Product-Catalyzed Aldol Reaction between Trimethylsilyl Enolates and Aldehydes

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Abstract: Aldol reactions between trimethylsilyl ketene acetals and aldehydes by using a catalytic amount of alkoxide anion proceeded smoothly to afford the corresponding aldols in DMF, indicating that the initially-formed aldolate anion effectively worked to catalyze the reaction. The "product-catalyzed aldol reaction", a new class Lewis base-catalyzed aldol reaction, between trimethylsilyl ketene acetals and aldehydes was performed successfully by the use of aldolate anion as a Lewis base catalyst.

Keywords: aldol reaction; autocatalysis; Lewis base; silicates; silyl ketene acetals

Introduction

The aldol reaction is one of the most fundamental reactions in synthetic organic chemistry to form carbon–carbon bonds effectively.[1] After a crossed aldol reaction between aldehydes and silyl enolates promoted by Lewis acids such as titanium tetrachloride was reported from our laboratory,[2] silyl enolates have been recognized as convenient and useful nucleophiles and are employed frequently in the construction of carbon skeletons.[3] In recent years, activation of silyl enolates having an enhanced Lewis acidic silicon atom with Lewis bases has intensively been studied: e.g., Denmark et al. introduced a Lewis base-catalyzed aldol reaction of trichlorosilyl enolates with aldehydes by using phosphoramides, a Lewis base,[4] while Hosomi and co-workers reported a reaction by using a combination of dimethylsilyl enolate and $CaCl_2$ in dry or aqueous DMF solvent.[5]

In order to activate simple and commonly employed silyl enolates such as trimethylsilyl (TMS) enolates, new methods of the activation with a Lewis base catalyst by formation of the hypervalent silicon intermediates were reported from our laboratory.[6] In this method, nitrogen- or oxygen-containing organic anions generated from amines, amides or carboxylic acids were considered to behave as useful Lewis base catalysts. This means that various organic compounds such as amides and carboxylic acids could be used as the precursors of Lewis base catalysts. Then, in order to extend the usefulness of organic anions as Lewis bases in organic synthetic reactions, the use of alkoxide anions was considered. In this report, a catalytic aldol reaction between TMS enolates and aldehydes promoted by alkoxide anions as a Lewis base catalyst is described.[7]

Results and Discussion

In the first place, the aldol reaction between benzaldehyde and TMS enolate **1** was studied by using lithium benzylate as a Lewis base catalyst, which proceeded smoothly to afford the corresponding aldol in high yield even when 3 mol % of lithium benzylate was used (Table 1, Entries 1–3), indicating that the alkoxide anions were a useful Lewis base catalyst for promotion of the reaction. After screening several Lewis base catalysts, it was observed that alkoxides such as *tert*-butoxide or phenoxide worked well as base catalyst when lithium, sodium, potassium, or ammonium ions were present as counter cations, and the lithium was the most effective of these. It was interesting to note that the yields of the above aldol reaction were dependent mainly on the nature of the counter cation but not on the nucleophilicity of the alkoxide anions.

The effect of acceptor aldehydes was examined by using alkoxide anions in DMF and TMS enolate **1** was found to react smoothly with various aromatic aldehydes to afford the corresponding aldols in high yields (Table 2). Aromatic aldehydes having an electron-donating group also reacted smoothly to afford aldols in high yields. On the other hand, aromatic aldehydes having an electron-withdrawing group and aliphatic aldehydes such as 3-phenylpropionaldehyde gave the corresponding aldols in moderate yields. When a conjugated aldehyde was used, the corresponding 1,2-adduct was obtained as a major product and the yields turned out to be excellent even when aldehydes having a basic function were employed.

