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Practical and robust method for stereoselective preparations of ketene silyl (thio)acetal derivatives and NaOH-catalyzed crossed-Claisen condensation between ketene silyl acetals and methyl esters

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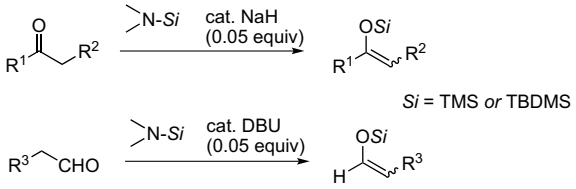
ABSTRACT

We developed an efficient, practical, and robust method for stereoselective preparations of (*Z*)-ketene trimethylsilyl (TMS) thioacetals from thioesters and alkyl (1*Z*)- or (1*Z*,3*E*)-1,3-bis(TMS)-dienol ethers from alkyl β-ketoesters. The former preparation was performed by convenient procedure (LDA–TMSCl, 0–5 °C, 2.5 h), while the latter preparation involved convenient method A (2NaHMDS–2TMSCl) and cost-effective method B (NaH, NaHMDS–2TMSCl). The first catalytic NaOH-catalyzed crossed-Claisen condensation between ketene silyl acetals and methyl esters proceeded successfully to give a variety of α-monomethyl β-ketoesters and inaccessible α,α-disubstituted β-ketoesters. For further extension, a couple of Claisen-aldol tandem reactions of the obtained β-ketoester analogues utilizing $TiCl_4$ and $TiCl_4$–Bu_3N reagents smoothly proceeded with good to excellent stereoselectivity.

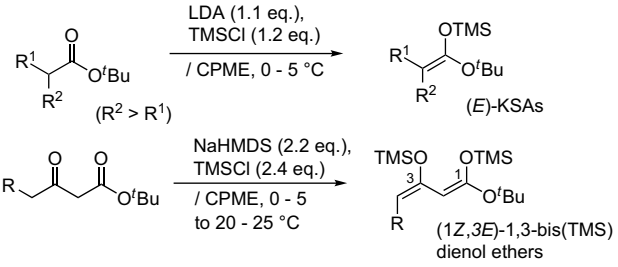
1. Introduction

Ketene silyl acetals (KSAs) as well as enol silyl ethers are widely employed as reactive precursors of carboxylic esters in a broad range of organic syntheses, e.g., the Mukaiyama aldol and Michael reactions, the Diels–Alder reaction, Ireland–Claisen rearrangement, etc.[1] The most conventional preparations of these silyl ethers from ketones and aldehydes use an R_3SiCl(*or* OTf)–amine (e.g., Et_3N) or R_3SiCl–amide (e.g., LDA) agent. We previously described the first catalytic base-promoted preparation of enol silyl ethers; NaH functioned for ketones and DBU did for aldehydes (Scheme 1).[2] Recently, a practical and robust method for regio- and stereoselective preparation of (*E*)-TMS-KSAs and β-ketoester-derived *tert*-butyl (1*Z*,3*E*)-1,3-bis(TMS)dienol ethers was reported (Scheme 2).[3] As a synthetic application of these silyl enolates, methyl and *tert*-butyl ester-derived KSAs were utilized for the first base-catalyzed crossed-Claisen condensation with simple methyl esters (Scheme 3).[4]

In connection with these topics, we present herein three subjects: (i) a new practical preparation of relevant (*Z*)-ketene silyl thioacetals (KSTAs), (ii) that of alkyl (1*Z*)- or (1*Z*,3*E*)-1,3-bis(TMS)-dienol ethers, (iii) full details of NaOH-catalyzed crossed-Claisen condensation,[4] and (iv) titanium-mediated Claisen–aldol tandem reactions of the obtained β-ketoester analogues.



Scheme 1. Base-catalyzed preparation of enol silyl ethers from ketones and aldehydes.



Scheme 2. Practical and robust method for preparing (*E*)-KSAs and *tert*-butyl (1*Z*,3*E*)-1,3-bis(TMS)dienol ethers.

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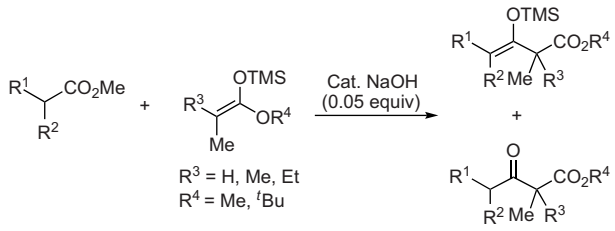


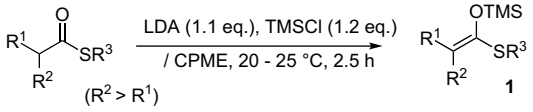
Scheme 3. NaOH-catalyzed crossed-Claisen condensation of KSAs with simple methyl esters.

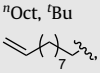
2. Results and discussion

2.1. Practical and robust preparation of ketene silyl thioacetals (KSTAs)

KSTAs **1** are relevant isosteres of KSAs. Since parent carboxylic thioesters have several characteristic features compared with the corresponding esters due to mild reactivity and specific useful functionalization,[5] practical preparations of **1** are therefore desirable for natural product synthesis and process chemistry. Initially, we examined the reaction using *S*-*tert*-butyl thioesters to prepare KSTA **1a**–**e** following the standard procedure for preparing KSAs under identical conditions [LDA, TMSCl, CPME (cyclopentyl methyl ether) solvent,[6] 0–25 °C].[3] As expected, the desired reaction proceeded smoothly to give **1a**–**e** (Table 1, entries 1–5). Further favorable features are as follows. (i) *n*-Octyl and phenyl thioester substrates could be used with the present method (entries 6–14); undesirable side *self*-Claisen condensation between two thioesters was sufficiently suppressed, in clear contrast to the case of methyl, ethyl, and phenyl esters. (ii) Consistent *Z*-stereoselectivity was obtained in every case examined, especially for the substrates bearing bulky R^2 group. (iii) In the case of α,α-disubstituted substrates, a couple of practical purification procedures, distillation, and column chromatography using Florisil® were applicable.

Table 1
Stereoselective preparation of (*Z*)-KSTAs **1**



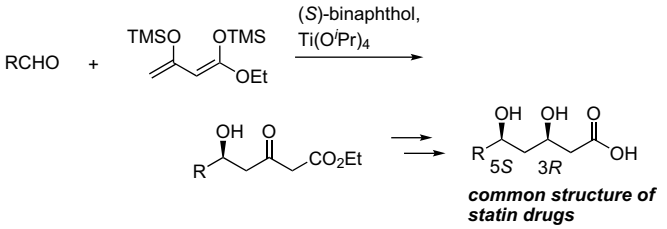
Entry	R^1, R^2, R^3	Product	Yield[a]/%		*Z*/*E*[b]
			Distillation	Florisil®	
1	H, Me, ^{t}Bu	**1a**	78		89:11
2	H, ^{n}Bu, ^{t}Bu	**1b**	70		97:3
3	H, ^{n}Oct, ^{t}Bu	**1c**	73		93:7
4	H,  , ^{t}Bu	**1d**	78		88:12
5	Me, Me, ^{t}Bu	**1e**	78		—
6	H, Me, ^{n}Oct	**1f**	85		93:7
7	H, ^{n}Bu, ^{n}Oct	**1g**	74		73:27
8	H, ^{i}Pr, ^{n}Oct	**1h**	80		98:2
9	H, Allyl, ^{n}Oct	**1i**	74		—[c]
10	Me, Me, Ph	**1j**	77	73	—
11	Me, Me, ^{n}Oct	**1k**	86	85	—
12	–$(CH_2)_5$–, ^{n}Oct	**1l**	79	74	—
13	Et, ^{n}Bu, ^{n}Oct	**1m**	68	73	—[c]
14	Me, OTBS ^{n}Oct	**1n**		94	99:1

[a] Isolated.
[b] Determined by ^{1}H NMR of the crude product.
[c] Not determined.

2.2. Practical and robust preparation of alkyl (1*Z*)- and (1*Z*,3*E*)-1,3-bis(TMS)dienol ethers

β-Ketoester-derived 1,3-bis(TMS)-dienol ethers **3** are useful and attractive KSA derivatives. Extensive studies by Langer's group revealed the utility of various 1,3-bis(TMS)dienol ethers of β-dicarbonyl compounds. The impressive progress in this area was reviewed:[7] precursors for Mukaiyama aldol reaction,[8] cyclopentannulation,[9] benzannulation,[10] oxabicyclo[3.2.1]octan-3-one formation,[11] tetrahydrofuran formation,[12] furanone formation,[13] Michael addition,[14] [4+2]- or [3+3]-cycloaddition,[15] Claisen-type reactions,[16] etc.[17]

As depicted in Scheme 4, Soriente's group disclosed a notable Ti(O^iPr)$_4$-BINOL-catalyzed asymmetric aldol addition of **3a** to aldedydes,[18] which is a promising candidate for the process route to synthesize the key common component of HMG-CoA reductase inhibitors (statin drugs)[19] such as pravastatin, simvastatin, atorvastatin, and pitavastatin.



Scheme 4. Synthesis of statin drugs utilizing asymmetric aldol addition using alkyl (1*Z*)-1,3-bis(TMS)dienol ethers as the key step.

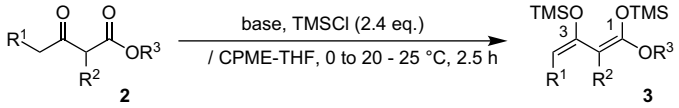
The most general method for preparing **3** involves a two-step sequence: TMSCl–Et_3N and TMSCl–LDA at −78 °C.[10,20] Although our previous method (Scheme 2) involved the use of *tert*-butyl β-ketoesters, we reinvestigated the possibility of using other, more accessible *alkyl* (Me and ^{i}Pr) β-ketoesters **2**. This objective is based on the conventional Weiler's protocol for dianion generation using **2**,[21] which can be performed at a practical temperature (0–5 °C); initial monoanion formation of the active methylene position suppresses the side *self*-Claisen condensation between β-ketoesters **2** due to intermolecular anion–anion repulsion. As anticipated, the desired *methyl* and *isopropyl* (1*Z*)-1,3-bis(TMS)-KSAs **3** were successfully produced from **2**; Table 2 lists the successful results. The salient features are as follows. (i) Two methods, A (2 equiv of NaHMDS) and B (each 1 equiv of NaH and NaHMDS), are available. (ii) Both methods were performed under practical conditions (CPME solvent,[6] 0–25 °C). (iii) The more cost-effective method B produced a slightly better yield than method A in every case examined. (iv) The reaction using methyl and isopropyl 3-oxopentanoates was slightly less 1*Z*-selective (entries 1–3) than that using the *tert*-butyl analogue. (v) Consistent and excellent 1*Z*/3*E*-stereoselectivity was obtained in the case of R^1-substituted 1,3-bis(TMS)-KSAs **3d**–**3i** (entries 4–9). (vi) R^1-, R^2-Disubstituted KSA **3j** also exhibited an excellent 1*Z*/3*E* ratio (>99:1) based on the chemical shift data of **3g** and NOESY measurement (entry 10). (vii) The plausible mechanism for 1*Z*/3*E*-stereoselectivity is consistent with the reported speculation.[3] (viii) Several trials to prepare 1,3-bis(TMS)-KSTAs, however, failed.

Thus, the present simple, practical, and robust method will provide an easy access for preparing various (1*Z*)- and (1*Z*/3*E*)-1,3-bis(TMS)-KSAs **3**.

