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Transition-Metal-Free Reduction of *α*-Keto Thioesters with Hydrosilanes at Room Temperature: Divergent Synthesis through Reagent-Controlled Chemoselectivities

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Abstract. The combination of hydrosilanes with a Brønsted or Lewis acid as a promoter can be used for the reagent-controlled chemoselective reduction at room temperature of conjugated C=C bond, enone moiety, or the carbonyl of (β,γ-unsaturated) α-keto thioesters, providing facile access to β,γ-saturated α-keto thioesters, α-hydroxy thioesters, or silyl ethers. The reaction pathway and the chemoselectivity can be fine-tuned through the judicious choice of the hydrosilane or the reaction conditions. The reactions tolerate a wide range of functional groups including labile thioesters and the products are generally obtained in moderate to excellent yields. Unsymmetrical thioethers can also be synthesized using PMHS and catalytic $B(C_6F_5)_3$ via reductive deoxygenation of both the carbonyl groups. The applicability has been highlighted by the amine-mediated and coupling reagent-free syntheses of saturated α-keto amides from β,γ-unsaturated α-hydroxy thioesters and β,γ-saturated *α*-keto thioesters.

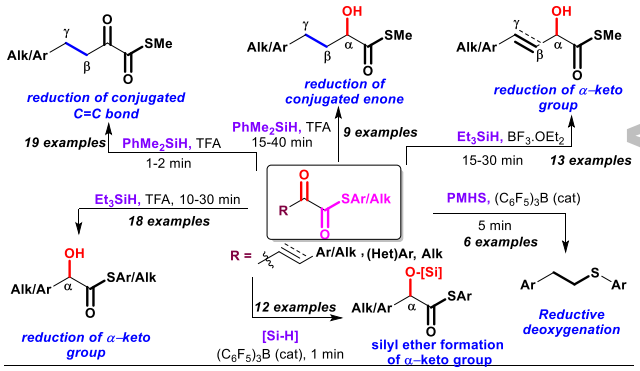
Keywords: α-Keto thioesters; Reduction; Chemoselective; Hydrosilylation; Lewis acids

Introduction

α-Hydroxy or keto thioesters are expedient intermediates for functional group transformations and have long been of interest to synthetic organic chemists.[1] They are often found as intermediates in biochemical processes, such as in acetyl group transfer reactions assisted by coenzyme A[2] and the native chemical ligation (NCL) method to connect peptides.[3] These processes are facilitated due to the greater reactivity towards nucleophiles of thioesters compared to oxoesters, ascribed to the smaller orbital overlap between the sulfur atom and the carbonyl group in the former. Notwithstanding the usefulness of α-hydroxy or keto thioesters either as synthetic intermediates or in pharmaceutical products,[4] their widespread application has been hamstrung by the lack of a general method for synthesis.

Since β,γ-unsaturated *α*-keto thioesters are easy to synthesise, methods for their selective reduction hold promise for easy access of α-hydroxy or keto thioesters. The selective reduction of C-C double bonds and ketones to C-C single bonds and alcohols is indeed an important transformation in organic chemistry.[5] But common reducing agents such as molecular hydrogen,[6] aluminium hydrides and borohydrides[7] often suffer from low selectivity in the presence of other more reducible functional groups. On the other hand, hydrosilanes are mild, practical, and selective reducing agents[8] that can be activated by Brønsted[9] and Lewis acids,[10] or bases,[11] or by transition metals.[12] More importantly their reactivity can be fine-tuned by changing the substituents on the silicon atom. We were therefore attracted by the possibility of using inexpensive and commercially available hydrosilanes for the chemoselective reduction of the conjugated C=C bond or keto group of β,γ-unsaturated *α*-keto thioesters,[13] which may lead to the formation of valuable synthetic intermediates.

Herein we describe the transition metal and base-free,[14] reagent-controlled chemoselective reduction of various functionalities of β,γ-unsaturated α-keto



Scheme 1. Chemoselective reduction of (β,γ-unsaturated) *α*-keto thioesters using hydrosilanes at room temperature.

