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The Invention of Radical Reactions. Part XXIV.[1] Relative Rates of Acylation and Radical Deoxygenation of Secondary Alcohols.+

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Abstract: Secondary alcohols were transformed into various thiocarbonyl derivatives. Reduction of these compounds using tributyltin hydride and an initiator afforded the corresponding deoxy-compounds. Half-life and competitive measurements showed that all these reactions were fast and could be run to completion.

Deoxygenation of alcohols, especially secondary alcohols, using radical processes was a good synthetic challenge. Such reactions have many advantages over analogous ionic procedures in complex Natural Products. The original Barton-McCombie reaction[2] has found many applications[3]. Radical deoxygenation of primary and tertiary alcohols is also possible[4]. Recently the tributyltin hydride normally used has been replaced by a variety of silane procedures[5].

In our original paper[2] we had examined the thiobenzoyl, the xanthate and the thioimidazolide functions. All of them gave efficient deoxygenation of secondary alcohols, but the rates of these reactions under competitive circumstances were not determined. The thiobenzoyl group was conveniently introduced by Vilsmeier chemistry, the xanthate by reaction of the corresponding anion with CS_2 and then methyl iodide and the thioimidazolide by use of freshly prepared thiocarbonyl bis-imidazolide. The latter reagent was convenient for alcohols where anion formation was precluded by other base sensitive functional groups in the molecules. Normally xanthates prepared using NaH or, better, and at lower temperature, butyl lithium[6], were the cheapest and most convenient procedure. Thiocarbonates, especially five-membered thiocarbonates also permit deoxygenation of one of the original alcohol functions[7].

More recent studies by Robins and his colleagues[8] have shown that phenylthiocarbonyl chloride was also a convenient reagent to produce phenoxythiocarbonyl derivatives which were readily deoxygenated with tributyltin hydride. Further developments were the introduction of halogenated phenylthiocarbonyl reagents[9] some of which are now available commercially[10].

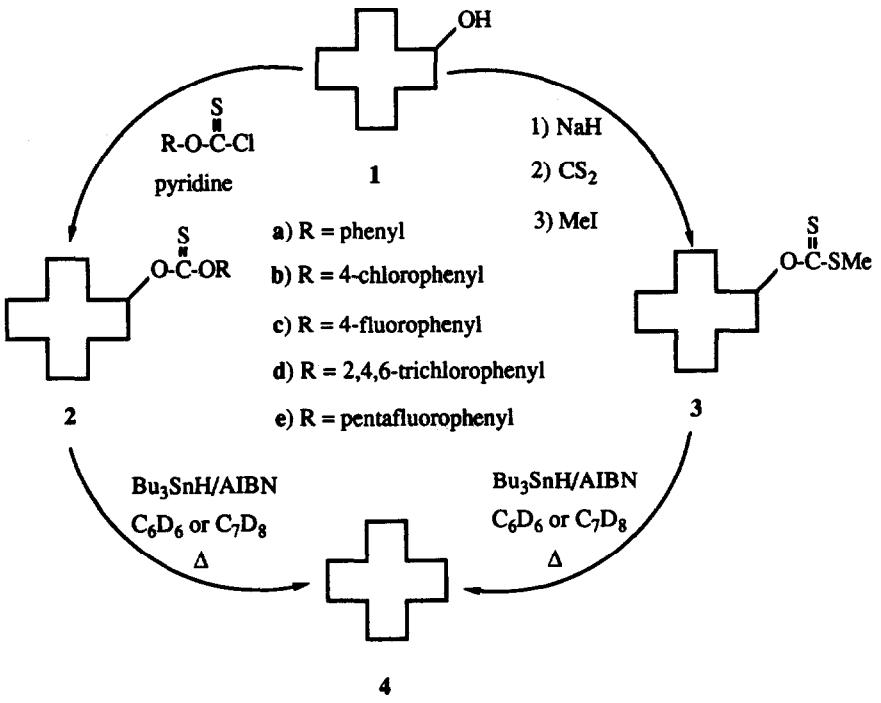
+ Dedicated with affection and respect to my successor Prof. Charles W. Rees, F.R.S., on the occasion of his retirement from the Hofmann Chair of Chemistry at Imperial College.

Derek H. R. Barton

Since no comparative rate measurements had been reported for any of the deoxygenation reactions, we thought it important to remedy this situation. It is difficult to make reliable rate measurements on radical chain reactions on single compounds, but by careful attention to detail we have been able to measure by N.M.R. procedures half-lives of both the thiocarbonyl derivatives and of the tributyltin hydride at the same time (Table 1). We compared cyclododecyl derivatives because of their non-volatility. The phenoxythiocarbonyl derivative **2a** was compared with 4-chloro-, 4-fluoro-, 2,4,6-trichloro- and pentafluoro- phenoxythiocarbonyl analogues **2b**, **2c**, **2d** and **2e** respectively. For comparison the xanthate **3** was also studied (Scheme 1).

