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Copper(I) Zeolites as Heterogeneous and Ligand-Free Catalysts: [3+2] Cycloaddition of Azomethine Imines

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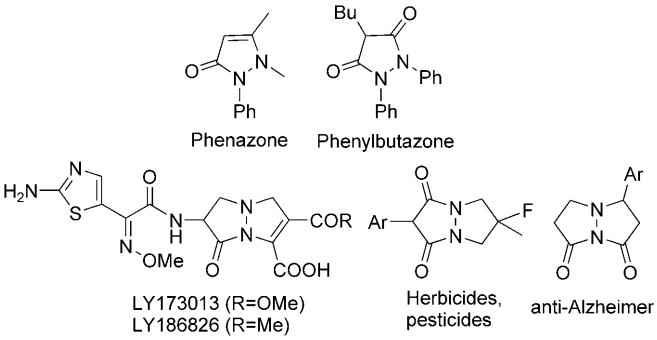
Abstract: Copper(I)-exchanged zeolites were used as heterogeneous ligand-free catalysts for [3+2] cycloaddition of azomethine ylides, which allows versatile, efficient, and highly regioselective synthesis of pyrazolone derivatives. These cheap and easy-to-prepare catalysts exhibit wide scope and compatibility with functional groups. They are very simple to use, easy to remove (by simple filtration), and recyclable (up to six times without loss of activity).

Keywords: click chemistry · copper · cycloaddition · heterogeneous catalysis · zeolites

Introduction

Pyrazolone heterocycles and especially dihydropyrazolones are widely used as dyes for various applications in the food, textile, photography, and cosmetics industries.[1] Some of these heterocycles exhibit useful biological properties, for example, phenazone (Scheme 1) was one of the first synthetic drugs. The corresponding saturated pyrazolidin-3-ones exhibit similar properties, as exemplified by the anti-inflammatory drug phenylbutazone (Scheme 1),[1] but they have also been investigated as β-lactam mimics towards new antibiotics.[2,3] In the latter context, N,N-bicyclic derivatives, especially tetrahydropyrazolo[1,2-*a*]pyrazolones (e.g., LY in Scheme 1) have been investigated since the late 1980s as analogues of penicillin and cephalosporin antibiotics.[2,3] These bicyclic heterocycles proved to have other important and useful bioactivities, and they have been developed as herbicides and pesticides,[4] antitumor agents,[5] calcitonin agonists,[6] and as potent drugs for treatment of cognitive dysfunctions such as Alzheimer's disease (Scheme 1).[7]



Scheme 1. Examples of biologically active dihydropyrazolones, pyrazolidin-3-ones, and N,N-bicyclic pyrazolidin-3-one derivatives

Because of this broad interest, several routes have been developed for the synthesis of pyrazolidin-3-ones and their N,N-bicyclic derivatives. The most common method relies on 1,3-dipolar cycloaddition of azomethine imines, especially for the formation of N,N-bicyclic pyrazolidinone derivatives.[1] Described as early as 1968 by Dorn et al., the latter route requires harsh conditions and usually leads to mixtures of regioisomers in variable yields [Scheme 2, Eq. (a)].[8] Most 1,3-dipolar cycloadditions have been improved by copper catalysis,[9] and Fu et al. recently reported that copper(I) iodide in the presence of certain amines catalyzes such [3+2] cycloadditions and dramatically enhances their regioselectivity [Scheme 2, Eq. (b)].[10] The obvious analogy between the conditions used by Fu et al. and the improved cycloaddition in the Meldal–Sharpless copper(I)-catalyzed version of the Huisgen cycloaddition of azides[11] led us to consider applying copper(I) zeolites as catalysts in

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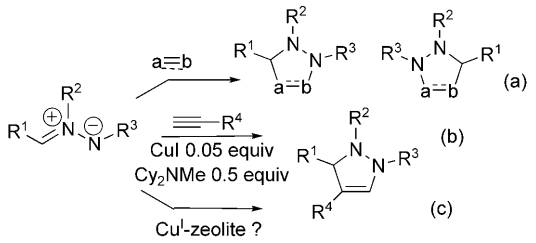
Supporting information for this article (detailed experimental procedures for **1a–j** and NMR spectra of all new compounds) is available on the WWW under http://dx.doi.org/10.1002/chem.200802191.



Scheme 2. Cycloaddition of azomethine imines.

the cycloaddition of azomethine imines. As successfully shown for the "click" Huisgen reaction,[12] we reasoned that the zeolite framework could act as ligand toward copper(I) that stabilizes this inherently labile species and thus avoid the addition of stabilizing and activating ligands [Scheme 2, Eq. (c)]. Furthermore, the inherent heterogeneous nature of zeolites should greatly facilitate product recovery (through simple filtration) and catalyst recycling.

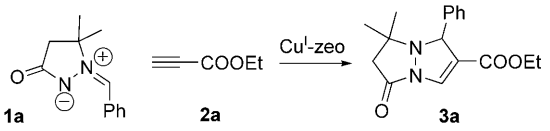
In this context and in connection with our current studies on zeolites as catalysts in organic synthesis,[12,13] we explored the cycloaddition of azomethine imines derived from pyrazolidinones in the presence of copper(I) zeolites. We report here that copper(I) zeolites indeed act as ligand-free catalysts for the cycloaddition of azomethine imines and we detail here the scope of this first zeolite-catalyzed cycloaddition of azomethine imines [Scheme 2, Eq. (c)].

Results and Discussion

Reaction conditions: In an initial series of experiments, we examined the behavior of the readily accessible (*Z*)-1-benzylidene-5,5-dimethyl-3-oxo-1-pyrazolidinium-2-ide (**1a**) with ethyl propiolate (**2a**) in the presence of Cu^I-modified USY zeolite under various conditions (Table 1). This zeolite was selected first, since it proved efficient for several other reactions[12,13] and its large pores can accommodate several molecules.

