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Lewis acid-mediated reactions of 1-cyclopropyl-2-arylethanone derivatives with diethyl 2-oxomalonate and ethyl 2-oxoacetate

Xiang-Ying Tang, Min Shi *

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China

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ABSTRACT

TMSOTf-mediated reactions of 2-aryl-1-(1-phenylcyclopropyl)ethanones **1** with diethyl 2-oxomalonate **2** afford a novel method for the synthesis of spiro-γ-lactone derivatives **3** in good to excellent yields via a sequential reaction involving a nucleophilic ring-opening reaction of the cyclopropane by H_2O, an aldol-type reaction and a cyclic transesterification mediated by Lewis acid. On the other hand, we found that TMSOTf-mediated reactions of 1-cyclopropyl-2-arylethanones **1** with ethyl 2-oxoacetate **4** could also provide the corresponding spiro-γ-lactone derivatives **5** in moderate yields along with another spiro-γ-lactone derivatives **6** derived from the reaction of **1** with two molecules of ethyl 2-oxoacetate. The plausible reaction mechanisms have also been provided on the basis of control experiments.

1. Introduction

Cyclopropane containing compounds, as versatile building blocks in organic synthesis, have been well understood.[1] The ring-opening reactions of cyclopropyl ketones are synthetically useful protocols in the construction of complex product structures that have been studied extensively thus far.[2] Previously, we reported Lewis acids $SnCl_4$ and TMSOTf-mediated reactions of cyclopropyl alkyl ketones with α-ketoesters and cyclopropyl aryl ketones with allenic esters to afford novel methods for the synthesis of 1,6-dioxa-spiro[4.4]non-3-en-2-ones with high stereoselectivities as well as dihydrofuro[2,3-*h*]chromen-2-one and 2,3-dihydrobenzofuran-4-ol derivatives in moderate to good yields under mild conditions (Scheme 1).[3] It is well known that spiro-γ-lactones constitute an important class of oxygen-containing heterocyclic compounds and such groups can be found in many biologically active natural products (Fig. 1).[4] Therefore, it is necessary to further explore such synthetic method for the construction of biologically important spiro-γ-lactone derivatives from simple or commercially available starting materials. In this paper, we wish to report the full details on the Lewis acid-mediated reactions of 1-cyclopropyl-2-arylethanone derivatives with diethyl 2-oxomalonate and ethyl 2-oxoacetate for the construction of functionalized 1,6-dioxa-spiro[4.4]non-3-en-2-one skeletons under mild conditions along with the mechanistic explanations on the basis of previous literature and control experiments.

2. Results and discussion

As shown in our previous communication,[3a,d] a plausible mechanism for the formation of 1,6-dioxa-spiro[4.4]non-3-en-2-one derivatives has been proposed on the basis of a ring-opening reaction of 1-cyclopropyl alkyl ketone, intramolecular aldol-type reaction as well as cyclic transesterification.[3a,d] However, this reaction suffers from a drawback on the substrate scope, that is, the substrates should contain a substitute on the cyclopropyl ring to control the reaction pathway, affording the corresponding spiro-γ-lactone in high yield (Scheme 1). To extend the scope and limitations of this reaction, we envisaged that if using diethyl 2-oxomalonate **2** (1.0 equiv), in which the carbonyl group is activated by two carboxyl groups, as the substrate to react with 1-cyclopropyl-2-phenylethanone **1a** (1.0 equiv) in the presence of TMSOTf (1.0 equiv), the corresponding spiro-γ-lactone derivative **3a** could be also formed under the standard conditions. To our delight, it was found that the corresponding 1,6-dioxa-spiro[4.4]non-3-en-2-one derivative **3a** was obtained as a sole product in good yield (81%) within 12 h in 1,2-dichloroethane (DCE) at 60 °C (Table 1, entry 1). Inspirited by this result, we next started to optimize the reaction conditions by changing Lewis acids and the ratio of the substrates and employed Lewis acid (**1a**/**2a**/Lewis acid). The results of these experiments are summarized in Table 1. $SnCl_4$ was first examined because it performed very well in our previous work.[3a] However, we found that

* Corresponding author. Fax: +86 21 64166128.
E-mail address: mshi@mail.sioc.ac.cn (M. Shi).

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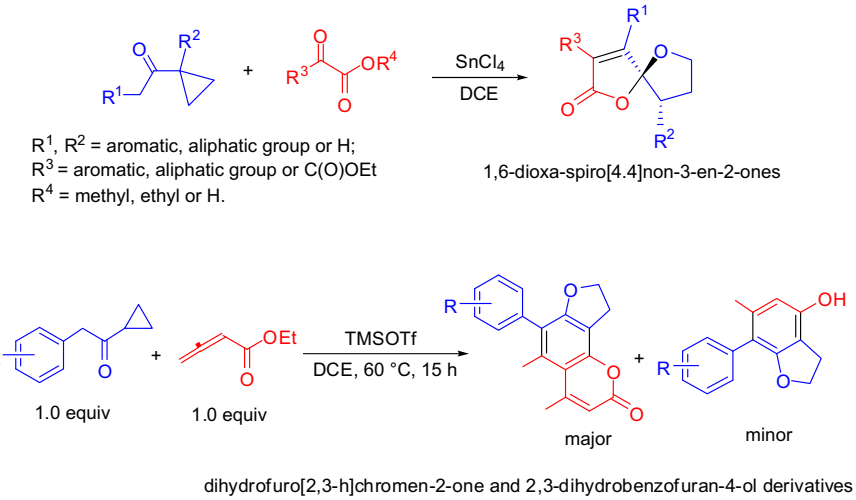


Scheme 1. $SnCl_4$ and TMSOTf-mediated reactions of 1-cyclopropyl alkyl ketones with α-ketoesters and cyclopropyl aryl ketones with allenic esters.

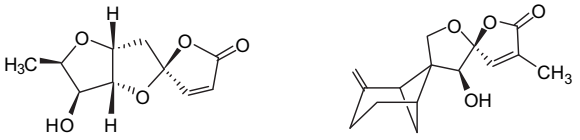
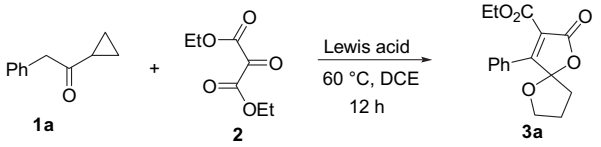


Figure 1. Important compounds bearing a spiro-γ-lactone moiety.

Table 1
Reactions of 1-cyclopropyl-2-phenylethanone (**1a**) and diethy1 2-oxomalonate (**2**) mediated by various Lewis acids



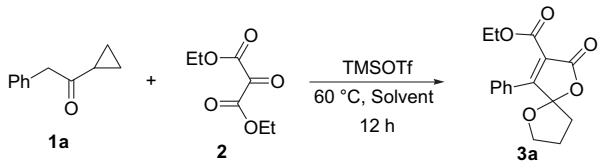
Entry	**1a**/**2**/Lewis acid	Lewis acid	Yield[a] (%)
			3a
1	1:1:1	TMSOTf	81
2	1:1:1	$SnCl_4$	—[b]
3	1:1:1	$TiCl_4$	Complex[c]
4	1:1:1	$Bi(OTf)_2Cl$	47
5	1:1:1	$InCl_3·4H_2O$	72
6	1:1:1	$BF_3·Et_2O$	7
7	1:1:1	$Nd(OTf)_3$	35
8	1:1:1	$Sc(OTf)_3$	39
9	1:1:1	HOTf	51
10	1:1.5:1	TMSOTf	81/(74)[d]
11	1:3:1	TMSOTf	82
12	*1.5:1:1.5*	*TMSOTF*	*97*

[a] Isolated yields.
[b] A product mixture was obtained.
[c] The reaction became disordered and **3a** was not formed.
[d] TMSOTf (0.5 equiv) was used.

using $SnCl_4$ (**1a**/**2a**/$SnCl_4$=1:1:1) as the Lewis acid in this reaction afforded a complex product mixtures on the basis of ^1H NMR spectroscopic data (Table 1, entry 2). Using $TiCl_4$ as the promoter provided the similar result without the formation of **3a** (Table 1, entry 3). When other Lewis acids such as $Bi(OTf)_2Cl$, $InCl_3·4H_2O$, $BF_3·Et_2O$, $Nd(OTf)_3$ and $Sc(OTf)_3$ were used as the promoters under the standard conditions, the reactions proceeded smoothly to give **3a** in 7–72% yields (Table 1, entries 4–8). Brønsted acid trifluoromethanesulfonic acid CF_3SO_3H (TfOH) could also promote this reaction very well, but affording **3a** in 51% yield (Table 1, entry 9). Thereby, TMSOTf was the best promoter among all these examined Lewis and Brønsted acids. Further investigation by changing the ratio of the starting materials and TMSOTf revealed that using the ratio of **1a**/**2**/TMSOTf as 1.5:1:1.5 afforded the corresponding **3a** in 97% yield under otherwise identical conditions (Table 1, entries 10–12).

