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O-Alkyl *S*-3,3-Dimethyl-2-oxobutyl Dithiocarbonates as Versatile Sulfur-Transfer Agents in Radical C(sp^3)–H Functionalization

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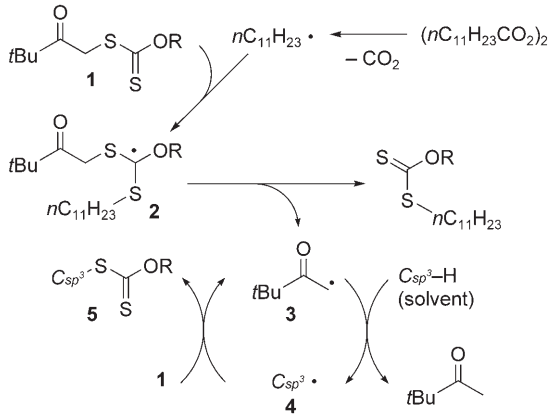
Dedicated to Prof. Miguel Yus on the occasion of his 60th birthday

Abstract: Boiling of the title compounds in ethereal solvents or cycloalkanes in the presence of a radical initiator leads to radical C(sp^3)–H functionalization, by which a sulfur atom is introduced into the ethereal solvents at the oxygenated carbon atom or into the cycloalkanes. Both acyclic and cyclic ethers, such as [18]crown-6 and [D_8]THF, undergo the sulfur transfer. The reaction is useful for the synthesis of monothioacetals, thiols, and sulfides from simple starting materials.

Keywords: C–H activation · C–S bond formation · dithiocarbonates · radical reactions · sulfur transfer

Introduction

Selective and efficient functionalizations of unreactive C–H bonds have been actively investigated.[1] Among them, functionalizations of C(sp^3)–H bonds are more difficult than those of C(sp^2)–H and C(sp)–H bonds because of the lack of a proximal π system. To realize the difficult C(sp^3)–H functionalization, radical processes are quite useful as they take advantage of homolytic hydrogen abstraction.[2] Although the formation of C–C[3], C–O[4], C–N,[5] and C–halogen bonds[6] by intermolecular radical C–H functionalization is well-documented, there are few reports on C–S bond formation.[7–9] Herein, we disclose new reagents for efficient C–S bond formation by radical C–H functionalization.



Scheme 1. Plausible mechanism for C–S bond formation by radical C–H functionalization.

Results and Discussion

The new reagents **1** were designed based on the radical chemistry of dithiocarbonate (Scheme 1).[8,10] An undecyl radical, thermally generated from dilauroyl peroxide, would attack the sulfur atom of the thiocarbonyl group in **1** to generate the radical **2**. Liberation of the 3,3-dimethyl-2-oxobutyl radical **3** would then take place with concomitant formation of *O*-alkyl *S*-undecyl dithiocarbonate. The electron-deficient radical **3** would be reactive enough to abstract hydrogen homolytically from a molecule of solvent such as ethers and cycloalkanes. The electron-rich radical **4** would react with **1** to complete the conversion of the initial C(sp^3)–H bond into a C(sp^3)–S bond and to regenerate **3**.

The preparation of **1** was facile. The reaction of chloropinacolone with potassium *O*-ethyl dithiocarbonate in acetone afforded **1a** quantitatively (Scheme 2). Other dithiocarbon-

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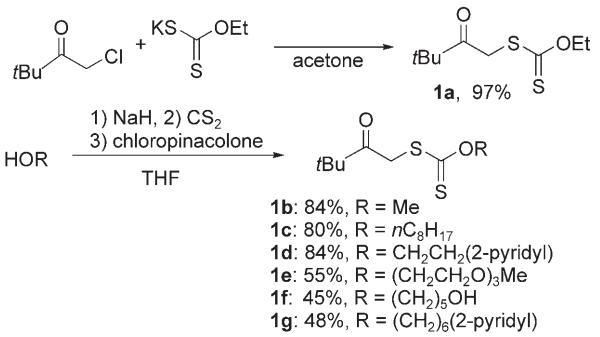
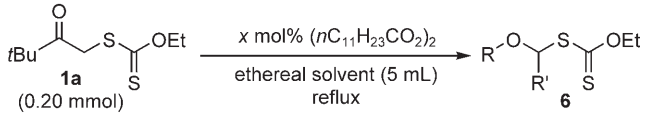
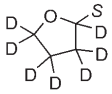


Scheme 2. Preparation of sulfur-transfer agents.

Table 1. C–S bond formation by using sulfur-transfer agents **1a** through radical C–H functionalization of ethereal solvents.



Entry	Solvent	x	B.p. [°C]	t [min]	**6**	Yield[a] [%]
1	1,4-dioxane	10	101	30	 **6a**	90
2	tetrahydropyran	20	88	100	 **6b**	76
3	tetrahydrofuran (THF)	10	66	120	 **6c**	90
4	dipropyl ether	15	88	120	 **6d**	69
5	1,2-dimethoxy-ethane	10	84	100	 **6e**  **6f**	93 (71:29)[b]
6	2,2-dimethyl-1,3-dioxolane	10	92	120	 **6g**	77
7	diethyl ether	20[c]	34	180	 **6h**	2
8	diethyl ether	10	100[d]	60	**6h**	69
9	[D8]THF	10	66	120	 [D7]**6c**	15
10	[D8]THF	15	120[d]	60	[D7]**6c**	79

[a] Based on **1a**. [b] The ratio of **6e** to **6f**. [c] Triethylborane was used. [d] Microwave heating in a sealed vial. S = SC(S)OEt.

