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DABCO catalyzed reaction of various nucleophiles with activated alkynes leading to the formation of alkenoic acid esters, 1,4-dioxane, morpholine, and piperazinone derivatives

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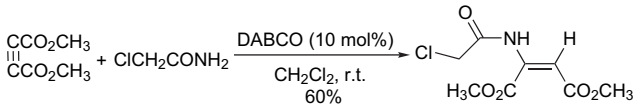
Abstract—The reaction of acids, alcohols, acylamides, 1,2-diols, 1,2-diamines or amino alcohols with activated alkynes catalyzed by 1,4-diazabicyclo[2.2.2]octane (DABCO) was systematically investigated. A series of unsaturated alkenoic acid esters or heterocycles were formed in the reaction of monobasic or dibasic nucleophiles in excellent yields, respectively.

1. Introduction

The organocatalytic carbon–carbon bond-forming reaction involving the addition of nucleophiles to activated alkynes has been drawing increasing attention.[1] Several organic catalysts have been investigated in detail in recent years.[2] Among them, DABCO, a tertiary amine base with weak basicity and moderate hindrance, has been widely used as a potential catalyst in a broad range of organic reactions, such as Hillman–Baylis reaction,[3] cyclopropanation,[4] heterocycle formation,[5] and other transformations. In our recent investigations on DABCO catalyzed reaction of α-halo carbonyl compounds with dimethyl acetylenedicarboxylate (DMAD), it was found that the Michael addition product rather than desired cyclization product was formed in moderate yield using 2-chloroacetamide as the substrate (Scheme 1).[5e]



Scheme 1.

On the basis of this observation and previous investigations,[6] we considered DABCO as a potential catalyst for the reaction of nucleophiles with activated alkynes. As a part of our continuing investigation on DABCO catalyzed organic reactions, we decided to look closer into this type of the reaction.[5d,e] A series of nucleophiles, such as alcohols, acylamides, acids, 1,2-diols, 1,2-diamines, and amino alcohols were selected to demonstrate the scope of the reaction and excellent results were obtained. On one hand, the reaction between DMAD and alcohols, acylamides or acids proceeded smoothly and rapidly at room temperature to give α,β-unsaturated carbonyl compounds in excellent yields. On the other hand, using dibasic nucleophiles, such as 1,2-diols, 1,2-diamines, and amino alcohols as the substrates, different cycloaddition products were obtained under the same conditions. Herein the full details of our research including the scope of the reaction, suitable reaction conditions, and selectivity optimization, along with the corresponding possible reaction mechanisms were reported.

2. Results and discussion

In an initial experiment, the reaction of alcohols with DMAD in the presence of a catalytic amount of DABCO (10 mol %) was examined. In a typical procedure, DMAD (0.5 mmol), DABCO (0.05 mmol), and alcohols (0.5 mmol) in CH_2Cl_2 were stirred for 10 min at room temperature and gave unsaturated alkenoic acid esters facilely by flash on chromatography on silica column. The reaction appeared to be general with a number of alcohols affording conjugate addition products in excellent yields (Table 1, entries 1–5), but it suffered from a drawback of stereoselectivity. Most of the reactions gave the final products as a pair of (*E*)-

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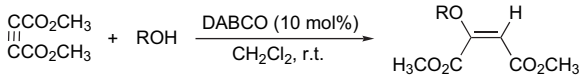
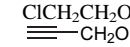
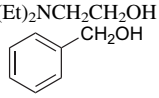
Table 1. Reaction of alcohols with DMAD[a]



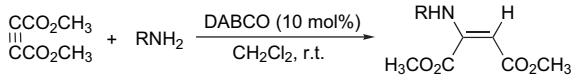
Entry	ROH	Product	Yield/%[b]	*E*/*Z*[c]
1	CH_3OH	**1**	88	20:80
2	$ClCH_2CH_2OH$	**2**	95	30:70
3		**3**	91	45:55
4	$(Et)_2NCH_2CH_2OH$	**4**	92	*E*
5		**5**	90	40:60

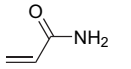
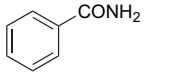
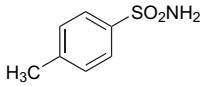
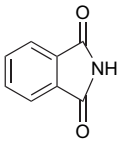
[a] All the reactions were performed at room temperature and completed within 10 min.
[b] Isolated yields.
[c] The (*E*)- and (*Z*)-isomers were separated by silica gel column chromatography.

and (*Z*)-isomers (Table 1, entries 1–3 and 5). These two isomers can be easily separated by column chromatography. An exception appeared when $Et_2NCH_2CH_2OH$ was used as the substrate. The product **4** was obtained with dominant (*E*)-selectivity (Table 1, entry 4). The structure and stereochemistry of the products were determined on the basis of their elemental analysis, mass spectrometry (MS), ^{1}H NMR, ^{13}C NMR, and IR data. The ^{1}H NMR spectral data of the products exhibited two isomers (except for product **4**) and both of them displayed characteristic resonance pattern with appropriate chemical shift. For example, the ^{1}H NMR spectrum of product **1** showed three single sharp lines at 3.76, 3.85, and 3.95 ppm for three methoxy groups in the (*Z*)-isomer and three singlets at 3.71, 3.75, and 3.89 ppm for the (*E*)-isomer. The olefinic proton in the (*Z*)-isomer resonated at 6.19 ppm, while the olefinic proton in the (*E*)-isomer resonated at 5.21 ppm. It was in agreement with the values reported in the previous literature.[7] In all the ^{1}H NMR spectra, (*E*)-isomer displayed a signal as a single sharp resonance at about 5.21–5.37 ppm for the olefinic proton. The ^{1}H NMR chemical shift of the (*Z*)-form was similar to that of the (*E*)-isomer, except for the olefinic proton, which was at about 6.19–6.36 ppm (see Section 4).

Although amine reacted with activated alkynes quickly and no base catalyst was needed,[8] we found that the same reaction of acylamides was very sluggish in the absence of a base catalyst. However, in the presence of a catalytic amount of DABCO (10 mol %), various acylamides could undergo a smooth reaction with activated alkynes at room temperature and gave the corresponding unsaturated alkenoic acid esters in moderate yields with excellent stereoselectivity. Only the (*E*)-form isomers were isolated in all the reactions of various acylamides with DMAD (Table 2, entries 1–5). Though the reaction showed optimal stereoselectivity, most of the yields were lower comparing to that of alcohols. It could be attributed to the following two reasons: (i) The reaction could not proceed completely even longer reaction time (24 h) and higher temperature (reflux) were adopted; (ii) complex side products were formed in company with the generation of unsaturated alkenoic acid esters. In each ^{1}H NMR spectrum of the products, a singlet was observed at about 5.54–5.74 ppm for the olefinic proton (except for product **10**). These shifts were similar to those observed in the previous literature.[7]

Table 2. Reaction of acylamides with DMAD[a]



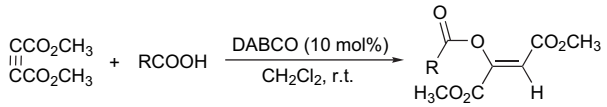
Entry	RNH_2 (or NH)	Product	Yield/%[b]	*E*/*Z*[c]
1	$ClCH_2CONH_2$	**6**	60	*E*
2		**7**	30	*E*
3		**8**	51	*E*
4		**9**	71	*E*
5		**10**	85	*E*

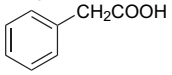
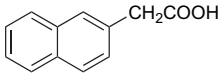
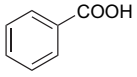
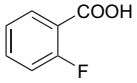
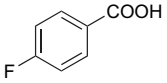
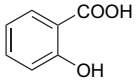
[a] All the reactions were performed at room temperature and the reaction time was extended to 12 h.
[b] Isolated yields.
[c] Determined by ^{1}H NMR (300 MHz) spectra.

