Trifluoromethanesulfonic Acid, an Unusually Powerful Catalyst for the Michael Addition Reaction of β-Ketoesters under Solvent-Free Conditions

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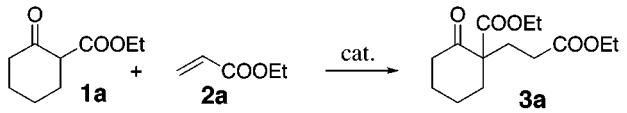
The Michael addition reaction is widely recognized as one of the most important carbon−carbon bond forming reactions in organic synthesis and can generally be carried out with a strong base.[1] However, the base-catalyzed method sometimes suffers from disadvantages of incompatibility with base-sensitive functionality and the occurrence of other side reactions such as auto-condensations and retro-Michael type decompositions. To circumvent these problems, considerable attention has recently been focused on the use of Lewis acid catalysts, including transition metal complexes.[2] We are generally interested in the use of lanthanide(III) trifluoromethanesulfonates [$Ln(OTf)_3$] as water-tolerant Lewis acid catalysts and recently reported that the Michael addition reactions of β-keto esters were efficiently catalyzed by $Yb(OTf)_3$ under high pressure or on silica gel supports.[3]

Although these methods are useful for properly reactive substrates, there are still some limitations. For example, reactions between β-keto esters and ethyl acrylate are only successful at high pressure and the reactions using cyclic enones as Michael acceptors under $Yb(OTf)_3/SiO_2$-catalyzed conditions invariably take a long time. In our continuing efforts to overcome these difficulties, we accidentally found that direct exposure of Michael donors and acceptors to a $Yb(OTf)_3$ catalyst provided the desired adducts, albeit in somewhat lower yields.[3] This result prompted us to investigate the possibility of whether trifluoromethanesulfonic acid (TfOH) itself can act as an active catalyst for performing this type of Michael addition reaction. Whereas this very strong acid has been used for carbon−carbon bond formation, taking advantage of its mildness, nonoxidative character, and ease of handling,[4,5] a TfOH-catalyzed Michael addition reaction has not yet been reported, to the best of our knowledge. We accomplished this feat by incorporating the novel feature of solvent-free conditions.[6, 7]

To find the optimum conditions, the Michael addition reaction of β-keto ester **1a** with 1.2 equiv of ethyl acrylate (**2a**) was carried out in the presence of a variety of Lewis and Brønsted acids (Table 1). The highest catalytic activity was attained for the reaction using 0.3 equiv of TfOH at room temperature: the reaction proceeded smoothly within 5 h to give **3a** in 92% yield (Table 1, entry 2). This result clearly reflects the remarkable activity of TfOH, since it is known that **2a** is usually the least reactive of several Michael acceptors under normal Lewis acid-catalyzed conditions (except for our high-pressure version).[3,8] It should be pointed out that the use of less TfOH retarded the reaction progress due to the competitive polymerization of **2a** (Table 1, entries 3 and 4) and no catalytic activity was observed in CH_2Cl_2 solution even after a prolonged reaction time (Table 1, entry 5).

Table 1. Effect of Various Lewis and Brønsted Acids for the Michael Addition Reaction of 1a with 2a



entry	catalyst	time (h)	yield (%)[b]
1[c]	$Yb(OTf)_3$ (0.1 equiv)	24	81
2	TfOH	5	92
3	TfOH (0.1 equiv)	72	25 (66)
4	TfOH (0.2 equiv)	72	63
5[d]	TfOH	72	trace[e]
6	$BF_3{\cdot}OEt_2$	72	9 (76)
7	$TiCl_4$	72	trace[e]
8	$ZnCl_2$	72	5 (90)
9	H_2SO_4	72	41 (44)
10	60% $HClO_4$	72	5 (70)

[a] Unless otherwise noted, 1.2 equiv of **2a** and 0.3 equiv of the catalyst were used under solvent-free conditions. [b] Isolated yields. Yields in parentheses are recovery of **1a**. [c] See ref 3. [d] Solvent (CH_2Cl_2) was used. [e] Unreacted **1a** was mostly recovered.