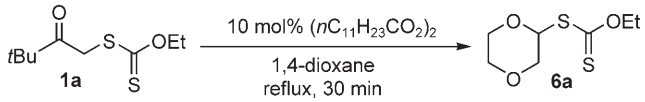
Abstract in Japanese:
表題化合物をエーテル系溶媒中あるいはシクロアルカン中ラジカル開始剤存在下加熱すると、エーテル酸素の隣の炭素上あるいはシクロアルカン内の sp^3 炭素– 水素結合が sp^3 炭素– 硫黄結合に置き換わる。本手法はモノチオアセタール、チオール、スルフィドの合成法として有用である。

ates **1b–g** were prepared in high yields from the corresponding alcohols, carbon disulfide, and chloropinacolone in a one-pot manner.

Dithiocarbonate **1a** was heated in boiling dioxane in the presence of 10 mol% of dilauroyl peroxide for 30 min to provide **6a** in 90% yield (Table 1, entry 1). The reaction of tetrahydropyran was less efficient and required a larger amount of the initiator as well as a longer reaction time (Table 1, entry 2). The lower reactivity of tetrahydropyran could be due to the slower hydrogen-abstraction step[11] as well as its relatively low boiling point (88°C). THF and acyclic dipropyl ether underwent the sulfur-transfer reaction smoothly (Table 1, entries 3 and 4). The regioselectivity in the reaction of 1,2-dimethoxyethane was moderate: a separable mixture of **6e** and **6f** in the ratio 71:29 was produced in high combined yield (Table 1, entry 5). Sulfur transfer to diethyl ether was difficult due to its low boiling point (Table 1, entry 7). This difficulty could be overcome by performing the reaction in a sealed vial with microwave heating at 100°C (Table 1, entry 8). Microwave heating in a sealed vial was applicable to the carbon–deuterium bond activation of [D_8]THF, wherein a considerable kinetic isotope effect was observed (Table 1, entries 9 and 10). The conversion of [D_8]THF is useful for the synthesis of deuterated tetrahydrofuran derivatives such as [D_6]γ-butyrolactone.[12]

The above reaction should be performed under highly diluted conditions (Table 2). Although reaction with a concentration of 0.040 M provided a 90% yield of **6a** (Table 2, entry 1), reaction with a concentration of 0.10 M resulted in a slight decrease in yield (Table 2, entry 2). A much higher concentration, 1.0 M, led to unsatisfactory yield with the recovery of a large amount of **1a** (Table 2, entry 3). The use of benzene as a cosolvent to minimize the amount of dioxane resulted in failure (Table 2, entry 4). The reaction can be performed on a large scale to provide **6a** in excellent yield with 90% recovery of dioxane by simple evaporation (Table 2, entry 5).

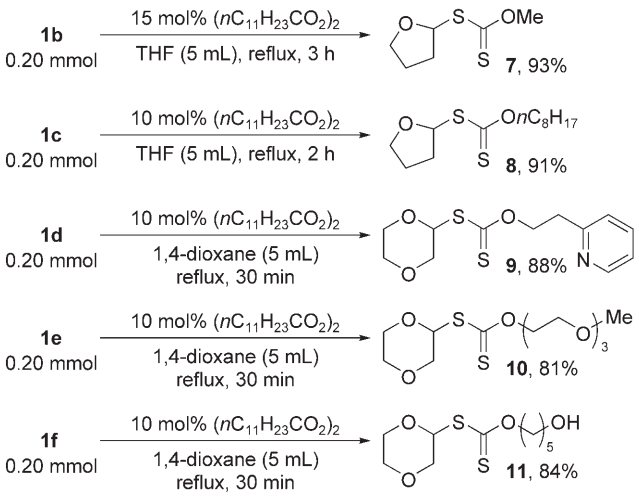
Table 2. Effect of concentration and scale on the reaction in dioxane.



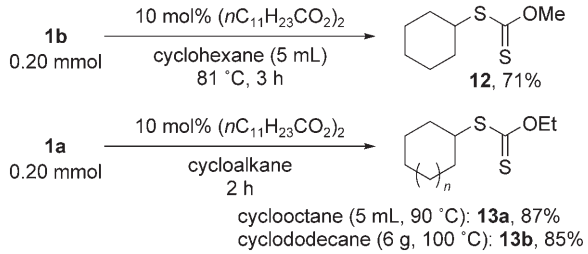
Entry	**1a** [mmol]	Dioxane [mL]	[**1a**] [M]	Yield [%]	Recovered **1a** [%]
1	0.20	5.0	0.040	90	0
2	2.0	20	0.10	83	3
3	1.0	1.0	1.0	19	70
4	0.20	0.40	0.037[a]	6	90
5	20	500	0.040	88	0

[a] Benzene (5.0 mL) was used as a cosolvent.