Next, we attempted to study the solvent effect in this reaction. In the presence of TMSOTf, the reactions were conducted in various solvents at 60 °C for 12 h. The results of these investigations are outlined in Table 2. Toluene and dichloromethane (DCM) benefited this reaction quite well, producing **3a** in 96% and 88% yields, respectively (Table 2, entries 1 and 2). Using CH_3CN and tetrahydrofuran (THF) as the solvents produced **3a** in 38% and 10% yields, respectively, presumably due to that a nitrogen atom or an oxygen atom could weakly coordinate with the Lewis acid to deactivate its catalytic ability (Table 2, entries 3 and 4). However, other solvents such as dimethyl sulfoxide (DMSO) and *N*,*N*-dimethylformamide (DMF) gave complex product mixtures rather than the clean formation of **3a** (Table 2, entries 5 and 6).

Table 2
Solvent effects in the reaction of 1-cyclopropyl-2-phenylethanone (**1a**) with diethyl 2-oxomalonate (**2**) mediated by TMSOTf

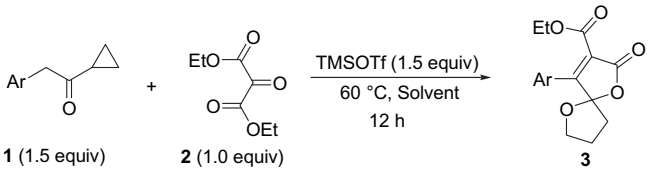


Entry	**1a**/**2**/TMSOTf	Solvent	Yield[a] (%)
			3a
1	1.5:1:1.5	$PhCH_3$	96
2	1.5:1:1.5	DCM	88
3	1.5:1:1.5	CH_3CN	38
4	1.5:1:1.5	THF	10
5	1.5:1:1.5	DMSO	Complex[b]
6	1.5:1:1.5	DMF	Complex[b]

[a] Isolated yields.
[b] The reaction became disordered and **3a** was not formed.

With these optimized reaction conditions in hand, we next turned our interest to examine the reaction generality by using a variety of 1-cyclopropyl-2-arylethanones **1** under these optimal conditions. The results are shown in Table 3. As for 1-cyclopropyl-

Table 3
Reactions of Various cyclopropyl benzyl ketones (**1**) with diethyl 2-oxomalonate (**2**) mediated by TMSOTf



Entry	Ar	Yield[a] (%)
		3
1	**1b**, *p*-ClC_6H_4	**3b**, 97
2	**1c**, *p*-BrC_6H_4	**3c**, 99
3	**1d**, *p*-FC_6H_4	**3d**, 96
4	**1e**, *m*-FC_6H_4	**3e**, 97
5	**1f**, *o*-BrC_6H_4	**3f**, 82
6	**1g**, *m*-MeC_6H_4	**3g**, 99
7	**1h**, *p*-MeC_6H_4	**3h**, 96
8	**1i**, *o*-MeC_6H_4	**3i**, 66

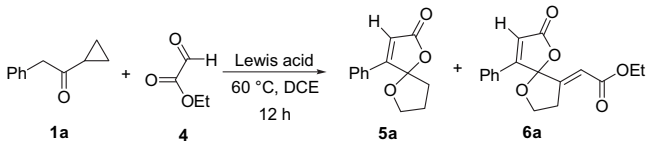
[a] Isolated yields.

2-arylethanones **1b–e** and **1g**,**h** having electron-withdrawing or electron-donating group on the benzene rings at the *para*- or *meta*-position, the corresponding 1,6-dioxa-spiro[4.4]non-3-en-2-one derivatives **3b–e** and **3g**,**h** were obtained in excellent yields (Table 3, entries 1–4 and 6,7). For 1-cyclopropyl-2-arylethanones **1f** and **1i** bearing an electron-withdrawing Br atom or a moderately electron-donating methyl group on the benzene rings at the *ortho*-position, the corresponding 1,6-dioxa-spiro[4.4]non-3-en-2-one derivatives **3f** and **3i** were obtained in 82% and 66% yields, respectively (Table 3, entries 5 and 8). The yields of **3f** and **3i** are slightly lower than those of **3b–e** and **3g**,**h** perhaps due to the steric effect of the *ortho*-substituted groups of the starting materials **1f** and **1i**.

Moreover, we also attempted to explore the Lewis acid-mediated reactions of 1-cyclopropyl-2-arylethanones **1** with ethyl 2-oxoacetate **4** since we envisioned that a similar reaction pathway might be able to take place smoothly to give the corresponding spiro-γ-lactone derivative in good yield as well. Under the standard reaction conditions established above, we investigated the reaction of 1-cyclopropyl-2-phenylethanone **1a** with ethyl 2-oxoacetate **4** in DCE at 60 °C in the presence of TMSOTf and found that the desired spiro-γ-lactone product **5a** was indeed provided in 63% yield, but interestingly along with another new product **6a** in 11% yield, which was assigned by the spectroscopic and analytic data (Table 4, entry 1). Therefore, our next purpose was to optimize the reaction conditions to produce both of the products **5a** and **6a** in higher yields similarly by changing the Lewis or Brønsted acids as well as the ratio of the starting materials and Lewis acid. The results of these experiments are summarized in Table 4. Brønsted acid TfOH could also promote this reaction smoothly as anticipated to give **5a** and **6a** in 64% total yield (Table 4, entry 2). When Lewis acids $Bi(OTf)_2Cl$, $InCl_3\cdot 4H_2O$ and $Sc(OTf)_3$ were used in this reaction, the corresponding products **5a** and **6a** were gained in 22–38% yields and 6–13% yields, respectively (Table 4, entries 3, 6 and 9). Using $SnCl_4$ as the promoter afforded a complex product mixture on the basis of the ^1H NMR spectrum (Table 4, entry 4). Other Lewis acids such as $TiCl_4$, $Ni(OAc)_2$ and $Yb(OTf)_3$ were not suitable in this reaction, leading to disordered reaction mixtures (Table 4, entries 5, 7, 8 and 10). Finally, we found that increasing the amount of ethyl 2-oxoacetate **4** to 2 equiv afforded the corresponding products **5a** and **6a** in 68% and 14% yields, respectively (82% total yield) (Table 4, entry 11).