The reactivities of the above enolate towards aldehydes are similar to those reported previously in our Lewis base-catalyzed aldol reaction in dry DMF. However, this was not the case with the enolates derived

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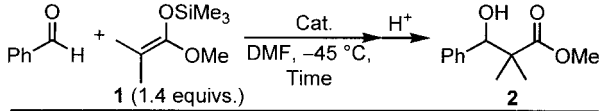
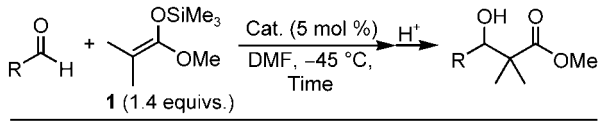
Table 1. Alkoxide anion mediated aldol reaction of TMS enolate **1** and PhCHO.

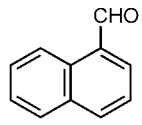
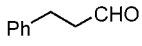
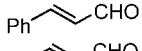
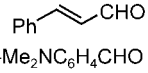
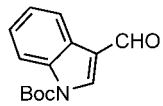


Entry	Cat.	Cat. [mol %]	Time [h]	Yield [%][a,b]
1	BzlOLi	10	3	98
2	BzlOLi	5	5	97
3	BzlOLi	3	5	97
4	MeONa	9	5	77 (19)
5	EtONa	9	5	75 (16)
6	*t*-BuOLi	5	2	96 (4)
7	*t*-BuOK	5	5	81 (13)
8	PhOLi	5	2	97
9	$PhONBu_4$	5	2	77 (13)

[a] Yield was determined by ^{1}HNMR analysis (270 MHz) using 1,1,2,2,-tetrachloroethane as an internal standard.
[b] In parentheses, starting material recovered.

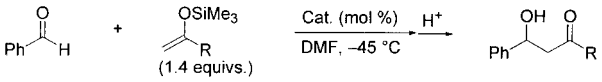
Table 2. Alkoxide anion-mediated aldol reactions of TMS enolate **1** and aldehydes.

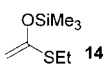
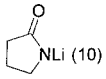
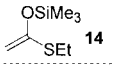
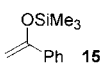
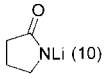
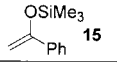


Entry	Aldehyde	Cat.	Time [h]	Product	Yield[a,b] [%]
1	*p*-MeC_6H_4CHO	BzlOLi	6	**3**	94
2	*p*-$MeOC_6H_4CHO$	BzlOLi	5	**4**	97
3	*p*-BrC_6H_4CHO	BzlOLi	5	**5**	82 (17)
4	*p*-ClC_6H_4CHO	BzlOLi	5	**6**	75 (24)
5	*p*-CNC_6H_4CHO	BzlOLi	6	**7**	81 (11)[c]
6		BzlOLi	4	**8**	88 (9)[c]
7		BzlOLi	5	**9**	65[c]
8		BzlOLi	4	**10**	89 (5:1)[d]
9		$PhONBu_4$	2	**10**	91 (5.3:1)[d]
10	*p*-$Me_2NC_6H_4CHO$	BzlOLi	5	**12**	95[e]
11	*p*-$Me_2NC_6H_4CHO$	$PhONBu_4$	2	**12**	quant[e]
12		BzlOLi	5	**13**	95[e]

[a] Yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2,-tetrachloroethane as an internal standard.
[b] In parentheses, starting material recovered.
[c] Yield of isolated product.
[d] In parentheses, the ratio of 1,2-adduct (**10**):1,4-adduct (**11**).
[e] Product was obtained as a TMS aldolate without carrying out a desilylation step.

Table 3. Lewis base-catalyzed aldol reaction of TMS enolates and PhCHO.



