# Resolution and Rotational Barriers of Quinolinone and Acridone Sulfenamide Derivatives: Demonstration of the S−N Chiral Axis

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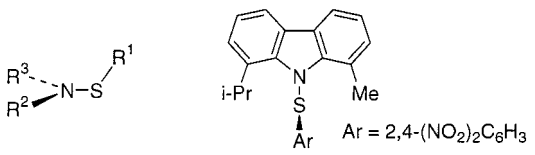
Achiral (**8a**) and chiral (**8b**) *N*-(2,4-dinitrobenzenesulfenyl)acridone derivatives were synthesized. Addition of the chiral solvating agent (*S*)- 2,2,2-trifluro-1-(anthryl)ethanol to **8a** rendered the enantiotopic groups on the acridone ring diastereotopic and anisochronous, thus allowing the estimation of a lower limit for the rotational barrier about the S−N bond (18.7 kcal mol$^{-1}$) by NMR spectroscopy. **8b** and the previously reported chiral sulfenamide **5** (Raban, M.; Martin, V. A.; Craine, L. *J. Org. Chem.* **1990**, *55*, 4311) were resolved on a Chiracel OD HPLC column. This constitutes the first resolution of stereostable enantiomers of a compound in which the chirality is due only to the presence of the S−N chiral axis. The rotational barriers of both compounds are nearly equal (22.7−22.8 kcal mol$^{-1}$ at 303.7 K) and are the largest determined to date for the rotation about the S−N bond in sulfenamides. The relatively high enantiomerization barrier for **8b** is remarkable since the peri positions are unsubstituted.

## Introduction

Sulfenamides of the general formula **1** adopt a conformation in which the $R^1SN$ and $R^2NR^3$ planes are on average nearly perpendicular, and hence, the S−N bond constitutes a chiral axis as long as $R^2 \neq R^3$.[1] The objective of the present work is to directly demonstrate the chirality of the S−N axis by optical resolution and isolation of *stereostable* enantiomers, owing their optical activity to the presence of the S−N chiral axis.




**1** **2**

When the nitrogen is pyramidal and its two substituents are different ($R^2 \neq R^3$) four stereoisomeric forms (two enantiomeric pairs) are possible. Enantiomerization of a given form requires both torsion (T) around the S−N bond and inversion (I) of the nitrogen atom (Figure 1).[2] If the nitrogen atom is nearly planar or inverts rapidly, enantiomerization is dominated by torsion about the S−N bond.[3a,b] Two diastereomeric rotational pathways exist, depending on whether in the transition state the S−R bond adopts a *syn*-periplanar arrangement with the $R^2$ or the $R^3$ substituent (Chart 1).

The magnitude of the rotational barrier in sulfenamides depends on a combination of steric and electronic effects. Electron withdrawing substituents on the sulfur atom and bulky substituents on the nitrogen are known to increase the torsional barrier.[1] In most cases examined to date the rotational barriers were not sufficiently high to allow for the resolution of enantiomers, and hence were measured using only NMR methods.[4] We have recently described the first enantiomeric resolution of a system (**2**) which owes its chirality to the sulfenamide chiral axis and the determination of its optical activity.[5] However, the enantiomers of **2** proved to be stereostable only at 0 °C. The nitrogen atom in sulfenamide **2** is nearly planar due to conjugation with the aromatic system, and the enantiomerization process consists almost entirely of a T process. The two bulky substituents flanking the S−N bond hinder the T process, thus raising the rotational barrier.[6] The enantiomerization barrier of **2** (determined

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(1) For reviews on the stereochemistry of sulfenamides see: (a) Kost, D.; Raban, M. in *The Chemistry of Sulphenic Acids and their Derivatives*, Patai, S., Ed., Wiley, Chichester, 1990, ch 2. (b) Raban, M.; Kost, D. in *Acyclic Organonitrogen Stereodynamics*, Lambert, J. B.; Takeuchi, Y., Ed., VCH: New York, 1992; p. 57. (c) Raban, M.; Kost, D. *Tetrahedron* **1984**, *40*, 3345.

(2) For a discussion of dynamic processes in a similar model system see: Kost, D.; Aviram, K.; Raban, M. *J. Org. Chem.* **1989**, *54*, 4903.

(3) (a) Symmetry arguments indicate that, precluding accidental degeneracy, in a chiral sulfenamide (with $R^2 \neq R^3$) the nitrogen and the three atoms connected to it should not lie exactly on the same plane. The symmetry operations necessary to force such arrangement are either a symmetry plane ($\sigma$) passing through the four atoms or a $C_2$ axis collinear with the R−N or N−S bonds. Since the molecule belongs to the $C_1$ point group, neither symmetry operation can be present and a planar arrangement cannot be enforced. For a discussion on symmetry arguments see: Mislow, K. *Introduction to Stereochemistry*, W. A. Benjamin, NY, 1965; p. 8. (b) A similar stereochemical analysis applies also for a time scale under which the nitrogen inversion process is fast relative to the torsion around the S−N bond.

(4) A barrier equal to or higher than 23 kcal mol$^{-1}$ is usually sufficient to separate two interconverting species at 298 K (Kessler, H. *Angew. Chem., Int. Ed. Eng.* **1970**, *9*, 219).

(5) Ben-David Blanca, M.; Maimon, E.; Kost, D. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2216.

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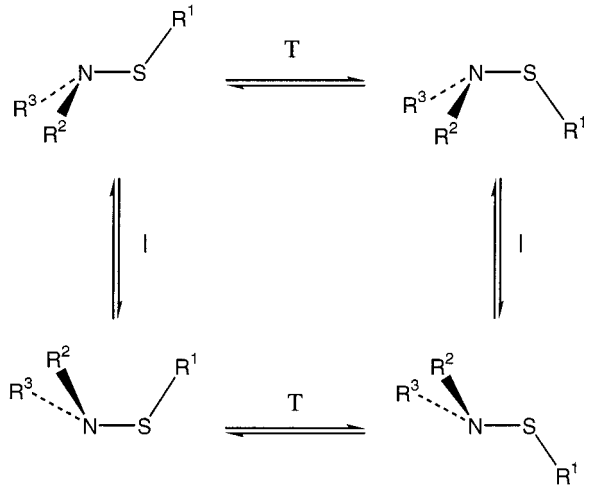
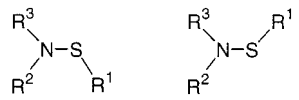


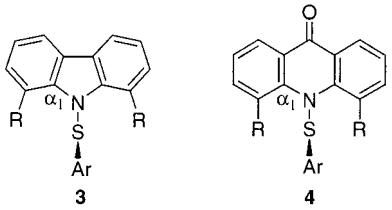
**Figure 1.** Interconversion graph of the four isomeric forms (two enantiomeric pairs) of a sulfenamide derivative with a pyramidal nitrogen atom. Pairs of forms located at opposite corners of the graph represent enantiomers. Nitrogen inversion and torsion about the S−N bond are denoted by the letters "I" and "T", respectively.