Under these optimal conditions, we next examined the reactions of many other 1-cyclopropyl-2-arylethanones **1** with ethyl

Table 4
Reactions of 1-cyclopropyl-2-phenylethanone (**1a**) and diethyl 2-oxomalonate (**4**) mediated by various Lewis acids



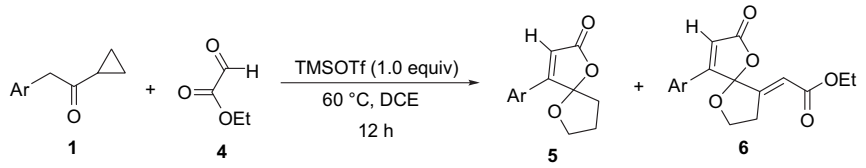
Entry	**1a**/**4**/Lewis acid	Lewis acid	Yield[a] (%)	
			5a	**6a**
1	1:1:1	TMSOTf	63	11
2	1:1:1	HOTf	48	16
3	1:1:1	$Bi(OTf)_2Cl$	38	13
4	1:1:1	$SnCl_4$	—[b]	
5	1:1:1	$TiCl_4$	Complex[c]	
6	1:1:1	$InCl_3\cdot 4H_2O$	22	6
7	1:1:1	$Ni(OAc)_2$	Complex[c]	
8	1:1:1	$Cu(OTf)_2$	Complex[c]	
9	1:1:1	$Sc(OTf)_3$	26	8
10	1:1:1	$Yb(OTf)_3$	Complex[c]	
11	1:2:1	TMSOTf	68	14

[a] Isolated yields.
[b] A product mixture was obtained.
[c] The reaction became disordered and **3a** was not formed.

2-oxoacetate **4** and the results of these experiments are outlined in Table 5. As can be seen from Table 5, for 1-cyclopropyl-2-arylethanones **1b–d** having substituents (Cl, Br and F atoms) on the benzene rings at the *para*-position, the corresponding 1,6-dioxa-spiro[4.4]non-3-en-2-one derivatives **5b–d** were obtained as the major products in moderate yields together with the minor products **6b–d** in 20–28% yields (Table 5, entries 1–3). When the substrates **1e** and **1j** bearing substituents (F atom or CF_3 group) on the benzene rings at the *meta*-position, the yields of the major spiro-γ-lactone products **5e** and **5h** were 59% and 50% along with 30% and 15% yields of the minor spiro-γ-lactone products **6e** and **6h**, respectively (Table 5, entries 4 and 7). As for 1-cyclopropyl-2-arylethanones **1f**, **1i** and **1k** having *ortho*-substituted groups on the benzene rings, the formation of spiro-γ-lactone products **5f**, **5g** and **5i** was significantly affected, leading to the spiro-γ-lactones **5f**, **5g** and **5i** in 29–47% yields, while the spiro-γ-lactone products **6f**, **6g** and **6i** were obtained in relatively higher yields (Table 5, entries 5, 6 and 8). Such reaction outcomes suggest that the sterically hindered 1-cyclopropyl-2-arylethanone can change the reaction pathway and subsequently affect the product distribution.

In our previous work, a presumed reaction mechanism in the reaction of cyclopropyl hexyl ketone with α-ketoester has been proposed.[3a,d] We considered that the reaction pathway is mainly controlled by the steric effect. As shown in Scheme 2 using cyclopropyl hexyl ketone as the model (R^1=C_5H_{11}, path a), intermediate **A** is first formed from the ring-opening reaction of cyclopropyl hexyl ketone (R^2=H) with ambient H_2O in the presence of Lewis acid.[3a,b] Then, intermediate **B**[3a] is formed as a mixture of *E*- and *Z*-isomers from the aldol condensation of intermediate **A** with α-ketoester at the C-3 position. Thus, product **C**[3a] can be formed after an intramolecular transesterification process via intermediate *E*-**B**.[5] The highly conjugated product *E*-**E**[3a] can be formed by dehydration of intermediate **D**,[3a] which itself can be derived from a Bradsher type cyclization reaction (or a Friedel–Crafts reaction) of **C**.[3a,5] On the other hand, product *Z*-**E**[3a] can be formed from *Z*-**B**[3a] via dehydration of intermediate **D′**,[3a] which itself can be produced via an intramolecular cyclization of intermediate **C′**[3a] derived from hydrolysis of *Z*-**B**.[3a] Alternatively, if the aldol-type reaction takes place at the C-5 position in γ-hydroxyketone **A** (path b), another intermediate, **F**,[3a] would be formed along with regeneration of an equivalent of H_2O, which can react with **1** to initiate the next reaction cycle. Intramolecular nucleophilic attack by the terminal

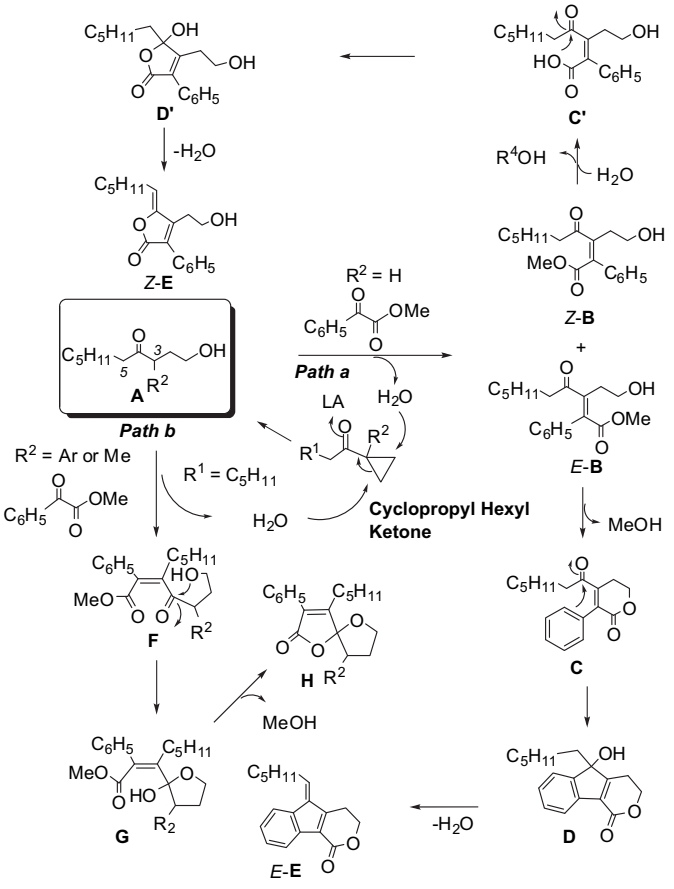
Table 5
Reactions of various cyclopropyl benzyl ketone (**1**) and diethyl 2-oxomalonate (**2**) mediated by TMSOTf



1 **4** **5** **6**

Entry	Ar	Yield[a] (%)	
		5	**6**
1	**1b**, *p*-ClC_6H_4	**5b**, 60	**6b**, 24
2	**1c**, *p*-BrC_6H_4	**5c**, 61	**6c**, 28
3	**1d**, *p*-FC_6H_4	**5d**, 72	**6d**, 20
4	**1e**, *m*-FC_6H_4	**5e**, 59	**6e**, 30
5	**1f**, *o*-BrC_6H_4	**5f**, 36	**6f**, 32
6	**1i**, *o*-MeC_6H_4	**5g**, 47	**6g**, 36
7	**1j**, *m*-$CF_3C_6H_4$	**5h**, 50	**6h**, 15
8	**1k**, *o*-ClC_6H_4	**5i**, 29	**6i**, 40

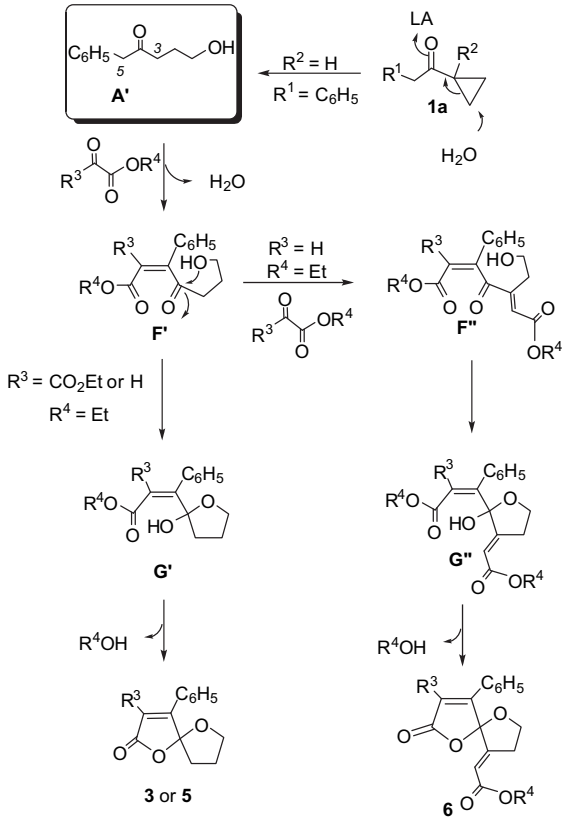
[a] Isolated yields.