No reaction took place without catalyst whatever the solvent (Table 1, entry 1). As reported,[10] CuI alone was not a good catalyst in dichloromethane, only giving the expected adduct **3a** in very low yield (Table 1, entry 2). Under similar conditions, Cu^I-USY was a better catalyst providing **3a** in modest yield but in a clean reaction (Table 1, entry 3). Better yields were achieved in dichloromethane at reflux (Table 1, entries 4 and 5), but on prolonged reaction some degradation occurred (Table 1, entry 5). Surprisingly, dichloroethane did not help and was even deleterious, with modest conversion (Table 1, entries 6 and 7) even after prolonged reaction time (Table 1, entry 8). Increasing solvent polarity seemed to help, since in THF **3a** was again obtained and isolated in good yield within reasonable reaction time (Table 1, entry 9). However, in more polar or in protic solvents, the reaction was again very slow whatever the temperature, and degradation occurred (Table 1, entries 10 and 11). Warm toluene proved to be the best choice, allowing the adduct **3a** to be isolated in high yield after a few hours, while the reaction performed at room temperature was again very slow (Table 1, entry 13 versus entry 12). Control experiments under these conditions with untreated H-USY confirmed the dramatic role of copper(I) loaded into the zeolite, since no transformation occurred (Table 1, entry 14).

Table 1. Screening conditions for the Cu^I-USY-catalyzed cycloaddition of **1a** with ethyl propiolate.[a]



1a **2a** **3a**

Entry	Catalyst	Solvent	*T* [°C]	*t* [h]	Recovered **1a** [%][b]	Yield of **3a** [%][b]
1	none	CH_2Cl_2[c]	20	24	98	0
2	CuI	CH_2Cl_2[c]	20	20	80–95	traces
3	Cu^I-USY	CH_2Cl_2	20	24	54	40
4	Cu^I-USY	CH_2Cl_2	40	24	42	55
5	Cu^I-USY	CH_2Cl_2	40	60	–	60[d]
6	Cu^I-USY	$Cl(CH_2)_2Cl$	20	24	96	traces
7	Cu^I-USY	$Cl(CH_2)_2Cl$	60	24	71	20
8	Cu^I-USY	$Cl(CH_2)_2Cl$	60	72	61	26
9	Cu^I-USY	THF	60	12	30	60
10	Cu^I-USY	MeCN	60	24	–	27[d]
11	Cu^I-USY	MeOH	60	72	–	20[d]
12	Cu^I-USY	PhMe	20	24	87	traces
13	Cu^I-USY	PhMe	60	4	–	90
14	H-USY	PhMe	60	72	98	0

[a] Reaction performed on 1 mmol of **1a** and 1.2 mmol of **2a** in 2 mL of solvent with 7–10 mg of Cu^I-zeolite (i.e., approximately 5 mol% of Cu^I[15]). [b] Yields of isolated pure product. [c] THF, acetonitrile, toluene, and methanol were also examined without success. [d] Some degradation occurred.

Catalyst screening: In the search for the optimal zeolite catalyst, Cu^I-USY was compared to four other representative zeolites. Zeolites H-Y, H-MOR, H-ZSM5, and H-β were modified by treatment with CuCl[14] and used as catalysts in the same reaction under the above conditions (Table 2).

As already observed for the cycloaddition of azides,[12a–c] all modified zeolites proved to efficient catalysts for Dorn cycloaddition, giving the expected adduct **3a** in good to high yields (69–95%; Figure 1). As expected for a reaction in

Table 2. Catalyst screening for cycloaddition of **1a** with ethyl propiolate.[a]

Entry	Catalyst	Yield [%]	Topology	Pore diameter [Å]	Si/Al ratio	Acidic sites [mmol g^{-1}]
1	Cu^I-USY	95	cage-type	7.4×7.4	2.8	4.39
2	Cu^I-Y	95	cage-type	7.4×7.4	1.5	6.67
3	Cu^I-β	69	channel-type	7.6×6.4 5.5×5.5	12.5–17.5	0.90–1.23
4	Cu^I-ZSM5	80	channel-type	5.1×5.5 5.3×5.6	15	1.04
5	Cu^I-MOR	89	channel-type	6.5×7.0 3.4×3.8	10.3	1.48

[a] Reaction conditions: 1 mmol of **1a** and 1.2 mmol of **2a** in 2 mL of toluene at 60°C for 4 h in the presence of 7–10 mg of Cu^I-zeolite. [b] Yields determined by NMR spectroscopy with internal standard.

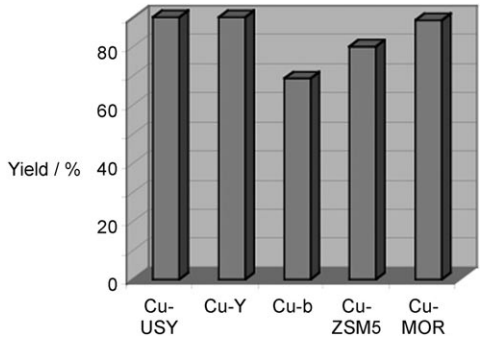


Figure 1. Efficiency of Cu-zeolite-catalyzed cycloaddition in dependence on zeolite nature.

which two molecules must meet within zeolite pores, cage-type zeolites having larger pore size were better catalysts than the smaller channel zeolites (Figure 1). However, size discrimination was clearly not the sole factor since Cu mordenite, which has the smallest pores in one of its channel systems, proved almost as effective as Cu-Y and Cu-USY (Figure 1).

Unexpectedly, it seemed that the catalyst efficiency of the modified zeolites could be correlated to the Si/Al ratio (Figure 2). The lower the Si/Al ratio, the better the catalyst.

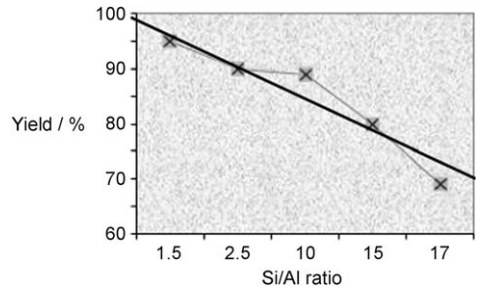


Figure 2. Efficiency of Cu-zeolite-catalyzed cycloaddition in dependence on zeolite Si/Al ratio.

