DOI: 10.1002/chem.201000930

Stereocontrolled Synthesis of Spiro[*n*.2]alkenes by Ring Contraction of Fused-Cyclobutanols

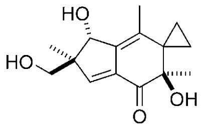
Kiyosei Takasu,* Yuuki Nagamoto, and Yoshiji Takemoto*[a]

Abstract: An unusual ring-contraction rearrangement to give spirocyclopropanes from fused cyclobutanols (see scheme) has been developed. It is found that the strain energy of the substrates derived from an additional fused ring and the stereoelectronic effect of the migrating σ bond are important factors. It is noteworthy that the rearrangement proceeds in a stereospecific manner. Moreover, the method provides a spiro(cyclopropane–indane) framework from tricyclo[6.3.0.02,5]undecane, which corresponds to illudane and the protoilludane skeleton.

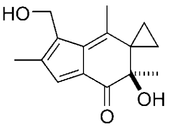
Keywords: rearrangement · ring contraction · small ring systems · spiro compounds · stereocontrolled synthesis

Introduction

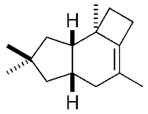
Small ring systems are an important topic in organic chemistry and afford considerable attention from theoretical, synthetic, and medicinal perspectives. Spirocyclic compounds have also attracted synthetic and medicinal chemists because of their characteristic structure. Spiro[*n*.2]alkanes and alkenes are found in naturally occurring substances,[1] such as illudins. Illudin S (**1**) was first discovered as an antibiotic from the Jack O'Lantern mushroom *Omphalotus olearius.* Irofulven (**2**), which is a hemi-synthetic analogue derived from illudin S, has been developed as an anticancer drug candidate, and is currently in phase II clinical trials for use in solid tumor treatments.[2] On the basis of the structures of its metabolites and structure–activity relationship studies, it has been proposed that the spirocyclopropyl structure plays a key function in anticancer action.[3] Illudins were postulated to be biosynthesized through 6-protoilludene (**3**) by a ring-contraction rearrangement.,[4,5] This biosynthetic mechanism led us to believe that the spiro[*n*.2]alkenes skeleton would be chemically transformed from fused cyclobutanols.



illudin S (**1**)



irofulven (**2**)



6-protoilludene (**3**)

Due to the inherent ring strains of small ring systems, interesting aspects of their reactivity have been well exploited.[6,7] For example, ring-expansion rearrangement reactions have been well studied. Furthermore, relief of the ring strain is known to produce cyclobutane and cyclopentane compounds from cyclopropane and cyclobutane derivatives, respectively, by the migration of a C–C bond in the ring system.[8] Conversely, the reversal rearrangement reaction (ring contraction), which produces a smaller ring system, is also possible.[6c,9] Olah et al. have summarized the nature of cyclopropylcarbinyl cations, which can be rearranged into cyclobutyl cations, and their reactivity.[10] However, studies concerning the selective formation of cyclopropyl compounds from cyclobutanes are rare for thermodynamic reasons.[11] We believe that an increase in strain energy of a cyclobutane substrate through the installation of an additional ring would induce the ring-contraction rearrangement in a cyclopropane compound (Scheme 1). Thus, a planar conformation of the sp^2 carbocation on the bridgehead of fused-cyclobutane **C** would be thermodynamically unfavorable owing to conformational restriction. PM3 level calculations estimate the heat of formation (ΔH_f) of the monocyclic cyclobutyl cation **A** and the corresponding cyclopropylcarbinyl cation **B** to be 190.17 and 192.60 kcal mol^{-1}, respectively. On the other hand, the ΔH_f for cations possessing bicyclo[4.2.0]octane **C** and spiro[4.2]octane **D** were calculated to be

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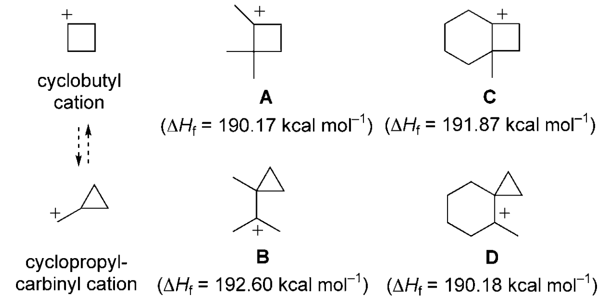
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201000930.



