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Highly Stereoselective Syntheses of Spiroacetal Enol Ethers, (*E*)- and (*Z*)-Methoxycarbonylmethylene-1, 6-dioxaspiro[4.5]decanes

Hiroaki Toshima,* Hisateru Aramaki, Yoshinori Furumoto, Shintaro Inamura, and Akitami Ichihara*

Department of Bioscience and Chemistry, Faculty of Agriculture, Hokkaido University, Sapporo 060-8589, Japan

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Abstract: (*E*)- and (*Z*)-2-methoxycarbonylmethylene-1,6-dioxaspiro[4.5]decanes have been synthesized from an acyclic keto alcohol possessing an alkynoate part *via* intramolecular conjugate addition. Under thermodynamically controlled conditions using *t*-BuOK in THF, the (*E*)-isomer could be obtained in 52:1 ratio. When a catalytic amount of $Pd(OAc)_2$ was used in benzene, the (*Z*)-isomer could be obtained in 95:1 ratio.

INTRODUCTION

Polyacetylenic metabolites are widespread in several plant families and are utilized as chemotaxonomical markers.[1] Within the tribe *Anthemideae* of the family *Asteraceae* (*Compositae*), the genus *Chrysanthemum* and the closely related genera produce acetylenic spiroacetal enol ethers, for example, **1**-**4**.[2,3,4] They are classified into three types, diol derivatives, epoxides, and olefins, with respect to the functional group of 2-enolic tetrahydrofuran. Polyacetylenes may generally play various ecological roles (nematicidal, antibiotic, insect repellent, etc.) and exhibit various biological activities. Although the biological activities of **1** and **2** have not been examined, (*E*)-**3** has been reported to exhibit antifeedant, antiphlogistic, and spasmolitic activities.[5,6,7] There are many kinds of spiroacetals as substructures of natural products, and great efforts have been made to construct them.[8] However, as regards spiroacetal enol ethers such as **1**-**4**, much attention has not been paid from a synthetic point of view. Although a few syntheses of **3** and **4** have been reported, their yields and geometrical selectivity are not always satisfactory.[9,10,11] In this paper, we describe the highly stereoselective construction of spiroacetal enol ethers as model compounds[12] directed toward total syntheses of naturally occurring acetylenic spiroacetal enol ethers.

Our biomimetic route constructing 2-enol ether-type 1, 6-dioxaspiro[4.5]decanes (**6*E*** and **6*Z***) is shown in Scheme 1. An acyclic substrate **5a** would be in equilibrium with a hemiacetal **5b** possessing both an acceptor part (alkynoate) and a donor part (hemiacetal hydroxyl group). Therefore, hemiacetalization and subsequent conjugate addition would provide **6*E*** and **6*Z*** under appropriate conditions. The methoxycarbonyl group would act effectively not only for conjugate addition but also for keeping the exo-enol system by conjugation. Our strategy would apply to the construction of more oxygenated compounds such as **1** and **2**.

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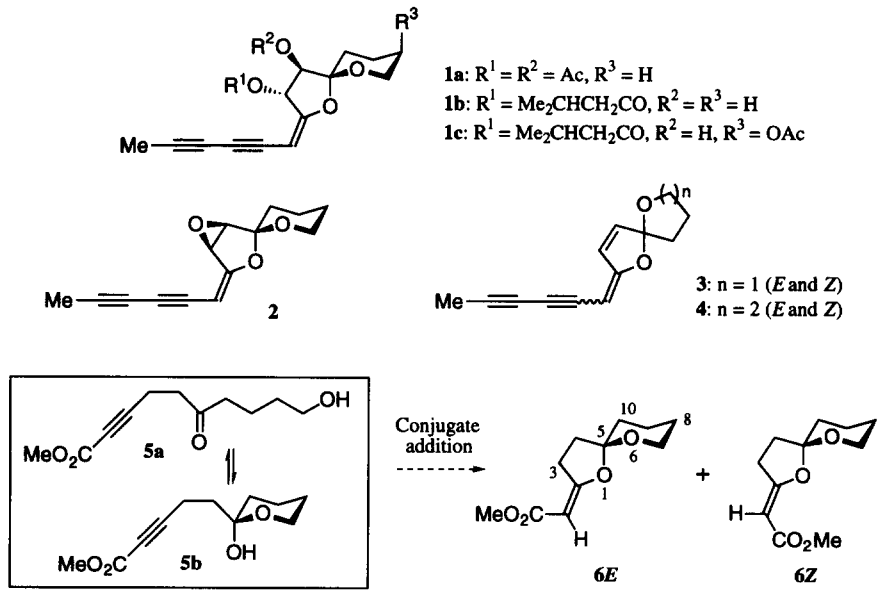


Scheme 1

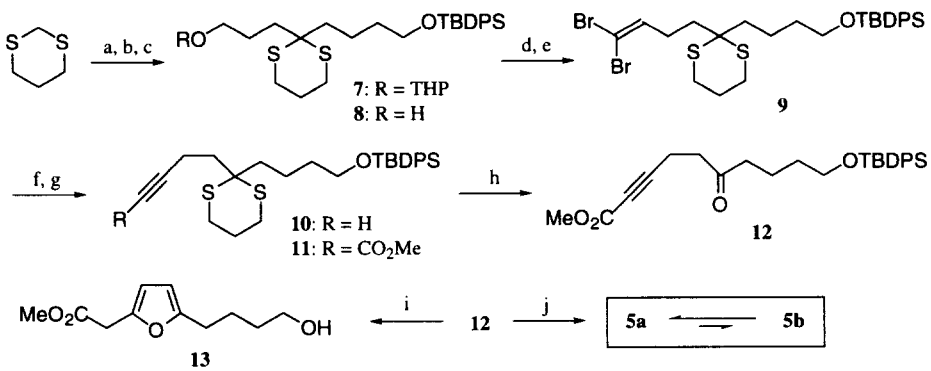
RESULTS AND DISCUSSION

Synthesis of the Acyclic Substrate

1,3-Dithianyl anion was alkylated by a C_3-alkyl halide to give a mono-alkylated 1,3-dithiane, whose anion was subsequently alkylated by a C_4-alkyl halide to give **7** in 84% yield (Scheme 2). Although the one-pot dialkylation gave **7**, the yield was lower than that obtained by the stepwise method. Selective deprotection of the THP group of **7** with a catalytic amount of PPTS in EtOH gave alcohol **8** in 96% yield. Oxidation of **8** and subsequent dibromoolefination with CBr_4 and Ph_3P gave **9** in 71% yield. Acetylene **10** was obtained by treating **9** with *n*-BuLi (2 eq.) in 96% yield. The lithium acetylide, again generated by treating **10** with *n*-BuLi (1 eq.), was trapped by methyl chloroformate to give labile alkynoate **11**, whose dithioacetal was deprotected immediately with NCS/$AgNO_3$ in aq. CH_3CN to give keto alkynoate **12** in 78% yield. Although the lithium acetylide generated from **9** could be trapped by methyl chloroformate to give **11** in one pot, the reproducibility of the stepwise method is better than that of the one-pot method.