Since this ratio is linked to the number of acidic sites, and thus to the number of copper ions in the zeolites, such correlation could correspond to the accessibility of the reagents to copper ions. The activity of copper loaded in zeolites is known to be dependent on its location within zeolite framework.[16]

Catalyst recycling: An important and useful feature of any heterogeneous catalyst is its recovery and recyclability. The Cu-modified zeolites used in the present study could easily be recovered through a simple filtration over Nylon membrane. A simple washing process allowed the organic materials and the zeolite to be recovered.

Recyclability was examined by performing the cycloaddition reaction between the azomethine ylide **1a** and ethyl propiolate (**2a**) several times with the same Cu^{I}-USY catalyst. After each run, the catalyst was recovered by filtration and regenerated by heating before being reused in the next run.[17] As shown in Figure 3, the Cu^{I}-USY catalyst could be recycled at least up to six times without dramatic changes. It seems, however, that every two runs a slight decrease in yield occurred, but the catalyst was still active after the sixth reuse, still giving the product with a reasonable 75% yield.

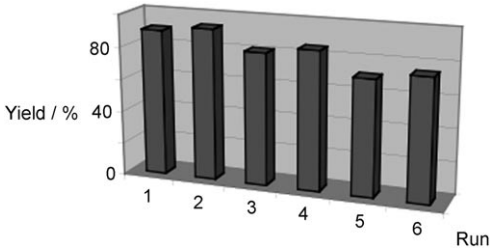
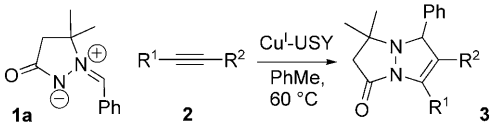


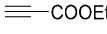
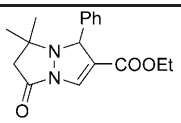
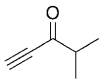
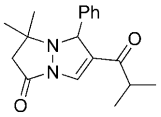
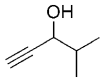
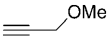
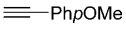
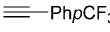
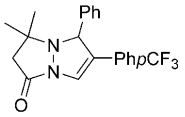
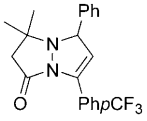
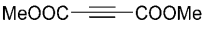
Figure 3. Cu^{I}-USY recycling and reuse for the cycloaddition of **1a** with ethyl propiolate.

Scope and limitations: In one series of experiments, the readily available (*Z*)-1-benzylidene-5,5-dimethylpyrazolidin-3-one ylide (**1a**) was treated with various alkynes **2a–i** bearing different groups in the presence of Cu^{I}-USY as catalyst (Table 3). As for the Dorn cycloaddition and the version of Fu et al., alkynes bearing an electron-withdrawing group proved to be most reactive. Ethyl propiolate (**2a**) gave the expected adduct **3a** in high yield and high regioselectivity (Table 3, entry 1). Propargylic ketones such as **2b** were also good dipolarophiles under these conditions, giving the corresponding diketo bicycle **3b** in high yield (Table 3, entry 2). The latter was however slightly lower than with propiolates (Table 3, entry 2 versus entry 1). Nevertheless, a single isomer was also detected in this case, that is, the regioselectivity of this Cu^{I}-zeolite catalyzed cycloaddition is high. The corresponding propargylic alcohol **2c** did not give the expected adduct, even after prolonged reaction time (Table 3, entry 3). To be sure that this lack of transformation was not due to some size discrimination by the zeolite, the simplest methyl propargyl ether (**2d**) was used under the same conditions (Table 3, entry 4). Since no reaction took place in this case and hyperconjugation slightly decreases the electron density on the alkyne, such Cu^{I}-zeolite-catalyzed cycloaddition clearly requires acetylenic derivatives bearing strongly electron withdrawing groups.

To check the extent of such electronic effects, we subjected phenylacetylene (**2e**) and derivatives thereof bearing electron-donating (**2f**) or electron-withdrawing groups at the *para* position (**2g**) to the same conditions. Parent compound **2e** and compound **2f** having an electron-donating substituent did not react (Table 3, entries 5 and 6). Compound **2e** was also a poorly reactive alkyne under the conditions of Fu et al.; it required heating and longer reaction time and gave a mixture of diastereoisomers. In contrast, 4-trifluoromethylphenylacetylene (**2g**) exhibiting an electron-withdrawing group rapidly underwent cycloaddition in good

Table 3. Cu^{I}-zeolite catalyzed cycloaddition of pyrazolidinone ylide **1a** with various alkynes **2**.[a]



Entry	Dipolarophile		t [h]	Yield [%][b,c]	Adduct
1		**2a**	4	90	 **3a**
2		**2b**	4	77	 **3b**
3		**2c**	4	0[d]	–
4		**2d**	4	0[d]	–
5		**2e**	48	0[d]	–
6		**2f**	4	0[d]	–
7		**2g**	4	68	 **3c** (**3c**/**4** 70:30)  **4**
8		**2h**	48	0[f]	–
9		**2i**	48	0[f]	–

[a] Reactions performed with 1 equiv of **1a**, 1.2 equiv of **2**, and 5 mol% Cu^{I}-USY,[15] in 2 mL of toluene at 60 °C. [b] Yields of isolated pure product. [c] Only one regioisomer was formed and isolated unless otherwise noted. [d] No further transformation on prolonged reaction time, and the starting materials were recovered. [e] The starting materials were essentially recovered. [f] Decomposition occurred, and unidentified byproducts were formed.

yield (Table 3, entry 7 versus entries 5 and 6). However, two regioisomers were produced, of which the major one **3c** was that solely observed in the preceding reactions (Table 3, entry 7 versus entries 1 and 2). The two isomers **3c** and **4** could be easily distinguished by ^{1}H NMR spectroscopy, through the multiplicity of their vinylic and benzylic protons.

Disubstituted alkynes **2h** and **2i** could not be transformed into the corresponding bicyclic heterocycles, and only degradation products formed after prolonged reaction time (Table 3, entries 8 and 9).

