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Axially Chiral 2-Arylimino-3-aryl-thiazolidine-4-one Derivatives: Enantiomeric Separation and Determination of Racemization Barriers by Chiral HPLC

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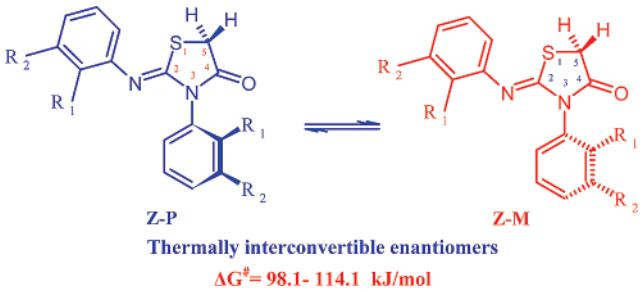

Axially chiral 2-arylimino-3-aryl-thiazolidine-4-ones have been synthesized as racemic mixtures, and each mixture with the exception of 2-(*o*-chlorophenyl)imino-3-(*o*-chlorophenyl)-thiazolidine-4-one has been converted to the corresponding 5-benzylidene-2-arylimino-3-aryl-thiazolidine-4-one racemates by reaction with benzaldehyde. The thermally interconvertible enantiomers of each compound have been obtained by enantioselective HPLC separation on columns Chiralpak AD-H and Chiralcel OD-H, and the barriers to racemization have been found to be 98.1−114.1 kJ/mol. The barriers determined were compared to those of structurally related compounds to provide evidence for the stereochemistry of the aryl imino bond.

Introduction

2-Arylimino-3-aryl-thiazolidine-4-one derivatives display anticonvulsive, antifungal, antiviral, and antibacterial pharmacological activities.[1−9] Several five-membered heterocyclic compounds containing N and S heteroatoms have been shown to react with aldehydes[10] and ketones[11] to give the corresponding biologically important 5-arylidene derivatives.[10,12−17]

The 2-*o*-arylimino-3-*o*-aryl-thiazolidine-4-ones and the corresponding 5-arylidene derivatives reported in this work (compounds **2**−**5** and **7**−**9**) (Scheme 1) are axially chiral and are of interest because of our ongoing studies on sterically constrained rotation about the C−N single bonds in *N*-(*o*-aryl) heterocyclic

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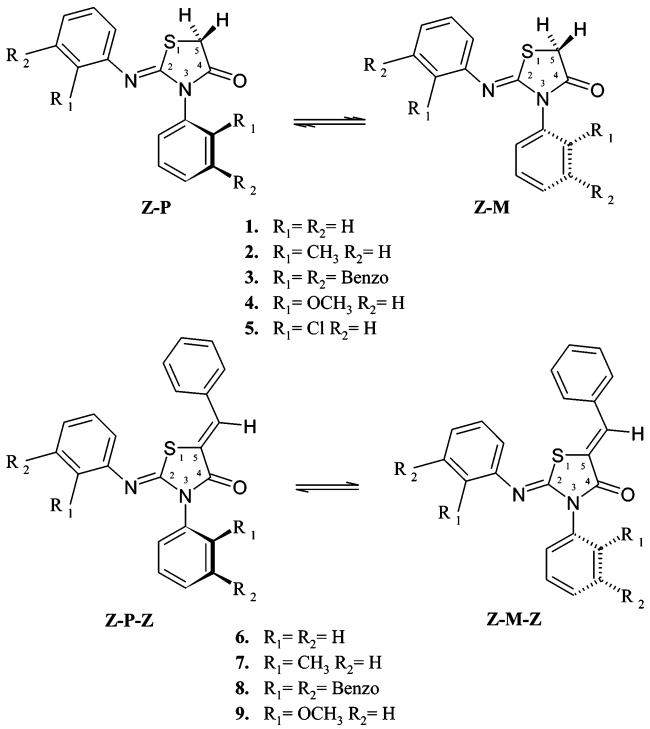
SCHEME 1



compounds.[18−24] In these compounds, the $N_{3(sp^2)}-C_{aryl}$ bond rotation is hindered, and partial rotation around it gives rise to *M* and *P* enantiomers. The chiral nature of each compound from **2** to **5** (Scheme 1) was revealed by the diastereotopic nature of the protons on carbon 5, which gives rise to the AB-type splitting pattern in the ^{1}H NMR spectra. On the other hand, although there are no such probes available within molecules **7**−**9** (Scheme 1) for the proof of chirality, the diastereomeric complexation with the optically active auxiliary (*S*)-(+)-1-(9-antryl)-2,2,2-trifluoro ethanol ((*S*)-TFAE) served to differentiate the enantiomers by ^{1}H NMR. The chiral HPLC enabled micropreparative separation of the thermally interconvertible enantiomers of compounds **2**−**5** and **7**−**9** (Scheme 1), and thus the barriers to rotation around the $N_{3(sp^2)}-C_{aryl}$ bond could be determined.

Results and Discussion

2-Arylimino-3-aryl-thiazolidine-4-ones: ^{1}H NMR Results. Compounds **1**−**5** of these series have the following stereochemical features: The rotation around the N_3-C_{aryl} bond (Scheme 1) is sterically encumbered by the presence of the carbonyl group or the aryl imino bond on the heterocyclic ring, and thus these molecules assume nonplanar ground states. Among these compounds, **2**−**5** are chiral due to the dissymmetry brought about by *o*-substituents, the N_3-C_{aryl} bond being the chiral axis. The 180° rotation about this bond in **2**−**5** results in the formation of *M* and *P* enantiomers (Scheme 1).

Furthermore, the stereochemistry of the aryl imino bond should also be clarified, because it could, in principle, have the possibility to exist in *E* or *Z* configurations, or as a mixture of both. The *ortho*-unsubstituted compound **1**, which lacks a chiral axis, was initially investigated for that purpose. ^{1}H and ^{13}C NMR spectra of this compound taken in five different solvents (Table 1) at temperatures between −80 and 110 °C in DMF-d_7 and −70 and 100 °C in toluene-d_8 displayed the expected signals for the presence of only one isomer. This isomer has been assigned the *Z* configuration (Scheme 1) in which the phenylimino ring is transoidal to the aryl ring on N_3 and is thus expected to form the more stable diastereomer.

