Synthesis of Tetrahydro- and Dihydropyridines by Hetero Diels-Alder Reactions of Enantiopure α,β-Unsaturated Sulfinimines

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Intermolecular hetero Diels-Alder reactions of the enantiopure sulfinimine **11** with the enol ethers **12–16** at 20 °C and 11 kbar lead to the tetrahydropyridines **18–22** in high yield, with very good to good *endo*/*exo* selectivities, and with an induced diastereoselectivity of up to 2.1:1. The sulfinyl group in the adducts can be removed with MeLi followed by treatment with acetyl chloride or dimethyl sulfate. According to this procedure, **21** gives either *N*-acetyltetrahydropyridine **29** or the *N*-methyldihydropyridine **32**. The intramolecular Diels-Alder reaction of **26** yields **27**, which is transformed into **33** and **34**, respectively.

Introduction

The synthesis of 6-membered N heterocycles is of general interest since they often show a pronounced biological activity. One of the most versatile methods for preparing such compounds is the hetero Diels-Alder reaction using either aza-dienophiles or aza-dienes.[1] Thus, α,β-unsaturated sulfonimines have been employed for the preparation of tetrahydropyridines.[2] In these reactions, however, racemic products are obtained since the starting material is achiral. Herein we describe the use of α,β-sulfinimines in inter- and intramolecular hetero Diels-Alder reactions leading to the formation of N heterocycles. Sulfinimines are interesting substrates in synthesis[3] since they can be obtained in enantiopure form from menthyl toluenesulfinate.[4] They show many similarities with vinyl sulfoxides, which have already been employed in asymmetric Diels-Alder reactions.[5] In these reactions, good asymmetric inductions are obtained as a result of a stereoelectronic stabilization due to the syncoplanar orientation of the S−O group and the C−C double bond.[6][7] On the other hand, formation of a chelate with a Lewis acid allows a reversal of the facial selectivity.

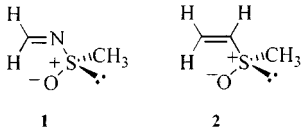
Results and Discussion

Calculations on the Conformation of Sulfinimines

For vinyl sulfoxide **2**, it was shown that the syncoplanar orientation of the S−O group and the C−C double bond as the ground-state conformation is stabilized by 1.7 kcal mol^{-1}.[6][7] We assumed that the conformation of sulfinimines might be controlled by similar effects as found for the vinyl sulfoxides and calculated the rotational potential energy surface (PES) of sulfinimine **1** with the B3LYP functional[8] and the 6-311+G* basis set.[9]

However, at 6.1 kcal mol^{-1}, the B3LYP/6-311+G* energy of the second local minimum **1b** relative to **1a** is not only more than three times as high as that calculated for the vinyl sulfoxide **2**, but is also only 0.2 kcal mol^{-1} lower in energy than the transition structure **1d** that separates the minima **1a** and **1b**. Moreover, the second transition structure **1c** is found to be twice as high in energy as in the case of the vinyl sulfoxide **2**. This clearly demonstrates that there must be an additional stabilizing factor for the syncoplanar conformation **1a** in the sulfinimines. Second-order perturbation analysis theory of the Fock matrix in the NBO[10] basis shows that the $\pi_{C=N}$-σ^*_{S-CH3}, $\pi_{C=N}$-Rd_S, $\pi^*_{C=N}$-σ_{S-CH3}, and the $\pi^*_{C=N}$-n_S interactions contribute to the stabilization of **1a** with the same order of magnitude as the corresponding interactions for the vinyl sulfoxide. The additional stabilization of **1a** is in fact the result of the n_N-σ^*_{S-O} interaction, which further stabilizes the ground-state

Scheme 1



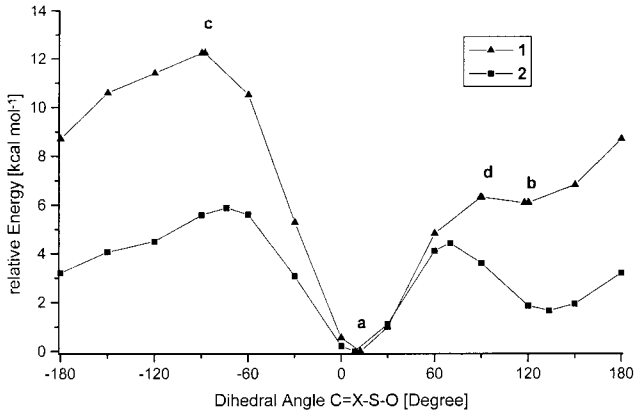
1 **2**

Table 1. Energies of the conformers of **1** and **2**

Structure	Dihedral angle C=X−S−O	B3LYP/6-311+G* energy [au]	Relative energy [kcal mol^{-1}]
1a	12°	−607.39871	0
1b	117°	−607.38900	6.1
1c (TS)	−88°	−607.37921	12.2
1d (TS)	89°	−607.38865	6.3
2a	9°	−591.34498	0
2b	133°	−591.34233	1.7
2c (TS)	−74°	−607.33560	5.9
2d (TS)	70°	−607.33792	4.4

