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Radical-Based Deoxygenation of Aliphatic Alcohols via Thioxocarbamate Derivatives

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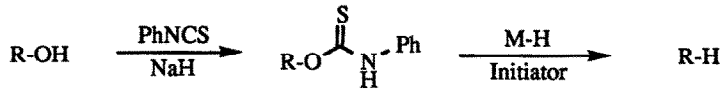
Abstract: *N*-Phenylthioxocarbamates, obtained from the reaction of alcohols with phenyl isothiocyanate in the presence of NaH, were reduced with various silanes such as triethylsilane, triphenylsilane, and tris(trimethylsilyl)silane, as well as tributylstannane under radical conditions to give deoxygenated products of the corresponding alcohols in excellent yields. The reaction was applicable to not only simple aliphatic alcohols but also sugars and nucleosides. Regio- and stereoselective deuteration using deuteriosilanes and deuteriostannane was also examined under the similar conditions.

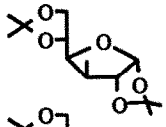
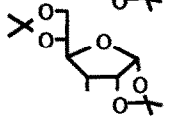
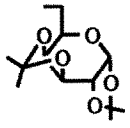
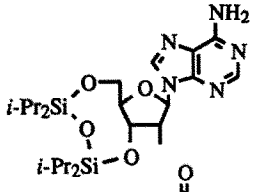
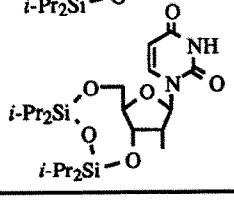
Deoxygenation of aliphatic alcohols plays an important role in organic synthesis. Since deoxygenated derivatives of sugars, nucleosides, and many other related compounds often exhibit biological activities, the methods of selective removal of hydroxy group are fundamental technique for researching biologically active compounds. Furthermore, deoxygenation methods provide chiro-economic routes for the synthesis of complex molecules, because carbohydrates can be regarded as cheap chiral starting materials. These deoxygenation reactions can be carried out effectively under radical conditions rather than ionic conditions for the synthesis of sensitive polyfunctionalized molecules.[1] Generally, radical deoxygenations are accomplished by reduction of *O*-thiocarbonyl derivatives of the corresponding alcohols.[2] Therefore, many derivatizing reagents are developed, of which substituted phenyl chlorothioxocarbonates[3-5] and diimidazolyl thioketone[6] are found to be effective and versatile reagents. However, these reagents have disadvantages of relatively expensive and low stability to moisture.

We have recently shown that acetyl isothiocyanate, prepared *in situ* from acetyl chloride and potassium thiocyanate, reacted readily with aliphatic alcohols, providing the corresponding *N*-acetylthioxocarbamates in good yields and these adducts were effectively deoxygenated using tributylstannane or triphenylsilane under radical conditions.[7] Sugars and nucleosides were not transformed into the adducts under similar conditions. In our preliminary communication,[8] bis(tributyltin)oxide (BTO) was used as an activator of alcohols for the addition reaction. BTO was not also adapted to the addition reaction of sugars and nucleosides to these compounds and, moreover, BTO was believed to be one of highly toxic compounds. Therefore, we examined other promoters for these reactions. In this paper, we would like to describe an addition reaction of a wide variety of alcohols containing sugars and nucleosides to phenyl isothiocyanate in the presence of sodium hydride and a reduction of the derived thioxocarbamates using various silanes and Bu_3SnH under radical conditions. A deoxydeuteration of aliphatic alcohols using deuteriosilanes and tributyldeuteriostannane was also examined in views of synthetic and mechanistic standpoints.



1 2

Table 1. *N*-Phenylthioxocarbamate **1** and Its Deoxygenated Product **2**

Run	R		**1** (%)	Deoxygenation Reaction M-H (2 eq.)	Initiator (0.2 eq.)	Temp (°C)	Time (h)	**2**[a] (%)
1	1-Dodecyl	(a)	90	TMS_3SiH	AIBN	80	5	84
2	Cyclododecyl	(b)	99	Et_3SiH	DTBP	140[b]	5	75
3				Ph_3SiH	DTBP	125[c]	3	90
4					Et_3B[d]	r.t.	0.2	93
5				TMS_3SiH	AIBN	80	0.5	95
6					Et_3B[d]	r.t.	0.2	89
7				Bu_3SnH	AIBN	80	3	88
8	1-Adamantyl	(c)	97	TMS_3SiH	AIBN	80	1	85
9		(d)	91	TMS_3SiH	AIBN	80	2	99
10		(e)	99	TMS_3SiH	AIBN	80	8	82
11		(f)	95	TMS_3SiH	AIBN	80	8	85
12		(g)	75	TMS_3SiH	AIBN	80	2	97
13		(h)	78	TMS_3SiH	AIBN	80	2	93

a) Determined by GC (runs 1-7) or isolation (runs 8-13).
b) Reaction was carried out in a sealed tube.
c) Reaction was carried out in refluxing octane.
d) 1.2 equivalent of Et_3B was used.

