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Dibromomethane as one-carbon source in organic synthesis: microwave-accelerated α-methylenation of ketones with dibromomethane and diethylamine

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Dedicated to Professor Chun-Chen Liao of National Hsing Hua University on the occasion of his 60th birthday

Abstract—The reactivity of aryl alkyl ketone with a preheated mixture of dibromomethane and diethylamine is poor and gives an α-methylenation product in very low yield even under refluxing condition. It can be accelerated dramatically by microwave irradiation. Under microwave condition, the cyclic 1,3-dicarbonyls, aryl alkyl ketones, heteroaryl alkyl ketones and acyclic benzyl ketone give α-methylenation products in modest to good yields. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

The α-methylenation of the ketone functionality is an important transformation in organic synthesis because α-methylene ketones are useful synthetic intermediates. This structural moiety is often found in biologically active natural products.[1] One of the most useful methods to prepare α-methylene ketones is through the formation of the corresponding Mannich base[2] followed by deamination. The deamination has been investigated using either free Mannich bases[3] or the corresponding quaternary ammonium derivatives.[4] In some modified examples, both the Mannich reaction and deamination can also be carried out in the same flask.[5] Recently, we reported that the reactive intermediate generated from the reaction of Et_2NH and CH_2Br_2 is effective in transforming the corresponding mono-substituted ozonides **1′** or aldehydes **2** to the α-substituted acroleins **3**.[6] Thus, α-alkyl-, α-alkoxy-, and α-amidoacroleins can be prepared in good yields (Eq. (1)). Mechanistically, Mannich base should be formed followed by the deamination of β-diethylaminoaldehyde leading to the formation of α-substituted acroleins in the same flask. It is a general, facile and economic method to synthesize α-methylene aldehydes in one pot fashion. This newly developed reaction condition shows the use of dihalomethane as one-carbon source in organic synthesis. In order to explore its synthetic utility further, we applied this reaction condition to the ketone functionality aiming to develop an effective one-pot reaction to prepare the α-methylene ketones. In this report, we describe a microwave-accelerated, one pot process for the α-methylenation of ketones.

2. Results and discussions

2.1. Reaction of 1,3-dicarbonyls or alkyl aryl ketones with a preheated mixture of CH_2Br_2 and Et_2NH

A mixture of Et_2NH (6 mol equiv.) and CH_2Br_2 (25 mol equiv.) was heated at 55°C for 1.5 h. This preheated mixture was treated with cyclic β-keto ester **4** (1 mol equiv.) in CH_2Cl_2 at rt for 19 h to give the corresponding α-methylenation ketone **4a** in 64% yield (Eq. (2)). Compound **4a** prefers to exist as its enol form as judged from its enolic proton chemical shift (δ 12.1 ppm) and its integrated intensity by ^1H NMR. On the other hand, under similar condition, the acyclic 1,3-dicarbonyl compounds such as ethyl acetoacetate (**5**), diethyl malonate (**6**), or dibenzoylmethane (**7**), gave 1,5-dicarbonyl products (**5a**–**7a**) instead of the corresponding α-methylene ketones in modest yields (Eqs. (3)–(5)). Presumably, the α-methylene ketone is first formed as an intermediate in each reaction, which may undergo further 1,4-addition with activated methylene compounds (**5**–**7**) to give the corresponding 1,5-dicarbonyl compounds (**5a**–**7a**). Interestingly,

Keywords: α-methylenation; microwave-accelerated reaction; α-methylene ketones; Mannich bases; dibromomethane; diethylamine.

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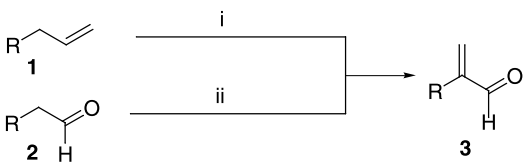
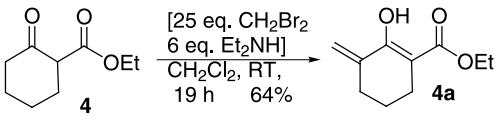
we could isolate the byproduct **6b** in Eq. (4) in 4% yield as a mixture of the diastereomers, which could result from the addition of product **6a** to the diethyl methylenemalonate intermediate. When 2,4-pentanedione (**7′**) was treated under the above reaction condition used at rt or even at −78°C, the reaction became very complicated and no desired product was isolated (Eq. (5)).



(1)

Reagents and conditions: (i) (a) O_3, CH_2Cl_2, −78°C; (b) preheated mixture of Et_2NH and CH_2Br_2 (mol ratio 5:15); (ii) preheated mixture of Et_2NH and CH_2Br_2 (mol ratio 3:15).



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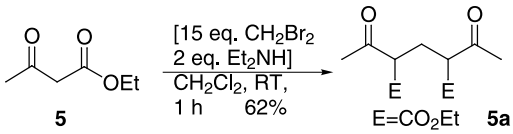

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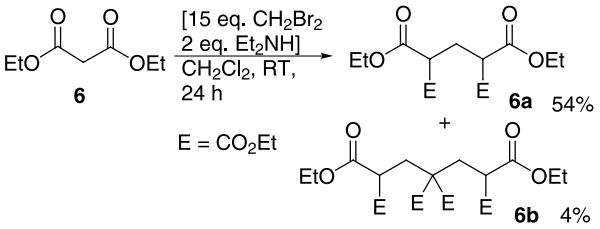

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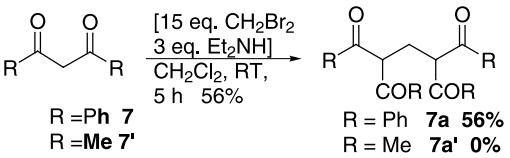

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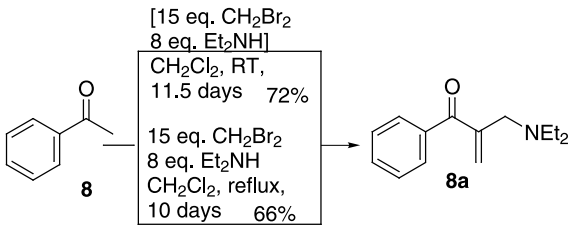
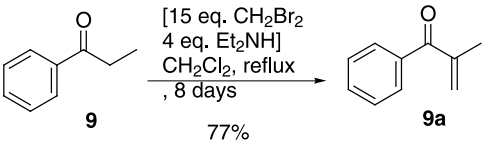


(6)



(7)

When the preheated mixture of Et_2NH (8 mol equiv.) and CH_2Br_2 (15 mol equiv.) was treated with acetophenone (**8**) in CH_2Cl_2 at rt, the α-methylene ketone **8a** was obtained in 72% yield. However, it took 11.5 days to complete the reaction (Eq. (6)). The formation of product **8a** was resulted from two Mannich base formations from acetophenone before the deamination. We tried to improve this reaction by raising the reaction temperature. When a mixture of acetophenone (**8**), Et_2NH and CH_2Br_2 in CH_2Cl_2 was heated to reflux, it still needed 10 days to give 66% yield of the α-methylene ketone **8a** (Eq. (6)). Under the refluxing condition for 8 days, propiophenone (**9**) gave the α-methylene ketone **9a** in 77% yield (Eq. (7)). In comparison with aliphatic aldehyde (Eq. (1)) or active methylene compounds (Eqs. (2)–(5)), the reactivities of the aryl alkyl ketones are poor in the preheated mixture of Et_2NH and CH_2Br_2 (Eqs. (6) and (7)). Thus, special effort should be made in order to reduce the reaction time, improve the chemical yield, and generalize the application of this methodology.

2.2. Microwave-accelerated α-methylenation of ketones in CH_2Cl_2 under constant pressure mode

The use of microwave oven to accelerate the reaction rate is becoming an important and useful technique in organic synthesis.[7] Therefore, we tried to improve the α-methylenation of ketone in the present study by employing microwave irradiation. MDS-2000 microwave oven (from CEM Company) was used in this part of study. Several reaction parameters, such as the internal temperature and pressure of the reaction vessel, the irradiation power and time, can be set automatically from the control panel on the microwave oven before the irradiation.

