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Indium-Trichloride Catalyzed Michael Reaction of Silyl Enol Ethers with α,β-Unsaturated Carbonyl Compounds under Neat Condition

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Abstract

In the presence of a catalytic amount of indium (III) trichloride ($InCl_3$) (20 mol%), ketene silyl enol ethers react quickly with α, β-unsaturated ketones and esters to afford the corresponding Michael adducts in moderate to good yields. Indium(III) trichloride can be recovered and reused without decrease in yields.

Keywords: Michael reaction; indium trichloride; neat condition.

Introduction

The development of new methodology for the assembly of complex molecules in water or neat conditions is one of the most challenging areas in organic synthesis. This is because reactions of this nature allow the synthesis of complex molecules under environmentally friendly conditions. In addition, water soluble substrates can be used directly and the protection and deprotection of acidic protons can be avoided[1].

On the other hand, despite extensive global research effort, most of the organic reactions still have to be carried out in toxic and flammable organic solvents. Hence, there is an urgent need to develop safe, practical and environmentally friendly processes. Among the many methods, the environmentally-friendly goal of making organic compounds without using solvents has become increasing popular[2].

Michael reaction is an important reaction for carbon-carbon bond formation reaction in modern organic synthesis. Traditional Michael reactions were conducted under basic

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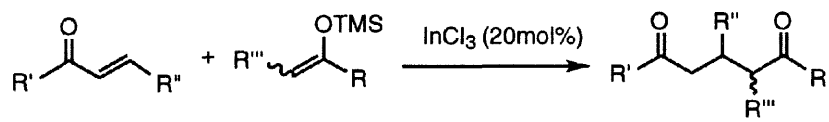
conditions[3]. Recently, the Lewis acid catalyzed variation has also been developed which allows the reaction to be carried out under pseudo-acidic conditions[4-14]. Although many Lewis acids have been found to catalyze this reaction, they still have the following limitiations: (1) It often requires a stoichiometric amount of Lewis acid as promoter. (2) Acid sensitive compounds such as methyl vinyl ketone is prone to polymerize under these conditions[15]. (3) Most of these Lewis acids have practical disadvantage such as moisture-sensitivity and thus the reaction has to be carried out under strict anhydrous conditions. (4) Reported Lewis acids rarely show a wide range of efficiency over various silyl enol ethers and reagents. Therefore, there is still a need for a convenient procedure to promote the Michael addition reactions of silyl enolethers to α,β-unsaturated carbonyl compounds under neutral conditions.

Recent research from our group has shown that commercially available indium trichloride ($InCl_3$) is a mild water-tolerant Lewis acid which functions as a highly efficient catalyst for the Mukaiyama-aldol reactions[16], Diels-Alder reactions[17], Aldol type Mannich reaction[18] and amine Michael reaction[19] under neat conditions and/or in water. These reactions can be performed under mild conditions (either neat for water-insoluble aldehydes or in water for water-soluble aldehydes), and the catalyst, indium trichloride can be recovered and reused after the reactions are completed. The unique features of indium trichloride have prompted us to investigate further applications of $InCl_3$ as catalyst in other Lewis acid-mediated C-C bond formation reactions. We present here indium trichloride as being a highly efficient catalyst for the conjugate additions of silyl enol ethers with α,β-unsaturated esters or ketones in the absence of solvent (Scheme 1). Furthermore, the solid catalyst can be recovered and reused without decrease in yield.



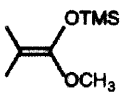
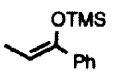
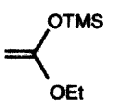
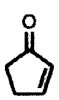
Scheme 1

Results and Discussion

The experimental procedure is very simple: silyl enol ethers were added into a mixture of enones/alkenoates and $InCl_3$. Generally, in the presence of 20 mol% indium trichloride, the Michael reactions proceeded very smoothly at room temperature or lower temperature under neat condition. The reactions were clean (except in Table 2, entry 4) and the corresponding Michael products were obtained in moderate to high yields in all cases. The results are summarized in Table 1 and 2.

