The Effect of Pressure on Sigmatropic Rearrangements of Seven-Membered Conjugated Systems. [3,3] and [1,9] Sigmatropies

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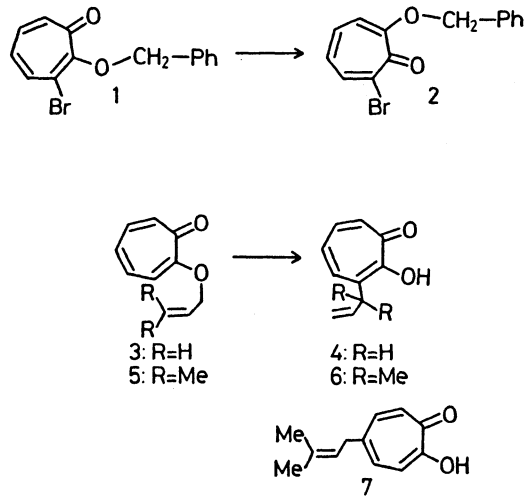
The kinetic features of the [1,9] sigmatropy (with 2-benzyloxy-3-bromotropone) and the [3,3] sigmatropy (with 2-allyloxytropone and 2-[(3-methyl-2-butenyl)oxy]tropone) were investigated under various pressures (1 to 1600 bar). The activation volume of [1,9] sigmatropy was of the same order as those of [1,5] sigmatropy of cyclopentadienes. The activation volume of [3,3] sigmatropy of more sterically-hindered substrate was more negative than that of the unhindered one.

Studies of the sigmatropic rearrangement have attracted considerable interest. Its mechanistic aspects and applications to organic syntheses have been investigated continuously.[1] However, although it is recognized in general that the high-pressure technique is a powerful synthetic method, investigations of sigmatropies under high-pressure conditions still remain unexplored. The sigmatropies of troponoids are unique in view of their interesting π-electron arrangement. A tautomerism of 2-acetoxytropones has been known for a long time,[2] and a kinetic analysis for the process by means of ^{13}C NMR spectroscopy was carried out by Masamune et al., [3a] who proposed an ionic mechanism. Recently, we showed[4] that the migration of the acetyl group[3] of 2-acetoxytropones between their C-1 and C-2 is a concerted [1,9] sigmatropy (acetotropy) by the kinetic analysis using temperature-variable ^{13}C NMR spectroscopy. Consequently, the kinetic analysis of various sigmatropic rearrangements under high-pressure conditions should be worthwhile. Herein, we describe, in addition to our preliminary presentation[5] of [1,9] sigmatropy of 2-benzyloxy-3-bromotropone,[6] the effect of pressure on the [3,3] sigmatropy of troponoids. A determination of the activation volume is essential in order to evaluate the synthetic aspect of any pressure effect. Previously, such studies were limited to [1,5] sigmatropy of cyclopentadiene derivatives[7] and 2-alkoxypridine *N*-oxide[8] and [3,3] sigmatropy of benzenoids and acyclic compounds.[9]



Scheme 1.

Results and Discussion

[1,9] Sigmatropy. The thermally-allowed [1,5] sigmatropies are well-known with cyclopentadienes. However, the next higher thermally-allowed electrocyclic systems, [1,9] process, are not so common. The concept of a [1,9] sigmatropy was introduced into troponoid chemistry by Harrison et al. when they observed a thermal rearrangement of 2-benzyloxy-3-bromotropone (**1**) to 7-benzyloxy-2-bromotropone (**2**).[6] Harrison et al. have also carried out a kinetic study of this rearrangement and expressed a view to favor a [1,9] process on the basis of the value of the activation energy (E_a).[6] However, it is known that E_a of sigmatropies varies from 27 to 210 kJ mol^{-1}, depending on the nature of the substrates.[10] Therefore, the conclusion drawn by Harrison deserves further investigation. We decided to examine the sigmatropy by means of a kinetic analysis. The results are summar-

Table 1. The Rate Constants ($10^7 k$/s^{-1}) of the Rearrangement of **1** at Various Temperatures

Solv.	Temperature/°C			
	110	120	130	140
Cumene	1.17±0.16	2.94±0.16	4.91±0.16	25.1±0.1
1-Hexanol	4.22±0.07	10.0±0.3	26.6±0.4	49.3±0.3