Acetophenone (**8**) was used as a starting material to find out the optimal irradiation condition for the α-methylenation reaction. Several factors such as the mole ratio of acetophenone/Et_2NH/CH_2Br_2, the power of the microwave irradiation, the maximum internal pressure of the reaction vessel and irradiation time were investigated and their results were shown in Table 1. A mixture of acetophenone (**8**) (1 mol equiv.), CH_2Br_2 (15 mol equiv.) and Et_2NH

Table 1. Reaction of acetophenone (**8**) CH_2Br_2 and Et_2NH in CH_2Cl_2 under microwave irradiation at constant pressure to give product **8a**

Entry	Mol ratio (**8**/CH_2Br_2/Et_2NH_2)	Microwave condition[a]			**8a** (%)	**8**[b] (%)
		Power level (%)	Vessel pressure (psi)	Irradiation time (min)		
1	1:15:4	30	30	30	12	33
2	1:4:8	30	30	30	50	18
3	1:4:8	30	30	60	51	16
4	1:6:12	30	30	120	62	0
5	1:6:12	100	60	5		
		50	60	30[c]	62	0

[a] CEM Model MDS-2000 microwave oven was used.
[b] Recovered starting material.
[c] Microwave power was set at 100% level for 5 min and then 50% level for another 30 min.

(4 mol equiv.) in 5 mL of CH_2Cl_2 were put in the reaction vessel where the maximum internal pressure was set at 30 psi. The reaction mixture was irradiated by 30% power of microwave for 30 min. The α-methylene ketone **8a** was isolated in 12% yield while 33% of the acetophenone was recovered (entry 1, Table 1). Under similar microwave condition, the changing mole ratio of CH_2Br_2 and Et_2NH from 15:4 to 4:8, improved the yield of the α-methylene ketone **8a** to 50% (entry 2). The mole ratio of CH_2Br_2 and Et_2NH was kept at 4:8 and we found that the longer irradiation time (60 min) do not improve the yield at all (entry 3). When the mole ratio of CH_2Br_2 and Et_2NH was raised to 6:12, the starting material **8** was consumed completely after 120 min irradiation and the α-methylene ketone **8a** was isolated in 62% yield (entry 4). During the irradiation, the reaction temperature in the sealed sample container was raised to 80–82°C gradually. Under this condition, we found that 120 min reaction time is necessary. The shorter reaction time resulted in the incompletion of the reaction. Although we have found the irradiation condition for complete conversion of acetophenone to the desired product, the irradiation time is too long to be applied for practical purposes.

In order to shorten the irradiation time, the internal pressure of the reaction vessel was raised to 60 psi. Moreover, the reaction mixture was irradiated by 100% power (630 W) for 5 min followed by 50% power for 30 min. The first 5 min irradiation was proposed to generate the reactive species from Et_2NH and CH_2Br_2 efficiently. This reactive intermediate may decompose before reacting with acetophenone under conditions of long irradiation. Therefore, 50% power irradiation was performed at the second stage. Thus, when a mixture of acetophenone (**8**) (1 mol equiv.), CH_2Br_2 (6 mol equiv.) and Et_2NH (12 mol equiv.) in 5 mL of CH_2Cl_2 was irradiated by microwave under the above described microwave condition, the reaction was complete and we were able to isolate the product **8a** in 62% yield (entry 5, Table 1; entry 1, Table 2). During the irradiation, the reaction temperature in the sealed sample container ranges from 100 to 110°C as indicated by the temperature sensor. In comparison, the results of entry 5 in Table 1 and Eq. (6) indicate that the microwave irradiation can improve the reaction rate dramatically. The results of entries 4 and 5 in Table 1 indicate that raising the reaction temperature by increasing the power level of the microwave irradiation can also shorten the reaction time efficiently. Therefore, we tried to investigate the scope of the α-methylenation of ketone by this two-stage microwave irradiation condition and their results are shown in Table 2.

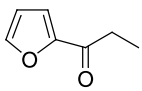
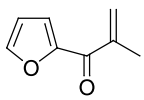
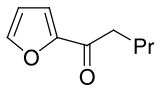
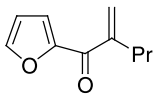
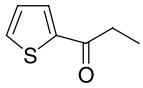
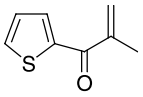
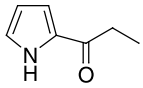
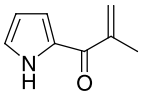
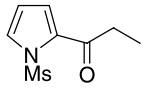
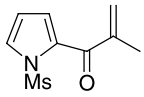
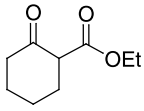
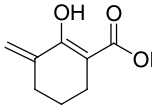
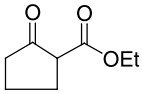
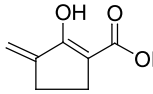
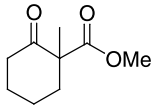
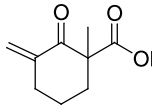
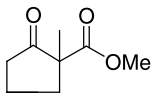
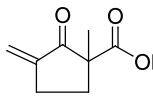
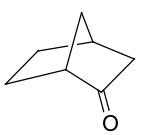
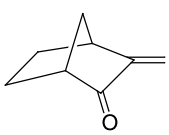
The aryl alkyl ketones, such as phenyl ethyl ketone (**9**), phenyl benzyl ketone (**10**) and 1-naphthyl ethyl ketone (**11**), can undergo α-methylenation under the above described two-stage microwave irradiation condition in good yields within 20–25 min (entries 2–4, Table 2). α-Tetralone (**12**) can also undergo α-methylenation to give the desired product **12a** in 49% yield (entry 5). The product **12a** could be purified by silica gel column chromatography. Compound **12a** in mixed solvents of hexane and ethyl acetate was shown as a clean spot as monitored by silica gel thin layer chromatography. This suggests that **12a** is stable in the diluted solution. After the concentration, we found that enone **12a** and dimer **12b** existed as an equilibrium mixture in $CDCl_3$ by ^1H NMR.

We wished to test the microwave-accelerated α-methylenation reaction of heteroaryl alkyl ketones, such as 2-furyl ethyl ketone (**13**), 2-furyl butyl ketone (**14**), 2-thienyl ethyl ketone (**15**) and found that these ketones can undergo α-methylenation under the above described two-stage microwave irradiation condition in good yields within 20 min (entries 6–8, Table 2). However, when (1*H*-pyrrol-2-yl) ethyl ketone (**16**) was subjected to the microwave irradiation under similar condition for 35 min, the α-methylenation product **16a** was obtained only in 20% yield and 72% of the starting material **16** was recovered. The polarities of the product **16a** and starting material **16** are almost the same so that it is difficult to separate them by column chromatography. Therefore, the reaction conversion and chemical yield are estimated by the integration of the ^1H NMR peak (entry 9). It is not clear why the reactivity of the pyrrole-derived ketone **16** is poor in the α-methylenation reaction as compared to those furan- or thiophene-derived ketones (entries 6–8 vs 9). We tried to protect the N–H on the pyrrole ring of compound **16** to the corresponding *N*-mesylate **17** with an idea to avoid the NH interfering in the reaction. When 1-(1-methanesulfonyl-1*H*-pyrrol-2-yl)-propan-1-one (**17**), CH_2Br_2, and Et_2NH in CH_2Cl_2 was irradiated with microwave (50% power, 60 psi) under the constant pressure condition for 40 min, the α-methylenation product was isolated in 41% yield and 37% of the starting material was recovered (entry 10). Apparently, the low reactivity of the pyrrole-derived ketone is not overcome by this structural modification. We also tried to solve this problem by raising the mole ratio of CH_2Br_2 and Et_2NH from 6:12 to 12:24, the α-methylene ketone **17a** was obtained in 75 and 7% of the starting material was recovered. Apparently, the yield is improved by the presence of more reagents. Following the reaction condition shown in entry 10 except the solvent was changed to CH_3CN, we isolated the desired product in 64% yield. When this reaction proceeded in the microwave, the internal reaction temperature was raised to 145°C. Our solution for this problem will be also described in the next section.

The cyclic ketones with α-alkoxycarbonyl moiety, such as ethyl 2-cyclohexanonecarboxylate (**4**) and ethyl 1-methyl-2-oxocyclohexanecarboxylate (**19**) can react with CH_2Br_2, Et_2NH in CH_2Cl_2 under two-stage microwave irradiation condition to give the corresponding α-methylenation products in good yield in 20 min (entries 11 and 13). However, under similar condition, methyl 2-cyclopentanonecarboxylate (**18**) gave very complicated products and no α-methylenation product was formed (entry 12). The α-position of compound **18** is substituted with methyl group to give ethyl 1-methyl-2-oxocyclopentanecarboxylate (**20**). Interestingly, compound **20** gave 82% of the α-methylenation product **20a** under our standard microwave condition in 20 min (entry 14).

