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HIGHLY STEREOSELECTIVE SYNTHESIS OF (Z)- OR (E)-DOUBLE BONDS WITH CONFORMATIONAL CONTROL IN [3,3]SIGMATROPIC RING EXPANSION OF 8-MEMBERED THIONOCARBONATES

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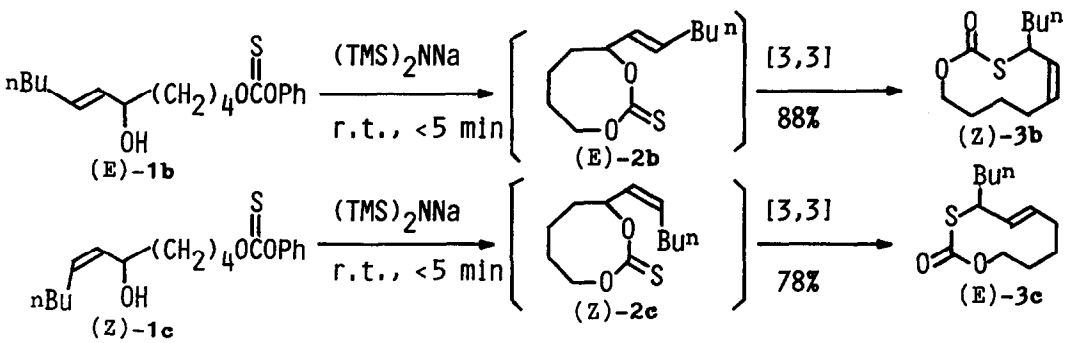
Summary: The highly stereoselective synthesis of (Z)- or (E)-double bonds in 10-membered thiolcarbonates was successfully conducted by controling the chairlike-boatlike transition states in the [3,3]sigmatropic rearrangement of 8-membered thionocarbonates.

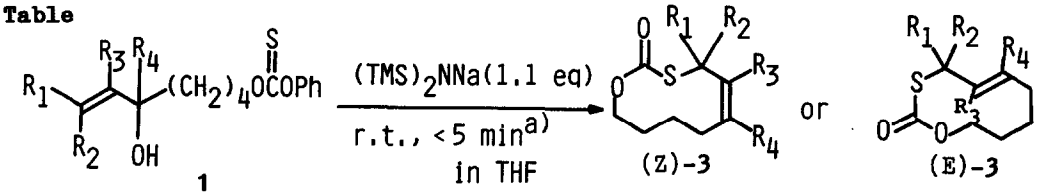
Exclusive (E)-selectivity of the created double bond by [3,3]sigmatropic rearrangement is extensively used in organic synthesis.[1] The strong preference for a chairlike conformation in the transition state for the rearrangement of acyclic systems serves as a basis for predicting product stereochemistry.[1a] The highly stereoselective synthesis of (Z)[2]- or (E)-double bonds in 10-membered thiolcarbonates **3** was achieved in this study by controling chairlike-boatlike transition states in the [3,3]sigmatropic rearrangement of 8-membered thionocarbonates **2**.



The treatment of a diol monothionocarbonate **1a** with sodium bis-(trimethylsilyl)amide [$(TMS)_2NNa$] results in the formation of an 8-membered thionocarbonate intermediate **2** followed by spontaneous [3,3]sigmatropic ring expansion to give the 10-membered thiolcarbonate **3a** containing a (Z)-double bond[2] (Table, run 1) and also, the relationship between the ring size

of cyclic thionocarbonates and geometry of the created double bond has been clarified.[3,4] In this context, the relationship between a substituent pattern in the allylic system of substrate **1** and product geometry was also determined. The results are summarized in Table. Reaction[5] of **1b** having a n-butyl group at the R_1 position with $(TMS)_2NNa$[4] instantly gave a (Z)-10-membered thiolcarbonate **3b**[6] in 88% yield (run 2).[7] Capillary GLC analysis[8] showed **3b** to have 100% isomeric purity. Examination of **3b** by ^{1}H-NMR after derivatization to the corresponding allylic thiolcarbamate **4b**[9] [^{1}H-NMR ($CDCl_3$) δ 5.28 (t, 11.0 Hz), 5.43 (ddd, 11.0, 8.2, 7.1 Hz)] indicated **3b** to possibly be the (Z)-isomer. The same treatment of **1c** (R_2=n-butyl) provided (E)-**3c** with 100% isomeric purity[8] and its ^{1}H-NMR[10] spectrum showed the presence of the (E)-double bond [($CDCl_3$) δ 5.48 (ddd, 15.3, 11.8, 3.5 Hz), 5.13 (ddd, 15.3, 10.0, 1.8 Hz)](run 3).