When a solution of cyclododecanol (10 mmol), phenyl isothiocyanate (1.1 equiv.), and NaH (1.1 equiv.) in THF (10 ml) was stirred at room temperature overnight, cyclododecyl *N*-phenylthioxocarbamate (**1b**) was isolated by a flash chromatography in 99% yield. The reduction of **1b** with Bu_3SnH (2 equiv.) in dry benzene (0.05 M) was carried out at 80°C in the presence of catalytic amount (20 mol%) of azobisisobutyronitrile (AIBN) for 3 h. Direct GC analysis of the reaction mixture exhibited the production of cyclododecane (**2b**) in 88% yield (Table 1, run 7). Substituted phenyl and ethyl isothiocyanates were also entried as derivatizing reagents and the corresponding thioxocarbamates were obtained in good yields (71-86%). However, these adducts were unsuitable for subsequent reductive reaction. The reduction of *N*-4-methoxyphenyl and *N*-4-fluorophenylthioxocarbamates of cyclododecanol under similar conditions gave cyclododecane in 57 and 76% yields, respectively. A similar treatment of *N*-ethyl derivative gave no deoxygenated product at all. These remarkable substituent effects were rationalized by the radicophilicity of the thiocarbonyl groups according to an electronic nature of a substituent on the nitrogen atom. The deoxygenations of **1b** with triethylsilane, triphenylsilane, and tris(trimethylsilyl)silane (TMS_3SiH) using di-*tert*-butyl peroxide (DTBP), AIBN, and triethylborane were also examined as these silicon reagents were more preferable in ecological and toxicological viewpoints. The representative results are shown in Table 1 (runs 2-6). The reduction of **1b** with Et_3SiH required higher temperature (140°C) to obtain a satisfactory yield (75%, run 2). Ph_3SiH was not so effective to lower the reaction temperature (125°C, run 3). In our reaction (run 5), TMS_3SiH, which was recognized to an alternative of Bu_3SnH,[9] was found to be effective even at 80°C to give cyclododecane in 95% yield. It was previously demonstrated that Et_3B facilitated the silane and stannane reduction at low temperature.[5b-c,7,10,11] Thus, a hexane solution of Et_3B (0.3 mmol) was added to a solution of **1b** (0.25 mmol) and TMS_3SiH (0.5 mmol) in benzene (5 ml) at room temperature, and then the mixture being stirred for 0.2 h afforded cyclododecane in 89% yield (run 6). Dry oxygen as an air (30 ml) should be injected to make the reaction complete. Ph_3SiH was also effective for Et_3B-induced deoxygenation reaction (run 4). Et_3SiH was not reactive under the conditions used. It is likely due to the Si-H bond strength. From these findings, TMS_3SiH was also proved to be most effective reducing agent in our case, and TMS_3SiH-AIBN system was mainly used for the following examinations because of the convenience of the operation.

Addition and deoxygenation reactions of other alcohols containing sugars and nucleosides using phenyl isothiocyanate and TMS_3SiH were similarly investigated. As shown in Table 1, the treatments of these alcohols with phenyl isothiocyanate in the presence of NaH gave the corresponding *N*-phenylthioxocarbamates **1a,c-h** in good yields (75-99%). The structures of the adducts were confirmed by IR, ^1H NMR, ^{13}C NMR and mass spectrometries, and the absence of the thiol carbamate, a rearranged isomer of the thioxocarbamate, was also approved. A radical deoxygenation of *N*-phenylthioxocarbamates **1** with TMS_3SiH was carried out at 80°C using AIBN to afford the corresponding deoxygenated products in excellent yields (82-99%). The reaction course was monitored by GC and TLC analyses. The product analyses were performed by comparing with the authentic samples using GC-MS and ^1H NMR spectroscopies, and the yields obtained by isolation or by GC using tridecane as an internal standard are also listed in Table 1. Generally, the deoxygenation of primary alcohol derivatives needed higher temperature, because the stability of primary radical would be relatively lesser than the secondary radical.[5b-c,7] In runs 1 and 11, only the prolonged reaction time (5-8 h) was required for the reduction of 1-dodecyl and 6-galactopyranosyl derivatives (**1a** and **1f**) to obtain the deoxygenated products in satisfactory yields (84 and 85%). With tertialy alcohol such as 1-adamantanol, the addition reaction followed by the deoxygenation reaction also gave the corresponding hydrocarbon in a high yield (85%, run 8). While the reduction of 3-glucofuranosyl derivative **1d** gave 3-deoxyglucofuranose **2d** in 99% yield (run 9), 3-allofuranosyl derivative **1e** needed longer reaction time (8 h) for the deoxygenation to give the same product in 82% yield (run 10). The lesser reactivity of **1e** was rationalized by the steric hindrance for the attacking of silyl radical from α-face.[12] In order to achieve a regiospecific 2'-deoxygenation of nucleosides, 1,1,3,3,-tetraisopropyldisiloxy (TIPS) group for a selective protection of 3' and 5' hydroxy groups was employed. Thus, 3',5'-*O*-TIPS-adenosine and uridine, after the functionalization with phenyl isothiocyanate at 2'-position, were subjected to the reduction conditions to furnish the corresponding 2'-deoxynucleosides **2g** and **2h** in 97 and 93% yields, respectively (runs 12 and 13).