In compounds **2**−**5**, the N_3-C_{aryl} bond is a chiral axis, and therefore the protons on C-5 are diastereotopic. In fact, all of the compounds from **2** to **5** gave AB-type splitting patterns for the C-5 protons (Table 1, Figure 1), and the AB spectra for these compounds were also found to show a strong solvent dependence (Table 1). The least resolution of the diastereotopic protons was observed in methanol-d_4. Figure 2 shows the AB splittings for 2-(*o*-chlorophenyl)imino-3-(*o*-chlorophenyl)-thiazolidine-4-one, **5**, in various solvents.

The presence of further AB splittings of the C-5 protons for a given compound in this series would indicate the existence of *E* and *Z* isomerization in the C═N bond and/or another hindered rotation about the $N_{imino}-C_{aryl}$ bond. The fact that only one AB was observed for each compound was an indication that only the enantiomers *Z-M* and *Z-P* existed and the $N_{imino}-C_{aryl}$ bond rotation is free in the temperature range studied (−60 to 100 °C in toluene-d_8 and DMF-d_7).

When the 2D-NOESY and 2D-COSY spectra of the compounds in toluene-d_8 were compared, the cross-peak patterns observed between the protons in both spectra were the same, suggesting that there were no through-space interactions between the two phenyl rings.

Enantioselective HPLC. Because compounds **2**−**5** have been found to exist as racemates of interconvertible enantiomers *Z-M* and *Z-P*, barriers to rotation (enantiomerization) about the N_3-C_{aryl} bond have been investigated.

The enantiomers, 50% each as shown by the integrations of the UV peaks on the chromatogram, have been resolved or enriched micropreparatively on cellulose- or amylose-based columns Chiralpak AD-H and Chiralcel OD-H at 7 °C under the conditions given in Table 2. The resolved or enriched enantiomers were then subjected to thermal racemization (Figure 3) to find out the rate constant for their interconversion. Each enantiomer was kept in a constant temperature bath in ethanol solution, and at certain time intervals the racemization of each enantiomer was quenched by immersing its ethanol solution in an ice bath, and 30 μL of sample was withdrawn and injected into the chiral column. The ratios of the enantiomers (Figure 3a) were found by integration of the UV peaks (λ = 254 nm) on the chromatogram. A plot of $\ln([M] - [M]_{eq})/[M]_0 - [M]_{eq})$ versus time (Figure 3b) gave first-order rate constants for interconversion, and substitution of the rate constants into the Eyring equation $\Delta G^{\#} = RT \ln(k_b/kh)$ provided the barriers to enantiomerization. The barriers found have been listed in Table 2.

Energy barriers to rotation found in these compounds, as expected, were associated with the relative sizes of the *ortho* substituents. The larger was the *o*- substituent, the larger

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TABLE 1. 400 MHz ^{1}H NMR Spectral Data for the Compounds Studied in Different Solvents at 25 °C

	solvent	protons on C-5 ppm	aromatic ppm	*o*-methyl ppm	*o*-methoxy ppm	benzylidene-H
1	DMF-d_7	4.41	7.01−7.72			
	$CDCl_3$	3.99	6.90−7.54			
	methanol-d_4	3.98	6.77−7.43			
	toluene-d_8	2.75	7.16−7.41			
	benzene-d_6	2.64	6.59−6.98			
2	DMF-d_7	$\delta_A = 4.51$ $\delta_B = 4.42$	6.96−7.58	2.46 and 2.25		
	methanol-d_4	$\delta_A = 4.15$ $\delta_B = 4.12$	6.78−7.41	2.29 and 2.09		
	$CDCl_3$	$\delta_A = 4.02$ $\delta_B = 4.01$	6.79−7.38	2.32 and 2.11		
	toluene-d_8	$\delta_A = 3.03$ $\delta_B = 2.98$	6.80−7.05	1.94 and 1.84		
3	DMF-d_7	$\delta_A = 4.69$ $\delta_B = 4.53$	7.19−8.30			
	methanol-d_4	$\delta_A = 4.32$ $\delta_B = 4.23$	7.01−8.08			
	$CDCl_3$	$\delta_A = 4.09$ $\delta_B = 4.05$	6.93−7.92			
	toluene-d_8	$\delta_A = 3.26$ $\delta_B = 3.20$	7.05−7.94			
4	DMF-d_7	$\delta = 4.24$	6.79−7.48		3.89 and 3.76	
	$CDCl_3$	$\delta_A = 4.01$ $\delta_B = 3.96$	6.82−7.44		3.89 and 3.78	
	methanol-d_4	3.97 and 3.96	6.67−7.39		3.79 and 3.67	
	toluene-d_8	$\delta_A = 3.12$ $\delta_B = 2.99$	6.50−7.28		3.44 and 3.33	
	benzene-d_6	$\delta_A = 2.82$ $\delta_B = 2.68$	6.21−7.07		2.98 and 3.03	
5	DMF-d_7	$\delta_A = 4.45$ $\delta_B = 4.38$	7.01−7.75			
	$CDCl_3$	$\delta_A = 4.11$ $\delta_B = 4.04$	6.93−7.60			
	methanol-d_4	$\delta = 4.09$	6.85−7.52			
	toluene-d_8	$\delta_A = 3.06$ $\delta_B = 2.90$	6.60−7.29			
	benzene-d_6	$\delta_A = 2.76$ $\delta_B = 2.58$	6.29−7.06			
6	$CDCl_3$		6.96−7.57			7.84
7	$CDCl_3$		6.78−7.42	2.27 and 2.06		7.77
	$CDCl_3$[a]		6.64−7.39	2.29 and 2.27		7.79
	benzene-d_6		6.58−7.05	1.78 and 1.93		7.67
	benzene-d_6[a]		6.55−6.88	1.87, 1.85, 1.84, 1.83		7.58
8	$CDCl_3$		7.05−8.04			7.89
9	$CDCl_3$		6.87−7.48		3.89 and 3.77	7.79
	benzene-d_6		6.24−7.13		2.99	7.62
	benzene-d_6[a]		6.11−6.67		3.01, 2.97, 2.96, 2.94	7.51

[a] 1:6 equiv of (*S*)-TFAE was used.

