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Diastereoselective Michael Additions of *N*-Boc-2-(*tert*-butyldimethylsiloxy)pyrrole to 2-(Arylsulfinyl)-1,4-benzoquinones

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Reactions of 2-(arylsulfinyl)-1,4-benzoquinones **1a**−**c** with *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole **2** have been studied under different catalytic conditions. Under $BF_3{\cdot}OEt_2$ catalysis, reactions were completely stereoselective leading to the Michael-type adducts **3**, whereas in the presence of $SnCl_4$ diastereomeric mixtures of the pyrrolo[3,2-*b*]benzofuranes **5** and **6** were obtained. The latter products result from a tandem process involving the Michael reaction followed by an intramolecular cyclization of the intermediates **3** and **4**, the first step being hardly stereoselective. Reactions catalyzed by $Eu(fod)_3$ evolved in a highly stereoselective manner yielding the products **3** or **5** depending on the electronic density of the arylsulfinyl group.

Introduction

Optically pure sulfinyl quinones have proved to be efficient dienophiles in Diels−Alder reactions[1] mainly due to the high ability of the sulfoxide to control the regiochemistry, as well as the endo and π-facial selectivities of the cycloadditions with a wide range of dienes.[2] Additionally, the use of sulfinyl quinones has allowed the synthesis of interesting cage compounds,[2a,3] as well as the enantioselective synthesis of several angucyclinones.[4] Nevertheless, the use of sulfinyl quinones as diastereoselective Michael acceptors is a largely unexplored field despite the wide synthetic potential of this transformation. The first example of a diastereoselective addition to an optically pure sulfinyl quinone was reported by Brimble et al.,[5] who obtained furobenzofuranes by reaction with 2-trimethylsiloxyfuran (TMSOF) as a nucleophile. The mechanism proposed to explain these moderately stereoselective reactions involved the conjugated addition of TMSOF to the 2-arylsulfinyl-1,4-benzoquinones as a step toward the intramolecular cyclization to the corresponding 3a,8b-dihydro-7-hydroxy-8-(arylsulfinyl)furo[3,2-*b*]benzofuran-2(3*H*)-one (Scheme 1).[6] The diastereomeric excesses ranged between 60 and 80% for *p*-tolyl and 2-methoxynaphthylsulfoxides but increased up to 96% with the bulky *tert*-butylsulfinyl group in the starting quinone.[6]

The synthetic utility of this process would be even higher if the intermediate 5-arylfuran-2-ones could be isolated and purified before evolving into the furo[3,2-*b*]benzofuran ring system. However, this was unsuccessful due to their high reactivity. Therefore, we reasoned that the use of other heterocyclic systems, precursors of intermediates that would be less prone to cyclization, would allow their isolation. For this purpose, *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (TBSOP), the nitrogen analogue of TMSOF, was chosen as a candidate to develop a new entry to the α,β-unsaturated butyrolactam skeletons (**3** and **4** in Scheme 2), since their reactivity is expected to be lower than that of the

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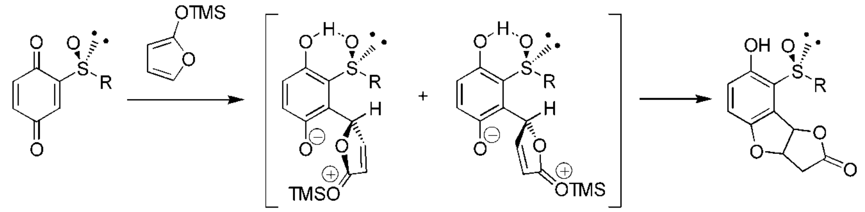
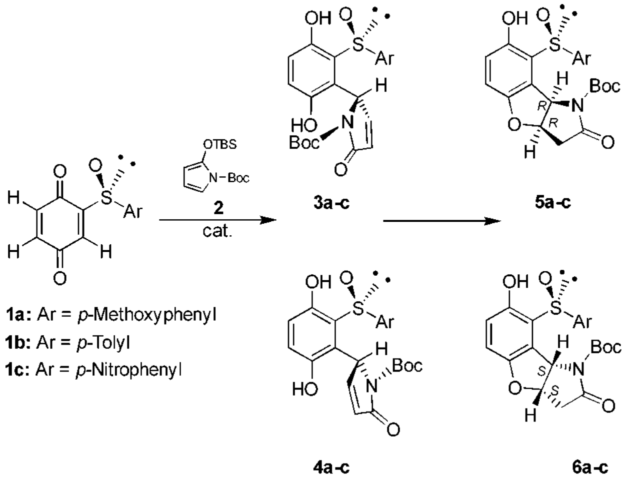
SCHEME 1



SCHEME 2



corresponding lactones depicted in Scheme 1. These lactam skeletons are present in several therapeutic agents[7] and some natural products exhibiting interesting biological properties.[8] The interest in these compounds is related to their use as substrates for inter or intramolecular conjugated additions, leading to pyrrolo[3,2-*b*]benzofurans, which are present in compounds such as BODIPY dyes[9] and the alkaloid phalarine.[10] Several examples of TBSOP as a nucleophile have been reported and illustrate the successful addition to carbonyl-related compounds[11] such as aldehydes, imines, and heteroatom-stabilized carbenium ions. However, the first example of its Michael addition to α-methylene lactones has been described just recently.[12]

We report herein the results obtained for the conjugate addition of *N*-Boc-2-(*tert*-butyldimethylsiloxy)pyrrole **2** to 2-(arylsulfinyl)-1,4-benzoquinones bearing electron-donating [**1a** (Ar = *p*-OMe-C_6H_4) and **1b** (Ar = *p*-Me-C_6H_4)] and electron-withdrawing groups [**1c** (Ar = *p*-NO_2-C_6H_4)] at the arylsulfinyl moiety using different catalysts (Scheme 2). These processes allow both the synthesis of the *N*-Boc derivatives of 5-aryl-substituted pyrrol-2-ones **3** and **4** by a simple Michael-type reaction and the preparation of the tricyclic butyrolactams **5** and **6** resulting from a tandem process involving the subsequent intramolecular conjugated addition of the pyrrolones **3** and **4**.

