# Asymmetric Transformation of *N*-Nitrosamines by Inclusion Crystallization with Optically Active Hosts

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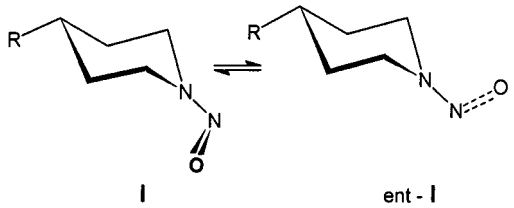
Several *N*-nitrosopiperidines with chirality solely due to a hindered rotation about the N−N bond were resolved to enantiomers by inclusion crystallization with optically active diols (TADDOLs). The absolute configuration of the guest nitrosamines was deduced from the X-ray crystal structures of the inclusion complexes. The enclathrated nitrosamines were liberated by a competitive complexation of the host diols with piperazine. The optical activity of the resolved nitrosamines is manifested by their CD spectra. A simple chirality rule was proposed for a rationalization of the observed Cotton effect sign corresponding to the n−$\pi$* electronic transition. The optically active nitrosamines are configurationally labile compounds and gradually racemize in solution but they are indefinitely stable in the solid state. The first-order kinetics of the racemization in solution allowed us to assign the N−N rotation barriers by simple polarimetric measurements.

## Introduction

*N*-Nitrosamines are known to be strong carcinogenic and mutagenic agents and therefore are the subject of continuing interest for biological chemists.[1] These compounds are also useful synthetic intermediates for a preparation of various N,N-bonded functionalities.[2] Furthermore, owing to their easy lithiation, followed by reaction with electrophiles and subsequent denitrosation, they can be used for the electrophilic substitution of the secondary amines at the α-carbon in a regio- and stereoselective manner.[3] A hindered rotation about the N−N bond, being a consequence of a partial double-bond character between two adjacent nitrogens, results in many intriguing stereochemical features of this class of compounds.[4] A substitution of the nitroso group at the nitrogen atom of the secondary amines lowers their symmetry and in the absence of any improper symmetry axis such simple molecules such as *N*-nitrosopiperidine (**1**) and its substituted analogues **2**−**7** are chiral. It should be noted that the chirality of the compounds **2**−**7** results solely from the restricted N−N rotation and interconversion between the enantiomers occurs by rotation of the nitroso group. Since the corresponding energy barrier is relatively high (23−25 kcal/mol)[5] it seems reasonable to expect that isolation of stereoisomers should be possible at ambient temperature. The optical resolution of this kind of compound would afford potential chiral auxiliaries for asymmetric synthesis and useful models for studying chiroptical spectra of the nitrosamino chromophore. Owing to a weak long-wavelength absorption near 370 nm, nitrosamines can be considered as chromophoric derivatives of the secondary amines, and their circular dichroism (CD) may be useful for configurational and conformational assignments of the parent amines. Therefore, a great deal of efforts has been devoted toward explanation of the Cotton effect sign of the nitrosamino chromophore.[6]

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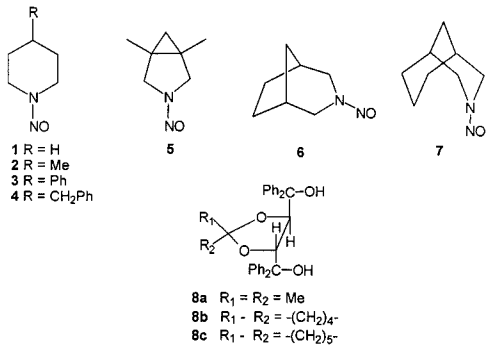


In this paper we describe a simple method of separation of the nitrosamines **3**−**7** into enantiomers by enclathration with the chiral hosts (*R*,*R*)-**8a**, (*R*,*R*)-**8b**, or (*R*,*R*)-**8c**.[7] The absolute configuration of the guest molecules was assigned by X-ray crystallographic studies of the corresponding inclusion crystals. We also report the CD spectra of the complexed as well as the liberated nitrosamines.

## Results and Discussion

The optical resolution of racemates devoid of any additional functional groups is a serious task and cannot be achieved by classical methods.[8] The inclusion crystallization of racemic compounds with optically active hosts is a technique that receives increasing significance in recent years.[9] An important contribution to this field has been made by Toda and co-workers,[10] and other Japanese groups.[11] Recently, we have been able to resolve simple *N*-nitrosopiperidines **1** and **2** by inclusion in the crystal matrixes of cholic and deoxycholic acids.[12] However, attempts to use this method for resolution of compounds **3**−**7** failed. Clearly, these molecules are too big to fit to the empty channels in the crystal lattices of the bile acids and do not form inclusion crystals. These observations prompted us to check the efficiency of some other hosts as resolving agents.