Apart from **1a**, dithiocarbonates **1b–f** also effected sulfur transfer to ethereal solvents (Scheme 3). Owing to the high chemoselectivity of the radical reaction, the basic pyridyl group of **1d** and the hydroxy group of **1f** did not influence the efficiency of the reaction.



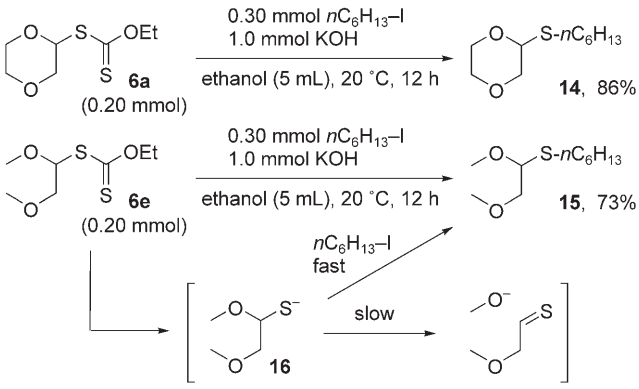
Scheme 3. Reactions with other sulfur-transfer agents.



Scheme 4. Reactions of cycloalkanes.

The sulfur-transfer reaction from **1** to cycloalkanes provides a mild and efficient way for the synthesis of cycloalkanethiol derivatives (Scheme 4). Although a large excess of cycloalkane was necessary, it can be recovered. For instance, when cyclododecane was used, it was recovered in 98% yield. The reaction of other alkanes such as hexane and methylcyclohexane proceeded, albeit with little regioselectivity.

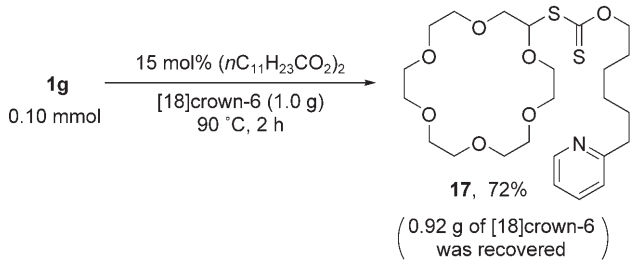
The transformations of dithiocarbonates **6a** and **6e** were examined (Scheme 5). These compounds were converted



Scheme 5. Transformations of products **6**.

into hexylthioacetals **14** and **15**, respectively, by the action of potassium hydroxide and 1-iodohexane[13] in ethanol. Notably, the possible fragmentation of intermediate **16** was slow enough to allow it to react with 1-iodohexane.

The present method was applied to the functionalization of [18]crown-6 (Scheme 6). Owing to the involatile and highly polar nature of the crown ether, the isolation of **17**



Scheme 6. Functionalization of a crown ether.

required size-exclusion chromatography. Although the expensive crown ether was used as a solvent, 92% of it was recovered during the purification procedure. The product **17** is a new "lariat ether"[14] that interacts more strongly with cations than the parent crown ether. By taking advantage of the variability of the *O*-alkyl group, this procedure offers a new method for the synthesis of crown ethers with a functionalized side arm.

Conclusions

We have developed an efficient sulfur-transfer agent. The reagent enables direct transformations of ethereal solvents and cycloalkanes into monothioacetals, thiols, and sulfides.

Experimental Section

General

Unless otherwise noted, all reactions were carried out with conventional glassware. Microwave-assisted reactions were performed with a focused microwave unit (Biotage Initiator™). The maximum irradiation power is 400 W. Each reaction was run in a 5-mL glass pressure vial, which is a commercially available and special vial for the Biotage Initiator™. It took 2–3 min to reach the indicated temperatures. After that, controlled microwave irradiation started and was continued for 60 min to keep the reaction temperature constant.

^{1}H (500 MHz) and ^{13}C NMR (125.7 MHz) spectra were recorded in $CDCl_3$ on a Varian UNITY INOVA 500 spectrometer. Chemical shifts (δ) are in parts per million relative to tetramethylsilane at 0.00 ppm for ^{1}H and relative to $CDCl_3$ at 77.0 ppm for ^{13}C unless otherwise noted. IR spectra were recorded on a Shimadzu FTIR-8200PC spectrometer. Mass spectra were obtained on a JEOL Mstation 700 spectrometer. TLC analysis was performed on commercial glass plates with a 0.25-mm layer of Merck silica gel 60F_{254}. Silica gel (Wakogel 200 mesh) was used for column chromatography. Gel-permeation chromatography (GPC) was performed with an LC-908 instrument (Japan Analytical Industry Ltd., two in-line JAIGEL-2H, toluene, 10 mL min^{-1}, UV and refractive-index detectors). Elemental analysis was carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, starting materials were readily available from commercial suppliers and were used without further purification. Ethereal solvents were purchased from Wako Pure Chemicals just prior to use and were used as received.