Results and Discussion

The synthesis of the racemic sulfinyl quinones **1a** and **1c** was carried out by oxidation of the corresponding sulfenyl derivatives.[2h] Enantiomerically pure sulfinyl quinone **1b**[13] and TBSOP **2**[11a,14] were prepared according to previously reported procedures.

The results obtained in reactions of compounds **1a**−**c** with **2** under thermal conditions and in the presence of the catalysts ($ZnBr_2$, BF_3·OEt_2, Eu(fod)$_3$, or $SnCl_4$) are collected in Scheme 2 and Table 1. All reactions were performed in CH_2Cl_2 at −90 °C.[15] Under thermal conditions (Table 1, entries 1−3), all the reactions afforded almost equimolecular mixtures of the two 5-arylpyrrol-2-ones epimers at C-5 (**3** and **4**, Scheme 2). They result from a Michael-type process where the pyrrole **2** attacks the most electrophilic C-3 position of the sulfinyl quinones **1**. The yields of these reactions were moderate to low, and the separation of the epimers was difficult due to the presence of significant amounts of *N*-Boc-pyrrol-2-(5*H*)-one. Fortunately, both reactivity and stereoselectivity were substantially improved when these reactions were conducted under Lewis acid catalysis. With $ZnBr_2$ as the catalyst (Table 1, entries 4−6) the diastereoisomeric excesses decreased as the electron-withdrawing power of the substituent at arylsulfinyl group increased [88 for **1a** (OMe), 66 for **1b** (Me), and 12 for **1c** (NO_2)]. The reactivity of the sulfinyl quinones was also dependent on the nature of such a substituent in catalyzed reactions, and as should be expected, it was considerably higher for the nitro derivative **1c**. Despite these improvements, the yields of these reactions remained low.

The best results were obtained by using BF_3·OEt_2 as catalyst (Table 1, entries 7−10). With 1.6 equiv of **2**, the stereoselectivity was complete in all cases, and the isolated yields were higher than 67% starting from **1a** and **1c**, whereas from **1b** the yield decreased to 40% (33% of the starting quinone **1b** was recovered). The use of 2.2

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[15] *N*-Boc-2-(*tert*-butyldimethylsiloxy)pyrrole **2** evolves into *N*-Boc-pyrrol-2(5*H*)-one at higher temperatures.

TABLE 1. Reactions of 2-(Arylsulfinyl)-1,4-benzoquinones (1) with TBSOP (2) in CH_2Cl_2 at −90 °C

entry	substrate	**2**[a]	catalyst (equiv)	time (h)	**3**/**4**	de (%)	**5**/**6**	de (%)	yield (%)
1	**1a**	1.6		6	51:49	2			30[b]
2	**1b**	2.2		6	55:45	10			58[b]
3	**1c**	1.6		6	51:49	2			14[b]
4	**1a**	1.6	$ZnBr_2$ (2)	0.4	94:6	88			25[c]
5	**1b**	2.2	$ZnBr_2$ (2)	0.4	83:17	66			24[c]
6	**1c**	1.6	$ZnBr_2$ (2)	0.05	56:44	12			25[c]
7	**1a**	1.6	$BF_3{\cdot}OEt_2$ (5)	0.4	100:0[d]	100			70 (**3a**)[e]
8	**1b**	1.6	$BF_3{\cdot}OEt_2$ (5)	0.4	100:0[d]	100			40 (**3b**)[e,f]
9	**1b**	2.2	$BF_3{\cdot}OEt_2$ (5)	0.4	91:9	82			64 (**3b**),[e] 6 (**4b**)[e]
10	**1c**	1.6	$BF_3{\cdot}OEt_2$ (5)	0.05	100:0[d]	100			67 (**5c**)[e,g]
11	**1a**	1.6	Eu(fod)$_3$ (2)	0.4	100:0[d]	100			70 (**3a**)[e]
12	**1b**	2.2	Eu(fod)$_3$ (2)	0.4			93:7	86	70 (**5b**)[e]
13	**1b**	2.2	Eu(fod)$_3$ (1.5)	0.4	4:1	60	76:19	60	70[b]
14	**1b**	2.2	Eu(fod)$_3$ (1.0)	0.4	37:37	0	13:13	0	72[b]
15	**1c**	1.6	Eu(fod)$_3$ (2)	0.05			90:10	80	40 (**5c**)[e]
16	**1a**	1.6	$SnCl_4$ (2)	0.4			53:47	6	27 (**5a**),[e] 23 (**6a**)[e]
17	**1b**	2.2	$SnCl_4$ (2)	0.4			62:38	24	28 (**5b**),[e] 17 (**6b**)[e]
18	**1c**	1.6	$SnCl_4$ (2)	0.05			57:43	14	40[c]

[a] Number of equivalents used in the reaction. [b] Combined yields estimated by ^1H NMR. [c] Isolated combined yields. [d] Only one diastereoisomer could be detected in the ^1H and ^{13}C NMR spectra of the crude reaction. [e] Isolated yields of pure compounds. [f] **1b** (33%) was recovered. [g] See text.

equiv of **2** gave **3b** in better yield but the stereoselectivity decreased (82% de; Table 1, entry 9). Nevertheless, the mixture of **3b** and **4b** obtained was easily separated and purified by flash chromatography. We have also observed a similar behavior for other reactions from **1b**, and therefore, the experiments with this substrate were performed with 2.2 equiv of **2** instead of the 1.6 equiv used for **1a** and **1c**. Compound **3c** was characterized as a sole diastereoisomer by ^1H NMR (78% estimated yield) from the crude reaction mixture since it evolved almost quantitatively into the tricyclic butyrolactam **5c** upon purification by flash chromatography (Table 1, entry 10), this process being completely diastereoselective. This result demonstrates that cyclization of **3c** was easier than that of **3a** and **3b**, which remained unchanged during purification.