With an intention to expand the scope of this conjugate addition, we tested various acids in this reaction and got excellent results surprisingly. In spite of longer reaction time required, the present method seemed to be perfect in terms of stereoselectivity. Only the (*Z*)-form isomers were isolated in all the reactions of various acids with DMAD (Table 3, entries 1–8). Moreover, the reaction had perfect selectivity in cases of more than one nucleophilic groups presented in the acids. For example, in the reaction of 2-hydroxybenzoic acid, only COOH group participated and gave the desired product with dominate (*Z*)-form (Table 3, entry 8). It should be an acidity-controlled process and the selectivity was determined by the pK_a value of the nucleophile. Nucleophilic groups with lower pK_a value will participate in the reaction first. The structure of the product was characterized by spectroscopic analysis. In each ^{1}H NMR spectrum of the products, the olefinic proton resonated at 6.66–6.82 ppm corresponding to the proposed (*Z*)-isomer. Furthermore, the structure and stereoselectivity of the products were established unambiguously by X-ray analysis of **17** as representative example (Fig. 1).[9] To the best of our knowledge, there is no such nucleophilic conjugate addition process involving acids to activated alkynes that has been reported in the literature so far.

The reaction of other activated alkynes was also investigated, such as benzyl propiolate, methyl propiolate with acids, alcohols or acylamides. It was found that excellent results were obtained under the same conditions (0.5 mmol of benzyl propiolate, 0.5 mmol of nucleophiles, and 0.05 mmol of DABCO, CH_2Cl_2, at room temperature). The reaction proceeded smoothly and rapidly (within 10 min) to give conjugate addition products in excellent yields with better stereoselectivities than that of DMAD (Table 4). Most of the reaction gave (*E*)-form alkenoic acid esters as the main product. The ^{1}H NMR spectrum of (*E*)-form isomer displayed two doublets with J=12.3 Hz for the two olefinic

Table 3. Reaction of acids with DMAD[a]



Entry	RCOOH	Product	Yield /%[b]	*E*/*Z*[c]
1	CH_3COOH	**11**	94	*Z*
2	$CH_3(CH_2)_2COOH$	**12**	99	*Z*
3		**13**	91	*Z*
4		**14**	85	*Z*
5		**15**	88	*Z*
6		**16**	78	*Z*
7		**17**	88	*Z*
8		**18**[d]	76	*Z*

[a] All the reactions were performed at room temperature and completed within 6 h.
[b] Isolated yields.
[c] Determined by ^{1}H NMR (300 MHz) analysis.
[d] The reaction time need to be extended to 24 h.

protons, while the chemical shift of the (*Z*)-form appeared with J=6.6 Hz. It was in agreement with the proposed (*E*)- and (*Z*)-isomers, respectively.

A proposed mechanism for this reaction was outlined in Scheme 2 based on the previous investigation of Nozaki Kyoko et al.[10] Initially, the zwitterionic intermediate **a**,[11] formed from DABCO and DMAD, deprotonated the nucleophile to form the corresponding intermediates **b** and **c**. Subsequent Michael addition of **b** to **c** gave intermediate **d**, which then eliminated DABCO to afford the final product. According to the proposed reaction mechanism, ethyl

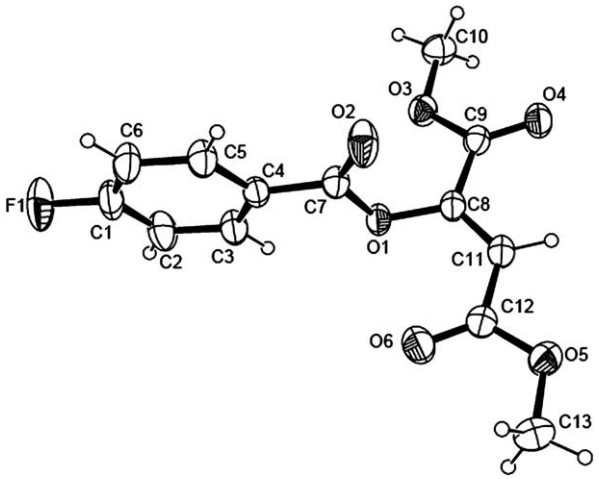
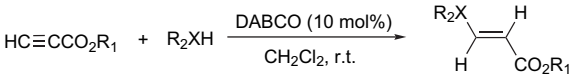
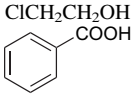
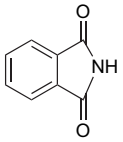


Figure 1. X-ray structure of **17**.

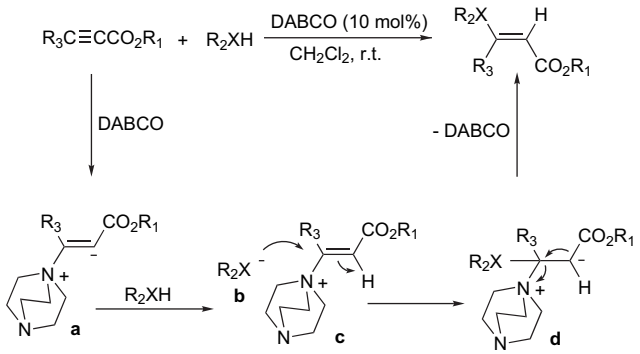
Table 4. Reaction of various nucleophiles with methyl or benzyl propiolate[a]



Entry	R_1	R_2XH	Product	Yield /%[b]	*E*/*Z*[c]
1	Bn	$ClCH_2CH_2OH$	**19**	99	95:5
2	Bn		**20**	98	*E*
3	Bn		**21**	99	*E*
4	CH_3	$ClCH_2CH_2OH$	**22**	90	90:10

[a] All the reactions were performed at room temperature and completed within 10 min.
[b] Isolated yields.
[c] Determined by ^{1}H NMR (300 MHz) spectra.

3-phenylpropiolate should also perform the same reaction with alcohols, acylamides or acids. However, the reaction did not take place even when the reaction mixture was heated to reflux or the reaction time was prolonged to 48 h.

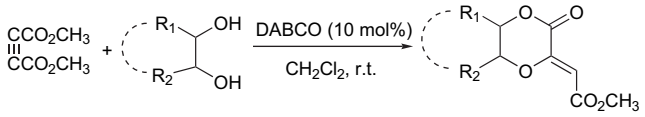


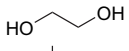
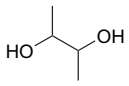
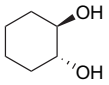
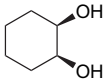
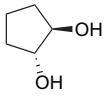
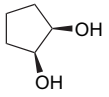
Scheme 2. Plausible mechanism for the reaction of various nucleophiles with activated alkynes.

Further scope exploration revealed that 1,2-diols were another class of suitable nucleophiles for this reaction. Interestingly, 1,2-diols on treatment with DMAD in the presence of a catalytic amount of DABCO (10 mol %) in CH_2Cl_2 afforded 1,4-dioxane derivatives in good to excellent yields. The reaction appeared to be general with a number of 1,2-diols. The results using this mild and straightforward procedure were shown in Table 5. The structure of the product was revealed by ^{1}H and ^{13}C NMR analyses. In addition, the NMR-based structure was confirmed by X-ray crystallographic analysis of **23** as representative example (Fig. 2).[12] All the reactions proceeded extremely fast and completed within 10 min. The formation of 1,4-dioxane derivatives involved a Michael addition of 1,2-diol to DMAD and a subsequent intramolecular esterification. Further study revealed that this reaction did not take place in the absence of DABCO, which suggested that the tertiary amine was required as a catalyst in this procedure.

