Montmorillonite-mediated hetero-Diels–Alder reaction of alkenes and *o*-quinomethanes generated *in situ* by dehydration of *o*-hydroxybenzyl alcohols

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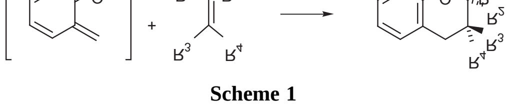
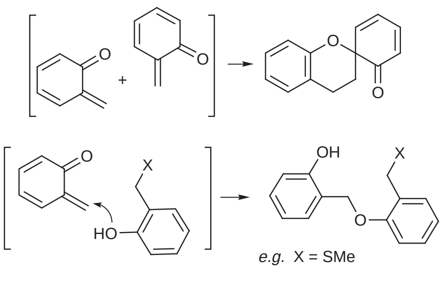
Received (in Cambridge, UK) 25th January 1999, Accepted 9th March 1999

The intermolecular hetero-Diels–Alder reaction of *in situ*-generated *o*-quinomethanes and unactivated alkenes has been accomplished through a wet montmorillonite catalyst in a $LiClO_4$–$MeNO_2$ solution to give good yields of varied chromane skeletons.

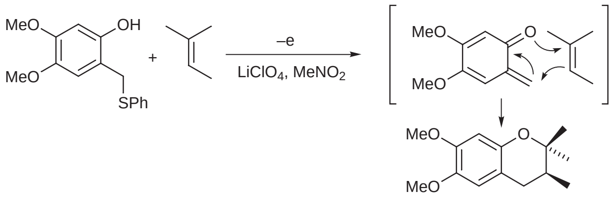
o-Quinomethanes play an important role as the heterodiene in the construction of a wide variety of chromane skeletons *via* hetero-Diels–Alder reaction with alkenes (Scheme 1). The generation and cycloaddition of *o*-quinomethanes has been extensively investigated, including pyrolysis of *o*-hydroxybenzyl alcohols,[1] one-electron oxidation of *o*-substituted phenols,[2] desilylation of an *o*-hydroxybenzyl alcohol disilyl ether,[3] and dehydrogenation of allylphenols with DDQ.[4] However, as the *o*-quinomethanes are generally very unstable, they must be trapped by highly active, electron-rich alkenes, by intramolecular reactions, or under high-temperature conditions. Furthermore, by-products of the homo-Diels–Alder reaction, Michael addition, or Friedel–Crafts reaction of *o*-quinomethanes have also often been obtained with desired products (Scheme 2).[5] On the other hand, it has been proposed that many natural products can be generated *via* the intermolecular cycloaddition of *o*-quinomethanes and aliphatic alkenes.[6] Biogenetically, it has been proposed that *o*-quinomethanes are produced by the dehydration of the corresponding *o*-hydroxybenzyl alcohols or benzylic oxidation of the corresponding *o*-cresol derivatives.[7] Biomimetic mild reaction media in which *o*-quinomethanes are generated and trapped efficiently by unactivated aliphatic alkenes have therefore been sought. Recently, we performed the intermolecular hetero-Diels–Alder reaction of electrochemically generated electon-rich *o*-quinomethanes and unactivated aliphatic alkenes to construct some natural product skeletons, but the *o*-quinomethanes were limited to stable ones possessing electron-donating groups (Scheme 3). Accordingly we have further investigated the biomimetic facile method for the generation and cycloaddition reaction of *o*-quinomethanes, and found that a catalytic amount of wet montmorillonite in a $LiClO_4$–$MeNO_2$ solution efficiently generated *o*-quinomethanes by the dehydration of the corresponding *o*-hydroxybenzyl alcohol. The reaction media showed a remarkable acceleration property in the generation and intermolecular cycloaddition of the unstable *o*-quinomethanes with varies unactivated alkenes.



Scheme 1



Scheme 2



Scheme 3

Under the usual dehydration conditions of benzyl alcohols using Lewis acids or Brønsted acids, salicyl alcohol and 2-methylbut-2-ene **3** gave the corresponding cycloadducts **10** and **11** in very low yields (Table 1). On the other hand, a catalytic amount of dry montmorillonite K 10 in $MeNO_2$ gave the desired cycloadducts in 26.8%, and the addition of $LiClO_4$ effectively increased the yield to 54.8%. Furthermore, the reaction proceeded to give **10** and **11** (6 : 1) almost quantitatively by using wet montmorillonite K 10 in the presence of $LiClO_4$ in $MeNO_2$ at ambient temperature. The wet montmorillonite did not work well in other solvents, even in the presence of $LiClO_4$. Accordingly, the targeted reactions with varied alkenes were performed in $MeNO_2$ in the presence of an *o*-hydroxybenzyl alcohol, wet montmorillonite, and $LiClO_4$ at ambient temperature.† Styrenes gave excellent yields of the corresponding flavanes, while unactivated aliphatic alkenes simply gave chromanes and spirochromanes in good yields (Table 2). Some products were obtained due to skeleton rearrangement of the alkene moieties (Scheme 4).