2.3. NaOH-catalyzed crossed-Claisen condensation between ketene silyl acetals (KSAs) and methyl esters

Our longstanding interests in Ti(Zr)-Claisen condensations[22] prompted us to investigate *catalytic* crossed-Claisen condensations.[23] This section describes full details of a previous

Table 2
Stereoselective preparation of (1*Z*)- and (1*Z*,3*E*)-1,3-bis(TMS)dienol



Entry	R^1, R^2, R^3	Product	Method A[a]			Method B[b]		
			Yield[c]/%	1*Z*/1*E*[d]	1*Z*, 3*E*/1*Z*, 3*Z*[d]	Yield[c]/%	1*Z*/1*E*[d]	1*Z*, 3*E*/1*Z*, 3*Z*[d]
1	H, H, Me	**3a**	60	90:10		69	91:9	
2	H, H, ^{i}Pr	**3b**				85	94:6	
3	H, H, ^{t}Bu	**3c**	76	>99:1[e]		87	>99:1	
4	Me, H, Me	**3d**	75		>99:1	91		93:7
5	Me, H, ^{i}Pr	**3e**				92		93:7
6	Me, H, ^{t}Bu	**3f**	90		96:4[e]	94		>99:1
7	Et, H, Me	**3g**				81		>99:1
8	 , H, Me	**3h**	71		63:37	68		91:9
9	^{i}Pr, H, Me	**3i**	72		>99:1	78		>99:1
10	Et, Et, Me	**3j**			>99:1[f]	88		>99:1

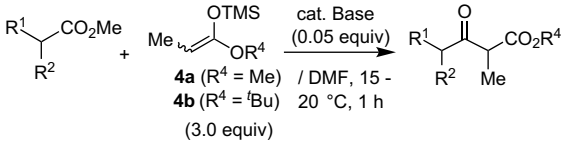
[a] NaHMDS (2.8 equiv) was used as the base.
[b] NaH (1.4 equiv) and NaHMDS (1.4 equiv) were used as the base.
[c] Isolated.
[d] Determined by ^{1}H NMR of the crude product.
[e] Reported data.[3]
[f] Not determined.

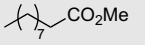
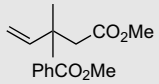
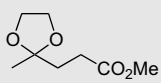
communication of NaOH-catalyzed crossed-Claisen condensation using KSAs[4] and a new extension on the reaction using an α-TBSO-substituted KSA.

The major problem of the traditional Claisen condensation lies in the difficulty in controlling the direction of the reaction; the reaction of a mixture of two different esters, each of which possesses α-hydrogens, generally affords all four products. This crucial issue was resolved by Ti-crossed-Claisen condensations between methyl esters and acid chlorides,[22c,d,f] and between KSAs and acid chlorides.[22e,23] As depicted in Scheme 3, the present NaOH-catalyzed crossed-Claisen condensation using KSAs derived from both α-monomethyl and α,α-disubstituted esters afforded a variety of the corresponding β-ketoesters.

The initial base screening was guided by the reaction of KSA **4a** with methyl decanoate (Table 3). Among alkali metal hydroxides (MOH, M=Li, Na, K; 0.05 equiv), NaOH had the best result. In contrast, no reaction proceeded using K_2CO_3 and TBAF (entries 1 and 2). The use of the KSA **4b** derived from *tert*-butyl propanoate increased the yield (entry 3), because the undesirable self-Claisen condensation was sufficiently circumvented. Thus, the reaction using **4b** with some methyl esters proceeded in moderate to good yields (entries 3–6).

Table 3
Crossed-Claisen condensation between methyl esters and KSAs **4a** and **4b** derived from methyl and *tert*-butyl propanoates



Entry	Ester	KSA	Base	Yield[a] /%
1		**4a**	LiOH, KOH, K_2CO_3, TBAF,	Trace
2		**4a**	NaOH	48
3		**4b**	NaOH	64
4		**4b**	NaOH	58
5	$PhCO_2Me$	**4b**	NaOH	61
6		**4b**	NaOH	57

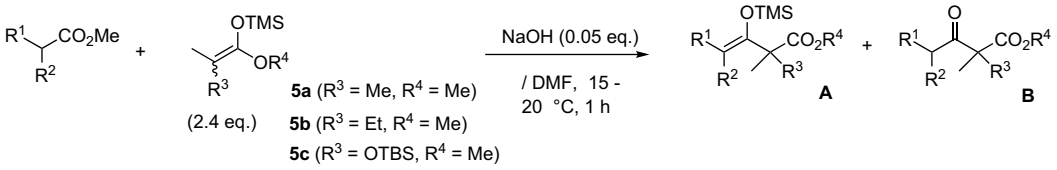
[a] Isolated.

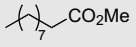
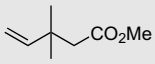
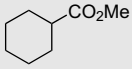
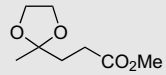
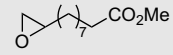
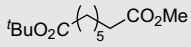
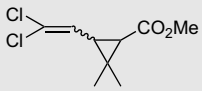
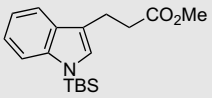
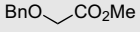
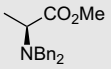
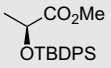
Next, we focused our attention on the reaction of KSAs **5** derived from α,α-disubstituted esters. The retro-Claisen condensation of α,α-disubstituted β-ketoesters usually predominates, because the reversible equilibrium barely shifts from the parent esters to β-ketoesters due to the fact that β-ketoesters lack the ability to force the formation of the stable β-ketoester enolate.

To overcome this problem, we examined the reaction between KSAs **5a**–**c** derived from α,α-dialkylated esters and methyl esters. Table 4 lists the successful results for the preparation of a variety of inaccessible β-ketoesters **6**–**17**. The salient features are as follows. (i) Surprisingly, the crossed-Claisen condensation using KSAs **5a**–**c**, which looked like less reactive nucleophiles than KSAs **4a**, **b**, proceeded smoothly and the yields were good to excellent in every case examined. (ii) As an apparent tendency, the reaction using linear esters (R^2=H) predominantly gave silyl enolates **A** of the parent β-ketoesters **B**, whereas that of branched esters (R^1 and $R^2 \neq$H) exclusively afforded **B**. (iii) Silyl enolates **A** was easily converted to **B** on treatment with TBAF or aqueous 1 M HCl. (iv) Several functionalities, such as an acetal, an epoxide, a *tert*-butyl ester, a cyclopropane, and an indole, and a benzyloxy, tolerated the reaction conditions (entries 12–20). (v) Feature (ii) ensures that the use of optically active methyl lactate and alanine methyl ester analogs will not racemize during the reaction, because the sp^3 stereogenic center will be maintained. Indeed, two optically active substrates underwent the reaction without racemization (entries 23 and 24).

Scheme 5 shows a plausible reaction mechanism (catalytic cycle) as exemplified by the reaction between KSA **5a** and α-unsubstituted linear methyl ester **18**. First, the ester enolate **19** generated by HO^- condenses with **18** to give the β-ketoester **20** with the elimination of MeO^-. Next, MeO^- attacks **5a** to give **19**, which in turn condenses with **20** to give ketone enolate **21**. Ketone enolate **21** receives the TMS group from **5a** to give the desired TMS enolate **22** by reforming **19**. Thus, more than 2 equiv of KSA was required to complete the reaction.

Table 4
NaOH-catalyzed crossed-Claisen condensation between methyl esters and KSAs **4**



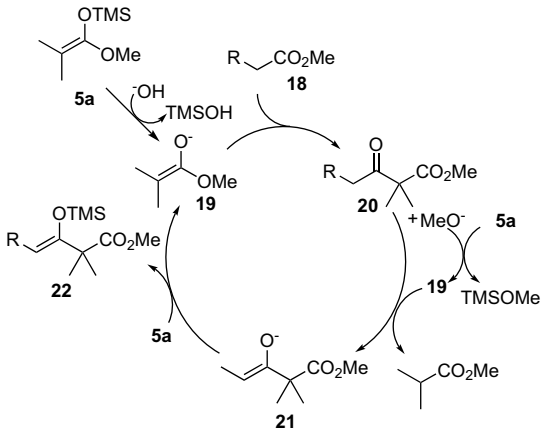
Entry	Ester	KSA	Yield[a]/%	Product (**A**/**B**)
1		**5a**	99	**6a** (82:18)
2		**5b**	98	**6b** (92:8)
3[b]		**5c**	89	**6c** (1:>99)
4		**5a**	88	**7a** (59:41)
5		**5b**	87	**7b** (93:7)
6[b]		**5c**	76	**7c** (1:>99)
7	$PhCO_2Me$	**5a**	85[c]	**8a** —
8		**5b**	94[c]	**8b** —
9		**5a**	83	**9a** (1:>99)
10		**5b**	82	**9b** (1:>99)
11[b]		**5c**	71	**9c** (1:>99)
12		**5a**	88[d]	**10a** (77:23)
13		**5b**	91[d]	**10b** (86:14)
14[b]		**5c**	76	**10c** (>99:1)
15		**5a**	83	**11a** (42:58)
16		**5b**	92	**11b** (27:73)
17		**5a**	85	**12a** (51:49)
18		**5b**	90	**12b** (54:46)
19		**5a**	89	**13a** (1:>99)
20		**5b**	88	**13b** (1:>99)
21		**5a**	67[e]	**14**
22		**5a**	83	**15** (98:2)
23		**5a**	85[f,g]	**16** (1:>99)
24		**5a**	89[f,h]	**17** (1:>99)

[a] Isolated.
[b] KSA (3.0 equiv), NMP solvent, 20–25 °C, 3 h.
[c] KSA (1.2 equiv). TBAF was added to the crude product to deprotect TMS and TBS groups.
[d] Reaction time is 3 h.
[e] Because the products **A** and **B** were not separable, the mixture was treated with 1 M HCl to convert **A** to **B**.
[f] Reaction temperature is 0–5 °C.
[g] 97% ee by HPLC analysis.
[h] 95% ee by HPLC analysis.

2.4. Titanium-mediated aldol reactions of newly produced β-ketoesters and their TMS enolates

For further useful functionalization of both the obtained α,α-dialkylated β-ketoesters **B** and their TMS enolates **A** in Table 4, Mukaiyama aldol reaction using **A** (method A) and Ti-direct aldol reaction[24] using **B** (method B) were performed. Table 5 lists these successful results. All six reactions smoothly proceeded to give the desired adducts **23**–**25**; R^1=octyl substrate predominantly gave *syn* aldol adducts (entries 1–4), whereas R^1=benzyloxy substrate gave *anti* aldol adducts (entries 5 and 6). This stereoselectivity were significantly enhanced by the Ti-direct method using hexanal (entries 3 and 4). Scheme 6 depicts our *syn* and *anti* switch proposal that the *syn* mechanism utilizes the conventional six-membered chair transition state in the case of **6a**, whereas the *anti* mechanism utilizes a benzoyloxy-coordination boat mechanism in the case of **15a**.[25]

In conclusion, we developed (i) practical preparations of ketene silyl thioacetals (KSTAs) and alkyl (1*Z*)- or (1*Z*,3*E*)-1,3-bis(TMS)dienol ethers, (ii) a mild, catalytic, practical NaOH-catalyzed crossed-Claisen condensation giving a variety of β-ketoesters, and (iii) further functionalization utilizing two Ti-aldol reactions. These studies will provide new useful protocols for organic synthesis.



Scheme 5. Proposed reaction mechanism of NaOH-catalyzed crossed-Claisen condensation.

3. Experimental

3.1. General

NMR spectra were recorded on a JEOL DELTA300 spectrometer, operating at 300 MHz for ^{1}H NMR and 75 MHz for ^{13}C NMR. Chemical shift (δ ppm) were reported downfield from tetramethylsilane (0 ppm) for ^{1}H NMR and were reported in the scale relative to $CDCl_3$ (77.00 ppm) for ^{13}C NMR. IR spectra were recorded on JASCO FT/IR-8000 and/or FT/IR-5300 spectrophotometer. Mass spectra were measured on a JEOL JMS-T100LC spectrometer.