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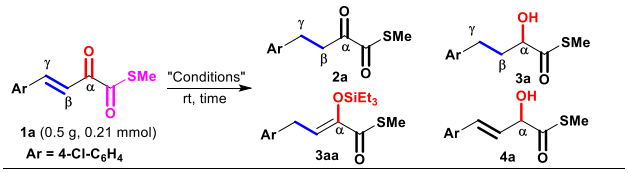
thioesters under hydrosilylation conditions at room temperature (Scheme 1). The reaction pathway and the chemoselectivity can be controlled by judicious choice of the reaction conditions. For example, preferential reduction of the C=C bond may be effected with $PhMe_2SiH$ in TFA, while that of the α-keto group to hydroxy may be brought about by Et_3SiH in $BF_3.OEt_2$. Moreover, aryl or alkyl substituted α-keto thioesters may undergo selective keto reduction either with Et_3SiH in TFA or with various hydrosilanes in presence of catalytic $B(C_6F_5)_3$.[15] On the other hand, reductive deoxygenation of both the carbonyl groups may be performed using PMHS and catalytic $B(C_6F_5)_3$, offering a method to synthesize unsymmetrical thioethers.

Results and Discussion

To optimize the reaction conditions for the chemoselective reductions of the conjugated C=C bond or the keto group of enones, a combination of commercially available hydrosilane and a Brønsted or Lewis acid was reacted with **1a** as a model substrate (Table 1; see also the Supporting Information). The starting materials were completely decomposed within two minutes in the presence of Polymethylhydrosiloxane (PMHS) as a hydride source and trifluoroacetic acid (TFA) as the promoter (entry 1), ascribed to the difficulty in precise determination of actual hydride content in PMHS.[8f] But we were pleased to observe that tetramethyldisiloxane (TMDS), containing two proximal Si-H bonds, could reduce the conjugated double bond selectively in TFA to furnish saturated α-keto thioester (**2a**) in 60% yield (entry 2). The best yield with high chemoselectivity was achieved with 1 equiv of $PhMe_2SiH$, affording **2a** in 83% yield within a minute (entry 3). Further increase in the amount of

Table 1. Optimization studies for **2a**, **3a**, and **4a**.[a]



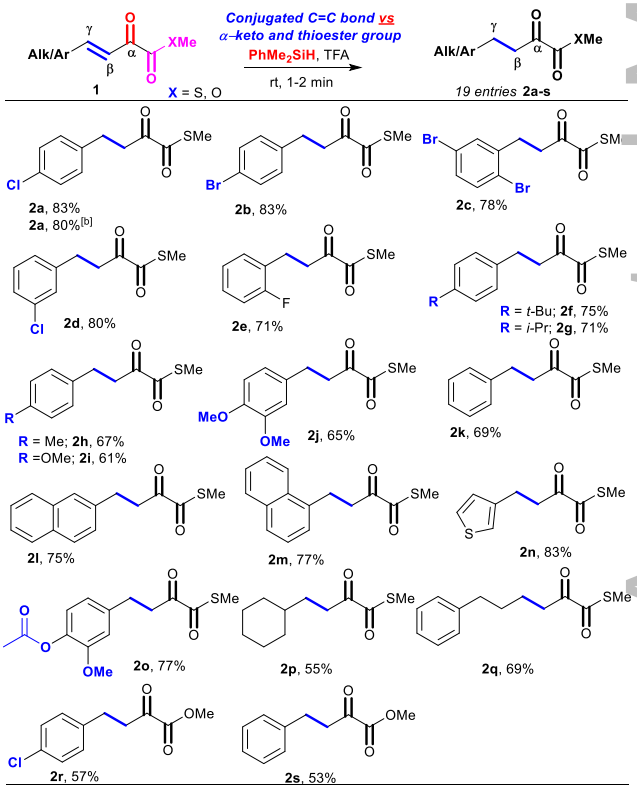
entry	Reaction Conditions	Yield (%) of 2a	3a	3aa	4a
1[b]	PMHS (1 eq), TFA (1 mL), 2 min	n.d.	n.d.	n.d.	n.d.
2	TMDS (1 eq), TFA (1 mL), 5 min	60	10	n.d.	10
3	**$PhMe_2SiH$** (1 eq), TFA (1 mL), 1 min	**83**	trace	n.d.	trace
4	**$PhMe_2SiH$** (3 eq), TFA (1 mL), 20 min	trace	**81**	n.d.	n.d.
5	Et_3SiH (1 eq), TFA (1 mL), 3 min	n.d.	n.d.	20	14
6	Et_3SiH (1 eq). $BF_3.OEt_2$ (1 eq), DCM, 1.5 h	n.d.	trace	n.d.	60
7	**Et_3SiH** (2.5 eq). $BF_3.OEt_2$ (1 eq), DCM, 35 min	n.d.	trace	n.d.	**85**
8	$PhMe_2SiH$ (2.5 eq). $BF_3.OEt_2$ (1 eq), DCM, 1 h	n.d.	trace	n.d.	58
9[c]	TMDS (2.5 eq), $BF_3.OEt_2$ (1 eq), DCM, 5 h	n.d.	n.d.	n.d.	n.d.

