Pergamon

Tetrahedron, Vol. 52, No. 8, pp. 2705-2716, 1996

0040-4020/96 $15.00 + 0.00

0040-4020(95)01019-X

The Invention of Radical Reactions. Part XXXV.[1] A Novel Radical Fission Reaction of *N*-Sulfonylthioxocarbamates.

Derek H. R. Barton,* Giovanni Fontana and **Yun Yang**

Department of Chemistry, Texas A&M University, College Station, Texas 77843-3255, U.S.A.

Abstract: A novel radical fission reaction of *N*-sulfonylthioxocarbamates, obtained from the reactionof alcohols with methanesulfonyl- and toluenesulfonyl isothiocyanates, to give the corresponding *O*-alkylthioxocarbamates, is described.

INTRODUCTION

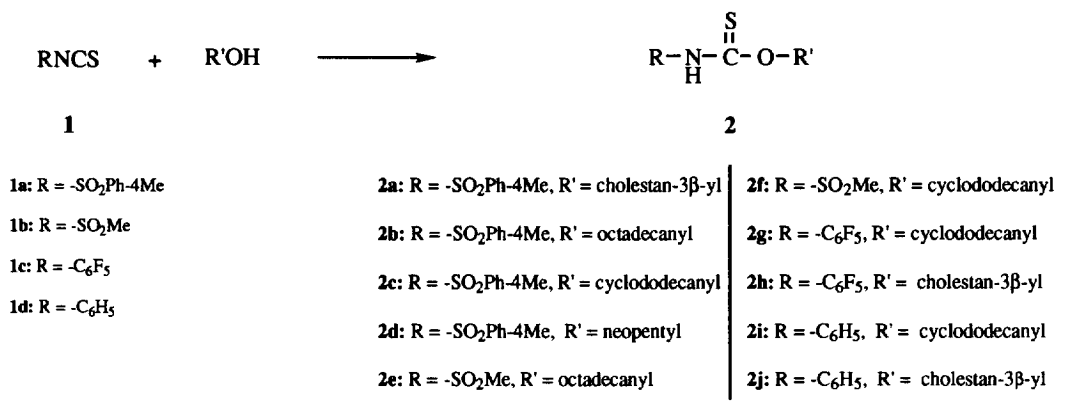
The deoxygenation of alcohols, especially secondary alcohols, has became an important reaction in synthetic chemistry.[2] In many complex molecules the radical induced process, originally introduced by Barton and McCombie,[3] is a milder and more efficient reaction than ionic type counterparts. The original work[3] used xanthates, thiocarbonylimidazolides and thionobenzoates, all with equal success. Recently, other derivatizing reagents have been developed in which substituted phenyl chlorothioxocarbonates[4-6] are used with high efficiency in the deoxygenation of alcohols.

A new type of alcohol deoxygenation has recently been reported[7] in which treatment of an alcohol with ethyl, phenyl or trimethylsilylmethyl isothiocyanates gave the corresponding thioxocarbamates. Reduction with triethylsilane in sealed tubes afforded the deoxygenated products. However, bis(tributyltin)oxide was used to activate alcohols for the addition reaction. It has also been reported that *N*-acylthioxocarbamates, prepared from alcohols and acyl isothiocyanates, can be deoxygenated under radical conditions.[8] Better results were obtained by reacting alcohols with phenyl isothiocyanate in the presence of NaH to give N-phenylthioxocarbamates. Reduction with various silanes and Bu_3SnH under radical conditions gave deoxygenated products.[9]

RESULTS

We investigated other isothiocyanate derivatives, the formation of which did not require activation and proceeded under neutral conditions. In this paper, we describe the addition reaction between alcohols and methanesulfonyl- and toluenesulfonyl isothiocyanates (**1a**,**1b**),[10-13] pentafluorophenyl isothiocyanate (**1c**)[14] and phenyl isothiocyanate (**1d**) to give the corresponding thioxocarbamates (**2a-2j**). Previously alcohols have

been reported to react very slowly with isothiocyanates at room temperature.[15] However, benzenesulfonyl isothiocyanate[16] reacts with ethanol and 2-propanol to give ethyl-*N*- and isopropyl-*N*-benzenesulfonylthioxocarbamates, respectively. Also pentafluorophenyl isothiocyanate reacts readily to give **2g** and **2h**.



Scheme 1

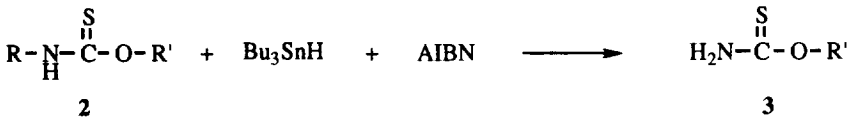
Table 1. Preparation of thioxocarbamates **2**

Run	RNCS	Alcohol	Solvent	Temp/ °C	Time(h)	2 (%)[a]
1	**1a**	Cholestan-3β-ol	C_6H_6	80	8	**2a** (98)
2	**1a**	1-Octadodecanol	C_6H_6	r.t.	12	**2b** (90)
3	**1a**	1-Octadodecanol	C_6H_6	80	4	**2b** (98)
4	**1a**	Cyclododecanol	C_6H_6	80	8	**2c** (98)
5	**1a**	Neopentanol	C_6H_6	r.t.	12	**2d** (90)
6	**1a**	Neopentanol	C_6H_6	80	4	**2d** (98)
7	**1b**	1-Octadodecanol	CH_2Cl_2	r.t.	4	**2e** (80)
8	**1b**	Cyclododecanol	C_6H_6	80	12	**2f** (90)
9	**1c**	Cyclododecanol	C_5H_5N	r.t.	24	**2g** (70)
10	**1c**	Cholestan-3β-ol	C_5H_5N	r.t.	24	**2h** (81)
11	**1d**	Cyclododecanol	THF	r.t.	24	**2i** (90)
12	**1d**	Cholestan-3β-ol	THF	r.t.	24	**2j** (75)

a) Isolated Yield

Interesting results were also obtained when the sulfonyl isothiocyanates (**1a**, **1b**) were added to a solution of alcohol in dry benzene and refluxed overnight to give the corresponding thioxocarbamates (**2a** - **2f**) in very high yields (**Scheme 1, Table 1**). It is important to point out that these sulfonyl isothiocyanates react with primary alcohols at room temperature to give the corresponding thioxocarbamates (**2b**, **2d**, **2e**) in high yields.