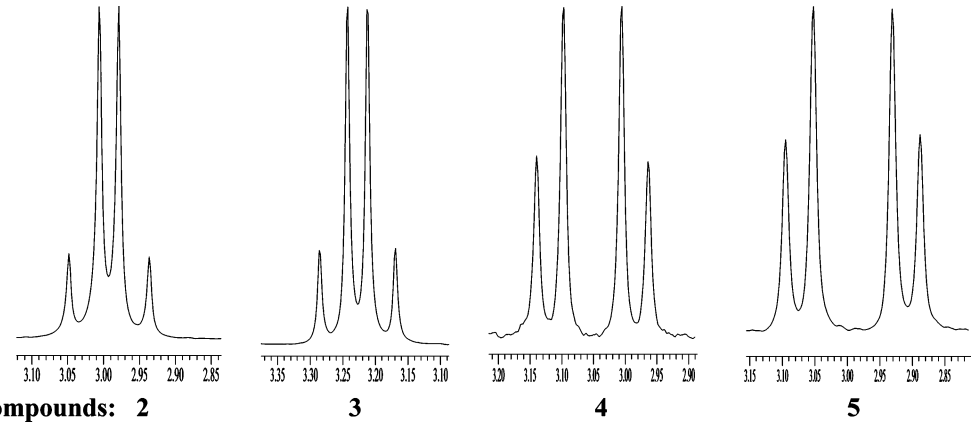

FIGURE 1. AB splittings of compounds **2**−**5** in toluene-d_8.

was the barrier. Although the van der Waals radius of chlorine is smaller than that of a methyl group, compound **5** (110.7 kJ/mol) showed a barrier greater than that of compound **2** (106.2 kJ/mol). Electrostatic repulsions between the lone pairs of the carbonyl oxygen and the chlorine atom are expected to make the rotation around the N_3−aryl bond more hindered, thus causing a larger barrier for this compound, which is in fact observed in structurally similar systems.[22] The naphthyl group on N_3 in compound **3** has introduced a greater barrier to rotation than an *ortho*-tolyl group present in **2**. The *ortho*-methoxy substituent gave rise to a lower barrier than an *ortho*-methyl group as has been observed previously.[21,22,24]

The energy barriers to enantiomerization found for the compounds have been compared to those of structurally similar systems to gather further evidence regarding the stereochemistry of the imino bond. The energy barrier for compound **2** was compared to that of 3-(*o*-tolyl)rhodanine, **11**. It was anticipated that there would not be as big an energy difference in rotational barriers between compound **2** with *Z* configuration and compound **11** because the imino nitrogen would not to be expected to hinder the rotation about N_3−aryl more than a sulfur atom (Figure 4). On the other hand, if the compound had an *E* configuration, the imino aryl would be expected to give rise to greater steric hinderence. Comparison of the barriers (106.2 kJ/

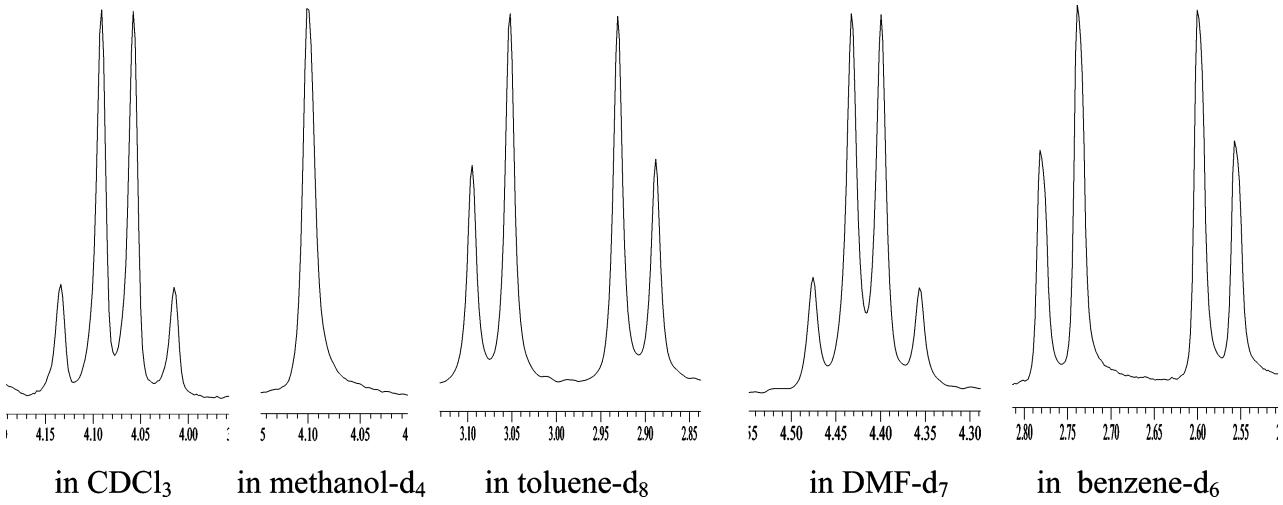

FIGURE 2. AB splittings for compound **5** in various solvents.

