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# Conformational studies by dynamic NMR. 33. Possible applications of the magic angle spinning technique for identifying meso and racemic conformers in the solid state

D. Casarini, L. Lunazzi, and Dante Macciantelli

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authors.[12,16] With isobutyl, this may be due to preferential backside migration of methyl from a more stable gauche form of the diazonium ion precursor rather than hydride migration from a more crowded conformer. The unusual behavior of these poorly solvated cations has been attributed to kinetic rather than the usual thermodyanamic factors.[20,21]

That primary unsolvated cations can be formed upon photolysis is not surprising since this method has been used to generate quite a number of high-energy cations difficult to prepare solvolytically, including bridgehead[5] and vinyl[22,23] (but not alkynyl[24]) cations.

The substitution pattern found from alkyl iodide photolysis with toluene also resembles that observed from cationic alkylation systems (Table IV)[12,25] and are somewhat different from alkyl radical substitution patterns.[26] This coupled with the lack of significant products resulting from the common benzylic hydrogen abstraction with toluene in most of the photolyses suggests that free-radical involvement in these reactions is minimal. However, photolysis with triethylamine additive did give rise to some radical coupling products, perhaps due to electron transfer from exited triethylamine to the alkyl iodide followed by loss of iodide.[27]

## Conclusions

The alkylation observed upon photolyses of primary alkyl halides in the presence of aromatic substrates is best explained as involving high-energy cations, which are trapped before they can undergo common hydride rearrangements.

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**Registry No.** PrI, 107-08-4; *i*-PrI, 75-30-9; BuI, 542-69-8; *sec*-BuI, 513-48-4; *i*-BuI, 513-38-2; *t*-BuI, 558-17-8; *i*-BuBr, 78-77-3; *t*-BuBr, 507-19-7; $I(CH_2)_4Me$, 628-17-1; $Et_2CHI$, 1809-05-8; $I(CH_2)_5Me$, 638-45-9; $MeCH(I)(CH_2)_3Me$, 18589-27-0; PrCHIEt, 31294-91-4; $I(CH_2)_6Me$, 4282-40-0; PhH, 71-43-2; PhMe, 108-88-3; PhOMe, 100-66-3.

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(22) McNeeley, S. A.; Kropp, P. J. *J. Am. Chem. Soc.* **1976**, *98*, 4319.
(23) Suzuki, T.; Kitamura, T.; Sonoda, T.; Kobayashi, S.; Taniguchi, H. *J. Org. Chem.* **1981**, *46*, 5324.
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(25) Olah, G. A.; Overchuck, N. A.; *J. Am. Chem. Soc.* **1965**, *87*, 5786.
(26) Kurz, M. E.; Frank, F. J.; Stronach, C., unpublished work.
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# Conformational Studies by Dynamic NMR. 33.[1] Possible Applications of the Magic Angle Spinning Technique for Identifying Meso and Racemic Conformers in the Solid State

D. Casarini and L. Lunazzi*

*Dipartimento di Chimica Organica, Università, 40136 Bologna, Italy*

Dante Macciantelli

*CNR, I.Co.C.E.A., Ozzano Emilia, Italy*

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The $^{13}C$ magic angle spinning NMR spectrum of a meso compound in the solid often displays a different number of lines with respect to its racemic isomer. Usually the meso isomers that have a symmetric conformation in the crystal are expected to yield the same spectral multiplicity as in solution (e.g., *meso*-2,3-dimethylsuccinic acid). Exceptions might in principle occur in the few cases when the center of molecular symmetry is not coincident with a center of crystallographic symmetry: examples of this type, however, were not encountered in the present work. On the other hand the isomeric racemic derivatives are normally expected to have solid-state spectra with a larger number of lines than in solution (e.g., *d,l*-2,3-dimethylsuccinic acid). In a very limited number of cases solid-state spectra with unsplit lines can be encountered: an example (*trans*-1,2-cyclohexanedicarboxylic acid) is reported here and discussed. In the case of *N,N'*-diisopropyl-*N,N'*-dimethyl-1,5-naphthyldiamine (1) the $^{13}C$ solution spectrum at −90 °C does show the existence of two conformers with unequal proportions: one of them being meso, the other racemic. The solid-state spectrum of 1 shows that some of the lines of the major conformer are split into two with respect to the solution spectrum whereas those of the minor conformer are unsplit, as in solution. On this basis the racemic structure has been tentatively assigned to the major conformer and the meso structure to the minor conformer. In favorable circumstances, as those here reported, these features might possibly be helpful in discriminating meso from racemic conformers when they cannot be physically separated nor investigated by X-ray diffraction.