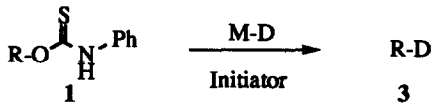


Table 2. Deuterated Product 3 Obtained by the Reduction of *N*-Phenylthioxocarbamate 1

Run	Adduct 1	M-D	Initiator (eq.)	Temp (°C)	Time (h)	3[a] (%)	D-content[b] (%)	Selectivity[c] (α/β)
1	**1b**	Ph_3SiD	DTBP (0.2)	130[d]	5	92	18	-
2[e]						83	50	-
3		$(Me_3Si)_3SiD$	AIBN (0.2)	80	2	83	80	-
4[e]						95	85	-
5			Et_3B (1.2)	r.t.	1	85	41	-
6		Bu_3SnD	AIBN (0.2)	80	3	98	98	-
7	**1d**	Bu_3SnD	AIBN (0.2)	80	4	96	98	15/85
8	**1e**	Bu_3SnD	AIBN (0.2)	80	10	21	100	13/87
9	**1h**	Bu_3SnD	AIBN (0.2)	80	4	74	100	86/14

a) Determined by GC (runs 1-5) or isolation (runs 6-9).

b) Determined by mass spectrometry using selected ion monitoring mode (runs 1-6) or ^1H NMR (runs 7-9).

c) Determined by ^1H NMR.

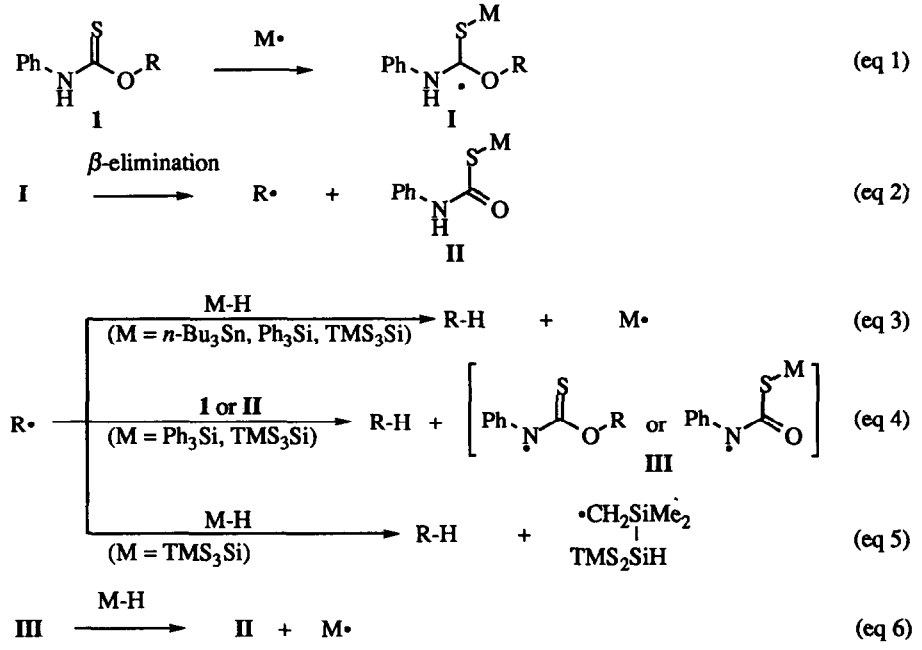
d) Reaction was carried out in refluxing chlorobenzene.

e) Starting thioxocarbamate **1b** was treated with MeOD prior to the reaction.

