Pergamon

Tetrahedron 55 (1999) 3479–3488

TETRAHEDRON

Conversion of Esters and Lactones to Ethers *via* Thionoesters and Thionolactones Using Reductive Radical Desulfurization

Doo Ok Jang,* Seong Ho Song, and Dae Hyan Cho

Department of Chemistry, Yonsei University, Wonju, 220-710, Korea

Dedicated to the memory of Professor Derek H. R. Barton

Received 26 August 1998; revised 7 October 1998; accepted 9 October 1998

Abstract: Various thionoesters and thionolactones are readily reduced into the corresponding ethers in high isolated yields by radical desulfurization with organotin hydrides and Et_3B under mild reaction conditions.

INTRODUCTION

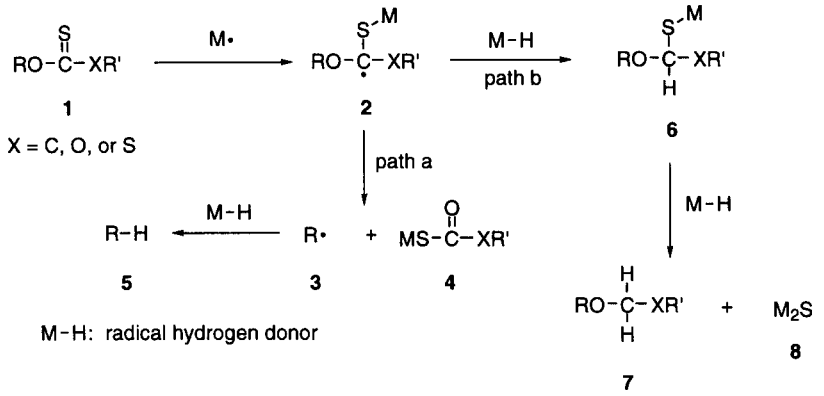
While a number of methods are available for the synthesis of esters and lactones,[1] the process for the preparation of ethers and cyclic ethers are relatively rare. The construction of cyclic ether skeletons, especially medium- and large- rings, is required frequently in natural product chemistry.[2] The preparation of such systems remains the difficult problems in organic synthesis since ring closure is difficult due to unfavourable entropy factors and transannular interactions.[3] Therefore, it is quite interesting to develop a general methodology for the preparation of ethers from esters and lactones. There have been several research efforts to obtain the ethers from the corresponding esters and lactones. The conversion of esters and lactones into the ethers can be accomplished directly with DIBAL-H/Et_3SiH/$BF_3{\cdot}OEt_2$,[4] $NaBH_4$/$BF_3{\cdot}OEt_2$,[5] $HSiCl_3$/$^tBuOO^tBu$,[6] manganese acetyl complexes/$PhSiH_3$,[7] or titanocene complexes/Et_3SiH/Amberlyst 15[6,8] Esters and lactones can also be transformed into the corresponding ethers indirectly *via* the thiono derivatives by the reaction with Raney nickel,[9] or nucleophiles, methyl iodide, and Ph_3SnH/AIBN consequently.[10]

Most recently, it was reported that thionoesters and thionolactones could be reduced giving the ethers with large excess triphenyltin hydride, which is expensive and offers difficulties to remove from the desired products.[11] We report herein the process for the desulfurization of thionoesters and thionolactones that can be accomplished more effectively under milder reaction conditions.

Thiocarbonyl functionality has been widely employed in radical reactions, especially in radical deoxygenation of alcohols. The radicophilic sulphur of thiocarbonyl group is attacked by a radical to generate a radical intermediate **2**, which is fragmented affording an alkyl radical **3** eventually leading to the deoxygenated product **5** (Scheme 1, path a).[12] When the radical hydrogen donor is very reactive and high in

0040-4020/99/$ - see front matter
PII: S0040-4020(98)01156-9

concentration, the radical intermediate **2** will capture a hydrogen from a radical hydrogen donor M-H before fragmentation to give the corresponding ether derivative **7** (path b). According to the scheme 1, there are several important factors to obtain the ether **7** from the thionoester **1** such as the reactivity and the concentration of the radical hydrogen donors, and the reaction temperature. We have thought that the controlled temperature is the most important factor to get the ether **7** from the thionoester **1** efficiently.