When the reactions were performed in the presence of Eu(fod)$_3$ (Table 1, entries 11−15) the results depended on the starting quinone and the amount of catalyst. Thus, when 2 equiv of Eu(fod)$_3$ was used, Michael adduct **3a** (Table 1, entry 11) was formed as the only product from **1a**, whereas a mixture of pyrrolo[3,2-*b*]benzofuranes **5** and **6** were isolated, after flash chromatography, from **1b** and **1c** (Table 1, entries 12 and 15).[16] The stereoselectivity decreased when the electron-withdrawing character of the substituent at arylsulfinyl group increased (as in the reactions catalyzed by $ZnBr_2$), the lowest de being higher than 80% (Table 1, entry 15). This could be due to the relative reactivity of the substrates (**1c** > **1b** > **1a**), easily rationalized from the electronic character of the arylsulfinyl group. The number of equivalents of Eu(fod)$_3$ has a significant influence on the stereoselectivity (Table 1, entries 12−14). The best de were obtained using 2 equiv of the catalyst (the use of 4 equiv of catalyst did not influence the stereoselectivity), while with 1.5 equiv the de decreased to 60% (Table 1, entry 13) and became zero by using just 1 equiv of the catalyst (Table 1, entry 14). In the latter case, a 50:50 mixture of **3b** and **4b** (53% yield) was also detected by ^1H NMR.

Under $SnCl_4$ catalysis, sulfinyl quinones **1a**, **1b**, and **1c** afforded, after flash chromatography of the reaction mixture,[16] varying mixtures of tricyclic butyrolactams **5** and **6** (Table 1, entries 16−18). Low diastereoselectivities were obtained in all cases with de ranging between 6 and 24%. Mixtures of epimers **5** and **6** obtained under the conditions described in the entries 16 and 17 could be separated and purified by flash chromatography. In contrast, all attempts to achieve the chromatographic separation of **5c** and **6c** mixture were unsuccessful.

Next, we investigated the synthesis of some pyrrolo[3,2-*b*]benzofuranes **5** and **6** by cyclization of the corresponding Michael adducts **3** and **4** in the presence of Eu(fod)$_3$ or $SnCl_4$. Treatment of compound **3a** with $SnCl_4$ at −90 °C, after 2 h, afforded tricyclic butyrolactam **5a** in an almost quantitative yield as the only product. Similarly, pure compounds **3b** and **4b** exclusively evolved into compounds **5b** and **6b**, respectively, in the presence of Eu(fod)$_3$ or $SnCl_4$.[17] The reaction mixture of **3b**/**4b** (91:9; Table 1, entry 9) was directly treated with Eu(fod)$_3$ or $SnCl_4$ to give the corresponding tricyclic butyrolactams **5b**/**6b** in a 91:9 ratio. These results suggested that cyclization of 5-arylpyrrol-2-ones **3** and **4** into tricyclic butyrolactames **5** and **6** is completely stereoselective as it was expected from their intramolecular character, and therefore, the de's observed for the direct transformation of quinones **1** into pyrrolo[3,2-*b*]benzofuranes **5** and **6** are indicative of the stereoselectivity of the initial nucleophilic addition. Moreover, these results have allowed the chemical correlation between compounds **3** and **4** with **5** and **6**, respectively.

The configurational assignment of the compounds **3**−**6**, shown in Scheme 2, was based on NMR studies. Thus, unequivocal conclusions could be drawn from the NOE experiments performed on pure samples of compounds **5b** and **6b**. The selective irradiation on bridgehead proton

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(16) In reactions performed under Eu(fod)$_3$ and $SnCl_4$ conditions, the ^1H NMR spectra of the crude reactions showed broad signals that did not allow quantification of the product ratio before removing the catalyst by filtration through silica gel.

(17) All the attempts to achieve cyclization of **3b** with 10% HCl afforded a complex mixture that we were unable to identify (see ref 6).

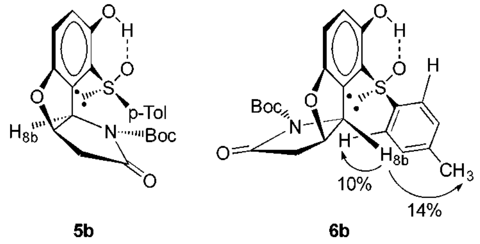


FIGURE 1. Stereochemistry and NOE values observed for compounds **5b** and **6b**.