## Introduction

Compounds existing in the meso and racemic (*d,l*) forms yield different NMR spectra in solution. The spectra differ in the chemical shifts and, to a lesser extent, in the coupling constants but in most cases display the same number of lines and the same multiplicity. As a consequence the structure often cannot be assigned on the basis of this spectral evidence.

When the meso and racemic compounds can be separated, other methods (e.g., X-ray diffraction) help in obtaining the correct assignment. However if the two forms interconvert rapidly into each other, i.e., when the meso

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(1) Part 31. Bonini, B. F.; Grossi, L.; Lunazzi, L.; Macciantelli, D. *J. Org. Chem.* **1986**, *51*, 517. Part 32. Casarini, D.; Lunazzi, L.; Placucci, G.; Macciantelli, D. *J. Org. Chem.*, in press.

**Table I. $^{13}$C NMR Chemical Shifts (in ppm with Respect to TMS) of the Two Conformers of *N*,*N*′-Diisopropyl-*N*,*N*′-dimethyl-1,5-naphthyldiamine (1) in Solution ($CD_2Cl_2$ at −90 °C) and in the Solid State (Room Temperature)[a]**

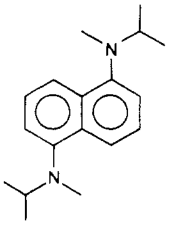
| compd | phase | C-1,5 | C-9,10 | other aromatics | | | NCH | $NCH_3$ | $CH_3$ | $CH_3$ |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 (minor) | solution | $149.4_5$ | 129.5 | 124.1 | 117.8 | 116.1 | $54.2_5$ | $31.0_5$ | 20.4 | $13.6_5$ |
| 1 (major) | solution | 149.3 | 129.7 | 124.0 | $117.5_5$ | 114.7 | $54.2_5$ | 30.6 | 20.4 | $13.9_5$ |
| **1a** (meso) | solid | 151.4 | 133.0 | 125.0 | 119.6 | 118.3 | 54.6 | 34.8 | 20.6 | 14.1 |
| **1b** (racemic) | solid | 151.4 | 131.6 | 125.5 | 120.9 | 116.8 | 54.6 | 32.5 | 20.6 | 16.0 |
| | | | | 124.5 | 119.6 | | | 31.7 | | 15.4 |

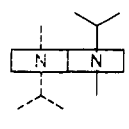
[a] Spectra were recorded at 75.47 MHz.

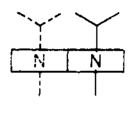
and racemic forms are conformers rather than configurational isomers, physical separation is impossible and unambiguous assignment of the structure cannot be easily achieved. In the present work it is shown that the solid-state NMR spectra of racemic and meso compounds may display different multiplicities. This feature could possibly be used as a guideline for a tentative assignment of their structure in favorable circumstances.

## Results and Discussion

An example illustrating the situation mentioned above is offered by *N*,*N*′-diisopropyl-*N*,*N*′-dimethyl-1,5-naphthyldiamine (1). This molecule does not stay in a planar conformation[2] since the dynamic planes containing the fast inverting *i*-Pr-N-Me moieties are significantly twisted with respect to the plane of the naphthalene ring. Both the $^1$H and $^{13}$C NMR solution spectra of 1 at low temperature display two groups of signals corresponding to a pair of conformers with a relative intensity of 4:1 (Figure 1). In both conformers the methyls of the isopropyl groups yield two signals at low temperature: they are in fact anisochronous since the twisted conformation creates chiral centers.[2] The existence of two such centers produces the meso and the racemic (*d,l*) conformers **1a** and **1b** that interconvert rapidly at room temperature, thus making the separation impossible.


