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バージョン：

権利関係：

Pressure Effect on the Cycloaddition of Tropone to 2,3-Dihydrofuran¹⁾

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The cycloaddition of tropone to 2, 3-dihydrofuran was examined under high pressure, to give all the possible four Diels-Alder adducts and two [8+2] cycloadducts, being different from those of 1, 1-diethoxyethenes. The ratio of [4+2]/[8+2] cycloadducts were pressure dependent.

Introduction

The cycloaddition to tropones, known as 2π -,²⁾ 4π -,^{3,4)} 6π -,⁵⁾ and 8π -⁶⁾ cycloaddends, is becoming an important process in organic synthesis. This may well be attributable to a recent progress in the high-pressure chemistry. Previously, we revised the results of cycloadditions of tropone (**1**) to 1,1-diethoxyethene (**A**)⁷⁾ to have oxygen substituent at C-9 of 8,9-dihydrohomobarrelenones. Interestingly, this was consistent to the mode of second step of 2:1-cycloadducts of **1** to 2-methoxyfuran (**B**)⁸⁾. On a contrary, our recent study with the high-pressure Diels-Alder reaction of **1** with ethoxyethene (**C**) showed a formation of all possible four [4+2] cycloadducts (dihydrohomobarrelenones) and two [8+2] cycloadducts.⁹⁾

We have now extended a high-pressure cycloaddition to **1** to 2,3-dihydrofuran (**2**), a cyclic analogue of **A**, to investigate the pressure effect on the stereo-selectivity and peri-selectivity. The results showed pressure dependent product distributions for *endo/exo*-ratio of the [8+2] cycloadducts as described herein.

Results and Discussion

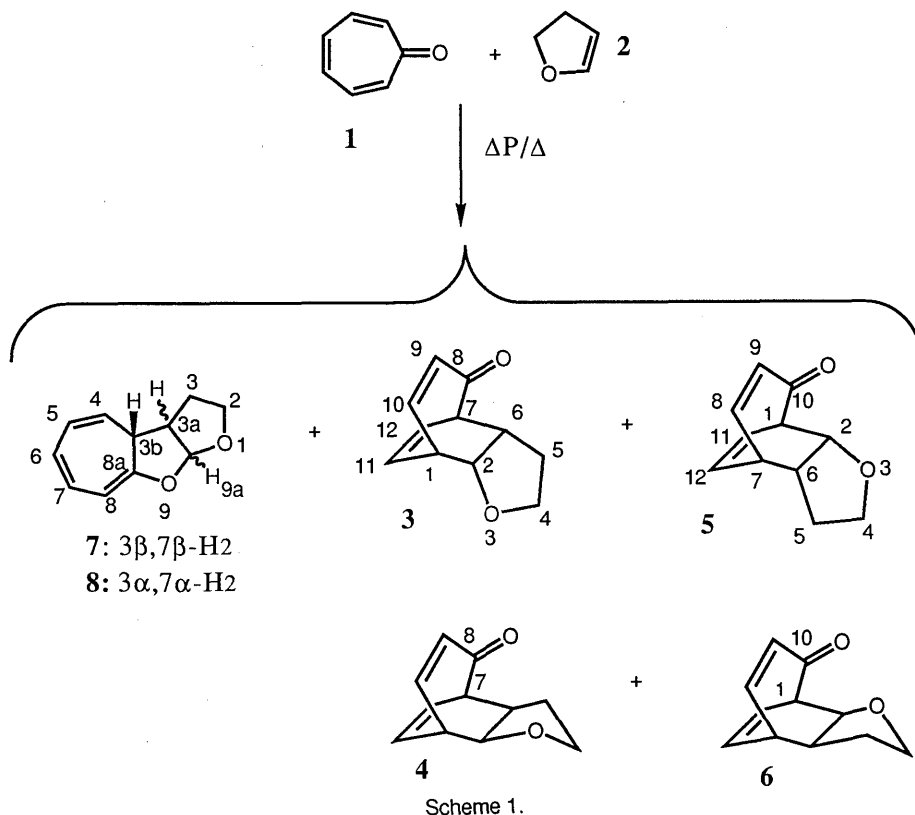
Thermal High-Pressure Cycloaddition. When **1** and **2** were heated at 100°C under 5000 bar (1 bar = 10⁵ Pa) for 10h, 58% of **1** was consumed to give 1:1-adducts (**3-8**).