[a] *Reaction Conditions*: **1a** (0.05 g, 0.21 mmol, 1.0 equiv) under the reaction conditions at rt (25 - 30 °C). n.d. = not detected.
[b] Starting material decomposed.
[c] Starting material recovered.

hydrosilane to 3 equiv resulted in a complete reduction of the conjugated enone to furnish the saturated α-hydroxy thioester (**3a**) in good yield (entry 4). Next we tried to use Et_3SiH as the hydride source, but this furnished **3aa** and **4a** in low yields in place of **2a** or **3a** (entry 5). However, replacing the Brønsted with a Lewis acid ($BF_3.OEt_2$) afforded **4a** in moderate yields, enhanced further by changing the amount of Et_3SiH to 2.5 equiv (entry 7). Other hydrosilanes, such as $PhMe_2SiH$ showed some activity but gave significantly lower yields (entry 8), while TMDS was completely inactive (entry 9).

Under the optimal reaction conditions (entry 3, Table 1), the substrate scope and generality for the chemoselective reduction of the conjugated C=C bond in presence of thioester and keto group was investigated. As shown in Table 2, β,γ-unsaturated α-keto thioesters carrying aromatic, heterocyclic, or fused aryl rings at the γ-position were selectively reduced with 1 equiv of $PhMe_2SiH$ in TFA at ambient temperature in moderate to good yields within a minute (**2a-o**). Substrates having alicyclic or aliphatic groups at the same position were also found to be compatible under the standard reaction conditions (**2p-q**). Notably, replacement of the thioester group with an oxoester was also feasible, furnishing the expected products (**2r-s**) in moderate yields.[16] It is

Table 2. Chemoselective reduction of the conjugated C=C bond for accessing β,γ-saturated *α*-keto thioesters and esters.[a]



[a] *Reaction conditions*: **1** (0.05 g, 1.0 equiv), $PhMe_2SiH$ (1.0 equiv), trifluoroacetic acid (1.0 mL), rt (25 - 30 °C) for 1-2 min.
[b] The reaction was carried out in 2 mmol batch size.

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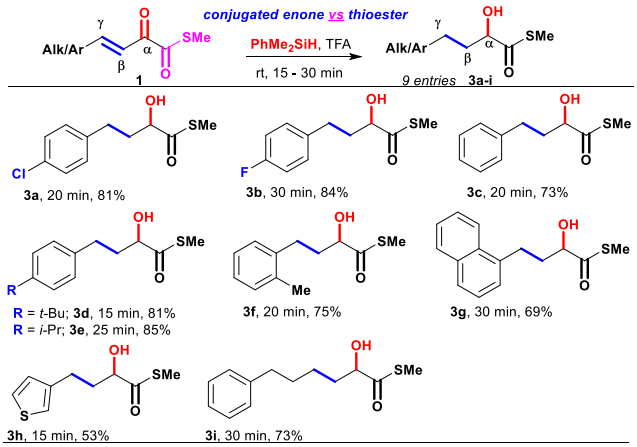
interesting to note that functional groups that are vulnerable to reducing conditions, such as thioester, keto, oxoester, acetoxy, and C(sp^2)-halogen bonds were unaffected, highlighting the mildness and versatility of the method. Additionally, a gram-scale experiment could be performed to isolate **2a** in good yields without special precautions (Table 2).

We next examined the scope and viability of the conjugated enone reduction (Table 3). Under the optimized reaction conditions (Table 1, entry 4), a range of β,γ-unsaturated α-keto thioesters bearing aromatic rings at γ-position underwent smooth conversion to saturated α-hydroxythioesters in good yields (**3a-g**). The 3-thienyl substituted thioester also furnished the expected product **3h**, albeit in moderate yields. Even a β,γ-unsaturated α-keto thioester substituted with an alkyl group at γ-position proved amenable to the reduction (**3i**).