3.1.1. 1-tert-Butylthio-1-(trimethylsiloxy)propene (**1a**)[26]

BuLi (1.58 M in hexane, 10.4 mL, 16.5 mmol) was added to a stirred solution of ^{i}Pr$_2$NH (2.53 mL, 18.0 mmol) in cyclopentyl methyl ether (CPME) (11 mL) at 0–5 °C under an Ar atmosphere, followed by being stirred at the same temperature for 0.5 h. *S-tert*-Butyl propanethioate (2.19 g, 15 mmol) in CPME (4 mL) was added to the mixture at the same temperature for 6 min, followed by being stirred for 0.5 h. TMSCl (2.28 mL, 18.0 mmol) was added to the mixture for 2 min, followed by being stirred for 0.5 h. Then, the mixture was warmed up to 20–25 °C, followed by being stirred at same temperature for 1.5 h. The reaction mixture was poured into ice-water and hexane, which was extracted with hexane. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by distillation to give the desired product (2.56 g, 78%).

(*Z* Isomer) Colorless oil; bp 47–48 °C/1.5 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (9H, s), 1.37 (9H, s), 1.73 (3H, d, *J*=6.9 Hz), 5.28 (1H, q, *J*=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 14.7, 31.7, 46.7, 115.3, 145.6; IR (neat) 2963, 2922, 1628, 1363, 1254, 1168, 1140, 1113, 1067, 943, 874, 758 cm^{-1}.

3.1.2. 1-tert-Butylthio-1-(trimethylsiloxy)-1-hexene (**1b**)[27]

Following the procedure for preparing KSTA **1a**, the reaction of *S-tert*-butyl hexanethioate (7.53 g, 40 mmol) gave the desired product **1b** (7.29 g, 70%).

(*Z* Isomer) Colorless oil; bp 45–48 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (9H, s), 0.89 (3H, t, *J*=6.9 Hz), 1.24–1.38 (4H, m), 1.37 (9H, s), 2.09–2.25 (2H, m), 5.20 (1H, t, *J*=7.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 14.0, 22.3, 28.9, 31.7, 32.2, 46.3, 121.0, 145.0; IR (neat) 2961, 2924, 2861, 1620, 1458, 1251, 1167, 1124, 878, 847 cm^{-1}.

3.1.3. 1-tert-Butylthio-1-(trimethylsiloxy)-1-decene (**1c**)

Following the procedure for preparing KSTA **1a**, the reaction of *S-tert*-butyl decanethioate (9.78 g, 40 mmol) gave the desired product **1e** (9.25 g, 73%).

(*Z* Isomer) Colorless oil; bp 94–97 °C/0.4 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (9H, s), 0.87 (3H, t, *J*=6.5 Hz), 1.16–1.39 (12H, m), 1.36 (9H, s), 2.08–2.23 (2H, m), 5.21 (1H, t, *J*=7.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 14.1, 22.7, 29.2, 29.3, 29.5, 30.0, 31.7, 31.9, 46.3, 121.1, 144.9; IR (neat) 2959, 2924, 2855, 1620, 1458, 1363, 1252, 1125, 874, 845, 756 cm^{-1}.

3.1.4. 1-tert-Butylthio-1-(trimethylsiloxy)-1,10-undecadiene (**1d**)

Following the procedure for preparing KSTA **1a**, the reaction of *S-tert*-butyl 10-undecenethioate (7.70 g, 30 mmol) gave the desired product **1d** (7.69 g, 78%).

(*Z* Isomer) Colorless oil; bp 96–99 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (9H, s), 1.20–1.42 (10H, m), 1.36 (9H, s), 1.93–2.08 (2H, m), 2.09–2.24 (2H, m), 4.84–5.04 (2H, m), 5.20 (1H, t, *J*=7.6 Hz), 5.81 (1H, ddt, *J*=6.5 Hz, 10.3 Hz, 17.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 28.9, 29.1, 29.1, 29.2, 29.3, 29.9, 31.7, 33.8, 46.3, 114.1, 121.0, 139.2, 145.0; IR (neat) 2961, 2926, 2857, 1620, 1252, 1362, 1167, 1126, 909, 872 cm^{-1}.

3.1.5. 1-tert-Butylthio-2-methyl-1-(trimethylsiloxy)propene (**1e**)[28]

Following the procedure for preparing KSTA **1a**, the reaction of *S-tert*-butyl 2-methylpropanethioate (3.58 g, 22.3 mmol) gave the desired product **1e** (3.06 g, 78%).

Colorless oil; bp 63–65 °C/6.8 mmHg. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.19 (9H, s), 1.32 (9H, s), 1.73 (3H, s), 1.88 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.8, 18.8, 22.2, 31.6, 47.4, 126.4, 138.2; IR (neat) 2963, 2861, 1628, 1456, 1363, 1254, 1148, 1055, 901, 864 cm^{-1}.

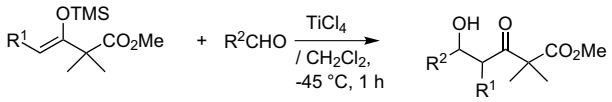
3.1.6. 1-Trimethylsiloxy-1-octylthio-1-propene (**1f**)

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl propanethioate (2.02 g, 10 mmol) gave the desired product **1f** (2.14 g, 85%).

(*Z* Isomer) Colorless oil; bp 58–60 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (9H, s), 0.87 (3H, t, *J*=6.5 Hz), 1.13–1.50 (10H, m), 1.50–1.67 (2H, m), 1.65 (3H, d, *J*=6.9 Hz), 2.64 (2H, t, *J*=7.2 Hz), 4.98 (1H, q, *J*=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ −0.1,

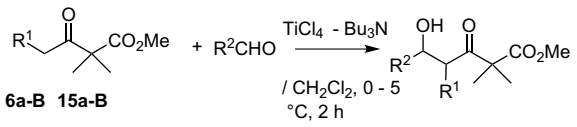
Table 5
Ti-Aldol reactions of crossed-Claisen adduct **A** and **B** with aldehydes[a,b]

Method A (Mukaiyama Aldol Reaction)[a]



6a-A: R^1 = *n*-Oct **15a-A**: R^1 = OBn

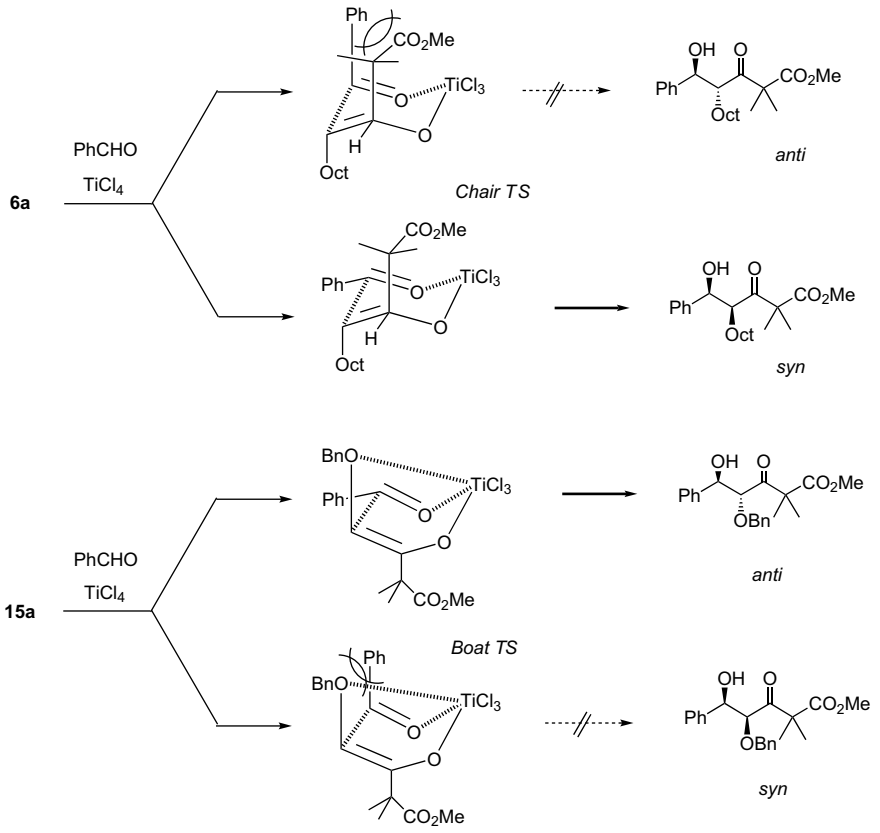
Method B (Ti - Direct Aldol Reaction)[b]



6a-B 15a-B

Entry	R^1	R^2	Method	Product	Yield[c]/%	*syn*/*anti*[d]
1	Octyl[e]	Ph	A	**23**	73	93:7
2			B	**23**	78	93:7
3		Pentyl	A	**24**	80	72:28
4			B	**24**	83	>99:1
5	BnO[f]	Ph	A	**25**	67	25:75
6			B	**25**	80	2:98

[a] Molar ratio; **A**/aldehydes/$TiCl_4$=1.0:1.2:1.2.
[b] Molar ratio ; **9B**/aldehydes/$TiCl_4$/Bu_3N=1.0:1.2:1.2:1.4.
[c] Isolated.
[d] Determined by ^{1}H NMR.
[e] Compound **9A** (*E*/*Z*=1:>99) was used.
[f] Compound **9A** (*E*/*Z*=5:95) was used.



Scheme 6. Proposed mechanism of stereoselective Ti-mediated aldol addition.

13.3, 14.1, 22.6, 28.8, 29.1, 30.1, 30.6, 31.8, 107.9, 145.0; IR (neat) 2959, 2857, 1698, 1636, 1458, 1252, 1159, 1064, 947, 873, 846 cm^{-1}.

*3.1.7. 1-Trimethoxysiloxy-1-octylthio-1-hexene (**1g**)*

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl butanethioate (2.44 g, 10 mmol) gave the desired product **1f** (2.36 g, 74%).

(*Z* Isomer) Colorless oil; bp 81–83 °C/0.2 mmHg; ^1H NMR (300 MHz, $CDCl_3$): δ 0.22 (9H, s), 0.79–0.96 (6H, m), 1.15–1.44 (14H, m), 1.49–1.64 (2H, m), 2.64 (2H, t, *J*=7.2 Hz), 4.97 (1H, t, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.6, 14.0, 14.1, 22.2, 22.4, 22.6, 27.8, 28.8, 29.2, 30.1, 30.7, 31.8, 32.3, 114.2, 144.3; IR (neat) 2957, 2926, 2855, 1624, 1508, 1458, 1252, 874, 847 cm^{-1}.

*3.1.8. 1-Trimethylsiloxy-3-methyl-1-octylthio-1-butene (**1h**)*

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl 3-methylbutanethioate (2.30 g, 10 mmol) gave the desired product **1h** (2.42 g, 80%).

(*Z* Isomer) Colorless oil; bp 79–81 °C/0.2 mmHg; ^1H NMR (300 MHz, $CDCl_3$): δ 0.23 (9H, s), 0.88 (3H, t, *J*=6.9 Hz), 0.96 (6H, d, *J*=9.7 Hz), 1.11–1.43 (10H, m), 1.45–1.64 (2H, m), 2.50 (3H, m), 4.82 (1H, d, *J*=9.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.0, 14.1, 22.6, 23.4, 28.2, 28.7, 29.2, 30.1, 30.6, 31.8, 122.1, 142.6; IR (neat) 2959, 2928, 2857, 1626, 1466, 1419, 1379, 1362, 1252, 1161, 1117, 881, 849, 756 cm^{-1}.

