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Stabilization and activation of unstable propynal in the zeolite nanospace and its application to addition reactions

Daijiro Hayashi, Yuta Igura, Yoichi Masui, Makoto Onaka*

Propynal (HC=C-CHO) having both a C=C triple bond and a formyl group in a molecule is a promising building block, but its labile property to easily polymerize often narrows its application for organic synthesis. In a similar way to unstable molecules, such as formaldehyde and acrolein, propynal is also stabilized and remains unchanged in the supercages of the Na-Y zeolite for over 30 days at ambient temperature, where the carbonyl oxygen atoms of the propynal coordinate to sodium ions in Na-Y which was proved by a ¹³C-DD/MAS-NMR analysis. In addition, the propynal adsorbed in the zeolite is sufficiently activated to allow unprecedented reactions; i.e., (1) The 1,3-dipolar cycloaddition with electron-deficient α -diazocarbonyl compounds, (2) the 1,4-addition with mono-, di-, and trimethoxy-substituted benzenes, and (3) the [2 + 2] cycloaddition of unactivated cycloalkenes. The nanospace of the zeolites keeps the products from dimerization during reaction (1) and from successive side-reactions in reaction (2). Quantum chemical calculation demonstrated that reaction (3) proceeds via a one-step-like non-concerted mechanism to afford the corresponding [2 + 2] cycloadducts. The three reactions can produce valuable synthetic intermediates retaining both a formyl group and a C=C double bond.

go in and out have been applied as catalysts or promoters not

only to gas-phase transformations of petrochemicals-based materials, but also to liquid-phase organic reactions for fine

chemicals synthesis for decades.³ We have been interested

and engaged in probing the behaviors of easily polymerizable

or short-lived organic molecules such as formaldehyde,

acrolein and secondary benzylic cations confined in the zeolite

pores at ambient temperature as well as developing their

molecular transformations from the viewpoint of synthetic

organic chemistry.^{4,5,6} We discovered that the zeolites can

stabilize and activate the molecules adsorbed in the pores. For

example, capturing polymerizable formaldehyde and acrolein

in the supercages of the faujasite zeolite Na-Y and preserving

them in monomer forms at ambient temperature for days.

Our quantum chemical calculation studies disclosed how such

labile molecules interacted with the zeolite pores and why

they were so stabilized:⁷ The calculated models showed that

three molecules of the monomeric formaldehyde and one

molecule of 1,3,5-trioxane, a cyclic trimer of formaldehyde,

encapsulated in the supercage of Na-Y were at equilibrium in

favour of the former. The reason is that the former is more

advantageous than the latter in terms of the coordination

energy of formaldehyde monomers to sodium ions in the Na-Y.

It was also discovered that the stabilized aldehydes in Na-Y

were sufficiently activated to react with some nucleophiles,

such as olefins and aromatics, to give homoallylic alcohols through the Prins reactions of formaldehyde as well as 3-

arylpropanals via the 1,4-addition reactions to acrolein.⁴

Introduction

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Alkynes conjugated with a carbonyl group, such as esters or ketones, are widely utilized for organic synthesis. Propynal (HC≡C-CHO), also known as propargyl aldehyde or propiolaldehyde, is the simplest conjugated ynal, and its addition to the C=C triple bond can lead to a product having both a formyl group and a C=C double bond. As a consequence, propynal is considered to be one of the versatile building blocks for the construction of valuable organic compounds,-but its use in organic synthesis has been scarce compared with those of related acetylenic carbonyl compounds such as alkyl propiolate and 3-butyn-2-one. One crucial reason is the instability of propynal, which easily polymerizes even at -20 °C without any catalyst, or even at -78 °C in the presence of bases like pyridine.¹ Therefore, a reaction promoter, which can suppress the propynal polymerization, is highly demanded to broaden the applications of propynal in organic synthesis.

In order to shield labile compounds from the exterior circumstances and to survive them, artificial organic cage compounds, such as hemicarcerands, cavitands, and networked molecular capsules, have been developed.² Inorganic zeolites composed of open subnano-sized pore systems where organic substrates and products are allowed to

E-mail: conaka@mail.ecc.u-tokyo.ac.jp

Graduate School of Arts and Sciences, The University of Tokyo, Komaba, Meguroku, Tokyo 153-8902, Japan.

