mL) at ambient temperature, and the resulting solution was stirred for 4 h. The reaction mixture was poured into ice–water, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Filtration followed by concentration gave a crude product, which was subjected to column chromatography (silica gel/hexane–ethyl acetate 20:1) to give **5a** (0.13 g) in 76% yield.

2-(Phenylthio)butane (5a): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 1.02 (t, J = 6 Hz, 3 H), 1.29 (d, J = 6 Hz, 3 H), 1.34–1.82 (m, 2 H), 3.20 (m, J = 6 Hz, 1 H), 7.20–7.50 (m, 5 H).

1-Phenyl-2-(phenylthio)propane (5b): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 1.27 (d, J = 6 Hz, 3 H), 2.60 (ABX, J = 8 Hz, 14 Hz, 1 H), 3.02 (ABX, J = 5 Hz, 14 Hz, 1 H), 3.24–3.68 (m, 1 H), 7.04–7.72 (m, 10 H); MS, m/z (M^+) calcd for $C_{15}H_{16}S$ 228.0973, found 228.0972.

2-Methyl-1-(phenylthio)propane (6c): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 1.02 (d, J = 7 Hz, 6 H), 1.86 (m, J = 6 Hz, 1 H), 2.79 (d, J = 7 Hz, 2 H), 6.96–7.68 (m, 5 H).

2-Methyl-1-(phenylthio)butane (6d): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 1.00 (t, J = 7 Hz, 6 H), 1.48–2.00 (m, 3 H), 2.82 (dd, J = 8 Hz, 12 Hz, 1 H), 2.94 (dd, J = 6 Hz, 12 Hz, 1 H), 7.16–7.44 (m, 5 H); MS, m/z (M^+) 180.

2-Methyl-1-(phenylthio)octane (6e): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 1.00–1.90 (m, 17 H), 2.56–3.04 (m, 2 H), 7.54–7.74 (m, 5 H); MS, m/z (M^+) calcd for $C_{15}H_{24}S$ 236.1599, found 236.1594.

[(Phenylthio)methyl]cyclopentane (6f): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 0.66–2.24 (m, 11 H), 2.71 (d, J = 6 Hz, 2 H), 7.00–7.38 (m, 5 H).

Intramolecular Friedel–Crafts Reaction of 7. The following procedure for the preparation of **8a** is representative. Under argon atmosphere, $SnCl_4$ (0.28 mL, 2.40 mmol) was added to a solution of **7a** (0.31 g, 1.03 mmol) in CH_2Cl_2 (5 mL), and the resulting solution was stirred for 6 h at ambient temperature. The reaction mixture was poured into ice–water, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Filtration followed by concentration gave a crude product, which was subjected to column chromatography (silica gel/hexane–ethyl acetate 20:1) to give **8a** (0.20 g) in 76% yield as colorless liquid. The ratio of *trans*-**8a**/*cis*-**8a** was found to be 58/42 (from *anti*-**7a**/*syn*-**7a** = 51/49) or 95/5 (from *anti*-**7a**/*syn*-**7a** = 88/12) by GLC analyses.

1-Methyl-2-(phenylthio)-1,2,3,4-tetrahydronaphthalene (8a): ^1H NMR (100 MHz, $CDCl_3$) δ for *trans*-**8a** 1.40 (d, J = 7 Hz, 3 H), 3.23–3.50 (m, 1 H); δ for *cis*-**8a** 1.27 (d, J = 7 Hz, 3 H for *cis*-**8a**), 3.60 (m, 1 H for *cis*-**8a**); the following signals were observed in both isomers: 1.63–2.38 (m, 2 H), 2.48–3.20 (m, 3 H), 7.04–7.50 (m, 9 H); MS, m/z (M^+) calcd for $C_{17}H_{18}S$ 254.1129, found 254.1152.

Other **8** were prepared in the same way. Physical and spectral data are summarized.

6,7-Dimethoxy-1-methyl-2-(phenylthio)-1,2,3,4-tetrahydronaphthalene (8b): liquid; ^1H NMR (100 MHz, $CDCl_3$) δ for *trans*-**8b** 1.39 (d, J = 7 Hz, 3 H); δ for *cis*-**8b** 1.27 (d, J = 7 Hz, 3 H); the following signals were observed in both isomers: 1.65–2.32 (m, 2 H), 2.50–3.18 (m, 3 H), 3.28–4.05 (m, 1 H), 3.87 (s, 6 H), 6.55 (s, 1 H), 6.61 (s, 1 H), 7.00–7.50 (m, 5 H); IR 1260, 1520 cm^{-1}; MS, m/z (M^+) calcd for $C_{19}H_{22}O_2S$ 314.1340, found 314.1291; trans/cis = 48/52 (HPLC).

***trans*-6,7-Dimethoxy-1-phenyl-2-(phenylthio)-1,2,3,4-tetrahydronaphthalene (*trans*-8c)**: yellow liquid. These *trans*- and *cis*-**8c** were separated by column chromatography; ^1H NMR (100 MHz, $CDCl_3$) δ 1.65–2.20 (m, 2 H), 2.70–3.10 (m, 2 H), 3.60–3.80 (m, 1 H), 3.66 (s, 3 H), 3.86 (s, 3 H), 4.14 (d, J = 4 Hz, 1 H), 6.26 (s, 1 H), 6.60 (s, 1 H), 6.94–7.42 (m, 10 H); IR 1260, 1500 cm^{-1}.