Table 2. Activation parameters of the Rearrangement of **1** at 130 °C

Solv.	ΔH^*/kJ mol^{-1}	ΔS^*/J mol^{-1} K^{-1}	ΔG^*/kJ mol^{-1}
Cumene	128±4	−47±11	147±9
1-Hexanol	106±3	−92±7	143±5

Table 3. The Rate Constants of Each Rearrangement at Various Pressures

Material		Solv.	Pressure/bar				
			1	400	800	1200	1600
1[a]	$10^7k/s^{-1}$	IB	4.91±0.16	5.48±0.01	6.19±0.18	7.24±0.08	8.28±0.03
1[a]	$10^6k/s^{-1}$	HA	2.66±0.04	2.93±0.08	3.38±0.20	3.62±0.05	4.04±0.22
3[b]	$10^5k/s^{-1}$	BB	2.30±0.02	2.61±0.02	2.82±0.02	3.07±0.02	3.20±0.01
5[b]	$10^5k/s^{-1}$	BB	6.49±0.04	8.40±0.04	9.30±0.07	11.2±0.1	12.5 ±0.1

IB: cumene, HA: 1-hexanol, BB: bromobenzene.
a) At 130 °C, b) At 120 °C.

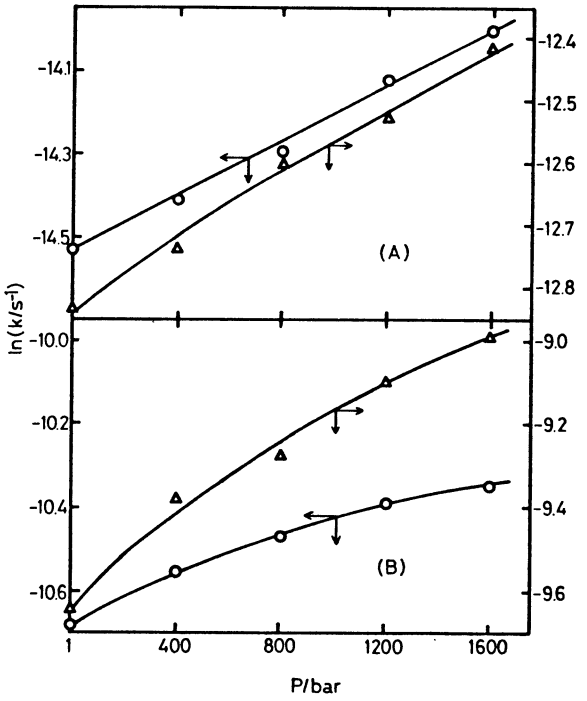


Fig. 1. Pressure dependence of $\ln k$.
(A): **1** at 130 °C, ○; in cumene, △; in 1-hexanol. (B): ○; **3** at 120 °C in bromobenzene, △; **5** at 120 °C in bromobenzene.

ized in Table 1. The activation parameters obtained at 130 °C are listed in Table 2.

Each activation parameter in both solvents, isopropylbenzene (cumene) and 1-hexanol, showed a similar tendency to those of a typical [1,5] sigmatropy operating within the range of temperature.[10] The activation entropies ($\Delta S^{\ddagger}$) obtained at 130 °C were −47 and −92 J mol^{-1} K^{-1} in cumene and 1-hexanol, respectively. As a general tendency, the stronger the solvation, the more negative $\Delta S^{\ddagger}$ is expectable from the pressure effect on this rearrangement. This indicates a weak, but not negligible, contribution of a polarized structure in the transition state. The activation free energy ($\Delta G^{\ddagger}$) remained nearly constant in both solvents as a result of the compensation effect between $\Delta S^{\ddagger}$ and the activation enthalpy ($\Delta H^{\ddagger}$).[11] Then, we investigated the high-pressure kinetic analysis of this [1,9] sigmatropy of **1** to **2**.