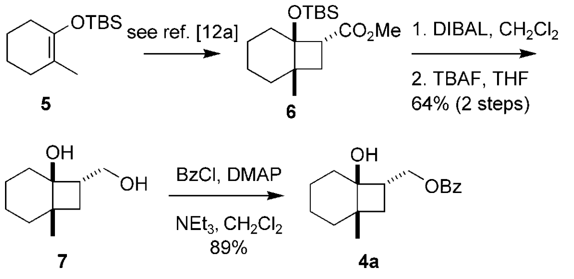
Scheme 1. PM3 calculated heat of formation of tertiary cyclobutyl cations **A** and **C** and cylopropylcarbinyl cations **B** and **D**.

191.87 and 190.18 $kcal\,mol^{-1}$, respectively. Herein, we describe the unusual ring-contraction reaction of fused-cyclobutanols to produce spirocyclic cyclopropanes, spiro[*n*.2]alkenes, as well as provide mechanistic insight. To the best of our knowledge, stereocontrolled methods giving spiro[*n*.2]alkenes with substituents on cyclopropane ring, which would be a useful skeleton in medicinal and synthetic chemistry, are limited.[12]

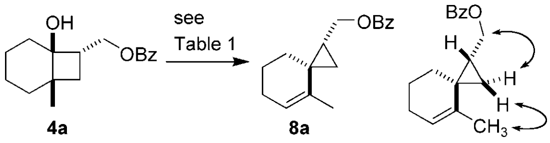
Results and Discussion

Cyclobutanol substrates **4a–j** were prepared from silyl enol ethers in several steps. A typical synthetic route of **4a**, which corresponds to a precursor of **C** (Scheme 1), is summarized in Scheme 2. Siloxycyclobutane **6** was synthesized from silyl enol ether **5** and methyl acrylate by a Tf_2NH-catalyzed [2+2] cycloaddition, which was previously developed by us, to give substituted cyclobutanes in a concise manner.[13] Reduction of the ester moiety of **6**, followed by desilylation, gave diol **7**. Selective protection of the primary hydroxyl group of **7** afforded **4** in a good yield.

With a series of cyclobutanols in hand, we examined the ring-contraction reaction of **4a** under conditions for the formation of the cyclobutyl cation (Scheme 3). When **4a** was treated with several acid catalysts, such as concentrated H_2SO_4, $TsOH{\cdot}H_2O$, and $BF_3{\cdot}OEt_2$, a complex mixture was obtained but no cyclopropane compound was detected. Next, we presumed that the transformation of the hydroxyl group of **4a** into a good leaving group would induce the desired rearrangement (Table 1). Under the conditions of Sc^{III}-catalyzed acetylation,[14] the desired cyclopropane **8a** was formed in 41% yield but the major product was the corresponding acetate (Table 1, entry 1). Treatment of **4a** with methanesulfonyl chloride (MsCl; 4.5 equiv) in the presence of excess amounts of 2,6-lutidine gave positive results (Table 1, entries 2–4). These results indicate that polar solvents are preferable for the reaction. By using 2,6-lutidine as a solvent, the ring contraction proceeded smoothly, producing **8a** in 70% yield (Table 1, entry 5). When the reaction was performed using smaller amounts of the reagent or at a lower temperature, the chemical yield of **8a** was reasonable, but the reaction required a longer time to go to completion (Table 1, entries 6 and 7). In all cases, spiro[4.2]octene **8a** was obtained as a single diastereomer, the structure and stereochemistry of which were determined by 2D NMR spectroscopy experiments. It should be noted that no compounds which could be formed by the rearrangement of another σ bond were detected. When thionylchloride ($SOCl_2$) was employed as a reagent, compound **8a** was obtained in approximately 55%. Although the reaction proceeded rapidly even at room temperature, it produced structurally undefined by-products (≈10%) that were hard to separate from **8a** (Table 1, entry 8).



Scheme 2. Typical procedure for the preparation of substrate **4a**. TBS = *tert*-butyldimethylsilyl, DIBAL = diisobutylaluminum hydride, TBAF = tetra-*n*-butylammonium fluoride, Bz = benzoyl, DMAP = 4-dimethylaminopyridine.



Scheme 3. Ring-contraction rearrangement of **4a** and selected NOE correlations of **8a**.

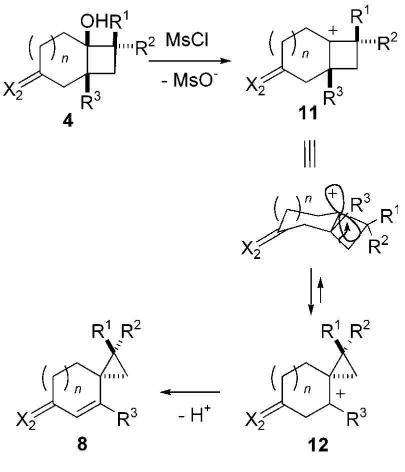
Table 1. Optimization of reaction conditions.