Table



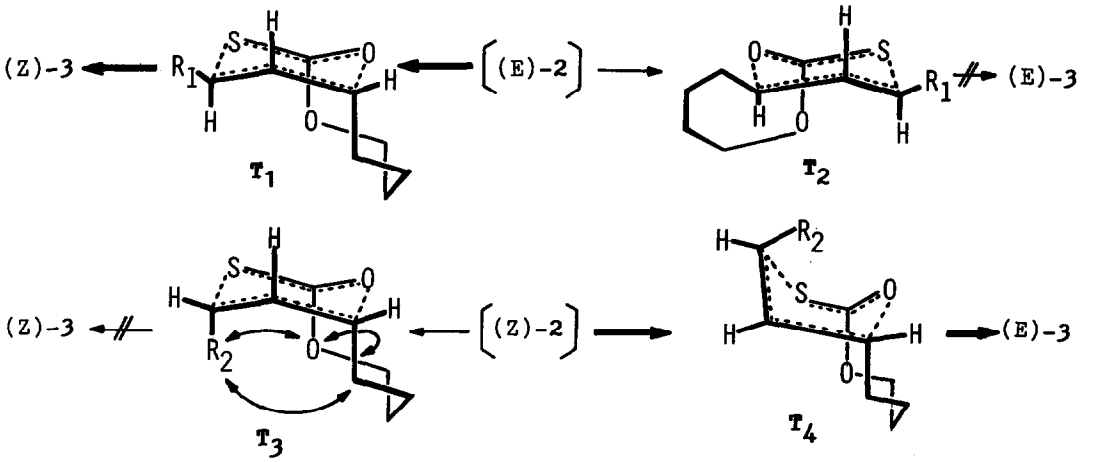
Run	1n[b]	R^1	R^2	R^3	R^4	T.S.[c]	Product[f]	Yield (%)[h]
1	**1a**	H	H	H	H	C[d]	(Z)-**3a**	78[i]
2	**1b**	nC_4H_9	H	H	H	C	(Z)-**3b**	88
3	**1c**	H	nC_4H_9	H	H	B[e]	(E)-**3c**	78
4	**1d**	CH_3	H	H	H	C	(Z)-**3d**[g]	58
5	**1e**	H	CH_3	H	H	B	(E)-**3e**[g]	60
6	**1f**	H	H	CH_3	H	C	(Z)-**3f**	74
7	**1g**	H	H	H	CH_3	C	(Z)-**3g**	76[j]
8	**1h**	CH_3	CH_3	H	H	B	(E)-**3h**	65
9	**1i**	nC_4H_9	H	H	CH_3	C	(Z)-**3i**	77

a) Unless otherwise stated, the reactions were carried out according to reference 5. b) see reference 4. c) T.S.: Transition State. d) C: Chairlike Transition State. e) B: Boat-like Transition State. f) Unless otherwise stated, complete isomeric purity was determined by ^{1}H-NMR and capillary GLC analysis.[8] g) Isomeric purity was determined by GLC analysis after conversion to the corresponding allylic thiolcarbamate **4**.[3,9] h) Isolated yield of purified product. i) See references 3 and 4. j) $(TMS)_2NK$ (1.0 eq.) was used under 10^{-1}M condition.

Substrates **1d** and **1e**, each a methyl group instead of a n-butyl group at the R_1 and R_2 positions similarly afforded isomeric pairs of (Z)-**3d** and (E)-**3e** in 58% and 60% yields, respectively (runs 4 and 5). Interestingly, it is thus evident that the respective olefin geometry in the starting materials is converted to the opposite geometry with complete isomeric purity. In runs

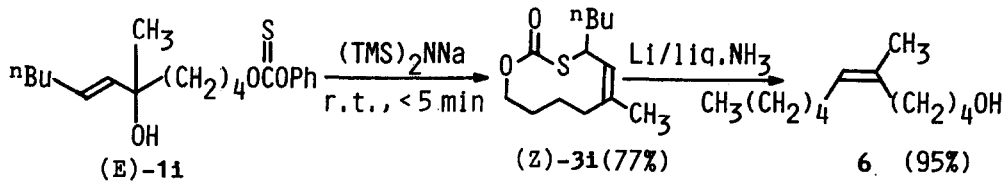
6 (R_3=CH_3) and 7 (R_4=CH_3), the reactions proceeded in the same manner to give only (Z)-isomers (**3f** and **3g**) as **1a**. The substrate **1h**, in which the R_1 and R_2 positions were occupied by methyl groups, gave only (E)-**3h** (run 8), as expected. Consequently, the geometry of the product appears to be highly dependent on the substituent pattern in the allylic system of the substrates. It should also be noted that each reaction provided a (Z)- or (E)-double bond with geometric integrity in 10-membered thiolcarbonates.