**Chart 1**



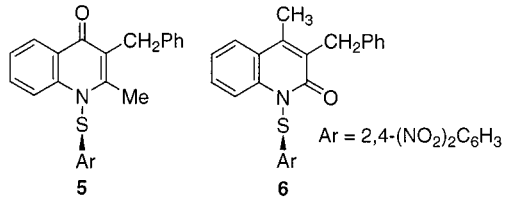
from the coalescence of the methyl signals in the $^1$H NMR spectrum) was $\Delta G^{\ddagger} = 21.0$ kcal mol$^{-1}$ ($C_6D_5NO_2$, 417 K). After 24 min at 0 °C the resolved sample had completely racemized. In the present study we sought to demonstrate the chirality generated by the sulfenamide chiral axis *directly* by preparing and resolving *stereostable* enantiomers. Chirality would then be manifested in the persistent optical activity of the enantiomers, by contrast to previously investigated sulfenamides, in which both chirality and rotational barriers could only be observed and determined by NMR methods.

Isolation of enantiomers which are stereostable at the laboratory time scale demands a higher barrier of rotation around the S−N bond. Two alternative routes for further increasing the enantiomerization barrier come to mind. The first route involves retaining the central scaffold of the amino part of the sulfenamide (the carbazole unit) and increasing the bulk of the substituents at the peri positions flanking the sulfenamide bond.[7] A different approach involves creating a more crowded environment about the S−N bond by changing the relative disposition of the peri substituents. This can be achieved, for example, by the formal replacement of the central five membered ring of the carbazole moiety of **3** by a six membered ring (e.g., **4**). The smaller exocyclic $\alpha_1$ angles in **4** should result in a closer disposition of the peri substituents to the sulfenamide bond.[8] The increased repulsive steric interaction between the peri substituents



**3** **4**

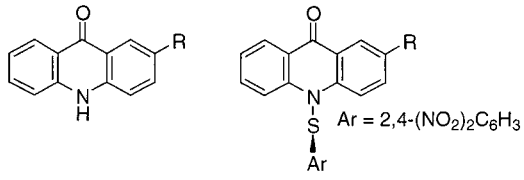
and the S−Ar group in the rotational transition state is expected to yield higher rotational barriers. Notably, evidence on related compounds suggests that such systems might possess substantial rotational barriers *even in the absence of peri substituents* (i.e., R = H in **4**). Raban and co-workers have shown that although the 2-quinolinone sulfenamide **6** has an enantiomerization barrier of only 16.9 kcal mol$^{-1}$, in the 4-quinolinone derivative **5** this barrier is higher than 22 kcal mol$^{-1}$.[9] The different barrier heights of **5** and **6** were interpreted as indicating that in both cases the lower energy rotational pathway involves passage of the dinitrophenyl group near the Me (or C=O) substituent (an "exo" passage). It was concluded that the passage near the peri hydrogen introduces severe steric interactions leading to a barrier in excess of 22 kcal mol$^{-1}$.[9] In this paper, we report the preparation, resolution of enantiomers, and determination of the enantiomerization barrier of a chiral acridone sulfenamide derivative lacking any peri substituent, and of sulfenamide **5**.



**5** **6**

## Results and Discussion

**Structural Considerations and Synthesis.** Two acridone sulfenamide derivatives lacking peri substituents were chosen as targets: **8a** and **8b**. In both cases the acridone nitrogen is expected to be nearly planar due to conjugation of its lone pair with the aromatic system. The isopropyl group in **8b** was introduced to serve two purposes: (i) to desymmetrize the acridone moiety rendering the molecule chiral and (ii) to serve as a prochiral probe capable of "sensing" the chirality of the molecule and allowing NMR monitoring of the enantiomerization process.



**7a** R = H **8a** R = H
**7b** R = *i*-Pr **8b** R = *i*-Pr

(6) The 2,4-dinitrophenyl substituent was chosen since the rotational barrier of sulfenamides N-substituted by this group is *higher* than when substituted by the more crowded 2,4,6-trinitrophenyl group. See: Raban, M.; Yamamoto, G. *J. Am. Chem. Soc.* **1977**, *99*, 4160; *J. Am. Chem. Soc.* **1979**, *101*, 5890.

(7) Preliminary attempts to synthesize sulfenamide derivatives by reaction of the anions of crowded carbazoles with 2,4-dinitrobenzenesulfenyl chloride proved unsuccessful. Apparently, the increased steric crowding hinders the formation of the sulfenamide bond.

(8) ZINDO calculations of the 2-isopropyl derivatives of **4** and **3** (Ar = 2,4-$(NO_2)_2C_6H_3$) indicate that in the first compound the $\alpha_1$ angle should be 7° smaller than in the second. (Maimon, E. M.Sc. thesis, Ben Gurion University, 1993).

(9) Raban, M.; Martin, V. A.; Craine, L. *J. Org. Chem.* **1990**, *55*, 4311.

