Notes

Novel Access to Thioacylsilanes with Benzotriazole-Mediated Methodology

Alessandro Degl'Innocenti* and Antonella Capperucci

Centro C.N.R. Composti Eterociclici e loro Applicazioni and Dipartimento di Chimica Organica, via G. Capponi 9, 50121 Firenze, Italy

Daniela C. Oniciu

Alchem Laboratories Corporation, 13305 Rachael Boulevard, Alachua, Florida 32615

Alan R. Katritzky*

Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, Florida 32611-7200

katritzky@chem.ufl.edu

Received July 31, 2000

Introduction

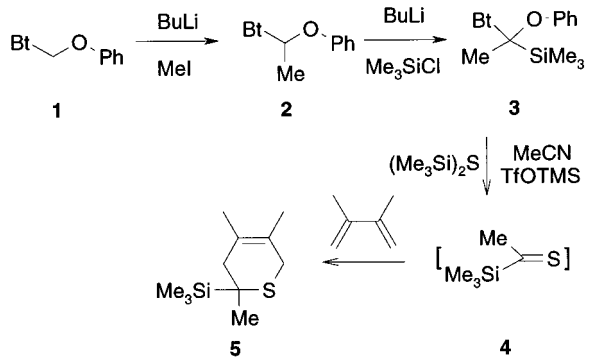
Thioformyl- and thioacetyl-silanes are successful intermediates for thiocarbonyl-containing compounds,[1−3] and useful building blocks for polyfunctionalized molecules. Besides being synthetic equivalents of thioaldehydes, thioacylsilanes[4] are characterized by the high reactivity of the carbon−sulfur double bond toward nucleophiles, electrophiles, and cycloaddition reactions, which lead to various compounds containing the Si−C−S unit.[5] Thus, thioacylsilanes react with organolithium reagents to yield vinyl sulfides,[6] and cycloadd to 1,3-dipoles,[6a,7] dienes,[4,6b,8] heterodienes,[9] and, under photoinduced conditions, olefins.[10] Silyl thioketones can be transformed into silyl sulfines and thioaldehyde *S*-oxides[11] and be used as spin-trapping agents.[12] Enethiolizable thioacylsilanes can afford 2-silyl thiacycloalkenes or *Z*-α-silyl sulfides, convertable by protiodesilylation into *Z*-vinyl sulfides, which are precursors of thioannulated cyclopentenes and thiofunctionalized enones.[13]

Novel routes to thioacylsilanes are of considerable interest, and a general entry was recently reported, using a hexamethyldisilathiane-based thionation procedure.[14,15] We now present an alternative method for the generation of thioacylsilanes using benzotriazole chemistry.

Results and Discussion

1-(Benzotriazol-1-yl)-1-phenoxyalkanes **1** and **2** were prepared as described previously (Scheme 1).[16] 1-(Benzotriazol-1-yl)-1-methylthioalkanes **7a**,**b**,**f**,**g** were obtained from (benzotriazol-1-yl)methyl methyl thioether (**6a**) by reactions with BuLi followed by alkyl halides or aldehydes, as described elsewhere.[17] 1-(Benzotriazol-1-yl)-1-thioalkane derivatives **7c** and **7e** were prepared according to known procedures.[18−20] Reactions of derivatives **2** and **7a**−**e** with BuLi and subsequent treatment with trimethylchlorosilane afforded the -trimethylsilyl-benzotriazoles **3** and **8a**−**d**, respectively (Schemes 1 and 2).

Scheme 1



(1) Capperucci, A.; Degl'Innocenti, A.; Scafato, P.; Spagnolo, P. *Phosphorus, Sulfur Silicon* **1997**, *120&121*, 165.

(2) Capperucci, A.; Degl'Innocenti, A.; Scafato, P. in *Recent Research Developments in Synthetic Organic Chemistry*; Pandalai, S. G., Ed.; Transworld Research Network: India, 1998; p 171.

(3) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A. *J. Organomet. Chem.* **1998**, *567*, 181. Bonini, B. F.; Fochi, M. in *Advances in Sulfur Chemistry*; Rayner, C. M., Ed.; JAI: Stamford, 2000; Vol. 2, p 1.

(4) (a) Bonini, B. F.; Fochi, M. *Rev. Heteroatom. Chem.* **1997**, *16*, 46−67. (b) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A.; Varchi, G. *Tetrahedron Lett.* **1999**, *40*, 6473−6476.