On the basis of the above encouraging results, we used this concept to devise a new one-step approach to the synthesis

Table 5. Reaction of 1,2-diols with DMAD[a]



Entry	1,2-Diol	Product	Yield/%[b]
1		**23**	80
2		**24**	96
3		**25**	60
4		**26**	74
5		**27**	58
6		**28**	60

[a] All the reactions were performed between DMAD (0.5 mmol), 1,2-diols (3 mmol), and DABCO (0.05 mmol) at room temperature and completed within 10 min.
[b] Isolated yields.

of morpholine derivatives from amino alcohols. As we expected, excellent result was obtained in the reaction of equimolar amount of 2-aminoethanol with DMAD under above conditions (Table 6, entry 1). The structure of the product was deduced from its elemental analysis, mass spectrometry (MS), and ^{1}H and ^{13}C NMR spectroscopic data. The ^{1}H NMR spectrum showed a sharp singlet at 3.71 ppm for three methoxy group protons and a broad peak at 8.37 ppm for NH group proton. The olefinic proton resonated at 5.66 ppm corresponding to the proposed (*Z*)-isomer. On top of this, a triplet at 4.50–4.54 ppm and a multiplet at 3.50–3.55 ppm were readily attributable to CH_2 bonding to oxygen and CH_2 bonding to NH group, respectively. It was worthy of note that this reaction could take place in the absence of DABCO. It was demonstrated that the NH_2 group in the amino alcohol played the same role as DABCO in this

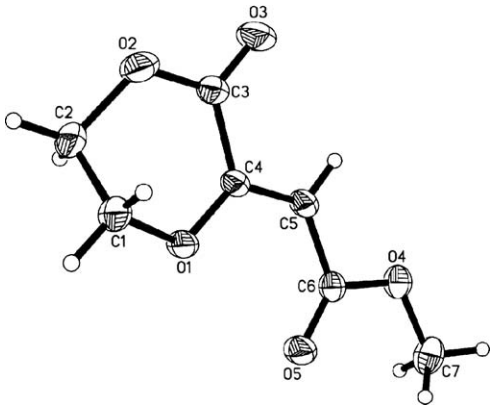
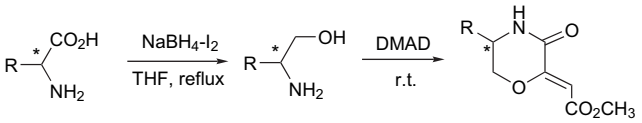
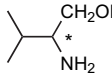
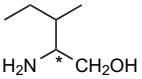
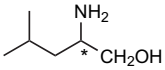
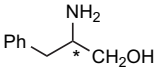
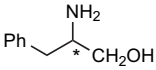
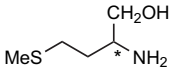
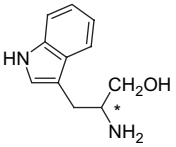
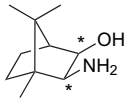


Figure 2. X-ray structure of **23**.

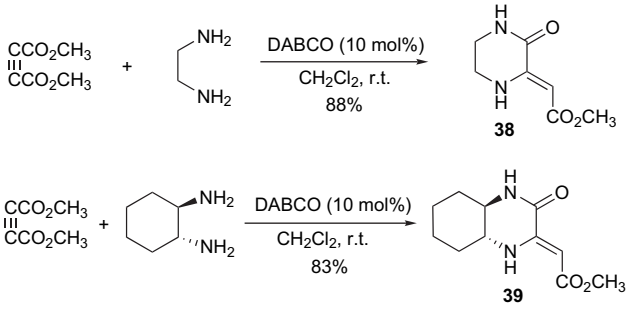
Table 6. Reaction of amino alcohols with DMAD[a]



Entry	Amino acid	Amino alcohol	Product Yield/%[b]	$[\alpha]_D^{20c}$
1	—	$NH_2CH_2CH_2OH$	**29** (80)	—
2	D-Valine		**30** (96)	−58
3	L-Isoleucine		**31** (60)	+109
4	L-Leucine		**32** (74)	+70
5	L-Phenylalanine		**33** (58)	+7
6	D-Phenylalanine		**34** (60)	−7
7	D-Methionine		**35** (80)	−56
8	DL-Tryptophane		**36** (90)	—
9	—		**37** (61)	−38

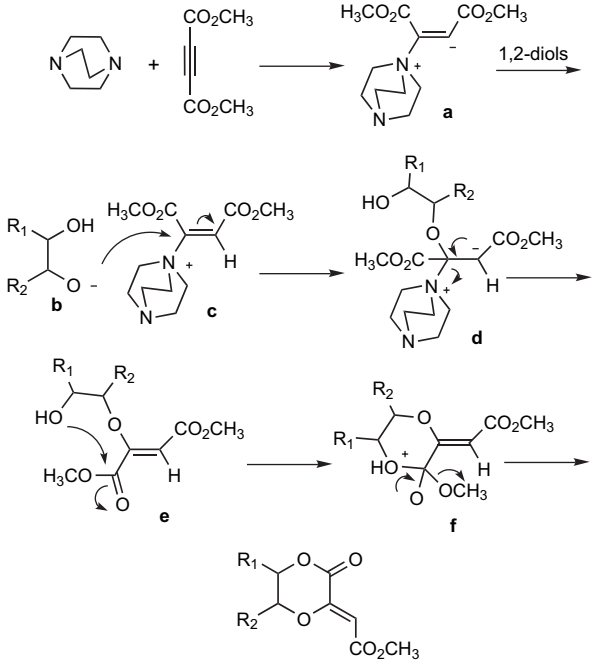
[a] All the reactions were performed between equimolar DMAD and amino alcohols at room temperature and completed within 10 h.
[b] Isolated yields.
[c] $[\alpha]_D$ in $CHCl_3$ (c=1).

reaction. It served not only as a reactant, but also as a catalyst in this reaction. A series of amino alcohols, which were readily prepared from commercial available amino acids,[13] were tested in this process to afford the corresponding morpholines (Table 6, entries 2–8). The reaction was found to be general with respect to various amino alcohols and morpholine derivatives were obtained in high yields. Moreover, we were pleased to find that this technique could also be extended to provide bicyclic morpholine in good yield (Table 6, entry 9). An attractive feature of this synthetic approach was that the incorporation of morpholine C3-substitution was facilitated by the aide availability of natural and unnatural α-amino acids. Similarly, 1,2-diamines, such as ethane-1,2-diamine and cyclohexane-1,2-diamine, could also react with DMAD in the absence of DABCO under the identical conditions to afford piperazinone derivatives in excellent yields (88% and 83%, respectively, Scheme 3). The present process was more efficient with primary 1,2-diamine or amino alcohol having primary NH_2 group, while secondary 1,2-diamine or amino alcohol with secondary NH_2 group did not work in this manner. For example, treatment of *N*1,*N*2-dimethylethane-1,2-diamine or L-prolinol with DMAD did not give the expected products under the same conditions.