From these findings, the present procedure was approved to be applicable to not only simple primary, secondary, and tertialy alcohols but also some kinds of sugars and nucleosides. And these results led us to examine a deoxydeuteration of aliphatic hydroxy compounds such as sugars and nucleosides via *N*-phenylthioxocarbamate **1**. Triphenyldeuteriosilane, tris(trimethylsilyl)deuteriosilane, and tributyldeuteriostannane were employed as deuterium atom sources. The results are compiled in Table 2. The treatment of cyclododecyl *N*-phenylthioxocarbamate (**1b**) with Bu_3SnD in refluxing benzene in the presence of AIBN for 3 h furnished deuteriocyclododecane (**3b**) in 98% yield. The isotopic distribution was determined by mass spectrometry using selected ion monitoring (SIM) mode and the deuterium incorporation was 98% for **3b** (run 6). In a reaction of **1b** with Ph_3SiD using DTBP at 130°C, however, only 18% of deuterium incorporation for **3b** was observed (run 1), suggesting the possibility of hydrogen abstraction from N-H moiety by cyclododecyl radical. Actually, 83% of **3b** with 50% of deuterium content was obtained under the similar conditions by the treatment of **1b** with MeOD prior to the deoxydeuteration (run 2). As TMS_3SiH was appeared to be one of the most effective reducing reagents under the conditions used, TMS_3SiD was also examined as a deuteration reagent. It gave the product containing 80% of deuterium (run 3). As a prior treatment of **1b** with MeOD was not so effective to improve the deuterium incorporation (85%, run 4), it was likely that another hydrogen source would be methyl group in TMS_3SiD. In fact, the deuteration of cyclododecyl 4-fluorophenylthioxocarbonate,[5b] in which an active hydrogen was not involved, gave **3b** in 80% yield with 78% of deuterium content under the similar conditions. The attempted deuteration of **1b** using TMS_3SiD-Et_3B system also resulted in insufficient deuteration yield (41%, run 5). In this case, Et_3B and/or Et radical are considered to be hydrogen source(s) for the hydrogen abstraction process by R radical.[7] Consequently, Bu_3SnD was found to be the most suitable reagent for the deoxydeuteration reactions. Using Bu_3SnD-AIBN system, we examined the stereoselective deuteration of sugars and nucleosides. The *N*-phenylthioxocarbamates **1d**, **1e**, and **1h** were subjected to the deoxydeuteration reaction to afford deuterated products **3** and the results are also summarized in Table 2. With **1d**, the yield (96%) and D-content (98%) of the product **3d** were excellect and the stereoselectivity of the deuterium substitution at 3-position was moderate (α/β = 15/85, run 7). Allofuranosyl derivative **1e** gave also **3d** in low yield (21%, run 8)

and the ratio of α/β deuterium substitution was 13/87, which was accorded with that in run 7. These results indicate that the reaction certainly proceeds through free radical chain process in which the approach of the bulky Bu_3SnD to the C-3 radical occurs with *ca* 85% stereoselectivity on the less hindered β-face. In the case of uridine derivative **1h**, Bu_3SnD predominantly attacks the C-2' radical from α-face of the furanosyl ring (α/β = 86/14, run 9) to avoid the steric hindrance of the heterocyclic moiety.[3,11]

In mechanistic considerations of the reaction, the pathway was postulated to be shown in Scheme. Namely, metal radical attacks the thiocarbonyl group to give the adduct **I** (eq 1) which undergoes β-elimination to genarate R radical (eq 2) in accordance with Barton's proposal.[5c,13] In our case, hydrogen abstraction by R radical from metal hydride (eq 3), N-H moiety (eq 4), and methyl group in TMS_3SiD (eq 5) would be competitive. With Bu_3SnH and TMS_3SiH, the D-incorporation content of **3b** shows that eq 3 occurs predominantly, and eq 5 is also included as an important course in the case of TMS_3SiH. When Ph_3SiH is used as a reducing reagent, the reaction shown in eq 4 predominates and the amyl radical **III** presumably regenerates the silyl radical (eq 6).



Scheme. Postulated Reaction Mechanism

In conclusion, phenyl isothiocyanate was proved to be effective and versatile derivatizing reagent of aliphatic alcohols and the derived *N*-phenylthioxocarbamates were readily deoxygenated using various silanes, especially TMS_3SiH, as well as tributylstannane under radical conditions to afford deoxygenated products in excellent yields. The reaction was applicable to not only simple aliphatic alcohols but also sugars and nucleosides. The procedure using Bu_3SnD provides a convenient method for the deoxydeuteration of the aliphatic alcohols and the stereoselectivity of the deuterium substitution on sugar moiety was found to be over 85%.