Surprising results were obtained from the reduction of these products (**2a** - **2f**) with Bu_3SnH (1.1 eq) at 80 °C by adding catalytic amounts (0.2-0.4 eq) of AIBN. There were formed the unexpected *O*-alkylthioxocarbamates (thiourethanes) in excellent yields (**3a** - **3d**) with no deoxygenated products (**Scheme 2, Table 2**). The reduction of compounds (**2g** - **2j**) was not studied in depth. Analogous work has already been reported.[7]



2 **3**

3a: R' = Cholestan-3β-yl | **3c**: R' = Cyclododecanyl
3b: R' = Octadecanyl | **3d**: R' = Neopentyl

Scheme 2

Table 2. Reduction of thioxocarbamates **2**[a]

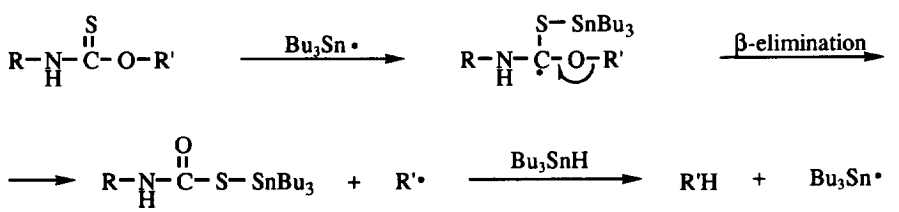
Run	RNH-CS-OR'	Bu_3SnH/AIBN	Time(h)	Product	Yield (%)[b]
1	**2a**	1.1 / 0.2	3	**3a**	98
2	**2b**	1.1 / 0.3	3	**3b**	95
3	**2c**	1.1 / 0.3	3	**3c**	98
4	**2d**	1.1 / 0.2	3	**3d**	90
5	**2e**	1.1 / 0.4	3	**3b** / alcohol	23 / 67
6	**2f**	1.1 / 0.4	1	**3c**	90

a) general conditions : refluxing in benzene.

b) isolated yield.

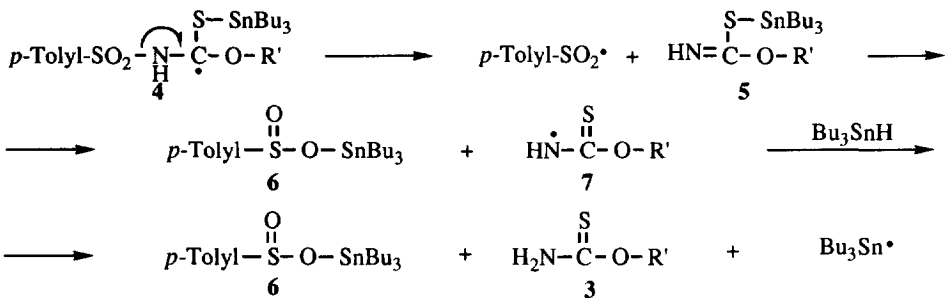
DISCUSSION AND MECHANISM

The formation of the thioxocarbamates **3a-3d** was unexpected. The normal course[2] of the reaction (**Scheme 3**) would be deoxygenation, or recovery of the starting material.



Scheme 3

In the case of the *N*-sulfonylthioxocarbamates (**2a-2f**) no deoxygenated products were observed. Instead the alkyl thioxocarbamates (**3a-3d**) were formed in excellent yields. Clearly, an S-N bond rather than C-O bond fission had taken place with consequent absence of the expected deoxygenation. The regioselectivity of fragmentation of the initial adduct radical **4** (**Scheme 4**) depends on the bond dissociation energies of the bond to be cleaved and that of the double bond to be formed and on the relative stability of the forming radical.



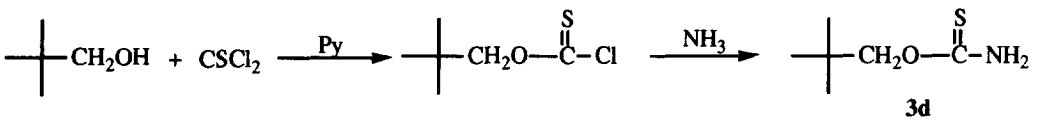
Scheme 4

We supposed that the formation of stable sulfonyl radicals could direct the fragmentation to the "opposite side". The sulfonyl radical, particularly the *p*-tolylsulfonyl radical, is stabilized compared to an alkyl radical so the difference with respect to the normal pathway can be understood. The mesyl radical is less stabilised than the *p*-tolylsulfonyl analogue. The more hindered secondary derivative fragments better (**Entry 6, Table 2**) than the primary analogue (**Entry 5, Table 2**). From the latter the alcohol is recovered, presumably by hydrolysis during the workup procedure. Another example of this abnormal behaviour has been reported.[23b]

According to **Scheme 4** the initial radical **4** fragments into the sulfonyl radical and intermediate **5**. It is the further reaction of the sulfonyl radical with **5** that affords the tributyltin sulfinate **6** and the nitrogen radical **7**. The latter reacts with the tin hydride to give the product **3** and reforms the tributyltin radical.

The course of the reaction with **2d** was studied by low temperature NMR experiments[17] using Et_3B/O_2 as initiator in toluene- D_8. After addition of O_2 at -20 °C, immediately the ^{119}Sn-NMR showed only one peak at -17 ppm (NMR spectrometer referenced to external Me_4Sn; δ= 0.00 ppm)[18] and the complete disappearance of the Bu_3SnH signal. Warming the reaction mixture first to 0 °C and then to 20 °C did not show any changes (although at 20 °C the peak became broad). ^{1}H and ^{13}C NMR analyses also showed that the reaction was complete. Similar results were obtained when compound **2d** was treated with Bu_3SnH/AIBN in C_6D_6 at 80 °C. This suggests that the reaction is very fast and forms only one compound containing a Sn-residue without the formation of an intermediate. The tin containing product was identified as the sulfinate **6** by comparison with an authentic sample synthesized according to the literature.[19] Thus the reaction of tributyltin chloride with sodium p-tolylsulfinate gave **6** (98%). The infra-red spectrum of this compound, compared with the data reported in literature[19] for triphenyltin *p*-toluenesulfinate showed the presence of the sulfinate group and not the sulfonyl group.

