Regiospecific Introduction of Two Carbon Moieties into the Vicinal Positions of Cyclopentadiene and Synthesis of C_9-Terpene Lactones

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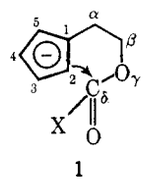
A method for the regiospecific introduction of two carbon moieties into the vicinal positions of cyclopentadiene was developed. The key step is a noval intramolecular cyclization of a carbonate of cyclopentadienylethanols prepared by the ring opening reaction of epoxides with cyclopentadienyl anion. Cyclopentadienylethanols were obtained in high yields by employing the reaction system in which both the starting material and products exist as a form of stable cyclopentadienyl anion. Carbonate esters of cyclopentadienylethanols gave vicinally disubstituted cyclopentadiene, i.e., cyclopentadienolactones, in high yields by treatment with a base, via a six-membered cyclic intermediate. The methylation of the anion of the cyclopentadienolactone intermediately formed was also studied and was applied to the synthesis of C_9-terpene lactones, onikulactone and mitsugashiwalactone. The positions of the double bonds in the cyclopentadienolactones and their methylated derivatives were confirmed by NMR analyses.

Several kinds of biologically active natural compounds, such as prostaglandins, jasmonoids, pyrethroids, iridoids, etc., have in common a five-membered ring bearing differentiated carbon side chains in the vicinal positions.[1] Although cyclopentadiene is the most simple and reactive five-membered carbocyclic precursor suitable for the synthesis of these cyclopentanoids, there have been few methods for selective introduction of two carbon moieties to the vicinal positions of this diene. Cyclopentadiene is thermally unstable and dimerizes easily at the ambient temperature. In addition, the methylenic protons of cyclopentadiene are very mobile,[2] making it very difficult to isolate cyclopentadiene derivatives free of olefin isomers.[3] Accordingly, in the case of reaction of monosubstituted cyclopentadienes, lower temperatures are required in order to avoid the undesired Diels–Alder type reaction products.[4,5]

On the other hand, metal salts of cyclopentadiene are thermally stable as they have 6π electrons in a ring and can be handled at relatively high temperature.[6] For example, sodium cyclopentadienide is stable below 300 °C under an inert atmosphere and is readily protonated with weak acids to regenerate free cyclopentadiene. Thus, if there is a favorable method to introduce two carbon moieties into the 1 and 2 positions of the five-membered ring, an alkaline metal cyclopentadienide would serve as a readily available starting material for many kinds of naturally occurring cyclopentanoid compounds.

It is very difficult to obtain only one isomer by the reaction of alkylcyclopentadiene with an electrophile.[7] The success of a synthesis based on monosubstituted cyclopentadiene is contingent upon the regiospecific introduction of the second side chain. This can be realized by modifying the initially introduced side chain, followed by its intramolecular reaction with the five-membered ring. When the side chain of the cyclopentadienyl anion has an electrophilic carbon at the δ position, the intramolecular reaction with the C-2 position on the five-membered ring is expected because of the steric preference of the six-membered cyclic transition state (1),[8]



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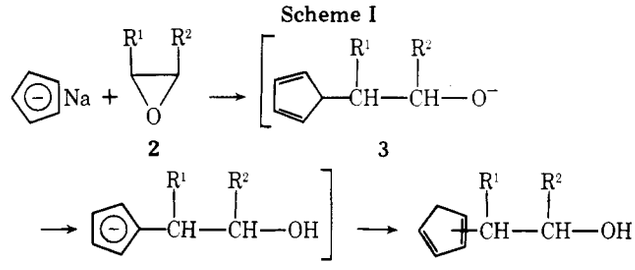
resulting in the formation of the vicinally disubstituted cyclopentadiene. The present method of synthesis of vicinally substituted cyclopentadiene derivatives consists of convenient stepwise reactions, i.e., preparation of cyclopentadienylethanol derivatives (**5**) by ring-opening reaction of epoxides with cyclopentadienyl anion and the successive intramolecular cyclization of the carbonate esters of the alcohols.

The first side chain should have such a functional group that does not react with a carbanion in its native form and can easily be attached to an electrophilic group. Thus hydroxyethyl group was employed. The reaction of cyclopentadiene with an epoxide in the presence of a small amount of potassium *tert*-butoxide has been reported to give cyclopentadienylethanol, but the yield of the monomer was low.[5,9] This is due to the dimerization and/or the polymerization of the starting material and the product during the reaction. An attractive way to suppress the undesirable side reactions is to keep cyclopentadiene and the product in a form of thermally stable cyclopentadienyl anion throughout the reaction and to isolate the acidified product at lower temperature. Thus, cyclopentadienylethanol derivatives (**5**) were obtained