*3.1.9. 1-Trimethoxysiloxy-1-octylthio-1,4-pentadiene (**1i**)*

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl 4-pentenethioate (2.84 g, 10 mmol) gave the desired product **1i** (2.36 g, 74%).

(*Z* Isomer) Colorless oil; bp 71–73 °C/0.1 mmHg; ^1H NMR (300 MHz, $CDCl_3$): δ 0.24 (9H, s), 0.88 (3H, t, *J*=6.9 Hz), 1.11–1.42 (10H, m), 1.44–1.65 (2H, m), 2.53–2.69 (2H, m), 2.72–2.94 (2H, m), 4.86–5.10 (3H, m), 5.66–5.88 (1H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.1, 14.1, 22.6, 28.7, 29.1, 30.1, 30.6, 31.8, 32.4, 43.2, 110.8, 114.2, 137.2, 145.9; IR (neat) 2959, 2928, 2855, 1698, 1638, 1624, 1509, 1458, 1252, 1150, 868, 847 cm^{-1}.

*3.1.10. 2-Methyl-1-trimethylsiloxy-1-phenylthio-1-propene (**1j**)*[29]

Following the procedure for preparing KSTA **1a**, the reaction of *S*-phenyl 2-methylpropanethioate (1.80 g, 10 mmol) gave the desired product **1j** (1.93 g, 77%) by distillation. Florisil® column chromatography (hexane) purification gave **1j** (1.84 g, 73%).

Colorless oil; bp 58–60 °C/0.2 mmHg; ^1H NMR (300 MHz, $CDCl_3$): δ 0.11 (9H, s), 1.18 (3H, s), 1.92 (3H, s), 7.09–7.16 (1H, m), 7.22–7.29 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.4, 18.7, 124.1, 125.2, 127.4, 128.7, 135.3, 135.9.

*3.1.11. 2-Methyl-1-trimethylsiloxy-1-octylthio-1-propene (**1k**)*[22d]

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl 2-methylpropanethioate (1.95 g, 9 mmol) gave the desired product **1k** (2.23 g, 86%) by distillation. Florisil® column chromatography (hexane) purification gave **1k** (2.21 g, 85%).

Colorless oil; bp 58–60 °C/0.2 mmHg; ^1H NMR (300 MHz, $CDCl_3$): δ 0.22 (9H, s), 0.88 (3H, t, *J*=6.5 Hz), 1.08–1.43 (10H, m), 1.47–1.59 (2H, m), 1.68 (3H, s), 1.83 (3H, s), 2.60 (2H, t, *J*=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.4, 14.0, 18.6, 20.9, 22.7, 28.7, 29.2, 29.7, 31.7, 31.8, 120.2.

*3.1.12. 1-Trimethylsiloxy-1-octylthiomethylenecyclohexane (**1l**)*

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl cyclohexanethiocarboxylate (1.80 g, 7 mmol) gave the desired product **1l** (1.82 g, 79%) by distillation. Florisil® column chromatography (hexane) purification gave **1l** (1.70 g, 74%).

Colorless oil; bp 66–68 °C/0.2 mmHg; ^1H NMR (300 MHz, $CDCl_3$): δ 0.22 (9H, s), 0.88 (3H, t, *J*=6.9 Hz), 1.17–1.42 (10H, m), 1.42–1.58 (2H, m), 2.16–2.25 (2H, m), 2.31–2.40 (2H, m), 2.61 (2H, t,

J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 14.1, 22.6, 26.7, 28.0, 28.5, 28.7, 29.2, 31.4, 31.6, 31.8, 128.4; IR (neat) 2926, 2855, 1630, 1449, 1252, 1130, 1091, 918, 846 cm^{-1}.

*3.1.13. 2-Ethyl-1-trimethylsiloxy-1-octylthio-1-hexene (**1m**)*

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl 2-ethylhexanethioate (2.72 g, 10 mmol) gave the desired product **1m** (2.52 g, 73%) by distillation. Florisil® column chromatography (hexane) purification gave **1m** (2.34 g, 68%).

Colorless oil; bp 87–89 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.23 (9H, s), 0.79–1.00 (9H, m), 1.16–1.42 (14H, m), 1.47–1.61 (2H, m), 2.01–2.15 (2H, m), 2.16–2.30 (2H, m), 2.61 (2H, t, J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 12.5, 13.8, 14.1, 22.7, 22.9, 25.4, 28.8, 29.2, 29.3, 30.1, 31.2, 31.5, 31.7, 31.9, 130.8; IR (neat) 2959, 2928, 2856, 1686, 1624, 1458, 1252, 1150, 1092, 882, 845 cm^{-1}.

*3.1.14. 2-(tert-Butyldimethylsiloxy)-1-trimethylsiloxy-1-octylthio-1-propene (**1n**)*

Following the procedure for preparing KSTA **1a**, the reaction of *S*-octyl 2-(*tert*-butyldimethylsiloxy)propanethioate (665 mg, 2 mmol) gave the desired product **1n** (762 mg, 94%) by Florisil® column chromatography (hexane).

(*Z* Isomer) Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.15 (6H, s), 0.22 (9H, s), 0.88 (3H, t, J=6.9 Hz), 0.96 (9H, s), 1.16–1.43 (10H, m) 1.46–1.62 (2H, m), 1.85 (3H, s), 2.62 (2H, t, J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ −4.0, 0.4, 1.6, 14.1, 18.1, 22.6, 25.9, 28.9, 29.2, 29.7, 31.7, 31.8, 129.8, 140.7; IR (neat) 2928, 2856, 1686, 1464, 1372, 1252, 1154, 833 cm^{-1}.

3.2. General procedure for the preparation of β-ketoester-derived 1,3-bis(TMS)-dienol ethers 3

3.2.1. Method A of Table 2

A β-ketoester (10.0 mmol) was added to a stirred suspension of NaH (14.0 mmol) in CPME (50 mL) at 0–5 °C under an Ar atmosphere, followed by being stirred at the same temperature for 0.5 h. After evolution of H_2 gas ceased, NaHMDS (1.9 M in THF, 7.4 mL, 14 mmol) was added to the mixture for 5–8 min, followed by being stirred at the same temperature for 0.5 h. TMSCl (3.0 mL, 24.0 mmol) was added to the mixture for 5–8 min., followed by being stirred for 0.5 h. Then, the mixture was warmed up to 20–25 °C, followed by being stirred at same temperature for 1.5 h. The reaction mixture was poured into ice-water and hexane, which was extracted with hexane. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by distillation to give the desired product.

3.2.2. Method B of Table 2

A β-ketoester (10.0 mmol) was added to a stirred solution of NaHMDS (1.9 M in THF, 14.7 mL, 28.0 mmol) in CPME (20 mL) at 0–5 °C under an Ar atmosphere, followed by being stirred at same temperature for 0.5 h. TMSCl (3,0 mL, 24.0 mmol) was added to the mixture for 5–8 min, followed by being stirred for 0.5 h. Then, the mixture was warmed up to 20–25 °C, followed by being stirred at same temperature for 1.5 h. The reaction mixture was poured into ice-water and hexane, which was extracted with hexane. The organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The obtained crude oil was purified by distillation to give the desired product.

(*Note*: after finishing this work, hexane or heptane solvent instead of CPME was found to be available.)

*3.2.3. 1,3-Bis(trimethylsiloxy)-1-methoxybuta-1,3-diene (**3a**)*

[Method A] The reaction of methyl 3-oxobutanoate (1.16 g, 10 mmol) gave the desired product **1** (1.56 g, 60%). [Method B] (1.79 g, 69%).

Colorless oil; bp 43–45 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.21 (9H, s), 0.24 (9H, s), 3.55 (3H, s), 3.94 (1H, d, J=1.4 Hz), 4.14 (1H, d, J=1.4 Hz), 4.47 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.2, 0.4, 54.9, 77.57, 89.2, 153.4, 158.6; IR (neat) 2964, 1708, 1652, 1444, 1388, 1252, 1196, 1093 cm^{-1}.

*3.2.4. 1,3-Bis(trimethylsiloxy)-1-isopropoxybuta-1,3-diene (**3b**)*

[Method B] The reaction of isopropyl 3-oxobutanoate (1.44 g, 10 mmol) gave the desired product **3b** (2.45 g, 85%).

Colorless oil; bp 46–47 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.17 (9H, s), 0.25 (9H, s), 1.26 (6H, d, J=6.2 Hz), 3.91 (1H, d, J=1.4 Hz), 4.12 (1H, d, J=1.4 Hz), 4.22 (1H, sep, J=6.2 Hz), 4.47 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.2, 0.6, 21.7, 70.2, 78.6, 88.9, 153.6, 156.1; IR (neat) 2978, 2961, 1716, 1649, 1385, 1252, 1221, 1188, 1113, 1064, 1014, 922, 847 cm^{-1}.

*3.2.5. 1,3-Bis(trimethylsiloxy)-1-tert-butoxybuta-1,3-diene (**3c**)*[3]

[Method A] Ref. 3. [Method B] The reaction of methyl 3-oxobutanoate (1.58 g, 10 mmol) gave the desired product **3c** (2.63 g, 87%).

Colorless oil; bp 65–67 °C/0.5 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.15 (9H, s), 0.21 (9H, s), 1.38 (9H, s), 4.21 (1H, d, J=1.0 Hz), 4.25 (1H, d, J=1.0 Hz), 4.54 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.2, 0.6, 28.7, 79.0, 85.9, 103.4, 146.3, 152.4; IR (neat) 2978, 2912, 1657, 1612, 1368, 1300, 1254, 1136, 1107, 1053, 939, 908, 852 cm^{-1}.

*3.2.6. 1,3-Bis(trimethylsiloxy)-1-methoxypenta-1,3-diene (**3d**)*

[Method A] The reaction of methyl 3-oxopentanoate (1.30 g, 10 mmol) gave the desired product **3** (2.06 g, 75%). [Method B] (2.50 g, 91%).

Colorless oil; bp 78–80 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (9H, s), 0.17 (9H, s), 1.50 (3H, d, J=6.9 Hz), 3.58 (3H, s), 4.04 (1H, s), 4.64 (1H, q, J=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.4, 0.6, 12.8, 55.0, 73.7, 102.7, 126.9, 146.1, 157.6; IR (neat) 2959, 1665, 1252, 1219, 1088, 978, 845 cm^{-1}.

*3.2.7. 1,3-Bis(trimethylsiloxy)-1-isopropoxypenta-1,3-diene (**3e**)*

[Method B] The reaction of isopropyl 3-oxopentanoate (1.58 g, 10 mmol) gave the desired product **3e** (2.78 g, 92%).

Colorless oil; bp 80–82 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.15 (9H, s), 0.21 (9H, s), 1.28 (6H, d, J=6.2 Hz), 1.49 (3H, d, J=6.9 Hz), 4.02 (1H, s), 4.26 (1H, sep, J=6.2 Hz), 4.62 (1H, q, J=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.4, 0.8, 12.8, 21.7, 70.0, 74.9, 102.5, 146.4, 154.9; IR (neat) 2963, 2912, 1655, 1373, 1309, 1252, 1217, 1159, 1107, 1065, 920, 845 cm^{-1}.

*3.2.8. 1,3-Bis(trimethylsiloxy)-1-tert-butoxypenta-1,3-diene (**3f**)*

[Method A] Ref. 3. [Method B] The reaction of *tert*-butyl 3-oxopentanoate (1.72 g, 10 mmol) gave the desired product **3** (2.98 g, 94%).

Colorless oil; bp 56–57 °C/0.3 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.15 (9H, s), 0.21 (9H, s), 1.38 (9H, s), 1.50 (3H, d, J=6.9 Hz), 4.41 (1H, s), 4.63 (1H, t, J=6.9 Hz), 4.62 (1H, q, J=6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.4, 0.7, 12.7, 28.6, 79.0, 85.9, 103.4, 146.3, 152.4; IR (neat) 2978, 2912, 1657, 1368, 1300, 1254, 1136, 1107, 1053, 939, 908, 852 cm^{-1}.