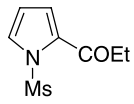
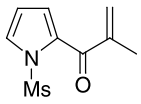
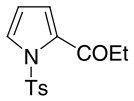
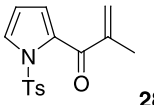
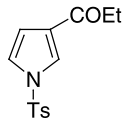
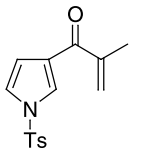
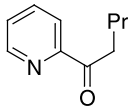
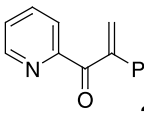
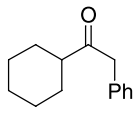
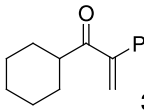
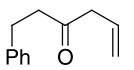
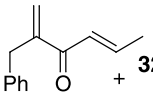
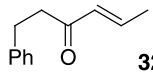
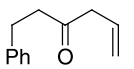
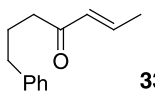
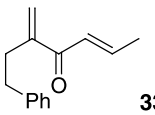
In the case of 2-norbornanone (**21**), the corresponding Mannich base (**21a′**) was formed in 49% yield and there is no α-methylenation product formation. Compound **21a′** was smoothly transformed to the α-methylenation product **21a**

Table 2. Reaction of ketones, CH_2Br_2 and Et_2NH in CH_2Cl_2 by microwave irradiation under constant pressure mode

Entry	Starting material	Power (%)	Pressure (psi)	Time (min)	Product	Yield[a] (%)
1	$PhCOCH_3$ **8**	100 50	60 60	5 30[b]	$PhCOC(CH_2)CH_2NEt_2$ **8a**	62
2	$PhCOCH_2Me$ **9**	100 50	60 60	5 15	$PhCOC(CH_2)Me$ **9a**	62
3	$PhCOCH_2Ph$ **10**	100 50	60 60	5 15	$PhCOC(CH_2)Ph$ **10a**	82
4	1-Naphthyl-COEt **11**	100 50	60 60	5 20	1-Naphthyl-$COC(CH_2)Me$ **11a**	69
5	 **12**	100 50	60 60	5 15	 **12a**	49[c]
6	 **13**	100 50	60 60	5 15	 **13a**	68
7	 **14**	100 50	60 60	5 15	 **14a**	66
8	 **15**	100 50	60 60	5 15	 **15a**	76
9	 **16**	100 50	60 60	5 30	 **16a**	20[d]
10	 **17**	50	60	40	 **17a**	41[e]
11	 **4**	100 50	60 60	5 15	 **4a**	84
12	 **18**	100 50	60 60	5 15	 **18a**	0[f]
13	 **19**	100 50	60 60	5 15	 **19a**	85
14	 **20**	100 50	60 60	5 15	 **20a**	82
15	 **21**	100 50	60 60	5 15	 **21a**	41[g]

[a] Isolated yields were reported.
[b] Microwave power was set at 100% level for 5 min and then 50% level for another 30 min.
[c] Compound **12a** will dimerize to give compound **12b** in $CDCl_3$.
[d] Recovered 72% of the starting material **16**.
[e] Recovered 37% of the starting material **17**.
[f] Very complicated mixtures were formed and no starting material left.
[g] Mannich base **21a**′ was formed as the produced in 49% yield. It can be converted to compound **21a** in 84% by stirring in a slurry of silica gel in dichloromethane at rt for 10 h.

Table 3. α-Methylenation of ketone by microwave irradiation under constant temperature mode

Entry	Starting material (SM)	Mole ratio ($SM/CH_2Br_2/Et_2NH$)	Power (%)	Temp. (°C)	Time (min)	Product	Yield[a]	Recovered SM (%)[a]
1	 **17**	1:12:24	50	180	30[b]	 **17a**	0	0
2		1:12:24	30	130	30		60	18
3	 **28**	1:12:24	30	180	30		57	17
4		1:24:48	30	100	30	 **28a**	71	12
5		1:24:48	30	100	30		81	4
6	 **29**	1:24:48	30	130	30	 **29a**	59	7
7	 **30**	1:24:48	30	80	30	 **30a**	72	0
8		1:12:24	30	80	20		81	0
9	 **31**	1:6:12	30	80	10	 **31a**	68	0
10	 **32**	1:6:12	30	80	10	 **32a** +  **32b**	25 24	0 0
11	 **32**	1:6:12	30	80	20	**32a** **32b**	15 7	0 0
12	 **33**	1:6:12	30	80	20	 **33a**	11	15

CEM MARS 5™ Microwave-accelerated reaction system was used. Its magnetron tube supplies 300 W.
[a] Isolated yields were reported.
[b] Microwave power was set at 50% level, the temperature inside the sealed sample vessels was set at 180°C and the reaction was irradiated for 30 min.

in 84% yield by stirring a slurry of **21a′** and silica gel in hexane at rt for 12 h (entry 15).

Although our microwave-accelerated α-methylenation methodology can be applied to the aryl alkyl ketones, heteroaryl alkyl ketones, and several cyclic ketones quite successfully (Tables 1 and 2), there are still some limitations to this reaction. For example, by using the above described microwave condition, no reaction occurs with the unactivated acyclic ketones such as 1-acetylferrocene (**22**), 4-heptanone (**23**), 1,5-diphenyl-3-pentanone (**24**), cyclohexyl *n*-butyl ketone (**25**), cyclohexyl 3-phenylpropyl ketone (**26**), and cyclohexyl 2-phenylethyl ketone (**27**). More effort is needed to overcome these obstacles.

2.3. Microwave-accelerated α-methylenation of ketones in CH_3CN under constant temperature mode

As described above, pyrrolyl ketones (**16**) and (**17**) gave the α-methylenation product in poor yield under constant

pressure (60 psi) process (entries 9 and 10, Table 2). From the temperature sensor, it was observed that the reaction temperature ranged between 100 and 110°C. The incompleteness of these two reactions may be due to the reaction temperature that is not high enough. We tried to raise the reaction temperature during the microwave irradiation by changing the reaction condition from the constant pressure condition to the constant temperature mode. Furthermore, we chose to use a solvent of a higher dielectric constant, such as CH_3CN, since it can absorb microwave more efficiently. A new CEM MARS 5™ microwave oven was used to carry out the constant temperature irradiation process as outlined below.

A mixture of N-mesylated propionyl pyrrole **17**, CH_2Br_2 and Et_2NH (their mole ratio is 1:12:24) in CH_3CN was placed in a sealed Teflon container. The maximum internal temperature of the container was set at 180°C and the reaction mixtures were irradiated in the CEM MARS 5™ microwave oven at 50% power level for 30 min. Unfortunately, the reaction became very complicated. There is no desired product and no starting material was recovered (entry 1, Table 3). Apparently, the reaction condition is too harsh to give the desired product. Therefore, we set the internal temperature at 110°C under 30% microwave power level. We found that the yield of the desired product **17a** was improved to 58%, and 20% of the starting material was recovered. When the internal reaction temperature was raised from 110 to 130°C, the desired product **17a** was slightly improved to 60%, and 18% of the starting material was recovered (entry 2, Table 3) Under similar condition, N-tosylated propionyl pyrrole **28** gave desired product **28a** in 57% yield and 17% of the starting material was recovered (entry 3). In order to push the reaction to complete, we employed the microwave irradiation condition used in entry 3 except that the mole ratio of ketone **28**/CH_2Br_2/Et_2NH was increased. When their mole ratio was changed from 1:12:24 to 1:24:48, the desired product **28a** was obtained in 71% yield, and 12% of the starting material was recovered (entry 4). When their mole ratio was changed to 1:36:72, the desired product **28a** was obtained in 81% yield and 4% of the starting material was recovered (entry 5). A mixture of 1-[1-(toluene-4-sulfonyl)-1*H*-pyrrol-3-yl]propan-1-one (**29**), CH_2Br_2 and Et_2NH (their mole ratio is 1:24:48) in CH_3CN was irradiated in the microwave oven at 30% power level for 30 min, the desired product was obtained in 59% yield and 7% of the starting material was recovered (entry 6). Although we have improved the yield of α-methylenation for the pyrrole-derived ketones by using this constant temperature approach, the reactants are still not consumed completely. On the other hand, when a mixture of 1-(pyridin-2-yl)pentan-1-one (**30**), CH_2Br_2 and Et_2NH (their mole ratio is 1:24:48) in CH_3CN was irradiated in the microwave oven at 30% power level (its maximum internal temperature was set at 80°C) for 30 min, the desired product **30a** was obtained in 72% yield (entry 7). It is still not clear why the pyrrole-derived ketones (**16**, **17** and **28**) are much more reluctant to undergo α-methylenation in comparison with furan-, thiophene- or pyridine-derived (**13**–**15** and **30**) ketones.