The products, **3**, and **4**, obtained in 15 and 13% yields, respectively, revealed a similarity with the reported ¹H and ¹³C NMR spectra of 9-ethoxybicyclo[3.2.2.]nona-3,6-dien-ones.⁶⁾ In the ¹H NMR of **3**, two proton signals on the bridge-head carbons appeared at $\delta = 3.42$ (dd) and 3.51 (ddd), respectively, spin-coupled to the vicinal methine protons on the ring junctures; the latter with the methine proton on the ethereal

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carbon at $\delta = 4.44$ (dd) showed $J = 2.0$ Hz, and the former with the C-7 methine proton signal at 3.42 did $J = 2.0$ Hz, and the former with the C-7 methine proton signal at 3.42 did $J = 1.8$ Hz. Therefore, those observations clearly indicate that **3** is the *endo*-adduct. The coupling sequence was confirmed by the two-dimensional H-H COSY experiment;⁹⁾ a methine proton signal for H-6 ($\delta = 2.81$) was correlated with those of H-7 and H-12 ($\delta = 3.42$ and 6.13) while a signal ascribable to the methine proton on the ethereal carbon, H-2 ($\delta = 4.44$), showed correlations to those of H-1 and H-11 ($\delta = 3.51$ and 6.51) (Fig. 1). Therefore, the structure of **3** could be deduced as *endo*-3-oxatricyclo[5.3.2.0^{2,6}]dodeca-9,11-dien-8 one.

The ¹H NMR spectrum of **4** showing the ethereal methine proton signal at $\delta = 4.39$ (dd) with a relatively large vicinal coupling constant ($J = 5.5$ Hz) with the bridge-head proton deduced to be *exo*-3-oxatricyclo[5.3.2.0^{2,6}]dodeca-9,11-dien-8-one.

The ¹H NMR spectra of other Diels-Alder adducts, **5** and **6**, *endo*- and *exo*-3-oxatricyclo[5.3.2.0^{2,6}]dodeca-8,11-dien-10-ones, clarified their structures; i.e. in **5**, the signal ascribable to the methine proton on the ethereal carbon appeared at $\delta = 4.45$ (d, $J = 8.4$ Hz) indicating to be the *endo*-adduct, and in **6** the corresponding signal is at $\delta = 4.39$ (dd, $J = 8.8, 7.0$ Hz), indicating to be the *exo*-adduct.

The structures of **7** and **8**, the [8+2]cycloadducts, were also elucidated from the ¹H

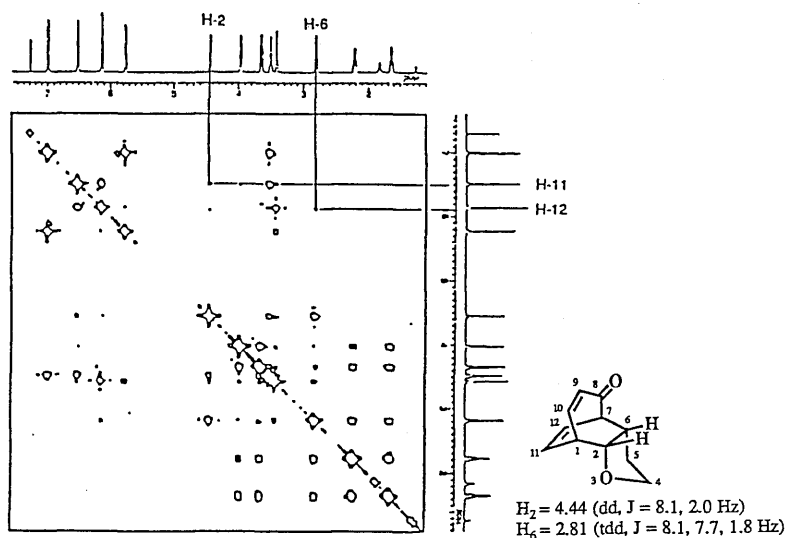


Fig. 1 Two-Dimensional NMR Spectrum of **3**.