Table 1.

Indium Trichloride-Mediated Michael Reaction of enones with sily enol ethers

Entry	Enones	Silyl Enol Ethers	Conditions	Yields%[a](*Anti/Syn*)
1	 I	 1	r.t., 1 h	0
2	I	1	$InCl_3$ (20 mol%), r.t., 1/2 h	67
3	I	 2	$InCl_3$ (20 mol%), 0 °C to r.t.	82
4	I	 3	$InCl_3$ (20 mol%), r.t., 1/2 h	86 (65:35)
5	I	 4	r.t., 1 h	0
6	I	4	$InCl_3$ (20 mol%), r.t., 1/2 h	90 (65:35)[b]
7	I	 5	$InCl_3$ (20 mol%), 0°C (5h), r.t.(2h)	66
8	 II	1	$InCl_3$ (20 mol%), r.t., 1/2 h	60
9	II	2	$InCl_3$ (20 mol%), 0 °C, 1/2 h	80
10	II	3	$InCl_3$ (20 mol%), r.t., 1/2 h	45 (52:48)[b]
11	II	4	$InCl_3$ (20 mol%), r.t., 1/2 h	67 (58:42)[b]
12	II	5	$InCl_3$ (20 mol%), 0°C (5h), r.t.(2h)	64[c] (57:43)[b] 63
13	 III	1	$InCl_3$ (20 mol%), r.t., 2 mins	68
14	III	2	$InCl_3$ (20 mol%), 0 °C(1h)	12
15	III	3	$InCl_3$ (20 mol%), r.t., 1/2 h	51
16	III	4	$InCl_3$ (20 mol%), -30 °C to r.t.	48
17	III	5	$InCl_3$ (20 mol%), 0°C (1/2h), r.t.(1h)	18

a. Isolated yields.

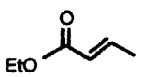
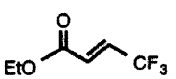
b. Diastereomeric ratio was determined by ^1H and/or ^{13}C NMR and the relative stereochemistries of the products have not been assigned.

c. The yield of 2nd run. $InCl_3$ was recovered and reused: after removal of water under reduced pressure, recovered $InCl_3$ was dried in 150 °C oven for 2 h before reused.

The results in Table 1 show that $InCl_3$ is such a mild Lewis acid that even acid-sensitive substrates such as 2-cyclopentenone and methyl vinyl ketone (MVK) can work very well under the catalysis of $InCl_3$ (Table 1, entries 8 to 17). Because of the high reactivity of MVK, its reactions with active silyl enol ethers such as 2 and 5 are extremely exothermic which resulted in lower yields (Table 1, entries 14 and 17). The simple diastereoselectivities of these reaction are moderate (Table 1, entries 4, 6, 10 and 11).

Table 2

Michael reaction of alkenoates with silyl enol ethers:

Entry	Alkenoates	Silyl Enol Ethers	Conditions	Yields(%)[a] (*Anti/Syn*)
1	 IV	2	r.t., 1 h	0
2	IV	2	$InCl_3$ (20 mol%), r.t., 1/2 h	90
3	IV	1	$InCl_3$ (20 mol%), r.t., 24 h	64
4	IV	4	$InCl_3$ (20 mol%), r.t., 15 h	14[b] (30:70)[c]
5	 V	2	$InCl_3$ (20 mol%), r.t., 17 h	37

a. Isolated yields.
b. 0.4 mmol 2-(1-cyclopentanol)-cyclopentanone was isolated. In this reaction, 1 mmol silyl enol ether was added.
c. Diastereomeric ratio was determined by ^1H and/or ^{13}C NMR and the stereochemistry of the products has not been assigned.