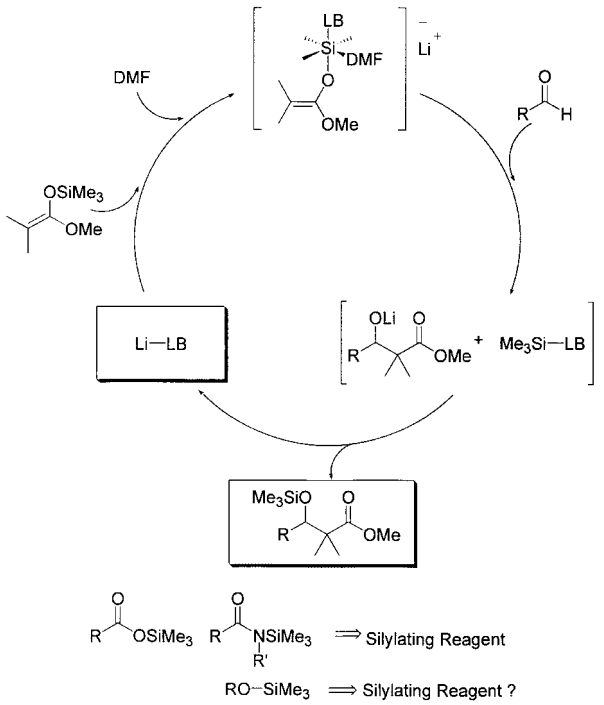
Entry	Silyl Enolate	Cat. [mol %]	Product	Yield[a] [%]
1	 **14**	 NLi (10)	**16**	95
2	 **14**	BnOLi (5)	**16**	40
3	 **15**	 NLi (10)	**17**	81
4	 **15**	BnOLi (5)	**17**	n.d.[b]

[a] Yield was determined by ^{1}H NMR analysis (270 MHz) using 1,1,2,2,-tetrachloroethane as an internal standard.
[b] Not detected.

from thioesters and ketones when alkoxide anions were used as the Lewis base. The aldol reaction of benzaldehyde with the TMS enolate generated from *S*-ethyl ethanethioate **14** in the presence of 5 mol % of lithium benzylate afforded the corresponding aldol only in 40% yield whereas the yield was 95% when 10 mol % of lithium 2-pyrrolidone was used under the same reaction conditions. On the other hand, when the aldol reaction of benzaldehyde and TMS enolates generated from acetophenone **15** was tried in the presence of 5 mol % of lithium benzylate, the corresponding aldol adduct was not detected. On the other hand, the corresponding aldol was formed in 81% yield by using 10 mol % of lithium 2-pyrrolidone (Table 3).

Then, the catalytic cycle of this reaction, especially the regeneration step of the Lewis base catalyst, was studied in order to explain the reactivity difference of silyl enolates by using alkoxide anion and our previously reported Lewis bases. In the reported Lewis base-catalyzed aldol reaction, the mode of regeneration of the catalyst was described; that is, the formed silylated Lewis base worked as a silylating reagent and a silyl group transfer from the silylated Lewis base to the aldolate anion led to form the corresponding silylated aldol together with simultaneous regeneration of the Lewis base and the catalytic cycle was completed (Scheme 1). This assumption was verified by the experiment in which smooth silylation of lithium aldolate **18** by TMS 2-pyrrolidone **19** took place to afford the silylated aldol **20** in high yield. However, the possibility of the above-mentioned silyl transfer in the case of using alkoxide anions was still questionable since the generated silyl ethers are not so reactive in most cases.

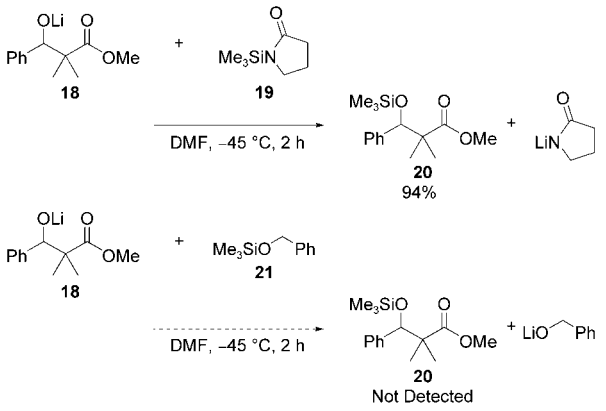
Then, the silylation of lithium aldolate **18** with benzyl TMS ether **21** was examined to verify the possibility of



Scheme 1.