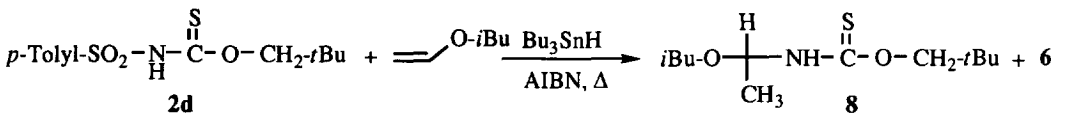
The *O*-neopentylthioxocarbamate (**3d**) was also compared with an authentic sample synthesized according to **Scheme 5.** According to the literature, *O*-alkylthiocarbamates can also be synthesized in low to moderate yields from alkylcyanates with hydrogen sulfide[20] or from (alkoxythiocarbonylthio)acetic acid and ammonia.[21]



Scheme 5

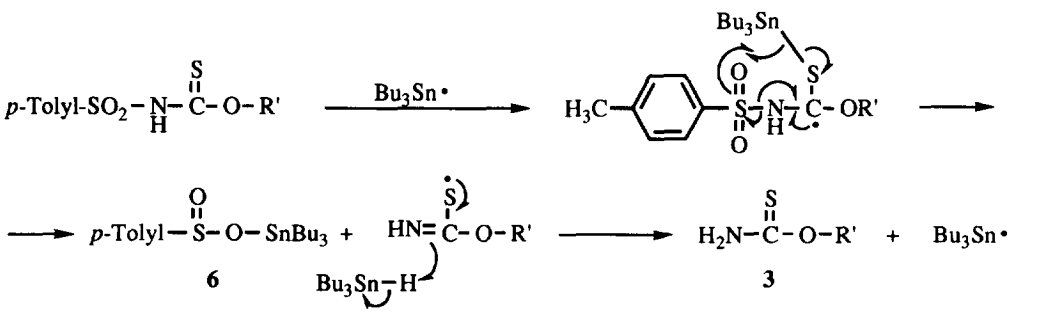
In order to confirm the proposed mechanism of this reaction we tried to trap the *p*-tolylsulfonyl radical, which is formed in the reaction, with ethyl vinyl ether and isobutyl vinyl ether. It is known that this radical can be trapped in the presence of such vinyl ethers.[22]

No trapping products were observed between *p*-tolylsulfonyl radical and vinyl ethers, but the *O*-alkylthioxocarbamate reacted to give the adduct **8** (79%) as well as **6** (**Scheme 6**). The identity of the adduct **8** was confirmed by ^1H, ^{13}C and APT NMR experiments. Moreover, after acid hydrolysis (CF_3COOH) of **8**, ^1H and ^{13}C NMR analyses showed the presence of *i*-butanol, CH_3CHO and compound **3d**.



Scheme 6

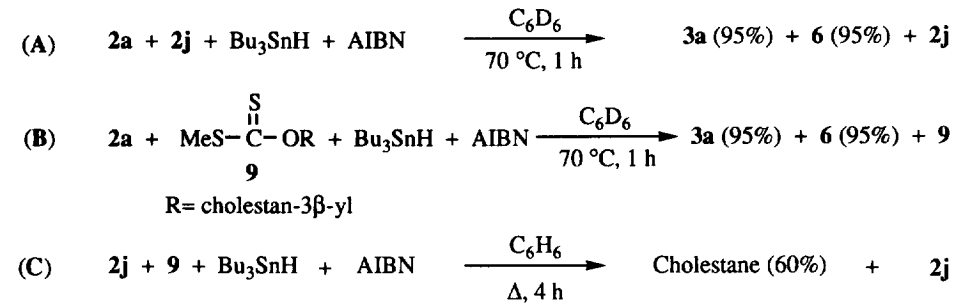
The radical mechanism of the reaction was further confirmed by some blank experiments. They showed that the reaction requires the presence of Bu_3SnH. However, it can also occur in the absence of AIBN at a much slower rate than in its presence. From these findings the reaction pathway was postulated to be concerted with a six membered ring intermediate as shown in **Scheme 7**.



Scheme 7

In order to investigate the scope and the limitations of this reaction, we performed several competition experiments between the cholestan-3β-yl derivative **2a** and the analogous methyl xanthate[2,23] and *N*-phenylthioxocarbamate[9] derivatives.

When the equimolar mixture of **2a** and **2j** was treated with one equivalent of Bu_3SnH under radical conditions at 70 °C , a rapid reaction took place and only compound **2a** reacted. No cholestane was produced and *O*-cholestanylthioxocarbamate (**3a**) and tributyltin sulfinate **6** were produced in very high yield (95%) (**Scheme 8, Reaction A**).



Scheme 8

The same result was obtained when an equimolar mixture of **2a** and xanthate **9** was treated with one equivalent of Bu_3SnH under the same reaction conditions. No cholestane was observed and only compound **2a** reacted to give **3a** (95%) and **6** (95%) (**Scheme 8, Reaction B**). Finally, the competition experiment between xanthate **9** and **2j** showed that under refluxing conditions only the xanthate **9** reacted to give the cholestane (60%) while **2j** did no react at all (**Scheme 8, Reaction C**).

This series of competitive experiments indicated that the reactivity of these compounds with Bu_3SnH/AIBN is in the order: **2a** >> **9** >>**2j**. It is also interesting to note that at the temperature of 70 °C only compound **2a** reacted very quickly whereas methyl xanthate **9** has to be refluxed in benzene for several hours.