⁺Electronic Supplementary Information (ESI) available: Data of products and calculation, Tables S1-S2, Scheme S1, and Structure determination of [2 + 2] cycloadducts. See DOI: 10.1039/x0xx00000x

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 $\label{eq:scheme1} \textbf{Scheme1} \ \textbf{Three types of propynal reaction discussed in this study}.$

We further discovered that in place of a stoichiometric amount of the Na-Y zeolite, a catalytic amount of acidic zeolites, such as H-Y and H-Beta, promoted the 1,4-addition of benzene derivatives to acrolein at much lower temperatures.⁵ In order to suppress the self-polymerization of acrolein in the study, we developed two protocols to maintain the concentration of acrolein in the zeolite pores as low as possible; i.e., (1) the slow *in-situ* generation of acrolein from its oligomeric precursor in the zeolite pores, and (2) competitive adsorption of a suitable solvent into the zeolite pores.

Considering our findings described above, we presume that 1) Na-Y-encapsulated propynal remains in the monomer form, and 2) the acid sites of Na-Y and H-Y promote three types of reaction with propynal as shown in Scheme 1:

Pyrazoles are recognized as the core structures in a broad variety of bioactive compounds, such as insecticides, antibacterial agents and anticancer drugs, and they are generally prepared through the reactions of 1,3-dicarbonyl compounds with hydrazine derivatives (Scheme 2a).⁸ The 1,3-dipolar cycloadditions of propynal to azides, the Huisgen cycloaddition, have been reported to produce triazole derivatives (Scheme 2b),⁹ but there were only three reports^{9,10,11} about the reactions of propynal with diazo compounds to form pyrazoles (Scheme 2c).

The 1,4-addition of benzene derivatives to propynal afford cinnamaldehyde derivatives having a terminal formyl group and an internal C=C double bond, but there have been no precedents. The cinnamaldehydes turn out to be the key



Scheme 2 (a) The synthesis of pyrazoles from 1,3-dicarbonyl compounds with hydrazines and (b) the precedent 1,3-dipolar cycloaddition of propynal with a diazo compound.⁹



Scheme 3 Typical synthetic methods for aromatic α , β -unsaturated aldehydes: (a) The Horner-Emmons reaction,¹⁹ (b) the Heck reaction,²⁰ and (c) the precedent 1,4-addition reaction of an aromatic to propynal.²¹

starting materials for the syntheses of γ -butyrolactones,¹² γ , δ unsaturated- δ -lactones,¹³ γ -lactams,¹⁴ cyclopentenes,¹⁵ carboxylate esters,¹⁶ and β^2 -amino acids,¹⁷ which are induced by the N-heterocyclic carbene (NHC) catalysis. As Bode pointed out, however, the cinnamaldehydes are not commercially available, so they have to be prepared through troublesome multiple steps or by the use of precious coupling catalysts (Supplementary Information Scheme S1).¹⁸ For example, cinnamaldehydes can be prepared through the reaction of benzaldehydes with the Horner-Emmons reagent followed by the conversion of the ester to the aldehyde (Scheme 3a),¹⁹ or through the Heck reaction of bromobenzenes with acrolein (Scheme 3b).²⁰ Only one report about the 1,4-addition of aromatics to propynal was published in 1986 using furan as a nucleophile and formic acid as both the promoter and the solvent (Scheme 3c).²¹ A few reports were published on the 1,4-addition of benzene derivatives to α , β -unsaturated carbonyl compounds having a terminal triple bond,²² but no example with heterogeneous catalysts.

The [2 + 2] cycloaddition of alkynes to alkenes is one of the important methods to synthesize cyclobutenes which have been used not only as valuable synthetic intermediates, but also as monomers for polymerization.²³ For example, the [2 + 2] cycloaddition of methyl propiolate to unactivated alkenes catalyzed by aluminium chloride was intensively studied by Snider,²⁴ indicating that monosubstituted and 1,2-disubstituted alkenes mainly gave [2 + 2]-type cycloadducts rather than ene-type adducts. The [2 + 2] cycloadducts tend to cause ring opening reactions with heat to give unsaturated carbonyl compounds, so the [2 + 2] cycloaddition should be performed as mildly as possible. Only one example of the [2 + 2] cycloaddition with propynal was reported by Hafner using