*3.2.9. 1,3-Bis(trimethylsiloxy)-1-methoxy hexa-1,3-diene (**3g**)*

[Method B] The reaction of methyl 3-oxohexanoate (1.44 g, 10 mmol) gave the desired product **3** (2.34 g, 81%).

Colorless oil; bp 45–46 °C/0.2 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (9H, s), 0.21 (9H, s), 0.94 (3H, t, J=7.6 Hz), 1.92 (2H, quin, J=7.6 Hz), 3.57 (3H, s), 4.06 (1H, s), 4.57 (1H, t, J=7.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 0.6, 14.8, 20.8, 55.0, 73.8, 110.9, 144.8, 157.6; IR (neat) 2961, 2908, 1718, 1655, 1387, 1252, 1221, 1165, 1127, 1092, 982, 920, 847, 760 cm^{-1}.

*3.2.10. 1,3-Bis(trimethylsiloxy)-1-methoxy-trideca-1,3,12-triene (**3h**)*

[Method A] The reaction of methyl 3-oxodec-12-enoate (2.40 g, 10 mmol) gave the desired product **3h** (2.73 g, 71%). [Method B] (2.59 g, 68%).

Colorless oil; bp 87–89 °C/0.1 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (9H, s), 0.18 (9H, s), 1.11–1.55 (10H, m), 1.78–2.13 (4H, m), 3.56 (3H, ×7/10, s), 3.68 (3H, ×3/10, s), 4.07 (1H, s), 4.57 (1H, ×7/10, d, J=7.6 Hz), 4.81, (1H, −3/10, d, J=7.6 Hz) 4.83–5.05 (2H, m), 5.80 (1H, ddt, J=6.9, 10.3, 16.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.2, 0.3, 0.6, 27.1, 27.4, 28.9, 29.1, 29.2, 29.3, 29.4, 30.2, 33.8, 51.8, 55.0, 73.9, 76.6, 77.0, 77.4, 109.0, 110.9, 114.1, 139.1, 139.2, 144.2, 145.2, 157.5; IR (neat) 2926, 2855, 1655, 1252, 1211, 1091, 978, 849 cm^{-1}.

*3.2.11. 1,3-Bis(trimethylsiloxy)-1-methoxy-5-methylhexa-1,3-diene (**3i**)*

[Method A] The reaction of methyl 5-methyl-3-oxohexanoate (1.58 g, 10 mmol) gave the desired product **3i** (2.18 g, 72%). [Method B] (2.36 g, 78%).

Colorless oil; bp 63–69 °C/0.1 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.16 (9H, s), 0.22 (9H, s), 0.94 (6H, d, J=6.5 Hz), 2.21–2.46 (1H, m), 3.56 (3H, s), 4.10 (1H, s), 4.42 (1H, d, J=9.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.3, 0.7, 23.6, 26.9, 55.0, 73.7, 117.1, 143.6, 157.5; IR (neat) 2959, 2869, 1665, 1252, 1208, 1088, 978, 845 cm^{-1}.

*3.2.12. 1,3-Bis(trimethylsiloxy)-1-methoxy-2-ethylhexa-1,3-diene (**3j**)*

[Method B] The reaction of methyl 2-ethyl-3-oxohexanoate (2.40 g, 10 mmol) gave the desired product **3i** (2.79 g, 88%).

Colorless oil; bp 63–69 °C/0.1 mmHg; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.14 (9H, s), 0.21 (9H, s), 0.94 (3H, t, J=7.2 Hz), 0.95 (3H, t, J=7.6 Hz), 2.05 (2H, q, J=7.2 Hz), 2.06 (2H, quin, J=7.6 Hz), 3.52 (3H, s), 4.57 (1H, t, J=7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 0.2, 0.4, 13.8, 14.4, 18.9, 20.9, 56.2, 102.2, 114.0, 145.3, 151.0; IR (neat) 2963, 2934, 2903, 2874, 1655, 1252, 1211, 1173, 1115, 1084, 1046, 961, 920, 845, 666 cm^{-1}.

*3.2.13. Methyl 2,2-dimethyl-3-(trimethylsiloxy)dodec-3-enoate (**6a-A**) and methyl 2,2-dimethyl-3-oxododecanoate (**6a-B**)*

1-Methoxy-1-trimethylsiloxy-2-methyl-1-propene (**5a**, 418 mg, 2.4 mmol) was added to a stirred solution of methyl decanoate (186 mg, 1.0 mmol) and NaOH (2 mg, 0.05 mmol) in DMF (0.2 mL) at 20–25 °C under an Ar atmosphere, followed by being stirred at the same temperature for 1 h. The mixture was quenched with water, which was extracted twice with ether. The combined organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by SiO_2 column chromatography (hexane/AcOEt=80:1) to give the desired products **6a-A** (267 mg, 81%) and **6a-B** (46 mg, 18%).

*Compound **6a-A***. Colorless oil; ^{1}H NMR: δ 0.17 (9H, s), 0.88 (3H, t, J=6.9 Hz), 1.21–1.36 (12H, m), 1.30 (6H, s), 1.97 (2H, q, J=6.9 Hz), 3.66 (3H, s), 4.60 (1H, t, J=6.9 Hz); ^{13}C NMR: δ 0.8, 14.1, 22.7, 24.4, 26.1, 29.3, 29.4, 29.5, 29.7, 31.8, 48.4, 51.9, 106.6, 152.6, 176.5; IR (neat) 2924, 2857, 1740, 1667, 1252, 1153, 845 cm^{-1}.

*Compound **6a-B***. Colorless oil; ^{1}H NMR: δ 0.88 (3H, t, J=6.9 Hz), 1.14–1.32 (12H, m), 1.36 (6H, s), 1.52–1.61 (2H, m), 2.43 (2H, t, J=7.2 Hz), 3.72 (3H, s); ^{13}C NMR: δ 14.1, 20.3, 21.9, 22.6, 23.8, 29.1, 29.3, 29.4, 31.85, 37.9, 52.4, 55.6, 174.3, 208.1; IR (neat) 2921, 2857, 1747, 1716, 1466, 1267, 1150 cm^{-1}.

*3.2.14. Methyl 2-ethyl-2-methyl-3-(trimethylsiloxy)dodec-3-enoate (**6b-A**) and methyl 2-ethyl-2-methyl-3-oxododecanoate (**6b-B**)*

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl decanoate (186 mg, 1.0 mmol) and 1-methoxy-1-trimethylsiloxy-2-methyl-1-butene (**5b**, 452 mg, 2.4 mmol) gave the desired products **6b-A** (309 mg, 90%) and **6b-B** (21 mg, 8%).

*Compound **6b-A***. colorless oil; ^{1}H NMR: δ 0.16 (9H, s), 0.80 (3H, t, J=7.6 Hz), 0.88 (3H, t, J=6.9 Hz), 1.23–1.35 (12H, m), 1.24 (3H, s), 1.71 (1H, dq, J=7.6, 13.4 Hz), 1.78 (1H, dq, J=7.6, 13.4 Hz), 1.88–2.07 (2H, m), 3.65 (3H, s), 4.56 (1H, t, J=6.9 Hz); ^{13}C NMR: δ 0.9, 8.8, 14.1, 20.5, 22.7, 26.1, 28.7, 29.3, 29.4, 29.5, 29.8, 31.9, 51.7, 52.5, 107.5, 151.4, 176.1.; IR (neat) 2926, 2855, 1738, 1665, 1252, 1148, 1125, 1103, 847 cm^{-1}.

*Compound **6b-B***. Colorless oil; ^{1}H NMR: δ 0.82 (3H, t, J=7.6 Hz), 0.88 (3H, t, J=6.9 Hz), 1.21–1.28 (12H, m), 1.31 (3H, s), 1.53–1.61 (2H, m), 1.80 (1H, dq, J=7.6, 14.1 Hz), 1.94 (1H, dq, J=7.6, 14.1 Hz), 2.36 (1H, dt, J=6.9, 17.2 Hz), 2.43 (1H, dt, J=6.9, 17.2 Hz), 3.72 (3H, s); ^{13}C NMR: δ 8.6, 14.1, 18.3, 22.7, 23.8, 27.7, 29.1, 29.3, 29.4, 29.4, 31.9, 38.3, 52.2, 60.0, 173.8, 208.0; IR (neat) 2928, 2856, 1745, 1715, 1460, 1244, 1148 cm^{-1}.

*3.2.15. Methyl 2-hydroxy-2-methyl-3-oxododecanoate (**6c**)*

2-(*tert*-Butyldimethylsiloxy)-1-methoxy-1-(trimethylsiloxy)-1-propene (**5c**, 436 mg, 1.5 mmol) was added to a stirred solution of methyl decanoate (93 mg, 0.5 mmol) and NaOH (1 mg, 0.03 mmol) in *N*-methylpyrrolidone (NMP) (0.1 mL) at 20–25 °C under an Ar atmosphere, followed by being stirred for 3 h. Water was added to the mixture, which was extracted with diethyl ether. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. To the obtained crude product in THF (0.5 mL), 1 M TBAF solution in THF (1 mL) was added at 0–5 °C under an Ar atmosphere, followed by being stirred for 1 h. Water was added to the reaction mixture, which was extracted with AcOEt. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica gel column chromatography (hexane/AcOEt=4:1) to give the desired product **6c** (119 mg, 89%).

Colorless oil; ^{1}H NMR: δ 0.87 (3H, t, J=6.9 Hz), 1.17–1.36 (12H, m), 1.52–1.65 (2H, m), 1.59 (3H, s), 2.53 (1H, dt, J=17.9, 7.2 Hz), 2.64 (1H, dt, J=17.9, 7.2 Hz), 3.79 (3H, s), 4.21 (1H, br s); ^{13}C NMR: δ 14.1, 21.9, 22.6, 23.5, 29.0, 29.2, 29.3, 29.4, 31.8, 36.3, 53.2, 80.9, 171.9, 207.2; IR (neat) 3470, 2986, 2926, 2856, 1750, 1456, 1265, 1159 cm^{-1}.

*3.2.16. Methyl 2,2,5,5-tetramethyl-3-(trimethylsiloxy)hept-3,6-dienoate (**7a-A**) and methyl 2,2,5,5-tetramethyl-3-oxohept-6-enoate (**7a-B**)*

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl 3,3-dimethyl-4-pentenoate (142 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired products **7a-A** (147 mg, 52%) and **7a-B** (76 mg, 36%).

*Compound **7a-A***. Colorless oil; ^{1}H NMR: δ 0.16 (9H, s), 1.16 (6H, s), 1.31 (6H, s), 3.66 (3H, s), 4.52 (1H, s), 4.86 (1H, dd, J=1.4, 10.7 Hz), 4.96 (1H, dd, J=1.4, 17.5 Hz), 5.95 (1H, dd, J=10.7, 17.5 Hz); ^{13}C NMR: δ 1.7, 25.2, 28.5, 36.8, 49.0, 52.0, 109.5, 114.1, 147.9, 151.6, 176.6; IR (neat) 2957, 1717, 1468, 1264, 1150 cm^{-1}.

*Compound **7a-B***. Colorless oil; ^{1}H NMR: δ 1.11 (6H, s), 1.32 (6H, s), 2.45 (2H, s), 3.71 (3H, s), 4.90 (1H, dd, J=1.4, 10.7 Hz), 4.93 (1H, dd, J=1.4, 17.5 Hz), 5.91 (1H, dd, J=10.7, 17.5 Hz); ^{13}C NMR: δ 21.9, 26.9, 35.9, 48.7, 52.3, 56.1, 110.4, 147.2, 174.2, 206.1; IR (neat) 2959, 1738, 1655, 1252, 1148, 1121, 845 cm^{-1}.