NMR spectra; both **7** and **8** revealed signals ascribable to five consecutive protons on the seven-membered rings, which indicate the carbon framework having a cycloheptatriene structure. In addition, C-9a- β proton signal of **7** appeared at $\delta = 5.72$ (d) which only coupled to the proton at C-3a- β , $\delta = 2.27$ (ddt), whose magnitude of vicinal coupling constant ($J = 9.1$ Hz) to the methine proton on the cycloheptatriene (at C-3b) was consistent as the *cis-endo*-isomer. Thus, the remaining isomer, **8**, should be the *trans-exo*-isomer. This was additionally confirmed by the nuclear Overhauser effect (NOE) measurements; the C-4 vinyl proton showed a clear increase of the signal height by irradiation with the frequency of C-3a- α methylene proton signal. On the other hand, C-3b proton of **7** showed an NOE with C-3a- β methine proton.¹⁰⁾

The attempted isomerization of these [4+2] cycloadducts, **3**, **4**, **5** and **6**, were investigated by heating in toluene at 100°C under 5000 bar for 5 h; the each starting compound was recovered in more than 95%, and no isomer could be detected. The same was true when the [8+2] cycloadducts, **7** and **8**, were respectively heated under similar conditions to recover 87% of the starting materials. In addition to this, as could be seen in Table 1, the ratio of [4+2]/[8+2] at 140°C under 5000 bar were constant within experimental error for the whole time course, up to ca. 60%, of the reaction.

Thus; there was no mutual isomerization taken place, and it is clear that [4+2] and [8+2] cycloadducts are formed independently.

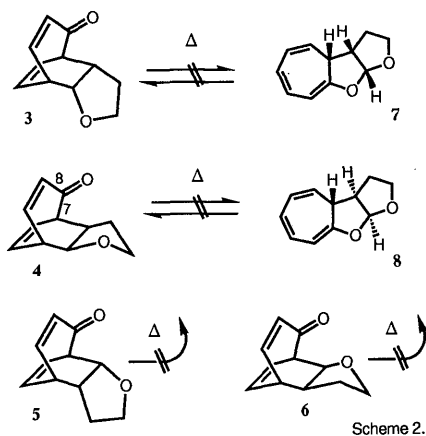


Table 1. Time Course in Product Distributions of the Cycloaddition of **1** to **2** at 100°C under 5000 bar in Toluene.

Time/h	Conversion/%	Ratio of [4+2]/[8+2]
3	18	2.0 ₅
5	25	2.1 ₄
7	37	2.0 ₃
10	58	1.9 ₁

Pressure Effect of the Cycloaddition. At first, the high-pressure conditions greatly improved the reaction; for the thermal addition of **1** and **2** under the ordinary pressure, much longer time was required, i.e., ca. 70 h for 10%-conversion of **1** at 100°C.

In addition, as could be seen in Table 2, the periselectivity was pressure dependent; the ratio of [4+2]cycloadducts over [8+2]cycloadducts were increased with increasing pressure. While within the [4+2]cycloadducts, relative yields were constant between 1 and 5000 bar.

On the other hand, the ratio of endo/exo-[8+2]cycloadducts changed with pressure (Table 3).

Table 2. Pressure Effect for the Periselectivity in the Cycloaddition of **1** to **2** at 140°C.

Pressure/bar	Time/h	Conversion/%	Yields		Ratio
			[4+2]	[8+2]	[4+2]/[8+2]
1	70	10	36	64	0.5 ₆
2000	8	24	66	34	1.9 ₄
5000	7	37	67	33	2.0 ₃

Table 3. Respective Product Distributions for [4+2]and [8+2]Cycloadducts of **1** to **2** under Various pressures.