Scheme I



	R^1	R^2
a	H	H
b	H	CH_3
c	H	n-C_6H_{13}
d	$-(CH_2)_4-$	

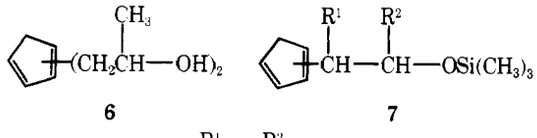
in high yields by adding epoxides very slowly to a solution of excess cyclopentadienide in dimethoxyethane (DME) with reflux, followed by treatment of the reaction mixture with aqueous ammonium chloride at 0 °C[10] (Table I). Fortunately, because the equilibrium between the alkoxy anion (**3**) and the cyclopentadienyl anion (**4**) lies so far to **4**,[11] no excess base was required to convert **3** into the form of cyclopentadienyl anion. The intermediacy of anion **4** was confirmed by isolation of bis(2-hydroxy-1-propyl)cyclopentadiene (**6**), conducting the reaction using some excess of propylene oxide (**2b**) to cyclopentadienyl anion. The attack of cyclopentadienyl anion on

Table I. Preparation of Cyclopentadienylethanol Derivatives and Their Cyclization Products

Epoxide	R^1	R^2	5 Bp, °C (mmHg)	5 Yield,[a] %	8 Bp, °C (mmHg)	12 Yield,[b] %	16 Bp, °C (mmHg)
2a	H	H	37 (0.08)	76	49–50 (0.08)	68	58–60 (0.04)
2b	H	CH_3	44 (0.1)	91	59–60 (0.2)	69	65 (0.04)
2c	H	n-C_6H_{13}	68 (0.05)	80	91–93 (0.06)	74	110 (0.02)
2d		$-(CH_2)_4-$	72 (0.25)	81	97–98 (0.04)	75	100 (0.03)

[a] Yields were determined by integration of the NMR spectra of the products based on epoxides. [b] Yields were determined by integration of the NMR spectra of the products based on carbonates 8.

epoxides occurred exclusively at the less hindered center as indicated by the isolation of **5** upon treatment of **4** with ammonium chloride.[12] Furthermore, when anion **4** was treated with trimethylsilyl chloride, the silyl ethers **7** were obtained in good yields.[10] Carbonate esters (**8**) were easily prepared by treating **5** with ethyl chloroformate in the presence of pyridine in DME.[10]



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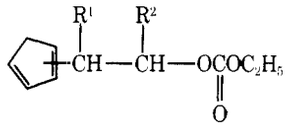

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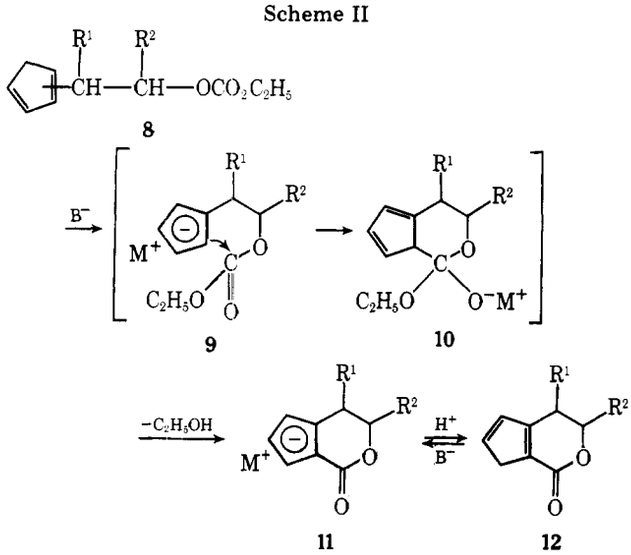
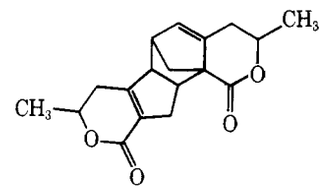
The second side chain was introduced by the reaction of carbonates (**8**) with a base. When 2-cyclopentadienyl-1-methylethyl ethyl carbonate (**8b**) was treated with sodium hydride in DME at 0–30 °C, cyclopentadienyl anion (**9b**) was formed immediately and cyclized as expected to give anion **11b**, which exhibited NMR signals at δ 5.31 (m, 1 H), 5.65 (q, 1 H) and 6.05 (q, 1 H). The structure of anion **11b** was indicated by its conversion to 4-methyl-2-oxo-3-oxabicyclo-[4.3.0]nona-1(6),7-diene (**12b**) upon acidification of the reaction mixture.

Scheme II



The cyclopentadienolactone (**12b**) was isolated as a colorless oil by column chromatography on silica gel and the structure was confirmed by spectral data and some chemical reactions. The presence of a lactone ring was confirmed by the infrared absorptions at 1710, 1215, and 1085 cm^{-1}. The integration of the quartet at δ 6.63 and 6.93 in the NMR spectrum indicated that the cyclopentadiene ring had two olefinic protons. On standing at room temperature, **12b** dimerized to form **13** as stable crystals. Compound **12b** also underwent the Diels–Alder reaction with dimethyl acetylenedicarboxylate in benzene at 80 °C to give the adducts **14** and **15** in a ratio of 3:2 (total yield of 55%). The results of hydrogenation of **12b** provided further evidence in confirmation of the cyclopentadiene ring. The unsaturated lactone (**12b**) reacted with 2 molar equiv of hydrogen using platinum oxide catalyst in ethanol to give 4-methyl-2-oxo-3-oxabicyclo[4.3.0]nonane (**16b**) in a quantitative yield.