(5) Bonini, B. F. *Phosphorus, Sulfur, Silicon* **1993**, *74*, 31−45.

(6) (a) Bonini, B. F.; Mazzanti, G.; Zani, P.; Barbaro, G.; Battaglia, A.; Giorgianni, P.; Maccagnani, G.; Macciantelli, D. *J. Chem. Soc., Perkin Trans.* 1 **1986**, 381−385. (b) Bonini, B. F.; Mazzanti, G.; Zani, P.; Maccagnani, G. *J. Chem. Soc., Perkin Trans.* 1 **1989**, 2083−2088. (c) Bonini, B. F.; Maccagnani, G.; Masiero, S.; Mazzanti, G.; Zani, P. *Tetrahedron Lett.* **1989**, *30*, 2677−2680.

(7) Bonini, B. F.; Maccagnani, G.; Mazzanti, G.; Atwa, A. I. A.; Zani, P. *Heterocycles* **1990**, *31*, 47−57.

(8) (a) Bonini, B. F.; Lenzi, A.; Maccagnani, G.; Barbaro, G.; Giorgianni, P.; Macciantelli, D. *J. Chem. Soc., Perkin Trans.* 1 **1987**, 2643−2646. (b) Bonini, B. F.; Mazzanti, G.; Zani, P.; Maccagnani, G. *J. Chem. Soc. Chem. Commun.* **1988**, 365−367. (c) Bonini, B. F.; Busi, F.; de Laet, R. C.; Mazzanti, G.; Thuring, J. W. J. F.; Zani, P.; Zwanenburg, B. *J. Chem. Soc., Perkin Trans.* 1 **1993**, 1011−1018.

(9) (a) Carisi, P.; Mazzanti, G.; Zani, P.; Barbaro, G.; Battaglia, A.; Giorgianni, P. *J. Chem. Soc., Perkin Trans.* 1 **1987**, 2647−2651. (b) Bonini, B. F.; Masiero, S.; Mazzanti, G.; Zani, P. *Tetrahedron Lett.* **1991**, *32*, 2971−2974.

(10) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A.; Zani, P. *J. Chem. Soc., Perkin Trans.* 1 **1995**, 2039−2044.

(11) Barbaro, G.; Battaglia, A.; Giorgianni, P.; Bonini, B. F.; Maccagnani, G.; Zani, P. *J. Org. Chem.* **1990**, *55*, 3744−3748.

(12) (a) Alberti, A.; Bonini, B. F.; Pedulli, G. F. *Tetrahedron Lett.* **1987**, *28*, 3737−3740. (b) Alberti, A.; Benaglia, M.; Bonini, B. F.; Pedulli, G. F. *J. Chem. Soc., Faraday Trans.* 1 **1988**, *84*, 3347−3358. (c) Alberti, A.; Benaglia, M.; Vismara, E. *Res. Chem. Intermed.* **1989**, *11*, 117−126.

(13) (a) Bonini, B. F.; Comes-Franchini, M.; Mazzanti, G.; Ricci, A.; Rosa-Fauzza, C.; Zani, P. *Tetrahedron* **1996**, 52, 4803−4816. (b) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A. *Tetrahedron Lett.* **1994**, *35*, 9227−9228. (c) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Peri, F.; Ricci, A. *J. Chem. Soc., Perkin Trans.* 1 **1995**, 2039−2044. (d) Bonini, B. F.; Comes-Franchini, M.; Fochi, M.; Mazzanti, G.; Ricci, A. *Tetrahedron* **1997**, *53*, 7897−7910.

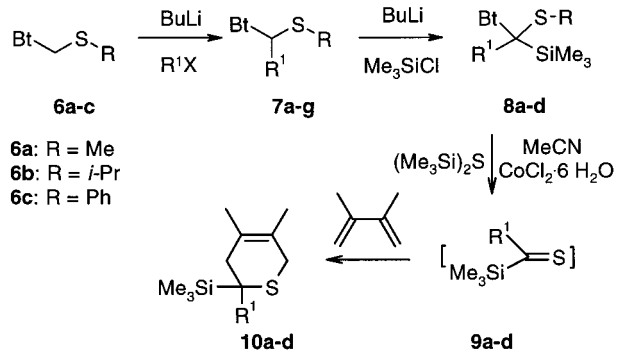
(14) (a) Degl'Innocenti, A.; Scafato, P.; Capperucci, A.; Bartoletti, L.; Spezzacatena, C.; Ruzziconi, R. *Synlett* **1997**, 361. (b) Ricci, A.; Degl'Innocenti, A.; Capperucci, A.; Reginato, G. *J. Org. Chem.* **1989**, *54*, 19−20.