Syntheses

1a (Scheme 2): Under an atmosphere of argon, potassium *O*-ethyl dithiocarbonate (0.96 g, 6.0 mmol) was added to a solution of 1-chloro-3,3-dimethyl-2-butanone (0.66 mL, 5.0 mmol) in acetone (15 mL). The mixture was stirred for 1 h at ambient temperature and then poured into water (20 mL). The product was extracted with hexane/ethyl acetate (5:1, 3× 10 mL). The combined organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. Silica-gel column chromatography (hexane/ethyl acetate = 5:1) afforded analytically pure *O*-ethyl *S*-3,3-dimethyl-2-oxobutyl dithiocarbonate (**1a**) as a pale-yellow oil (1.1 g, 4.9 mmol, 97%). IR (neat): $\tilde{\nu}$ = 2969, 1716, 1477, 1366, 1223, 1114, 1047, 1001 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9H), 1.41 (t, J = 7.0 Hz, 3H), 4.28 (s, 2H), 4.63 ppm (q, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.8, 26.7, 42.6, 44.4, 70.5, 207.3, 213.9 ppm; elemental analysis: calcd (%) for $C_9H_{16}O_2S_2$: C 49.06, H 7.32; found: C 49.15, H 7.11.

1b (Scheme 2): The preparation of *O*-methyl *S*-3,3-dimethyl-2-oxobutyl dithiocarbonate (**1b**) is representative for **1c**–**g**. Under an atmosphere of argon, methanol (0.33 mL, 8.0 mmol) was added to a suspension of sodium hydride (60 wt% in oil, 0.24 g, 6.0 mmol) in THF (10 mL). The mixture was stirred for 40 min at ambient temperature. Carbon disulfide (0.48 mL, 8.0 mmol) in THF (5 mL) was then added at 0°C, and the mixture was soon warmed to room temperature. After 2 h, 1-chloro-3,3-dimethyl-2-butanone (0.66 mL, 5.0 mmol) was added at 0°C, and the mixture was soon warmed to room temperature. After a further 3 h, the mixture was poured into water (20 mL). The product was extracted with hexane/ethyl acetate (5:1, 3×10 mL). The combined organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. Silica-gel column chromatography (hexane/ethyl acetate = 20:1–10:1) afforded analytically pure **1b** as a yellow oil (0.87 g, 4.2 mmol, 84%). IR (neat): $\tilde{\nu}$ = 2969, 1717, 1477, 1437, 1367, 1226, 1157, 1071, 1053, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9H), 4.17 (s, 3H), 4.29 ppm (s, 2H); ^{13}C NMR ($CDCl_3$): δ = 26.6, 42.9, 44.4, 60.5, 207.3, 214.7 ppm; elemental analysis: calcd (%) for $C_8H_{14}O_2S_2$: C 46.57, H 6.84; found: C 46.63, H 6.67.

1c: *O*-Octyl *S*-3,3-dimethyl-2-oxobutyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2959, 2921, 2854, 1717, 1467, 1347, 1248, 1232, 1087, 1046 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 3H), 1.25 (s, 9H), 1.22–1.36 (m, 8H), 1.36–1.43 (m, 2H), 1.75–1.82 (m, 2H), 4.28 (s, 2H), 4.56 ppm (t, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 22.6, 25.8, 26.7, 28.2, 29.1, 29.1, 31.7, 42.6, 44.4, 74.8, 207.4, 214.0 ppm; elemental analysis: calcd (%) for $C_{15}H_{28}O_2S_2$: C 59.16, H 9.27; found: C 59.22, H 9.34.

1d: *S*-3,3-Dimethyl-2-oxobutyl *O*-2-(2-pyridyl)ethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2968, 1716, 1592, 1476, 1437, 1367, 1228, 1214, 1072, 1051, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.22 (s, 9H), 3.27 (t, J = 7.0 Hz, 2H), 4.24 (s, 2H), 4.97 (t, J = 7.0 Hz, 2H), 7.17 (ddd, J = 7.5, 5.0, 1.0 Hz, 1H), 7.22 (ddd, J = 7.5, 1.0, 1.0 Hz, 1H), 7.63 (ddd, J = 7.5, 7.5, 2.0 Hz, 1H), 8.55 ppm (ddd, J = 5.0, 2.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 26.6, 36.8, 42.6, 44.3, 73.0, 121.8, 123.5, 136.5, 149.5, 157.3, 207.3, 213.5 ppm; elemental analysis: calcd (%) for $C_{14}H_{19}NO_2S_2$: C 56.53, H 6.44; found: C 56.79, H, 6.42.

1e: *S*-3,3-Dimethyl-2-oxobutyl *O*-3,6,9-trioxadecyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2968, 2875, 1717, 1478, 1366, 1221, 1109, 1053, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9H), 3.39 (s, 3H), 3.55–3.58 (m, 2H), 3.65–3.71 (m, 6H), 3.82–3.86 (m, 2H), 4.29 (s, 2H), 4.69–4.73 ppm (m, 2H); ^{13}C NMR ($CDCl_3$): δ = 26.6, 42.7, 44.3, 59.0, 68.4, 70.5, 70.5, 70.7, 71.9, 73.1, 207.2, 213.9 ppm; elemental analysis: calcd (%) for $C_{14}H_{26}O_5S_2$: C 49.68, H 7.74; found: C 49.42, H 7.76.