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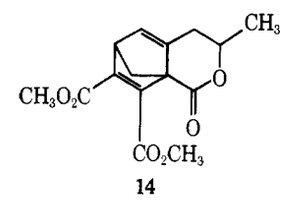

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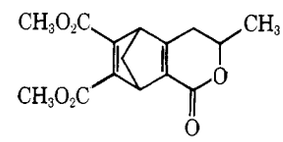

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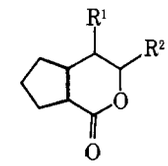

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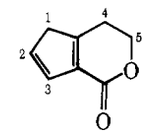
The positions of unsaturated bonds in the five-membered ring were finally confirmed by NMR analysis of nonsubstituted cyclopentadienolactone (**12a**), as shown in Table II: the coupling constants were compared with those of methylcyclopentadiene (**19** and **20** shown in Table II.)[3] The possible structures of the reaction product of **6a** with sodium hydride other than **12a** which are consistent with the chemical shifts and integration of the NMR spectrum are **17** and **18**, positional isomers of the double bonds in the five-membered ring. Assignment of H_1–H_5 is unambiguous from their chemical shifts. The coupling constant J_{14} in **17** is expected to have almost the same value as J_{12} in 1-methylcyclopentadiene (**19**). But, in fact, the observed value was 3 Hz, while J_{12} in **19** has been reported to be 0.2 Hz. Thus, structure **17** is very unlikely. The value of 3 Hz for J_{14} is accounted for by both structure **12a** and **18**. In spite of the same positional relationship between two olefinic protons (H_2–H_3) in **18** and H_2–H_5 in 2-methylcyclopentadiene (**20**), the observed coupling constant for two olefinic protons (5.4 Hz) differs from J_{25} in **20** (1.8 Hz). This fact excludes the possibility of structure **18**. On the other



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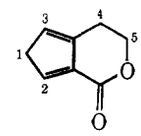

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Table II. ^{1}H NMR Chemical Shifts and Coupling Constants for Cyclopentadiene Derivatives[a]

		H_1	H_2	H_3	H_4	H_5
12a	δ	3.27	6.76	6.55	2.70	4.39
	$\Delta\delta$[b]	3.15	0.93	0.69	1.66	2.14
		$J_{12} = J_{13} = 1.0$ $J_{14} = 3.0$ $J_{23} = 5.4$				
21	δ	3.01	5.78	2.10	2.72	4.34
	$\Delta\delta$[b]	1.17	1.07	2.26	1.46	1.88
22	δ	3.10	6.30	1.98	2.64	4.36
	$\Delta\delta$[b]	3.30	0.95	0.68	1.50	2.04
19	δ[c]	2.70	1.98	6.00	6.25	6.07
		$J_{12} = 0.2$ $J_{45} = 5.4$ $J_{14} = 1.5$ $J_{15} = 1.4$				
20	δ[c]	2.79	5.83	1.91	6.23	6.23
		$J_{13} = 2.0$ $J_{25} = 1.8$ $J_{45} = 5.4$				

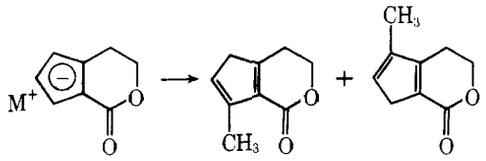
[a] Taken on a Varian HA-100 spectrometer in CCl_4. [b] Shift differences of the corresponding signals with and without $Eu(fod)_3$. [c] Data obtained on a Varian HA-100 spectrometer for neat liquid; see ref 3.

hand, the coupling constant between H_4 and H_5 in **20**, of which the positional relationship is the same as that of H_2–H_5 in **12a**, has been reported to be 5.4 Hz, which is identical with the observed value. The fact that J_{14} in **12a** (3 Hz) is in fairly good agreement with J_{13} in **20** (2 Hz) also supports the presented structure. Thus, structure **12a** is the only one that is consistent with all the spectral data. This is accounted for by the fact that the olefinic bonds in **12** are located so that the longest resonance with the carbonyl group is possible. In our knowledge, it is the first example that a disubstituted cyclopentadiene can be isolated without any isomers.