Michael addition of silyl enol ethers to alkenoates has seldom been reported although it is the basis of Du Pont's Group transfer polymerization process (GTP)[20]. From the results of Table 2, we find that: (1) $InCl_3$ is an efficient catalyst for this reaction too. The yields are dependent on the reactivity of silyl enol ethers and reagents (For silyl enol ethers: 2 > 1 > 4; and IV > V). (2) In the presence of $InCl_3$, silyl enol ether 4 reacts with its decomposed product (cyclopentanone) faster than with the alkenoates which causes much lower yields (entry 4).

The key features of the indium trichloride catalyzed Michael reaction are as follows: (1) In the absence of indium trichloride (Table 1, entries 1 and 5; Table 2, entry 1), no Michael product was observed indicating that $InCl_3$ is essential for the success of these reactions. (2) In every case, the reactions proceeded smoothly under extremely mild conditions (almost neutral) to give the corresponding 1,5-dicarbonyl compounds in good yields. (3) Strict anhydrous and non-protic conditions were not required, where the neat condition is found to be the simplest and the most facile. And only catalytic amount of $InCl_3$

(20 mol%) was required to complete the reaction. (4) Only the 1,4-addition product was formed and no 1,2-addition product was observed. (5) The diastereoselectivities of the reactions are moderate (Table 1, entries 4, 6, 10 and 11; Table 2, entry 4). (6) After these reactions were completed, indium trichloride can be recovered and reused. The yield of 2nd run using recovered $InCl_3$ is almost comparable to that of 1st run (Table 1, entry 11). (7) $InCl_3$ is highly efficient for a wide range of various silyl enolates derived from both esters and ketones and Michael acceptors including the cyclic enones, acyclic enones as well as alkenoates.

In conclusion, we have demonstrated that indium trichloride is a mild and efficient Lewis acid catalyst in a wide range of conjugate addition of silyl enolethers to enones/acrylates under neat conditions. Especially noteworthy is that the mild conditions employed enable the conjugate addition to work even with acid sensitive compounds such as methyl vinyl ketone. The experimental procedures are very simple and no special precaution is necessary. Only catalytic amount of commercially available $InCl_3$ is needed and it is recoverable. Since Michael reaction has been widely used in modern synthetic chemistry[21], this newly developed methodology will no doubt find wide applications for the syntheses of complex molecules. Efforts to apply this methodology for the synthesis of prostaglandins are ongoing in our group.

Experimental section

General Procedure. NMR spectra were recorded on Bruker ACF 300 NMR or AMX 500 NMR. MS sepectra were obtained with Hewlett-Packard 5890A gas chromatograph. HR-mass spectra (EI) were obtained with V.G. Micromass 7035. IR spectra were measured with a Perkin-Elmer 1600 FTIR spector. Column chromatograghy was performed on silica gel, Merck grade 60 (40-63 μm particle size). All the solvents were distilled before use. Silyl enol ethers were prepared according to the references (**3** and **5**)[22] or purchased from Fluka (**1**, **2** and **4**). Enone **I** (Fluka) and **III** (Fluka) were distilled before use. **II** (Fluka), **IV** (Fluka), **V** (Aldrich) and indium trichloride (Aldrich) were purchased and used directly.

General procedure for Michael addition: e.g. (Table 1, entry 2): 2-Cyclohexen-1-one (48 mg, 48.4 μL, 0.5 mmol) and indium trichloride (22.1 mg, 0.1 mmol, 20 mol%) were stirred at r.t. for 15 mins and then silyl enol ether **1** (192.3 mg, 1 mmol) was added. The resulting mixture was stirred at r.t. for 1/2 h and then 3 mL distilled water was added. The suspension was stirred at r.t. for 1/2 h, extracted with ethyl acetate and purified in the usual manner. The corresponding product was obtained in 67 % yield (72 mg) after silica gel column chromatography.

According to former reports, some of these Michael adducts are known compounds and are easily identified by comparison of ^1H, ^{13}C NMR, MS and IR data. Data below corresponds to entries in Table 1.