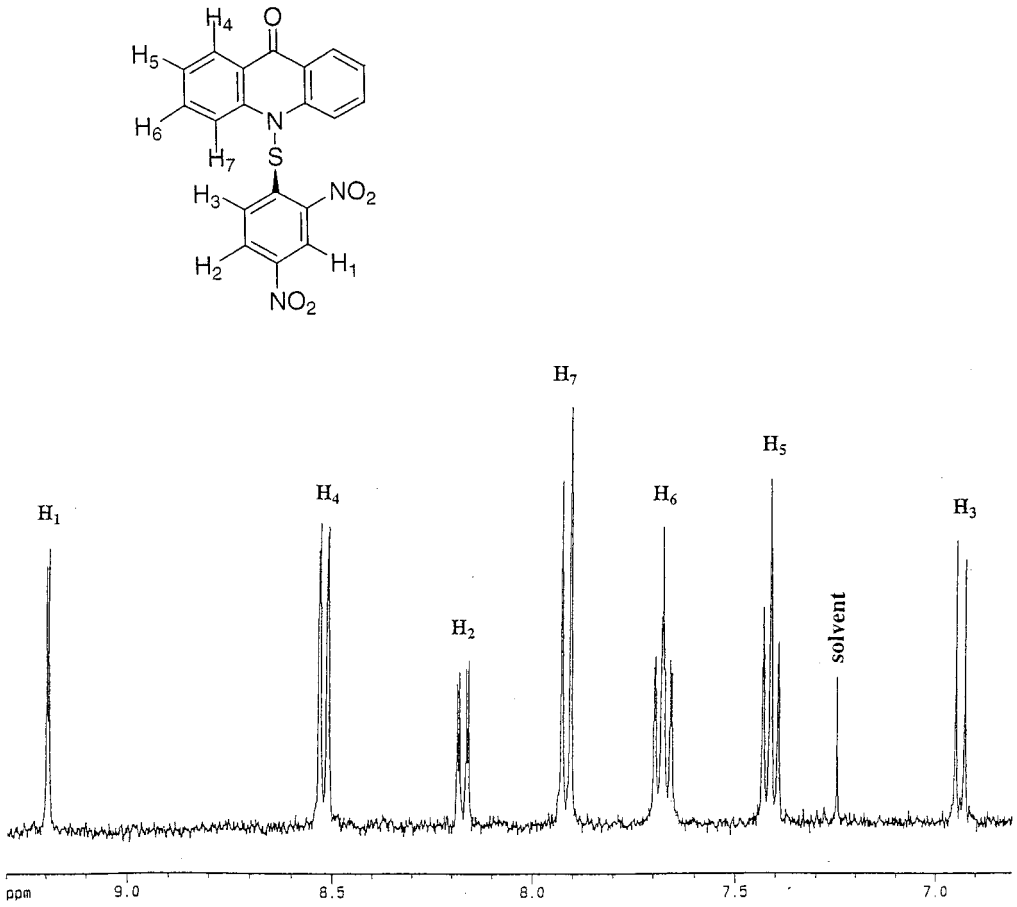
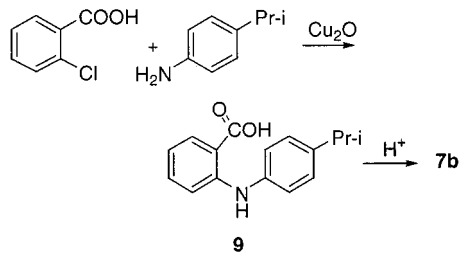



**Figure 2.** $^1$H NMR (400 MHz, $C_2D_2Cl_4$) of the achiral sulfenamide **8a**.

**Scheme 1**




**9**

Isopropyl acridone (**7b**) was prepared according to Scheme 1.[10] Acridones **7a** and **7b** were deprotonated with KH, and the resulting anions were treated with 2,4-dinitrobenzenesulfenyl chloride yielding the yellow sulfenamides **8a** and **8b**.[11] Sulfenamide **5** was prepared by a minor modification of the literature procedure.[9,12]

**NMR Spectra.** Sulfenamide **8a** displays in the $^1$H NMR spectrum (400 MHz, $CDCl_3$, rt) seven aromatic signals (Figure 2). Assignment of the aromatic signals of **8a** and **8b** was carried out on the basis of their coupling pattern and in the case of **8b**, by COSY and NOESY experiments. Notably, the peri protons vicinal to the nitrogen ($H_7$ in Figure 2), which in the parent acridones **7a** and **7b** resonate at ca. 7.3 ppm, are shifted downfield by ca. 0.6 ppm in the sulfenamides **8a** and **8b** as a result of their proximity to the dinitrophenyl ring.

The isopropyl methyl groups of **8b** are accidentally isochronous in $CDCl_3$, but become anisochronous in acetone-$d_6$ or DMF-$d_7$ solutions although they are separated by only 1.3 and 1.9 Hz, respectively, at 400 MHz (Figure 3). The rather similar shift of the signals is due to their relatively large distance from the sulfenamide chiral axis. The anisochrony of the isopropyl methyl groups is evidence that at room temperature **8b** exists in a "frozen" chiral conformation (relative to the NMR time scale).

**Rotational Barrier of Sulfenamide 8a.** Sulfenamide **8a** is achiral and a 180° rotation around the S−N bond results in homomerization which mutually exchanges the two phenylene rings. These rings are enantiotopic under slow rotation (on the NMR time scale) around the sulfenamide bond, and homotopic under fast rotation. Since enantiotopic groups are isochronous under achiral conditions, the rotational process is "invisible" and cannot be followed by NMR. Enantiotopic groups can be rendered anisochronous in a chiral nonracemic medium, and therefore the homomerization process of **8a** could be followed in such a medium. Addition of the chiral solvating agent (CSA) (*S*)-2,2,2-trifluoro-1-(anthryl)ethanol (**10**)[13] to a $C_2D_2Cl_4$ solution of **8a** resulted in noticeable splitting of the acridone protons in the 400 MHz $^1$H NMR spectrum, while the dinitrophenyl protons remained unsplit as expected. The largest splitting ($\Delta\delta$ = 18.7 Hz) was observed for the $H_5$ protons (Figure 4). Due to partial

(10) (a) Agranat, I.; Tapuhi, Y. *J. Am. Chem. Soc.* **1978**, *100*, 5604. (b) Allen, C. F. H.; McKee, G. H. W. *Org. Synt.* Coll. Vol. II, p 15.

(11) We were unable to prepare by this method the dinitrobenzenesulfenyl derivative of peri-substituted acridones, probably due to steric hindrance effects of the alkyl substituent on the nitrogen atom.

(12) The "c" and "d" arrows of Scheme 1 in ref 9 should point to the structures **13** and **12**, respectively, and not as depicted.

(13) Pirkle, W. H.; Beare, S. D. *J. Am. Chem. Soc.* **1969**, *91*, 5150.

