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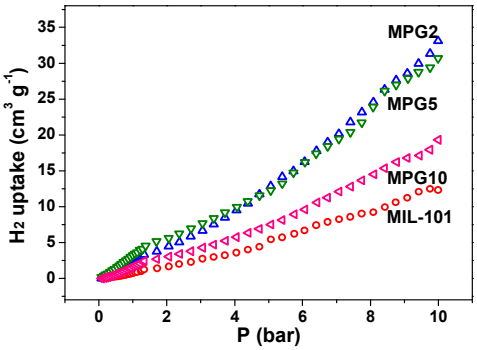
Graphical abstract

Composites of Pt-doped graphene oxide (GO) and a chromate-organic framework (MIL-101) were prepared through the in-situ solvent-thermal method. The significant enhancement of hydrogen storage capacities at ambient temperature for the composites with low Pt/GO contents can be attributed reasonably to the spillover mechanism in such system.



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ARTICLE

A facile synthesis of β-amino carbonyl compounds through an aza-Michael addition reaction under solvent-free conditions†

Cite this: DOI: 10.1039/xoxxoooooox

Received ooth January 2013,
Accepted ooth January 2013

DOI: 10.1039/xoxxoooooox

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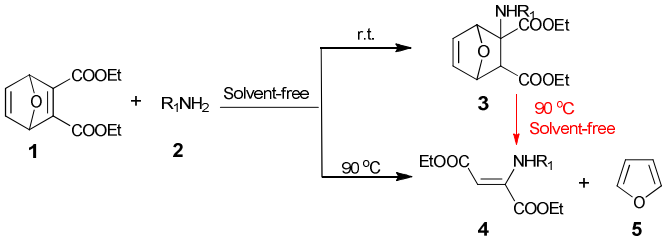
An efficient and eco-friendly process for the synthesis of β-amino carbonyl compounds was introduced in this paper. The oxanorbornene β-amino esters and β-enamine esters were successfully prepared from oxabornene and amines by using solvent-free aza-Michael addition reaction in the absence of any catalyst. Oxanorbornene β-amino esters were the major product at room temperature, but higher temperature e.g. 90 °C led to the formation of β-enamine esters. In addition, all the target compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, and HR-MS. A possible reaction pathway was also proposed.

Introduction

β-Amino carbonyl structural units exist extensively in natural products and bioactive compounds.[1] They are usually used as intermediates for the preparation of amino alcohols, diamines, β-amino acid derivatives and other nitrogen-containing molecules.[2] As a result, the synthesis and application have received a great deal of recent attention in the field of organic chemistry and medicinal chemistry.[3]

The Mannich-type reaction could be a useful and practical protocol for constructing β-amino carbonyl units.[4] Unfortunately, harsh reaction conditions and longer reaction time are commonly required.[5] On the other hand, aza-Michael addition reaction, addition of an amine to an electron deficient alkene, offers an easy access to β-amino carbonyl compounds.[6,7] To date, a number of synthetic approaches to β-amino carbonyl compounds have been established through aza-Michael addition.[8] A variety of catalysts, such as acetic acid, boric acid,[9] ionic liquid,[10] cyclodextrin, transition metal,[11] lanthanide halides, triflates or silica gel, solid salts and quaternary ammonium salt, have been developed for this purpose.[12] However, drawbacks including use of expensive reagents or organic solvents, or an excess of catalyst and high temperature still exist.[13] Thus, the development of an efficient and environmentally benign protocol could be highly desirable for the synthesis of β-amino carbonyl compounds.

Herein, an efficient and eco-friendly procedure for the synthesis of β-amino carbonyl compounds from oxabornene and amine via aza-Michael addition as depicted in Scheme 1 was disclosed without use of any catalyst and solvent. Oxanorbornene β-amino esters **3** and (Z)-β-enamine esters **4** were successfully prepared at r.t. and 90 °C, respectively.



Scheme 1 Synthesis of β-amino carbonyl compounds **3** and **4**

Results and discussion

To establish the synthetic process for β-amino carbonyl compounds from oxabornene **1** and amines **2** through solvent-free aza-Michael addition reaction, the reaction of oxabornene **1** and 1-phenylpiperazine **2a** were initially selected as a model reaction. As a result, diethyl 2-(4-phenylpiperazin-1-yl)-7-oxabicyclo [2.2.1]hept-5-ene-2,3-dicarboxylate **3a** was obtained as the product. As shown in Table 1, acetone, THF, DCE and toluene as the solvent, the reaction gave poor results (Table 1, entries 1–4). To be delighted, the reaction ran well at r.t. without solvent under other identical conditions, leading to 75% isolated yield of **3a** (entry 5). Accordingly, the solvent-free aza-Michael addition reaction was chosen for the further investigation.

