110205-68-0; **3**, 110269-17-5; **3** (amine deriv), 110205-69-1; **4**, 104343-30-8; **6**, 104343-31-9; **7a**, 104419-28-5; **7b**, 104343-32-0; **7c**, 104343-35-3; **8**, 104419-80-9; **9**, 110205-70-4; **10**, 110205-71-5; $Ph_3P{=}CH_2$, 3487-44-3; α-glucosidase, 9001-42-7; sucrose, 9001-57-4; maltase, 9001-42-7; trehalase, 9025-52-9; glucoamylase, 9032-08-0; α-amylase, 9000-90-2; 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl bromide, 4196-35-4; 2,3,4,6-tetra-*O*-α-D-glucopyranosyl bromide, 572-09-8.

Conformational Studies by Dynamic NMR. 32.[1] Enantiomerization of Chiral Conformers in Hindered Naphthylamines and Naphthyl Nitroxides

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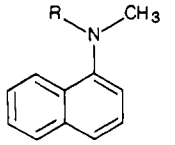
Observation of anisochronous NMR signals in *N*-alkyl-*N*-methyl-1-naphthylamines at low temperature indicates that these molecules adopt a twisted conformation (yielding enantiomeric conformers at the equilibrium) as opposed to the corresponding *N*-alkyl-*N*-methyl-2-naphthylamines which give two planar (thus achiral) conformers. The barriers to enantiomerization in 1-naphthylamines have been measured by line-shape analysis for those amines containing prochiral substituents. The use at low temperature of one of the Pirkle's chiral alcohols as a discriminating agent allowed these barriers to be measured even in absence of prochiral groups. Related alkyl 1-naphthyl nitroxides were also shown to prefer a twisted conformation, but the enantiomerization barriers are too low to be measured by ESR. Examination of a much more hindered nitroxide (2-*tert*-butyl-1-naphthyl ethyl nitroxide) showed that the methylenic hydrogens were anisochronous even at room temperature, indicating that this radical exists as a racemic mixture. The existence of an exponential relationship between the free energies of enantiomerization in the 1-naphthylamines and the nitrogen hyperfine splittings in the analogous nitroxides allowed the barrier for *N*,*N*-dimethyl-1-naphthylamine to be estimated. This barrier could not be measured directly because of the symmetry of the amine.

Introduction

Hindered aromatic amines may adopt a conformation whereby the dynamic plane containing the rapidly inverting nitrogen atom is twisted with respect to the plane of the aromatic ring.[2] In the case of *N*,*N*-diisopropyl-1-naphthylamine,[3] for instance, this arrangement is revealed at low temperature by two different (anisochronous[4]) NMR signals, corresponding to the two methyls within each isopropyl moiety. The anisochrony of these *gem*-methyls is due to the fact that the molecular plane of symmetry is not a plane of symmetry for the sensor group (i.e., the prochiral isopropyl moiety)[4] in a twisted conformation. Accordingly in naphthylamines with two different N-bonded groups, two possible situations may occur. When the molecule is not hindered and a planar conformation is preferred, two conformers in different proportions should be observable: in each of the two conformers the prochiral substituents,[4] if present, would display isochronous geminal groups. On the other hand, in naphthylamines where steric requirements force the molecule into a nonplanar conformation, only one conformer will be observed and prochiral substituents, if present, will display anisochronous geminal groups. In this arrangement the compound is actually a racemic mixture of a pair of enantiomeric conformers that might in principle be detected in a chiral environment. We report here the barriers to enantiomerization for this class of compounds as well as examples of direct detection of their enantiomeric conformers in a chiral medium at low temperature.

Results and Discussion

In the present work the *N*-alkyl-*N*-methyl-1-naphthylamines **1**–**6** were investigated, together with the *N*-isopropyl-*N*-methyl-2-naphthylamine (**7**) by variable-temperature ^1H and ^{13}C NMR spectroscopy.



1, R = Me
2, R = CH_2Me
3, R = CH_2Bu-*t*
4, R = $CHMe_2$
5, R = $CHEt_2$
6, R = *t*-Bu

Dynamic NMR of Naphthylamines. As a typical example the ^{13}C NMR spectrum of **4** displays, at −95 °C, two different methyl signals (ratio 1:1) for the isopropyl moiety and single signals for both NCH and NCH_3. By way of contrast the 2-isomer (**7**) displays (at −148 °C) two lines (ratio 6.5:1) for the NCH carbons and single lines (clearly due to overlapping) for the methyl groups. The less hindered compound **7** thus prefers a quasi-planar

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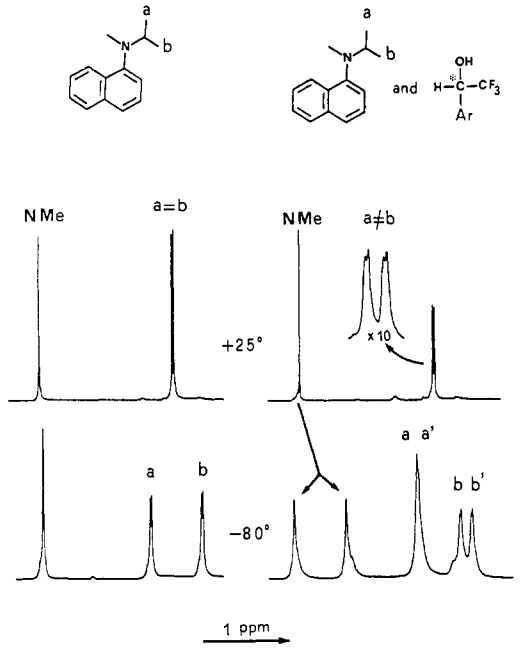
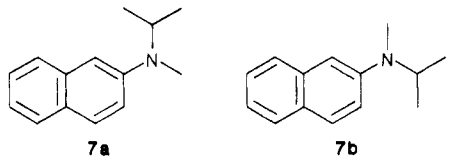