Pressure/bar	[4+2]				Ratio 3+5/4+6	[8+2]		Ratio 7/8
	3	5	4	6		7	8	
1	50	8	36	6	1.3 ₈	67	33	2.0 ₃
2000	49	9	36	6	1.3 ₈	65	35	1.8 ₆
5000	51	6	39	4	1.3 ₃	58	42	1.3 ₈

Increased formation of *endo*-[8 + 2]cycloadduct (**8**) over *exo*-[8 + 2]cycloadduct, **7**, under higher pressure conditions is noteworthy. Evidently, the transition state leading to **8** was more sterically hindered than that of **7**. It has been known that the pressure acceleration is larger for the more sterically hindered than that of **7**. It has been known that the pressure acceleration is larger for the more sterically hindered reactants,¹¹⁾ and more significant effect was observed for polar reactants and solvent. The desolvation process, being required to encounter the cycloaddends, should become critical by increasing pressures. And, this is important in a rigid, polar cycloaddend such as **2**. As an acyclic substrate, ethoxythene⁶⁾ showed no significant effect, and this could be explained in terms of their conformationally mobile transition states leading to [8 + 2]adducts.¹²⁾

Finally, 8-*exo*-oxygenated dihydrohomobarrelenone (**6**), which should have larger transition barrier, was not detectable when the reaction was carried out at room temperature, 25°C. An example of this category was recently reported.^{12a)}

Experimental

The NMR spectra were measured with JEOL GSX and 270H GSX 500 spectrometers in CDCl₃, unless otherwise specified, and the chemical shifts expressed were in δ units. Mass spectra were measured with a JEOL 01SG-2 spectrometer. The UV spectra were measured by the use of a Hitachi U-3200 spectrophotometer in methanol. The IR spectra were taken as liquid films inserted between NaCl plates using a JASCO IR-700 spectrometer. The stationary phase for the column chromatography was Wakogel C-300 and the elution solvents were mixture of hexane and ethyl acetate.

High-Pressure Cycloaddition of 1 and 2. A toluene solution (2 ml) of **1** (212 mg), **2** (280 mg) was heated at 100°C under 5000 bar for 10 h. The mixture was then separated by means of silica-gel column and high-pressure liquid (Microporasil, ethyl acetate and hexane) chromatography to give the products:¹³⁾

3: A colorless oil, 68 mg; 19.3%. Found: M. W., 176.0836 (M⁺). Calcd for C₁₁H₁₂O₂; 176.0836. ¹H NMR δ = 1.66 (1H, ddt, J = 12.1, 9.9, 7.7 Hz), 2.22 (1H, dddd, J = 12.1, 8.1, 5.9, 2.6 Hz), 2.81 (1H, tdd, J = 8.1, 7.7, 1.8 Hz), 3.42 (1H, dd, J = 7.3, 1.8 Hz), 3.51 (1H, ddd, J = 8.8, 7.7, 2.6 Hz), 3.65 (1H, ddd, J = 9.9, 8.8, 5.9 Hz), 3.97 (1H, ddd, J = 8.8, 8.1, 2.9 Hz), 4.44 (1H, dd, J = 8.1, 2.0 Hz), 5.76 (1H, dd, J = 11.0, 2.0 Hz), 6.13 (1H, ddm, 8.4, 7.7 Hz), 6.51 (1H, ddm, J = 8.4, 8.1 Hz), and 6.99 (1H, dd, J = 11.0, 8.8 Hz). ¹³C NMR δ = 33.2, 40.0, 41.8, 56.7, 69.7, 82.3, 126.0, 130.8, 136.9, 149.4, and 196.2. MS m/z (%): 176 (M⁺, 54), 158 (13), 147 (13), 131 (19), 120 (18), 107 (100), 91 (53), 77 (28), 70 (45), 65 (21), 51 (25), 42 (30), 39 (42), and 26 (21). IR ν : 3048, 2942, 2862, 1670, 1632, 1386, 1080, and 715 cm⁻¹. UV $\lambda_{\max}^{\text{MeOH}}$ = 216 nm (ϵ = 7200), 282 (700), and 343 (300).