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Scheme 4 Only one example of the [2 + 2] cycloaddition with propynal. $^{\rm 25}$

cyclopenta[*cd*]azulene which has a large dipole moment (Scheme 4).²⁵

Experimental section

Zeolites and materials

Powdery Na-Y (Si/Al=2.75, HSZ-320NAA) and H-Y (Si/Al=15, HSZ-371HUA) were obtained from the Tosoh Corporation (Japan). Powdery SiO₂-Al₂O₃ (Si/Al=5.3, JRC-SAL-2) was provided by the Catalysis Society of Japan. The cation exchange capacity of the zeolites is generally the same as the aluminium content in the zeolite framework,²⁶ so we simply calculated the aluminium contents of the Na-Y and H-Y from the Si/Al ratio of each zeolite to be 4.0 mmol g⁻¹ and 1.1 mmol g⁻¹, respectively. The Na-Y and H-Y were activated at 400 °C / <26 Pa for 4 h and 2 h just before use, respectively.

Propynal was synthesized according to Sauer's report.²⁷ α -Diazoacetophenone and 1-diazo-3,3-dimethyl-2-butanone were synthesized as previously reported by Shioiri.²⁸ The other reactants were commercially available (Supplementary Information Section I) and purified before use.

General procedure for the 1,3-dipolar cycloaddition of α -diazocarbonyl compounds

To the activated Na-Y (1.0 g) in a 30-mL flask was added CH₂Cl₂ (10 ml) and propynal (1.0 mmol), and the suspension was stirred for 30 min at room temperature (RT) prior to the reaction. To the suspension was then added an α diazocarbonyl compound (1.5 mmol), and the reaction mixture was continuously stirred for a specific reaction time at RT. To the reaction mixture was then added methanol (5 mL) and the mixture was stirred for 10 min. The Na-Y was removed by filtration through a 10–16 μm sintered glass funnel, and washed with methanol and ethyl acetate. After the filtration through a Celite pad with ethyl acetate, the filtrate was concentrated under reduced pressure. The recrystallization from ethyl acetate produced a pyrazole compound as a white solid. The residue of the product in the solution part was purified on silica gel to afford the additional pyrazole. The isolated yield was calculated based on the propynal amount.

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DOI: 10.1039/C7CY01161J Procedure for the 1,4-addition of methoxybenzenes with propynal

In the case of anisole or 1,3-dimethoxybenzene as a nucleophile, the procedure for each experiment is described in Table 2 or Table 3.

In Scheme 5, to the activated Na-Y (1.0 g) in a 30-mL flask was added 1,3,5-trimethoxybenzene (10 g). After the suspension was stirred for 10 min at 100 °C, propynal (1.0 mmol) was added over a period of one minute. After the reaction was completed in 3 h, the reaction vessel was placed in an ice-water bath, and ethanol (5 mL) was added. The mixture was stirred for 10 min, then the Na-Y was removed by filtration through a 10–16 μ m sintered glass funnel, and washed with ethanol and ethyl acetate. To the combined filtrate was added triphenylmethane as an internal standard substance, and the mixture was analyzed by gas chromatography (GC). The reaction yield was calculated based on the propynal amount.

General procedure for the [2 + 2] cycloaddition of alkenes with propynal

To the activated Na-Y (1.0 g) in a 30-mL flask was added CH_2Cl_2 (10 ml) and propynal (1.0 mmol), and the suspension was stirred for 30 min at RT prior to the reaction. To the suspension was then added an alkene (3.0 mmol), and the reaction mixture was continuously stirred for a specific reaction time at RT. To the reaction mixture was then added methanol (5 mL) and the mixture was stirred for 10 min. The Na-Y was removed by filtration through a 10–16 μ m sintered glass funnel, and washed with methanol and ethyl acetate. After the filtration through a Celite pad with ethyl acetate, the combined filtrate was concentrated under reduced pressure. This crude product was analyzed by NMR with triphenylmethane as the internal standard. The reaction yield was calculated based on the propynal amount.