In Table 3, the rate constants for the rearrangement of **1** to **2** at various pressures at 130 °C are listed. The activation volume ($\Delta V^{\ddagger}$) was evaluated with Eq. 1 by using a linear function of $\ln k$ vs. pressure (P).

$$\Delta V^{\ddagger} = -RT(\partial \ln k/\partial P)_T, \quad (1)$$

The rates were accelerated with pressure; in cumene, the logarithm of the rate constants was linear to the pressure (correlation coefficient r: 0.998), but in 1-hexanol, it showed a curvature (Fig. 1 (A)). If one neglects the difference toward compressibility between the ground and transition states by assuming this rearrangement to be a unimolecular reaction, one reason of this behavior must be the contribution of a somewhat polarized transition state. This contribution may alter the degree of solvation in 1-hexanol under high pressure. Thus, from Eq. 1, $\Delta V^{\ddagger}$ were evaluated by a linear function in the case of cumene and a quadratic function in the case of 1-hexanol (tabulated in Table 4). The solvent effect on $\Delta V^{\ddagger}$ was very small and the above-mentioned solvation effect on the transition state was very weak. The rate constant at atmospheric pressure in 1-hexanol (dielectric constant ε=13.3 D) was five-times larger than that in cumene (ε=2.4 D). This magnitude of the rate enhancement is just similar to that of the Diels-Alder reaction of isoprene to maleic anhydride,[12] where the rate was about eight times larger in nitromethane (ε=38.6 D) than that in ethyl acetate (ε=6.06 D). These results show that the rearrangement of **1** to **2** is a concerted process, i.e., [1,9] sigmatropy. At the same time, the effect of pressure on [1,9] sigmatropy is similar to that of the other typical sigmatropy.

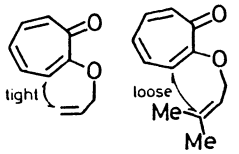
Consequently, from the temperature, pressure, and solvent effects, the present rearrangement is undoubtedly a concerted [1,9] sigmatropy.

[3,3] Sigmatropy. The Claisen rearrangement of tropolone derivatives has been a focus of attention. As early as in 1953, Sebe et al. carried out pioneering work, and reported some fundamental features.[13] However, Kitahara's studies on natural product syntheses, nootkatin and procerin,[14] have revealed a limitation of the process, i.e., the yields of the Claisen products, prenylated products, were only a few %. This was later explained by ourselves, i.e., the proto-Claisen thermolysates of the γ-substituted allyl ethers of tropolones cause another thermally-allowed fragmentation to tropolones and diene via the $[_s6_\pi + _s2_\pi + _s2_\sigma]$ electro-

cyclic reaction.[15] Intramolecular Diels-Alder reactions of the proto-products from the substituted troponyl allyl ethers found by Harrison et al.[16] and Schmid et al.[17] also constitute a limitation of the Claisen rearrangement. Nevertheless, the Claisen rearrangement of troponoids may be competitive with other electrocyclic reactions, and it is interesting from a theoretical point of view.

As a typical [3,3] sigmatropy, Claisen rearrangements of 2-allyloxytropone (**3**) to 3-allyltropolone (**4**) and 2-[(3-methyl-2-butenyl)oxy]tropone (**5**) to thermolysates (**6** and **7**) were carried out. Prior to high-pressure kinetics, authentic samples of thermolysates were prepared and isolated as 2-methoxytropone derivatives, i.e., 3-allyl-2-methoxytropone (**8**), 2-allyl-7-methoxytropone (**9**), 2-methoxy-3-(1,1-dimethyl-2-propenyl)tropone (**10**), 2-methoxy-7-(1,1-dimethyl-2-propenyl)tropone (**11**), and 2-methoxy-5-(3-methyl-2-butenyl)tropone (see Experimental). The rates of reactions under various pressures were measured by high-pressure liquid chromatography (HPLC) of the product mixture after treatment with ethereal diazomethane.

Table 3 shows the pressure effect on Claisen rearrangements of **3** and **5**. At 1 bar, the rate constant of **5** was three-times larger than that of **3**. This is predictable in terms of an electron-releasing effect of the methyl groups of **5**; however, the effect of this electronic character on the solvation term must be very small in this concerted reaction.[18] As shown in Fig. 1 (B), the acceleration with pressure was much larger in the case of **5** than **3**. By using a quadratic function of pressure to express this dependence $\Delta V^{\ddagger}$ was evaluated (listed in Table 4). Evidently, the rearrangement of **5**, being more sterically hindered at the reaction center, was more accelerated with pressure than that of **3**, being less hindered. There have been several discussions about a pressure effect on the steric hindrance to Menshutkin reaction.[19,20] Le Noble and Asano found that, by volume criterion, the transition state of Menshutkin reaction is more product-like as the reaction is more hindered. In other words, more hindered Menshutkin reactions tend to become more accelerated with pressure. This is consistent to a postulation by Hammond.[20] In order to explain the results, one has to consider the difference of the bulkiness of the reactant. That is, in order to cause a rearrangement, a reactant having a bulky substituent must be contracted



3 5

$|\Delta V^{\ddagger}| < |\Delta V^{\ddagger}|$

Scheme 2.