***cis*-6,7-Dimethoxy-1-phenyl-2-(phenylthio)-1,2,3,4-tetrahydronaphthalene (*cis*-8c)**: yellow liquid; ^1H NMR (100 MHz, $CDCl_3$) δ 1.84–2.10 (m, 2 H), 2.80–3.00 (m, 2 H), 3.60–3.80 (m, 1 H), 3.66 (s, 3 H), 3.86 (s, 3 H), 4.40 (d, J = 3 Hz, 1 H), 6.36 (s, 1 H), 6.60 (s, 1 H), 7.00–7.36 (m, 10 H); IR 1260, 1500 cm^{-1}; MS, m/z (M^+) calcd for $C_{24}H_{24}O_2S$ 376.1497, found 376.1513.

6,7-Dimethoxy-1-(3′-oxobutyl)-2-(phenylthio)-1,2,3,4-tetrahydronaphthalene (8d): yellow liquid; 1H NMR (100 MHz, $CDCl_3$) δ 2.08 (s, 3 H), 2.36–3.05 (m, 10 H), 3.82 (s), 3.90 (s), 3.96 (s), 6.84 (s, 1 H), 7.00 (s, 1 H), 7.05–7.44 (m, 5 H); IR 1260, 1510, 1710 cm^{-1}; MS, m/z (M^+) calcd for $C_{22}H_{26}O_3S$ 370.1603, found 370.1601.

Reaction of 9 with Lewis Acid. To a solution of **9** (0.17 g, 0.56 mmol) in CH_2Cl_2 (5 mL) was added $SnCl_4$ (0.16 mL, 1.37 mmol), and the resulting solution was stirred for 6 h at room temperature. The usual workup followed by column chromatography gave **8a** (0.07 g) in 49% yield.

Reaction of 21 with $AlCl_3$ and Allyltrimethylsilane. A mixture of *trans*-**21** (434 mg, 1.83 mmol), allyltrimethylsilane (995 mg, 8.72 mmol), and powdered $AlCl_3$ (564 mg, 4.23 mmol) in 10 mL of CH_2Cl_2 was refluxed for 1 h. The reaction mixture was poured into ice–water, and the aqueous layer was extracted with CH_2Cl_2 three times. The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. Filtration followed by concentration gave a crude product, which was subjected to column chromatography (silica gel/hexane–ethyl acetate 20:1) to give *trans*-**3o** (230 mg) in 54% yield as colorless liquid: ^1H NMR (250 MHz, $CDCl_3$) δ 1.05–2.15 (m, 10 H), 2.63–2.70 (m, 1 H), 2.80 (dt, J = 3.67 Hz, 10.4 Hz, 1 H), 5.03 (d, J = 8.5 Hz, 1 H), 5.06 (d, J = 18 Hz, 1 H), 5.71–5.88 (m, 1 H), 7.15–7.47 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 25.51, 26.47, 31.81, 34.33, 38.60, 41.63, 52.08, 116.48, 126.71, 128.73, 132.47, 136.45; MS, m/z (M^+) calcd for $C_{15}H_{20}S$ 232.1286, found 232.1208.

Methoxy(phenylthio)(trimethylsilyl)methane as a One-Carbon Homologation Reagent: Efficient 1,4-Addition of a Formyl or a Carboxy Anion Equivalent to Cyclic α-Enones Concomitant with in Situ α-Alkylation

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Efficient 1,4-addition of a formyl and carboxy anion equivalent is realized by use of [methoxy(phenylthio)(trimethylsilyl)methyl]lithium. Of further synthetic value is consecutive α-alkylation by in situ trapping of intermediary enolates with various alkyl halides. The reaction proceeds highly regioselectively, thus no α'-isomers are formed, and highly stereoselectively, thus trans α,β-dialkylation products of more than 95% purity are formed. The unique selectivity is ascribed to chelation by the proximate methoxy group to the lithium. The new method is applied to sarkomycin synthesis.

Introduction

The 1,4-addition of acyl anion equivalents to α,β-unsaturated systems has received extensive attention on account of facile accessibility to 1,4-dicarbonyl compounds. In particular, sulfur-stabilized reagents played a central role in this field.[1] Nevertheless, there appeared a limited

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number of formyl anion equivalents, the simplest form among the above class of equivalents. The formyl group is synthetically promising because it undergoes various carbon–carbon bond formations was well as functional-group transformations. The first hurdle to overcome for this purpose is to establish exclusive 1,4-addition free from 1,2-addition. α-Heterosubstituted organometallics have given many solutions to this problem. However, more synthetically desired is to make use of intermediary enolates for one-pot introduction of electrophiles at the α-position, especially when using cyclic α-enones which lead to versatile key compounds in natural product synthesis.[2] In fact, electrophiles such as aldehydes and some Michael acceptors have been successfully incorporated, but alkylation has proven rather difficult to achieve due to faster enolate ion equilibration between α and α′ forms. For example, with organocopper reagents, α,β-dialkylation of 2-cyclohexenones was realized only for limited cases, while contamination by α′-alkylation was unavoidable in the case of 2-cyclopentenones whose enolates undergo more rapid equilibration.[3] These drawbacks have been bypassed occasionally by transmetalation of the intermediary enolates with organotin compounds.[4] The enolate ion equilibration also causes cis–trans isomerization in α,β-dialkylation. Therefore, the stereocontrol of the 1,4-addition mode is another important problem in this field.