4: A colorless oil; 52.3 mg; 14.9%. Found: M. W., 176.0837 (M⁺). ¹H NMR δ = 1.52 (1H, dddd, J = 12.5, 9.5, 9.2, 7.7 Hz), 1.99 (1H, dddd, J = 12.5, 9.2, 6.2, 2.6 Hz), 2.83 (1H, qd, J = 9.2, 6.2 Hz), 3.64 (1H, tm, J = 8.4 Hz), 3.75 (2H, m), 4.07 (1H, ddd, J = 8.8, 7.7, 2.6 Hz), 4.39 (1H, dd, J = 9.2, 5.5 Hz), 5.88 (1H, dd, J = 11.0, 2.2 Hz), 6.17 (1H, dd, J = 8.4, 7.3 Hz), 6.41 (1H, dd, J = 8.4, 7.3 Hz) and 6.96 (1H, dd, 11.0, 8.0

Hz). ^{13}C NMR $\delta = 29.9, 41.3, 42.5, 57.0, 69.9, 83.8, 129.4, 131.2, 136.3, 152.4$ and 197.5 . MS m/z (%): 176 (M^+ , 64), 157 (15), 147 (13), 131 (18), 107 (100), 91 (31), 77 (16), 70 (39), 42 (19), and 39 (20). IR ν : 3046, 2944, 2868, 1664, 1630, 1390, 1216, 1074, 1039, 880, 842, 731 and 680 cm^{-1} .

5: A colorless oil, 8.0 mg; 2.3%. Found: M. W., 176.0836 (M^+). ^1H NMR $\delta = 1.61$ (1H, ddt, $J = 12.1, 10.3, 8.1$ Hz), 2.09 (1H, dddd, $J = 12.1, 8.4, 5.9, 2.6$ Hz), 2.99 (1H, tdm, $J = 8.4, 8.1$ Hz), 3.24 (1H, dd, $J = 8.4, 7.3$ Hz), 3.65 (1H, ddd, $J = 10.3, 8.4, 5.9$ Hz), 3.74 (1H, dm, $J = 7.3$ Hz), 3.98 (1H, td, $J = 8.1, 2.6$ Hz), 4.45 (1H, d, $J = 8.4$ Hz), 5.67 (1H, dm, $J = 11.0$ Hz), 6.16 (1H, DD, $J = 8.4, 7.3$ Hz), 6.50 (1H, dd, $J = 8.4, 7.3$ Hz), and 7.11 (1H, dd, $J = 11.0, 8.4$ Hz). ^{13}C NMR $\delta = 33.1, 39.3, 45.5, 59.6, 69.7, 79.9, 127.4, 129.4, 135.9, 153.5,$ and 194.9 . MS m/z (%): 176 (M^+ , 37), 107 (100), 91 (14), 70 (46), 42 (16), and 39 (11). IR ν : 3050, 2962, 2856, 1667, 1630, 1384, 1260, 1082, and 800 cm^{-1} .

6: A colorless oil; 5.4 mg; 1.5%. Found: M. W., 176.0837. ^1H NMR $\delta = 1.75$ (1H, dddd, 12.5, 8.8, 7.5, 7.0 Hz), 2.09 (1H, dddd, $J = 12.5, 9.2, 6.6, 3.0$ Hz), 2.74 (1H, tdd, $J = 8.8, 6.6, 5.5$ Hz), 3.42 (1H, ddd, $J = 8.4, 8.2, 5.5$ Hz), 3.69 (1H, td, $J = 8.8, 3.3$ Hz), 4.0 (2H, br m), 4.39 (1H, dd, $J = 8.8, 7.0$ Hz), 5.90 (1H, dm, $J = 11.0$ Hz), 6.02 (1H, dd, $J = 8.4, 7.3$ Hz), 6.57 (1H, dd, $J = 8.2, 7.3$ Hz), and 6.93 (1H, dd, $J = 11.0, 8.4$ Hz). ^{13}C NMR $\delta = 29.8, 40.9, 45.5, 58.0, 69.5, 80.3, 125.8, 132.2, 139.8, 151.0$ and 195.4 . MS m/z (%): 176 (M^+ , 62), 175 (56), 131 (28), 117 (21), 107 (100), 104 (29), 91 (52), 77 (42), 70 (49), 55 (21), 51 (25), 42 (24), and 39 (38). IR ν : 3014, 2930, 1695, 1666, 1216, 1082, 756, and 667 cm^{-1} .