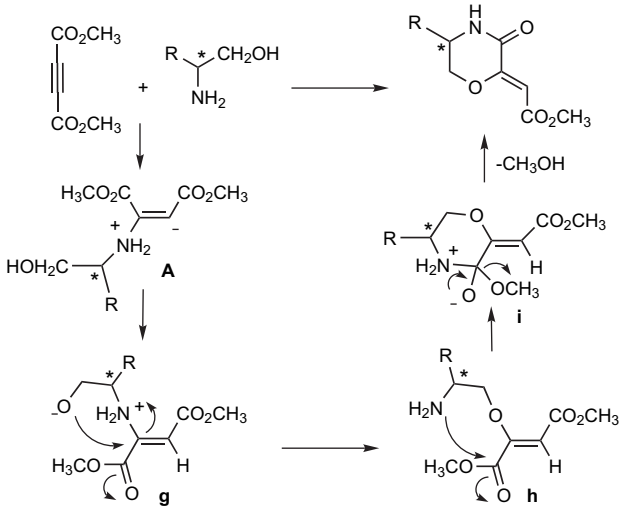


Scheme 3. Reaction of 1,2-diamines with DMAD.

The mechanisms of these reactions have not been unequivocally established, but two plausible explanations were proposed in Schemes 4 and 5. In the reaction of 1,2-diol or 1,2-diamines with DMAD, it might also involve the initial generation of a zwitterionic intermediate **a** between DABCO and DMAD (Scheme 4), which was readily protonated by one of the two protons of the nucleophile to yield intermediates **b** and **c**. Subsequent Michael addition of **b** to **c** formed intermediate **d**. It underwent the elimination of DABCO to form intermediate **e**, which was followed by intramolecular esterification in the presence of DABCO to produce the corresponding 1,3-dioxane derivatives and regenerate DABCO to accomplish the catalytic cycle. In the reaction of amino alcohol with DMAD, similarly, zwitterionic intermediate **A** generated from the addition of amino alcohol to DMAD (Scheme 5) underwent a second Michael addition of the OH group, which was followed by the leaving of NH_2 group. Subsequent intramolecular amidization led to the final morpholine derivatives. The slow transformation step of **h** to **i** was assumed to be the rate determining step, accounting for the longer reaction time required for the final product.



Scheme 4. Plausible mechanism for the reaction of 1,2-diols or 1,2-diamines with DMAD.



Scheme 5. Plausible mechanism for the reaction of amino alcohols with DMAD.

Further comparison studies demonstrated that DABCO was the optimal catalyst for the addition of acids and cyclization of 1,2-diols. Triphenylphosphine, which was commonly employed in the traditional conjugate addition reaction, was ineffective in promoting these reactions under the same conditions. Triethylamine and 4-methylmorpholine gave the lowered yields.

3. Conclusion

In the present work, we reported an excellent catalyst, DABCO, for the reaction of nucleophiles with some activated alkynes. The procedure provided an easy access to unsaturated alkenoic acid ester derivatives and various heterocycles in good to excellent yields under mild reaction conditions. This process expanded not only the scope of organocatalyst catalyzed carbon–carbon bond-forming reaction but also unprecedented approaches to heterocycle formations.

4. Experimental

4.1. General

All reagents were used directly as obtained commercially unless otherwise noted. Melting points were determined on a microscopic apparatus and were uncorrected. Column chromatography was carried out on silica gel. ^{1}H NMR spectra were recorded at 300 MHz in $CDCl_3$ and ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded by the EI method. Nicolet AVATAR 360 FTIR spectrometer was used for IR spectra. HRMS spectra were obtained with a Bruker APEX II instrument.

4.2. Typical procedure for the reaction of various nucleophiles with DMAD. Using alcohol as an example

DMAD (0.5 mmol), DABCO (0.05 mmol), and alcohol (0.5 mmol, 3 mmol for 1,2-diol, 0.5 mmol for other nucleophiles) were stirred in CH_2Cl_2 (4 ml) at room temperature for 10 min. (The reaction time needed to be extended

to 10 h for the reaction of amino alcohols and 6 h for acids.) The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on silica column to give final products.

4.2.1. Dimethyl 2-methoxyfumarate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.19 (s, 1H), 3.95 (s, 3H), 3.85 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.9, 163.4, 155.0, 107.9, 61.2, 53.0, 51.9. MS (EI, 70 eV): *m/z* (%)=174 (M^+, 2.58), 159 (20.46), 143 (48.67), 115 (67.41), 69 (100). Known compound.[7a]

4.2.2. Dimethyl 2-methoxymaleate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.21 (s, 1H), 3.89 (s, 3H), 3.75 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=166.2, 163.9, 162.4, 93.0, 56.9, 52.9, 51.5. MS (EI, 70 eV): *m/z* (%)=174 (M^+, 4.7), 159 (17.2), 143 (51.1), 115 (55), 69 (100). Known compound.[7a]

4.2.3. Dimethyl 2-(2-chloroethoxy) fumarate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.30 (s, 1H), 4.34–4.38 (t, *J*=6 Hz, 2H), 3.85 (s, 3H), 3.77–3.81 (t, *J*=6 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.3, 162.9, 153.3, 110.6, 73.2, 52.8, 51.7, 42.2. MS (EI, 70 eV): *m/z* (%)=222 (M^+, 0.64), 207 (0.45), 191 (15.05), 163 (41.83), 127 (36.58), 101 (61.28), 69 (100). Anal. Calcd for $C_8H_{11}ClO_5$: C, 43.16; H, 4.98. Found: C, 43.34; H, 4.54. IR (KBr): 2956, 2852, 1728, 1643, 1269.

4.2.4. Dimethyl 2-(2-chloroethoxy) maleate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.22 (s, 1H), 4.09–4.13 (t, *J*=6 Hz, 2H), 3.90 (s, 3H), 3.76–3.79 (t, *J*=5.7 Hz, 2H), 3.71 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=166.0, 163.5, 160.9, 94.2, 69.4, 53.0, 51.6, 40.3. MS (EI, 70 eV): *m/z* (%)=222 (M^+, 0.49), 207 (0.15), 191 (8.71), 163 (22.19), 127 (16.43), 101 (49.94), 69 (100). Anal. Calcd for $C_8H_{11}ClO_5$: C, 43.16; H, 4.98. Found: C, 43.12; H, 4.68. IR (KBr): 2956, 2851, 1751, 1717, 1630, 1212, 1154.

4.2.5. Dimethyl 2-(prop-2-ynyloxy) fumarate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.36 (s, 1H), 4.91 (s, 2H), 3.85 (s, 3H), 3.77 (s, 3H), 2.58 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 163.1, 151.9, 111.5, 77.1, 77.0, 60.2, 53.0, 51.8. MS (EI, 70 eV): *m/z* (%)=198 (M^+, 1.25), 183 (0.63), 167 (12.10), 139 (74.73), 111 (60.55), 69 (100). Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.32; H, 5.34. IR (KBr): 2958, 2852, 1733, 1633, 1256, 1116.

4.2.6. Dimethyl 2-(prop-2-ynyloxy) maleate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.37 (s, 1H), 4.60 (s, 2H), 3.89 (s, 3H), 3.72 (s, 3H), 2.66 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=165.8, 163.3, 159.7, 95.1, 77.8, 75.4, 57.4, 52.9, 51.6. MS (EI, 70 eV): *m/z* (%)=198 (M^+, 0.60), 183 (0.43), 167 (18.84), 139 (66.80), 111 (52.50), 69 (100). Anal. Calcd for $C_9H_{10}O_5$: C, 54.55; H, 5.09. Found: C, 54.57; H, 5.04. IR (KBr): 2954, 2853, 1748, 1714, 1630, 1144.