Several examples demonstrating the general feasibilty of the present method are shown in Table 2. Ethyl acrylate (**2a**) reacted with various β-keto esters in nearly quantitative yields (Table 2, entries 5, 8, 11, 13, and 14), and even with nonactivated cyclohexanones such as 2-methylcyclohexanone (**1i**) and 2,6-dimethylcyclohexanone (**1j**), reasonable yields of the product were obtained (Table 2, entries 15 and 16).[9] Due to the more reactive nature of ethyl acetoacetate (**1d**), the reaction with **2a** resulted in a complex mixture (Table 2, entry 9). Instead, ethyl 2-methylacetoacetate (**1e**) reacted quite smoothly

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Table 2. TfOH-Catalyzed Michael Addition Reaction of β-Keto Esters (E = COOEt)[a]

entry	donor	acceptor	time (h)	product	yield[b] (%)
1			6		50[c]
2[d]	**1a**		19		79
3[e]		**2b**	8	**3b**	87
4[f]	**1a**	**2c**	24	**3c**	79[g]
5	**1b**	**2a**	5	**3d**	99
6[e]	**1b**	**2b**	8	**3e**	88
7[f]	**1b**	**2c**	60	**3f**	72(9)[g]
8	**1c**	**2a**	10	**3g**	97
9	**1d**	**2a**	54	**3h**	--[h]
10[f]	**1d**	**2c**	24	**3i**	75 (2)[g]
11	**1e**	**2a**	2	**3j**	93
12	**1f**	**2a**	42	**3k**	51[i]
13	**1g**	**2a**	2	**3l**	94
14	**1h**	**2a**	1	**3m**	92
15	**1i**	**2a**	36	**3n**	64[j]
16	**1j**	**2a**	48	**3o**	78[g]

[a] Unless otherwise noted, 1.2 equiv of the Michael acceptor and 0.3 equiv of TfOH were used under solvent-free conditions. [b] Isolated yield based on the starting Michael donor. Yields in parentheses are recovery of the Michael donor. [c] A Robinson annulated compound (13%) was also obtained. See ref 10. [d] 0.02 equiv of TfOH was used. [e] Solvent (CH_2Cl_2) was used, and in total 2.7−3.3 equiv of **2b** was added. [f] Solvent (CH_3CN) was used, and in total 1.5 equiv of **2c** was added. [g] A 1:1 diastereomeric mixture. [h] A complex mixture of products was obtained. [i] Considerable amounts of byproducts were formed. [j] Only a trace amount of the regioisomer was detected by GC. See ref. 9.

to afford the desired adduct **3j** in 93% yield (Table 2, entry 11). Conformationally flexible α-acetyl-γ-butyrolactone (**1f**) was exceptionally unreactive with **2a** and, after 42 h, 51% of **3k** was isolated along with a considerable quantity of byproducts (Table 2, entry 12).

In contrast, when methyl vinyl ketone (**2b**) was used as the Michael acceptor, the reaction of **1a** took place violently under TfOH-catalyzed solvent-free conditions, giving 50% of adduct **3b** along with a small amount (13%) of a Robinson annulated compound (Table 2, entry 1).[10] The use of less amount of TfOH could improve the yield of **3b** (79%), but the reaction was very slow (Table 2, entry 2). Under these harsh conditions, polymerization of **2b** proved to be unavoidable. This was also true for 2-cyclopentenone (**2c**). Therefore, for these meaningly sensitive substrates, the use of CH_2Cl_2 or CH_3CN as the solvent[11] and the gradual addition of an excess of the reagents were essential for improving the product yields (Table 2, entries 3, 4, 6, 7, and 10).

The role of TfOH in these Michael addition reactions can be attributed to its strong proton-donating ability (pK_a value is <-11),[12] which enhances both the nucleophilicity of β-keto esters via their enol forms and the electrophilicity of the acceptor molecules.[4] In the latter case, the polymerization side reaction becomes a serious drawback. However, this difficulty can be overcome by conducting the reaction under carefully controlled conditions in the presence of an appropriate organic solvent. This newly discovered method apparently shows a remarkable contrast with the Lewis acid-catalyzed method. The catalytic activity of Lewis acids mainly relies on their coordinating character to assemble both Michael donors and acceptors on their coordination surface. On the other hand, TfOH, in principle, can activate these substrates through protonation, so that the reactivity of Michael acceptors is essentially independent of their *s-cis* or *s-trans* conformation. Despite the extreme activity of TfOH, however, no reaction was observed with acrylonitrile, ethyl methacrylate, ethyl crotonate, or ethyl cinnamate.[13]

