2-methylfuran. A sample, 233 mg in 10 mL of THF at 0 °C, was treated with 6 equiv of Me_3SiCl followed by 4 equiv of LTMP in 10 mL of THF. After 0.5 h, the mixture was quenched by adding it to Skelly-solv and washing with buffer (3 × 20 mL). Evaporation and chromatography (30 g of neutral alumina, 10% ether/Skelly-solv with 1% triethylamine) gave two products, **28** (oil, 177 mg, 54%) and **29** (oil, 68 mg, 24%.)

28: ^1H NMR δ 0.30 (s, 9 H), 1.91 (s, 3 H), 6.75 (d, 1 H, J = 5.5 Hz, vinyl), 6.93 (m, 3 H, 2 Ar and 1 vinyl), 7.14 (m, 2 H); MS/Cl calcd for $C_{14}H_{18}OSi$ 230.1126, found 230.1129.

29: ^1H NMR δ 0.09 (s, 9 H), 1.92 (s, 3 H), 5.70 (s, 1 H, bridgehead), 6.89 (s, 1 H, vinyl), 6.95 (m, 2 H), 7.16 (m, 2 H); MS/Cl found 230.1130.

(21) The benzyne was generated by slow concurrent addition (two separatory funnels) of anthranilic acid (13.7 g in DME solvent) and ethyl nitrile (20 mL) to a refluxing solution of 2-methylfuran (70 mL) in DME (70 mL.) Distillation gave 9.3 g (59%) of **27**: bp 59 °C (0.4 torr); ^1H NMR δ 1.91 (s, 3 H), 5.61 (d, 1 H, J = 2 Hz, bridgehead), 6.75 (d, 1 H, J = 5.5 Hz, vinyl proximal to methyl), 6.95 (m, 3 H, 2 Ar and 1 vinyl), 7.15 (m, 2 H).

Acknowledgment. Financial support of this work by the University of California Cancer Research Coordinating Committee is gratefully acknowledged. We thank Randy Jackson for carrying out the preparation of **27**, Dr. Ata Shirazi for obtaining the difference NOE spectra of **24**, and Dr. Hugh Webb for obtaining MS spectra.

Dynamic Stereochemistry of Imines and Derivatives. 19. Mutarotation and *E*–*Z* Isomerization of Chiral Imines in [$^2H_4$]Methanol Solution[1]

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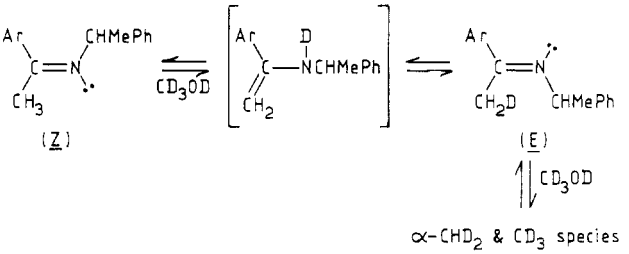
NMR studies indicate that the origin of the mutarotation of optically active *N*-[1-phenylethylidene]-1-phenylethylamine (**1**) and *N*-[1-(1′-naphthyl)ethylidene]-1-phenylethylamine (**2**) in CD_3OD solution is *E*–*Z* isomerization and not tautomerization to the enamine as proposed previously for imine **1**. An equilibrium overshoot effect was observed during the isomerization of imine **2**. It is concluded that the *E*–*Z* isomerization probably proceeds via a thermodynamically unstable enamine which is not observable by NMR. A second dynamic process occuring in **2** is assigned to atropisomerism about the naphthyl–imino bond in the hindered (*Z*)-imine.

The mutarotation of chiral imines derived from optically pure 1-phenylethylamine has been extensively studied over the past 15 years by Perez-Ossorio and co-workers.[2-6] The origin of the mutarotation was rationalized either in terms of *E*–*Z* isomerization or a restricted rotation around bonds between the imino group and substituents.[2-5] Recently an alternative explanation involving imine → enamine tautomerization alone has been advanced in this journal[6] to account for the observed mutarotation of imine **1** in methanol solvent. In support of this hypothesis it was reported[6] that the ^{13}C NMR spectrum of imine **1** on standing in CD_3OD solution was essentially that expected for the enamine tautomer.