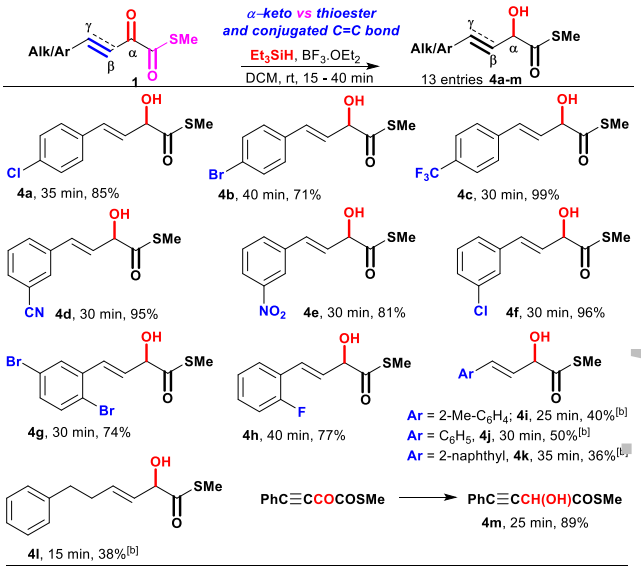
Table 3. Reduction of the conjugated enone for accessing β,γ-saturated α-hydroxy thioesters.[a]



[a] *Reaction conditions*: **1** (0.05 g, 1.0 equiv), $PhMe_2SiH$ (3.0 equiv), TFA (1.0 mL), rt.

We next investigated the substrate scope for the considerably more challenging chemoselective reduction of the keto group of β,γ-unsaturated α-keto thioesters with Et_3SiH in $BF_3.OEt_2$ (entry 7, Table 1) in the presence of conjugated C-C double or triple bond and thioester group (Table 4). Substrates containing electron-withdrawing substituents in the aromatic ring delivered the corresponding products (**4a-h**) in good to nearly quantitative yields. However, the presence of an electron-donating group in the aromatic ring decreased the yield to 40% (**4i**). The outcome may be ascribed to the decrease in electrophilicity of the carbonyl group. The same trend was also observed in case of phenyl, naphthyl, or alkyl (-CH_2CH_2Ph) substituents at the γ-position of β,γ-unsaturated α-hydroxy thioesters (**4j-l**). However, a β,γ-alkynyl derivative was found to be compatible to the reaction, and delivered the product (**4m**) in excellent yields.

Table 4. Switched chemoselectivity in reduction of the keto group of β,γ-unsaturated α-keto thioesters.[a]

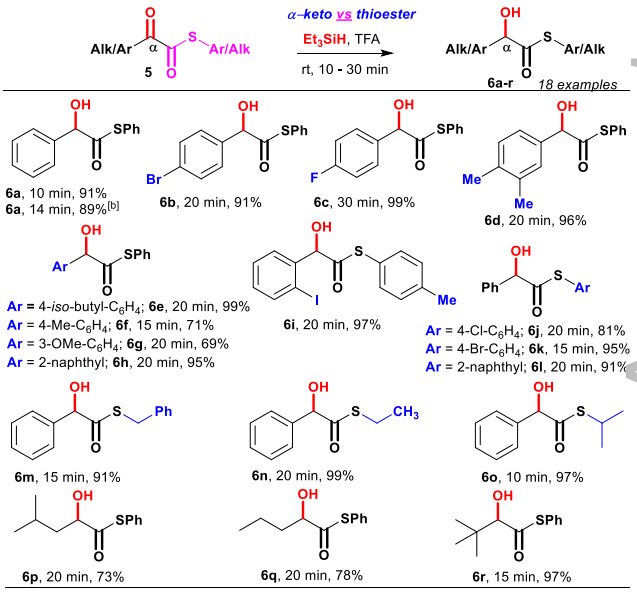


[a] *Reaction conditions*: **1** (0.05 g, 1.0 equiv), Et_3SiH (2.5 equiv), $BF_3.OEt_2$ (1.0 equiv), dry DCM (1.5 mL), rt, 15 - 40 min.

[b] Along with the products **4** and the unreacted starting materials **1**, minor amounts of compounds **2** and **3** were also formed.

Encouraged by the above results, we extended the possibility of the reduction of the α-keto group with aryl- or alkyl-substituted α-keto thioesters rather than styryl-substituted ones (Table 5). Optimization with

Table 5. Chemoselective reduction of the keto group of α-keto thioesters using Et_3SiH in TFA.[a]



[a] *Reaction Condition*: **5** (0.05 g, 1.0 equiv), Et_3SiH (2.0 equiv), and trifluoroacetic acid (1.0 mL), rt.

[b] The reaction was carried out in 1.8 mmol batch size.

