Thermal Racemization of Thiaheterohelicenes

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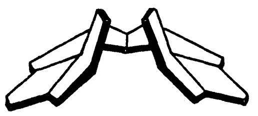
Thermal racemizations of four thiaheterohelicenes (TH) with alternant thiophene and benzene rings were examined and compared with those of carbohelicenes (CH). The racemization rate of [5]TH was very fast at room temperature, and the rates of [7]TH and [9]TH were found to be 1/5 to 1/50 times slower than the corresponding CH having a similar internal angle. The $\Delta S^{\neq}$ values obtained by temperature-variable experiments showed a large difference between [7]TH (-103.9 ± 4.8 JK^{-1} mol^{-1}) and [9]TH (-66.3 ± 4.0), suggesting different conformations in the transition state. CNDO calculations on the transitional conformations of [5]TH demonstrated that a geometry, such as that distorting the benzene rings, has a lower energy than a geometry such as that twisting the thiophene ring. Based upon these results, the conformations in the transition states for the THs are inferred.

Reports on the racemization of carbohelicenes (CH) were very surprising in view of the flexibility of the angularly fused benzene rings.[1] Despite their structural overcrowding, the free energies of the activation ($\Delta G^{\neq}$) for the reactions did not seem to be too large to override a severe transition path: [8]CH, 181.9; [9]CH, 188.3kJ mol^{-1} at 543 K. Thus, the racemization is thought to occur via an achiral transition state in which the deformations spread over the entire molecule so as to prevent a local severe strain, accompanied by much motional freedom. Lindner calculated the energy differences between the ground state and some assumed transition states for a [6]CH molecule by the π-SCF-force-field method, and argued that the most plausible geometry for a transition state is that in which the terminal portions of the molecule are in a face-to-face position with each other (Figure).[2] So far, only a few heterohelicenes, partially composed of heteroaromatics, were investigated regarding racemizations.[3] However, they were confined to hexa homologs which do not complete a full turn and, hence, do not reveal the distinct effect of heteroaromatics on the reaction.

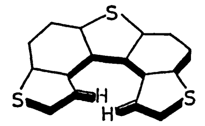
As a part of the study on the properties and structures of thiaheterohelicene (TH), we examined the thermal racemizations of TH containing alternant thiophene and benzene rings. We wish to describe here the kinetic results of the reactions and to discuss their transition states by referring to our CNDO calculation on the transition state models. A comparison of CH with TH in the transition states is also made while focusing on the influence of the heteroaromatics.

Experimental

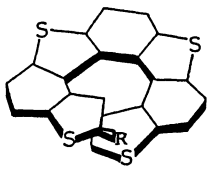
Syntheses[4] and optical resolutions[5] of the thiaheterohelicenes studied have been reported in the foregoing publications. Optical rotations were measured on a JASCO DIP-180 digital polarimeter or a JASCO J-20A automatic recording spectropolarimeter. Chromatograms of THs were recorded on a Waters Model 204 HPLC system. CNDO calculations[6] were performed on a FACOM M-160F computer.



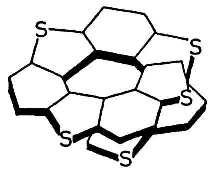
[6]CH



[5]TH



[7]TH



[9]TH

R = H, Me

Racemization reactions of chiral TH were carried out in a mesitylene solution in a tube sealed under a nitrogen atmosphere. Tubes of the solution were thermostated in an oil bath and the reaction progress was pursued by measuring the optical rotation at given time intervals. The reactions were also followed by measuring changes in the absorption spectra and HPLC peaks.

Results and Discussion

The ease of racemization depends on the winding degree of the helix, i.e. the extent of the intramolecular overlap, which can be estimated with the internal angle (IA) of the TH molecules[3] studied here: [9]TH, 465; [7]TH and 2-methyl[7]TH, 360; and [5]TH, 255°.[7] Thus, it is expected that [5]TH should racemize rapidly in solution, although the structure in crystals retains a rigid helix.[8] In fact, HPLC using a column containing (+)TAPA-bonded silica gel (TAPA: 2-(2,4,5,7-tetranitro-9-fluorenylideneaminooxy)-propionic acid) could not be used to separate the enantiomers of [5]TH at -14°C. Several recyclings or a lowering of the temperature to -24°C caused a slight separation between *P* and *M* enantiomers[9] (Fig. 1). All attempts to isolate the enantiomers were, however, unsuccessful, even at lowered temperatures, suggesting a low activation energy for the racemization of [5]TH.