Previous work in these laboratories has shown that in CD_3OD solution, imines closely related to **1** undergo *E*–*Z* isomerization with concomitant deuteration of the vinylic methyl group.[7] It was suggested[7] that the isomerization proceeded via a transient enamine intermediate which was less energetically stable than the imine and was not observed in the NMR spectra. Accordingly the proposal[6] that the enamine tautomer of imine **1** was more stable than the imine in CD_3OD solution was of considerable interest and merited further investigation in the light of related studies reported here.

Imine **2**, which is structurally related to **1**, exhibited mutarotation following dissolution of the crystals in CH_3OH at ambient temperature; $[\alpha]_D$ decreased exponentially from ca. +277° to +133°. The mutarotation was much slower in CD_3OD and gave a markedly nonexponential plot of optical rotation vs. time (Figure 1). A parallel ^1H NMR study of the imine in CD_3OD showed a change in the *E*:*Z* the distribution with time which closely followed the profile of the mutarotation curve (Figure 1). Spectra recorded a few minutes after dissolution indicated that the crystalline form of imine **2** consisted exclusively of the *Z* isomer. On standing in CD_3OD the compound slowly equilibrated to a final isomer distribution *Z*:*E* = 78:22, and the close correspondence of the curves in Figure

Scheme I



† Queen's University.
‡ University of Birmingham.

(1) Part 18: Boyd, D. R.; Campbell, R. M.; Coulter, P. B.; Grimshaw, J.; Neill, D. C.; Jennings, W. B. *J. Chem. Soc., Perkin Trans. 1* **1985**, 849.
(2) Melendez, E.; Perez-Ossorio, K.; Sanchez del Olmo, V. *An. Quim.* **1970**, *66*, 87.
(3) Garcia Ruano, J. L.; Perez-Ossorio, R. *An. Quim.* **1975**, *71*, 93.
(4) Alcaide, B.; Lago, A.; Perez-Ossorio, R.; Plumet, J. *J. Chem. Res., Synop.* **1982**, 173.
(5) Lopez-Mardomingo, C.; Perez-Ossorio, R.; Plumet, J. *J. Chem. Res., Synop.* **1983**, 150.
(6) Arjona, O.; Perez-Ossorio, R.; Perez-Rubalcaba, A.; Plumet, J.; Santesmases, M. J. *J. Org. Chem.* **1984**, *49*, 2624.
(7) Jennings, W. B.; Boyd, D. R. *J. Am. Chem. Soc.* **1972**, *94*, 7187.

0022-3263/86/1951-0992$01.50/0

Table I. NMR Data for Imines 1–3[a]

compd	solvent	^{1}H chemical shifts[b]			^{13}C chemical shifts			
		NCH*Me*	*Me*C=N	NC*H*	NCH*Me*	*Me*C=N	NC*H*	*C*=N
1 (*E*)	$CDCl_3$	1.54 (d)	2.27 (s)	4.84 (q)	25.1	15.5	59.8	163.4
1 (*Z*)	$CDCl_3$	1.41 (d)	2.32 (s)	4.43 (q)	24.6	29.3	60.8	167.3
1 (*E*)	CD_3OD	1.54 (d)	2.25 (s)	4.89 (q)	24.8	16.1[c]	61.0	167.4
1 (*Z*)	CD_3OD	1.40 (d)	2.30 (s)	4.45 (q)	24.1	28.3[c]	61.8	171.2
2 (*E*)	$CDCl_3$	1.66 (d)	2.34 (s)	4.94 (q)	25.1	20.4	60.6	167.1
2 (*Z*)[d]	$CDCl_3$	1.37 (d), 1.38 (d)	2.40 (s), 2.42 (s)	4.15 (q), 4.20 (q)	24.4, 24.6	29.5, 29.6	61.9, 62.1	167.0, 167.4
2 (*E*)	CD_3OD	1.63 (d)	*e*	5.15 (q)	24.4	*e*	61.4	171.0
2 (*Z*)[d]	CD_3OD	1.36 (d)	*e*	4.25 (q)	23.9, 24.2	*e*	62.7, 62.9	170.6, 170.9
3 (*Z*)	$CDCl_3$	1.34 (d)	2.79[f]	4.34 (q)	25.1	39.3[g]	60.4	174.5
3 (*Z*)	CD_3OD	1.34 (d)	2.82[f]	4.31 (q)	24.4	39.7[g]	61.4	177.7

[a] Only the alkyl resonances are given (the aromatic region was very complex). [b] Signal multiplicity given in parenthesis; J = 6.5 Hz in all cases cited. [c] Very low intensity septuplet owing to deuteration of this carbon atom. [d] A mixture of atropisomers (see text). [e] Signal not evident owing to deuteration. [f] Septuplet signal from Me_2CH, J = 6.9 Hz. [g] Signal from Me_2CH.