Table 4. The Activation Volumes of Each Rearrangement

Material	1	1	3	5
Solv.	IB	HA	BB	BB
$\Delta V^{\ddagger}$/cm^{3}mol^{-1}	−11.1±0.7	−10.1±0.5	−10.6±0.3	−18.2±1.0

IB: cumene, HA: 1-hexanol, BB: bromobenzene.

to a greater extent than that having a non-bulky one. As a result, the $\Delta V^{\ddagger}$ value for the more hindered rearrangement must be more negative (Scheme 2).

The Claisen rearrangement of **5** was much more accelerated with pressure than that of unsubstituted **3**, due to the contribution of two additional methyl groups. If there were more crowded substituents at the reaction center, the Claisen rearrangement might be more pressure-accelerated to give a more negative $\Delta V^{\ddagger}$ value than the ordinary [3,3] sigmatropy ($-18 < \Delta V^{\ddagger} < -7$).[9]

Experimental

Materials. Solvents were carefully purified by dehydration and distillation under N_2 atmosphere. All materials were prepared by the known procedures, and purified by silica-gel column chromatography. Recrystallizations for a solid sample were performed by using the solvents indicated in parentheses. The NMR spectra were measured in $CDCl_3$ solutions, and the chemical shifts were expressed in δ units with the internal standard, Me_4Si. The IR spectra were taken in $CHCl_3$ solutions.

Kinetic Measurements. The apparatus for kinetic runs was the same as used in our previous studies.[21] The reaction temperature was controlled within ±0.5 °C. The progress of the reaction was monitored by high-pressure liquid chromatography [Nippon Waters Model 244 apparatus] by the increase of product formations. In the case of Claisen rearrangements of **3** and **5**, tropolone derivatives were methylated with ethereal CH_2N_2 prior to analysis.

[1,9] Sigmatropy of 1 (Preparative). A cumene solution of **1** (mp 44—45 °C (from benzene-hexane) (lit,[6] 43—44 °C); 254 mg) was heated in a sealed tube at 150 °C for 24 h. The mixture was chromatographed on a silica-gel column to give the desired product:

2: Mp 94—95 °C (from benzene-hexane) (lit,[6] 96—97 °C).

Claisen Rearrangement of 3 (Preparative). Characterization of the Thermolysate (4) as its Methyl Ethers (8 and 9). A toluene solution of **3** (bp 60 °C/0.3 Torr (1 Torr=133.22 Pa)) (177 mg) was refluxed for 8 h. The mixture was then heated in vacuo to remove the solvent and the residue was chromatographed on a silica-gel column with benzene-EtOAc (1 : 1) to give **4** [colorless crystals, mp 42—43 °C (hexane-EtOAc) (lit,[22] 43—44 °C); 49.5 mg; 60%] and the recovered **3** (95.1 mg). The **4** was treated with ethereal diazomethane. Silica-gel column chromatography of the mixture with benzene-EtOAc (5 : 1) afforded methylated derivatives:

8: A pale yellow oil; 15 mg. Found: *m/z* 176.0836. Calcd for $C_{11}H_{12}O_2$: M, 176.0837; ^{1}H NMR δ=3.44 (2H, dt, *J*=6.6, 1.5 Hz), 3.91 (3H, s), 5.09 (1H, dtd, *J*=16.1, 1.5, 1.1 Hz), 5.10 (1H, dtd, *J*=11.0, 1.5, 1.1 Hz), 5.91 (1H, ddt. *J*=16.1, 11.0, 6.6 Hz), and 6.8—7.2 (4H, m). ^{13}C NMR δ=38.9, 58.9, 116.7, 129.7, 135.3, 135.4, 137.1, 137.7, 138.6, 163.9, and 181.8. IR ν; 1620, 1580, and 1275 cm^{-1}.