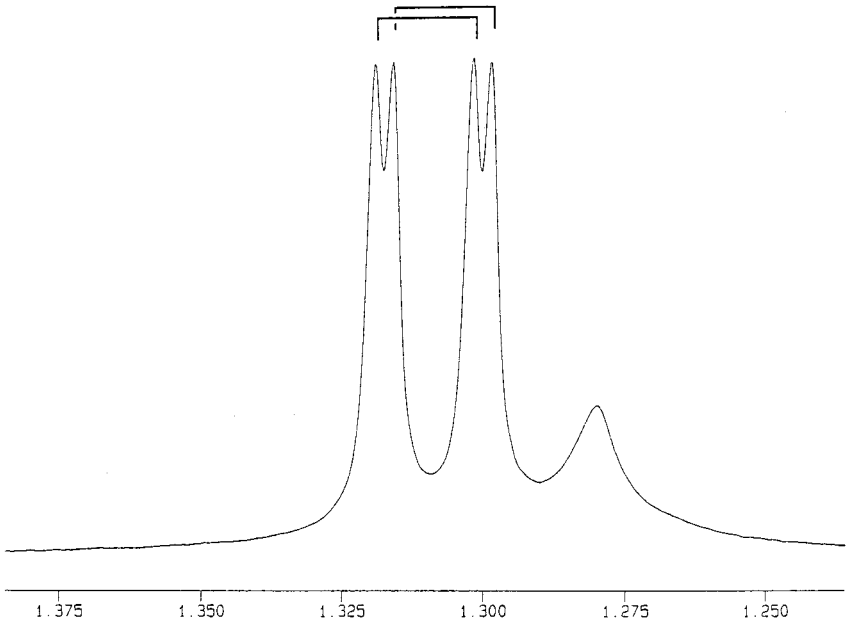
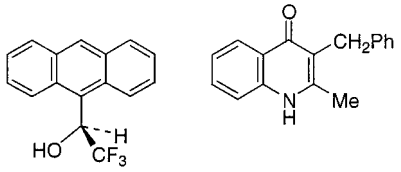



**Figure 3.** $^1$H NMR (400 MHz, acetone-$d_6$) spectrum of **8b** (expansion of the isopropyl methyl region). The two partially overlapping doublets correspond to the diastereotopic isopropyl methyl groups.

overlap of the triplets of each proton, their combined patterns form a quartet.




**10** **11**

Upon raising the temperature of **8a** in the presence of **10** the two $H_5$ signals merged (Figure 4). This process can be attributed either to a fast rotation (on the NMR time scale) around the S−N bond (a homomerization) or to a weaker association between the chiral additive and **8a**. Since the $\Delta\delta$ value between the two $H_5$ protons diminished upon raising the temperature and none of the line shape changes characteristic of a coalescence process were observed (line broadening, formation of a plateau between the coalescing signals), it may be concluded that the observed process is due to a weaker association. On the basis of the chemical shift difference at room temperature ($\Delta\delta$ = 6 Hz) and the highest temperature at which separate signals could be distinguished for the two $H_5$ protons (350 K), a lower limit of $\Delta G^{\ddagger} > 18.7$ kcal mol$^{-1}$ could be estimated for the rotational barrier of **8a**.

**High-Temperature NMR Studies of 5 and 8b.** The enantiomerization barriers of **5** and **8b** can be determined from the rate of exchange of the diastereotopic protons (the methylene protons of the benzyl group in **5** and the isopropyl methyl groups in **8b**) at a given temperature.

Raban and co-workers reported that at 300 MHz in 4:1 *o*-dichlorobenzene-$d_4$/toluene-$d_8$ solution the diastereotopic methylene proton signals of **5** do not undergo any line broadening or coalescence up to 423 K. On the basis of these data, a lower limit of 22 kcal mol$^{-1}$ was estimated for the enantiomerization barrier of **5**.[9] To obtain a better estimate of the lower limit of its enantiomerization barrier, additional high-temperature NMR studies of **5** were conducted. The experiments were initially conducted in *o*-dichlorobenzene-$d_4$ solution at 446 K. At high temperatures the compound substantially decomposed to its starting material **11**. To minimize the exposure of **5** to high temperatures, the NMR probe was preheated to 446 K using an ethylene glycol sample standard. The ethylene glycol was replaced by a sample of **5** and the NMR spectrum determined after thermal equilibrium had been achieved (10−15 min). Under these conditions, ca. 50% of the compound decomposed but the unreacted **5** displayed two signals for the benzylic diastereotopic protons, indicating that the enantiomerization process was slow on the NMR time scale. From the chemical shift difference (19.9 Hz) between the proton signals and their mutual coupling constant ($J$ = 15.3 Hz), a lower limit of 49 s$^{-1}$ can be estimated for the exchange rate at 446 K by the Kurland equation.[14a] From this rate constant a lower limit of 23.0 kcal mol$^{-1}$ was estimated for the enantiomerization barrier.

The high-temperature NMR studies of **8b** were conducted in DMF-$d_7$. Increasing the sample temperature resulted in broadening of the partially overlapping isopropyl methyl signals and coalescence. Partial decomposition of the sample was observed during the high-temperature studies. From the chemical shift difference of the isopropyl methyls ($\Delta\delta$ = 1.9 Hz) the rate of exchange ($k$ = 4.2 s$^{-1}$) at the coalescence temperature (394 K) corresponding to a barrier of $\Delta G^{\ddagger}$ = 22.1 kcal mol$^{-1}$ was estimated by the Gutowsky-Holm equation.[14b] Due to the proximity of the two partially overlapping doublets, the error introduced by the use of the Gutowsky-Holm equation can be relatively large.[15] Full line shape analysis of the spectra at 380, 384, 389, and 394

(14) (a) Kurland, R. J.; Rubin, M. B.; Wise, W. B. *J. Chem. Phys.* **1964**, *40*, 2426. (b) Gutwosky, H. S.; Holm, C. H. *J. Chem. Phys.* **1956**, *25*, 1228.

(15) For a critical examination of the validity of the coalescence methods see: Kost, D.; Carlson, E. H.; Raban, M. *J. Chem. Soc., Chem. Commun.* **1971**, 656; Kost, D.; Zeichner, A. *Tetrahedron Lett.* **1974**, 4533.