4.2.7. Dimethyl 2-(2-(diethylamino) ethoxy) maleate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=5.21 (s, 1H), 3.90–3.95 (t, *J*=6.6 Hz, 2H), 3.88 (s, 3H), 3.70 (s, 3H), 2.81–2.85 (t, *J*=6.6 Hz, 2H), 2.54–2.61 (q, *J*=7.2 Hz, 4H), 1.01–1.05 (t, *J*=7.2 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=166.1, 163.8, 161.7, 93.1, 68.7, 52.6, 51.3, 50.5, 47.6. MS (EI, 70 eV): *m/z* (%)=259 (M^+, 0.44), 244 (0.92), 100 (15.08), 86 (100). Anal. Calcd for $C_{12}H_{21}NO_5$: C, 55.58; H, 8.16; N, 5.40. Found: C, 55.37; H, 8.02; N, 5.56. IR (KBr): 2956, 2926, 2851, 1754, 1719, 1627, 1209, 1150.

4.2.8. Dimethyl 2-(benzyloxy) fumarate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.31–7.45 (m, 5H), 6.25 (s, 1H), 5.19 (s, 2H), 3.81 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.5, 163.3, 153.6, 136.0, 128.4, 128.3, 128.1, 110.2, 74.9, 52.7, 51.6. MS (EI, 70 eV): *m/z* (%)=250 (M^+, 0.55), 218 (0.63), 191 (1.33), 159 (2.20), 91 (100). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.10; H, 5.22. IR (KBr): 2953, 2849, 1729, 1640, 1266, 742, 698.

4.2.9. Dimethyl 2-(benzyloxy) maleate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.36–7.38 (m, 5H), 5.29 (s, 1H), 4.91 (s, 2H), 3.88 (s, 3H), 3.69 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=166.2, 163.8, 161.5, 134.0, 128.7, 127.8, 94.0, 71.8, 52.9, 51.6. MS (EI, 70 eV): *m/z* (%)=250 (M^+, 0.14), 218 (0.44), 191 (1.35), 159 (3.24), 91 (100). Anal. Calcd for $C_{13}H_{14}O_5$: C, 62.39; H, 5.64. Found: C, 62.39; H, 5.52. IR (KBr): 2954, 1752, 1725, 1637, 1203, 1131, 826.

4.2.10. Dimethyl 2-(2-chloroacetamido) maleate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=11.03 (s, 1H), 5.64 (s, 1H), 4.14 (s, 2H), 3.83 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.0, 164.8, 163.9, 142.4, 104.3, 53.4, 52.4, 42.4. MS (EI, 70 eV): *m/z* (%)=235 (M^+, 5.36), 237 (1.85), 204 (11.46), 206 (3.76), 176 (100), 178 (30.74). Anal. Calcd for $C_8H_{10}ClNO_5$: C, 40.78; H, 4.28; N, 5.94. Found: C, 40.61; H, 4.01; N, 5.65. IR (KBr): 3285, 2956, 2851, 1746, 1694, 1638, 1295, 1223.

4.2.11. Dimethyl 2-(acrylamido) maleate. White powder, mp 57–58 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=10.45 (s, 1H), 5.87–6.46 (m, 3H), 5.54 (s, 1H), 3.88 (s, 3H), 3.78 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.4, 164.1, 162.9, 143.8, 130.2, 129.4, 101.5, 53.1, 51.9. MS (EI, 70 eV): *m/z* (%)=213 (M^+, 3.39), 182 (3.63), 154 (35.25), 55 (100). Anal. Calcd for $C_9H_{11}NO_5$: C, 50.70; H, 5.20; N, 6.57. Found: C, 50.51; H, 5.13; N, 6.65. IR (KBr): 3302, 2954, 2852, 1745, 1692, 1633, 1283, 1220.

4.2.12. Dimethyl 2-(benzamido) maleate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=11.24 (s, 1H), 7.47–7.96 (m, 5H), 5.60 (s, 1H), 3.92 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.8, 164.5, 144.5, 133.1, 131.8, 128.9, 127.8, 101.2, 53.1, 51.9. MS (EI, 70 eV): *m/z* (%)=263 (M^+, 5.55), 232 (4.71), 204 (82.65), 105 (100). Anal. Calcd for $C_{13}H_{13}NO_5$: C, 59.31; H, 4.98; N, 5.32. Found: C, 59.19; H, 5.28; N, 5.20. IR (KBr): 3291, 2954, 2851, 1746, 1684, 1631, 1289, 1220, 774, 708.

4.2.13. Dimethyl 2-(tosylamino) maleate. White powder, mp 65–66 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=10.25 (s, 1H), 7.80–7.83 (d, *J*=8.1 Hz, 2H), 7.32–7.35 (d, *J*=8.4 Hz, 2H), 5.74 (s, 1H), 3.81 (s, 3H), 3.75 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.2, 162.9, 144.2, 143.6, 137.2, 129.4, 127.1, 103.4, 53.1, 52.1, 21.5.

MS (EI, 70 eV): *m/z* (%)=313 (M^+, 0.85), 282 (0.13), 189 (5.19), 164 (19.42), 155 (30.23), 91 (100). Anal. Calcd for $C_{13}H_{15}NO_6S$: C, 49.83; H, 4.83; N, 4.47. Found: C, 49.61; H, 4.76; N, 4.17. IR (KBr): 3116, 2955, 2844, 1747, 1682, 1627, 1272, 1230, 1161, 837.

4.2.14. Dimethyl 2-(1,3-dioxoisoindolin-2-yl) maleate. White powder, mp 104–105 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.78–7.95 (m, 4H), 7.18 (s, 1H), 3.87 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=165.5, 163.1, 162.3, 134.5, 132.0, 131.6, 128.6, 124.1, 53.5, 52.4. MS (EI, 70 eV): *m/z* (%)=289 (M^+, 8.61), 258 (5.89), 230 (100), 104 (97.83), 76 (81.30). Anal. Calcd for $C_{14}H_{11}NO_6$: C, 58.13; H, 3.83; N, 4.84. Found: C, 58.36; H, 4.10; N, 4.55. IR (KBr): 2956, 2924, 2853, 1732, 1659, 720.

4.2.15. Dimethyl 2-acetoxy fumarate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.69 (s, 1H), 3.86 (s, 3H), 3.77 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.7, 163.1, 161.4, 146.5, 116.8, 53.1, 51.9, 20.2. MS (EI, 70 eV): *m/z* (%)=202 (M^+, 0.07), 171 (4.40), 143 (46.92), 101 (77.55), 69 (55.10), 43 (100). Anal. Calcd for $C_8H_{10}O_6$: C, 47.53; H, 4.99. Found: C, 47.59; H, 4.73. IR (KBr): 2957, 2852, 1779, 1732, 1662, 1280, 1162.

4.2.16. Dimethyl 2-(butyryloxy) fumarate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.68 (s, 1H), 3.84 (s, 3H), 3.76 (s, 3H), 2.54–2.59 (t, *J*=6.9 Hz, 2H), 1.74–1.81 (m, 2H), 1.01–1.06 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.4, 163.1, 161.5, 146.6, 116.7, 53.0, 51.9, 35.3, 17.9, 13.3. MS (EI, 70 eV): *m/z* (%)=230 (M^+, 0.09), 199 (1.24), 171 (1.97), 129 (1.76), 71 (100). Anal. Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 51.93; H, 5.72. IR (KBr): 2961, 2880, 1773, 1732, 1664, 1279, 1102.