The chiral diols (*R*,*R*)-**8a**, (*R*,*R*)-**8b**, and (*R*,*R*)-**8c**, known as TADDOLs (α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols), are easily accessible from (+)-tartaric acid.[13] They have found a broad application in asymmetric synthesis[13a,14] and enantioselective photocyclizations in the solid state.[15] There are also several examples of successful optical resolutions of racemic ketones,[16a] lactones,[16b] pyrazolines,[16c] and amino and hydroxy esters[16d] by enclathration with these hosts. We found that they are also very useful for our purpose. Thus the 1:1 inclusion complexes of the nitrosamines **3**−**7** with the diols (*R*,*R*)-**8a**−**c** were prepared by cocrystallization of the equimolar amounts of the corresponding compounds from a mixture of toluene and hexane at room temperature. However, the compound **3**, after choosing a proper component proportion, forms 1:1 or 2:1 host−guest complexes with **8b**, as evidenced by $^1$H NMR spectra.

The X-ray diffraction studies of the inclusion complexes **3·8b**, **4·8a**, **4**·2**(8b)**, **5·8a**, **6·8a**, **6·8c**, and **7·8b** were performed to assign the absolute configuration of the guest nitrosamine molecules and to estimate the enantioselectivity of the inclusion crystallization. The structures of **3·8b**, **4·8a**, **4**·2**(8b)**, and **7·8b** revealed that the nitroso group in the guest nitrosamines is disordered over two positions; however, the occupancy factors of these orientations substantially differ from 0.5, indicating a significant enrichment of the nitrosamine sample in one enantiomer. The enantiomer ratio estimated from the occupancy factors for **7·8b** is of 85:15, whereas in the case of **3·8b**, **4·8a**, and **4**·2**(8b)** it is close to 3:1. A different pattern of disorder was observed in the crystal structures of **6·8a** and **6·8c**, where the bicyclic skeleton of the guest molecule occupies two different positions and the NO group is fixed in one orientation. In both cases the same enantiomer is preferentially complexed by the chiral hosts, and the estimated stereoisomer ratio is about 3:2. Fortunately, no obvious guest disorder was detected in the crystal of **5·8a**, and it is very likely that only one enantiomer of the guest nitrosamine is selectively incorporated into the host matrix. Elucidation of the crystal packing of **5·8a** (Figure 1) reveals that the presence of the intermolecular hydrogen bonding between the N═O oxygen and the hydroxyl group of the host, which favors one of the two possible orientations of the nitroso group, is responsible for a selective inclusion of the one enantiomer of **5**. In this case, during the formation of the **5·8a** crystals (also **5·8b**, as evident from the CD data), a whole quantity of the racemate was converted into one enantiomer. This process can be considered as an example of a complete asymmetric transformation.[17] It is important to note that the asymmetric transformation occurs also during the inclusion crystallization of the remaining nitrosamines, since in all cases the yields of the resolution exceeds 50%. This is apparently due to a configurational lability of the nitrosamines studied.

Since the configurations of host compounds **8a**−**c** are known, the absolute configurations of the guest molecules can be easily deduced from the X-ray crystal structures of the complexes **3·8b**, **4**·2**(8b)**, **5·8a**, **6·8a**, **6·8c**, and **7·8b**. Thus, the *R* configuration was assigned to (−)-**3** and (−)-**4**, whereas (−)-**5**, (+)-**6**, and (−)-**7** assume the *Z*, *E*, and *Z* configuration (geometric enantiomerism),[18] respectively (Figure 2). The configuration of the guest molecules in the remaining complexes can be easily elucidated from

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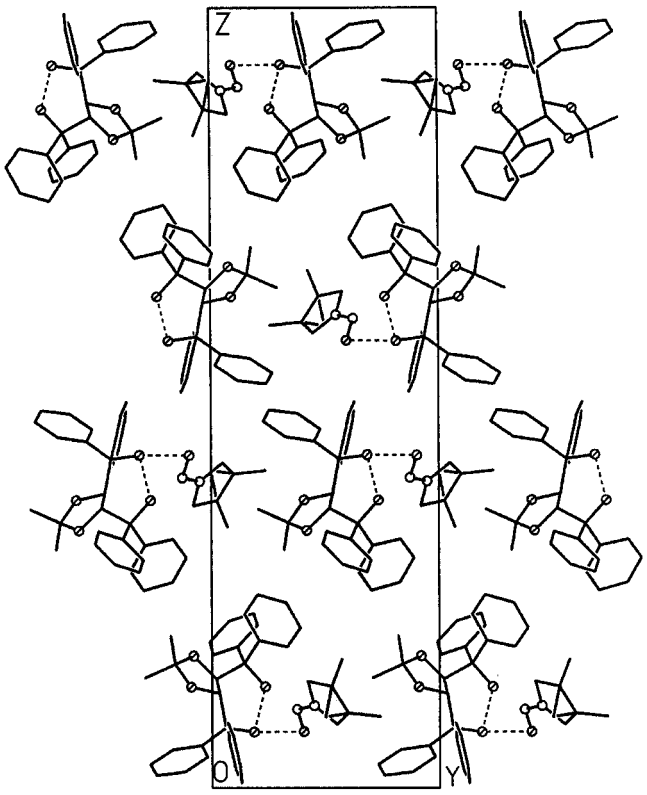


**Figure 1.** X-ray crystal structure of the complex of **5·8a** viewed along the *x*-axis. Broken lines represent the hydrogen bonds.