In a second series of experiments, various pyrazol-3-one ylides **1b–j** were treated with the most reactive alkyne under our conditions, that is, ethyl propiolate (**2a**; see Table 3) in the presence of Cu^{I}-USY as catalyst (Table 4). The unsubstituted (*Z*)-1-benzylidenepyrazol-3-one ylide (**1b**) proved to be as reactive as its disubstituted analogue **1a** and gave the expected adduct with ethyl propiolate (**3d**) over 4 h and in high yield (Table 4, entry 1).

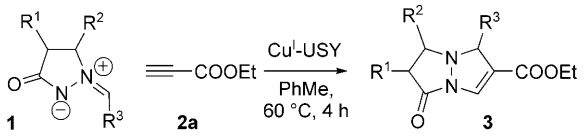
The mono-substituted (*Z*)-1-benzylidene-5-methylpyrazol-3-one ylide **1c** also gave the expected adduct **3e**. The yield was, however, lower due to some degradation of this adduct (Table 4, entry 2 versus entry 1). Interestingly, a single regio- and diastereoisomer was isolated. The NOESY correlations revealed a *syn* relative stereochemistry for the methyl and phenyl groups in this adduct (Scheme 3). Such stereochemical relationship in **3e** suggested propiolate addition *anti* to the methyl group in **1c** (Scheme 3).

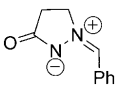
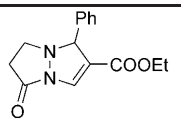
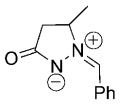
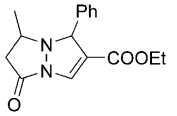
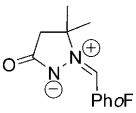
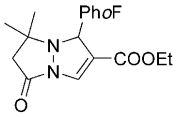
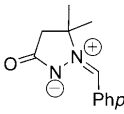
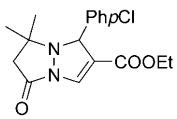
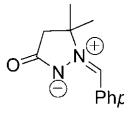
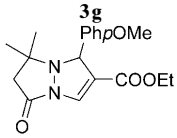
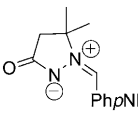
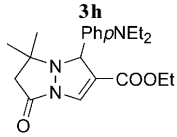
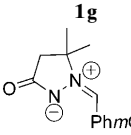
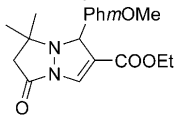
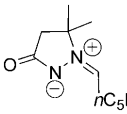
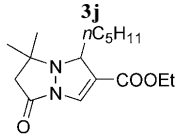
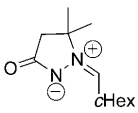
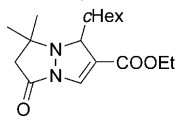
The nature of the substituent at the dipole end was varied in order to explore the frontier orbital control typical of uncatalyzed [3+2] cycloadditions. Benzaldehyde derivatives bearing electron-donating or -withdrawing groups were thus condensed with 5,5-dimethylpyrazol-3-one to give a series of pyrazol-3-one ylides with variously substituted phenyl groups at the 1-position.

Halogenated derivatives **1d** and **1e** reacted as readily as their parent compound **1a** to yield the corresponding adducts **3f** and **3g** in the same reaction time and with similar high yields (Table 4, entries 3 and 4, versus Table 1, entry 1). Interestingly, the fluorinated compound having the more electron-withdrawing group gave the highest yield, while the less electronegative chloride gave the lowest (Table 4, entry 3 versus 4), and this suggests a correlation between reaction efficiency and the electronic properties of the substituent. This effect was confirmed by the reaction of compounds bearing electron-donating groups of increasing strength. The *para*-methoxyphenyl derivative **1f** indeed gave the expected cycloadduct **3h**, but in lower yield than achieved with the halogenophenyl derivatives **1d** and **1e** (Table 4, entry 5 versus entries 3 and 4). The *para*-aminophenyl derivative **1g** proved far less reactive and only approximately one-third of the starting material was converted within the same duration, giving the corresponding adduct **3i** in modest yield (Table 4, entry 6).

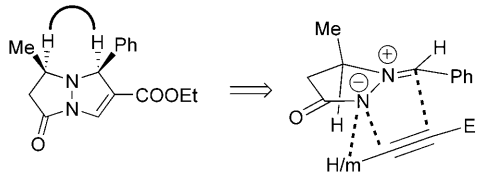
These results clearly showed the influence of electronic effects on the Cu^{I}-zeolite-catalyzed cycloaddition of pyrazol-3-one ylides. The more electron-withdrawing the substituent at the dipole end, the more efficient the reaction and the

Table 4. Cu^{I}-USY-catalyzed cycloaddition of various **1** with ethyl propiolate.[a]



Entry	Dipolarophile	Yield [%][b,c]	Adduct
1	 **1b**	80	 **3d**
2	 **1c**	63	 **3e**
3	 **1d**	90	 **3f**
4	 **1e**	82	 **3g**
5	 **1f**	67	 **3h**
6	 **1g**	30[d,e]	 **3i**
7	 **1h**	70	 **3j**
8	 **1i**	63	 **3k**
9	 **1j**	50[f]	 **3l**

[a] Reactions performed with 1 equiv of **1**, 1.2 equiv of **2a**, and 5 mol% Cu^{I}-USY[15] in 2 mL of toluene at 60°C. [b] Yields of isolated pure product. [c] Only one regioisomer was formed and isolated. [d] No further transformation on prolonged reaction time. [e] The starting materials were essentially recovered. [f] Decomposition occurred, and unidentified byproducts were formed.



Scheme 3. NOESY correlations establishing the relative stereochemistry of **3e** and suggesting possible transition states.

better the yield over the same reaction time (Table 4, entries 3–6). However, an experiment carried out with the *meta*-methoxyphenyl-substituted ylide **1h** revealed that such electronic influence might not be the sole parameter. Indeed, **1h** reacted as effectively as its *para*-substituted analogue **1f**, despite the weaker electronic effect of the methoxy group at that position (Table 4, entry 7 versus entry 5).