CONCLUSION

We have shown that the methanesulfonyl- and toluenesulfonyl isothiocyanates react readily with alcohols providing the corresponding thioxocarbamates **2a-2f** in high yields. These adducts react very quickly with Bu_3SnH under radical conditions to afford the corresponding *O*-alkylthioxocarbamates **3** and tributyltin sulfinate derivatives in excellent yields.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 881 spectrophotometer. ^1H and ^{13}C NMR spectra were determined for solutions in deuterochloroform (unless specified otherwise) with TMS as internal reference on Varian Gemini 200, Varian XL 200E or Varian XL 200 spectrometers. ^{119}Sn NMR spectra were obtained on a Varian XL 200 with Me_4Sn as external reference.[18] Microanalyses were performed by Atlantic Microlab, Inc., Norcross, Georgia. Thin-layer chromatography (TLC) was performed on aluminium sheets precoated with silica gel (Merck, Kieselgel 60 F-254). Column chromatography was performed on silica gel (Merck, Kieselgel 60 230-400 mesh). Solvents were used either as purchased or dried and purified by standard methodology under argon.

Other reference compounds and starting materials were purchased from Aldrich Chemical Co., Inc., Milwaukee, WI.

Toluenesulfonyl isothiocyanate (1a). A mixture of *p*-toluenesulfonamide (17.1 g, 0.1 mol) and potassium hydroxide (11.8 g, 0.21 mol) in carbon disulfide (200 mL; distilled over P_2O_5) was refluxed for 6h under argon. Evaporation *in vacuo* of the excess CS_2 afforded a pale orange solid. Water was removed azeotropically by adding benzene (200 mL) and distilling. To this mixture was added dropwise a solution of phosgene (14.85 g, 0.15 mol) in dry benzene (40 mL) during 1h while stirring at 0 °C under a nitrogen atmosphere. The resulting mixture was then allowed to warm to room temperature and stirred overnight. Filtration of the mixture followed by evaporation of the solvent gave a residue which was purified by vacuum distillation to afford the title compound **1a** (11.2 g, 52%) as a pale yellow oil : b.p. 85 °C/0.05 mmHg, (lit.[11] b.p. 109 °C/0.4mmHg); IR (neat): 1881, 1356, 1166 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.85 (2H, d, J = 8.3 Hz), 7.40 (2H, d, J = 8.3 Hz), 2.28 (3H, s); ^{13}C-NMR ($CDCl_3$, δ, ppm): 155.9 (NCS), 146.2, 136.3, 130.0, 127.2, 21.7.

Cholestan-3β-yl *N*-toluenesulfonyl thioxocarbamate (2a). To a stirred solution of cholestan-3β-ol (1 g, 2.57 mmol) in dry benzene (100 mL) at room temperature was added dropwise a solution of toluenesulfonyl isothiocyanate **1a** (0.60 g, 2.83 mmol) in dry benzene (10 mL) and the resulting mixture was stirred and heated at reflux overnight. Evaporation of the solvent and recrystallization from dichloromethane/hexanes gave the thioxocarbamate **2a** (1.52 g, 98%) as white crystals : m.p. 190-191 °C; IR (KBr): 3170, 2923, 1580, 1429, 1320, 1276 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.55 (1H, s, NH), 7.85 (2H, d, J = 7.5 Hz), 7.33 (2H, d, J = 7.5 Hz), 5.05 (1H, m), 2.45 (3H, s), 2.0-0.6 (47H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 186.0, 145.2, 135.5, 129.5, 128.6, 83.6, 56.3, 56.2, 54.0, 44.3, aliphatics; Anal. Calcd for $C_{35}H_{55}NO_3S_2$: C, 69.83; H, 9.20; N, 2.33; S, 10.65. Found: C, 69.83; H, 9.29; N, 2.31; S, 10.73 %.

***n*-Octadodecyl *N*-toluenesulfonyl thioxocarbamate (2b).** To a solution of 1-octadecanol (0.5 g, 1.85 mmol) in dry benzene (80 mL) was added a solution of isothiocyanate **1a** (0.41 g, 1.94 mmol) in dry benzene (10 mL) at room temperature . The reaction mixture was stirred for 12h at room temperature under an inert atmosphere. After removal of the solvent, the crude product was purified by recrystallization from dichloromethane/hexanes to give the thioxocarbamate **2b** (0.81 g; 90%) as a white solid. The reaction was also carried out at reflux temperature to afford, after recrystallization, the product **2b** in excellent yield (0.88 g; 98%): m.p. 80-81 °C; IR (KBr): 3236, 2906, 2837, 1582, 1418, 1343, 1194, 1139 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.82 (1H, s, NH), 7.86 (2H, d, J = 8.3 Hz), 7.34 (2H, d, J = 8.3 Hz), 4.36 (2H, t, J = 7.5 Hz), 2.45 (3H, s), 1.6 (2H, m), 1.26 (30H, m), 0.88 (3H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 187.1, 145.3, 135.4, 129.6, 128.5, 73.8, 31.9, 29.5; Anal. Calcd for $C_{26}H_{45}NO_3S_2$: C, 64.54; H, 9.37; N, 2.89; S, 13.25. Found: C, 64.64; H, 9.41; N, 2.94; S, 13.30 %.

Cyclododecyl *N*-toluenesulfonyl thioxocarbamate (2c). To a stirred solution of cyclododecanol (0.5 g, 2.71 mmol) in dry benzene (80 mL) was added a solution of isothiocyanate **1a** (0.64 g, 2.98 mmol) in dry benzene (10 mL). The reaction mixture was stirred and refluxed for 8h under argon. After solvent evaporation, the product was purified by recrystallization from dichloromethane/hexanes to give the thioxocarbamate **2c** (1.06 g; 98%) as a white solid: m.p. 126-128 °C; IR (KBr): 3053, 2929, 2854, 1580, 1439, 1345, 1281, 1197 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.76 (1H, s, NH), 7.85 (2H, d, J = 8.3 Hz), 7.33 (2H, d, J = 8.3 Hz), 5.4 (1H, m), 2.45 (3H, s), 1.75-1.0 (23H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 186.5, 145.1, 135.6, 129.5, 128.4, 83.4, 28.3, 23.8, 23.6, 23.3, 23.1, 21.7, 20.5; Anal. Calcd for $C_{20}H_{31}NO_3S_2$: C, 60.41; H, 7.85; N, 3.52; S, 16.13. Found: C, 60.38; H, 7.92; N, 3.65; S, 16.26 %.