Figure 1. Left (top): proton NMR (300 MHz) spectrum in CD_2Cl_2 of the methyl region of **4** at room temperature. Left (bottom): the same spectrum at −80 °C displaying anisochronous methyls in the isopropyl group. Right (top): the same spectrum in the presence of a chiral auxiliary agent (*l*-$ArCF_3CHOH$, Ar = 9-anthryl) at room temperature. Right (bottom): at −80 °C the chiral auxiliary discriminates the two enantiomeric conformers.

arrangement, since its NMR spectrum corresponds to that of the syn and anti conformers **7a** and **7b** in a 6.5:1 proportion. Line-shape analysis yields the barrier for the



7a **7b**

syn–anti interconversion between the two planar conformers ($\Delta G^{\ddagger}$ = 7.0 kcal mol^{-1}).

The different spectral behavior of **7** and **4** indicates that the latter exists in a conformation lacking any element of symmetry, that is, a racemic mixture of the two enantiomers, **4a** and **4b**, is present:

4a **4b**

On raising the temperature the enantiomers interconvert rapidly and the barrier to the enantiomerization was measured by monitoring the anisochronous methyls of the isopropyl group. Similar behavior was observed by ^1H NMR for the pairs of anisochronous methylenic hydrogens of **2** and **3** and by ^{13}C NMR for the carbons in the β-position with respect to nitrogen in **5**.

Enantiomeric conformers of this type could yield, in principle, different NMR spectra in a chiral environment,[5,6] at a temperature sufficiently low that the enantiomerization process is frozen. Attempt to discriminate **4a** and **4b** at −90 °C by means of optically active lanthanide shift reagents[6,7] failed, probably for steric reasons.[8,9] However,

Table I. Barrier to Enantiomerization ($\Delta G^{\ddagger}$ in kcal mol^{-1}) Measured by Line-Shape Analysis from the NMR Spectra (H-1 or C-13) of Amines 2–6. The Syn–Anti Interconversion Barrier for the β-Isomer of 2, i.e., *N*-Isopropyl-*N*-methyl-2-naphthylamine (7) Is Also Reported

compound	$\Delta G^{\ddagger}$	solvent	temp (°C)	nucleus
2 (R = Et)	8.3	CD_2Cl_2	−95; −105	H-1
	8.8[a]		−88	H-1
3 (R = CH_2Bu-*t*)	9.4	CHF_2Cl	−54	H-1
4 (R = $CHMe_2$)	10.3	CD_2Cl_2	−50	C-13
	10.7[a]		−47	H-1
5 (R = $CHEt_2$)	9.5	CD_2Cl_2	−75	C-13
6 (R = Bu-*t*)	19.1[a]	toluene-d^8	+52	H-1
	5.8[b]	CHF_2Cl	−136; −140	C-13
7	7.0	CHF_2Cl	−131	C-13

[a] These values have been obtained in the presence of an optically active Pirkle alcohol (see text). [b] The barrier refers to the N-inversion process (see text) measured at 75.47 MHz.

addition to **4** of an enantiomerically pure Pirkle's alcohol[10] [*l*-2,2,2-trifluoro-1-(9-anthryl)ethanol: $ArCHCF_3OH$, with Ar = 9-anthryl] yields, at −80 °C, two different spectra (^1H, 300 MHz) due to the diastereomeric interactions of the enantiomeric conformers **4a** and **4b** with the alcohol. In Figure 1 (left-hand side) is shown the methyl region of the ^1H spectrum of **4** at 25 °C (top) and −80 °C (bottom) in the absence of the chiral alcohol. The methyl signals of the isopropyl groups split at low temperature whereas the signal due to *N*-methyl group remains unsplit. Addition of the chiral alcohol (right-hand-side spectrum) does not affect the NMe signal at room temperature (top) since the enantiomers exchange rapidly, but it does induce a small splitting of the isopropyl methyl groups (see the tenfold expanded scale). The latter effect is *not* due to chiral discrimination but is a result of the formation of a solvating complex between the amine **4** and the optically active alcohol[5a] where the methyls of the isopropyl group of the amine are anisochronous (methyl *a* different from methyl *b*). At −80 °C (bottom right-hand side) the two chiral conformers no longer exchange rapidly on the NMR time scale and the enantiotopic NMe groups therefore become diastereotopic owing to the *d*–*l* and *l*–*l* diastereomeric interaction with the chiral alcohol. The same occurs for the pairs of doublets of the isopropylic methyl groups. This should yield four different pairs of signals (labeled a, b, a′, b′) but two of them are accidentally degenerate (a and a′) and so the signals appear as three pairs of doublets in a 2:1:1 ratio. At intermediate temperature the NMe signals coalesce. The enantiomerization barrier can therefore be determined by monitoring the signals of groups that are not prochiral. Analogous results were obtained in the case of **2** (R = Et). The comparison of the $\Delta G^{\ddagger}$ values obtained in the presence and in the absence of this chiral auxiliary indicate that in **2** and **4** the values are slightly higher (8.8 and 10.7 kcal mol^{-1}, respectively) than those determined in CD_2Cl_2 alone (viz. 8.3 and 10.3 kcal mol^{-1}, respectively see Table I). These differences are analogous to those observed for barriers measured in different solvents.[11–13]