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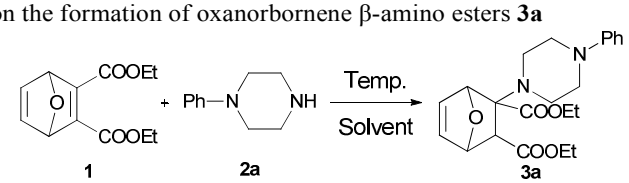
† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

Table 1 Effect of solvent, temperature and role of molar-ratio on the formation of oxanorbornene β-amino esters **3a**



1 2a 3a

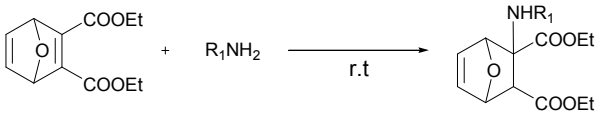
Entry	Solvent	1:2a	Temp. (°C)	Time	Yield (%)[a]
1	Acetone	1:1.5	r.t	12 h	60
2	THF	1:1.5	r.t	12 h	59
3	DCE	1:1.5	r.t	12 h	64
4	Toluene	1:1.5	r.t	12 h	62
5	Solvent-free	1:1.5	r.t	30 min	75
6	Solvent-free	1:1.5	30	30 min	70
7	Solvent-free	1:1.5	50	30 min	63
8	Solvent-free	1:1.5	70	30 min	48
9	Solvent-free	2:1	r.t	1 min	53
10	Solvent-free	1:1	r.t	1 min	51
11	Solvent-free	1:1.5	r.t	1 min	75
12	Solvent-free	1:2	r.t	1 min	83
13	Solvent-free	1:3	r.t	1 min	68

[a] Isolated yield by neutral alumina column chromatography.

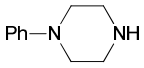
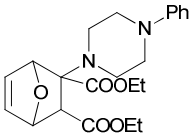
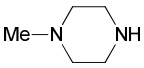
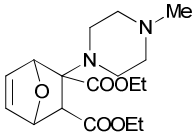
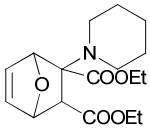
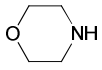
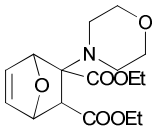
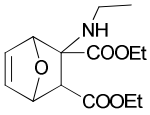
The temperature has detrimental effect on the formation of oxanorbornene β-amino ester **3a**. The yield decreased from 75% to 48% as the temperature went from r.t. up to 70 °C (Table 1, entries 5–8), indicating oxanorbornene β-amino ester may have poor stability at higher temperature. Interestingly, 1 min was enough to get better **3a** yield (entry 11 *vs.* 5); On the other hand, excellent yield up to 83% was reached at 1:2 molar ratio of **1** to **2a** (entries 9-13).

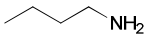
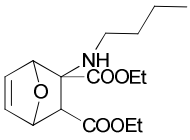
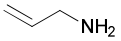
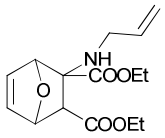
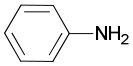
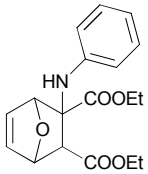
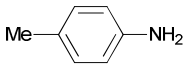
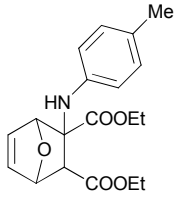
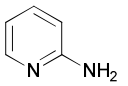
The applicability of various amines on solvent-free aza-Michael addition reaction was further investigated. The results showed that it is a general method to produce oxanorbornene β-amino esters **3** as listed in Table 2. Aliphatic amines have higher activity than aromatic counterparts (Table 2, entries 1-7 *vs.* 8-10), especially cyclic amines, ran much faster (entries 1-4), being in well agreement with the literature reuslts.[14] Whereas, longer reaction time was needed for aromatic amines for completing the reaction (entries 8-10), probably due to the electronic and steric effect. The yield of oxanorbornene β-amino esters **3** was also affected by the basicity and steric factor of the amino group and the nature of the carbonyl group (entries 3, 5 and 8).