**1**


**1a** (meso)


**1b** (racemic)

A line shape analysis of the pair of $^{13}$C signals of the $NCH_3$ group, as well as of one of the pairs of the aromatic CH signals, yields an activation energy for the interconversion process of 10.8 ± 0.15 kcal mol$^{-1}$. This value matches, as expected, the barrier obtained at the coalescence temperature (−33 °C) by monitoring the $^{13}$C signals of the anisochronous methyls of the two isopropyl groups in the major conformer. Unambiguous assignment of the meso and racemic structures to the two conformers cannot however be achieved[3] since both spectra have, as mentioned, the same number of signals (Table I) with the same multiplicity. The differences in the chemical shifts (Table I) do not allow an absolute structural correlation to be achieved.

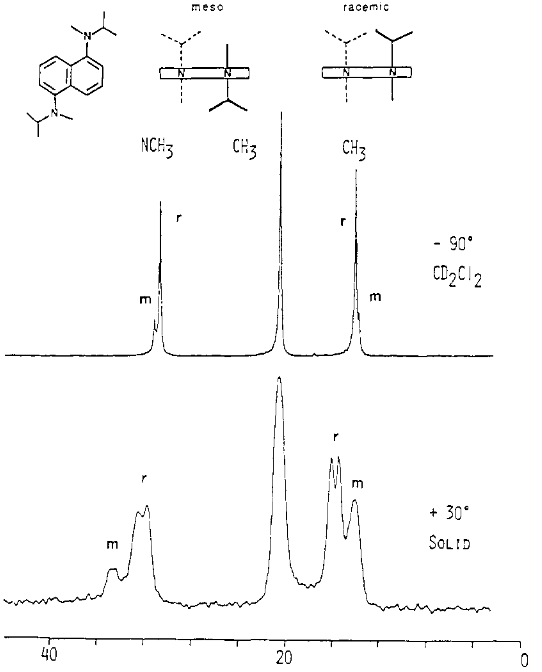


**Figure 1.** Methylic region of the $^{13}$C NMR spectrum (75.47 MHz) of *N*,*N*′-diisopropyl-*N*,*N*′-dimethyl-1,5-naphthyldiamine (1) in $CD_2Cl_2$ at −90 °C (upper) showing the existence of the racemic (r) and meso (m) conformer in a 4:1 ratio. Underneath is reported the corresponding spectrum in the solid state at +30 °C. The splitting of the lines at ~16 and ~32 ppm suggests that the asymmetric racemic structure corresponds to the more abundant conformer. Scale in ppm.

All the attempts of obtaining, by slow recrystallization from various solvents, crystals suited for X-ray diffraction failed: a direct determination of the structure of 1 could not therefore be achieved. In order to obtain indications concerning the most likely assignment of the meso and racemic conformers detected in solution, we made use of solid-state NMR spectroscopy.

A high-resolution $^{13}$C NMR spectrum of a crystalline material may present a multiplicity different from that observed in solution, owing to the effect of crystal packing. In some cases this feature can be related to the molecular symmetry and can thus be of some help in discriminating conformers of different symmetry.

In the solid in fact the intermolecular interactions between optically active (or racemic) systems are diastereomeric[4a] or, as other authors prefer to call them, chirodiastaltic.[4b] As a consequence optically active or racemic systems quite often display, in the solid-state $^{13}$C NMR spectra, a pair of equally intense signals for those equivalent carbons that are not related by a plane or a center

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(2) Casarini, D.; Lunazzi, L.; Macciantelli, D. *Tetrahedron Lett.* **1984**, *25*, 3641.

(3) Use of chiral discriminating agents is ineffective in this situation. Addition of optically active Pirkle's alcohols such as *l*-2,2,2-trifluoro-1-(9-anthryl)ethanol ($CF_3CHArOH$, where Ar = 9-anthryl) to a solution of 1 at −90 °C in $CD_2Cl_2$ did split the $^1$H NMR signals of *both* conformers. Interaction with the optically active alcohol does not occur simultaneously at both chiral centers, thus destroying the symmetry of the meso conformer which behaves, in these conditions, in a manner analogous to a racemic mixture.

(4) (a) Jacques, J.; Collet, A.; Wilen, S. H. *Enantiomers, Racemates and Resolution*; Wiley: New York 1981. (b) Craig, D. P.; Mellor, D. P. *Top. Curr. Chem.* **1976**, *63*, 1.