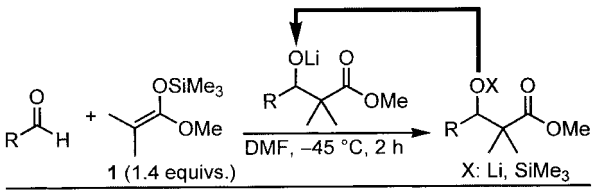
this silyl transfer under the reaction conditions mentioned above, but no such transfer was observed (Scheme 2). This means that the regeneration of Lewis base catalyst never takes place in the presence of alkoxide anions. However, the reaction proceeded if a catalytic amount of an activator such as alkoxide anion was used. It was assumed then that the initially formed aldolate anion activated this reaction because the aldolate anion was also considered as a kind of alkoxide anion. Then, the aldol reaction of benzaldehyde and **1** was tried by using 10 mol % of the lithium aldolate **18** as a Lewis base catalyst and the reaction proceeded smoothly to afford the corresponding aldol in excellent yield as expected (Table 4, Entry 1): that is, the aldolate anion promoted this reaction, and that the difference of reactivities mentioned above is attributed to the reaction pathways which proceeded *via* a different mechanism.

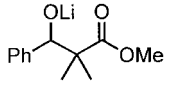
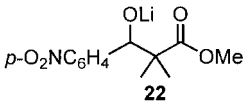
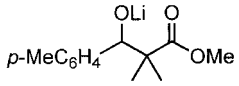
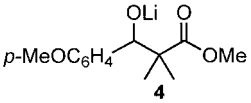
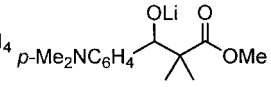
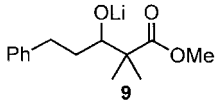
Thus, from an environmental point of view, "the product-catalyzed aldol reaction" has great advantages because it is not necessary to discard the catalyst or to separate it from the produced aldol adduct since the product obtained was the catalyst itself. Furthermore, this product-catalyzed aldol reaction was investigated by using the corresponding lithium aldolate as a Lewis base catalyst (Table 4). When an aromatic aldehyde having either an electron-donating group or a basic part was used, the corresponding aldol adduct was obtained in excellent yield. In the case when an aromatic aldehyde having a strong electron-withdrawing group or an aliphatic aldehyde was used, the aldol adduct was produced in low to moderate yields, respectively.



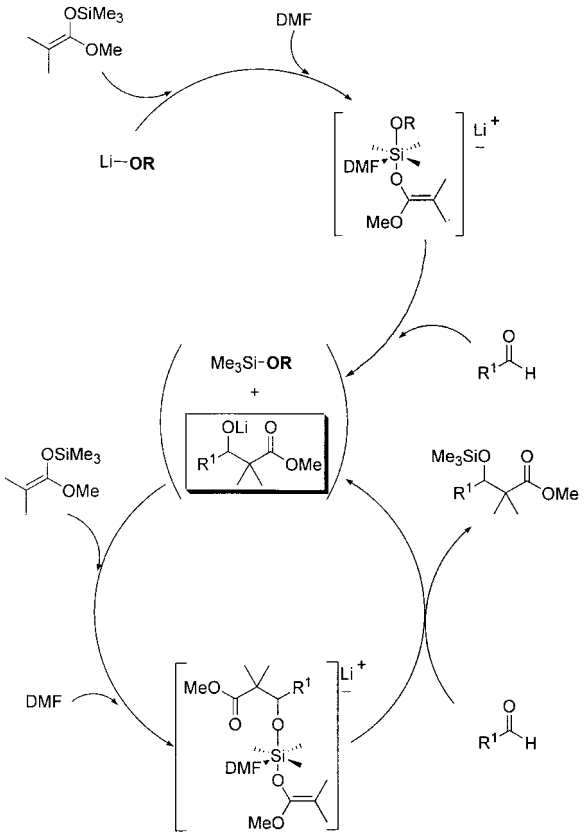
Scheme 2.

