December, 1987] Bull. Chem. Soc. Jpn., 60, 4335—4338 (1987)

The Kinetic Evidence of the Concerted [1,9] Sigmatropy for the Acetyl Migration in the 2-Acetoxytropones. The NMR Spectral Analysis of the Seven-Fold Degenerated Acetotropy of Hexaacetoxytropone

Hitoshi Takeshita,* Akira Mori, Hiroyasu Watanabe,† Tomoyuki Kusaba,†
Shigeru Sugiyama, and Mitsuaki Kodama††
Institute of Advanced Material Study, 86, Kyushu University, Kasuga-koen, Kasuga, Fukuoka 816
†Graduate School of Engineering Sciences, 39, Kyushu University, Kasuga-koen, Kasuga, Fukuoka 816
††Pharmaceutical School of Tokushima Bunri University, Yamashirocho, Tokushima, 770
(Received May 11, 1987)

"The acetotropy" of 2-acetoxytropones was shown to be a concerted [1,9] sigmatropic process on the basis of a kinetic analysis. A little substituent effect for the activation free energy of the acetyl migration was recognized. Preferred tautomers of polyacetoxytropones were those having the carbonyl group at inner positions. As an extreme case, a "Merry-Go-Round"-type rearrangement was operative in hexaacetoxytropone.

Currently, we have developed a preparation method for polyacetoxytropones from polyhalotropones.[1)] By this method, we have synthesized several polyacetoxytropones, including hexaacetoxytropone (**1**). The ^{1}H NMR of **1** revealed only one methyl signal in the ^{1}H NMR spectrum at room temperature, indicating the operation of a seven-fold symmetric degenerated [1,9] acetyl migration. This paper deals with a kinetic analysis with variable temperature ^{13}C NMR spectra of **1** and its related derivatives in order to ascertain the concerted nature of this rearrangement. The term, [1,9] sigmatropy, was first introduced in the literature by Harrison et al.[2)] for a benzyl group migration in the isomerization of 2-benzyloxy-3-bromotropone to 2-benzyloxy-7-bromotropone.[3)]

The acetyl migration in the 2-acetoxytropones was previously reported by Masamune et al.[4)] and by Minkin et al.[5)] Masamune et al. proposed an ionic mechanism which is assisted by the polarization of tropone carbonyl to form a delocalized 6π system in a seven-membered ring; however, at the same time, they inconsistently mentioned a small medium effect for the reaction rates. When we noticed a formation of the same thermolysates in the same product distribution[6)] in the thermal homolytic rearrangement of 2-(2-furylmethoxy)-4-isopropyltropone and 2-(2-furylmethoxy)-6-isopropyltropone, we thought that prior to rearrangement, these ethers mutually isomerized via an electrocyclic process, a further example of the [1,9] alkyl shift process.[2)] In view of the similarity, the acetotropy, the rearrangement of the acyl groups between two oxygens of C-1 and C-2 positions of tropolones, may well be concerted, too. Herein, we will show unequivocal evidence for the concerted mechanism of the acetotropy, that is the [1,9] sigmatropy.[7)]

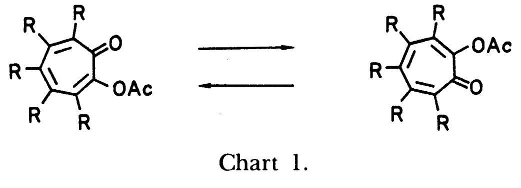
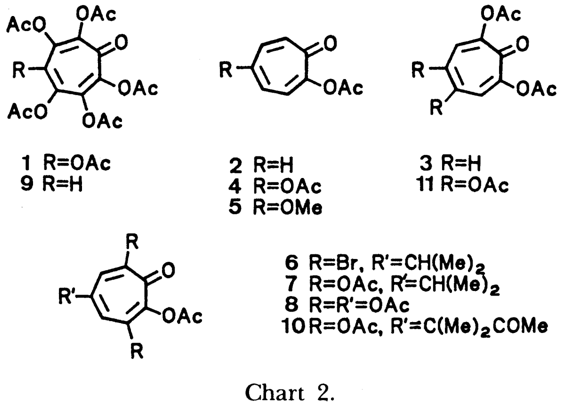


Chart 1.