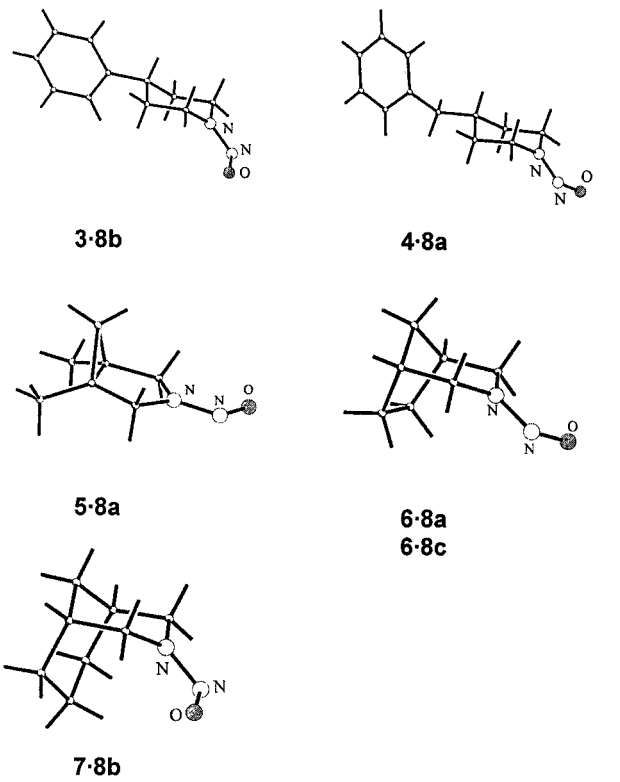


**Figure 2.** Molecular structures of the guest nitrosamines in (a) **3·8b**, (b) **4**·2(**8b**), (c) **5·8a**, (d) **6·8c**, and (e) **7·8b** showing the absolute configuration of the major enantiomer.

the corresponding CD spectra by a comparison of their Cotton effect sign with that of the compounds of the known absolute stereochemistry.

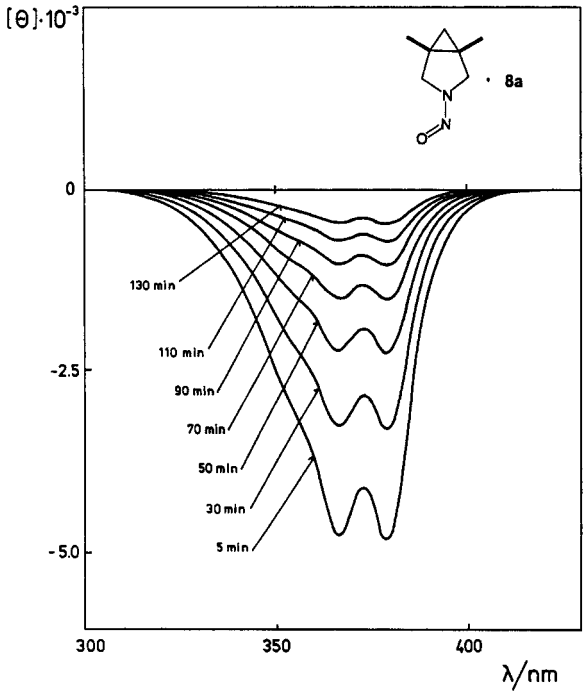


**Figure 3.** Decay of the CD signal of the **5·8a** solution in toluene at 22 °C.

The nitrosamines **3**−**7** were of particular value for us because they are easily crystallizing species and could retain their optical activity upon isolation in the enantiomeric form over a long period of time at room temperature. Column chromatography or fractional distillation are commonly used for the separation of guest compounds from the host diols **8a**−**c**.[9,15a] Evidently neither of these techniques is suitable for unstable or rapidly racemizing compounds such as nitrosamines. Therefore, bearing in mind the reported strong affinity of **8a**−**c** to secondary amines,[19] we developed a new and simple procedure for the liberation of the enclathrated nitrosamines. It can be accomplished by a competitive complexation of the host diols with piperazine. This diamine forms with **8b** a very stable 1:2 complex of high symmetry (trigonal, space group $P3_221$), which is almost insoluble in nonpolar solvents. The optically active nitrosamines **3**−**7** were isolated by a treatment of the inclusion complexes with piperazine in $Et_2O$ at 0 °C, followed by a filtration of the precipitated piperazine complex, evaporation of the solvent, and crystallization of the product. Obviously, all these operations should be carried out as quickly as possible to avoid a significant loss of the optical activity of the nitrosamines. The optical activity of the complexed and the liberated guest compounds can be detected by the CD measurements in solution (Figures 3 and 4). Since the nitrosamine n−$\pi$* band does not interfere with the absorption of the phenyl chromophore in the host diols, the shape of the CD curves in both cases are essentially the same (Table 1).