**Table II. Solution and Solid-State $^{13}C$ NMR Chemical Shifts (in ppm from TMS) of the Meso and Racemic Isomers of 2,3-Dimethylsuccinic Acid (2 and 3, Respectively), of *cis*- and *trans*-2,3-Cyclohexanedicarboxylic Anhydride (4 and 5, Respectively), and of *cis*- and *trans*-2,3-Cyclohexanedicarboxylic Acid (6 and 7, Respectively)**

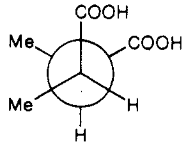
| compd | phase | CO | CH | $CH_2$ | $CH_2$ | $CH_3$ |
|---|---|---|---|---|---|---|
| **2** (meso) | solution[a] | 177.9 | 42.0 | | | 14.6 |
| | solid | 182.8 | 42.4 | | | 16.3 |
| **3** (racemic) | solution[a] | 178.7 | 41.1 | | | 13.2 |
| | solid | 182.7 | 41.0 | | | 9.9 |
| | | | 42.4 | | | 16.3 |
| **4** (cis) | solution[b] | 172.9 | 40.4 | 23.7 | 21.9 | |
| | solid | 173.1 | 38.1 | 23.6 | 20.5 | |
| | | 174.5 | 39.8 | 24.3 | 21.5 | |
| | | 175.1 | 40.1 | 25.0 | 21.5 | |
| | | 175.3 | 40.5 | 27.2 | 21.9 | |
| **5** (trans) | solution[b] | $170.3_5$ | 46.9 | 25.2 | 24.9 | |
| | solid | 170.6 | 42.1 | 22.5 | 21.5 | |
| | | | 42.9 | | | |
| **6** (cis) | solution[c] | 176.7 | 42.2 | 26.0 | 23.5 | |
| | solid | 182.0 | 41.8 | 25.6 | 22.9 | |
| | | 182.8 | 42.6 | 28.8 | | |
| **7** (trans) | solution[c] | 177.9 | 44.7 | 28.8 | 25.1 | |
| | solid | 183.2 | 41.4 | 29.1 | 25.7 | |

[a] In $CDCl_3$/acetone-$d_6$. [b] In $CDCl_3$. [c] In $CDCl_3/CD_3OD$.

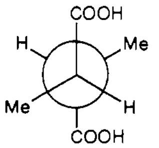
of symmetry.[5] On the other hand in the meso forms the same carbons are related through a plane or a center of symmetry, and if this relationship is maintained in the solid, the pairs of symmetry related carbons are expected to give in the majority of cases single signals, as they do in solution.[6]

The possibility of a different spectral behaviour for a meso and a racemic isomer in the solid has been checked by recording the cross polarization (CP) magic angle spinning (MAS) $^{13}C$ spectra of the meso (**2**) and *d,l* (**3**) isomers of 2,3-dimethylsuccinic acid (HOOCCHMeCHMeCOOH). Whereas the spectrum of **2** yields three lines corresponding to the CO, CH, and Me carbons (Table II), in the spectrum of **3** the lines of the CH and Me carbons are split into two (Figure 2). The fact that the two carbonylic carbons of **3** give a single signal is due to the accidental degeneracy of their chemical shifts.

In order to observe a different multiplicity between a meso (that has a plane or a center of symmetry) and a racemic isomer it is obviously necessary that the meso adopt a symmetric conformation in the crystal: only in this way can the dynamic solution symmetry (where different conformers, including the asymmetric ones, may be populated) be maintained in the solid state, where exchange among conformers rarely occurs. Therefore from the spectrum of Figure 2 it can also be inferred that of the two possible conformers gauche (**2a** and anti (**2b**), the latter is the only one which is populated in the solid.



**2a** (gauche)



**2b** (anti)

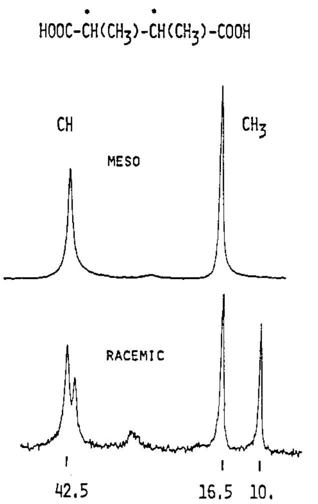


Figure 2. Aliphatic region of the $^{13}C$ NMR solid-state spectra (67.92 MHz) of the two isomers of the 2,3-dimethylsuccinic acid. The meso isomer **2** yields a single line for each pair of carbons (upper trace). The racemic isomer **3** gives two lines for the same carbons (lower trace) since in this isomer the pairs of CH and of $CH_3$ carbons are not related by a plane or a center of symmetry. The unequal intensities of the lines within each doublet in the spectrum of **3** are due to impurities of **2** present in the sample. Scale in ppm.