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Experimental

Melting points were determined with a Yamato MP-21 melting point apparatus and are uncorrected. GC measurements were performed on a Ohkura GC-103C and a GL Sciences GC-380 gas chromatograph using a 50 m × 0.25 mm methyl silicone capillary column (Quadrex). TLC was carried out on Merck silica gel 60 F_{254}. Flash column chromatography was performed on Merck silica gel 60 (230-400 mesh). Infrared spectra were recorded on a Perkin Elmer 1720X infrared spectrometer. ^1H and ^{13}C NMR spectra were measured in $CDCl_3$ solutions on a Varian UNITY-400 spectrometer. All chemical shifts are reported as δ values (ppm) relative to residual chloroform (7.26 ppm) and the central peak of deuteriochloroform (77.00 ppm). Mass spectra were obtained on a JEOL JMS-AX-500 spectrometer with DA7000 data system. GC-MS was measured with the direct combination of GC (Hewlett-Packard GC 5890 Series II with a 25 m × 0.25 mm methyl silicone capillary column) and a JEOL JMS-AX-500 spectrometer. Selected ion monitoring (SIM) method was used to determine isotopic distribution in the deuterated products, focussing on M^+ and $(M + 1)^+$ ions.

Most of starting materials and reagents were commercial products and were purified if necessary. Tributyldeuteriostannane and triphenyldeuteriosilane were prepared by reducing the corresponding chlorides with lithium aluminium deuteride in ether or tetrahydrofuran. Tris(trimethylsilyl)deuteriosilane was prepared according to the literature.[14] Solvents were distilled over sodium in the presence of benzophenone.

Preparation of *N*-Phenylthioxocarbamate 1. Typically, to a solution of cyclododecanol (1.84 g, 10 mmol) and phenyl isothiocyanate (1.49 g, 11 mmol) in dry THF (10 ml) was added NaH (60% in oil, 0.44 g, 11 mmol) and the reaction was monitored by TLC. When the reaction was complete, the solvent was removed *in vacuo* and the residue was partitioned between CH_2Cl_2 (50 ml) and H_2O (50 ml). The organic layer was separated and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel. Elution with hexane/AcOEt (9/1) gave cyclododecyl *N*-phenylthioxocarbamate (**1b**, 3.15 g, 99%) as a colorless solid. The analytical sample was obtained by recystallization from hexane as colorless plates, mp 115-116°C. IR (KBr) 3177, 3031, 2937, 2848, 1594, 1543, 1494, 1472, 1397, 1330, 1223, 1197, 1145, 1043, 1010 cm^{-1}. ^1H NMR δ 1.32-1.90 (m, 22 H), 5.68 (m, 1 H), 7.13-7.35 (m, 5 H), 8.22 (br, 1 H). ^{13}C NMR δ 21.1, 23.4, 23.6, 24.2, 24.5, 29.1, 81.8, 121.9, 125.2, 128.9, 137.6, 188.6. HRMS (EI) *m/z* 319.1997 (M^+, $C_{19}H_{29}ONS$ requires 319.1970).