The X-ray structure of the racemic nitrosamine **4** revealed that this compound crystallizes in the enantiomorphous space group $P2_12_12_1$. Usually it means that the racemic mixture forms a conglomerate, i.e., a mechanical

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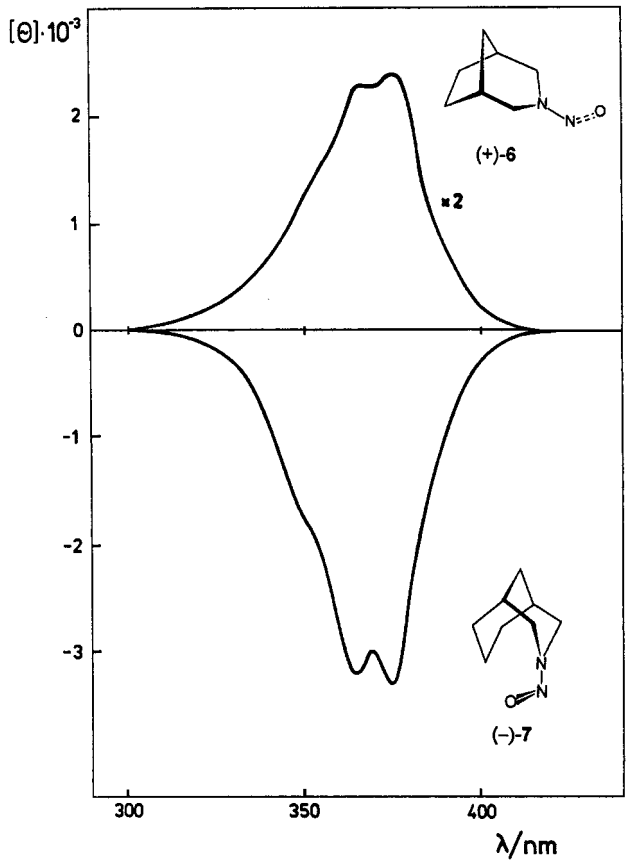


**Figure 4.** CD spectra of the nitrosamines (+)-**6** and (−)-**7** in cyclohexane−dioxane (9:1).

**Table 1. Circular Dichroism (CD) Data**

| compd | solvent[a] | CD $\lambda$, nm ([Θ])[b] |
|---|---|---|
| (−)-**3** | CyD | 376 (−510) |
| **3**·**8a** | PhMe | 373 (−2170) |
| **3**·**8b** | PhMe | 373 (−1290) |
| **3**·**8c** | PhMe | 373 (−580) |
| (−)-**4** | CyD | 373 (−1200) |
| **4**[c] | MeOH | 354 (655) |
| **4**·**8a** | PhMe | 372 (1230) |
| **4**·**8b** | PhMe | 372 (−1880) |
| **4**·2(**8b**) | PhMe | 371 (−1550) |
| (+)-**5** | CyD | 381 (2700) |
| **5**·**8a** | PhMe | 383 (−5000) |
| | KBr | 346 (−1840)[d] |
| **5**·**8b** | PhMe | 383 (6100) |
| (+)-**6** | CyD | 378 (1260) |
| **6**·**8a** | PhMe | 373 (1160) |
| **6**·**8b** | PhMe | 373 (1740) |
| **6**·**8c** | PhMe | 373 (880) |
| (−)-**7** | CyD | 376 (−3350) |
| **7**·**8a** | PhMe | 373 (4700) |
| **7**·**8b** | PhMe | 374 (−8500) |

[a] CyD = cyclohexane-dioxane (9:1). [b] Molecular ellipticity in deg $cm^2$ $dmol^{-1}$, measured immediately after dissolution of the sample. [c] CD of the monocrystal obtained by recrystallization of racemate from toluene−hexane. [d] Approximate value determined by considering the weight concentration (KBr density 2.75 g $cm^{-3}$).

mixture of homochiral crystals and each single crystal contains only one enantiomer. Thus, a spontaneous generation of a molecular chirality occurs during the crystallization.[17,20] In some cases, however, the chiral crystal can be composed of optical antipodes participating in unequal proportions, since due to a disorder, the same site in the crystal can be occupied by the enantiomeric molecules. This situation is exemplified by the crystals