TABLE 2. Rate Constants and Energy Barriers to Rotation about the N_3–Aryl Bond of Compounds 2−5, 7−9

compounds	T (K)[h]	k (s^{-1})	$\Delta G^{\#}$ (kJ/mol)	$\Delta G^{\#}$ (kcal/mol)
2[a]	333	1.5×10^{-4}	106.2 ± 0.7	25.4 ± 0.2
3[b]	333	2.5×10^{-5}	111.2 ± 0.7	26.6 ± 0.2
4[c]	308	1.5×10^{-4}	98.1 ± 0.7	23.4 ± 0.2
5[d]	343	1.0×10^{-4}	110.7 ± 0.7	26.4 ± 0.2
7[e]	333	1.0×10^{-4}	107.4 ± 0.7	25.7 ± 0.2
8[f]	343	3.0×10^{-5}	114.1 ± 0.7	27.2 ± 0.2
9[g]	308	5.0×10^{-5}	100.9 ± 0.7	24.1 ± 0.2

[a] Column, Chiralcel OD-H; eluent, hexane:ethanol (95%:5%, v/v); α, 1.27; column temperature, 280 K. [b] Column, Chiralpak AD-H; eluent, ethanol:hexane (70%:30%, v/v); α, 1.17; column temperature, 280 K. [c] Column, Chiralcel OD-H; eluent, hexane:ethanol (95%:5%, v/v); α, 1.12; column temperature, 280 K. [d] Column, Chiralcel OD-H; eluent, hexane:ethanol (95%:5%, v/v); α, 1.15; column temperature, 280 K. [e] Column, Chiralcel OD-H; eluent, hexane:ethanol (60%:40%, v/v); α, 1.19; column temperature, 280 K. [f] Column, Chiralcel OD-H; eluent, hexane:ethanol (60%:40%, v/v); α, 1.14; column temperature, 280 K. [g] Column, Chiralpak AD-H; eluent, hexane:ethanol (95%:5%, v/v); α, 1.10; column temperature, 280 K. [h] Temperature at which the thermal racemization has been carried out.

mol for compound **2** and 109.3 kJ/mol for compound **11**) supports the assignment of *Z* configuration to the C═N bond. Similar comparisons were performed by Roussel et al. in identifying structurally relevant compounds.[25]

The energy barrier of compound **3** was compared to those of 3-(α-naphthyl)-2,4-thiazolidinedione,[24] **12**, and 3-(α-naphthyl)-rhodanine,[24] **13** (Figure 4). Comparison of the rotational barriers (111.2 kJ/mol for **3**, 105. 9 kJ/mol for **12**, and 111.3 kJ/mol for **13**) revealed that the barrier is higher than would be expected from just the steric requirements alone for a nitrogen atom, which would suggest that the aryl imino ring is also contributing to the barrier to rotation in compound **3**.

5-Benzylidene-2-arylimino-3-aryl-thiazolidine-4-ones. The α,*β*-unsaturated carbonyl compounds, 5-benzylidene-2-arylimino-3-aryl-thiazolidine-4-ones, **6**−**9** (Scheme 1), have been synthesized from the corresponding 2-arylimino-3-aryl-thiazolidine-4-ones, **1**−**4** (Scheme 1), by the reaction of benzaldehyde in the presence of sodium acetate in acetic acid.[10] Compound **5**, 2-(*o*-chlorophenyl)imino-3-(*o*-chlorophenyl)-thiazolidine-4-one, however, was found to be unreactive under these conditions despite longer reflux times.

^{1}H NMR in the Presence of a Chiral Auxiliary. The formation of the 5-benzylidene bond (Scheme 1) was shown by disappearance of the diastereotopic protons at C-5 of the precursor compounds (and also by disappearance of the protonated C-5 carbon in the ^{13}C NMR). The 5-benzylidene bond is known to have a *Z*-configuration from X-ray studies of structurally similar compounds.[26] In the present work, only one benzylidene-H was observed, which displayed a signal around 7.8 ppm. This was assigned to the benzylidene-H of the *Z* isomer, which is highly deshielded due to the magnetic anisotropy effect of the carbonyl bond syn to it (Scheme 1). The chiral natures of compounds **7** and **9** were confirmed by ^{1}H NMR spectroscopy, which were obtained in the presence of the optically active chiral auxiliary (*S*)-(+)-1-(9-antryl)-2,2,2-trifluoro ethanol ((*S*)-TFAE). These compounds were selected as representatives of this series because they contain a CH_3 group, which would give rise to different signals in the diastereomeric association complexes that are expected to form by noncovalent interactions (hydrogen bonds) between the hydroxyl group of (*S*)-TFAE and oxygen atoms of the heterocyclic ring as well as $\pi-\pi$ stacking interactions between the anthryl group and aryl ring (Figure 5).

In the case of compound **7**, two peaks were observed for *ortho*-methyl groups in the ^{1}H NMR spectrum at 1.93 and 1.78 ppm in the absence of (*S*)-TFAE in benzene-d_6, whereas in the presence of (*S*)-TFAE four peaks were present for *ortho*-methyl groups at 1.87, 1.85, 1.84, and 1.83 ppm, which provided evidence for the chiral nature of compound **7**. The 2D-NOESY results (DMF-d_7) obtained for **2**, which is structurally related to compound **7**, showed that the methyl group that appeared relatively upfield was the one on the N_{imino}−aryl ring, whereas the methyl signal that appeared more downfield was due to the one on the N_3−aryl ring (Figure 6). Based on this result, for compound **7**, the signal at 1.78 ppm in the absence of (*S*)-TFAE was assigned to the methyl group on the N_{imino}−phenyl ring and the signal at 1.93 ppm to the methyl on N_3−phenyl. Correspondingly, of the four singlets observed in the presence of (*S*)-TFAE (Figure 7), the peaks at 1.84 and 1.83 ppm were assigned to the N_{imino}−phenyl methyls, and those at 1.87 and 1.85 ppm, which were better resolved, were consistent with the

