JOC Article
pubs.acs.org/joc

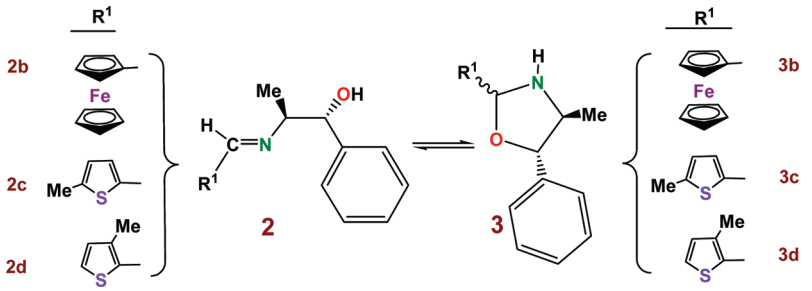
Study of the Effect Induced by the Substituents on the Ring−Chain Tautomerism of Schiff Bases Derived from Norephedrine

Daniel Talancón, Ramon Bosque, and Concepción López*

Departament de Quimica Inorgànica, Facultat de Quimica, Universitat de Barcelona, Martí i Franquès 1-11, 08028 Barcelona, Spain

conchi.lopez@qi.ub.es

Received February 22, 2010



The solution behavior and the spectroscopic properties of the novel Schiff bases (1*S*,2*R*)-R^{1}CH=NCH-(Me)CH(OH)Ph [with R^1 = ferrocenyl-[Fc (**2b**)], 5- or 3-methylthienyl [hereafter referred to as 5-MeTf and 3-MeTf (**2c** and **2d**), respectively]] are reported. NMR studies show the existence of a tautomeric equilibrium between these imine forms (**2b**−**d**) and 2-substituted 4-methyl-5-phenyloxazolidines. The comparison of the results reveals that the molar ratios imine/oxazolidines (*K*): (a) are solvent and temperature dependent, (b) are higher than that obtained for (1*S*,2*R*)-PhCH=NCH(Me)CH(OH)Ph (**2e**), (c) are strongly affected by the nature of the R^1 group, and (d) increase according to the sequence Ph < Fc < 5-MeTf < 3-MeTf. Density functional theory (DFT) calculations on the open forms (imines **2b**−**e**) and on the diastereomers of the closed forms (2-substituted 4-methyl-5-phenyl oxazolidines) have also been carried out in order to rationalize the differences detected in the solution behavior of **2b**−**d** and their analogue with R^1 = Ph (**2e**).

Introduction

Ring−chain tautomeric equilibria involving 1,3-O,N-heterocyclic systems have generated great interest in the past few years.[1−6] In this type of process, an imino alcohol undergoes a reversible intramolecular C−H activation of the −OH group giving 1,3-oxazines or oxazolidines (via a *6*- or a *5-endo-trig* process, respectively) (Scheme 1, **A** and **B**). This type of tautomerism affects the reactivity of the species involved, and this property is important not only in view of their utility in organic synthesis but also in physical and medical chemistry.[2]

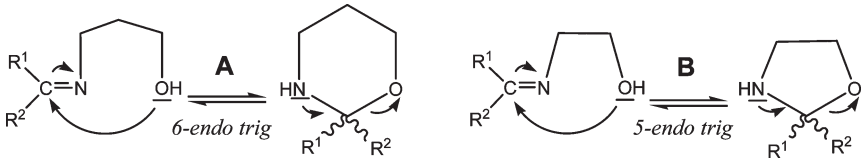
On the other hand, despite the increasing importance of ferrocene-containing heterocycles in organic and organometallic synthesis, in homogeneous catalysis and/or in supramolecular chemistry as well as of chiral ligands and their transition-metal compounds in metal-catalyzed asymmetric synthesis, in biochemistry, or even in drug development, chiral ferrocene derivatives containing 1,3 O,N-heterocycles with ring−chain tautomerism are not common.[5,6]

We have recently reported the synthesis of 2-ferrocenyl-2,4-dihydro-1*H*-benzo[*d*][1,3]oxazine (**1a**) and the tautomeric

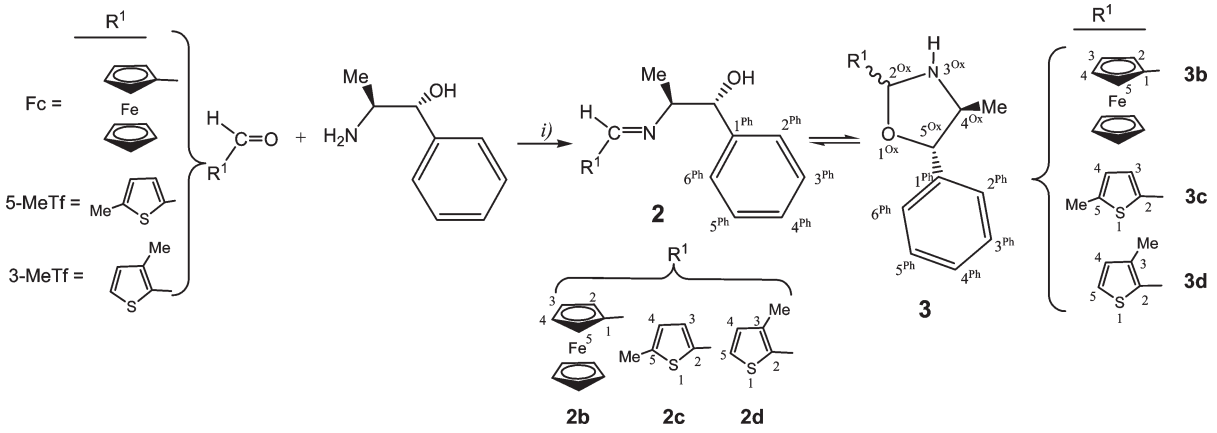
(1) Valters, R. E.; Flitsch, W. *Ring-Chain Tautomerism*; Plenum Press: New York, 1985.
(2) (a) Lázár, L.; Fülöp, F. *Eur. J. Org. Chem.* **2003**, 3025–3042. and references cited therein. (b) Szatmári, I.; Martinek, T. A.; Lázár, L.; Koch, A.; Kleinpeter, E.; Neuvonen, K.; Fülöp, F. *J. Org. Chem.* **2004**, *69*, 3645–3653.
(3) For recent contributions in this field: (a) Keiko, N. A.; Vchislo, N. V.; Stepanova, L. G.; Larina, L. I.; Chuvashev, Y. A.; Funtikova, E. A. *Chem. Heterocycl. Compd.* **2008**, *44*, 1466–1471. (b) Pihlaja, K.; Juhasz, M.; Kivelä, H.; Fülöp, F. *Rapid. Commun. Mass Spectrosc.* **2008**, *22*, 1510–1518. (c) Juhasz, M.; Lázár, L.; Fülöp, F. *J. Heterocycl. Chem.* **2007**, *44*, 1465–1473. (d) Peng, L.-J.; Liu, Z.-Q.; Wang, J.-T.; Wu, L.-M. *Tetrahedron Lett.* **2007**, *48*, 7418–7421. (e) Selambarom, J.; Smadja, J.; Thomas, O.; Parrot, I.; Martínez, J.; Pavia, A. A. *Int. J. Pept. Res. Ther.* **2005**, *11*, 267–270. (f) Strong, E. T. J.; Cardile, S. A.; Brazeau, A. L.; Jennings, M. C.; McDonald, R.; Jones, N. D. *Inorg. Chem.* **2008**, *47*, 10575–15086. (g) Caputo, C. A.; Jones, N. D. *Dalton Trans.* **2007**, 4627–4640.
(4) Cardile, S. A.; Jennings, M. C.; Jones, N. D. *Dalton Trans.* **2006**, 4672–4678.