The (Z) selectivity in the R_1 substituted examples (runs 2 and 4) can be explained by the chairlike transition state (T_1)[3,4] which disposes a pseudo-1,3-diaxial interaction rather than the more strained transition



state (T_2) that would lead to (E)-3. Such an rearrangement via transition state (T_2) has been shown to occur only when cyclic thionocarbonate is 9-membered or larger.[4] With **1f** and **1g** (R_3=CH_3 or R_4=CH_3), the geometry may be explained on the basis of the transition state (T_1) (runs 6 and 7). The substrate (runs 3,5 and 8) bearing an R_2 substituent rearranges exclusively to give an (E)-isomer through a boatlike transition state (T_4),[1a] since the chairlike transition state (T_3) would have severe pseudo-1,3-diaxial interactions leading to the opposite geometry.

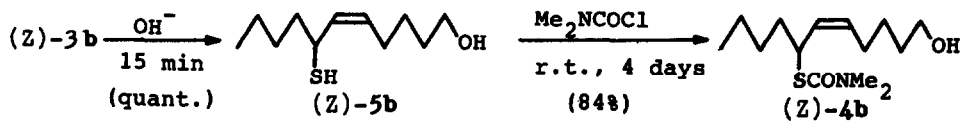
The hydrolysis[3,9] of (Z)-3 or (E)-3 obtained above with sodium hydroxide in aqueous methanol at room temperature gave (Z)- or (E)-allylic thiols 5 with liberation of carbon dioxide in quantitative yields. Treatment of (E)-**1i** having two alkyl groups with $(TMS)_2NNa$ afforded (Z)-**3i** in 77% yield (run 9). Subsequent treatment of (Z)-**3i** with lithium in liquid ammonia readily gave a (Z)-trisubstituted olefin **6** (95%) with a versatile alcohol function at the terminal position with a 95% retention of the stereochemistry. The reductive desulfurization of (Z)-**3i** obviously indicates the possible synthetic use of the present method for producing (Z)-alkenol sex pheromones.[11]



(E)-1i (Z)-3i(77%) 6 (95%)

References and Notes

1. a) F.E.Ziegler, Chem.Rev., **88**, 1423 (1988); b) S.Blechert, Synthesis, **1989**, 71.
2. For (Z)-selectivity in the [3,3]sigmatropic rearrangement; K.Nonoshita, H.Banno, K.Maruoka and H.Yamamoto, J.Am.Chem.Soc., **112**, 316 (1990).
3. S.Harusawa, T.Kurokawa, H.Fujii, R.Yoneda and T.Kurihara, Chem.Pharm. Bull., **37**, 2567 (1989).
4. S.Harusawa, H.Fujii, H.Osaki, R.Yoneda and T.Kurihara, Chem.Pharm. Bull. submitted.
5. To a dry THF (50 ml, 10^{-2}M) solution of 1 (0.5 mM) was added rapidly a 1M THF solution of $(TMS)_2NNa$ (0.55 ml) at room temperature under N_2. The reaction went to completion instantly. The ordinary workup and purification on silica gel gave pure 3 and trace amounts of dimeric product.
6. **3b**: ^{1}H-NMR (δ in $CDCl_3$) 0.89 (3H, t, 7.5 Hz), 1.17-1.82 (10H, br), 2.05 (1H, br d, 11.0 Hz), 2.62 (1H, br q, 11.0 Hz), 3.76 (1H, ddd, 11.8, 6.5, 4.2 Hz), 4.26 (1H, q, 10.0 Hz), 4.95 (1H, dt, 11.8, 3.5 Hz), 5.20-5.40 (2H, m).
7. Refluxing of 6-heptene-1,5-diol with 1,1'-thiocarbonyldi-2,2'-pyridone (1.1 eq) in toluene for 15 h afforded (Z)-**3b** and (E)-**3b** at a ratio of 82:18 in 53% yield (reference 4).
8. Capillary GLC analyses were carried out using a FS-WCOT OV-1701 column (0.25 mm i.d. x 25 m, programmed at 80-210 °C, 5 °C/min).
9. (Z)-**3b** was converted to the (Z)-**4b** according to the reference 3.



10. **3c**: ^{1}H-NMR (δ in $CDCl_3$) 0.89 (3H, t, 7.5 Hz), 1.18-1.60 (8H, br), 1.70-2.02 (3H, br), 2.22-2.38 (1H, br), 3.59 (1H, td, 11.8, 2.0 Hz), 3.87 (1H, dt, 10.0, 7.6 Hz), 5.01 (1H, dd, 11.8, 5.9 Hz), 5.13 (1H, ddd, 15.3, 10.0, 1.8 Hz), 5.48 (1H, ddd, 15.3, 11.8, 3.5 Hz).
11. K.Mori, "The Total Synthesis of Natural Products," Vol. 4, John Wiley & Sons, New York, 1981, p.1.

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