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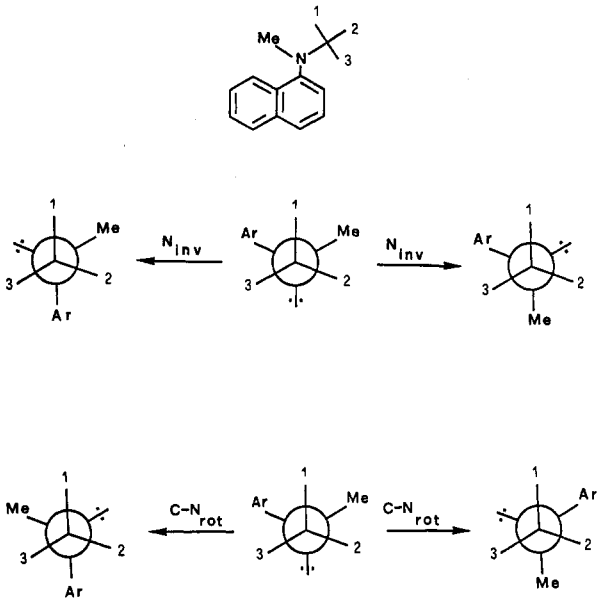
Scheme I. Diagram Showing the Three Possible Conformational Arrangements Obtained by N-Inversion (Top), Starting from the Formula in the Center. The Three Possible Conformational Arrangements Obtained by C–N Rotation, Starting from the Same Formula, Are Shown Underneath. The Environments Contributing to the Chemical Shifts of the Three Methyls (Labeled 1, 2, 3) Are the Same for the Two Processes (Ar Represents the 1-Naphthyl Moiety)



An interesting extension of this experiment is the possibility that enantiomerization barriers could be measured even in the absence of the prochiral groups. For instance in compound **6** (R = *t*-Bu) neither of the groups bonded to nitrogen (methyl and *t*-Bu) can give anisochronous signals. However, addition of the chiral alcohol splits the NMe signal into two lines that eventually broaden and coalesce on raising the temperature. The value obtained in this way ($\Delta G^{\ddagger}$ = 19.1 kcal mol^{-1}) could not have been measured in an achiral medium.

In the amines **2–5** the effects due to nitrogen inversion could not be observed since the prochiral groups yield anisochronous signals at temperatures higher than those required to measure the N-inversion barrier. However in the case of **6** (R = *t*-Bu), where there are no prochiral groups, this barrier could be determined. The ^{13}C signals of the methyls in the *tert*-butyl group are split at −152 °C (75.47 MHz in CHF_2Cl) into two lines with a 2:1 intensity ratio. This implies that the three methyls have different chemical shifts, two of them being accidentally coincident. The methyls can become nonequivalent only when *both* N-inversion and N-Bu-*t* rotation are slow.[14] They will all be equivalent if either rotation or N-inversion is fast (Scheme I). The $\Delta G^{\ddagger}$ value of 5.8 kcal mol^{-1} obtained by line-shape simulation thus corresponds to the lower of these two barriers.[14,15] In unhindered amines it is known that rotation about the N–C bond has a lower barrier than N-inversion,[16] but in amines having a *tert*-butyl group bonded to nitrogen, it has been recognized that isolated

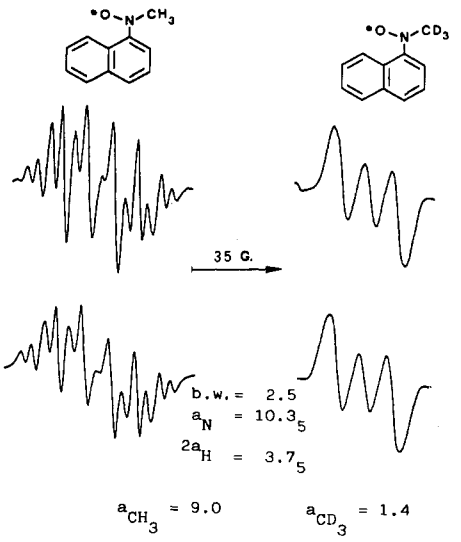
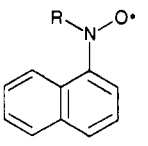


Figure 2. Experimental (top) ESR spectra of nitroxide **9** (left) and of its deuteriated derivative (right) in toluene. The computed spectra reported underneath were obtained with the same band with (b.w. = 2.5 G).

rotation about the N-Bu-*t* is slower than N-inversion.[15,17] Accordingly, the barrier measured in **6** (5.8 ± 0.15 kcal mol^{-1}) corresponds essentially to a N-inversion process (or to an inversion accompanied by a concomitant rotation[17]). This value is expected to be the highest N-inversion barrier in this series of compounds since in **6** (R = *t*-Bu) there is little conjugation between the nitrogen atom and the ring owing to the bulkiness of the *tert*-butyl group. In the less hindered amines **1–5** the contribution to conjugation, albeit quite small, would make the N-inversion barrier even lower than in **6**: N-inversion in conjugated aromatic amines (e.g. 1.6 kcal mol^{-1} in aniline[18]) is in fact undetectable by NMR. It thus seems a good approximation to represent this enantiomerization process as due essentially to the rotation of the plane containing a fast inverting nitrogen, with negligible coupling with the N-inversion process.