(15) Degl'Innocenti, A.; Capperucci, A.; Scafato, P.; Mecca, T.; Reginato, G.; Mordini, A. *Synlett* **1999**, 1739.

(16) Katritzky, A. R.; Lang, H.; Wang, Z.; Lie, Z. *J. Org. Chem.* **1996**, *61*, 7551.

10.1021/jo0011585 CCC: $19.00
Published on Web 12/07/2000

Scheme 2

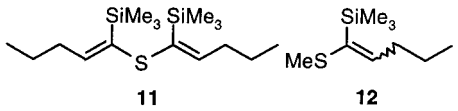


7,8,9,10a: R = Me, R^1 = *n*-Bu,
7,8,9,10b: R = Me, R^1 = $PhCH_2$
7,8,9,10c: R = *i*-Pr, R^1 = *cyclo*-C_5H_9
7,8,9,10d: R = Me, R^1 =$SiMe_3$
7e: R = Ph, R^1 =H
7f: R = Me, R^1 = PhCHOH
7g: R = Me, R^1 = (*cyclo*-C_6H_{11})CHOH

Benzotriazole derivatives **3** and **8a**−**d** reacted with hexamethyldisilathiane (HMDST) in the presence of TfOTMS or cobalt dichloride hexahydrate as a Lewis acid to afford the corresponding thioacylsilanes **4** and **9a**−**d**, which were trapped with 2,3-dimethyl-1,3-butadiene as their adducts **5** and **10a**−**d** (Schemes 1 and 2).

Reactions of the butyl, benzyl, and cyclopentyl derivatives **8a**−**c** afforded the corresponding silylated cycloadducts **10a**−**c** in good yields upon treatment with HMDST and 2,3-dimethyl-1,3-butadiene in the presence of $CoCl_2$ (Scheme 2). However, the O-derivative **3** required the addition of the more oxophilic TfOTMS to furnish the cycloadduct **5** in 51% yield. By contrast, the use of TfOTMS in the case of **8a** led to mixtures of di(1-trimethylsilyl-1-pentenyl)sulfide (**11**) and isomers of 1-trimethylsilyl-1-methylthio-1-pentene (**12**).

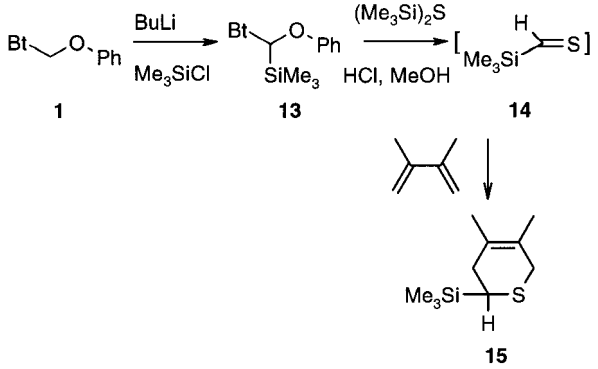
Earlier attempts to prepare bis-trimethylsilylthioketone failed: no reactions of disilylated 1,3-dioxanes under previously reported conditions[14] have afforded a bis-silyl thioketone. α-Bis(trimethylsilyl)benzotriazol-1-ylmethyl methyl thioether (**8d**) reacted smoothly with HMDST in the presence of 2,3-dimethyl-1,3-butadiene and various catalysts, such as $CoCl_2$, TfOTMS, $TiCl_4$, and even HCl in methanol as a solvent. GC/MS analyses of the reaction mixtures indicated that the bis(trimethylsilyl)dihydrothiopyran **10d** was the sole or main product, but workup led to its decomposition.



