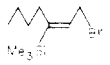
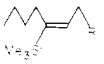
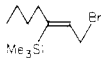
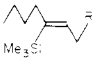
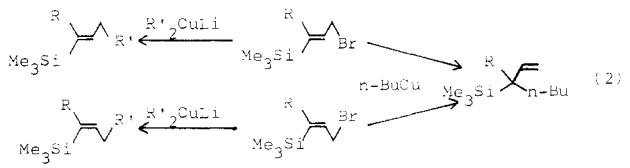
Table II. Reactions of 3-(Trimethylsilyl)allylic Bromides with Alkylcopper Reagents[a]

starting material (R = n-Bu)	alkylcopper RCu (equiv)	products and yield,[b] %	
		 20	 21
	n-BuCu (2)	0	100
	n-BuCu·BF_3 (2)	0	100
	PhCu (2)	16[c]	82[c]
	sec-BuCu (3)	100	0
	t-BuCu (2)	100	0
		 22	 21
	n-BuCu (2.5)	0	100

[a] Reactions were done under the identical conditions (with those in Table I). [b] The products were isolated pure by chromatography unless otherwise noted. [c] Determined by NMR.

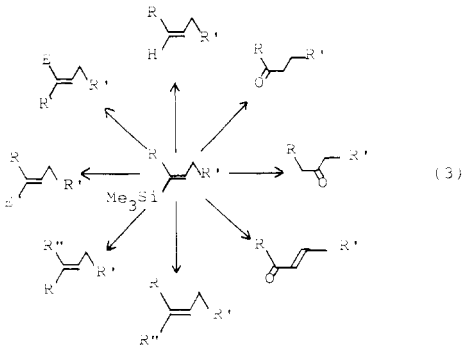
straightforwardly S_N2 products (entries 5 and 6, Table I), while, irrespective of stereochemistries of allylic bromides, the corresponding reactions with either *n*-butylcopper or *n*-BuCu·BF_3[10] provided exclusively same S_N2' product, **21** (Table II). This is, to our knowledge, the first instance where clear and sharp distinction of reaction paths exists between reactions of dialkylcuprates and alkylcoppers (eq 2).



(2)

Unfortunately, though, the difference faded gradually as the alkyl groups on copper became larger (Table II). Thus, with *sec*- or *tert*-butyl groups, even the corresponding alkylcopper reagents were effective for S_N2 reactions, but with *n*-butyl or phenyl groups, use of cuprate reagents was necessary for S_N2 product formation (Table I).

In conclusion, γ-(trimethylsilyl)allylic bromides are superb substrates for regiospecific S_N2 functionalization and the resulting stereodefined alkenylsilanes are valuable synthetic intermediates convertible to a number of functional groups of variable oxidation states[2,11] (eq 3).



(3)

(10) Maruyama, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1977**, *99*, 8068.
(11) (a) Hudrlik, P. F.; Peterson, D.; Rona, R. J. *J. Org. Chem.* **1975**, *40*, 2263. Hudrlik, P. F.; Hudrlik, A. M.; Rona, R. J.; Misra, R. N.; Withers, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 1993. (b) Hirao, T.; Yamada, N.; Ohshiro, Y.; Agawa, T. *Chem. Lett.* **1982**, 1977.

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Registry No. **6** (R = *n*-Bu), 89828-12-6; **6** (R = *n*-C_6H_{13}), 89828-13-7; **7** (R = *n*-Bu), 89828-14-8; **8**, 89828-15-9; **9**, 89828-16-0; **10**, 89828-17-1; **11**, 89828-18-2; **12**, 89828-11-5; **13**, 89828-19-3; **14**, 89828-20-6; **15**, 89828-21-7; **16**, 89828-22-8; **17**, 89828-23-9; **18**, 89828-24-0; **19**, 89828-25-1; **20** (R = *sec*-Bu), 89828-26-2; **20** (R = *t*-Bu), 89828-27-3; **21** (R = *n*-Bu), 89828-28-4; **21** (R = Ph), 89828-29-5; $NaCH(CO_2Et)_2$, 34727-00-9; $LiCu(n\text{-}Bu)_2$, 24406-16-4; *sec*-BuCu, 89828-30-8; *t*-BuCu, 56583-96-1; $LiCuPh_2$, 23402-69-9; *n*-BuCu, 34948-25-9; *n*-BuCu·BF_3, 68079-35-6; PhCu, 3220-49-3.