The desired acyclic substrate **5a** would be obtained by desilylation and, furthermore, we expected that desilylation of **12** with anhydrous *n*-Bu_4NF in THF would directly provide ***6E*** and ***6Z*** *via* the resulting ammonium alkoxide. When **12** was treated with *n*-Bu_4NF in THF, **5a/5b** could not be obtained, but ***6E*** (9%) and ***6Z*** (< 4%) could be obtained along with major product **13**. The structures of ***6E*** and ***6Z*** were elucidated by their ^1H- and ^{13}C-NMR spectra. One olefinic proton, two allylic protons, one pair of olefinic carbons and one acetal carbon were observed in the respective isomers. The geometry of ***6E*** and ***6Z*** was determined from the ^1H-^1H NOE experiments. When the olefinic proton (δ 4.88) of ***6Z*** was irradiated, the two allylic protons were enhanced. When the olefinic proton (δ 5.32) of ***6E*** was irradiated, no proton was enhanced. Furthermore,

the chemical shift of the olefinic proton of **6*E*** was closely similar to those of naturally occurring (*E*)-spiroacetal enol ethers.[2] While **6*E*** and **6*Z*** were minor products, furan derivative **13** was the major product (34%). The structure of **13** was determined from the fact that two olefinic protons in the ^{1}H-NMR spectrum and two pairs of olefinic carbons in the ^{13}C-NMR spectrum were observed. Under this condition, enolization of the ketone and subsequent conjugate addition of the resulting enolic hydroxyl group might proceed preferentially to give **13**. A similar cyclization providing furan derivatives with NaH, starting from keto alkynoates lacking a hydroxyl group, has recently been reported.[13] Therefore, other desilylating reagents were applied to **12**. Among them, HF·pyridine gave **5a** in the highest yield (94%), as an equilibrium mixture of *ca.* 8:1 with hemiacetal **5b**. In the ^{1}H-NMR spectrum of a mixture of **5a** and **5b**, the hydoxymethyl protons of **5a** were observed at δ 3.63 ppm as a triplet, and the corresponding methylene protons of **5b** were observed at δ 3.85-3.96 ppm as a multiplet. In this way, the preparation of the desired substrate for spirocyclization was completed.



(a) *n*-BuLi / THF, then $Br(CH_2)_3OTHP$, 96% (b) *n*-BuLi / THF, then $I(CH_2)_4OTBDPS$, 88% (c) PPTS / EtOH 96% (d) DMSO, SO_3·pyr., Et_3N / CH_2Cl_2 (e) CBr_4, Ph_3P / CH_2Cl_2, 71%, 2 steps (f) *n*-BuLi / THF, 96% (g) *n*-BuLi / THF, then $ClCO_2Me$ (h) NCS, $AgNO_3$ / 10% aq. CH_3CN, 78%, 2 steps (i) n-Bu_4NF / THF, 34% (j) HF·pyr. / CH_3CN, 94% [**5a**:**5b** = 8:1]

Scheme 2

Construction of Spiroacetal Enol Ethers

From the fact that a small amount of **6*E*** and **6*Z*** was obtained from **12** *via* the ammonium alkoxide, the activation of the donor part as the alkoxide was considered to be a promising approach for the construction of **6*E*** and **6*Z***. Therefore, various non-aqueous basic conditions were examined for an equilibrium mixture of **5a** and **5b**, and the results are shown in Table 1. Most of the reactions proceeded in moderate or high yields in both stoichiometric and catalytic cases. When alkaline metal hydrides were used, the geometrical selectivity was poor (*E*:*Z* = 1.9-3:1, entries 1-5). Effects of the counter cation (Li^+, Na^+ and K^+: entries 1-3) and the solvent (THF, DMSO and DMF: entries 2, 4 and 5) did not appear clearly. Although only the case of using LiH (entry 1) took a long time, the geometrical selectivity was not influenced and was similar to those of entries 2-4. It seemed that isomerization of cyclized products would not occur in entries 1-5. When NaOMe was used in MeOH, the geometrical selectivity did not appear (*E*:*Z* = 1:1, entry 6). However, when a stoichiometric amount of *t*-BuOK in THF or *t*-BuOH was used, the (*E*)-selectivity increased greatly (*E*:*Z* = 52:1, entry 7; *E*:*Z* = 25:1, entry 8). In contrast to the stoichiometric reactions with *t*-BuOK, the catalytic reactions resulted in poor

selectivity (*E*:*Z* = 2:1, entry 10; *E*:*Z* = 1:1.2, entry 11). The geometrical selectivity was also decreased by using a catalytic amount of NaH (*E*:*Z* = 1.5:1, entry 9, cf. entry 2). Although the conditions synthesizing monocyclic 2-methylene-tetrahydrofurans from alkynoate alcohols[14] also gave **6*E*** and **6*Z***, the yield was moderate and the geometrical selectivity was also poor (*E*:*Z* = 1.1:1, entry 12; *E*:*Z* = 3:1, entry 13). These conditions induced a side reaction to form furan derivative **13** and unknown products. When NaH (1.0 eq.) was used in *t*-BuOH, the reaction was completed in 5 min to give **6*E*** and **6*Z*** in 1:2.4 ratio (entry 14). In the initial process monitored by TLC analysis, **6*Z*** was produced more preferentially than the ratio attained at the end of the reaction. Prolongation of the reaction time resulted in giving the reverse geometrical selectivity (*E*:*Z* = 32:1, entry 15) similar to that of entry 8. These results suggested that: (1)*t*-BuOH as the proton source acted to give **6*Z*** kinetically, (2) isomerization to the thermodynamically more stable **6*E*** occurred in the presence of *t*-BuONa generated *in situ*, and (3) the reactions using *t*-BuOK (entries 7 and 8) were also controlled thermodynamically. In this way, the highly (*E*)-selective method (entry 7) for constructing a spiroacetal enol ether was developed.

Table 1. Construction of spiroacetal enol ethers under basic conditions

Entry	Conditions Base (eq.) / Solvent / Temp. / Time	Yield (%)	Product ratio 6*E* : 6*Z*
1	LiH (1.0) / THF / 4 °C - r.t. / 24 h	80	1.9 : 1
2	NaH (1.0) / THF / 4 °C / 10 min	91	3 : 1[a)]
3	KH (1.0) / THF / 4 °C / 5 min	77	2 : 1[a)]
4	NaH (1.0) / DMSO / r.t. / 10 min	92	2.3 : 1
5	NaH (1.0) / DMF / 4 °C / 10 min	95	2.5 : 1
6	NaOMe (1.0) / MeOH / 4 °C - r.t. / 30 min	95	1 : 1[a)]
7	*t*-BuOK (1.0) / THF / 4 °C / 10 min	73	52 : 1
8	*t*-BuOK (1.0) /*t*-BuOH / r.t. / 5 min	97	25 : 1
9	NaH (0.1) / THF / 4 °C / 10 min	99	1.5 : 1
10	*t*-BuOK (0.1) / THF / 4 °C / 10 min	99	2 : 1
11	*t*-BuOK (0.1) /*t*-BuOH / r.t. / 10 min	96	1 : 1.2
12	KOH (1.0) / MeOH / r.t. / 22 h	66	1.1 : 1
13	DBU (1.0) / toluene / reflux / 3 h	44	3 : 1
14	NaH (1.0) /*t*-BuOH / r.t. / 5 min	90	1 : 2.4
15	NaH (1.0) /*t*-BuOH / r.t. / 36 h	40	32 : 1

a) The ratio was determined after chromatographic separation. The other cases were based on the integration by ^{1}H-NMR.