Contrary to our earlier thinking[9], the xanthate reacted faster than any of the phenoxythiocarbonyl derivatives. Of the latter the unsubstituted phenoxythiocarbonyl derivative **2a** was slightly faster than the 2,4,6-trichloro analogue **2d** and the 4-fluorophenyl derivative **2c**. The 4-chlorophenyl **2b** and especially the pentafluorophenyl **2e** analogues were slower than phenyl by a factor of 2 (± 0.5).

In order to confirm these interesting results a series of competition experiments was carried out in which all derivatives of type **2** were competed against the xanthate **3**. The conversion of the xanthate **3** was limited to about 50% so as to make comparison more reliable. The data in Table 2 broadly confirm the data given in Table 1.



Scheme 1

Table 1 Half-life measurements of cyclododecanol derivatives **2a-e** and **3** in the deoxygenation reaction with tributyltin hydride + AIBN[a].

Thiocarbonyl compound	**2** (or **3**) $t_{1/2}$ (sec)	Bu_3SnH $t_{1/2}$ (sec)	$t_{1/2}$ (**2**) / $t_{1/2}$ (**3**)
2a	33.2	47.1	1.54
2b	51.0	49.8	2.37
2c	37.7	35.3	1.75
2d	36.5	29.6	1.70
2e	81.2	92.0	3.78
3	21.5	24.8	-

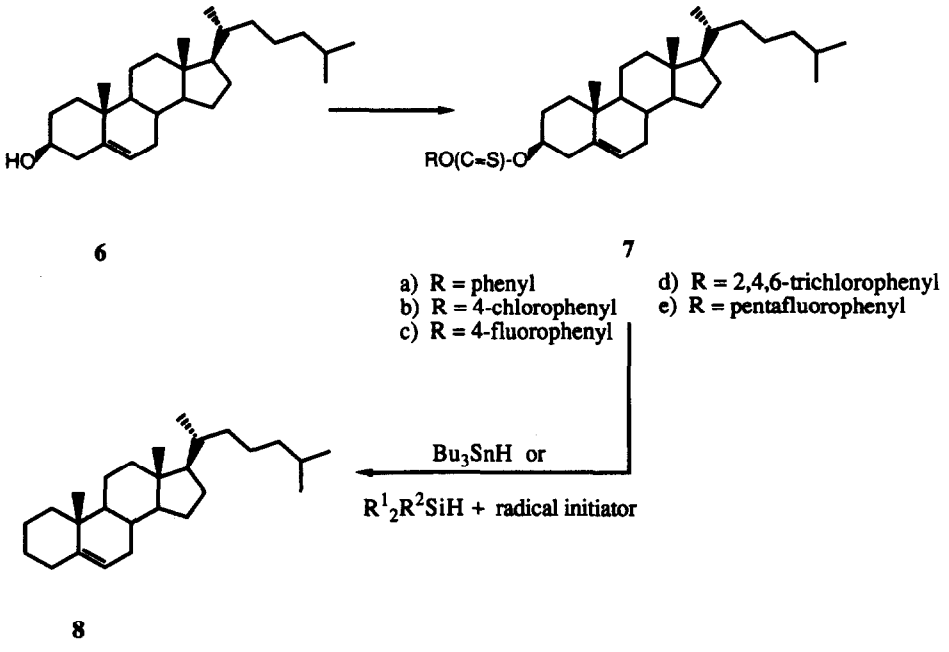
[a] in C_6D_6 at 100°C.

Table 2 Competition experiments between thiocarbonyl compounds **2** and the xanthate **3** in the radical deoxygenation reaction with tributyltin hydride + AIBN.

Thiocarbonyl compound	**2** $t_{1/2}$ (sec)[a]	**3** $t_{1/2}$ (sec)[a]	Bu_3SnH $t_{1/2}$ (sec)	**2** $t_{1/2}$ / **3** $t_{1/2}$	Unreacted **2** (%)	Unreacted **3** (%)
2a	53.0	14.1	14.2	3.75	87	50
2b	57.3	15.5	17.3	3.69	85	44
2c	95.1	18.3	18.0	5.21	91	51
2d	117[b]	17.5[b]	17.2[b]	6.68	93	51
2d	144	17.6	17.3	8.21	94	48
2e	76.0	29.9	27.2	2.54	82	55
2e	77.6	30.4	27.9	2.55	82	54

[a] in C_6D_6 at 110°C. [b] in C_7D_8 at 110°C.

We have also compared the kinetics of acylation of cholesterol as a model compound with chlorothionoformates (Scheme 2).