ESR of Naphthyl Nitroxides. From the discussion of the NMR experiments it is clear that the barrier for **1** (R = Me) cannot be measured, owing to the symmetry of the molecule. A possible way of circumventing this problem and finding the barrier for **1** is to establish a relationship between the $\Delta G^{\ddagger}$ values of **2–6** and other parameters in analogous derivatives: the unknown value can then be estimated by extrapolation.

Suitable derivatives for such a comparison were found the nitroxides **8–14** where an oxygen atom has taken the place of the methyl group of amines **1–6**. These nitroxides



8, R = H
9, R = Me
10, R = CH_2Me
11, R = CH_2Bu-*t*
12, R = $CHMe_2$
13, R = $CHEt_2$
14, R = *t*-Bu

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Table II. Hyperfine Splitting Constants (Gauss) and g Factors of Nitroxides 8–16 Obtained at Room Temperature in Toluene

	a_N	a_{CH_n}	a_{ring}	$a_{H(N)}$	g factor
8 (R = H)	9.7_5		4.7_5 (2 H)	11.7_5	2.0050
9 (R = Me)	10.3_5	9.0 (CH_3)	3.7_5 (2 H)		2.0056_5
10 (R = Et)	11.0	7.5 (CH_2)	3.2_5 (2 H)		2.0058
11 (R = CH_2Bu-*t*)	10.9	6.1_5 (CH_2)	2.6 (1 H)		2.0059
			3.2 (1 H)		
12 (R = $CHMe_2$)	11.7	2.8_5 (CH)	2.8_5 (2 H)		2.0060
13 (R = $CHEt_2$)	11.3	<1.8 (CH)[a]	3.0 (2 H)		2.0062_5
14 (R = *t*-Bu)	13.5				2.0063
15	11.5	3.0 (CH)	3.0 (1 H)		
16	14.1	11.9 (CH)			2.0063_5
		15.5 (CH)[b]			

[a] At room temperature this splitting is less than the line width but becomes 3.0 G at 120 °C. [b] Reference 22.

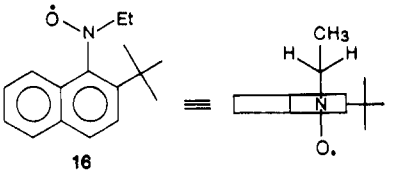
were obtained by oxidation of the corresponding amines. A typical ESR spectrum is shown in Figure 2 in the case of R = Me (**9**); the corresponding spectrum of the deuteriated (R = CD_3) derivative is also displayed. Spectral simulations were performed in both cases by using the same hyperfine splittings and line width: only the CH_3 splitting of **9** was reduced by a factor of 6.5 in the deuteriated derivative to allow for the H/D gyromagnetic ratio.

The hyperfine splitting constants and the *g* factors are collected in Table II. The two smallest splittings in nitroxides **8–13** were assigned to positions 2,4 of the naphthalene ring. Substitution of H-4 in nitroxide **12** with a bromine atom yields the nitroxide **15** where one of the two small splittings is missing (Table II). It is thus conceivable that also the ortho-like position 2 has a splitting similar to that of the para-like position 4.

These nitroxides are expected to stay in a twisted conformation where the angle between the dynamic plane containing[19] the NO moiety and that of the naphthalene ring changes according to the bulkiness of R. Nitroxide **14** has in fact a much larger a_N splitting and much smaller aromatic hydrogen splittings (a_H) than its less crowded β-isomer:[20] the a_N value should thus increase and the a_H values decrease when the conjugation is less efficient.

Evidence of increasing twist angles in **8–14** is also offered by the trend of the *g* factors (Table II). The latter values depend[21] upon the spin–orbit coupling of the unpaired electron in the π orbital of the NO moiety with the doubly occupied MO's of the nitrogen and oxygen atoms. The larger the twist angle, the smaller the delocalization of the unpaired electron on the naphthalene, the spin density on NO thus increases, and so increases the spin–orbit coupling and the *g* factor.

If the 1-naphthylalkyl nitroxides prefer a twisted conformation, one might expect that nitroxide **10** (R = Et) would exhibit anisochronous methylenic hydrogens. The fact that this feature was not observed (Table II) could be due either to accidental degeneracy or to an enantiomerization barrier much lower than that in the corresponding tertiary amines **1–6** (methyl is bulkier than oxygen). As a consequence even at the lowest attainable temperature fast interconversion could make the methylenic hydrogens isochronous. To prove that this is actually the case 2-*tert*-butyl-1-naphthyl ethyl nitroxide (**16**) was examined.