As an application of the novel intramolecular cyclization reaction of carbonates of cyclopentadienylethanol derivatives, a total synthesis of C_9-terpene lactones, onikulactone (**23**) and mitsugashiwalactone (**24**), was investigated.[13] These two lactones, which were isolated by Sakan et al. as the biologically active principles of *Boshniakia rossica* Hult and *Menyanthes trifoliata* L., have a highly attractive physiological action on the Felidae and Chrysopidae.[14] The key step of the synthesis of these compounds is methylation of the anion **11a** to prepare 9-methyl-2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (**21**). The reaction conditions were examined using several kinds of metal salts of **12a** (M = Li, Na, K, MgBr, Tl). The sodium salt and potassium salt were prepared directly by the reaction of **8a** with the hydride of the metals. The lithium salt and bromomagnesium salt were obtained by treating the free lactone (**12a**) with *n*-butyllithium or ethylmagnesium bromide, respectively. Metal exchange reactions were also effective in preparation of the bromomagnesium and thallium salts, using active magnesium bromide[15] or thallium sulfate, respectively. Among these metal salts, only the thallium salt is stable in air and isolated as a white solid. In an inert atmosphere, all but the bromomagnesium salt are stable to water.

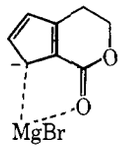
Methylation of **11a** with methyl iodide or dimethyl sulfate at 0 °C–room temperature was accompanied by some undesirable side reactions, such as polymethylation, which is considered to occur via anion exchange between methylated compounds (**21** or **22**) and nonmethylated anion (**11a**). However, a good yield (50%) of monomethylated product **21** [along

Scheme III



11a **21** **22**

with the isomer **22** (17%)] was obtained by the reaction of **11a** (M = Na) with methyl fluorosulfonate[16] at −70 °C. The bromomagnesium salt of **12a** gave exclusively the isomer **21** in a yield of 35% without formation of the isomer **22** (38% of free lactone **12a** was recovered). This is accounted for by the fact that the chelation of the metal to the carbonyl group of the lactone ring (**25**) localizes the anionic center of the five-



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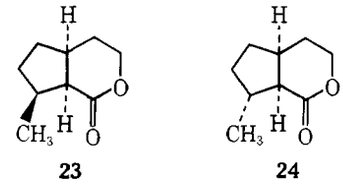
membered ring to the position that favors the formation of **21**. The positional isomers **21** and **22** were isolated separately and their structures were determined by NMR spectra (Table II). Signals due to only one olefinic proton and allylic methyl protons demonstrate that the methyl groups of **21** and **22** are attached to olefinic carbons. The methylenic protons (H_4) of **21** coupled only with H_5 and appeared in a triplet, but the corresponding signal of **22** was complicated as it coupled with two kinds of methylenic protons, H_1 and H_5. The similarity of the splitting pattern of the signals of H_4 of **22** and **12a** suggests the structural resemblance of these two compounds. As the observed shift differences in Table II show, the effect of shift reagent, tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III) [$Eu(fod)_3$], is different to two isomers. Since the shift reagent associates with the carbonyl group, the signal of methyl protons shifted further than any others in the case of **21**, but in the case of **22**, the shift of the signal of the methylenic protons of the five-membered ring (H_1) was the maximum. All of these data invoke us to conclude that the structures of the methylated compounds are **21** and **22**, including the positions of the double bonds in the five-membered ring, as shown in Scheme III.

Hydrogenation of **21** on platinum oxide in ethanol at ambient pressure and temperature gave a mixture of racemic onikulactone (**23**) and mitsugashiwalactone (**24**) in a ratio of 1:1.8, in a yield of 93%, which were isolated by gas chromatography and identified by comparison of NMR, IR, and mass spectra with those of the natural products. Thus, onikulactone (**23**) and mitsugashiwalactone (**24**) were synthesized from the



23 **24**

readily available carbonate (**8a**) in only two steps, via methylation of anion **11a**.

Some of the advantages of the present procedure for introduction of two carbon moieties are that (a) two carbon–carbon bonds are formed regiospecifically in the vicinal positions of the cyclopentadiene ring; (b) since resulting disubstituted cyclopentadienes are in the anionic form, it is possible to subject them to further reactions with electrophiles without isolation; (c) lactones **12** include no positional isomers of

double bonds, although the starting materials, carbonates 8, are mixtures of two positional isomers;[10] (d) compound 12 still has a reactive cyclopentadiene ring and lactone ring, which can be utilized to further conversion. Considering these advantages, the present technique could be applied to the synthesis of a wide variety of cyclopentanoid natural products.

Experimental Section

Boiling points and melting points were uncorrected. Proton magnetic resonance spectra were obtained on Varian T-60 and HA-100 instruments and infrared spectra were obtained with neat samples, unless otherwise stated, on a Hitachi EPI-Ge spectrometer. Mass spectra were obtained on a Hitachi RMU-6E spectrometer at 100 °C and 70 eV. Elemental analyses were performed on a Micro Elemental Analyzer of Mitamura Riken.