Various carbonate salts were next examined and the results are shown in Table 2. The (*Z*)-selective reaction proceeded, except for entry 8. The geometrical selectivities were low in entries 1-7 (*E*:*Z* = 1:1.8-2.6), and high in entries 9-12 (*E*:*Z* = 1:10-25). When 10 eq. each of a carbonate salt (counter cation: Li^+, Na^+, K^+, Cs^+ and Ca^{2+}, corresponding to entries 1-5) was used in the aqueous medium (MeOH-H_2O) [14], the geometrical selectivity decreased slightly in that order. While the stoichiometry of Li_2CO_3 (10 or 1.0 eq.) did not affect the geometrical selectivity (*E*:*Z* = 1:2.6, entry 1; *E*:*Z* = 1:2.4, entry 6), the use of THF as a co-solvent resulted in a decrease (*E*:*Z* = 1:1.8, entry 7). When Li_2CO_3 (1.0 eq.) was used in MeOH, the reaction took a long time and proceeded in almost no selectivity (entry 8) because of the insolubility or low solubility of Li_2CO_3 in MeOH. When Ag_2CO_3 was used,[15] the geometrical selectivity increased greatly but the yield was low,

because the reaction also gave many unknown products (entries 9-12). The stoichiometry of Ag_2CO_3 (10 eq. or 1.0 eq.) affected the geometrical selectivity (*E*:*Z* = 1:11, entry 9; *E*:*Z* = 1:25, entry 10). When aprotic solvents (THF and benzene) were used, both reactions gave almost similar selectivity (*E*:*Z* = 1:11, entry 11; *E*:*Z* = 1:10, entry 12). The character of Ag^+ as a soft Lewis acid would mechanistically influence the geometrical selectivity, and Ag^+ would activate the acceptor part by coordination to the triple bond.

Table 2. Construction of spiroacetal enol ethers with carbonate salts

Entry	Conditions MCO_3 (eq.) / Solvent / Temp. / Time	Yield (%)	Product ratio[a] **6*E*** : **6*Z***
1	Li_2CO_3 (10) / MeOH-H_2O (1:1) / r.t. / 40 min	70	1 : 2.6
2	Na_2CO_3 (10) / MeOH-H_2O (1:1) / r.t. / 50 min	65	1 : 2.5
3	K_2CO_3 (10) / MeOH-H_2O (1:1) / r.t. / 15 min	65	1 : 2
4	Cs_2CO_3 (10) / MeOH-H_2O (1:1) / r.t. / 25 min	90	1 : 1.8
5	$CaCO_3$ (10) / MeOH-H_2O (1:1) / r.t. / 4 days	40	1 : 1.5
6	Li_2CO_3 (1.0) / MeOH-H_2O (1:1) / r.t. / 11 h	65	1 : 2.4
7	Li_2CO_3 (1.0) / THF-H_2O (1:1) / r.t. / 9 h	55	1 : 1.8
8	Li_2CO_3 (1.0) / MeOH / r.t. / 7 days	65	1.2 : 1
9	Ag_2CO_3 (10) / MeOH-H_2O (1:1) / r.t. / 18 h	30	1 : 11
10	Ag_2CO_3 (1.0) / MeOH-H_2O (1:1) / r.t. / 4 days	25	1 : 25
11	Ag_2CO_3 (1.0) / THF / r.t. / 13 days	15	1 : 11
12	Ag_2CO_3 (1.0) / benzene / r.t. / 13 days	25	1 : 10

a) The ratio was determined based on the integration by ^{1}H-NMR.

In order to establish the method for synthesizing (*Z*)-spiroacetal enol ethers such as **3*Z*** and **4*Z***, other reagents containing soft transition metal cations were next examined because Ag_2CO_3 gave good (*Z*)-selectivity. All the reactions were carried out in benzene, and the results are shown in Table 3. When $AgClO_4$ (1.0 eq.) was used, **6*E*** was obtained preferentially in high geometrical selectivity (*E*:*Z* = 28:1, entry 1) in contrast to when using Ag_2CO_3. In both cases of using $HgCl_2$ (1.0 eq.) and $Hg(OAc)_2$ (1.0 eq.),[16] the reactions also gave high (*E*)-selectivity (*E*:*Z* = 21:1, entry 2; *E*:*Z* = 15:1, entry 3); however, the yields were low. When $PdCl_2$ (1.0 eq.) was used, only the yield was increased; however, (*E*)-selectivity was not changed (*E*:*Z* = 15:1, entry 4). A dramatic change occurred when a catalytic amount of $Pd(OAc)_2$ was used (entries 5-7).[17-20] Although the yield was moderate, the (*Z*)-selectivity was very high (*E*:*Z* = 1:40, entry 5; *E*:*Z* = 1:56, entry 6) and the maximum ratio reached 1:95 in a 100-mg scale reaction (entry 7). By decreasing the amount of $Pd(OAc)_2$ from 0.2 to 0.01 or 0.02 eq., a long time was required to complete the reaction, but the (*Z*)-selectivity was clearly increased. In these cases, it was assumed that **6*Z*** was mechanistically formed *via* the anti-mode addition and rarely isomerized. In the cases of entries 1-4, the reaction medium would become acidic, and isomerization to the thermodynamically more stable **6*E*** would be caused by the acidity. Therefore, Et_3N (1.0 eq.) was added for each of entries 1-4 as a scavenger of the resulting acid (entries 8-11). (*E*)-Selectivity was decreased (*E*:*Z* = 2:1, entry 8) as we expected, and the yield was improved to 85%. Although (*E*)-selectivity was also decreased in entry 10 (*E*:*Z* = 7:1), the yield was still low. In contrast to entry 4, the addition of Et_3N resulted in decreasing not only (*E*)-selectivity (*E*:*Z* = 3.4:1) but also the yield in entry 11. When $HgCl_2$ (1.0 eq.) was used with Et_3N (entry 9), the spot corresponding to **6*Z*** was detected on TLC analysis without that of **6*E***; however, there was

no olefinic proton in the ^{1}H-NMR spectrum of the isolated product by preparative TLC. In the case of entry 2, such a phenomenon did not occur. Since the product seemed to be an organomercury compound, reductive treatment with $NaBH_4$ in an alkaline medium was carried out to give **6*E*** and **6*Z*** in 32:1 ratio and in 30% overall yield. A (*Z*)-organomercury compound would be first formed *via* the anti-mode addition, and the next reduction would be considered not to proceed with complete retention of the geometry. In this way, the highly (*Z*)-selective method (entry 7) for constructing a spiroacetal enol ether was developed.