Results and discussion

Capture and stabilization of propynal in Na-Y zeolite

For the effective organic synthesis using propynal, it is desired to keep propynal from polymerizing. Labile carbonyl compounds, such as formaldehyde and acrolein, were found to be stabilized in the monomer form in the Na-Y pores, so propynal is also thought to be applicable.⁴ Propynal vaporized in a stream of nitrogen was adsorbed on powdery Na-Y at 0 °C and the actual amount of the adsorbed propynal in 1.0 g of Na-Y was 3.8 mmol, which is hereafter referred to as propynal(3.8)@Na-Y.

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To confirm that propynal was in the monomer form in the Na-Y, the propynal(3.8)@Na-Y sample was analyzed by ¹³C-DD/MAS-NMR spectroscopy. Propynal(3.8)@Na-Y showed three distinctive peaks at 182.5, 88.4 and 81.2 ppm which were assigned to the C¹, C³ and C² carbons of propynal, respectively (Fig.1b). The ¹³C chemical shift values of C¹ and C³ for the propynal(3.8)@Na-Y showed the low-field shift by 6.0

and 5.8 ppm, respectively, than those of propynal Ain CDCI (Fig.1a). On the other hand, the ¹³C chemical Shift Values of CC^3 for the propynal (3.8)@Na-Y showed a slightly high-field shift compared with that of propynal in CDCI₃. Such chemical shifts of the C¹, C², and C³ were also observed in the ¹³C-DD/MAS-NMR spectrum of acrolein adsorbed on Na-Y,⁵ proving that the carbonyl oxygen atoms of propynal strongly coordinate to the Lewis acidic sodium ions in the zeolite pores. Surprisingly, after storage for 30 days at ambient temperature, the propynal (3.8)@Na-Y sample remained unchanged without any formation of polymerized products (Fig.1c).

1,3-Dipolar cycloaddition of α -diazocarbonyl compounds with propynal.

We reported the Na-Y promoted the 1,3-dipolar cycloaddition of ethyl α -diazoacetate to alkynes having electron-withdrawing groups such as esters as well as keto and formyl groups.¹¹ For example, propynal smoothly reacted with ethyl α -diazoacetate (1a) to afford the corresponding pyrazole 2a. Pyrazoles with a formyl group are known to be in equilibrium with their dimer.²⁹ Indeed, a mixture of the monomer (2a) and dimer (3a) was detected by 13 C NMR in DMSO- d_6 at RT (Fig.2a); the two sets of signals at 74.7 and 75.2 ppm in the ¹³C NMR spectrum were assigned as the C-OH of two diastereomers of 3a. 2a was also assigned by comparison with the NMR spectrum at 60 °C in which only 2a was included (Fig.2b). Since the size of 3a was too large to be accommodated in the pores, we expected that the monomer product 2a would stay in the Na-Y pores. To determine whether 2a or 3a was present in the Na-Y during the 1,3-dipolar cycloaddition, we evacuated the reaction mixture including Na-Y and analyzed it with ¹³C-CP/MAS-NMR at RT (Fig.2c). The C-OH peaks of 3a at around 75 ppm were



Fig. 2 ¹³C NMR spectra of **2a** and **3a**. (a) A mixture of **2a** and **3a** in DMSO- d_6 at RT, (b) only **2a** in DMSO- d_6 at 60 °C, and (c) **2a** preferentially adsorbed in the Na-Y by ¹³C-CP/MAS-NMR at RT.

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Table 1

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1,3-Dipolar cycloaddition of α -diazocarbonyl compounds to

| Entry | 1 : R | Additive | Time (h) | Yield ^b (%) |
|-------|--------------------------|----------|----------|------------------------|
| 1 | 1 | Na-Y | 1 | 83 |
| 2 | Ia: OEt | — | 1 | 30 |
| 3 | 4 h · Dh | Na-Y | 1 | 93 |
| 4 | 10: PN | — | 1 | 1 |
| 5 | | Na-Y | 24 | 90 |
| 6 | 1c : <i>t</i> -Bu | — | 24 | 6 |

 a Reaction conditions: 1 (1.5 mmol), propynal (1.0 mmol), additive (1.0 g), CH₂Cl₂ (10 mL), RT. b Isolated yield of both 2 and 3. 2 includes two prototropic tautomers.³⁰

lost, and the carbonyl carbon peak of **2a** was observed at around 185 ppm, indicating that **2a** rather than **3a** favourably stayed in the Na-Y.