Published on Web 04/20/2010 DOI: 10.1021/jo100255k

SCHEME 1. ***6-Endo* and *5-Endo-Trig* Processes**



SCHEME 2[a]



[a]Key: (i) in refluxing benzene (for **2b**) or ethanol (for **2c** and **2d**).

equilibrium between **1a** and the imino alcohol [(η^5-C_5H_5)Fe-[(η^5-C_5H_4)CH=N(C_6H_4-2-CH_2OH)]] (**2a**).[5] Furthermore, the study of the reactivity of **1a** with palladium(II) salts or complexes has allowed us to isolate heterodi- and heterotrimetallic compounds with one or two ferrocenyl units, some of which exhibit outstanding electrochemical behavior.[7]

In view of this, and as a part of a project directed toward the synthesis of chiral ligands derived from ferrocene[8] or achiral derivatives with (N,X) (X = N, S or O) heterocycles,[9] in this work we present (a) the synthesis of the diastereomerically pure Schiff bases (1*S*,2*R*)-R^1CH=NCH(Me)CH(OH)Ph [with R^1 = ferrocenyl- (**2b**), 5- or 3-methylthienyl (**2c** and **2d**, respectively)], (b) a comparative study of the solution behavior of imines **2b**−**d** that reveals the existence of a tautomeric equilibrium between these imines and their closed forms (2-substituted-4-methyl-5-phenyloxazolidines), and (c) a theroretical study based on DFT calculations that has allowed us to establish the influence of the nature of the R^1 group on this ring−chain tautomerism.

Results and Discussion

Treatment of ferrocenecarboxaldehyde with an equimolar amount of (1*S*,2*R*)-H_2NCH(Me)CH(OH)Ph (norephedrine) in refluxing benzene (Scheme 2) produced a deep red solution that gave, after concentration, an oily material (hereafter referred to as **2b**).

Its IR spectrum showed a narrow and intense band at 1638 cm^{-1}, which falls in the range reported for related ferrocenylaldimines of general formula [(η^5-C_5H_5)Fe[(η^5-C_5H_4)CH=NR^2]] [with R^2 = −CH(R^3)CH_2OH, (R^3 = H, Me or ^{i}Pr)],[8a,b,10] thus suggesting that **2b** was [(η^5-C_5H_5)Fe-[(η^5-C_5H_4)CH=NCH(Me)CH(OH)Ph]]. The high-resolution ESI mass spectrum of **2b** showed a peak at m/z = 348.1043 that agrees with that expected for the [[M] + H]$^+$ cation [$C_{20}H_{21}FeNO$, m/z = 348.1051].

Previous studies have shown that the condensation of ferrocenecarboxaldehyde with chiral amines such as H_2NCH(R^4)CH_2OH (R^4 = Me or ^{i}Pr) or (*R*)-H_2NCH(Me)($C_{10}H_7$) does not modify the absolute configuration of the stereocenters;[8a−c] on this basis, we assumed that **2b** is the (1*S*,2*R*) isomer.

The ^{1}H NMR spectrum of **2b** in $CDCl_3$ at 298 K showed three sets of superimposed signals, thus suggesting the presence of at least three species in solution. This behavior differs from those reported for [(η^5-C_5H_5)Fe[(η^5-C_5H_4)CH=NR^2]] [with R^2 = −CH(R^3)CH_2OH (R^3 = H, Me or ^{i}Pr)],[8a,b,10] for which only the imine form was present in solution. The resonances due to the major component agreed with those expected for the

(5) Pérez, S.; López, C.; Caubet, A.; Roig, A.; Molins, E. *J. Org. Chem.* **2005**, *70*, 4857–4860.
(6) Krieg, R.; Wyrwa, R.; Möllmann, U.; Görls, H; Schönecker, B. *Steroids* **1998**, *63*, 531–541.
(7) Pérez, S.; López, C.; Caubet, A; Solans, X.; Font-Bardía, M.; Roig, A.; Molins, E. *Organometallics* **2006**, *25*, 596–601.
(8) (a) López, C.; Caubet, A.; Pérez, S.; Solans, X.; Font-Bardía, M.; Roig, A.; Molins, E. *Chem. Commun.* **2004**, 540–541. (b) López, C.; Caubet, A.; Pérez, S.; Solans, X.; Font-Bardía, M. *Eur. J. Inorg. Chem.* **2006**, 3974–3984. (c) Benito, M.; López, C.; Solans, X.; Font-Bardía, M. *Tetrahedron: Asymmetry* **1998**, *9*, 4219–4238. (d) Moyano, A.; Rosol, M.; Moreno, R. M.; López, C.; Maestro, M. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1865–1869. (e) Platero, A. E.; Pérez, S.; López, C.; Solans, X.; Font-Bardía, M.; van Leeuwen, P. W. N. M.; van Strijdonck, G. P. F.; Freixa, Z. *J. Organomet. Chem.* **2007**, *692*, 4215–4226. (f) Moreno, R. M.; Catasús, M.; López, C.; Moyano, A. *Eur. J. Org. Chem.* **2008**, 2388–2396. (g) Gibert, L.; González, A.; Granell, J.; López, C. *Tetrahedron: Asymmetry* **2002**, *13*, 983–988. (h) López, C.; Caubet, A.; Bosque, R.; Solans, X.; Font-Bardía, M. *J. Organomet. Chem.* **2002**, *645*, 146–151. (i) González, A.; Granell, J.; López, C. *J. Organomet. Chem.* **2001**, *637*−*639*, 116–125.
(9) (a) Pou, D.; Platero, A. E.; Pérez, S.; López, C.; Solans, X.; Font-Bardía, M.; van Leeuwen, P. W. N. M.; van Strijdonck, G. P. F.; Freixa, Z. *J. Organomet. Chem.* **2007**, *692*, 5017–5025. (b) González, A.; López, C.; Solans, X.; Font-Bardía, M. *J. Organomet. Chem.* **2008**, *693*, 2877–2886.
(10) López, C.; Caubet, A.; Solans, X.; Font-Bardía, M. *J. Organomet. Chem.* **2000**, *598*, 87–102.

