Restricted Rotation Involving the Tetrahedral Carbon. XVII. Isolation of Three "Diastereomeric" Rotamers of a Triptycene Type Compound and Stereoselectivity in the Synthesis[1]

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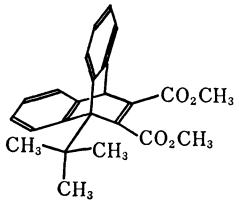
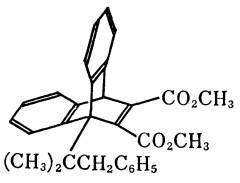
Three rotameric forms of 2,3-dichloro-9-(1,1-dimethyl-2-phenylethyl)-11,12-bis(methoxycarbonyl)-9,10-dihydro-9,10-ethenoanthracene (**3**) were isolated as stable entities at room temperature. The structural assignment of the rotamers based on the PMR characteristics. Since the synthesis of **3** produced only the *ap* form, another reaction involving benzyne was carried out to test the generality of the stereoselectivity. Thus the *ap* form and the *sc* form of 2,3-dichloro-9-(1,1-dimethyl-2-phenylethyl)triptycene (**4**) were prepared separately. Equilibration of isomers of **4** was carried out and the barrier to isomerization was obtained as 36.6 kcal/mol.

A triptycene type compound (**1**) was found to possess an extremely high barrier to rotation about the bond between the *t*-butyl group and the skeleton.[2] As an extention, racemic and *meso* forms of **2** were isolated[3] and the racemic form was resolved into enantiomers.[1]

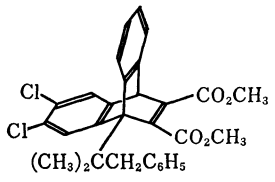


(**1**)

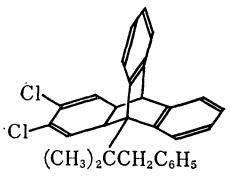


(**2**)

Since **2** has no asymmetric carbon atom, optical resolution was necessary to isolate all the possible rotational isomers. However, if a like compound has a center of asymmetry, the frozen rotation should result in the formation of stable diastereomers, although the compound has only one asymmetric center. If this is the case, the three isomers should be separated by physical means such as chromatography. We wish to report, in the first half of this paper, the realization of such expectation: three isomers of 2,3-dichloro-9-(1,1-dimethyl-2-phenylethyl)-11,12-bis(methoxycarbonyl)-9,10-dihydro-9,10-ethenoanthracene (**3**) were isolated by chromatography.[4]

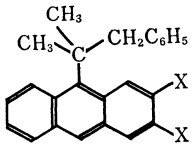


(**3**)



(**4**)

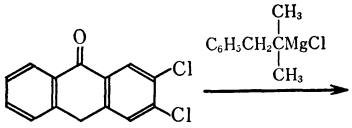
The second half of this paper is mainly concerned with the stereoselectivity in the Diels-Alder type reaction of 9-(1,1-dimethyl-2-phenylethyl)anthracene (**5**) and its 2,3-dichloro derivative (**6**). Since the reaction of **5** with dimethyl acetylenedicarboxylate is known to produce the *meso* form almost exclusively[1,3] and **6** was found to react similarly, it must be interesting to see the generality of the stereoselectivity. We wish to report that the Diels-Alder reaction of **6** as well as **5** is really stereoselective and rotameric *sc* (*dl*) and *ap* (*meso*) forms of a triptycene derivative can be prepared separately.[5]



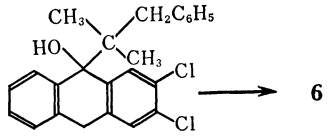
X=H (**5**)
X=Cl (**6**)

Results and Discussion

The required anthracene **6** was prepared by Grignard reaction between 2,3-dichloroanthrone (**7**) and 1,1-dimethyl-2-phenylethylmagnesium chloride followed by dehydration.

