate followed by 10 mL of methanol. The solvent was evaporated and the residue was chromatographed on silica gel. Note that although the chroman and starting ethers usually have very similar R_f 's on silica, progress is visible by TLC since the ether and chroman stain different colors with *p*-anisaldehyde. ¹HNMR data or literature references for all products in Table 1 are provided in footnote 8.

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References and Notes:

1. In this paper the [i,j] sigmatropic shift notation is used, although it is not intended to imply concertedness of the rearrangements discussed.

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¹HNMR: 2: see ref. 2b. 4: δ 6.57 (s, 1H), 6.48 (s, 1H), 5.28 (s, 1H), 5.12 (t, 1H), 3.30 (d, 2H), 2.24 (s, 3H),
2.21 (s, 3H), 1.79 (s, 3H), 1.70 (s, 3H). 5: δ 6.60 (s, 1H), 6.55 (s, 1H), 2.64 (t, 2H), 2.28 (s, 3H), 2.24 (s, 3H),
1.86 (t, 2H), 1.36 (s, 6H). 6: δ 6.76-6.64 (m, 3H), 5.30 (t, 1H), 4.85 (s, 1H), 3.76 (s, 3H), 3.33 (d, 2H), 1.77 (s,
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and 9: see ref. 2b. 10: see Von Borgulya, J.; Madeja, R.; Fahrni, P.; Hansen, H.-J.; Schmid, H. Helv. Chim. Acta
1973, 56, 14. 11: δ 6.52 (s, 1H), 6.47 (s, 1H), 4.76 (m, 1H), 3.22 (m, 1H), 2.28 (s, 6H), 1.48 (d, 3H), 1.10 (d, 3H).

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