Entry	Reagents	Solvent	T [°C]	t [h][a]	Yield of **8a** [%]
1	Ac_2O (5.0 equiv), $Sc(OTf)_3$ (4 mol%)	MeCN	50	6	41
2	MsCl (4.5 equiv), 2,6-lutidine (6.0 equiv)	MeCN	50	5	42
3	MsCl (4.5 equiv), 2,6-lutidine (6.0 equiv)	DCE	80	3	31
4	MsCl (4.5 equiv), 2,6-lutidine (6.0 equiv)	DMF	50	5	41
5	MsCl (4.5 equiv)	2,6-lutidine	50	2	70
6	MsCl (2.0 equiv)	2,6-lutidine	50	10	65
7	MsCl (4.5 equiv)	2,6-lutidine	RT	8	69
8	$SOCl_2$ (2.5 equiv), Et_3N (5.0 equiv)	CH_2Cl_2	RT	0.25	≈55[b]

[a] Reaction time was determined when complete consumption of **4a** was monitored on TLC. [b] Inseparable by-products were contained. Ac = acetyl, Tf = trifluoromethanesulfonyl, Ms = methanesulfonyl, DCE = 1,2-dichloroethane, DMF = dimethylformamide

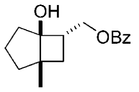
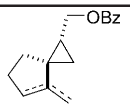
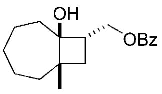
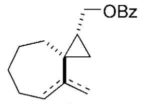
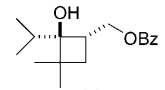
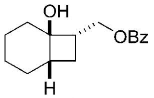
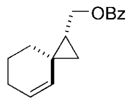
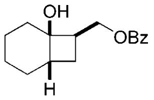
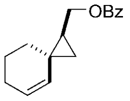
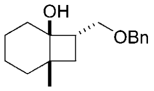
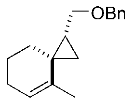
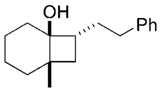
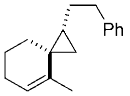
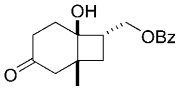
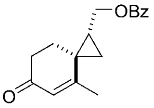
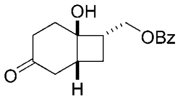
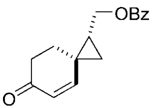
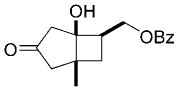
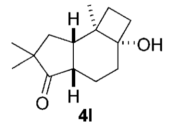
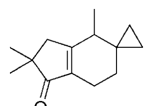
Having established the optimal conditions for the ring-contraction reaction, we intended to determine its scope and limitations with respect to cyclobutanols with various fused rings and substituents (Table 2). Reactions of bicyclo[3.2.0]heptanol **4b** and [5.2.0]nonanol **4c** gave the corresponding spirocyclopropanes **8b** and **8c**, respectively, in good yields (Table 2, entries 1 and 2). Different from the reaction of bicyclo[4.2.0]octanol **4a**, which gave *endo*-olefin **8a**, compounds **8b** and **8c** were obtained as mixtures of *endo*- and *exo*-olefinic isomers. On the other hand, no rearrangement occurred in the reaction of monocyclic cyclobutanol **4d** (Table 2, entry 3). It should be mentioned that the rearrangement proceeded in a stereospecific manner. Thus, diastereoisomeric bicyclo[4.2.0]octanols **4e** and **4f** gave the spiro[4.2]octenes **8e** and **8f**, respectively, in moderate yields as a single isomer (Table 2, entries 4 and 5). Compounds **4g** and **4h**, with ether and alkyl side chains, respectively, on the cyclobutane ring, also afforded the corresponding spirocyclic compounds in moderate to good yields (Table 2, entries 6 and 7). The result indicates that the contribution of the oxygen atom in stabilizing the cationic intermediate is not crucial. Substrates **4i** and **4j**, which have carbonyl groups on the cyclohexane ring, underwent rearrangement smoothly to give spirocyclic enones **8i** and **8j**, respectively, in moderate to high yields (Table 2, entries 8 and 9). On the contrary, in the reaction of bicyclo[3.2.0]heptanone **4k**, only the chloride with an enol sulfonate moiety (**9k**) was obtained in 50% yield. No desired spirocyclopropane was observed under the conditions tested (Table 2, entry 10). To elucidate the effect of a benzoyloxymethyl substituent on the reactivity, the tricyclic substrate **4l**, which has no substituent on the cyclobutane ring was prepared. The reaction proceeded to give cyclopropane **8l** in 50% yield along with chloride **10l** in 30% yield (Table 2, entry 11). Formation of **10l** indicates that the reaction proceeds through the generation of a cyclobutyl cation via the mesylate of **4l**. It is noteworthy that the reaction of **4l** into **8l** is reasonably consistent with the proposed biosynthetic route of illudins from protoilludanes.[4]