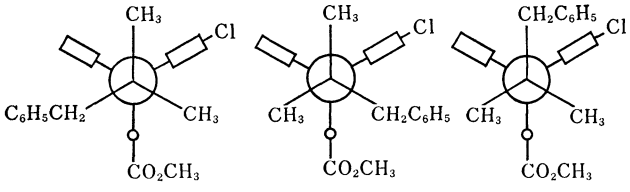


(**7**)



Diels-Alder reaction between **6** and dimethyl acetylenedicarboxylate was carried out by heating the substrates in toluene. Chromatography of the product followed by recrystallization gave pure compound in 42% yield which was a sole isomer, as judged from the PMR data (see Table 1). If one considers the mechanical loss during the purification processes this yield must be taken as an indication of high selectivity of the reaction.

The assignment of the structure caused trouble, because there are three possible isomers and only one



(**3a**) *M-sc* Form (**3b**) *P-sc* Form (**3c**) *ap* Form

(only the 9-(*R*) forms are shown)

was isolated. Thus, in order to obtain other isomers, thermal equilibration was carried out.

The equilibration of rotational isomers (**3a**, **3b**, and **3c**) was reached within 8 hr by heating an *o*-dichlorobenzene solution of **3** at 150 °C. A half-life of **3** under these conditions was *ca.* 2 hr, although it was not possible to run the kinetic study due to the heavy overlap of the signals concerned. The isomer ratio at the equilibrium was estimated to be 3 : 3 : 2.

The equilibrated mixture was chromatographed on silica gel, benzene being used as an eluent. Separation of the least populated isomer was not difficult by this means, because it was eluted most sluggishly among the isomers. This isomer gave identical spectral data with the one obtained by the Diels-Alder reaction and is named Isomer C. Separation of the remaining two isomers was tedious but spectroscopically pure isomers were obtained by repeating the chromatographic operations ten times.* These were named Isomers A and B, respectively, according to the ease of elution. Heating these isomers in *o*-dichlorobenzene caused redistribution of the isomers and afforded the equilibrium mixtures with the identical composition, as judged from the PMR spectra. Thus the rotational isomers could be separated by physical means, because they correspond to diastereomers with each other in spite of the fact that they have only one asymmetric carbon atom.

The PMR data are summarized in Table 1. Theoretically two methyls and two benzyl methylene protons should be nonequivalent because they are located closely to the chiral center. Some peaks showed coincidence of the chemical shifts in one solvent, although they appeared as two different ones in another solvent.

Having all the possible isomers in hand, we may proceed to the assignment of the structures. The PMR spectral data in Table 1 did not seem to be helpful because the differences in chemical shifts of various corresponding signals were too small to draw a definite conclusion. Fortunately however, examination of the whole region of the PMR spectra indicated that there were typical differences in the patterns of signals at the lowest part of the aromatic region. Since the severe steric effect is given by the 9-*t*-alkyl group, the peri protons are expected to give signals at the low field due to the compression effect. The integrated areas (2H) correspond well to the number of the peri protons also.

For the assignment of the structure, comparison of

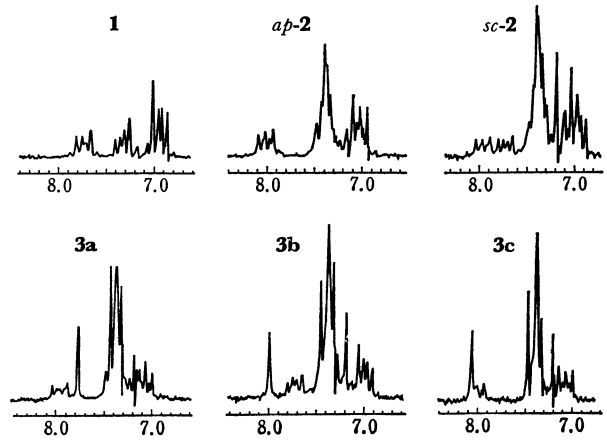
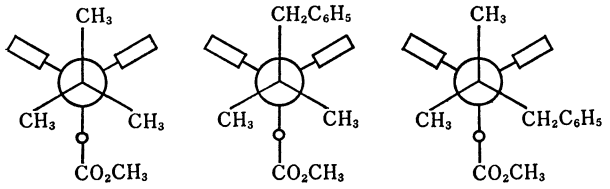


Fig. 1. Shapes of the peri proton signals.



