[3,3]Sigmatropic Ring Expansion of Cyclic Thionocarbonates. VI.[1] Regioselective Wohl-Ziegler Bromination of 10-Membered Thiolcarbonates

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Wohl-Ziegler bromination of 10-membered thiolcarbonates (3) gave regioselectively 7-bromocyclic thiolcarbonates (4). The structure of 4a was unambiguously established by an X-ray crystallographic analysis.

Keywords [3,3]sigmatropic ring expansion; 10-membered thiolcarbonate; Wohl-Ziegler bromination; cyclic thionocarbonate; sodium bis(trimethylsilyl)amide; X-ray analysis

We have reported that treatment of diol monothionocarbonates (**1**) having an (*E*)-double bond with lithium[1] or sodium bis(trimethylsilyl)amide results in the formation of 8-membered thionocarbonates (**2**) followed by spontaneous [3,3]sigmatropic rearrangements to give 10-membered thiolcarbonates (**3**) containing a (*Z*)-double bond.[2a–d]

We have examined the applicability of 10-membered thiolcarbonates (**3**) in organic synthesis, and have found that they are easily converted into (*Z*)-allylic sulfides[2a,d] or (*Z*)-trisubstituted olefins.[2b] Further, the sexual pheromone of yellow scale insect, (*E*)-6-isopropyl-3,9-dimethyl-5,8-decadienyl acetate, has been successfully synthesized by the [3,3]sigmatropic ring expansion of 8-membered thionocarbonates and these reactions.[1]

Dauben and McCoy[3] demonstrated that the mechanism of Wohl-Ziegler bromination[4] was of the free-radical type. On the othe hand, it is known that a divalent sulfur atom stabilizes a radical on a carbon atom adjacent to the sulfur atom.[5] Therefore, we anticipated that a Wohl-Ziegler bromination of 10-membered thiolcarbonate (**3a**) would proceed to give the 4-brominated product (**5a**), which would be useful as a substrate for introduction of alkyl substituents at C_4.[2b] We wish to report here on the regioselective bromination of 10-membered thiolcarbonates (**3**).

When the 10-membered thiolcarbonate (**3a**) (R=H) was allowed to react with *N*-bromosuccinimide (NBS) in the presence of dibenzoyl peroxide in refluxing carbon tetrachloride (CCl_4) for 2 h, the Wohl-Ziegler bromination proceeded smoothly to give a bromide (**4a**) as stable crystals in 85% yield, as a single product.

Assignment of the proton nuclear magnetic resonance (^{1}H-NMR) signals of **4a** was performed on the basis of decoupling experiments as follows. Irradiation of overlapped vinyl protons at δ 5.6 led to the variation of peaks