  1434−193X/98/0808−1629 $ 17.50+.50/0

Figure 1. B3LYP/6-311+G* rotational potential energy surface of **1** and **2**

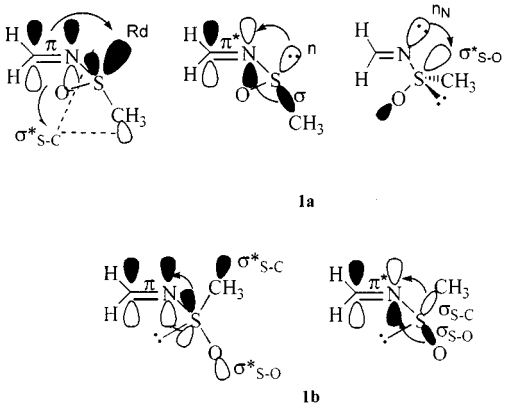


conformation by 3.9 kcal mol^{-1}, giving rise to a shortening of the N−S bond from 1.80 A in **1b** to 1.78 A in **1a**. The X-ray structure of sulfinimine **3** corresponds very well with the calculations on **1a**; the C=N−S−O dihedral angles deviate by only 6°.

The negative results indicate that in these Diels-Alder reactions with inverse electron demand, the LUMO energies and coefficients of the sulfinimines **3** and **5** are not appropriate. We therefore calculated the LUMO energies of **3** and **4** by the PM3 method[11] and obtained values of −0.9 and −1.0 eV, respectively. The respective LUMO coefficients of **3** and **4** were found to be −0.44 and −0.22 at C-3, and −0.37 and −0.18 at the nitrogen atoms. Since the LUMO energy of **3** is only slightly higher than that of the corresponding sulfonimine **4**, and the LUMO coefficients of **3** at C-3 and at the nitrogen atom are twice as high as those found for **4**, these calculations offer no explanation as to the lack of reactivity of **3** compared to **4**. Indeed, the calculations serve only to illustrate the limited reliability of such semiempirical approaches in the realm of hypervalent sulfur compounds.

For Diels-Alder reactions of 1-oxa-1,3-butadienes, we have previously demonstrated the accelerating effect of an electron-withdrawing group at the 3-position of the diene, which causes a decrease of the LUMO energy and favourable coefficients.[12] We therefore prepared **11**, bearing a cyano group at the 3-position of the 1-azabutadiene moiety,

Figure 2. Stabilization of **1a** and **1b**



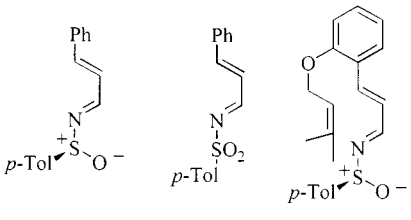
interaction	stabilisation [kcal mol^{-1}]
$\pi_{C\text{-}N}$-$\sigma^*_{S\text{-}CH3}$	1.4
$\pi_{C\text{-}N}$-Rd_S	1.4
$\sigma_{S\text{-}CH3}$–$\pi^*_{C\text{-}N}$	2.0
n_S-$\pi^*_{C\text{-}N}$	1.5
n_N-$\sigma^*_{S\text{-}O}$	**3.9**
Σ	10.2

interaction	stabilisation [kcal mol^{-1}]
$\pi_{C\text{-}N}$-$\sigma^*_{S\text{-}CH3}$	0.7
$\pi_{C\text{-}N}$-$\sigma^*_{S\text{-}O}$	2.6
$\sigma_{S\text{-}CH3}$–$\pi^*_{C\text{-}N}$	0.8
$\sigma_{S\text{-}O}$-$\pi^*_{C\text{-}N}$	<0.5
Σ	4.1