Table 3. Construction of spiroacetal enol ethers with transision metal salts

Entry	Conditions MX (eq.) / Solvent / Temp. / Time	Yield (%)	Product ratio[a] **6*E*** : **6*Z***
1	$AgClO_4$ (1.0) / benzene / r.t. / 1 h	40	28 : 1
2	$HgCl_2$ (1.0) / benzene / r.t. / 37 h	10	21 : 1
3	$Hg(OAc)_2$ (1.0) / benzene / r.t. / 8 days	20	15 : 1
4	$PdCl_2$ (1.0) / benzene / r.t. / 3 days	70	15 : 1
5	$Pd(OAc)_2$ (0.2) / benzene / r.t. / 15 h	55	1 : 40
6	$Pd(OAc)_2$ (0.01) / benzene / r.t. / 7 days	65	1 : 56
7	$Pd(OAc)_2$ (0.02) / benzene / r.t. / 7 days[b]	61	1 : 95
8	$AgClO_4$ (1.0) / benzene / r.t. / 30 min[c]	85	2 : 1
9	$HgCl_2$ (1.0) / benzene / r.t. / 3 days[c]	30	32 : 1[d]
10	$Hg(OAc)_2$ (1.0) / benzene / r.t. / 8 days[c]	5	7 : 1
11	$PdCl_2$ (1.0) / benzene / r.t. / 3 days[c]	15	3.4 : 1

a) The ratio was determined based on the integration by ^{1}H-NMR.
b) The reaction was carried out at a 100-mg scale.
c) Triethylamine (1.0 eq.) was added.
d) After cyclization, the product was treated with $NaBH_4$ in Et_2O-aq.NaOH.

Isomerization and Reaction Mechanism of Spiroacetal Enol Ethers

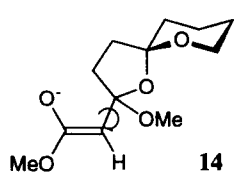
It was considered that the high (*E*)-selectivity would be caused by the thermodynamic control. Therefore, the isomerization process was studied, and the results are shown in Table 4. When **6*Z*** was treated with NaH (1.0 eq.) in THF, no isomerization was observed except for producing by-products on TLC analysis (entry 1). Therefore, the cyclizations using alkaline metal hydrides (entries 1-5 in Table 1) were controlled by kinetic protonation. Aqueous NH_4Cl used upon work-up and/or the starting material itself would act as the proton source, because the catalytic reaction (entry 9 in Table 1) proceeded completely to give a quantitative yield. When **6*Z*** was treated with NaOMe (1.0 eq.) in MeOH over a period of 4 days, isomerization to **6*E*** occurred (*E*:*Z* = 7:1, entry 2). In the case of the reaction starting from **6*E***, **6*Z*** was clearly detected under the same conditions (*E*:*Z* = 15:1, entry 3). It seemed that the reactions did not attain completely to the equilibrium state, because both reactions gave a different ratio. Conjugate addition of NaOMe forming enolate anion **14** would be the rate-determining step, and **6*E*** and **6*Z*** would be in equilibrium *via* **14**. Although the ester corresponding to **14** could not be detected, β-elimination would give **6*E*** and **6*Z***. While the cyclization using NaOMe was completed in 30 min (entry 6 in Table 1), isomerization using the same base took a very long time. Therefore, the cyclization was mainly controlled by kinetic protonation to give **6*E*** and **6*Z*** in 1:1 ratio. By using *t*-BuOK (1.0 eq.) in THF, **6*Z*** underwent isomerization rapidly to give **6*E*** in 30:1 ratio at r.t. (entry 4) and in 70:1 at 4 ℃ (entry 5). Therefore, the cyclization using a stoichiometric amount of *t*-BuOK (entries 7 and 8 in Table 1)

involved the isomerization process, and the results were based on thermodynamic control. However, the cyclization using a catalytic amount of *t*-BuOK (entries 10 and 11 in Table 1) would not involve (or slightly involve) the isomerization process to give poor selectivity because a sufficient amount of *t*-BuOK for isomerization would not be regenerated after cyclization. When **6*Z*** was treated with LDA in THF at -78 ℃, **6*E*** was also obtained in 73:1 ratio after protonation by adding H_2O (entry 6). In the case of using D_2O instead of H_2O, a mixture of **6*E*** and its partially deuterated product (**6*E*-*d***, *ca.* 20%) at the allylic position was obtained, and the structure was determined by the ^{1}H-NMR and mass spectra (HR-EIMS: calcd. for $C_{11}H_{15}DO_4$ (M^+) *m/z* 213.1111, found 213.1095). These results suggested that dienolate anion **15** would be formed as an intermediate of isomerization. Further study to substantiate the formation of intermediate **15** is in progress. A reductive condition using $NaBH_4$ in an alkaline medium resulted in no isomerization (entry 7). Therefore, **6*E*** was selectively obtained *via* the intermediate generated from the organomercury compound under such a condition (entry 9 in Table 3). Under the weakly basic condition using Cs_2CO_3 in aqueous medium, a slight isomerization from **6*Z*** to **6*E*** proceeded in 60 min (*E*:*Z* = 1:4.8, entry 8). The mechanism would be almost similar to that of entry 2 *via* conjugate addition and β-elimination. Therefore, the cyclization using a carbonate salt in aqueous medium (entries 1-8 in Table 2) slightly involved the isomerization process.

Table 4. Isomerization of spiroacetal enol ethers

Entry	SM	Conditions[a] Base or Acid (eq.) / Solvent / Temp. / Time	Product ratio[b] **6*E*** : **6*Z***
1	**6*Z***	NaH (1.0) / THF / r.t. / 10 min	No isomerization
2	**6*Z***	NaOMe (1.0) / MeOH / r.t. / 4 days	7 : 1
3	**6*E***	NaOMe (1.0) / MeOH / r.t. / 3 days	15 : 1
4	**6*Z***	*t*-BuOK (1.0) / THF / r.t. / 1 min	30 : 1
5	**6*Z***	*t*-BuOK (1.0) / THF / 4 °C / 1 min	70 : 1
6	**6*Z***	LDA (2.0) / THF / -78 °C / 60 min	73 : 1
7	**6*Z***	$NaBH_4$ (1.0) / Et_2O-aq. NaOH (1:1) / r.t. / 60 min	No isomerization
8	**6*Z***	Cs_2CO_3 (10) / MeOH-H_2O (1:1) / r.t. / 60 min	1 : 4.8
9	**6*Z***	CSA (0.2) / benzene / r.t. / 60 min	20 : 1
10	**6*Z***	Et_3N·HCl (1.0) / benzene / r.t. / 60 min	1 : 6.1
11	**6*Z***	AcOH (0.02) / benzene / r.t. / 60 min	1 : 59

a) All reactions were carried out at 10-mg scale, and the yields were more than 70% after usual work-up.
b) The ratio was determined based on the integration by ^{1}H-NMR.