Results and Discussion

Acetotropy of 2-Acetoxytropone and Its Acetoxy Derivatives. At first, the kinetics of the acetotropy of 2-acetoxytropone (**2**) were analyzed in order to make a comparison with the reported data.[4)] Table 1 shows that both data were in accord within experimental error. Unexpectedly, 2,7-diacetoxytropone (**3**)[9)] did not operate the acetotropy and its ^{1}H NMR signals retained their sharpness at a temperature between −50 and +100 °C, while 2,5-diacetoxytropone (**4**)[9)] showed smooth acetotropy. Therefore, the acetyl migration is operative only between tautomers having the same degree of thermodynamic stability. In other words, in the case of **3**, a symmetrical 2,7-diacetoxy structure is much more stable than the unsymmetrical 2,3-diacetoxy structure. As will be shown in later, this applies to consecutively substituted polyacetoxytropones; the predominant tautomers in that category possess the carbonyl carbon as such having two adjacent acetoxyl groups (the "inner positions"). Further examples of acetotropy were obtained from 2-acetoxy-5-methoxytropone (**5**), 2-acetoxy-3,7-dibromo-5-isopropyltropone (**6**),[1)] 2,3,7-triacetoxy-5-isopropyltropone (**7**),[1)] 2,3,5,7-tetraacetoxytropone (**8**),[1)] pentaacetoxytropone (**9**),[1)] and 2,3,7-triacetoxy-5-(1,1-dimethyl-2-oxopropyl)tropone (**10**):[1)] From the NMR spectros-



1 R=OAc
9 R=H

2 R=H
4 R=OAc
5 R=OMe

3 R=H
11 R=OAc

6 R=Br, R'=CH(Me)$_2$
7 R=OAc, R'=CH(Me)$_2$
8 R=R'=OAc
10 R=OAc, R'=C(Me)$_2$COMe

Chart 2.

copy, the acetotropy of **7** or **10** is operative only with an acetyl group between C-1 and C-2 oxygens, while **8** mainly exists as a tautomeric 1 : 1-mixture of **8b** and **8c**, and **9** was a mixture of **9b**, **9c**, **9d**, and **9e** (13 : 37 : 37 : 13). The absence of tautomers having the carbonyl carbon at the "outer position" in these polyacetoxytropones simplified the kinetic analyses. A notable case was that of 2,4,5,7-tetraacetoxytropone (**11**)[1] which showed no acetotropy at all.

Acetotropy of Hexaacetoxytropone. Now, it is noteworthy that **1**[1,10] exhibited a seven-fold symmetric, "Merry-Go-Round"-type degenerated acetotropy; at +50.2 °C, **1** exhibited only one methyl signal (20.05) and one carbonyl signal (167.47). However, the signals of tropone ring carbons were undetectable due to the broadenings by the chemical exchange. At −0.5 °C, these tropone ring signals were still undetectable, while the methyl signal (20.02) and the acetyl carbonyl signals (167.74 and 168.02) became broadened. At −15.4 °C, the spectrum changed to show three acetyl carbonyl signals (167.79, 168.03, and 168.35), three tropone ring signals (140.59, 145.61, and 149.17), and an unresolved methyl signal (20.14). At −60.1 °C, the exchange ceased; i.e., the methyls (20.13, 20.22, and 20.44), tropone ring signals (140.91, 146.17, and 149.45), the tropone carbonyl (169.00), and acetyl carbonyl signals (168.56, 168.82, and 169.18).

Kinetic Analyses of the Acetotropy. The kinetic data of these acetoxytropones are compiled in Table 1. In all cases, the activation free energies ($\Delta G^{\neq}$) were not much different, in spite of the different polarity and electronic effect of the substituents and different solvent polarity. Should an ionic intermediate be involved, the $\Delta G^{\neq}$ must become smaller to large extent by increasing the number of electron-releasing acetoxyl groups, and even by the polarity of the solvents. Consequently, the figures obtained by the present experiments were not consistent with an ionic mechanism. Previously, Harrison et al. proposed that the