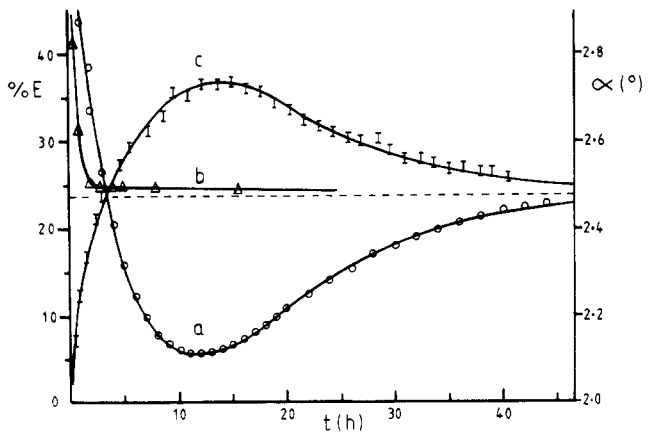


Figure 1. Plots of the optical rotation (α) vs. time following dissolution of **2** in (a) CD_3OD and (b) CH_3OH, and (c) the percent E isomer vs. time in CD_3OD at ca. 27 °C. Sample concentration 0.020 g cm^{-3}.

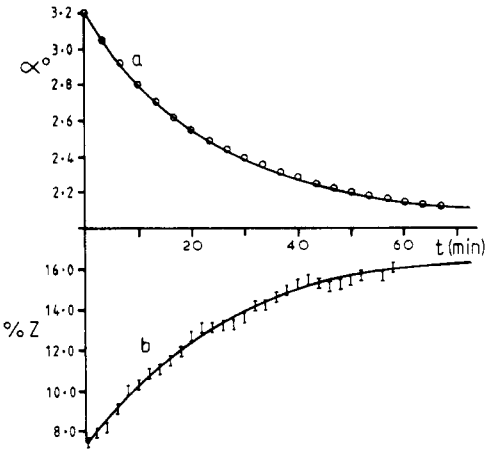


Figure 2. Plots of (a) the optical rotation, α, and (b) the percent Z isomer vs. time following dissolution of 1 in CD_3OD at 22 °C. Sample concentration 0.040 g cm^{-3}.

1 establishes that this process is also responsible for the mutarotation. The close correspondence of the ^{1}H and ^{13}C NMR signals of the major and minor components (including the observation of ^{13}C=N signals from both components) (Table I) clearly shows that the minor component is indeed the E isomer.

The anomalous equilibration curve obtained in CH_3OH (Figure 1) showing an increase in the proportion of the E isomer beyond its equilibrium value to a maximum of 38% after ca. 12 h, followed by a gradual reduction to 22%, is an "equilibrium overshoot" phenomenon[8] induced by a kinetic deuterium isotope effect. In CD_3OD the $Z \rightarrow E$ isomerization proceeds via exchange of the vinylic methyl protons (Scheme I) and the reverse process ($E \rightarrow Z$) is retarded in the earlier stages of the equilibration by deuterium isotope effects as discussed elsewhere for related imines.[8] An optical rotation equilibrium overshoot was also evident during the mutarotation in CD_3OD (Figure 1) for the same reason, and this provided a more accurate method of analysis than NMR measurement of the E–Z ratio. In agreement with this explanation no overshoot was observed during mutarotation in CH_3OH (Figure 1) and the isomerization is faster in this solvent owing to the absence of retarding deuterium isotope effects.