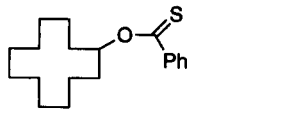


Scheme 1

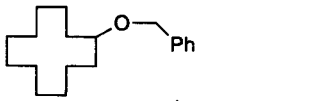
RESULTS AND DISCUSSION

Desulfurization with Ph_3SnH

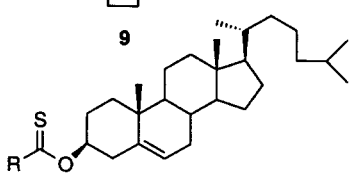
Cyclododecyl thionobenzoate (**9**) was treated with Ph_3SnH (2.2 equiv.), Et_3B (1.0 equiv.) in dry toluene under argon at room temperature to furnish the corresponding ether **9a** in 97% yield (Table 1, entry 1). Cyclododecane that is deoxygenated product of **9** was not detected. When the amount of Et_3B was decreased, more reaction time was needed to finish the reaction, and the yield was somewhat lowered (entry 2). The reaction was optimised to use a small amount of Et_3B (0.5 equiv.) without affecting the yield of the desired product. Various thionoesters and thionolactones were prepared and transformed into the corresponding ethers. When thionobenzoate of cholesterol **10** was reduced under the conditions, cholesteryl benzyl ether (**10a**) was obtained in 85% yield along with cholesterol in 9% yield that was produced by Ph_3SnH acting as a Lewis acid (entry 4), while cholesteryl thioacetate (**11**) afforded cholesteryl ethyl ether (**11a**) in 93% yield without detecting cholesterol (entry 5). A thionoacetyl derivative of primary alcohol **12** was also reduced to the corresponding ether **12a** in high isolated yields under the reaction conditions (entry 6). The process was applied for the preparation of cyclic ethers from thionolactones. Transformation of primary and secondary-derived thionolactones into the corresponding cyclic ethers can be accomplished in high isolated yields without observing ring-opened by-products (entries 7-9). Even tertiary alcohol-derived thionolactone **17** can be transformed to the cyclic ether **17a** in high yields though a large amount of Ph_3SnH is required (entries 7-9). α,β-Unsaturated thionolactone **18** was intact under the reaction conditions (entry 12).



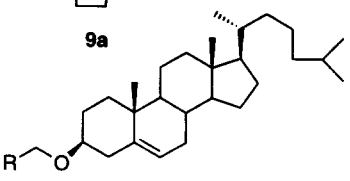
9



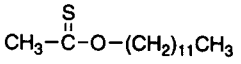
9a



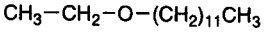
10: R = Ph
11: R = CH_3



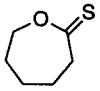
10a: R = Ph
11a: R = CH_3



12

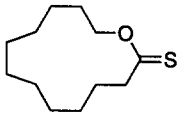


12a

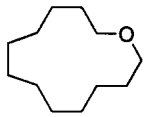


13

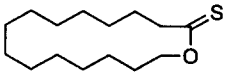
13a



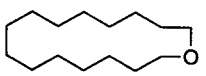
14



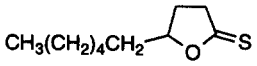
14a



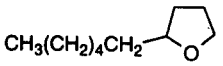
15



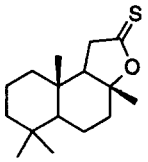
15a



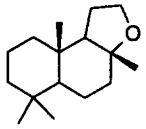
16



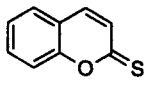
16a



17



17a



18

Table 1. Reduction of Thionoesters and Thionolactones with Ph_3SnH (2.2 equiv.) and Et_3B at Room Temperature.

Entry	Substrate	Et_3B (equiv.)	Time (min)	Product	Yield (%)[a]
1	**9**	1.0	30	**9a**	97[b]
2	**9**	0.1	60	**9a**	85[b]
3	**9**	0.5	30	**9a**	91[b]
4	**10**	0.5	15	**10a**	85 (9)[c]
5	**11**	0.5	40	**11a**	93
6	**12**	0.5	60	**12a**	95
7	**14**	0.5	60	**14a**	89
8	**15**	0.5	40	**15a**	90
9	**16**	0.5	60	**16a**	97
10	**17**[d]	0.5	60	-[e]	
11	**17**[d]	1.0	40	**17a**	92
12	**18**	0.5	120		NR[f]

[a]Isolated yield. [b]Analyzed by GC. [c]Cholesterol. [d]5 equiv. of Ph_3SnH was used. [e]1:1 Adduct with Ph_3SnH was observed. [f]No reaction.