2: **3-(2-Oxo-2-phenylethyl)cyclohexanone**[14]: mp. 70-72 °C; *Rf* 0.31 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 7.91-7.88 (m, 2H), 7.55-7.47 (m, 1H), 7.45-7.40 (m, 2H), 3.05-2.76 (m, 2H), 2.52-1.94 (m, 7H), 1.76-1.62 (m,1H), 1.48-1.38 (m,1H); ^{13}C NMR ($CDCl_3$) δ 210.49, 198.28, 136.85, 133.09, 128.55, 127.91, 47.62, 44.55, 41.10, 34.74, 31.00, 24.79; IR (KBr plate) 1711.0, 1679.9 cm^{-1}; HRMS calcd for $C_{14}H_{16}O_2$ 216.1150, found 216.1158.

3: **3-(1-Methoxycarbonyl-1-methylethyl)cyclohexanone**[23]: oil; *Rf* 0.43 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 3.62 (s, 3H), 2.36-1.93 (m, 6H), 1.77-1.70 (m, 1H), 1.57-1.50 (m, 1H), 1.39-1.30 (m, 1H), 1.11 (s, 3H), 1.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 211.08, 177.21, 51.70, 45.75, 45.14, 43.17, 41.06, 26.24, 24.98, 21.98, 21.66; IR (KBr plate) 1725.1, 1708.9, 1137.6 cm^{-1}; HRMS calcd for $C_{11}H_{18}O_3$ 198.1256, found 198.1270.

4: **3-(1-Methyl-2-oxo-2-phenylethyl)cyclohexanone**[24]: oil; *Rf* 0.44 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 7.92-7.87 (m, 2H), 7.55-7.51 (m, 1H), 7.45-7.41 (m, 2H), 3.47-3.41 (m, 1H), 2.46-1.35 (m, 9H), 1.17 (d, J = 6.9 Hz, 3Hx0.35), 1.13 (d, J = 6.9 Hz, 3Hx0.65); ^{13}C NMR ($CDCl_3$): for major product:δ 210.80, 203.24, 136.66, 133.10, 128.66, 128.08, 45.09, 44.51, 41.20, 41.07, 29.82, 24.96, 14.22; for minor product: 210.65, 203.05, 136.66, 133.10, 128.66, 128.08, 46.20, 44.67, 41.07, 40.95, 27.28, 24.75, 13.81; IR (KBr plate) 1709.9, 1678.2 cm^{-1}; HRMS calcd for $C_{15}H_{18}O_2$ 230.1307, found 230.1301.

6: **3-(2-Cyclopentanone)cyclohexanone**: oil; *Rf* 0.22 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 2.47-1.99 (m, 11H), 1.80-1.45 (m, 5H); ^{13}C NMR ($CDCl_3$) for major product:δ 219.27, 210.78, 52.95, 44.58, 41.10, 38.81, 38.29, 29.03, 25.92, 25.05, 20.41; for minor product:δ 219.27, 210.78, 53.31, 46.00, 41.10, 38.89, 38.16, 27.38, 25.45, 25.05, 20.41; IR (KBr plate) 1726.6, 1708.6 cm^{-1}; HRMS calcd for $C_{11}H_{16}O_2$ 180.1150, found 180.1137.

7: **3-Ethoxycarbonylmethylcyclohexanone**: oil; *Rf* 0.36 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 4.12 (q, J = 7.2 Hz, 2H), 2.45-1.38 (m, 9H), 2.29 (d, J = 4.1 Hz, 2H), 1.24 (t, J =7.2Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 210.30, 171.63, 60.35, 47.32, 40.95, 40.87, 35.47, 30.76, 24.67, 14.10; IR (KBr plate) 1725.9, 1709.9, 1155.8 cm^{-1}; HRMS calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1086.