2-Cyclopentadienylethanol (5a). To a solution of 15.7 g (178 mmol) of sodium cyclopentadienide[6] in 75 ml of DME was added a solution of 0.84 g (19 mmol) of ethylene oxide in 20 ml of DME, under vigorous stirring at 83 °C over a 6.5-h period, and the solution was stirred for an additional 30 min at the same temperature. The solution was cooled in an ice–water bath, neutralized with an aqueous solution of ammonium chloride, separated, and extracted with ether. The organic layer was dried over anhydrous magnesium sulfate and concentrated to about 10 ml. The yield of **5a** was confirmed by integration of three olefinic protons in the NMR spectrum of the product vs. the signal of a predetermined amount of added benzene as internal standard (76% based on ethylene oxide). 2-Cyclopentadienylethanol (**5a**) was isolated as a mixture of positional isomers of the double bond by distillation as a colorless oil: bp 30–37 °C (0.08 mm); NMR (CCl_4) δ 2.57 (t, 2, CH_2 adjacent to cyclopentadiene ring), 2.83 (m, 2, CH_2 of the ring), 3.67 (t, 3, CH_2OH), 6.0–6.7 (m, 3, olefinic H); mass spectrum *m/e* (rel intensity) 66 (49), 77 (87), 79 (100), 91 (28), and 110 (40) (molecular ion).

In a preparative scale experiment, using 1 mol of sodium cyclopentadienide and 0.5 mol of ethylene oxide in 700 ml of DME, fairly good yields (45–55%) were obtained according to the same procedure.

1-Cyclopentadienyl-2-propanol (5b). To a solution of 15.8 g (180 mmol) of sodium cyclopentadienide[6] in 55 ml of DME was added a solution of 1.03 g (17.8 mmol) of propylene oxide in 10 ml of DME, under vigorous stirring at 83 °C over a 5-h period and the solution was stirred for an additional 30 min at the same temperature. The solution was cooled in an ice–water bath, neutralized with an aqueous solution of ammonium chloride, separated, and extracted with ether. The organic layer was dried over anhydrous magnesium sulfate and concentrated to about 10 ml. The yield of **5b** was confirmed by integration of three olefinic protons in the NMR spectrum of the product vs. the signal of a predetermined amount of added benzene as internal standard (91% based on propylene oxide). 1-Cyclopentadienyl-2-propanol (**5b**) was isolated as a mixture of positional isomers of the double bond by distillation, yielding 1.63 g (74%) of colorless oil: bp 44 °C (0.1 mm); NMR (CCl_4) δ 2.57 (d, 3, CH_3), 2.51 (m, 2, CH_2 of the side chain), 2.61 (s, 1, OH), 2.86 (m, 2, CH_2 of the ring), 3.83 (sextet, 1, CHOH) 6.0–6.3 (m, 3, olefinic H); IR 3350 (OH), 2960 (CH_3), 2900 (CH_2), 1120 cm^{-1} (C–O); mass spectrum *m/e* (rel intensity) 45 (80), 79 (87), 80 (100), and 124 (24) (molecular ion).

Anal. Calcd for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.23; H, 9.82.

The other cyclopentadienylethanol derivatives (**5c,d**) were prepared by the same way using the corresponding epoxides (**2c,d**).

1-Cyclopentadienyl-2-propanol Trimethylsilyl Ether (7b). To a refluxing solution of sodium cyclopentadienide, prepared from 8 ml (107 mmol) of cyclopentadiene and 2.3 g (100 mmol) of sodium, in 50 ml of DME was added a solution of 1.74 (30 mmol) of propylene oxide in 10 ml of DME, stirring vigorously under an atmosphere of argon, over a 5-h period. To the resulting solution, cooled in an ice–water bath, was added dropwise a solution of 3.30 g (30 mmol) of trimethylsilyl chloride in 15 ml of DME over a period of 30 min and the reaction mixture was stirred for an additional 30 min at room temperature. Ether (150 ml) was added and the organic layer was washed with an aqueous solution of ammonium sulfate. The organic layer was separated, dried over anhydrous magnesium sulfate, and concentrated to about 10 ml. The yield of **7b** was determined to be 3.80 g (65%) by integration of three olefinic protons in the NMR spectrum as mentioned above. Then **7b** was isolated by distillation as a colorless oil: bp 75 °C (14 mm); NMR (CCl_4) δ 0.27 (m, 9, $SiCH_3$), 1.32 (d, 3, CH_3), 2.7 (m, CH_2 of the side chain), 3.05 (m, 2, CH_2 of the ring), 4.08 (sextet, 1, CHOH), 6.1–6.7 (m, 3, olefinic H).

Isolation of Bis(2-hydroxypropyl)cyclopentadiene (6). To a vigorously stirred solution of 2.72 g (31 mmol) of sodium cyclopentadienide in 20 ml of DME, a solution of 5.80 g (100 mmol) of propylene oxide in 10 ml of DME was added slowly over a period of 5.5 h under an atmosphere of argon at 83 °C. The reaction mixture was cooled in an ice–water bath, neutralized with aqueous ammonium chloride, and extracted with ether. After drying over anhydrous magnesium sulfate, the solvent was removed under reduced pressure. Distillation yielded 1.33 g (24% based on sodium cyclopentadienide) of **6** as a colorless oil: bp 117 °C (0.3 mm); NMR ($CDCl_3$) δ 1.17 (d, 6, CH_3), 2.4 (m, 4, CH_2 of the side chain), 2.9 (m, 2, CH_2 of the ring), 3.9 (m, 2, CHOH), 6.0–6.4 (m, 2, olefinic H); mass spectrum *m/e* (rel intensity) 45 (90), 79 (89), 80 (100), 91 (47), 94 (77), 138 (38), and 182 (6) (molecular ion).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 73.02; H, 9.71.