Table 2 Preparation of various oxanorbornene β-amino esters **3** through solvent-free aza-Michael addition reaction at r.t.



1 2 3

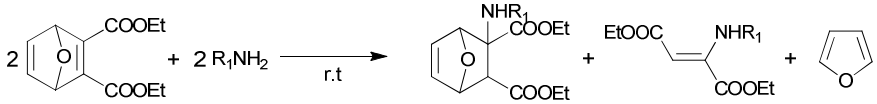
Entry	Amine **2**	Product **3**		Time	Isolated Yield (%)[a]
1		**3a**		1 min	83
2		**3b**		1 min	86
3		**3c**		1 min	89
4		**3d**		1 min	97
5		**3e**		0.5 h	76

6		**3f**		1 h	54
7		**3g**		5 h	93
8		**3h**		12 h	62
9		**3i**		10 h	78
10		**3j**	-	24 h	Trace

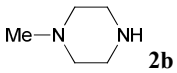
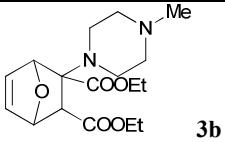
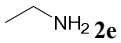
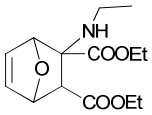
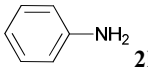
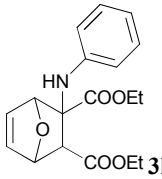
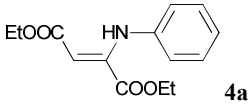
[a] The molar ratio of oxabornene **1** to amines **2** was 1:2; Isolated yield by neutral alumina column chromatography; The progress of the reaction was monitored by TLC.

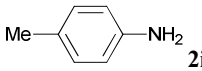
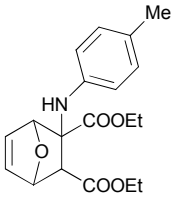
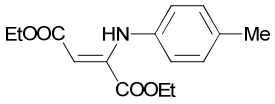
Unexpectedly, (Z)-β-enamine esters **4** and furan **5** can be obtained during the solvent-free aza-Michael addition reaction. When aliphatic amines as the substrates, e.g. **2b** and **2e**, just a trace amount of β-enamine ester **4** was formed and oxanorbornene β-amino ester **3** became the major product (Table 3, entries 1 and 2). In the case of aromatic amines, the yield of product **4** was slightly increased (entries 3 and 4). Those results encouraged us to further explore the reaction in order to develop novel access to β-amino carbonyl compound **4**.

Table 3 Preparation of β-amino carbonyl compounds **3** and **4** through solvent-free aza-Michael addition reaction at r.t.



1 **2** **3** **4** **5**

Entry	Amine **2**	Time	Product **3**	**3** Yields (%)[a]	Product **4**	**4** Yields (%)
1	 **2b**	1 min	 **3b**	86	-	Trace
2	 **2e**	0.5 h	 **3e**	76	-	Trace
3	 **2h**	12 h	 **3h**	62	 **4a**	12

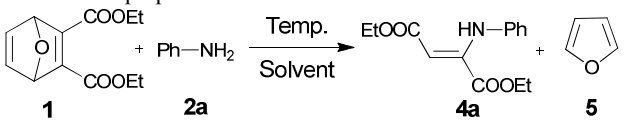
4	 **2i**	10 h	 **3i**	78	 **4b**	8

[a] The molar ratio of oxabornene **1** to amines **2** was 1:2; Isolated yield by neutral alumina column chromatography; The progress of the reaction was monitored by TLC.