(**1'**) (*ap*-**2**) (*sc*-**2**)

* The PMR spectral charts of these compounds are given in a short communication.[4]

Table 1. Physical properties and PMR data of the isomers of **3**

Isomer	A	B	C
Assignment	**3a**	**3b**	**3c**
Mp (°C)	oil	oil	215.5—216.5
Chromatographic behavior	eluted first	eluted second closely behind the first	eluted last
Relative population at equilibrium (152 °C)	3	3	2
PMR data			
Solvent / Assignment	$CDCl_3$ / C_6D_6	$CDCl_3$ / C_6D_6	$CDCl_3$ / C_6D_6
C-CH_3	1.80 / 1.63	1.77 / 1.67	1.71 / 1.72
	/ 1.80	1.88 / 1.94	1.80 / 1.89
O-CH_3	3.74 / 3.33	3.74 / 3.33	3.68 / 3.28
	3.77 / 3.47	3.77 / 3.47	3.75 / 3.40
C-CH_2	3.60 q / 3.80	3.50 q / 3.77	3.69 q / 3.49 q
	J=14.1 Hz, $\Delta\nu$=15.6 Hz	J=14.1 Hz, $\Delta\nu$=12.1 Hz	J=14.6 Hz, $\Delta\nu$= 8.7 Hz / J=14.4 Hz, $\Delta\nu$=11.8 Hz
10-H	5.49 / 5.44	5.49 / 5.44	5.49 / 5.44
1-H	7.76 / 7.75	7.99 / 8.04	8.05 / 8.05
8-H	7.9 m / 7.9 m	7.7 m / 7.7 m	8.0 / 8.0 m

the chemical shifts and/or shapes of the signals with the model compounds may be helpful. Thus the peri proton signal shapes of the isomers are shown in Fig. 1 together with those of **1**, *ap*-**2**, and *sc*-**2**.

Inspection of the Newman-type projections of **1** and **2** reveals that the peri protons in **1** are equivalent because they are both located between two methyls, and those in *ap*-**2** are also equivalent because they are both placed between a methyl and a benzyl group. On the other hand, peri protons in *sc*-**2** are not equivalent: one is placed between two methyls and the other between a methyl and a benzyl group. The spectra in Fig. 1 conform with this expectation and it can now be concluded that the multiplet signal centered at δ 7.7 corresponds to a peri proton placed between two methyl groups and the multiplet centered at δ 8.0 to a peri proton placed between a methyl and a benzyl groups.

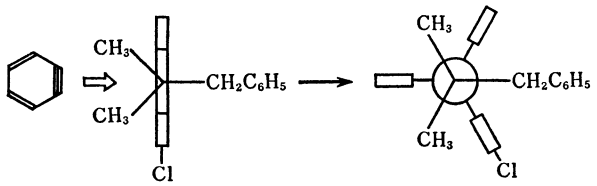
Now that the isomers in question have a chlorine atom ortho to the peri proton, the assignment may be possible by taking advantage of the substituent. Fortunately a chloro substituent in the aromatic ring is known to give little effect on the chemical shift of the protons ortho to it.[6] The chloro substituents in **3** will cause the appearance of an apparent singlet of the peri proton because they erase the ortho and meta couplings and the para coupling is small. Thus it may be assumed that a peri proton ortho to the chloro group gives a singlet at about the same chemical shift with the corresponding protons in **1** and **2**.