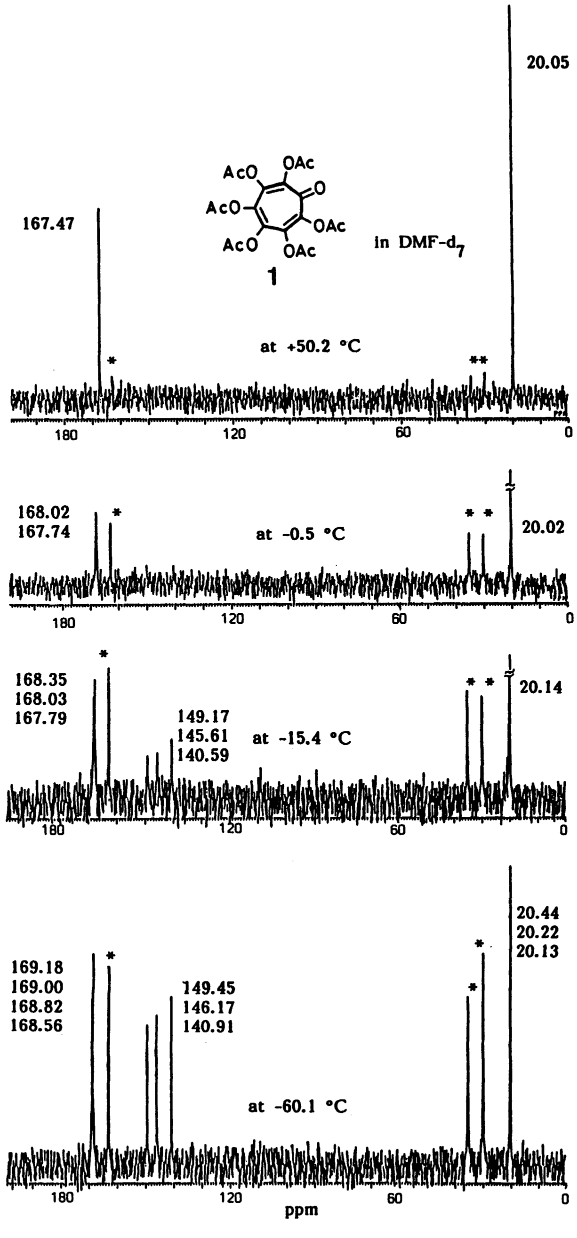


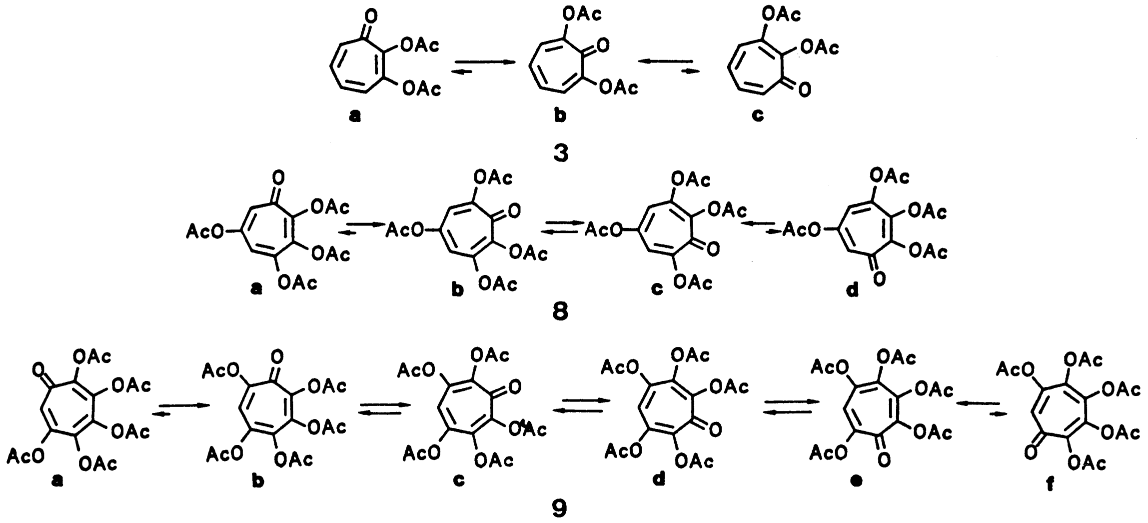
Fig. 1.