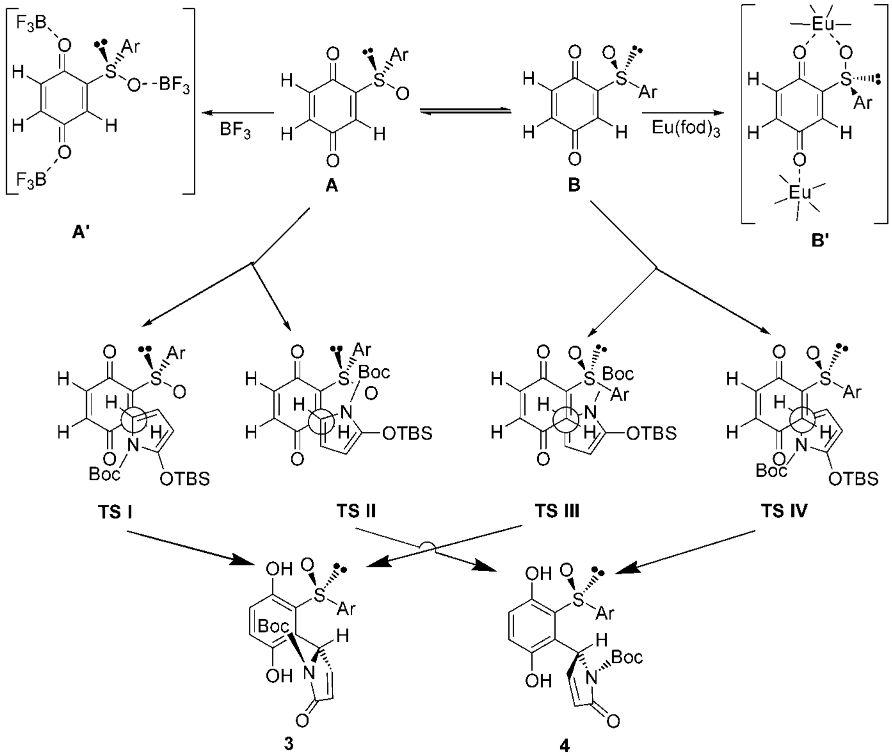
H_{8b} for compound **6b** showed a relevant 10% and 14% NOE enhancements between this proton and both the ortho protons and the methyl group of the *p*-tolyl residue, respectively (see Figure 1). These NOE effects are absent in the case of **5b**. Assuming that the spatial arrangements of the *p*-tolyl group in **5b** and **6b** are those depicted in Figure 1 (conformations stabilized by intramolecular hydrogen bond[18]), the observed NOE effects allowed us to unequivocally assign their relative configuration and therefore that of their respective precursors **3b** and **4b**.

The stereoselectivity observed under different conditions, which must be identical to that of the Michael-type reaction even when compounds **5** and **6** were obtained (the cyclization is completely stereoselective), can be rationalized as follows. The most stable conformations around the C−S bond for sulfinyl quinones **1** must be **A** and **B** rotamers (Scheme 3), favored on electronic and steric grounds.[19] Assuming a steric approach control, the favored approach of the TBSOP **2** would take place from the least hindered face of the sulfinyl quinones **1**, the top side for **A** and the bottom one for **B**, through four possible transition states depicted in Scheme 3.

As the steric interaction of the *N*-Boc and S(O)Tol groups is higher than with the quinonic oxygen, **TS I** and **TS IV** are more stable than **TS II** and **TS III**. The presumably similar stability of **TS I** and **TS IV** suggests that the low de observed under thermal conditions could be a consequence of a significant participation of A and B rotamers, the first one being slightly predominant. In the presence of an excess of $BF_3{\cdot}OEt_2$, an almost complete shift of the conformational equilibria toward **A**-type rotamers by formation of the species **A′** has been postulated (Scheme 3).[19] The evolution of **A′** into **3** through a transition state similar to **TS I** would explain the complete stereselectivity observed in these reactions. By contrast, under $Eu(fod)_3$ catalysis the formation of a chelated species (B′ in Scheme 3) has also been postulated.[19] The second equivalent of the bulky $Eu(fod)_3$ significantly increased the size of the quinonic oxygen and, therefore, the magnitude of their interaction with the *N*-Boc group during the attack of compound **2**. Moreover, the *N*-Boc/SOTol interaction must be lower in **B′** than in **B** due to the different spatial arrangement of the aryl group in both rotamers (see Scheme 3). These facts would account for the fact that the reaction of **2** with **B′** took place preferentially through transition states similar to **TS III** (thus also yielding compounds **3** as the major ones[20]) despite the fact that **TS IV** was the favored one in uncatalyzed reactions of the **B** rotamers.[21] This explanation is in accord with the low stereoselectivity obtained when the amount of $Eu(fod)_3$ is lower than 2 equiv (Table 1, entries 13 and 14). Additionally, the low de achieved with $SnCl_4$ suggests that several of the conformations and transition states indicated in Scheme 3 must be operative.

At this point, it is of interest to note that the sense of the stereoselectivity observed in reactions with compound **2** is the opposite to that obtained with TMSOF.[6] Thus, starting from (*S*)-**1b** the configuration induced at the new

SCHEME 3



stereogenic center of the major isomer **3** was *S* with pyrrole **2** (see above), whereas it was *R* with the furan derivative.[6] This is easily explained taking into account that the change of the fragment *N*-Boc (in TBSOP) into an oxygen atom (in TMSOF) modifies the relative stability of the TS depicted in Scheme 3, because of the smaller size and higher charge density of the oxygen (see ref 6 for a more detailed discussion of the furan derivatives). Similar changes in the stereoselectivity have been observed in other nucleophilic additions of TMSOF and TBSOP to the carbonyl group of sugar derivatives.[11×bb]

Conclusion

We have demonstrated that the reactions of *N*-Boc-2-(*tert*-butyldimethylsiloxy)pyrrole **2** with 2-(arylsulfinyl)-1,4-benzoquinones **1a**−**c** evolve in a completely stereoselective manner into the Michael adducts **3** when they are catalyzed by $BF_3·OEt_2$. These compounds can be cyclized into the corresponding pyrrolo[3,2-*b*]benzofuranes **5** with $SnCl_4$ or $Eu(fod)_3$ in quantitative yields with complete stereoselectivities. The reactions of **1b** and **1c** with $Eu(fod)_3$ directly yield the pyrrolo[3,2-*b*]benzofuranes **5** in a high stereoselective manner (mixtures of **5** and **6** were obtained under $SnCl_4$ catalysis) according to tandem reactions involving Michael addition followed by intramolecular cyclization.