Table 4. Product-catalyzed aldol reaction of TMS enolate **1** and aldehydes.



Entry	R	Catalyst ([mol %]) Product		Yield[a] [%]
1	Ph	 **2**	(5)	quant.
2	*p*-$O_2NC_6H_4$	 **22**	(5)	32 (57)[b]
3	*p*-MeC_6H_4	 **3**	(5)	94
4	*p*-$MeOC_6H_4$	 **4**	(8)	quant.
5	*p*-$Me_2NC_6H_4$	 **12**	(6)	quant.[c]
6	$Ph(CH_2)_2$	 **9**	(5)	70

[a] Yield was determined after desilylation by ^1H NMR analysis (270 MHz) using 1,1,2,2,-tetrachloroethane as an internal standard.
[b] In parentheses, starting material recovered.
[c] Product was obtained as a TMS aldolate without carrying out a desilylation step.



Scheme 3.

By taking these results into consideration, a catalytic cycle for this reaction is proposed as shown in Scheme 3. An alkoxide anion, a Lewis base catalyst, firstly coordinates to the silicon atom of TMS enolate to form a pentacordinated hypervalent silicate and further coordination of DMF forms a highly nucleophilic hexacordinated hypervalent silicate. The reactivity of the enolate, therefore, increases sufficiently to attack the aldehyde to form the lithium aldolate and TMS ether of the alcohol. In the next step, the lithium aldolate thus generated similarly activates the TMS enolate to form the silylated aldol and lithium aldolate, and consequently a catalytic cycle is established. When aldolate anion is used as Lewis base catalyst, the reaction proceeds *via* the latter pathway to complete the "product-catalyzed aldol reaction".

Conclusion

It is reported that the Lewis base-catalyzed aldol reaction between TMS ketene acetals and aldehydes by using an alkoxide anion can be successfully performed. This shows that the initially formed aldolate anion behaves as a useful catalyst for this reaction. Thus, a product-catalyzed aldol reaction between TMS ketene acetals and aldehydes has been established by using the aldolate anion as a Lewis base catalyst.

Experimental Section

General Remarks

All melting points were determined on a Yanagimoto micro melting point apparatus (Yanaco MP-S3) and are not corrected. Infrared (IR) spectra were recorded on a Horiba FT300 FT-IR spectrometer. ^{1}H NMR spectra were recorded on a JEOL JNM EX270L (270 MHz) spectrometer; chemical shifts (δ) are reported in parts per million relative to tetramethylsilane. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. ^{13}C NMR spectra were recorded on an EX270L (68 MHz) spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million relative to tetramethylsilane, with the solvent resonance as the internal standard ($CDCl_3$; $\delta = 77.0$ ppm). Analytical TLC was performed on Merck preparative TLC plates (silica gel 60 GF_{254}, 0.25 mm). Column chromatography was carried out on Merck silica gel 60 (0.063–0.200 mm). Preparative thin-layer chromatography (PTLC) was carried out on silica gel Wakogel B-5F. Reactions were carried out under an argon atmosphere in dried glassware. DMF was dried with P_2O_5 and then distilled from CaH_2 under reduced pressure and dried (molecular sieves, 4 Å). All reagents were purchased from Tokyo Kasei Kogyo, Kanto Chemical, Kokusan Chemical, Wako Pure Chemical Industries or Aldrich Chemical. Aldehydes were used after purification by distillation or recrystallizaion. Silyl enolates were prepared by the usual methods.