Interestingly, when a mixture of cyclohexyl-2-phenylethanone (**31**), CH_2Br_2 and Et_2NH (their mole ratio is 1:12:24) in CH_3CN was irradiated in the microwave oven at 30% power level (its maximum internal temperature was set at 80°C) for 20 min, the desired product **31a** was obtained in 81% yield (entry 8). When the mole ratio of ketone **31**, CH_2Br_2 and Et_2NH was decreased to 1:6:12, the desired product **31a** was obtained in 68% yield in 10 min (entry 9). These results indicate that the reactivity of the acyclic ketone **31** is much better than those compounds **22**–**27** mentioned above. The phenyl group located α- to the keto group may facilitate the enolization of the ketone **31**. This enolization is crucial to the Mannich base formation. Therefore, we chose to check the reactivity of a ketone containing a vinyl group α to the ketone such as **32**. When a mixture of the ketone **32**, CH_2Br_2 and Et_2NH (their mole ratio is 1:6:12) was irradiated by microwave for 10 min, the α-methylene enone **32a** and the enone **32b** were obtained in 25 and 24% yields, respectively (entry 10). Under this reaction condition, the double bond of compound **32** is isomerized preferentially to form the conjugated ketone **32b**, which then undergoes α-methylenation to give the dienone **32a**. This assumption is also confirmed by the result of entry 12 in which the conjugated ketone gave the α-methylenation product. We tried to irradiate the reaction mixture for longer time (20 min) in order to see whether we could convert **32b** to **32a** more efficiently. Unfortunately, both compounds **32b** and **32a** were obtained in lower yield (entry 11). It is possible that dienone **32a** is not a stable compound and it may decompose under the reaction condition.

3. Conclusions

The reaction of acyclic β-keto esters (**5**–**7**) reacted with a preheated mixture of dibromomethane and diethylamine afforded the 1,5-dicarbonyl compounds in modest to good yields. On the other hand, under similar condition, the cyclic β-keto ester (**4**) afforded the α-methylenation product (**4a**) in good yield. The α-methylenation of the aryl alkyl ketones with a preheated mixture of dibromomethane and diethylamine needs rather long reaction time even at refluxing condition. This type of reaction can be accelerated dramatically by microwave irradiation. Under microwave condition (either constant pressure or constant temperature mode), the cyclic 1,3-dicarbonyls, aryl alkyl ketones, heteroaryl alkyl ketones and acyclic benzyl ketone gave modest to good yields of the α-methylenation products, except dialkyl ketones.

4. Experimental

Materials were obtained from commercial suppliers and used without further purification. Melting points were determined by using a Thomas–Hoover melting point apparatus and were uncorrected. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX400 spectrometer, and chemical shifts were given in ppm downfield from tetramethylsilane (TMS). IR spectra were taken with a Perkin–Elmer 682 spectrophotometer and only noteworthy absorptions were listed. Mass spectra were measured on a VG Trio-2000GC/MS spectrometer by electronic impact at 70 eV (unless otherwise indicated).

High Resolution Mass Spectroscopy (HRMS) was measured on a JEOL JMS-HX 110 (National Hsing-Hua University) or VG-11-250J (Academia Sinica) Mass Spectrometer. Some of the reactions described were carried out using a CEM Model MDS-2000 oven equipped with a pressure monitoring device and a MetriCorp fiberoptic temperature-monitoring device. The magnetron tube supplies 630 W. Effective power level of 0–100% of this value are available as a train of timed pulses. The MDS-2000 unit is designed so that irradiation stops when a predetermined pressure is reached; thus, the pressure monitor functions as a baristat and controls the reaction temperature indirectly. The experiments were performed in sealed Teflon acid digestion vessels. CEM MARS 5™ Microwave-accelerated reaction system was used in Section 2.3 of this study. We choose the magnetron tube supplies with 300 W. Microwave-immune Thermo-Optic™ system for in situ measurement and control of temperature inside sealed sample vessels. The pressure sensor provides an 'in-vessel' pressure measurement up to 1500 psi.

4.1. General procedure for the α-methylenation of ketone at rt

A mixture of Et_2NH (2 mmol) and CH_2Br_2 (15 mmol) was heated to 55°C for 1.5 h and then cooled to rt. To a solution of ethyl acetoacetate (**5**) (1 mmol) in 5 mL of CH_2Cl_2, a preheated mixture of Et_2NH–CH_2Br_2 was added at rt. After the reaction was complete (1 h), the reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give the desired product **5a** in 62% yield.

4.2. General procedure for the α-methylenation of ketone under refluxing condition

A mixture of acetophenone (**8**) (1 mmol), Et_2NH (8 mmol) and CH_2Br_2 (15 mmol) in 5 mL of CH_2Cl_2 were heated up to reflux for 10 days. After the reaction was complete, the reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give the desired product **8a** in 66% yield.

4.3. General procedure for the α-methylenation of ketone under microwave irradiation at constant pressure in CH_2Cl_2

To a solution of acetophenone (**8**) (1 mol equiv.) in 5 mL of CH_2Cl_2 in Teflon container, CH_2Br_2 (6 mol equiv.) and Et_2NH (12 mol equiv.) were added. The container was sealed in the acid digestion vessel and was placed into microwave. The microwave oven (a CEM Model MDS-2000) was programmed so that the maximum internal pressure of the sealed Teflon container would not be over 60 psi, the reaction mixture was irradiated by 100% power for 5 min followed by 50% power for 30 min. The vessel was cooled to rt and the contents were concentrated to give the crude residues. To the crude mixture, ether was added and most of the ammonium salts were precipitated out. After filtration, the filtrate was concentrated, chromatographed on the silica gel column to give the α-methylenated product **8a** in 62% yield.

4.4. General procedure for the α-methylenation of ketone under microwave irradiation at constant temperature in CH_3CN

To a solution of ketone **30** (1 mol equiv.) in 5 mL of CH_3CN in Teflon container, CH_2Br_2 (24 mol equiv.) and Et_2NH (48 mol equiv.) were added. The container was sealed in the acid digestion vessel and was placed into microwave (a CEM MARS 5™). The microwave was programmed so that the maximum internal temperature would not be over 80°C, the reaction mixture was irradiated at 30% power for 30 min. The vessel was cooled to rt and the contents were concentrated to give the crude residues. To the crude mixture, ether was added and most of the ammonium salts were precipitated out. After filtration, the filtrate was concentrated, chromatographed on the silica gel column to give the desired product **30a** in 72% yield.

4.4.1. Ethyl 2-hydroxy-3-methylene-1-cyclohexene-1-carboxylate (4a). *Method I*. Following the general procedure for the α-methylenation of ketone at rt for 19 h, the product **4a** was prepared in 64% yield.

Method II. Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **4a** was prepared in 84% yield. TLC R_f=0.90 (EtOAc/hexane=1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (t, J=7.2 Hz, 3H, $-CH_3$), 1.68 (quin, J=6.1 Hz, 2H), 2.34–2.44 (m, 4H), 4.23 (q, J=7.2 Hz, 2H, $-OCH_2-$), 5.17 (s, 1H, $=CH_2$), 5.81 (s, 1H, $=CH_2$), 12.09 (s, 1H, $-OH$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1 (2°), 22.6 (2°), 23.5 (2°), 31.4 (2°), 60.5 (2°, $-OCH_2-$), 100.1 (4°, O=C–*C*=), 115.5 (2°, $=CH_2$), 138.7 (4°, $CH_2=C-$), 163.9 (4°, $-C-OH$), 172.9 (4°, C=O); IR (KBr, neat): 2930 (C–H), 1627 (C=O), 1579, 1395, 1347, 1319, 1257, 1188, 1033 cm^{-1}; MS (*m*/*z*, relative intensity): 182 (M^+, 81), 153 (20), 136 (85), 108 (100), 79 (40); HRMS calcd for $C_{10}H_{14}O_3$ 182.0943, found 182.0939.