1f: *O*-5-Hydroxypentyl *S*-3,3-dimethyl-2-oxobutyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 3368 (br), 2938, 2869, 1714, 1477, 1367, 1229, 1048, 1001 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9H), 1.46–1.53 (m, 2H), 1.55–1.66 (m, 3H), 1.80–1.87 (m, 2H), 3.67 (t, J = 6.5 Hz, 2H), 4.28 (s, 2H), 4.59 ppm (t, J = 6.5 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 22.2, 26.6, 28.0, 32.2, 42.6, 44.3, 62.5, 74.4, 207.4, 214.0 ppm; elemental analysis: calcd (%) for $C_{12}H_{22}O_3S_2$: C 51.77, H 7.96; found: C 51.94, H 8.13.

1g: *S*-3,3-Dimethyl-2-oxobutyl *O*-6-(2-pyridyl)hexyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2934, 2858, 1717, 1590, 1475, 1434, 1366, 1227, 1049, 999, 749 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 9H), 1.37–1.49 (m, 4H), 1.70–1.83 (m, 4H), 2.79 (t, J = 7.5 Hz, 2H), 4.28 (s, 2H), 4.55 (t, J = 7.0 Hz, 2H), 7.10 (ddd, J = 7.5, 5.0, 1.0 Hz, 1H), 7.14 (ddd, J = 7.5, 1.0, 1.0 Hz, 1H), 7.59 (ddd, J = 7.5, 7.5, 2.0 Hz, 1H), 8.53 ppm (ddd, J = 5.0, 2.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 25.7, 26.7, 28.1, 28.9, 29.6, 38.3, 42.7, 44.4, 74.6, 120.9, 122.7, 136.2, 149.2, 162.2, 207.4, 214.0 ppm; elemental analysis: calcd (%) for $C_{18}H_{27}NO_2S_2$: C 61.15, H 7.70; found: C 61.27, H 7.93%.

Transformation of the C–H bond of the solvent into a C–S bond: The synthesis of *O*-ethyl *S*-2-oxacyclopentyl dithiocarbonate (**6c**; Table 1, entry 3) is representative. Under an atmosphere of argon, a solution of **1a** (44 mg, 0.20 mmol) and dilauroyl peroxide (DLP; 8.0 mg, 0.020 mmol) in THF (5.0 mL) was stirred for 2 h while heated at reflux. The mixture was then cooled to room temperature, diluted with acetone, dried over sodium sulfate, filtered, and concentrated in vacuo. Silica-gel column chromatography (hexane/ethyl acetate = 20:1–10:1) afforded analytically pure **6c** as a yellow oil (34 mg, 0.18 mmol, 90%). IR (neat): $\tilde{\nu}$ = 2980, 2871, 1458, 1364, 1292, 1219, 1112, 1042, 933 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.44 (t, J = 7.5 Hz, 3H), 1.90–2.13 (m, 3H), 2.37–2.46 (m, 1H), 3.90–4.02 (m, 2H), 4.61–4.73 (m, 2H), 6.17 ppm (dd, J = 7.5, 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 24.6, 31.7, 68.4, 69.6, 88.3, 213.2 ppm; elemental analysis: calcd (%) for $C_7H_{12}O_2S_2$: C 43.72, H 6.29; found: C 43.99, H 6.31.

6a: *O*-Ethyl *S*-2,5-dioxacyclohexyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2967, 2920, 2855, 1447, 1220, 1111, 1045, 893, 869 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.44 (t, J = 7.5 Hz, 3H), 3.70–3.81 (m, 3H), 3.88 (dd, J = 12.0, 3.0 Hz, 1H), 4.04 (dd, J = 12.0, 3.0 Hz, 1H), 4.07–4.13 (m, 1H), 4.63–4.73 (m, 2H), 5.92 ppm (dd, J = 3.0, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 63.6, 66.7, 69.7, 70.3, 84.2, 211.7 ppm; elemental analysis: calcd (%) for $C_7H_{12}O_3S_2$: C 40.36, H 5.81; found: C 40.59, H 5.67.

6b: *O*-Ethyl *S*-2-oxacyclohexyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2941, 2859, 1441, 1218, 1105, 1057, 1038, 1010, 882, 714 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.43 (t, J = 7.0 Hz, 3H), 1.58–1.70 (m, 2H), 1.70–1.77 (m, 2H), 1.84–1.91 (m, 1H), 2.02–2.10 (m, 1H), 3.70–3.76 (m, 1H), 3.93–3.99 (m, 1H), 4.61–4.72 (m, 2H), 5.89 ppm (dd, J = 5.5, 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 21.6, 25.3, 30.7, 65.6, 69.9, 86.1, 212.4 ppm; elemental analysis: calcd (%) for $C_8H_{14}O_2S_2$: C 46.57, H 6.84; found: C 46.81, H 6.89.