2-Cyclopentadienylethyl Ethyl Carbonate (8a). To a magnetically stirred solution of 1.10 g (10 mmol) of cyclopentadienylethanol (**5a**) and 1.02 g (13 mmol) of pyridine in 20 ml of DME, a solution of 1.30 g (12 mmol) of ethyl chloroformate in 5 ml of DME was added dropwise (15 min) at 0 °C/ Stirring was continued for 2 h at room temperature. Water was added to the reaction mixture to dissolve white precipitates and the organic layer was diluted with 50 ml of ether and separated. The carbonate **8a** was obtained on evaporation of the solvent in a quantitative yield (1.90 g). No impurity was detected on NMR analysis. Distillation gave an analytical sample as a colorless oil: bp 49–50 °C (0.08 mm); NMR (CCl_4) δ 1.43 (t, 3, CH_3), 2.67 (m, 2, $C_5H_5CH_2$–), 2.96 (m, 2, CH_2 of the ring), 4.1 (t + q, 4, $-CH_2OCO_2CH_2$–), 6.1–6.4 (m, 3, olefinic H): IR 3030 (=CH), 1740 (C=O), 1260, 1010 cm^{-1} (COC); mass spectrum *m/e* (rel intensity) 91 (52), 92 (100), 93 (20), and 182 (1) (molecular ion).

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.87; H, 7.69. Found: C, 65.92; H, 7.74.

The other carbonates (**8b–d**) were prepared according to the same procedure in quantitative yields.

2-Oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (12a). Sodium hydride in mineral oil (50%, 0.53 g, 11 mmol) was washed with three 10-ml portions of *n*-hexane and suspended in 10 ml of DME. To this suspension, a solution of 1.82 g (10 mmol) of 2-cyclopentadienylethyl ethyl carbonate (**8a**) in 15 ml of DME was added over a 30-min period, stirring at 0 °C under an atmosphere of argon. Evolution of hydrogen was observed simultaneously with adding of the ester. The reaction mixture was diluted with 25 ml of DME and when the generation of hydrogen was ceased, the temperature of the solution was raised to ca. 40 °C and thg solution was stirred for 3 h. An aqueous solution of ammonium chloride was added to the reaction mixture cooled in an ice–water bath. Ether (50 ml) was added and the organic layer was separated, washed with brine, and dried over anhydrous magnesium sulfate. The solution was concentrated in vacuo to ca. 10 ml and cyclopentadienolactone (**12a**) was determined by NMR (68%). An analytical sample was obtained by purification on a column chromatograph (silica gel). Elution with ether–*n*-hexane (1:1 v/v) gave **12a** as a colorless oil: NMR (CCl_4) δ 2.70 (heptet, 2), 3.27 (m, 2), 4.39 (t, 2), 6.53, 6.80 (AB q, 2); IR 3020 (=CH), 1710 (C=O), 1215, 1085 cm^{-1} (COC); mass spectrum *m/e* (rel intensity) 78 (95), 91 (100), 92 (85), 106 (41), and 136 (88) (molecular ion).

Other cyclopentadieno-δ-lactone derivatives (**12b–d**) were prepared according to the same procedure as mentioned above.

Dimer of 4-Methyl-2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (13). Crude **12b** (ca. 1.5 g, 10 mmol) was allowed to stand at room temperature for 6 days. White solid was separated from the viscous oil. Recrystallization from ethanol gave **13** (ca. 0.5 g) as white crystals: mp 152–154 °C; NMR ($CDCl_3$) δ 1.60 (d, 3, CH_3), 1.65 (d, 3, CH_3), 1.93 (s, 2), 1.9–2.7 (m, 6), 3.15 (broad s, 2), 3.95 (m, 1), 4.40 (m, 2, CHOH), 5.93 (t, 1, olefinic H); IR (KBr disk) 1730, 1715, 1280, 1090 cm^{-1}; mass spectrum *m/e* (rel intensity) 78 (55), 105 (68), 106 (69), 150 (78), 151 (100), and 300 (4) (molecular ion).

Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.64; H, 6.69.