4.4.2. Diethyl 2,4-diacetylpentanedioate (5a). Following the general procedure for the α-methylenation of ketone at rt for 1 h, the product **5a**[8] was prepared in 62% yield as a mixture of two diastereomers. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.23–1.35 (m, 6H, $2OCH_2CH_3$), 2.05–2.50 (m, 2H), 2.04 (s, 3H, CH_3CO), 2.07 (s, 3H, CH_3CO), 3.55 and 3.69 (t, J=7.2 Hz, 2H), 4.13–4.26 (m, 4H, $2OCH_2CH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.8 (1°, OCH_2CH_3), 25.2 (2°), 28.9 (1°, CH_3CO), 29.1 (1°, CH_3CO), 56.4 (3°), 56.5 (3°), 61.4 (2°, OCH_2CH_3), 168.8 (4°, C=O), 201.9 (4°, C=O); IR (KBr, neat): 3433 (overtone of 1719 cm^{-1}), 1719, 1359, 1244, 1148 cm^{-1}; MS (*m*/*z*, relative intensity): 272 (M^+, 3), 230 (35), 181 (32), 143 (34), 130 (100); HRMS calcd for $C_{13}H_{20}O_6$ (M^+) 272.1260, found 272.1259.

4.4.3. Diethyl 2,4-bis(ethoxycarbonyl)pentanedioate (6a) and diethyl 2,4,4,6-tetrakis(ethoxycarbonyl)heptanedioate (6b). Following the general procedure for the α-methylenation of ketone at rt for 24 h, the product **6a** was obtained in 54% yield and product **6b** was obtained in 4% yield.

Compound **6a**.[9] ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, J=7.1 Hz, 12H), 2.47 (t, J=7.5 Hz, 2H), 3.47 (t, J=7.5 Hz,

2H), 4.20 (q, J=7.1 Hz, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9 (1°), 27.3 (2°), 49.4 (3°), 61.6 (2°), 168.5 (4°, C=O); IR (KBr, neat): 3451, 1729, 1442, 1367, 1282, 1179, 1096 cm^{-1}; MS (*m/z*, relative intensity): 332 (M^+, 2), 287 (43), 258 (15), 241 (41), 173 (100), 160 (23), 127 (45); HRMS calcd for $C_{15}H_{24}O_8$ (M^+) 332.1471, found 332.1476.

Compound **6b**.[10] ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.21–1.30 (m, 18H), 2.55 (d, J=5.9 Hz, 4H), 3.55 (t, J=5.9 Hz, 2H, $-CH_2CHC$=O), 4.07–4.24 (m, 12H, O–CH_2); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.7 (1°), 13.8 (1°), 32.0 (2°), 48.1 (3°), 55.5 (4°), 61.6 (2°), 168.9 (4°, C=O), 169.9 (4°, C=O); IR (KBr, neat): 3063, 2982, 2939, 1727, 1442, 1366, 1286, 1188, 1095, 1017 cm^{-1}; MS (60 eV; *m/z*, relative intensity): 505 (M^++1, 3), 459 (M^+−OEt, 30), 413 (31), 332 (70), 287 (42), 173 (100); HRMS calcd for $C_{21}H_{31}O_{11}$ ($M^+-OCH_2CH_3$) 459.1866, found 459.1872.

4.4.4. 2,4-Dibenzoyl-1,5-diphenylpentan-1,5-dione (7a). Following the general procedure for the α-methylenation of ketone at rt for 5 h, the product **7a**[11] was prepared in 56% yield as a white solid; mp 179–180°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.77 (t, J=7.0 Hz, 2H), 5.75 (t, J=7.0 Hz, 2H), 7.44–7.62 (m, 12H), 8.14 (d, J=7.8 Hz, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 28.9 (2°), 54.0 (3°), 128.8 (3°), 129.0 (3°), 133.9 (3°), 135.4 (4°), 196.6 (4°, C=O); IR (KBr): 3059, 2936, 1689, 1594, 1182, 951 cm^{-1}; MS (*m/z*, relative intensity): 461 (M^++1, 2), 442 (M^+−18, 12), 355 (M^+−COPh, 100), 337 (40); HRMS calcd for $C_{24}H_{19}O_3$ (M^+−COPh) 355.1335, found 355.1330.

4.4.5. 2-(Diethylaminomethyl)-1-phenyl-2-propen-1-one (8a). *Method I*. Following the general procedure for the α-methylenation of ketone under the refluxing condition in CH_2Cl_2 for 10 days, the product **8a**[12] was prepared in 66% yield.

Method II. Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 30 min, the product **8a**[12] was prepared in 62% yield. TLC (EtOAc/hexane=1:10) R_f=0.12; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.01 (t, J=7.2 Hz, 6H, $-CH_2CH_3$), 2.54 (q, J=7.2 Hz, 4H, $-CH_2CH_3$), 3.44 (s, 2H, N–CH_2), 5.67 (s, 1H, =CH_2), 5.99 (s, 1H, =CH_2), 7.41–7.48 (m, 2H), 7.50–7.55 (m, 1H), 7.75–7.80 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.6 (1°), 47.8 (2°, CH_2CH_3), 55.1 (2°, –N–CH_2), 126.5 (2°, C=CH_2), 128.8 (3°), 130.2 (3°), 132.9 (3°), 138.3 (4°), 147.0 (4°, –C=CH_2), 198.7 (4°, C=O); IR (KBr, neat): 3064, 2971, 1652 (C=O), 1315, 1111, 1068 cm^{-1}; MS (*m/z*, relative intensity): 217 (M^+, 30), 216 (10), 202 (62), 200 (100), 188 (30), 105 (72), 86 (100), 72 (30); HRMS calcd for $C_{14}H_{19}ON$ (M^+) 217.1467, found 217.1469.

4.4.6. 2-Methyl-1-phenylpropenone (9a). *Method I*. Following the general procedure for the α-methylenation of ketone under refluxing condition in CH_2Cl_2 for 8 days, the product **9a**[13] was prepared in 77% yield.

Method II. Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **9a**[13] was prepared in 62% yield. TLC (EtOAc/hexane=1:10) R_f=0.62; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.07 (s, 3H, CH_3), 5.61 (s, 1H, =CH_2), 5.90 (s, 1H, =CH_2), 7.40–7.44 (m, 2H), 7.49–7.54 (m, 1H), 7.70–7.73 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.6 (1°), 126.9 (2°, =CH_2), 128.1 (3°), 129.3 (3°), 131.9 (3°), 137.7 (4°), 143.8 (4°, C=CH_2), 198.3 (4°, C=O); IR (KBr, neat): 3068, 2976, 2921, 1691 (C=O), 1659, 1599, 1452, 1332, 1203 cm^{-1}; MS (*m/z*, relative intensity): 146 (M^+, 12), 136 (18), 107 (30), 105 (81), 91 (32), 89 (30), 77 (100); HRMS calcd for $C_{10}H_{10}O$ (M^+) 146.0732, found 146.0739.

4.4.7. 1,2-Diphenyl-2-propen-1-one (10a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **10a**[13,14] was prepared in 82%. TLC R_f=0.73 (EtOAc/hexane=1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (s, 1H, =CH_2), 6.07 (s, 1H, =CH_2), 7.34–7.41 (m, 3H), 7.42–7.45 (m, 4H), 7.51–7.60 (m, 1H), 7.90–7.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.8 (2°, =CH_2), 127.0 (3°), 127.8 (3°), 128.4 (3°), 128.6 (3°), 130.0 (3°), 133.0 (3°), 137.0 (3°), 137.1 (4°), 148.3 (4°, C=CH_2), 197.5 (4°, C=O); IR (KBr, neat): 3059, 3022, 2930, 1673 (C=O), 1604, 1573, 1258, 1217, 1143, 1005, 982, 761 cm^{-1}; MS (*m/z*, relative intensity): 208 (M^+, 11), 165 (2), 106 (4), 105 (56), 103 (13), 102 (11), 77 (97), 51 (100), 50 (36); HRMS calcd for $C_{15}H_{12}O$ 208.0888, found 208.0884.