Scheme 2

Thus, acylation of **6** with chlorothionoformates **5a-e** resulted in the formation of **7a-e**, respectively. The conversion of **6** to **7** can be made quantitative; the only contaminant present is some diaryl thionocarbonate, removed by crystallization from dichloromethane/hexanes. Compounds of type **7** are easily deoxygenated to the corresponding hydrocarbon **8** by using the Barton-McCombie methodology[2].

We have shown recently, however, that various primary[4d] and secondary alcohols can be deoxygenated with diphenylsilane,[5c,5d] phenylsilane,[5e] triphenylsilane[5c] and triethylsilane,[5f] respectively. Dixanthates of 1,2-diols can also be deoxygenated to the corresponding olefins by this method.[5d,5f]

Half-life measurements revealed that the pentafluorophenyl chlorothionoformate **5e**[9,10] reacted much faster than the unsubstituted phenyl reagent **5a**[8]; the half-life of the acylation of cholesterol **6** with pentafluorophenyl chlorothionoformate **5e** being 0.5 min at 25°C. The results, summarized in Table 3 show that the halogenated reagents **5b**, **5c** and **5e** have shorter half-lives in the acylation reaction than **5a** with the same

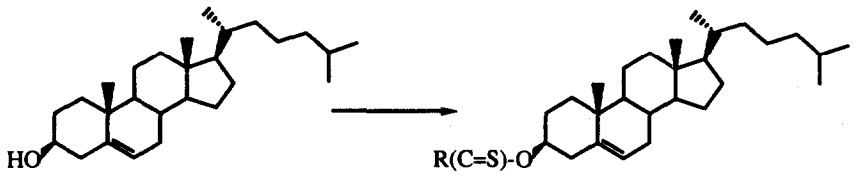
substrate **6**. The variation in rates for the deoxygenation reaction (Table 1) is over a limited range (about 4), but the variation in acylation rate (Table 3) is much greater (about 50). Hence, it is clear that the pentafluorophenyl derivative **5e** will be the reagent of choice for (at least) hindered hydroxyl groups. However, from the economic point of view the xanthate remains the preferred work horse. New methods of xanthate formation are under investigation.

Table 3 Acylation of cholesterol **6** with chlorothionoformates **5a-e**[a].

Thiocarbonyl compound **5** R	Product **7**	m.p.[b] [°C]	Yield[e] [%]	$t_{1/2}$ [min]
phenyl (5a)	**7a**	157-158	84	3.26
4-chlorophenyl (5b)	**7b**	183-184	76	1.47
4-fluorophenyl (5c)	**7c**	160-161	94	1.53
2,4,6-trichloro-phenyl (5d)	**7d**	155-156[c]	43[d]	27.0
pentafluorophenyl (5e)	**7e**	150-152	82	0.50

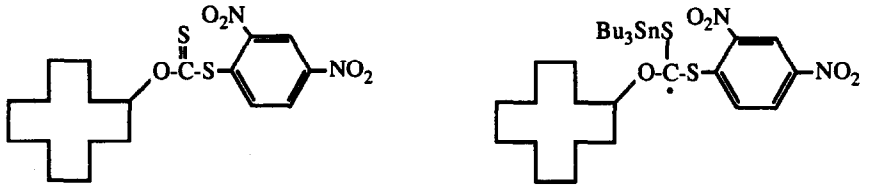
[a] samples taken and analyzed at intervals up to 40 min, depending on the rate of the given reaction.
[b]dichloromethane/hexanes, except where noted.
[c]dichloromethane/EtOH.
[d]fractional crystallization (4 times) to remove the ArO(C=S)OAr byproduct.
[e]yield of isolated crystallized products.

Cholesterol **6** was also transformed to the corresponding thiocarbamate **9b** *via* the xanthate **9a**[2] by the method of Barton et al.[11] However, this compound remained mostly unchanged in the attempted deoxygenation reaction with AIBN and tributyltin hydride and failed to give cholest-5-ene **8**. Similarly, the dithiocarbonate **10**[12] failed to give the desired deoxygenated product (cyclododecane). It appears that in the initially formed adduct radical **11** the C(Ar)-S bond breakage was the favoured one instead of the C-O bond breakage in the radical beta-elimination (Scheme 3). The latter would have resulted in the formation of the desired cyclododecyl radical and, after quenching, this radical could have furnished the desired hydrocarbon (cyclododecane).



6 **9**

a) R = MeS
b) R = Et_2N



10 **11**

Scheme 3

Experimental

General Procedures and Starting Materials.

Melting points were determined with a Kofler hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 881 spectrophotometer. UV-VIS spectra were recorded on a Beckman DU-7 spectrometer. ^1H and ^{13}C NMR spectra were determined for solutions in deuterochloroform (unless specified otherwise) with TMS internal reference on Varian Gemini 200, Varian XL 200E or Varian XL 400 instruments. Mass spectra were obtained on a VG Analytical 70S high resolution double focusing magnetic sector mass spectrometer with attached VG 11/250J data system in the EI or FAB mode. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Solvents were used either as purchased or dried and purified by standard methodology under dry, pure argon. Other reference compounds and starting materials were purchased from Aldrich Chemical Co., Inc., Milwaukee, Wisconsin.