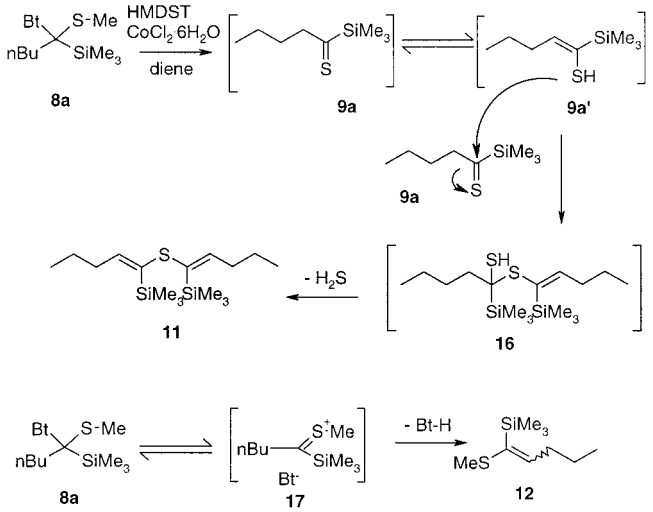
11 **12**

Interestingly, compound **13** was rather inert in the present reaction conditions. Thus, attempted reactions of **13** with HMDST in the presence of $CoCl_2$, TfOTMS, or even BF_3 etherate or $TiCl_4$ led only to recovery of starting material. However, generation of the thioformylsilane **14** and its trapping with 2,3-dimethylbutadiene to give adduct **15** was achieved efficiently by using HCl in methanol as the solvent (Scheme 3).

Scheme 3



Scheme 4. Proposed Mechanism for the Formation of Compounds 11 and 12

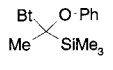
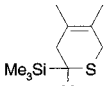
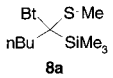
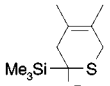
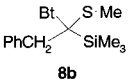
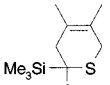
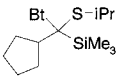
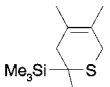
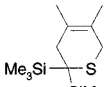
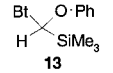
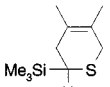


As mentioned above, contrary to what was observed in other cases, cyclohexadiene was inefficient as a trapping agent in these reactions; in the case of the butyl derivative **8a**, it led to the formation of sulfide **11** as the main product. Even the stronger Lewis acid $TiCl_4$ with **8a** and cyclohexadiene gave the isomeric olefin **12**, arising from benzotriazole elimination, as the only product isolated. Scheme 4 depicts our rationalization of this occurrence: reaction of the Bt-derivative **8a** in the present conditions affords initially thioacylsilane **9a**, which further reacts as its enethiol **9a′**, through a carbophilic pathway, with more **9a** to afford adduct **16**. This pathway was previously described in the literature.[4a] Compound **16**, upon loss of H_2S, gives the isolated divinyl sulfide **11**. The isomers of 1-trimethylsilyl-1-methylthio-1-pentene (**12**) arise from benzotriazole elimination in the starting material (Scheme 4).

As documented in the Experimental Section, upon standing, the 1-(benzotriazol-1-yl) pent-1-yl ether **8a** partially rearranged into the corresponding (1-benzotriazol-2-yl)pent-2-yl analogue. Such rearrangement between isomeric pairs of compounds of type RX-CH(R^1)-Bt^1 ⇆ RX-CH(R^1)-Bt^2 are common.[21−25] However, such

(17) Katritzky, A. R.; Oniciu, D. C.; Ghiviriga, I.; Soti, F. *J. Org. Chem.* **1998**, *63*, 2110.
(18) Katritzky, A. R.; Ghiviriga, I.; Oniciu, D. C.; Soti, F. *J. Heterocycl. Chem.* **1996**, *33*, 1927.
(19) Katritzky, A. R.; Perumal, S.; Kuzmierkiewicz, W.; Lue, P.; Greenhill, J. V. *Helv. Chim. Acta* **1991**, *74*, 1924.
(20) Katritzky, A. R.; Afridi, A. S.; Kuzmierkiewicz, W. *Helv. Chim. Acta* **1991**, *74*, 1931.
(21) Smith, J. L. R.; Saad, J. S. *J. Chem. Soc., Perkin Trans. 1* **1975,** 1181.

Table 1. Summary of Results

Entry	Reagent	Catalyst	Product	Yield (%) [a]
1	 **3**	TfOTMS	 **5**	51
2	 **8a**	$CoCl_2 \cdot 6H_2O$	 **10a**	64
3	 **8b**	$CoCl_2 \cdot 6H_2O$	 **10b**	58
4	 **8c**	$CoCl_2 \cdot 6H_2O$	 **10c**	40 [b]
5	 **8d**	$CoCl_2 \cdot 6H_2O$	 **10d**	55 [b]
6	 **13**	HCl/MeOH	 **15**	42

[a] Yield of isolated product. [b] GC yield.

isomerization is of little significance from a purely preparative point of view, as Bt^1 and Bt^2 isomers of type $RX\text{-}CH(R^1)\text{-}Bt$ show essentially similar reactivity, particularly in reactions involving ion pair intermediates of type $RX^+{=}CHR^1Bt^-$.