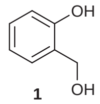
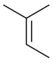
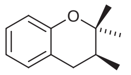
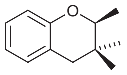
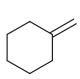
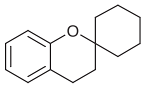
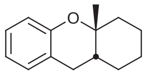
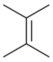
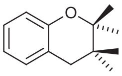
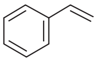
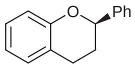
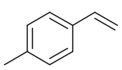
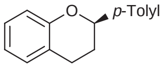
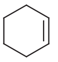
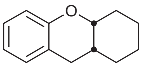
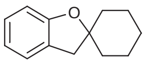
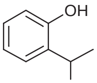
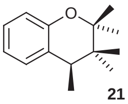
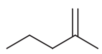
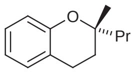
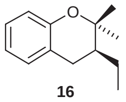
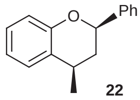
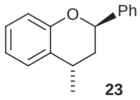
In the present reaction media, the dehydration reaction may be accelerated on the wide surface of montmorillonite, and the

Table 1 Effect of catalysts and reaction media on the cycloaddition of **3** and *o*-quinomethane generated by the dehydration of salicyl alcohol **1**[a]

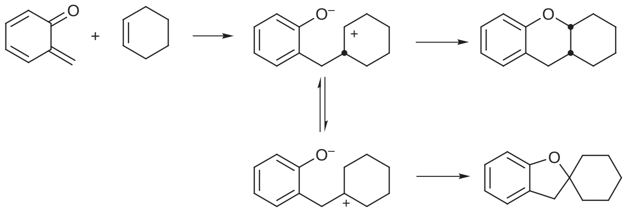
Solvent	Catalyst	Additive	Yield (%)
CH_2Cl_2	$TiCl_4$[b]	none	12.7
CH_2Cl_2	BF_3/Et_2O[b]	none	13.7
CH_2Cl_2	$ZnCl_2$[b]	none	1.8
CH_2Cl_2	MsOH[b]	none	17.1
CH_2Cl_2	P_2O_5[b]	none	10.6
MeCN	wet mont.[c]	$LiClO_4$[e]	12.1
Et_2O	wet mont.	$LiClO_4$	trace
CH_2Cl_2	wet mont.	$LiClO_4$	trace
$MeNO_2$	wet mont.	none	15.8
$MeNO_2$	dry mont.[d]	none	26.8
$MeNO_2$	dry mont.	$LiClO_4$	54.8
$MeNO_2$	wet mont.	$LiClO_4$	> 99

[a] 20 mg of **1** and 3 equiv. of **3** were dissolved in 2.0 ml of solvent. [b] 1.5 equiv. of catalyst was added. [c] 20 mg of montmorillonite and 36 mg of water were added to 2 ml of solvent. [d] 20 mg of montmorillonite was added to 2.0 ml of solvent. [e] 200 mg of $LiClO_4$.

Table 2 Montmorillonite-mediated cycloaddition of *o*-quinomethanes and alkenes[a]

Substrate	Alkene	Products	Yield (%)	Substrate	Alkene	Products	Yield (%)
 **1**	 **3**	 **10**  **11** (**10**:**11**=6:1)	>99	**1**	 **7**	 **17**  **18** (**17**:**18**=1.7:1)	78
1	 **4**	 **12**	>99	**1**	 **8**	 **19**	94
				1	 **9**	 **20**	>99
1	 **5**	 **13**  **14** (**13**:**14**=2:1)	>99	 **2**	**4**	 **21**	76
1	 **6**	 **15**  **16** (**15**:**16**=4:1)	85	**2**	**8**	 **22**  **23** (**22**:**23**=2:1)	79

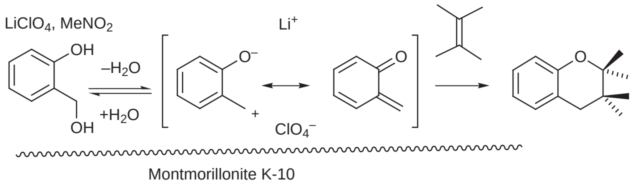
[a] 2-Hydroxybenzyl alcohol (20 mg) and 3 equiv. of alkene were dispersed in 2.0 ml of 0.1 M $LiClO_4$–$MeNO_2$ in the presence of 20 mg of montmorillonite and 36 mg of water. The reaction mixture was allowed to stand at ambient temperature for 48 h.



Scheme 4

addition of water might regulate the acidic decomposition and polymerization of starting materials. $LiClO_4$ is expected to stabilize the *in situ*-generated zwitterion, which is an equivalent of the *o*-quinomethane (Scheme 5). Furthermore, the products are easily extracted from the reaction media with *n*-hexane, and the catalytic solvent system can be reused many times. Employing the hetero-Diels–Alder reaction of *o*-quinomethanes in $LiClO_4$–$MeNO_2$ mediated by wet montmorillonite K 10 is applicable to the formation of a variety of chromanes. In these cases involving unsubstituted, unstable *o*-quinomethanes, the cycloaddition reactions with unactivated alkenes proceeded smoothly to give cycloadducts, including those which are difficult to obtain in high yields *via* other methods.

This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas (No. 283, 'Innovative Synthetic Reactions') from the Ministry of Education, Science, Sports and Culture, Japan.



Scheme 5

Notes and references

† *General procedure:* Montmorillonite K 10 (Aldrich) and water were dispersed in 5 ml of $MeNO_2$, and salicyl alcohol **1** (25 mg), styrene **8** (63 mg) and $LiClO_4$ (50 mg) were dissolved in the solution. The reaction mixture was allowed to stand at ambient temperture for 48 h under air atmosphere. After the reaction was completed, products were extracted with *n*-hexane. The *n*-hexane was removed *in vacuo* after drying with Mg_2SO_4, and the residue was then separated by silica gel column chromatography (*n*-hexane–AcOEt) to give the cycloadduct **19** in 94% yield.

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Communication 9/00657E