Desulfurization with $^nBu_3SnH$

Cyclododecyl thiobenzoate (**9**) was used as a model compound to find out the optimal conditions for the desulfurization of the thiocarbonyl functionality with $^nBu_3SnH$. When **9** was treated with $^nBu_3SnH$ (2.2 equiv.), Et_3B (0.25 equiv.), and O_2 (0.25 equiv.) at room temperature, only the half-reduced mixed thioketal was obtained (Table 2, entry 1). It shows that while the addition of $^nBu_3SnH$ to the thiocarbonyl group proceeds at room temperature, the second step, the reduction of carbon-sulphur bond of mixed thioketal does not proceed with $^nBu_3SnH$ at room temperature. Based on the observation, the reaction was carried out with Et_3B-O_2 at room temperature until **9** reacted completely. Another portion of Et_3B-O_2 was added and then the reaction temperature was increased to 80 °C giving the corresponding ether **9a** in 77% yield along with 9% yield of the deoxygenated product, cyclododecane (entry 2). Without adding O_2, although it was required much longer reaction time, the reduction of thionoester was proceeded to give 98% of the ether **9a** (entry 3). Finally, we have found that AIBN (azobisisobutyronitrile) is very effective radical initiator for the second step in the reduction of thionoester **9**. When the thionoester **9** was treated with $^nBu_3SnH$ (3.0 equiv.) and Et_3B (0.5 equiv.) without O_2 at room temperature for 1.5 h, and then AIBN (0.25 equiv.) at 85 °C for 1.5 h consequently, 85% yield of the ether **9a** was obtained (entry 4). Thionoesters **10**, **11** and **12** were reduced effectively in high isolated under the conditions (entries 5-7). The process can be applied for the conversion of medium- and large-thionolactones into the corresponding cyclic ethers. Primary alcohol-derived

thionolactones **13**, **14**, and **15** gave the cyclic ethers **13a**, **14a**, and **15a** in high isolated yields without observing ring-opened by-products, respectively (entries 8-10). Secondary alcohol-derived thionolactone **16** can also be transformed to the cyclic ether **16a** smoothly under the conditions (entry 11). Even tertiary alcohol-derived thionolactone **17** gave the corresponding ether **17a** in high yield though a large amount of $^{n}Bu_3SnH$ was required (entry 12). However, α,β-unsaturated thionolactone **18** was not reduced under the reaction conditions.

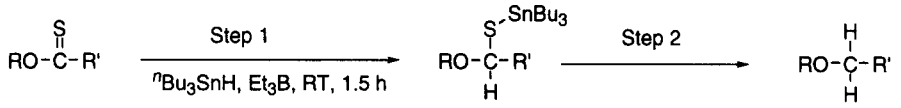


Table 2. Reduction of Thionoesters and Thionolactones with $^{n}Bu_3SnH$.

Entry	Substrate	Step 1		Step 2			Product	Yield (%)[c]
		$^{n}Bu_3SnH$ (equiv.)	Et_3B (equiv.)	Initiator (equiv.)	Temp (°C)	Time (h)		
1	**9**	2.2	0.25[a]		RT	4	-[b]	
2	**9**	3.0	1.0[a]	Et_3B(1.0)[a]	80	6	**9a**	77[d] (9)[e]
3	**9**	3.0	1.0		80	27	**9a**	98[d]
4	**9**	3.0	0.5	AIBN (0.25)	85	1.5	**9a**	85[d]
5	**10**	3.0	0.5	AIBN (0.25)	85	2.0	**10a**	93
6	**11**	3.0	0.5	AIBN (0.25)	85	1.0	**11a**	93
7	**12**	3.0	0.5	AIBN (0.25)	85	0.5	**12a**	94
8	**13**	3.0	0.5	AIBN (0.25)	85	1.5	**13a**	98[f]
9	**14**	3.0	0.5	AIBN (0.25)	85	1.0	**14a**	92
10	**15**	3.0	0.5	AIBN (0.25)	85	1.5	**15a**	98
11	**16**	3.0	0.5	AIBN (0.25)	85	1.0	**16a**	91
12	**17**	5.0	0.5	AIBN (0.25)	85	3.0	**17a**	87

[a]The same mole equiv. of O_2 was added. [b]1:1 Adduct with $^{n}Bu_3SnH$ was observed. [c]Isolated yield. [d]Measured by GC. [e]Cyclododecane. [f]Measured by NMR.

CONCLUSIONS

We have developed an efficient method for the desulfurization of thionoesters and thionolactones. Since the thionoesters and thionolactones can be obtained readily from the corresponding esters and lactones with Lawesson's reagent, this process is a general method for the conversion of esters and lactones to the corresponding ethers. The procedure can be applied to the synthesis of medium- and large cyclic ethers that are not easily prepared. From a practical point of view, the process can be carried out without using an excess of radical hydrogen donors which are expensive, and difficult to remove from the desired products.