The proposed reaction mechanism of the ring-contraction rearrangement is summarized in Scheme 4. After the sulfonylation of the tertiary hydroxyl group of **4**, the corresponding carbocationic intermediate **11** can be generated.[15] Then,

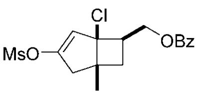


Scheme 4. Proposed mechanism for the ring-contraction rearrangement.

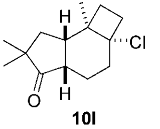
Table 2. Scope of ring-contraction rearrangement.[a]

Entry	Substrates	Products	Yield [%]
1	 **4b**	 **8b**	63 (*endo*/*exo* = 3:1)[d]
2	 **4c**	 **8c**	62 (*endo*/*exo* = 1:10)[d]
3	 **4d**	–	0
4	 **4e**	 **8e**	43
5	 **4f**	 **8f**	42
6	 **4g**	 **8g**	70
7	 **4h**	 **8h**	49
8[b]	 **4i**	 **8i**	82
9	 **4j**	 **8j**	58
10	 **4k**	–	0[e]
11[c]	 **4l**	 **8l**	50[f]

[a] Reactions were carried out using **4** (0.10 mmol) and MsCl (4.5 equiv) in 2,6-lutidine (1 M) at 50 °C for 2-20 h, unless otherwise mentioned. [b] at 70 °C. [c] MsCl (4.5 equiv), NEt_3 (6.0 equiv) in CH_2Cl_2 at 0 °C to RT. [d] The ratios (*endo*/*exo*) were determined by ^1H NMR spectroscopy. [e] **9k** was obtained as a major product in 58% yield. [f] **10l** was obtained as a by-product in 30% yield.



9k



10l

the adjacent C−C bond to the cation in the cyclobutane ring of **11** can rearrange to give spirocyclic cation **12**. Finally, irreversible deprotonation would result in spiro[*n*.2]alkene **8**. The preferable production of spirocyclopropanes from fused cyclobutanols can be explained as follows: A release of strain energy of the cyclobutyl cation can act as a driving force for the rearrangement because the sp^2-like geometry of the carbocation on the cyclobutane ring (**11**) would be unfavorable compared with that on the medium-sized ring (**12**). In this respect, migration of R^1–R^3 substituents, which also result in the formation of the corresponding cyclobutyl cation intermediates, can be ruled out. Moreover, strain energy of a fused system itself would be a trigger to rearrange into a spiro system with migration of a C−C bond in cyclobutane ring. Clearly, no rearrangement was detected in the reaction of the monocyclic system (Table 2, entry 3). Beyond our expectations, the desired rearrangement also proceeds in the reaction of **4e**, **4f**, and **4j** ($R^3 = H$), although secondary cation **12** would be generated as an intermediate from tertiary cation **11** (Table 2, entries 4, 5, and 9). A carbonyl group in the cyclohexane ring (substrates **4i** and **4j**) would accelerate the final elimination step and, therefore, resulted in higher yields of **8**.

Next, we considered stereoelectronic effects on the reactivity to learn why rearrangement does not occur in the reaction of substrate **4k**. X-ray crystallographic structures of **4i** and **4k** and their Newman projections viewed along the ring juncture are shown in Figure 1.[16] The reaction begins with the generation of the carbocation intermediate **11**. The structure of **11** should be comparable to that of the substrate **4** because a tetrahedral conformation (sp^2-hybridyzed carbon) of the cationic carbon atom at the ring-juncture position would be more unstable than an sp^3-like tetrehedral one. Thus, the orientation of the *p* orbital of cation **11** would be approximated to that of the hydroxyl σ bond of **4**. It is found that the dihedral angle between the hydroxyl substituent and the migrating C−C bond of **4i** is approximately 137°. Namely, the *p* orbital and the σ_{C-O} bonding of intermediate **11** would overlap to some degree and, therefore, the rearrangement produces **8i**. In contrast, the angle for **4k** is almost perpendicular (102°), which would rule out rearrangement. Suitable crystals for X-ray analysis of the other substrates **4** could not be obtained, but X-ray crystallographic analysis of cyclobutanols **13b** and **13j**, which are synthetic intermediates of **4b** and **4j**, respectively, were performed. The dihedral angle between the C−OH bond and the C−C bond for **7b** and **13j** are 126 and 143°, respectively (see the Supporting Information). The observation would agree with the results that **4b** and **4j** proceed ring-contraction reaction.