Catalyst Preparation

To a solution of alcohol or aldol (0.63 mmol) in Et_2O (5.5 mL) was added MeLi in Et_2O (1.20 M, 0.5 mL, 0.6 mmol) at 0 °C and the mixture was stirred for 30 minutes to prepare 0.1 M solution of lithium alkoxide or lithium aldolate.

General Procedure for Lithium Alkoxide- or Lithium Aldolate-Catalyzed Aldol Reaction

An ether solution of the lithium alkoxide or aldolate (0.1 M, 0.2 mL, 0.02 mmol) was evaporated under reduced pressure and the residue was dissolved in DMF (0.4 mL). This solution was cooled to −45 °C and a solution of a silyl enolate (0.56 mmol) in DMF (0.6 mL) was added at −45 °C. After the mixture was stirred for 5 minutes at −45 °C, a solution of aldehyde (0.4 mmol) in DMF (1.4 mL) was added slowly over 5 minutes. The reaction mixture was stirred for an appropriate time at −45 °C and then saturated aqueous NH_4Cl was added. The mixture was extracted with Et_2O. After evaporation of the solvent, the residue was dissolved in a mixture of aqueous HCl (1.0 M, 2 mL) and THF (6 mL). The mixture was stirred for 30 minutes, extracted with Et_2O, and the organic layer was washed with brine, dried over Na_2SO_4. After filtration of the mixture and evaporation of the solvent, the crude product was purified by column chromatography to afford the corresponding aldol. Products and yields were as reported in the text.

***Methyl 3-Hydroxy-2,2-dimethyl-3-phenylpropionate* (2):** White powder; mp 67.1 °C; IR (neat): $\nu = 3394$, 2985, 1704, 1450, 1281, 1149, 1049 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$):

δ = 1.11 (s, 3H), 1.14 (s, 3H), 3.12 (d, *J* = 4.1 Hz, 1H), 3.72 (s, 3H), 4.90 (d, *J* = 4.0 Hz, 1H), 7.22–7.47 (m, 5H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 19.0, 23.0, 47.7, 52.1, 78.6, 127.6, 127.7, 139.9, 178.2.

***Methyl 3-Hydroxy-2,2-dimethyl-3-(4-methylphenyl)propionate* (3):** White powder; mp 70.0 °C; IR (neat): ν = 3502, 2950, 1730 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.08 (s, 3H), 1.12 (s, 3H), 2.32 (s, 1H), 3.05 (s, 1H), 3.69 (s, 3H), 4.83 (s, 1H), 7.09–7.18 (m, 4H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 19.0, 21.0, 22.8, 47.7, 51.9, 78.4, 127.4, 128.3, 137.0, 137.2, 178.1.

***Methyl 3-Hydroxy-3-(4-methoxyphenyl)-2,2-dimethylpropionate* (4):** White powder; mp 81.2 °C; IR (neat): ν = 3502, 2985, 1720 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.07 (s, 3H), 1.12 (s, 3H), 3.05 (s, 1H), 3.70 (s, 3H), 3.78 (s, 3H), 4.83 (s, 1H), 6.83 (m, 2H), 7.20 (m, 2H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 18.9, 22.8, 47.7, 51.9, 55.1, 78.1, 113.0, 128.6, 132.1, 159.0, 178.1.

***Methyl 3-(4-Bromophenyl)-3-hydroxy-2,2-dimethylpropionate* (5):** White powder; mp 70.8 °C; IR (neat): ν = 3471, 3410, 2978, 1705 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.07 (s, 3H), 1.11 (s, 3H), 3.24–3.44 (br s, 1H), 3.70 (s, 3H), 4.82 (s, 1H), 7.14–7.17 (m, 2H), 7.42–7.45 (m, 2H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 19.0, 22.7, 47.5, 52.1, 77.8, 121.5, 129.3, 130.8, 138.9, 177.9.