Diels-Alder Reactions of α,β-Unsaturated Sulfinimines

Since the aforementioned calculations had shown the sulfinimines to be conformationally rigid, we expected them to give high asymmetric induction in hetero Diels-Alder reactions, even in the absence of a chelating Lewis acid. The reaction of the α,β-unsaturated sulfinimine **3** with ethyl vinyl ether seemed to be a suitable starting point for our investigations since it is known that α,β-unsaturated sulfonimines such as **4** cyclize with ethyl vinyl ether at 12 kbar in high yield with *endo* selectivity.[2] However, we found that even after heating the reactants to 60°C under high pressure up to 11 kbar for 48 h, the desired cycloadduct was not formed. Addition of Lewis acids such as $AlClMe_2$, $AlCl_2Me$, $SnCl_4$ or TMSOTf at −78°C did not change the picture; only decomposition of the enol ether was observed. The intramolecular Diels-Alder reaction of **5** was likewise unsuccessful under the conditions mentioned above.

Scheme 2

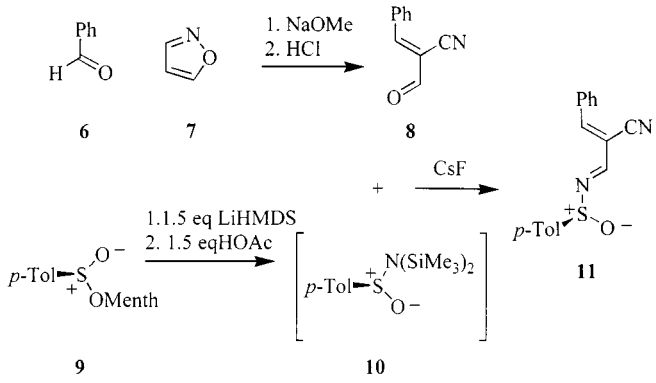


3 4 5

from the aldehyde **8** and menthyl toluenesulfinate **9**. The aldehyde **8** was synthesized from benzaldehyde **6** and isoxazole **7**.[13] The usual procedure for the synthesis of sulfinimines reported by Davis,[4] in which an excess of the aldehyde is added to the crude mixture of **10** after the addition of LiHMDS to **9**, proved to be unsuitable for the synthesis

of sulfinimine **11**. We suspect that a Michael addition of the formed menthoxide to the aldehyde **8** occurred. However, upon addition of acetic acid to the crude mixture of **10**, the desired sulfinimine **11** was obtained in high yield. Using this procedure, it was not necessary to employ an excess of the aldehyde **8**.

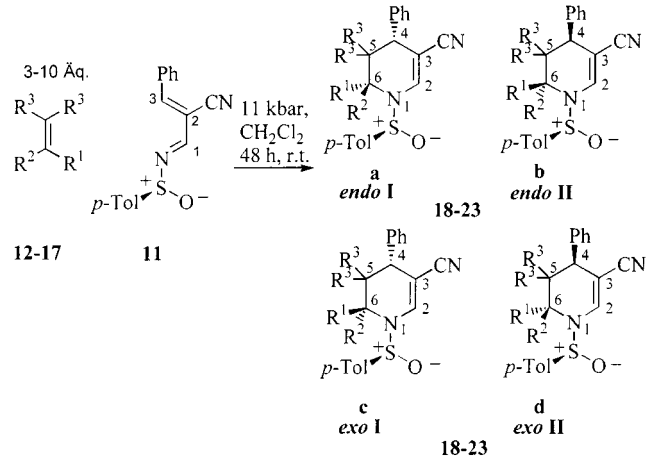
Scheme 3



6 **7** **8** **9** **10** **11**

Cycloadditions of **11** to various electron-rich dienophiles **12**−**16** at room temperature under a pressure of 11 kbar gave the cycloadducts **18**−**22** in almost quantitative yields (Table 2). In those cases where the dienophiles could not be removed by distillation, thus necessitating chromatographic purification, the yields of the isolated products were around 80%. Dienophiles without electron-donating substituents, such as the simple alkene **17**, did not react. In most cases, the *endo* products were formed highly preferentially, the exceptions being the reaction of **14**, which contains a bulky *tert*-butoxy group, and that of **16**, which has a methyl group at C-1 of the enol ether. In contrast, the induced diastereoselectivities were found to be rather low, ranging from 1.1:1 to 2.3:1 for the *endo* products, with a preferential attack *anti* to the *p*-tolyl group. Some of the major products could be separated by column chromatography. The reaction of **11** and **12** was also performed using different Lewis acids at atmospheric pressure. However, decomposition of the enol ether occurred prior to product formation.

