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H-type Zeolite-Catalyzed 1,4-Addition of Benzene Derivatives to Labile Acrolein

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Abstract

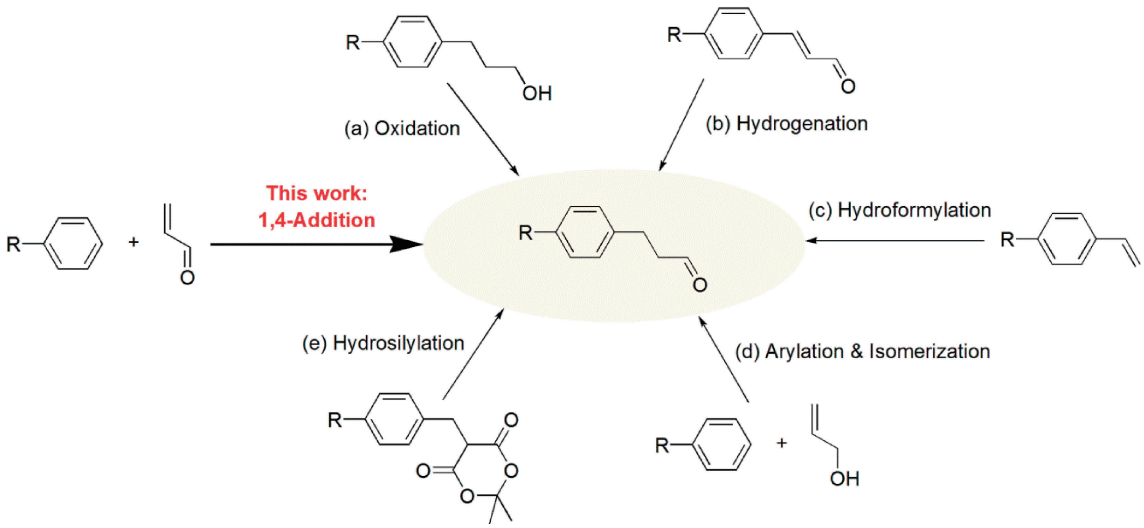
The 1,4-addition of benzene derivatives to acrolein is a straightforward way to synthesize 3-arylpropanals. A survey of acid catalysts for the 1,4-addition of methoxy-substituted benzenes to acrolein revealed that H-Beta and H-Y were the most suitable catalysts. We hypothesized three side-reactions: (1) the double 1,4-addition of acrolein to the starting benzene derivatives, (2) the Friedel–Crafts-type alkylation to the desired product, and (3) the self-polymerization of acrolein. The type (3) side-reaction was inhibited by two different methods which kept the concentration of acrolein low in the reaction mixture or in the zeolite pores. First, acrolein monomers were in situ generated through the gradual monomerization of an acrolein cyclic trimer. Second, using a reaction solvent lowered the acrolein concentration in the zeolite pores due to the competitive adsorption. We discovered that the content of monomeric acrolein in a solvent was closely related to the polarity of the solvent. Actually, both methods improved the yields for the 1,4-additions of 1,3-dimethoxybenzene to acrolein. Other electron-rich benzene derivatives, such as phenol and *N*,*N*-dimethylaniline, were also applicable to the 1,4-addition reactions.

1. Introduction

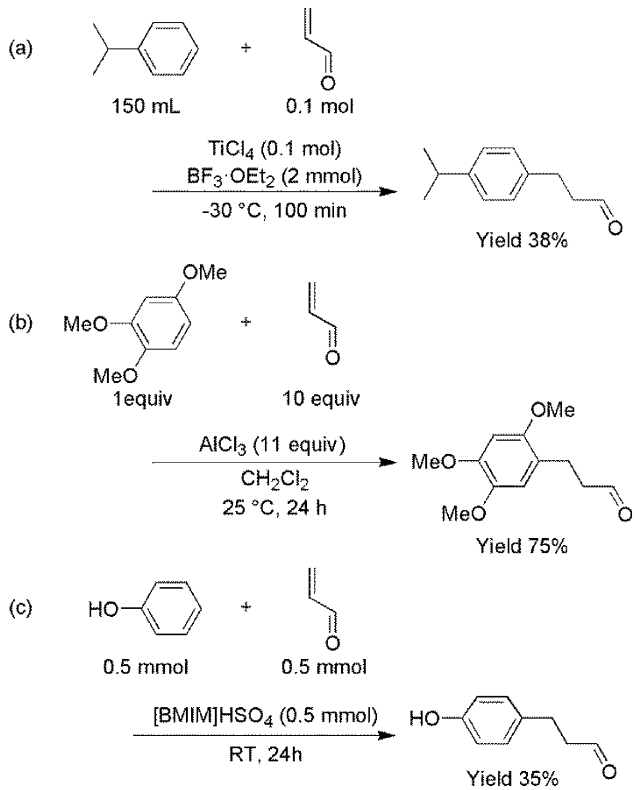
Acrolein is the smallest unsaturated aldehyde as a useful electrophile through 1,4-addition (the Michael addition) to extend a three-carbon unit holding a formyl group on its edge.[1] However, acrolein so easily polymerizes that it has a limited potential for fine chemical syntheses, especially in lab-scale experiments in comparison with other relatively stable α,β-unsaturated carbonyl compounds. The 1,4-additions to acrolein usually proceed using powerful nucleophiles, such as 1,3-dicarbonyl compounds,[2–4] nitroalkanes,[5] and secondary amines,[6,7] in the presence of bases, such as 1,8-diazabicyclo[5.4.0]undec-7-ene,[6] Al_2O_3,[2] and alkali metal ion exchanged zeolites.[3] On the other hand, the 1,4-addition of aromatic compounds to acrolein requires suitable acid catalysts in order to activate the electrophile because it is usually difficult to abstract a proton from the aromatic ring to activate the nucleophile under basic conditions. Electron-rich heteroaromatic compounds, such as indole[8] and furan[8b,9] are mainly employed as aromatic donor reagents.

The 1,4-addition of benzene derivatives to acrolein is a one-step aromatic substitution reaction to generate 3-arylpropanals as compared with the other routes, such as (a) oxidation of 3-arylpropan-1-ol,[10] (b) selective hydrogenation of cinnamyl aldehydes,[11] (c) hydroformylation of styrenes,[12] (d) arylation of allylic alcohols followed by isomerization,[13] and (e) hydrosilylation of cyclic malonates[14] (Scheme 1).

The previous 1,4-addition of benzene derivatives to acrolein has been found only in the following three articles, indicating a limited substrate scope for the reaction: Alkyl-substituted benzenes, such as toluene, cumene, and *tert*-butylbenzene, added



Scheme 1. Various synthetic routes for 3-arylpropanals.



Scheme 2. Previous studies of the 1,4-addition of benzene derivatives to acrolein.

to acrolein using a stoichiometric amount of $TiCl_4$, in up to a 38% yield (Scheme 2a).[15] The stoichiometric use of $AlCl_3$ converted a highly electron-rich nucleophile, 1,2,4-trimethoxybenzene, into 3-arylpropanal in moderate yield (Scheme 2b).[16] As the third example, the selective *para*-alkylation of phenol rather than the oxa-Michael addition of phenol was conducted using an acidic ionic liquid in the poor yield of 35% (Scheme 2c).[17]

The 1,4-addition of benzene derivatives to α,β-unsaturated carbonyl compounds such as ketones, esters, and amides typically proceeds using stoichiometric amounts of metal halides, such as $AlCl_3$[16,18] and $TiCl_4$,[15] or the catalytic use of $AuCl_3$.[8b,19] In the case of the metal halides, large amounts of metal hydroxides as well as hydrogen halides are produced as by-products after work-up with aqueous bases. Therefore, performing the reaction using heterogeneous catalysts is preferred in terms of the green chemistry concept. Among the heterogeneous catalysts, zeolites having relatively large pores are very promising for the 1,4-addition reactions because the zeolites have practical advantages of easy separation from the organic products, safe handling and recyclability.