8: **3-(2-Oxo-2-phenylethyl)cyclopentanone**[14]: mp. 66-68 °C; *Rf* 0.30 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 7.94-7.91 (m, 2H), 7.58-7.55 (m, 1H), 7.54-7.41 (m,

1H), 3.18-3.03 (m, 2H), 2.80-1.55 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 218.46, 198.47, 136.80, 133.12, 128.56, 127.86, 44.74, 43.83, 38.17, 32.59, 29.31; IR (KBr plate) 1729.0, 1682.4 cm^{-1}; HRMS calcd for $C_{13}H_{14}O_2$ 202.0994, found 202.0995.

9: **3-(1-Methoxycarbonyl-1-methylethyl)cyclopentanone**[14]: oil; *Rf* 0.41 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 3.65 (s, 3H), 2.49-1.94 (m, 6H), 1.68-1.54 (m, 1H), 1.18 (s, 3H), 1.17 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 218.07, 177.10, 51.68, 44.95, 43.71, 40.33, 38.71, 24.31, 22.57, 22.47; IR (KBr plate) 1725.4, 1712.5, 1263.4, 1191.9, 1144.2 cm^{-1}; HRMS calcd for $C_{10}H_{16}O_3$ 184.1099, found 184.1128.

10: **3-(1-Methyl-2-oxo-2-phenylethyl)cyclopentanone**: oil; *Rf* 0.35 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 7.98-7.92 (m, 2H), 7.61-7.54(m, 1H), 7.51-7.44 (m, 2H), 3.50-3.41 (m, 1H), 2.61-1.43 (m, 7H), 1.27 (d, J = 7.0 Hz, 3Hx0.48), 1.22 (d, J = 7.0 Hz, 3Hx0.52); ^{13}C NMR ($CDCl_3$) For major product:δ 218.36, 203.27, 136.46, 133.18, 128.69, 128.13, 45.54, 42.54, 39.86, 38.37, 28.15, 16.63; For minor product: δ 218.14, 203.18, 136.29, 133.18, 128.69, 128.13, 45.58, 43.65, 39.38, 38.66, 27.03, 15.73; IR (KBr plate) 1737.6, 1676.6 cm^{-1}; HRMS calcd for $C_{14}H_{16}O_2$ 216.1150, found 216.1155.

11: **3-(2-Cyclopentanone)cyclopentanone**: oil; *Rf* 0.21 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 2.64-1.89 (m, 10H), 1.84-1.56 (m, 4H); ^{13}C NMR ($CDCl_3$): for major product:δ 219.56, 218.36, 52.12, 41.95, 38.40, 38.05, 36.82, 27.71, 27.09, 20.50; for minor product:δ 219.46, 218.76, 52.77, 43.33, 38.40, 36.98, 27.22, 26.91, 20.50; IR (KBr plate) 1726.2, 1163.4 cm^{-1}; HRMS calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0989.

12: **3-Ethoxycarbonylmethylcyclopentanone**: oil; *Rf* 0.35 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 4.12(q, J = 7.1 Hz, 2H), 2.42 (d, J = 4.1 Hz, 2H), 2.61-2.12 (m, 5H), 1.90-1.81 (m, 1H), 1.64-1.48 (m, 1H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 218.12, 171.86, 60.32, 44.41, 39.56, 38.10, 33.30, 29.01, 14.05; IR (KBr plate) 1736.0, 1190.1, 1158.2, 1029.6 cm^{-1}; HRMS calcd for $C_9H_{14}O_3$ 170.0943, found 170.0938.

13: **1-Phenyl-1,5-hexanedione**[14]: mp. 63-65°C; *Rf* 0.42 (hexane/ethyl acetate = 3/1); ^1H NMR ($CDCl_3$) δ 7.97-7.95 (m, 2H), 7.56-7.54(m, 1H), 7.48-7.46(m, 2H), 3.02 (t, J = 7.0 Hz, 2H), 2.57 (t, J = 7.0 Hz, 2H), 2.15 (s, 3H), 2.05-2.01 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 208.51, 199.78, 136.85, 133.10, 128.63, 128.06, 42.62, 37.42, 29.83, 18.24; IR (KBr plate) 1709.4, 1675.8 cm^{-1}. HRMS calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0991.