A sample of imine 1 prepared in this laboratory showed physical characteristics and mutarotation behaviour similar to those reported previously. Thus, in CD_3OD at 22 °C $[\alpha]_D$ decreased steadily from an initial value of +88° to a final constant value of +50° (Figure 2). Information

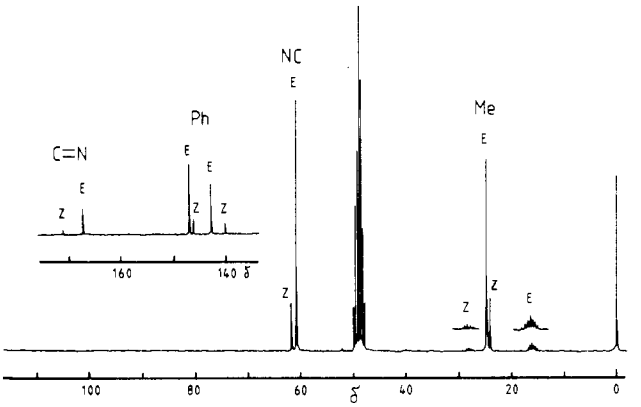


Figure 3. 62.8-MHz ^{13}C NMR spectrum of 1 in CD_3OD. The multiplet at δ 49 is from the solvent and most of the complex aromatic signals (δ 125–135) are not shown.

regarding the origin of the mutarotation was obtained by recording ^{1}H NMR spectra of the solution as a function of time. An NMR spectrum of neat liquid 1 showed the presence of E and Z isomers in the ratio 95:5%. On dissolution in CD_3OD at 22 °C the proportion of the Z isomer increased steadily from 5% to a final new equilibrium value of 18% in this solvent. The exponential curve for the isomer distribution vs. time was in close correspondence with the mutarotation curve (Figure 2). Additionally, the first-order rate constants for the equilibration derived from the NMR data, $k_f + k_r = 5.5 \times 10^{-4}$ s^{-1}, were in agreement with those for mutarotation, $k_f + k_r = 5.7 \times 10^{-4}$ s^{-1} at 22 °C. These results are in acceptable accord with the previously reported[6] rate constants for mutarotation,

(8) Boyd, D. R.; Al-Showiman, S.; Jennings, W. B.; Wilson, V. E. *J. Chem. Soc., Chem. Commun.* **1985**, 443.

Table II. Equilibrium Isomer Distribution of Imine 1 in Various Solvents[a]

solvent	Z%	E%
neat liquid	5	95
[$^2H_6$]dimethyl sulfoxide	5	95
[$^2H_6$]benzene	6	94
[$^2H_6$]acetone	6	94
[$^2H_3$]acetonitrile	6	94
tetrachloromethane	10	90
[^2H]chloroform	10	90
2-methyl-2-propenol	11	89
methanol	18	82

[a] Measured at 35 °C in 0.5 M solutions by ^1H NMR.

$k_f + k_r = 4.76 \times 10^{-4}$ at 25 °C. Clearly the mutarotation arises from the *E–Z* isomerization. The role of the enamine is merely that of a transient intermediate in the imine isomerization process.[7,8] The ^{13}C and ^1H NMR spectra of the present sample of imine **1** in CD_3OD showed no signals attributable to an enamine tautomer, even after standing for a week (Figure 3). The reported signal[6] at δ 60.6 assigned to the $=CD_2$ carbon of the enamine is at unusually high field for an alkene carbon but corresponds closely with a signal at δ 61.0 (Table I) assigned in the present investigation to the NCH carbon of the (*E*)-imine. The vinylic methyl carbon signals of both imine isomers were essentially absent in CD_3OD solution owing to deuteration of the attached protons. However, two low-intensity septuplets (arising from deuterium coupling) were detected at δ 16.1 (*E* isomer) and 28.3 (*Z* isomer) after long accumulation (Figure 3). These signals appeared as singlets (δ 16.9 and 28.6) with normal intensities when the ^{13}C NMR spectra were recorded in CH_3OH solution, but no $=CH_2$ signal of the enamine was detected. The observation of a $^{13}C{=}N$ signal from the minor component and the correspondence of the other signals with those expected[9] for a (*Z*)-imine clearly establishes that this is indeed the minor component.