Scheme 2. Proposed mechanism for the reaction of cyclopropyl hexyl ketone with α-ketoester.

hydroxyl group at the ketone group can take place, leading to the corresponding cyclic intermediate **G**[3a] containing a hemiacetal hydroxyl group. From intermediate **G**, the corresponding product **H** can be formed via an intramolecular transesterification. If $R^2 \neq H$, the aldol condensation of intermediate **A** with α-ketoester at the C-3 position is blocked out due to the steric effect and therefore, path a is shut down and the corresponding spiro-γ-lactone product can be obtained exclusively.

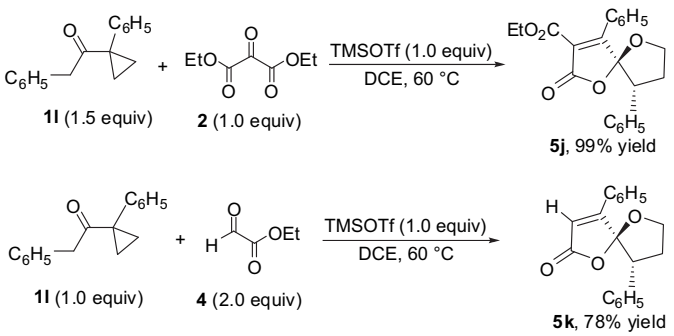
When 1-cyclopropyl-2-phenylethanone **1a** (R^2=H), which is a more common substrate than the substituted 1-cyclopropyl-2-phenylethanone (R^2 is not a hydrogen atom, $R^2 \neq H$), is treated with diethyl 2-oxomalonate and ethyl 2-oxoacetate, the spiro-γ-lactone product **3** or **5** can also be formed through the same reaction route via intermediates **A**′, **F**′ and **G**′ shown in Scheme 3 (intermediates **A**, **F** and **G** in Scheme 2). Besides the normal product **5**, the reaction of **1a** with ethyl 2-oxoacetate leads to a new product **6**. The reaction pathway has been shown in Scheme 3. The intermediate **F**″, derived from an aldol reaction of **F**′ and another molecule of diethyl 2-oxomalonate, is first formed. Intramolecular nucleophilic attack by the terminal hydroxyl group at the ketone group affords the corresponding cyclic intermediate **G**″, which produces the product **6** via an intramolecular transesterification (Scheme 3).



Scheme 3. Proposed mechanism for the reaction of cyclopropyl keto **1a** with diethyl 2-oxomalonate and ethyl 2-oxoacetate.

Now we can explain the steric and electronic effects of this reaction. When R^1 is an alkyl group and R^3 is an aryl or alkyl group, the reaction pathway is not exclusive because the reaction can take place at both of the C-3 and C-5 position in intermediate **A** or **A′** to give the corresponding product mixtures. Only if the C-3 position is blocked by an aryl or alkyl group ($R^2 \neq H$), the aldol reaction can take place exclusively at the C-5 position and therefore, the spiro-γ-lactone is the major product. When R^1 is an aryl group, the situation is quite complicated. Since in this case, the C-5 position is much more reactive to undergo the aldol reaction than that of the C-3 position,[3b,6] the condensation of 1-cyclopropyl-2-arylethanone with diethyl 2-oxomalonate in which the carbonyl group is activated by two carboxyl groups exclusively takes place at the C-5 position to give the corresponding spiro-γ-lactone product in higher yield. Moreover, the steric effect cannot be completely ignored in this case. If R^3 is an aryl group, the aldol reaction at the C-5 position becomes difficult and a product mixtures can be obtained through path a and path b at the same time.[7] If R^3 is a hydrogen atom, the aldol reaction of intermediate **F′** with another molecule of ethyl 2-oxoacetate can easily take place to generate product **6**.

Two control experiments were conducted by treatment of 2-phenyl-1-(1-phenylcyclopropyl)ethanone **1l** with diethyl 2-oxomalonate and ethyl 2-oxoacetate under the standard conditions, the corresponding spiro-γ-lactones **5j** and **5k** were obtained as the sole products in 99% and 78% yields, respectively (Scheme 4). The phenyl group at the C-3 position blocked out the aldol reaction of intermediate **F′** with another molecule of ethyl 2-oxoacetate, affording the spiro-γ-lactone **5k** exclusively.



Scheme 4. Two control experiments.

In conclusion, we have further explored a reaction process involving a sequential ring-opening reaction of cyclopropyl alkyl ketones by H_2O, followed by one intermolecular aldol-type reaction and a cyclic transesterification in the reaction of 1-cyclopropyl-2-arylethanone derivatives with diethyl 2-oxomalonate and ethyl 2-oxoacetate mediated by Lewis acid, which affords an efficient synthetic protocol for the preparation of functionalized 1,6-dioxa-spiro[4.4]non-3-en-2-one skeletons in good yields. Moreover, two kinds of spiro-γ-lactone products were obtained at the same time in the TMSOTf-mediated reactions of 1-cyclopropyl-2-arylethanone derivatives with ethyl 2-oxoacetate. A detailed overview on the whole reaction mechanism has been provided. The reaction scope is also extended to 1-cyclopropyl-2-arylethanones, which do not have a substituent at the C3-position. Thus, many new functionalized spiro-γ-lactone derivatives can be synthesized easily. Further work directed at elucidation of the detailed mechanisms of this process and the application of it to the synthesis of spiro-γ-lactone containing natural products are currently in progress.

3. Experimental section

3.1. General remarks

Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively. Mass and HRMS spectra were recorded by EI methods. Organic solvents used were dried by standard methods when necessary. Satisfactory CHN microanalyses were obtained with an analyzer. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with silica gel coated plates. Flash column chromatography was carried out using silica gel at increased pressure.

3.2. General procedure for the reaction of 1-cyclopropyl-2-arylethanones with diethyl 2-oxomalonate

1-Cyclopropyl-2-arylethanones **1** (0.3 mmol), ethyl buta-2,3-dienoate (0.2 mmol), TMSOTf (0.3 mmol) and DCE (3.0 mL) were added into a Schlenk tube. The reaction mixture was stirred at 60 °C for 12 h. The solvent was removed under reduced pressure and then the residue was purified by a flash column chromatography.

3.3. General procedure for the reaction of 1-cyclopropyl-2-arylethanones with ethyl 2-oxoacetate

1-Cyclopropyl-2-phenylethanones **1** (0.3 mmol), ethyl 2-oxoacetate (0.6 mmol), TMSOTf (0.3 mmol) and DCE (3.0 mL) were added into a Schlenk tube. The reaction mixture was stirred at 60 °C for 12 h. The solvent was removed under reduced pressure and then the residue was purified by a flash column chromatography.

*3.3.1. Compound **3a**.* A white solid. Mp 193–195 °C. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.21 (t, J=7.2 Hz, 3H, CH_3), 1.97–2.09 (m, 2H), 2.20–2.39 (m, 2H), 4.12–4.20 (m, 1H), 4.26 (q, J=7.2 Hz, 2H, CH_2), 4.33–4.38 (m, 1H), 7.42–7.52 (m, 3H, Ar), 7.57 (d, J=7.5 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 24.3, 35.3, 61.7, 71.1, 113.7, 122.6, 128.1, 128.5, 129.1, 130.9, 161.4, 163.1, 165.5; IR (CH_2Cl_2): ν 3064, 2981, 2967, 2897, 1778, 1716, 1648, 1465, 1442, 1378, 1323 cm^{-1}; MS (EI) m/z (%): 288 [M^+] (16.8), 202 (45.5), 174 (66.8), 171 (15.3), 130 (30.9), 129 (83.1), 103 (14.1), 102 (100). Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66%; H, 5.59%. Found: C, 66.60%; H, 5.73%.