Conditions and materials: Benzene-d_6 (F-1816) and toluene-d_8 (F-1023) (Cambridge Isotope Laboratories) were degassed (freeze-thaw 4 times) and stored under dry argon. The solvents were then used without further purification. A standard solution of AIBN (33 mmole/l) was prepared by placing 0.108 g (0.660 mmole) of AIBN in a dry 2.00 ml volumetric flask. The flask was fitted with a rubber septum and flushed with dry argon. The solution was made to volume with benzene-d_6 and stored in the dark in the freezer until used. Tributyltin hydride (Aldrich HX-05613HX) was analyzed for purity prior to use (^{1}H NMR) and calculated to 79%. The reagent was used without further purification; compensating to give one equivalent of usable hydride. n-Propyl acetate (Aldrich 00816EX) was used as an internal reference for ^{1}H-NMR analysis of reaction solutions and is stable in these reaction conditions. All reaction samples were analyzed via ^{1}H-NMR relative to n-propyl acetate.

Half-life measurement: 0.500 mmol (0.1372 g) S-methyl-O-cyclododecyl dithiocarbonate **2** was placed in a dry 5 ml volumetric flask. The flask was fitted with a rubber septum and flushed with dry argon. Approximately 2 ml of solvent (degassed benzene-d_6) was then added followed by 21µl n-propyl acetate (0.180 mmol) and 170 µl of 79% $HSnBu_3$ (0.500 mmol). The solution was then made close to volume and equilibrated in a large water bath at 25°C. Then 50.0 µl (0.0165 mmol) of the above AIBN solution was added and the solution made to volume. Aliquots (0.75 ml) of this solution were then transferred *via* syringe into six separate flame-dried 5 mm NMR tubes under dry argon. The final concentration of reagents were: 0.100 M xanthate **2**, 0.100 M $HSnBu_3$, 3.3 mM AIBN, 36 mM n-propyl acetate. The six NMR tubes were equilibrated in a large water bath at 25°C. A large rapidly stirred oil bath (> 1000 ml) was pre-equilibrated at 100°C using an accurate thermostatic controller. The sample tubes were quickly wiped dry and placed in the oil bath and the timer started. Samples were removed at the appropriate times and rapidly quenched by cooling in an ice acetone bath.

Competition experiments: For the competition experiments samples were prepared in a manner identical to that for the half-life measurements; however 0.500 mmol of the aryl thionocarbonate **2** was placed in the dry 5.00 ml volumetric flask in addition to 0.500 mmol of **3**.

Phenyl chlorothionoformate **5a**: This reagent is commercially available (Aldrich); however it is readily prepared in high yield *via* a modification of the procedure of Germaise *et al.*[13] Phenol (18.82 g, 0.20 mmol) was dissolved in conc. aqueous NaOH solution (0.21 mmol) and subsequently diluted to near 1 M. The aqueous sodium phenoxide solution was added dropwise with stirring (room temperature, 1 hr) to a solution of thiophosgene (25.23 g, 16.8 ml, 2.2 mmol) in chloroform or dichloromethane (160 ml). Following complete addition the reaction was allowed to stir for one hour more. The organic layer was then removed and washed first with saturated aqueous $NaHCO_3$ solution; followed by water (twice), and finally brine. After drying over anhydrous magnesium sulfate, the solvent and unreacted thiophosgene were evaporated together at reduced pressure (40°C water bath, aspirator vacuum); occasionally adding fresh solvent to facilitate the removal of the orange thiophosgene. The small amount of the diphenyl thionocarbonate that is invariably formed in this reaction

is readily precipitated in hexanes (200 ml). Filtration and evaporation of the hexanes provides the product in high yield and >90% purity (^{1}H NMR). Fractional distillation (52°C/0.55 mm) gave pure phenyl chlorothionoformate (85%, >95% purity by ^{1}H NMR) which appeared identical (IR, ^{1}H NMR, ^{13}C NMR) to an authentic sample (Aldrich 99%, lot No. EW10118EW).

4-Chlorophenyl chlorothionoformate **5b**: This compound is commercially available; however for our purposes this compound was also prepared in the same manner as the phenyl derivative above. Distillation (87°C/9 mm) gave the product in 94% yield (>95% purity, ^{1}H NMR), and was identical (IR, ^{1}H NMR, ^{13}C NMR) to an authentic sample (Lancaster Synthesis, lot No. 90866-00-641).