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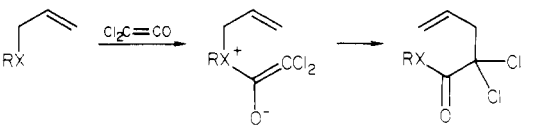
Macrolide Synthesis via Dichloroketene Ring Expansion

Summary: The reaction of allyl sulfides with dichloroketene followed by [3,3] sigmatropic rearrangement has been adapted for the efficient ring expansion of α-alkenyl cyclic sulfides.

Sir: Belluš and Malherbe have described a remarkable [3,3] sigmatropic rearrangement of allyl ethers or sulfides upon treatment with dichloroketene:[1]



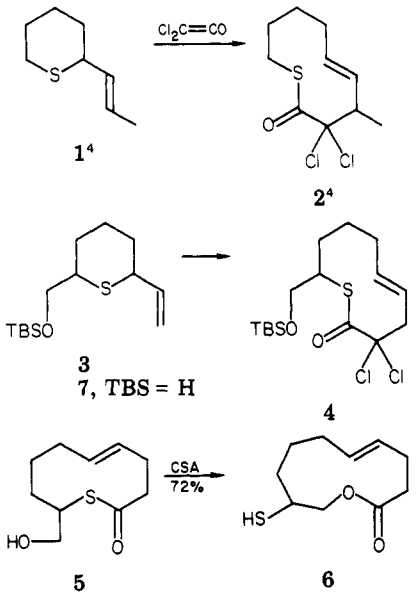
It occurred to us that this reaction should also be applicable to the synthesis of medium or large ring thiolactones from cyclic α-alkenyl sulfides that are available by sulfur ylide ring expansion techniques.[2] In particular, we were interested in potential applications where the rearranged product would contain an ω-hydroxyalkyl substituent because thiolactones of this type have been shown to rearrange to seven–ten-membered mercapto lactones by S to O acyl transfer.[3] The key steps correspond to Scheme I, **3** to **4** (dichloroketene ring expansion) and **5** to **6** (S to O acyl transfer). After our work was well under way, Belluš et al. published an apparently close analogy to the desired [3,3] sigmatropic ring expansion, the conversion of **1** into **2**, but in a disappointing yield of 8%.[4] Although we have not repeated this specific example, our results suggest that a modified dichloroketene ring expansion procedure (reflux during slow addition of excess Cl_3CCOCl) gives consistently good yields. The method has been used to prepare ω-hydroxyalkyl thiolactones **5** and **12**, which provide convenient access to 11- and 14-membered lactones, respectively, by S to O acyl transfer.

The starting material **3** for both lactone series was available from previous work.[5] Treatment of **3** with $Cl_2C{=}C{=}O$, generated in situ by syringe pump addition