7: A colorless oil; 40.7 mg; 11.6%. Found: M. W., 176.0844. ^1H NMR $\delta = 1.30$ (1H, ddt, $J = 13.1, 9.5, 7.9$ Hz), 1.61 (1H, ddt, $J = 13.1, 7.7, 4.7$ Hz), 2.27 (1H, ddt, $J = 9.5, 9.1, 4.7$ Hz), 2.79 (1H, ddt, $J = 9.1, 4.0, 2.0$ Hz), 3.55 (1H, ddd, $J = 8.3, 7.9, 4.7$ Hz), 3.60 (1H, ddd, $J = 8.3, 7.9, 7.7$ Hz), 4.67 (1H, dd, $J = 9.9, 4.0$ Hz), 5.72 (1H, d, $J = 4.7$ Hz), 5.79 (1H, dd, $J = 7.2, 2.0$ Hz), 6.05 (1H, ddd, $J = 9.9, 6.0, 2.0$ Hz), 6.12 (1H, dd, $J = 11.0, 6.0$ Hz), and 6.25 (1H, dd, $J = 11.0, 7.2$ Hz). ^{13}C NMR $\delta = 26.9, 42.2, 44.4, 69.1, 97.4, 111.9, 118.5, 123.4, 128.2, 129.2$ and 154.8 , MS m/z (%): 176 (M^+ , 93), 175 (20), 147 (29), 131 (22), 117 (27), 107 (99), 91 (57), 77 (24), 70 (100), 51 (20), 42 (31), and 39 (31). IR ν : 3014, 2974, 2878, 1639, 1597, 1478, 1460, 1243, 1183, 1080, 955, 935, 752, and 704 cm^{-1} . UV $\lambda_{\text{max}}^{\text{MeOH}} = 208\text{ nm}$ ($\epsilon = 10800, \text{sh}$), 279 (20000) and 301 (1200).

8: A colorless oi; 30.9 mg; 8.8%. Found: M. W., 176.0836. ^1H NMR $\delta = 1.88$ (1H, ddt, $J = 12.5, 5.5, 1.8$ Hz), 2.20 (1H, m), 2.39 (1H m), 3.11 (1H, m), 3.89 (1H, ddd, $J = 11.0, 8.8, 5.5$ Hz), 4.06 (1H, ddd, $J = 8.8, 8.4, 1.8$ Hz), 5.03 (1H, dd, $J = 9.2, 4.0$ Hz), 5.68 (1H, d, $J = 6.6$ Hz), 6.02 (1H, d, $J = 5.1$ Hz), 6.12 (1H, ddd, $J = 9.2, 5.9, 1.8$ Hz), 6.24 (1H, dd, $J = 11.0, 5.9$ Hz), and 6.44 (1H, dd, $J = 11.0, 6.6$ Hz). ^{13}C NMR $\delta = 33.1, 47.2, 48.7, 67.4, 95.3, 112.3, 121.3, 123.8, 126.7, 129.5,$ and 152.5 . MS m/z (%): 176 (M^+ , 58), 147 (13), 131 (13), 107 (100), 941 (27), 77 (15), 70 (58), 69 (16), 51 (13), 42 (24), and 39 (16). IR ν : 3014, 2970, 2897, 1640, 1383, 1357, 1179, 1073, 1028, 963 and 712. UV $\lambda_{\text{max}}^{\text{MeOH}} = 277\text{ nm}$ ($\epsilon = 16000$) and 241 (2300).