***Methyl 3-(4-Chlorophenyl)-3-hydroxy-2,2-dimethylpropionate* (6):** White powder; mp 63.2 °C; IR (neat): ν = 3471, 2978, 1720 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.08 (s, 3H), 1.12 (s, 3H), 3.21 (s, 1H), 3.71 (s, 3H), 4.85 (s, 1H), 7.18–7.36 (m, 4H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 19.0, 22.8, 47.6, 52.1, 77.9, 127.9, 129.0, 133.5, 138.4, 178.0.

***Methyl 3-(4-Cyanophenyl)-3-hydroxy-2,2-dimethylpropionate* (7):** White powder; mp 96.0 °C; IR (neat): ν = 3479, 2985, 2229, 1728 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): d = 1.09 (s, 3H), 1.13 (s, 3H), 3.59–3.68 (m, 1H), 3.71 (s, 3H), 4.95 (d, *J* = 4.3 Hz, 1H), 7.38–7.48 (m, 2H), 7.55–7.66 (m, 2H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 19.1, 22.3, 47.6, 52.1, 77.5, 111.2, 118.6, 128.3, 131.3, 145.5, 177.5.

***Methyl 3-Hydroxy-2,2-dimethyl-3-(naphthalen-1-yl)propionate* (8):** Colorless oil; IR (neat): ν = 3471, 2946, 1720 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.07 (s, 3H), 1.24 (s, 3H), 3.72 (s, 3H), 5.92 (s, 1H), 7.42–7.51 (m, 3H), 7.65–7.68 (m, 1H), 7.77–7.86 (m, 2H), 8.13–8.16 (m, 1H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 18.9, 23.7, 48.7, 52.1, 73.0, 123.7, 124.9, 125.2, 125.7, 125.7, 128.2, 128.7, 131.7, 133.4, 136.2, 178.4.

***Methyl 3-Hydroxy-2,2-dimethyl-5-phenylpentanoate* (9):** Colorless oil; IR (neat): ν = 3465, 2939, 1720 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.16 (s, 3H), 1.18 (s, 3H), 1.53–1.81 (m, 2H), 2.51 (s, 1H), 2.59–2.70 (m, 1H), 2.90–3.00 (m, 1H), 3.60–3.67 (m, 1H), 3.68 (s, 3H), 7.15–7.31 (m, 5 H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 20.3, 22.4, 32.8, 33.6, 47.1, 51.9, 76.0, 125.8, 128.4, 128.5, 142.1, 178.2.

***Methyl (E)-3-Hydroxy-2,2-dimethyl-5-phenylpent-4-enoate* (10):** Colorless oil; IR (neat): ν = 3409, 2970, 1720, 1458, 1265, 1134, 971, 748, 702 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.23 (s, 3H), 1.24 (s, 3H), 2.75–2.89 (br s, 1H), 3.72 (s, 3H), 4.29–4.44 (m, 1H), 6.21 (dd, *J* = 7.1, 15.8 Hz, 1H), 6.64 (d, *J* = 15.8 Hz, 1H), 7.23–7.40 (m, 5H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 20.0, 22.8, 47.2, 52.1, 77.8, 126.5, 127.4, 127.8, 128.5, 132.9, 136.5, 177.9.

***Methyl 2,2-Dimethyl-3-phenyl-5-oxopentanoate* (11):** Colorless oil; IR (neat): ν = 3464, 1712 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.10 (s, 3H), 1.16 (s, 3H), 2.69 (ddd, *J* = 1.3, 4.3, 16.8 Hz, 1H), 2.98 (ddd, *J* = 2.6, 10.9, 16.8 Hz, 1H), 3.62 (dd, *J* = 4.3, 10.9 Hz, 1H), 3.66 (s, 3H), 7.16–7.32 (m, 5H), 9.53 (dd, *J* = 1.3, 2.6 Hz, 1H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 21.3, 24.3, 44.8, 46.1, 46.7, 51.9, 127.3, 128.2, 129.4, 139.0, 177.3, 201.3.