Although **2a** was obtained even without Na-Y in 30% yield, α -diazoacetophenone (**1b**) and 1-diazo-3,3-dimethyl-2butanone (**1c**), which are less reactive to the 1,3-dipolar cycloaddition than α -diazoacetate, were not able to form pyrazoles without Na-Y (Table 1, entries 2, 4, and 6). With Na-Y, however, the α -diazoketones were converted into **2a**, **2b**, and **2c** in greater than 83% yields (Table 1, entries 1, 3, and 5). In these Na-Y promoted 1,3-dipolar cycloadditions, propynal is thought to be activated by the coordination of the carbonyl oxygen atoms to the Lewis acidic sodium ions in the zeolite pores and undergo additions to the α -diazocarbonyl compounds.¹¹

1,4-Addition of benzene derivatives to propynal

As we previously reported that the 1,4-additions of benzene derivatives to acrolein were mediated by Na-type or H-type zeolites,^{4b,5} we expected that the Na-Y and/or H-Y would also promote the similar 1,4-additions of benzene derivatives to propynal. First, we carried out the reaction of an excess amount (10 mL) of anisole having an electron-donating methoxy group (**4a**) with propynal (1.0 mmol) as shown in Table 2. One gram of Na-Y slightly promoted the 1,4-addition at 140 °C, but had no affect at 80 °C (Table 2 entries 1 and 2). Surprisingly, the catalytic use of acidic H-Y (0.1 g) was found to facilitate the 1,4-addition to afford **5a** in 35% yield (Table 2 entry 3) accompanied by some successive side-reactions.^{22b,31} The present addition reaction is also considered to proceed inside the H-Y pores in a similar way to the acidic zeolite-catalyzed 1,4-addition of benzene derivatives to acrolein,

 Table 2
 1,4-Addition of anisole to propynal^a



| Entry | (g) | (g) | (°C) | (h) | Yield [®] (%) | para:ortho |
|-----------------------|-----|------|------|-----|------------------------|------------|
| 1 ^b | 1.0 | _ | 80 | 1 | <1 | — |
| 2 ^b | 1.0 | _ | 140 | 4 | 14 | 82:18 |
| 3 | _ | 0.10 | 80 | 12 | 35 | 85:15 |
| 4 ^{<i>c</i>} | _ | 0.10 | 80 | 12 | 22 | 84:16 |
| 5 | 1.0 | 0.10 | 80 | 12 | 43 | 80:20 |
| 6 ^{<i>c</i>} | 1.0 | 0.10 | 80 | 12 | 42 | 81:19 |

^{*a*} Reaction conditions: **4a** (10 mL), propynal (1.0 mmol). ^{*b*} Reaction mixture was stirred for 0.5 h at RT prior to the reaction. ^{*c*} Propynal was added using a syringe pump over 11 h. ^{*d*} Yield was determined by GC analysis.

which was proved to proceed even after the exterior surface of the acidic zeolite was selectively poisoned by using a bulky base.⁵ We then envisaged that the coexisting Na-Y would probably work as a reservoir which could entrap **5a** and keep **5a** from any side-reactions induced by the acidic H-Y. Indeed, the combined use of Na-Y (1.0 g) and a catalytic amount of H-Y (0.1 g) increased the yield to 43% (Table 2 entry 5).³² The slow addition of propynal to **4a** in the presence of only H-Y using a syringe pump did not improve the yield of **5a**, but the slow addition in the presence of Na-Y and H-Y similarly increased the yield (Table 2 entries 4 and 6).

We next conducted the reaction of an excess amount (10 mL) of 1,3-dimethoxybenzene (**4b**) having cooperative *orthopara* influences by the two methoxy groups. The 1,4-addition of **4b** to propynal (1.0 mmol) was promoted by Na-Y (1.0 g) to give **5b** in 47% yield including the exclusive 4-adduct (Table 3, entry 1). A by-product (**6b**) derived from the 1,2-addition was also obtained in 2% yield. The combined use of Na-Y and H-Y showed almost the same catalytic activity as the use of Na-Y (Table 3, entry 3). The slow addition of propynal improved the yields to around 60% (Table 3, entries 2 and 4).