Adduct of 12b and Dimethyl Acetylenedicarboxylate (14 and 15). A solution of 1.5 g (10 mmol) of crude **12b** and 3.0 g (21.2 mmol) of dimethyl acetylenedicarboxylate in 20 ml of benzene was refluxed for 12 h. The solvent was removed under reduced pressure and the residue was column chromatographed twice on silica gel. Elution with ether-*n*-hexane (4:1 v/v) gave 0.96 g (33% from carbonate **8b**) of **14** and 0.67 g (22% from carbonate **8b**) of **15**. The former (**14**): NMR ($CDCl_3$) δ 1.42 (d, 3, CH_3), 2.3–2.7 (m, 4), 3.75 (s + m, 7, CO_2CH_3, *t*-CH), 4.7 (m, 1, OCH), 6.52 (broad s, 1, olefinic H); mass spectrum *m/e* (rel intensity) 59 (33), 105 (33), 150 (32), 177 (18), 195 (20), 229 (17), 231 (18), and 292 (100) (molecular ion). The latter (**15**) was recrys-

tallized from ethanol to give white crystals: mp 105–106 °C; NMR ($CDCl_3$) δ 1.42 (d, 3, CH_3), 2.3–2.7 (m, 4), 3.87 (s, 6, CO_2CH_3), 4.1 (m, 1), 4.4 (m, 1) 4.7 (sextet, 1, OCH); mass spectrum *m/e* (rel intensity) 59 (54), 66 (36), 79 (39), 105 (58), 150 (70), 151 (72), 242 (32), 245 (39), 274 (100), and 292 (48) (molecular ion).

Anal. Calcd for $C_{15}H_{16}O_6$: C, 61.64; H, 5.52. Found: C, 61.55; H, 5.52.

Preparation of the Bromomagnesium Salt of 2-Oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (25) from 12a and Ethylmagnesium Bromide. To a stirred solution of 0.15 g (3.8 mmol) of cyclopentadienolactone (**12a**) in 20 ml of THF was added a solution of 0.75 g (5.6 mmol) of ethylmagnesium bromide in 20 ml of THF under an atmosphere of argon at 8 °C. The solution was stirred for 45 min. The yield of the bromomagnesium salt (**25**) was determined by the integration of three protons on the five-membered ring in the NMR spectrum at δ 5.31, 5.65, and 6.05 (92%).

Preparation of 25 from Sodium 2-Oxo-3-oxabicyclo[4.3.0]-nona-1(6),7-diene (11a, M = Na) and Magnesium Bromide. To a solution of 8.5 mmol of **11a** (M = Na) in 20 ml of DME was added slowly a solution of 0.6 g (9.4 mmol) of *n*-butyllithium in 6 ml of *n*-hexane at ca. −50 to −55 °C to quench ethanol, which was inevitably formed as the by-product of the reaction preparing **11a** (M = Na) from carbonate (**8a**) and sodium hydride. Stirring was continued for 15 min at the same temperature and the mixture was allowed to stand at room temperature. To a slurry of magnesium bromide prepared from 0.48 g (20 mmol) of magnesium powder, 3.76 g (20 mmol) of ethylene bromide, and 30 ml of THF was added dropwise a solution of sodium salt of cyclopentadienolactone (**11a**, M = Na, 8.5 mmol) at 50 °C. The reaction mixture was cooled to room temperature and filtered off. The yield of the bromomagnesium salt (**25**) was determined by the integration of the NMR spectrum as mentioned above (42%). The formation of **25** was confirmed by the derivation to lactone (**12a**) by adding water to the filtrate. Since the sodium salt (**11a**, M = Na) is stable in water, the quantity of obtained lactone (**12a**) is equivalent to that of the bromomagnesium salt (**11a**, M = MgBr).

Preparation of the Thallium Salt of 2-Oxo-3-oxabicyclo-[4.3.0]nona-1(6),7-diene (11a, M = Tl). To a solution of 1.10 g (2.2 mmol) of thallium sulfate in 10 ml of water was added slowly a solution of 4.3 mmol of sodium 2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-dienide (**11a**, M = Na) in 15 ml of DME below 28 °C and the reaction mixture was stirred at room temperature. Filtration and washing with methanol gave the thallium salt of 2-oxo-3-oxabicyclo[4.3.0]nona-1(6),-7-diene (**11a**, M = Tl) (1.2 g, 84%): mp 165 °C dec; NMR (Me_2SO-d_6) δ 2.64 (t, 2, CH_2 adjacent to the five-membered ring), 4.20 (t, 2, CH_2 adjacent to oxygen), 5.6 (m, 2, five-membered ring), 6.03 (q, 1, five-membered ring); IR 3020, 1665 cm^{-1}.

Anal. Calcd for $C_8H_7O_2Tl$: C, 28.31; H, 2.06. Found: C, 28.81; H, 2.35.