Bis(4-chlorophenyl) thionocarbonate: Previously isolated during the work-up of a reaction mixture in a reaction similar to the one above. White crystalline solid, mp: 132-34°C (CH_2Cl_2/MeOH), (lit. mp: 158-158.5°C from benzene/ethanol)[14]. ^{1}H NMR: 7.11-7.19 (m, 2H), 7.36-7.40 (m, 2H). ^{13}C NMR: 123.2 (s, 2C), 129.8 (s, 2C), 132.4 (s, 1C), 151.8 (s, 1C), 194.1 (s, 1C, C=S).

O-Cyclododecyl-S-methyl xanthate **3**: Cyclododecanol **1** (4.61 g, 25 mmol) was placed in a 100 ml round bottom flask and azeotropically dried (50 ml benzene was evaporated at reduced pressure). The flask was then fitted with a magnetic stirrer bar and a rubber septum and flushed with dry nitrogen. THF (50 ml) was added and the solution cooled to 0°C. Butyl lithium (25.5 mmol; 2.5 M/hexanes) was slowly introduced *via* syringe with constant stirring. Carbon disulfide (40 mmol) was added immediately thereafter in a similar manner. The ice bath was then removed and the orange solution allowed to slowly warm to room temperature. After standing 3 hr the solution was again cooled to 0°C and methyl iodide (30 mmol) added in one portion (mildly exothermic reaction). The nearly colorless solution was worked up in the usual manner: diluted with CH_2Cl_2 (150 ml), washed with water, 3% HCl solution and water again, saturated aqueous $NaHCO_3$ solution, water and brine. The organic layer was separated, dried over anhydrous magnesium sulfate and evaporated in vacuum. The crude product was again dissolved in a minimal amount of CH_2Cl_2 and filtered through silica gel washing with hexanes (approx. 150 ml) to remove traces of unreacted cyclododecanol. Crystallization (4x, CH_2Cl_2/MeOH) gave the pure product (77% after the first crystallization), (61%, mp 47.0-47.5°C). ^{1}H NMR: 1.35-1.45 (m, 18H, 2(H3-H11)), 1.59-1.93 (m, 4H, H2, H2', H12, H12'), 2.53 (s, 3H, SMe), 5.84 (tt, 1H, H1, $^3J_{H1\text{-}H2} = {}^3J_{H1\text{-}H12} = 9.0$ Hz; $^3J_{H1\text{-}H2'} = {}^3J_{H1\text{-}H12'} = 5.0$ Hz). ^{13}C NMR: 18.7 (s, 2C), 21.0 (s, 1C), 23.2 (s, 2C), 23.4 (s, 2C), 23.7 (s, 2C), 24.0 (s, 2C), 28.7 (s, 2C), 82.8 (s, 1C), 215.3 (s, 1C, C=S). IR: 2934, 2864, 1221, 1047 cm^{-1}. UV: $\lambda_{max} = 275$ nm; $\varepsilon = 8390$. Calcd for $C_{14}H_{26}OS_2$ C 61.26, H 9.55, S 23.36; found C 61.11, H 9.57, S 23.32%.

O-Cyclododecyl-O'-phenyl thionocarbonate **2a**: Cyclododecanol **1** (1.84 g, 10.0 mmol) was placed in a 50 ml round bottom flask and azeotropically dried (25 ml benzene was evaporated at reduced pressure). The flask was then fitted with a magnetic stir-bar and a rubber septum and flushed with dry nitrogen. Dry dichloromethane (20 ml) was then added followed by phenyl chlorothionoformate (1.8432 g, 10.0 mmol) and dry pyridine (0.9492 g, 0.97 ml, 12 mmol). Precipitation of pyridine hydrochloride was observed almost immediately. After 10 min the reaction mixture was worked up in the usual manner (see above). Recrystallization (3 times, CH_2Cl_2/MeOH)

gave the pure product (83% after the first crystallization), m.p. 60-61°C. ^{1}H NMR: 1.30-1.55 (m, 18H, 2(H3-H11)), 1.65-1.99 (m, 4H, H2, H2', H12, H12'), 5.51 (tt, 1H, H1, $^3J_{H1-H2} = {}^3J_{H1-H12} = 7.0$ Hz; $^3J_{H1-H2'} = {}^3J_{H1-H12'} = 4.9$ Hz), 7.06-7.13 (m, 2H, ArH), 7.21-7.31 (m, 1H, ArH), 7.35-7.45 (m, 2H, ArH). ^{13}C NMR: 21.0 (s, 1C), 23.2 (s, 2C), 23.4 (s, 2C), 23.7 (s, 2C), 24 (s, 2C), 28.6 (s, 2C), 84.0 (s, 1C) 112.1 (s, 2C), 126.4 (s, 1C), 129.4 (s, 2C), 153.4 (s, 1C), 194.6 (s, 1C). IR: 2938, 2863, 1489, 1256, 1199 cm^{-1}. UV: λmax = 210 nm; ε = 7000. Calcd for $C_{19}H_{28}O_2S$ C 71.21, H 8.81, S 10.00; found C 71.16, H 8.83, S 9.90%.