The next step is to develop a mild method to convert the masked function into a formyl group, which often is not tolerated under the ordinary conditions used for deprotection. A number of potential formyl anion equivalents proved effective for the 1,4-addition,[5] but only a part of these reaction products were actually derivatized to formyl compounds. The cyano[5a] and nitromethyl[5b] groups were employed as masked formyl synthon earlier. Later, Cohen disclosed a more practical two-step conversion of the tris(phenylthio)methyl group via dithioacetals.[5f] These compounds were also deprotected by Italian workers.[5n] Ogura reported a photochemical method involving the (methylthio)(*p*-tolylsulfonyl)methyl group.[5i]

The 1,4-addition of a carboxy anion is another interesting process but has met with less success. This may be ascribed to the higher oxidation state of the carboxy group as compared with other carbonyl groups, and hence the more forced conditions are needed for unmasking. Orthothioformyl groups were converted into carboxy or alkoxycarbonyl groups with the aid of mercuric salts.[6] Successive treatment with mCPBA and concentrated hydrochloric acid in refluxing ethanol effected transformation of the (methylthio)(*p*-tolylsulfonyl)methyl moiety to a methylthiocarbonyl group.[5i] Trost revealed BCl_3-promoted generation of esters from the 2-alkoxybenzo-1,3-dithiole 1,1,3,3-tetraoxide moiety.[7]

Scheme I

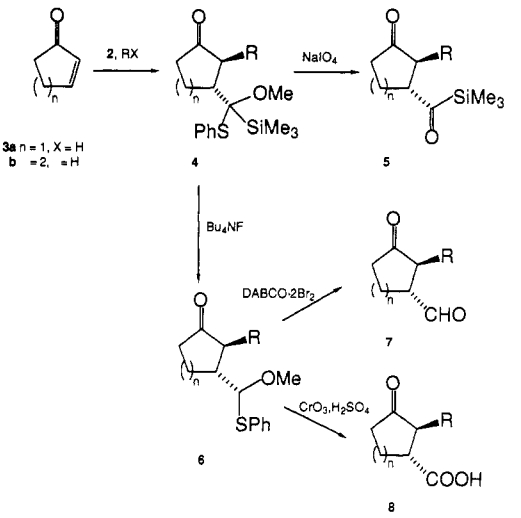
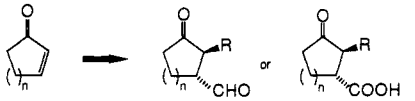


Table I. 1,4-Addition Concomitant with α-Alkylation and Conversion to Silylcarbonyl Compounds

α-enone	RX	4, %	5, % (trans/cis)[a]
3a	CH_3I	**4a**, 98	**5a**, 91 (>99)
	C_2H_5I	**4b**, 48	**5b**, 67 (>99)
	$CH_2{=}CHCH_2Br$	**4c**, 82	**5c**, 73 (95:5)
	$CH{\equiv}CCH_2Br$	**4d**, 95	**5d**, 90 (96:4)
3b	CH_3I	**4e**, 65	**5e**, 83 (>99)
(**3a**	H_2O	**4i**, 86)	

[a] Based on GLC analysis.

In the context of our studies on synthetic applications of methoxy(phenylthio)methane[8] and its silylated derivative 1,[9] we have found that [methoxy(phenylthio)(trimethylsilyl)methyl]lithium (**2**) undergoes clean 1,4-addition to cyclic α-enones concomitant with in situ α-alkylation. The products thus obtained are converted into the formyl and carboxy derivatives under mild conditions, consequently allowing facile 1,4-addition of formyl and carboxy groups in a highly regio- and stereoselective manner as shown below. In this paper we describe the details of these procedures and furthermore a novel synthesis of sarkomycin as an application of this new method.[10]



Results and Discussion

1,4-Addition. Treatment of α-enones, **3a** and **3b**, with **2**[11] (2 equiv) in the presence of HMPA (10 equiv) at −78 °C for 30 min and subsequently with alkyl halides (2.4 equiv) at −40 °C for 30 min in THF afforded the α,β-disubstituted cycloalkanones **4** (Scheme I and Table I). No 1,2-addition products were detected. As [methoxy(phe-

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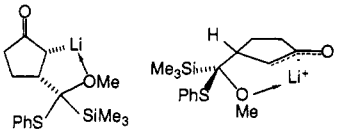
nylthio)methyl]lithium gives rise to 1,2- and 1,4-addition in a 6:4 ratio, the trimethylsilyl group in **2** apparently plays an important role for the 1,4-preference. This is accounted for by the α-silicon effect to stabilize an adjacent carbanion.[12] The stabilized (or soft) carbanion favors 1,4-addition.[1b] Consistent with other 1,4-addition reactions as discussed by Krief,[1b] HMPA is crucial in this case, too. The 1,2-addition of **2** in the absence of HMPA was reported.[11b] The in situ alkylation of the enolate was conducted at −40 °C because of sluggishness below this temperature. The 1,4-addition is frequently induced upon raising the reaction temperature as a result of equilibrium shift from the 1,2-addition products. Although no concrete evidence is available to confirm the irreversibility in the present case, the kinetic control is suggested by the exclusive formation of the 1,4-addition product **4i** when the enolate is trapped with water at −78 °C. The in situ alkylation of the intermediary enolates is smoothly achieved to give the α,β-dialkylation products **4** free from both the α'-counterparts and stereoisomers, the trans stereochemistry being clarified later.