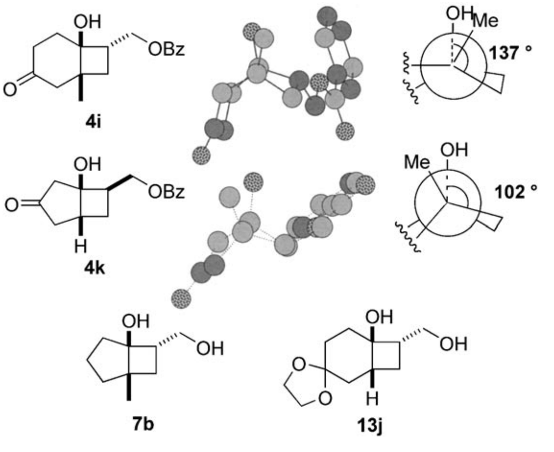


Figure 1. X-ray structures and Newman projections of **4i** and **4k** along with the structures of **7b** and **13j**.

Conclusion

An unusual ring-contraction rearrangement that gives spirocyclic cyclopropanes from fused cyclobutanols is described. It was found that the strain energy of the substrates derived from an additional fused ring and the stereoelectronic effect of the migrating σ bond were important factors. It is noteworthy that the rearrangement proceeds in a stereospecific manner. Moreover, we demonstrated the biomimetic synthesis of **8l** from **4l**, which corresponds to illudane and the protoilludane skeleton, respectively. Further studies involving the synthesis of illudines and the biological evaluation of synthetic **8** are ongoing in our laboratory.

Experimental Section

General: All reactions were carried out under a positive atmosphere of argon in dried glassware unless otherwise noted. Solvents and materials were obtained from commercial suppliers and used without further purification. Column chromatography was performed on Merck silica gel 60 (230–400 mesh). Reactions and chromatography fractions were analyzed by employing precoated silica gel plates (Merck Silica Gel 60 F_{254}). All melting points were measured on a YANACO MP-500P micro melting point apparatus and are uncorrected. IR spectra were measured on a JASCO FT/IR-410 spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on JEOL AL-400 or JEOL ECP-500 instruments with tetramethylsilane as internal standard. Low- and high-resolution mass spectra were recorded on JEOL JMS-01SG-2 or JMS-HX/HX 110A mass spectrometers. X-ray crystal analyses were performed on a Rigaku RAPID-S diffractometer.

General procedure for ring-contraction rearrangement of 4: MsCl (0.45 mmol) was added to a solution of **4** (0.10 mmol) in 2,6-lutidine (0.10 mL) at ambient temperature under an argon atmosphere. After being stirred at 50 °C, the resulting mixture was quenched with a saturated aqueous solution of NH_4Cl. The aqueous layer was extracted with AcOEt three times. The combined organic layers were washed with brine, dried with Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel chromatography (hexane/AcOEt) to give **8**.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methylspiro[2.5]oct-4-en (8a)**: Colorless oil, ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.06$ (d, $J = 7.5$ Hz, 2H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.44 (dd, $J = 7.5, 7.5$ Hz, 2H), 5.51 (s, 1H), 4.55 (dd, $J = 11.5, 6.9$ Hz, 1H), 4.27 (dd, $J = 11.5, 8.0$ Hz, 1H), 2.15–2.05 (m, 2H), 1.75–1.69 (m, 2H), 1.64–1.58 (m, 3H), 1.42 (s, 3H), 1.10 (dd, $J = 8.6, 5.2$ Hz, 1H), 0.40 ppm (t, $J = 5.2$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 166.7$, 135.3, 132.8, 130.5, 129.6, 128.3, 123.4, 65.6, 29.5, 25.9, 25.3, 22.4, 20.0, 18.2, 16.3 ppm; IR (neat): $\tilde{\nu} = 2926$, 2857, 1719 cm^{-1}; LRMS