**Table 2. Free Energies of Activation ($\Delta G^{\ddagger}$) for the N−N Rotation of *N*-Nitrosamines[a]**

| compd | solvent | $T$ (°C) | $t_{1/2}$ (min) | $\Delta G^{\ddagger}$ (kcal/mol) |
|---|---|---|---|---|
| (−)-**3** | $C_6H_6$ | 22 | 50 | 22.2 |
| | MeOH | 23 | 38 | 22.1 |
| (−)-**4** | $C_6H_6$ | 22 | 45 | 22.1 |
| | MeOH | 22 | 54 | 22.2 |
| (+)-**5** | $C_6H_6$ | 23 | 80 | 22.5 |
| | MeOH | 22 | 100 | 22.4 |
| (+)-**6** | $C_6H_6$ | 22 | 510 | 23.5 |
| | MeOH | 21 | 1140 | 23.9 |
| (−)-**7** | $C_6H_6$ | 21 | 465 | 23.4 |
| | MeOH | 22 | 2690 | 24.5 |

[a] The errors on $\Delta G^{\ddagger}$ are of ±0.2 kcal/mol.

of **4**, where the observed enantiomer ratio of 3:2 apparently results from the nitroso group disorder. Therefore, after dissolution of a monocrystal of **4** in MeOH, we were able to observe a Cotton effect of a moderate intensity near 355 nm in the CD spectrum (Table 1). The configuration of the major enantiomer can be easily assigned by a comparison of its CD sign with that of the complex **4**·**8a**.

The CD curves of the complexed as well as the liberated nitrosamines in hydrocarbon solvents are characterized by relatively strong Cotton effects near 370 nm, corresponding to the n−$\pi$* transition of the NNO chromophore. Owing to a rapid racemization of the nitrosamines, their intensity gradually decreases in solution and, in most cases, vanishes completely after 3−4 h at room temperature (Figure 3). An exceptional behavior is observed in the case of the compounds **6** and **7**, which need about 3−4 days for a complete racemization in methanolic solution. This effect can be attributed to a steric interaction between the nitroso group and the *endo*-hydrogens at C-6 and/or C-7 of the bicyclic skeletons that slows down the rotation about the N−N bond. Furthermore, it proves that the steric hindrance may be caused not only by the nitroso oxygen but also by the NO nitrogen lone pair. The significant steric requirements of the nitrogen lone pair in the NO group has been reported on several occasions[4b,21] and supported by the molecular mechanics (MM2) calculations.[6] It is noteworthy that the racemization of **6** and **7** is much slower in polar than hydrocarbon solvents. Probably a solvation increases the effective bulkiness of the polar NO group, enhancing in this way its steric interaction with the neighboring substituents. In contrast, the rates of racemization of monocyclic compound **3** and **4** are almost solvent independent. The rates of racemization assessed from simple polarimetric measurements follow the first-order kinetics (Table 2). The calculated activation energy barriersto the N−N rotation $\Delta G^{\ddagger}$ are comparable to those obtained from the variable temperature NMR experiments.[5]

A correlation between the molecular geometry and the Cotton effect sign for many chromophores is offered by sector or helicity rules. However, the so-called "lowered-symmetry" sector rule (Figure 5), that predicts correctly

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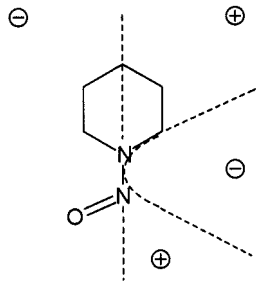

**Figure 5.** The *N*-nitrosamine "lowered symmetry" sector rule".[22] The signs refer to upper sectors.

the n−$\pi$* CD sign of many nitrosamines,[6,22] is apparently not useful for the compounds **1**−**7**. According to this rule the piperidine ring in **1**−**4** or the related bicyclic skeletons in **3**−**7**, that are symmetrically disposed about the nodal plane, contribute negligibly to the Cotton effect, and therefore only weak CD magnitudes are expected for these compounds. Instead, the observed CD bands are of moderate or strong intensity. On the other hand, the crystal structures of nitrosamines revealed that the molecular skeletons of **1**−**7** are not exactly symmetric in respect to the nodal plane containing the N−N bond and therefore should contribute to the Cotton effect. The deformations of the molecular skeletons in nitrosamines are due to a steric interaction between the nitroso oxygen and the neighboring $C_\alpha$ substituents, as illustrated by the CNN bond angles differing substantially from 120° (e.g., they are of 112.0 and 125.5° in **4**). It is also known that the nitrosamine CD is extremely sensitive to any twisting of the chromophore or a pyramidal distortion of the amino nitrogen. The inherent chirality of the NNO chromophore acquired in this way may exert a strong contribution to the magnitude and sign of the Cotton effect.[23] However, the crystal structures of the host−guest complexes do not show any appreciable deviations of the nitrosamino group from planarity, as indicated by the CNNO torsional angles of 0.6 and −176.8° observed for **5**·**8a**,[24] whereas the remaining complexes exhibit even smaller distortions of the chromophore from planarity. Similarly, the crystal structure of the uncomplexed compound (+)-**7** revealed that the nitrosamine group is nearly planar (CNNO of 0.9 and 179.9°). On the other hand, the chromophore in **4** is appreciably twisted (the CNNO torsional angles are of −1.3 and 173.8°). Furthermore, according to the reported MNDO calculations,[25] the potential energy surface of the nitrosamine moiety around the energy minimum is flat, and for this reason it seems reasonable to expect that small deviations of the chromophore from planarity are also possible in solution. Obviously, these facts make application of the sector rule for the compounds studied rather complicated. Therefore, we propose to use a very simple chirality rule (Figure 6) for predictions of the n−$\pi$* CD sign of *N*-nitrosopiperidines. It explains correctly the observed sign of the Cotton effect for all of the compounds studied, the solid-state CD of *N*-nitrosopiperidine (**1**), and the solution spectra of 4-methyl- (**2**) and *cis*-2,6-dimethyl-*N*-nitrosopiperidines reported previously,[12] as well as the CD of many other *N*-nitrosopiperidines,[26] provided that the ring substituents contribution do not overweigh that of the piperidine moiety. Apparently the exceptional stereochemistry of the compound **5**, assuming a nonchair conformation, causes the contribution of the methyl substituents to outweigh that of the cyclopropyl ring and determines the CD sign. There is some analogy with the reported chiroptical spectra of cyclopropyl ketones, where the three-membered ring exerts antioctant contribution to the n−$\pi$* Cotton effect.[27]