Recently, we reported that once small, labile organic compounds, such as formaldehyde and acrolein, were encapsulated in a Na-type zeolite, they were able to remain as monomers in the zeolite cavities for a long time even at ambient temperature.[8c,20] Our quantum chemical calculations of models of zeolite-encapsulated formaldehyde and 1,3,5-trioxane, a cyclic trimer of formaldehyde, revealed that the equilibrium between three molecules of formaldehyde and one molecule of 1,3,5-trioxane inside Na-Y lies to the former.[21] This is because the three formaldehyde molecules are not only advantageous in terms of entropy, but are also more thermodynamically stabilized by the coordination to sodium ions in the zeolite than the 1,3,5-trioxane. The zeolite-entrapped aldehydes were not only well stabilized in the zeolite pores, but also demonstrated to be sufficiently activated to react with some nucleophiles, such as olefins and indoles, to produce homoallylic alcohols through the Prins reaction and 3-(1*H*-indol-3-yl)propanal via 1,4-addition, respectively.[8c,20] As another example of the acrolein activated by Na-Y, the 1,4-addition to anisole successfully proceeded to yield 3-(4′-methoxyphenyl)propanal.[8c] In this case, however, a *large* amount of Na-Y and harsh anisole reflux conditions were required to obtain the 1,4-addition product in a fair yield. To perform this reaction in the presence of a *catalytic* amount of a zeolite under much milder conditions, we focused on using acidic H-type zeolites instead of Na-type zeolites.

When these acidic zeolites are used, we always have to keep in mind that acrolein easily polymerizes under acidic conditions. Once part of the acrolein polymerizes in the zeolite

pores, the complete extraction of organic compounds with organic solvents from the zeolite pores as well as the quantitative analysis of the products, intact acrolein and polymers would be difficult. The acrolein polymerization can be suppressed by keeping the concentration of acrolein low. For this purpose, two protocols were attempted: (1) The gradual formation of an acrolein monomer through the in situ monomerization of a cyclic trimer of acrolein, and (2) the proper selection of a specific solvent.

A cyclic trimer of acrolein, 2,4,6-trivinyl-1,3,5-trioxane, is a 1,3,5-trioxane on which three vinyl units are substituted at the 2,4,6-carbons on the trioxane ring.[22] Trioxane derivatives are expected to be monomerized under acidic conditions to generate the labile aldehydes,[23] but there have been no reports about the use of the trioxane derivative as a source of acrolein as well as the generation of aldehydes at an appropriate rate. We presumed that the gradual monomerization of the trimer would supply acrolein to a reaction system in a preferable concentration.

Derouane reported that in the liquid-phase reactions catalyzed by zeolites, the concentration of reactants and/or products in the zeolite pores were different from that in the solution part due to the competitive adsorption of reactants, products, and solvent into the zeolites.[24] This selective adsorption is mainly governed by the polarity of each compound, and thus the choice of the solvent affects the concentration of reactants and products in the zeolite pores.[25] The solvent effect is responsible for the reaction rates, because a solvent competes with reactants to diffuse in the zeolite pores, and to be adsorbed on the active sites.[26] That is to say, in a highly polar solvent, the concentration of reactant is low in the zeolite pores, and the reaction rate is decreased. Moreover, limiting the contact time of products with the active sites in a highly polar solvent can reduce the reaction rate of the consecutive reaction.[26a] By exploiting this competitive adsorption effect of the solvent, we expect that the solvent choice would lessen the undesired acrolein polymerization.

2. Experimental

2.1 Zeolites and Materials. Na-Y (Si/Al = 2.8, HSZ-320NAA), H-Y (Si/Al = 15, HSZ-371HUA), and H-Mor (Si/Al = 120, HSZ-690HOA) as powders were obtained from the Tosoh Corporation (Tokyo, Japan). H-Beta (Si/Al = 75, JRC-Z-HB150) and SiO_2–Al_2O_3 (Si/Al = 5, JRC-SAL-2) as powders were provided by the Catalysis Society of Japan. The cation-exchange capacity of the zeolites is generally the same as the aluminum content in the zeolite framework,[27] so we simply calculated the aluminum contents of Na-Y, H-Y, and H-Beta from the Si/Al ratio of each zeolite to be 4.0, 1.1, and 0.22 mmol g^{-1}, respectively. Each zeolite was activated at 400 °C/<26 Pa for 2 h just before use.

2.2 Procedures. 2.2.1 General Procedure for the 1,4-Addition of Benzene Derivatives to Acrolein: To the activated H-type zeolite (0.10 g) in a 10-mL flask was added a benzene derivative (10 mL or 10 g) of a reactant as well as a solvent at the specified reaction temperature. After the mixture was stirred for more than 10 min, acrolein (1.0 mmol) was added over a period of one minute. After the reaction was completed, the reaction vessel was placed in an ice-water bath, and ethanol (5 mL) was added. The mixture was stirred for 10 min, and then the H-type zeolite was removed by filtering through a 10–16 μm sintered glass funnel, washed with ethanol (20 mL) and ethyl acetate (20 mL). To the combined filtrate was then added an internal standard substance, and the mixture was analyzed by gas chromatography (GC). The reaction yields by GC analysis were calculated based on the amount of the added acrolein. When a decreased amount (10 or 1.0 mmol) of a benzene derivative was used, a benzene derivative in a certain solvent (10 mL) was added to the activated H-Beta zeolite (0.10 g) in a 10-mL flask. The yields of only **2g** and **2h** were obtained by isolation.

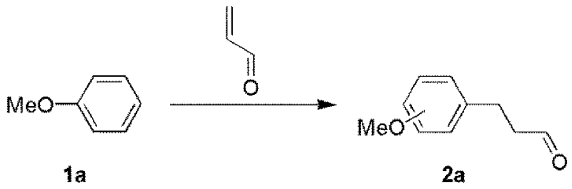
2.2.2 Time-Course Measurements of the Amount of Intact Acrolein: From a mixture of acrolein (1.0 mmol), cyclohexane (40 μL), and solvent (5 mL) was collected an aliquot (0.1 mL). This aliquot was diluted with 1-propanol (1 mL) to analyze by GC. To the activated H-Beta (0.10 g) in a 10-mL flask was added the remaining mixture (ca. 5 mL) and solvent (5 mL). After the flask was immersed in a water bath at RT, the mixture was stirred. Each aliquot (0.2 mL) was periodically picked up from the mixture. The aliquot was diluted with 1-propanol (1.5 mL) and filtered through a 0.2 μm syringe filter. The filtrate was analyzed by GC, and the area ratio of cyclohexane to acrolein in each sample was compared with that of the starting one.

3. Results and Discussion

3.1 Comparison between Acid Catalysts for the 1,4-Addition of Anisole to Acrolein. We previously reported that the addition of anisole (**1a**) to acrolein was induced by Na-Y in a fair yield (Table 1, Entry 1),[8c] but that for the reaction to proceed it required a large excess amount of anisole playing the roles of both a reactant and a solvent, a large amount of Na-Y (1.0 g) and the high reaction temperature of 154 °C. We then searched for a much better catalytic system using homogeneous and heterogeneous catalysts under much milder reaction conditions for the 1,4-addition.