Other *N*-phenylthioxocarbamates **1a,c-h** were similarly prepared. The yields are listed in Table 1 and the physical and spectral data are as follows. **1a**: colorless needles (hexane), mp 48-49°C. IR (KBr) 3227, 2960, 2920, 2849, 1599, 1549, 1495, 1445, 1413, 1363, 1337, 1212, 1039 cm^{-1}. ^1H NMR δ 0.88 (t, J = 6.9 Hz, 3 H), 1.26-1.42 (m, 18 H), 1.78 (m, 2 H), 4.56 (br, 2 H), 7.17-7.34 (m, 5 H), 8.31 (br, 1 H). ^{13}C NMR δ 13.9, 22.6, 26.0, 28.6, 29.2, 29.3, 29.48, 29.52, 29.6 (2 C), 31.9, 72.5, 122.2, 125.5, 129.0, 137.5, 189.2. HRMS (EI) *m/z* 321.2133 (M^+, $C_{19}H_{31}ONS$ requires 321.2126). **1c**: colorless needles (hexane), mp 173-174°C. IR (KBr) 3192, 3024, 2902, 1594, 1538, 1490, 1448, 1349, 1314, 1294, 1191, 1102, 1055 cm^{-1}. ^1H NMR δ 1.69 (m, 6 H), 2.24 (br, 3 H), 2.47 (d, J = 2.6 Hz, 6 H), 7.11-7.33 (m, 5 H), 8.01 (br, 1 H). ^{13}C NMR δ 31.5, 36.2, 41.5, 87.8, 121.9, 125.0, 128.9, 137.8, 186.1. HRMS (EI) *m/z* 287.1296 (M^+, $C_{17}H_{21}ONS$ requires 287.1344). **1d**: amorphous solid. IR (KBr) 3279, 2988, 1598, 1543, 1448, 1376, 1337, 1217, 1164, 1078 cm^{-1}. ^1H NMR δ 1.27 (s, 3 H), 1.33 (s, 3 H), 1.41 (s, 3 H), 1.55 (s, 3 H), 3.92-4.34 (m, 4 H), 4.83 (br, 1 H), 5.76 (br, 1 H), 5.87 (br, 1 H), 7.15-7.61 (m, 5 H), 8.37 (br, 1 H). ^{13}C NMR δ 25.2, 26.3, 26.8 (2 C), 67.4, 72.6, 80.1, 83.2, 83.6, 105.0, 109.5, 112.5, 123.0, 126.3, 129.2, 137.0, 187.4. HRMS (EI) *m/z* 395.1414 (M^+, $C_{19}H_{25}O_6NS$ requires 395.1403). **1e**: amorphous solid. IR (KBr) 3280, 2986, 1598, 1538, 1448, 1386, 1191 cm^{-1}. ^1H NMR δ 1.32 (s, 3 H), 1.36 (s, 6 H), 1.56 (s, 3 H), 3.77-4.27 (m, 4 H), 5.06 (br, 1 H), 5.57 (br, 1 H), 5.85 (br, 1 H), 7.15-7.60 (m, 5 H), 8.35 (br, 1 H). ^{13}C NMR δ 25.2, 26.3, 26.66, 26.70, 66.0, 75.6, 77.5, 77.6, 78.9, 104.4, 110.0, 113.2, 122.7, 125.9, 128.9, 137.2, 187.2. HRMS (EI) *m/z* 395.1417 (M^+, $C_{19}H_{25}O_6NS$ requires 395.1403). **1f**: colorless crystals (hexane-benzene), mp 126-127°C. IR (KBr) 3259, 3056, 2988, 2935, 1598, 1544, 1260, 1013 cm^{-1}. ^1H NMR δ 1.35 (s, 6 H), 1.47 (s, 3 H), 1.50 (s, 3 H), 4.26-4.78 (m, 4 H), 4.36 (dd, J = 5.0, 2.5 Hz, 1 H), 4.64 (dd, J = 7.8,

2.5 Hz, 1 H), 5.59 (d, J = 5.0 Hz, 1 H), 7.15-7.57 (m, 5 H), 8.34 (br, 1 H). ^{13}C NMR δ 24.5, 25.0, 26.0, 26.1, 66.2, 70.6, 70.9, 71.2, 77.2, 96.4, 108.9, 109.8, 121.6, 125.4, 129.1, 137.3, 188.4. HRMS (EI) m/z 395.1411 (M^+, $C_{19}H_{25}O_6NS$ requires 395.1403). **1g**: colorless needles (hexane-benzene), mp 172-174°C. IR (KBr) 3320, 3171, 2946, 2868, 1641, 1599, 1520, 1467, 1385, 1328, 1180, 1040 cm^{-1}. ^{1}H NMR δ 1.06-1.14 (m, 28 H), 3.98-4.16 (m, 3 H), 5.56 (br, 1 H), 6.03 (br, 1 H), 6.16 (br, 2 H), 6.35 (d, J = 5.5 Hz, 1 H), 7.16-7.48 (m, 5 H), 7.91 (s, 1 H), 8.26 (s, 1 H), 9.22 (br, 1 H). ^{13}C NMR δ 12.7, 12.9, 13.1, 13.3, 16.9, 17.0, 17.1, 17.22, 17.29, 17.32, 17.35, 17.43, 61.3, 70.1, 82.5, 83.1, 88.0, 120.5, 122.0, 125.8, 129.2, 137.1, 140.3, 149.6, 153.2, 155.6, 187.3. HRMS (EI) m/z 644.2590 (M^+, $C_{29}H_{44}O_5N_6Si_2S$ requires 644.2632). **1h**: amorphous solid. IR (KBr) 3240, 2946, 2868, 1692, 1600, 1543, 1499, 1464, 1387, 1271, 1221, 1181, 1040 cm^{-1}. ^{1}H NMR δ 1.00-1.14 (m, 28 H), 3.90 (br, 1 H), 4.15 and 4.02 (AB, J = 13.0 Hz, 2 H), 4.72 (br, 1 H), 5.71 (br, 2 H), 6.15 (d, J = 4.9 Hz, 1 H), 7.15-7.55 (m, 6 H), 8.67 (br, 1 H), 8.76 (br, 1 H). ^{13}C NMR δ 12.7, 12.9, 13.0, 13.4, 16.8, 16.95, 17.01, 17.1, 17.22. 17.25, 17.3, 17.4, 60.5, 68.9, 81.6, 82.6, 90.4, 102.5, 122.5, 125.9, 129.1, 137.1, 140.7, 149.5, 162.6, 187.2. HRMS (EI) m/z 443.1670 [(M - PhNHCS - i-Pr + H)$^+$, $C_{18}H_{31}O_7N_2Si_2$ requires 443.1670].