*3.2.17. Methyl 2-ethyl-2,5,5-trimethyl-3-(timethylsiloxy)hept-3,6-dienoate (**7b-A**) and methyl 2-ethyl-2,5,5-trimethyl-3-oxohept-6-enoate (**7b-B**)*

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl 3,3-dimethyl-4-pentenoate (142 mg, 1.0 mmol) and **5b** (452 mg, 2.4 mmol) gave the desired products **7b-A** (242 mg, 81%) and **7b-B** (14 mg, 6%).

*Compound **7b-A***. Colorless oil; ^{1}H NMR: δ 0.15 (9H, s), 0.80 (3H, t, J=7.6 Hz), 1.16 (3H, s, J=6.9 Hz), 1.67 (3H, s), 1.24 (3H, s), 1.72 (1H, dq, J=7.6, 13.8 Hz), 1.77 (1H, dq, J=7.6, 13.8 Hz), 4.86 (1H, dd, J=1.4, 10.7 Hz), 4.97 (1H, dd, J=1.4, 17.4 Hz), 5.96 (1H, dd, J=10.7, 17.4 Hz);

^{13}C NMR: δ 1.8, 8.5, 21.5, 28.3, 28.7, 28.8, 37.0, 51.8, 52.9, 109.5, 115.6, 148.0, 149.9, 176.3; IR (neat) 2965, 1736, 1651, 1252, 1115, 847 cm^{-1}.

Compound ***7b-B***. Colorless oil; ^{1}H NMR: δ 0.81 (3H, t, *J*=7.6 Hz), 0.87 (3H, t, *J*=6.9 Hz), 1.11 (6H, s), 1.28 (3H, s), 1.75 (1H, dq, *J*=7.6, 13.8 Hz), 1.92 (1H, dq, *J*=7.6, 13.8 Hz), 2.40 (1H, d, *J*=17.6 Hz), 2.48 (1H, dd, *J*=17.6 Hz), 3.71 (3H, s), 4.90 (1H, dd, *J*=1.4, 10.7 Hz), 4.93 (1H, dd, *J*=1.4, 17.5 Hz), 5.92 (1H, dd, *J*=10.7, 17.5 Hz); ^{13}C NMR: δ 8.6, 18.1, 26.9, 27.7, 35.9, 49.2, 52.2, 60.5, 110.4, 147.3, 173.6, 205.9; IR (neat) 2971, 2883, 1716, 1460, 1242, 1150 cm^{-1}.

3.2.18. *Methyl 2-hydroxy-2,5,5-trimethyl-3-oxohept-6-enoate (**7c**)*

Following the procedure for preparing **6c**, the reaction between methyl 3,3-dimethyl-4-pentenoate (71 mg, 0.5 mmol) and **5c** (436 mg, 1.5 mmol) gave the desired product **7c** (81 mg, 76%).

Colorless oil; ^{1}H NMR: δ 1.13 (6H, s), 1.56 (3H, s), 2.56 (1H, d, *J*=17.5 Hz), 2.68 (1H, d, *J*=17.5 Hz), 3.78 (3H, s), 4.20 (1H, br s, OH), 4.93 (1H, dd, *J*=10.7, 1.0 Hz), 4.95 (1H, dd, *J*=17.5, 1.0 Hz), 5.89 (1H, dd, *J*=17.5, 10.7 Hz); ^{13}C NMR: δ 21.8, 26.8, 27.0, 36.0, 47.0, 53.2, 81.3, 110.9, 146.6, 171.8, 205.3; IR (neat) 3478, 2961, 1755, 1732, 1451, 1263, 1163, 1041, 916 cm^{-1}.

3.2.19. *Methyl 2,2-dimethyl-3-oxo-3-phenylpropanoate (**8a**)*

Following the procedure for preparing **6a-B**, the reaction between methyl benzoate (136 mg, 1.0 mmol) and **5a** (214 mg, 1.2 mmol) gave the desired product **8a** (175 mg, 85%).

Colorless oil; ^{1}H NMR: δ 1.55 (6H, s), 3.64 (3H, s), 7.39–7.45 (2H, m), 7.49–7.55 (1H, m), 7.80–7.84 (2H, m); ^{13}C NMR: δ 23.9, 52.5, 53.2, 128.5, 132.7, 135.1, 137.3, 175.6, 197.5; IR (neat) 2996, 2951, 1740, 1686, 1271, 1142, 708 cm^{-1}.

3.2.20. *Methyl 2-ethyl-2-methyl-3-oxo-3-phenylpropanoate (**8b**)*

Following the procedure for preparing **6a-B**, the reaction between methyl benzoate (136 mg, 1.0 mmol) and **5b** (226 mg, 1.2 mmol) gave the desired product **8b** (194 mg, 94%).

Colorless oil; ^{1}H NMR: δ 0.82 (3H, t, *J*=7.6 Hz), 1.51 (3H, s), 2.05 (1H, dq, *J*=7.6, 14.1 Hz), 2.10 (1H, dq, *J*=7.6, 14.1 Hz), 3.63 (3H, s), 7.38–7.44 (2H, m), 7.49–7.54 (1H, m), 7.80–7.84 (2H, m); ^{13}C NMR: δ 8.2, 20.5, 29.3, 52.3, 57.3, 128.4, 128.5, 132.6, 135.7, 174.9, 197.5; IR (neat) 2976, 2951, 1738, 1684, 1449, 1250, 1130, 702 cm^{-1}.

3.2.21. *Methyl 3-cyclohexyl-2,2-dimethyl-3-oxopropanoate (**9a**)*[21]

Following the procedure for preparing **6a-B**, the reaction between methyl cyclohexanoate (142 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired product **9a** (176 mg, 83%).

Colorless oil; ^{1}H NMR: δ 1.17–1.48 (5H, m), 1.35 (6H, s), 1.58–1.79 (5H, m), 2.58 (1H, tt, *J*=3.4, 11.4 Hz), 3.71 (3H, s); ^{13}C NMR: δ 21.7, 25.6, 30.2, 47.4, 52.2, 56.0, 174.3, 211.2; IR (neat) 2936, 1746, 1711, 1453, 1265, 1150, 993 cm^{-1}.

3.2.22. *Methyl 3-cyclohexyl-2-ethyl-2-methyl-3-oxopropanoate (**9b**)*

Following the procedure for preparing **6a-B**, the reaction between methyl cyclohexanoate (142 mg, 1.0 mmol) and **5b** (452 mg, 2.4 mmol) gave the desired product **9b** (186 mg, 82%).

Colorless oil; ^{1}H NMR: δ 0.81 (3H, t, *J*=7.6 Hz), 1.16–1.47 (5H, m), 1.31 (3H, s), 1.58–1.78 (5H, m) 1.76 (1H, dq, *J*=7.6, 14.1 Hz), 1.96 (1H, dq, *J*=7.6, 14.1 Hz), 2.56 (1H, tt, *J*=3.4, 11.4 Hz), 3.71 (3H, s); ^{13}C NMR: δ 8.6, 17.9, 25.6, 27.3, 29.9, 30.4, 47.5, 52.0, 60.4, 173.6, 211.1; IR (neat) 2936, 1744, 1709, 1453, 1244, 1148 cm^{-1}.

3.2.23. *Methyl 3-cyclohexyl-2-hydroxy-2-methyl-3-oxopropanoate (**9c**)*

Following the procedure for preparing **6c**, the reaction between methyl cyclohexanoate (71 mg, 0.5 mmol) and **5c** (436 mg, 1.5 mmol) gave the desired product **9c** (76 mg, 71%).

Yellow oil; ^{1}H NMR: δ 1.12–1.48 (5H, m), 1.51–1.84 (5H, m), 1.58 (3H, s), 2.85 (1H, tt, *J*=11.4, 3.4 Hz), 3.77 (3H, s), 4.24 (1H, br s); ^{13}C NMR: δ 21.8, 25.4, 25.4, 25.5, 29.4, 29.5, 45.0, 53.1, 80.8, 171.8, 210.0; IR (neat) 3474, 2934, 1720, 1450, 1265, 1149, 1114, 1059, 993 cm^{-1}.

3.2.24. *Methyl 2,2-dimethyl-5-(2-methyl-1,3-dioxolane-2-yl)-3-(trimethylsiloxy)pent-3-enoate (**10a-A**) and methyl 2,2-dimethyl-5-(2-methyl-1,3-dioxolane-2-yl)-3-oxopentanoate (**10a-B**)*

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl 3-(2-methyl-1,3-dioxolane-2-yl)propanoate (174 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired products **10a-A** (214 mg, 68%) and **10a-B** (63 mg, 20%).

Compound ***10a-A***. Colorless oil; ^{1}H NMR: δ 0.18 (9H, s), 1.30 (3H, s), 1.32 (6H, s), 2.32 (2H, d, *J*=6.9 Hz), 3.65 (3H, s), 3.89–3.96 (4H, m), 4.73 (1H, t, *J*=6.9 Hz); ^{13}C NMR: δ 0.9, 23.6, 24.4, 36.0, 48.5, 51.9, 64.7, 101.1, 110.0, 154.7, 176.2; IR (neat) 2982, 2882, 1738, 1254, 1136, 845 cm^{-1}.

Compound ***10a-B***. Colorless oil; ^{1}H NMR: δ 1.30 (3H, s), 1.37 (6H, s), 1.93–1.98 (2H, m) 2.51–2.56 (2H, m), 3.71 (3H, s), 3.86–3.97 (4H, m); ^{13}C NMR: δ 22.1, 23.8, 32.5, 32.7, 52.4, 55.6, 64.6, 109.2, 174.2, 207.6; IR (neat) 2982, 2882, 1738, 1254, 1136, 845 cm^{-1}.

3.2.25. *Methyl 2-ethyl-2-methyl-5-(2-methyl-1,3-dioxolane-2-yl)-3-(trimethylsiloxy)pent-3-enoate (**10b-A**) and methyl 2-ethyl-2-methyl-5-(2-methyl-1,3-dioxolane-2-yl)-3-oxopentanoate (**10b-B**)*

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl 3-(2-methyl-1,3-dioxolane-2-yl)propanoate (174 mg, 1.0 mmol) and **5b** (452 mg, 2.4 mmol) gave the desired products **10b-A** (259 mg, 78%) and **10b-B** (34 mg, 13%).

Compound **10b-A**. Colorless oil; ^{1}H NMR: δ 0.17 (9H, s), 0.81 (3H, t, *J*=7.6 Hz), 1.25 (3H, s), 1.30 (3H, s), 1.74 (1H, dq, *J*=7.6, 13.4 Hz), 1.80 (1H, dq, *J*=7.6, 13.4 Hz), 2.29 (1H, dd, *J*=6.5, 14.6 Hz), 2.38 (1H, dd, *J*=7.6, 14.6 Hz), 3.65 (3H, s), 3.92–3.95 (4H, m), 4.69 (1H, dd, *J*=6.5, 7.6 Hz); ^{13}C NMR: δ 0.9, 8.8, 20.5, 23.7, 28.7, 36.0, 51.7, 52.6, 64.7, 102.2, 110.4, 153.5, 175.9; IR (neat) 2978, 2884, 1736, 1667, 1252, 1123, 849 cm^{-1}.

Compound ***10b-B***. Colorless oil; ^{1}H NMR: δ 0.82 (3H, t, *J*=7.6 Hz), 1.30 (3H, s), 1.32 (3H, s), 1.81 (1H, dq, *J*=7.6, 14.1 Hz), 1.90–2.02 (2H, m), 1.95 (1H, dq, *J*=7.6, 14.1 Hz), 2.42–2.61 (2H, m), 3.65 (3H, s), 3.86–3.97 (4H, m); ^{13}C NMR: δ 8.6, 18.4, 23.9, 27.8, 32.7, 33.0, 52.3, 60.0, 64.6, 109.2, 173.6, 207.4; IR (neat) 2982, 2883, 1743, 1715, 1246, 1150, 1055 cm^{-1}.