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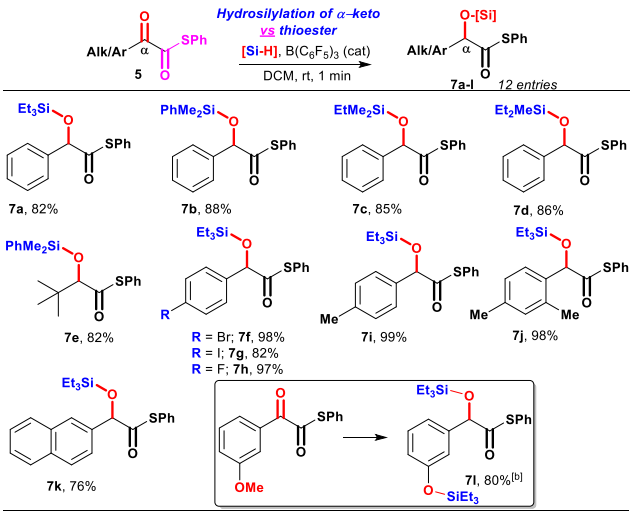
different hydrosilanes and a promoter showed that 2 equiv of Et_3SiH in TFA can be used for accessing α-hydroxy thioesters **6** with high selectivity (see the Supporting Information). As summarized in Table 5, regardless of the electronic properties of the substituents in the aryl- or alkyl- group at the α-position or in the thiol component of α-keto thioesters, products **6a-o** were always obtained in good to nearly quantitative yields. Even thioesters containing α-alkyl substituents delivered the corresponding products smoothly (**6p-r**).

During the optimization studies on **6a**, we observed that adding 1 mol% of $B(C_6F_5)_3$ to a DCM solution of **5a** containing 2 equiv of Et_3SiH, resulted in the chemoselective formation of the silyl ether of the α-hydroxy thioester (**7a**) within a minute. This encouraged us to undertake a thorough investigation (Table 6) to find that replacement of the Et_3SiH with other hydrosilanes also delivered the corresponding silyl ether products in good to excellent yields (**7b-d**). Even a thioester bearing a *tert*-butyl group at the *α*-position was also found to be compatible for the reaction (**7e**). The generality of this redction was further explored with triethylsilane as the hydride source (**7f-k**). Not surprisingly, an anisole derivative underwent demethylation[17] to form the corresponding silyl ether derivative, along with chemoselective hydrosilylation at the α-keto group (**7l**).

Table 6. Chemoselective formation of the silyl ether derivatives of α-hydroxy thioesters.[a]

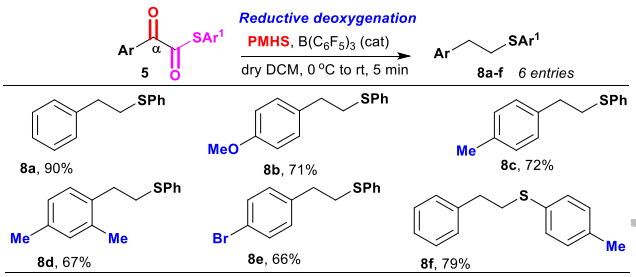


[a] *Reaction Condition*: **5** (0.05 g, 1.0 equiv), silane reagents (2.0 equiv), $B(C_6F_5)_3$ (1 mol%), dry DCM (1.0 mL), rt.

[b] 4.0 equiv Et_3SiH and $B(C_6F_5)_3$ (1 mol%) was used.

Interestingly, by replacing Et_3SiH with PMHS as the hydride source, we noticed the formation of unsymmetrical thioethers (**8a-f**) in good to excellent yields via reductive deoxygenation of the carbonyl groups of the *α*-keto thioesters (Table 7).[18a-d] Unsymmetrical thioethers are classically prepared by the alkylation of thiols under basic conditions.[18e] We envision that these transition metal- and base-free reaction conditions will be complementary to the existing methods, particularly for the synthesis of base-sensitive compounds.