Table 1. Kinetic Data of Acetotropy of Several Acetoxytropones

Compd.	$\Delta H^{\neq}$/kJ mol^{-1}	$\Delta S^{\neq}$/J mol^{-1} K^{-1}	$\Delta G^{\neq}_{298}$/kJ mol^{-1}	$r^{a)}$
I: **2** b)	42.6±2.5	−15.5±8.8	47.2±5.0	0.998
c)	34.3±2.1	−42.2±7.5	46.4±4.2	0.997
d)	(45.1)	(−8.3)	(47.7)	
6 b)	48.1±4.2	−8±16	50.2±8.8	0.994
7 b)	51.0±5.4	−11±20	54±12	0.991
10 b)	53.1±8.4	−4±31	54±18	0.981
c)	40.5±5.0	−43±18	53±11	0.985
II: **1** b)	41.0±6.3	−35±28	51±15	0.988
4 b)	39.3±2.5	−41.8±7.9	51.8±5.0	0.998
c)	37.2±2.1	−43.5±7.1	50.2±4.2	0.998
5 b)	37.6±2.5	−54±11	53.5±5.4	0.996
c)	40.1±1.7	−47.7±6.3	53.5±5.4	0.998
8 b)	39.3±3.8	−59±14	56.8±7.9	0.989
c)	38.0±2.0	−57.3±7.9	54.8±4.2	0.995
9 b)	44.7±7.9	−35±28	55±16	0.975

a) Correlation coefficient of Eyring plot. b) Measured in DMF-d_7. c) Measured in $CDCl_3$. d) Ref. 4.

Equilibrium of Polyacetoxytropones



Scheme 1.

acetotropy of 2-acetoxytropones proceeds via an ionic intermediate in view of its small $\Delta G^{\neq}$;[2] however, their proposal seems to lack a sound basis. The figures of $\Delta G^{\neq}$ for [1,5] sigmatropies determined to date are in very wide range (27 to 210 kJ mol^{-1}),[11] and no definite conclusion should be drawn only from the $\Delta G^{\neq}$.

On the other hand, the activation entropies ($\Delta S^{\neq}$) should provide available information; the negative and small $\Delta S^{\neq}$ for the present acetotropies are in the range of many precedent figures of [1,5] sigmatropies;[11] also, the migration of the acetyl group must proceed via a concerted mechanism, i.e., [1,9] sigmatropy, but not via a radical mechanism which should show the positive $\Delta S^{\neq}$.

Further, an introduction of the oxygen functions into 5-position made the $\Delta S^{\neq}$ significantly larger negative in DMF (ε=36.7); if one looks at **2** and **4**, which showed most reliable parameters, $\Delta S^{\neq}$ are −16 J mol^{-1} K^{-1} for the former and −42 J mol^{-1} K^{-1} for the latter. Unfortunately, errors for other substrates are quite large, and it is not suitable for intensive discussions. However, if each compound could be classified as in Table 1, a very interesting tendency would be noticed. An average $\Delta S^{\neq}$ of **2**, **6**, **7**, and **10** (Group I) is −9 J mol^{-1} K^{-1}, the other hand, −45 J mol^{-1} K^{-1} in the case of other derivatives (Group II). All 2-acetoxytropones have the large negative $\Delta S^{\neq}$ (−42 to −57 J mol^{-1} K^{-1}) in chloroform (ε=4.70). This means that as far as the 2-acetoxytropones concern, the transition state of the acetotropy is less polar than the initial state. Particularly, the initial state of Group II compounds is less polar and less solvated than the initial state of Group I derivatives. The same classification might be true for $\Delta H^{\neq}$, owing to the results of compensation effect between $\Delta S^{\neq}$ and $\Delta H^{\neq}$.

Namely, polarized 6π contribution stabilizes the initial state in respect of tight solvation, but does not stabilize the transition state; therefore, polarized carbonyl oxygen does not assist but retard the rearrangement. This invalidates the Masamune's mechanism.

It will be interesting to compare these kinetic features to those of the isomerization of 2-benzyloxy-3-bromotropone to 2-benzyloxy-7-bromotropone, for which, we have recently established the concerted nature, the [1,9] sigmatropy, by an intensive high-pressure kinetic analysis.[3] Namely, in that rearrangement, the $\Delta S^{\neq}$, (−47 and −92 J mol^{-1} K^{-1} in isopropylbenzene (IP, ε=2.4) and 1-hexanol (ε=13.3), respectively), showed a weak, but not negligible, polarized contribution at the transition state. The value of $\Delta S^{\neq}$ of the present acetotropy in less polar chloroform is in the same range with the $\Delta S^{\neq}$ of that [1,9] sigmatropy in IP. These similarities did not contradict the view of a concerted mechanism for the acetotropy, i.e., the [1,9] sigmatropy. However, the $\Delta S^{\neq}$ in polar solvents were considerably different; $\Delta S^{\neq}$ of that benzyl migration (−92 J mol^{-1} K^{-1}) was more negative than the $\Delta S^{\neq}$ of the present acetotropy (−9 J mol^{-1} K^{-1}). The difference is surely attributable to a solvation effect in the transition states for the former and the initial states for the latter.[3]

All the findings supported the rearrangement of the acetyl group in the 2-acetoxytropones being the [1,9] sigmatropy, which could not be expected in benzenoid derivatives such as 2-acetoxybenzaldehyde.