16

Its ESR spectrum at room temperature shows indeed two different methylenic splittings (Table II) that do not coalesce even at 120 °C:[22] in **16**, in fact, the *R,S* conformational enantiomers do not interconvert, as in **10**, owing to the hindrance of the *tert*-butyl group in position 2. This hindrance also increases the twist angle between the NO moiety and the naphthalene ring making negligible the a_H ring splittings and increasing the a_N splitting with respect to **10**. Actually the nitrogen splitting in **16** (a_N = 14.1 G) is even larger than that in **14** (13.5 G), thus suggesting that a "perpendicular" conformation is adopted. It is thus conceivable that in the homogeneous series **14–8** the decreasing bulkiness of R causes the nitrogen splitting to decrease more or less monotonically (Table II). The a_N values can thus become a measure of the twist angle between the planes containing Ar and RNO. The relationship between the a_N values of nitroxides **9–14** and the $\Delta G^{\ddagger}$ values of the analogous amines **1–6** cannot however be a linear one. This is because as the bulkiness of R increases, the twist angle will approach its maximum value of about 90°. The a_N splittings cannot therefore increase indefinitely but must eventually reach a limiting value. On the contrary, the $\Delta G^{\ddagger}$ values of the amines can, in principle, increase without limit if the bulkiness of R is continuously augmented. The two quantities are thus expected to be exponentially related in that, near the limiting value of the twist angle, large variations of $\Delta G^{\ddagger}$ will correspond to a smaller and smaller variation of a_N as this quantity asymptotically approaches its limit. The experimental values[23] collected in Tables I and II obey the relationship

$$\Delta G^{\ddagger} = 0.37 \exp(0.29 a_N)$$

with a correlation coefficient equal to 0.96. Introduction in this equation of the a_N splitting of nitroxide **8** (10.3_5 G) yields a $\Delta G^{\ddagger}$ value for amine **1** (R = Me) equal to 7.3 kcal mol^{-1}.

An estimate of the barrier, not otherwise measurable, has been thus obtained for the symmetric amine **1**.

Experimental Section

Unless otherwise indicated the ^1H NMR spectra were taken at 60 MHz and the ^{13}C NMR spectra at 25.16 MHz.

Materials. The tertiary *N,N*-dialkyl-1-naphthylamines can be prepared according to a general method which is described in detail for the case of **4**.

***N*-Isopropyl-*N*-methyl-1-naphthylamine (4).** To an ethereal 2 M solution of phenyllithium (37 mL, 75 mmol) was slowly (20 min) added a solution of *N*-isopropyl-*N*-methylamine (10 mL, 96 mmol) in anhydrous ether (25 mL). The temperature increased spontaneously to 40 °C and the system was left for 45 min under stirring. A solution of 1-bromonaphthalene (7 mL, 50 mmol) in anhydrous ether (25 mL) was subsequently added dropwise (15 min) and allowed to reflux overnight. The cooled mixture was treated with water and left overnight under stirring. Two phases were separated and the organic layer was washed many times, dried, and concentrated. The residue was distilled in vacuo (0.5

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(22) The larger of the two a_H splittings changes remarkably with the temperature (16.4 G at −40 °C and 14.5 G at 120 °C) but the line width of the spectrum remains essentially the same.

(23) In the equation a value of 18.5 rather than 19.1 kcal mol^{-1} was used for the barrier of **6** to correct for the effect of the chiral auxiliary on the barrier.

mmHg) and the 80–115 °C fraction (4.6 g) was passed through a silica gel column (eluent petroleum ether/ether 95:5) to yield 4 g of the pure compound: ^{1}H NMR (CCl_4, 300 MHz) δ 1.15 (6 H, d, CH_3CH) 2.75 (3 H, s, NCH_3) 3.63 (1 H, sept, $CHMe_2$) 7.05 (1 H, m, H-2) 7.2–7.5 (4 H, br m, Ar) 7.70 (1 H, m, H-5) 8.20 (1 H, m, H-8); ^{13}C NMR (CD_2Cl_2) δ 19.4 (2 C, CH_3) 33.8 (NCH_3) 54.6 (NCH) 116.3, 121.9, 123.5, 124.2, 124.8 (2 C), 127.4, 134.0 (quat) 140.2 (quat) 149.0 (quat). Anal. Calcd for $C_{14}H_{17}N$: C, 84.42; H, 8.54; N, 7.03. Found: C, 85.0; H, 8.7; N, 6.8.

Through a mechanism probably involving a benzyne-like intermediate this method,[24] in addition to **4**, also affords a substantial amount of the isomeric derivative **7** (*N*-isopropyl-*N*-methyl-2-naphthylamine): ^{1}H NMR (CCl_4) δ 1.18 (6 H, d, CH_3CH), 2.80 (3 H, s, NCH_3), 4.15 (1 H, sept, $CHMe_2$), 6.75–7.8 (7 H, br m, Ar); ^{13}C NMR (CHF_2Cl, −80 °C) δ 19.4 (2 C, CH_3), 30.1 (NCH_3), 51.0 (NCH), 108.4, 117.9, 118.9, 127.4 (2 C), 128.0 (quat), 128.6, 129.8, 136.2 (quat), 149.8 (quat).