Since Isomer A, which is eluted first, gives a sharp signal at δ 7.7 and a multiplet centered at δ 8.0, it should have two kinds of peri protons: one is ortho to a chloro group and placed between two methyl groups and the other is placed between a methyl and a benzyl group. **3a**, which is the *M*-*sc* form, is qualified to meet the above conditions. Thus Isomer A is the *M*-*sc* form. Likewise, Isomer B which is eluted closely behind Isomer A is concluded to have a peri proton which is ortho to a chloro substituent and placed between a methyl and a benzyl group and another peri proton which is placed between two methyl groups. Thus isomer B is **3b** which is the *P*-*sc* form. Isomer C should possess both peri protons placed between a benzyl and a methyl group and thus is the *ap* form (**3c**).

After the establishment of the structural assignment, the composition of the equilibrium mixture may be compared with the data of **1** which gave $K=3.0$ at various temperatures in favor of the *sc* form.[3,4] Since **3a** and **3b** are the *sc* forms and **3c** the *ap*, the sum of **3a** and **3b** may be taken in discussing the thermal stability of the isomers. Then the ratio is obtained as *sc* : *ap* $=3:1$ which coincides with the equilibrium constant of **1**. From these data, it may be concluded that the two chloro groups in compound **3** play little role in determining the thermodynamic stability. This is so probably because the chloro groups are located distantly from the *t*-alkyl group. The same population of the *M*-*sc* and *P*-*sc* forms is another indication that the remote chloro groups have scarce effect on the stability.

The almost exclusive formation of the *ap* form in the Diels-Alder reaction is interesting. This stereoselectivity matches that obtained in the reaction of **5** with dimethyl acetylenedicarboxylate, in which *ca.* 85% of the product was the one formed by the attack from the least hindered side. A possible explanation was described in a preceding paper.[1] Although it may be possible to postulate that the rotation about the C_9–C_{alkyl} bond is frozen, the postulate is not consistent with the facts that no anomaly is found in PMR spectra and the selectivity is not exclusive in the case of **5**. Some steric and electronic effects may be responsible in causing the results.

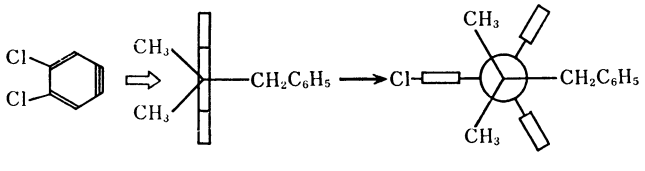
It is then tempting to investigate the scope of the selectivity. Accordingly Diels-Alder reaction between **6** and benzyne was carried out. If the reaction is really stereoselective, an expected product is the *sc* form (*dl* form), because the attack of benzyne from the least hindered side will proceed as depicted in scheme 1. Only one product was isolated indeed. A PMR spectrum of the product shows the presence of a non-equivalent set of methyls and that of benzyl methylene protons to indicate that it is really an *sc*-form. The peri proton signals are also consistent with this assignment and the following signals are found: a multiplet centered at δ 7.73 corresponding to 1 H which is placed between two methyl groups, a multiplet centered at δ 7.95 corresponding to 1 H which is placed between a methyl and a benzyl group, and a sharp singlet at δ 8.03 corresponding to 1 H which is ortho to a chloro substituent and placed between a methyl and benzyl group.



(*sc*-**4**)

Scheme 1.

The stereoselectivity discussed above seemed to open up a way for the synthesis of individual rotational isomers. If the combination of **6** and benzyne gives the *sc* (or *dl*) isomer, the combination of **5** and 4,5-dichlorobenzyne should give the *ap* (or *meso*) form (Scheme 2). The actual synthesis proceeded as expected and a sole product was obtained, of which structure was evident from the PMR data: one methyl signal (δ 2.02, 6H), a sharp singlet (δ 3.86) for the benzyl methylene, two peri protons (a multiplet centered at δ 7.95) placed between a methyl and a benzyl group, and one peri proton (δ 7.78) which is ortho to a chloro substituent and placed between two methyl groups.