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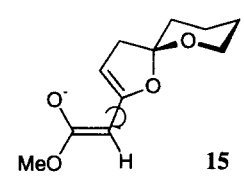

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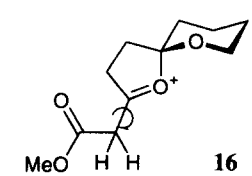

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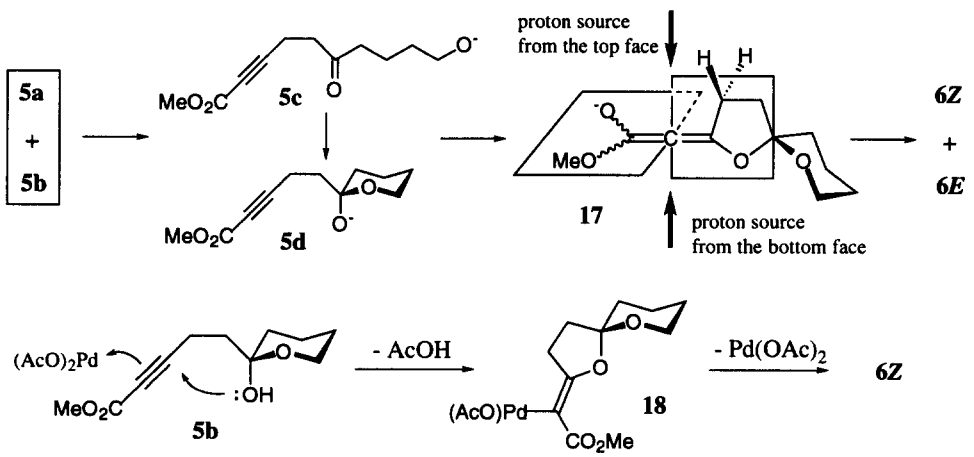
Under the acidic condition using CSA (0.2 eq.) in $CHCl_3$, isomerization proceeded smoothly in 60 min to give **6*E*** (*E*:*Z* = 20:1, entry 9). Oxonium ion intermediate **16** would be generated by protonation for the enol-part. While a slight isomerization proceeded in 60 min under the condition using Et_3N·HCl (1.0 eq.) in benzene (*E*:*Z* = 1:6.1, entry 10), isomerization was rarely detected under the condition using a catalytic amount

(0.02 eq.) of AcOH (*E*:*Z* = 1:59, entry 1). Therefore, the geometrical selectivity of most of the entries in Table 3 is mechanistically rationalized based on the anti-mode addition and the acidic isomerization.

The electronic repulsion between the lone-pair electrons of the ring oxygen and that of the ester carbonyl oxygen might reduce the thermodynamic stability of **6Z**. The MOPAC calculations (with PM3 parameter using CAChe™ work system) were carried out for both *s-cis* and *s-trans* conformers of **6E** and **6Z**. The result shows that the energy (= heat of formation) of **6E** (*s-cis*: -167.007 kcal/mol) is lower than that of **6Z** (*s-cis*: -164.963 kcal/mol). This result supports the assumption that **6E** is thermodynamically more stable than **6Z**. The mole fraction, calculated from ΔE (2.044 kcal/mol) at 298 K, is *E*:*Z* = *ca.* 30:1. This ratio is approximately identical with the experimental ratio (entries 8 and 15 in Table 1; entry 1 in Table 3; and entry 4 in Table 4).

By treating an equilibrium mixture of **5a** and **5b** with a base in non-aqueous medium, primary alkoxide **5c** and hemiacetal alkoxide **5d** are generated, and then allenolate anion **17** would be formed[21] *via* intramolecular conjugate addition (Scheme 3).[22] The diastereofacial selectivity of protonation for **17** reflects the geometrical selectivity under kinetic conditions. Protonation from the top or bottom face provides **6Z** or **6E**, respectively. While the allylic methylene group might act as a slight steric hindrance, the ring oxygen would have an electronic effect. An ionic proton source such as aq. NH_4Cl (used for work-up) tends to approach from the bottom face to give **6E** preferentially (entries 1-5 in Table 1). A large proton source such as *t*-BuOH (used as solvent) tends to approach from the top face to give **6Z** preferentially in the initial kinetic process (entry 14 in Table 1). It seems that a lipophilic interaction between the methylene group and *t*-BuOH would be induced rather than the steric hindrance.



Scheme 3

When carbonate salts were used in aqueous medium (entries 1-7 in Table 2), an allenol intermediate corresponding to **17** would be formed and undergo protonation from the top face to give **6Z** preferentially. It seems that a small non-ionic proton source such as MeOH or H_2O (used as solvent) is rarely subject to the steric hindrance of the methylene group. There is a little possibility that the chelation of metal cations by the ring oxygen and the ester carbonyl oxygen might prevent the isomerization of **6Z**. In any event, no marked

differentiation of the diastereoface of **17** or the corresponding allenol could be achieved under the conditions examined.

By using soft transition metal salts, the addition of the hemiacetal hydroxy group in **5b** proceeds mechanistically *via* the *anti*-mode addition to give a vinylic metal compound (for example, such as **18**, entry 5-7 in Table 3). Protonolysis of **18** proceeds with retention of the geometry to give **6Z** and with reproduction of the catalyst, $Pd(OAc)_2$.[17,18] After production of **6Z** under the kinetically controlled conditions, the acidity derived from the resulting acid in the reaction medium controls the final geometrical selectivity.

CONCLUSION

We have established highly stereoselective methods for constructing (*E*)- and (*Z*)-2-methoxycarbonylmethylene-1,6-dioxaspiro[4.5]decanes (**6*E*** and **6*Z***) from an equilibrium mixture of acyclic keto alcohol **5a** and hemiacetal **5b** possessing an alkynoate part *via* intramolecular conjugate addition. The mechanisms were proposed from the results of isomerization study. The thermodynamic stability of *s-cis* conformation in **6*E*** was supported by MOPAC calculation, and reflected actually the geometrical selectivity. Under the thermodynamically controlled condition using a stoichiometric amount of *t*-BuOK (1.0 eq.) in THF, (*E*)-isomer **6*E*** could be obtained exclusively in 52:1 ratio. Under the kinetically controlled condition using a catalytic amount of $Pd(OAc)_2$ (0.02 eq.) in benzene, (*Z*)-isomer **6Z** could be obtained exclusively in 95:1 ratio. Both conditions would be applied to the construction of more functionalized spiroacetal enol ethers and also become the key reaction for the synthesis of natural products such as **1**, **2** and **4** with the complementarity of geometrical selectivity. Furthermore, both homologues of **6*E*** and **6Z**, (*E*)- and (*Z*)-2-methoxycarbonylmethylene-1,6-dioxaspiro[4.4]nonanes relating to **3*E*** and **3Z**, have already been synthesized under the basic conditions.[12] Synthetic study of **1a** is now in progress. Natural and synthetic non-natural spiroacetal enol ethers are expected to exhibit various biological activities.