Experimental Section

General Methods. Melting points were measured in open capillary tubes and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ at 300 and 75 MHz, respectively. IR spectra are reported in cm^{-1}. For thermal, $BF_3·OEt_2$, and $ZnBr_2$ catalytic conditions, diastereoisomeric ratios were determined from integration of well-separated signals in the ^1H NMR spectra of the crude reaction mixtures (H′-4 and H′-5 for compounds **3** and **4** and from H-8b for compounds **5** and **6**). In reactions performed in the presence of $Eu(fod)_3$ and $SnCl_4$, product ratios were determined after filtration through a silica gel pad.

All reactions were monitored by thin-layer chromatography on precoated sheets of silica gel 60 F-254, and flash column chromatography was performed with silica gel 60 (230−400 mesh). Eluting solvents are indicated in the text. Apparatus for inert atmosphere experiments were dried by flaming in a stream of dry argon. Dry THF was distilled from sodium/benzophenone ketyl. CH_2Cl_2 was dried over P_2O_5. $BF_3·OEt_2$ was distilled from $CaCl_2$. $ZnBr_2$ was flamed in the reaction flask, in a stream of dry argon prior to use. For routine workup, hydrolysis was carried out with water, extractions were performed with CH_2Cl_2, and the organic phases were dried over $MgSO_4$.

General Procedure for Thermal Michael-Type Reactions. Method A. To a solution of the corresponding sulfinyl quinone **1a**−**c** (0.15 mmol) in dry CH_2Cl_2 (4 mL) was added *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (**2**) in CH_2Cl_2 (1 mL), under argon, over 20 min (see Table 1 for the reaction conditions). After the mixture was stirred for 6 h at −90 °C, the solvent was removed under reduced pressure. Yields and diastereoisomeric ratios for the Michael adducts were calculated from the ^1H NMR spectra of the crude reaction mixtures and summarized in Table 1.

General Procedure for Lewis Acid Michael-Type Reactions. Method B. To a solution of the corresponding sulfinyl quinone **1a**−**c** (0.15 mmol) in dry CH_2Cl_2 (4 mL) was added the appropriate Lewis acid under argon (see Table 1 for the reaction conditions). The mixture was stirred for 1 h at room temperature and cooled at −90 °C, and then *N*-(*tert*-butoxycarbonyl)-2-(*tert*-butyldimethylsiloxy)pyrrole (**2**) in dry CH_2Cl_2 (1 mL) was added over 20 min. After the time required in each case and workup, the resulting material was purified by flash chromatography (AcOEt/hexane, 2:1 for compounds **3a**,**b**, **4b**, **5a**, **6a**, and **5c**; AcOEt/hexane,1:2 for compounds **5b** and **6b**). Yields and diastereoisomeric ratios of the adducts are summarized in Table 1.

(5*S,*SS**)-*N*-(*tert*-Butoxycarbonyl)-5-[3′,6′-dihydroxy-2-(*p*-methoxyphenylsulfinyl)phenyl]pyrrol-2(5*H*)-one (3a).** Diastereoisomerically pure **3a** was obtained from (±)-**1a** following method B (in the presence of $ZnBr_2$, $BF_3·OEt_2$, or $Eu(fod)_3$) as a white solid: mp 140−142 °C (CH_2Cl_2/hexane); ^1H NMR δ 1.30 (s, 9H), 3.85 (s, 3H), 5.79 (t, 1H, $J = 1.9$ Hz), 5.94 and 6.00 (2dd, 2H, $J = 1.9, 6.0$ Hz), 6.86 and 7.07 (2d, 2H, $J = 8.9$ Hz), 7.01 and 7.72 (AA′BB′ system, 4H), 10.93 (s, 1H); ^{13}C NMR δ: 27.8, 55.6, 59.5, 83.6, 116.4, 119.8, 115.2 (2C), 129.7 (2C), 120.8, 122.2, 127.3, 134.2, 147.7, 144.8, 148.7, 149.1, 153.4, 170.1; EI-MS *m*/*z* (rel intensity) 417 ($M^+ - CO$,1), 192 (31), 171 (100), 155 (23), 141 (42), 139 (97), 109 (6); HMRS (EI) calcd for $C_{22}H_{23}NO_7S$ − Boc (M^+ − Boc) 346.0736, found 346.0749. Anal. Calcd for $C_{22}H_{23}NO_7S$: C, 59.32; H, 5.20; N, 3.14; S, 7.20. Found: C, 59.19; H, 5.19; N, 3.14.

(5*R,*SS**)-*N*-(*tert*-Butoxycarbonyl)-5-[3′,6′-dihydroxy-2-(*p*-methoxyphenylsulfinyl)phenyl]pyrrol-2(5*H*)one (4a).** Compound **4a** was detected, along with **3a**, in the ^1H NMR spectra of the crude reaction mixture from (±)-**1a** following method A: ^1H NMR δ 1.29 (s, 9H), 3.83 (s, 3H), 5.69−5.75 (m, 1H), 5.85−5.92 (m, 2H), 6.79−7.00 (m, 3H), 7.68 (part B of AA′BB′ system, 2H), 10.02 (s, 1H).