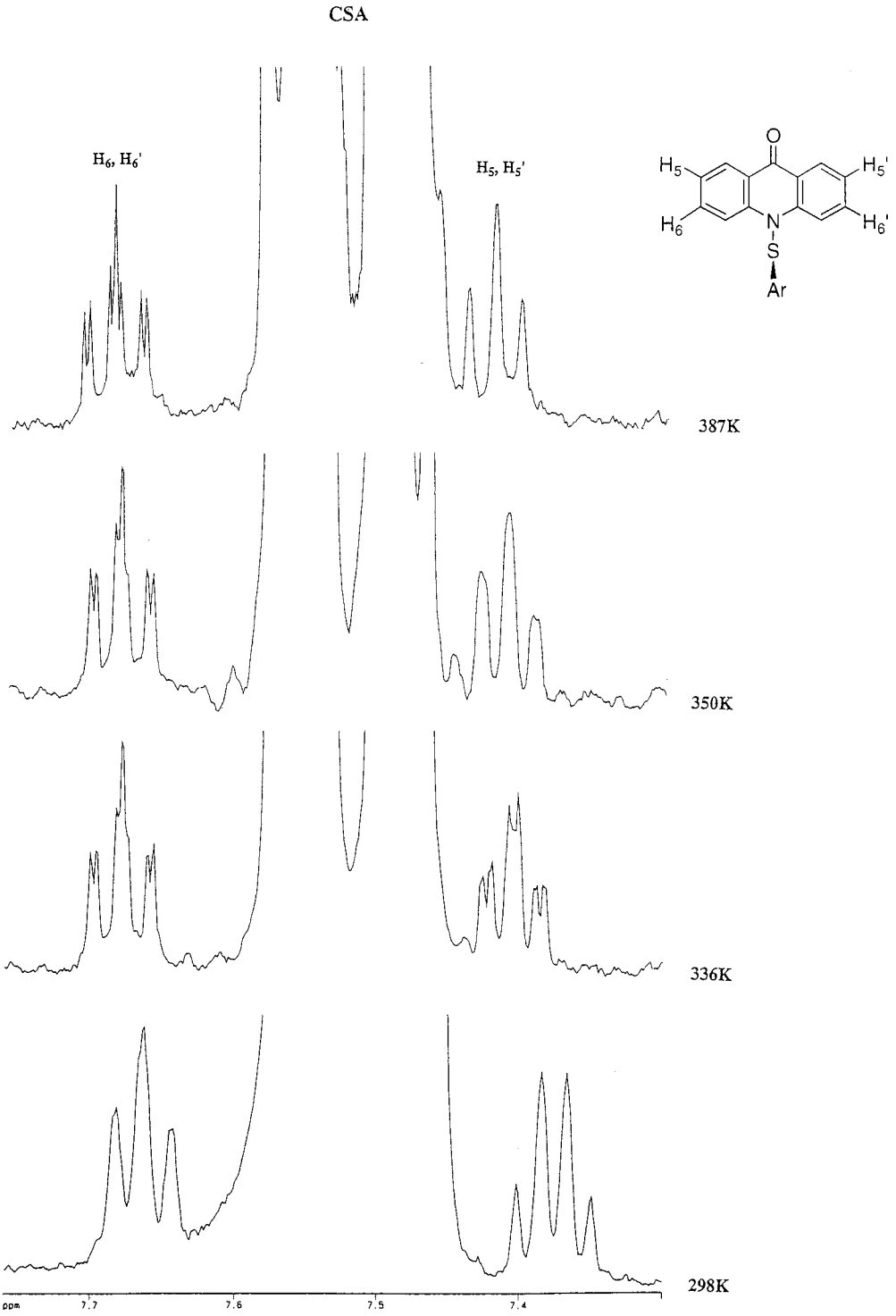
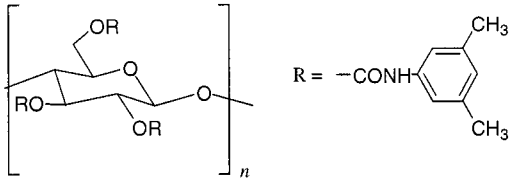



**Figure 4.** $^1$H NMR (400 MHz, $C_2D_2Cl_4$) spectra of a 1:15 mixture of **8a** and the chiral solvating agent **10** at different temperatures. The strong signals in the middle of the spectrum correspond to the chiral solvating agent.

K was conducted with the gNMR program.[16] The simulation provided rate constants of 2, 2.5, 3.0, and 4.0 $s^{-1}$, respectively, which correspond to a barrier of $\Delta G^{\ddagger} = 22.0 \pm 0.1$ kcal $mol^{-1}$.

**Resolution and Enantiomerization Barriers.** Initial attempts to resolve the sulfenamide **8b** by enantioselective HPLC were conducted at room temperature using a Chiracel OD (**12**) column (eluent: hexane/EtOH 8:2). Although the two enantiomers were resolved, the chromatogram displayed a plateau between the peaks of the enantiomers, indicating that some enantiomerization took place during the time scale of the resolution.[17]




**12**

(16) gNMR v4.1.0. Cherwell Scientific Publishing: Oxford, UK.

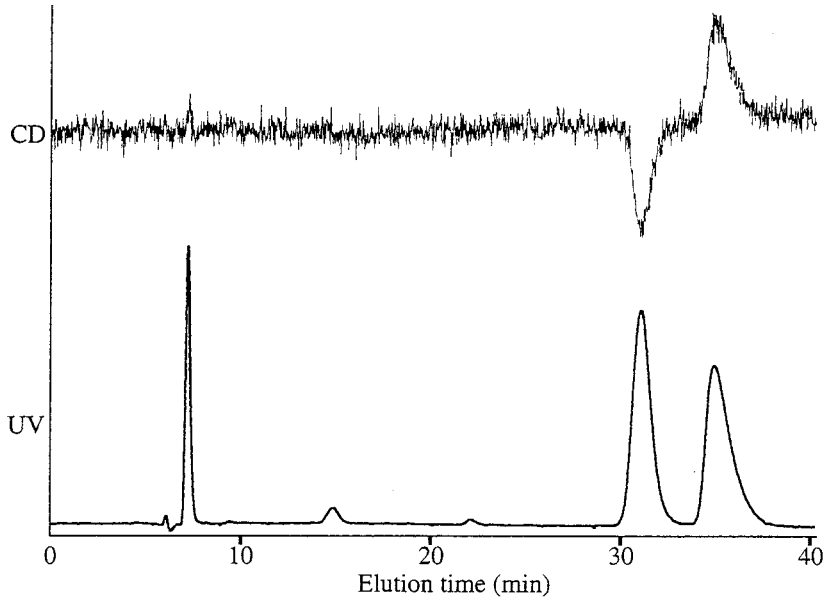



**Figure 5.** Chromatogram of the enantioseparation of **8b** by HPLC on Chiralcel OD at 10 °C. The opposite signs of the CD peaks of the resolved sample indicate that the species separated indeed correspond to enantiomeric forms.