Finally, the above technique was applied to the diastereoselective Michael addition reaction using **1k**,[14] **1l**, **2d**, and **2e**[15] as the chiral substrates with (−)-menthol or (−)-8-phenylmenthol as the common chiral auxiliary[16] (Table 3). In these examples, the Michael addition reactions were considerably slower than the standard reaction employing **1a** and **2a**. This is probably due to the rather sterically crowded menthyl moiety. Although essentially no asymmetric induction was observed for the combination of **1a** and **2d** or **1k** and **2a** (Table 3, entries

(9) GC analyses revealed that only a trace amount of the regioisomer was formed in the reaction of **1i** and **2a**. A similar phenomenon was also observed for the reaction using NaOEt. The results indicate that in this acid-catalyzed alkylation well-known Saytzeff-type orientation of an enolic double bond was predominant. See: Ingold, C. K. *Structure and Mechanism in Organic Chemistry*, 2nd ed.; Cornell University Press: Ithaca, 1969; p 819.

(10) The use of 0.3 equiv of TfOH/Tf_2O (1:1) as a cocatalyst under similar conditions (rt, 6 h) gave a somewhat better yield (23%) of the Robinson adduct but **3b** in 24% yield.

(11) No significant differences in product yields were observed in these solvents.

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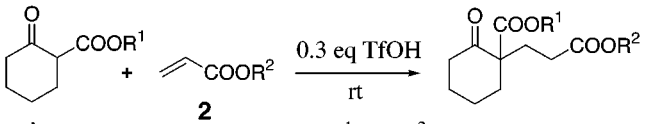
Table 3. Diastereoselective Michael Addition Reaction Using Chiral Menthyl Esters



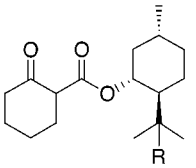
1 **2**

3p: R^1=Et, R^2=(-)-Menthyl
3q: R^1=Et, R^2=(-)-8-Phenylmenthyl
3r: R^1=(-)-Menthyl, R^2=Et
3s: R^1=(-)-8-Phenylmenthyl, R^2=Et

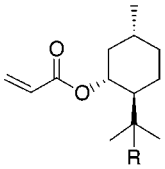
entry	1	2	product	time (h)	yield (%)[a]	ratio of diastereomers
1	**1a**	**2d**	**3p**	11	86	52:48[b]
2	**1a**	**2e**	**3q**	38	49 (42)	69:31[c]
3	**1k**	**2a**	**3r**	7	87	50:50[c]
4	**1l**	**2a**	**3s**	8	78 (18)	68:32[c]

[a] Isolated yields. Yields in parentheses are recovery of **1**. [b] Determined by chiral HPLC analysis (Chiralcel OD) after conversion to **3a**. [c] Determined by ^{1}H and ^{13}C NMR analyses.

1 and 3), the moderate diastereoselectivity could be attained for the reaction between **1a** and **2e** or **1l** and **2a** (Table 3, entries 2 and 4). This is in striking contrast to cases utilizing alumina-supported reactions[17] or chiral imine technology.[18] The results imply that no significant electrostatic interaction between those reagents was present in our system.



1k: R = H
1l: R = Ph



2d: R = H
2e: R = Ph

In conclusion, we succeeded in developing a novel method to effect the Michael addition reaction of β-keto esters (**1**) with ethyl acrylate (**2a**) in the presence of TfOH as a strong Brønsted acid catalyst under solvent-free conditions. For relatively reactive Michael acceptors such as methyl vinyl ketone (**2b**) and 2-cyclopentenone (**2c**), the reactions occurred best in CH_2Cl_2 or CH_3CN. It should be noted that the method does not require any metal salts and hence it might be of great value as an environmentally friendly process.[19] We believe that the method offers considerable advantages for producing several types of Michael adducts in view of its high efficiency, operational simplicity, and convenient workup procedure, although there are some limitations for the usable substrates having no acid sensitive functionality. Work is in progress to expand the synthetic utility of this method.

Experimental Section

General Remarks. Commercially available reagents were used without purification. For general experimental information, see our previous paper.[20] The structures of the Michael adducts **3a**,[21] **3b**,[6b] **3d**,[22] **3e**,[6b] **3g**,[23] **3i**,[24] **3j**,[25] **3m**,[26] and **3n**[27] were confirmed by comparison with published data.