*3.3.2. Compound **3b**.* A yellow solid. Mp 76–78 °C. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.24 (t, J=7.2 Hz, 3H, CH_3), 1.92–2.08 (m, 2H), 2.20–2.41 (m, 2H), 4.11–4.18 (m, 1H), 4.30 (q, J=7.2 Hz, 2H, CH_2), 4.33–4.39 (m, 1H), 7.43 (d, J=8.7 Hz, 2H, Ar), 7.54 (d, J=8.7 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 24.2, 35.3, 61.8, 71.1, 113.4, 122.9, 127.5, 128.8, 129.6, 137.1, 161.1, 162.0, 165.1; IR (CH_2Cl_2): ν 3061, 2986, 2964, 2897, 1788, 1715, 1647, 1592, 1489, 1443, 1377, 1321 cm^{-1}; MS (EI) m/z (%): 322 [M^+] (12.7), 236 (17.8), 210 (22.0), 208 (63.1), 163 (55.4), 138 (33.3), 136 (100.0), 99 (17.2). Anal. Calcd for $C_{16}H_{15}ClO_5$: C, 59.54%; H, 4.68%. Found: C, 59.62%; H, 4.62%.

*3.3.3. Compound **3c**.* A white solid. Mp 79–81 °C. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.24 (t, J=7.2 Hz, 3H, CH_3), 1.93–2.09 (m, 2H), 2.20–2.37 (m, 2H), 4.11–4.18 (m, 1H), 4.28 (q, J=7.2 Hz, 2H, CH_2), 4.32–4.39 (m, 1H), 7.47 (d, J=8.4 Hz, 2H, Ar), 7.60 (d, J=8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 24.3, 35.3, 61.8, 71.1, 113.4, 122.9, 125.6, 128.0, 129.8, 131.7, 161.1, 162.1, 165.1; IR (CH_2Cl_2): ν 3050, 2972, 2904, 1769, 1722, 1641, 1585, 1490, 1453, 1369, 1326 cm^{-1}; MS (EI) m/z (%): 366 [M^+] (13.0), 254 (72.1), 252 (68.1), 207 (57.9), 182 (97.6), 180 (100.0), 147 (52.3), 120 (82.8). Anal. Calcd for $C_{16}H_{15}BrO_5$: C, 52.34%; H, 4.12%. Found: C, 52.60%; H, 4.02%.

*3.3.4. Compound **3d**.* A yellow solid. Mp 78–80 °C. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.24 (t, J=7.2 Hz, 3H, CH_3), 1.94–2.14 (m, 2H), 2.20–

2.38 (m, 2H), 4.17 (q, J=7.8 Hz, 1H), 4.28 (q, J=7.2 Hz, 2H), 4.33–4.40 (m, 1H), 7.15 (dd, J=8.1, 9.0 Hz, 2H, Ar), 7.62 (dd, J=6.6, 9.0 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 24.3, 35.4, 61.9, 71.1, 113.5, 115.8 (d, J_{C-F}=21.7 Hz), 122.7, 125.2 (d, J_{C-F}=3.6 Hz), 130.7 (d, J_{C-F}=8.6 Hz), 161.4, 162.1, 164.1 (d, J_{C-F}=251.7 Hz), 165.3; IR (CH_2Cl_2): ν 3110, 2983, 2961, 2895, 1775, 1715, 1650, 1598, 1509, 1468, 1377, 1229 cm^{-1}; MS (EI) m/z (%): 306 [M$^+$] (9.4), 220 (22.8), 192 (43.6), 189 (10.4), 148 (18.0), 147 (66.2), 120 (100.0), 69 (12.6). Anal. Calcd for $C_{16}H_{15}FO_5$: C, 62.74%; H, 4.94%. Found: C, 62.85%; H, 4.90%.

3.3.5. Compound ***3e***. A yellow solid. Mp 113–115 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.23 (t, J=7.2 Hz, 3H, CH_3), 1.99–2.15 (m, 2H), 2.22–2.38 (m, 2H), 4.12–4.20 (m, 1H), 4.28 (q, J=7.2 Hz, 2H), 4.33–4.40 (m, 1H), 7.18–7.24 (m, 1H, Ar), 7.30–7.37 (m, 2H, Ar), 7.41–7.48 (m, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 24.3, 35.3, 61.9, 71.2, 113.5, 115.3 (d, J_{C-F}=23.4 Hz), 117.9 (d, J_{C-F}=21.3 Hz), 123.5, 124.2 (d, J_{C-F}=2.8 Hz), 130.3 (d, J_{C-F}=8.4 Hz), 131.0 (d, J_{C-F}= 9.0 Hz), 161.1, 161.6, 162.3 (d, J_{C-F}=246.2 Hz), 165.1; IR (CH_2Cl_2): ν 3070, 2989, 2905, 1782, 1717, 1610, 1582, 1487, 1442, 1378, 1348, 1269 cm^{-1}; MS (EI) m/z (%): 306 [M$^+$] (16.8), 241 (23.7), 220 (32.6), 192 (43.7), 148 (29.9), 147 (89.7), 120 (100.0), 99 (17.4). Anal. Calcd for $C_{16}H_{15}FO_5$: C, 62.74%; H, 4.94%. Found: C, 62.73%; H, 4.73%.

3.3.6. Compound ***3f***. A yellow solid. Mp 72–74 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.07 (t, J=7.2 Hz, 3H, CH_3), 1.94–2.09 (m, 2H), 2.23–2.37 (m, 2H), 3.86–3.93 (m, 1H), 4.09–4.26 (m, 2H), 4.30–4.33 (m, 1H), 7.30–7.34 (m, 1H, Ar), 7.40–7.42 (m, 2H, Ar), 7.67 (d, J=8.1 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.5, 24.3, 34.7, 61.4, 71.3, 112.8, 121.6, 127.1, 128.8, 130.8, 131.2, 132.5, 159.6, 164.8, 166.1; IR (CH_2Cl_2): ν 3068, 2985, 2940, 2905, 1778, 1723, 1610, 1585, 1473, 1435, 1378, 1345, 1263 cm^{-1}; MS (EI) m/z (%): 366 [M$^+$−Br] (40.1), 259 (33.7), 241 (100.0), 209 (31.6), 207 (32.0), 182 (38.7), 180 (40.7), 128 (21.4). Anal. Calcd for $C_{16}H_{15}BrO_5$: C, 52.34%; H, 4.12%. Found: C, 52.37%; H, 3.99%.

3.3.7. Compound ***3g***. A yellow solid. Mp 93–95 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.21 (t, J=7.2 Hz, 3H, CH_3), 2.02–2.09 (m, 2H), 2.19–2.33 (m, 2H), 2.39 (s, 3H, CH_3), 4.11–4.19 (m, 1H), 4.22–4.30 (m, 2H), 4.32–4.39 (m, 1H), 7.29–7.36 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.7, 21.3, 24.3, 35.4, 61.6, 71.1, 113.7, 122.5, 125.2, 128.4, 128.7, 129.1, 131.7, 138.2, 161.5, 163.2, 165.5; IR (CH_2Cl_2): ν 3046, 2982, 2890, 1774, 1713, 1643, 1438, 1374, 1345, 1321, 1271 cm^{-1}; MS (EI) m/z (%): 302 [M$^+$] (12.6), 216 (17.3), 188 (48.1), 144 (10.7), 143 (49.0), 117 (12.4), 116 (100.0), 115 (15.2). Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.54%; H, 6.00%. Found: C, 67.67%; H, 6.04%.