**Table 1. Enantiomerization Rate Constants (*k*) and Kinetic Activation Parameters for the S−N Rotation of 5 and 8b**

| | $T$ (K) | $k$ ($s^{-1}$) | $\Delta G^{\ddagger}$ (kcal $mol^{-1}$) |
|---|---|---|---|
| **5**[a] | 293.6 | $6.63 \times 10^{-5}$ | 22.8 |
| | 298.6 | $1.34 \times 10^{-4}$ | 22.8 |
| | 303.7 | $2.62 \times 10^{-4}$ | 22.8 |
| | 308.7 | $4.78 \times 10^{-4}$ | 22.8 |
| | 313.7 | $9.38 \times 10^{-4}$ | 22.7 |
| **8b**[b] | 288.6 | $3.59 \times 10^{-5}$ | 22.8 |
| | 293.7 | $6.60 \times 10^{-5}$ | 22.8 |
| | 303.7 | $2.88 \times 10^{-4}$ | 22.7 |
| | 308.7 | $5.97 \times 10^{-4}$ | 22.7 |
| | 313.7 | $1.14 \times 10^{-3}$ | 22.6 |

[a] $\Delta H^{\ddagger} = 23.3$ kcal $mol^{-1}$, $\Delta S^{\ddagger} = 1.80$ cal $K^{-1}$ $mol^{-1}$. [b] $\Delta H^{\ddagger} = 24.6$ kcal $mol^{-1}$, $\Delta S^{\ddagger} = 6.19$ cal $K^{-1}$ $mol^{-1}$.

Baseline separation of the enantiomers was obtained at 10 °C (Figure 5). The racemization of resolved samples of **5** and **8b** was followed by CD at different temperatures (Figure 6).[18] Excellent first order rate plots were obtained from the CD data. The kinetic data are collected in Table 1. The Gibbs free energies of activation of both compounds are nearly equal (22.8−22.7 kcal $mol^{-1}$ at 303.7 K) and are ca. 2 kcal $mol^{-1}$ larger than the values determined for the enantiomerization of **2** by the coalescence method ($\Delta G^{\ddagger} = 21.0$ kcal $mol^{-1}$). The increase in the rotational barrier can be ascribed to the increase in the central ring size from five membered in **2** to six membered in **5** and **8b**. The relatively high enantiomerization barrier of **8b** is remarkable since the peri positions are unsubstituted. Since the rotational barriers of **8a** and **8b** should be similar, it must be concluded that the spectral changes observed upon heating of a sample of **8a** in the presence of **10** (see above) must be due to weaker association at the elevated temperature.

It was previously observed that the racemization barrier determined by following the decay of the CD spectra of **2** was lower than the barrier measured by NMR spectroscopy.[5] This could indicate that under the CD irradiation a photochemically induced racemization pathway is operative.[19] Solutions of resolved samples of **5** and **8b** were kept in the dark at 293.2 and 288.2 K, respectively, and the progress of the enantiomerization at those temperatures was followed by enantioselective HPLC. The rate constants obtained for **5** and **8b** ($6.66 \times 10^{-5}$ and $3.70 \times 10^{-5}$ $s^{-1}$, respectively) were practically equal to those obtained at the same temperatures by following the process by CD ($6.63 \times 10^{-5}$ and $3.59 \times 10^{-5}$ $s^{-1}$, Table 1), indicating that there is no photochemical contribution to the racemization process in either of the two compounds.

**Exo vs Peri Rotational Transition States in the Chiral Sulfenamide 5.** Two diastereomeric transition states are possible for **5**, involving the passage of the dinitrophenyl group near the peri hydrogen (a peri transition state) or near the methyl group (an exo transition state). The large difference between the enantiomerization barriers of **5** and **6** was previously interpreted as indicating that in both compounds the lowest energy enantiomerization pathway (threshold pathway) involves the exo transition state.[9] However, although the large difference in barriers obviously rules out a common peri transition state for both compounds (the barriers in that case should be similar), an additional possibility is that the threshold enantiomerization pathways for the two compounds are different, namely exo for **6** and peri for **5**.

The two diastereomeric transition states for the enantiomerization of **8b** are expected to possess essentially similar energies. In those transition states the repulsive steric interactions involving a peri hydrogen and the rotating ring should be similar to those present in the peri transition state of **5**. The nearly equal enantiomer-

(17) For a discussion of the peak coalescence phenomena in enantioselective chromatography see: Schurig, V. *Chirality* **1998**, *10*, 140. See also: Gasparrini, F.; Lunazzi, L.; Mazzanti, A.; Pierini, M.; Pietrusiewicz, K. M.; Villani, C. *J. Am. Chem. Soc.* **2000**, *122*, 4776.

(18) The slope of a plot of ln(ee) vs time affords the racemization rate which is twice the enantiomerization rate ($k_{rac} = 2\ k_{enant}$).

(19) See for example: Okamoto, Y.; Honda, S.; Yuki, H.; Nakamura, H.; Iitaka, Y.; Nozoe, T. *Chem. Lett.* **1984**, 1149.