EXPERIMENTAL

General Methods. ^1H- and ^{13}C-NMR spectra were recorded with a JEOL JNM-EX-270 spectrometer (^1H: 270 MHz; ^{13}C: 67.8 MHz), and chemical shifts are reported as δ (ppm) values relative to internal tetramethylsilane or the residual proton of deuterated solvent. IR spectra were measured with a Perkin Elmer System 2000 FT-IR spectrometer. Mass spectra were recorded with a JEOL JMS-AX500 spectrometer or a JEOL JMS-SX102A spectrometer. Melting point values were obtained with a Yanaco micro-melting point apparatus MP-30 and are uncorrected. Column chromatography was carried out with Silica gel 60 (spherical, 70-140 mesh ASTM, KANTO CHEMICAL). Silica gel 60 F_{254} precoated plates were used for analytical TLC (catalog no. 5715, Merck) and preparative TLC (catalog no. 5744, Merck).

2-(3-Tetrahydropyranyloxypropyl)-1,3-dithiane. To a stirred solution of 1,3-dithiane (1.74 g, 14.4 mmol) in dry THF (25 ml) was added dropwise *n*-BuLi (9.5 mL, 16.0 mmol, as 1.68 M hexane solution) at -40 ℃ under an argon atmosphere. The solution was stirred for 3 h at -20 ℃ and then cooled to -78 ℃. To the resulting solution of 2-lithio-1,3-dithiane was added dropwise a solution of 1-bromo-3-(tetrahydropyranyloxy)-propane (3.22 g, 14.4 mmol) in dry THF (5.8 ml) at -78 ℃. The mixture was stirred for 24 h at -20 ℃ to

complete monoalkylation. After the addition of sat. aq. NH_4Cl (50 ml), the mixture was extracted with EtOAc (50 ml x 3). The combined extracts was washed with brine (50 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 4/1) to give 2-(3-tetrahydropyranyloxypropyl)-1,3-dithiane (3.63 g, 96 %) as a colorless oil: IR (film) 2941, 2900, 2870, 1465, 1451, 1441, 1423, 1384, 1362, 1366, 1352, 1323, 1276, 1260, 1243, 1201, 1185, 1156, 1136, 1121, 1076, 1034, 987, 905, 969, 814 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.47-1.95 (11H, m), 2.12 (1H, m), 2.77-2.94 (4H, m), 3.37-3.54 (2H, m), 3.75 (1H, m), 3.84 (1H, m), 4.07 (1H, t, J = 6.4 Hz), 4.58 (1H, t, J = 3.5 Hz); EI-MS *m/z* 262 (M^+, 4.2), 177 (M^+-C_5H_9O, 100), 161 (M^+-$C_5H_9O_2$, 36.4), 85 (77.8); HR-EI-MS calcd. for $C_{12}H_{22}O_2S_2$ (M^+) *m/z* 262.1061, found 262.1041.

2-(4-tert-Butyldiphenylsilyloxybutyl)-2-(3-tetrahydropyranyloxypropyl)-1,3-dithiane (**7**). To a stirred solution of 2-(3-tetrahydropyranyloxypropyl)-1,3-dithiane (8.31 g, 31.7 mmol) was added dropwise *n*-BuLi (21.8 mL, 34.8 mmol, as 1.60 M hexane solution) at -40 ℃ under an argon atmosphere. The stirring was continued for 5.5 h at -20 ℃. To the resulting solution of 2-alkyl-2-lithio-1,3-dithiane was added dropwise a solution of 1-(*tert*-butyldiphenylsilyloxy)-4-iodobutane (17.8 g, 40.5 mmol) in dry THF (30 ml) at -78 ℃. The mixture was stirred for 24 h at -20 ℃ to complete dialkylation. The same work-up as described above and silica gel column chromatography (hexane/EtOAc = 8/1) gave **7** (16.0 g, 88 %) as a colorless oil: IR (film) 2938, 2858, 1590, 1472, 1463, 1454, 1441, 1428, 1388, 1362, 1352, 1275, 1261, 1239, 1200, 1184, 1159, 1137, 1112, 1034, 998, 989, 908, 969, 823 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.04 (9H, s), 1.44-2.03 (18H, m), 2.70-2.89 (4H, m), 3.40 (1H, m), 3.50 (1H, m), 3.67 (2H, t, J = 6.1 Hz), 3.75 (1H, m), 3.86 (1H, m), 4.58 (1H, t, J = 3.3 Hz), 7.34-7.46 (6H, m), 7.63-7.72 (4H, m); EI-MS *m/z* 573 (MH^+, 0.48), 572 (M^+, 1.03), 515 (M^+-C_4H_9, 13.4), 471 (M^+-$C_5H_9O_2$, 13.4), 323 (100), 199 (33.2), 85 (72.1); HR-EI-MS calcd. for $C_{32}H_{48}O_3SiS_2$ (M^+) *m/z* 572.2814, found 572.2841.

2-(4-tert-Butyldiphenylsilyloxybutyl)-2-(3-hydroxypropyl)-1,3-dithiane (**8**). A mixture of **7** (1.52 g, 2.64 mmol) and PPTS (66.3 mg, 0.26 mmol) in EtOH (60 ml) was stirred for 6 days at r.t. After addition of $NaHCO_3$ (60 mg), the mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 4/1) to give **8** (1.24 g, 96 %) as a colorless oil: IR (film) 3392, 2998, 2933, 2858, 1589, 1472, 1462, 1455, 1428, 1390, 1361, 1324, 1275, 1239, 1188, 1111, 1008, 999, 937, 909, 823 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.05 (9H, s), 1.45-1.75 (7H, m), 1.82-2.03 (6H, m), 2.72-2.89 (4H, m), 3.66 (2H, t, J = 5.9 Hz), 3.68 (2H, t, J = 5.9 Hz), 7.34-7.46 (6H, m), 7.63-7.72 (4H, m); EI-MS *m/z* 489 (MH^+, 0.25), 488 (M^+, 0.55), 431 (M^+-C_4H_9, 12.2), 323 (100), 199 (43.4); HR-EI-MS calcd. for $C_{27}H_{40}O_2SiS_2$ (M^+) *m/z* 488.2239, found 488.2239.

2-(4-tert-Butyldiphenylsilyloxybutyl)-2-(4,4-dibromo-3-butenyl)-1,3-dithiane (**9**). To a stirred solution of **8** (3.80 g, 7.77 mmol), DMSO (5.56 ml, 77.7 mmol), and Et_3N (11.0 ml, 78.0 mmol) in CH_2Cl_2 (15 ml) was added portionwise SO_3·pyridine complex (6.31 g, 38.9 mmol). After being stirred for 20 min at r.t., the reaction mixture was partitioned between water (50 ml) and ether (50ml). The organic layer was washed with brine (50 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give a crude aldehyde, which was used for the next reaction without further purification. To a prepared solution of Ph_3P (8.40 g, 31.1