Though Na-Y (1.0 g) gave **2a** in 66% yield under harsh conditions at the reflux temperature of anisole (154 °C, Entry 1), the catalytic use of Na-Y (0.1 g) at 60 °C did not induce **2a** (Entry 2). The catalytic use of H-Y (0.1 g) successfully gave **2a** even at 60 °C in 77% yield with an 87% *para*-selectivity (Entry 3). In this reaction, the turnover number (TON) is defined as the **2a** amount divided by the total amount of exchangeable cations in the zeolite which is simply calculated from the Si/Al ratio of the zeolite. The TON of Entries 1 and 3 were 0.2 and 7, respectively, proving that the protons in the zeolite H-Y functioned as a real catalyst. Amorphous silica alumina showed only the low catalytic activity of 8% yield (Entry 4). Homogeneous catalysts of (±)-10-camphorsulfonic acid and BF_3·OEt_2 showed no or poor activities in 0% and 26% yields, respectively (Entries 5 and 7). The stoichiometric use of $AlCl_3$ resulted in only a 17% yield of **2a** (Entry 6). It was reported that $AlCl_3$ showed a moderate activity for the 1,4-addition of anisole to methyl vinyl ketone (MVK, Supporting Information Scheme S1),[18a] though MVK is a less electrophilic α,β-unsaturated carbonyl compound than acrolein.[4] $AlCl_3$ was considered to accelerate the acrolein polymerization rather than the formation of **2a**.

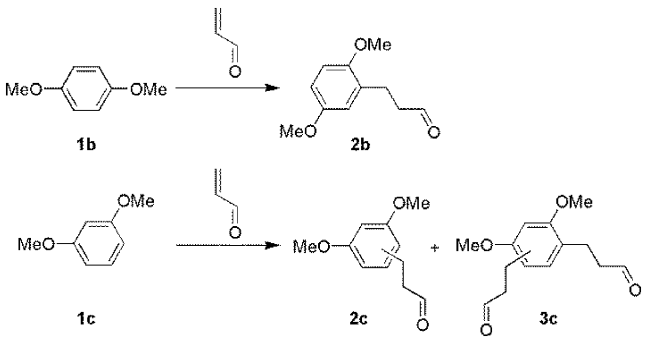
Table 1. 1,4-Addition of anisole to acrolein with homogeneous or heterogeneous catalysts[a)]



1a **2a**

Entry	Catalyst	Amount	Temp./°C	Time/h	Yield[b)]/%	*para*:*ortho*	TON[c)]
1[d)]	Na-Y	1.0 g	154	12	66	84:16	0.2
2	Na-Y	0.1 g	60	3	0	—	0
3	H-Y	0.1 g	60	3	77	87:13	7
4	SiO_2–Al_2O_3	0.1 g	60	3	8	85:15	—
5[e)]	CSA[f)]	0.1 mmol	60	0.3	0	—	0
6[e)]	$AlCl_3$	1.0 mmol	−30	0.5	17	86:14	0.2
7[e)]	BF_3•OEt_2	0.1 mmol	60	3	26	84:16	3

a) Reaction conditions: anisole (10 mL), acrolein (1.0 mmol). b) No 1,2-addition products were formed in any case. c) Turnover number (the amount of **2a**/the total amount of exchangeable cations in zeolite). d) Data were quoted from ref. 8c. e) Anisole (5 mL). f) (±)-10-Camphorsulfonic acid.



Scheme 3. Methoxy-substituted benzenes **1b** and **1c** and their 1,4-adducts **2b**, **2c**, and **3c**.

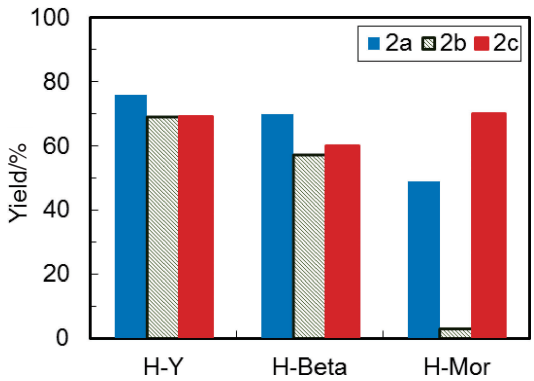


Figure 1. 1,4-Addition of methoxy-substituted benzenes **1a**–**1c** to acrolein with H-type zeolites. Reaction conditions: **1a**–**1c** (10 mL or 10 g), acrolein (1.0 mmol), H-type zeolite (0.10 g), 3 h. Reaction temperature was 60 °C (**2a** and **2b**) or RT (**2c**).

The preferable 1,4-addition reaction to the acrolein polymerization using H-Y should be partly attributed to the initial high concentration of anisole in the zeolite pores. Before the addition of acrolein, a mixture of H-Y and anisole was stirred for a certain time to fill the zeolite pores with anisole molecules. This addition protocol would keep the acrolein diluted in the zeolite pores at the beginning of the reaction.

3.2 Effects of the Zeolite Type. The appropriate zeolites for the 1,4-addition to acrolein were explored among the 12-membered ring zeolites, such as H-Y, H-Beta, and H-Mor, whose pore sizes are large enough to accommodate the reactants. In addition to anisole **1a**, two isomeric dimethoxybenzenes **1b** and **1c** were selected (Scheme 3 and Figure 1). By using H-Y, H-Beta, and H-Mor, **2a** and **2c** were obtained in moderate yields. H-Y and H-Beta gave **2b** in moderate yields, while H-Mor only showed a low activity. The one-dimensional pores of H-Mor have narrower spaces than the three-dimensional ones of H-Y and H-Beta. Due to the steric effect on the bulky transition state leading to **2b** inside the one-dimensional Mor pores, the activation energy for **2b** in H-Mor was higher than that in H-Y or H-Beta, resulting in the poor yield. There was also the steric effect on the bulky transition state leading to **2c** inside the Mor pores, but **1c** has a much higher reactivity to acrolein than **1b** due to the cooperative *ortho*–*para* orientation of the two methoxy groups at the 1,3-positions, so H-Mor produced a fair yield of **2c**.

The results under the optimized conditions for H-Y or H-Beta are summarized in Table 2 (Supporting Information Figure S1). **2a** was obtained in 79% and 83% in only 15 min by using H-Beta and H-Y, respectively. H-Beta showed a higher *para*-selectivity than H-Y (90% vs. 85%, Entries 1 and 2). The 1,4-addition of **1c** with H-Y displayed a higher yield of **2c** than H-Beta, but both zeolites had similar excellent regioselectivities to *para*-**2c** (Entries 5 and 6). In case of the **2b** synthesis, however, H-Beta showed a much higher yield than did H-Y (77% vs. 69%, Entries 3 and 4). Based on the results in Figure 1 and Table 2, we judged that H-Beta exhibited a slightly higher catalytic activity than H-Y. Hereafter, all the 1,4-additions were conducted using H-Beta.

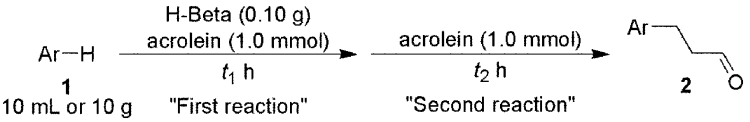
3.3 Deactivation of Zeolite during the Reaction. H-Beta was able to catalyze the 1,4-addition to acrolein, but gave the desired products in only moderate 64–79% yields of **2a**–**2c** (Table 2, Entries 1, 3, and 5), so H-Beta was considered to be deactivated during the reactions by the strong adsorption of by-

Table 2. 1,4-Addition of methoxy-substituted benzenes to acrolein with H-Beta or H-Y[a)]

Entry	Reactant	Zeolite catalyst	Temp. /°C	Time /h	Product[b)]	Yield /%	Regioselectivity of **2**[c)]/%
1	**1a**	H-Beta	80	0.25	**2a**	79	90
2	**1a**	H-Y	80	0.25	**2a**	83	85
3	**1b**	H-Beta	80	3	**2b**	77	—
4	**1b**	H-Y	60	3	**2b**	69	—
5	**1c**	H-Beta	0	3	**2c**	64	98
6	**1c**	H-Y	RT	3	**2c**	69	97

a) Reaction conditions: methoxy-substituted benzenes **1a**–**1c** (10 mL or 10 g), acrolein (1.0 mmol), zeolite (0.10 g). b) **3c** was obtained in 6% and 7% yields in Entries 5 and 6, respectively. Only a trace amount of the dialkylated product **3a** was observed by GC, and **3b** was not detected. c) Regioselectivity of the *para*-adduct for **2a** and that of the 4-adduct for **2c**.