4.2.17. 13 Dimethyl 2-(2-phenylacetoyloxy) fumarate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.29–7.36 (m, 5H), 6.68 (s, 1H), 3.90 (s, 2H), 3.78 (s, 3H), 3.67 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.5, 163.1, 161.4, 146.4, 132.5, 129.5, 128.5, 127.3, 117.1, 53.1, 52.0, 40.3. MS (EI, 70 eV): *m/z* (%)=278 (M^+, 0.02), 247 (0.38), 219 (0.20), 118 (17.35), 91 (100). Anal. Calcd for $C_{14}H_{14}O_6$: C, 60.43; H, 5.07. Found: C, 60.39; H, 5.32. IR (KBr): 2953, 2924, 2853, 1773, 1729, 1664, 1279, 1102, 789, 689.

4.2.18. Dimethyl 2-(2-(naphthalen-6-yl) acetoyloxy) fumarate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.40–8.08 (m, 7H), 6.66 (s, 1H), 4.32 (s, 2H), 3.68 (s, 3H), 3.58 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.4, 163.1, 161.4, 146.4, 133.7, 132.0, 129.1, 128.6, 128.3, 126.3, 125.8, 125.4, 123.8, 117.2, 53.0, 51.9, 38.2. MS (EI, 70 eV): *m/z* (%)=328 (M^+, 9.61), 297 (0.30), 168 (100), 141 (73.02), 115 (67.61). Anal. Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.88; H, 4.95. IR (KBr): 2954, 2849, 1774, 1730, 1664, 1279, 1105, 789, 689.

4.2.19. Dimethyl 2-(benzoxy) fumarate. White powder, mp 40–42 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.14–8.16 (d, *J*=7.2 Hz, 2H), 7.61–7.65 (t, *J*=7.5 Hz, 1H), 7.47–7.52 (t, *J*=7.5 Hz, 2H), 6.79 (s, 1H), 3.84 (s, 3H), 3.70 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=163.6, 163.0, 161.5, 146.8, 133.9, 130.3, 128.5, 128.0, 117.0, 53.1, 52.0. MS (EI, 70 eV): *m/z* (%)=264 (M^+, 0.49), 2.33 (0.74), 205 (0.11), 105 (100), 77 (42.36). Anal. Calcd for $C_{13}H_{12}O_6$: C, 59.09; H, 4.58. Found: C, 59.37; H, 4.34. IR (KBr): 2956, 2848, 1736, 1664, 1279, 1104, 707, 669.

4.2.20. Dimethyl 2-(2-fluorobenzoxy) fumarate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.17–8.13 (m, 4H), 6.80 (s, 1H), 3.87 (s, 3H), 3.73 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.1, 163.0, 161.4, 160.7, 146.4, 135.8, 135.7, 132.6, 124.2, 117.3, 116.9, 116.6, 116.5, 53.2, 52.1. MS (EI, 70 eV): *m/z* (%)=282 (M^+, 0.27), 251 (0.59), 223 (0.36), 123 (100), 95 (19.92). HRMS (EI) calcd for $C_{13}H_{11}FO_6$: (M+Na) 305.0432. Found: 305.0431. IR (KBr): 2957, 1733, 1279, 756.

4.2.21. Dimethyl 2-(4-fluorobenzoxy) fumarate. White powder, mp 69–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.15–8.20 (m, 2H), 7.15–7.21 (t, *J*=8.7 Hz, 2H), 6.79 (s, 1H), 3.86 (s, 3H), 3.72 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=168.0, 164.6, 163.0, 162.6, 161.5, 146.7, 133.2, 133.0, 124.3, 117.2, 116.0, 115.7, 53.2, 52.0. MS (EI, 70 eV): *m/z* (%)=282 (M^+, 0.35), 251 (0.58), 223 (0.15), 123 (100), 95 (29.54). HRMS (EI) calcd for $C_{13}H_{11}FO_6$: (M+Na) 305.0432. Found: 305.0437. IR (KBr): 2964, 1732, 1273, 856, 759.

4.2.22. Dimethyl 2-(2-hydroxybenzoxy) fumarate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=9.99 (s, 1H), 6.94–8.01 (m, 4H), 6.82 (s, 1H), 3.88 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.1, 162.9, 162.0, 161.3, 146.0, 136.9, 130.8, 119.7, 117.8, 110.9, 53.4, 52.3. MS (EI, 70 eV): *m/z* (%)=280 (M^+, 0.37), 249 (0.68), 221 (0.90), 121 (100). Anal. Calcd for $C_{13}H_{12}O_7$: C, 55.72; H, 4.32. Found: C, 55.83; H, 4.48. IR (KBr): 3239, 2957, 2851, 1732, 1699, 1653, 1293, 1156, 759.

4.2.23. (*E*)-Benzyl 3-(2-chloroethoxy) acrylate. White powder, mp 40–41 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.59–7.63 (d, *J*=12.3 Hz, 1H), 7.30–7.36 (m, 5H), 5.26–5.30 (d, *J*=12.3 Hz, 1H), 5.15 (s, 2H), 4.03–4.07 (t, *J*=6 Hz, 2H), 3.66–3.70 (t, *J*=5.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.0, 161.8, 136.2, 128.4, 128.0, 97.1, 70.5, 65.6, 41.2. MS (EI, 70 eV): *m/z* (%)=240 (M^+, 0.44), 195 (21.69), 160 (32.72), 133 (100), 91 (99.32). Anal. Calcd for $C_{12}H_{13}ClO_3$: C, 59.88; H, 5.44. Found: C, 59.69; H, 5.66. IR (KBr): 1709, 1627, 1132, 963, 751, 698.

4.2.24. (*Z*)-Benzyl 3-(2-chloroethoxy) acrylate. White powder, mp 50–51 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.26–7.40 (m, 5H), 6.56–6.59 (d, *J*=6.9 Hz, 1H), 5.15 (s, 2H), 4.93–4.96 (d, *J*=7.2 Hz, 1H), 4.24–4.28 (t, *J*=6 Hz, 2H), 3.72–3.76 (t, *J*=6.3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.7, 158.9, 136.3, 128.4, 128.0, 127.9, 96.5, 96.4, 74.9, 65.4, 42.2. MS (EI, 70 eV): *m/z* (%)=240 (M^+, 3.17), 195 (7.77), 160 (4.66), 133 (96.92), 91 (100). Anal. Calcd for $C_{12}H_{13}ClO_3$: C, 59.88; H, 5.44. Found: C, 59.67; H, 5.56. IR (KBr): 1709, 1634, 1157, 1134, 745, 697.

4.2.25. (*E*)-2-((Benzyloxy) carbonyl) vinyl benzoate. White powder, mp 79–81 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.56–8.60 (d, *J*=12.3 Hz, 1H), 7.32–8.11 (m, 10H), 5.93–5.97 (d, *J*=12.6 Hz, 1H), 5.22 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=165.9, 162.4, 150.2, 135.8,

134.3, 130.3, 128.7, 128.5, 128.2, 127.6, 106.0, 66.2. MS (EI, 70 eV): *m/z* (%)=282 (M^+, 0.02), 177 (1.49), 160 (2.76), 105 (100). Anal. Calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.15; H, 5.11. IR (KBr): 1744, 1708, 1655, 1261, 1106, 959, 755, 700, 679.

4.2.26. (*E*)-Benzyl 3-(1,3-dioxoisoindolin-2-yl) acrylate. White powder, mp 108–109 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.23–7.97 (m, 10H), 6.97–7.02 (d, J=15 Hz, 1H), 5.22 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=166.9, 165.4, 135.9, 135.2, 131.4, 128.5, 128.2, 124.2, 108.3, 66.3. MS (EI, 70 eV): *m/z* (%)=307 (M^+, 3.59), 261 (36.67), 200 (98.52), 91 (100). Anal. Calcd for $C_{18}H_{13}NO_4$: C, 70.35; H, 4.26; N, 4.56. Found: C, 70.18; H, 4.39; N, 4.27. IR (KBr): 2956, 1751, 1717, 1630, 1212, 1153, 971, 764, 676.