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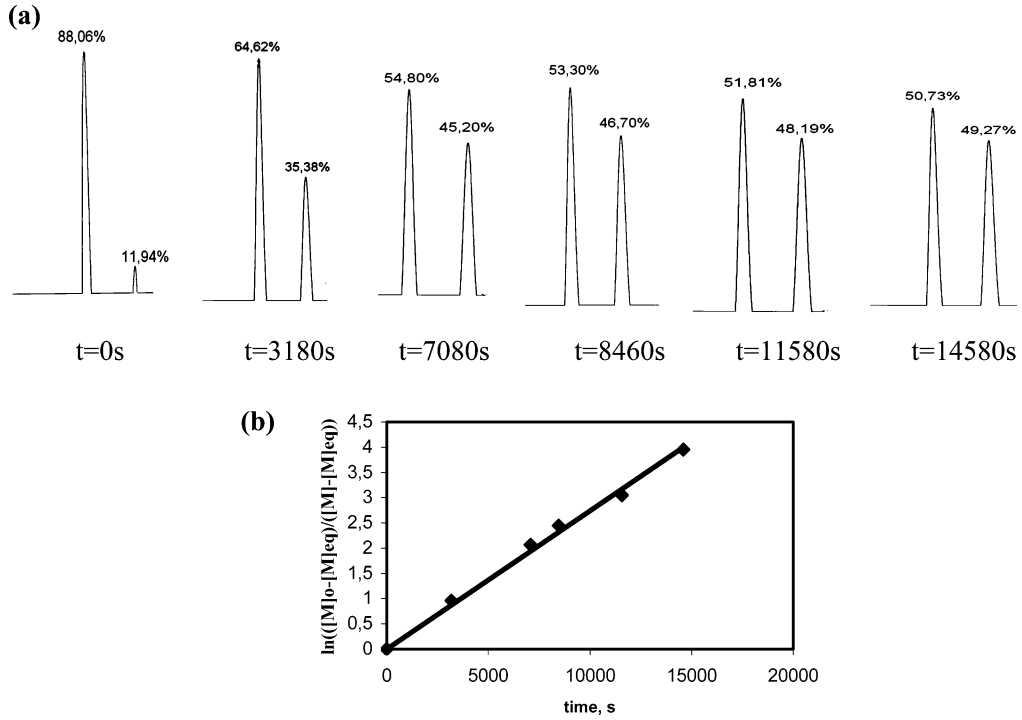

FIGURE 3. (a) The chromatograms taken to follow thermal racemization process of compound **2** at 333 K (column, Chiralcel OD-H; eluent, hexane:ethanol (95%:5%, v/v); flow rate, 0.6 mL/min; retention times, t_1, 30.64 min, t_2, 37.28 min; α, 1.27; column temperature, 280 K). (b) The plot of $\ln(([M]_0 - [M]_{eq}/[M] - [M]_{eq}))$ versus time at 333 K for compound **2**.

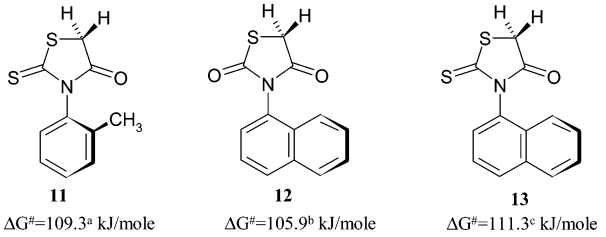

FIGURE 4. Structures and the energy barriers of structurally related compounds. (a) Column, Chiralcel OD-H; eluent, hexane:ethanol (95%:5%, v/v); α, 1.08; at 333 K. Racemization has been done in ethanol. (b) Reference 24. (c) Reference 24.

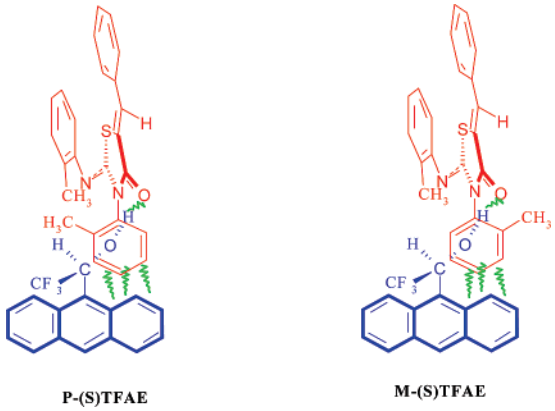

FIGURE 5. The proposed solvation model for compound **7**, based on the known stereostructure of (*S*)-TFAE where the hydroxyl and the carbinyl hydrogens are on the same side and $-CF_3$ is nearly orthogonal to the plane of the antryl ring.[27]

methyls attached to the N_3−phenyl ring. The proposed solvation model (Figure 5) accounts for the difference in chemical shifts for the methyl groups in the association complexes. In this solvation model, when the association complex has the *P* conformation, the *ortho*-methyl group on the N_3−aryl ring resides in the shielding zone of the antryl and would be expected to be more shielded. In the case of the *M* conformation, the N_3−methyl is located outside of the shielding zone of the antryl ring (Figure 5), and therefore this methyl group will be expected to be more deshielded as compared to the (*P*)-N_3−methyl group. Thus, among the diastereomeric pairs *M*-(*S*)-TFAE and *P*-(*S*)-TFAE, the CH_3 groups of *P*-(*S*)-TFAE are expected to be more shielded (Figure 7). The chemical shift differences were found to be 0.01 ppm for the N_{imino}−methyl groups and 0.02 ppm for the N_3−methyl groups in benzene-d_6. In $CDCl_3$, the presence of (*S*)-TFAE did not give rise to additional peaks for *ortho*-methyl groups (2.29 and 2.27 ppm).

In the case of compound **9**, the two *ortho*-methoxy groups were not differentiated in the absence of (*S*)-TFAE and gave a signal corresponding to 6 hyrogens at 2.99 ppm in benzene-d_6. In the presence of (*S*)-TFAE, four well-resolved peaks (Figure 7) were observed. For this compound, there is the added possibility of additional interactions between the oxygen of the methoxy group and the carbinyl or hydroxyl H of the (*S*)-TFAE, which might contribute to better resolution of the $-OCH_3$ signals.