[D_7]**6c**: *S*-1,3,3,4,4,5,5-Heptadeuterio-2-oxacyclopentyl *O*-ethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2982, 2239, 1221, 1114, 1062, 1044, 1004, 972 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.43 (t, J = 7.0 Hz, 3H), 4.65 (dq, J = 11.0, 7.0 Hz, 1H), 4.69 ppm (dq, J = 11.0, 7.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 23.6 (quint, J = 20.3 Hz), 30.9 (quint, J = 20.3 Hz), 67.6 (quint, J = 22.3 Hz), 69.6, 88.0 (t, J = 26.8 Hz), 213.2 ppm; elemental analysis: calcd (%) for $C_7H_3D_7O_2S_2$: C 42.18, H+D 9.60; found: C 41.99, H+D 9.54.

6d: *O*-Ethyl *S*-1-propoxypropyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2965, 2936, 2877, 1462, 1208, 1108, 1053, 1011, 916 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 0.92 (t, J = 7.5 Hz, 3H), 1.05 (t, J = 7.5 Hz, 3H), 1.43 (t, J = 7.0 Hz, 3H), 1.56–1.64 (m, 2H), 1.92–2.04 (m, 2H), 3.45 (dt, J = 9.5, 6.5 Hz, 1H), 3.69 (dt, J = 9.5, 6.5 Hz, 1H), 4.61–4.70 (m, 2H), 5.49 ppm (dd, J = 6.5, 5.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 10.2, 10.6, 13.8, 22.6, 29.8, 69.6, 71.2, 93.8, 214.6 ppm; elemental analysis: calcd (%) for $C_9H_{18}O_2S_2$: C 48.61, H 8.16; found: C 48.89, H 7.95.

6e: *O*-Ethyl *S*-1,2-dimethoxyethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2988, 2931, 2829, 1457, 1448, 1215, 1111, 1048 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.44 (t, J = 7.5 Hz, 3H), 3.45 (s, 3H), 3.52 (s, 3H), 3.70–3.77 (m, 2H), 4.62–4.72 (m, 2H), 5.66 ppm (dd, J = 6.5, 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 57.5, 59.4, 70.0, 74.5, 91.8, 213.3 ppm; elemental analysis: calcd (%) for $C_7H_{14}O_3S_2$: C 39.98, H 6.71; found: C 40.26, H 6.51.

6f: *O*-Ethyl *S*-2,5-dioxahexyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2982, 2924, 1454, 1366, 1308, 1221, 1101, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.44 (t, J = 7.0 Hz, 3H), 3.38 (s, 3H), 3.54–3.57 (m, 2H), 3.71–3.74 (m, 2H), 4.68 (q, J = 7.0 Hz, 2H), 5.40 ppm (s, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 59.0,

68.9, 70.2, 71.4, 76.8 (overlapped with the signal of $CDCl_3$), 213.1 ppm; elemental analysis: calcd (%) for $C_7H_{14}O_3S_2$: C 39.98, H 6.71; found: C 40.15, H 6.70.

6g: *O*-Ethyl *S*-3,3-dimethyl-2,4-dioxacyclopentyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2988, 2937, 1453, 1383, 1373, 1222, 1147, 1114, 1066, 1044, 952, 837 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.42 (d, J = 1.0 Hz, 3H), 1.43 (t, J = 7.0 Hz, 3H), 1.48 (d, J = 1.0 Hz, 3H), 4.21 (dd, J = 9.5, 3.0 Hz, 1H), 4.43 (dd, J = 9.5, 5.5 Hz, 1H), 4.64 (dq, J = 10.5, 7.0 Hz, 1H), 4.67 (dq, J = 10.5, 7.0 Hz, 1H), 6.15 ppm (dd, J = 5.5, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 25.6, 26.3, 69.7, 70.4, 84.8, 112.0, 212.6 ppm; elemental analysis: calcd (%) for $C_8H_{14}O_3S_2$: C 43.22, H 6.34; found: C 43.10, H 6.59.

6h: *S*-1-Ethoxyethyl *O*-ethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2978, 2930, 1444, 1374, 1252, 1212, 1107, 1052 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.21 (t, J = 7.0 Hz, 3H), 1.43 (t, J = 7.0 Hz, 3H), 1.69 (d, J = 6.5 Hz, 3H), 3.57 (dq, J = 9.5, 7.0 Hz, 1H), 3.77 (dq, J = 9.5, 7.0 Hz, 1H), 4.61–4.70 (m, 2H), 5.63 ppm (q, J = 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.7, 14.9, 22.9, 64.9, 69.6, 88.2, 214.1 ppm; elemental analysis: calcd (%) for $C_7H_{14}O_2S_2$: C 43.27, H 7.26; found: C 43.16, H 7.06.

7: *O*-Methyl *S*-2-oxacyclopentyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2980, 2943, 2879, 1436, 1223, 1153, 1049, 924 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.91–2.12 (m, 3H), 2.37–2.46 (m, 1H), 3.91–4.03 (m, 2H), 4.20 (s, 3H), 6.17 ppm (dd, J = 7.5, 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 24.6, 31.7, 59.9, 68.4, 88.5, 214.0 ppm; elemental analysis: calcd (%) for $C_6H_{10}O_2S_2$: C 40.42, H 5.65; found: C 40.65, H 5.54.