Had in fact the gauche conformation (**2a**) been preferred, the spectrum of the meso isomer **2** would have exhibited the same kind of splitting observed in **3**, since conformation **2a** does not possess any element of symmetry. This conclusion matches the results of an X-ray investigation[7] which indicates the anti as the only populated conformation for the *meso*-2,3-dimethylsuccinic acid (**2**) in the solid.

The possibility that in some molecules the meso derivative loses its dynamic element of symmetry by adopting, in the crystal, an asymmetric conformation should never be neglected. Such an example is offered by *meso*-tartaric acid which, in the crystal, is known to have a gauche conformation lacking any element of symmetry.[8] In the solid, however, the unit cell of the *meso*-tartaric acid contains pairs of *d* and *l* gauche conformers.[8] Accordingly the lines of its solid-state NMR spectrum are all split, as are those of the optically active and of the racemic tartaric acid.[5] When such a situation occurs the information obtained from the solid-state NMR spectrum is not useful for discriminating between meso and racemic configurations. The existence of a splitting, however, indicates that the conformation adopted by the meso derivative is asymmetric; a result that agrees with the X-ray diffraction structure.[8] This conclusion, although valid in the present case and possibly in many other circumstances, should not be unduly generalized since another situation could be, in principle, responsible for the splitting, even when a symmetric conformation is adopted in the solid. This might happen when the meso derivative occupies a site in the crystal which does not possess the full symmetry of the molecule (site symmetry lower than molcular symmetry).[9,10] Although the center of molecular symmetry is very often retained as a crystallographic center, the possibility that in some cases the two centers do not coincide has to be considered. In this event split signals can be observed even for those pairs of nuclei related by a center of molecular symmetry.

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(5) Hill, H. D. W.; Zens, A. P.; Jacobus, J. *J. Am. Chem. Soc.* **1979**, *101*, 7090.

(6) Lipmaa, E. T.; Alla, M. A.; Pehk, T. J.; Engelhardt, G. *J. Am. Chem. Soc.* **1978**, *100*, 1930.

(7) Sirigu, A.; Temussi, P. A.; Ganis, P.; Corradini, P. *Ric. Sci.* **1967**, *37*, 676.

(8) Bootsma, G. S.; Schoone, J. C. *Acta Crystallogr.* **1967**, *22*, 522.

(9) Lyerla, J. R.; Yannoni, C. S. *Acc. Chem. Res.* **1982**, *15*, 208.

(10) Fyfe, C. A. *Solid State NMR for Chemists*; C.F.C.: Guelph, 1984; pp 454–455.

Another example where a meso derivative adopts an asymmetric conformation in the solid state is offered by *cis*-1,2-cyclohexanedicarboxylic anhydride (**4**) that corresponds to a meso form having, in solution, a dynamic plane of symmetry due to the fast ring reversal. In the solid state, on the contrary, there is not such a plane since the axial carbonyl group does not exchange with the equatorial one: derivative **4**, therefore, is not a meso compound in the solid state. A spectrum having more signals than the four lines observed in solution should therefore be expected. The same feature is also expected for its trans isomer (**5**), since the latter corresponds to a racemic form with both carbonyl groups in the two equatorial positions. A split solid state spectrum has been actually observed for **5** (Table II) in that the CH signal turns out to be a doublet (the CO signals are degenerate and the two $CH_2$ signals are to broad to allow detection of a further spitting). Also the spectrum of **4** displays, as predicted, more lines than in solution: however, whereas in most cases each carbon with a different chemical environment would yield a single signal, in **4** the eight different carbons yield 16 lines. This apparently depends upon the fact that the asymmetric unit in the crystalline powder of **4** employed in the NMR experiment does not correspond to a single molecule but rather to a pair of molecules, although the X-ray diffraction indicates that one molecule is the asymmetric unit in the single crystal of **4** ($Z = 4$, space group $P2_12_12_1$) where only one of the two possible enantiomers was found to be present.[11] On the other hand, the corresponding acid [i.e., *cis*-1,2-cyclohexanedicarboxylic acid (**6**)] displays, as normally expected, eight lines for the eight different carbons (two methylenic carbons yielding degenerate signals, seven lines are actually reported in Table II).