To establish the synthetic process for (Z)-β-enamine esters **4**, a variety of reaction parameters and the results are summarized in Table 4. THF, toluene, acetone and DMF as the solvent, yields of diethyl 2-(phenylamino)fumarate **4a** were found to be in the range of 27% to 63% at 90 °C for 24 h (Table 4, entries 1-4). Surprisingly, better yield was achieved for 6 h under solvent-less conditions (entries 5 *vs.* 1-4), suggesting solvent-free was favourable for the reaction. In addition, higher temperature is beneficial for the generation of β-amino ester **4a**. The yield of **4a** reached to 77% at 90 °C (entries 5). Further increasing the reaction temperature to 110 °C had negative effect on **4a** yield (entries 10). And excellent yield was achieved at 1:2 molar ratio of **1** to **2a** (entries 5 *vs.* 11-14)**.**

The generality of the reaction was examined and the results are presented in Table 5. A wide range of amines **2** reacted with oxabornene **1** to afford (Z)-β-enamine esters **4a**–**4f**. The reactions with alkylamine were easier to perform (Table 4, entries 3-6) in 0.5 h or 1 min. But aromatic amines needed longer time to react, as the weaker activity (entries 1-2 *vs.* 3-6). Generally, cyclic amines can produce enamines faster than open-chain amines (entries 4-6 *vs.* 3).

Table 4 Effect of solvent reagent, temperature and molar ratio of materials on preparation of **4a**

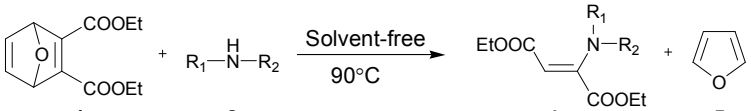


1 **2a** **4a** **5**

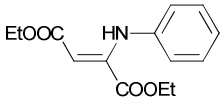
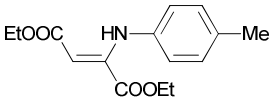
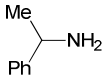
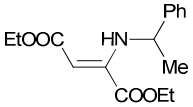
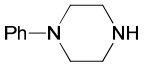
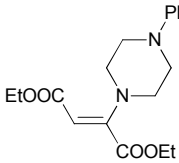
Entry	Solvent	**1**:**2a**	Temp. (°C)	Time	Yield/%[a]
1	THF	1:2	90	24 h	63
2	Toluene	1:2	90	24 h	41
3	Acetone	1:2	90	24 h	27
4	DMF	1:2	90	24 h	27
5	Solvent-Free	1:2	90	6 h	77
6	Solvent-Free	1:2	r.t	5 d	62
7	Solvent-Free	1:2	30	4 d	65
8	Solvent-Free	1:2	50	3 d	70
9	Solvent-Free	1:2	70	17 h	72
10	Solvent-Free	1:2	110	6 h	65
11	Solvent-Free	2:1	90	38 h	13
12	Solvent-Free	1:1	90	36 h	44
13	Solvent-Free	1:1.5	90	19 h	59
14	Solvent-Free	1:3	90	5 h	72

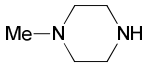
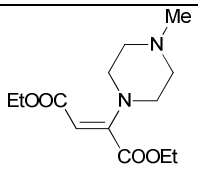
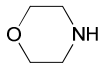
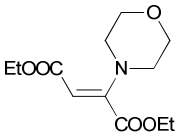
[a] Isolated yield by alumina column chromatography;
The progress of the reaction was monitored by TLC.

Table 5 Synthesis of (Z)-β-enamine esters **4** under solvent-free condition at 90 °C



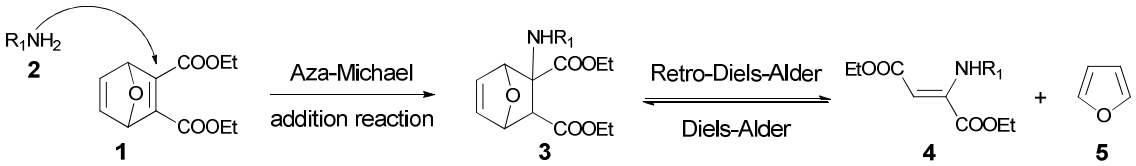
1 **2** **4** **5**

Entry	Amine **2**	Product **4**		Time	Isolated Yield (%)[a]
1	$PhNH_2$	**4a**		6 h	77
2	*p*-$MePhNH_2$	**4b**		4 h	54
3		**4c**		0.5 h	42
4		**4d**		1 min	70

Entry	Amine **2**	Product **4**	Time	Isolated Yield (%)[a]
5		**4e** 	1 min	61
6		**4f** 	1 min	73

[a] The molar ratio of oxabornene **1** to amines **2** was 1:2; Isolated yield by neutral alumina column chromatography; The progress of the reaction was monitored by TLC.