Pyrazol-3-one ylides **1i** and **1j** substituted by alkyl group at the dipole end also gave the corresponding adducts **3k** and **3l** (Table 4, entries 8 and 9). Under the same conditions, these 1-alkylidenepyrazol-3-one ylides reacted almost the same as the methoxyphenyl-substituted derivative **1f**, as expected from a dipole bearing a slightly electron donating group (Table 4, entry 8 versus entry 5). In the case of cyclohexyl derivative **1j**, some decomposition occurred and led to a reduced yield of the adduct and to side products (Table 4, entry 9).

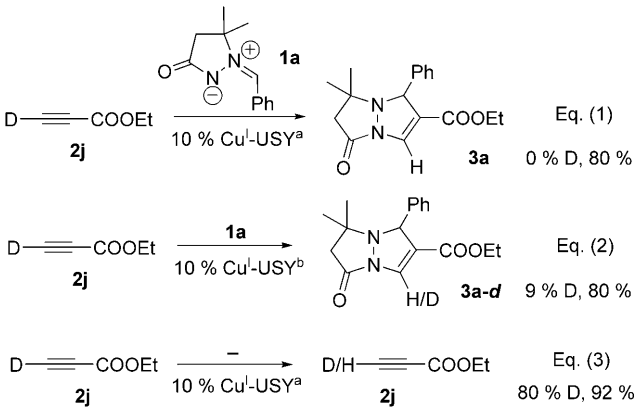
Mechanism: As for other copper(I)-catalyzed [3+2] cycloadditions, copper acetylides have been postulated as intermediates.[9–11] Whether the mechanism of the present copper(I)-zeolite catalyzed Dorn cycloaddition is similar could easily be checked through experiments with deuterated alkynes. With such starting materials, no deuterium should be recovered in the adduct if copper acetylides are involved.

Ethyl deuteropropriolate (**2j**) was thus prepared and treated with ylide **1a** in the presence of a catalytic amount of Cu^{I}-USY. The bicyclic heterocycle **3a** was obtained with a yield similar to the one previously obtained (see Table 3, entry 1), but no deuterium could be found in this adduct [Scheme 4, Eq. (1)]. This result is in favor of acetylide formation during the course of the reaction, as are the results obtained with disubstituted alkynes.

However, H/D exchange in ethyl deuteropropriolate prior to the cycloaddition could not be excluded in zeolites. Indeed, copper(I)-USY prepared at 350°C still contains approximately 20% of protons in its active sites. Therefore, these residual acidic protons could be responsible for some H/D exchange with relatively labile protons.

To check this hypothesis, **2j** was subjected to the same conditions but without any dipole. Only a slight decrease in deuterium content was observed [Scheme 4, Eq. (3)], that is, H/D exchange occurred to an extent which corresponds to the amount of protons remaining in Cu^{I}-USY.

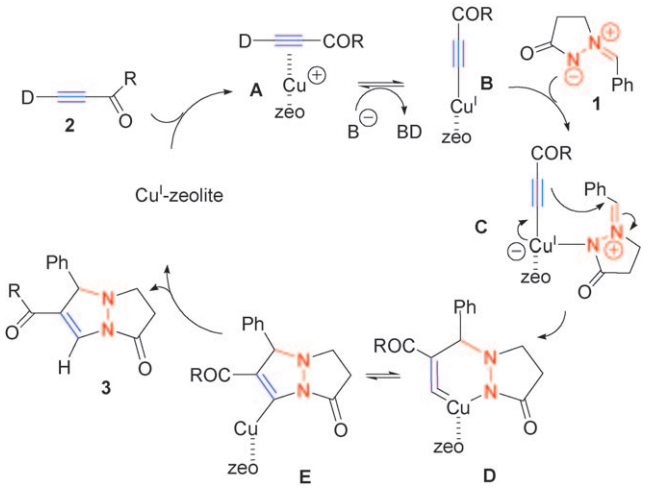
Further, **2j** was again treated with ylide **1a** but in the presence of deuterated copper(I) zeolite.[18] No H/D ex-



Scheme 4. Cycloadditions with deuterated ethyl propriolate catalyzed by either regular copper(I) zeolite (a) or deuterated copper(I)-zeolite (b).

change can occur on **2j** if the starting zeolite is already deuterated. The deuterium label should thus be retained during the reaction if no other process occurs, but should disappear if acetylide is formed. Cu^{I}-USY obtained from a deuterated zeolite.[18] catalyzed the cycloaddition as well as regular Cu^{I}-USY, but loss of deuterium was observed [Scheme 4, Eq. (2)].

These results clearly showed that the mechanism of the copper-zeolite catalyzed cycloaddition of azomethine imines is similar to those other copper-catalyzed cycloadditions, and probably involves a copper acetylide.[9–11] The copper acetylide (**B** in Scheme 5) is probably produced from the initial π complex **A** through hydrogen (deuterium) abstraction. The base able to do so could be the azomethine ylide **1**, but not the zeolite oxygen atoms, since **2j** was mostly recovered in the presence of zeolite alone [see Scheme 4, Eq. (3)]. The thus-formed copper acetylide would then interact with the azomethine ylide, most probably through the negatively charged nitrogen atom, giving cuprate-like complex (**C**). This would then rearrange to a putative six-membered metallacycle, which could evolve to a bicyclic vinyl copper species, which on hydrolysis yields the adduct **3**. Other routes, such as nucleophilic addition of the azomethine ylide to the propiolate unit in **A**, **B**, or **C**, which should also give **E**, can not be ruled out at this stage.



Scheme 5. Proposed mechanism for copper(I)-zeolite-catalyzed cycloaddition of azomethine ylide with activated alkyne.

Conclusion

We have shown for the first time that copper(I)-modified zeolites can be used as catalysts for [3+2] cycloaddition of pyrazol-3-one ylides with alkynes. This heterogeneous method offers mild and efficient access to tetrahydropyrazolo[1,2-*a*]pyrazol-3-ones with a reasonably wide scope, tolerates various functional groups, and gives high regioselectivity. Moreover, this heterogeneous copper(I)-modified zeolite catalyst can be reused six times without significant loss of activity. Experiments with labeled materials suggested a mechanism involving a copper acetylide as intermediate.