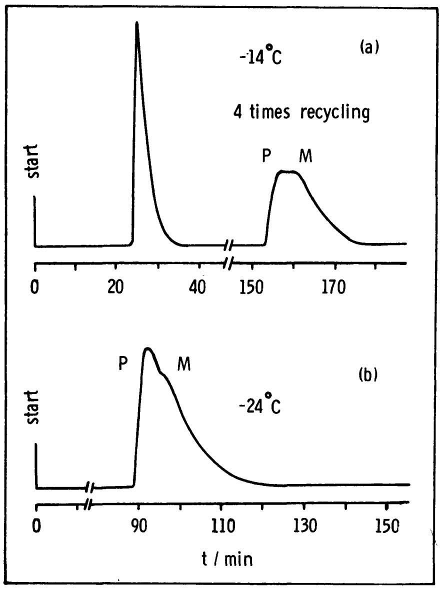


Fig. 1. Resolutions of the enantiomers of [5]TH by HPLC. (+)TAPA-bonded silica-gel column, $CH_2Cl_2/n\text{-}C_6H_{14}=4/1$, monitored at 254 nm, (a) flow rate 2 ml min^{-1}, and (b) 1 ml min^{-1}.

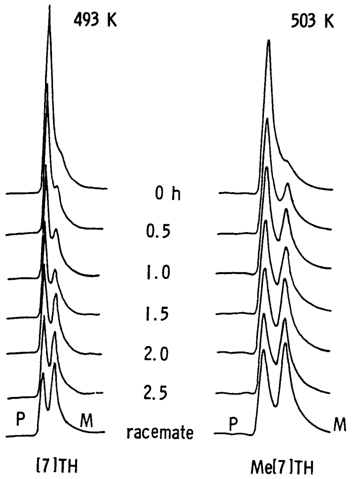


Fig. 2. Time course of HPLC peaks of [7]TH and 2-Me[7]TH. (+)TAPA-bonded silica-gel column, $CH_2Cl_2/n\text{-}C_6H_{14}=1/1$, flow rate 1 ml min^{-1}, and monitored at 254 nm.

Figure 2 illustrates the time course of the HPLC peaks for reactions of [7]TH and 2-Me[7]TH. During every reaction time, no peak except for those illustrated was observed, indicating that no meaningful side reaction took place and that all the changes in the optical rotations could be regarded as racemization processes.

The first-order rate constant k_r and the activation parameters were obtained from the following equations by least-squares treatments,

$$k_r = 1/2\,t\ln(\alpha_0/\alpha_t),$$
$$\Delta G^{\neq} = RT[\ln(k/h) - \ln(k_r/T)],$$
$$\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\neq},$$

Table 1. k_r and $\Delta G^{\neq}$ of Racemization at 500 K

	Internal angle	$k_r \times 10^6$	$\Delta G^{\neq}$
	deg.	s^{-1}	kJ mol^{-1}
[7]TH	360	124	162.0
Me[7]TH	360	113	162.4
[9]TH	465	0.021	198.1
[6]CH[a]	360	668	154.3
[8]CH[a]	480	1.10	181.9

a) The values are cited from Ref. 1.

Table 2. Activation Parameters of Racemization

	$\Delta H^{\neq}$	$-\Delta S^{\neq}$
	kJ mol^{-1}	JK^{-1} mol^{-1}
[7]TH	110.0±2.8	103.9±4.8
Me[7]TH	120.7±2.8	83.3±4.6
[9]TH	164.9±2.2	66.3±4.0
[6]CH[a]	146.4	17.6
[8]CH[a]	171.5	19.2

a) The values are cited from Ref. 1.

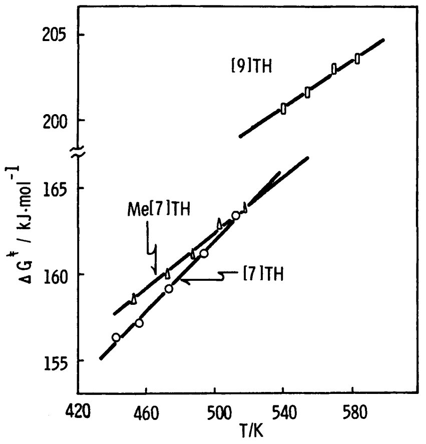


Fig. 3. Temperature dependence of $\Delta G^{\neq}$.

where α_0 and α_t are the optical rotation at time 0 and t, respectively. The k_r's and the free energies of the activation ($\Delta G^{\neq}$) at 500 K are tabulated in Table 1, together with the calculated IA values. The effect of a methyl substituent at the 2-position in a [7]TH molecule seems to be relatively small. It is notable that the rate of [9]TH becomes much smaller than that of [7]TH by about 1/5900 times with a large $\Delta G^{\neq}$ value by 36.1 kJ mol^{-1}. Compared with the k_r of carbohelicene having a similar IA value, the k_r of [7]TH is 1/5.4 times smaller than that of [6]CH, and [9]TH (which possesses the smaller IA than [8]CH) shows a k_r that is 1/52 times slower as a result of the larger $\Delta G^{\neq}$ by 16.2 kJ mol^{-1}. These results demonstrate that TH molecules hold more rigid skeleton than CH molecules.