14: **Methyl 2,2-dimethyl-5-oxohexanoate**[14]: oil; *Rf* 0.41 (hexane/ethyl acetate = 3/1) ^1H NMR ($CDCl_3$) δ 3.66 (s, 3H), 2.40 (t, J = 8.0 Hz, 2H), 2.14 (s, 3H), 1.80 (t, J = 8.0 Hz, 2H), 1.17 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 208.15, 177.77, 51.71, 41.44, 39.32, 33.79, 29.82, 25.02; IR (KBr plate) 1726.7, 1712.6, 1195.7, 1137.5 cm^{-1}. HRMS calcd for $C_9H_{16}O_3$ 172.1099, found 172.1115.

15: **2-Methyl-1-phenyl-1,5-hexanedione**: oil; *Rf* 0.50 (hexane/ethyl acetate = 3/1); ^{1}H NMR ($CDCl_3$) δ 7.98-7.96 (m, 2H), 7.58-7.55 (m, 1H), 7.49-7.46 (m, 2H), 3.59-3.52 (m, 1H), 2.56-2.49 (m, 1H), 2.43-2.37 (m, 1H), 2.10 (s, 3H), 2.12-2.05 (m, 1H), 1.79-1.72 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 208.42, 203.82, 136.43, 133.08, 128.72, 128.34, 40.84, 39.49, 29.95, 27.14, 17.50; IR (KBr plate) 1712.1, 1678.3 cm^{-1}; HRMS calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1148.

16: **2-(3-Oxobutyl)cyclopentanone**[14]: oil; *Rf* 0.23 (hexane/ethyl acetate = 3/1); ^{1}H NMR ($CDCl_3$) δ 2.61-2.46 (m, 2H), 2.33-1.42 (m, 9H), 2.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 220.75, 208.36, 47.87, 41.07, 37.96, 29.76, 29.66, 23.58, 20.50; IR (KBr plate) 1722.2, 1710.7 cm^{-1}; HRMS calcd for $C_9H_{14}O_2$ 154.0994, found 154.1000.

17: **Ethyl 5-oxohexanoate:** oil; *Rf* 0.35 (hexane/ethyl acetate = 3/1); ^{1}H NMR ($CDCl_3$) δ 4.12 (q, J = 7.2 Hz, 2H), 2.50 (t, J = 7.2 Hz, 2H), 2.32 (t, J = 7.2 Hz, 2H), 2.14 (s, 3H), 1.93-1.84 (m, 2H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 207.90, 173.04, 60.22, 42.36, 33.14, 29.77, 18.79, 14.09; IR (KBr plate) 1727.5, 1712.1, 1156.9 cm^{-1}; HRMS calcd for $C_8H_{14}O_3$ 158.0943, found 158.0952.

The following data corresponds to entries in Table 2.

2: **5-Ethyl-1-methyl-2,2,3-trimethyl-1,5-pentanedioate:** oil; *Rf* 0.65 (hexane/ethyl acetate = 6/1); ^{1}H NMR ($CDCl_3$) δ 4.13 (q, J = 7.1 Hz, 2H), 3.66 (s, 3H), 2.40-2.28 (m, 2H), 2.06-1.97 (m, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.13 (s, 3H), 1.12 (s, 3H), 0.89 (d, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 177.49, 172.82, 60.07, 51.44, 45.20, 37.16, 36.95, 21.79, 21.73, 14.86, 13.97; IR (KBr plate) 2978.5, 1734.6, 1258.3, 1186.1, 1134.1 cm^{-1}; HRMS (M $C_{11}H_{20}O_4$): calcd. for $C_{10}H_{17}O_3^+$ [(M-CH_3O)$^+$] 185.1178, found 185.1173 (4); calcd. for $C_9H_{15}O_3^+$ [(M-C_2H_5O)$^+$] 171.1021, found 171.1048 (12).