An NMR study of the equilibrium isomer ratio of imine **1** in several solvents shows that the proportion of the *Z* isomer is unusually high in methanol (Table II). Although many factors could influence the solvent effect on the equilibrium, the *Z* isomer may form a stronger hydrogen bond to methanol as the nitrogen lone pair may be somewhat less sterically hindered in this isomer.[10] The smaller solvent effect in 2-methyl-2-propanol might be associated with weaker hydrogen bonding in both isomers due to the increased steric bulk of the solvent molecules.

Unlike imine **2**, no evidence of an equilibrium overshoot effect was seen during the mutarotation or *E–Z* isomerization of imine **1** in CD_3OD (Figure 2). The size of the overshoot will be dependent on the precise value of the isotopic rate constants for any given substrate, but the absence of any detectable overshoot in **1** may be associated with the fact that a significant proportion (5%) of the minor *Z* isomer was present initially in this liquid imine (which could not be obtained in the same ultrapure form as crystalline imine (**2**)).

Imine **3** also showed mutarotation in CD_3OD solution at 24 °C as reported previously, though the magnitude of the effect ($[\alpha]_D$ decreased from −136° to −130°) was much smaller than in imines **1** and **2**. ^1H NMR studies on **3** showed a barely detectable proportion of the minor *E* isomer either in the neat liquid (≤1.5%) or in CD_3OD solution (3%). Thus the very small change in $[\alpha]_D$ with time possibly reflects the very small change in the *E*:*Z* ratio upon dissolution in CD_3OD. Small amounts of hydrolysis brought about by traces of D_2O in the CD_3OD could also contribute to the small mutarotation observed in imine **3**.

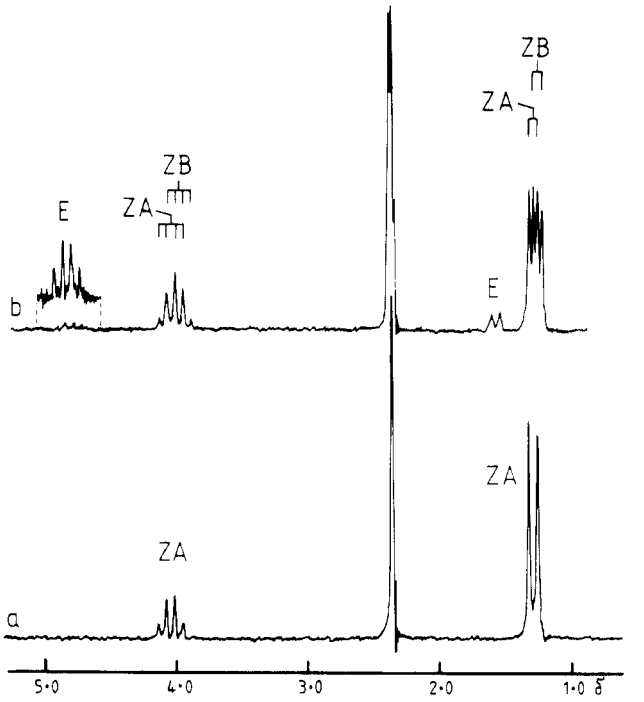
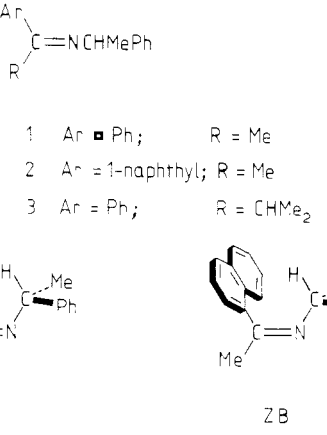


Figure 4. 100-MHz ^1H NMR spectra of **2** in CCl_4 at −15 °C: (a) freshly dissolved, (b) after equilibration.

In addition to *E–Z* isomerism, the ^1H NMR spectra of compound **2** in most solvents (e.g., CCl_4) show a further complication involving doubling of the alkyl signals of the Z isomer (Table I). This effect was not evident in 100-MHz spectra recorded in CD_3OD. The latter observation is due to an accidental coincidence of the ^1H signals since the ^{13}C NMR spectrum in CD_3OD showed that most of the alkyl carbon resonances of the Z isomer were split into two components with approximately equal intensity (Table I). The signal doubling is ascribed to atropisomerism about the 1-naphthyl-imino single bond in the sterically congested *Z* isomer. This give rise to two diastereoisomers (ZA and ZB) owing to the presence of the chiral N-alkyl group. In line with expectations, the crystals of **2** consist



of a single pure atropisomer of the (*Z*)-imine. This was established by recording NMR spectra on a dissolving crystalline sample below 0 °C (Figure 4a). Spectra recorded at this temperature following warming of the sample to 40 °C for ca. 20 min showed equilibration of the

(9) Jennings, W. B.; Wilson, V. E.; Boyd, D. R.; Coulter, P. B. *Org. Magn. Reson.* **1983**, *21*, 279.