Conclusions

Table 1 summarizes the experimental results. The methodology described in this paper provides a general method for the synthesis of silylated thiocarbonyl compounds, and represents an extension to the synthesis of silylated thioaldehydes by the reaction of hexamethyldisilathiane with silyl acetals.[14] The pathway described above enables the direct preparation of silylated thioketones and eliminates the tedious synthesis of their silyl acetal precursors. Other significant advantages of the present methodology over previous methods include the readily available starting materials and simple procedures.

Experimental Section

General. Melting points were determined with a hot-stage apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as the internal standard for ^1H (60 and 200 MHz) or the solvent as the internal standard for ^{13}C (22.5 and 50 MHz). Tetrahydrofuran was distilled under nitrogen immediately prior to use from sodium/benzophenone. All reactions with air-sensitive compounds were carried out under an argon atmosphere. Column chromatography was conducted with silica gel 230 mesh. TLC was performed on precoated silica gel 60 F_{254} plates. Benzotriazol-1-ylalkyl phenyl ethers **1**−**3** and **13** were prepared according to the literature procedures.[16] (Benzotriazol-1-yl)methyl methyl thioether (**6a**)[17] and benzotriazole derivatives **7a**−**g**[18−20] were prepared by the procedures previously reported.

2-Methyl-2-trimethylsilyl-4,5-dimethyl-3,6-dihydro-2*H*-thiopyran (5). A mixture of 1-(benzotriazol-1-yl)-1-phenoxy-1-trimethylsilylethane (**3**) (30 mg, 0.1 mmol), 2,3-dimethyl-1,3-butadiene (41 mg, 0.5 mmol), and HMDST (36 mg, 0.2 mmol) in 0.5 mL of CH_3CN was treated at room temperature with $CF_3SO_3SiMe_3$ (0.02 mmol, 5 μL) under inert atmosphere. Progress of the reaction was monitored by GC/MS analysis. After 6 h the reaction mixture was quenched with saturated NH_4Cl, extracted with diethyl ether, and dried over Na_2SO_4. After removal of the solvent, the product was purified by chromatography on silica gel (cyclohexane) affording 11 mg of pure product (51%). ^1H NMR ($CDCl_3$, 200 MHz) δ: 0.08 (s, 9 H), 1.28 (s, 3 H), 1.66 (bs, 3 H), 1.72 (bs, 3 H), 1.76 (bd, 1 H, partially overlapped with peak at 1.72 ppm), 2.44 (bd, 1 H), 2.71 (bd, 1 H), 3.26 (bd, 1 H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: −4.3, 19.7, 20.8, 21.6, 26.4, 36.9, 39.9, 122.1, 125.2. MS *m*/*z* (%): 214 (M^+, 1), 199 (2), 141 (9), 109 (25), 108 (100), 92 (28), 73 (80). Anal. Calcd for $C_{11}H_{22}SSi$: C, 61.61; H, 10.34. Found: C, 61.52; H, 10.42.

General Procedure for the Silylation of α-Benzotriazolylalkyl Thioethers 7a−d. To a solution of the appropriate (benzotriazol-1-yl)methyl derivative (50 mmol) in THF (200 mL) at −78 °C under nitrogen was added BuLi (2.22 M in hexane, 23.6 mL, 52.5 mmol) over a period of 5 min. After 10 min, a solution of trimethylchlorosilane (60 mmol) in THF (10 mL) was added. The mixture was stirred at −78 °C for 2 h and then was allowed to warm to room temperature and stirred for an additional 12 h. The reaction was quenched with saturated ammonium chloride (100 mL) and extracted with methylene chloride (3 × 50 mL), and the combined extracts were washed with water (2 100 mL) and dried ($MgSO_4$). After the solvent was removed by rotary evaporation, the residue was subjected to column chromatography to give the pure product.