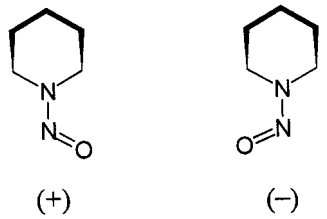

**Figure 6.** The proposed helicity rule for *N*-nitrosopiperidines.

In conclusion, the above results illustrate a great potentiality of the inclusion crystallization for a preparation of the optically active compounds that are inaccessible by classical methods of racemate resolution. Furthermore, in the case of the configurationally labile molecules an asymmetric transformation may occur during the crystallization that may lead to isolation of one enantiomer with yields exceeding 50%. Another advantage of the method is a possibility of the storing of the configurationally unstable substances in the form of host−guest complexes for long periods without loss of their optical activity. The proposed simple technique of liberation of the guest *N*-nitrosamines from the inclusion complexes by the competitive complexation with piperazine may be used also for other species. The optical activity of the guest molecules can be studied by measuring the CD spectra either in solution or in the solid state without liberation from the inclusion complexes,[28] provided that there is no coincidence between absorption regions of the host and guest compounds.

## Experimental Section

$^1$H and $^{13}$C NMR spectra were obtained at 300 and 50 MHz, respectively. The deuterated solvents were used as an internal lock for $^1$H and $^{13}$C NMR. CD spectra were recorded using a 10 mm path length and sample concentrations $3.0-5.5 \times 10^{-3}$ mol $L^{-1}$. Racemic *N*-nitrosamines **3**, **4**, **5**, and **7** were obtained following the literature methods.[4b,29] Host compounds **8a**−**c** were prepared according to the literature procedures.[13a]

**Preparation of the Crystalline Inclusion Compounds**. A solution of the suitable host compound **8a**−**c** with the respective racemic nitrosamine **3**−**7** in toluene-hexane (4:1) was kept at room temperature for 4 h. The precipitated crystals were collected by suction, washed with hexane, and dried.

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Host−guest stoichiometry was determined by $^1$H NMR integration.

**(*S*)-1-Nitroso-4-phenylpiperidine (3)**. To a stirred suspension of the inclusion complex **3·8b** (mp 127−128 °C) (1.20 g, 1.75 mmol) in ethyl ether (30 mL) was added a solution of piperazine (0.26 g, 30 mmol) in ethyl ether at 0 °C. After stirring for 15 min, the mixture was concentrated to a small volume at reduced pressure and diluted with pentane (20 mL). The precipitated crystals of the piperazine complex were filtered and washed with pentane. The filtrate was washed with a cold 15% aqueous solution of citric acid (15 mL), dried ($Na_2SO_4$), and evaporated to dryness at 0 °C. The residue was recrystallized from ethyl ether−pentane at 0 °C: yield 0. 26 g (78%); mp 66−67 °C (lit.[29b] racemate mp 64.5−65.5 °C); $[\alpha]^{21}_D$ −50.2 (*c* 1, $C_6H_6$); $^1$H NMR ($CDCl_3$) $\delta$ 7.36−7.18 (complex m, 5 H), 5.24 (ddt, $J$ = 13.7, 4.6 and 2.4 Hz, 1 H), 4.91 (ddt, $J$ = 13.3, 4.6 and 2.4 Hz, 1 H), 3.78 (td, $J$ = 13.0 and 3.2 Hz, 1 H), 2.92 (tt, $J$ = 12.2 and 3.3 Hz, 1 H), 2.61 (td, $J$ = 13.3 and 3.3 Hz, 1 H), 2.14 (m, 1 H), 1.94 (m, 1 H), 1.88 (qd, $J$ = 12.8 and 4.6 Hz, 1 H), 1.55 (qd, $J$ = 12.8 and 4.6 Hz, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 144.0, 128.7, 126.8, 126.6, 50.3, 42.3, 39.2, 33.5, 31.9.