(FAB): m/z: 257 $[M^++H]$; elemental analysis calcd (%) for $C_{17}H_{20}O_2$: C 79.65, H 7.86; found: C 79.72, H 8.13.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methylspiro[2.4]hept-4-ene (8b: major isomer)**: Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=8.06$ (dd, $J=8.3$, 1.7 Hz, 2H), 7.56 (t, $J=7.5$ Hz, 1H), 7.45 (dd, $J=8.3$, 7.5 Hz, 2H), 5.41 (s, 1H), 4.48 (dd, $J=11.7$, 7.1 Hz, 1H), 4.17 (dd, $J=11.7$, 8.0 Hz, 1H), 2.44–2.36 (m, 2H), 2.18–2.11 (m, 1H), 1.96–1.83 (m, 1H), 1.50–1.46 (m, 1H), 1.42 (d, $J=1.9$ Hz, 3H), 1.00 (dd, $J=9.0$, 5.1 Hz, 1H), 0.49 ppm (t, $J=5.1$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=166.7$, 141.2, 132.8, 130.5, 129.6, 128.3, 124.1, 66.8, 35.0, 29.8, 29.0, 17.9, 15.1, 11.5 ppm; IR (neat): $\tilde{\nu}=2948$, 2852, 1718 cm^{-1}; LRMS (FAB): m/z: 243 $[M^++H]$; elemental analysis calcd (%) for $C_{17}H_{20}O_2$: C 79.65, H 7.86; found: C 79.72, H 8.13.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methylenespiro[2.6]nonane (8c: major isomer)**: Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=8.07$ (d, $J=7.6$ Hz, 2H), 7.57 (t, $J=7.0$ Hz, 1H), 7.44 (dd, $J=7.6$, 7.0 Hz, 2H), 5.51 (s, 1H), 4.71 (s, 1H), 4.65 (s, 1H), 4.57 (dd, $J=11.7$, 6.3 Hz, 1H), 4.27 (dd, $J=11.7$, 9.3 Hz, 1H), 2.39–2.28 (m, 2H), 1.80–1.69 (m, 2H), 1.67–1.49 (m, 6H), 1.40–1.36 (m, 1H), 1.05 (dd, $J=9.0$, 5.1 Hz, 1H), 0.51 ppm (t, $J=5.1$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=166.7$, 155.7, 132.8, 130.4, 129.6, 128.3, 109.1, 65.9, 35.9, 33.3, 29.9, 29.0, 28.9, 27.4, 25.3, 19.7 ppm; IR (neat): $\tilde{\nu}=2925$, 2853, 1719 cm^{-1}; LRMS (FAB): m/z: 271 $[M^++H]$; elemental analysis calcd (%) for $C_{18}H_{22}O_2$: C 79.96, H 8.20; found: C 80.15, H 8.44.

(1*R,3*S**)-1-Benzoyloxymethylspiro[2.5]oct-4-ene (8e)**: Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=8.06$ (d, $J=8.6$ Hz, 2H), 7.55 (t, $J=7.3$ Hz, 1H), 7.44 (dd, $J=8.6$, 7.3 Hz, 2H), 5.68 (td, $J=10.0$, 3.6 Hz, 1H), 5.00 (td, $J=10.0$, 2.0 Hz, 1H), 4.55 (dd, $J=11.7$, 6.6 Hz, 1H), 4.27 (dd, $J=11.7$, 8.8 Hz, 1H), 2.09–2.04 (m, 2H), 1.80–1.69 (m, 3H), 1.65–1.51 (m, 1H), 1.33–1.25 (m, 1H), 0.83 (dd, $J=8.8$, 4.9 Hz, 1H), 0.40 ppm (t, $J=4.9$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=166.7$, 134.7, 132.8, 130.5, 129.6, 128.3, 126.2, 65.5, 28.0, 25.1, 23.8, 22.9, 22.2, 19.2 ppm; IR (neat): $\tilde{\nu}=2928$, 1718 cm^{-1}; LRMS (FAB): m/z: 242 $[M^+]$; HRMS (FAB): m/z: calcd for $C_{16}H_{18}O_2$ $[M^+]$: 242.1307, found: 242.1306.