It seems thus possible to suggest that in many cases the meso isomers are likely to yield, in the solid state, the same unsplit spectrum observed in solution, provided they adopt in the crystal a symmetric conformation; on the other hand their racemic isomers are normally expected to have the single signals of their solution spectra split into a greater number of lines.[12]

There is, however, a possible exception to this last statement, which might occur in the case of a racemic compound having a C-2 molecular axis coincident with a C-2 crystallographic axis of symmetry. Such a situation is expected to be relatively rare since the great majority (~70%) of racemic compounds crystallize[4a] in the space groups $P2_1/c$ and $P\bar{1}$ where there is not a crystallographic axis C-2. For instance, the racemic tartaric acid as well as the *cis*-1,2-cyclohexanedicarboxylic acid (**6**), which possess a C-2 molecular axis of symmetry, yield split NMR spectra since they both crystallize in the $P\bar{1}$ space group.[5,13a] Furthermore not all the racemic compounds have a C-2 molecular axis of symmetry. In addition, even when a racemic derivative with a binary molecular axis crystallizes in one of the less frequently encountered space groups possessing a C-2 crystallographic axis, the two axes might not be coincident. An example is offered by the racemic 2,3-dimethylsuccinic acid (**3**): although its space group[7] is $P2/c$ (which has a crystallographic binary axis) its solid-state NMR spectrum displays two different signals for the pairs of carbons related by the axis C-2 (Figure 2 and Table II).

The probability of observing an unsplit NMR spectrum in a racemic derivative is therefore rather low and, in practice, is restricted to some of the compounds crystallizing in the $C2/c$ space group since its statistical frequency is not negligible (~15%).[4a] An example could be found in the case of the *trans*-1,2-cyclohexanedicarboxylic acid (**7**). This racemic derivative crystallizes in fact in the $C2/c$ group and the molecular C-2 axis is retained as a crystallographic element of symmetry.[13b] Accordingly the corresponding NMR spectrum displays, in the solid state, only four sharp signals for the four pairs of carbons, as in the solution spectrum (Table II): the asymmetric unit corresponds here to half a molecule.

Having explored some of the possible features that can be expected for the solid-state $^{13}C$ NMR spectra of meso and racemic compounds of known configuration, an attempt was made to interpret the spectrum of **1** on the basis of the different symmetry of its meso and racemic conformers.

The solid-state CP-MAS $^{13}C$ spectrum of the methylic region of **1** (taken at room temperature) is shown in Figure 1 underneath the corresponding signals recorded in solution at −90°C. In the solid the two conformers **1a** and **1b** do not interconvert at room temperature, so that distinguishable spectra can be observed for the meso and the racemic forms. The chemical shifts[14] and the conformer ratio in the crystal are similar to those observed in solution. In the solid, however, *two aliphatic* and *two aromatic* carbons of the major conformer have their signals split into two (Table I). On the contrary the signals of the minor conformer are unsplit.[16] Since in this case the structure of the meso conformer (**1a**) entails a center of symmetry, the spectral features seem to indicate that the most likely assignment is that where the meso structure (**1a**) corresponds to the minor conformer with unsplit signals and the racemic structure (**1b**) to the major conformer with split signals.

The possibility that the conformer meso adopts, even in the solid, the idealized centrosymmetric arrangement of the type **1a** that entails a center of symmetry is supported by the structure reported for a similar flexible molecule, i.e., *N*,*N*′-diisopropyl-1,5-naphthyldiamine (**8**).

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[11] Powel, A.; Woller, K. H.; Strumpel, M.; Luger, P. *Cryst. Struct. Commun.* **1982**, *11*, 647.

[12] Great care has to be taken to avoid the trap of an asymmetric racemic structure yielding an unsplit spectrum (which thus mimics a meso derivative) owing to the accidental degeneracy of the spectral lines. Since the line width in the solid is relatively broad (normally 30–60 Hz) this possibility should not be neglected. The smaller the number of carbons in the moleoule, the greater is the risk that such an event might occur.