Barriers to Enantiomerization. Chromatographic separations of the enantiomers of **7** and **8** were performed on Chiralpak OD-H, and that of **9** on Chiralcel AD-H under the conditions given in Table 2. To determine the barriers to enantiomerization, the resolved enantiomers were subjected to thermal racemization as has been described previously in the text, and the barriers for compounds **7**, **8**, and **9** were found as 107.4, 114.1, and 100.9 kJ/mol (Table 2), respectively. Although the 5-benzylidene derivatization is not close to the internal rotation site, the rotational barriers in **7**−**9** were found to be 2−3 kJ/mol larger

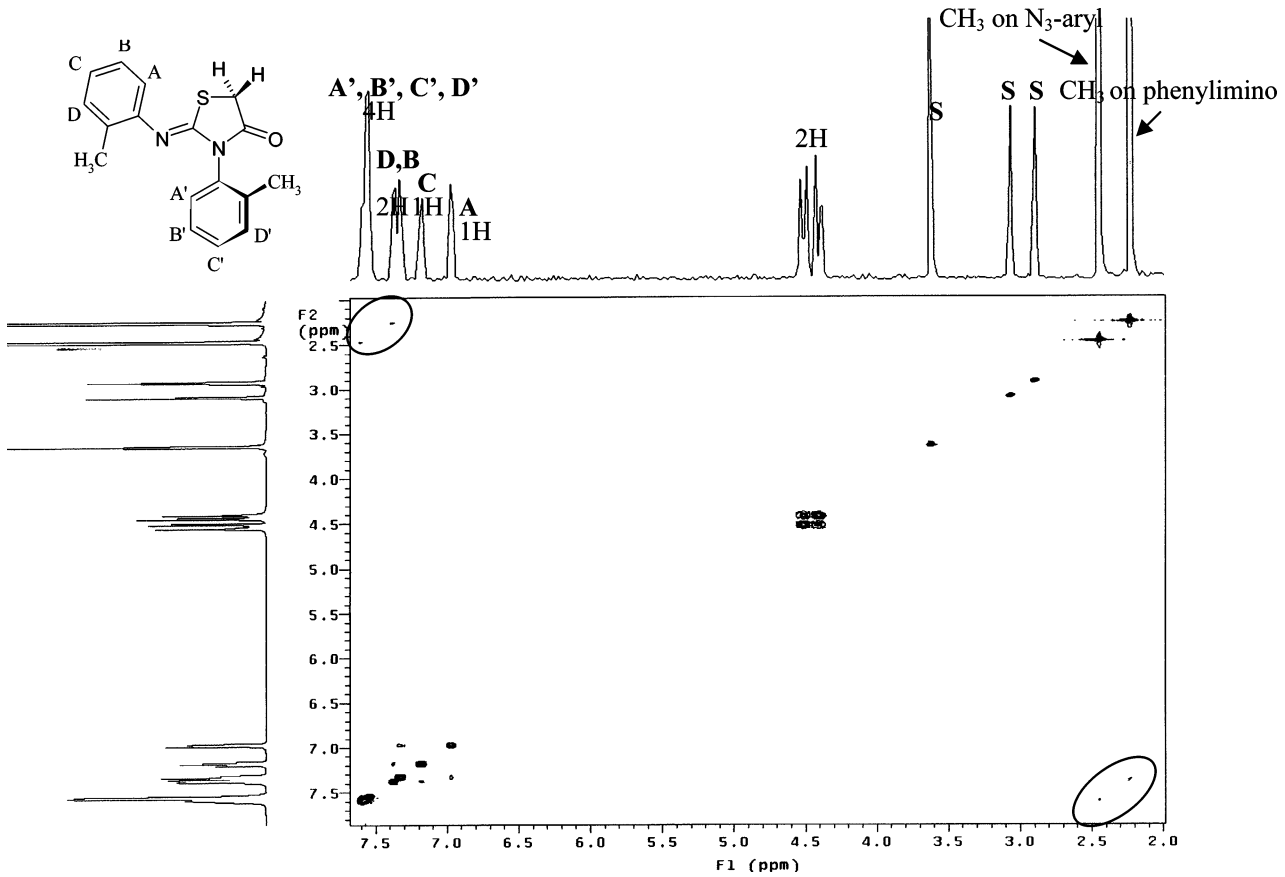

FIGURE 6. 2D-NOESY spectrum of compound **2** in DMF-d_7 (S: solvent).

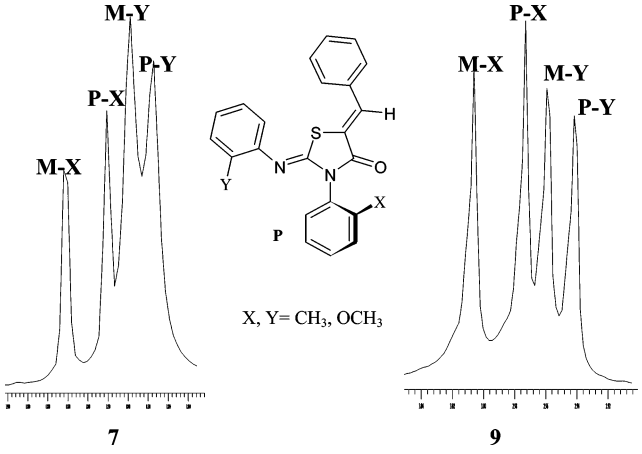

FIGURE 7. ^{1}H NMR signals of *ortho*-methyl and *ortho*-methoxy groups of compounds **7** and **9** in the presence of 6 equiv of (*S*)-TFAE in benzene-d_6.

than their corresponding 2-arylimino-3-aryl-thiazolidine-4-ones, **2**−**4**. This increase in barrier height may be due to the partial single bond character and the negative charge that the carbonyl oxygen takes upon conjugation with the α−β double bond.