Derivatives **2–6** were also obtained by reacting the appropriate secondary 1-naphthylamine with methyl iodide. For **3**, **5**, and **6** butyllithium rather than phenyllithium was employed. The raw materials were not distilled but chromatographed on a silica gel column using petroleum ether or petroleum ether/ether 95:5 as eluent. The compounds were identified as follows.

***N*-Ethyl-*N*-methyl-1-naphthylamine (2)**: ^{1}H NMR (CCl_4) δ 1.0 (3 H, t, CH_3CH_2), 2.7 (3 H, s, NCH_3), 2.95 (2 H, q, CH_2Me), 6.8–7.8 (6 H, br m, Ar), 8.2 (1 H, m, H-8); ^{13}C NMR ($CDCl_3$) δ 12.7 (CH_3, 41.6 (NCH_3), 51.5 (NCH_2), 115.7, 123.1, 124.1, 125.1, 125.7 (2 C), 128.2, 135.0 (quat) 150.4 (quat), one quaternary carbon was not detected. Anal. Calcd for $C_{13}H_{15}N$: C, 84.32; H, 8.11; N, 7.57. Found: C, 83.8; H, 8.3; N, 7.2.

***N*-(2,2-Dimethylpropyl)-*N*-methyl-1-naphthylamine (3)**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (9 H, s, $C(CH_3)_3$), 2.89 (3 H, s, NCH_3), 3.09 (2 H, s, NCH_2), 7.25–7.6 (5 H, m, Ar), 7.81 (1 H, br d, H-5) 8.41 (1 H, br d, H-8). Anal. Calcd for $C_{16}H_{21}N$: C, 84.58; H, 9.25; N, 6.17. Found: C, 85.0; H, 9.0; N, 6.5.

***N*-Methyl-*N*-pent-3-yl-1-naphthylamine (5)**: ^{1}H NMR (CCl_4) δ 0.93 (6 H, t, CH_3CH_2), 1.50 (4 H, m, CH_2Me), 2.73 (3 H, s, NCH_3) 3.10 (1 H, m, $CH(Et)_2$), 6.8–7.8 (6 H, br m, Ar), 8.1 (1 H, m, H-8); ^{13}C NMR (CD_2Cl_2, 0 °C) δ 11.75 (2 C, CH_3), 23.7 (2 C, CH_2) 33.5 (NCH_3), 65.7 (NCH), 117.5, 122.3, 124.7, 124.8, 125.7, 125.9, 128.6, 129.0 (quat), 135.0 (quat), 150.3 (quat); MS, molecular ion at *m/e* 227.16759, calcd 227.16739.

***N*-Methyl-*N*-*tert*-butyl-1-naphthylamine (6)**: ^{1}H NMR (CCl_4) δ 1.15 (9 H, s, $(CH_3)_3C$), 2.80 (3 H, s, NMe), 7.3–7.8 (6 H, br m, Ar), 8.6 (1 H, m, H-8); ^{13}C NMR (CHF_2Cl, −30 °C, 75.47 MHz) δ 27.6 (3 C, $(CH_3)_3C$) 38.3 (NCH_3), 56.7 ($C(CH_3)_3$), 125.6, 126.4, 126.45, 126.8 (2 C), 127.05, 128.9, 129.2 (quat), 135.6 (quat) 150.9 (quat); MS, molecular ion at *m/e* 213.15229, calcd 213.15175.

The secondary *N*-alkyl-1-naphthylamines used to generate the nitroxides **9–15** or to undergo further alkylation to yield the tertiary *N*-alkyl-*N*-methyl-1-naphthylamines **2–6** were prepared according to the following procedures.

***N*-Methyl-1-naphthylamine**[25] (mass spectrum, *m/e* 157 (M^+)), ***N*-ethyl-1-naphthylamine**[26] (bp 143–145 °C/4 mmHg, mass spectrum, *m/e* 171 (M^+)), and ***N*-isopropyl-1-naphthylamine** (bp 125–127 °C/1.5 mmHg, mass spectrum *m/e* 185 (M^+)) were obtained by reacting 1-naphthylamine with the appropriate alkyl iodide (CD_3I was used for labeling the *N*-methyl-1-naphthylamine; the deuteriated compound had a mass spectrum *m/e* 160 (M^+)) with molar ratio amine/iodide = 1.0–1.2. The reactions were carried out respectively for 6, 24, and 48 h in toluene at 60–80 °C. Sodium hydroxide was employed to recover the free amines from the ammonium salts. The raw materials were purified on a silica gel column (petroleum ether/ether 9:1 as eluent).

***N*-Isopropyl(4-bromo-1-naphthyl)amine** used to generate nitroxide **15** was obtained in the same way by reacting 4-bromo-1-naphthylamine with isopropyl iodide (molar ratio 1:2) in refluxing chloroform for 5 h: ^{1}H NMR (CCl_4) δ 1.13 (6 H, d, CH_3CH), 3.5 (1 H, sept, $CHMe_2$), 3.95 (1 H, br s, NH), 6.25 (1 H, d, H-2), 7–7.7 (4 H, br m, Ar), 8.1 (1 H, m, H-8); ^{13}C NMR ($CDCl_3$) δ 22.6 (2 C, CH_3), 44.5 (CH), 105.8, 120.15, 125.2, 126.9, 127.8, 130.3, 132.3 (quat), two quaternary carbons were not observed.