[13] (a) Benedetti, E.; Pedone, C.; Allegra, G. *J. Phys. Chem.* **1970**, *74*, 512. (b) Benedetti, E.; Corradini, P.; Pedone, C.; Post, B. *J. Am. Chem. Soc.* **1969**, *91*, 4072.

[14] In solution the N-$CHMe_2$ rotation is always rapid, even at −90 °C, and the methyls of the isopropyl groups become anisochronous (both in the meso and *d*,*l* conformers) in that chiral centers are created at low temperature. The nonequivalence of these methyls in the solid is due on the other hand, to a "frozen" N-$CHMe_2$ rotation.[15] The fact that the chemical shift difference remains similar seems however to indicate that the rotational arrangement adopted in the solid by the isopropyl moiety is also the most populated in solution.

[15] Grombridge, C. J.; Harris, R. K.; Packer, K. J.; Say, B. J.; Tanner, S. F. *Chem. Commum.* **1980**, 174.

[16] The splitting of the NMe signal could be due, rather than to the lacking of symmetry, to the failure of the magic angle spinning in completely removing the dipolar coupling between $^{13}C$ and $^{14}N$ that has a substantial quadrupolar moment.[15,17–20] This interpretation is supported by the slight asymmetry of this doublet and by the observation that the shape of the corresponding signal in the minor conformer (that should not be split in absence of a C–N interaction) could be better computer simulated by a pair of lines (rather than by a single line) having the same width (60 Hz) as the lines of the major conformer and an internal separation of 40 Hz. Of course such interpretation cannot account for the other splittings observed in the major conformer.

[17] Opella, S. J.; Frey, M. H.; Cross, T. A. *J. Am. Chem. Soc.* **1979**, *101*, 5856.

[18] Zumbulyadis, N.; Henrichs, P. M.; Young, R. H. *J. Chem. Phys.* **1981**, *75*, 1603.

[19] Kessler, H.; Zimmerman, G.; Förster, H.; Engel, J.; Oepen, G.; Sheldrick, W. S. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 1053.

[20] Diaz, L. E.; Morin, F.; Mayne, C. L.; Grant, D. M.; Chang, C. *Magn. Reson. Chem.* **1986**, *24*, 167.

The X-ray diffraction shows[21] in fact that 8 has a centrosymmetric structure with the center of molecular symmetry coincident with the center of crystallographic symmetry ($Z = 2$, space group $P2/c$).

On warming the crystal of 1 below its melting point (83 °C) the signals of the two conformers broaden and eventually coalesce (+72 °C) in a way similar to that observed, albeit at much lower temperature, in solution. Above 72 °C the splittings detected at room temperature for the signals of the major conformer (racemic) also disappear. This is the consequence of the fact that the molecule, as a whole, has now a dynamic center of symmetry, and, accordingly, a single signal is expected for each pair of symmetry related carbons, as previously discussed. On further raising the temperature the compound melts, eventually yielding the same spectrum observed in solution at room temperature.

## Conclusion

The observation of a different multiplicity in the solid-state NMR spectra of symmetric and asymmetric molecules can be used, in favorable circumstances, as a possible guideline for attempting the assignment of meso and racemic structures to pairs of conformers that cannot be separated. Although this approach can give useful indications when X-ray diffraction cannot be employed, it is by no means an unambiguous method since crystal-packing effects, in addition to molecular symmetry, are also responsible for the multiplicity of the spectral lines observed in the solid-state NMR spectra. Nonetheless the method is expected to work in the majority of cases because of the statistical abundance of the favorable space groups where the crystals of meso and racemic derivatives can give different NMR spectra.[4a]