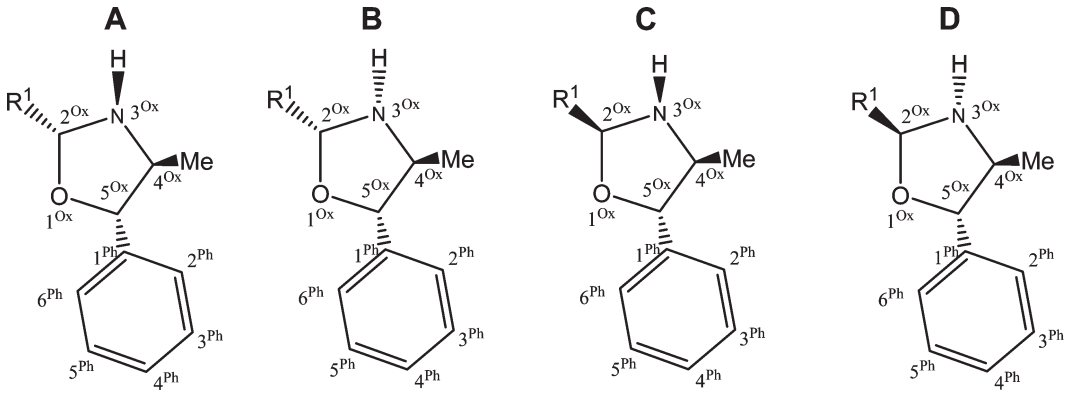


FIGURE 1. Schematic view of the four possible diastereomers of the 2-substituted 4-methyl-5-phenyloxazolidines **3** where R^1 represents Fc, 5-MeTf, 3-MeTf, or Ph. Compounds **A** and **B** (or **C** and **D**) differ exclusively on the absolute configuration of the heterocyclic nitrogen.

aldimine **2b** and the [^{1}H−^{1}H]-NOESY spectrum in $CDCl_3$ at 298 K indicated the existence of NOE contacts between the imine proton and those of the −CH(Me)− unit, indicating that **2b** is in the *anti*-(*E*) form. This agrees with the results obtained for other ferrocenylaldimines, which also adopt this form in solution as well as in the solid state.[11]

The analyses of the remaining signals observed in the ^{1}H NMR spectrum suggested, according to the references,[12] the presence of two of the diastereomers of the 4-methyl-2-(ferrocenyl)-5-phenyloxazolidines (Scheme 2) generated by a *5-endo-trig* process. It should be noted that (a) the formation of the oxazolidines generates a new stereogenic carbon center (C^2) and (b) the hydrogen of the −NH unit may be located on two different sites. Consequently, four diastereomers of the oxazolidine could be formed in the cyclization process (Figure 1, **A**−**D**). (The four diastereomers **A**−**D** may exist in the solid state or when these oxazolidines act as N-donor ligands in coordination complexes; see, for instance, ref 4. However, in solution the proton of the >NH unit is expected to interchange, and thus, the interconversion between isomers **A** and **B** (or **C** and **D**) will probably occur).

Since the ^{1}H NMR spectrum of **2b** in $CDCl_3$ at 298 K indicated the coexistence of the open-chain form **2b** and two of the isomers of the cyclic form **3b** [herein after referred to as $\mathbf{3b_I}$ and $\mathbf{3b_{II}}$ (major and minor isomer, respectively)], we decided to study this tautomeric process in detail. In order to achieve this goal, several NMR experiments were performed. In all of the experiments, the samples used were dissolved in the appropriate deuteriated solvent, and the solution was allowed to stand for some time to be sure that the equilibrium was reached. The relative molar ratio imine/oxazolidines was $K_{Fc} = 5.4$ (where the subscript of *K* refers to the R^1 group: Fc, 5-MeTf, 3-MeTf, or Ph; the relative abundance of the imine and oxazolidine forms was determined by integration of well-separated signals due to the protons of the imine unit (of **2b**) and the "N−CH(ring)−O" (of $\mathbf{3b_I}$ and $\mathbf{3b_{II}}$)).

Variable-temperature (233 K ≤ *T* ≤ 298 K) ^{1}H NMR studies in $CDCl_3$ indicate that the oxazolidine form was slightly favored at lower temperatures,[13] but the molar ratios $\mathbf{3b_I}/\mathbf{3b_{II}}$ did not change substantially upon cooling.[14] The van't Hoff plot (log K_{Fc} versus $1/T$) gave $\Delta H° = 2.5$ kJ mol^{-1} and $\Delta S° = 22.3$ J mol^{-1} K^{-1}. The value of $\Delta H°$ is rather small, and this can be consistent with the tiny variation detected for K_{Fc} upon cooling.[13] The $\Delta S°$ value is slightly greater than that reported for the tautomeric equilibrium between the imine: (C_5H_4N)-2-CH=NCH(^{i}Pr)CH_2OH and the diastereomers of the oxazolidines ($\Delta S° = 15$ J mol^{-1} K^{-1}).[4a]

When the spectrum was recorded in acetone-d_6 at 298 K, the molar ratio imine/oxazolidines ($K_{Fc} = 17.2$) was greater than that obtained in $CDCl_3$ ($K_{Fc} = 5.4$) and the value reported for the equilibrium between the imine **2a** and the 2-ferrocenyl-2,4-dihydro-1*H*-benzo[*d*][1.3]oxazine (imine/oxazine = 2.5, under identical experimental conditions).[5] The later finding agrees with Baldwin's rules,[15] which establish that the formation of 1,3-oxazines (via the *6-endo-trig* process) is more favored than formation of the 1,3-oxazolidines (Scheme 1).

To elucidate whether the extent of the tautomeric equilibrium could be tuned by the solvent, ^{1}H NMR spectra were registered also at 298 K in benzene-d_6, methanol-d_4, and DMSO-d_6. The results obtained revealed that the equilibrium is solvent dependent[16] and the percentage of the imine form **2b** increases accordingly to the following sequence: benzene-d_6 < $CDCl_3$ < acetone-d_6 < methanol-d_4 < DMSO-d_6.