The plausible mechanism for the formation of oxanorbornene β-amino esters **3** and (Z)-β-enamine esters **4** was also proposed on the basis of the experimental results. As showed in scheme 2, the reaction of the amine and oxabornene **1** generate the oxanorbornene β-amino ester **3** through aza-Michael addition reaction. Subsequently, **3** goes at higher temperature through retro-Diels-Alder reaction to produce (Z)-β-enamine esters **4**. This is understandable that the thermodynamic product **4** forms at higher temperature; while oxanorbornene β-amino ester **3** is a major product at room temperature. Indeed, compound **4a** and **5** were obtained from thermal degradation of **3h** at 90 °C, identified by spectroscopy (see Supporting Information).



Scheme 2 Plausible mechanism for solvent-free aza-Michael addition reaction

Experimental

General Method

All compounds were fully characterized by spectroscopic techniques. The NMR spectra were recorded on a Bruker-Avance 400 MHz spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz) with tetramethylsilane (TMS) as the internal standard (δ 0.0 ppm), chemical shifts (δ) are expressed in ppm, and J values are given in Hz. Deuterated $CDCl_3$ was used as a solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using neutral alumina. The melting points were determined on an XT-4A melting point apparatus and are uncorrected. HRMS was performed on an Agilent LC-MSD TOF instrument.

All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on neutral alumina.

Preparatiotion of diethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate **1**.

Diethyl acetylenedicarboxylate 12 mmol and furan 60 mmol were placed in a sealed tube, which was heated at 100 °C for 20 hours. The reaction mixture was distilled under vacuum. The endoxide was obtained as a light yellow oil.[16]

General Procedure for the Synthesis of oxanorbornene β-amino esters 3 through solvent-free aza-Michael addition reaction

A schlenk was charged with **1** (0.4 mmol, 95.3 mg), amine **2** (0.8 mmol), and the solution was stirred for 1 minute to 6 days at room temperature until the **1** was completely consumed. The mixture was purified by flash column chromatography. The desired compounds (**3a**–**3j**) were formed from **1** in yields: 54-97%.

The Data of the oxanorbornene β-amino esters 3.

Diethyl- 2-(4-phenylpiperazin-1-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3a):

Yield 83%; Yellow oil; IR (KBr) ($\nu_{max,}$ cm^{-1}) 3447, 2333, 1731, 1597, 1452, 1263, 1127, 1136, 1060, 860, 755, 568 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23 (2H, m), 6.91-6.83 (3H, m), 6.59-6.57 (1H, m), 6.25-6.23 (1H, m), 5.31 (1H, s), 5.24 (1H, s), 4.23-4.11 (4H, m), 3.42 (1H, s), 3.08-2.93 (8H, m), 1.34-1.31 (3H, t, J = 7.1 Hz), 1.29-1.25 (3H, t, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 169.9, 151.3, 140.7, 135.0, 129.2, 120.0, 116.2, 81.2, 80.2, 78.2, 61.2, 61.0, 53.3,50.2, 48.2, 14.6, 14.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{28}N_2O_5Na^+$ [(M+Na)$^+$], 423.1890; found, 423.1885.

Diethyl- 2-(4-methylpiperazin-1-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3b):

Yield 86%; Yellow oil; IR (KBr) ($\nu_{max,}$ cm^{-1}) 3447, 3136, 2838, 2345, 1733, 1455, 1378, 1266, 1127, 1056, 859, 808, 558 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.53-6.51 (1H, m), 6.17-6.16 (1H, m), 5.23-5.17 (2H, m), 4.20-4.09 (4H, m), 3.35-3.34 (1H, m), 2.82 (4H, m), 2.20-2.19 (7H, m), 1.30-1.23 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 169.8, 140.5, 134.8, 81.0, 79.9, 77.9, 60.9, 60.7, 55.8, 53.0, 46.0, 14.3, 14.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{28}N_2O_5Na^+$ [(M+Na)$^+$], 423.1890; found, 423.1885.

Diethyl 2-(piperidin-1-yl)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3c):

Yield 89%; White solid; mp: 81-82 °C; IR (KBr) ($\nu_{max,}$ cm^{-1}) 3448, 3134, 2332, 1728, 1452, 1265, 1126, 1061, 860, 568 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.54-6.53 (1H, m), 6.20-6.18(1H, m), 5.29 (1H, s), 5.18 (1H, s), 4.25-4.11 (4H, m), 3.36 (1H, s), 2.72-2.67 (4H, m), 1.46-1.36 (6H, m), 1.32-1.26 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3, 170.3, 140.6, 135.2, 81.3, 80.2, 80.1, 79.1, 60.0, 60.9, 60.8, 53.0, 50.6, 49.3, 27.0,

24.6, 14.6, 14.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{17}H_{25}NO_5Na^+$ [(M+Na)$^+$], 346.1624; found, 346.1622.