Experimental Section

General: All starting materials were commercial and were used as received; pyrazolidin-3-ones **1a–j** were prepared according to known procedures (see Supporting Information for details).[19] The reactions were monitored by thin-layer chromatography on silica plates (silica gel 60 F_{254}, Merck) by using UV light and *p*-anisaldehyde for visualization. Column chromatography was performed on silica gel 60 (0.040–0.063 mm, Merck) with ethyl acetate/cyclohexane as eluent. Evaporation of solvents was conducted under reduced pressure below 30 °C unless otherwise noted. Melting points were measured in open capillary tubes and are uncorrected. IR spectra were recorded with a Perkin-Elmer FTIR 1600 spectrometer (KBr disk). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance 300 or 400 spectrometers. Chemical shifts are reported relative to residual solvent as an internal standard ($CDCl_3$: 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C; CD_3OD: 3.31 ppm for ^{1}H and 49.15 ppm for ^{13}C). Carbon multiplicities were determined by DEPT135 experiments. Electron impact (EI) and electrospray ionization (ESI) low/high-resolution mass spectra (MS) were obtained from the mass spectrometry department of the Service Commun d'Analyses, Institut de Chimie, Strasbourg.

Preparation of Cu^{I}-USY and other Cu^{I} zeolites: Commercial NH_4-USY was loaded in an oven and heated at 550 °C for 4 h giving H-USY. 1 g of H-USY and 475 mg of CuCl (1.1 equiv) were mixed in a mortar and charged into a closed reactor. Heating the mixture of powders at 350 °C for 3 d under a nitrogen flow quantitatively yielded Cu^{I}-USY. The same procedure was applied to other zeolites.[14] Such modified zeolites have been characterized.[14]

General procedure for Cu^{I}-zeolite catalyzed [3+2] cycloaddition of azides and terminal alkynes: Pyazolidin-3-one ylide **1** (0.4 mmol, 1.0 equiv) and then alkyne **2** (0.48 mmol, 1.2 equiv) were added to a suspension of Cu^{I}-USY (7 mg, 0.05 equiv)[15] in 2 mL of toluene. After 4 h of stirring at 60 °C (unless otherwise stated), the mixture was cooled to room temperature, and the catalyst was removed by filtration over Nylon membrane (0.20 μm). Solvent evaporation provided the resulting crude product. Column chromatography was performed when necessary.

Ethyl 6,7-dihydro-7,7-dimethyl-5-oxo-1-phenyl-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3a): Yellow oil, 90 % yield. ^{1}H NMR ($CDCl_3$): δ = 7.52 (d, J = 1.5 Hz, 1H), 7.46–7.43 (m, 2H), 7.37–7.27 (m, 2H), 5.45 (d, J = 1.5 Hz, 1H), 4.13–3.98 (m, 2H), 2.86 (d, J = 15.9 Hz, 1H), 2.37 (d, J = 15.9 Hz), 1.24 (s, 3H), 1.15 (t, J = 7.0 Hz, 3H), 1.14 ppm (s, 3H);

^{13}C NMR ($CDCl_3$): δ = 166.6, 166.4, 142.0, 129.2, 128.3, 127.8, 127.7, 117.3, 64.5, 64.4, 60.3, 49.4, 24.9, 19.0, 14.0 ppm; FTIR (neat): 3556, 3074, 2979, 2937, 1686, 1596, 1544, 1502, 1455, 1404, 1374, 1355, 1318, 1275, 1252, 1222, 1208, 1169, 1115, 1094, 1039, 1025, 994, 976, 919 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{17}H_{20}N_2O_3$: 323.1366 [M+Na^+]; found: 323.1372.

6-Isobutyryl-3,3-dimethyl-5-phenyl-2,3-dihydropyrazolo[1,2-a] pyrazol-1(5*H*)-one (3b): Yellow oil, 77% yield. M.p. 129°C; ^{1}H NMR ($CDCl_3$): δ = 7.50 (d, J = 1.5 Hz, 1H), 7.42–7.39 (m, 2H), 7.34–7.24 (m, 3H), 5.51 (d, J = 1.5 Hz, 1H), 2.93–2.85 (m, 2H), 2.38 (d, J = 15.6 Hz, 1H), 1.21 (s, 3H), 1.15 (s, 3H), 1.04 (d, J = 6.6 Hz, 3H), 0.98 ppm (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 200.0, 167.3, 142.1, 128.3, 128.0, 127.6, 125.1, 64.5, 49.3, 37.0, 24.9, 19.7, 18.9, 18.4 ppm; FTIR (neat): 3081, 3058, 3029, 2965, 2930, 2871, 1719, 1674, 1638, 1578, 1534, 1495, 1464, 1455, 1394, 1374, 1363, 1339, 1310, 1289, 1271, 1211, 1151, 1120, 1099, 1084, 1043, 1029, 1008, 988, 943 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{18}H_{22}N_2O_2$: 321.1573 [M+Na^+]; found: 321.1555.

3,3-Dimethyl-5-phenyl-6-(4-trifluoromethylphenyl)-2,3-dihydropyrazolo-[1,2-*a*]pyrazol-1(5*H*)-one (3c): Yellow oil, 49% yield. ^{1}H NMR ($CDCl_3$): δ = 7.42 (m, 10H), 5.66 (d, J = 1.5 Hz, 1H), 2.90 (d, J = 15.6 Hz, 1H), 2.39 (d, J = 15.6 Hz, 1H), 1.32, (s, 3H), 1.17 ppm (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 164.1, 141.3, 135.8, 131.1, 128.9, 128.2, 127.4, 125.4, 125.3, 124.4, 119.1, 66.0, 64.1, 63.6, 50.0, 49.8, 29.4, 25.2, 19.5 ppm; FTIR (neat): $\tilde{\nu}$ = 2975, 2930, 1713, 1667, 1617, 1557, 1495, 1445, 1410, 1371, 1321, 1235, 1162, 1108, 1064, 1016, 959, 923 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{21}H_{19}F_3N_2O$: 411.1081 [M+K^+]; found: 411.1242.