Reduction of *N*-Phenylthioxocarbamate 1. Deoxygenation of 1,2:5,6-di-*O*-isopropylidene-3-(*N*-phenylthioxocarbamoyl)-α-D-glucofuranose (**1d**) using TMS_3SiH-AIBN is representative. A solution of **1d** (0.195 g, 0.5 mmol), TMS_3SiH (0.248 g, 1 mmol), and AIBN (0.0164 g, 0.1 mmol) in benzene (10 ml) was refluxed under argon atmosphere for 2 h. The progress of the reaction was monitored by GC and TLC analyses. The crude product obtained after removal of the solvent was purified by flash chromatography (hexane/AcOEt = 9/1) affording pure 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**2d**, 0.122 g, 99%) as a colorless oil. The structure was confirmed by comparing with the reported ^{1}H NMR and mass spectra in the literatures.[3b,12] ^{1}H NMR δ 1.32 (s, 3 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 1.51 (s, 3 H), 1.77 (ddd, J = 13.5, 10.2, 4.8 Hz, 1 H), 2.18 (dd, J = 13.5, 4.4 Hz, 1 H), 3.79-3.85 (m, 1 H), 4.08-4.19 (m, 3 H), 4.76 (dd, J = 4.8, 3.7 Hz, 1 H), 5.82 (d, J = 3.7 Hz, 1 H). ^{13}C NMR δ 25.2, 26.2, 26.5, 26.8, 35.6, 67.3, 77.2, 78.8, 80.5, 105.8, 109.6, 111.4. HRMS (EI) m/z 229.1054 [(M - Me)$^+$, $C_{11}H_{17}O_5$ requires 229.1076].

Other *N*-phenylthioxocarbamates **1a-c,e-h** were deoxygenated under analogous conditions as shown in Table 1 and the structures of the products were confirmed by comparing with GC, NMR, and mass spectra of the authentic materials and/or the reported data.[3b,5c,12] **2f**: colorless oil. ^{1}H NMR δ 1.26 (d, J = 6.6 Hz, 3 H), 1.33 (s, 3 H), 1.35 (s, 3 H), 1.47 (s, 3 H), 1.52 (s, 3 H), 3.92 (dq, J = 1.9, 6.6 Hz, 1 H), 4.08 (dd, J = 7.9, 1.9 Hz, 1 H), 4.29 (dd, J = 5.1, 2.4 Hz, 1 H), 4.59 (dd, J = 7.9, 2.4 Hz, 1 H), 5.52 (d, J = 5.1 Hz, 1 H). ^{13}C NMR δ 15.9, 24.6, 24.9, 26.08, 26.10, 63.6, 70.2, 71.2, 73.8, 96.7, 108.3, 109.1. HRMS (EI) m/z 229.1044 [(M - Me)$^+$, $C_{11}H_{17}O_5$ requires 229.1076]. **2g**: colorless viscous oil. ^{1}H NMR δ 1.01-1.12 (m, 28 H), 2.64 (ddd, J = 13.2, 8.9, 7.3 Hz, 1 H), 2.71 (ddd, J = 13.2, 7.5, 2.6 Hz, 1 H), 3.89 (m, 1 H), 4.03 (dd, J = 12.4, 3.3 Hz, 1 H), 4.06 (dd, J = 12.4, 4.3 Hz, 1 H), 4.95 (m, 1 H), 5.71 (br, 2 H), 6.29 (dd, J = 7.3, 2.6 Hz, 1 H), 8.03 (s, 1 H), 8.32 (s, 1 H). ^{13}C NMR δ 12.7, 13.0, 13.2, 13.5, 16.9, 17.0, 17.1, 17.2, 17.3, 17.37, 17.39, 17.5, 40.3, 62.4, 70.7, 83.4, 85.4, 120.5, 139.1, 149.4, 153.0, 155.6. HRMS (EI) m/z 493.2583 (M^+, $C_{22}H_{39}O_4N_5Si_2$ requires 493.2541). **2h**: colorless viscous oil. ^{1}H NMR δ 0.90-1.10 (m, 28 H), 2.24 (ddd, J = 13.2, 6.9, 1.4 Hz, 1 H), 2.49 (ddd, J = 13.2, 10.5, 6.9 Hz, 1 H), 3.76 (m, 1 H), 4.00 (dd, J = 13.2, 2.8 Hz, 1 H), 4.13 (dd, J = 13.2, 2.0 Hz, 1 H), 4.43 (m, 1 H), 5.69 (d, J = 8.1 Hz, 1 H), 6.04 (dd, J = 6.9, 1.4 Hz, 1 H), 7.78 (d, J = 8.1 Hz, 1 H), 9.29 (br, 1 H). ^{13}C NMR δ 12.6, 13.0 (2 C), 13.5, 16.8, 16.91, 16.92, 17.0, 17.2, 17.25, 17.34, 17.4, 40.1, 60.5, 67.8, 84.4, 85.2, 101.8, 139.6, 150.1, 163.3. HRMS (EI) m/z 471.2328 [(M + H)$^+$, $C_{21}H_{39}O_6N_2Si_2$ requires 471.2347], 427.1711 [(M - i-Pr)$^+$, $C_{18}H_{31}O_6N_2Si_2$ requires 427.1721].