Neopentyl *N*-toluenesulfonyl thioxocarbamate (2d). To a stirred solution of neopentyl alcohol (1 g, 11.34 mmol) in dry benzene (20 mL) was added a solution of isothiocyanate **1a** (2.66 g, 12.34 mmol) in dry benzene (20 mL) under an inert atmosphere. The reaction mixture was stirred for 12 h at room temperature. Evaporation of the solvent and recrystallization from dichloromethane/hexanes gave the thioxocarbamate **2d** (3.08 g; 90%) as a white solid.When the reaction was carried out under reflux conditions, a very high yield was obtained (3.35 g; 98%): m.p. 115-118 °C; IR (KBr): 3252, 3078, 2965, 2883, 1592, 1455, 1362, 1148 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.80 (1H, s, NH), 7.87 (2H, d, J = 8.5 Hz), 7.34 (2H, d, J = 8.5 Hz), 4.07 (2H, s), 2.44 (3H, s), 0.88 (9H, s); ^{13}C-NMR ($CDCl_3$, δ, ppm): 187.4, 145.2, 135.5, 129.7, 128.0, 83.1, 31.6, 26.2; Anal. Calcd for $C_{13}H_{19}NO_3S_2$: C, 51.80; H, 6.35; N, 4.64; S, 21.28. Found: C, 51.77; H, 6.40; N, 4.64; S, 21.21 %.

Methanesulfonyl isothiocyanate (1b). A mixture of methylsulphonamide (8.1 g, 0.085 mol) and potassium hydroxide (9.64 g, 0.17 mol) in carbon disulfide (100 mL) was refluxed for 6 h under argon atmosphere. Carbon disulfide was distilled off. The residue was an orange-colored half-solid. Water was removed by adding benzene (150 mL) and azeotropic distillation until ca. 100 mL of benzene was distilled off. To this mixture was added a solution of phosgene (13.6 g, 0.14 mol) in dry benzene (40 mL) during 1 h. The resulting mixture was left to stand at room temperature for 5h during which time the sticky half-solid at the bottom was stirred with a spatula. There was a gradual heat and gas evolution and the orange half-solid turned into a white powder at the end of the reacion. It was filtered under argon and the filtrate concentrated. Vacuum distillation gave the pure product (3.2 g; 27%) as a yellow oil : b.p. 104-105 °C/17mmHg, (lit.[11] b.p. 104 °C/18mmHg).

***n*-Octadodecyl *N*-methanesulfonyl thioxocarbamate (2e).** To a solution of methanesulfonyl isothiocyanate **1b** (0.25 g, 1.05 mmol) in dry dichloromethane (5 mL) was added 1-octadecanol (0.48 g, 1.05 mmol) and the resulting mixture was stirred at room temperature for 4 h. Evaporation of the solvent and recrystallization from dichloromethane/hexanes gave the thioxocarbamate **2d** (0.58 g; 80%) as colorless crystals: m.p. 82-84 °C; IR (KBr): 3273, 2910, 2846, 1439, 1344, 1198, 1157, 965, 840 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.78 (1H, s, NH), 4.52 (2H, br.s.), 3.35 (3H, s), 1.79 (2H, q, J = 6.8 Hz), 1.25 (28H, br.s) 0.88 (3H, t, J = 6.8 Hz); ^{13}C-NMR ($CDCl_3$, δ, ppm): 187.3, 73.6, 41.7, 31.9, 29.7, 29.5, 29.4, 29.3, 29.1, 28.1, 22.7, 14.0; Anal. Calcd for $C_{20}H_{41}NO_3S_2$: C, 58.92; H, 10.14. Found: C, 58.99; H, 10.12 %.

Cyclododecyl *N*-methanesulfonyl thioxocarbamate (2f). Cyclododecanol (0.94 g, 5.1 mmol) was added to a solution of methanesulfonyl isothiocyanate **1b** (0.74 g, 5.35 mmol) in dry benzene (10 mL). The reaction mixture was refluxed for 12 h under an inert atmosphere. Evaporation of the solvent and recrystallization from dichloromethane/hexanes gave the thioxocarbamate **2f** (1.4 g; 90%) as colorless crystals: m.p. 120-121 °C; IR (KBr): 3253, 2917, 2878, 1418, 1344, 1275, 1198, 1125, 955, 844 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.61 (1H, s), 5.58 (1H, m), 3.32 (3H, s), 1.95-1.60 (4H, m), 1.50-1.29 (18H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 186.8, 83.5, 42.0, 28.5, 24.1, 23.9, 23.3, 23.1, 20.8; Anal. Calcd for $C_{14}H_{27}NO_3S_2$: C, 52.30; H, 8.46. Found: C, 52.06; H, 8.43 %.

Pentafluorophenyl isothiocyanate (1c). Thiophosgene (30 g, 0.3 mol) in chlorobenzene (30 mL) was added dropwise to a solution of pentafluoroaniline (20.5 g, 0.112 mol) in chlorobenzene (100 mL) and DMF (2 mL) over 40 min. A red solution was formed along with slight heat and voluminous gas evolution. It was heated at 90 °C for 1 h, then at 80 °C for 3 h. The mixture was cooled and filtered via a canulla under argon. Hydrogen chloride and excess thiophosgene were evaporated off. The remaining solution was fractionally distilled using a Vigreux column to give product **1c** (20.7 g; 82%) as a colorless liquid: b.p. 68 °C/4.5 mmHg, (lit.[14] b.p. 71 °C/10 mmHg).

Cyclododecyl *N*-pentafluorophenyl thioxocarbamate (2g). To a solution of cyclododecanol (1.66 g, 9.0 mmol) in pyridine (40 mL) was added pentafluorophenyl isothiocyanate **1c** (2.2 g, 9.8 mmol). The color of the solution instantly turned orange and darkened as the reaction proceeded. After stirring at room temperature for 24 h, the solution was evaporated *in vacuo*. The residue was chromatographed on silica gel (eluent: ethyl acetate/hexanes 1/9) and further purified by recrystallization from dichloromethane/hexanes to give the thioxocarbamate **2g** (3.0 g; 81%) as colorless crystals: m.p. 111-113 °C; IR (KBr): 3103, 2843, 1482, 1183, 1125, 989 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.20 (1H, br. s), 5.58 (1H, m), 1.85-1.15 (22H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 189.5, 145.7, 143.3, 140.2, 138.2, 135.3, 112.2, 82.5, 28.6, 24.0, 23.7, 23.3, 23.1, 20.7; Anal. Calcd for $C_{19}F_5H_{24}NOS$: C, 55.73; H, 5.91. Found: C, 55.83; H, 5.94.