3,3-Dimethyl-5-phenyl-7-(4-trifluoromethylphenyl)-2,3-dihydropyrazolo-[1,2-*a*]pyrazol-1(5*H*)-one (4): Yellow oil, 19% yield. ^{1}H NMR ($CDCl_3$): δ = 7.72–7.26 (m, 9H), 5.44 (d, J = 2.4 Hz, 1H), 2.39 (d, J = 2.1 Hz, 1H), 3.03 (d, J = 15.3 Hz, 1H), 2.45 (d, J = 15.3 Hz, 1H), 1.36 (s, 3H), 1.17 ppm (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 165.6, 142.2, 130.2, 128.7, 128.3, 128.2, 127.5, 127.4, 125.8, 124.9, 116.1, 107.7, 64.2, 62.7, 50.9, 26.9, 20.4 ppm; FTIR (neat): $\tilde{\nu}$ = 2976, 2928, 1707, 1667, 1619, 1555, 1484, 1444, 1410, 1370, 1320, 1215, 1162, 1107, 1063, 1016, 959 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{21}H_{19}F_3N_2O$: 373.1522 [M+H^+]; found: 373.1550.

Ethyl 6,7-dihydro-5-oxo-1-phenyl-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3d): Yellow oil, 80% yield. ^{1}H NMR ($CDCl_3$): δ = 7.51–7.52 (m, 1H), 7.39–7.25 (m, 5H), 5.14 (s, 1H), 4.13–3.97 (m, 2H), 3.43–3.35 (m, 1H), 3.05–3.01 (m, 1H), 2.96–2.84 (m, 1H), 2.79–2.71 (m, 1H), 1.13–1.10 ppm (m, 3H); ^{13}C NMR ($CDCl_3$): δ = 164.3, 163.3, 138.3, 128.7, 128.5, 128.4, 128.2, 118.3, 73.4, 60.6, 52.0, 36.1, 14.3 ppm.

Ethyl 6,7-dihydro-7-methyl-5-oxo-1-phenyl-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3e): Yellow solid, m.p. 92–93°C, 63% yield. ^{1}H NMR ($CDCl_3$): δ = 7.46–7.23 (m, 5H+1H), 5.14 (d, J = 1.6 Hz, 1H), 4.10–3.94 (qd, J = 7,1 Hz, 11 Hz, 2H), 3.41 (qdd, J = 6, 6.2, 12.1 Hz, 1H), 2.72–2.54 (m, 2H), 1.10 (t, J = 7.1 Hz, 3H), 1.05 ppm (d, J = 6 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ?166.17, 163.45, 140.96, 128.84, 128.3, 128.09, 127.97, 117.82, 117.6, 63.58, 60.35, 42.94, 17.43, 14.04 ppm; FTIR (neat): $\tilde{\nu}$ = 3075, 2971, 2928, 1693, 1596, 1429, 1302, 1245, 1184, 1102, 1012, 957, 928, 899, 867, 843 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{18}N_2O_3$: 309.1215 [M+Na^+]; found: 309.1365.

Ethyl 1-(2-fluorophenyl)-6,7-dihydro-7,7-dimethyl-5-oxo-1*H*,5*H*-pyrazolo-[1,2-*a*]pyrazole-2-carboxylate (3f): Yellow solid, 90% yield. M.p 104°C; ^{1}H NMR ($CDCl_3$): δ = 7.59 (d, J = 1.5 Hz, 1H), 7.49–7.43 (m, 1H), 7.28–7.23 (m, 1H), 7.18–7.13 (m, 2H), 7.07–7.00 (m, 1H), 5.86 (d, J = 1.2 Hz), 4.13–3.98 (m, 2H), 2.83 (d, J = 15.9 Hz, 1H), 2.39 (d, J = 15.6 Hz, 1H), 1.28 (s, 3H), 1.17 (s, 3H), 1.11 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 166.2, 163.3, 161.9, 158.6, 129.9, 129.2, 124.4, 116.2, 115.3, 115.0, 64.4, 60.4, 57.0, 49.3, 26.8, 24.6, 19.1, 13.9 ppm; FTIR (neat): $\tilde{\nu}$ = 2978, 2932, 1697, 1603, 1556, 1489, 1440, 1384, 1362, 1322, 1288, 1256, 1223, 1204, 1172, 1119, 1094, 1035, 1010, 937 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{17}H_{19}FN_2O_3$: 341.1272 [M+Na^+]; found: 341.1226.

Ethyl 1-(4-chlorophenyl)-6,7-dihydro-7,7-dimethyl-5-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3g): Yellow oil, 82% yield. ^{1}H NMR ($CDCl_3$): δ = 7.50 (d, J = 1.2 Hz, 1H), 7.42–7.15 (m, 4H), 5.44 (d, J = 1.2 Hz, 1H), 4.14–4.00 (m, 2H), 2.87 (d, J = 15.6 Hz, 1H), 2.40 (D, J = 15.6 Hz, 1H), 1.23 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H), 1.13 ppm (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 166.2, 163.7, 140.6, 133.6, 129.2, 138.5, 116.8, 64.3, 63.9, 60.4, 49.3, 24.9, 19.0, 14.0 ppm; FTIR (neat): $\tilde{\nu}$ = 2979, 2932, 1699, 1602, 1573, 1541, 1497, 1454, 1384, 1367, 1322, 1211, 1174, 1089, 1029, 1015, 978, 934 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{17}H_{19}ClN_2O_3$: 373.0729 [M+K^+]; found: 373.0887.