(*ap*-**4**)

Scheme 2.

The equilibration between *ap*-**4** and *sc*-**4** proceeded sluggishly: no isomer was detected after heating either *ap*-**4** or *sc*-**4** in *o*-dichlorobenzene at the boiling point for 60 hr. Apparently, the higher temperature was needed to cause equilibration in the practical rate. The choice of a solvent caused trouble, however. A high boiling solvent tends to have the higher viscosity at room temperature, causing the difficulty in PMR spectroscopy. 1-Chloronaphthalene was chosen as a solvent from these aspects.

In principle, the population of each isomer can be determined by careful integration of the methyl or other signals. In practice, however, due to the heavy overlap of the signals, it was not possible to obtain the population directly from the simple integration. Thus calibration curves were drawn by the procedure described in the experimental section and first order rate constants k_1 (*ap*→*sc*) and equilibrium constants K were obtained at four temperatures in the range of 211—259 °C. The results are given in Table 2.

Table 2. Rates of isomerization of *ap*-**4** and the equilibrium constants for *ap*-**4** ⇌ *sc*-**4**

T °C	k_1 (s^{-1})	K
259	4.1×10^{-4}	2.0
245	1.6×10^{-4}	2.0
232	7.5×10^{-5}	2.0
211	1.3×10^{-5}	2.0

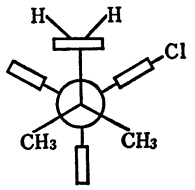
Table 3. Kinetic parameters for isomerization *ap*-**4** → *sc*-**4**

E_a=36.6 kcal/mol	ΔH=35.7 kcal/mol
log A=11.7	ΔS=−7.9 eu

Arrhenius and Eyring plots of k_1's gave the good linear relationship and thermodynamic parameters were obtained as shown in Table 3. The Arrhenius activation energy of 36.6 kcal/mol is one of the highest barriers to the isomerization of this type.[7] Interconversions of the atropisomers may be most reasonably assumed to proceed through rotation about the axis bond, although other possibilities such as a retro-Diels-Alder reaction and ionic or radical type fission-recombination mechanisms cannot be ruled out. Then this barrier is one of the highest to rotation about a C_{sp^3}–C_{sp^3} bond.

The equilibrium constant remained constant throughout the temperature range examined. Thus the equilibrium is controlled by the entropy factor. Indeed there are two enantiomeric *sc* forms which are energetically identical. In this case also, two chloro groups in a benzo group seems to give little effect on the enthalpy of the atropisomers.

Finally we wish to comment on the conformation of the benzyl group in the compounds studied here. The typical features of the PMR spectra are that 1) a peri proton gauche to the benzyl group gives the signal at *ca.* δ 8.0 which is lower by *ca.* 0.3 ppm than a peri proton *trans* to the benzyl and 2) the coupling constants of the benzyl methylenes are *ca.* 14 Hz. These features are best explained if one assumes the conformation such as **8**, because, in this conformation, the peri protons gauche to the benzyl group are located in the deshielding region of the benzene ring and the coupling constants agree with the theoretical value of this conformation.[9] Molecular models support this conformation on the ground of the steric effect and a fact that the chemical shifts of the methyl groups in *ap*-**4** are close to that of the methyl groups of 9-*t*-butyltriptycene may be another support, because the methyls are located in the region where little anisotropy effect of the benzene ring is expected.



(**8**)

Experimental

2,3-Dichloroanthrone. A suspension of 39 g (0.14 mol) of 2,3-dichloroanthraquinone[9] and 8 g of red phosphorus in 1.5 l of acetic acid and 66 ml of hydriodic acid was heated under reflux for 5 hr. The resulted mixture was concentrated by removal of *ca.* 700 ml of the solvent by distillation and the concentrate was cooled to room temperature. The solid was collected by filtration and extracted with 300 ml of boiling benzene. The benzene extract was cooled to give 26 g (70%) of yellow crystals, mp 198—200 °C. This compound was directly used for the next synthesis.