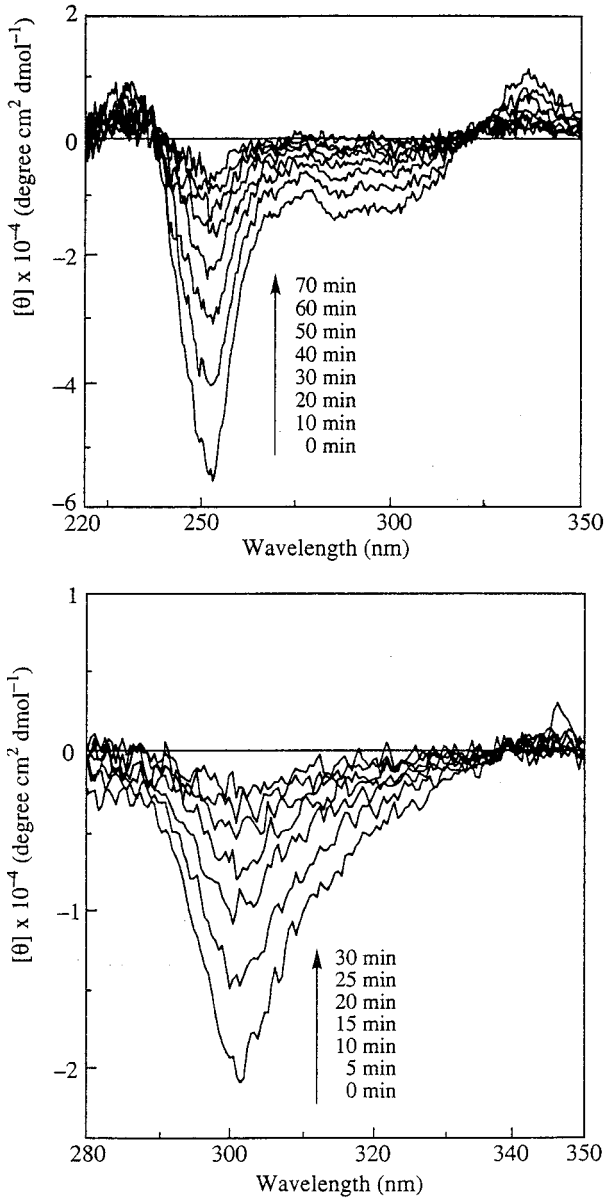



**Figure 6.** Decay of the CD spectra of resolved samples of **5** (top, in 2:8 hexane/ethanol at 303.7 K) and **8b** (bottom, in 6:4 hexane/ethanol at 308.7 K).

ization barriers determined for **5** and **8b** suggest (disregarding ground-state effects) that the rotating rings experience rather similar steric environments in the rotational transition states of both compounds. It may be concluded that the peri pathway is operative in **5**, and that either the peri and exo pathways are similar in energy, or that the enantiomerization proceeds largely via the peri transition state.

## Conclusions

Enantiomeric resolution of **5** and **8b**, which owe their chirality to the presence of the S−N chiral axis, was accomplished on an enantioselective HPLC column. Thus, the chirality generated by the S−N chiral axis, in the absence of any other stereogenic unit, has been directly demonstrated. First-order rate constants for the enantiomerization process were determined. Sulfenamide derivatives of acridone possess substantially higher rotational barriers than their carbazole analogues, even in the absence of bulky peri substituents, suggesting a significant effect of the exocyclic angle ($\alpha_1$) size on steric congestion. The enantiomerization barriers of **5** and **8b** represent the highest barriers determined to date for the sulfenamide bond.

## Experimental Section

**Chromatographic Resolutions.** Resolution of the sulfenamides **5** and **8b** were conducted using a Chiracel OD column (25 × 0.46 cm i.d.) and a UV/CD JASCO CD-1595, 254 nm detector. The resolutions were conducted at 0 °C (**5**) or 10 °C (**8b**) using 20:80 (**5**) or 60:40 (**8b**) hexane/EtOH mixtures as eluents and a flow rate of 0.5 mL/min. The determination of the enantiomeric excess by HPLC was conducted at 0 °C.

**NMR Experiments.** Temperatures were measured using ethylene glycol spectra, and are assumed accurate within ±1 K.[20] To minimize the sample decomposition in the high-temperature studies, the NMR probe was heated to the desired temperature with an ethylene glycol sample, which was replaced by the sulfenamide sample once the temperature was achieved. NMR spectra were recorded after 15 min to ensure thermal equilibration of the sample.

***N*-(2,4-Dinitrobenzenesulfenyl)acridone (8a).** Dry THF (25 mL) was added via a syringe to a flask charged with acridone (0.195 g, 1 mmol) and potassium hydride (0.06 g, 1.5 mmol) under an argon atmosphere. After the evolution of hydrogen ceased, the flask was cooled to −78 °C and a solution of 0.282 g (1.2 mmol) of 2,4-dinitrobenzenesulfenyl chloride in 15 mL of dry THF was added dropwise. The flask was allowed to warm to room temperature over 18 h, the THF was evaporated and the reaction mixture partitioned between chloroform and water. The organic layer was dried (anhydrous $MgSO_4$) and evaporated and the residue chromatographed (silica gel, eluent: $CHCl_3$) to yield 0.18 g (46%) pure **8a** as a yellow solid: mp 220 °C dec; $^1$H NMR ($CDCl_3$, 300.13 MHz) $\delta$ 9.27 (d, $J$ = 2.3 Hz, 1 H), 8.60 (dd, $J$ = 7.9 Hz, 1.4 Hz, 2H), 8.21 (dd, $J$ = 8.9 Hz, 2.4 Hz, 1H), 7.97 (d, $J$ = 8.5 Hz, 2H), 7.69 (dt, $J$ = 7.9 Hz, 1.7 Hz, 2H), 7.44 (t, $J$ = 7.8 Hz, 2 H), 6.98 (d, $J$ = 9.0 Hz, 1 H) ppm; $^{13}$C NMR (DMSO-$d_6$, 100.1 MHz) $\delta$ 176.96, 146.13, 145.50, 143.46, 143.36, 134.78, 128.95, 126.87, 125.08, 123.56, 123.51, 121.18, 118.02 ppm; CI MS *m*/*z* (rel intensity) 393.9 ($MH^+$).

***N*-(4-Isopropylphenyl)anthranilic Acid (9).** A mixture of 22.7 mL (0.166 mol) of *p*-isopropyl aniline (cumidine), 4.1 g (0.026 mol) of *o*-chlorobenzoic acid, 4.1 g (0.03 mol) of anhydrous $K_2CO_3$, and 0.1 g of copper(I) oxide was refluxed for 2 h. The excess aniline was removed by steam distillation. 2 g of charcoal and 20 mL of water were added to the brown residue, and the mixture was boiled for 15 min and filtered. A mixture of 3 mL of concentrated HCl and 6 mL of water was added to the stirred filtrate. The purple-brown acid which precipitated after cooling was filtered and purified by dissolving in a hot solution of 2.5 g $Na_2CO_3$ in 100 mL water, adding 2.5 g of charcoal, boiling for 10 min, filtering and acidifying. The yield of the beige acid was 4.2 g, 63%: mp 170−174 °C (lit.[10a] mp 172−174 °C); $^1$H NMR ($CDCl_3$, 400.13 MHz) $\delta$ 9.27 (br s, 1 H, NH), 8.05 (dd, $J$ = 8.1, 1.4 Hz, 1 H), 7.35 (dt, $J$ = 7.7 Hz, 1.5 Hz, 1 H), 7.24−7.16 (m, 6 H), 6.73 (dt, $J$ = 7.0 Hz, 1.1 Hz, 1 H), 2.88−2.95 (q, $J$ = 7.0 Hz, 1 H), 1.28 (d, $J$ = 6.9 Hz, 6 H) ppm; $^{13}$C NMR ($CDCl_3$, 100.1 MHz) $\delta$ 173.19, 149.56, 145.16, 137.95, 135.22, 132.61, 127.43, 123.71, 116.79, 113.99, 109.97, 33.72, 24.15 ppm.