Ethyl 6,7-dihydro-1-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3h): Yellow oil, 67% yield. ^{1}H NMR ($CDCl_3$): δ = 7.49 (d, J = 1.5 Hz, 1H), 7.36 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 5.43 (d, J = 1.5 Hz, 1H), 4.12–3.97 (m, 2H), 3.80 (s, 3H), 2.85 (d, J = 15.9 Hz, 1H), 2.37 (d, J = 15.6 Hz, 1H), 1.40 (s, 3H), 1.23 (s, 3H), 1.16 ppm (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ = 166.2, 163.7, 159.1, 134.1, 128.9, 117.4, 113.6, 64.2, 63.9, 60.3, 55.1, 49.4, 26.8, 24.9, 19.9, 14.0 ppm; FTIR (neat): $\tilde{\nu}$ = 3079, 2964, 2933, 1728, 1686, 1600, 1511, 1459, 1439, 1409, 1374, 1358, 1324, 1282, 1245, 1224, 1200, 1169, 1119, 1097, 1034, 1001, 979, 930 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{18}H_{22}N_2O_4$: 353.1472 [M+Na^+]; found: 353.1462.

Ethyl 1-(4-diethylaminophenyl)-6,7-dihydro-7,7-dimethyl-5-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3i): Yellow oil, 30% yield. ^{1}H NMR ($CDCl_3$): δ = 7.47 (d, J = 1.5 Hz, 1H), 7.21 (d, J = 8.7 Hz, 2H), 6.62 (d, J = 8.4 Hz, 2H), 5.36 (d, J = 1.5 Hz, 1H), 4.14–3.99 (m, 2H), 3.31 (q, J = 7.1 Hz, 4H), 2.85 (d, J = 15.6 Hz, 1H), 2.35 (d, J = 15.6 Hz, 1H), 1.21–1.11 ppm (m, 15H); ^{13}C NMR ($CDCl_3$): δ = 166.6, 163.9, 147.4, 128.9, 128.6, 128.4, 117.7, 111.4, 64.3, 64.0, 60.2, 49.5, 44.2, 24.9, 19.0, 14.1, 12.6 ppm; FTIR (neat): $\tilde{\nu}$ = 2968, 2927, 2869, 1721, 1697, 1596, 1571, 1518, 1454, 1412, 1381, 1370, 1356, 1319, 1286, 1254, 1230, 1191, 1167, 1150, 1116, 1089, 1035, 1005, 978, 940 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{21}H_{29}N_3O_3$: 394.2101 [M+Na^+]; found: 394.2026.

Ethyl 6,7-dihydro-1-(3-methoxyphenyl)-7,7-dimethyl-5-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3j): Yellow oil, 70% yield. ^{1}H NMR ($CDCl_3$): δ = 7.51 (d, J = 1.8 Hz, 1H), 7.26–7.21 (m, 1H), 7.03–6.99 (m, 2H), 6.83–6.79 (m, 1H), 5.43 (d, J = 1.5 Hz, 1H), 4.13–3.98 (m, 2H), 3.80 (s, 3H), 2.85 (d, J = 15.6 Hz, 1H), 2.47 (d, J = 15.6 Hz, 1H), 1.22 (S, 3H), 1.15 ppm (t, J = 14.4 Hz, 6H); ^{13}C NMR ($CDCl_3$): δ = 166.5, 163.6, 159.0, 143.6, 129.2, 129.0, 120.2, 117.1, 113.5, 113.1, 64.4, 60.3, 55.2, 49.3, 24.9, 19.0, 14.0 ppm; FTIR (neat): $\tilde{\nu}$ = 2976, 2935, 2836, 1695, 1599, 1544, 1489, 1463, 1435, 1384, 1362, 1318, 1258, 1223, 1202, 1174, 1150, 1118, 1097, 1038, 1009, 951 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{18}H_{22}N_2O_4$: 353.1472 [M+Na^+]; found: 353.1449.

Ethyl 6,7-dihydro-7,7-dimethyl-5-oxo-1-pentyl-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole-2-carboxylate (3k): Yellow oil, 63% yield. ^{1}H NMR ($CDCl_3$): δ = 7.42 (d, J = 1.5 Hz), 4.42–4.38 (m, 1H), 4.22–4.19 (m, 2H), 3.11–3.06 (m, 1H), 2.79 (d, J = 15.6 Hz, 1H), 2.28 (d, J = 15.6 Hz, 1H), 1.72 (s, 3H), 1.66–1.58 (m, 2H), 1.35–1.25 (m, 7H), 1.03 (s, 3H), 0.90–0.85 ppm (m, 3H); ^{13}C NMR ($CDCl_3$): δ = 171.0, 168.9, 131.4, 116.1, 65.1, 60.6, 60.3, 48.8, 35.5, 31.7, 24.9, 24.4, 22.5, 18.2, 14.2 ppm; FTIR (neat): $\tilde{\nu}$ = 2957, 2931, 2871, 1699, 1606, 1543, 1466, 1405, 1362, 1332, 1253, 1203, 1173, 1118, 1097, 1081, 1023, 948 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{16}H_{26}N_2O_3$: 317.1836 [M+Na^+]; found: 317.1842.

Ethyl 1-cyclohexyl-6,7-dihydro-7,7-dimethyl-5-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]-pyrazole-2-carboxylate (3l): Yellow oil, 50% yield. M.p. 99°C; ^{1}H NMR ($CDCl_3$): δ = 7.44 (s, 1H), 4.18–4.13 (m, 4H), 2.73 (d, J = 15.3 Hz, 1H), 2.20 (d, J = 15.3 Hz, 1H), 1.70–1.67 (m, 2H), 1.61–1.58 (m, 2H), 1.47–1.44 (m, 2H), 1.26–1.16 (m, 8H), 1.08–1.03 (m, 3H), 0.92 ppm (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 170.9, 164.2, 133. 2, 114.1, 65.8, 65.4, 48.1, 41.3, 30.2, 26.4, 26.3, 26.2, 26.1, 24.9, 17.6, 14.2 ppm; FTIR (neat): $\tilde{\nu}$ = 3085, 2926, 2852, 1735, 1684, 1603, 1410, 1383, 1371, 1354, 1329, 1315, 1299, 1287, 1266, 1257, 1223, 1207, 1173, 1117, 1103, 1030, 1000, 976, 923 cm^{-1}; HRMS (ESI): m/z: calcd for $C_{17}H_{26}N_2O_3$: 329.1836 [M+Na^+]; found: 329.1803.

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