Cholestan-3β-yl *N*-pentafluorophenyl thioxocarbamate (2h). A solution of cholestanol (0.5 g, 1.29 mmol) and pentafluorophenyl isothiocyanate **1c** (0.32 g, 1.4 mmol) in pyridine (20 mL) was stirred at room temperature for 24 h. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel (eluent: ethyl acetate/hexanes 1/9) and further purified by recrystallization from dichloromethane/hexanes to give the thioxocarbamate **2h** (0.57 g; 72%) as colorless crystals: m.p. 178-180 °C; IR (KBr): 3138, 2936, 1493, 1334, 1209, 1143, 982 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.68 (1H, br. s), 5.26 (1H, m), 2.10-0.50 (47H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 189.2, 145.6, 143.2, 140.4, 138.2, 135.3, 112.2, 83.1, 56.3, 56.2, 54.1, 44.5, 42.5, 39.9, aliphatics; Anal. Calcd for $C_{34}F_5H_{48}NOS$: C, 66.53; H, 7.88. Found: C, 66.61; H, 7.88.

Cyclododecyl *N*-phenylthioxocarbamate (2i). To a solution of cyclododecanol (1 g, 5.42 mmol) and phenylisothiocyanate **1d** (0.81 g, 5.96 mmol) in dry THF (10 mL) was added NaH (60% dispersion in oil, 0.238 g, 5.96 mmol) and the resulting mixture was stirred at room temperature for 24 h under an inert atmosphere. After removing the solvent, the crude product was partitioned between CH_2Cl_2 (50 mL) and H_2O (50 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent evaporated. The product was purified by flash chromatography on silica gel (eluent: ethyl acetate/hexanes 1/9) to afford the title compound **2i** (1.59 g, 92%) as a colorless solid. An analytical sample was obtained by recrystallization from dichloromethane/hexanes as colorless plates : m.p. 121-123 °C, (lit.[9] m.p. 115-116 °C).

Cholestan-3β-yl *N*-phenylthioxocarbamate (2j). To a solution of cholestan-3β-ol (3.89 g, 10 mmol) in dry THF (20 mL) was added phenyl isothiocyanate **1d** (1.49 g, 11 mmol) followed by the addition of NaH (60% dispersion in oil, 0.44 g, 11 mmol). The reaction was stirred at room temperature for 24 h under an argon atmosphere. After removing the solvent, the residue was dissolved in CH_2Cl_2 (80 mL) and the organic layer was washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure.The residue was purified by flash chromatography on silica gel (eluent: ethyl acetate/hexanes 1/9) to afford the title compound **2j** (3.93 g; 75%) as a colorless solid. An analytical sample was obtained by recrystallization from dichloromethane/hexanes to give colorless plates: m.p. 180-181 °C; IR (KBr): 3310, 2927, 1590, 1442, 1317, 1170, 1006 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 8.52 (1H, br, NH), 7.35-7.13 (5H, m), 5.35 (1H, m), 2.0-0.6 (47H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 187.8, 137.6, 129.0, 125.2, 121.9, 56.4, 56.2, 54.2, 44.5, 42.6, 39.9, 39.5, aliphatics; Anal. Calcd for $C_{34}H_{53}NOS$: C, 77.96; H, 10.19; N, 2.67; S, 6.12. Found: C, 77.69; H, 10.25; N, 2.65; S, 5.97 %.

General Procedure for Reduction with Bu_3SnH / AIBN.

A typical procedure is described for the reduction of Cholestan-3β-yl *N*-toluenesulfonyl thioxocarbamate (**2a**)

***O*-Cholestanylthioxocarbamate (3a).** To a solution of thioxocarbamate **2a** (0.24 g, 0.4 mmol) in dry benzene (20 mL) was added Bu_3SnH (0.128 g, 0.44 mmol) under argon. The solution was heated to reflux

and treated at 30-min. intervals with 150-μL portions of a solution of 150 mg of AIBN in 3 mL of dry benzene during reflux. The reaction was monitored by TLC. When the reaction was complete, the solvent was removed under vacuum and the product was isolated by flash chromatography on silica gel (eluent: ethyl acetate/hexanes 2/8) to afford cholestan-3β-ylthioxocarbamate **3a** (0.176 g; 98%) as a colorless solid. An analytical sample was obtained by recrystallization from dichloromethane/hexanes to give colorless plates: m.p. 216-217 °C; IR (KBr): 3407, 3257, 3158, 2904, 1586, 1432, 1391, 1079 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.5 (1H, br.s), 6.0 (1H, br.s), 5.2 (1H, m), 2.05-0.6 (47H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 191.9, 81.4, 56.4, 56.2, 54.2, 44.5, 42.6, 40.0, aliphatics; Anal. Calcd for $C_{28}H_{49}NOS$: C, 75.10; H, 11.02; N, 3.13; S, 7.16. Found: C, 74.96; H, 11.08; N, 3.07; S, 7.25 %.

Other O-Alkylthioxocarbamates **3b, 3c, 3d** were prepared from the corresponding *N*-toluenesulfonyl thioxocarbamates **2b, 2c, 2d** with Bu_3SnH / AIBN under the same conditions. In every case the ^{1}H and ^{13}C analyses of the crude mixture showed the presence of tributyltin p-toluenesulfinate **6** in a ratio 1:1 with respect to the *O*-alkylthioxocarbamate. The yields are listed in **Table 2** and physical and spectral data are as follows:

***O*-Octadecanylthioxocarbamate (3b).** Purification by column chromatography on silica gel (eluent: ethyl acetate/hexanes 2/8) gave compound **3b** (95%). An analytical sample was obtained by recrystallization from dichloromethane/hexanes to give colorless needles: m.p. 90-91 °C; IR (KBr): 3381, 3252, 3164, 2904, 1606, 1418, 1278 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.45 (1H, br.s), 6.0 (1H, br.s), 4.4 (2H, t, J = 6.7 Hz), 1.25 (32H, s), 0.9 (3H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 192.0, 72.1, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3,, 28.5, 25.8, 22.7, 14.1.; Anal. Calcd for $C_{19}H_{39}NOS$: C, 69.24; H, 11.92; N, 4.25; S, 9.73. Found: C, 69.09; H, 11.89; N, 4.22; S, 9.79 %.