Table 3. Catalytic activity of H-Beta by an additional 1,4-addition reaction[a)]



Entry	Reactant	Temp. /°C	t_1/h (First reaction)	t_2/h (Second reaction)	Total amount of **2**/mmol	Ratio[b)]
1	**1a**	80	0.25	2	1.40	1.78
2	**1b**	80	3	24	1.23	1.61
3	**1c**	0	3	24	1.18	1.85

a) Reaction conditions: **1a**–**1c** (10 mL or 10 g), acrolein (1.0 mmol + 1.0 mmol), H-Beta (0.10 g). b) The ratio of the total amount of **2** after the second reaction to the yield of **2** after the first reaction which was adopted from Table 2.

products having higher molecular weights or multifunctional groups, which would be generated by the self-polymerization of acrolein, the poly-1,4-additions of **1** to acrolein, and other types of consecutive reactions.[28]

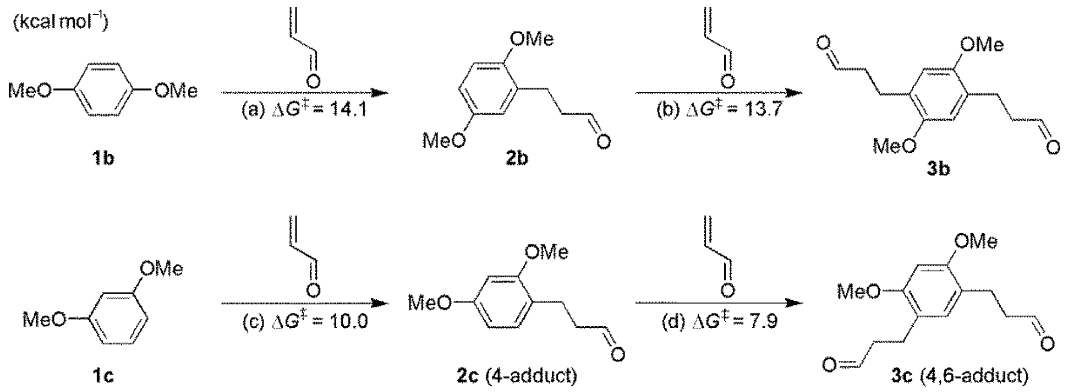
We investigated whether or not H-Beta was deactivated during the reaction as follows: After the first trial of the reaction for t_1 hours according to the reaction conditions shown in Table 3, to the reaction mixture was added one millimole of acrolein and the mixture was continued to be stirred for t_2 hours as the second reaction. The total amount of the product **2** was obtained by GC after the second reaction was completed. We calculated the ratio of the total yield of **2** after the second reaction to the yield of **2** after the first one which was adopted from the yield in Table 2. Using this ratio, we can compare the catalytic activity of H-Beta between the first and second reactions. For example, the ratio of 1.60 indicates that in the second reaction, the catalyst H-Beta maintains three fifths of the catalytic activity for the second run. Based on the ratios in Table 3, we concluded that H-Beta was not completely deactivated but still had a sufficient catalytic ability to induce the 1,4-addition to acrolein.

We proposed the reason why we only obtained the desired products **2** in moderate yields as follows: (1) Two types of consecutive reactions from the desired product would occur; the poly-1,4-additions of **1** to acrolein and the Friedel–Crafts-type additions of **1** to the formyl group in **2**, and (2) the self-polymerization of acrolein would competitively take place. We now show that (1) and (2) actually occur, and provide solutions to suppress them.

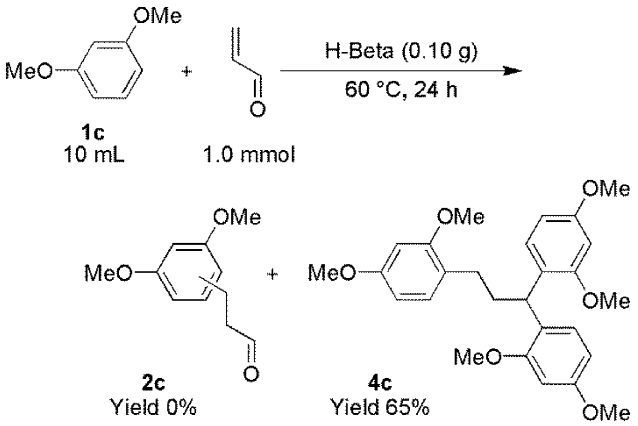
3.4 Consecutive Reactions from the Desired Product. The poly-1,4-addition of **1** to acrolein is feasible because the nucleophilicity of a monoalkylated benzene gets enhanced compared with that of the starting benzene compound. In fact, the dialkylated product **3c** was produced and isolated in 6% yield, while **3b** was not detected by GC (Table 2). Tri- or tetra-alkylated products were not observed for any of the benzene derivatives. There some possibility that such polyalkylated products would get clogged in the zeolite pores and never be extracted from the pores.[29]

We compared the activation energies between the monoalkylation and the dialkylation of **1b** as well as **1c** with acrolein by a computational chemical approach to judge if the dialkylation preferentially occurs. In order to simplify the quantum chemical calculations, a protonated dimethyl ether was employed to simulate a Brønsted acid site in the H-type zeolite framework. The reactions of each benzene derivative of **1b**, **2b**, **1c**, and **2c** with a protonated acrolein were estimated by the calculations (Scheme 4, Supporting Information Section V). The activation energy of step (d) ($\Delta G^{\ddagger} = 7.9\,\mathrm{kcal\,mol^{-1}}$) was $2.1\,\mathrm{kcal\,mol^{-1}}$ lower than that of step (c) ($\Delta G^{\ddagger} = 10.0\,\mathrm{kcal\,mol^{-1}}$), while that of step (a) ($\Delta G^{\ddagger} = 14.1\,\mathrm{kcal\,mol^{-1}}$) and step (b) ($\Delta G^{\ddagger} = 13.7\,\mathrm{kcal\,mol^{-1}}$) were close to each other. Though the 1,4-addition of **2c** is expected to easily proceed based on the calculations, **3c** was only obtained in 6% yield (Table 2, Entry 5). Therefore, we can conclude that the 1,4-addition of **2b** to acrolein scarcely proceeds.

The Friedel–Crafts reaction of **2** with two molar equivalents of **1** may take place at the formyl carbon of **2** through dehydra-



Scheme 4. Computed activation energies for the 1,4-addition (calculated at M06-2X/6-311G(d,p) level).



Scheme 5. Friedel–Crafts reaction of **2c** with **1c**.