1-(Benzotriazol-1-yl)-1-trimethylsilylpent-1-yl Methyl Thioether (8a). 1-(Benzotriazol-1-yl)pent-1-yl methyl thioether (**7a**) (2.35 g, 10 mmol) was dissolved in 50 mL of THF, and a solution of BuLi 2 N in hexane (5.25 mL, 10.5 mmol) was added at −78 °C under nitrogen and with stirring. Ten minutes later, trimethylsilyl chloride (1.20 g, 1.40 mL, 11 mmol) was added, and the reaction mixture was stirred at −78 °C for 2 h and at rt for 12 h. The reaction was quenched with 100 mL of sodium chloride 5%. The layers were separated, and the aqueous layer was extracted with diethyl ether (3 25 mL). The combined organic extracts were dried over magnesium sulfate, and the solvent was removed in vacuo. The residue (3.01 g) was flash chromatographed on silica gel (175 g) eluting with benzene:ethyl acetate 95:5. The expected product was separated as an oil (2.54 g) in 84% yield. It partially rearranged on standing at room temperature to the Bt-2 isomer: ^1H NMR 0.35 (s, 9 H), 0.95 (t, J = 7.4 Hz, 3 H), 1.20−1.50 (m, 4 H), 2.10 (s, 3 H), 2.15−2.25 (m, 2 H), 7.30−7.40 (m, 2 H), 7.70−7.80 (m, 2 H). Distinct signals of the Bt-1 isomer (20%): 0.45 (s, 1 H), 0.80 (t, J = 7.2 Hz, 3 H), 7.35−7.45 (m, 2 H), 8. 10 (d, J = 8.2 Hz, 2 H), 8. 20 (d, J = 8.2 Hz, 2 H); ^{13}C NMR 0.91, 13.1, 15.5, 24.7, 29.7, 38.1, 70.6, 115.5, 119.7, 121.8, 127.4, 135.2, 145.2.

General Procedure for the Synthesis of Thioacylsilane Adducts 10a−d Starting from 1-(Benzotriazol-1-yl)-1-trimethylsilylmethyl Thioethers 8a−d. A solution containing the appropriate 1-(benzotriazol-1-yl)-1-trimethylsilyl methyl thioether (0.1 mmol), 2,3-dimethyl-1,3-butadiene (0.5 mmol), and HMDST (0.2−0.4 mmol) in CH_3CN (0.5 mL) was treated at room temperature in inert atmosphere with a solution of $CoCl_2 \cdot 6H_2O$ (0.1 mmol) in CH_3CN (0.5 mL). Progress of the reaction was monitored by GC/MS analysis. The reaction mixture was quenched with saturated NH_4Cl, extracted with diethyl ether, and dried (Na_2SO_4) and the solvent removed under vacuum. The

(22) Katritzky, A. R.; Yannakopoulou, K.; Kuzmierkiewicz, W.;Aurrecoechea, J. M.; Palenik, G. J.; Koziol, A. E.; Szczesniak, M.; Skarjune, R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 225.
(23) Katritzky, A. R.; Rachwal, S.; Rachwal, B.; Steel, P. J. *J. Org. Chem.* **1992**, *57*, 4932.
(24) Katritzky, A. R.; Kuzmierkiewicz, W.; Perumal, S. *Helv. Chim. Acta* **1991**, *74*, 1936.
(25) Katritzky, A. R.; Perumal, S.; Fan, W.-Q. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2059.

crude product was then purified by preparative TLC on silica gel using hexane as an eluent.

2-Butyl-2-trimethylsilyl-4,5-dimethyl-3,6-dihydro-2*H*-thiopyran (10a). Following the general procedure, starting from 30 mg (0.1 mmol) of **8a**, 16 mg of pure **10a** were obtained (64%). ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 0.09 (s, 9H), 0.89 (bt, 3H), 1.25−1.33 (m, 4H), 1.51−1.55 (m, 2H), 1.67 (bs, 3H), 1.71 (bs, 3H), 1.89 (bd, 1H), 2.41 (bd, 1H), 2.68 (bd, 1H), 3.12 (bd, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ: −2.7, 14.0, 19.4, 20.7, 23.5, 26.9, 28.8, 30.2, 35.3, 38.6, 122.3, 125.5. MS *m*/*z* (%): 256 (M^+, 0.1), 183 (4), 150 (19), 107 (31), 95 (35), 73 (100). Anal. Calcd for $C_{14}H_{28}SSi$: C, 65.55; H, 11.00. Found: C, 65.40; H, 11.12.

Supporting Information Available: Experimental procedures and ^{1}H and ^{13}C NMR and GC/MS spectral data for compounds **8b**−**d**, **10b**−**d**, **13**, and **15**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0011585