(5*S*,*SS*)-*N*-(*tert*-Butoxycarbonyl)-5-[3′,6′-dihydroxy-2-(*p*-tolylsulfinyl)phenyl]pyrrol-2(5*H*)-one (3b). Compound **3b** was obtained from (+)-(S*S*)-**1b** following method B (in the presence of $ZnBr_2$ or $BF_3·OEt_2$) as a pink solid: mp 126−128 °C (CH_2Cl_2/hexane); $[\alpha]_D$ +47 (*c* 1.0, $CHCl_3$); ^1H NMR δ 1.31 (s, 9H), 2.43 (s, 3H), 5.85 (t, 1H, $J = 1.6$ Hz), 6.01 and 6.05 (2dd, 2H, $J = 1.6, 6.0$ Hz), 6.87 and 7.13 (2d, 2H, $J = 9.0$ Hz), 7.35 and 7.66 (AA′BB′ system, 4H), 10.82 (s, 1H); ^{13}C NMR δ 21.6, 27.8, 59.5, 83.7, 116.6, 119.9, 120.8, 122.4, 127.3, 127.2 (2C), 130.8 (2C), 140.0, 143.9, 144.9, 148.8, 149.2, 153.5, 171.0; IR ν_{max} 1773, 1372, 829, 727; EI-MS *m*/*z* (rel intensity) 330 ($M^+ + 1$ − Boc, 19), 314 (4), 192 (70), 139 (43), 125 (100), 101 (5); HMRS (EI) calcd for $C_{22}H_{23}NO_6S$ − Boc (M^+ − Boc) 330.0811, found 330.0800.

(5*R*,*SS*)-*N*-(*tert*-Butoxycarbonyl)-5-[3′,6′-dihydroxy-2-(*p*-tolylsulfinyl)phenyl]pyrrol-2(5*H*)-one (4b). Compound **4b** was obtained from (+)-(S*S*)-**1b** following method B ($BF_3·OEt_2$) as a white solid: mp 166−168 °C (methanol/hexane); $[\alpha]_D$ +76 (*c* 1.0, methanol); ^1H NMR δ 1.30 (s, 9H), 2.36 (s, 3H), 5.79 (t, 1H, $J = 1.5$ Hz), 6.00 and 6.03 (2dd, 2H, $J = 1.5, 6.1$ Hz), 6.74 and 6.80 (2d, 2H, $J = 8.9$ Hz), 7.28 and 7.60

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(18) The presence of the hydrogen bonding was evident from the ^1H NMR spectra of **5b** and **6b**, where the phenolic proton appears very deshielded at 10.45 and 10.50 ppm, respectively.

(19) A more detailed discussion about the conformational behavior of sulfinyl quinones, as well as the influence of catalysts such as BF_3 or $Eu(fod)_3$ on the rotamer's population, can be found in: Carreño, M. C.; García Ruano, J. L.; Urbano, A. *J. Org. Chem*. **1992**, *57*, 6870 and references therein.

(20) A complete inversion of the π-facial selectivity was observed in Diels−Alder reactions of compounds **1** under $BF_3·OEt_2$ and $Eu(fod)_3$ catalysis (see ref 19). In this case, the increase in the size of the quinonic oxygen, quite higher in B′ than in B, had no significant consequence on the stereochemical course of the cycloadditions, almost exclusively controlled by the orientation of the arylsulfinyl group, which is the opposite one for B′ (favored under $Eu(fod)_3$ catalysis) and A′ (favored in the presence of $BF_3·OEt_2$).

(21) Another plausible mechanism to accounting for the formation of the compounds **3** and **4**, alternative to the Michael addition, would assume a Diels−Alder reaction as the first step followed by a retro-aldol-type fragmentation. According this mechanism, the influence of the catalyst on the π-facial selectivity of this cycloaddition,[20] would lead to the predominant formation of compounds **3** and **4** when reactions were catalyzed by $BF_3·OEt_2$ or $Eu(fod)_3$. Therefore, the fact that compounds **3** were obtained as the major ones under both catalytic conditions allowed us to reject this alternative mechanism.

(AA′BB’system, 4H), 8.95 (s, 1H), 10.49 (s, 1H); ^{13}C NMR δ 21.5, 27.9, 59.4, 82.7, 117.4, 120.7, 120.5, 121.8, 127.4, 127.1 (2C), 130.7 (2C), 140.2, 143.7, 144.4, 148.5, 149.1, 153.2, 170.5; IR $\nu_{\max}$ 1774, 1369, 824, 761; EI-MS *m*/*z* (rel intensity) 329 ($M^+ -$ Boc, 10), 311 (40), 91 (31), 57 (100), 41 (69); HMRS (EI) calcd for $C_{22}H_{24}NO_6S$ ($M^+ + 1$) 430.1340, found 430.1324.

(5*S,S*S**)-*N*-(*tert*-Butoxycarbonyl)-5-[3′,6′-dihydroxy-2-(*p*-nitrophenylsulfinyl)phenyl]pyrrol-2(5*H*)-one (3c).** Compound **3c** was detected in the ^{1}H NMR spectra of the crude reaction mixture from (±)-**1c** following method B ($BF_3{\cdot}OEt_2$): ^{1}H NMR δ 1.30 (s, 9H), 6.15 and 6.18 (2dd, 2H, $J = 1.0$, 2.1, 6.1 Hz), 6.2 (dd, 1H, $J = 1.0$, 2.1 Hz, **H**-C5), 6.85 and 7.13 (2d, 2H, $J = 8.8$ Hz), 7.90 and 8.40 (AA′BB′ system, 4H), 9.91 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 28.0, 60.5, 84.0, 120.5, 121.4, 123.4, 125.0, 124.5 (2C), 127.1, 127.8 (2C), 133.5, 145.0, 145.4, 149.3, 149.7, 153.4, 169.1; EI-MS *m*/*z* (rel intensity) 337 (1), 309 (8), 156 (100), 140 (6), 124 (29), 111 (5).