(10) For a related observation see Bjorgo, J.; Boyd, D. R.; Watson, C. G.; Jennings, W. B.; Jerina, D. M. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1081.

atropisomers and of the *E* and *Z* isomers (Figure 4b). In fact the atropisomers equilibrated much more rapidly than isomerization occurs around the imino bond. When a sample of **2** in [$^2H_8$]toluene solution was warmed to ca. 90 °C, the signals of the atropisomers ZA and ZB broadened and coalesced owing to the onset of fast rotation of the 1-naphthyl group on the NMR time scale. Application of the graphical procedure of Jaeschke et al.[11] to the coalescing NCH*Me* doublets ($\Delta\nu$ = 1.8 Hz, line width in the absence of exchange = 0.65 Hz) gave k = 3.2 s^{-1} and $\Delta G^{\ddagger}$ = 20.5 kcal mol^{-1} at the coalescence temperature of 89 °C. The barrier is similar to that measured previously ($\Delta G^{\ddagger}$ = 20.4 kcal mol^{-1}) for 1-naphthyl rotation in a related imine derived from 1-acetylnaphthalene using a prochiral *N*-isopropyl substituent to monitor the process.[12] The atropisomerization probably also accounts for a very rapid initial decrease in optical rotation of imine **2** observed in the first few minutes after dissolution in CD_3OD. This preceded the much slower *E*–*Z* isomerization process depicted in Figure 1 and corresponds to a half-life in the region of 1 min at 28 °C and a $\Delta G^{\ddagger}$ value of ca. 20 kcal mol^{-1}. This estimate is in good agreement with the naphthyl rotation barrier determined in [$^2H_8$]toluene solution by dynamic NMR.

(11) Jaeschke, A.; Muensch, H.; Schmid, H. G.; Friebolin, H.; Mannschreck, A. *J. Mol. Spectrosc.* **1969**, *31*, 14.
(12) Boyd, D. R.; Al-Showiman, S.; Jennings, W. B. *J. Org. Chem.* **1978**, *43*, 3335.

Experimental Section

Mutarotation studies were carried out by using a Perkin-Elmer Model 241 automatic polarimeter equipped with a thermostatically controlled (±0.5 °C) cell and a chart recorder. NMR spectra were obtained on a Bruker WH-90, Bruker WM-250, or a Varian XL-100 spectrometer.

The imines were obtained by condensation of the appropriate ketone with optically pure 1-phenylethylamine using either a Dean–Stark trap and refluxing xylene containing a trace of *p*-toluenesulfonic acid,[6] or the $TiCl_4$ catalyzed method.[12]

N-[1-Phenylethylidene]-1-phenylethylamine (**1**) prepared from (*S*)-(−)-1-phenylethylamine had bp 110–115 °C (0.005 mm) [lit.[6] bp 123 °C (1.0 mm)] and $[\alpha]_D$ +74° ($CHCl_3$).

N-[1-(1′-Naphthyl)ethylidene]-1-phenylethylamine (**2**) prepared from (*R*)-(+)-1-phenylethylamine had bp 120–125 °C (0.01 mm), mp 85–86 °C, and $[\alpha]_D$ +95° ($CHCl_3$). Anal. Calcd for $C_{20}H_{19}N$: C, 87.9; H, 7.0; N, 5.1. Found: C, 88.0; H, 7.2; N, 5.15.

N-(1-Phenyl-2-methylpropylidene)-1-phenylethylamine (**3**) prepared from (*S*)-(−)-1-phenylethylamine had bp 114–115 °C (0.01 mm) [lit.[6] bp 121 °C (0.4 mm)] and $[\alpha]_D$ −130° ($CHCl_3$).

^1H and ^{13}C NMR data for imines 1–3 are given in Table I.