8: *O*-Octyl *S*-2-oxacyclopentyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2925, 2855, 1460, 1224, 1043, 934 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 3H), 1.22–1.37 (m, 8H), 1.37–1.45 (m, 2H), 1.77–1.84 (m, 2H), 1.90–2.12 (m, 3H), 2.36–2.46 (m, 1H), 3.90–4.02 (m, 2H), 4.54–4.64 (m, 2H), 6.16 ppm (dd, J = 7.5, 3.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 14.1, 22.6, 24.6, 25.8, 28.1, 29.1, 29.1, 31.7, 31.8, 68.4, 73.9, 88.3, 213.4 ppm; elemental analysis: calcd (%) for $C_{13}H_{24}O_2S_2$: C 56.48, H 8.75; found: C 56.68, H 8.50.

9: *S*-2,5-Dioxacyclohexyl *O*-2-(2-pyridyl)ethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2967, 2855, 1592, 1475, 1438, 1229, 1214, 1126, 1056, 893, 869 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 3.30 (t, J = 7.0 Hz, 2H), 3.66–3.77 (m, 3H), 3.83 (dd, J = 12.0, 3.5 Hz, 1H), 3.98 (dd, J = 12.0, 3.0 Hz, 1H), 4.03–4.09 (m, 1H), 5.00 (t, J = 7.0 Hz, 2H), 5.83 (dd, J = 3.5, 3.0 Hz, 1H), 7.17 (ddd, J = 7.5, 5.0, 1.0 Hz, 1H), 7.23 (ddd, J = 7.5, 1.0, 1.0 Hz, 1H), 7.63 (ddd, J = 7.5, 7.5, 2.0 Hz, 1H), 8.56 ppm (ddd, J = 5.0, 2.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 36.8, 63.6, 66.6, 69.7, 72.9, 84.1, 121.8, 123.5, 136.5, 149.6, 157.4, 211.5 ppm; elemental analysis: calcd (%) for $C_{12}H_{15}NO_3S_2$: C 50.50, H 5.30; found: C 50.76, H 5.36.

10: *S*-2,5-Dioxacyclohexyl *O*-3,6,9-trioxadecyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2873, 1450, 1240, 1221, 1126, 1109, 1057, 894, 868 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 3.39 (s, 3H), 3.55–3.58 (m, 2H), 3.64–3.69 (m, 4H), 3.69–3.74 (m, 3H), 3.75–3.80 (m, 2H), 3.85–3.91 (m, 3H), 4.04 (dd, J = 12.0, 3.0 Hz, 1H), 4.07–4.13 (m, 1H), 4.70–4.79 (m, 2H), 5.92 ppm (dd, J = 3.0, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 59.1, 63.6, 66.7, 68.4, 69.8, 70.6, 70.6, 70.8, 71.9, 73.0, 84.5, 212.0 ppm; elemental analysis: calcd (%) for $C_{12}H_{22}O_6S_2$: C 44.15, H 6.79; found: C 44.27, H 6.82.

11: *O*-5-Hydroxypentyl *S*-2,5-dioxacyclohexyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 3398 (br), 2938, 2861, 1457, 1232, 1126, 1049, 893, 868 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.44 (br s, 1H), 1.47–1.55 (m, 2H), 1.59–1.68 (m, 2H), 1.82–1.90 (m, 2H), 3.67 (t, J = 6.0 Hz, 2H), 3.69–3.80 (m, 3H), 3.88 (dd, J = 12.0, 3.0 Hz, 1H), 4.03 (dd, J = 12.0, 3.0 Hz, 1H), 4.08–4.15 (m, 1H), 4.63 (t, J = 6.5 Hz, 2H), 5.91 ppm (dd, J = 3.0, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 22.2, 27.9, 32.1, 62.5, 63.5, 66.7, 69.7, 74.2, 84.1, 211.7 ppm; elemental analysis: calcd (%) for $C_{10}H_{18}O_4S_2$: C 45.09, H 6.81; found: C 45.12, H 6.66.

12: *S*-Cyclohexyl *O*-methyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2933, 2854, 1448, 1435, 1218, 1151, 1078, 1067, 998 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.23–1.35 (m, 1H), 1.38–1.53 (m, 4H), 1.58–1.66 (m, 1H), 1.71–1.80 (m, 2H), 2.02–2.11 (m, 2H), 3.63–3.70 (m, 1H), 4.16 ppm (s, 3H); ^{13}C NMR ($CDCl_3$): δ = 25.5, 25.9, 32.3, 49.1, 59.7, 215.4 ppm; elemental analysis: calcd (%) for $C_8H_{14}OS_2$: C 50.49, H 7.41; found: C 50.49, H 7.16.