EXPERIMENTAL

General Procedures and Starting Materials. Melting points were determined with a Fisher-Jones melting point apparatus and were uncorrected. IR spectra were recorded on a Mattson Genesis series spectrophotometer. ^1H and ^{13}C NMR spectra were determined for solutions in $CDCl_3$ with TMS internal reference on a Varian Gemini 300 NMR spectrometer. Mass spectra were determined on a Hewlett-Packard GC/MS 5972 series. Gas chromatography (GC) measurements were performed on a Hewlett-Packard 5890 gas chromatograph on 30-m capillary columns. Microanalyses were performed at Hanwha Group R&E Center. Thin-layer chromatography (TLC) was performed on 0.25 mm silica gel plates (Merk, Kieselgel 60F-254). Column chromatography was performed on silica gel (Merk, Kieselgel 60, 230-400 mesh). Solvents were used either as purchased or dried and purified by standard methodology under argon. Starting materials were purchased from Aldrich Chemical Co.

Cyclododecyl Thiobenzoate (9). Cyclododecyl benzoate (4.5g, 15.6 mmol) and Lawesson's reagent (12.6 g, 31.3 mmol) in xylenes (50 mL) under argon were heated to reflux for 48 h. After cooling, the solvent was removed in vacuum and the reaction mixture was chromatographed on silica gel (hexanes) to yield **9** (3.95 g, 83%) as a yellow solid: mp 90-92 °C ($EtOH/CH_2Cl_2$); IR (KBr) 2936, 2848, 1450, 1316, 1248, 1174, 1149, 1073, 1016, 895 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30-1.63 (m, 18H), 1.71-2.00 (m, 4H), 5.89-6.01 (m, 1H), 7.32-7.42 (m, 2H), 7.46-7.55 (m, 1H), 8.11-8.19 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 21.2 (2C), 23.5 (2C), 23.6 (2C), 24.2, 24.4 (2C), 28.8 (2C), 80.9, 128.2 (2C), 129.0 (2C), 132.7, 139.3, 211.2; MS *m/e* (rel inten) 166 (M^+-OC(S)Ph, 31), 138 (4), 123 (8), 109 (24), 96 (57), 82 (86), 67 (100), 55 (76), 41 (44). Anal. Calcd for $C_{19}H_{28}OS$: C, 74.95; H, 9.27; S, 10.53. Found: C, 74.49; H, 9.90; S, 10.27.

5α-Cholester-3β-yl Thiobenzoate (10). Cholester-3β-yl benzoate (3.5 g, 7.13 mmol) and Lawesson's reagent (5.76 g, 14.3 mmol) in xylenes (50 mL) under argon were heated to reflux for 72 h. After cooling, the solvent was removed in vacuum and the reaction mixture was chromatographed on silica gel (hexanes) to yield **10** (1.44 g, 40%) as a yellow solid: mp 164-167 °C ($EtOH/CH_2Cl_2$) (lit.[13] 164-166 °C); IR (KBr) 2936, 1450, 1379, 1268, 1247, 1024 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.66-2.68 (m, 43H), 5.38-6.62 (m, 2H), 7.34-7.43 (m, 2H), 7.42-7.58 (m, 1H), 8.13-8.20 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 12.1, 19.0, 19.6, 21.3, 22.8, 23.1, 24.1, 24.5, 27.3, 28.3, 28.5, 32.1, 32.2, 36.0, 36.4, 37.0, 37.1, 37.6, 39.8, 40.0, 42.6, 50.3, 56.4, 56.9, 81.9, 123.4, 128.2 (2C), 129.0 (2C), 132.8, 139.1, 139.6, 211.3.

5α-Cholester-3β-yl Thioacetate (11). Cholester-3β-yl acetate (3.5 g, 8.16 mmol) and Lawesson's reagent (6.59 g, 16.3 mmol) in xylenes (50 mL) under argon were heated to reflux for 72 h. After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/EtOAc (9:1) to give **11** (2.7 g, 74%) as a white solid: mp 138-139 °C ($MeOH/CH_2Cl_2$) (lit.[14] 140-142 °C); IR (KBr) 2938, 1463, 1362, 1275, 1253, 1216, 1027 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.64-2.52 (m, 43H), 3.55(s, 3H), 5.19-5.37 (m, 1H), 5.39-5.44 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 12.1, 19.0, 19.6, 21.3, 22.8, 23.1,

24.1, 24.5, 27.1, 28.2, 28.4, 32.1, 35.4, 36.0, 36.4, 36.9, 37.1, 37.4, 39.8, 40.0, 42.6, 50.3, 56.4, 56.9, 81.8, 123.3, 139.5, 219.4.