3: **Ethyl 3-methyl-5-oxo-5-phenylvalerate:** oil; *Rf* 0.54 (hexane/ethyl acetate = 6/1); ^{1}H NMR ($CDCl_3$) δ 7.98-7.95 (m, 2H), 7.59-7.43 (m, 3H), 4.13 (q, J = 7.1 Hz, 2H), 3.11 (dd, J = 5.8, 16.1 Hz, 1H), 2.83 (dd, J = 7.6, 16.1 Hz, 1H), 2.71-2.64 (m, 1H), 2.42 (dd, J = 6.6, 15.2 Hz, 1H), 2.30 (dd, J = 7.0, 15.2 Hz, 1H), 1.25 (t, J = 7.1 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 199.14, 172.43, 136.99, 132.91, 128.47, 128.01, 60.15, 44.75, 41.07, 26.80, 19.97, 14.12; IR (KBr plate) 1731.4, 1682.2 cm^{-1}; HRMS calcd. for $C_{14}H_{18}O_3$ 234.1256, found 234.1251.

4: **2-(2-Ethoxycarbonyl-1-methylethyl)cyclopentanone:** oil; *Rf* 0.40 (hexane/ethyl acetate = 6/1); ^{1}H NMR ($CDCl_3$) δ 4.15-4.06 (m, 2H), 2.52-1.62 (m, 10H), 1.27-1.21 (m, 3H), 1.01 (d, J = 6.8 Hz, 3Hx0.7), 0.85 (d, J = 6.8 Hz, 3Hx0.3); ^{13}C NMR ($CDCl_3$) δ major product: 219.78, 172.71, 60.15, 53.43, 39.07, 38.46, 29.70, 26.08, 20.45, 17.57, 14.09; minor product: 219.90, 172.50, 60.15, 52.85, 39.82, 38.86, 29.43, 24.72, 20.33,

16.22, 14.95; **IR (KBr plate)** 1735.3 cm^{-1}; HRMS calcd. for $C_{11}H_{18}O_3$ 198.1256, found 198.1245.

5: **5-Ethyl-1-methyl-2,2-dimethyl-3-trifloromethyl-1,5-pentanedioate:** oil; *Rf* 0.51 **(hexane/ethyl acetate = 6/1)**; ^1H NMR ($CDCl_3$) δ 4.17 (q, J = 7.1 Hz, 2H), 3.70 (s, 3H), 3.57-3.49 (m, 1H), 2.54 (dd, J = 17.1, 6.3 Hz, 1H), 2.43 (dd, J = 17.1, 5.3 Hz, 1H), 1.26 (t, J = 7.1Hz, 3H), 1.20 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 176.13, 171.06, 61.25, 52.35, 45.61 (q, J = 25 Hz), 43.18, 30.57, 30.54, 23.94, 20.95, 14.06; IR (KBr plate) 1738.5 cm^{-1}; HRMS (M $C_{11}H_{17}O_4F_3$): calcd. for $C_{10}H_{14}O_3F_3^+$ [(M-CH_3O)$^+$] 239.0895, found 239.0899 (8); calcd. for $C_9H_{12}O_3F_3^+$ [(M-C_2H_5O)$^+$] 225.0739, found 225.0738 (29).

Entry 4 (side-product): **2-(1-Cyclopentanol)cyclopentanone**: oil; *Rf* 0.21 **(hexane/ethyl acetate = 6/1)**; ^1H **NMR** ($CDCl_3$) δ 3.25 (s, 1H), 2.40-1.51 (m, 15H); ^{13}C NMR ($CDCl_3$) δ 222.49, 82.23, 56.73, 39.14, 38.51,36.26, 26.25, 23.68, 23.48, 20.20; IR (KBr plate) 1728.5, 1154.4, 991.3 cm^{-1}; HRMS calcd. for $C_{10}H_{16}O_2$ 168.1150, found: 168.1153.

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