Registry No. (*E*)-**1**, 100483-17-8; (*Z*)-**1**, 100483-18-9; (*E*)-**2**, 100430-66-8; (*Z*)-**2**, 100430-65-7; (*Z*)-**3**, 100483-19-0; $PhCOCH_3$, 98-86-2; $PhCOCH(CH_3)_2$, 611-70-1; (*S*)-1-phenylethylamine, 2627-86-3; (*R*)-1-phenylethylamine, 3886-69-9; 1-acetylnaphthalene, 941-98-0.

2,2′-Dicarbomethoxy-9,9′-bitriptycyl. Synthesis, Conformational Stability, and Separation and Identification of the Conformers[1]

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The synthesis of 2,2′-dicarboxy-9,9′-bianthryl (**6d**) was achieved in four steps from 2-chloroanthrone (**7**). Resolution with quinidine yielded optically pure **6d**, which was converted to the corresponding dimethyl ester (**6c**) with CH_2N_2. Optically pure **6c** was converted to 2,2′-dicarbomethoxy-9,9′-bitriptycyl (**5c**) with excess anthranilic acid and *n*-butyl nitrite. Compound **5c** was shown to be conformationally stable. The anti (**5c′**) and gauche (**5c″**, **5c‴**) conformers were separated and identified. A precise value of the rotational barrier of **5c** could not be measured, but a minimum value of 55 kcal/mol was established. The gauche conformer was shown to be only 30% optically pure. This is taken to indicate that the rate of addition of the second benzyne, in the conversion of **6c** to **5c**, and the rate of rotation about the central bond in the monoadduct, 2-carbomethoxy-9-(2′-carbomethoxy-9′-anthracyl)triptycene (**9**), are of comparable magnitudes.

Restricted rotation between sp^3 hybridized carbon atoms has been the subject of considerable activity over the past 20 years. Many attempts have been made to devise systems with high rotational barriers, to separate conformers, and to examine the factors which influence rotational barriers, both experimentally and theoretically.[2] Generally, larger interfering substituents result in larger barriers. However, Ōki and co-workers have shown that rotational barriers can decrease as the interfering groups become larger. This effect has been attributed to ground-state strain and molecular distortion, which leads to sequential rather than simultaneous passage of groups past each other.[2b,3] Most of the reported examples of conformationally stable substituted ethanes contain a 1-substituted bicyclo[2.2.2]octatriene backbone (**1**), e.g., **2**,[4] **3**,[5] and **4**,[6] which insures that three of the six interfering substituents are directed toward the other three.

Early on, we chose to study the 9,9′-bitriptycyl system **5**.[7] In contrast to compounds of the type illustrated by

(1) This work was supported in part by grants from the National Science Foundation (GP 3511, GP 6404), the City University of New York, and the City College Faculty Senate Committee on Research and Publication.
(2) Many publications are worthy of mention. The following review articles contain pertinent references. (a) Long, D. A. *J. Mol. Struct.* **1985**, *126*, 9. (b) Ōki, M. In "Topics in Stereochemistry"; Allinger, N. L., Eliel, E. L., Wilen, S. H., Eds.; John Wiley and Sons: New York, 1983; Vol. 14.
(3) (a) Yamamoto, G.; Ōki, M. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2219. (b) Yamamoto, G.; Tanaka, A.; Suzuki, M.; Morita, Y.; Ōki, M. *Ibid.* **1984**, *57*, 891. (c) Yamamoto, G.; Ōki, M. *Ibid.* **1983**, *56*, 2082. (d) Yamamoto, G.; Suzuki, M.; Ōki, M. *Ibid.* **1983**, *56*, 809. (e) Yamamoto, G.; Suzuki, M.; Ōki, M. *Ibid.* **1983**, *56*, 306.
(4) Iwamura, H. *J. Chem. Soc., Chem. Commun.* **1973**, 232.
(5) Yamamoto, G.; Ōki, M. *J. Chem. Soc., Chem. Commun.* **1974**, 713.
(6) Ōki, M.; Yamamoto, G. *Chem. Lett.* **1972**, 45.
(7) Koukotas, C.; Mehlman, S. P.; Schwartz, L. H. *J. Org. Chem.* **1966**, *31*, 1970.

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