3.3.8. Compound ***3h***. A yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.24 (t, J=7.2 Hz, 3H, CH_3), 1.97–2.14 (m, 2H), 2.19–2.36 (m, 2H), 2.40 (s, 3H, CH_3), 4.09–4.16 (m, 1H), 4.28 (q, J=7.2 Hz, 2H), 4.32–4.39 (m, 1H), 7.25 (d, J=8.4 Hz, 2H, Ar), 7.48 (d, J=8.4 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.8, 21.4, 24.3, 35.6, 61.7, 71.1, 113.7, 122.0, 126.2, 128.3, 129.2, 141.7, 161.8, 162.9, 165.7; IR (CH_2Cl_2): ν 2984, 2901, 1787, 1727, 1648, 1611, 1565, 1512, 1455, 1372, 1322, 1238 cm^{-1}; MS (EI) m/z (%): 302 [M$^+$] (10.8), 216 (13.8), 189 (8.7), 188 (52.2), 143 (39.8), 117 (12.9), 116 (100.0), 115 (20.9); HRMS (EI) calcd for $C_{17}H_{18}O_5$ (M$^+$) requires 302.1154, found: 302.1151.

3.3.9. Compound ***3i***. A yellow solid. Mp 113–115 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.06 (t, J=7.2 Hz, 3H, CH_3), 1.90–2.04 (m, 2H), 2.19–2.32 (m, 2H), 2.25 (s, 3H, CH_3), 3.84–3.91 (m, 1H), 4.08–4.18 (m, 2H), 4.25–4.31 (m, 1H), 7.22–7.36 (m, 4H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.6, 19.8, 24.2, 34.2, 61.4, 71.1, 113.4, 124.1, 125.3, 126.7, 126.9, 129.4, 130.0, 135.7, 160.2, 165.2, 168.1; IR (CH_2Cl_2): ν 2984, 2901, 1787, 1727, 1648, 1611, 1565, 1512, 1455, 1372, 1322, 1238 cm^{-1}; MS (EI) m/z (%): 302 [M$^+$] (10.8), 216 (13.8), 189 (8.7), 188 (52.2), 143 (39.8), 117 (12.9), 116 (100.0), 115 (20.9); HRMS (EI) calcd for $C_{17}H_{18}O_5$ (M$^+$) requires 302.1154, found: 302.1155.

3.3.10. Compound ***5a***. A yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.16–2.28 (m, 3H), 2.33–2.44 (m, 1H), 4.27–4.43 (m, 2H), 6.35 (s, 1H, CH), 7.42–7.49 (m, 3H, Ar), 7.62–7.65 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.2, 35.8, 70.6, 114.8, 117.2, 127.7, 129.0, 129.5, 131.1, 162.1, 169.4; IR (CH_2Cl_2): ν 2981, 2900, 1765, 1718, 1621, 1574, 1495, 1448, 1376, 1296, 1209, 1178 cm^{-1}; MS (EI) m/z (%): 216 [M$^+$] (13.5), 171 (9.0), 160 (7.0), 130 (15.7), 129 (5.8), 103 (12.6), 102 (100.0), 76 (8.0); HRMS (EI) calcd for $C_{13}H_{12}O_3$ (M$^+$) requires 216.0786, found: 216.0793.

3.3.11. Compound ***6a***. A yellow solid. Mp 75–77 °C. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.25 (t, J=7.2 Hz, 3H, CH_3), 3.26–3.39 (m, 1H), 3.46–3.54 (m, 1H), 4.06–4.24 (m, 2H), 4.34–4.43 (m, 1H), 4.53–4.59 (m, 1H), 5.75 (t, J=2.7 Hz, 1H, CH), 6.56 (s, 1H, CH), 7.39–7.47 (m, 3H, Ar), 7.50–7.53 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.1, 30.7, 60.7, 69.2, 112.8, 115.9, 117.6, 128.0, 128.6, 129.0, 131.6, 156.1, 160.4, 165.6, 168.7; IR (CH_2Cl_2): ν 2982, 2906, 1769, 1716, 1677, 1622, 1575, 1495, 1449, 1375, 1331, 1290 cm^{-1}; MS (EI) m/z (%): 300 [M$^+$] (9.4), 176 (74.8), 148 (31.1), 147 (41.0), 131 (61.4), 102 (43.4), 91 (41.2), 69 (100.0); HRMS (EI) calcd for $C_{17}H_{16}O_5$ (M$^+$) requires 300.0998, found: 300.0996.

3.3.12. Compound ***5b***. A yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.16–2.32 (m, 3H), 2.35–2.45 (m, 1H), 4.26–4.33 (m, 1H), 4.36–4.43 (m, 1H), 6.34 (s, 1H, CH), 7.43 (d, J=9.0 Hz, 2H, Ar), 7.57 (d, J=9.0 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.2, 35.8, 70.6, 114.6, 117.7, 128.0, 129.0, 129.3, 137.3, 160.8, 169.1; IR (CH_2Cl_2): ν 2982, 2958, 1767, 1719, 1622, 1593, 1492, 1407, 1375, 1338, 1247, 1179 cm^{-1}; MS (EI) m/z (%): 250 [M$^+$] (11.2), 138 (30.2), 137 (11.8), 136 (100.0), 101 (12.3), 75 (9.6), 43 (14.3), 42 (16.0); HRMS (EI) calcd for $C_{13}H_{11}O_3Cl$ (M$^+$) requires 250.0397, found: 250.0402.

3.3.13. Compound ***6b***. A yellow solid. Mp166–168 °C. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25 (t, J=7.2 Hz, 3H, CH_3), 3.25–3.33 (m, 1H), 3.43–3.50 (m, 1H), 4.09–4.23 (m, 2H), 4.35–4.41 (m, 1H), 4.52–4.57 (m, 1H), 5.71 (t, J=2.8 Hz, 1H, CH), 6.54 (s, 1H, CH), 7.39 (dd, J=2.4, 6.8 Hz, 2H, Ar), 7.45 (dd, J=2.4, 6.8 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 30.6, 60.8, 69.3, 112.6, 116.0, 118.1, 127.1, 129.3, 129.4, 137.9, 155.8, 159.1, 165.5, 168.4; IR (CH_2Cl_2): ν 3082, 3060, 3028, 1769, 1719, 1659, 1621, 1598, 1578, 1447, 1317, 1277, 1248 cm^{-1}; MS (EI) m/z (%): 334 [M$^+$] (5.4), 138 (32.3), 137 (9.6), 136 (100.0), 101 (10.3), 58 (11.1), 53 (9.7), 43 (33.8); HRMS (EI) calcd for $C_{17}H_{15}O_5Cl$ (M$^+$) requires 334.0608, found: 334.0609.

3.3.14. Compound ***5c***. A yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.17–2.35 (m, 3H), 2.39–2.43 (m, 1H), 4.25–4.31 (m, 1H), 4.36–4.41 (m, 3H), 6.34 (s, 1H, CH), 7.49 (d, J=8.8 Hz, 2H, Ar), 7.59 (d, J=8.8 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 24.2, 35.8, 70.7, 114.6, 117.8, 125.8, 128.5, 129.2, 132.3, 161.0, 169.0; IR (CH_2Cl_2): ν 3096, 2981, 1765, 1717, 1621, 1587, 1487, 1403, 1339, 1310, 1247, 1179 cm^{-1}; MS (EI) m/z (%): 294 [M$^+$+1] (12.9), 182 (94.6), 108 (100.0), 102 (23.6), 101 (41.5), 75 (26.1), 43 (20.4), 42 (28.4); HRMS (EI) calcd for $C_{13}H_{11}O_3Br$ (M$^+$) requires 293.9892, found: 293.9894.