**2-Isopropylacridone (7b).** A mixture of 3.2 g (12.5 mmol) of **9** and 10 mL of concentrated sulfuric acid was heated on a boiling water bath for 4 h. The mixture was poured slowly into 100 mL of boiling water with stirring and after boiling for 5 additional min filtered by suction. The yellow-brown paste was boiled for 10 min with a solution of 3 g of $Na_2CO_3$ in 40 mL of water, and the crude product was filtered and washed with water. The greenish solid was recrystallized from hot DMSO and washed with $CHCl_3$ to give 0.6 g (65%) of **7b**: mp 265 °C;

(20) Van Geet, A. L. *Anal. Chem.* **1968**, *40*, 2227.

$^1$H NMR ($CDCl_3$, 400.13 MHz) $\delta$ 8.49 (d, $J$ = 7.6 Hz, 1 H), 8.33 (d, $J$ = 1.8 Hz, 1 H), 8.24 (s, 1 H, NH), 7.63 (dt, $J$ = 8.4, 1.5 Hz, 1 H), 7.56 (dd, $J$ = 8.5, 2.0 Hz, 1 H), 7.31−7.24 (m, 3 H), 3.05 (q, $J$ = 6.9 Hz, 1 H), 1.31 (d, $J$ = 6.9 Hz, 6 H) ppm; $^{13}$C NMR ($CDCl_3$, 100.1 MHz) $\delta$ 176.57, 140.93, 140.68, 139.19, 133.10, 132.52, 125.92, 122.08, 120.63, 120.24, 120.19, 117.35, 117.15, 32.83, 23.78 ppm.

***N*-(2,4-dinitrobenzenesulfenyl)-2-isopropylacridone (8b).** Under an argon atmosphere, 25 mL of dry THF were added via a syringe to a flask charged with 0.2 g (0.84 mmol) of **7b** and 0.05 g (1.25 mmol) of KH. After evolution of hydrogen had ceased, the flask was cooled to −78 °C and a solution of 0.233 g (1 mmol) of 2,4-dinitrobenzenesulfenyl chloride in 15 mL of dry THF was added dropwise. The flask was allowed to warm to room temperature over 18 h, the THF was evaporated, and the reaction mixture partitioned between chloroform and water. The organic layer was dried over anhydrous $MgSO_4$, and the solvent was evaporated. The sulfenamide was purified by chromatography (silica gel, eluent: $CHCl_3$) to yield 0.3 g (55%) of pure **8b** as a bright orange solid: mp 218−220 °C (from acetonitrile); $^1$H NMR ($CDCl_3$, 400.13 MHz) $\delta$ 9.26 (d, $J$ = 2.3 Hz, 1 H), 8.60 (dd, $J$ = 8.0 Hz, 1.5 Hz, 1 H), 8.44 (d, $J$ = 2.2 Hz, 1 H), 8.21 (dd, $J$ = 9.0 Hz, 2.4 Hz, 1 H), 7.95 (d, $J$ = 8.6 Hz, 1 H), 7.88 (d, $J$ = 8.9 Hz, 1 H), 7.67 (dt, $J$ = 8.5 Hz, 1.4 Hz, 1 H), 7.57 (dd, $J$ = 8.9 Hz, 2.2 Hz, 1 H), 7.41 (t, $J$ = 7.3 Hz, 1 H), 6.97 (d, $J$ = 9.0 Hz, 1 H), 3.07 (q, $J$ = 7.0 Hz, 1 H), 1.32 (d, $J$ = 6.9 Hz, 6 H) ppm; $^{13}$C NMR ($CDCl_3$, 100.1 MHz) $\delta$ 177.87, 147.00, 146.00, 144.93, 143.27, 141.52, 134.62, 133.74, 128.73, 128.32, 125.41, 125.17, 124.27, 124.19, 123.83, 121.94, 117.09, 116.89, 33.50, 23.87 ppm; CI MS, $m/z$ 435.9 ($MH^+$). Anal. Calcd: C, 60.68; H, 3.93; N, 9.65. Found: C, 60.38; H, 4.17; N, 9.86.

**3-Benzyl-2-methyl-4(1*H*)-quinolinone (11).** The compound was prepared by a minor modification of the literature procedure.[9] A mixture of 8.8 g (0.04 mol) of ethyl 2-benzylacetoacetate, 3.72 g (0.04 mol) of distilled aniline, 12 g of anhydrous $CaSO_4$ (Drierite), 0.08 mL of glacial acetic acid, and 12 mL of absolute ethanol was refluxed for 5 h. The reaction mixture was filtered, the solids were washed with ethanol, and the combined filtrates were evaporated. Distillation of impurities took place when the mixture was heated to 140 °C at 5 mmHg using a sand bath. Cyclization occurred when heating the sand bath to 280 °C for 20 min. After cooling, the mixture solidified and the crude quinolinone was treated with charcoal in boiling ethanol, filtered and recrystallized from absolute ethanol to yield 4.7 g (48%) **11**, mp 284−6 °C (lit.[9] mp 290.5−294.5 °C).

Reaction of the potassium salt of **11** with 2,4-dinitrobenzenesulfenyl chloride according to the literature procedure[9] afforded **5**.

**Acknowledgment.** We thank Dr. Roy Hoffman for assistance with the NMR experiments.

**Supporting Information Available:** $^1$H NMR spectrum of **8a** in DMSO-$d_6$. This material is available free of charge via the Internet at http://pubs.acs.org.

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