4.4.8. 1-(1-Naphthyl)-2-methylpropenone (11a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 25 min, the product **11a** was prepared in 69%. TLC R_f=0.83 (EtOAc/hexane=1:20, developed twice); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.16 (s, 3H, $-CH_3$), 5.65 (s, 1H, =CH_2), 6.00 (s, 1H, =CH_2), 7.45–7.52 (m, 4H), 7.88 (dd, J=6.2, 3.2 Hz, 1H), 7.93 (d, J=7.8 Hz, 1H), 7.98 (dd, J=6.2, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.5 (1°), 124.2 (2°, C=CH_2), 125.5 (3°), 126.3 (3°), 126.6 (3°), 127.0 (3°), 128.3 (3°), 130.2 (3°), 130.5 (3°), 130.8 (4°), 133.6 (4°), 136.7 (4°), 145.6 (4°, C=CH_2), 200.0 (4°, C=O); IR (KBr, neat): 3050, 2921, 1659 (C=O), 1511, 1452, 1323, 1093, 798, 780 cm^{-1}; MS (*m/z*, relative intensity): 196 (M^+, 13), 181 (20), 168 (16), 155 (35), 127 (100), 126 (35), 101 (15), 77 (38); HRMS calcd for $C_{14}H_{12}O$ 196.0888, found 196.0884.

4.4.9. 2-Methylene-3,4-dihydro-2*H*-naphthalen-1-one (12a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **12a**[13,15] was prepared in 49% yield. Compound **12a** is stable in mixed solvents of hexane and ethyl acetate and it will dimerize to give compound **12b** during concentration.

Compound **12a**. TLC (EtOAc/hexane=1:10) R_f=0.45; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.80–2.88 (m, 2H, CH_2), 2.99 (t, J=6.8 Hz, 2H, CH_2), 5.44 (s, 1H, =CH_2), 6.23 (s, 1H, =CH_2), 7.24–7.49 (m, 3H), 8.11 (dd, J=7.6, 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 29.7 (2°), 31.7 (2°), 121.7 (2°, C=CH_2), 126.7 (3°), 126.8 (3°), 128.5 (3°), 133.1 (4°), 143.4 (4°), 144.1 (4°), 187.5 (4°, C=O); IR (KBr, neat): 3059, 2921, 1696 (C=O), 1599, 1152, 1092 cm^{-1}; MS; HRMS calcd for $C_{11}H_{10}O$ (M^+) 158.0732, found 158.0729.

Dimer **12b**. TLC (EtOAc/hexane=1:10) R_f=0.45; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.82–1.96 (m, 1H), 2.10–2.40 (m, 5H), 2.40–2.50 (m, 1H), 2.70–3.00 (m, 4H), 3.15–3.25 (m, 1H), 7.06–7.48 (m, 7H), 8.03 (d, J=7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.8 (2°), 26.3 (2°), 27.1 (2°), 28.1 (2°), 28.6 (2°), 33.4 (2°), 77.8 (4°), 107.9 (4°), 121.3 (3°), 126.8 (3°), 127.3 (3°), 127.4 (3°), 127.5 (3°), 129.0 (3°), 129.2 (3°), 132.2 (3°), 132.3 (4°), 134.0 (3°), 136.5 (4°), 143.4 (4°), 143.6 (4°), 196.2 (4°, C=O); IR (KBr, neat): 3059, 2921, 1696 (C=O), 1599, 1152, 1092 cm^{-1}; MS (*m/z*, relative intensity): 316 (M^+, 50), 159 (98), 156 (10), 154 (100), 136 (95), 115 (50), 107 (48), 91 (56), 89 (48), 77 (62); HRMS calcd for $C_{22}H_{20}O_2$ (M^+) 316.1464, found 316.1469.

4.4.10. 1-(2-Furyl)-2-methylpropenone (13a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **13a**[16] was prepared from 1-furan-2-yl-propan-1-one (**13**)[17] in 68% yield. TLC R_f=0.46 (EtOAc/hexane=1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.07 (s, 3H, $-CH_3$), 5.78 (s, 1H, $=CH_2$), 5.81 (s, 1H, $=CH_2$), 7.12 (dd, J=4.9, 3.8 Hz, 1H), 7.65–7.67 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3 (1°), 112.6 (3°), 121.6 (3°), 122.9 (2°, $=CH_2$), 143.7 (4°), 148.4 (3°), 153.2 (4°, $C=CH_2$), 175.0 (4°, C=O); IR (KBr, neat): 1710 (C=O), 1678 cm^{-1}; MS (*m/z*, relative intensity): 136 (M^+, 72), 124 (100), 96 (26), 68 (55); HRMS calcd for $C_8H_8O_2$ 136.0524, found 136.0522.

4.4.11. 1-(2-Furyl)-2-propylpropenone (14a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **14a** was prepared from 1-(furan-2-yl)pentan-1-one (**14**)[18] in 66% yield. TLC R_f=0.79 (EtOAc/hexane=1:10); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J=5.8 Hz, 3H, $-CH_3$), 1.49 (sextet, J=7.1 Hz, 2H, $-CH_2CH_2CH_3$), 2.42 (t, J=7.1 Hz, 2H, $-CH_2-$), 5.71 (s, 1H, $=CH_2$), 5.89 (s, 1H, $=CH_2$), 6.52 (dd, J=3.5, 1.8 Hz, 1H, 4-furan-H), 7.12 (dd, J=3.5, 0.6 Hz, 1H, 3-furan-H), 7.64 (dd, J=1.6, 0.7 Hz, 1H, 5-furan-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7 (1°), 21.3 (2°, $-CH_2CH_3$), 34.3 (2°), 111.8 (3°), 119.7 (3°), 123.1 (2°, $=CH_2$), 147.0 (3°), 148.1 (4°, $-C=CH_2$), 152.1 (4°), 184.5 (4°, C=O); IR (KBr, neat): 3123, 2958, 2865, 1650 (C=O), 1567, 1470, 1392, 1237, 1028, 766 cm^{-1}; MS (*m/z*, relative intensity): 164 (M^+, 16), 149 (12, M^+-CH_3), 146 (15), 135 (34, $M^+-C_2H_5$), 122 (26), 121 (17), 95 (100), 94 (21), 93 (18), 67 (33), 53 (27); HRMS calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0835.

4.4.12. 1-(2-Thienyl)-2-methylpropenone (15a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **15a**[19] was prepared from 1-(thiophen-2-yl)-propan-1-one (**15**)[20] in 76% yield. TLC R_f=0.55 (EtOAc/hexane=1:20); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (s, 3H), 5.74 (t, J=0.9 Hz, 1H, $=CH_2$), 5.85 (t, J=1.1 Hz, 1H, $=CH_2$), 7.31 (dd, J=4.8, 3.8 Hz, 1H), 7.61–7.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.6 (1°), 122.9 (2°, $=CH_2$), 128.5 (3°), 134.5 (3°), 136.7 (3°), 143.7 (4°), 145.5 (4°), 180.7 (4°, C=O); IR (KBr, neat): 1712 (C=O), 1688 cm^{-1}; MS (*m/z*, relative intensity): 152 (M^+, 22), 140 (100), 112 (8), 84 (56); HRMS calcd for C_8H_8OS 152.0296, found 152.0291.

4.4.13. 2-Methyl-1-(1*H*-pyrrol-2-yl)propenone (16a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 35 min, the product **16a** was prepared from 2-propionyl-pyrrole (**16**)[21] in 20% yield and 72% of the starting material **16** was recovered. TLC R_f=0.36 (4 times EtOAc/hexane=1:10); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.05 (s, 3H, $-CH_3$), 5.66 (qu, J=1.5 Hz, 1H, $=CH_2$), 5.83 (qu, J=1.1 Hz, 1H, $=CH_2$), 6.28–6.29 (m, 1H, pyrrole-2-H), 6.86–6.88 (m, 1H, pyrrole-3-H), 7.07–7.08 (m, 1H, pyrrole-5-H), 9.45 (brs, 1H, N–H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.9 (1°), 110.7 (3°), 118.1 (3°), 122.6 (2°, $=CH_2$), 124.8 (3°), 130.8 (4°), 143.7 (4°), 186.5 (4°, C=O); IR (KBr, neat): 3277 (N–H), 2958, 2924, 1628 (O=C), 1591 (s), 1541, 1407, 1258, 1139, 1105, 1301 cm^{-1}; MS (*m/z*, relative intensity): 135 (M^+, 72), 124 (11), 94 (100), 66 (10), 39 (15); HRMS calcd for C_8H_9NO 135.0684, found 135.0676.