A more highly electron-rich benzene derivative, 1,3,5trimethoxybenzene (4c), also reacted with propynal to give 5c in 43% under the same reaction conditions of Table 3, Entry 1 (Scheme 5 and Supplementary Information Table S1). These results indicated that 4b and 4c had a sufficient nucleophilic reactivity to add to propynal induced by a relatively weak Lewis acid promoter of Na-Y, and that a more strongly acidic catalyst like H-Y was required to promote the 1,4-addition of the less nucleophilic 4a than 4b and 4c. Phenol and N,Ndimethylaniline with more electron-donating groups, such as OH and NMe₂, than a methoxy group were not converted into the corresponding cinnamaldehyde derivatives. The amine group was considered to work as a base (a conjugate acid of *N*,*N*-dimethylaniline; p*K*a = 5.01, 25 °C in water³³) to promote the polymerization of propynal because one drop of propynal turned the N,N-dimethylaniline solution brown. It was concluded that a methoxy group is inert to propynal, and that

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^a Reaction conditions: **4b** (10 mL), propynal (1.0 mmol). ^b Reaction mixture was stirred for 0.25 h at RT prior to the reaction. ^c Propynal was added using a syringe pump over 1 h. ^d Yield was determined by GC analysis. ^e Yield was calculated by the effective carbon number based on GC. ^f The major isomer was the 4-adduct, and the minor one having the same mass number was also detected in less than a few percent.



Scheme 5 1,4-Addition of 1,3,5-trimethoxybenzene to propynal. The yield was determined by GC analysis.

methoxy-substituted benzenes are proper carbon nucleophiles for the reactions of propynal.

[2+2] Cycloaddition of alkenes to propynal

The [2 + 2] cycloaddition of alkenes to propynal has not yet been reported, but we predicted that the Lewis acid property of Na-Y might be sufficient to induce the [2 + 2] cycloaddition. As cyclohexene (7a) prefers the [2 + 2] cycloaddition to the ene reaction,²⁴ **7a** underwent the cycloaddition to propynal which was activated by Na-Y and the other acidic additives in Table 4 and Supplementary Information Table S2. Using SiO₂-Al₂O₃ or H-Y as a Brønsted acid catalyst, 8a was obtained in ca. 10% yields (Table 4, entries 2 and 3). Although AlCl₃ and EtAlCl₂ were reported to be suitable Lewis acid catalysts for the [2 + 2] cycloaddition to methyl propiolate²⁴, which is more stable to Lewis acids than propynal, they were not applicable to the labile propynal (Table 4, entries 4 and 5). Na-Y gave the highest yield of 8a among the five catalysts (23%, Table 4, entry 6) although the yield was not satisfactory.³⁴ The use of polar

Table 4 [2 + 2] Cycloaddition of cyclohexene to propynal under different reaction conditions^a

| 7a 1.0 mmol 7a 1.0 mmol 7a 8a | | | | | | |
|---|---------------------|------------|------------|----------|------------------------|--|
| Entry | Additive | Amount | Solvent | Time (h) | Yield ^c (%) | |
| 1 | _ | - | 7a | 209 | 0 | |
| 2 | $SiO_2-Al_2O_3^{b}$ | 1.3 g | CH_2CI_2 | 1 | 10 | |
| 3 | H-Y | 0.1 g | CH_2Cl_2 | 24 | 5 | |
| 4 | AICI ₃ | 1.0 equiv. | CH_2CI_2 | 8 | 0 | |
| 5 | EtAICl ₂ | 0.5 equiv. | CH_2CI_2 | 8 | 0 | |
| 6 | Na-Y | 1.0 g | CH_2Cl_2 | 72 | 23 | |
| 7 | Na-Y | 1.0 g | AcOEt | 72 | 0 | |
| 8 | Na-Y | 1.0 g | CH₃CN | 72 | 0 | |
| 9 | Na-Y | 1.0 g | 7a | 72 | 9 | |

^a Reaction conditions: **7a** (3.0 mmol), propynal (1.0 mmol), CH₂Cl₂ (10 mL), and an additive at RT. ^b JRC-SAL-2, Si/AI = 5.3. ^c Yield was determined by the ¹H NMR analysis of the reaction mixture.



Scheme 6 [2 + 2] Cycloaddition of vinyl ethers to propynal with the yields based on the ¹H NMR analysis of the reaction mixtures.