mmol) and CBr_4 (5.26 g, 15.5 mmol) in CH_2Cl_2 (85 ml) at 0 ℃, a solution of the crude aldehyde in CH_2Cl_2 (10 ml) was added. After being stirred for 60 min at 0 ℃, the reaction mixture was washed with sat. aq. $NaHCO_3$ (80 ml) and brine (80 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crystalline residue (Ph_3P=O) was removed by filtration with hexane-EtOAc (20:1). The combined filtrate and washings were concentrated under reduced pressure to give an oily residue. Purification by silica gel column chromatography (hexane/EtOAc = 4/1) gave **9** (3.55 g, 71 %, 2 steps) as a colorless oil: IR (film) 3070, 3048, 2932, 2857, 1589, 1472, 1462, 1428, 1389, 1361, 1262, 1110, 1029, 1097, 822, 804, 741, 702 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.05 (9H, s), 1.45-1.63 (4H, m), 1.79-2.06 (6H, m), 2.14-2.26 (2H, m), 2.70-2.91 (4H, m), 3.68 (2H, t, J = 5.9 Hz), 6.40 (1H, t., J = 7.5 Hz), 7.34-7.46 (6H, m), 7.63-7.72 (4H, m); EI-MS *m/z* 644 (M^+, 0.27; $^{81}Br^{81}Br$), 642 (M^+, 0.31; $^{79}Br^{81}Br$), 640 (M^+, 0.16; $^{79}Br^{79}Br$), 587 (M^+-C_4H_9, 60.7; $^{81}Br^{81}Br$), 585 (M^+-C_4H_9, 100; $^{79}Br^{81}Br$), 583 (M^+-C_4H_9, 40.5; $^{79}Br^{79}Br$), 199 (79.9); HR-EI-MS calcd. for $C_{24}H_{29}O^{79}Br^{81}BrSiS_2$ (M^+-C_4H_9) *m/z* 584.9775, found 584.9807.

2-(4-tert-Butyldiphenylsilyloxybutyl)-2-(3-butynyl)-1,3-dithiane (**10**). To a stirred solution of **9** (1.02 g, 1.59 mmol) in dry THF (3.2 ml) was added dropwise *n*-BuLi (2.06 mL, 3.50 mmol, as 1.7 M hexane solution) at -78 ℃ under an argon atmosphere. The mixture was stirred for 60 min at -78 ℃, and allowed to warm to r.t. After addition of sat. aq. NH_4Cl (20 ml), the mixture was extracted with EtOAc (20 ml). The organic extract was washed with brine (20 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 19/1) to give **10** (0.72 g, 94%) as a colorless oil: IR (film) 3295, 3071, 3049, 2932, 2907, 2858, 2119, 1472, 1427, 1389, 1275, 1111, 823 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.05 (9H, s), 1.48-1.60 (4H, m), 1.78 (2H, m), 1.83-2.04 (2H, m), 2.32 (2H, m), 2.72 (2H, m), 2.87 (2H, m), 3.67 (2H, t, J = 5.9 Hz), 7.34-7.46 (6H, m), 7.63-7.72 (4H, m); EI-MS *m/z* 483 (MH^+, 1.07), 482 (M^+, 2.34), 425 (M^+-C_4H_9, 100), 199 (61.6); HR-EI-MS calcd. for $C_{28}H_{38}OSiS_2$ (M^+) *m/z* 482.2133, found 482.2161.

Methyl 10-(tert-butyldiphenylsilyloxy)-6-oxo-2-decynoate (**12**). To a stirred solution of **10** (966 mg, 2.00 mmol) in dry THF (20 ml) was added dropwise *n*-BuLi (1.25 mL, 2.10 mmol, as 1.68 M hexane solution) at -78 ℃ under an argon atmosphere. After 60 min, the resulting acetylide was treated with $ClCO_2Me$ (0.19 ml, 2.40 mmol) at -78 ℃. The reaction mixture was stirred for 60 min at -78 ℃ and allowed to warm to r.t. After the addition of sat. aq. NH_4Cl (15 ml), the mixture was extracted with EtOAc (15 ml). The organic extract was washed with brine (15 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give **11**, which was used for the next reaction without further purification. To a prepared solution of NCS (1.07 g, 8.00 mmol) and $AgNO_3$ (1.54 g, 9.00 mmol) in 30% aq. CH_3CN (30 ml) at -5 ℃, a solution of **11** in CH_3CN (15 ml) was added. The mixture was stirred for 15 min. To this mixture was successively added sat. aq. $Na_2S_2O_3$ (2 ml), sat. aq. $NaHCO_3$ (2 ml), and brine (2 ml) at 1-min intervals. The resulting mixture was filtered through a Celite pad, and the filter cake was washed with hexane-$CHCl_3$ (1:1). The organic layer of the filtrate was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/EtOAc = 6/1) to give **12** (701 mg, 78%, 2 steps) as a colorless oil: IR (film) 3072, 3050, 3015, 3000, 2954, 2933, 2859, 2241, 1723, 1715, 1590, 1487, 1472, 1463, 1429, 1390, 1362, 1331, 1257, 1191, 1112, 1029, 1007, 998, 924, 823, 743, 704

cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.05 (9H, s), 1.49-1.74 (4H, m), 2.40 (2H, t, *J* = 7.3 Hz), 2.58 (2H, m), 2.67 (2H, m), 3.65 (2H, t, *J* = 6.1 Hz), 3.74 (3H, s), 7.34-7.46 (6H, m), 7.63-7.72 (4H, m); EI-MS *m/z* 419 (M^+-CH_3O, 6.11), 393 (M^+-C_4H_9, 86.4), 199 (100); HR-EI-MS calcd. for $C_{24}H_{25}O_4Si$ (M^+-C_4H_9) *m/z* 393.1522, found 393.1539.

2-(4-Hydroxybutyl)-5-(methoxycarbonylmethyl)-furan (**13**). To a solution of **12** (52 mg, 0.11 mmol) in THF (1.0 ml) was added *n*-Bu_4NF (0.20 ml, 0.20 mmol, as 1.0 M THF solution) at 0 ℃. The mixture was stirred for 30 min. After the addition of sat. aq. $NaHCO_3$ (10 ml), the mixture was extracted with CH_2Cl_2 (10 ml x 3). The combined extracts were washed with brine (10 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (benzene/EtOAc = 2/1) to give **13** (8.0 mg, 34%) as a colorless oil: IR (film) 3392, 2945, 2867, 1747, 1645, 1568, 1436, 1344, 1273, 1226, 1122, 1060, 1015, 956, 890, 832, 788 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.61-1.74 (7H, m), 2.63 (2H, t, *J* = 7.2 Hz), 3.65 (2H, m), 3.72 (3H, s), 5.93 (1H, d, *J* = 3.0 Hz), 6.09 (1H, d, *J* = 3.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 24.00, 27.50, 31.90, 33.75, 52.00, 62.40, 105.60, 108.32, 145.44, 155.44, 169.95; EI-MS *m/z* 212 (M^+, 99.9), 194 (M^+-H_2O, 7.3), 166 (M^+-C_2H_6O, 49.8), 153 (M^+-CO_2CH_3, 100), 135 (47.4), 111 (68.5), 107 (78.0), 94 (41.2); HR-EI-MS calcd. for $C_{11}H_{16}O_4$ (M^+) *m/z* 212.1049, found 212.1051.