Typical Experimental Procedure for the Synthesis of 3a. TfOH (0.6 mmol) was added dropwise to a mixture of ethyl 2-oxocyclohexanecarboxylate (**1a**) (2.0 mmol) and ethyl acrylate (**2a**) (2.4 mmol) at 0 °C, and the resultant yellow mixture was allowed to stand at room temperature for 5 h. When the reaction was finished, the mixture turned brown. The cooled mixture was diluted with CH_2Cl_2 and neutralized by the addition of the minimum amount of Et_3N. Concentration and purification by silica gel column chromatography gave the desired Michael adduct **3a**[21] in 92% yield.

The followings are new compounds.

Ethyl 2-oxo-1-(3-oxocyclopentyl)cyclohexanecarboxylate (3c): a 1:1 mixture of the two diastereomers; colorless oil; IR (neat) 1742, 1711 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28 and 1.29 (totally 3H, t, J = 7.1 Hz), 1.48−1.70 (3H, m), 1.77−1.87 (2H, m), 1.93−2.11 (2H, m), 2.12−2.25 (2H, m), 2.27−2.38 (2H, m), 2.40−2.60 (3H, m), 2.62−2.77 (1H, m), 4.17−4.31 (2H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 22.6, 24.1 and 25.0 (pair), 27.2(7) and 27.3(3) (pair), 34.2 and 34.3 (pair), 38.3 and 38.6 (pair), 40.2 and 40.8 (pair), 40.9(0) and 40.9(2) (pair), 41.4, 61.4-(8) and 61.4(9) (pair), 62.3 and 62.6 (pair), 170.8 and 170.9 (pair), 207.0(7) and 207.1(0) (pair), 217.7 and 217.9 (pair); HRMS calcd for $C_{14}H_{20}O_4$ + H 253.1439, found 253.1429.

Ethyl 2-oxo-1-(3-oxocyclopentyl)cyclopentanecarboxylate (3f): a 1:1 mixture of the two diastereomers; colorless oil; IR (neat) 1744, 1726 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26 and 1.27 (totally 3H, t, J = 7.1 Hz), 1.54−1.83 (1H, m), 1.91−2.06 (4H, m), 2.10−2.40 (5H, m), 2.42−2.56 (2H, m), 2.83−2.94 (1H, m), 4.18, 4.20 (totally 2H, q, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 19.6 (1) and 19.6 (5) (pair), 24.3 and 25.2 (pair), 30.4 and 30.8 (pair), 38.3 and 38.4 (pair), 38.5 and 38.7 (pair), 40.1, 40.2 and 40.9 (pair), 61.7, 61.8 and 62.1 (pair), 170.5, 214.0 and 214.1 (pair), 217.3 and 217.4 (pair); HRMS calcd for $C_{13}H_{18}O_4$ + H 239.1283, found 239.1302.

Ethyl 3-(1-acetyl-2-oxo-3-oxolanyl)propanoate (3k): colorless oil; IR (neat) 1767, 1732, 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26 (3H, t, J = 7.1 Hz), 2.05 (1H, dt, J = 12.9, 9.0 Hz), 2.16−2.28 (3H, m), 2.35 (3H, s), 2.40−2.47 (1H, m), 2.88 (1H, ddd, J = 12.9, 7.1, 3.4 Hz), 4.14 (2H, q, J = 7.1 Hz), 4.17 (1H, dt, J = 9.0, 7.1 Hz), 4.33 (1H, dt, J = 9.0, 3.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 25.6, 29.2, 29.3, 29.7, 60.5, 60.9, 66.1, 171.8, 175.0, 202.0; HRMS calcd for $C_{11}H_{16}O_5$ + H 229.1076, found 229.1062.

Ethyl 3-(2-(ethoxycarbonyl)-1-oxoindan-2-yl)propanoate (3l): colorless oil; IR (neat) 1738, 1713, 1609 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.21, 1.23 (each 3H, t, J = 7.3 Hz), 2.21−2.47 (4H, m), 3.07, 3.70 (each 1H, d, J = 17.3 Hz), 4.10, 4.17 (each 2H, q, J = 7.1 Hz), 7.41 (1H, dt, J = 7.8, 0.7 Hz), 7.49 (1H, dt, J = 7.8, 1.0 Hz), 7.64 (1H, dt, J = 7.8, 1.0 Hz), 7.77 (1H, dt, J = 7.8, 0.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.8, 13.9, 29.5, 29.6, 37.0, 59.3, 60.3, 61.4, 124.5, 126.2, 127.7, 134.8, 135.3, 152.5, 170.4, 172.4, 201.7; HRMS calcd for $C_{17}H_{20}O_5$ 304.1311, found 304.1327.