13a: *S*-Cyclooctyl *O*-ethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2922, 2851, 1473, 1445, 1210, 1144, 1111, 1055 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.42 (t, J = 7.0 Hz, 3H), 1.49–1.66 (m, 8H), 1.67–1.82 (m, 4H), 2.01–2.09 (m, 2H), 3.87 (tt, J = 9.5, 4.0 Hz, 1H), 4.64 ppm (q, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.8, 25.4, 26.0, 26.9, 31.9, 50.0, 69.4, 214.9 ppm; elemental analysis: calcd (%) for $C_{11}H_{20}OS_2$: C 56.85, H 8.67; found: C 57.00, H 8.64.

13b: *S*-Cyclododecyl *O*-ethyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2935, 2862, 2851, 1469, 1445, 1211, 1111, 1055 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.28–1.54 (m, 18H), 1.43 (t, J = 7.0 Hz, 3H), 1.59–1.67 (m, 2H), 1.74–1.82 (m, 2H), 3.80–3.86 (m, 1H), 4.64 ppm (q, J = 7.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 13.8, 22.6, 23.3, 23.6 (2C), 23.7, 29.9, 47.1, 69.5, 215.2 ppm; elemental analysis: calcd (%) for $C_{15}H_{28}OS_2$: C 62.45, H 9.78; found: C 62.68, H 10.01.

Transformation of dithiocarbonate into thioether (Scheme 5): The synthesis of 2-hexylthio-1,4-dioxane (**14**) is representative. Under an atmosphere of argon, ground potassium hydroxide (56 mg, 1.0 mmol) was added to a solution of **6a** (42 mg, 0.20 mmol) and 1-iodohexane (0.044 mL, 0.30 mL) in ethanol (5.0 mL). The mixture was stirred for 12 h at ambient temperature and then poured into water (10 mL). The product was extracted with hexane/ethyl acetate (10:1, 3×10 mL). The combined organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. Silica-gel column chromatography (hexane/ethyl acetate = 10:1) afforded analytically pure **14** as a colorless oil (36 mg, 0.18 mmol, 86%). IR (neat): $\tilde{\nu}$ = 2958, 2927, 2855, 1456, 1260, 1126, 1119, 1085, 1070, 908, 870 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 3H), 1.24–1.35 (m, 4H), 1.35–1.44 (m, 2H), 1.56–1.68 (m, 2H), 2.60–2.73 (m, 2H), 3.58 (dd, J = 12.0, 7.0 Hz, 1H), 3.63–3.74 (m, 3H), 3.90 (dd, J = 12.0, 3.0 Hz, 1H), 4.06–4.11 (m, 1H), 4.80 ppm (dd, J = 7.0, 3.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.5, 28.5, 30.1, 30.5, 31.4, 64.5, 66.4, 69.9, 80.4 ppm; elemental analysis: calcd (%) for $C_{10}H_{20}O_2S$: C 58.78, H 9.87; found: C 58.98, H 9.60.

15: 3-Hexylthio-2,5-dioxahexane: IR (neat): $\tilde{\nu}$ = 2927, 2857, 1467, 1188, 1133, 1101, 926, 763 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 0.89 (t, J = 7.0 Hz, 3H), 1.22–1.34 (m, 4H), 1.34–1.42 (m, 2H), 1.53–1.63 (m, 2H), 2.56 (t, J = 7.5 Hz, 2H), 3.41 (s, 3H), 3.46 (s, 3H), 3.60 (dd, J = 10.5, 4.5 Hz, 1H), 3.65 (dd, J = 10.5, 8.0 Hz, 1H), 4.53 ppm (dd, J = 8.0, 4.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.5, 28.2, 28.6, 30.4, 31.4, 55.7, 59.1, 75.2, 85.5 ppm; elemental analysis: calcd (%) for $C_{10}H_{22}O_2S$: C 58.21, H 10.75; found: C 58.27, H 10.50.

17: *S*-2,5,8,11,14,17-Hexaoxacyclooctadecyl *O*-6-(2-pyridyl)hexyl dithiocarbonate: IR (neat): $\tilde{\nu}$ = 2929, 2860, 1590, 1569, 1473, 1436, 1352, 1225, 1119, 1048 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.37–1.49 (m, 4H), 1.70–1.86 (m, 4H), 2.79 (t, J = 8.0 Hz, 2H), 3.63–3.94 (m, 22H), 4.56 (t, J = 7.0 Hz, 2H), 5.79 (dd, J = 7.5, 3.5 Hz, 1H), 7.10 (ddd, J = 7.5, 5.0, 1.0 Hz, 1H), 7.14 (ddd, J = 7.5, 1.0, 1.0 Hz, 1H), 7.59 (ddd, J = 7.5, 7.5, 2.0 Hz, 1H), 8.52 ppm (ddd, J = 5.0, 2.0, 1.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 25.7, 28.1, 28.9, 29.6, 38.2, 69.5, 69.9, 70.6, 70.6, 70.6, 70.7, 70.8, 70.8, 70.9, 71.1, 73.2, 74.0, 90.9, 120.9, 122.7, 136.3, 149.2, 162.1, 213.4 ppm; HRMS: m/z calcd for $C_{24}H_{40}NO_7S_2$: 518.2246 $[MH]^+$; found: 518.2255; elemental analysis: calcd (%) for $C_{24}H_{39}NO_7S_2$: C 55.68, H 7.59; found: C 55.39, H 7.82.

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