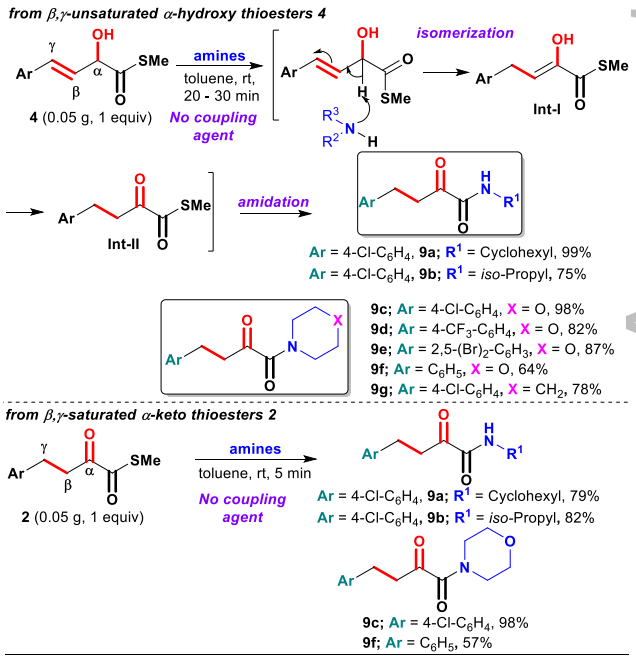
Table 7. Synthesis of unsymmetrical thioethers via reductive deoxygenation of the carbonyl groups.[a]



[a] *Reaction Condition*: **5** (0.05 g, 1.0 equiv), PMHS (2.0 equiv), $B(C_6F_5)_3$ (1 mol%), DCM.

The synthetic utility of the developed β,γ-unsaturated α-hydroxy thioesters **4** was demonstrated by metal- and coupling reagent-free, primary or secondary amine-mediated synthesis of β,γ-saturated α-keto amides (**9a-g**) in good to nearly quantitative yields (Scheme 2). Based on earlier reports, the reaction is believed to proceed through the amine-catalyzed isomerization of allylic alcohols[19] via **Int-I** to **Int-II**, which underwent amidation to yield the desired products. It is noteworthy that α-keto amides (**9a-b,c,f**) could also be synthesized from β,γ-saturated *α*-keto thioesters under the same optimized conditions in good to excellent yields (Scheme 2).[20]

Scheme 2. Amine-mediated syntheses of β,γ-saturated α-keto amides from β,γ-unsaturated α-hydroxy thioesters **4** and β,γ-saturated α-keto thioesters **2**.



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Conclusion

In conclusion, we have developed a reagent-controlled highly chemoselective reduction of various functionalities of β,γ-unsaturated α-keto thioesters at room temperature. The reaction pathway can be steered by the judicious choice of the reaction conditions. The conjugated C=C bond can be selectively reduced with $PhMe_2SiH$ in TFA, and the α-keto group using Et_3SiH in combination with $BF_3.OEt_2$. Aryl or alkyl substituted α-keto thioesters can be selectively reduced to α-hydroxy thioesters or silyl ether derivatives under hydrosilylation conditions in good to quantitative yields. On the other hand, unsymmetrical thioethers can be synthesized via reductive deoxygenation of both the carbonyl groups with PMHS and catalytic $B(C_6F_5)_3$. To demonstrate the potentiality of the method, amine-mediated and coupling reagent-free syntheses of saturated α-keto amides from β,γ-unsaturated *α*-hydroxy thioesters and β,γ-saturated *α*-keto thioesters have also been carried out successfully.

Experimental Section

General Procedure and Representative Examples

General Procedure for the Synthesis of 2a-p: γ-Substituted β,γ-unsaturated α-keto thioesters **1** (0.05 g, 1 equiv) were dissolved in trifluoroacetic acid (1.0 mL). Then dimethylphenylsilane ($PhMe_2SiH$; 1.0 equiv) was added to the reaction mixture which was allowed to stir at the room temperature for 1-2 min under argon atmosphere. After completion of the reaction (TLC), water was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified using silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **2a-p**.

***S*-methyl 4-(4-chlorophenyl)-2-oxobutanethioate 2a:** Prepared according to the general procedure discussed above: R_f = 0.3; eluent, EtOAc/*n*-hexane (2%); yellow liquid (0.042 g, 83%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25 (d, J = 8.4 Hz, 2 H), 7.13 (d, J = 8.4 Hz, 2 H), 3.13 (t, J = 7.8 Hz, 2 H), 2.92 (t, J = 6.9 Hz, 2 H), 2.34 ppm (s, 3 H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 193.9, 191.6, 138.4, 132.1, 129.7 (2 CH), 128.6 (2 CH), 37.9 (CH_2), 28.2 (CH_2), 11.2 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1720, 1667, 1492, 1091, 847, 814, 741 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{11}{}^{35}ClO_2SNa$ [M + Na]$^+$: 265.0066; found: 265.0061.