Ethyl 3-(1,3-dimethyl-2-oxocyclohexyl)propanoate (3o): a 1:1 mixture of the two diastereomers; colorless oil; IR (neat) 1736, 1703 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.98(6) (1.5H, d, J = 6.6 Hz), 0.99(2) (1.5H, d, J = 6.3 Hz), 1.00 and 1.18 (totally 3H, s), 1.24(9) and 1.25(0) (totally 3H, t, J = 7.1 Hz), 1.22−1.38 (1H, m), 1.49−2.00 (6H, m), 2.00−2.10 (1H, m), 2.24−2.42 (2H,

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m), 2.62 (0.5H, sextet, J = 6.3 Hz), 2.65 (0.5H, sextet, J = 6.6 Hz), 4.11 and 4.12 (totally 2H, q, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1 and 14.2 (pair), 14.8(8) and 14.9(0) (pair), 21.0 and 21.2 (pair), 22.1 and 23.0 (pair), 29.1 and 29.5 (pair), 32.4 and 33.3 (pair), 36.4 and 36.6 (pair), 38.9 and 40.8 (pair), 41.0 and 41.2 (pair), 47.5 and 48.1 (pair), 60.2 and 60.5 (pair), 173.3 and 174.1 (pair), 216.2 and 216.3 (pair); HRMS calcd for $C_{13}H_{22}O_3$ + H 227.1647, found 227.1651.

(1*R*,2*S*,5*R*)-(+)-8-Phenylmenthyl 2-Oxocyclohexanecarboxylate (1l). This compound was prepared from **1a** and (−)-8-phenylmenthol in a similar manner to that described in the literature for the preparation of **1k**:[14] mp 73.5−74.5 °C; $[\alpha]^{25}_D$ +3.0 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.84; H, 9.17.

Menthyl 3-(1-ethoxycarbonyl-2-oxocyclohexyl)propanoate (3p): a mixture of the two diastereomers; colorless oil; IR (neat) 1732, 1717 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.74 and 0.75 (totally 3H, d, J = 6.8 Hz), 0.80−1.40 (3H, m), 0.88 (3H, d, J = 6.6 Hz), 0.90 (3H, d, J = 5.9 Hz), 1.27 (3H, t, J = 7.1 Hz), 1.31−1.40 (1H, m), 1.42−1.52 (2H, m), 1.60−1.71 (4H, m), 1.74−2.04 (5H, m), 2.12−2.26 (2H, m), 2.32−2.54 (4H, m), 4.18−4.23 (2H, m), 4.66 (1H, dt, J = 11.0, 4.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 16.3, 20.7, 22.0, 22.5, 23.5, 26.2(3) and 26.2(5) (pair), 27.5, 29.6, 29.8, 31.3, 34.2, 36.1(5) and 36.1(9) (pair), 40.9, 41.0, 47.0, 60.0, 61.4, 74.2, 171.7, 172.6, 207.5; HRMS calcd for $C_{22}H_{36}O_5$ 380.2563, found 380.2567.

The diastereoselectivity was determined after conversion to the corresponding ethyl ester **3a** (*p*-TsOH, EtOH, reflux, 24 h), which was further analyzed by chiral HPLC (Chiralcel OD, elution with hexane/2-propanol = 99:1).[28]

8-Phenylmenthyl 3-(1-ethoxycarbonyl-2-oxocyclohexyl)-propanoate (3q): a 69:31 mixture of the two diastereomers; colorless oil; $[\alpha]^{25}_D$ +27.8 (*c* 1.1, $CHCl_3$); IR (neat) 1734, 1711, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.86 (3H, d, J = 6.6 Hz), 1.20, 1.30 (each 3H, s), 0.85−2.05 (20H, m), 2.35−2.50 (3H, m), 4.10−4.25 (2H, m), 4.80 (1H, m), 7.14 (minor) and 7.26 (major) (totally 5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.1, 21.8, 22.5, 25.0, 26.6, 27.4, 27.9, 29.1 and 29.2 (pair), 29.3(6) and 29.4-(2) (pair), 31.2, 34.5, 35.8 and 36.0 (pair), 39.6, 41.0, 41.7, 50.2-(9) and 50.3(1) (pair), 59.8 and 59.9 (pair), 61.2(8) and 61.3(1) (pair), 74.1 and 74.2 (pair), 125.0, 125.4 (×2), 127.9 (×2), 151.5, 171.5(5) and 171.6(0) (pair), 172.2(2) and 172.2(4) (pair), 207.3 and 207.4 (pair); HRMS calcd for $C_{28}H_{40}O_5$ + H, 457.2954, found 457.2959.