The comparison of the solution behavior of **2b** and those of (*S* or *R*)-[(η^5-C_5H_5)Fe(η^5-C_5H_4)CH=NCH(Me)CH_2OH],[8a,b] which do not undergo the formation of the 1,3-N,O heterocycle in benzene-d_6, $CDCl_3$, acetone-d_6, or DMSO-d_6, suggests that the presence of the phenyl group in the geminal carbon of

(11) (a) López, C.; Sales, J.; Solans, X.; Zquiak, R. *J. Chem. Soc., Dalton Trans.* **1992**, 2321–2328. (b) Bosque, R.; López, C.; Sales, J.; Solans, X.; Font-Bardía, M. *J. Chem. Soc., Dalton Trans.* **1994**, 735–745. (c) López, C.; Bosque, R.; Solans, X.; Font-Bardía, M. *New J. Chem.* **1996**, *20*, 1285–1292.

(12) (a) Hetényi, A.; Szakonyi, Z.; Klika, K. D.; Pihlaja, K.; Fülöp, F. *J. Org. Chem.* **2003**, *68*, 2175–2184. (b) Star, A.; Fuchs, B. *J. Org. Chem.* **1999**, *64*, 1166–1172. (c) Fülöp, F.; Pihlaja, K.; Neuvonen, K.; Bernáth, G.; Argay, G.; Kálmán, A. *J. Org. Chem.* **1993**, *58*, 1967–1969. (d) Neuvonen, K.; Fülöp, F.; Neuvonen, H.; Koch, A.; Kleinpeter, E.; Pihlaja, K. *J. Org. Chem.* **2001**, *66*, 4132–4140. (e) Lázár, L.; Lakatos, A. G.; Fülöp, F.; Bernáth, G.; Riddell, F. G. *Tetrahedron* **1997**, *53*, 1081–1088. (f) Riddell, F. G.; Arumugan, S.; Fülöp, F.; Bernáth, G. *Tetrahedron* **1992**, *48*, 4979–4984. (g) Fülöp, F.; Bernáth, G.; Mattinen, J.; Pihlaja, K. *Tetrahedron* **1989**, *45*, 4317–4325. (h) Vainiotalo, P.; Ronkanen, S.; Fülöp, F.; Pihlaja, K. *Tetrahedron* **1990**, *46*, 3683–3692. (i) Astudillo, M. E. A.; Chokotho, N. C. J.; Jarvis, T. C.; Johnson, C. D.; Lewis, C. C.; McDonnell, P. D. *Tetrahedron* **1985**, *41*, 5919–5928. (j) McDonagh, A. F.; Smith, H. E. *J. Org. Chem.* **1968**, *33*, 1–8.

(13) The ratio **2b**/($\mathbf{3b_I}$ and $\mathbf{3b_{II}}$) was $K_{Fc} = 5.40$, 4.64, 4.44, and 4.02 for $T = 298$, 273, 253, and 233 K, respectively.

(14) The molar ratio $\mathbf{3b_I}/\mathbf{3b_{II}}$ was 1.57, 1.66, 1.75, and 1.82 for $T = 298$, 273, 253, and 233 K, respectively.

(15) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734–736.

(16) Molar ratio **2b**/($\mathbf{3b_I}$ and $\mathbf{3b_{II}}$) = 4.8 (in benzene-d_6) and 18.9 (in methanol-d_4), but in DMSO-d_6 the signals due to $\mathbf{3b_I}$ or $\mathbf{3b_{II}}$ were not detected in the ^{1}H NMR spectrum of **2b** at 298 K, thus suggesting that if present in solution their abundance should be extremely low.

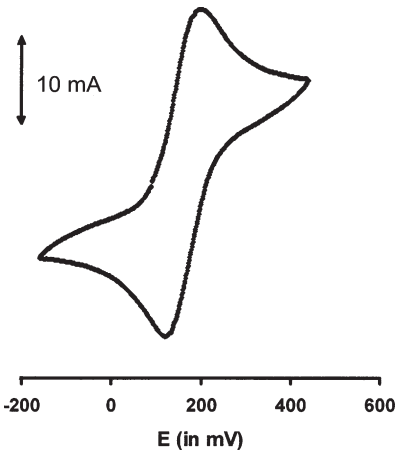


FIGURE 2. Cyclic voltammogram of a freshly prepared solution of **2b** (10^{-3} M) in acetonitrile at 298 K and at a scan speed $v = 100$ mV s^{-1}. [Summary of electrochemical parameters: anodic (E_{pa}), cathodic (E_{pc}) and half-wave potential ($E_{1/2}$): $E_{pa} = 206$ mV, $E_{pc} = 120$ mV, $E_{1/2} = 163$ mV); separation between peaks: $\Delta E = E_{pa} - E_{pc} = 86$ mV, and intensity ratio $I_{pa}/I_{pc} = 1.03$].

the −OH functionality is important as to induce the formation of the cyclic forms.

In order to fulfill the characterization of **2b**, and due to the ongoing interest on the electrochemical properties of ferrocene derivatives, we also undertook electrochemical studies of **2b**. Cyclic voltammetric studies of freshly prepared solutions (10^{-3} M) in CH_3CN[17] using $(Bu_4N)[PF_6]$ at different scan rates, v (from 5 to 100 mV s^{-1}), were carried out. The cyclic voltammogram of **2b** (Figure 2) exhibited an anodic peak with a directly associated reduction in the reverse scan and the intensities ratio was close to 1 ($I_{pa}/I_{pc} = 1.03$). All these findings are consistent with those expected for a simple reversible one-electron-transfer process.

For **2b**, the ΔE value departs from the constant value of 59 mV (theoretically expected for an electrochemically reversible one-electron step oxidation−reduction process[18]), suggesting that a structural reorganization takes place on oxidation. The half-wave potential $E_{1/2}$ falls in the range reported for related ferrocenylaldimines.[8a,b,10,11c,19]

Since the ^{1}H NMR spectrum of **2b** in acetonitrile-d_3[17] revealed that in this solvent the tautomeric equilibrium is strongly displaced toward the open form (**2b**), the results obtained from the electrochemical studies are consistent with a greater electron-withdrawing effect of the imine group when compared with that of the oxazolidine unit.

Previous studies on ring−chain tautomeric equilibria involving imines and 1,3-N,O-heterocycles have shown that frequently the relative abundance between the closed and open chain forms is strongly dependent on the nature of the substituents.[1−3,5,6,20] In view of the solution behavior of **2b** and since examples of ring−chain tautomerism involving thienylimines and 2-thienyloxazolidines have not been reported so far, we decided to study the condensation reaction between (1*S*,2*R*)-(+)-H_2NCH(Me)CH(OH)Ph and the aldehydes ($R^5C_4H_2S$)CHO, in which the >C(O) unit is bound to a thienyl ring that has a Me group on position 5 or 3 (R^5 = 5-Me or 3-Me).