General Procedure for the Synthesis of 3a-i: γ-Substituted β,γ-unsaturated α-keto thioesters **1** (0.05 g, 1 equiv) were dissolved in trifluoroacetic acid (1.0 mL), and dimethylphenyl silane ($PhMe_2SiH$; 3.0 equiv) was added to the reaction mixture that was allowed to stir at the room temperature for 15-30 min under argon atmosphere. After completion of the reaction (TLC), water was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified by silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **3a-i**.

***S*-methyl 4-(4-chlorophenyl)-2-hydroxybutanethioate 3a:** Prepared according to the general procedure discussed above: R_f = 0.3; eluent, EtOAc/*n*-hexane (10%); colourless solid (0.041 g, 81%); mp 49-51 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.25 (d, J = 8.4 Hz, 2 H), 7.14 (d, J = 8.4 Hz, 2 H), 4.24 (dd, J = 9.0, 4.2 Hz, 1 H), 2.85 (br. s., 1 H), 2.75 - 2.79 (m, 1 H), 2.71 - 2.75 (m, 1 H), 2.32 (s, 3 H), 2.10 - 2.16 (m, 1 H), 1.93 ppm (dtd, J = 14.4, 8.4, 6.0 Hz, 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 204.3, 139.4, 131.9, 129.9 (2 CH), 128.6 (2 CH), 76.7, 36.6 (CH_2), 30.3 (CH_2), 11.2 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 3429, 1678, 1489, 1088, 814, 609 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{13}{}^{35}ClO_2SNa$ [M + Na]$^+$: 267.0226; found: 267.0226.

General Procedure for the Synthesis of 4a-m: γ-Substituted β,γ-unsaturated α-keto thioesters **1** (0.05 g, 1 equiv) were dissolved in dry DCM (1.0 mL), and triethyl silane (Et_3SiH; 2.5 equiv) and $BF_3.OEt_2$ (1.0 equiv) were added successively to the reaction mixture which was allowed to stir at the room temperature for 15-40 min under argon atmosphere. After completion of the reaction (TLC), water was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified by silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **4a-m**.

***S*-methyl (*E*)-4-(4-chlorophenyl)-2-hydroxybut-3-enethioate 4a:** Prepared according to the general procedure discussed above: R_f = 0.3; eluent, EtOAc/*n*-hexane (15%); light yellow liquid (0.043 g, 85%). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.32 (d, J = 9.0 Hz, 2 H), 7.29 (d, J = 8.4 Hz, 2 H), 6.76 (dd, J = 15.6, 0.6 Hz, 1 H), 6.20 (dd, J = 15.6, 6.6 Hz, 1 H), 4.89 (dd, J = 0.6, 6.6 H, 1 H), 3.41 (br. s., 1 H), 2.35 ppm (s, 3 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 202.0, 134.4, 134.0, 132.7, 128.9 (2 CH), 128.0 (2 CH), 125.9, 78.5, 11.5 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 3429, 1678, 1489, 1088, 968, 814 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{11}H_{12}{}^{35}ClO_2S$ [M + H]$^+$: 243.0246; found: 243.0250 and $C_{11}H_{12}{}^{37}ClO_2S$ [M + H]$^+$: 245.0217; found: 245.0220.

General Procedure for the Synthesis of 6a-r: α-Keto thioesters **5** (0.05 g, 1 equiv) were dissolved in trifluoroacetic acid (1.0 mL), and triethyl silane (Et_3SiH; 2.0 equiv) was added to the reaction mixture which was allowed to stir at the room temperature for 20-30 min under argon atmosphere. After completion of the reaction (TLC), water was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified by silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **6a-r**.

***S*-phenyl 2-(4-bromophenyl)-2-hydroxyethanethioate 6b:** Prepared according to the general procedure discussed above: R_f = 0.3; eluent, EtOAc/*n*-hexane (10%); light yellow solid (0.046 g, 91%); mp 77-79 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.55 (d, J = 8.4 Hz, 2 H), 7.39 - 7.44 (m, 3 H), 7.35 - 7.37 (m, 4 H), 5.29 (s, 1 H), 3.72 ppm (br. s., 1 H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$): δ = 200.0, 136.6, 134.6 (2 CH), 132.0 (2 CH), 129.8, 129.4 (2 CH), 128.8 (2 CH), 126.2, 123.2, 79.3 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1690, 1480, 968, 834, 792 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{14}H_{11}{}^{79}BrO_2SNa$ [M + Na]$^+$: 344.9561; found: 344.9544 and *m/z* calcd for $C_{14}H_{11}{}^{81}BrO_2SNa$ [M + Na]$^+$: 346.9541; found: 346.9521.