***Methyl 3-[4-(Dimethylamino)phenyl]-2,2-dimethyl-3-(trimethylsiloxy)propionate* (12):** White powder; mp 80.1 °C; IR (neat): ν = 2978, 1728, 1612, 1519, 1458, 1349, 1250, 1073 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = −0.07 (s, 9H), 1.00 (s, 3H), 1.09 (s, 3H), 2.91 (s, 6H), 3.65 (s, 3H), 4.87 (s, 1H), 6.59 (d, *J* = 8.7 Hz, 2H), 7.31 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = −0.1, 18.8, 21.9, 40.5, 49.2, 51.5, 79.0, 111.3, 128.4, 128.5, 149.8, 177.6.

***Methyl 3-{1-[(tert-Butoxy)carbonyl]-1H-indol-3-yl}-2,2-dimethyl-3-(trimethylsiloxy)propionate* (13):** Colorless oil; IR (neat): ν = 2978, 1736, 1458, 1373, 1257, 1149, 1280, 856, 756 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = −0.04 (s, 9H), 1.09 (s, 3H), 1.25 (s, 3H), 1.68 (s, 9H), 3.67 (s, 3H), 5.26 (s, 1H), 7.12–7.37 (m, 2H), 7.43 (s, 1H), 7.68–7.84 (m, 1H), 7.99–8.22 (m, 1H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = −0.2, 19.9, 21.9, 28.2, 49.7, 51.7, 74.1, 83.7, 114.9, 120.8, 121.5, 122.3, 124.0, 129.9, 135.2, 149.7, 168.1, 177.2.

***Ethyl (S)-3-Hydroxy-3-phenylpropanethioate* (16):** Colorless oil; IR (neat): ν = 3502, 3425, 2970, 2924, 1682 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.25 (t, *J* = 7 Hz, 3H); 2.84–3.04 (m, 4H), 3.11–3.17 (br s, 1H), 5.12–5.21 (m, 1H), 7.23–7.40 (m, 1H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 14.6, 23.5, 52.5, 70.8, 125.5, 127.7, 128.4, 142.2, 198.7.

***3-Hydroxy-1,3-diphenylpropan-1-one* (17):** Colorless oil; IR (neat): ν = 3548, 3425, 1673 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 3.37 (d, *J* = 6 Hz, 2H), 5.34 (t, *J* = 6 Hz, 1H), 7.29–7.58 (m, 8H), 7.81–8.12 (m, 2H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 47.4, 70.0, 125.7, 127.7, 128.1, 128.6, 128.7, 133.6, 136.5, 142.9, 200.2.

***Methyl 2,2-Dimethyl-3-(trimethylsiloxy)-3-phenypropionate* (20):** Colorless oil; IR (neat): ν = 2947, 1736, 1458, 1257, 1134, 1095 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = −0.05 (s, 9H), 0.99 (s, 3H), 1.12 (s, 3H), 3.67 (s, 3H), 4.97 (s, 1H), 7.49–7.64 (m, 5H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = −0.08, 19.1, 23.0, 49.0, 51.6, 79.2, 127.6, 127.7, 140.8, 177.3.

***Methyl 3-Hydroxy-2,2-dimethyl-3-(4-nitrophenyl)propionate* (21):** White crystals; mp 114.5 °C; IR (neat): ν = 3517, 2985, 1712, 1519 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 1.13 (s, 3H), 1.15 (s, 3H), 3.74 (s, 3H), 5.01 (s, 1H), 7.41–7.62 (m, 2H), 8.09–8.32 (m, 2H); ^{13}C NMR (68.7 MHz, $CDCl_3$): δ = 19.2, 22.7, 47.6, 52.3, 77.7, 122.9, 128.6, 147.3, 147.6, 177.7.

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