Treatment of the (1*S*,2*R*)-(+)-norephedrine with the corresponding aldehyde ($R^5C_4H_2S$)CHO under reflux in ethanol gave (after workup) a pale yellow solid (R^5 = 5-Me) and a gummy material (for R^5 = 3-Me). These products were identified as the imines [R^1CH=NCH(Me)CH(OH)Ph] with R^1 = 5-MeTf (**2c**) or 3-MeTf (**2d**) (Scheme 2). Based on the same criteria as for **2b** (see above), we assumed that the isolated products were the (1*S*,2*R*) isomers.

The ^{1}H NMR spectrum of **2c** in $CDCl_3$ at 298 K also indicated the coexistence of the imine (**2c**) and two diastereomers of the closed forms [**3c$_I$** and **3c$_{II}$** (major and minor isomers, respectively), Scheme 2], but the molar ratio imine/oxazolidines ($K_{5\text{-MeTf}} = 16.7$) was significantly greater than for R^1 = Fc ($K_{Fc} = 5.4$), thus suggesting that replacement of the ferrocenyl unit by the 5-methylthienyl group produces a displacement of the equilibrium toward the open form. Further NMR studies showed that the relative abundance of the closed forms (**3c$_I$** and **3c$_{II}$**) in $CDCl_3$ increased slightly at low temperatures.[21] Similar to what happened for **2b**, the $K_{5\text{-MeTf}}$ values were also solvent dependent.[22]

In contrast with the results obtained for **2b** and **2c**, the ^{1}H NMR spectrum of **2d** [under identical experimental conditions ($CDCl_3$ at 298 K)] showed four sets of signals, of relative intensities 100.0:10.1:2.7:1.8, indicating the presence of at least four species in solution. Signals due to the two major components (**2d$_I$** and **2d$_{II}$**), as well as their chemical shifts and multiplicities, were consistent with those expected for [(3MeC_4H_2S)CH=NCH(Me)CH(OH)Ph] in the *anti*-(*E*) form. It should be noted that further NMR studies of **2d** showed that the molar ratio (**2d$_I$**/**2d$_{II}$**) did not vary substantially when $CDCl_3$ was replaced by acetone-d_6, methanol-d_4, benzene-d_6, or DMSO-d_6.[23]

Imines **2c** and **2d** differ in the location of the substituent. In **2d**, the Me group is closer to the imine unit than in **2c**; this may introduce significant steric effects which could hinder the free rotation around the C_{ipso}(thienyl)−C_{imine} bond. The use of molecular models supports this hypothesis, and consequently, we assumed that the duplicity of the signals could be attributed to two rotamers of the imine

(17) The ^{1}H NMR spectrum (400 MHz) of a freshly prepared solution of **2b** in acetonitrile-d_3 at 298 K indicated the presence of **2b**, **3b$_I$**, and **3b$_{II}$** in a molar ratio of **2b**/(**3b$_I$** and **3b$_{II}$**) = 51.

(18) Brown, E. R.; Sandifer, J. R. In *Physical Methods in Chemistry. Electrochemical Methods*; Rossiter, B. W., Hamilton, J. H., Eds.; Wiley: New York, 1986; Vol. 4, Chapter 4.

(19) Bosque, R.; López, C.; Sales, J. *Inorg. Chim. Acta* **1996**, *244*, 141–145.

(20) (a) Fülöp, F.; Bernáth, G.; Pihlaja, K. *Adv. Heterocycl. Chem.* **1997**, *69*, 349–477 and references cited therein. (b) Valters, R. E.; Fülöp, F.; Korbonits, D. *Adv. Heterocycl. Chem.* **1996**, *66*, 1–403. (c) Valters, R. E.; Fülöp, F.; Korbonits, D. *Adv. Heterocycl. Chem.* **1995**, *64*, 251–321. (d) Hetényi, A.; Szakonyi, Z.; Klika, K. D.; Pihlaja, K.; Fülöp, F. *J. Org. Chem.* **2003**, *68*, 2175–2182. (e) Szatmári, I.; Martinek, T. A.; Lázar, L.; Fülöp, F. *Tetrahedron* **2003**, *59*, 2877–2844. (f) Allaway, C. L.; Daly, M.; Nieuwenhuyzen, M.; Saunders, G. C. *J. Fluorine Chem.* **2002**, *115*, 91–99. (g) Szakonyi, Z.; Fülöp, F.; Bernáth, G.; Evanics, F.; Riddell, F. G. *Tetrahedron* **1998**, *54*, 1013–1020. (h) Riddell, F. G.; Rogerson, M.; Fülöp, F.; Bernáth, G. *Magn. Reson. Chem.* **1995**, *33*, 600–603. (i) Saeed, A. A. H. *J. Heterocycl. Chem.* **1982**, *19*, 113–115. (j) McDonagh, A. F.; Smith, H. E. *J. Chem. Soc., Chem. Commun.* **1966**, 374–375.

(21) In $CDCl_3$, $K_{5\text{-MeTf}} = 9.1$ (at 233 K) and 16.7 (at 298 K), respectively.

(22) At 298 K, $K_{5\text{-MeTf}} = 15.6$ (in benzene-d_6), 16.7 (in $CDCl_3$), and 32.3 (in acetone-d_6). In DMSO-d_6 the typical resonances due to the protons of the forms (**3c$_I$** and **3c$_{II}$**) were not detected.

(23) Molar ratio **2d$_I$**/**2d$_{II}$** wasobtained by integration of the singlets due to the imine protons (in the range 8.2 ppm < δ < 8.5 ppm) detected in the ^{1}H NMR spectra (500 MHz) of (1*S*,2*R*)-[(3Me-C_4H_2S)CH=NCH(Me)-CH(OH)Ph] (**2d**) in different solvents. The values obtained at 298 K were as follows: 9.7 (methanol-d_4), 9.9 ($CDCl_3$), 10.2 (acetone-d_6), 10.6 (DMSO-d_6), and 10.7 (benzene-d_6).

form (hereafter referred to as $\mathbf{2d_I}$ and $\mathbf{2d_{II}}$; we will return to this point latter on).

It should be noted that the set of resonances assigned to the two remaining and minor components present in solutions of [(3MeC$_4$H$_2$S)CH=NCH(Me)CH(OH)Ph] in $CDCl_3$ at 298 K suggested also the presence of two oxazolidine forms ($\mathbf{3d_I}$ and $\mathbf{3d_{II}}$), but their relative abundance was smaller ($K_{3\text{-MeTf}} = 20.4$) than when R^1 was 5-MeTf ($K_{5\text{-MeTf}} = 16.7$) or Fc ($K_{Fc} = 5.4$).