## Experimental Section

***N,N'*-Diisopropyl-*N,N'*-dimethyl-1,5-naphthyldiamine (1).** To an ethereal solution (10 mL) of 2.5 g (10.3 mmol) of *N,N'*-diisopropyl-1,5-naphthyldiamine (8) kept at −30 °C was added dropwise 19 mL of a 1.2 M solution of PhLi (23 mmol) in ether and left to react for 3–4 h. A yellow precipitate was observed. Subsequently a solution of 2 mL (30 mmol) of methyl iodide in 5 mL of ether was added and the system allowed to react for 3 h. The temperature was then increased to 0 °C, and water was added. The system was extracted with ether, dried, and evaporation of the solvent in vacuo left a residue (3.5 g) that was passed through a silica column (eluent, petroleum ether/ether, 9:1) to yield 1.2 g of 1 (mp 83–84 °C) as well as the monomethylated derivative and unreacted starting material, which were further reacted in the same way to obtain an additional amount of 1: mass spectrum, $m/e$ 270 ($M^+$); $^1$H NMR ($CCl_4$) $\delta$ 1.1 (d, $J$ = 11 Hz, 12 H, $CH_3CH$), 2.7 (s, 6 H, $NCH_3$), 3.55 (sept, $J$ = 11 Hz, 2 H, $NCHMe_2$), 6.9–8 (m, 6 H, Ar); $^{13}$C NMR ($CDCl_3$) $\delta$ 18.6 ($CH_3$), 33.3 ($NCH_3$), 54.2 (NCH), 116.7 (CH), 119.0 (CH), 124.6 (CH), 129.0 (C quat), 149.0 (NC quat). Anal. Calcd for $C_{18}H_{26}N_2$: C, 79.94; H, 9.70; N, 10.36. Found: C, 79.4; H 10.0; N, 10.5.

***N,N'*-Diisopropyl-1,5-naphthyldiamine (8). Method a.** A solution of commercially available 1,5-naphthyldiamine (10 g, 63 mmol) and isopropyl iodide (16 mL, 158 mmol) in 50 mL of dimethylformamide was refluxed overnight. Additional isopropyl iodide (16 mL) was added and further reacted overnight at 90 °C. The insoluble residue was filtered off, and the solution was concentrated, treated with water (50 mL), extracted with ether, and dried. Evaporation of the solvent yielded a residue that was dissolved in petroleum ether: the insoluble residue was filtered off and the solution chromatographed on a silica column (petroleum ether/ether, 9:1) to yield 2.8 g of the compound (mp 135–137 °C from ethanol).

**Method b.** To a boiling solution of 10.3 g (65 mmol) of 1,5-naphthyldiamine in 300 mL of ethanol was added a mixture of triethylamine (20.2 g, 200 mmol) and isopropyl iodide (34 g, 200 mmol) and allowed to react for 6 h. Additional isopropyl iodide (8 g) was then introduced and the reaction carried out for a further 2 h. The solvent was evaporated, and water was added to dissolve most of the solid residue. After extraction with chloroform the solid residue still present was filtered off. The chloroform solution was dried, and evaporation of the solvent yielded a residue that was chromatographed on a silica column by using benzene as eluent: 3.5 g of the desired compound was obtained: mass spectrum, $m/e$ 242 ($M^+$); $^1$H NMR ($CDCl_3$) $\delta$ 1.3 (d, $J$ = 11 Hz, 12 H, $CH_3CH$), 3.8 (sept, $J$ = 11 Hz, 2 H, $NCHMe_2$), 4.2 (br s, 2 H, NH), 6.5–7.5 (m, 6 H, Ar); $^{13}$C NMR ($CDCl_3$) $\delta$ 22.8 ($CH_3$), 44.3 (NCH), 105.1 (CH), 108.3 (CH), 124.5 (C, quat), 125.2 (CH), 142.9 (NC quat). Anal. Calcd for $C_{16}H_{22}N_2$: C, 79.27; H, 9.16; N, 11.56. Found C, 79.9; H, 9.5; N, 11.2.

**NMR Measurements.** The $^{13}$C NMR spectra in solution were run on a Bruker CXP-300 spectrometer (high-field NMR service of CNR, Bologna) at 75.47 MHz. In the low-temperature experiments the temperature was monitored by substituting the sample with a sealed tube containing acetone-$d_6$ and $CHF_2Cl$. The chemical shifts of this sample are known to be temperature dependent and had been previously calibrated.[1,22] The solid-state spectra were recorded either at 75.47 MHz (Bruker CXP-300) or at 67.92 MHz (JEOL 270). Thanks are due to S. Aime (Turin), H. Förster (Karlsruhe), and A. Hasenindle (Freiburg, FRG) who kindly ran some of the spectra. A few hundred transients were accumulated, the delay time was about 30 s and the spinning rate 2.5 kHz. Owing to its low melting point (32 °C) the CP-MAS spectrum of 4 has been run at low temperatures (+20 and −40 °C).

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