Conclusion

In the work described here, sterically hindered 2-arylimino-3-aryl-thiazolidine-4-ones and 5-benzylidene-2-arylimino-3-aryl-thiazolidine-4-ones have been synthesized where the *N*-*o*-aryl-substituted derivatives are axially chiral. The chiral nature of the compounds has been shown by observation of either (i) diastereotopic protons on the heterocycles or (ii) diastereomer formation via supramolecular interactions in the presence of optically active auxiliary (*S*)-TFAE in ^{1}H NMR. The enantiomers of the chiral derivatives that have been synthesized as racemates have been resolved or enriched by micropreparative enantioselective HPLC, and the barriers to enantiomerization have been determined by thermal racemization. Now that the enantiomers of **2**−**5** and **7**−**9** have been found to be separable, asymmetric reactions via steric control of the *N*-*o*-aryl group will be worth trying on single enantiomers of these compounds.

Experimental Section

General Procedure for the Preparation of Compounds 1−5. Compounds **1**−**5**, 2-arylimino-3-aryl-thiazolidine-4-ones, were synthesized by the reaction of the corresponding *N*,*N*′-diarylthioureas and α-bromoacetic acid.[28] The appropriate *N*,*N*′-diarylthiourea and α-bromoacetic acid were refluxed for 6 h in absolute ethanol in the presence of sodium acetate. At the end of this period, the crude product was purified by recrystallization from ethanol.[28]

2-Phenylimino-3-phenyl-thiazolidine-4-one (1). The compound was synthesized according to the general procedure using 1.14 g (0.005 mol) of *N*,*N*′-diphenylthiourea, 0.84 g (0.006 mol) of α-bromoacetic acid, 0.49 g (0.006 mol) of sodium acetate, and 50 mL of ethanol. After recrystallization from ethanol, 2-phenylimino-3-phenyl-thiazolidine-4-one was obtained as bright white crystals. Yield: 0.60 g (44.8%). mp: 175−176 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54−6.90 (m, 10H), 3.99 (s, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 155.1, 148.3−121.1, 33.1 ppm.

(28) Doğan, İ.; İçli, S. *Spectrosc. Lett.* **1983**, *16*, 499.

Anal. Calcd for $C_{15}H_{12}ON_2S$: C, 67.14; H, 4.51; N, 10.44; S, 11.95. Found: C, 67.52; H, 4.72; N, 10.65; S, 11.87. IR (KBr): 1630, 1579 cm^{-1}. UV−vis (EtOH) λ_{max} 223 (log ϵ 4.27), 269 (log ϵ 3.71) nm.

2-(*o*-Tolyl)imino-3-(*o*-tolyl)-thiazolidine-4-one (2). The compound was synthesized according to the general procedure using 0.64 g (0.0025 mol) of *N*,*N*′-di-(*o*-tolyl)thiourea, 0.42 g (0.003 mol) of α-bromoacetic acid, 0.25 g (0.003 mol) of sodium acetate, and 50 mL of ethanol. After recrystallization from ethanol, 2-(*o*-tolyl)-imino-3-(*o*-tolyl)-thiazolidine-4-one was obtained as white crystals. Yield: 0.41 g (55.4%). mp: 154−155 °C. ^{1}H NMR (400 MHz, DMF-d_7): δ 7.58−6.96 (m, 8H), 4.51 and 4.42 (AB quartet, 1H each, J_{AB} = 17 Hz), 2.46 (s, 3H), 2.25 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 171.4, 154.1, 147.0−120.0, 33.3, 18.0, 17.9 ppm. Anal. Calcd for $C_{17}H_{16}ON_2S$: C, 68.90; H, 5.44; N, 9.45; S, 10.82. Found: C, 68.96; H, 5.55; N, 9.59; S, 10.72. IR (KBr): 1631, 1603 cm^{-1}. UV−vis (EtOH) λ_{max} 212 (log ϵ 4.46), 270 (log ϵ 3.62) nm.

2-(α-Naphthyl)imino-3-(α-naphthyl)-thiazolidine-4-one (3). The compound was synthesized according to the general procedure using 1.64 g (0.005 mol) of *N*,*N*′-di-(α-naphthyl)thiourea, 0.84 g (0.006 mol) of α-bromoacetic acid, 0.49 g (0.006 mol) of sodium acetate, and 50 mL of ethanol. After recrystallization from ethanol, 2-(α-naphthyl)imino-3-(α-naphthyl)-thiazolidine-4-one was obtained as a light pink colored and very fine crystalline powder. Yield: 0.46 g (25.0%). mp: 180−181 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93−7.92 (m, 14H), 4.09 and 4.05 (AB quartet, 1H each, J_{AB} = 17 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9, 166.4, 144.5−115.2, 33.4 ppm. Anal. Calcd for $C_{23}H_{16}ON_2S$: C, 74.97; H, 4.38; N, 7.60; S, 8.70. Found: C, 74.73; H, 4.58; N, 7.72; S, 8.52. IR (KBr): 1630, 1511 cm^{-1}. UV−vis (EtOH) λ_{max} 241 (log ϵ 5.49), 293 (log ϵ 5.35) nm.

2-(*o*-Methoxyphenyl)imino-3-(*o*-methoxyphenyl)-thiazolidine-4-one (4). The compound was synthesized according to the general procedure using 2.16 g (0.0075 mol) of *N*,*N*′-di-(*o*-methoxyphenyl)-thiourea, 1.25 g (0.009 mol) of α-bromoacetic acid, 0.75 g (0.009 mol) of sodium acetate, and 50 mL of methanol. After recrystallization from ethanol, 2-(*o*-methoxyphenyl)imino-3-(*o*-methoxyphenyl)-thiazolidine-4-one was obtained as a white fine crystalline powder. Yield: 0.30 g (12.2%). mp: 194−195 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06−6.93 (m, 8H), 4.01 and 3.96 ppm (AB quartet, 1H each, J_{AB} = 17 Hz), 3.89 (s, 3H), 3.78 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6, 155.6, 155.2−112.5, 56.3, 56.1, 33.3 ppm. Anal. Calcd for $C_{17}H_{16}O_3N_2S$: C, 62.18; H, 4.91; N, 8.53; S, 9.76. Found: C, 62.18; H, 4.93; N, 8.59; S, 9.59. IR (KBr): 1631, 1502 cm^{-1}. UV−vis (EtOH) λ_{max} 213 (log ϵ 4.56), 279 (log ϵ 3.97) nm.