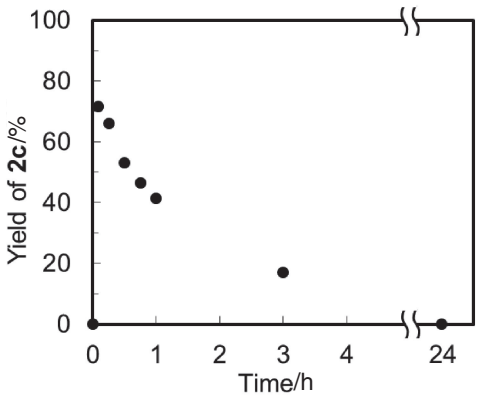
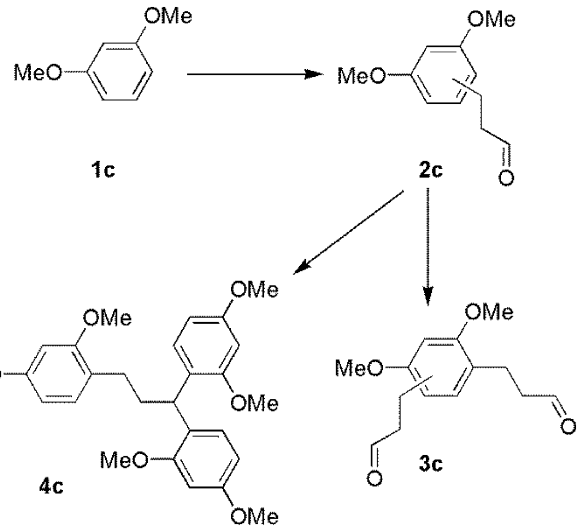
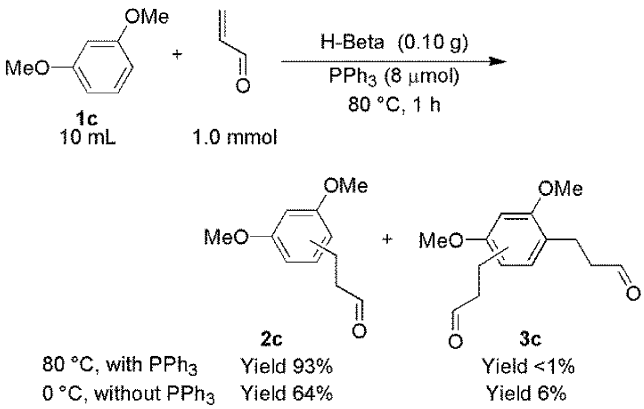


Figure 2. The time-course measurement for the formation and consumption of **2c**. Conditions: **1c** (10 mL), acrolein (1.0 mmol), H-Beta (0.10 g), 60 °C.



Scheme 6. Two types of consecutive reactions from **2c**.



Scheme 7. Treatment with or without PPh_3 in 1,4-addition reaction of **1c** to acrolein.

tion to form **4**.[30] In fact, the formation of a by-product **4c** was observed only for the Friedel–Crafts reaction of **2c** with **1c** at 60 °C (Scheme 5), in which the amount of **2c** rapidly increased at the beginning, and then gradually decreased as shown in Figure 2.

These two types of consecutive reactions from **2c** might preferentially occur on the outer surface of H-Beta, because the dimensions of **3c** and **4c** are larger than the pore size of H-Beta (Scheme 6). We expected that poisoning the acid sites on the outer surface of H-Beta with a base compound precluded the formations of **3c** and **4c**. Since a bulky base, triphenylphosphine (PPh_3), is often used to selectively poison the outer surface of H-Beta, not the inner one,[31] we attempted the 1,4-addition in the presence of a catalytic amount of PPh_3, which was about one-third of the total amount of the acid sites included in H-Beta (Scheme 7). The addition of PPh_3 effectively increased the yield of **2c** to 93%, and concurrently decreased the yield of **3c** to <1% compared with those under the conditions without PPh_3 (Table 2, Entry 5). The positive suppression of the consecutive reactions directly indicated that

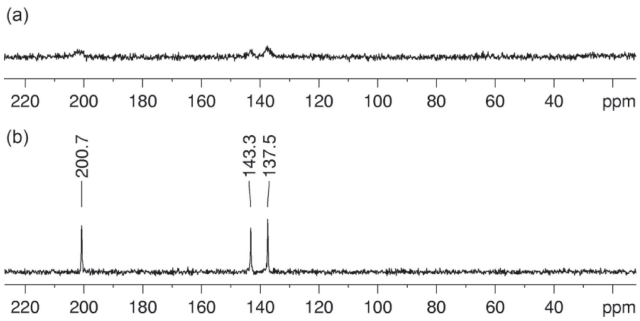


Figure 3. ^{13}C DD/MAS NMR spectra of acrolein adsorbed zeolites. (a) Acrolein(1.1)@H-Y, 8192 scans, (b) acrolein(1.2)@Na-Y, 1024 scans.

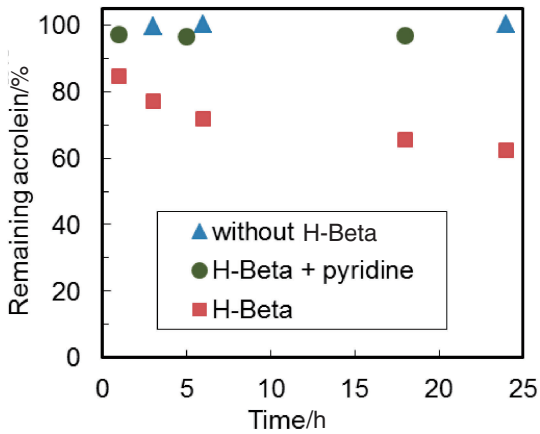


Figure 4. The time-course analysis of the remaining acrolein monomer amount in toluene with or without H-Beta. Common conditions: toluene (10 mL) and acrolein (1.0 mmol) at RT. (▲): without H-Beta; (■): with H-Beta (0.10 g); (●): with H-Beta (0.10 g) and pyridine (0.02 mmol). The acrolein monomer amounts were determined by GC using an internal standard.

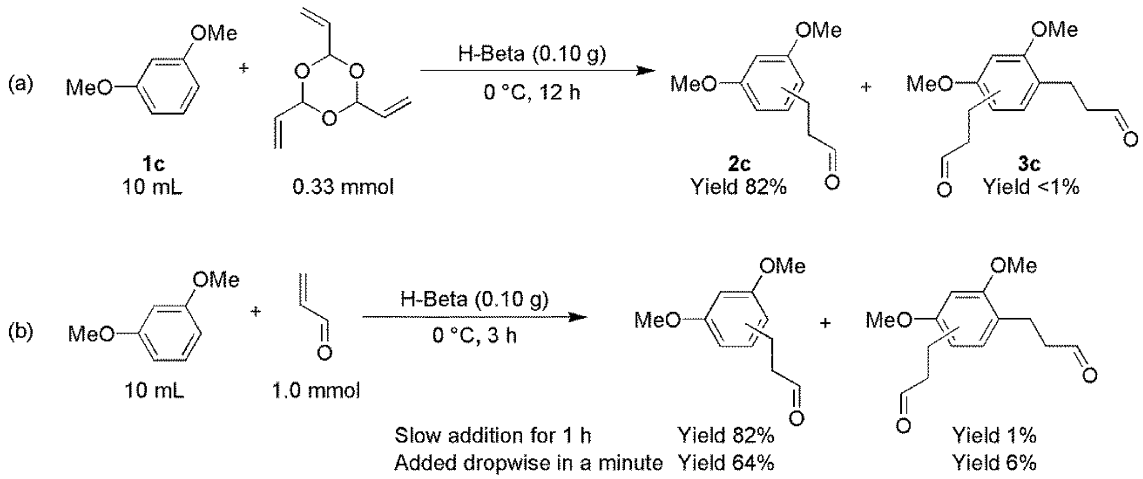
the consecutive reactions mainly proceeded on the outer surface of H-Beta, and that **2c** was formed inside the zeolite pores.[32]

3.5 Self-Polymerization of Acrolein. H-type zeolites are considered to necessarily accelerate the prompt self-polymerization of acrolein due to their intrinsic, strongly acidic character, so the acrolein adsorbed on H-Y was analyzed by ^{13}C DD/MAS NMR spectroscopy. The acrolein adsorbed on H-Y is hereafter referred to as acrolein(*n*)@H-Y in which *n* stands for the millimoles of added acrolein per one gram of zeolite. As a control, acrolein was also adsorbed on Na-Y, which was represented as acrolein(*n*)@Na-Y, because Na-Y can preserve acrolein molecules in the monomer form at ambient temperature for a long time.[8c] Acrolein(1.2)@Na-Y showed only three sharp peaks at 200.7, 143.3, and 137.5 ppm which were assignable to the C1, C3, and C2 of acrolein, respectively (Figure 3b, Supporting Information Figure S2). This clearly explained the fact that the acrolein monomers were maintained in the pores of Na-Y. On the contrary, acrolein(1.1)@H-Y showed three weak, broad peaks of C1, C3, and C2 as shown in Figure 3a. The acrolein polymerization processes would be very complicated because both the vinyl and formyl groups in the acrolein molecule would participate in the self-polymerization.[33] The expected signals for the polymeric by-products of acrolein were not observed by ^{13}C DD/MAS NMR (Figure 3a) as well as ^{13}C CP/MAS NMR.[34] We concluded that a part of the acrolein monomer was still present in the zeolite pores, but that it was difficult for the ^{13}C MAS NMR technique to detect and quantify the formation of acrolein polymers at such a low concentration level.