Seebach et al. reported that the reaction of [bis(methylthio)(trimethylsilyl)methyl]lithium with **3a** and **3b** provided the regioisomers as well as the stereoisomers.[5d] This reagent differs from **2** in possessing no methoxy group. We, hence, assume that the high regio- and stereoselectivities result from the *C*-lithio enolate (A) or the conjugated enolate (B) where the lithium ion is located on the same side of the incoming nucleophile.[13] In either structure, the equilibrium is biased in favor of the α-isomer by the methoxy chelation. Furthermore, these structures enhance the thermal stability of an enolate, which survives even at 0 °C, and the reactivity of the α-carbon toward electrophiles.[14]



A B

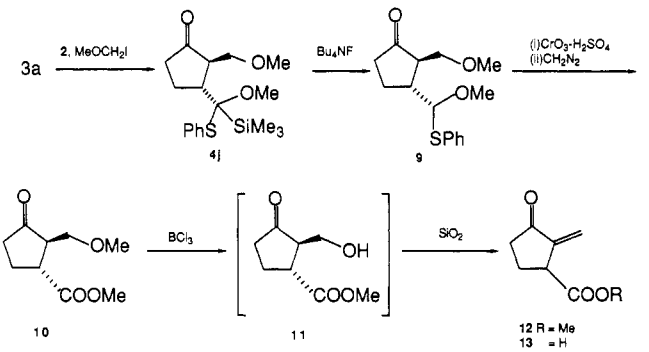
GLC of the 1,4-addition products thus obtained exhibited two peaks, which, however, proved not to arise from the cis–trans isomers associated with the α- and β-carbons but to be attributable to the diastereomerism induced by incorporation of a new chiral center, the methoxy(phenylthio)(trimethylsilyl)methyl carbon, since $NaIO_4$ oxidation of **4** provided silylcarbonyl derivatives **5** exhibiting essentially a single GLC peak (Table I). Then, **5a** was subjected to 400-MHz ^1H NMR analysis. The vicinal coupling constant between the methine protons attached to the α- and β-carbons, respectively, was found to be 10.3 Hz, a quite reasonable value for the trans isomer of vicinally disubstituted cyclopentanones.[3] By analogy with this result, the trans structures are most plausible for other compounds.

Conversion to Aldehydes and Carboxylic Acids. First, we manipulated **4** through various oxidations to directly arrive at the desired compounds. All attempts, however, failed, and silylcarbonyl derivtives **5** were produced in most cases. The trimethylsilyl group of **4** was then initially removed by action of Bu_4NF to give monothioacetals **6** (Scheme I). Since we had disclosed a mild oxidative method for transforming monothioacetals to aldehydes,[15] **6** was subjected to this reaction. Unfortunately, however, none of the oxidants employed previously (mCPBA, $NaIO_4$, and SeO_2–H_2O_2) were effective. Finally we found that the 1,4-diazabicyclo[2.2.2]octane·$2Br_2$ adduct (DABCO·$2Br_2$)[16] served quite well to convert **6** to aldehydes **7**. On the other hand, Jones' oxidation of **5** according to our previous method[15] furnished the desired carboxylic acids **8**. These results are compiled in Table II. Consequently, we have established efficient methods for 1,4-addition of formyl and carboxy groups to α-enones.

Table II. Conversion of 4 into Aldehydes 7 and Carboxylic Acids 8 via 6

4	6, %	7, %	8, %
4a	92	83	72
4b	77	71	65
4c	82	40	82
4d	95	41	70
4e	82	75	54

Scheme II



Formal Synthesis of Sarkomycin.[17] To exemplify the utility of this new method we synthesized sarkomycin (**13**) (Scheme II). Exposure of **3a** to **2** (2 equiv) in the presence of HMPA (10 equiv) in THF at −78 °C for 2 h and subsequently to iodomethyl methyl ether[18] at 0 °C for 30 min furnished the 1,4-addition product **4j** in 71% yield. Desilylation of **4j** gave a 71% yield of monothioacetal **9**, which was then converted into the ester **10** through Jones' oxidation followed by esterification in 69% yield. Treatment of **10** with BCl_3 in dichloromethane afforded a 95% crude yield of the hydroxy ketone **11**, which was contaminated by a small amount (ca. 10%) of the dehydration product **12**. Fortunately, purification of the crude **11** was unnecessary because the mixture was converted into pure **12** by treating the mixture with silica gel for 1 h before column chromatography. Hydrolysis of **12** to sarkomycin (**13**) has been achieved.[19]

Experimental Section

NMR spectra were recorded on Hitachi R-24B, JEOL JNM-FX 100, and JEOL GSX-400 spectrometers operating at 60, 100, and 400 MHz, respectively, for ^1H spectra and at 25 MHz for ^{13}C spectra. Chemical shifts are given in ppm relative to Me_4Si as

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an internal standard. Mass spectra were obtained with a JEOL JMS-DX 303-HF mass spectrometer using electron impact ionization. Column chromatography was performed on Kieselgel 60 (70–230 mesh) (E. Merck). Thin-layer chromatography was carried out on Merck Kieselgel 60 F_{254}. GLC analysis was performed on Shimadzu GC-8A with 2% Silicone OV 17 on Chromosorb W (3.2 p × 2000). All the solvents were purified by standard methods before use. All reactions involving organometallic reagents were conducted under a nitrogen atmosphere.