Diethyl 2-morpholino-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3d):

Yield 97%; Yellow oil; IR (KBr) ($\nu_{max,}$ cm^{-1}) 3447, 3134, 2332, 1730, 1453, 1262, 1122, 1061, 860, 553 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.58-6.57 (1H, dd, J = 5.8, 1.6 Hz), 6.23-6.21 (1H, dd, J = 5, 1.7 Hz), 5.26-5.23 (2H, d, J = 9.5 Hz), 4.28-4.11 (4H, m), 3.61-3.59 (4H, t, J = 4.5 Hz), 3.38 (1H, s), 2.86-2.82 (2H, m), 2.74-2.73 (2H, m), 1.60 (1H, s), 1.35-1.25 (7H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.1, 169.8, 140.8, 134.9, 81.2, 79.8, 78.3, 67.8, 61.2, 60.9, 53.3, 49.7, 48.7, 14.6, 14.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{16}H_{23}NO_6Na^+$ [(M+Na)$^+$], 348.1417; found, 348.31407.

Diethyl 2-(ethylamino)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3e):

Yield 76%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3447, 2980, 2357, 1733, 1457, 1377, 1257, 1126, 1061, 859, 709, 558 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.73-6.71 (1H, dd, J = 5.8, 1.7 Hz), 6.36-6.34 (1H, dd, J = 5.8, 1.8 Hz), 5.07-5.06 (1H, m), 4.79 (1H, m), 4.14-4.09 (4H, m), 3.07-3.05 (1H, d, J = 4.3 Hz), 2.81-2.78 (1H, m), 2.65-2.60 (1H, m), 1.78 (1H, s), 1.26-1.22 (6H, t, J = 7.1 Hz), 1.17-1.13 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 170.4, 137.7, 132.8, 85.5, 80.3, 75.6, 61.1, 60.8, 55.9, 39.8, 15.6, 14.2, 14.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{14}H_{21}NNaO_5^+$ [(M+Na)$^+$], 306.1312; found, 306.1316.

Diethyl 2-(butylamino)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3f):

Yield 54%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3381, 2357, 1734, 1664, 1460, 1259, 1127, 860, 550 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.73-6.71 (1H, dd, J = 5.8, 1.6 Hz), 6.36-6.34 (1H, dd, J = 5.8, 1.8 Hz), 5.08-5.06 (1H, m), 4.79 (1H, m), 4.14-4.09 (4H, m), 3.06-3.05 (1H, d, J = 4.3 Hz), 2.80-2.73 (1H, m), 2.58-2.52 (1H, m), 1.84 (1H, s), 1.53-1.46 (2H, m), 1.38-1.33 (2H, m) 1.26-1.22 (6H, m), 0.90 (3H, t, J = 7.28 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 170.6, 137.8, 133.0, 85.6, 80.4, 75.7, 61.3, 60.9, 60.0, 45.3, 32.5, 20.5, 14.3, 14.1, 14.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{16}H_{25}NO_5Na^+$[(M+Na)$^+$], 334.1624; found, 334.1625.

Diethyl 2-(allylamino)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3g):

Yield 93%; colorless oil; IR (KBr) ($\nu_{max,}$ cm^{-1}) 3323, 2985, 1734, 1659, 1606, 1459, 1376, 1254, 1170, 1062, 914, 859, 786, 710, 554 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.75-6.74 (1H, dd, J = 5.8, 1.7 Hz), 6.35-6.33 (1H, dd, J = 5.8, 1.8 Hz), 5.98-5.88 (1H, m), 5.23-5.18 (1H, m), 5.11-5.07 (2H, m), 4.80-4.79 (1H, m), 4.16-4.08 (4H, m), 3.46-3.41(1H, m), 3.24-3.19 (1H, m), 3.08 (1H, d, 4.3 Hz), 2.00 (1H, s), 1.26-1.22 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 170.4, 137.9, 136.0, 132.8, 116.7, 85.8, 80.4, 75.5, 61.3, 60.9, 55.9, 48.5, 14.2, 14.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{15}H_{22}NO_5^+$[(M+H)$^+$], 296.1498; found, 296.1501.