**(*S*)-1-Nitroso-4-phenylmethylpiperidine (4)**. The nitrosamine (−)-**4** was obtained from the complex **4·8b** (mp 131 °C) in a manner similar to that of compound **3**; mp 62−63 °C (lit.[29a] racemate mp 54−57 °C); $[\alpha]^{21}_D$ −67.2 (*c* 1.25, $C_6H_6$); $^1$H NMR ($CDCl_3$) $\delta$ 7.33−7.13 (complex m, 5 H), 5.03 (ddt, $J$ = 13.7, 4.6 and 2.3 Hz, 1 H), 4.74 (ddt, $J$ = 13.3, 4.6 and 2.3 Hz, 1 H), 3.61 (tdd, $J$ = 12.5, 3.3 and 1.0 Hz, 1 H), 2.58 (d, $J$ = 6.9 Hz, 2 H), 2.49 (tdd, $J$ = 12.5, 3.8 and 1.0 Hz, 1 H), 1.94 (m, 2 H), 1.75 (m, 1 H), 1.40 (m, 1 H), 1.09 (m, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 139.5, 129.0, 128.4, 126.2, 49.9, 42., 38.8, 37.8, 32.2, 30.6.

**(*E*)-3-Nitroso-1,5-dimethyl-3-azabicyclo[3.1.0]hexane (5).** The nitrosamine (−)-**5** was obtained from the complex **5·8b** (mp 88−91 °C) in a manner similar to that of compound **3**; mp 30−31 °C (lit.[29c] racemate mp 28 °C); $[\alpha]^{20}_D$ +33 (*c* 1, MeOH); $^1$H NMR ($CDCl_3$) $\delta$ 4.56 (d, $J$ = 11.9 Hz, 1 H), 4.19 (d, $J$ = 14.0 Hz, 1 H), 4.06 (dq, $J$ = 11.9 and 1.4 Hz, 1 H), 3.11 (dq, $J$ = 14.0 and 1.5 Hz, 1 H), 1.27 (s, 3 H), 1.22 (s, 3 H), 0.46 (dt, $J$ = 5.4 and 1.5 Hz, 1 H), 0.39 (d, $J$ = 5.4 Hz, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 57.8, 52.8, 23.9, 23.5, 21.9, 14.7, 14.6.

**(*E*)-3-Nitroso-3-azabicyclo[3.2.1]octane (6).** Racemic nitrosamine **6** was obtained by nitrosation of 3-azabicyclo[3.2.1]-octane hydrochloride[30] with $HNO_2$; mp 115−117 °C (hexane); $^1$H NMR ($CDCl_3$) $\delta$ 4.77 (ddt, $J$ = 13.8, 2.9 and 1.4 Hz, 1 H), 4.53 (ddt, $J$ = 12.9, 3.2 and 1.7 Hz, 1 H), 3.79 (dd, $J$ = 12.9 and 1.4 Hz, 1 H), 2.59 (dd, $J$ = 13.8 and 1.4 Hz, 1 H), 2.47 (m, 1 H), 2.33 (m, 1 H), 1.80−1.55 (complex m, 5 H), 1.27 (m, 1 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 57.9, 47.9, 36.9, 34.2, 33.8, 27.7, 26.9. Anal. Calcd for $C_7H_{12}N_2O$ (140): C, 59.98; H, 8.62; N, 19.98. Found: C, 60.03; H, 8.55; N, 19.88. The nitrosamine (+)-**6** was obtained from the complex **6·8b** (mp 140−141 °C) in a manner similar to that of compound **3**; mp102−108 °C; $[\alpha]^{22}_D$ +53 (*c* 1, $C_6H_6$).

**(*Z*)-3-Nitroso-3-azabicyclo[3.3.1]nonane (7)**. The nitrosamine (−)-**7** was obtained from the complex **7·8b** (mp 154−155 °C)[31] in a manner similar to that of compound **3**; mp 163−4 °C (lit.[4b] racemate mp 164−166 °C); $[\alpha]^{21}_D$ −104 (*c* 0.6, $C_6H_6$); $^1$H NMR ($CDCl_3$) $\delta$ 4.90 (d, $J$ = 14.6 Hz, 1 H), 4.78 (d, $J$ = 13.4 Hz, 1 H), 3.93 (m, 1 H), 2.73 (m, 1 H), 2.18 (m, 1 H), 2.08 (m, 1 H), 1.92 (m, 1 H), 1.86 (m, 2 H), 1.80−1.55 (complex m, 3 H), 1.40 (m, 2 H); $^{13}$C NMR ($CDCl_3$) $\delta$ 55.8, 45.0, 32.6, 31.2, 30.2, 28.4, 27.5, 18.7.