Preparation of Methoxy(phenylthio)(trimethylsilyl)methane (1).[9,11] To a THF solution (40 mL) of methoxy(phenylthio)methane (4.23 g, 30 mmol) was added BuLi (1.5 N hexane solution, 24 mL, 36 mmol) dropwise at −78 °C. The solution was stirred at −40 °C for 30 min and recooled to −78 °C. To this solution was added chlorotrimethylsilane (7.6 mL, 60 mmol) in one portion. The reaction mixture was stirred for 2 h at this temperature and quenched with water. Extraction with benzene, washing of the organic layer with water, and evaporation left a crude oil, which was distilled to give pure **1** (6.14 g, 91%): bp 75 °C/0.5 mm (lit.[11b] bp 65–70 °C/0.35 mm); ^{1}H NMR (CCl_4) δ 0.07 (s, 9 H), 3.27 (s, 3 H), 4.27 (s, 1 H), 6.87–7.20 (m, 3 H), 7.20–7.43 (m, 2 H).

1,4-Addition to 2-Cyclopentenone and 2-Cyclohexenone Followed by Alkylation. To a THF solution (15 mL) of **1** (1.356 g, 6.0 mmol) was added BuLi (1.5 N hexane solution, 4.4 mL, 6.6 mmol) at −78 °C. The solution was stirred at −40 °C for 30 min and cooled to −78 °C again. To this solution, HMPA (5.38 g, 30 mmol) and **3a** (246 mg, 3.0 mmol) were added dropwise and the resulting solution was stirred for 30 min at this temperature. Then, methyl iodide (1.022 g, 7.2 mmol) was added. The reaction mixture was warmed up to −40 °C and stirred for 30 min. Benzene and water were added. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. The residue was subjected to column chromatography (20:1 hexane–ethyl acetate) to give 3-[methoxy(phenylthio)(trimethylsilyl)methyl]-2-methylcyclopentanone (**4a**) (947 mg, 98%): ^{1}H NMR ($CDCl_3$) δ 0.11 (s, 2.6 H), 0.27 (s, 6.4 H), 1.06 (d, 0.8 H, J = 7.2 Hz), 1.13 (d, 2.2 H, J = 7.2 Hz), 1.63–2.70 (m, 6 H), 3.54 (s, 0.8 H), 3.57 (s, 2.2 H), 7.16–7.37 (m, 3 H), 7.37–7.61 (m, 2 H).

Anal. Calcd for $C_{17}H_{26}O_2SSi$: C, 63.30; H, 8.12. Found: C, 63.53; H, 8.16.

Other reactions were conducted analogously.

2-Ethyl-3-[methoxy(phenylthio)(trimethylsilyl)methyl]cyclopentanone (4b): ^{1}H NMR (CCl_4) δ 0.10 (s, 2.7 H), 0.30 (s, 6.3 H), 0.77 (br t, 3 H, J = 6.0 Hz), 1.03–2.73 (m, 8 H), 3.52 (s, 3 H), 6.93–7.50 (m, 5 H).

Anal. Calcd for $C_{18}H_{28}O_2SSi$: C, 64.24; H, 8.39. Found: 64.40; H, 8.61.

2-Allyl-3-[methoxy(phenylthio)(trimethylsilyl)methyl]cyclopentanone (4c): ^{1}H NMR ($CDCl_3$) δ 0.14 (s, 2.6 H), 0.29 (s, 6.4 H), 1.60–2.63 (m, 8 H), 3.59 (s, 3 H), 4.76–5.03 (m, 2 H), 5.27–5.71 (m, 1 H), 7.17–7.33 (m, 3 H), 7.33–7.54 (m, 2 H).

Anal. Calcd for $C_{19}H_{28}O_2SSi$: C, 65.47; H, 8.10. Found: C, 65.62; H, 8.39.

3-[Methoxy(phenylthio)(trimethylsilyl)methyl]-2-propargylcyclopentanone (4d): ^{1}H NMR ($CDCl_3$) δ 0.13 (s, 3.2 H), 0.36 (s, 5.8 H), 1.70–2.45 (m, 8 H), 2.51–2.70 (m, 1 H), 3.60 (s, 1.1 H), 3.63 (s, 1.9 H), 7.15–7.35 (m, 3 H), 7.35–7.57 (m, 2 H).

Anal. Calcd for $C_{19}H_{26}O_2SSi$: C, 65.85; H, 7.56. Found, C, 65.54; H, 7.87.