O-Cyclododecyl-O'-4-chlorophenyl thionocarbonate **2b**: Reaction analogous to the one above followed by recrystallization (CH_2Cl_2/MeOH) gave the desired product (81% after the first crystallization), m.p. 89.5-90.5°C. ^{1}H NMR: 1.29-1.55 (m, 18H, 2(H3-H11)), 1.65-1.99 (m, 4H, H2, H2', H12, H12'), 5.49 (tt, 1H, $^3J_{H1-H2} = {}^3J_{H1-H12} = 6.9$ Hz; $^3J_{H1-H2'} = {}^3J_{H1-H12'} = 5.0$ Hz), 7.04 (bd, 2H, ArH, $^3J \approx 8.7$ Hz), 7.36 (bd, 2H, ArH, $^3J \approx 8.7$ Hz). ^{13}C NMR: 21.4 (s, 1C), 23.7 (s, 2C), 23.9 (s, 2C), 24.2 (s, 2C), 24.5 (s, 2C), 29.1 (s, 2C), 84.8 (s, 1C), 124.0 (s, 2C), 130.0 (s, 2C), 132.3 (s, 1C), 152.2 (s, 1C), 194.7 (s, 1C, C=S). IR: 2936, 1484, 1277, 1195, 1086, 995 cm^{-1}. UV: λ_{max} = 228 nm; ε = 8000. Calcd. for $C_{19}H_{27}ClO_2S$ C 64.30, H 7.67, S 9.03; found C 64.93, H 7.71, S 8.98%.

O-Cyclododecyl-O'-4-fluorophenyl thionocarbonate **2c**: Reaction analogous to the one above followed by recrystallization (CH_2Cl_2/MeOH) gave the desired product (99.1% after the first crystallization), m.p. 49-50°C. ^{1}H NMR: 1.29-1.55 (m, 18H, 2(H3-H11)), 1.65-199 (m, 4H, H2, H2', H12, H12'), 5.49 (tt, 1H, $^3J_{H1-H2} = {}^3J_{H1-H12} = 7.0$ Hz; $^3J_{H1-H2'} = {}^3J_{H1-H12'} = 5.0$ Hz), 7.03 (s, 2H, H_{ortho}), 7.08 (d, 2H, H_{meta}, $^3J_{H-F} \approx 1$ Hz). ^{13}C NMR: 20.9 (s, 1C), 23.2 (s, 2C), 23.4 (s, 2C), 23.7 (s, 2C), 24.0 (s, 2C), 28.6 (s, 2C), 84.2 (s, 1C), 116.1 (d, 2C, $^2J_{C-F} = 23.8$ Hz), 123.5 (d, 2C, $^3J_{C-F} = 8.6$ Hz), 149.2 (d, 1C, $^4J_{C-F} = 2.9$ Hz), 160.5 (d, 1C, $^1J_{C-F} = 245.0$ Hz), 194.7 (s, 1C, C=S). IR: 2935, 2865, 2686, 1500, 1253, 1183 cm^{-1}. UV: λ_{max} = 210 nm; ε = 6700. Calcd. for $C_{19}H_{27}FO_2S$ C 67.42, H 8.04, S 9.47; found C 67.50, H 8.07, S 9.38%.

O-Cyclododecyl-O'(2.4.6-trichlorophenyl) thionocarbonate **2d**: Reaction analogous to the one above followed by recrystallization (CH_2Cl_2/MeOH) gave the desired product (87% after the first crystallization), m.p. 82.0-83.0°C. ^{1}H NMR: 1.29-1.60 (m, 18H, 2(H3-H11)), 1.65-2.02 (m, 4H, H2, H2', H12, H12'), 5.48 (tt, 1H, $^3J_{H1-H2} = {}^3J_{H1-H12} = 6.9$ Hz; $^3J_{H1-H2'} = {}^3J_{H1-H12'} = 5.0$ Hz), 7.38 (s, 2H, ArH). ^{13}C NMR: 21.4 (s, 1C), 23.7 (s, 2C), 23.9 (s, 2C), 24.2 (s, 2C), 24.4 (s, 2C), 29.1 (s, 2C), 85.9 (s, 1C), 129.2 (s, 2C), 130.4 (s, 2C), 132.7 (s, 1C), 145.4 (s, 1C), 191.2 (s, 1C, C=S). IR: 2936, 1484, 1277, 1195, 1086, 995 cm^{-1}. UV: λ_{max} = 233 nm; ε = 8500. Calcd. for $C_{19}H_{25}Cl_3O_2S$ C 53.85, H 5.95, S 7.56; found C 53.94, H 5.92, S 7.59%.