A time-course analysis of the acrolein monomer content in the suspended mixture of acrolein, H-Beta powder, and an organic solvent was an informative way to estimate the progress of the acrolein polymerization. We selected toluene as the solvent because toluene was unable to react with acrolein in the presence of H-Beta at RT due to its low nucleophilicity. The amount of the remaining acrolein monomer in the mixture was measured by GC analysis of each aliquot from the suspended mixture at the specified time (Figure 4). Although the acrolein monomer in the toluene solution was intact without H-Beta (▲), the content of the monomer with H-Beta (■) decreased to ca. 60% after 24 h. By contrast, the addition of 0.02 mmol of pyridine (●), which was an amount equal to the acid sites in H-Beta, almost inhibited the self-polymerization of acrolein. These results show that the acid sites in H-Beta are responsible for the acrolein polymerization. We then postulated that the acrolein polymerization should be the reason why the yields of **2a**–**2c** in Table 2 were only moderate and not excellent.

The acrolein polymerization was thought to be suppressed by lowering the acrolein concentration in the reaction mixture or in the zeolite pores, so that the following two tactics were proposed: (1) the slow formation of acrolein monomers through the in situ monomerization of an acrolein cyclic trimer (2,4,6-trivinyl-1,3,5-trioxane), and (2) the competitive adsorption effect of the solvent. We selected 1,3-dimethoxybenzene (**1c**) as a powerful nucleophile for the 1,4-addition to observe the efficiency of these two tactics.

3.6 The Slow Formation of Acrolein Monomers through the In situ Monomerization of an Acrolein Cyclic Trimer. We postulated that the slow formation of acrolein monomers was realized by the monomerization of the acrolein cyclic trimer gradually catalyzed by the acidic H-type zeolite. The acrolein cyclic trimer was synthesized from acrolein as previously reported (Supporting Information Section VI).[35] The use of the acrolein cyclic trimer in place of acrolein definitely improved the yield of **2c** up to 82%, and decreased the yield of **3c** to <1% as compared with the yield of Entry 5 in Table 2 and Scheme 8a. The time-course analysis showed that 43% of the acrolein cyclic trimer was present in the reaction mixture at 0.5 h, and 2% of that at 8 h (Figure 5). The one-hour slow addition of acrolein to the suspended mixture of H-Beta and **1c**, which is the simplest way to maintain the lower concentration of acrolein, was conducted. This method also increased the yield of **2c** to 82% as well as decreased the yield of **3c** to 1% (Scheme 8b). The in situ monomerization method of the acrolein cyclic trimer showed almost the same results for the 1,4-addition of **1c** as the slow addition method. The gradual monomerization of the cyclic trimer maintained a low monomer concentration in the mixture, and prevented not only the acrolein polymerization, but also the consecutive reaction of **2c** with acrolein.



Scheme 8. 1,4-Addition of **1c** to acrolein by lowering the acrolein concentration.

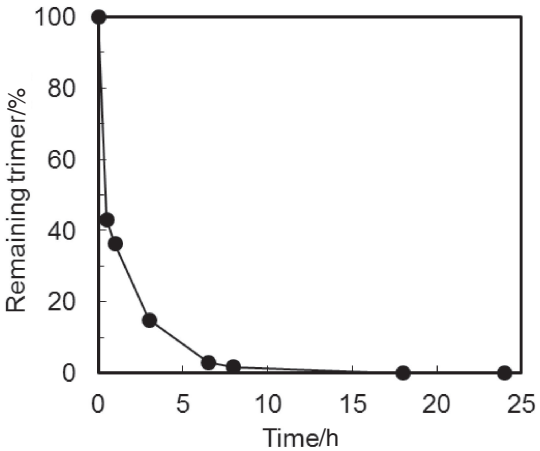


Figure 5. The time-course analysis of the remaining acrolein cyclic trimer. Conditions: **1c** (10 mL), acrolein cyclic trimer (0.33 mmol), H-Beta (0.10 g), 0 °C. The trimer amount was determined by GC.

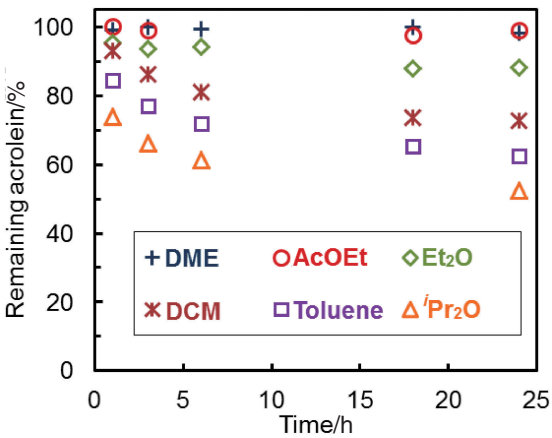


Figure 6. The time-course amount of the acrolein monomer in the presence of H-Beta. Conditions: solvent (10 mL), acrolein (1.0 mmol), H-Beta (0.10 g), RT. The conditions were the same as those in Figure 4.

3.7 Competitive Adsorption Effect of the Solvent. We presumed that the solvent choice could directly affect the acrolein concentration in the zeolite pores, because the acrolein and solvent molecules should be competitively adsorbed in the zeolite pores. Briefly, the higher the solvent polarity, the lower the acrolein concentration in the zeolite pores. Therefore, without any changes in the reagent amounts and in the addition protocol of acrolein to the mixture, the acrolein concentration in the reaction environment is expected to drop due to the competitive adsorption.

Six solvents, such as 1,2-dimethoxyethane (DME), ethyl acetate (AcOEt), diethyl ether (Et_2O), dichloromethane (DCM), toluene, and diisopropyl ether ($^iPr_2O$) were compared in light of the time-course amount of the remaining acrolein monomers (Figure 6). Nearly all of the acrolein remained after 24 h in DME (+) or AcOEt (○) even in the presence of H-Beta. In Et_2O (◇), ca. 90% of the acrolein survived after 24 h, but in $^iPr_2O$ (△), only ca. 50% of the acrolein was present after 24 h.

To evaluate the polarity of each solvent, the R_f value of acrolein was examined when an acrolein spot was developed on TLC on silica gel by each solvent which was diluted with hexane to 25% (v/v). The R_f values for the solvents were 0.44, 0.37, 0.23, 0.10, 0.06, and 0.17 in DME (+), AcOEt (○), Et_2O (◇), DCM (∗), toluene (□), and $^iPr_2O$ (△), respectively. The plots of the remaining amount of acrolein in each solvent at 24 h in Figure 6 versus the R_f value of acrolein are shown in Figure 7. The five plots, except for that of $^iPr_2O$,[36] showed a positive correlation between the R_f value of acrolein and the remaining acrolein amount. The R_f values for DME (+) and AcOEt (○) were higher than those for the other solvents, and nearly all of the added acrolein survived in DME and AcOEt. We postulated that the DME and AcOEt solvents competed with acrolein for the adsorption, and that they work well to lower the acrolein concentration in the zeolite pores.