General Procedure for the Synthesis of 7a-l: α-Keto thioesters **5** (0.05 g, 1 equiv) were dissolved in dry DCM (1.0 mL), and various silanes - Et_3SiH, $PhMe_2SiH$, $EtMe_2SiH$, and Et_2MeSiH (2.0 equiv) and $B(C_6F_5)_3$ (1 mol%) were added successively to the reaction mixture and allowed to stir at the room temperature for 1 min under argon atmosphere. After completion of the reaction (TLC), water was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue

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was purified by silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **7a-l**.

***S*-phenyl 2-phenyl-2-((triethylsilyl)oxy)ethanethioate 7a:** Prepared according to the general procedure discussed above: R_f = 0.3; eluent, EtOAc/*n*-hexane (2%); colourless liquid (0.061 g, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 7.2 Hz, 2 H), 7.30 - 7.37 (m, 8 H), 5.27 (s, 1 H), 0.97 - 1.01 (m, 9 H), 0.65 - 0.72 ppm (m, 6 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ = 201.5, 139.0, 134.8 (2 CH), 129.1 (2 CH), 129.1 (2 CH), 128.5 (2 CH), 128.4, 126.4 (2 CH), 80.5, 6.8 (3 CH_3), 4.8 ppm (3 CH_2); IR (KBr): $\tilde{\nu}_{max}$ = 1703, 1125, 1053, 1001, 742, 701, 687 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{20}H_{27}O_2SSi$ [*M* + H]$^+$: 359.1501; found: 359.1491 and *m/z* calcd for $C_{20}H_{26}O_2SSiNa$ [*M* + Na]$^+$: 381.1321; found: 381.1308.

General Procedure for the Synthesis of 8a-f: α-Keto thioesters **5** (0.05 g, 1 equiv) were dissolved in dry DCM (1.0 mL), and polymethylhydrosiloxane (PMHS; 2.0 equiv) and $B(C_6F_5)_3$ (1 mol%) were added successively to the reaction mixture at 0 °C under argon atmosphere. The reaction mixture was allowed to stir at the room temperature for 5 min. After completion of the reaction (TLC), water was added, and the product was extracted with DCM. The combined organic layers were dried over anhydrous Na_2SO_4 and filtered, and the filtrate was concentrated under reduced pressure to get a residue. The crude residue was purified using silica gel column chromatography [230−400; eluent: ethyl acetate/*n*-hexane] to obtain **8a-f**.

(2,4-dimethylphenethyl)(phenyl)sulfane 8d: Prepared according to the general procedure discussed above: R_f = 0.3; eluent, *n*-hexane (100%); colourless liquid (0.03 g, 67%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 7.5 Hz, 2 H), 7.30 (t, *J* = 6.9 Hz, 2 H), 7.20 (t, *J* = 7.2 Hz, 1 H), 7.04 (d, *J* = 7.5 Hz, 1 H), 6.95 - 6.98 (m, 2 H), 3.10 (t, *J* = 8.7 Hz, 2 H), 2.89 (t, *J* = 8.7 Hz, 2 H), 2.29 (s, 3 H), 2.24 ppm (s, 3 H); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 136.4, 136.1, 135.7, 135.3, 131.1, 129.2 (2 CH), 129.0, 128.9 (2 CH), 126.7, 125.9, 34.0 (CH_2), 32.7 (CH_2), 20.9, 19.1 ppm; IR (KBr): $\tilde{\nu}_{max}$ = 1442, 1261, 1026, 802, 736 cm^{-1}; HRMS (ESI): *m/z* calcd for $C_{16}H_{18}SNa$ [*M* + Na]$^+$: 265.1027; found: 265.1023.

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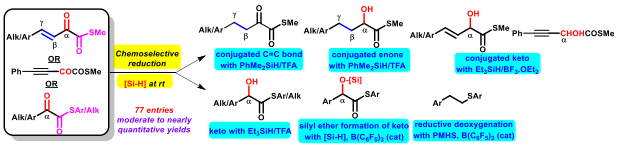
FULL PAPER

Transition-Metal-Free Reduction of α-Keto Thioesters with Hydrosilanes at Room Temperature: Divergent Synthesis through Reagent-Controlled Chemoselectivities

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Rajib Maity, Bhanuranjan Das, and Indrajit Das*



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