The studies presented here reveal that for the three systems under study with R^1 = Fc, 5-MeTf, or 3-MeTf the imine forms (1*S*,2*R*)-R^{1}CH=NCH(Me)CH(OH)Ph were the major component present in $CDCl_3$ solution at 298 K. This finding is in contrast with that reported for (1*S*,2*R*)-[PhCH=NCH(Me)-CH(OH)Ph] (**2e**)[12g] for which the ratio imine/oxazolidines was clearly smaller ($K_{Ph} = 0.36$) under identical experimental conditions).[24]

Comparison of results obtained from ^{1}H NMR studies of (1*S*,2*R*)-[R^{1}CH=NCH(Me)CH(OH)Ph] with R^1 = Fc, 3-MeTf, 5-MeTf, or Ph, in $CDCl_3$, 298 K, reveals that relative abundance of the imine form increases according to the sequence Ph < Fc < 5-MeTf < 3-MeTf. Furthermore, the variations detected in the chemical shift of the imine carbon in $CDCl_3$ [δ(−CH=N−) = 161.4 ppm (for **2e**), 160.6 (for **2b**), 153.9 ppm (for **2c**), 153.2 (for $\mathbf{2d_I}$), 154.3 ppm (for $\mathbf{2d_{II}}$)] provide conclusive evidence of the effect induced by the R^1 substituents on the electronic density of the >C=N− moiety. The difference between the values obtained for the two rotamers of **2d** ($\mathbf{2d_I}$ and $\mathbf{2d_{II}}$) suggests that these two species may exhibit different proclivity to undergo the *5-endo-trig* process to give the corresponding oxazolidines.

On the other hand, it should be noted that in **2d** the Me group is proximal to the imine unit, and thus, steric effects are expected to have greater importance than for **2c**. In particular this could (a) reduce the stability of the oxazolidines $\mathbf{3d_I}$ and $\mathbf{3d_{II}}$ when compared with their analogues $\mathbf{3c_I}$ and $\mathbf{3c_{II}}$, in which the methyl group is further away, and (b) hinder the free rotation of the thienyl ring in the oxazolines, leading to the existence of rotameric species in solution. (Molecular models of the four isomers of the oxazolidines showed that the presence of the Me group restricts the free rotation of the 3-MeTf unit in the cyclic forms. As consequence of this finding, the cyclic forms with R^1 = 3-MeTf were not included in the theoretical studies included in the following section.)

Theoretical Studies. In a first attempt to rationalize the influence of the R^1 group on the ring−chain tautomerism, we decided to undertake DFT calculations for the imines (1*S*,2*R*)-[R^{1}CH=NCH(Me)CH(OH)Ph] [with R^1 = Fc (**2b**), 5-MeTf (**2c**), 3-MeTf (**2d**), or Ph (**2e**)] and for the cyclic forms involved in this process (Figure 1A−D). Theoretical calculations were performed at the B3LYP computational level[25] with the Gaussian03 package[26] using the LANL2DZ basis set.[27] In the first step, geometries of imines (**2a**−**e**) and of the oxazolidine derivatives with R^1 = Ph, Fc, or 5-MeTf (types **A**−**D**, in Figure 1) were optimized, and afterward, the total energy of these molecules (E_T) was calculated.

Optimized geometries of imines **2b**, **2c**, and **2e** revealed the existence of an intramolecular interaction between the −OH moiety and the imine nitrogen. It has been reported that for 2-phenyloxazolidines the influence of the substituents on the aryl ring on position 2 upon the stability of the tautomers is controlled by several electronic factors involving this intramolecular O−H···N bond and the >C=N− group appear to be specially relevant.[2] The formation of the heterocycle requires the cleavage of the O−H···N interaction and thus, imines with stronger O−H···N bonds are expected to be less prone to undergo the *5-endo-trig* process. In the optimized geometries of **2b**, **2c**, and **2e**, the O−H bond length was identical (0.975 Å for the three imines), but the N···H distance increased according to the sequence Ph < 5-MeTf < Fc.[27] Thus, indicating a stronger N···H intramolecular interaction.

For **2d** two different optimized geometries were obtained, one of them being 1.51 kcal/mol more stable. This value is rather small in the gas phase; however, in solution the energy barrier between the two species could be high enough as to inhibit the free rotation of the C_{ipso}(thienyl)−C_{imine} bond and to allow the coexistence of the two rotamers ($\mathbf{2d_I}$ and $\mathbf{2d_{II}}$).

For the sets of compounds with a identical R^1, we also calculated the differences $(\Delta E_T)_i = [E_{T(oxazolidine)}]_i - [E_{T(imine)}]$ and the Boltzmann's distribution using the calculated energies of the molecules and T = 298 K (Table 1). In this equation, the subscript "i" refers to any of the four diastereomers **A**−**D** of the closed forms; that is to say $(\Delta E_T)_A = [E_{T(oxazoline)}]_A - [E_{T(imine)}]$, and this will be also applied to isomers **B**−**D**. Comparison of data revealed that the relative contribution of the imine form (n_{imine}) decreased according to the sequence 5-MeTf > Fc ≫ Ph, and for cyclic forms with identical R^1, the relative proportion of the four isomers (**A**−**D**) followed the trend **D** ≪ **C** < **B** < **A**.

It is well-known that in solution the amine proton of 1,3-(N,O) heterocycles interchanges,[28] and thus, the interconversion between isomers **A** and **B** (or **C** and **D**) of the oxazolidines under study is expected to occur. On these bases, we also calculated the total contribution of the pairs (**A** and **B**) and (**C** and **D**). Comparison of data presented in Table 1 revealed that (a) oxazolidines with a *cis*-arrangement of the phenyl and the R^1 group (**A** and **B** types) have a greater

(24) In order to compare the *K* ratios for compounds under study and that of their analogue with R^1 = Ph, under identical experimental conditions, we also studied the solution behavior of the imine (1*S*,2*R*)-[PhCH=NCH(Me)-CH(OH)Ph] (**2e**).

(25) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5692. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789.

(26) Frisch, M. J.; Trucks, G. W. Schlegel, H. B. Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision C.02*; Gaussian, Inc.: Wallingford, CT, 2004.

(27) (a) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 270–283. (b) Wadt, W. R.; Hay, P. J. *J. Chem. Phys.* **1985**, *82*, 284–298. (c) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299–310. (d) For C, H, and N, the D95 basis set is used : Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaefer, H. F.., III, Ed.; Plenum Press: New York, 1976; Vol. 3, p 1.

(28) The distances between the imine nitrogen and the hydrogen of the alcohol unit were 2.181 Å (R^1 = Ph), 2.165 Å (R^1 = 5-MeTf), and 2.145 Å (R^1 = Fc).