The diastereoselectivity was determined by ^{1}H and ^{13}C NMR analyses.

Ethyl 3-(1-menthyloxycarbonyl-2-oxocyclohexyl)propanoate (3r): a 1:1 mixture of the two diastereomers; colorless oil; IR (neat) 1736, 1713 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.74 and 0.75 (totally 3H, d, J = 7.1 Hz), 0.88 (3H, d, J = 6.8 Hz), 0.92 (3H, d, J = 6.6 Hz), 0.90−1.10 (2H, m), 1.24 and 1.25 (totally 3H, t, J = 7.1 Hz), 1.36−1.56 (3H, m), 1.60−1.74 (4H, m), 1.74−2.06 (6H, m), 2.12−2.28 (2H, m), 2.30−2.54 (4H, m), 4.11(9) and 4.12(1) (totally 2H, q, J = 7.1 Hz), 4.72(0) and 4.72(3) (totally 1H, dt, J = 10.7, 4.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.2, 15.5(7) and 15.6(3) (pair), 20.7(8) and 20.8(3) (pair), 21.9, 22.5, 22.7(8) and 22.8(3) (pair), 25.8 and 26.0 (pair), 27.5, 29.5(5) and 29.5 (9) (pair), 29.7 and 29.8 (pair), 31.4, 34.1, 36.0 and 36.1 (pair), 40.4 and 40.5 (pair), 41.0 and 41.1 (pair), 46.6 and 46. 7 (pair), 60.2 and 60.3 (pair), 60.4, 75.6(8) and 75.7(3) (pair), 171.2 and 171.3 (pair), 173.0 and 173.1 (pair), 207.4(8) and 207.5(2) (pair); HRMS calcd for $C_{22}H_{36}O_5$ 380.2563, found 380.2546.

The diastereoselectivity was determined by ^{1}H and ^{13}C NMR analyses.

Ethyl 3-(1-(8-phenylmenthyloxycarbonyl)-2-oxocyclohexyl)propanoate (3s): a 68:32 mixture of the two diastereomers; colorless oil; $[\alpha]^{27}_D$ +33.6 (*c* 1.1, $CHCl_3$); IR (neat) 1736, 1711, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.85−2.55 (23H, m), 0.86 and 0.88 (totally 3H, d, J = 6.8 Hz), 1.24 and 1.26 (totally 3H, s), 1.30 and 1.31 (totally 3H, s), 4.12 (2H, q, J = 7.1 Hz), 4.88 (1H, dt, J = 10.7, 4.1 Hz), 7.16 (minor) and 7.26 (major) (totally 5H, m); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.2(0) and 14.2-(3) (pair), 21.7 and 21.8 (pair), 22.1 and 22.5 (pair), 24.0 and 25.4 (pair), 27.1 and 27.2 (pair), 27.3 and 27.4 (pair), 28.4 and 28.7 (pair), 29.5 and 29.7 (pair), 30.0, 31.4, 34.3(7) and 34.4(3) (pair), 34.7 and 35.4 (pair), 40.0 and 40.2 (pair), 40.8 and 41.1 (pair), 41.4 and 41.5 (pair), 49.8 and 50.0 (pair), 60.0 and 60.3-(9) (pair), 60.4(2) and 60.5 (pair), 77.1 and 77.2 (pair), 125.3 and 125.4 (pair), 125.5 and 125.6 (pair, ×2), 128.0 and 128.1 (pair, ×2), 150.3 and 150.9 (pair), 171.2(1) and 171.2(4) (pair), 173.1, 207.3 and 207.4 (pair); HRMS calcd for $C_{28}H_{40}O_5$ + H 457.2954, found 457.2965.

The diastereoselectivity was determined by ^{1}H and ^{13}C NMR analyses.

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Supporting Information Available: Copies of NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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