***O*-Clododecanylthioxocarbamate (3c).** Purification by column chromatography on silica gel (eluent: ethyl acetate/hexanes 2/8) gave compound **3c** (98%). An analytical sample was obtained by recrystallization from dichloromethane/hexanes to give colorless needles: m.p. 121-122 °C; IR (KBr): 3349, 3254, 3161, 2923, 1603, 1421, 1299, 1083 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.80 (1H, br.s), 6.10 (1H, br.s), 5.48 (1H, m), 1.9-1.2 (22H, m); ^{13}C-NMR ($CDCl_3$, δ, ppm): 192.2, 80.4, 28.9, 23.8, 23.5, 23.4,, 23.1, 20.9.; Anal. Calcd for $C_{13}H_{25}NOS$: C, 64.15; H, 10.35; N, 5.75; S, 13.17. Found: C, 64.06; H, 10.31; N, 5.81; S, 13.15 %.

***O*-Neopentylthioxocarbamate (3d).** Purification by column chromatography on silica gel (eluent: ethyl acetate/hexane 2/8) gave compound **3d** (90%). An analytical sample was obtained by recrystallization from dichloromethane/hexanes to give colorless needles: m.p. 89-90 °C; IR (KBr): 3410, 3267, 3165, 2954, 2866, 1596, 1417, 1361, 1299, 1082 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.74 (1H, br.s), 6.15 (1H, br.s), 4.10 (2H, s), 0.97 (9H, s); ^{13}C-NMR ($CDCl_3$, δ, ppm): 192.9, 81.2, 31.5, 26.3; Anal. Calcd for $C_6H_{13}NOS$: C, 48.95; H, 8.89; N, 9.51; S, 21.78. Found: C, 49.01, ; H, 8.92, ; N, 9.42; S, 21.70 %.

Reduction of *n*-Octadodecyl *N*-methanesulfonyl thioxocarbamate (2e). A solution of compound **2e** (0.102 g, 0.25 mmol) and Bu3SnH (0.08 mL, 0.297 mmol) in dry benzene (5 mL) was refluxed for 3 h during which time a solution of AIBN (16 mg, 0.1 mmol) in benzene (1 mL) was added in four portions every half hour. Evaporation of the solvent followed by flash chromatography on silica gel (eluent: ethyl acetate / hexanes 1/9) gave *O*-octadecanylthiocarbamate **3b** (19 mg; 23 %) and *n*-octadodecanol (45 mg, 67%).

Reduction of Clododecyl *N*-methanesulfonyl thioxocarbamate (2f). A solution of compound **2f** (0.32 g, 1.1 mmol) and Bu3SnH (0.4 mL, 1.32 mmol) in dry benzene (20 mL) was refluxed for

1 h during which time a solution of AIBN (36 mg, 0.22 mmol) in benzene (0.5 mL) was added in two portions. Evaporation of the solvent followed by flash chromatography on silica gel (eluent: ethyl acetate / hexanes 1/9) gave pure *O*-cyclododecylthiocarbamate **3c** (0.23 g; 90%) as colorless crystals (*vide supra*).

Synthesis of Tributyltin *p*-Toluenesulfinate (6).[19] To a suspension of anhydrous sodium *p*-toluenesulfinate (3.56 g, 0.02 mol) in dry THF (150 mL) was added tributyltin chloride (6.50 g, 0.02 mol) at room temperature under an argon atmosphere. The progress of the reaction was monitored by TLC. After stirring for 4 days, the reaction mixture was filtered through a sintered glass funnel (40 M) in order to remove NaCl formed. Evaporation of the solvent afforded the tributyltin *p*-toluenesulfinate **4** (8.80 g; 98%) as a colorless, viscous oil: IR (neat): 2956, 2922, 2870, 2854, 1456, 1080, 981, 955, 864, 808, 674 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 7.44 (2H, d, J = 8.1 Hz), 7.19 (2H, d, J = 8.1 Hz), 2.36 (3H, s), 1.5 (6H, m), 1.2 (12H, m), 0.83 (9H, t, J = 7.1 Hz); ^{13}C-NMR ($CDCl_3$, δ, ppm): 149.8, 140.5, 129.1, 124.3, 27.9, 26.9, 21.2, 19.5, 13.5; ^{119}Sn-NMR (toluene-d_8, δ, ppm, refer. Me_4Sn, δ=0.00 ppm): -17 (-20 °C, sharp ; +20 °C br.); Anal. Calcd for $C_{19}H_{34}O_2SSn$: S, 7.20. Found: S, 6.98 %.

Synthesis of an Authentic Sample of *O*-Neopentylthioxocarbamate (3d). To a solution of neopentyl alcohol (2 g, 0.023 mol) and pyridine (4.6 mL) in dry CH_2Cl_2 (40 mL) was added thiophosgene (2.74 g, 0.0238 mol) at 0 °C under argon atmosphere. After stirring for 3 h at 0 °C, anhydrous ammonia was bubbled into the solution at 0 °C for 3 h. The solvent was removed and the reaction mixture was treated with ethyl ether (80 mL); washed with brine, dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography on silica gel (eluent: ethyl acetate/hexanes 2/8) and recrystallization from dichloromethane/hexanes gave compound **3d** (0.350 g, 10%) as colorless needles.
All physical and spectral data were identical to that previously reported for compound **3d** (*vide supra*).