The low acrolein concentration in the pores may disturb not only the self-polymerization of acrolein, but also the 1,4-addition. In fact, the solvent choice affected the efficiency for the 1,4-addition of **1c** (Table 4). We performed the reaction of 10 mmol of **1c** with 1.0 mmol of acrolein in 10 mL of each solvent in the presence of 0.1 g of H-Beta at 40 °C or under reflux. In DME and AcOEt, the yields of **2c** were improved to 76% and 75% at each optimized reaction time, respectively (Entries 1 and 2). Meanwhile, the yield was 64% when 76 mmol (10 mL) of **1c** was reacted with acrolein at 0 °C

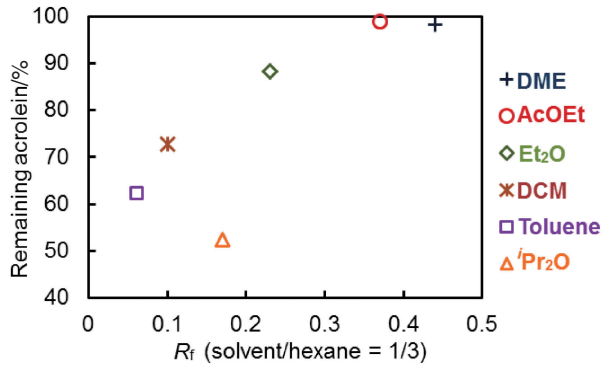
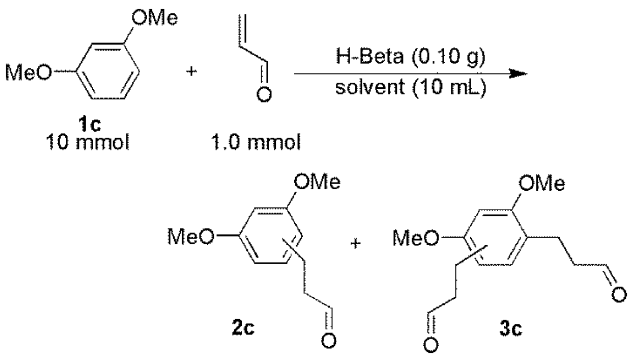


Figure 7. Remaining acrolein amounts vs. acrolein R_f values. The developing solvents were diluted with hexane to 25% (v/v). The data of the remaining acrolein amount at 24 h were quoted from Figure 6.

Table 4. Effects of solvents in H-Beta on the 1,4-addition of **1c** to acrolein[a)]



Entry	Solvent	Temp./°C	Time/h	Yield/%	
				2c[b)]	**3c**
1	DME	40	48	76	4
2	AcOEt	40	3	75	3
3	Et_2O	reflux	18	74	2
4	DCM	reflux	3	70	3
5	Toluene	40	3	58	3
6	$^iPr_2O$	40	6	52	3
7[c)]	**1c**	0	3	64	6

a) Reaction conditions: **1c** (10 mmol), acrolein (1.0 mmol), H-Beta (0.10 g), solvent (10 mL). b) Isomeric selectivity of 4-adduct was 93–98%. c) Data from Table 2, Entry 5.

(Entry 7). In Et_2O and DCM, the yields of **2c** also increased to 74% and 70% yields, respectively (Entries 3 and 4). On the other hand, the use of toluene and $^iPr_2O$ lowered the yield of **2c** to 58% and 52% yields, respectively (Entries 5 and 6). This tendency matches with the remaining acrolein amount in each solvent as shown in Figure 8. The reaction performed in AcOEt did not show as high a yield of **2c** as those by adding PPh_3 in Scheme 7 or in situ monomerizing the acrolein cyclic trimer in Scheme 8, but employing a solvent for the 1,4-addition has merits of reducing the amount of **1c**.

Unfortunately, performing the 1,4-addition to acrolein in the AcOEt solvent was not generally applicable to the other benzene derivatives, because the amount of the nucleophile **1** used was drastically reduced. For example, the yields of **2a** and **2b** in the AcOEt solvent decreased to 58% or 25%, respectively (Table 5). **1c** with a high nucleophilicity arising from the *ortho–para* orientation effects of the two methoxy groups can only realize an improvement in the yield of **2c**.

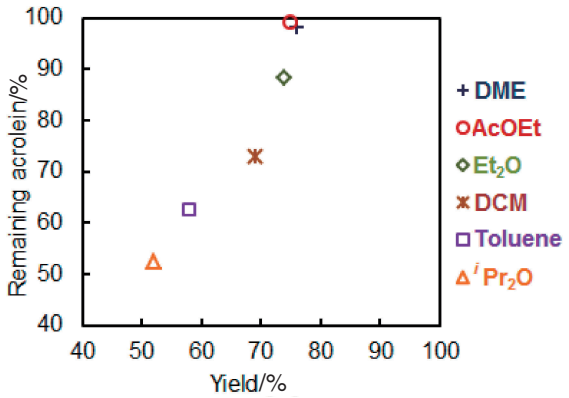
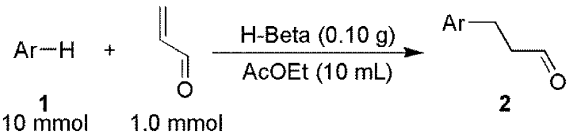


Figure 8. The remaining acrolein amounts vs. the yields of **2c**.

Table 5. Application of AcOEt solvent conditions to **1a** and **1b**[a)]

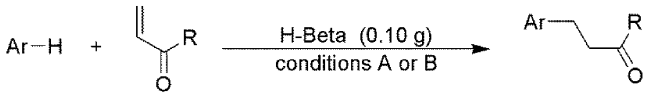


Entry	Reactant	Temp./°C	Time/h	Product[b)]	Yield/%
1	**1a**	60	24	**2a**[c)]	58
2	**1b**	reflux (77)	18	**2b**	25

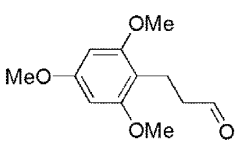
a) Reaction conditions: **1** (10 mmol), acrolein (1.0 mmol), H-Beta (0.10 g), AcOEt (10 mL). b) Dialkylated products **3a** and **3b** were not observed. c) The *para*-selectivity of **2a** was 93%.

3.8 Scope and Limitations of H-Beta-Catalyzed 1,4-Addition of Benzene Derivatives to Acrolein or MVK. We next investigated the scope and limitations of the 1,4-addition of the benzene derivatives to acrolein or methyl vinyl ketone (MVK) (Table 6). A bulky and highly electron-rich benzene derivative, 1,3,5-trimethoxybenzene (**1d**) was converted to **2d** in 81% yield under conditions B, where **1** (10 mmol) was reacted with acrolein (1.0 mmol) in AcOEt (10 mL) in the presence of H-Beta (0.10 g) (Entry 1). The 1,4-addition was also applicable to phenol (**1e**), yielding **2e** in 67% yield under the conditions B (Entry 2). An *ortho*-alkylated isomer of **2e** was not observed, but chroman-2-ol and its derivatives were obtained in a total of 7% yield.[30a,37] An oxa-Michael adduct, 3-phenoxypropanal, from **1e** was not formed.[38,39] The 1,4-addition of *N*,*N*-dimethylaniline (**1f**) catalytically proceeded to produce **2f** in 72% yield under conditions A, where acrolein (1.0 mmol) was reacted with **1** (10 mL) in the presence of H-Beta (0.10 g) without the use of AcOEt (Entry 3). An *ortho*-alkylated isomer of **2f** was not formed. Our computational chemical study also demonstrated that the bulky dimethylamino group interrupted the introduction of the 2-formylethyl substituent at the *ortho*-position (Supporting Information Section V). The 1,4-additions of alkyl substituted benzenes, such as **1g**, **1h**, and **1i**, to acrolein gave **2g**, **2h**, and **2i** only in low or no yields of 21%, 5%, and 0% yields, respectively, even at the higher reaction temperatures of more than 100 °C (Entries