3-[Methoxy(phenylthio)(trimethylsilyl)methyl]-2-methylcyclohexanone (4e): ^{1}H NMR (CCl_4) δ 0.41 (s, 4.4 H), 0.60 (s, 4.6 H), 1.22 (d, 1.5 H, J = 5.0 Hz), 1.35 (d, 1.5 H, J = 5.0 Hz), 1.52–3.17 (m, 8 H), 3.70 (s, 3 H), 7.30–7.85 (m, 5 H).

Anal. Calcd for $C_{18}H_{28}O_2SSi$: C, 64.24; H, 8.39. Found: C, 64.49; H, 8.53.

3-[Methoxy(phenylthio)(trimethylsilyl)methyl]cyclopentanone (4i): ^{1}H NMR (CCl_4) δ 0.17 (s, 9 H), 1.07–2.77 (m, 7 H), 3.43 (s, 3 H), 6.83–7.30 (m, 5 H).

Preparation of Silylcarbonyl Compounds 5. A mixture of **4a** (644 mg, 2 mmol) and $NaIO_4$ (642 mg, 3 mmol) in dioxane (8 mL)–water (2 mL) was stirred at room temperature for 3 h. The reaction mixture was diluted with benzene–water. The organic layer was washed with aqueous sodium thiosulfate and sodium bicarbonate solutions. Drying ($MgSO_4$), evaporation, and column chromatography (10:1 hexane–ethyl acetate) afforded 2-methyl-3-[(trimethylsilyl)carbonyl]cyclopentanone (**5a**) (360 mg, 91%)%: ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 9 H), 1.00 (d, 3 H, J = 6.7 Hz), 2.05–2.76 (m, 5 H), 3.11–3.44 (m, 1 H).

Anal. Calcd for $C_{10}H_{18}O_2Si$: C, 60.56; H, 9.15. Found: C, 60.67; H, 9.03.

Other compounds were obtained analogously.

2-Ethyl-3-[(trimethylsilyl)carbonyl]cyclopentanone (5b): ^{1}H NMR (CCl_4) δ 0.12 (s, 9 H), 0.67 (br t, 3 H), 1.03–2.50 (m, 7 H), 2.93–3.47 (m, 1 H).

Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.20; H, 9.53.

2-Allyl-3-[(trimethylsilyl)carbonyl]cyclopentanone (5c): ^{1}H NMR (CCl_4) δ 0.08 (s, 9 H), 1.00–2.68 (m, 7 H), 2.92–3.40 (m, 1 H), 4.47–5.70 (m, 3 H).

Anal. Calcd for $C_{12}H_{20}O_2Si$: C, 64.24; H, 8.98. Found: C, 64.13; H, 8.99.

2-Propargyl-3-[(trimethylsilyl)carbonyl]cyclopentanone (5d): ^{1}H NMR ($CDCl_3$) δ 0.29 (s, 9 H), 1.39–2.53 (m, 7 H), 2.61–2.88 (m, 1 H), 3.55–3.93 (m, 1 H).

Anal. Calcd for $C_{12}H_{18}O_2Si$: C, 64.82; H, 8.16. Found: C, 64.88; H, 8.10.

2-Methyl-3-[(trimethylsilyl)carbonyl]cyclohexanone (5e): ^{1}H NMR (CCl_4) δ 0.18 (s, 9 H), 0.73 (d, 3 H, J = 6.0 Hz), 1.00–2.40 (m, 7 H), 2.53–3.23 (m, 1 H).

Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 61.99; H, 9.47.

Preparation of Monothioacetals 6. A mixture of **4a** (161 mg, 0.5 mmol) and Bu_4NF (196 mg, 0.75 mmol) in DMF (8 mL)–water (1 mL) was stirred at room temperature for 1 h. The reaction mixture was diluted with benzene–water, and the organic layer was washed with water. Drying ($MgSO_4$), evaporation, and column chromatography (10:1 hexane–ethyl acetate) afforded 3-[methoxy(phenylthio)methyl]-2-methylcyclopentanone (**6a**) (115 mg, 92%): ^{1}H NMR ($CDCl_3$) δ 1.04 (d, 3 H, J = 5.7 Hz), 1.79–2.51 (m, 6 H), 3.37 (s, 0.8 H), 3.55 (s, 2.2 H), 4.60 (d, 0.8 H, J = 5.7 Hz), 4.75 (d, 0.2 H, J = 2.9 Hz), 7.14–7.37 (m, 3 H), 7.37–7.59 (m, 2 H).

Anal. Calcd for $C_{14}H_{18}O_2S$: C, 67.17; H, 7.25. Found: C, 67.20; H, 7.31.

Other compounds were obtained analogously.

2-Ethyl-3-[methoxy(phenylthio)methyl]cyclopentanone (6b): ^{1}H NMR ($CDCl_3$) δ 0.66–0.97 (m, 3 H), 1.21–2.59 (m, 8 H), 3.41 (s, 0.9 H), 3.47 (s, 2.1 H), 4.56 (d, 0.7 H, J = 6.0 Hz), 4.73 (d, 0.3 H, J = 5.2 Hz), 7.17–7.36 (m, 3 H), 7.36–7.57 (m, 2 H).

Anal. Calcd for $C_{15}H_{20}O_2S$: C, 68.15; H, 7.62. Found: C, 68.12; H, 7.67.