3.3.15. Compound ***6c***. A yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25 (t, J=7.2 Hz, 3H, CH_3), 3.24–3.34 (m, 1H), 3.44–3.50 (m, 1H), 4.08–4.23 (m, 2H), 4.35–4.41 (m, 1H), 4.51–4.57 (m, 1H), 5.71 (t, J=2.8 Hz, 1H, CH), 6.55 (s, 1H, CH), 7.37 (d, J=8.8 Hz, 2H, Ar), 7.56 (d, J=8.8 Hz, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 14.1, 30.6, 60.8, 69.3, 112.6, 116.0, 118.2, 126.3, 127.5, 129.4, 132.4, 155.7, 159.2, 165.5, 168.4; IR (CH_2Cl_2): ν 3085, 3062, 2983, 2905, 1774, 1719, 1676, 1618, 1588, 1561, 1474, 1375, 1209, 1171 cm^{-1}; MS (EI) m/z (%): 378 [M$^+$] (10.0), 341 (35.2), 182 (100.0), 180 (92.9), 102 (38.5), 101 (26.9), 91

(34.0), 43 (43.6); HRMS (EI) calcd for $C_{17}H_{15}O_5Br$ (M^+) requires 378.0103, found: 378.0106.

3.3.16. Compound ***5d***. A yellow oil. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 2.18–2.27 (m, 3H), 2.35–2.45 (m, 1H), 4.25–4.43 (m, 2H), 6.30 (s, 1H, CH), 7.12–7.17 (m, 2H, Ar), 7.62–7.67 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 24.2, 35.9, 70.6, 114.6, 116.2 (d, J_{C-F}=21.8 Hz), 117.1, 125.8 (d, J_{C-F}=3.5 Hz), 129.9 (d, J_{C-F}=8.6 Hz), 160.9, 164.2 (d, J_{C-F}=251.7 Hz), 169.2; IR (CH_2Cl_2): ν 3104, 2963, 2898, 1764, 1624, 1605, 1509, 1458, 1414, 1340, 1309, 1231, 1179 cm^{-1}; MS (EI) *m*/*z* (%): 234 [M^+] (8.0), 178 (4.5), 149 (5.1), 148 (9.9), 121 (12.4), 120 (100.0), 70 (4.8), 42 (13.8); HRMS (EI) calcd for $C_{13}H_{11}O_3F$ (M^+) requires 234.0692, found: 234.0689.

3.3.17. Compound ***6d***. A yellow oil. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.26 (t, *J*=6.9 Hz, 3H, CH_3), 3.27–3.37 (m, 1H), 3.42–3.53 (m, 1H), 4.09–4.22 (m, 2H), 4.34–4.43 (m, 1H), 4.52–4.59 (m, 1H), 5.72 (t, *J*=2.7 Hz, 1H, CH), 6.50 (s, 1H, CH), 7.09–7.27 (m, 2H, Ar), 7.50–7.55 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 30.6, 60.8, 69.2, 112.6, 116.0, 116.4 (d, J_{C-F}=21.9 Hz), 117.4, 124.9 (d, J_{C-F}=2.8 Hz), 130.3 (d, J_{C-F}=8.9 Hz), 155.9, 159.2, 164.4 (d, J_{C-F}=253.1 Hz), 165.6, 168.5; IR (CH_2Cl_2): ν 3104, 2983, 2905, 1827, 1769, 1719, 1677, 1623, 1605, 1561, 1510, 1375, 1288, 1237 cm^{-1}; MS (EI) *m*/*z* (%): 318 [M^+] (5.4), 289 (8.4), 141 (10.3), 139 (30.7), 121 (10.0), 120 (100.0), 111 (11.0), 75 (9.5); HRMS (EI) calcd for $C_{17}H_{15}O_5F$ (M^+) requires 318.0904, found: 318.0911.

3.3.18. Compound ***5e***. A yellow oil. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.19–2.29 (m, 3H), 2.36–2.44 (m, 1H), 4.28–4.34 (m, 1H), 4.37–4.42 (m, 1H), 6.35 (s, 1H, CH), 7.16–7.21 (m, 1H, Ar), 7.31–7.35 (m, 1H, Ar), 7.41–7.47 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 24.2, 35.8, 70.7, 114.5 (d, J_{C-F}=22.3 Hz), 114.6, 118.0 (d, J_{C-F}=20.5 Hz), 118.5, 123.6 (d, J_{C-F}=3.2 Hz), 130.7 (d, J_{C-F}=8.2 Hz), 131.5 (d, J_{C-F}=8.2 Hz), 160.8 (d, J_{C-F}=22.0 Hz), 162.7 (d, J_{C-F}=246.2 Hz), 168.9; IR (CH_2Cl_2): ν 3101, 2963, 2898, 1871, 1765, 1625, 1611, 1582, 1486, 1444, 1349, 1302, 1253 cm^{-1}; MS (EI) *m*/*z* (%): 234 [M^+] (12.2), 189 (8.2), 178 (8.0), 149 (10.4), 148 (12.9), 121 (21.9), 120 (100), 42 (19.1); HRMS (EI) calcd for $C_{13}H_{11}O_3F$ (M^+) requires 234.0692, found: 234.0693.

3.3.19. Compound ***6e***. A yellow oil. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.26 (t, *J*=7.2 Hz, 3H, CH_3), 3.25–3.36 (m, 1H), 3.43–3.51 (m, 1H), 4.09–4.22 (m, 2H), 4.35–4.42 (m, 1H), 4.56 (td, *J*=8.8, 2.8 Hz, 1H), 5.73 (t, *J*=2.8 Hz, 1H, CH), 6.56 (s, 1H, CH), 7.15–7.22 (m, 2H, Ar), 7.30–7.33 (m, 1H, Ar), 7.38–7.44 (m, 1H, Ar); ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ 32.6–32.6 (m, 1F); IR (CH_2Cl_2): ν 3103, 2983, 2906, 1775, 1720, 1677, 1625, 1611, 1582, 1487, 1446, 1375, 1223 cm^{-1}; MS (EI) *m*/*z* (%): 378 [M^+] (6.5), 289 (13.0), 201 (9.3), 173 (9.3), 148 (7.6), 133 (7.7), 121 (11.3), 120 (100.0); HRMS (EI) calcd for $C_{17}H_{15}O_5F$ (M^+) requires 318.0904, found: 318.0905.

3.3.20. Compound ***5g***. A yellow oil. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.93–2.06 (m, 2H), 2.19–2.38 (m, 2H), 2.35 (s, 3H, CH_3), 3.99–4.07 (m, 1H), 4.28–4.33 (m, 1H), 6.10 (s, 1H, CH), 7.22–7.35 (m, 3H, Ar), 7.48 (d, *J*=7.8 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 20.7, 24.2, 34.7, 70.7, 115.8, 121.6, 125.8, 127.8, 129.6, 129.9, 130.9, 136.5, 162.7, 169.7; IR (CH_2Cl_2): ν 3103, 3061, 2960, 2896, 1778, 1645, 1568, 1485, 1455, 1382, 1330, 1300, 1253, 1179 cm^{-1}; MS (EI) *m*/*z* (%): 230 [M^+] (4.5), 184 (5.1), 144 (11.0), 117 (11.1), 116 (100.0), 115 (53.4), 89 (5.8), 63 (4.9); HRMS (EI) calcd for $C_{14}H_{14}O_3$ (M^+) requires 230.0943, found: 230.0941.

3.3.21. Compound ***6g***. A yellow oil. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.27 (t, *J*=7.2 Hz, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.90–3.04 (m, 1H), 3.38–3.49 (m, 1H), 4.08–4.20 (m, 2H), 4.25–4.33 (m, 1H), 4.39–4.45 (m, 1H), 5.83 (t, *J*=3.0 Hz, 1H, CH), 6.32 (s, 1H, CH), 7.14–7.20 (m, 1H, Ar), 7.27–7.32 (m, 2H, Ar), 7.42 (d, *J*=3.0 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 21.5, 31.2, 60.7, 69.3, 114.2, 116.1, 122.0, 126.0, 128.0, 129.1, 130.1, 131.5, 137.4, 156.1, 160.4, 165.5, 169.2; IR (CH_2Cl_2): ν 3106, 3063, 2982, 2904, 1774, 1719, 1677, 1637, 1568, 1484, 1460, 1375, 1339, 1210 cm^{-1}; MS (EI) *m*/*z* (%): 314 [M^+] (1.5), 269 (4.1), 268 (5.1), 144 (6.5), 117 (10.3), 116 (100.0), 115 (30.9), 53 (4.9); HRMS (EI) calcd for $C_{18}H_{18}O_5$ (M^+) requires 314.1154, found: 314.1152.