Reduction of Neopentyl *N*-toluenesulfonyl Thioxocarbamate (2d) with Bu_3SnH / AIBN in the Presence of Isobutyl Vinyl Ether as a Radical trap. To a solution of neopentyl *N*-toluenesulfonyl thioxocarbamate **2d** (0.30 g, 1.0 mmol) in isobutyl vinyl ether (30 mL) was added Bu_3SnH (0.32 g, 1.1 mmol) under argon. The solution was heated to reflux and treated at 30 min. intervals with 4 portions of 200-μL (0.33 eq. in total) of a solution of 200 mg of AIBN in 3 mL of dry benzene during reflux. The reaction was monitored by TLC. After removing the isobutyl vinyl ether under reduced pressure, flash column chromatography on silica gel (eluent: ethyl ether/hexanes 2/8) afforded compound **8** (0.195 g; 79%) in a 1:1 ratio of two isomers and as a pale yellow oil: IR (neat): 3255, 2948, 2861, 1711, 1493, 1377, 1194, 1097, 1043 cm^{-1}; ^{1}H-NMR ($CDCl_3$, δ, ppm): 6.80 (1H, m), 6.45 (1H, m), 5.72 (1H, m), 5.22 (1H, m), 4.18 (2H, d, J = 2.9 Hz), 4.11 (2H, d, J = 3.2 Hz), 3.36 (2H, m), 3.15 (2H, m), 1.82 (2H, m), 1.41 (3H, d, J = 5.8 Hz), 1.36 (3H, d, J = 5.8 Hz), 1.00 (9H, s), 0.97 (9H, s), 0.90 (3H, d, J = 6.6 Hz), 0.88 (3H, d, J = 6.6 Hz); ^{13}C-NMR ($CDCl_3$, δ, ppm): 190.5, 189.9, 82.5, 81.4, 79.5, 79.4, 75.2, 74.9, 31.6, 31.4, 28.3, 26.5, 26.4, 21.4, 21.2, 19.2, 19.2; Anal. Calcd for $C_{12}H_{25}NO_2S$: C, 58.26; H, 10.18; N, 5.66; S, 12.96. Found: C, 58.38; H, 10.21; N, 5.51; S, 12.77 %.

Acknowledgments: We thank the N.I.H. and the Schering-Plough Corporation for the financial support which made this work possible.

REFERENCES

1. Part XXXIV: Barton, D. H. R.; Chern, C. Y.; Jaszberenyi, J. Cs. *Tetrahedron* **1995**, *51*, 1867.

2. Motherwell, W. B. and Crich, D. *Free Radical Chain Reactions in Organic Synthesis*, Academic Press, London, 1992. Barton, D. H. R. and Parekh, S. I., *Half a Century of Free Radical Chemistry*, Cambridge University Press, Cambridge, 1993. McCombie, S. W. Comprehensive Organic Synthesis, Eds. Trost, B.M. and Fleming I., Vol. 8 Ed. Fleming I., pp. 811-833, Pergamon Press, Oxford, 1991.
3. Barton, D. H. R.; McCombie, S.W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.
4. Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.* **1983**, *105*, 4059.
5. Hayashi, T.; Iwaoka, T.; Takeda, N.; Ohki, E. *Chem. Pharm. Bull.* **1978**, *26*, 1786.
6. a) Barton, D. H. R.; Blundell, P.; Dorchak, J.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron* **1991**, *47*, 8969. b) Barton, D. H. R.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1989**, *30*, 2619. c) Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1990**, *31*, 4681.
7. Nishiyama, K.; Oba, M.; Oshimi, M.; Sugawara, T,; Ueno, R. *Tetrahedron Lett.* **1993**, *34*, 3745.
8. Oba M.; Nishiyama, K. *Synthesis* **1994**, *6*, 624-8.
9. a) Oba M.; Nishiyama, K. *Tetrahedron* **1994**, *50*, 10193-10200. b) Okabe, M.; Sun, R.-C.; Scalone, M.; Jibilian, C. H.; Hutchings, S. D. *J. Org. Chem.* **1995**, *60*, 767-771.
10. Dickore, K.; Kuehle, E. German Patent 1,183,492 (Dec 17, 1964); *Chem. Abstr.* **1965**, *62*, 7691.
11. Dickore, K.; Kuehle, E. *Angew. Chem.* **1965**, *77*, 429; *Angew. Chem. Internat. Edit. Engl.* **1965**, *4*, 430.
12. Schaumann, E.; Sieveking, S.; Walter, W. *Tetrahedron* **1974**, *30*, 4147-4152.
13. Van Loock, E.; Vandensavel, J. M.; L'abbe, G.; Smets, G. *J. Org. Chem.* **1973**, *33*, 2916-2917.
14. Herkes, F. E. *J. Fluorine Chem.* **1979**, *13*, 1-21.
15. Dadieu, A. *Ber.* **1931**, *64B*, 358.
16. McFarland, J. W.; Houser, R. *J. Org. Chem.* **1968**, *33*, 340-343.
17. Barton, D. H. R.; Jang, D. O.; Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1990**, *31*, 3991-3994.
18. Harris, R. K.; Mann, B. E. ; Eds. "NMR and the Periodic Table", Ch.10, p. 390, Harris, R. K.; Kennedy, J. D.; McFarlane, W. Academic Press, London, **1978** and references cited therein.
19. a) Lindner, E.; Kunze, U.; Vitzthum, G.; Ritter, G.; Haag, A. *J. Organometal. Chem.* **1970**, *24*, 131-143. b) Lindner, E.; Kunze, U.; Ritter, G.; Haag, A. *J. Organometal. Chem.* **1970**, *24*, 119-129.
20. a) Jensen, K. A.; Due, M.; Holm, A.; Wentrup, C. *Acta Chem. Scand.* **1966**, *20*, 2091-2106. b) Jensen, K. A.; Holm, A. *Acta Chem. Scand.* **1964**, *18*, 826.
21. Jensen, K. A.; Due, M.; Holm, A. *Acta Chem. Scand.* **1965**, *19*, 438-442.
22. a) Barton, D. H. R.; Jaszberenyi, J. Cs.; Theodorakis, E. A. *Tetrahedron* **1992**, *48*, 2613-2626. b) Barton, D. H. R.; Csiba, M. A. Jaszberenyi, J. Cs. *Tetrahedron Lett.* **1994**, *35*, 2869-2872.
23. a) Barton, D. H. R.; Crich, D.; Lobberding, A.; Zard, S. Z. *J. Chem. Soc., Chem. Commun.*, **1985**, 646-647. b) Barton, D. H. R.; Crich, D.; Lobberding, A.; Zard, S. Z. *Tetrahedron* **1986**, *42*, 2329-2338.

(*Received in USA* 13 *September* 1995; *revised* 14 *November* 1995; *accepted* 15 *November* 1995)