2-Allyl-3-[methoxy(phenylthio)methyl]cyclopentanone (6c): ^{1}H NMR ($CDCl_3$) δ 1.17–2.59 (m, 8 H), 3.40 (s, 0.8 H), 3.47 (s, 2.2 H), 4.59 (d, 1 H, J = 5.7 Hz), 4.71–5.11 (m, 2 H), 5.29–5.77 (m, 1 H), 7.14–7.34 (m, 3 H), 7.34–7.56 (m, 2 H).

Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.57; H, 7.39.

3-[Methoxy(phenylthio)methyl]-2-propargylcyclopentanone (6d): ^{1}H NMR ($CDCl_3$) δ 1.50–2.87 (m, 9 H), 3.44 (s, 1 H), 3.50 (s, 2 H), 4.63 (d, 0.7 H, J = 6.0 Hz), 4.95 (d, 0.3 H, J = 3.7 Hz), 7.19–7.36 (m, 3 H), 7.36–7.59 (m, 2 H).

Anal. Calcd for $C_{16}H_{18}O_2S$: C, 70.04; H, 6.61. Found: C, 70.03; H, 6.59.

3-[Methoxy(phenylthio)methyl]-2-methylcyclohexanone (6e): ^{1}H NMR (CCl_4) δ 0.78 (d, 1.5 H, J = 7.0 Hz), 0.83 (d, 1.5 H, J = 7.0 Hz), 1.10–1.47 (m, 8 H), 3.10 (s, 1.5 H), 3.20 (s, 1.5 H), 4.52 (br s, 1 H), 6.83–7.40 (m, 5 H).

Anal. Calcd for $C_{15}H_{20}O_2S$: C, 68.14; H, 7.62. Found: C, 68.42; H, 7.69.

Preparation of Aldehydes 7. A mixture of **6a** (131 mg, 0.52 mmol) and DABCO·$2Br_2$ (143 mg, 0.52 mmol) in acetic acid (7 mL)–water (3 mL) was stirred at room temperature for 1 h. The reaction mixture was diluted with dichloromethane–water, and the organic layer was washed successively with water, $NaHCO_3$ solution, and water. Drying ($MgSO_4$), evaporation, and column chromatography (3:1 hexane–ethyl acetate) afforded 2-methyl-3-oxocyclopentanecarbaldehyde (**7a**) (55 mg, 83%): ^{1}H NMR ($CDCl_3$) δ 1.09 (d, 3 H, J = 6.9 Hz), 1.63–2.80 (m, 6 H), 9.94 (d, 1 H, J = 2.6 Hz); HRMS calcd for $C_7H_{10}O_2$ 126.0681, found 126.0665.

Other compounds were obtained analogously.

2-Ethyl-3-oxocyclopentanecarbaldehyde (7b): ^{1}H NMR ($CDCl_3$) δ 0.86 (t, 3 H, J = 7.4 Hz), 1.34–2.49 (m, 7 H), 2.63–2.97 (m, 1 H), 9.66 (d, 1 H, J = 2.6 Hz); HRMS calcd for $C_8H_{12}O_2$ 140.0838, found 140.0836.

2-Allyl-3-oxocyclopentanecarbaldehyde (7c): ^{1}H NMR ($CDCl_3$) δ 1.49–2.63 (m, 7 H), 2.69–3.03 (m, 1 H), 4.83–5.14 (m, 2 H), 5.31–5.83 (m, 1 H), 9.66 (d, 1 H, J = 2.2 Hz); HRMS calcd for $C_9H_{12}O_2$ 152.0837, found 152.0742.

3-Oxo-2-propargylcyclopentanecarbaldehyde (7d): ^{1}H NMR ($CDCl_3$) δ 1.77–2.77 (m, 8 H), 2.97–3.34 (m, 1 H), 9.83 (d, 1 H, J = 2.0 Hz); HRMS calcd for $C_9H_{10}O_2$ 150.0681, found 150.0680.

2-Methyl-3-oxocyclohexanecarbaldehyde (7e): ^{1}H NMR ($CDCl_3$) δ 1.06 (d, 3 H, J = 6.0 Hz), 1.57–2.87 (m, 8 H), 9.66 (d, 1 H, J = 2.3 Hz); HRMS calcd for $C_8H_{12}O_2$ 140.0867, found 140.0897.

Preparation of Carboxylic Acids 8. To an acetone solution (10 mL) of **6a** (375 mg, 1.5 mmol) was added dropwise the Jones' reagent (3 N aqueous solution) at 0 °C until the color of the reagent no more disappeared (total amount of the added reagent, 1.5 mL, 4.5 mmol). The solution was stirred for 1 h, and sodium bicarbonate solution was added. The mixture was shaken with benzene. The aqueous layer was separated, acidified slightly with 1 N HCl, and extracted with dichloromethane. The organic layer was dried ($MgSO_4$) and evaporated to leave 2-methyl-3-oxocyclopentanecarboxylic acid (**8a**) (153 mg, 72%): ^{1}H NMR ($CDCl_3$) δ 1.12 (d, 3 H, J = 6.6 Hz), 1.74–2.87 (m, 6 H), 10.8 (br s, 1 H).

Anal. Calcd for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.06; H, 7.14.

Other compounds were obtained analogously.