4.4.14. 1-(1-Methanesulfonyl-1*H*-pyrrol-2-yl)-2-methyl-propenone (17a). *Method I*. Following the general procedure for the α-methylenation of ketone under microwave irradiation at constant pressure for 40 min, compound **17a** was formed in 41% yield from 1-(1-methanesulfonyl-1*H*-pyrrol-2-yl)propan-1-one (**17**)[21] and recovered 27% of the starting material **17**.

Method II. Following the general procedure for the α-methylenation of ketone under microwave irradiation at constant temperature (130°C) for 30 min, compound **17a** was formed in 60% yield and recovered 18% of the starting material **17**. TLC R_f=0.36 (EtOAc/hexane=1:5); mp 81.5–82.5°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 3H), 3.77 (s, 3H), 5.89 (s, 1H, $=CH_2$), 5.90 (s, 1H, $=CH_2$), 6.27 (t, J=3.3 Hz, 1H, $-NCH=CH-$), 6.83 (dd, J=3.6, 1.7 Hz, 1H, $-NC=CH-$), 7.51 (dd, J=3.2, 1.7 Hz, 1H, $-NCH=CH-$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1 (1°), 43.8 (1°, SO_2CH_3), 110.1 (3°), 124.6 (3°), 127.5 (2°, $=CH_2$), 129.0 (3°), 132.6 (4°), 144.2 (4°), 187.0 (4°, O=*C*); IR (KBr): 3148, 3042, 2930, 1644 (C=O), 1540, 1363 (S=O), 1170 (S=O) cm^{-1}; MS (*m/z*, relative intensity): 213 (M^+, 26), 172 (38), 134 (50), 94 (100), 79 (19); HRMS calcd for $C_9H_{11}NO_3S$ (M^+) 213.0460, found 213.0459.

4.4.15. Methyl 3-methylene-1-methyl-2-oxocyclohexane-carboxylate (19a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **19a** was prepared in 85% yield. TLC R_f=0.49 (EtOAc/hexane=1:10); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (s, 3H), 1.79–1.86 (m, 3H), 1.97–2.47 (m, 3H), 3.59 (s, 3H, OCH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.71 (1°), 21.87 (2°), 23.28 (2°), 27.37 (2°), 38.89 (2°), 41.30 (2°), 57.77 (4°), 61.87 (1°, OCH_3), 173.74 (4°, C=O), 208.94 (4°, C=O); IR (KBr, neat): 2939, 1724 (C=O), 1457, 1268, 1245, 1180, 1153, 738 cm^{-1}; MS (*m/z*, relative intensity): 196 (M^+, 17), 184 (5), 156 (15), 141 (8), 128 (36), 113 (25), 102 (28), 82 (9), 69 (28), 55 (100); HRMS calcd for $C_{11}H_{16}O_3$ 196.1099, found 196.1093.

4.4.16. Methyl 3-methylene-1-methyl-2-oxocyclopentane-carboxylate (20a). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **20a** was prepared in 82% yield. TLC R_f=0.67 (EtOAc/hexane=1:5); ^{1}H NMR

(400 MHz, $CDCl_3$) δ 1.38 (s, 3H), 1.70–1.82 (m, 1H), 2.45–2.60 (m, 1H), 2.70–2.80 (m, 2H), 3.66 (s, 3H, $-OCH_3$), 5.44 (s, 1H, $=CH_2$), 6.10 (s, 1H, $=CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9 (1°), 26.6 (2°), 32.8 (2°), 52.6 (1°, $-OCH_3$), 56.3 (4°), 119.7 (2°, C=*C*H_2), 143.4 (4°, *C*=CH_2), 172.6 (4°, C=O), 203.1 (4°, C=O); IR (KBr, neat): 2949, 2847, 1733 (C=O), 1640, 1461, 1438, 1277, 1171, 738 cm^{-1}; MS (*m*/*z*, relative intensity): 168 (M^+, 3), 153 (2), 140 (44), 125 (28), 109 (30), 101 (14), 81 (73), 69 (87), 53 (100); HRMS calcd for $C_9H_{12}O_3$ 168.0786, found 168.0788.

4.4.17. 3-(Diethylaminomethyl)bicyclo[2.2.1]heptan-2-one (21a′). Following the general procedure for the α-methylenation of ketone under microwave condition at constant pressure for 20 min, the product **21a′** was prepared in 49% yield. TLC (EtOAc/hexane=1:5) R_f=0.2; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.95–1.00 (m, 6H, CH_3), 1.35–1.60 (m, 4H), 1.65–2.02 (m, 4H), 2.32–2.60 (m, 7H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 11.7 (1°), 24.2 (2°), 27.8 (2°), 34.8 (2°), 38.7 (3°), 47.0 (2°), 49.6 (3°), 51.6 (2°), 52.8 (3°), 219.7 (4°, C=O); IR (KBr, neat): 2967, 2875, 1742 (C=O), 1171, 1078 cm^{-1}; MS (*m*/*z*, relative intensity): 195 (M^+, 6), 95 (5), 87 (10), 86 (100), 79 (5); HRMS calcd for $C_{12}H_{21}ON$ (M^+) 195.1624, found 195.1625.

4.4.18. 3-Methylenebicyclo[2.2.1]heptan-2-one (21a). To a mixture of compound **21a′** (195 mg, 1 mmol) and silica gel (1 g) was added 5 mL of CH_2Cl_2. The slurry mixture was stirred at rt for 10 h and put on silica gel column chromatography to give compound **21a**[22] as a colorless oil in 84% yield. TLC (EtOAc/hexane=1:5) R_f=0.75; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.50–1.60 (m, 2H), 1.61–1.63 (m, 1H), 1.70–1.73 (m, 1H), 1.85–1.88 (m, 2H), 2.70 (brs, 1H, bridgehead-H), 3.11 (brs, 1H, bridgehead-H), 5.12 (s, 1H, $=CH_2$), 5.69 (s, 1H, $=CH_2$); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 24.3 (2°), 28.7 (2°), 37.5 (2°), 43.2 (3°), 49.8 (3°), 112.4 (2°, C=CH_2), 150.7 (4°, C=CH_2), 206.5 (4°, C=O); IR (KBr, neat): 2948, 2865, 1737 (C=O), 1654, 1452, 1387, 1253, 1065, 936, 770 cm^{-1}; MS (*m*/*z*, relative intensity): 122 (M^+, 90), 107 (30), 93 (80), 91 (65), 79 (100), 77 (80); HRMS calcd for $C_8H_{10}O$ (M^+) 122.0732, found 122.0738.

4.4.19. 2-Methyl-1-[1-(toluene-4-sulfonyl)-1*H*-pyrrol-2-yl]propenone (28a). Following the general procedure for the α-methylenation under microwave irradiation at constant temperature (100°C) for 30 min, compound **28a** was formed in 81% yield from 1-[1-(toluene-4-sulfonyl)-1*H*-pyrrol-2-yl]propan-1-one (**28**)[23] and recovered 4% of the starting material **28**. TLC R_f=0.63 (EtOAc/hexane=1:3); mp 90–91°C; ^1H NMR (400 MHz, $CDCl_3$) δ 1.97 (s, 3H, $-CH_3$), 2.42 (s, 3H, $-CH_3$), 5.81 (s, 1H, $=CH_2$), 5.83 (s, 1H, $=CH_2$), 6.28 (brd, *J*=2.8 Hz, 1H, –NCH=C*H*–), 6.71 (brd, *J*=1.3 Hz, 1H, –CN=C*H*–), 7.34 (d, *J*=8.0 Hz, 2H, –(CH$_3$)C=C*H*–), 7.64 (brs, 1H, –NC*H*=CH–), 7.94 (d, *J*=8.1 Hz, 2H, –SC=C*H*–); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1 (1°), 21.6 (1°, $-NCH_3$), 110.5 (3°), 123.3 (3°), 126.9 (2°, $=CH_2$), 128.2 (3°), 128.6 (3°), 129.5 (3°), 132.8 (4°), 136.3 (4°), 144.6 (4°), 144.8 (4°), 186.6 (4°, C=O); IR (KBr, neat): 1652 (C=O), 1366 (S=O), 1145 (S=O) cm^{-1}; MS (*m*/*z*, relative intensity): 289 (M^+, 5), 155 (20), 134 (43), 91 (100), 65 (27); HRMS calcd for $C_{15}H_{15}NO_3S$ (M^+) 289.0773, found 289.0774.