2,3-Dichloro-9-(1,1-dimethyl-2-phenylethyl)anthracene (**6**). To a chilled solution of a Grignard reagent prepared from 42 g (0.25 mol) of 1,1-dimethyl-2-phenylethyl chloride, was added 22.8 g (0.1 mol) of 2,3-dichloroanthrone powder in small portions during the course of 1 hr. The reaction mixture was decomposed with aqueous ammonium chloride. The ethereal solution was filtered and evaporated. The resulting oil was dissolved in 200 ml of carbon tetrachloride and heated with *ca.* 30 g of phosphorus pentoxide under reflux for 5 hr. The carbon tetrachloride solution was decanted and evaporated. The residue was chromatographed on alumina. Elution with 9 : 1 hexane–benzene gave 2.95 g (7.9%) of yellow fluorescent crystals, mp 121—123 °C. PMR (δ, CCl_4): 1.73 (6H, s), 3.63 (2H, s), 6.9—8.3 (12H, m). Found: C, 76.68; H, 5.11; Cl, 18.48%. Calcd for $C_{24}H_{20}Cl_2$: C, 75.99; H, 5.31; Cl, 18.69%.

ap-*2,3-Dichloro-9-(1,1-dimethyl-2-phenylethyl)-11,12-bis(methoxycarbonyl)-9,10-dihydro-9,10-ethenoanthracene* (**3c**). A solution of 1.53 g (4.0 mmol) of the anthracene (**6**) and 1 ml of dimethyl acetylenedicarboxylate in toluene was heated under reflux for 5 hr. The reaction mixture was chromatographed on silica gel with benzene as an eluent. Recrystallization of the product from benzene–methanol gave 0.87 g (42%) of colorless crystals, mp 215.5—216.5 °C. Found: C, 69.24; H, 5.07; Cl, 13.68%. Calcd for $C_{30}H_{26}O_4Cl_2$: C, 69.10; H, 5.03; Cl, 13.60%.

Isomerization of **3c** *and Separation of the Isomers.* Heating a solution of **3c** in *o*-dichlorobenzene at 152 °C for 10 hr caused equilibration of the rotamers, the composition being 3 : 3 : 2. The least populated isomer was the *ap* form. The solvent was evaporated *in vacuo* and the residue was taken up in benzene. The chromatographic behavior of the *ap* form was different enough to separate it from other two but those of *M-sc* and *P-sc* forms were quite close to

cause the heavy overlap of the chromatographic bands. Nonetheless it was possible to isolate pure *M-sc* and *P-sc* forms after repeated chromatographies. The *M-sc* form and *P-sc* form resisted crystallization but they showed no peaks attributable to impurities in PMR spectra. Heating either the *M-sc* or the *P-sc* form in *o*-dichlorobenzene at 152 °C caused isomerization and gave the equilibrium mixture of the identical composition with the one obtained from the *ap* form. This can be taken as another piece of evidence for the structures of the *sc* forms.

sc-*2,3-Dichloro-9-(1,1-dimethyl-2-phenylethyl)triptycene* (sc-**4**). To a boiling solution of 1.30 g (3.43 mmol) of **6** and 2 ml of isoamyl nitrite in *ca.* 20 ml of methylene chloride, was added a solution of 600 mg (4.4 mmol) of anthranilic acid in 10 ml of tetrahydrofuran over a period of 1 hr. The mixture was heated for another hour and then the solvent was evaporated. The residue was chromatographed on alumina with the use of 9 : 1 hexane-benzene as an eluent. Recrystallization of the product from tetrahydrofuran-methanol gave 1.29 g (83%) of colorless crystals, mp 215.5—216.5 °C. Found: C, 79.40; H, 5.47: Cl, 15.65%. Calcd for $C_{30}H_{24}Cl_2$: C, 79.12; H, 5.31; Cl, 15.57%. PMR (δ, $CDCl_3$): 1.99 (3H, s), 2.08 (3H, s), 3.75 and 3.89 (2H, q, J=14.6 Hz), 5.17 (1H, s), 6.7—7.6 (12H, m), 7.73 (1H, m), 7.95 (1H, m), 8.03 (1H, s).