Experimental

The compounds studied in this paper were prepared by means of reported procedures as indicated, except for 2-acetoxy-5-methoxytropone. Kinetic analysis of this process was performed by variable temperature ^{13}C NMR measurements at 100 MHz and 25 MHz in *N*,*N*-dimethylformamide-d_7 (DMF-d_7) or $CDCl_3$: Rate constants of the chemical exchange process were determined by broadened line-widths of the exchangeable signals at the half height. Natural line widths were obtained from the signals of C-5 or the narrowest signal for each compound.[8] The ^{13}C NMR spectra were measured with JMN GX 400 Model and FX 100 Model Spectrometers, JEOL. The chemical shifts (δ unit) were from the internal Me_4Si.

Preparation of 2-Acetoxy-5-methoxytropone (5). A mixture of Ac_2O (10 cm^3) and 5-methoxytropolone (214 mg)[9] was heated at 90 °C for 3.5 h. The solvent was removed in vacuo and the residue was chromatographed on a silica-gel column to give **5** [colorless crystals, mp 90—91 °C, 269 mg; 99%. Found: m/z 194.0576 (M$^+$). Calcd for $C_{10}H_{10}O_4$: M, 194.0578. ^{1}H NMR δ=2.29 (3H, s), 3.77 (3H, s), 6.4—6.6 (2H, dm, J=12 Hz), and 7.0—7.2 (2H, dm, J=12 Hz). ^{13}C NMR δ=20.9, 56.1, 105.6, 129.5, 134.7, 140.1, 151.1, 163.7, 169.4, and 178.1].

The starting material, tropolone, was provided by Sankyo Co. Ltd., Tokyo, to whom our thanks are due. Also, we thank the Ministry of Education, Science and Culture for a financial support, a Grant-in-Aid for Scientific Research to A. M. (No. 60470025).

References

1) H. Takeshita, A. Mori, and T. Kusaba, *Synthesis*, **1986**, 578; H. Takeshita, A. Mori, T. Kusaba, and H. Watanabe, *Bull. Chem. Soc. Jpn.*, **60**, 4325 (1987). A part of study has been presented at the 80th Annual Meeting of the Chem. Soc. Jpn. (Abstract Papers, II, Tokyo, April, 1985, p. 1265).

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

3) Recently, we have confirmed the concerted nature of the rearrangement by means of the high-pressure kinetic analysis. Discussion on the $\Delta S^{\neq}$ of this reaction was supported by activation volume and solvent effect. See S. Sugiyama, A. Mori, and H. Takeshita, *Chem. Lett.*, **1987**, 1247.

4) 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.

5) V. I. Minkin, L. P. Olekhnovich, and Y. A. Zhdanov, *Acc. Chem. Res.*, **14**, 210 (1981).

6) H. Takeshita and H. Mametsuka, *Heterocycles*, **22**, 663 (1984).

7) R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry" Verlag Chemie, GmbH, Weinheim/Bergstr., 1970, p. 117.

8) H. Gunther, J. Runsink, H. Schmickler, and P. Schmitt, *J. Org. Chem.*, **50**, 289 (1985).

9) T. Nozoe, S. Seto, S. Ito, M. Sato, and T. Katono, *Sci. Repts. Tohoku Univ., Ser. I*, **37**, 191 (1953).

10) It should be emphasized that the species involved in this acetotropy was not pentaacetoxytropolone (**A**), but **1**. Although, the difference for calculated carbon content, 0.71%, is larger than the experimental error, a discrimination of **A** and **1** on the basis of elemental analyses alone seems to be unconvincing. The ^{13}C NMR spectra at −60 °C firmly eliminated the possibility of **A**; three separated methyl signals were nearly 1:1:1 in peak heights.

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