Thermal Cycloaddition Reaction of 1 with 2 under Ordinary Pressure. A toluene solution (2 ml) of **1** (212 mg) and **2** (280 mg) was heated in sealed tube at 100 °C for 70 h. The mixture was chromatographed on a silica-gel column to give a mixture of **3**, **4**, **5**, and **6** (12 mg; 3%) and a mixture of **7** and **8** (21 mg; 6%) together with the recovered **1** (125 mg; 59%). Further fractionation was carried out by means of high-pressure liquid chromatography, and the product ratio was shown in Table 2 and 3.

Attempted Isomerization of Cycloadducts under 5000 bar. A toluene solution containing a mixture of [4+2] or [8+2] cycloadducts of cycloadducts (ca. 20 mg) was placed in a pressure vessel, and kept at 140 °C under 5000 bar for 10 h. The mixture was then, analyzed by HPLC, which every time showed only the starting cycloadducts.

References

- 1) A. Part of this study was preliminarily reported. See Z.-H. Li, A. Mori, H. Takeshita, and Y. Nagano, *Chem. Express*, **7**, 213 (1992).
- 2) H. Takeshita, Y. Wada, A. Mori, and T. Hatsui, *Chem. Lett.* **1973**, 335.
- 3) As the recent examples: G. Mehta and S. R. Karra, *J. Org. Chem.*, **54**, 2975 (1989); H. Meier, A. Pauli, and H. Kolshorn, *Chem. Ber.*, **122**, 101 (1989); G. R. Tian, S. Sugiyama, A. Mori, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **61**, 2398 (1988).
- 4) G. R. Tian, S. Sugiyama, A. Mori, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **61**, 1557 (1988); *ibid.*, **61**, 2393 (1988).
- 5) D. Forstmeyer, J. Bauer, E. Fontain, R. Herges, R. Herrmann, and I. Ugi, *Angew. Chem, Int. Ed. Engl.*, **27**, 1558 (1988); S. Itô, Y. Fujise, T. Okuda, and Y. Inoue, *Bull. Chem. Soc. Jpn.*, **39**, 1351 (1966); R. C. Cookson, B. V. Drake, J. Hudec, and A. Morrison, *Chem. Commun.*, **1966**, 15.
- 6) A. Mori, Z.-H. Li, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **63**, 2257 (1990).
- 7) T. S. Cantrell, *Tetrahedron Lett.*, **1975**, 907.
- 8) H. Takeshita, H. Nakashima, S. Sugiyama, and A. Mori, *Bull. Chem. Soc. Jpn.*, **61**, 573 (1988).
- 9) The measurement was carried out with a GSX 270 H Model spectrometer with the VCOSYN pulse sequence of the JEOL GSX series software.
- 10) The observed magnitudes of methine protons on the acetal carbons of **7** (d, $J=4.7$ Hz) and **8** (d, $J=5.1$ Hz) were somewhat smaller than normal vicinal coupling constants for *cis*-protons of the five-membered rings. However, these figures were in good accord to the similar [8+2] cycloadducts from **1** and ethoxyethene.⁴⁾ Similar values were reported for the vicinal couplings of protons on the acetal carbons of 5,7-dioxabicyclo[3.3.0]octane derivatives. See T. Mikami, A. Katoh, and O. Mitsunobu, *Tetrahedron Lett.*, **31**, 539 (1990).
- 11) R. van Eldik, T. Asano, and W. J. le Noble, *Chem. Rev.*, **88**, 549 (1975).
- 12) The other acyclic ethenes, acrylonitrile, has no tendency to form [8+2] cycloadduct; a) Z.-H. Li, A. Mori, and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **63**, 3713 (1990); b) S. Itô, H. Takeshita, and Y. Shoji, *Tetrahedron Lett.*, **1969**, 1815.
- 13) Combustion analysis of these cycloadducts failed due to thermal instability; even a Bulb-to-Bulb distillation caused a partial decomposition.