1-Dodecyl Thioacetate (12). 1-Dodecyl acetate (1.0 g, 3.44 mmol) and Lawesson's reagent (2.78 g, 6.88 mmol) in xylenes (30 mL) under argon were heated to reflux for 72 h. After cooling, the solvent was removed in vacuum and the reaction mixture was chromatographed on silica gel (hexanes) to give **12** (0.65 g, 62%) as a pale yellow oil: IR (neat) 2932, 2853, 1466, 1363, 1271, 1219, 1036 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (t, J = 6.3 Hz, 3H), 1.15-1.49 (m, 18H), 1.66-1.83 (m, 2H), 2.57 (s, 3H), 4.41(t, J = 6.9 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 14.3, 22.9, 26.2, 28.3, 29.5, 29.6, 29.7, 29.8, 29.9 (2C), 32.1, 34.7, 73.1, 220.3; MS *m/e* (rel inten) 244 (M^+, 2), 211 (23), 168 (110), 140 (10), 125 (12), 111 (22), 97 (32), 83 (23), 55 (11). Anal. Calcd for $C_{14}H_{28}OS$: C, 68.79; H, 11.55; S, 13.12. Found: C, 68.00; H, 11.52; S, 13.33.

2-Oxepanethione (13). A mixture of ε-caprolactone (1.5 g, 13.3 mmol) and Lawesson's reagent (7.8 g, 19.7 mmol) in toluene (30 mL) under argon was heated to reflux for 24 h. After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/EtOAc (8.2/1.8) to give **13** (1.07 g, 62%) as a pale yellow oil: IR (neat) 2933, 2859, 1474, 1435, 1391, 1295, 1244, 1168, 1066, 1026 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74-1.96 (m, 6H), 3.14-3.26 (m, 2H), 4.52 (t, J = 4.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 24.8, 28.2, 28.3, 45.9, 74.2, 227; MS *m/e* (rel inten) 130 (M^+, 100), 115 (2), 97 (9), 76 (11), 69 (24), 55 (17).

2-Oxacyclotridecanethione (14).[9b] A mixture of oxacyclotridecan-2-one (1.13 g, 5.67 mmol) and Lawesson's reagent (4.59 g, 11.4 mmol) in toluene (20 mL) under argon was heated to reflux for 48 h. After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/EtOAc (9.7/0.3) to give **14** (0.66 g, 54%) as a pale yellow oil: IR (neat) 2929, 2859, 1461, 1377, 1294, 1196, 1137 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15-1.50 (m, 14H), 1.62-1.80 (m, 4H), 2.70-2.85 (m, 2H), 4.40-4.50 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 24.7, 25.0, 25.6, 25.8, 25.9, 26.3, 26.6, 27.1, 27.5, 225.1; MS *m/e* (rel inten) 214 (M^+, 22), 182 (13), 163 (36), 137 (10), 121 (18), 97 (27), 81 (27), 69 (19), 55 (23), 41 (16). Anal. Calcd for $C_{12}H_{22}OS$: C, 67.24; H, 10.34; S, 14.96. Found: C, 67.72; H, 10.10; S, 14.20.

2-Oxacyclohexadecanethione (15). A mixture of oxacyclohexadecan-2-one (2.0 g, 8.32 mmol) and Lawesson's reagent (4.0 g, 9.98 mmol) in toluene (20 mL) under argon was heated to reflux for 72 h. After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/CH_2Cl_2 (7/3) to give **15** (1.63 g, 77%) as a pale yellow oil: IR (neat) 2924, 2856, 1455, 1373, 1278, 1200, 1099, 1069 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10-1.55 (m, 20H), 1.70-1.82 (m, 4H), 2.81 (t, J = 7.2 Hz, 2H), 4.45 (t, J = 5.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 25.5, 26.0, 26.1, 26.2, 26.4, 26.7, 27.1, 27.2, 27.3 (2C), 27.9, 28.1, 47.6, 72.5, 224.7; MS *m/e* (rel inten) 256 (M^+, 22), 223 (100), 205 (8), 179 (5), 165 (5), 149 (7), 135 (12), 109 (20), 97 (18), 83 (14), 55 (12), 41 (7). Anal. Calcd for $C_{15}H_{28}OS$: C, 70.25; H, 11.00; S, 12.50. Found: C, 70.36; H, 11.45; S, 12.26.

Thiocarbonyl Derivative of γ-Decanolactone (16). A mixture of γ-decanolactone (2.5 g, 14.7 mmol) and Lawesson's reagent (7.13 g, 17.6 mmol) in toluene (20 mL) under argon was heated to reflux for 24 h.