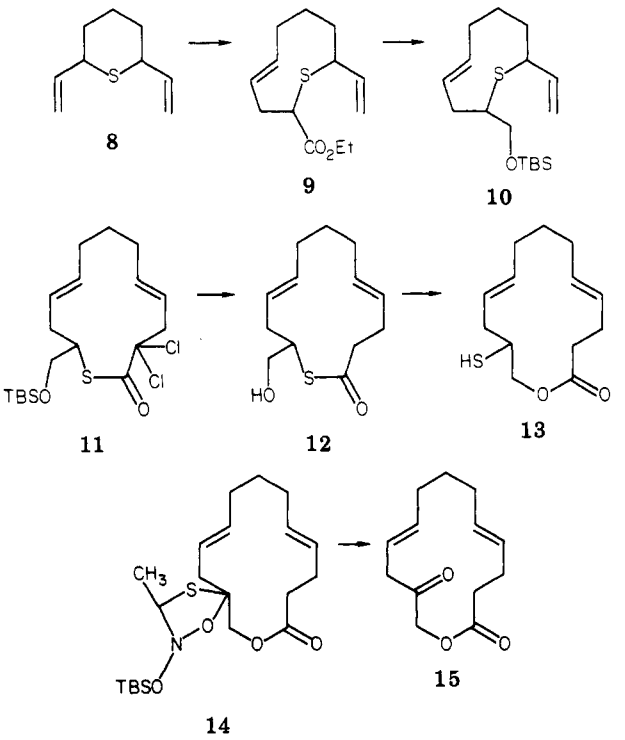
(1) Malherbe, R., Belluš, D. *Helv. Chim. Acta* **1978**, *61*, 3096.
(2) (a) Vedejs, E.; Hagen, J. P.; Roach, B. L.; Spear, K. L. *J. Org. Chem.* **1978**, *43*, 1185. (b) Vedejs, E.; Arco, M. J.; Powell, D. W.; Renga, J. M.; Singer, S. P. *Ibid.* **1978**, *43*, 4831. (c) Vedejs, E.; Dophin, J. M.; Mastalerz, H. *J. Am. Chem. Soc.* **1983**, *105*, 127.
(3) Vedejs, E.; Powell, D. W. *J. Am. Chem. Soc.* **1982**, *104*, 2046.
(4) Malherbe, R.; Rist, G.; Belluš, D. *J. Org. Chem.* **1983**, *48*, 860.
(5) Vedejs, E.; Arnost, M. J.; Hagen, J. P. *J. Org. Chem.* **1979**, *44*, 3230.

0022-3263/84/1949-1840$01.50/0

Scheme I



Scheme II



of 3 equiv of Cl_3CCOCl over several hours to 13 equiv of Zn–Cu couple in refluxing ether gave the ten-membered thiolactone **4**,[6] 75–85% isolated. After dechlorination (Zn/HOAc, 85 °C) and OTBS cleavage (CH_3CN + aqueous HF, 20 °C), the desired acyl-transfer substrate **5** was obtained, 85% overall. Rearrangement of **5** to mercapto lactone **6**[6] occurred upon heating in 5:1 hexane:CH_2Cl_2 + anhydrous camphorsulfonic acid (48 h; 70% isolated yield).

The sequence leading to 14-membered lactones begins with α,α'-divinylthiane (**8**), available from **7** by Swern oxidation and Wittig reaction with $Ph_3P{=}CH_2$ (74% overall). Three-carbon ring expansion to **9** occurs under standard conditions[2] ($CF_3SO_3CH_2CO_2Et$, CH_3CN; DBU, 85% yield) and gives a mixture of diastereomers (Scheme II). After reduction ($LiAlH_4$) and OH protection (TBSCl + DMAP, DMF) two diastereomers of **10** are obtained in >85% yield. Either diastereomer reacts with dichloroketene under the same conditions as before to afford the 13-membered thiolactone **11**,[6] 74%.

Dechlorination and OTBS cleavage as before results in the desired acyl-transfer substrate **12**. This substance is more labile than is **5** and rearranges in excellent yield to **13**[6] (96%) upon treatment with $TSOH{\cdot}H_2O$ in CH_2Cl_2 at room temperature.

To apply this technique to the synthesis of naturally occurring macrolides, it is desirable to convert the –CHSH– group of the acyl-transfer product into a carbonyl group. As detailed elsewhere, this can be done under very mild conditions by a method involving the photochemical fragmentation of the derived phenacyl sulfide into a thioketone.[7] Thus, treatment of **13** with phenacyl bromide/$(i\text{-}C_3H_7)_2NC_2H_5$ followed by sunlamp irradiation in the presence of the highly reactive thioketone scavenger $CH_3CH{=}^+N(O^-)OTBS$[8] affords **14** (80%), the [2 + 3] cycloadduct of thione + nitronate ester. Cleavage to **15** occurs smoothly at room temperature upon reaction of **14** with $Et_3NH^+F^-$ in THF. The NMR spectrum of **15**[9] confirms the trans,trans olefin geometry, which results from the sigmatropic ring-expansion steps.[10] The photochemical oxidation sequence has also been applied to **6** and converts the mercaptan into the corresponding ketone in 40% overall (unoptimized) yield.