4.4.20. 2-Methyl-1-[1-(toluene-4-sulfonyl)-1*H*-pyrrol-3-yl]propenone (29a). Following the general procedure for the α-methylenation under microwave irradiation at constant temperature (100°C) for 30 min, compound **29a** was formed in 60% yield from 1-[1-(toluene-4-sulfonyl)-1*H*-pyrrol-3-yl]propan-1-one (**29**)[23a,24] and recovered 7% of the starting material **29**. TLC R_f=0.67 (EtOAc/hexane=1:3); ^1H NMR (400 MHz, $CDCl_3$) δ 1.99 (s, 3H, $-CH_3$), 2.42 (s, 3H, $-CH_3$), 5.74 (s, 1H, $=CH_2$), 5.75 (s, 1H, $=CH_2$), 6.69 (dd, *J*=3.2, 1.6 Hz, 1H, –NCH=C*H*–), 7.14 (dd, *J*=3.3, 2.2 Hz, 1H, –NC*H*=CH–), 7.32 (d, *J*=8.3 Hz, 2H, –(CH$_3$)C=C*H*–), 7.60 (dd, *J*=3.7, 1.9 Hz, 1H, –NC*H*=CH–), 7.79 (d, *J*=8.3 Hz, 2H, –SC=C*H*–); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.5 (1°), 21.7 (1°, $-NCH_3$), 113.7 (3°), 121.4 (3°), 124.2 (2°, $=CH_2$), 125.3 (3°), 127.2 (3°), 127.5 (4°), 130.3 (3°), 135.3 (4°), 144.8 (4°), 145.9 (4°), 191.4 (4°, C=O); IR (KBr, neat): 3138, 1644 (C=O), 1531, 1173 (S=O) cm^{-1}; MS (*m*/*z*, relative intensity): 289 (M^+, 11), 155 (38), 91 (100), 65 (2); HRMS calcd for $C_{15}H_{15}NO_3S$ (M^+) 289.0773, found 289.0771.

4.4.21. 2-Propyl-1-(pyridin-2-yl)propenone (30a). Following the general procedure for the α-methylenation under microwave irradiation at constant temperature (80°C) for 30 min, compound **30a** was formed from 1-(pyridin-2-yl)-pentan-1-one (**30**)[25] in 72% yield. TLC R_f=0.55 (EtOAc/hexane=3:1); ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J*=7.4 Hz, 3H, $CH_2CH_2CH_3$), 1.54 (sextet, *J*=7.4 Hz, 2H, $CH_2CH_2CH_3$), 2.46 (t, *J*=7.4 Hz, 2H, $COCCH_2$), 5.95 (s, 1H, C=CH_2), 5.96 (s, 1H, C=CH_2), 7.41 (dd, *J*=5.2, 3.4 Hz, 1H), 7.79–7.82 (m, 2H), 8.65 (d, *J*=4.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8 (1°), 21.4 (2°), 33.9 (2°), 123.9 (2°, =*C*H_2), 125.7 (3°), 128.3 (3°), 136.8 (3°), 147.1 (4°), 148.5 (3°), 155.6 (4°), 196.0 (4°, C=O); IR (KBr, neat): 3058, 2966, 2930, 1664 (C=O), 1004 cm^{-1}; MS (*m*/*z*, relative intensity): 175 (M^+, 25), 149 (42), 146 (75), 106 (32), 84 (82), 78 (100), 71 (31); HRMS calcd for $C_{11}H_{13}NO$ (M^+) 175.0997, found 175.0997.

4.4.22. 1-Cyclohexyl-2-phenylpropenone (31a). Following the general procedure for the α-methylenation under microwave irradiation at constant temperature (80°C), compound **31a** was formed from cyclohexyl-2-phenylethanone (**31**)[26] in 81% yield. TLC R_f=0.44 (EtOAc/hexane=10:1); ^1H NMR (400 MHz, $CDCl_3$) δ 1.25–1.90 (m, 10H), 2.91–2.97 (m, 1H, –C*H*CO), 5.84 (s, 1H, $=CH_2$), 5.96 (s, 1H, $=CH_2$), 7.29–7.36 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6 (2°), 25.8 (2°), 28.9 (2°), 46.8 (3°), 122.0 (2°), 127.9 (3°), 128.0 (3°), 128.2 (3°), 137.4 (4°), 149.2 (4°), 206.2 (4°, C=O); IR (KBr, neat): 2930 (s), 2853 (s), 1679 (s, O=C) cm^{-1}. MS (*m*/*z*, relative intensity): 214 (M^+, 100), 171 (10), 149 (8), 141 (10), 133 (15), 132 (18), 110 (18); HRMS calcd for $C_{15}H_{18}O$ (M^+) 214.1358, found 214.1356.

4.4.23. 2-Benzylhexa-1,4-dien-3-one (32a) and 1-phenylhex-4-en-3-one (32b). Following the general procedure for the α-methylenation under microwave irradiation at constant temperature (80°C) for 20 min, phenylhex-5-en-3-one (**32**)[27] gave compound **32a** in 60% yield and **32b** in 18% yield.

Compound **32a**. ^1H NMR (400 MHz, $CDCl_3$) δ 1.90 (d, *J*=6.9 Hz, 3H, $-CH_3$), 3.66 (s, 2H, $-CH_2Ph$), 5.59 (s, 1H,

C═CH_2), 5.99 (s, 1H, C═CH_2), 6.62 (d, J=15.2 Hz, 1H, –COCH═CHMe), 6.89 (dq, J=15.3, 6.9 Hz, 1H, –COCH═CHMe), 7.17–7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3 (1°), 37.4 (2°), 124.7 (2°), 126.2 (3°), 127.1 (3°), 128.4 (3°), 129.1 (2°), 139.1 (4°), 143.8 (3°), 148.9 (4°), 191.6 (4°, C═O); IR (KBr, neat): 3027, 2925, 1725, 1667, 1620, 1290, 1073 cm^{-1}; MS (*m*/*z*, relative intensity): 186 (M^+, 5), 171 (10), 149 (95), 91 (65), 86 (71), 84 (100), 57 (45); HRMS calcd for $C_{13}H_{14}O$ (M^+) 186.1045, found 186.1046.

Compound **32b**.[28] ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.88 (d, J=6.8 Hz, 3H, –CH_3), 2.84–2.88 (m, 2H, CH_2), 2.92–2.96 (m, 2H, –COCH_2), 6.13 (d, J=15.7 Hz, 1H, –COCH═CHMe), 6.85 (dq, J=15.7, 6.8 Hz, 1H, –COCH═CHMe), 7.17–7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2 (2°), 30.0 (2°), 41.5 (2°), 126.0 (3°), 128.3 (3°), 128.4 (3°), 131.9 (3°), 141.3 (4°), 142.7 (3°), 199.3 (4°, C═O); IR (KBr, neat) 3054, 2925, 1672 (CO), 1632, 1265, 970 cm^{-1}; MS (*m*/*z*, relative intensity): 174 (M^+, 8), 149 (35), 97 (33), 91 (20), 86 (36), 84 (100), 71 (44), 69 (50), 57 (18); HRMS calcd for $C_{12}H_{14}O$ (M^+) 174.1045, found 174.1044.

4.4.24. 2-Phenethylhexa-1,4-dien-3-one (33a). Following the general procedure for the α-methylenation under microwave irradiation at constant temperature (80°C) for 20 min, compound **33a** was formed from 7-phenylhept-2-en-4-one (**33**)[29] in 11% yield and recovered 15% of the starting material **33**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92 (d, J=6.8 Hz, 3H, –CH_3), 2.64–2.67 (m, 2H), 2.74–2.78 (m, 2H), 5.66 (s, 1H, C═CH_2), 5.89 (s, 1H, C═CH_2), 6.62 (d, J=15.3 Hz, 1H, –COCH═CHMe), 6.89 (dq, J=15.3, 6.8 Hz, 1H, –COCH═CHMe), 7.17–7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.3 (1°), 33.4 (2°), 34.6 (2°), 123.8 (3°), 125.9 (3°), 127.3 (3°), 128.3 (3°), 128.5 (2°), 141.5 (4°), 143.6 (3°), 148.5 (4°), 192.1 (4°, O═C); IR (KBr, neat) 3026, 1667 (CO), 1619, 1442 cm^{-1}; MS (*m*/*z*, relative intensity): 200 (M^+, 25), 185 (28), 171 (23), 149 (8), 91 (78), 86 (71), 91 (100), 65 (18), 57 (5); HRMS calcd for $C_{14}H_{16}O$ (M^+) 200.1201, found 200.1202.

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