After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/EtOAc (9.5/0.5) to give **16** (1.09 g, 40%) as a yellow oil: IR (neat) 2929, 2857, 1455, 1355, 1314, 1236, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (t, 3H), 1.20-1.60 (m, 8H), 1.60-1.78 (m, 1H), 1.78-2.00 (m, 2H), 2.30-2.45 (m, 1H), 2.95-3.25 (m, 2H), 4.70-4.82 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.6, 25.3, 29.0, 29.7, 31.7, 35.0, 45.0, 91.2, 222.6; MS *m/e* (rel inten) 186 (M^+, 100), 153 (70), 135 (49), 111 (30), 97 (46), 83 (74), 69 (77), 55 (41), 41 (24). Anal. Calcd for $C_{10}H_{18}OS$: C, 64.47; H, 9.74; S, 17.21. Found: C, 64.44; H, 10.66; S, 17.39.

Thiocarbonyl Derivative of (3a*R*)-(+)-Sclareolide (17). A mixture of (3a*R*)-(+)-sclareolide (1.5 g, 6.0 mmol) and Lawesson's reagent (4.85 g, 12.0 mmol) in toluene (20 mL) under argon was heated to reflux for 24 h. After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/CH_2Cl_2(6/4) to give **17** (0.48 g, 30%) as a white solid: mp 167-170 °C ($MeOH/CH_2Cl_2$); IR (KBr) 2923, 2866, 1460, 1389, 1301, 1236, 1187, 1153 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80-2.20 (m, 24H), 2.72-2.96 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 15.5, 18.3, 21.0, 21.1 (2C), 33.3, 33.5, 36.7, 38.7, 39.6, 42.4, 43.6, 56.9, 59.9, 95.6, 222.6; MS *m/e* (rel inten) 266 (M^+, 87), 251 (20), 233 (15), 215 (8), 191 (70), 175 (25), 163 (16), 137 (32), 123 (87), 95 (91), 82 (100), 69 (78), 55 (28). Anal. Calcd for $C_{16}H_{26}OS$: C, 72.13; H, 9.84; S, 12.03. Found: C, 72.21; H, 10.22; S, 12.05.

2-Thiocoumarin (18). A mixture of coumarin (1.5 g, 10.3 mmol) and Lawesson's reagent (5.0 g, 12.4 mmol) in xylenes (20 mL) under argon was heated to reflux for 24 h. After cooling, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel eluting with hexane/EtOAc(9/1) to give **18** (0.82 g, 52%) as a yellow solid: mp 95-97°C ($EtOH/CH_2Cl_2$)(lit.[15] mp 98-100 °C); IR (KBr) 3008, 2930, 1606, 1415, 1251, 1205, 1127, 1094 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.18-7.64 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 116.9, 120.6, 125.7, 128.0, 129.8, 132.4, 134.7, 156.8, 198.2; MS *m/e* (rel inten) 162 (M^+, 70), 118 (100), 90 (14).

General Procedure for Desulfurization with Ph_3SnH and Et_3B. To a solution of a thionoester (0.4 mmol) and Ph_3SnH (0.88 mmol) in dry toluene (1 mL) was added Et_3B (0.2 mL, 1.0 M solution in *n*-hexane) under argon. The solution was stirred at room temperature. When the reaction was completed, the solvent was removed in vacuum and the product was isolated by column chromatography on silica gel.

General Procedure for Desulfurization with $^nBu_3SnH$ and Et_3B/AIBN. To a solution of a thionoester (0.4 mmol) and $^nBu_3SnH$ (1.0 mmol) in dry toluene (0.5 mL) was added Et_3B (0.2 mL, 1.0 M solution in *n*-hexane) under argon. The solution was stirred for 1.5 h at room temperature. To the solution was added AIBN (17 mg) and then the reaction mixture was allowed to stir at 85 °C for 1-2 h. The solvent was removed in vacuum and the product was isolated by column chromatography on silica gel.

Cyclohexyl Benzyl Ether (9a). Column chromatography on silica gel as a yellow oil: ($EtOH/CH_2Cl_2$); IR (neat) 3063, 3028, 2934, 2861, 1469, 1445, 1358, 1097, 1066, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20-1.90 (m, 22H), 3.50-3.60 (m, 1H), 4.50 (s, 2H), 7.20-7.50 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 19.9 (2C), 22.0 (2C), 22.2 (2C), 23.1, 23.5 (2C), 27.8 (2C), 69.2, 75.2, 126.3, 126.6 (2C), 127.2 (2C), 138.1; MS

m/e (rel inten) 274 (M^+, 2), 183 (11), 91 (100). Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 82.96; H, 11.25.