TABLE 1. Calculated $(\Delta E_T)_i$ Values [$(\Delta E_T)_i$ = E_T (for the Corresponding Oxazolidine Form)$_i$ − E_T (for the Imine Form)] in kcal/mol[a]

R^1	$(\Delta E_T)_A$	$(\Delta E_T)_B$	$(\Delta E_T)_C$	$(\Delta E_T)_D$	n_{imine}	n_A	n_B	n_C	n_D	$n_A + n_B$	$n_C + n_D$	Q_i	K_i
Ph	−5.37	−2.51	−4.59	−4.10	0.1	71.9	0.6	19.0	8.4	72.5	27.4	1.0×10^{-3}	0.36
Fc	−1.71	0.53	−1.02	−0.58	3.6	64.8	1.5	20.5	9.6	66.3	30.1	3.7×10^{-2}	5.4
5-MeTf	−1.88	0.82	−1.52	−0.87	2.5	58.3	0.6	32.1	6.5	58.9	38.6	2.6×10^{-2}	17.9

[a]Results obtained from the analyses of the contributions (in %) of the open form (n_{imine}) and for the closed forms (n_A, n_B, n_C, and n_D); total contributions of isomers **A** and **B** ($n_A + n_B$), where Ph and the R^1 group are in a *cis*-arrangement, and of the pair of compounds **C** and **D** ($n_C + n_D$) where these substituents are in a *trans*-arrangement. Calculated Q_i values were defined as the ratio between the contribution of the imine form (n_{imine}) over the total contribution of the closed forms **A**−**D** ($n_A + n_B + n_C + n_D$) and experimental K_i ratios obtained in $CDCl_3$ solution at 298 K. The labels **A**−**D** refer to the closed forms shown in Figure 1.

contribution than their corresponding *trans*-analogues (**C** and **D**) and (b) the *Q* ratios defined as [contribution of the imine form (n_{imine})/contributions of all closed forms (n_A+ n_B+ n_C+ n_D)] decrease according to the sequence Fc ≥ 5-MeTf ≫ Ph. This indicates that for R^1 containing the pentagonal rings [Tf or (η^5-C_5H_4)] the oxazolidine forms are less favored than when R^1 is Ph.

The solution studies revealed that in $CDCl_3$ at 298 K the imine/oxazolidine ratios decreased according to the sequence 5-MeTf > Fc ≫ Ph [*K*(in $CDCl_3$) = 16.7, 5.4, and 0.36, respectively). The main difference between this trend and that obtained for the *Q* ratio (Fc ≥ 5-MeTf ≫ Ph) arises from the order of the Fc and 5-MeTf derivatives. However, the differences between $(\Delta E_T)_i$ for R^1 = Fc and 5-MeTf for the same isomer of the oxazolidine are very small (≤0.5 kcal/mol), especially when compared with those obtained for $(\Delta E_T)_i$ with R^1 = Ph and Fc (or 5-MeTf). Furthermore, and as mentioned above, the optimized geometries of the imines suggest that for R^1 = Fc the O−H···N interaction is stronger than when R^1 is 5-MeTf.[27]

On the other hand, in solution other more subtle factors such as (a) the effective bulk of the pentagonal [5MeTf or (η^5-C_5H_4)] rings[29] and (b) the influence of the solvent could be important for modifying the magnitude of the [$(\Delta E_T)_i$ (for R^1 = Fc) − $(\Delta E_T)_i$ (for R^1 = 5-MeTf)] values obtained in the gas phase. The 5-MeTf substituent is bulkier than the (η^5-C_5H_4) ring,[30] and consequently, during the cyclization process steric effects induced by the 5-MeTf are expected to be greater than those produced by the Fc. These factors, as well as the influence of the temperature, could explain why in solution K_{Fc} is smaller than $K_{5\text{-MeTf}}$ (0.54 versus 16.7).

As can be easily seen in Table 1, for the three types of products the minimum $(\Delta E_T)_i$ values were found for the **A** isomer of the oxazolidines with the absolute configuration *S* on the stereogenic carbon (C^2) generated in the cyclization process. This suggests that **A** isomers are more stable. As mentioned above in solution the proton of the >NH unit is expected to interchange in solution.[28] On these bases, we assumed that the major ozaxolidine form present in the solutions of **2b**, **2c** ,and **2e** should correspond to the (2*R*,4*S*,5*R*) isomers, in which the phenyl and the R^1 unit are in a *cis*-arrangement.

(29) See, for instance: (a) Hurtado, M.; Contreras, J. G.; Matamala, A.; Mó, O.; Yañez, M. *New J. Chem.* **2009**, *32*, 2209–2217. (b) Riddell, F. G.; Anderson, J. E. *J. Chem. Soc., Perkin Trans. 2* **1977**, 588–591.

(30) In order to compare the effective bulk of the two pentagonal rings we calculated the perimeters (*p*) of the monosubstituted pentagonal rings [(η^5-C_5H_4) and thienyl] of the imine [(η^5-C_5H_5)Fe(η^5-C_5H_4)CH=$NCH_2(C_4H_3S)$] whose crystal structure has been reported before.[9a] The perimeter of the thienyl ring was 7.551 Å, clearly bigger than that of (η^5-C_5H_4) (*p*=7.123Å). In addition, the bond angle S−C_{ipso}−C(3) of the (C_4H_3S) unit (110.01°) is greater than the C(2)−C(1)−C(5) bond angle of the (η^5-C_5H_4) (108.5°). These values suggest that in **2c** (R^1 = 5-MeTf) the environment of the imine carbon is expected to be more crowded than in **2b**, where R^1 is Fc.

Conclusions

Three new imines of general formulas (1*S*,2*R*)-[R^1CH=NCH(Me)CH(OH)Ph] with R^1 = Fc (**2b**), 5-MeTf (**2c**), or 3-MeTf (**2d**) have been prepared and characterized. The study of their solution behavior has shown the existence of a ring−chain tautomerism between these imines (open forms) and two isomers of the corresponding 2-substituted 4-methyl-5-phenyl oxazolidines. As far as we know, examples of thienyl imines exhibiting this type of tautomerism in solution have not been described before. The results obtained from the study of these ring−chain tautomerisms indicated that (a) these processes are solvent and temperature dependent and (b) the displacement of these equilibria toward the closed forms increase according to the sequence 3-MeTf < 5-MeTf < Fc < Ph. Furthermore, the replacement of the 5-MeTf group by the 3-MeTf inhibits the free rotation around the C_{ipso} (3-MeTf)−C_{imine} bond and two rotameric species of (1*S*,2*R*)-[(3-MeTf)CH=NCH(Me)CH(OH)Ph] (**2d**) were detected in solution. The theoretical calculations undertaken for **2d** confirmed this result.

On the other hand, the results obtained from the DFT calculations revealed (a) the existence of an intramolecular O−H···N bond in the optimized geometries of the imines whose strength increased according to the sequence Ph < 5-MeTf < Fc and (b) that the comparison of the analyses of the Boltzmann's distribution for the imines and the four isomers of the oxazolidines with identical R^1 substituent explained why the molar ratios imine/oxazolidines decrease when the phenyl ring is replaced by the 5-MeTf or the Fc groups.