4,5-Dichloroanthranilic acid was obtained by hydrogenation of 4,5-dichloro-2-nitrobenzoic acid[10] and used for generation of dichlorobenzyne.

ap-*2,3-Dichloro-9-(1,1-dimethyl-2-phenylethyl)triptycene* (ap-**4**). Treatment of the anthracene (**6**) with 3,4-dichloroanthranilic acid and isoamyl nitrite in boiling methylene chloride-tetrahydrofuran, as described in the preparation of the *sc* form, caused precipitation of reddish brown solid which was found to be the corresponding diazonium carboxylate from the IR spectrum ($N^+{\equiv}N$, 2280 cm^{-1}). The solution contained *ca.* 7 : 3 mixture of the anthracene and the triptycene. Thus the decomposition of the diazonium salt seemed to require the higher temperature.

A mixture of 3.10 g (10 mmol) of the anthracene and 2.38 g of the diazonium salt (*ca.* 11 mmol) in 80 ml of chlorobenzene was heated at 100 °C for 1 hr. Evolution of gas and disappearance of the solid were observed. The solvent was evaporated and the residue was taken up in hexane. Chromatagraphy on alumina with the use of 9 : 1 hexane-benzene gave colorless crystals which were recrystallized from tetrahydrofuran-methanol. The *ap* form was obtained as colorless crystals, mp 200—201 °C, in 3.97 g (88%) yield. Found: C, 79.29; H, 5.53; Cl, 15.68%. Calcd for $C_{30}H_{24}Cl_2$: C, 79.12; H, 5.31; Cl, 15.57%. PMR (δ, $CDCl_3$): 2.02 (6H, s), 3.86 (2H, s); 5.17 (1H, s), 6.8—7.6 (12H, m), 7.78 (1H, s), 7.96 (2H, m).

Equilibration and Determination of Rates of Isomerization. *ap*-**4** was dissolved in 1-chloronaphthalene to make up 4.8 (w/w)% solution and sealed in an NMR sample tube. The sample tube was immersed in a boiling solvent bath and PMR spectra were determined at 34 °C with appropriate intervals. The solvents used for the bath and the boiling points were as follows: diphenyl ether 259 °C, diethylene glycol 245 °C, *m*-nitrotoluene 232 °C, nitrobenzene 211 °C.

A calibration curve was drawn by the following procedure. A 4.8 (w/w)% solution in 1-chloronaphthalene was prepared for each of the *ap* and the *sc* form. These two solutions were mixed in various ratios to make up solutions of which concentration remained 4.8 (w/w)% when the sum of both forms was taken. For each solution thus made up, the ratio of the apparent height of the methyl signals of the *ap* form to that of the lower field methyl signal of the *sc* form was observed and plotted against

$$-\log\left\{1-\left(1+\frac{1}{K}\right)\frac{[sc]}{[sc]+[ap]}\right\}$$

which was calculated from the known $[sc]/[ap]$ values. Using this calibration curve, the apparent height ratios observed in the kinetic run directly gave the

$$-\log\left\{1-\left(1+\frac{1}{K}\right)\frac{[sc]}{[sc]+[ap]}\right\}$$

values which were necessary for kinetic analysis. These values were plotted against time and the slope of the straight line produced the desired rate constants. The equilibrium constants at various temperatures were found to be constant, 2.0, within the experimental error.

Measurement of the Spectra. The PMR spectra were recorded on a Hitachi R-20B spectrometer operating at 60 MHz. Samples were dissolved either in $CDCl_3$ or in C_6D_6 to make up *ca.* 10 (w/w)% solutions, unless otherwise stated.

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