5α-Cholester-3β-yl Benzyl Ether (10a). Column chromatography on silica gel (eluent; hexanes : CH_2Cl_2, 1 : 1): mp 112-115 °C(EtOH/CH_2Cl_2) (lit.[14] 118-121 °C); IR 3063, 3027, 2950, 2866, 1737, 1461, 1098 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80-2.50 (m, 43H), 3.20-3.40 (m, 1H), 4.58 (s, 2H), 5.30-5.40 (m, 1H), 7.15-7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 12.1, 19.0, 19.6, 21.3, 22.8, 23.0, 24.1, 24.5, 28.2, 28.5, 28.7, 32.1, 32.2, 36.0, 36.4, 37.2, 37.5, 39.4, 39.8, 40.1, 42.6, 50.5, 56.4, 57.0, 70.2, 78.8, 121.8, 127.6, 127.7 (2C), 128.6 (2C), 139.3, 141.2.

5α-Cholester-3β-yl Ethyl Ether (11a).[16] Column chromatography on silica gel (eluent; hexanes : CH_2Cl_2, 6 : 4): mp 75-78 °C (EtOH/CH_2Cl_2); IR (KBr) 2950, 1462, 1375, 1239, 1107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80-2.40 (m, 46H), 3.08-3.22 (m, 1H), 3.53 (t, J = 7 Hz, 2H), 5.15-5.40 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 12.1, 15.9, 19.0, 19.6, 21.3, 22.8, 23.0, 24.1, 24.5, 28.2, 28.5, 28.7, 32.1, 32.2, 36.0, 36.4, 37.1, 37.5, 39.5, 39.8, 40.1, 42.6, 50.5, 56.4, 57.0, 63.4, 79.0, 121.7, 141.4.

1-Dodecyl Ethyl Ether (12a). Column chromatography on silica gel (eluent; hexanes : CH_2Cl_2, 7 : 3): oil; IR (neat) 2925, 2853, 1466, 1376, 1123 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8 (t, J = 6.3 Hz, 3H), 1.19 (t, J = 6.9 Hz, 3H), 1.26 (s, 18H), 1.50-1.62 (m, 2H), 3.40 (t, J = 6.9 Hz), 3.46 (q, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2, 15.4, 22.9, 26.4, 29.6, 29.6, 29.7, 29.8, 29.9 (2C), 30.0, 32.1, 66.2, 71.0; MS *m/e* (rel inten) 214 (M^+, 1), 168 (95), 140 (43), 125 (26), 111 (76), 97 (100), 83 (73), 69 (28), 59 (36). Anal. Calcd for $C_{14}H_{30}O$: C, 78.43; H, 14.10. Found: C, 77.74; H, 14.73.

Oxacyclotridecane (14a). Column chromatography on silica gel (eluent; hexanes : CH_2Cl_2, 8.5 : 1.5): oil; IR (neat) 2925, 2856, 1460, 1360, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30-1.50 (m, 10H), 3.45 (t, J = 4.8 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 25.0 (2C), 25.3 (2C), 26.2 (2C), 26.8 (2C), 28.8 (2C), 70.6 (2C); MS *m/e* (rel inten) 184 (M^+, 8), 166 (8), 138 (29), 123 (39), 110 (62), 96 (100), 82 (100), 69 (31), 55 (35). Anal. Calcd for $C_{12}H_{24}O$: C, 78.29; H, 13.12. Found: C, 78.03; H, 13.64.

Oxacyclohexadecane (15a). Column chromatography on silica gel (eluent; hexanes : CH_2Cl_2, 7 : 3): oil; IR (neat) 2926, 2854, 1459, 1351, 1119 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20-1.45 (m, 24H), 3.43 (t, J = 5.1 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 25.5, 26.5, 26.8, 27.4, 27.5, 27.6, 29.4, 70.2; MS *m/e* (rel inten) 226 (M^+, 1), 208 (14), 180 (12), 165 (5), 152 (19), 137 (25), 124 (38), 96 (98), 82 (100), 69 (34), 55 (28). Anal. Calcd for $C_{15}H_{30}O$: C, 79.58; H, 13.36. Found: C, 79.03; H, 13.60.

2-Hexyltetrahydrofuran (16a).[8] Column chromatography on silica gel (eluent; hexanes : EtOAc, 9.7 : 0.3): oil; IR (neat) 2929, 2856, 1456, 1373, 1069 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (t, J = 7 Hz, 3H), 1.20-1.65 (m, 11H), 1.80-2.00 (m, 3H), 3.62-3.90 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.3, 22.8, 26.0, 26.6, 29.6, 31.6, 32.1, 36.0, 67.8, 79.7; MS *m/e* (rel inten) 226 (M^+, 1), 208 (14), 180 (12), 165 (5), 152 (19), 137 (25), 124 (38), 96 (98), 82 (100), 69 (34), 55 (28).