9: Colorless crystals, mp 48—49 °C (benzene-hexane);

35 mg. Found: C, 74.87; H, 6.79%. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86%. ^{1}H NMR δ=3.52 (2H, d, J=6.6 Hz), 3.93 (3H, s), 5.10 (1H, dm, J=9.9 Hz), 5.15 (1H, dm, J=17.0 Hz), 5.99 (1H, ddt, J=17.0, 9.9, 6.6 Hz), 6.74 (1H, br d, J=9.4 Hz), 6.84 (1H, br t, J=9.4 Hz), 7.01 (1H, br t, J=9.4 Hz), and 7.37 (1H, br d, J=9.4 Hz); ^{13}C NMR δ=39.8, 56.3, 112.1, 117.0, 127.1, 131.0, 135.8 (2C), 147.9, 164.0, and 179.3. IR ν: 1640, 1595, and 1275 cm^{-1}.

Claisen Rearrangement of 5 (Preparative). Characterization of the Thermolysates (6 and 7) as Methyl Ethers (10, 11, and 12). A toluene solution (20 cm^3) of **5**[23] (527 mg) was similarly refluxed for 17 h. The mixture was then heated in vacuo to remove the solvent, and the residue was chromatographed on a silica-gel column with benzene-EtOAc (1 : 1) to give **10** (89.2 mg; 19%), **11** (166.6 mg; 36%), **12** (130.2 mg; 28%), 2-methoxytropone (38.4 mg; 11%), and the recovered **5** (67.1 mg):

10: A pale yellow oil. Found: m/z 204.1148. Calcd for $C_{13}H_{16}O_2$: M, 204.1149. ^{1}H NMR δ=1.47 (6H, s), 3.80 (3H, s), 4.94 (1H, dd, J=17.6, 1.1 Hz), 4.99 (1H, dd, J=10.6, 1.1 Hz), 6.12 (1H, dd, J=17.6, 10.6 Hz), 6.82 (1H, ddd, J=11.7, 7.6, 1.8 Hz), 7.05 (1H, dd, J=12.1, 1.8 Hz), 7.15 (1H, ddd, J=12.1, 7.6, 7.1 Hz), and 7.28 (1H, br d, J=11.7 Hz); ^{13}C NMR δ=28.0 (2C), 43.5, 57.8, 109.6, 128.2, 134.2, 135.3, 136.9, 144.8, 148.5, 165.7, and 182.6. IR ν: 1630, 1605, and 1290 cm^{-1}.

11: Colorless crystals, mp 49—50 °C (benzene-hexane); Found: C, 76.21; H, 7.94%. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90%. ^{1}H NMR δ=1.49 (6H, s), 3.86 (3H. s), 5.01 (1H, dd, J=10.6, 1.1 Hz), 5.02 (1H, dd, J=17.6, 1.1 Hz), 6.16 (1H, dd, J=17.6, 10.6 Hz), 6.57 (1H, d, J=9.5 Hz), 6.75 (1H, br t, J=9.5 Hz), 6.91 (1H, br t, J=9.5 Hz), and 7.39 (1H, d, J=9.5 Hz). ^{13}C NMR δ=27.1 (2C), 44.1, 56.3, 110.1, 110.8, 125.9, 130.4, 133.5, 147.7, 153.1, 163.1, and 180.9. IR ν: 1625 and 1270 cm^{-1}.

12: A yellow oil, MS m/z, 204 (M^+). ^{1}H NMR δ=1.71 (3H, s), 1.76 (3H, s), 3.25 (2H, d, J=7.3 Hz), 3.92 (3H, s), 5.23 (1H, tm, J=7.3 Hz), 6.71 (1H, d, J=10.3 Hz), 6.92 (1H, br d, J=10.3 Hz), 7.11 (1H, dd, J=12.5, 1.8 Hz), and 7.20 (1H, d, J=12.5 Hz); ^{13}C NMR δ=17.9, 25.8, 37.6, 56.1, 113.1, 121.5, 130.5, 134.6, 136.7, 139.3, 141.9, 163.8, and 180.2. IR ν: 1630, 1570, and 1250 cm^{-1}.

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References

1) Selected examples in the organic synthesis: J. S. Bindra and R. Bindra, "Creativity in Organic Syntheses," Academic Press, New York (1975); see also T. Shioiri and M. Shibasaki, "Organic Syntheses directed to Biologically Important Compounds," Kodansha, Tokyo (1985), p. 194.