Methyl 10-hydroxy-6-oxo-2-decynoate (**5a**). To a solution of **12** (397 mg, 0.882 mmol) in CH_3CN (1.8 ml) was added HF·pyr. (0.50 ml, 17.6 mmol) at 0 ℃. The mixture was stirred for 24 h. After addition of sat. aq. $NaHCO_3$ (10 ml), the mixture was extracted with CH_2Cl_2 (10 ml x 3). The combined extracts were washed with brine (10 ml), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (benzene/EtOAc = 2/1) to give **5a** (equilibrium mixture with **5b**, **5a**:**5b** = *ca.* 8:1, 175 mg, 94%) as a colorless oil: IR (film) 3419, 2952, 2933, 2859, 224, 1715, 1695, 1505, 1435, 1373, 1258, 1429, 1184, 1078, 954, 909, 817, 753 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.42-1.92 (5H, m), 2.49 (2H, t, *J* = 6.9 Hz), 2.60 (2H, m), 2.72 (2H, m), 3.63 (2H, t, *J* = 5.9 Hz), 3.74 (3H, s); ^{13}C-NMR ($CDCl_3$) δ 12.67, 19.61, 31.59, 39.64, 41.92, 52.33, 61.69, 72.62, 88.05, 153.76, 207.71; EI-MS *m/z* 212 (M^+, 2.72), 195 (M^+-OH, 13.4), 181 (M^+-CH_3O, 11.9), 180 (6.38), 153 (M^+-CH_3CO_2, 5.54), 101 (71.1), 83 (90.1), 55 (100); HR-EI-MS calcd. for $C_{11}H_{16}O_4$ (M^+) *m/z* 212.1048, found 212.1068.

Construction of **6E** *and* **6Z** *from an equilibrium mixture of* **5a** *and* **5b**.

Typical procedure A (entry 2 in Table 1). To a solution of **5a** and **5b** (60.8 mg, 286 μmol) in dry THF (2.0 ml) was added NaH (11.5 mg, 296 μmol, as 60% dispersion in oil) at 4 ℃. The mixture was stirred for 10 min at the same temperature. After the addition of sat. aq. NH_4Cl (2.0 ml), the mixture was extracted with EtOAc (5 ml x 3). The combined extract was washed with brine (5 ml) and concentrated under reduced pressure. The residue was separated by preparative TLC (hexane/EtOAc = 3/1) to give **6*E*** (41.6 mg, 68%) as colorless crystals and **6*Z*** (14.2 mg, 23%) as a colorless oil. According to procedure A, the other entries in Table 1 were carried out. Except for entries 2, 3 and 6, the product ratio was at first determined from the integration of crude mixture by ^{1}H-NMR, and then the yield was determined after purification by columun chromatography or preparative TLC.

Typical procedure B (entry 1 in Table 2). To a solution of **5a** and **5b** (10.0 mg, 50.0 μmol) in MeOH-H_2O (1:1, 2.0 ml) was added Li_2CO_3 (35.0 mg, 500 μmol) at r.t. The mixture was stirred for 50 min at the same temperature and then extracted with EtOAc (5 ml x 3). The combined extracts was successively washed with H_2O (5 ml) and brine (5 ml), and concentrated under reduced pressure to give a crude mixture of **6*E*** and **6*Z***. The geometrical selectivity (*E*:*Z* = 1:2.6) was determined from the integration by ^{1}H-NMR. The yield (70%) was determined as a mixture of **6*E*** and **6*Z*** after the purification by preparative TLC. According to procedure B, the other entries in Table 2 were carried out. In the cases of using Ag_2CO_3 (entries 9-12), the filtration of the reaction mixture through Celite pad was carried out before extraction.

Typical procedure C (entry 7 in Table 3). To a solution of **5a** and **5b** (100 mg, 470 μmol) in benzene (10 ml) was added $Pd(OAc)_2$ (2.10 mg, 9.4 μmol) at r.t. The mixture was stirred for 7 days at the same temperature and passed through a short silica gel columun with 1% Et_3N-EtOAc as eluent. The eluate was concentrated under reduced pressure to give a crude mixture of **6*E*** and **6*Z***. The geometrical selectivity (*E*:*Z* = 1:95) and the yield (61%) were detemined by the same method as already described. According to procedure C, the other entries in Table 3 were carried out.

Isomerization of **6E** *and* **6Z** *(Table 4).* According to typical procedure A for constructing **6*E*** and **6*Z***, entries 1-5 were carried out. According to typical procedure B, entries 7 and 8 were carried out. In entry 6, a solution of **6Z** in dry THF was added to a prepared LDA solution in dry THF. After the addition of H_2O, the mixture was extracted with EtOAc. In entries 9-11, the reaction mixture was partitioned between EtOAc and H_2O. The each organic layer was successively washed with H_2O and brine, and concentrated under reduced pressure to give a crude mixture. All the geometrical selectivities and yields (> 70%) were detemined by the same method as already described.

(E)-2-Methoxycarbonylmethylene-1,6-dioxaspiro[4.5]decane (**6*E***). mp 43-44 ℃; IR (film) 2949, 2880, 1710, 1651, 1646, 1436, 1376, 1359, 1317, 1286, 1257, 1229, 1205, 1191, 1160, 1118, 1094, 1075, 1046, 1007, 971, 941, 888, 859, 849 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.52-1.97 (7H, m), 2.08 (1H, ddd, *J* = 12.5, 9.2, 2.0 Hz), 3.03 (1H, dddd, *J* = 18.5, 10.6, 8.6, 2.0 Hz), 3.26 (1H, ddt, *J* = 18.5, 9.2, 2.0 Hz), 3.65 (3H, s), 3.67 (1H, m), 3.79 (1H, ddd, *J* = 15.2, 11.2, 4.0 Hz), 5.32 (1H, t, *J* = 2.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 19.91, 24.80, 29.53, 33.10, 35.82, 50.86, 63.16, 90.59, 110.08, 169.09, 176.05; EI-MS *m/z* 212 (M^+, 45.9), 181 (M^+-CH_3O, 36.4), 180 (53.7), 153 (7.86), 152 (15.6), 111 (100); HR-EI-MS calcd. for $C_{11}H_{16}O_4$ (M^+) *m/z* 212.1048, found 212.1044.

(Z)-2-Methoxycarbonylmethylene-1,6-dioxaspiro[4.5]decane (**6*Z***). IR (film) 2945, 2883, 1718, 1697, 1653, 1436, 1383, 1320, 1289, 1277, 1260, 1230, 1208, 1190, 1155, 1123, 1096, 1074, 1046, 1007, 993, 971, 951, 942, 896, 884, 853 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.56-2.14 (8H, m), 2.63 (1H, ddt, *J* = 17.2, 9.2, 2.0 Hz), 2.93 (1H, dddd, *J* = 17.2, 10.6, 8.6, 2.0 Hz), 3.67 (3H, s), 3.70 (1H, m), 3.94 (1H, ddd, *J* = 15.2, 11.2, 4.0 Hz), 4.88 (1H, t, *J* = 2.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 19.63, 24.53, 30.35, 32.81, 34.58, 50.44, 63.09, 88.75, 111.79, 166.06, 171.09; EI-MS *m/z* 212 (M^+, 48.5), 181 (M^+-CH_3O, 41.5), 180 (55.6), 153 (8.72), 152 (15.1), 111 (100); HR-EI-MS calcd. for $C_{11}H_{16}O_4$ (M^+) *m/z* 212.1048, found 212.1044.

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