Diethyl 2-(phenylamino)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3h):

Yield 62%; White solid; mp: 107-108 ^{o}C; IR (KBr) (ν_{max}, cm^{-1}) 3385, 2974, 2331, 1735, 1604, 1511, 1449, 1377, 1321, 1254, 1062, 1011, 859, 749, 689, 551 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.16 (2H, m), 6.84-6.80 (4H, m), 6.47-6.46 (1H, dd, J = 5.8, 1.9 Hz), 5.15-5.14 (1H, m), 5.06-5.05 (1H, m), 4.41 (1H, s), 4.20-4.09 (4H, m), 3.19 (1H, d, J = 4.4Hz), 1.30 (3H, t, J = 7.2 Hz), 1.15 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 169.8, 144.9, 138.3, 132.3, 129.1, 119.5, 115.8, 86.5, 80.6, 72.4, 61.9, 61.2, 58.2, 14.1, 14.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{22}NO_5^+$ [(M+H)$^+$], 332.1492; found, 332.1483.

Diethyl 2-(p-tolylamino)-7-oxabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate (3i):

Yield 78%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3386, 2356, 1730, 1519, 1454, 1257, 1126, 1061, 858, 814, 567 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (2H, d, J = 8.4 Hz), 6.79 (1H, dd, J = 5.8, 1.6 Hz), 6.74-6.71 (2H, m), 6.46 (1H, dd, J = 5.8, 1.8 Hz), 5.13-5.12 (1H, m), 5.04 (1H, s), 4.26 (1H, s), 4.19-4.09 (4H, m), 3.18 (1H, d, J = 4.4 Hz), 2.25 (3H, s), 1.29 (3H, t, J = 7.13 Hz), 1.17 (6H, t, J = 7.13 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.40, 142.5, 138.1, 132.5, 129.6, 129.1, 116.4, 86.3, 72.8, 61.9, 61.2, 58.1, 20.6, 14.2, 14.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{24}NO_5^+$[(M+H)$^+$], 346.1468; found, 346.1649.

General Procedure for the Synthesis of (Z)-β-enamine esters 4

A Schlenk was charged with diethyl 7-oxabicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate **1** (0.4 mmol, 95.3 mg), amine **2** (0.8 mmol), and the solution was stirred for 1 minute to 6 days at 90 ^{o}C until **1** was completely consumed. The mixture was purified by flash column chromatography. The desired compounds **4** were formed from **1** in yields 42-77%.

The Data of the (Z)-β-enamine esters 4.

Diethyl 2-(phenylamino)fumarate (4a):

Yield 77%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3279, 2984, 2344, 1735, 1668, 1607, 1498, 1382, 1274, 1208, 1137, 1039, 861, 755, 693, 553 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.68 (1H, s), 7.30-7.25 (2H, m), 7.11-7.07 (1H, m), 6.92 (2H, d, J = 7.7 Hz), 5.38 (1H, s), 4.22-4,13 (4H, m), 1.30 (3H, t, J = 7.1 Hz), 1.09 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 164.5, 148.5, 140.5, 129.2, 124.3, 121.1, 93.9, 62.2, 60.1, 14.5, 13.7. HRMS (TOF ES$^+$): m/z calcd for $C_{14}H_{17}NO_4Na^+$ [(M+Na)$^+$], 286.1050; found, 286.1055.

Diethyl 2-(*p*-tolylamino)fumarate (4b):

Yield 54%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3448, 2331, 1735, 1666, 1613, 1519, 1457, 1274, 1207, 1071, 859, 811, 551; 1H NMR (400 MHz, $CDCl_3$): δ 9.62 (1H, s), 7.07-7.05 (2H, m), 6.83-6.81 (2H, m), 5.32 (1H, s), 4.21-4.12 (4H, m), 2.29 (3H, s), 1.29 (3H, t, J = 7.1 Hz), 1.10 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 163.5, 147.9, 136.9, 133.1, 128.7, 120.3, 91.8, 61.1, 58.9, 19.9, 13.4, 12.8.