***N*-(2,2-Dimethylpropyl)-1-naphthylamine** (mass spectrum, *m/e* 213 (M^+)), ***N*-pent-3-yl-1-naphthylamine** (mass spectrum, *m/e* 213 (M^+)), and ***N*-*tert*-butyl-1-naphthylamine** (bp 140 °C/0.5 mmHg; mass spectrum, *m/e* 199 (M^+)) were obtained by reacting the appropriate alcohol with 1-naphthylamine. The reactions were carried out in an autoclave at high temperature (130–150 °C) for 24 or 48 h. When 2,2-dimethylpropanol and *tert*-butyl alcohol were employed the reaction was carried out under nitrogen pressure (50–90 atm). The reaction with *tert*-butyl alcohol also afforded as a secondary product the rearranged primary amine **(2-*tert*-butyl-1-naphthyl)amine**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.49 (9 H, s, $(CH_3)_3C$), 4.28 (2 H, br s, NH_2), 7.25 (1 H, d, H-4) 7.3–7.4 (2 H, m, H-6 and H-7), 7.47 (1 H, d, H-3), 7.71 (1 H, m, H-5), 7.80 (1 H, m, H-8). Evidence that for the latter compound the structure with the *tert*-butyl group in position 2 is correct is offered by the presence of the two mutually coupled doublets (AB group, J = 8.5 Hz) due to H-3 and H-4. Unambiguous assignment to H-4 of the doublet at 7.25 ppm (hence of that at 7.47 ppm to H-3) comes from the existence of an unresolved long range coupling[27] (which broaden the lines at 7.25) with H-8. Irradiation of the H-8 multiplet actually sharpens the lines at 7.25 ppm.

***N*-Ethyl(2-*tert*-butyl-1-naphthyl)amine**, used to generate nitroxide **16**, was prepared reacting at 120 °C 2-*tert*-butyl-1-naphthylamine with ethyl iodide in toluene (autoclave) for 18 h and treating the system with sodium hydroxide: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37 (3 H, t, CH_3CH_2), 1.50 (9 H, s, CH_3C), 3.16 (2 H, q, CH_2CH_3), 3.58 (1 H, br s, NH), 7.41 (2 H, br t, H-6 and H-7), 7.45 (1 H, d, H-4), 7.50 (1 H, d, H-3), 7.75 (1 H, m, H-5), 8.15 (1 H, m, H-8).

NMR Measurements. The NMR spectra at variable temperature were taken either with a Varian XL-100 (operating at 100 MHz for ^{1}H and 25.16 for ^{13}C) or with a Bruker CXP-300 spectrometer operating at 300 MHz for ^{1}H and 75.47 for ^{13}C. In the first instrument the temperature was monitored by substituting the sample with a thermistor; in the second one it was found more convenient to replace the examined samples with samples known to have temperature-dependent spectra. Methanol[28] was employed for the ^{1}H 300-MHz measurements and a mixture of CHF_2Cl/acetone-d_6 for the ^{13}C 75.47-MHz measurements.[1,29] In the experiments with the chiral auxiliary the required ratio between the components depends on the kind of the amine involved. For instance the 300-MHz ^{1}H signals of **2** were considerably split (264 Hz and 124 Hz for the methyl signals of the NMe and ethyl groups, respectively, at −110 °C in CD_2Cl_2) with an alcohol/amine ratio = 2.8/1. In the case of **3** an alcohol/amine ratio = 2/1 split the 300-MHz ^{1}H signal of the NMe group by 198 Hz, at −83 °C in CD_2Cl_2. In both **2** and **3** the separation of the shifts induced by the chiral alcohol decreased on raising the temperature,[5a,6] therefore the shift differences were monitored at six temperatures below the exchange region. Linear extrapolation of these differences at the coalescence (−88 °C for the methyl of the ethyl group in **2** and −47 °C for the methyl of the NMe group in **3**) yielded the shift differences (58 and 87 Hz, respectively) used to determine the rate constants, hence the $\Delta G^{\ddagger}$ values (Table I). In the case of **6** the splitting induced by the chiral auxiliary on the ^{1}H signal of the NMe group was much smaller, owing probably to steric effects. With an alcohol/amine ratio = 75/1 the separation of these signals was only 3.7 Hz at −10 °C (in toluene-d_8 at 300 MHz). The value increased to 4.6 Hz (at 6 °C) when the ratio was raised to 940/1. With such small differences the extrapolation method used in the case of **2** and **3** was far too inaccurate to obtain reliable shift differences at the coalescence. The following method was thus employed. The width of the lines under investigation (i.e. the methyl signals of the NMe group) was measured well below and above the temperature range of the exchange. The width of a reference line, not influenced by the

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exchange, was also measured at the same temperatures. The ratio of the line widths was then plotted as function of temperature, so that the ratios could be interpolated, at temperatures where exchange occurs. The use of the ratios guarantees that the results are not affected by variations of the spectrometer resolution at different temperatures. From the interpolated ratios and from the knowledge of the width of the reference line where exchange occurs, accurate values of the line width in absence of exchange were obtained for the pair of the NMe signals. The knowledge of the line widths allowed us to computer-simulate the line-shape in the coalescence region as a function of *both* the rate constant and the chemical shift difference. These two unknowns were thus simultaneously obtained with a satisfactory degree of accuracy, allowing the determination of a $\Delta G^{\ddagger}$ = 19.1 kcal mol^{-1} for the enantiomerization of **6**. Owing to the additional measurements required when the chiral auxiliary is employed, the errors on $\Delta G^{\ddagger}$ obtained in these conditions are larger: they were estimated to be ±0.3 kcal mol^{-1}. In the other cases the error is believed[1] to be ±0.15 kcal mol^{-1}.