The temperature dependences of $\Delta G^{\neq}$ are depicted in Fig. 3 and the activation enthalpies ($\Delta H^{\neq}$) and entropies ($\Delta S^{\neq}$) are listed in Table 2. As is apparent

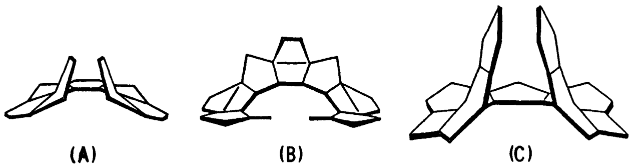


Fig. 4. The possible transitional geometries of [7]TH ((A) and (B)), and the plausible transitional geometry of [9]TH ((C)).

from the Table, a comparison between the two CHs exhibits an increasing $-\Delta S^{\neq}$ with an increasing $\Delta H^{\neq}$. This relationship between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ is generally observed in such a case as a series of homologs whose racemization could occur through the same kind of transitional geometries. On the other hand, the trend of $-\Delta S^{\neq}$ against $\Delta H^{\neq}$ in the TH series was found to be opposite; this might imply that [9]TH should take a different transitional geometry from that of [7]THs. Moreover, the most striking feature is the large difference of $-\Delta S^{\neq}$ values between CH and TH. In the racemization of a TH molecule, the entropy term contributes greatly to the free energy of the activation, suggesting a great loss of motional freedom in the transition state.

As for the transitional geometry of [7]TH racemization two conformations, (A) and (B), are thought possibly to exist (Fig. 4), as speculated in the literature.[2] Form (A) is produced by a distortion of the terminal thiophene rings, while (B) is formed by a distortion of the benzene portions. The kinetic results indicate that type (B) is more plausible since in this form the distortion should occur synchronously at the three sites to provide a greater entropy change than at the two sites in form (A). Regarding the [9]TH transition state, it may be no longer possible to hold form (B) on account of its larger extent of winding. Figure 4 (C) illustrates the plausible transitional geometry of the [9]TH racemization. In this geometry the number of the mainly distorted sites is two; this is more related to the smaller $-\Delta S^{\neq}$ value than that of [7]TH.

Table 3. Total Energies (E_T) of Some Conformations of the [5]TH Molecule. Refer to Fig. 5.

Conformation	r / Å	E_T / eV
(a) Ground State	2.11	−4141.17
(b) Plane	1.36	−4140.94
Distorted Ring		
(c) Thiophene	1.55	−4139.28
(d) Benzene	1.56	−4139.74

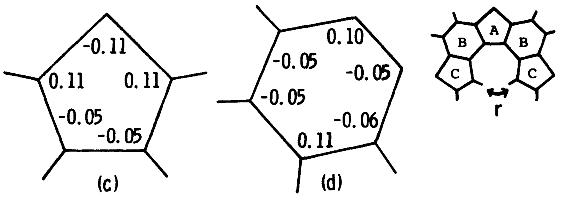


Fig. 5. Distorted conformations of [5]TH molecule. Distorted sites are (c) thiophene A ring and (d) benzene B rings. The figures in the rings are deviations (Å) from the least-squares plane.

Finally, we attempted to obtain CNDO-calculational support for the geometries mentioned above. However, the [7]TH and [9]TH molecules are so big that the energies could not converge to definite values. For the [5]TH molecule, the total energies were attained with iterative methods for the ground-state geometry determined by an X-ray analysis, and for a planar geometry having the same bond lengths, in which the terminal hydrogens are brought into close proximity with each other: 1.36 Å (Table 3, (a) and (b)). Interestingly, the energies of both conformations were found to be close; the increase in the conjugation energy, due to the planarity, would counteract the repulsion energy between the terminal hydrogens. Thus, the transition state of the [5]TH racemization can be supposed to be like a planar geometry.

Furthermore, a series of tentative calculations of the total energies of the [5]TH molecules was carried out using various hypothetical models in which only thiophene or benzene rings were distorted from the planar geometry. Figure 5 and Table 3 ((c) and (d)) show an example where two kinds of distorted molecules are chosen as being equal at a distance (r) between the terminal hydrogens. In every case, it was found that the energy obtained for the molecule with a distorted benzene became smaller than that of a molecule with a distorted thiophene. This implies that in order to hold the terminal moieties in the same separation, the distortion of the five-membered ring thiophene needs to have a higher energy than that of the six-membered ring benzene. This difference in the rigidity between thiophene and benzene ring might play a role in the transitional geometry of the [7]TH racemization.

In conclusion, thiaheterohelicenes manifest fairly different behaviors in thermal racemization reactions from carbohelicenes, presumably because of the existence of the heteroaromatics thiophene.

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7) IUPAC nomenclatures of the compounds studied are as follows; [5]TH thieno[3,2-*e*:4,5-*e*′]di[1]benzothiophene, [7]TH bisthieno[3′,2′:4,5]benzo[1,2-*b*:4,3-*b*′]di[1]benzothiophene, [9]TH bis[1]benzothieno[5′,4′:2,3]thieno[3,2-*e*:4,5-*e*′]di[1]benzothiophene.

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