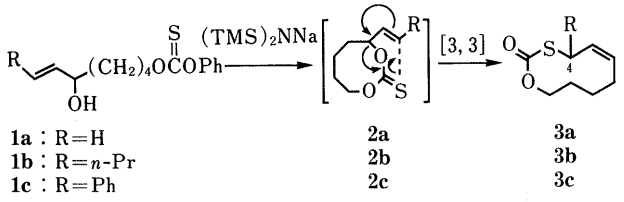

Chart 1

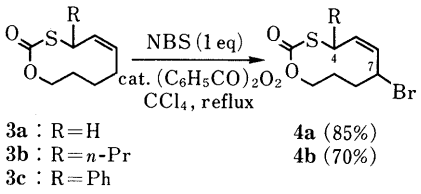

Chart 2

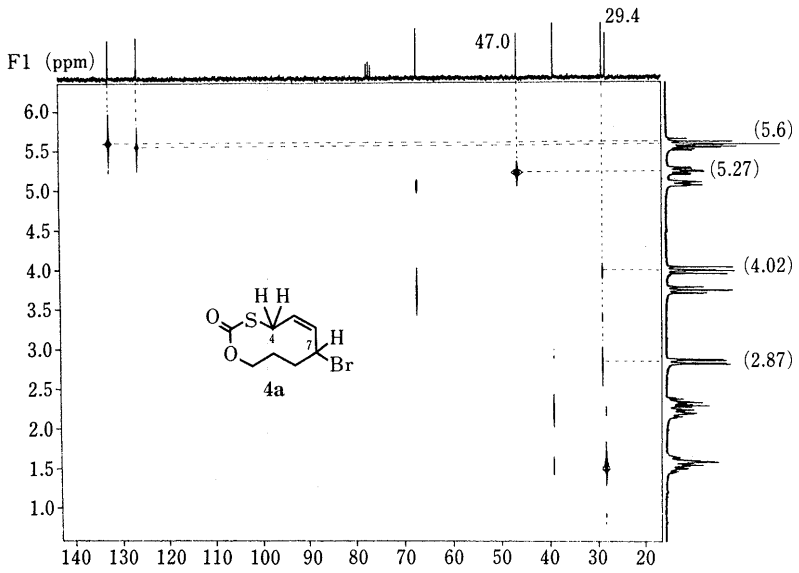

Fig. 1. ^{1}H–^{13}C Shift-Correlated 2-D NMR Spectrum of **4a** ($CDCl_3$)

at δ 2.87, 4.02 and 5.27, indicating these signals to be due to the three allylic protons at C_4 and C_7. The ^1H–^{13}C shift-correlated two dimensional NMR (2-D NMR) spectrum of **4a** showed that the sextet signal (J=10.5, 10.5 and 5.0 Hz) at δ 5.27 in the ^1H-NMR spectrum was correlated to a carbon resonance in the carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum at δ 47.0. The other peaks (δ 2.87 and 4.02) of the ^1H-NMR spectrum were correlated to a carbon resonance at δ 29.4 in the ^{13}C-NMR spectrum. Accordingly, the peak of δ 5.27 was assignable to the proton signal of >CHBr. However, the position of the bromine atom in the 10-membered ring still remained undetermined. Thus, the structure of **4a** was finally confirmed as (*Z*)-7-bromo-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one by an X-ray crystallographic analysis. A perspective view and Corey-Pauling-Koltun (CPK) molecular model are depicted in Fig. 2.

Conformational studies on cyclodecane and its simple derivatives have been reported[6] and these molecules predominantly have a boat-chair-boat conformation. In the case of **4a**, a distorted boat–chair–boat conformation is adopted in the solid state.

To investigate the regioselectivity of Wohl-Ziegler bromination of the 10-membered thiolcarbonates, **3b** and **3c** with a propyl or a phenyl group on C_4 were prepared according to the reported procedure.[2b,d] Wohl-Ziegler bromination of **3b** exclusively afforded a 7-bromo derivative (**4b**)[7] in 70% yield under similar conditions. The position of the bromo substituent in this case was easily determined from the ^1H-NMR spectrum (see Experimental). However, a similar treatment of **3c** with NBS in refluxing CCl_4 in the presence of dibenzoyl peroxide gave none of the desired brominated product, with only decomposed materials being obtained.

It is well known that sulfur and bromine atoms both have a large van der Waals radius (S: 1.65—2.09 A, Br: 1.78—1.92 A).[8] Actually, a marked steric crowding round about C_4 was observed by inspection of the CPK model of the 4-bromo compound (**5a**). Therefore, Wohl-Ziegler bromination of **3a,b** presumably proceeds *via* initial formation of radical intermediates, which exist in equilibrium with each other, followed by bromination to give the sterically unhindered 7-bromo derivatives (**4a,b**) (Fig. 3). However, we can not explain why a brominated product was not obtained in the case of **3c**.

In summary, the above results indicate that the regioselective bromination at the C_7-position of **3** is mainly due to the unique structure of the 10-membered thiolcarbonate and the radical stabilization by sulfur atom in these compounds is negligibly small.