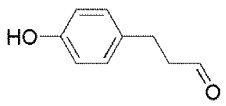
Table 6. Scope and limitations of H-Beta-catalyzed 1,4-additions of benzene derivatives to acrolein or MVK[a)]



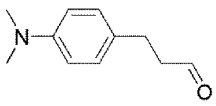
	1	R = H or Me		2
conditions A	10 mL	1.0 mmol		
conditions B	10 mmol	1.0 mmol	AcOEt 10 mL	



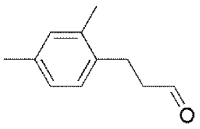
2d



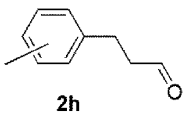
2e



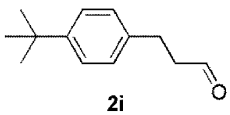
2f



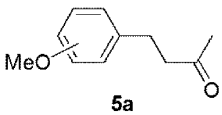
2g



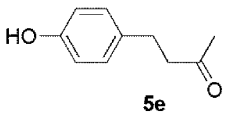
2h



2i



5a



5e

Entry	Reactant	R	Conditions	Temp./°C	Time[b)]/h	Product	Yield/%
1	**1d**	H	B	40	1	**2d**[c)]	81
2	**1e**	H	B	40	24	**2e**[d)]	67
3	**1f**	H	A	80	3	**2f**[e)]	72
4	**1g**	H	A	120	2	**2g**[f)]	21
5	**1h**	H	A	100	3	**2h**[g)]	5
6	**1i**	H	A	140	3	**2i**	0
7	**1a**	Me	A	80	0.25	**5a**[h)]	82
8	**1e**	Me	B	40	24	**5e**[i)]	29

a) Conditions A: **1** (10 mL), acrolein or MVK (1.0 mmol), H-Beta (0.10 g). Conditions B: **1** (10 mmol), acrolein or MVK (1.0 mmol), H-Beta (0.10 g), AcOEt (10 mL). b) Reaction time was optimized. c) Dialkylated product **3d** was obtained in 1% yield. d) Chroman-2-ol and its derivatives were obtained in ca. 7% yield. e) A *para*-alkylated product only. f) A positional isomer was too low in amount to identify. g) *Para*:*ortho* = 65:35. h) *Para*:*ortho* = 94:6. i) Neither the oxa-Michael adduct nor the *ortho*-alkylation isomer was obtained.

4–6). 4-(4′-Methoxyphenyl)butan-2-one (**5a**) was produced in the high yield of 82% by the reaction of **1a** with MVK, and the *para*-selectivity of **5a** was as high as 94% (Entry 7).[40] By contrast, the raspberry ketone (**5e**) was obtained from **1e** and MVK in the low yield of 29% under the conditions B (Entry 8).[17,40,41] Neither the oxa-Michael adduct nor *ortho*-alkylated isomer was obtained. Benzene derivatives, which bear strongly electron-donating groups such as methoxy, dimethylamino, and hydroxy groups, were applicable to the 1,4-addition to acrolein with H-Beta, but those which have poorly electron-donating groups, such as alkyl substituents, were hard to apply.

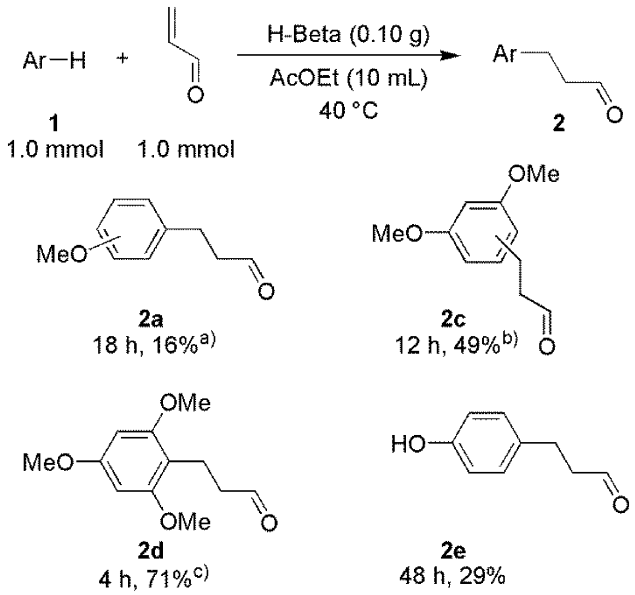
Using a reduced amount of **1** from 10 to 1.0 mmol, equimolar to acrolein, decreased the yield of **2** (Scheme 9). For example, **2c** and **2d** were obtained in moderate yields of 49% and 71%, respectively, but **2a** and **2e** were formed in low yields of 16% and 29%, respectively. The dialkylated product **3c** was drastically formed in up to 12% yield as compared with the reaction in 3% yield using 10 mmol of **1c** (Table 4, Entry 2). In the equimolar **1**–acrolein mixture, bulky by-products which resulted from the polyalkylation of **2** may also be formed and would get clogged in the zeolite pores.[29]

4. Conclusion

Zeolites H-Beta and H-Y were found to be suitable catalysts for the 1,4-addition of benzene derivatives **1** to acrolein. Due to the initial high concentration of **1** in the zeolite pores, the 1,4-addition exceeded the acrolein polymerization. With electron-rich benzene derivatives, 3-arylpropanals **2** were obtained in moderate yields, but the simple alkyl-substituted benzenes were not reactive enough for the 1,4-addition reactions (Tables 2 and 6).

Since H-Beta was not completely deactivated during the 1,4-addition (Table 3), the moderate yields in Table 2 were due to the consecutive reactions from **2** as well as the self-polymerization of acrolein. Two types of consecutive reactions from **2c** were observed and successfully suppressed by poisoning the acid sites on the outer surface of H-Beta with PPh_3 (Scheme 7), proving that **2c** was formed in the zeolite pores.

The self-polymerization of acrolein concurrently takes place during the 1,4-addition (Figure 4). To preclude the acrolein polymerization, we presented two protocols which helped lower the acrolein concentration. First, the in situ monomerization of an acrolein cyclic trimer with an acidic zeolite can realize a lower concentration of acrolein in the reaction system, leading to an increase in the yield of **2c** (Scheme 8). This tactic is expected to be useful for the gradual production of other types of reactive monomers from the corresponding 1,3,5-trioxane analogues as well as polyoxymethylene analogues. Second, the competitive adsorption of the solvent helps to maintain a low concentration of acrolein in the zeolite pores. In



Scheme 9. 1,4-Addition reaction under the equimolar conditions. a) 60 °C. b) Dialkylated product **3c** was obtained in 12% yield. c) Dialkylated product **3d** was obtained in 3% yield.

the DME or AcOEt solvent, nearly all of the acrolein remained intact (Figure 6), and the reaction yield of **2c** increased (Table 4, Entries 1 and 2). We observed a certain correlation between the remaining acrolein amount and the reaction yield of **2c** in each solvent (Figure 8), indicating that the competitive adsorption of the solvent inhibited the acrolein polymerization and enhanced the 1,4-addition to **2c**.

The computations were performed using Research Center for Computational Science, Okazaki, Japan.

Supporting Information

The Supporting Information contains experimental details and characterization results. This material is available on http://dx.doi.org/10.1246/bcsj.20150387.

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