3.2.26. *Methyl 2-hydroxy-2-methyl-5-(2-methyl-1,3-dioxolane-2-yl)-3-oxopentanoate (**10c**)*

Following the procedure for preparing **6c**, the reaction between methyl 3-(2-methyl-1,3-dioxolane-2-yl)propanoate (87 mg, 0.5 mmol) and **5c** (436 mg, 1.5 mmol) gave the desired product **10c** (92 mg, 76%).

Pale yellow oil; ^{1}H NMR: δ 1.30 (3H, s), 1.59 (3H, s), 1.99 (2H, t, *J*=7.2 Hz), 2.63 (1H, dt, *J*=17.9, 7.2 Hz), 2.73 (1H, dt, *J*=17.9, 7.2 Hz), 3.76 (3H, s), 3.82–3.96 (4H, m), 4.24 (1H, br s); ^{13}C NMR: δ 22.1, 23.8, 31.0, 32.6, 53.3, 64.6, 81.1, 109.0, 171.9, 206.9; IR (neat) 3470, 2986, 2957, 1724, 1452, 1381, 1261, 1149, 1045, 862 cm^{-1}.

3.2.27. *Methyl 2,2-dimethyl-11-(oxirane-2-yl)-3-(trimethylsiloxy)-undec-3-enoate (**11a-A**) and methyl 2,2-dimethyl-11-(oxirane-2-yl)-3-oxoundecanoate (**11a-B**)*

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl 9-(oxiran-2-yl)nonanoate (214 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired products **11a-A** (124 mg, 35%) and **11a-B** (137 mg, 48%).

Compound ***11a-A***. Colorless oil; ^{1}H NMR: δ 0.17 (9H, s), 1.22–1.61 (12H, m), 1.30 (6H, s), 1.93–2.00 (2H, m), 2.46 (1H, dd, *J*=5.2, 2.8 Hz), 2.74 (1H, dd, *J*=5.2, 4.1 Hz), 2.87–2.93 (1H, m), 3.66 (3H, m), 4.59 (1H, t, *J*=6.9 Hz); ^{13}C NMR: δ 0.8, 24.4, 25.9, 26.0, 29.3, 29.4, 29.6,

32.5, 47.1, 48.4, 51.9, 52.4, 106.5, 152.6, 176.5; IR (neat) 2930, 2856, 1738, 1666, 1460, 1253, 1155, 1099, 898, 848 cm^{-1}.

*Compound **11a-B***. Colorless oil; ^1H NMR: δ 1.21–1.60 (14H, m), 1.35 (6H, s), 2.42 (2H, t, J=7.2 Hz), 2.45 (1H, dd, J=2.8, 5.2 Hz), 2.74 (1H, dd, J=3.8, 5.2 Hz), 2.85–2.92 (1H, m), 3.71 (3H, s); ^{13}C NMR: δ 21.9, 23.8, 25.9, 29.1, 29.3, 29.3, 32.5, 37.9, 47.1, 52.4, 55.6, 174.3, 208.1; IR (neat) 2984, 2930, 2856, 1745, 1714, 1466, 1267, 1194, 1149 cm^{-1}.

3.2.28. Methyl 2-ethyl-2-methyl-11-(oxirane-2-yl)-3-(trimethylsiloxy)undec-3-enoate (*11b-A*) and methyl 2-ethyl-2-methyl-11-(oxirane-2-yl)-3-oxoundecanoate (*11b-B*)

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between methyl 9-(oxiran-2-yl)nonanoate (214 mg, 1.0 mmol) and **5b** (452 mg, 2.4 mmol) gave the desired products **11b-A** (92 mg, 25%) and **11b-B** (200 mg, 67%).

*Compound **11b-A***. Colorless oil; ^1H NMR: δ 0.16 (9H, s), 0.80 (3H, t, J=7.6 Hz), 1.23 (3H, s), 1.23–1.57 (12H, m), 1.70 (1H, dq, J=13.4, 7.6 Hz), 1.78 (1H, dq, J=13.4, 7.6 Hz), 1.87–2.06 (2H, m), 2.46 (1H, dd, J=5.2, 2.8 Hz), 2.74 (1H, dd, J=5.2, 4.0 Hz), 2.86–2.93 (1H, m), 3.65 (3H, s), 4.55 (1H, t, J=6.9 Hz); ^{13}C NMR: δ 0.9, 8.8, 20.5, 25.9, 26.1, 28.7, 29.2, 29.4, 29.7, 32.5, 47.1, 51.7, 52.4, 52.5, 107.4, 151.4, 151.5, 176.0; IR (neat) 2928, 2856, 1736, 1664, 1460, 1350, 1251, 1149, 941, 850, 756 cm^{-1}.

*Compound **11b-B***. Colorless oil; ^1H NMR: δ 0.82 (3H, t, J=7.6 Hz), 1.16–1.62 (14H, m), 1.30 (3H, s), 1.80 (1H, dq, J=14.1, 7.6 Hz), 1.94 (1H, dq, J=14.1, 7.6 Hz), 2.39 (1H, t, J=7.2 Hz), 2.31–2.48 (1H, m), 2.45 (1H, dd, J=5.2, 2.8 Hz), 2.74 (1H, dd, J=5.2, 4.1 Hz), 3.71 (3H, s); ^{13}C NMR: δ 8.6, 18.3, 23.8, 25.9, 27.7, 29.0, 29.3, 29.3, 32.4, 38.3, 47.1, 52.2, 52.3, 59.9, 173.7, 207.9; IR (neat) 2930, 2856, 1741, 1712, 1460, 1246, 1147, 1057, 835 cm^{-1}.

3.2.29. 10-tert-Butyl 1-methyl 2,2-dimethyl-3-(trimethylsiloxy)dec-3-enedioate (*12a-A*) and 10-tert-butyl 1-methyl 2,2-dimethyl-3-oxodecanedioate (*12a-B*)

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between 8-*tert*-butyl 1-methyl octanoate (244 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired products **12a-A** (168 mg, 44%) and **12a-B** (129 mg, 41%).

*Compound **12a-A***. Colorless oil; ^1H NMR: δ 0.17 (9H, s), 1.23–1.37 (4H, m), 1.30 (6H, s), 1.44 (9H, s), 1.50–1.65 (2H, m), 1.94–2.01 (2H, m), 2.20 (2H, t, J=7.9 Hz), 3.66 (3H, s), 4.59 (1H, t, J=6.9 Hz); ^{13}C NMR: δ 0.8, 24.4, 25.0, 25.9, 28.1, 28.8, 29.4, 35.6, 48.3, 51.8, 79.9, 106.2, 152.7, 173.2, 176.4; IR (neat) 2978, 2935, 2858, 1736, 1666, 1253, 1155, 846 cm^{-1}.

*Compound **12a-B***. Colorless oil; ^1H NMR: δ 1.18–1.38 (4H, m), 1.35 (6H, s), 1.43 (9H, s), 1.49–1.64 (4H, m), 2.19 (2H, t, J=7.6 Hz), 2.42 (2H, t, J=7.2 Hz), 3.72 (3H, s); ^{13}C NMR: δ 21.9, 23.6, 24.8, 28.0, 28.7, 28.8, 35.4, 37.7, 52.3, 55.5, 79.9, 173.1, 174.2, 207.9; IR (neat) 2980, 2937, 2864, 1712, 1460, 1367, 1259, 1157, 848, 734 cm^{-1}.

3.2.30. 10-tert-Butyl 1-methyl 2-ethyl-2-methyl-3-(trimethylsiloxy)-dec-3-enedioate (*12b-A*) and 10-tert-butyl 1-methyl 2-ethyl-2-methyl-3-oxodecanedioate (*12b-B*)

Following the procedure for preparing **6a-A** and **6a-B**, the reaction between 8-*tert*-butyl 1-methyl octanoate (44 mg, 1.0 mmol) and **5b** (452 mg, 2.4 mmol) gave the desired products **12b-A** (195 mg, 49%) and **12b-B** (135 mg, 41%).

*Compound **12b-A***. Colorless oil; ^1H NMR: δ 0.16 (9H, s), 0.79 (3H, t, J=7.6 Hz), 1.22 (3H, s), 1.25–1.39 (4H, m), 1.43 (9H, s), 1.50–1.65 (2H, m), 1.69 (1H, dq, J=13.8, 7.6 Hz), 1.77 (1H, dq, J=13.8, 7.6 Hz), 1.87–2.06 (2H, m), 2.19 (2H, t, J=7.2 Hz), 3.65 (3H, s), 4.55 (1H, t, J=7.2 Hz); ^{13}C NMR: δ 0.9, 8.8, 20.5, 25.0, 25.9, 28.1, 28.7, 28.8, 29.4, 35.6, 51.7, 52.5, 79.9, 107.2, 151.6, 173.2, 176.0; IR (neat) 2976, 2938, 1732, 1664, 1460, 1251, 1152, 1119, 844 cm^{-1}.

*Compound **12b-B***. Colorless oil; ^1H NMR: δ 0.81 (3H, t, J=7.6 Hz), 1.18–1.34 (4H, m), 1.30 (3H, s), 1.43 (9H, s), 1.49–1.62 (4H, m), 1.79 (1H, dq, J=14.1, 7.6 Hz), 1.94 (1H, dq, J=14.1, 7.6 Hz), 2.18 (2H, t, J=7.6 Hz), 2.37 (1H, dt, J=19.6, 7.2 Hz), 2.43 (1H, dt, J=19.6, 7.2 Hz), 3.71 (3H, s); ^{13}C NMR: δ 8.6, 18.3, 23.6, 24.9, 27.7, 28.1, 28.8, 28.8, 35.5, 38.2, 52.2, 59.9, 79.9, 173.1, 173.7, 207.8; IR (neat) 2969, 2946, 1716, 1460, 1367, 1248, 1153 cm^{-1}.

3.2.31. Methyl 3-[3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropyl]-2,2-dimethyl-3-oxopropnoate (*13a-B*)

Following the procedure for preparing **6a-B**, the reaction between methyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (223 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired product **13a-B** (261 mg, 89%).

Diastereomixture (ca. *trans*/cis 3:2); colorless oil; ^1H NMR: δ 1.11 (trans, 3H×3/5, s), 1.13 (cis, 3H×2/5, s), 1.18 (trans, 3H×3/5, s), 1.23 (cis, 3H×2/5, s), 1.34 (cis, 3H×2/5, s), 1.35 (trans, 3H×3/5, s), 1.36 (cis, 3H×2/5, s), 1.38 (trans, 3H×3/5, s), 1.86 (trans, 1H×3/5, d, J=5.5 Hz), 2.06 (cis, 1H×2/5, d, J=8.26 Hz), 2.12 (cis, 1H×2/5, dd, J=8.3, 8.3 Hz), 2.40 (trans, 1H×3/5, dd, J=5.5, 7.9 Hz), 3.73 (3H, s), 5.62 (trans, 1H×3/5, d, J=7.9 Hz), 6.32 (cis, 1H×2/5, d, J=8.3 Hz); ^{13}C NMR: δ 14.3, 19.2, 21.4, 21.7, 21.8, 22.5, 28.4, 30.8, 32.6, 33.6, 35.7, 36.7, 39.7, 52.5, 55.8, 56.4, 120.5, 122.0, 124.7, 126.7, 174.1, 174.2, 203.0, 203.7; IR (neat) 2980, 2955, 2937, 1741, 1699, 1462, 1386, 1263, 1149, 1101, 918, 881 cm^{-1}.