O-Cyclododecyl-O'(2.3.4.5.6-pentafluorophenyl) thionocarbonate **2e**: Reaction analogous to the one above followed by careful recrystallization (3 times, cold CH_2Cl_2/MeOH) gave the desired product. The crude yield is practically quantitative. The low melting point, however, makes crystallization complicated. First crop: 33%, m.p. 37.0-38.0°C. ^{1}H NMR: 1.33-1.55 (m, 18H, 2(H3-H11)), 1.61-2.09 (m, 4H, H2, H2', H12, H12'), 5.45 (tt, 1H, $^3J_{H1-H2} = {}^3J_{H1-H12} = 7.0$ Hz; $^3J_{H1-H2'} = {}^3J_{H1-H12'} = 5.0$ Hz). ^{13}C NMR: 20.8 (s, 1C),

23.2 (s, 2C), 23.4 (s, 2C), 23.7 (s, 2C), 24.0 (s, 2C), 28.5 (s, 2C), 86.7 (s, 1C), 127.3-128.2 (m, 1C), 135.0-135.9 (m, 1C), 136.9-137.8 (m, 0.5C), 138.4-139.1 (m, 1C), 140.0-140.9 (m, 1C), 141.9-142.5 (m, 0.5C), 142.6-144.1 (m, 1C), 191.5 (s, 1C, C=S). IR: 2940, 1520, 1200, 1255, 1142, 997 cm^{-1}. UV: λ_{max} = 231 nm; ε = 7600. Calcd. for $C_{19}H_{23}F_5O_2S$ C 55.67, H 5.67, S 7.71; found C 55.60, H 5.65, S 7.71%.

Acylation half-life determinations: Cholesterol **6** (crystallized four times from ethyl alcohol and dried in vacuum at 60°C for 24 hrs) (2.4166 g, 6.25 mmol), dibenzyl ether (internal reference compound, 238 µl) and dry pyridine (distilled from KOH, 506 µl) were dissolved in $CDCl_3$ in a 25 ml volumetric flask. From this solution 1.0 ml samples were transferred into flame dried NMR tubes, sealed with rubber septa. The tubes were then equilibrated in a water bath at 25°C. One equivalent of the corresponding acylating agent was added into each tube. The reactions were terminated (after 1, 2, 5, 15, 30 min., respectively) by rapid cooling in an acetone/dry ice bath, followed by the addition of 100 µl of concentrated aqueous HCl. The samples were stored at -25°C until the ^1H NMR measurements.

O-cholesteryl-O'-phenyl thionocarbonate **7a**: m.p. 157.2-158.8°C (methylene chloride/hexanes); Rf = 0.66 (hexanes:EtOAc = 7:1); ^1H NMR: (δ, $CDCl_3$) 0.6-2.8 (m, 43H), 5.1 (m, 1H, H3β), 5.51 (bd, 1H, H6, ^3J = 4.8 Hz), 7.05-7.15 (m, 2H, ArH), 7.20-7.35 (m, 1H, ArH), 7.35-7.50 (m, 2H, ArH). ^{13}C NMR: 11.85, 18.70, 19.28, 21.03, 22.55, 22.81, 23.79, 24.26, 27.02, 27.99, 28.20, 31.82, 31.89, 35.76, 36.15, 36.58, 36.78, 37.22, 39.49, 39.68, 42.28, 49.95, 56.08, 56.64, 84.26, 122.03 (2C), 123.38, 126.42, 129.43 (2C), 138.94, 153.29, 194.19; IR ($CHCl_3$): 2949, 1291, 1189, 1009 cm^{-1}; Calcd for $C_{34}H_{50}O_2S$ C 78.11, H 9.64, S 6.13, found C 78.05, H 9.67, S 6.20%.

O-cholesteryl-O'-(4-chlorophenyl) thionocarbonate **7b**: m.p. 183.2-184.4°C (methylene chloride/hexanes); Rf = 0.65 (hexanes:EtOAc = 7:1); ^1H NMR: (δ, $CDCl_3$) 0.6-2.8 (m, 43H), 5.09 (m, 1H, H3β), 5.44 (bd, 1H, H6, ^3J = 4.95 Hz), 7.0-7.1 (m, 2H, ArH), 7.3-7.4 (m, 2H, ArH); ^{13}C NMR (δ, $CDCl_3$): 11.84, 18.70, 19.27, 21.03, 22.55, 22.81, 23.79, 24.26, 26.99, 27.99, 28.20, 31.81, 31.89, 35.76, 36.15, 36.57, 36.75, 37.18, 39.49, 39.66, 42.27, 49.94, 56.08, 56.63, 84.57, 123.49 (3C), 129.55 (2C), 131.92, 138.82, 151.65, 193.78; IR ($CHCl_3$): 2951, 1294, 1187, 1007 cm^{-1}; Calcd for $C_{34}H_{49}ClO_2S$ C 73.28, H 8.86, S 5.75, found C 73.39, H 8.89, S 5.82%.