It should be noted that for the new products the NMR studies showed that the relative abundance of the closed forms in solution is rather small, especially if compared with the results obtained when R^1 = Ph. However, preliminary studies on the reactivity of (1*S*,2*R*)-[R^1CH=NCH(Me)CH(OH)Ph] (**2b**−**e**) in front of palladium(II) and platinum(II) complexes reveal that the proper selection of the solvent allows direction of the reactivity of the species involved in the tautomeric equilibria to the formation of (a) the coordination compounds in which these ions are bound to the nitrogen atom of the imine forms (**2b**−**e**) or (b) complexes where the oxazolidines act as N-donor ligands, thus providing a new synthetic route to this type of noncommon products,[4] with interesting applications.

Experimental Section

Preparation of the Compounds. (1*S*,2*R*)-(+)-[(η^5-C_5H_5)Fe-[(η^5-C_5H_4)CH=NCH(Me)CH(OH)(Ph)]] (2b). A mixture formed by ferrocenecarboxaldehyde (1.0 g, 4.67×10^{-3} mol) and 20 mL of benzene (which should be handled with caution) was stirred at 298 K for 20 min. After this period, the undissolved materials were removed by filtration. Afterward, (1*S*,2*R*)-(+)-norephedrine (0.71 g, 4.67×10^{-3} mol) was added to the filtrate.

The flask was then introduced on an ethylene glycol bath and connected to a Dean−Stark apparatus equipped with a condenser. Then, the reaction mixture was refluxed until ca. 10 mL of the azeotrope benzene−water had collected on the Dean−Stark apparatus. The hot solution was then filtered out, and the deep red filtrate was concentrated to dryness on a rotary evaporator. The oily residue obtained was dried in vacuum for 2 days (yield 1.58 g, 98%). Characterization data: HRMS-ESI(+) [H_2O/CH_3CN (1:1)] m/z = 348.1043, calcd for $[M + H]^+$ ($C_{20}H_{22}$-FeNO) m/z = 348.1051; IR data 1638 cm^{-1}, ν(>C=N−); $[\alpha]_D$ (c = 9.9 × 10^{-3} g/100 mL = +857); UV−vis data (c = 1.8 × 10^{-4} M) λ in nm [log ε (ε in M^{-1} cm^2)] = 457 (2.53), 326 (3.17), 274 (3.96), 230 (4.3).

(1*S*,2*R*)-(−)-[(5-Me-C_4H_2S)CH=NCH(Me)CH(OH)(Ph)]] (2c). 5-Methyl-thiophene-2-carbaldehyde (0.260 mL, 2.38 × 10^{-3} mol) was dissolved in 30 mL of ethanol, and then an equimolar amount of (1*S*,2*R*)-(+)-norephedrine (364 mg, 2.38 × 10^{-3} mol) was added. The reaction mixture was refluxed for 6 h and then filtered. The undissolved materials were discarded, and the filtrate was concentrated to dryness on a rotary evaporator. The residue was then dissolved in hexane, and slow evaporation of the solvent at 298 K produced a pale yellow solid that was collected, air-dried, and then dried in vacuum for 4 days (yield: 573 mg, 93%). Characterization data: HRMS-ESI(+) [H_2O/CH_3CN (1:1)] m/z = 260.1106, calcd for $[M + H]^+$ ($C_{15}H_{18}NOS$) m/z = 260.1109; IR data 1632 cm^{-1}, ν(>C=N−); $[\alpha]_D$ (c = 9.8 × 10^{-2} g/100 mL) = −61); UV−vis data in CH_2Cl_2 (c = 1.8 × 10^{-4} M) λ in nm [log ε (ε in M^{-1} cm^2)] = 292 (4.16), 262 (3.99), and 215 (3.65).

(1*S*,2*R*)-(−)-[(3-MeC_4H_2S)CH=NCH(Me)CH(OH)(Ph)]] (2d). This product was prepared following the same procedure as for **2c**, but using 3-methylthiophene-2-carbaldehyde (0.4 mL, 3.71 × 10^{-3} mol) and (1*S*,2*R*)-(+)-norephedrine (561 mg, 3.71 × 10^{-3} mol) as starting materials. In this case, concentration of the solution gave **2d** as a brownish gummy material (yield: 940 mg, 98%). Characterization data: HRMS-[ESI(+) H_2O/CH_3CN (1:1)], m/z = 260.1103, calcd for $[M + H]^+$ ($C_{15}H_{18}NOS$) m/z = 260.1109; IR data 1625 cm^{-1}, ν(>C=N−); $[\alpha]_D$ (c = 1 × 10^{-1} g/100 mL = −33); UV−vis data in CH_2Cl_2 (c = 1.8 × 10^{-4} M) λ in nm [log ε (ε in M^{-1} cm^2)] = 273 (4.5) and 221 (3.59).

Electrochemical Studies. Electrochemical data were obtained by cyclic voltammetry under nitrogen at ca. 298 K of a 10^{-3} M solution of **2b** in acetonitrile (HPLC grade) using (Bu_4N)[PF_6], (0.1 M) as supporting electrolyte and a potentiostat M263A from EGG instruments. Ferrocene was used as reference, and under these experimental conditions the standard error of the measured potentials was ±5 mV. The cyclic voltammograms were registered using scan speeds varying from υ = 10 mV s^{-1} to 100 mV s^{-1}.

Computational Studies. Calculations were carried out at the B3LYP computational level[25] with the Gaussian 98 package[26] using the LANL2DZ basis set.[27] Geometry optimizations were performed without symmetry restrictions. To improve the calculated geometry, polarization functions were added to the Dunning−Huzinaga full double basis set[31] for H, C, N, and S atoms, while for Pd and Pt the LANL2DZ basis set was used.[27]

Acknowledgment. This work was supported by the Ministerio de Ciencia y Tecnología of Spain (Grant No. CTQ2009-11501). D.T. is grateful to the same institution for a predoctoral (FPI) fellowship.

Supporting Information Available: Figures containing ^1H, $^3C[^1H]$ and $[^1H-^1H]$ NOESY of **2b−d**; UV−vis spectra of **2b−2e** in CH_2Cl_2 and optimized geometries of **2b**, **2c**, and **2e**, of the two rotamers of **2d**, and of the isomers of the ozaxolidines, tables containing ^1H and $^{13}C[^1H]$ NMR spectroscopic data for **2b−d** (at 298 K) in several deuterated solvents and calculated total energy and final atomic coordinates for the optimized geometries. This material is available free of charge via the Internet at http://pubs.acs.org.

(31) For C, H, and N, the D95 basis set is used: Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaefer, H. F., III, Ed.; Plenum Press: New York, 1976; Vol. 3, p 1.