Our earlier studies demonstrated the synthesis of seven–ten-membered lactones via S to O acyl transfer.[3] The new results extend the generality of this process for contruction of 11- or 14-membered lactones. There is also good reason to believe that efficient sulfide ring expansion with dichloroketene is a general reaction.[11,12] Application of these concepts to more complex substrates is under investigation.

Acknowledgment. This work was supported by NSF Grant CHE-8113026.

(6) Spectral characterization. **4**: IR (neat, cm^{-1}) 1681; 200-MHz NMR ($CDCl_3$, δ) 5.81–5.35 (2 H, m, J_{AB} = 15.8 Hz by decoupling), 3.29 (1 H, br, s), 3.11 (1 H, dd, J = 13.4 Hz, 2.8 Hz), 2.91 (1 H, dd, J = 13.4 Hz, 9.6 Hz), 2.24–1.35 (6 H, complex), 0.85 (9 H, S), 0.03 (6 H, S); correct exact mass. **6**: IR (neat, cm^{-1}) 1730; 200-MHz NMR ($CDCl_3$) δ 5.39 (1 H, ddd, J = 15.3 Hz, 6.0 Hz, 4.8 Hz), 5.25 (1 H, ddd, J = 15.3 Hz, 9.2 Hz, 5.0 Hz), 4.47 (1 H, dd, J = 10.8 Hz, 3.4 Hz), 3.58 (1 H, dd, J = 10.8 Hz, 10.8 Hz), 2.83–1.73 (7 H, complex), 1.36 (S-H, br, d, J = 7.8 Hz); correct exact mass. **11**: IR (neat, cm^{-1}) 1695, 1676; partial 200-MHz ($CDCl_3$, δ) 5.59 (1 H, dt, J = 15.6 Hz, 6.7 Hz), 5.38 (1 H, dd, J = 15.6 Hz, 5.6 Hz), 5.35–5.10 (2 H, m), 3.77 (1 H, dd, J = 13.3 Hz, 7.0 Hz), 3.74 (1 H, dd, J = 13.3 Hz, 2.9 Hz); correct exact mass. **13**: IR (neat, cm^{-1}) 1735; partial 200-MHz NMR ($CDCl_3$, δ) 5.52–5.28 (4 H, complex), 4.33 (1 H, dd, J = 11.2 Hz, 3.4 Hz), 3.90 (1 H, dd, J = 11.2 Hz, 7.8 Hz), 3.09 (1 H, m, J = 8.4 Hz by decoupling), 1.62 (S-H, d, J = 8.4 Hz); correct exact mass.

(7) Vedejs, E.; Perry, D. A. *J. Org. Chem.* **1984**, *49*, 573.

(8) Calvin, E. W.; Beck, A. K.; Bastani, B.; Seebach, D.; Kai, Y.; Dunitz, J. D *Helv. Chim. Acta* **1980**, *63*, 697.

(9) Characterization of **9**: IR (neat, cm^{-1}) 1752, 1737, 1721; 200-MHz NMR ($CDCl_3$, δ) 5.63 (1 H, dtt, J = 15.4 Hz, 6.7 Hz, 1.5 Hz), 5.50 (1 H, dtt, J = 15.5 Hz, 5.3 Hz, 2.5 Hz), 5.41 (1 H, dtt, J = 15.5 Hz, 3.9 Hz, 2.5 Hz), 5.30 (1 H, dtt, J = 15.4 Hz, 6.7 Hz, 1.3 Hz), 4.53 (2 H, S), 3.20 (2 H, ddt, J = 6.7 Hz, 1.3 Hz, 1.2 Hz), 2.59–1.45 (10 H, complex); correct exact mass.

(10) Both the [2,3] and [3,3] sigmatropic ring expansions usually afford (*E*)-alkenes in rings of nine or more members; see ref 2 and 4.

(11) We have previously used the dichloroketene ring expansion to prepare analogues of the C_1–C_9 segment of erythronolide. This more complex system reacts smoothly under the optimized dilution conditions for ketene generation.

(12) For a related reaction, see: Rosini, G.; Spineti, G. G.; Foresti, E.; Pradella, G. *J. Org. Chem.* **1981**, *46*, 2228.

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