O-cholesteryl-O'-(4-fluorophenyl) thionocarbonate **7c**: m.p. 160.0-161.3°C (methylene chloride/hexanes); Rf = 0.60 (hexanes:EtOAc = 7:1); IR ($CHCl_3$): 2951, 1294, 1187, 1007 cm^{-1}; ^1H NMR: (δ, $CDCl_3$) 0.6-2.8 (m, 43H), 5.09 (m, 1H, H3β), 5.44 (bd, 1H, H6, ^3J = 5.1 Hz), 7.0-7.1 (m, 4H, ArH); ^{13}C NMR (δ, $CDCl_3$): 11.85, 18.71, 19.27, 21.03, 22.56, 22.82, 23.81, 24.26, 27.00, 27.99, 28.21, 31.81, 31.89, 35.76, 36.16, 36.57, 36.77, 37.19, 39.49, 39.67, 42.28, 49.94, 56.09, 56.64, 84.47,116.14 (d, 2C, $^2J_{C\text{-}F}$ = 23.8 Hz), 123.44, 123.53 (d, 2C, $^3J_{C\text{-}F}$ = 8.7 Hz), 138.86, 149.1 (d, 1C, $^1J_{C\text{-}F}$ = 2.9 Hz), 160.54 (d, 1C, $^1J_{C\text{-}F}$ = 245.3

Hz), 194.19 (d, 1C, $^{6}J_{C\text{-}F}$ = 1.4 Hz); Calcd for $C_{34}H_{49}FO_2S$ C 75.51, H 9.13, S 5.93, found C 75.40, H 9.11, S 5.99%.

O-cholesteryl-O'-(2,4,6-trichlorophenyl) thionocarbonate **7d**: m.p. 155.3-155.7°C (methylene chloride/ethanol); Rf = 0.68 (hexanes:EtOAc = 7:1); IR ($CHCl_3$): 2951, 1302, 1172, 1130, 1005 cm^{-1}; ^{1}H NMR: (δ, $CDCl_3$) 0.6-2.8 (m, 43H), 5.07 (m, 1H, H3β), 5.45 (bd, 1H, H6, ^{3}J = 5.0 Hz), 7.38 (s, 2H, ArH); ^{13}C NMR (δ, $CDCl_3$): 11.86, 18.71, 19.29, 21.04, 22.56, 22.82, 23.81, 24.27, 26.83, 28.00, 28.21, 31.81, 31.90, 35.77, 36.14, 36.58, 36.73, 36.96, 39.50, 39.67, 42.29, 49.93, 56.09, 56.64, 85.57, 123.59, 128.72 (2C), 129.92 (2C), 132.30, 138.72, 144.68, 190.27; Calcd for $C_{34}H_{47}Cl_3O_2S$ C 65.22, H 7.57, S 5.12, found C 65.13, H 7.56, S 5.17%.

O-cholesteryl-O'-(pentafluorophenyl) thionocarbonate **7e**: m.p. 150-151°C (methylene chloride/ethanol); Rf = 0.77 (hexanes:EtOAc = 7:1); IR ($CHCl_3$): 2951, 1519, 1304, 1146, 998 cm^{-1}; ^{1}H NMR: (δ, $CDCl_3$) 0.6-2.8 (m, 43H), 5.04 (m, 1H, H3β), 5.46 (bd, 1H, H6, ^{3}J = 5.2 Hz); ^{13}C NMR (δ, $CDCl_3$): 11.84, 18.70, 19.26, 21.07, 22.55, 22.81, 23.85, 24.28, 26.79, 28.02, 28.23, 31.83, 31.93, 35.81, 36.20, 36.59, 36.74, 36.93, 39.53, 39.70, 42.31, 49.97, 56.15, 56.68, 86.79, 123.80, 138.54, 190.80 (aromatic carbons not resolved due to C-F multiple splitting and long relaxation times); Calcd for $C_{34}H_{45}F_5O_2S$ C 66.64, H 7.40, S 5.23, found C 66.52, H 7.42, S 5.28%.

3β-(N,N-Diethylaminothiocarbonyloxy)cholest-5-ene **9b**: Synthesized by the reported method for similar compounds[11] from the known **9a**.[2] Recrystallization (twice) from acetone gave the pure title compound as fine white needles in a 79% yield. M.p. 158-160°C (aceton); ^{1}H NMR: (δ, $CDCl_3$) 0.6-2.6 (m, cholesterol + 2 Me of the NEt_2 moiety, 49H), 3.45 (q, 2H, NEt_2, J = 7.12 Hz), 3.82 (q, 2H, NEt_2, J = 7.22 Hz), 5.12-5.34 (m, 1H, H3β), 5.35-5.48 (m, 1H, H6); Calcd for $C_{32}H_{55}NOS$ C 76.59, H 11.05, N 2.79, S 6.39, found C 76.67, H 11.06, N 2.70, S 6.48%.

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