(1*R,3*R**)-1-Benzoyloxymethylspiro[2.5]oct-4-ene (8f)**: Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=8.05$ (d, $J=7.1$ Hz, 2H), 7.56 (t, $J=7.3$ Hz, 1H), 7.44 (dd, $J=7.3$, 7.1 Hz, 2H), 5.78 (td, $J=10.0$, 3.7 Hz, 1H), 5.32 (td, $J=10.0$, 2.2 Hz, 1H), 4.46 (dd, $J=11.7$, 7.1 Hz, 1H), 4.20 (dd, $J=11.7$, 8.3 Hz, 1H), 2.10–2.06 (m, 2H), 1.81–1.69 (m, 2H), 1.65 (dd, $J=9.5$, 3.6 Hz, 1H), 1.38–1.32 (m, 1H), 1.29–1.22 (m, 1H), 0.90 (dd, $J=8.5$, 5.1 Hz, 1H), 0.65 ppm (t, $J=5.1$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=166.7$, 132.7, 130.6, 129.6, 129.6, 128.5, 128.3, 66.1, 34.5, 25.6, 25.3, 23.1, 22.3, 19.9 ppm; IR (neat): $\tilde{\nu}=2925$, 1714 cm^{-1}; LRMS (FAB): m/z: 242 $[M^+]$; HRMS (FAB): m/z calcd for $C_{16}H_{18}O_2$ $[M^+]$: 242.1307, found: 242.1303.

(1*R,3*R**)-1-Benzyloxymethylspiro[2.5]oct-4-ene (8g)**: Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.35$–7.32 (m, 4H), 7.28–7.26 (m, 1H), 5.49 (s, 1H), 4.56 (d, $J=12.0$, 1H), 4.50 (d, $J=12.0$, 1H), 3.54 (dd, $J=10.3$, 7.4 Hz, 1H), 2.09–2.02 (m, 2H), 1.77–1.61 (m, 3H), 1.51–1.42 (m, 2H), 1.40 (s, 3H), 1.02 (dd, $J=9.2$, 4.6 Hz, 1H), 0.25 ppm (t, $J=4.6$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=138.6$, 135.8, 128.3, 127.7, 127.5, 123.1, 72.7, 70.3, 29.5, 25.9, 24.8, 22.5, 21.0, 18.2, 16.3 ppm; IR (neat): $\tilde{\nu}=2926$, 2855 cm^{-1}; LRMS (FAB): m/z: 243 $[M^++H]$; elemental analysis calcd (%) for $C_{17}H_{22}O$: C 84.25, H 9.15; found: C 84.20, H 9.25.

(1*R,3*R**)-4-Methyl-1-[(2-phenyl)ethyl]spiro[2.5]oct-4-ene (8h)**: Colorless oil ; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.29$–7.25 (m, 2H), 7.20–7.16 (m, 3H), 5.47 (s, 1H), 2.71 (t, $J=8.0$, 1H), 2.09–2.02 (m, 2H), 1.84–1.76 (m, 1H), 1.70–1.54 (m, 4H), 1.49–1.44 (m, 1H), 1.37 (s, 3H), 1.12–1.05 (m, 1H), 0.93 (dd, $J=9.2$, 4.6 Hz, 1H), 0.05 ppm (t, $J=4.6$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=142.6$, 136.8, 128.4, 128.2, 125.6, 122.2, 36.4, 31.0, 29.6, 26.0, 24.7, 22.7, 21.6, 18.4, 18.0 ppm; IR (neat): $\tilde{\nu}=2922$, 2855 cm^{-1}; LRMS (FAB): m/z: 226 $[M^+]$; elemental analysis calcd (%) for $C_{17}H_{22}$: C 90.20, H 9.80; found: C 90.25, H 9.71.

(1*R,3*R**)-1-Benzoyloxymethyl-4-methyl-spiro[2.5]oct-4-en-6-one (8i)**: white solids; M.p. 57–58 °C (Hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.02$ (dd, $J=8.5$, 1.4 Hz, 2H), 7.58 (tt, $J=7.5$, 1.4 Hz, 1H), 7.45 (dd, $J=8.5$, 7.5 Hz, 2H), 5.97 (s, 1H), 4.75 (dd, $J=12.0$, 6.1 Hz, 1H), 4.21 (dd, $J=12.0$, 9.3 Hz, 1H), 2.58–2.43 (m, 2H), 2.12–1.98 (m, 2H), 1.88–1.80 (m, 1H), 1.70 (d, $J=1.2$ Hz, 3H), 1.35 (dd, $J=9.3$, 5.4 Hz, 1H), 0.81 (t, $J=5.4$ Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=199.1$, 166.4, 163.5, 133.2, 129.9, 129.5, 128.5, 127.7, 64.5, 36.8, 28.1, 26.3, 22.5, 19.3, 17.1 ppm; IR (neat): $\tilde{\nu}=2955$, 1717, 1665 cm^{-1}; LRMS (FAB): m/z: 271 $[M^++H]$; HRMS (FAB): m/z calcd for $C_{17}H_{19}O_3$ $[M^++H]$: 271.1334, found: 271.1331.