ESR Measurements. The spectra were recorded with a Varian E-4 spectrometer. The *g* factors were measured by comparison with a sample containing solid DPPH in sodium chloride (*g* 2.0037). The nitroxides **8–16** were obtained by oxidizing the corresponding amines with *m*-chloroperbenzoic acid in toluene. The samples were degassed in vacuo by the usual thaw–freezing technique. The molar ratio amine/peracid was about 5–10:1 and the concentrations of the amines ranged between 10^{-3} and 10^{-2} M. If an excess of peracid was used, a second nitroxide was sometimes observed. For instance in the case of *N*-isopropyl-1-naphthylamine a second ESR spectrum appeared, in addition to the spectrum of **12**. On raising the temperature (+100 °C) this second radical disappeared, whereas at low temperature (−100 °C) it became the dominant species. This second nitroxide had a_N = 13.5 G and $a_H(CH)$ = 3.5 G and no splittings from the ring hydrogens. Analogous results were obtained with *N*-ethyl-1-naphthylamine (the corresponding secondary species had a_N = 13.2$_5$ G and $a_H(CH_2)$ = 9.0 G). Probably an excess of peracid introduces the -OCOAr (Ar = *m*-chlorophenyl) group into position 2 (and in position 4) of the naphthalene ring.[30] The presence of a substituent in position 2 would make the RNO plane more twisted with respect to the naphthalene ring than in the unsubstituted nitroxides **10** and **12**. This feature would account for the increased a_N values and for the absence of ring splittings in the secondary radicals.

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Registry No. **1**, 86-56-6; **2**, 83777-94-0; **3**, 110014-40-9; **4**, 110014-41-0; **5**, 110014-42-1; **6**, 110014-43-2; **7**, 110014-44-3; **8**, 61899-23-8; **9**, 110014-45-4; **10**, 110014-46-5; **11**, 110014-47-6; **12**, 110014-48-7; **13**, 110014-49-8; **14**, 41085-50-1; **15**, 110014-50-1; **16**, 110014-51-2; *N*-isopropylmethanamine, 4747-21-1; 1-bromonaphthalene, 90-11-9; *N*-ethyl-1-naphthalenamine, 118-44-5; *N*-(2,2-dimethylpropyl)-1-naphthalenamine, 110014-52-3; *N*-(3-pentyl)-1-naphthalenamine, 110014-53-4; *N*-*tert*-butyl-1-naphthalenamine, 54961-92-1; 1-naphthalenamine, 134-32-7; iodoethane, 75-03-6; 2-iodopropane, 75-30-9; *N*-isopropyl-1-naphthalenamine, 4960-23-0; *N*-methyl-1-naphthalenamine, 2216-68-4; *N*-methyl-1-naphthalenamine-*methyl-d*, 110014-54-5; 4-bromo-1-naphthalenamine, 2298-07-9; *N*-isopropyl-4-bromo-1-naphthalenamine, 110014-55-6; 2,2-dimethylpropanol, 75-84-3; *tert*-butyl alcohol, 75-65-0; 2-*tert*-butyl-1-naphthalenamine, 110014-56-7; *N*-ethyl-2-*tert*-butyl-1-naphthalenamine, 110014-57-8.

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π-Facial Selectivity in Diels–Alder Reactions of Hexacyclo[10.2.1.0^{2,11}.0^{4,9}.0^{4,14}.0^{9,13}]pentadeca-5,7-diene-3,10-dione

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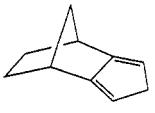
The reactions of the title diene (**2**) with olefinic dienophiles occur exclusively by attack on the carbonyl-bearing face of the diene component of **2**, while other dienophiles (benzyne, acetylenes, and azo compounds) exhibit mixed π-facial selectivities. X-ray crystal structures of the diene **5** and the diethyl azodicarboxylate adduct **47**, refined to conventional *R* values of 3.8% and 4.0%, respectively, are also reported.

Diels–Alder reactions of isodicyclopentadiene (**1**) and its derivatives have been extensively studied in recent years.[1] The origin of the observed π-facial selectivities



(1)

has been considered variously as resulting from product stabilities,[1b] polarizability effects,[1c] π-orbital tilting associated with σ/π interactions,[1d] and a combination of torsional and steric effects.[1e]

We now report a related study of the Diels–Alder reactions of the title diene (**2**) with a variety of dienophiles. This diene can undergo dienophile attack on either the carbonyl-bearing face of the diene to produce **3**, or on the opposite face to produce **4**. Although three Diels–Alder reactions of this diene had been previously reported,[2-4] the stereochemistry of the products was not known until our

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