(5*R,S*S**)-*N*-(*tert*-Butoxycarbonyl)-5-[3′,6′-dihydroxy-2-(*p*-nitrophenylsulfinyl)phenyl]pyrrol-2(5*H*)-one (4c).** Compound **4c** was detected, along with **3c**, in the ^{1}H NMR spectra of the crude reaction mixture obtained from (±)-**1c** following method A or B ($ZnBr_2$): ^{1}H NMR δ 1.29 (s, 9H), 5.99 (t, 1H, $J = 1.0$ Hz), 6.14−6.18 (m, 2H), 6.20 (dd, 1H, $J = 1.0$, 2.1 Hz), 6.85 and 7.13 (2d, 2H, $J = 8.8$ Hz), 7.90 and 8.40 (AA′BB′ system, 4H), 9.91 (s, 1H).

(3a*R,8b*R**,S*S**)-*N*-(*tert*-Butoxycarbonyl)-3a,8b-dihydro-7-hydroxy-8-(*p*-methoxyphenylsulfinyl)pyrrolo[3,2-*b*]benzofuran-2(3*H*)-one (5a).** Diastereoisomerically pure **5a** was obtained from (±)-**1a** following method B ($SnCl_4$) or by treatment of **3a** (0.03 mmol) in CH_2Cl_2 with $SnCl_4$ (0.06 mmol) at −90 °C as a white solid: mp 126−127 °C (CH_2Cl_2/hexane); ^{1}H NMR δ 1.56 (s, 9H), 2.91 and 2.97 (2dd, 2H, $J = 2.4$, 7.8, 18.9 Hz), 3.82 (s, 3H), 5.25 (dt, 1H, $J = 2.4$, 7.8 Hz), 5.63 (d, 1H, $J = 7.8$ Hz), 6.94 and 7.63 (AA′BB′ system, 4H), 7.18 and 7.21 (2d, 2H, $J = 8.8$ Hz), 10.19 (s, 1H); ^{13}C NMR δ 28.0, 39.1, 55.5, 62.9, 78.0, 84.5, 114.8, 115.0, 124.9 (2C), 125.1 (2C), 127.5, 127.7, 133.9, 148.1, 149.7, 151.1, 152.9, 170.6; HMRS (EI) calcd for $C_{22}H_{24}NO_7S$ ($M^+ + 1$) 446.1253, found 446.1273. Anal. Calcd for $C_{22}H_{23}NO_7S$: C, 59.32; H, 5.20; N, 3.14; S, 7.20. Found: C, 59.18; H, 5.21; N, 3.13.

(3a*S,8b*S**,S*S**)-*N*-(*tert*-Butoxycarbonyl)-3a,8b-dihydro-7-hydroxy-8-(*p*-methoxyphenylsulfinyl)pyrrolo[3,2-*b*]benzofuran-2(3*H*)-one (6a).** Compound **6a** was obtained from (±)-**1a** following method B ($SnCl_4$) as a white solid: mp 139−141 °C (CH_2Cl_2/hexane); ^{1}H NMR δ 1.55 (s, 9H), 2.82 and 2.88 (2dd, 2H, $J = 2.1$, 7.8, 18.8 Hz), 3.81 (s, 3H), 5.18 (dt, 1H, $J = 2.1$, 7.8 Hz), 5.59 (d, 1H, $J = 7.8$ Hz), 7.00 and 7.65 (AA′BB′ system, 4H), 7.17 and 7.20 (2d, 2H, $J = 8.5$ Hz), 10.24 (s, 1H); ^{13}C NMR δ 28.0, 39.1, 55.5, 62.9, 78.0, 83.5, 114.7 (2C), 117.7, 124.9, 125.1, 127.0, 127.7 (2C), 134.0, 147.9, 149.5, 151.1, 152.9, 170.8; HMRS (EI) calcd for $C_{22}H_{24}NO_7S$ ($M^+ + 1$) 446.1261, found 446.1273.

(3a*R*,8b*R*,S*S*)-*N*-(*tert*-Butoxycarbonyl)-3a,8b-dihydro-7-hydroxy-8-(*p*-tolylsulfinyl)pyrrolo[3,2-*b*]benzofuran-2(3*H*)-one (5b). Diastereoisomerically pure **5b** was obtained from (+)-(S*S*)-**1b** following method B (Eu(fod)$_3$) or by treatment of **3b** (0.03 mmol) in CH_2Cl_2 with Eu(fod)$_3$ (0.06 mmol) or $SnCl_4$ (0.06 mmol) at −90 °C as a white solid: mp 101−103 °C (CH_2Cl_2/hexane); $[\alpha]_D$ −100 (*c* 1.0, $CHCl_3$); ^{1}H NMR δ 1.58 (s, 9H), 2.38 (s, 3H), 2.87 and 2.99 (2dd, 2H, $J = 4.2$, 7.1, 18.3 Hz), 5.20 (dt, 1H, $J = 4.2$, 7.1 Hz), 5.78 (d, 1H, $J = 7.1$ Hz), 6.79 and 6.84 (2d, 2H, $J = 8.9$ Hz), 7.30 and 7.68 (AA′BB′ system, 4H), 10.45 (s, 1H); ^{13}C NMR δ 21.4, 28.0, 38.8, 62.5, 78.1, 84.7, 115.4, 121.3, 121.7, 122.2, 125.2 (2C), 130.2 (2C), 140.1, 142.2, 150.1, 155.3, 153.0, 169.9; CI-MS *m*/*z* (rel intensity) 429 (M^+, 1), 329 (2), 312 (7), 91 (13), 65 (13), 57 (69), 41 (100); HMRS (EI) calcd for $C_{22}H_{24}NO_6S$ ($M^+ + 1$) 430.1309, found 430.1324. Anal. Calcd for $C_{22}H_{23}NO_6S$: C, 61.52; H, 5.40; N, 3.26; S, 7.47. Found: C, 61.65; H, 5.37; N, 3.25.