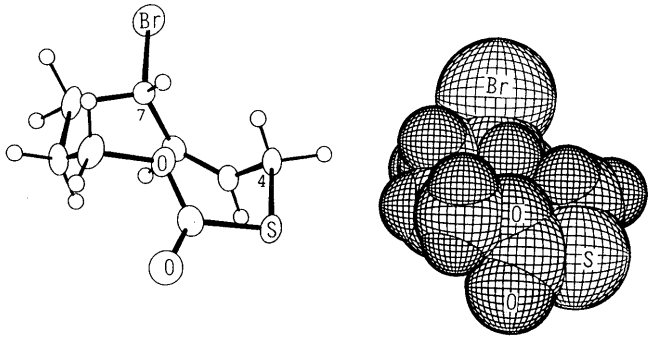

Fig. 2. Perspective View and CPK Molecular Model for **4a**

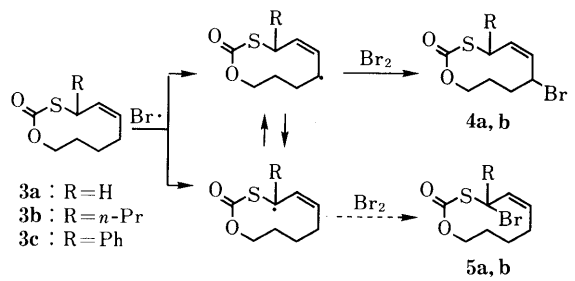

Fig. 3

Experimental

All melting points were measured on a Yanagimoto apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Shimadzu IR-435 spectrophotometer. ^1H- and ^{13}C-NMR spectra were taken with tetramethylsilane as an internal standard on a Varian Gemini-200 spectrometer in $CDCl_3$. Low-resolution (MS) and high-resolution mass spectra (HRMS) were obtained on a Hitachi M-80 instrument. Capillary gas liquid chromatography (GLC) analysis was carried out using an FS-WCOT OV-1701 column (0.25 mm i.d. × 25 m, programed at 120—220 °C, 4 °C/min). All reactions were carried out under a nitrogen atmosphere. For column chromatography, SiO_2 (Merck 9385) was used.

***O*-[(*E*)-5-Hydroxy-6-decenyl] *O*-Phenyl Thionocarbonate (1b)** A 1.7 M solution of *tert*-butyllithium (1.50 ml, 2.53 mM) in pentane was added to a solution of *trans*-1-iodo-1-pentene[9] (495 mg, 2.53 mM) in ether (5 ml) at −78 °C under argon. The reaction mixture was stirred for 0.5 h at the same temperature. *O*-4-Formylbutyl *O*-phenyl thionocarbonate[2d] (401 mg, 1.68 mM) in ether (5 ml) was added, and the reaction mixture was stirred at −78 °C for 0.5 h then at −20 °C for 0.5 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride. The ether solution was separated, dried over anhydrous $MgSO_4$, and evaporated *in vacuo*. The residue was purified by column chromatography (5% EtOAc in hexane) to give **1b** (274 mg, 53%) as an oil. IR ν_{max}^{film} cm^{-1}: 3400 (OH). ^1H-NMR δ: 0.89 (3H, t, J=7.3 Hz, CH_3), 1.16—1.70 (6H, br, 3 × CH_2), 1.83 (2H, quint, J=6.8 Hz, $C\underline{H}_2CH_2O$), 2.00 (2H, q, J=6.7 Hz, =$CHC\underline{H}_2$), 4.06 (1H, br, $C\underline{H}OH$), 4.51 (2H, t, J=6.5 Hz, CH_2O), 5.44 (1H, dd, J=15.3, 6.9 Hz, =$C\underline{H}CHOH$), 5.64 (1H, dt, J=15.3, 6.5 Hz, =$CHCH_2$), 7.02—7.48 (5H, m, ArH). MS *m/z*: 291 (M^+−OH). HRMS Calcd for $C_{17}H_{23}O_2S$: 291.1417. Found: 291.1411 (M^+−OH).