9-Methyl-2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (21) and 7-Methyl-2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (22). To a solution of sodium 2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-dienide (**11a**, M = Na, 23 mmol) in a mixture of 70 ml of DME and 50 ml of THF was added a solution of 3.70 g (32.4 mmol) of methyl fluorosulfonate in 40 ml of dry methylene chloride stirring at −70 °C over a period of 4.5 h and the reaction mixture was allowed to stand overnight at −70 °C. Gaseous ammonia was bubbled through the solution for 20 min at −70 °C, and the mixture was brought to room temperature. After the precipitates were filtered off, the filtrate was diluted with 250 ml of ether and washed three times with 20-ml portions of brine. Evaporation of the solvents at reduced pressure gave a reddish oil residue. Monomethylated products **21** and **22** were isolated by column chromatography on silica gel. Elution with *n*-hexane–ether (10:3 v/v) gave **21** and **22** as white crystals. **21**: mp 52–54 °C (from ether); yield 1.70 g (50%); R_f 0.49; IR (KBr disk) 1685, 1070 cm^{-1}; mass spectrum *m/e* (rel intensity) 51 (27), 77 (20), 78 (27), 91 (100), 92 (32), 105 (61), 106 (30), 119 (25), and 150 (34) (molecular ion).

Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.87; H, 6.50.

22: mp 58–60 °C (from *n*-hexane–ether); yield 0.58 g (14%); R_f 0.35; IR (KBr disk) 1700, 1265, 1090 cm^{-1}; mass spectrum *m/e* (rel intensity) 51 (23), 65 (21), 77 (24), 91 (100), 92 (21), 105 (74), 106 (19), 119 (20), 122 (18), 149 (5), and 150 (69) (molecular ion).

Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.78; H, 6.48.

Onikulactone (23) and Mitsugashiwalactone (24). A solution of 200 mg (1.33 mmol) of 9-methyl-2-oxo-3-oxabicyclo[4.3.0]nona-1(6),7-diene (**21**) in 15 ml of ethanol containing 20 mg of platinum oxide was stirred at room temperature under an atmosphere of hydrogen (1 atm) for 12 h. Filtration, followed by evaporation of ethanol, gave 190 mg (93%) of a mixture of saturated compounds as a colorless oil, bp 94–95 °C (0.45 mm).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.90; H, 8.77.

Onikulactone (**23**) and mitsugashiwalactone (**24**) were isolated in a ratio of 1:1.8 by GLC (20% SE-30, 2 m, 150 °C). Onikulactone (**23**): NMR (CCl_4) δ 0.99 (d, 3, CH_3), 0.9–3.0 (m, 9), 4.20 (m, 2, CH_2 of the lactone ring adjacent to oxygen); IR 2930, 2850, 1730, 1480, 1455, 1395, 1315, 1265, 1200, 1180, 1090, 1070 cm^{-1}; mass spectrum *m/e* (rel intensity) 41 (23), 55 (19), 67 (32), 68 (11), 69 (9), 81 (32), 82 (10), 95 (10), 99 (100), 112 (17), 125 (6), 126 (4), 139 (4), and 154 (9) (molecular ion). Mitsugashiwalactone (**24**): NMR (CCl_4) δ 1.15 (d, 3, CH_3), 0.9–2.8 (m, 9), 4.17 (m, 2, CH_2 of the lactone ring adjacent to oxygen); IR 2930, 2850, 1730, 1480, 1460, 1390, 1260, 1205, 1180, 1115, 1075 cm^{-1}; mass spectrum *m/e* (rel intensity) 41 (45), 55 (41), 67 (67), 68 (19), 69 (21), 81 (70), 82 (19), 99 (100), 112 (27), 125 (10), 126 (10), 139 (56), 153 (5), and 154 (19) (molecular ion).

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Registry No.—**2a,** 75-21-8; **2b,** 75-56-9; **2c,** 2984-50-1; **2d,** 286-20-4; **5a,** 51134-16-8; **5b,** 57383-30-9; **5c,** 57383-31-0; **5d,** 57383-32-1; **6,** 61258-90-0; **7b,** 57383-29-6; **8a,** 58147-99-2; **8b,** 58147-94-7; **8c,** 58147-98-1; **8d,** 58147-97-0; **11a**(M = Na), 61259-65-2; **11a**(M = Tl), 61278-52-2; **12a,** 58161-88-9; **12b,** 58237-61-9; **12c,** 58237-63-1; **12d,** 58237-64-2; **13,** 61259-66-3; **14,** 61259-67-4; **15,** 61259-68-5; **16a,** 5732-99-0; **16b,** 58237-62-0; **16c,** 58237-65-3; **16d,** 58237-66-4; **19,** 96-39-9; **20,** 3727-31-9; **21,** 60244-32-8; **22,** 60244-31-7; **23,** 60363-04-4; **24,** 60363-05-5; **25,** 61278-53-3; sodium cyclopentadienide, 38785-12-5; trimethylsilyl chloride, 75-77-4; ethyl chloroformate, 541-41-3; dimethyl acetylenedicarboxylate, 762-42-5; ethylmagnesium bromide, 925-90-6; magnesium bromide, 7789-48-2; thallium sulfate, 10031-59-1; methyl fluorosulfonate, 421-20-5.

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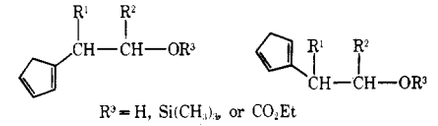

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