3.3.22. Compound ***5h***. A white solid. Mp 79–81 °C. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.14–2.26 (m, 3H), 2.31–2.45 (m, 1H), 4.27–4.33 (m, 1H), 4.38–4.44 (m, 1H), 6.41 (s, 1H, CH), 7.61 (t, *J*=8.0 Hz, 1H, Ar), 7.73–7.75 (m, 1H, Ar), 7.81–7.83 (m, 1H, Ar), 7.88 (br s, 1H, Ar); ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ 15.3 (s, 1F); IR (CH_2Cl_2): ν 3103, 2989, 2900, 1770, 1720, 1629, 1487, 1435, 1327, 1230, 1170, 1125, 1089 cm^{-1}; MS (EI) *m*/*z* (%): 284 [M^+] (15.2), 199 (17.2), 198 (12.7), 171 (25.0), 170 (100.0), 169 (15.0), 151 (17.6), 42 (40.2); HRMS (EI) calcd for $C_{14}H_{11}O_3F_3$ (M^+) requires 284.0660, found: 284.0655.

3.3.23. Compound ***6h***. A yellow oil. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.25 (t, *J*=7.2 Hz, 3H, CH_3), 3.23–3.34 (m, 1H), 3.46–3.53 (m, 1H), 4.11–4.22 (m, 2H), 4.38–4.43 (m, 1H), 4.57 (td, *J*=8.8, 2.8 Hz, 1H), 5.74 (t, *J*=2.8 Hz, 1H, CH), 6.63 (s, 1H, CH), 7.57 (t, *J*=7.2 Hz, 1H, Ar), 7.67–7.73 (m, 2H, Ar), 7.79 (br s, 1H, Ar); ^{19}F NMR ($CDCl_3$, 376 MHz, $CFCl_3$): δ 62.4 (s, 1F); IR (CH_2Cl_2): ν 3103, 2985, 2908, 1775, 1719, 1677, 1648, 1628, 1487, 1436, 1376, 1334 cm^{-1}; MS (EI) *m*/*z* (%): 378 [M^+] (6.5), 289 (13.0), 201 (9.3), 173 (9.3), 148 (7.6), 133 (7.7), 121 (11.3), 120 (100.0); HRMS (EI) calcd for $C_{18}H_{15}O_5F_3$ (M^+) requires 368.0872, found: 368.0868.

3.3.24. Compound ***5i***. A white solid. Mp 90–92 °C. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.95–2.07 (m, 2H), 2.24–2.35 (m, 2H), 4.02–4.08 (m, 1H), 4.30–4.35 (m, 1H), 6.39 (s, 1H, CH), 7.31–7.40 (m, 2H, Ar), 7.50–7.52 (m, 1H, Ar), 7.63–7.65 (m, 1H, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS) δ 24.2, 34.8, 70.8, 115.5, 123.3, 126.8, 129.1, 129.4, 130.3, 130.9, 133.2, 158.9, 169.3; IR (CH_2Cl_2): ν 3105, 3070, 2985, 2897, 1766, 1649, 1589, 1563, 1473, 1434, 1331, 1300, 1249, 1179, 1120 cm^{-1}; MS (EI) *m*/*z* (%): 250 [M^+] (10.8), 171 (11.1), 164 (20.1), 138 (33.0), 137 (12.2), 136 (100.0), 101 (15.6), 42 (16.0); HRMS (EI) calcd for $C_{13}H_{11}O_3Cl$ (M^+) requires 250.0397, found: 250.0403.

3.3.25. Compound ***6i***. A colourless oil. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 1.26 (t, *J*=7.2 Hz, 3H, CH_3), 2.97–3.07 (m, 1H), 3.35–3.43 (m, 1H), 4.07–4.23 (m, 2H), 4.30–4.36 (m, 1H), 4.44–4.49 (m, 1H), 5.91 (t, *J*=2.8 Hz, 1H, CH), 6.72 (s, 1H, CH), 7.27–7.38 (m, 2H, Ar), 7.49–7.52 (m, 1H, Ar), 7.63 (dd, *J*=2.0, 7.6 Hz, 1H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 14.1, 30.9, 60.6, 69.3, 113.8, 116.2, 124.3, 126.8, 128.2, 129.4, 130.9, 131.2, 133.6, 155.2, 156.3, 165.5, 168.7; IR (CH_2Cl_2): ν 3071, 2983, 2905, 1775, 1721, 1677, 1641, 1590, 1474, 1443, 1375, 1266 cm^{-1}; MS (EI) *m*/*z* (%): 334 [M^+] (5.6), 164 (15.9), 138 (36.4), 137 (11.8), 136 (100.0), 121 (14.3), 101 (12.2), 91 (18.1); HRMS (EI) calcd for $C_{17}H_{15}O_5Cl$ (M^+) requires 334.0608, found: 334.0605.

3.3.26. Compound ***5j***. A yellow oil. ^1H NMR ($CDCl_3$, 300 MHz, TMS) δ 1.11 (t, *J*=7.2 Hz, 3H, CH_3), 2.33–2.42 (m, 1H), 2.69–2.77 (m, 1H), 3.27–3.33 (m, 1H), 4.09–4.25 (m, 3H), 4.51 (t, *J*=8.4 Hz, 1H), 7.10–7.13 (m, 2H, Ar), 7.25–7.31 (m, 3H, Ar), 7.48–7.58 (m, 3H, Ar), 7.62–7.64 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 13.6, 30.0, 52.2, 69.4, 112.9, 123.4, 128.0, 128.4, 128.5, 128.6, 128.9, 129.5, 131.0, 133.2, 160.8, 163.0, 164.8; IR (CH_2Cl_2): ν 3063, 3030, 2983, 2903, 1779, 1730, 1650, 1602, 1573, 1496, 1446, 1373, 1346, 1315, 1259 cm^{-1}; MS (EI) *m*/*z* (%): 364 [M^+] (0.7), 129 (12.4), 119 (9.9), 118 (100.0), 117 (54.6), 115 (6.1), 103 (3.1), 102 (4.0); HRMS (EI) calcd for $C_{22}H_{20}O_5$ (M^+) requires 364.1311, found: 364.1306.

3.3.27. Compound ***5k***. A white solid. Mp 114–116 °C. ^1H NMR ($CDCl_3$, 400 MHz, TMS) δ 2.43–2.50 (m, 1H), 2.76–2.81 (m, 1H), 3.52–3.57 (m, 1H), 4.33–4.40 (m, 1H), 4.53–4.58 (m, 1H), 6.08 (s, 1H), 7.05–7.07 (m, 2H, Ar), 7.20–7.25 (m, 3H, Ar), 7.48–7.54 (m, 3H,

Ar), 7.67–7.70 (m, 2H, Ar); ^{13}C NMR ($CDCl_3$, 75 MHz, TMS) δ 29.4, 52.5, 68.9, 114.2, 118.5, 127.7, 127.8, 128.2, 128.9, 129.2, 129.9, 131.2, 133.7, 161.1, 168.6; IR (CH_2Cl_2): ν 3061, 3030, 2983, 2900, 1765, 1622, 1574, 1494, 1449, 1346, 1304, 1243, 1178, 1108, 1035 cm^{-1}; MS (EI) m/z (%): 292 [M$^+$] (0.4), 119 (10.2), 118 (100.0), 117 (68.9), 115 (8.2), 103 (5.8), 102 (14.4), 91 (8.2); HRMS (EI) calcd for $C_{19}H_{16}O_3$ (M$^+$) requires 292.1099, found: 292.1103.

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Supplementary data

Spectroscopic data of all the new compounds and the detailed descriptions of experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org. Supplementary data associated with this article can be found in online version, at doi:10.1016/j.tet.2009.09.003.

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6. The C-5 position is an activated methylene group because of the two substituents: phenyl and acyl groups.
7. When both the R^1 and R^3 were aryl groups, two products derived from path a and path b were obtained.