Et_3B Induced Deoxygenation of *N*-Phenylthioxocarbamate 1. A typical procedure is described for a reduction of cyclododecyl *N*-phenylthioxocarbamate (**1b**) with TMS_3SiH. To a solution of **1b** (0.08 g,

0.25 mmol) and TMS_3SiH (0.124 g, 0.5 mmol) in benzene (5 ml) was added a hexane solution of Et_3B (1.0 M, 0.3 ml, 0.3 mmol) at room temperature under argon atmosphere and dry air (30 ml) was introduced into the solution through a septum during 3 min. After stirring at room temperature for 10 min, the direct GC analysis of the reaction mixture using tridecane as an internal standard showed the formation of cyclododecane (**2b**) in 89% yield.

Deoxydeuteration of *N*-Phenylthioxocarbamate 1 with Bu_3SnD-AIBN. As an example, a deuteration of 2'-*O*-(*N*-phenylthioxocarbamoyl)-3',5'-*O*-TIPS-uridine (**1h**) with Bu_3SnD-AIBN is representative. A mixture of **1h** (0.124 g, 0.2 mmol), Bu_3SnD (0.117 g, 0.4 mmol), and AIBN (6.6 mg, 0.04 mmol) in benzene (4 ml) was refluxed under argon atmosphere for 4 h. After removal of the solvent, the residue was chromatographed on silica gel (hexane/AcOEt = 7/3) to afford 2'-deoxy-3',5'-*O*-TIPS-uridine (**3h**, 70.1 mg, 74%) as a viscous oil. The deuterium content (100%) and the stereoselectivity (α/β = 86/14) of the deuterium substitution at 2'-position were determined by ^1H NMR. ^1H NMR δ 0.90-1.11 (m, 28 H), 2.24 (d, J = 6.9 Hz, 0.86 H), 2.49 (dd, J = 10.5, 7.0 Hz, 0.14 H), 3.76 (m, 1 H), 4.01 (dd, J = 13.2, 2.9 Hz, 1 H), 4.13 (dd, J = 13.2, 2.0 Hz, 1 H), 4.43 (dd, J = 8.4, 7.0 Hz, 1 H), 5.69 (d, J = 8.1 Hz, 1 H), 6.03 (d, J = 1.4 Hz, 1 H), 7.78 (d, J = 8.1 Hz, 1 H), 8.68 (br, 1 H). ^{13}C NMR δ 12.6, 13.1 (2 C), 13.5, 16.8, 16.9, 17.0, 17.1, 17.26, 17.29, 17.4, 17.5, 39.8 (t, J = 20.1 Hz), 60.5, 67.7, 84.4, 85.3, 101.8, 139.6, 149.9, 162.8. HRMS (EI) *m/z* 472.2381 [$(M + H)^+$, $C_{21}H_{38}O_6N_2Si_2D$ requires 472.2409], 428.1776 [$(M - i\text{-}Pr)^+$, $C_{18}H_{30}O_6N_2Si_2D$ requires 428.1783].

1b,d,e were also subjected to the deoxydeuteration reaction and the yields, deuterium contents, and stereoselectivities of the deuterated products **3** are summarized in Table 2. The spectral data of **3d** are as follows. ^1H NMR δ 1.32 (s, 3 H), 1.36 (s, 3 H), 1.43 (s, 3 H), 1.51 (s, 3 H), 1.76 (m, 0.15 H), 2.17 (m, 0.85 H), 3.82 (m, 1 H), 4.08-4.19 (m, 3 H), 4.75 (d, J = 3.7 Hz, 1 H), 5.82 (d, J = 3.7 Hz, 1 H). ^{13}C NMR δ 25.2, 26.2, 26.5, 26.8, 35.3 (t, J = 19.9 Hz), 67.3, 77.3, 78.8, 80.5, 105.8, 109.6, 111.4. HRMS (EI) *m/z* 230.1133 [$(M - Me)^+$, $C_{11}H_{16}O_5D$ requires 230.1139].

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