(3a*S*,8b*S*,S*S*)-*N*-(*tert*-Butoxycarbonyl)-3a,8b-dihydro-7-hydroxy-8-(*p*-tolylsulfinyl)pyrrolo[3,2-*b*]benzofuran-2(3*H*)-one (6b). Diastereoisomerically pure **6b** was obtained from (+)-(S*S*)-**1b** following method B ($SnCl_4$) or by treatment of **4b** (0.03 mmol) in CH_2Cl_2 with Eu(fod)$_3$ (0.06 mmol) or $SnCl_4$ (0.06 mmol) at −90 °C as a white solid: mp 131−132 °C (CH_2Cl_2/hexane); $[\alpha]_D$ −25 °C (*c* 0.2, $CHCl_3$); ^{1}H NMR δ 1.56 (s, 9H), 2.37 (s, 3H), 2.86 and 2.98 (2dd, 2H, $J = 2.5$, 7.4, 18.8 Hz), 5.16 (dt, 1H, $J = 2.5$, 7.4 Hz), 5.58 (d, 1H, $J = 7.4$ Hz), 6.63 and 6.64 (2d, 2H, $J = 8.8$ Hz), 7.30 and 7.56 (AA′BB′ system, 4H), 10.05 (s, 1H); ^{13}C NMR δ 21.5, 28.1, 39.0, 62.6, 78.1, 84.6, 116.3, 121.3, 121.7, 122.1, 125.2 (2C), 130.3 (2C), 139.8, 141.9, 149.4, 155.1, 152.9, 169.5; EI-MS *m*/*z* (rel intensity) 429 (M^+, 1), 329 (2), 312 (7), 91 (13), 65 (13), 57 (69), 41 (100); HMRS (EI) calcd for $C_{22}H_{24}NO_6S$ (M^++1) 430.1322, found 430.1324. Anal. Calcd for $C_{22}H_{23}NO_6S$: C, 61.52; H, 5.40; N, 3.26; S, 7.47. Found: C, 61.51; H, 5.39; N, 3.25.

(3a*R,8b*R**,S*S**)-*N*-(*tert*-Butoxycarbonyl)-3a,8b-dihydro-7-hydroxy-8-(*p*-nitrophenylsulfinyl)pyrrolo[3,2-*b*]-benzofuran-2(3*H*)-one (5c).** Diastereoisomerically pure **5c** was obtained from (±)-**1c** following method B (Eu(fod)$_3$) as a white solid: mp 147−148 °C (CH_2Cl_2/hexane); ^{1}H NMR δ 1.57 (s, 9H), 2.94 and 3.05 (2dd, 2H, $J = 4.1$, 7.0, 18.5 Hz), 5.30 (dt, 1H, $J = 4.1$, 7.0 Hz), 5.91 (d, 1H, $J = 7.0$ Hz), 6.80 and 6.90 (2d, 2H, $J = 8.9$ Hz), 7.92 and 8.37 (AA′BB′ system, 4H), 9.77 (s, 1H); ^{13}C NMR δ 28.0, 38.7, 62.6, 77.6, 81.9, 116.5, 121.1, 122.6, 122.9, 124.5 (2C), 125.8 (2C), 134.5, 142.1, 150.1, 154.2, 153.1, 169.5; HMRS (EI) calcd for $C_{16}H_{13}N_2O_6S$ ($M^+ -$ Boc) 361.0485, found 361.0494. Anal. Calcd for $C_{21}H_{20}N_2O_8S$: C, 54.78; H, 4.38; N, 6.08; S, 6.96. Found: C, 54.72; H, 4.37; N, 6.10.

(3a*S,8b*S**,S*S**)-*N*-(*tert*-Butoxycarbonyl)-3a,8b-dihydro-7-hydroxy-8-(*p*-nitrophenylsulfinyl)pyrrolo[3,2-*b*]benzofuran-2(3*H*)-one (6c).** Compound **6c** was detected, along with **5c**, in the ^{1}H NMR spectra of the crude reaction mixture from (±)-**1c** following method B ($SnCl_4$): ^{1}H NMR δ 1.57 (s, 9H), 2.95 and 3.00 (2dd, 2H, $J = 2.6$, 7.3, 18.8 Hz), 5.21 (dt, 1H, $J = 2.6$, 7.3 Hz), 5.60 (d, 1H, $J = 7.3$ Hz), 6.85 and 6.86 (2d, 2H, $J = 8.9$ Hz), 7.89 and 8.28 (AA′BB′ system, 4H), 9.92 (s, 1H).

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Supporting Information Available: Copies of ^{1}H NMR spectra for compounds **3a**,**b**, **4b**, **5a**,**b**, **6a**,**b**, and **5c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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