(1*R,3*S**)-1-Benzoyloxymethylspiro[2.5]oct-4-en-6-one (8j)**: White solid; M.p. 65–66 °C (hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=8.03$ (d, $J=7.1$ Hz, 2H), 7.58 (t, $J=7.4$ Hz, 1H), 7.45 (dd, $J=7.4$, 7.1 Hz, 2H), 6.23 (d, $J=10.0$ Hz, 1H), 5.99 (d, $J=10.0$ Hz, 1H), 4.73 (dd, $J=12.0$, 5.8 Hz, 1H), 4.14 (dd, $J=12.0$, 9.3 Hz, 1H), 2.54 (td, $J=7.8$, 1.7 Hz, 1H), 2.17–2.10 (m, 1H), 2.06–1.99 (m, 1H), 1.73–1.66 (m, 1H), 1.18 (dd, $J=9.0$, 5.4 Hz, 1H), 0.95 (t, $J=5.4$ Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=199.2$, 166.4, 157.3, 133.2, 129.9, 128.5, 128.1, 64.4, 36.6, 26.4, 25.0, 23.9, 19.2 ppm; IR (neat): $\tilde{\nu}=2957$, 1717, 1672 cm^{-1}; LRMS (FAB): m/z: 257 $[M^++H]$; HRMS (FAB): m/z calcd for $C_{16}H_{17}O_3$ $[M^++H]$: 257.1178, found: 257.1182.

3,3,9-Trimethylbicyclo[4.3.0]nonan-1(5)en-4-one-8-spirocyclopropane (8l): Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta=2.49$ (dt, $J=18.3$, 3.1 Hz, 1H), 2.30–2.05 (m, 3H), 1.93–1.82 (m, 1H), 1.68 (td, $J=7.6$, 7.1 Hz, 1H), 1.12 (s, 3H) , 1.12 (s, 3H) , 1.11 (s, 3H), 0.96 ppm (ddd, $J=13.5$, 5.8, 2.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=203.3$, 174.1, 135.4, 45.4, 43.5, 40.8, 27.6, 25.3, 25.3, 21.3, 20.0, 16.5, 12.8, 9.8 ppm; IR (neat): $\tilde{\nu}=2928$,1699,1645 cm^{-1}; LRMS (FAB): m/z: 204 $[M^+]$; HRMS (FAB): m/z calcd for $C_{14}H_{20}O$ $[M^+]$: 204.1514, found: 204.1497.

Crystal data for 4i: Colorless needles (recryst. from hexane/AcOEt); $C_{17}H_{20}O_4$; monoclinic; space group $P2_1/n$; $a=11.7971(6)$, $b=7.5796(3)$, $c=17.7477(8)$ Å; $\beta=104.283(3)°$; $V=1537.90(12)$ Å^3; $Z=4$; $\rho_{calcd}=1.245$ g cm^{-3}; $R=0.0477$; $R_w=0.074$; GOF$=0.854$.

Crystal data for 4k: Colorless platelets (recryst. from hexane/AcOEt); $C_{16}H_{18}O_4$; triclinic; space group $P\bar{1}$; $a=6.7625(6)$, $b=9.4963(7)$, $c=11.2202(9)$ Å; $\beta=101.648(2)°$; $\beta=96.981(3)°$; $\beta=100.873(3)°$; $V=683.40(1)$ Å^3; $Z=2$; $\rho_{calcd}=1.333$ g cm^{-3}; $R=0.0780$; $R_w=0.1730$; GOF$=1.108$.

Acknowledgements

The work was supported by a Grant-in-Aid for Scientific Research and Targeted Proteins Research Program from Ministry of Education, Culture, Sports, Science, and Technology, Japan, the Astellas Foundation for Research on Metabolic Disorders, and the Tekeda Science Foundation.

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[15] As an alternative possible mechanism, a concerted S_N2-type rearrangement pathway can be proposed. Thus, both elimination of mesyl group and migration of C–C bond would occur concertedly to give spirocyclopropanes. Formation of chloride **10l** would suggest the formation of cationic intermediate **11**. Thus, a stepwise mechanism would be preferable. Further study in the reaction mechanism is ongoing.

[16] CCDC-758893 (**4i**), 758894 (**4k**) 758895 (**7b**) and 758896 (**13k**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Received: April 13, 2010