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Scheme 7 Three mechanisms for the [2 + 2] cycloadditions

solvents, such as AcOEt and CH_3CN , as well as an excess amount of **7a** in place of CH_2Cl_2 did not improve the yield (Table 4, entries 7–9).

We also employed more nucleophilic cyclic vinyl ethers as ynophiles, such as 3,4-dihydro-2H-pyran (**7b**) and 2,3-dihydrofuran (**7c**), yielding **8b** and **8c** in 31% and 27% yields, respectively (Scheme 6a and 6b). On the other hand, linear vinyl ethers (**7d**) did not produce the [2 + 2] cycloadduct (Scheme 6c).

For the [2 + 2] cycloaddition, the "one-step mechanism" and the "two-step mechanism" were proposed.³⁵ In general, the one-step reaction involves the concerted [$_{\pi}2_{a} + _{\pi}2_{s}$]-type orbital interaction, and the two-step reaction goes through a zwitterion intermediate in a non-concerted way. Concerning

the [2 + 2] cycloaddition of alkenes to methyl propiolate, Snider proposed the one-step concerted mechanism taking on a large degree polar character (Scheme 7a).²⁴ On the other hand, Huisgen concluded that the [2 + 2] cycloaddition proceeded through the two-step mechanism based on the kinetic and stereochemical evidence,³⁶ and most of reports by other researchers adopted the zwitterionic intermediacy (Scheme 7b).^{25,37}

To discuss the reaction mechanism for the [2 + 2] cycloaddition of **7b** to propynal, the transition state of this reaction was investigated. As a function of the length of the two bonds, C^1-C^8 and C^6-C^7 , the Gibbs free energy of each point was calculated at the B3LYP/6-311+G level (Fig. 3, Supplementary Information Section IV). Based on the



Fig. 3 The two-dimensional potential energy surface as a function of the length of two bonds (C^1-C^8 and C^6-C^7) created by the [2 + 2] cycloaddition of **7b** to propynal. The hypothetical reaction coordinate for the formation of **8b** is indicated by the blue projection. The ridge separating the reactants' and products' valleys is highlighted by the green curve.

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calculation, only one saddle point was found, which indicated that the reaction went through the one-step mechanism. At the saddle point, the length of the C^1-C^8 bond and the C^6-C^7 bond are 2.84 Å and 1.63 Å, respectively. Meanwhile, the length of the C^1-C^8 bond and the C^6-C^7 bond of the product **8b** are 1.54 Å and 1.53 Å, respectively. It is clear that at the saddle point, the C^6-C^7 bond nearly forms, while the C^1-C^8 bond hardly forms. These results indicated that the C^6 carbon on **7b** first attacks the C^7 carbon of propynal directly leading to a zwitterionic structure without any formation of an intermediate (Scheme 7c).³⁸

Conclusions

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Once propynal was adsorbed into the supercages of Na-Y, the labile aldehyde was stabilized and survived for over 30 days even at ambient temperature without self-polymerization. The Na-Y-adsorbed propynal showed low-field shifts of C^1 and C^3 in its ¹³C-DD/MAS-NMR, which indicated the coordination of a carbonyl oxygen atom of propynal to the sodium ion in the zeolite. In addition, the Na-Y-adsorbed propynal was sufficiently and concurrently activated to react with three types of ynophile which have been only rarely reported so far: (1) Three electron-deficient α -diazocarbonyl compounds underwent the 1,3-dipolar cycloaddition to propynal to afford the corresponding pyrazoles in good yields, (2)cinnamaldehyde derivatives were produced by the 1,4addition of the mono-, di-, and trimethoxy-substituted benzenes to propynal. Especially in the case of the reactions of anisole with propynal, the combined use of Na-Y and a catalytic amount of H-Y improved the yields because the Brønsted acid sites of H-Y catalyzed the addition reaction and the Na-Y functioned as a reservoir for the desired products and kept them from some consecutive side-reactions, and (3) the [2 + 2] cycloaddition of three cycloalkenes to propynal yielded the corresponding cyclobutenes. Our quantum chemical calculation demonstrated that the alkene first attacks propynal in the Michael addition-type fashion via the one-step-like nonconcerted mechanism. The three types of reaction can produce valuable products containing a formyl group and a C=C double bond.

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