**X-ray Diffraction Analysis**. The intensity data for the crystals have been collected using Kuma KM-4 diffractometer [**4**, **4·8a**, **5·8a**, **7·8b**, (+)-**7**] or Kuma CCD diffractometer [**4·2(8b)**, **6·8a**, **6·8c**]. The crystal structures were solved with SHELXS-97[32] and refined with SHELXL-97.[33] The crystal data for **3·8b** and **4·2(8b)** have been reported earlier;[7] however, we repeated the X-ray analysis of **4·2(8b)** at $T$ = 130 K.

Crystal data for $C_{12}H_{16}N_2O$ (**4**): orthorhombic, space group $P2_12_12_1$, $a$ = 6.076(1), $b$ = 8.203(2), $c$ = 22.713(5) Å, $V$ = 1132.1-(4) Å$^3$, $Z$ = 4, $\lambda$ = 0.71073 Å, $T$ = 292 K, $R_1$ = 0.0360, $wR_2$ = 0.0854 for 1161 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_{43}H_{46}N_2O_5$ (**4·8a**): monoclinic, space group $P2_1$, $a$ = 11.521(2), $b$ = 9.579(2), $c$ = 16.970(3) Å, $\beta$ = 98.08-(3)°, $V$ = 1854.2(6) Å$^3$, $Z$ = 2, $\lambda$ = 1.54178 Å, $T$ = 292 K, $R_1$ = 0.0392, $wR_2$ = 0.1038 for 2413 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_{76}H_{80}N_2O_9$ [**4·2(8b)**]: monoclinic, space group $C2$, $a$ = 35.368(2), $b$ = 8.5181(7), $c$ = 23.494(1) Å, $\beta$ = 117.810(6)°, $V$ = 6260.5(7) Å$^3$, $Z$ = 4, $\lambda$ = 0.71073 Å, $T$ = 130 K, $R_1$ = 0.0548, $wR_2$ = 0.0951 for 3759 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_{38}H_{42}N_2O_5$ (**5·8a**): orthorhombic, space group $P2_12_12_1$, $a$ = 9.722(2), $b$ = 10.021(2), $c$ = 34.550(7) Å, $V$ = 3366.0(12) Å$^3$, $Z$ = 4, $\lambda$ = 1.54178 Å, $T$ = 292 K, $R_1$ = 0.0570, $wR_2$ = 0.1658 for 2874 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_{38}H_{42}N_2O_5$ (**6·8a**): orthorhombic, space group $P2_12_12_1$, $a$ = 9.541(1), $b$ = 9.599(1), $c$ = 34.711(4) Å, $V$ = 3179.0(6) Å$^3$, $Z$ = 4, $\lambda$ = 0.71073 Å, $T$ = 120 K, $R_1$ = 0.0564, $wR_2$ = 0.1223 for 2944 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_{41}H_{46}N_2O_5$ (**6·8c**): monoclinic, space group $P2_1$, $a$ = 9.892(1), $b$ = 9.544(1), $c$ = 17.968(1) Å, $\beta$ = 96.79(1)°, $V$ = 1684.4(3) Å$^3$, $Z$ = 2, $\lambda$ = 0.71073 Å, $T$ = 100 K, $R_1$ = 0.0578, $wR_2$ = 0.1452 for 2714 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_8H_{14}N_2O$ [(+)**7**]: orthorhombic, space group $P2_12_12_1$, $a$ = 6.096(1), $b$ = 9.982(2), $c$ = 12.881(3) Å, $V$ = 783.8(3) Å$^3$, $Z$ = 4, $\lambda$ = 0.71073 Å, $T$ = 150 K, $R_1$ = 0.0306, $wR_2$ = 0.0666 for 676 independent reflections with $I > 2\sigma(I)$.

Crystal data for $C_{41}H_{46}N_2O_5$ (**7·8b**): orthorhombic, space group $P2_12_12_1$, $a$ = 12.719(2), $b$ = 14.799(3), $c$ = 18.470(4) Å, $V$ = 3476.6(12) Å$^3$, $Z$ = 4, $\lambda$ = 1.54178 Å, $T$ = 293 K, $R_1$ = 0.0373, $wR_2$ = 0.0993 for 2712 independent reflections with $I > 2\sigma(I)$.

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**Supporting Information Available:** X-ray crystallographic data for **4·8a**, **4·2(8b)**, **5·8a**, **6·8a**, **6·8c, 7·8b**, **4**, and (+)-**7** including ORTEP drawings, atomic positions, and atomic displacement parameters as well as a complete list of bond lengths and angles. This material is available free of charge via the Internet at http://pubs.acs.org.

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