4.2.27. (*E*)-Methyl 3-(2-chloroethoxy) acrylate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.58–7.62 (d, J=12.9 Hz, 1H), 5.23–5.28 (d, J=12.6 Hz, 1H), 4.09–4.13 (t, J=5.7 Hz, 2H), 3.73–3.77 (t, J=5.7 Hz, 2H), 3.71 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=167.7, 161.6, 97.1, 70.5, 51.2, 41.3. MS (EI, 70 eV): *m/z* (%)=164 (M^+, 17.0), 133 (100). Anal. Calcd for $C_6H_9ClO_3$: C, 43.78; H, 5.51. Found: C, 43.91; H, 5.11. IR (KBr): 2952, 1712, 1629, 1143.

4.2.28. (*Z*)-Methyl 2-(3-oxo-1,4-dioxan-2-ylidene) acetate. White powder, mp 105–106 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.19 (s, 1H), 4.60–4.63 (m, 2H), 4.37–4.40 (m, 2H), 3.75 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.2, 158.5, 150.0, 104.7, 66.5, 64.2, 51.4. MS (EI, 70 eV): *m/z* (%)=172 (M^+, 8.01), 141 (70.01), 69 (100). Anal. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.68. Found: C, 48.79; H, 4.81. IR (KBr): 2960, 1742, 1715, 1639, 1287, 1236, 1092.

4.2.29. (*Z*)-Methyl 2-(5,6-dimethyl-3-oxo-1,4-dioxan-2-ylidene) acetate. White powder, mp 77–78 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.14 (s, 1H), 4.41–4.46 (m, 1H), 4.06–4.11 (m, 1H), 3.72 (s, 3H), 1.37–1.42 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.7, 159.5, 150.2, 104.2, 78.7, 76.0, 51.7, 17.2, 16.5. MS (EI, 70 eV): *m/z* (%)=200 (M^+, 23.1), 169 (53.7), 69 (100). Anal. Calcd for $C_9H_{12}O_5$: C, 54.00; H, 6.04. Found: C, 54.24; H, 6.26. IR (KBr): 2959, 2917, 2850, 1734, 1701, 1646, 1279, 1237, 1070.

4.2.30. (*Z*)-Methyl 2-((4a*R*,8a*R*)-hexahydro-2-oxobenzo-[*b*][1,4]dioxin-3 (2*H*)-ylidene) acetate. White powder, mp 62–63 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.12 (s, 1H), 4.21–4.29 (m, 1H), 3.86–4.94 (m, 1H), 3.69 (s, 3H), 1.21–2.32 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 159.3, 150.6, 103.9, 79.5, 77.5, 51.4, 29.5, 29.1, 23.0, 22.8. MS (EI, 70 eV): *m/z* (%)=226 (M^+, 4.80), 195 (8.33), 101 (54.37), 69 (100). Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.64; H, 5.91. IR (KBr): 2947, 2865, 1742, 1712, 1641, 1259, 1188, 1072.

4.2.31. (*Z*)-Methyl 2-((4a*S*,8a*R*)-hexahydro-2-oxobenzo-[*b*][1,4]dioxin-3(2*H*)-ylidene) acetate. Sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.17 (s, 1H), 4.67–4.71 (m, 1H), 4.42–4.46 (m, 1H), 3.75 (s, 3H), 1.42–1.97 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.6, 159.2, 149.2, 103.9, 76.0, 73.0, 51.5, 28.3, 27.4, 21.0, 20.3. MS (EI, 70 eV): *m/z* (%)=226 (M^+, 9.81), 195 (19.09), 101 (46.37), 69 (100). Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.28; H, 5.94. IR (KBr): 2949, 2869, 1720, 1643, 1237, 1174, 1073.

4.2.32. (*Z*)-Methyl 2-((4a*R*,7a*R*)-tetrahydro-2-oxo-2*H*-cyclopenta[*b*][1,4]dioxin-3(4a*H*)-ylidene) acetate. White powder, mp 68–70 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.16 (s, 1H), 4.48–4.57 (m, 1H), 4.19–4.28 (m, 1H), 3.73 (s, 3H), 1.69–2.24 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 160.0, 150.7, 105.2, 80.6, 79.4, 51.6, 24.3, 24.0, 17.4. MS (EI, 70 eV): *m/z* (%)=212 (M^+, 26.09), 181 (72.38), 69 (100). Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.58; H, 5.75. IR (KBr): 2924, 1721, 1642, 1233, 1105.

4.2.33. (*Z*)-Methyl 2-((4a*S*,7a*R*)-tetrahydro-2-oxo-2*H*-cyclopenta[*b*][1,4]dioxin-3(4a*H*)-ylidene) acetate. White powder, mp 94–96 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=6.27 (s, 1H), 4.85–4.88 (m, 1H), 4.67–4.70 (m, 1H), 3.75 (s, 3H), 1.76–2.18 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=164.4, 158.4, 148.0, 105.3, 80.1, 76.1, 51.5, 29.0, 27.8, 19.2. MS (EI, 70 eV): *m/z* (%)=212 (M^+, 24.02), 181 (100), 69 (59.28). Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.64; H, 5.90. IR (KBr): 2956, 1709, 1642, 1239, 1087.

4.2.34. (*Z*)-Methyl 2-(3-oxomorpholin-2-ylidene) acetate. White powder, mp 79–80 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.37 (s, 1H), 5.66 (s, 1H), 4.50–4.54 (t, J=4.8 Hz, 2H), 3.71 (s, 3H), 3.50–3.55 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.4, 160.3, 144.4, 89.9, 67.3, 51.0, 38.4. MS (EI, 70 eV): *m/z* (%)=171 (M^+, 41.6), 140 (52.9), 68 (100). Anal. Calcd for $C_7H_9NO_4$: C, 49.12; H, 5.30; N, 8.18. Found: C, 49.22; H, 5.75; N, 8.24. IR (KBr): 3326, 2923, 1744, 1663, 1619, 1287, 1233.

4.2.35. (*Z*)-Methyl 2-((*R*)-5-isopropyl-3-oxomorpholin-2-ylidene) acetate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.51 (s, 1H), 5.56 (s, 1H), 4.26–4.46 (m, 2H), 3.66 (s, 3H), 3.22–3.29 (m, 2H), 1.76–1.88 (m, 1H), 0.97–1.03 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.4, 160.3, 144.0, 89.1, 69.4, 53.7, 50.8, 29.6, 18.6, 18.4. MS (EI, 70 eV): *m/z* (%)=213 (M^+, 16.3), 182 (8.9), 170 (100), 138 (97.9). Anal. Calcd for $C_{10}H_{15}NO_4$: C, 56.33; H, 7.09; N, 6.57. Found: C, 56.43; H, 7.20; N, 6.19. IR (KBr): 3310, 2965, 1747, 1664, 1620, 1265, 1237.

4.2.36. (*Z*)-Methyl 2-((*S*)-5-*sec*-butyl-3-oxomorpholin-2-ylidene) acetate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.55 (s, 1H), 5.61 (s, 1H), 4.33–4.51 (m, 2H), 3.71 (s, 3H), 3.38–3.43 (m, 1H), 1.57–1.70 (m, 2H), 1.25–1.34 (m, 1H), 0.94–1.01 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.4, 160.3, 144.0, 88.9, 69.3, 52.3, 50.8, 35.8, 25.1, 14.6, 10.8. MS (EI, 70 eV): *m/z* (%)=227 (M^+, 16.0), 196 (7.8), 170 (100), 138 (92.0). Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.14; H, 7.54; N, 6.16. Found: C, 58.23; H, 7.58; N, 5.82. IR (KBr): 3309, 2966, 1748, 1664, 1619, 1254, 1233.