2-Ethyl-3-oxocyclopentanecarboxylic acid (8b): ^{1}H NMR (CCl_4) δ 1.00 (t, 3 H, J = 6.0 Hz), 1.47–3.17 (m, 8 H), 9.17 (br s, 1 H).

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.32; H, 7.78.

2-Allyl-3-oxocyclopentanecarboxylic acid (8c): ^{1}H NMR ($CDCl_3$) δ 1.59–3.09 (m, 8 H), 4.89–5.26 (m, 2 H), 5.43–5.91 (m, 1 H), 10.41 (br s, 1 H).

Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.47; H, 7.06.

3-Oxo-2-propargylcyclopentanecarboxylic acid (8d): ^{1}H NMR ($CDCl_3$) δ 1.58–2.76 (m, 8 H), 3.03–3.41 (m, 1 H), 11.30 (br s, 1 H).

Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 65.27; H, 6.03.

2-Methyl-3-oxocyclohexanecarboxylic acid (8e): ^{1}H NMR (CCl_4) δ 1.07 (d, 3 H, J = 5.0 Hz), 1.43–2.68 (m, 8 H), 9.73 (br s, 1 H).

Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.27; H, 7.87.

2-(Methoxymethyl)-3-[methoxy(phenylthio)(trimethylsilyl)methyl]cyclopentanone (4j). To a THF solution (10 mL) of **2** (4 mmol) and HMPA (20 mmol) was added **3a** (164 mg, 2 mmol) at −78 °C. The solution was stirred at this temperature for 2 h. Iodomethyl methyl ether (1.03 g, 6 mmol) was added to this solution at −78 °C. After being stirred for 30 min at 0 °C, the reaction mixture was quenched with water at this temperature and extracted with benzene. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. Column chromatography of the residue (10:1 hexane–ethyl acetate) provided **4j** (500 mg, 71%): ^{1}H NMR (CCl_4) δ 0.00 (s, 2.7 H), 0.12 (s, 6.3 H), 1.03–2.23 (m, 6 H), 3.00 (s, 3 H), 3.43 (s, 3 H), 3.20–3.57 (m, 2 H), 7.27–7.50 (m, 5 H).

Anal. Calcd for $C_{18}H_{28}O_3SSi$: C, 61.32; H, 8.00. Found: C, 61.38; H, 7.86.

2-(Methoxymethyl)-3-[methoxy(phenylthio)methyl]cyclopentanone (9). A mixture of **4j** (428 mg, 1.22 mmol) and Bu_4NF (349 mg, 1.34 mmol) in DMF (8 mL)–water (1 mL) was stirred at room temperature for 1 h. The mixture was diluted with benzene–water. The organic layer was washed with water, dried ($MgSO_4$), and evaporated. Column chromatography of the residue (5:1 hexane–ethyl acetate) afforded **9** (266 mg, 78%): ^{1}H NMR (CCl_4) δ 1.20–2.40 (m, 6 H), 3.07 (s, 3 H), 3.28 (s, 3 H), 3.17–3.63 (m, 2 H), 4.52 (d, 0.3 H, J = 6.0 Hz), 4.65 (d, 0.7 H, J = 4.0 Hz), 7.07–7.55 (m, 5 H).

Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.26; H, 7.19. Found: C, 64.55; H, 7.10.

3-(Methoxycarbonyl)-2-(methoxymethyl)cyclopentanone (10). To an acetone solution (5 mL) of **9** (212 mg, 0.76 mmol) was added dropwise the Jones' reagent (3 N aqueous solution) at room temperature until the color of the reagent no more disappeared. After being stirred at this temperature for 1 h, the reaction mixture was diluted with dichloromethane–water. Evaporation of the organic layer provided crude carboxylic acid (98 mg), which was treated with excess diazomethane in ether at 0 °C for 1 h. Acetic acid was added dropwise until the color of diazomethane disappeared. The mixture was evaporated, and the residue was purified by column chromatography (5:1 hexane–ethyl acetate) to give **10** (97 mg, 69%): ^{1}H NMR (CCl_4) δ 1.22–2.42 (m, 6 H), 3.07 (s, 3 H), 3.50 (s, 3 H), 3.23–3.62 (m, 2 H).

Sarkomycin Methyl Ester (12). To a dichloromethane solution (5 mL) of **10** (122 mg, 0.66 mmol) was added BCl_3 (0.63 N dichloromethane solution, 3.12 mL, 1.97 mmol) at −10 °C. The mixture was stirred at this temperature for 4 h and diluted with water–dichloromethane. Drying ($MgSO_4$) and evaporation of the organic layer gave crude hydroxymethyl ester **11** contaminated by **12** (ca. 10% based on ^{1}H NMR spectrum). This product was kept on standing on a silica gel column for 1 h. Then, elution with 5:1 hexane–ethyl acetate provided **12** (59 mg, 57%): ^{1}H NMR ($CDCl_3$) δ 1.95–2.64 (m, 4 H), 3.60–3.94 (m, 1 H), 3.77 (s, 3 H), 5.54 (d, 1 H, J = 2.9 Hz), 6.19 (d, 1 H, J = 2.9 Hz); ^{13}C NMR (CDCl3) δ 22.96, 36.58, 45.80, 52.19, 120.18, 142.25, 172.67, 204.19.

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