3.2.32. Methyl 2-[3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropne-carbonyl]-2-methylbutanoate (*13b-B*)

Following the procedure for preparing **6a-B**, the reaction between methyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (223 mg, 1.0 mmol) and **5b** (452 mg, 2.4 mmol) gave the desired product **13b-B** (261 mg, 89%).

Diastereomixture (ca. major/minor 3:2); colorless oil; ^1H NMR: δ 0.76–0.90 (3H×3/5, m, +3H×2/5, m), 1.08–1.23 (6H×3/5, m, +6H×2/5, m), 1.30–1.38 (3H×3/5, m, +3H×2/5, m), 1.71–2.04 (1H×3/5, m, +2H×3/5, m, +2H×2/5, m), 2.05–2.17 (1H×2/5, m, +1H×2/5, m), 2.34–2.45 (1H×3/5, m), 3.73 (3H, s), 5.62 (1H×3/5, d, J=7.91 Hz), 6.25–6.35 (1H×2/5, m); ^{13}C NMR: δ 8.5, 8.6; 14.3, 17.8, 17.9, 18.2, 19.1, 22.5, 22.6, 27.5, 27.7, 28.4, 30.8, 30.8, 32.5, 32.7, 33.6, 34.0, 35.6, 35.7, 36.9, 37.0, 39.8, 40.0, 52.3, 60.1, 60.3, 60.6, 60.7, 120.4, 120.4, 122.2, 124.7, 126.8, 173.5, 173.6, 173.6, 173.7, 202.8, 203.3, 203.5, 203.7; IR (neat) 2955, 2881, 1739, 1699, 1458, 1244, 1149, 1099, 1051, 914, 879 cm^{-1}.

3.2.33. Methyl 5-(1H-indol-3-yl)-2,2-dimethyl-3-oxo-pentanoate (*14*)

Following the procedure for preparing **6a-B**, the reaction between 3-[(1-*tert*-butyldimethylsilyl)indol-3-yl]propanoate (318 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired crude product, which was added to a stirred solution of TBAF (2.0 mmol) in THF (3.0 mL) at 0–5 °C, followed by being stirred at 20–25 °C for 1 h. A similar work up gave the desired product **14** (183 mg, 67%).

Yellow oil; ^1H NMR: δ 1.33 (6H, s), 2.85 (2H, d, J=7.2 Hz), 3.07 (2H, d, J=7.2 Hz), 3.57 (3H, s), 6.98 (1H, d, J=2.0 Hz), 7.09–7.21 (2H, m), 7.35 (1H, d, J=7.9 Hz), 7.56 (1H, d, J=7.91 Hz), 7.91–8.06 (1H, br); ^{13}C NMR: δ 14.2, 19.6, 21.8, 38.8, 52.3, 55.6, 60.4, 111.1, 115.1, 118.6, 119.3, 121.6, 122.0, 127.1, 136.3, 174.1, 207.6; IR (neat) 3412, 2988, 2951, 1711, 1458, 1271, 1149, 1068, 744 cm^{-1}.

3.2.34. Methyl 4-(benzyloxy)-2,2-dimethyl-3-(trimethylsiloxy)-3-butenoate (*15*)

Following the procedure for preparing **6a-A**, the reaction between methyl 2-(benzyloxy)acetate (180 mg, 1.0 mmol) and **5a** (418 mg, 2.4 mmol) gave the desired product **15** (268 mg, 83%).

(*Z*/*E*=95:5); colorless oil; ^1H NMR: δ 0.11 (9H×19/20, s, *Z*), 0.17 (9H×1/20, s, *E*), 1.27 (6H, s), 3.66 (3H, s), 4.58 (2H×1/20, s, *E*), 4.73

(2H×19/20, s, *Z*), 5.73 (1H×19/20, s, *Z*), 5.84 (1H×1/20, s, *E*), 7.21–7.40 (5H, m); ^{13}C NMR: δ 0.6, 23.5, 46.3, 51.9, 73.9, 127.2, 127.6, 127.9, 128.3, 137.2, 139.0, 176.3; IR (neat) 2978, 1738, 1157, 848, 752 cm^{-1}.

3.2.35. (S)-Methyl 4-(dibenzylamino)-2,2-dimethyl-3-oxopentanoate (**16**)

Following the procedure for preparing **6a-B**, the reaction between methyl (*S*)-methyl 2-(dibenzylamino)propanoate (142 mg, 0.5 mmol) and **5a** (209 mg, 1.2 mmol) at 0–5 °C for 30 min gave the desired product **16** (150 mg, 85%).

HPLC analysis [flow rate 0.30 mL /min, solvent: hexane/2-propanol=99:1, t_R(racemic)=19.99 and 20.70 min, t_R(**16**)=19.27 min] 95% ee. Pale yellow oil; $[\alpha]_D^{23}$ −1.3 (*c* 1.16, $CHCl_3$); ^{1}H NMR: δ 1.20 (3H, d, *J*=6.9 Hz), 1.26 (3H, s), 1.28 (3H, s), 3.53 (3H, s), 3.55 (1H, d, *J*=13.8 Hz), 3.83 (1H, d, *J*=13.8 Hz), 3.90 (1H, q, *J*=6.9 Hz), 7.20–7.37 (10H, m); ^{13}C NMR: δ 10.4, 22.6, 22.7, 52.1, 54.1, 55.2, 57.4, 127.0, 128.2, 129.0, 139.3, 173.9, 209.1; IR (neat) 3028, 2982, 2939, 2841, 1743, 1709, 1454, 1383, 1267, 1151, 981 cm^{-1}.

3.2.36. (S)-Methyl 4-(tert-butyldiphenylsiloxy)-2,2-dimethyl-3-oxopentanoate (**17**)

Following the procedure for preparing **6a-B**, the reaction between methyl (*S*)-methyl 2-(*tert*-butyldiphenylsiloxy)propanoate (171 mg, 0.5 mmol) and **5a** (209 mg, 1.2 mmol) at 0–5 °C for 30 min gave the desired product **17** (184 mg, 89%).

HPLC analysis [flow rate 0.50 mL/min, solvent: hexane/2-propanol=99.5:0.5, t_R(racemic)=11.71 and 12.64 min, t_R(**17**)=11.57 and 12.45 min] 97% ee. Colorless oil; $[\alpha]_D^{24}$ +21.7 (*c* 1.11, $CHCl_3$); ^{1}H NMR: δ 1.07 (9H, s), 1.18 (3H, d, *J*=6.9 Hz), 1.33 (3H, s), 1.39 (3H, s)3.67 (3H, s), 4.46 (1H, q, *J*=6.9 Hz), 7.32–7.48 (6H, m), 7.60–7.73 (4H, m); ^{13}C NMR: δ 19.2, 21.8, 22.4, 22.7, 26.9, 52.1, 53.1, 74.5, 127.5, 127.8, 129.8, 130.0, 132.5, 133.8, 135.9, 135.9, 173.7, 209.6; IR (neat) 3073, 3051, 2936, 2893, 2860, 1750, 1711, 1589, 1473, 1383, 1263, 1190 cm^{-1}.

3.2.37. Mukaiyama aldol reaction (Table 5, method A): general procedure

$TiCl_4$ (40 μL, 0.36 mmol) was added to a stirred solution of an enol silyl ether (0.30 mmol) and an aldehyde (0.36 mmol) in CH_2Cl_2 (0.9 mL) at −45 °C under an Ar atmosphere, followed by being stirred at same temperature for 1 h. Water was added to the reaction mixture, which was extracted with AcOEt. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica gel column chromatography to give the desired product.

3.2.38. Ti-direct aldol reaction (Table 5, method B)

$TiCl_4$ (67 μL, 0.60 mmol) and Bu_3N (130 mg, 0.70 mmol) were successively added to a stirred solution of a β-ketoester (0.50 mmol) in CH_2Cl_2 (1.5 mL) at 0–5 °C under an Ar atmosphere, followed by being stirred at the same temperature for 0.5 h. Aldehyde (0.60 mmol) was added to the mixture at the same temperature. After stirring for 2 h, water was added to the mixture, which was extracted with AcOEt. The organic phase was washed with water, brine, dried (Na_2SO_4), and concentrated. The obtained crude product was purified by silica gel column chromatography to give the desired product.

3.2.39. Methyl 4-(hydroxy(phenyl)methyl)-2,2-dimethyl-3-oxododecanoate (**23**)

Colorless oil; ^{1}H NMR: δ 0.77–0.97 (1H, m), 0.85 (3H, t, *J*=6.9 Hz), 0.99–1.53 (12H, m), 1.33 (3H, s), 1.35 (3H, s), 1.53–1.75 (1H, m), 3.08–3.26 (1H, m), 3.73 (3H, s), 4.94 (1H, d, *J*=3.4 Hz), 7.20–7.40 (5H, m); ^{13}C NMR: δ 14.0, 21.7, 21.9, 22.0, 22.6, 26.3, 27.7, 29.1, 29.2, 29.8, 31.7, 52.5, 53.5, 54.0, 56.7, 73.0, 75.2, 125.9, 126.3, 127.4, 127.8, 128.3, 128.4, 141.6, 173.4, 212.7; IR (neat) 3520, 2928, 1736, 1703, 1265, 1030, 702 cm^{-1}.

3.2.40. Methyl 4-(1-hydroxyhexyl)-2,2-dimethyl-3-oxododecanoate (**24**)

Colorless oil; ^{1}H NMR: δ 0.78 (6H, m), 1.10–1.73 (22H, m), 1.40 (6H, s), 2.20–2.64 (1H, br s), 2.78–2.95 (1H, m), 3.62–3.76 (1H, m) 3.72 (3H, s); ^{13}C NMR: δ 13.99, 14.03, 22.00, 22.21, 22.27, 22.31, 22.54, 22.60, 25.73, 25.90, 26.23, 27.30, 28.33, 29.19, 29.33, 29.59, 29.73, 30.00, 31.70, 31.77, 34.39, 35.73, 51.60, 51.87, 52.35, 56.65, 56.90, 71.62, 72.02, 173.46, 173.50, 213.06, 213.79; IR (neat) 3524, 2928, 1739, 1703, 1466, 1149 cm^{-1}.

3.2.41. Methyl 4-(benzyloxy)-5-hydroxy-2,2-dimethyl-3-oxo-5-phenylpentanoate (**25**)

syn/*anti* 25:75; colorless oil; ^{1}H NMR: δ 1.19 (*anti*, 0.75×3H, s), 1.24 (*syn*, 0.25×3H, s), 1.30 (*syn*, 0.25×3H, s), 1.31 (*anti*, 0.75×3H, s), 3.37 (*anti*, 0.75×3H, s), 3.42 (*syn*, 0.25×3H), 3.99 (*syn*, 0.25×1H, d, *J*=10.7 Hz), 4.09 (*anti*, 0.75×1H, d, *J*=10.7 Hz), 4.22 (*anti*, 0.75×1H, d, *J*=6.2 Hz), 4.32 (*anti*, 0.75×1H, d, *J*=10.7 Hz), 4.34 (*syn*, 0.25×1H, d, *J*=10.7 Hz), 4.36 (*syn*, 0.25×1H, d, *J*=2.8 Hz), 5.06 (*anti*, 0.75×1H, d, *J*=6.2 Hz), 5.25 (*syn*, 0.25×1H, d, *J*=2.8 Hz), 7.01–7.17 (2H, m), 7.19–7.45 (8H, m); ^{13}C NMR: δ 20.9, 21.1, 22.2, 22.4, 51.8, 52.0, 53.3, 53.5, 73.1, 74.2, 74.5, 75.8, 86.2, 87.3, 126.1, 127.5, 127.5, 127.6, 127.9, 128.1, 128.1, 128.3, 136.6, 136.9, 139.7, 140.8, 173.3, 173.8, 208.3, 210.1; IR (neat) 3499, 2949, 1749, 1714, 1454, 1151, 702 cm^{-1}.

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