***O*-[(*E*)-5-Hydroxy-7-phenyl-6-heptenyl] *O*-Phenyl Thionocarbonate (1c)** A 1.6 M solution of *n*-butyllithium in hexane (0.75 ml, 1.2 mM) was added to a solution of (*E*)-β-styryltributyltin[10] in tetrahydrofuran (THF) (4 ml) at −78 °C. The generated wine-red solution was stirred for 0.5 h. *O*-4-Formylbutyl *O*-phenyl thionocarbonate[2d] (238 mg, 1 mM) in THF (3 ml) was added to the solution. The reaction was subsequently quenched by the addition of H_2O. The THF was evaporated off to give a residue, which was extracted with EtOAc–hexane (1 : 1). The extract was washed with H_2O and brine, dried over anhydrous Na_2SO_4 and then evaporated *in vacuo*. The residue was purified by column chromatography (18% EtOAc in hexane) to give **1c** (231 mg, 68%) as an oil. IR ν_{max}^{film} cm^{-1}: 1590 (C=C). ^1H-NMR δ: 1.48—1.97 (6H, br, 3 × CH_2), 4.31 (1H, br, $C\underline{H}OH$), 4.53 (2H, t, J=7.0 Hz, CH_2O), 6.20 (1H, dd, J=16.0, 7.0 Hz, =$C\underline{H}CH$), 6.59 (1H, d, J=16.0 Hz, $ArCH$=), 7.01—7.47 (10H, m, ArH). MS *m/z*: 325 (M^+−OH). HRMS Calcd for $C_{20}H_{21}O_2S$: 325.1261. Found: 325.1250 (M^+−OH).

***(Z)*-4-*n*-Propyl-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (3b)** A 1 M solution of $(TMS)_2NNa$ in THF (0.39 ml, 0.39 mM) was added rapidly to a solution of **1b** (111 mg, 0.36 mM) in THF (36 ml) at room temperature, and the mixture was stirred for 5 min. The reaction was quenched by the addition of H_2O and the solvent was evaporated under reduced pressure. The residue was extracted with EtOAc–hexane (1 : 1) and the extract was washed with H_2O and brine, dried over anhydrous Na_2SO_4 and then evaporated *in vacuo*. The residual oil was purified by column chromatography (5% EtOAc in hexane) to give **3b** (56 mg, 73%) as an oil. IR ν_{max}^{film} cm^{-1}: 1685 (C=O), 775. ^1H-NMR δ: 0.86 (3H, t, J=7.0 Hz, CH_3), 1.23—1.84 (8H, br, 4 × CH_2), 2.04 (1H, br d, J=13.9 Hz, =$CHC\underline{H}_aH_b$), 2.61 (1H, qt, J=10.8, 3.7 Hz, =$CHCH_a\underline{H}_b$), 3.75 (1H, ddd, J=11.7, 6.7, 5.0 Hz, $OC\underline{H}_aH_b$), 4.27 (1H, q, J=8.3 Hz, SCH), 4.93 (1H, dt, J=11.7,

3.8 Hz, OCH_aH_b), 5.19—5.39 (2H, m, CH=CH). MS *m/z*: 214 (M^+). HRMS Calcd for $C_{11}H_{18}O_2S$: 214.1026. Found: 214.1027. Capillary GLC analysis: t_R = 13.6 min.

(*Z*)-4-Phenyl-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (3c) A 1.0 M solution of $(TMS)_2NNa$ (0.58 ml, 0.58 mM) in THF was added to a solution of **1c** (200 mg, 0.58 mM) in THF (58 ml) at room temperature. The ordinary work-up followed by purification by column chromatography (5% EtOAc in hexane) afforded **3c** (73 mg, 50%) as a solid. Recrystallization from MeOH gave colorless pillars, mp 98—99 °C. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1680 (C=O). ^{1}H-NMR δ: 1.58—1.88 (4H, br, 2×CH_2), 2.05—2.21 (1H, br d, J=15.0 Hz, =CHCH_aH_b), 2.78 (1H, br q, J=15.0 Hz, =CHCH_aH_b), 3.87 (1H, ddd, J=11.0, 7.0, 5.0 Hz, OCH_aH_b), 4.97—5.17 (1H, m, OCH_aH_b), 5.39 (1H, td, J=11.0, 3.2 Hz, =CHCH_2), 5.51 (1H, d, J=11.0 Hz, SCH), 5.91 (1H, td, J=11.0, 2.2 Hz, =CHCHS), 7.22—7.41 (5H, m, ArH). MS *m/z*: 248 (M^+). *Anal.* Calcd for $C_{14}H_{16}O_2S$: C, 67.71; H, 6.49. Found: C, 67.48; H, 6.47.