4.2.37. Methyl 2-((*S*)-5-isobutyl-3-oxomorpholin-2-ylidene) acetate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.46 (s, 1H), 5.61 (s, 1H), 4.17–4.46 (m, 2H), 3.71 (s, 3H), 3.66–3.69 (m, 1H), 1.32–1.80 (m, 3H), 0.97–1.01 (t,

J=6.3 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.4, 160.2, 143.9, 89.2, 71.3, 50.8, 46.2, 39.7, 24.4, 22.8, 21.7. MS (EI, 70 eV): m/z (%)=227 (M^+, 15.43), 196 (7.72), 170 (100), 138 (93.98). Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.14; H, 7.54; N, 6.16. Found: C, 58.47; H, 7.15; N, 5.97. IR (KBr): 3310, 2957, 1748, 1666, 1619, 1253, 1227.

4.2.38. (*Z*)-Methyl 2-((*S*)-5-benzyl-3-oxomorpholin-2-ylidene) acetate. White powder, mp 83–84 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.36 (s, 1H), 7.20–7.39 (m, 5H), 5.65 (s, 1H), 4.22–4.43 (m, 2H), 3.74–3.80 (m, 1H), 3.68 (s, 3H), 2.85–2.87 (d, J=7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.1, 160.3, 143.4, 135.3, 129.0, 128.9, 127.4, 90.2, 70.2, 51.0, 49.7, 38.0. MS (EI, 70 eV): m/z (%)=261 (M^+, 6.51), 230 (2.83), 170 (100), 138 (89.10). Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.61; H, 5.88; N, 5.09. IR (KBr): 3315, 2949, 1740, 1667, 1622, 1238, 772, 698.

4.2.39. (*Z*)-Methyl 2-((*R*)-5-benzyl-3-oxomorpholin-2-ylidene) acetate. White powder, mp 74–75 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.36 (s, 1H), 7.20–7.39 (m, 5H), 5.65 (s, 1H), 4.22–4.42 (m, 2H), 3.77–3.79 (m, 1H), 3.68 (s, 3H), 2.84–2.87 (d, J=7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.0, 160.3, 143.4, 135.3, 129.0, 128.9, 127.4, 90.1, 70.2, 50.9, 49.6, 38.0. MS (EI, 70 eV): m/z (%)=261 (M^+, 5.17), 230 (2.67), 170 (91.84), 138 (100). Anal. Calcd for $C_{14}H_{15}NO_4$: C, 64.36; H, 5.79; N, 5.36. Found: C, 64.52; H, 5.76; N, 4.97. IR (KBr): 3321, 2947, 1740, 1667, 1622, 1238, 772, 699.

4.2.40. (*Z*)-Methyl 2-((*R*)-5-(2-(methylthio) ethyl)-3-oxomorpholin-2-ylidene) acetate. Oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.47 (s, 1H), 5.59 (s, 1H), 4.21–4.50 (m, 2H), 3.68–3.78 (m, 1H), 3.66 (s, 3H), 2.50–2.65 (m, 2H), 2.09 (s, 3H), 1.77–1.95 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.2, 160.1, 143.4, 89.9, 70.5, 50.9, 46.9, 30.5, 29.9, 15.4. MS (EI, 70 eV): m/z (%)=245 (M^+, 12.60), 214 (5.26), 170 (19.14), 138 (84.38), 61 (100). Anal. Calcd for $C_{10}H_{15}NO_4S$: C, 48.96; H, 6.16; N, 5.71. Found: C, 49.25; H, 6.39; N, 5.44. IR (KBr): 3307, 2949, 1745, 1666, 1619, 1269, 1240.

4.2.41. (*Z*)-Methyl 2-(5-((1*H*-indol-3-yl) methyl)-3-oxomorpholin-2-ylidene) acetate. Yellow powder, mp 59–61 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.40 (s, 1H), 8.31 (s, 1H), 7.54–7.56 (d, J=7.8 Hz, 1H), 7.36–7.39 (d, J=8.4 Hz, 1H), 7.13–7.25 (m, 3H), 5.65 (s, 1H), 4.27–4.49 (m, 2H), 3.88–3.91 (m, 1H), 3.67 (s, 3H), 2.90–3.11 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.3, 160.5, 143.6, 136.4, 126.7, 123.1, 122.5, 119.8, 118.2, 111.5, 109.3, 89.8, 70.8, 51.0, 48.4, 27.7. MS (EI, 70 eV): m/z (%)=300 (M^+, 3.02), 269 (0.42), 241 (2.00), 138 (4.20), 130 (100). Anal. Calcd for $C_{16}H_{16}N_2O_4$: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.76; H, 5.55; N, 9.12. IR (KBr): 3407, 2948, 1742, 1664, 1616, 1260, 1237, 744.

4.2.42. (*Z*)-Methyl 1,7,7-trimethylbicyclo[2.2.1]hepta-[*c*]2-((4a*S*,8a*R*)-3-oxomorpholin-2-ylidene) acetate. White powder, mp 87–90 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.44 (s, 1H), 5.75 (s, 1H), 4.42–4.45 (d, J=8.7 Hz, 1H), 3.71 (s, 3H), 3.59–3.62 (dd, J=8.4 Hz, J=3 Hz, 1H), 0.82–1.91 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.5, 159.1, 142.2, 89.7, 85.6, 55.4, 51.5, 50.9, 50.3, 47.5, 32.4, 25.4, 22.1, 19.7, 10.7. MS (EI, 70 eV): m/z (%)=279 (M^+, 17.22), 248 (3.55), 169 (17.17), 95 (100). Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.23; H, 8.01; N, 5.34. IR (KBr): 3292, 2954, 1738, 1664, 1628, 1258.

4.2.43. (*Z*)-Methyl 2-(3-oxopiperazin-2-ylidene) acetate. White powder, mp 169–170 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.29 (s, 1H), 7.87 (s, 1H), 5.59 (s, 1H), 3.70 (s, 3H), 3.42–3.55 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.8, 161.6, 148.9, 86.3, 50.7, 40.1, 38.9. MS (EI, 70 eV): m/z (%)=170 (M^+, 92.2), 139 (100), 110 (75.4). Anal. Calcd for $C_7H_{10}N_2O_3$: C, 49.41; H, 5.92; N, 16.46. Found: C, 49.18; H, 5.85; N, 16.12. IR (KBr): 3328, 3203, 3073, 2948, 1698, 1657, 1621, 1218.

4.2.44. (*Z*)-Methyl 2-((4a*R*,8a*R*)-hexahydro-3-oxopiperazin-2(1*H*,2*H*,4*H*)-ylidene) acetate. White powder, mp 188–189 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.08 (s, 1H), 7.63 (s, 1H), 5.59 (s, 1H), 3.69 (s, 3H), 3.10–3.25 (m, 2H), 1.37–1.98 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=170.8, 161.6, 149.1, 86.0, 55.4, 54.9, 50.7, 29.5, 29.4, 23.7, 23.4. MS (EI, 70 eV): m/z (%)=224 (M^+, 83.9), 193 (41.3), 41 (100). Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19; N, 12.49. Found: C, 59.01; H, 7.57; N, 12.26. IR (KBr): 3296, 3191, 3072, 2933, 1693, 1657, 1615, 1212.

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References and notes

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