(-)-Ambroxide (17a).[17] Column chromatography on silica gel (eluent; hexanes : EtOAc, 9 : 1): white solid; mp 73-75 °C; IR (KBr) 2919, 2869, 1455, 1381, 1124, 1005, 978 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.83 (s, 3H),

0.84 (s, 3H), 0.88 (s, 3H), 0.90-1.52 (m, 11H), 1.60-1.78 (m, 4H), 1.90-1.98 (m, 2H), 3.76-3.96 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 15.3, 18.6, 20.9, 21.4, 22.9, 33.3, 33.8, 36.4, 40.0, 40.2, 42.7, 57.5, 60.4, 65.2, 80.1; MS *m/e* (rel inten) 236 (M^+, 2), 221 (100), 203 (1), 177 (2), 151 (2), 137 (23), 121 (5), 109 (7), 97 (32), 81 (14), 55 (12).

ACKNOWLEDGEMENTS: We thank the Korea Science and Engineering Foundation (Grant No. 971-0302-015-2) for the financial support of this work.

REFERENCES

1. For some recent examples: a) Nicolaou. K. C.; Hwang, C. –K.; Duggan, M. E.; Reddy, K. B.; Marron, B. E.; McGarry, D. G. *J. Am. Chem. Soc.* **1986**, *108*, 6800. b) Overman, L. E.; Blumenkoph, T. A.; Castaneda, A.; Thopmpson, A. S. *J. Am. Chem. Soc.* **1986**, *108*, 3516. c) Carling, R. W.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1986**, 565. d) Kocienski, P. *J. Chem. Soc., Perkin Trans. I* **1985**, 2093. e) Paterson, I.; Mansuri, M. M. *Tetrahedron* **1985**, *41*, 3569. f) Schreiber, S.; Kelley, S. E. *Tetrahedron Lett.* **1984**, *25*, 1757. g) Jackson, W. P.; Ley, S. V.; Morton, J. A. *Tetrahedron Lett.* **1981**, *22*, 2601. h) Nicolaou, K. C. *Tetrahedron* **1977**, *33*, 683. i) Back, T. G. *Tetrahedron* **1977**, *33*, 3041. j) Masamune, S.; Bates, G. S.; Corcoran, J. W. *Angew Chem. Int. Ed. Engl.* **1977**, *16*, 585.
2. Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *3*, 1.
3. Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 102.
4. Kraus, G. A.; Frazier, K. A.; Roth, B. D.; Taschner, M. J.; Neuenschwander, K. *J. Org. Chem.* **1981**, *46*, 2417.
5. Pettit, G. R.; Piatok. D. M. *J. Org. Chem.* **1962**, *27*, 2127.
6. Tsurugi, J.; Nakao, R.; Fukumoto, T. *J. Am. Chem. Soc.* **1969**, *91*, 4587.
7. Mao, Z.; Gregg, B. T.; Culter, A. R. *J. Am. Chem. Soc.* **1995**, *117*, 10139.
8. Hansen, M. C.; Verdaguer, X.; Buchwald, S. L. *J. Org. Chem.* **1998**, *63*, 2360.
9. a) Barrett, A. G. M.; Lee, A. C. *J. Org. Chem.* **1992**, *57*, 2818. b) Bradshaw, J. S.; Jones, B. A.; Gebhard, J. S. *J. Org. Chem.* **1983**, *48*, 1127. c) Baxter, S. L.; Bradshaw, J. S. *J. Org. Chem.* **1981**, *46*, 831.
10. a) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Veale, C. A.; Furst, G. T. *J. Am. Chem. Soc.* **1987**, *109*, 2504. b) Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.
11. Nicolaou. K. C.; Sato, M.; Theodorakis, E. A.; Miller, N. D. *J. Chem. Soc., Chem. Commun.* **1995**, 1583.
12. Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1990**, *31*, 3991.
13. Achmatowicz, S.; Barton, D. H. R.; Magnus, P. D.; Poulton, G. A.; West, P. J. *J. Chem. Soc., Perkin Trans. I* **1973**, 1567.
14. Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. I* **1975**, 1574.
15. Koster, R; Kucznierz, R.; Seidel, G.; Betz, P. *Chem. Ber.* **1992**, *125*, 1023.
16. Heyl, B. L.; Tyrrell, D.; Lambeth, J. D. *J. Biol. Chem.* **1986**, *261*, 2743.
17. Martres, P.; Perfetti, P.; Zahra, J. –P.; Waegell, B. Giraudi, E.; Petrzilka, M. *Tetrahedron Lett.* **1993**, *34*, 629.