(*Z*)-7-Bromo-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (4a) A mixture of **3a** (244 mg, 1.42 mM), NBS (267 mg, 1.50 mM) and dibenzoyl peroxide (5 mg, 0.02 mM) in CCl_4 (20 ml) was refluxed for 2 h. After cooling, the insoluble material was fitered off and the filtrate was evaporated under reduced pressure to give a residue. Flash chromatography (10% EtOAc in hexane) gave **4a** (304 mg, 85%). Recrystallization from MeOH gave colorless prisms, mp 118—120 °C. IR ν_{max}^{Nujol} cm^{-1}: 1685 (C=O), 1220, 1130, 992. ^{1}H-NMR δ: 1.62 (2H, m, CH_2), 2.30 (2H, m, CH_2), 2.87 (1H, dd, J=12.5, 4.0 Hz, SCH_aH_b), 3.78 (1H, ddd, J=10.0, 10.0, 3.0 Hz, OCH_aH_b), 4.02 (1H, dd, J=12.5, 11.0 Hz, SCH_aH_b), 5.13 (1H, dt, J=10.0, 3.0 Hz, OCH_aH_b), 5.27 (1H, ddd, J=10.5, 10.5, 5.0 Hz, CHBr), 5.62 (2H, m, CH=CH). ^{13}C-NMR δ: 28.6, 29.4, 39.6, 47.0, 67.7, 126.8, 133.0, 168.8. MS *m/z*: 251 (M^++1). HRMS Calcd for $C_8H_{11}BrO_2S$: 249.9663. Found: 249.9652. *Anal.* Calcd for $C_8H_{11}BrO_2S$: C, 38.26; H, 4.42. Found: C, 38.20; H, 4.43.

(*Z*)-7-Bromo-4-*n*-propyl-7,8,9,10-tetrahydro-4*H*-1,3-oxathiecin-2-one (4b) A solution of **3b** (27 mg, 0.13 mM) in CCl_4 (2 ml) was refluxed with NBS (22 mg, 0.13 mM) and dibenzoyl peroxide (1 mg) for 3 h. The ordinary work-up gave **4b** (26 mg, 70%) as an oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1685 (C=O). ^{1}H-NMR δ: 0.95 (3H, t, J=7.0 Hz, CH_3), 1.19—1.72 (6H, br, CH_2×3), 2.10—2.44 (2H, br, CH_2CHBr), 3.73 (2H, m, OCH_aH_b), 4.22 (1H, ddd, J=10.8, 8.6, 5.7 Hz, SCH), 5.10 (1H, dt, J=11.1, 3.2 Hz, OCH_aH_b), 5.22 (1H, td, J=11.4, 4.8 Hz, CHBr), 5.34 (1H, t, J=10.8 Hz, SCHCH=), 5.56 (1H, t, J=10.8 Hz, BrCHCH=). ^{13}C-NMR δ: 13.6, 20.5, 28.4, 34.4, 39.2, 43.3, 47.2, 67.1, 130.7, 132.4, 169.7. MS *m/z*: 294 (M^+). HRMS Calcd for $C_{11}H_{17}BrO_2S$: 294.0112. Found: 294.0111.

X-Ray Structure Determination of the 4a Transparent, colorless, plate-like crystals were obtained from MeOH solution. Crystal data: $C_8H_{11}BrO_2S$, monoclinic, space group $P2_{1/n}$ a=13.035 (6), b=7.1999 (9), c=10.873 (3) A, β=105.35 (3)°, V=983.1 (5) A^3, Z=4, D_c=1.698 g cm^{-3}, μ=(CuK_α)=73.94 cm^{-1}, F(ooo)=504. In total, 1685 independent observed reflections [$(F^2>2\sigma(F^2)$] were measured on a Rigaku AFC automatic four-circle diffractometer using graphite-monochromated CuK_α radiation (λ=1.5418). Observed data were corrected for Lorentz and polarization effects. The structure was solved by the direct method using the program MULTAN 87. Anisotropic refinement was carried out for nonhydrogen atoms. Ideal positions of hydrogen atoms were calculated and included only for the calculation of structure factors. The final R value is 0.079.

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References and Notes

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