Diethyl 2-((1-phenylethyl)amino)fumarate (4c):

Yield 42%; Yellow oil; IR (KBr) ($\nu_{max,}$ cm^{-1}) 3449, 3134, 2981, 2356, 1733, 1662, 1605, 1453, 1372, 1264, 1209, 1132, 1045, 861, 779, 698, 564 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (1H, d, J = 6.7 Hz), 7.32-7.28 (2H, m), 7.23-7.19 (3H, m), 5.09 (1H, s), 5.07-5.00 (1H, m), 4.19-4.14 (2H, m), 4.08-4.03 (2H, m), 1.51 (3H, d, J = 6.9 Hz), 1.28 (3H, t, J = 7.1 Hz), 1.12 (3H, t, J = 7.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4, 163.8, 151.7, 145.0, 128.8, 127.3, 126.1, 88.5, 61.8, 59.5, 53.8, 24.9, 14.6, 14.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{16}H_{21}NO_4Na^+$[(M+Na)$^+$], 314.1362; found, 314.1364.

Diethyl 2-(4-phenylpiperazin-1-yl)fumarate (4d):

Yield 70%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3449, 2331, 1738, 1691, 1586, 1498, 1447, 1382, 1277, 1154, 1063, 858, 803, 755, 689, 548; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.26 (2H, m), 6.92-6.89 (3H, m), 4.83 (1H, s), 4.40-4.39 (2H, m), 4.14-4.09 (2H, m), 3.34-3.32 (4H, m), 3.24-3.22 (4H, m), 1.39 (3H, t, J = 7.2 Hz), 1.24 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.4, 165.6, 154.5, 150.7, 129.4, 120.8, 116.7, 87.5, 62.3, 59.6, 48.8, 47.1, 14.5, 14.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{25}N_2O_4Na^+$[(M+Na)$^+$], 333.1808; found, 333.1807.

Diethyl 2-(4-methylpiperazin-1-yl)fumarate (4e):
Yield 61%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3450, 2980, 2801, 2331, 1739, 1693, 1582, 1450, 1379, 1285, 1201, 1159, 1049, 1007, 801, 750, 552; ^1H NMR (400 MHz, $CDCl_3$): δ 4.68 (1H, s), 4.32-4.27 (2H, m), 4.03-3.98 (2H, m), 3.09 (3H, t, J = 5.1 Hz), 2.37-2.35 (4H, m), 2.21 (3H, s), 1.27 (3H, t, J = 7.2 Hz), 1.13 (3H, t, J = 7.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 164.4, 153.4, 85.8, 61.0, 58.2, 52.9, 45.8, 44.9, 13.3, 12.8; HRMS (TOF ES^+): *m/z* calcd for $C_{13}H_{22}N_2O_4Na^+[(M+Na)^+]$, 2931471; found, 293.1477.

Diethyl 2-morpholinofumarate (4f):
Yield 73%; Yellow oil; IR (KBr) (ν_{max}, cm^{-1}) 3451, 2980, 2330, 1739, 1694, 1585, 1444, 1380, 1276, 1158, 1113, 1041, 917, 861, 802, 748, 552; ^1H NMR (400 MHz, $CDCl_3$): δ 4.73 (1H, s), 4.34-4.29 (2H, m), 4.06-4.01 (2H, m), 3.69-3.66 (4H, m), 3.08 (4H, t, J = 4.9 Hz), 1.32-1.29 (3H, m), 1.19-1.15 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.2, 164.4, 153.7, 86.7, 64.9, 61.2, 58.5, 46.1, 13.4, 12.9; HRMS (TOF ES^+): *m/z* calcd for $C_{12}H_{19}NO_5Na^+[(M+Na)^+]$, 280.1155; found, 280.1161.

Conclusions

In summary, an efficient and eco-friendly protocol for the synthesis of β-amino carbonyl compounds through solvent-free aza-Michael addition reaction was disclosed. Meanwhile, two kinds of β-amino carbonyl compounds were obtained by tuning the reaction temperature. We believe these results stimulate further research efforts to develop β-amino carbonyl compounds and extend solvent-free aza-Michael addition reaction to pharmaceutical synthesis.

Acknowledgements

The work was supported by the National Natural Science Foundation of China (Nos. 21202142, 21162042), the Key Project of Chinese Ministry of Education (Nos. 212161) and the Opening Foundation of Key Laboratory of Chemistry in Ethnic-medicine Resources (Yunnan Nationalities University), Ministry of Education (MZY1115).

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