2) An acetylation of hinokitiol is known to give only one acetate, while methyl and *p*-toluenesulfonyl derivatives of hinokitiol are known to exist as two isolable isomers. The same was true for many other substituted derivatives. For these phenomena, Dr. Masafumi Yasunami, Tohoku University, has pointed out that carboxylates of tropolones exist as an equilibrating mixture at the ordinary temperature. For hinikitiol acetate, see T. Nozoe, "Dai Yuki Kagaku (Comprehensive Organic Chemistry)," ed by M. Kotake, Asakura Shoten, Tokyo (1961), Vol. 13, p. 164.

3) a) S. Masamune, A. V. Kemp-Jones, J. Green, D. L. Rabenstein, M. Yasunami, K. Takase, and T. Nozoe, *J. Chem. Soc., Chem. Commun.*, **1973**, 283; b) V. I. Minkin, L. P. Olekhnovich, and Y. A. Zhdanov, *Acc. Chem. Res.*, **14**, 210 (1981).

4) H. Takeshita, A. Mori, H. Watanabe, T. Kusaba, S. Sugiyama, and M. Kodama, *Bull. Chem. Soc. Jpn.*, **60**, 4335 (1987).

5) S. Sugiyama, A. Mori, and H. Takeshita, *Chem. Lett.*, **1987**, 1247.

6) R. M. Harrison, J. D. Hobson, and A. W. Midgley, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 2403.

7) E. M. Schulman, A. E. Merbach, M. Tutin, R. Weddinger, and W. J. le Noble, *J. Am. Chem. Soc.*, **105**, 3988 (1983).

8) W. J. le Noble and M. R. Daka, *J. Am. Chem. Soc.*, **100**, 5961 (1978).

9) C. Walling and M. Naiman, *J. Am. Chem. Soc.*, **84**, 2628 (1962); K. R. Brower, *ibid.*, **83**, 4370 (1961).

10) C. W. Spangler, *Chem. Rev.*, **76**, 187 (1976).

11) J. E. Leffer, *J. Org. Chem.*, **20**, 1202 (1955).

12) R. A. Grieger and C. A. Eckert, *Trans. Faraday Soc.*, **66**, 2579 (1970).

13) E. Sebe and S. Matsumoto, *Proc. Jpn. Acad.*, **29**, 207 (1953).

14) Y. Kitahara and M. Funamizu, *Bull. Chem. Soc. Jpn.*, **31**, 782 (1958); Y. Kitahara and T. Kato, *ibid.*, **37**, 895 (1964).

15) H. Takeshita, H. Mametsuka, and K. Uchida, *Chem. Lett.*, **1982**, 1061.

16) R. M. Harrison, J. D. Hobson, and M. M. Al Holly, *J. Chem. Soc. C*, **1971**, 3084; R. M. Harrison, J. D. Hobson, and A. W. Midgley, *J. Chem. Soc., Perkin Trans. 1*, **1973**, 1960.

17) A. Pride, J. Zindely, and H. Schmid, *Helv. Chim. Acta*, **57**, 1598 (1974).

18) H. Mametsuka, Ph. D. Thesis, Kyushu University, 1983; H. Takeshita, H. Mametsuka, and N. Matsuo, *Bull. Chem. Soc. Jpn.*, **55**, 1137 (1982).

19) W. J. le Noble and Y. Ogo, *Tetrahedron*, **26**, 4119 (1970), and the references cited therein.

20) W. J. le Noble and T. Asano, *J. Am. Chem. Soc.*, **97**, 1778 (1975).

21) S. Sugiyama and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **60**, 977 (1987).

22) H. Takeshita, I. Kouno, and K. Miyake, *Kyushu Daigaku Seisan Kagaku Kenkyusho Hokoku*, **66**, 1 (1977).

23) In the preparation of **5**, a by-product, a colorless oil, was obtained in 4% yield. Its ^{1}H NMR indicated its structure to be 5-(3-methyl-2-butenyl)-2-[(3-methyl-2-butenyl)oxy]tropone. Since **5** was quite stable at the preparative condition (50 °C for 24 h), it must be formed directly from **5** and prenyl bromide.[18]