2-(*o*-Chlorophenyl)imino-3-(*o*-chlorophenyl)-thiazolidine-4-one (5). The compound was synthesized according to the general procedure using 1.48 g (0.005 mol) of *N*,*N*′-di-(*o*-chlorophenyl)-thiourea, 0.84 g (0.006 mol) of α-bromoacetic acid, 0.49 g (0.006 mol) of sodium acetate, and 50 mL of ethanol. After recrystallization from ethanol, 2-(*o*-chlorophenyl)imino-3-(*o*-chlorophenyl)-thiazolidine-4-one was obtained as white crystals. Yield: 0.20 g (11.9%). mp: 166−167 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06−6.93 (m, 8H), 4.11 and 4.04 (AB quartet, 1H each, J_{AB} = 17 Hz) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 155.9, 145.2−122.1, 33.4 ppm. Anal Calcd for $C_{15}H_{10}ON_2SCl_2$: C, 53.42; H, 2.99; N, 8.31; S, 9.50. Found: C, 53.13; H, 3.11; N, 8.34; S, 9.12. IR (KBr): 1641, 1582 cm^{-1}. UV−vis (EtOH) λ_{max} 209 (log ϵ 4.40), 267 (log ϵ 3.44) nm.

General Procedure for the Preparation of Compounds 6−9. Compounds **6**−**9**, 5-arylidene-2-arylimino-3-aryl-thiazolidine-4-ones, were synthesized by refluxing appropriate 2-arylimino-3-aryl-thiazolidine-4-one with benzaldehyde in the presence of sodium acetate and acetic acid for 5 h.[4] The compounds were purified by recrystallization from ethanol.

5-Benzylidene-2-phenylimino-3-phenyl-thiazolidine-4-one (6). The compound was synthesized according to the general procedure using 0.4 g (0.0015 mol) of compound **1**, 0.19 g (0.0018 mol) of benzaldehyde, 0.14 g (0.0018 mol) of sodium acetate, and 10 mL of acetic acid. Yield: 0.39 g (73%). mp 200−202 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 1H), 7.57−6.96 (m, 15H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 151.1, 148.4−121.6, 121.3 ppm. Anal. Calcd for $C_{22}H_{16}ON_2S$: C, 74.13; H, 4.52; N, 7.86; S, 8.99. Found: C, 74.07; H, 4.83; N, 7.92; S, 8.80. IR (KBr): 1633, 1588 cm^{-1}. UV−vis (EtOH) λ_{max} 228 (log ϵ 4.26), 330 (log ϵ 4.32) nm.

5-Benzylidene-2-(*o*-tolyl)imino-3-(*o*-tolyl)-thiazolidine-4-one (7). The compound was synthesized according to the general procedure using 0.2 g (0.00067 mol) of compound **2**, 0.09 g (0.0008 mol) of benzaldehyde, 0.06 g (0.0008 mol) of sodium acetate, and 10 mL of acetic acid. Yield: 0.16 (62%). mp: 168−170 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.42−6.78 (m, 13H), 2.27 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 157.0, 147.2−120.2, 121.8, 18.0, 17.9 ppm. Anal. Calcd for $C_{24}H_{20}ON_2S$: C, 74.97; H, 5.24; N, 7.29; S, 8.33. Found: C, 74.74; H, 5.32; N, 7.49; S, 8.16. IR (KBr): 1635, 1600 cm^{-1}. UV−vis (EtOH) λ_{max} 231 (log ϵ 4.41), 329 (log ϵ 4.35) nm.

5-Benzylidene-2-(α-naphthyl)imino-3-(α-naphthyl)-thiazolidine-4-one (8). The compound was synthesized according to the general procedure using 0.2 g (0.00054 mol) of compound **3**, 0.07 g (0.00064 mol) of benzaldehyde, 0.05 g (0.00064 mol) of sodium acetate, and 10 mL of acetic acid. Yield: 0.14 (56%). mp: 250−252 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04−7.05 (m, 19H), 7.89 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.4, 133.2−122.4, 121.2 ppm. Anal. Calcd for $C_{30}H_{20}ON_2S$: C, 78.92; H, 4.41; N, 6.14; S, 7.02. Found: C, 78.30; H, 4.62; N, 6.05; S, 6.31. The combustion analysis for compound **8** deviates 0.62% in C and 0.71% in S, while the H and N results are acceptable (0.21% and 0.08%, respectively). The HPLC trace for this substance shows no impurities and has been provided as a part of the Supporting Information. No further samples of **8** are currently available; thus the analysis could not be repeated. IR (KBr): 1639, 1625 cm^{-1}. UV−vis (EtOH) λ_{max} 237 (log ϵ 5.20), 293 (log ϵ 4.68) nm.

5-Benzylidene-2-(*o*-methoxyphenyl)imino-3-(*o*-methoxyphenyl)-thiazolidine-4-one (9). The compound was synthesized according to the general procedure using 0.3 g (0.0009 mol) of compound **4**, 0.12 g (0.0011 mol) of benzaldehyde, 0.09 g (0.0011 mol) of sodium acetate, and 10 mL of acetic acid. Yield: 0.28 (73%). mp: 162−164 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.48−6.87 (m, 13H), 3.89 (s, 3H), 3.77 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6, 155.4, 151.4−110.0, 122.4, 56.2, 56.1 ppm. Anal. Calcd for $C_{24}H_{20}O_3N_2S$: C, 69.21; H, 4.84; N, 6.73; S, 7.69. Found: C, 69.29; H, 5.05; N, 6.84; S, 7.68. IR (KBr): 1646, 1606 cm^{-1}. UV−vis (EtOH) λ_{max} 222 (log ϵ 4.15), 330 (log ϵ 3.00) nm.

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Supporting Information Available: General methods and ^{1}H NMR spectra of **1**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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