Scheme 4



12-17 **11**

Table 2. Cycloaddition of **11** to various dienophiles **12**−**17**

Dienophile	Cycloadduct	R^1	R^2	R^3	Yield [%]	*exo*/*endo*	*endo* I/*endo* II (/*exo* I/*exo* II)
12	**18**	OEt	H	H	96	1:100	1.7:1
13	**19**	SPh	H	H	80	1:100	1.9:1
14	**20**	O*t*Bu	H	H	99	13:87	2.3:1(:0.3:0.2)
15	**21**	SMe	SMe	H	76	1:100	1.8:1
16	**22**	OMe	Me	H	98	24:76	1.1:1(:0.4:0.3)
17	**23**	Me	Me	Me	0	−	−

The structural assignment of the diastereomeric cycloadducts is representatively shown for **20**. It is based on an X-ray analysis of the minor *endo* adduct **20b**. The NOESY spectra of the two main products **20a** and **20b** both show a strong NOE between 4-H and 6-H, which is only possible if the two hydrogen atoms are in a *cis* orientation. A differentiation of the two *exo* products was not possible on the basis of the spectroscopic data; however, considering the facial selection in forming the *endo* product **20a**, it was assumed that the main *exo* product is also formed by an attack of the dienophile *anti* to the *p*-tolyl group.

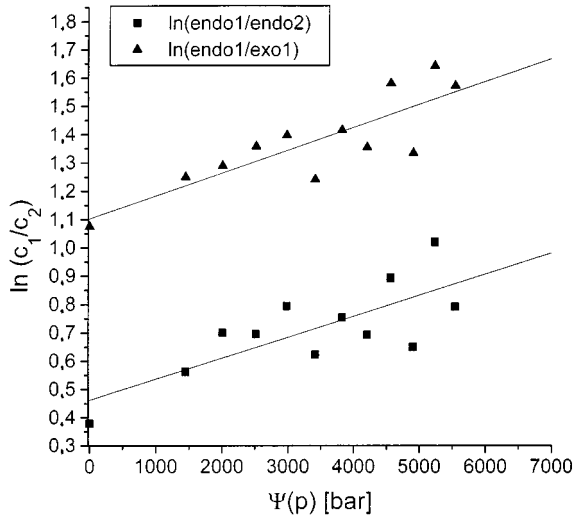
Pressure Dependence of the Diastereoselectivity

Recently, we observed a pronounced pressure dependence of up to $\Delta\Delta V^{\neq} = 7$ cm^3 mol^{-1} on the diastereoselectivities of cycloadditions of some 1-oxa-1,3-butadienes at high pressures.[14] Such an effect is only found if there is strong steric hindrance in the *endo* transition structure. The cycloaddition of **11** to *tert*-butyl vinyl ether was performed under various pressures ranging from 2 to 12 kbar. The ratio of the diastereomeric products **20a**−**d** was determined by analyzing the ^{1}H-NMR signals of the methyl group of the *p*-toluyl moiety and those of the *tert*-butoxy group. A marked decrease of the conversion rate with decreasing pressure was observed, which corresponds to the well known fact that Diels-Alder reactions have a strong negative activation volume $\Delta V^{\neq}$. According to El′yanow′s equation,[15] the differences of the activation volumes $\Delta\Delta V^{\neq}$ were determined from plots of ln(*endo* I/*endo* II) and ln(*endo* I/*exo* I) versus Ψ(p). A $\Delta\Delta V^{\neq}$ value of $-(2.0 \pm 0.4)$ cm^3 mol^{-1} was found for the formation of the *endo* I and *exo* I cycloadducts, which is consistent with the expected stabilization of the more crowded *endo* transition structure under high pressure. Somewhat unexpected, however, is the preferential formation of the *endo* I cycloadduct compared to *endo* II with a $\Delta\Delta V^{\neq}$(*endo* I − *endo* II) $= -(1.8 \pm 0.5)$ cm^3 mol^{-1}. This would imply that the attack of the dienophile *anti* to the tolyl group in **11**, the less hindered approach, is actually stabilized under high pressure.[16] Though the $\Delta\Delta V^{\neq}$ values are significant, they are too small to indicate a pronounced pressure-induced enhancement of the diastereoselectivity in these cycloadditions.

Intramolecular Hetero Diels-Alder Reactions of Sulfinimines 26

Intramolecular reactions often occur with a much higher stereoselectivity than the corresponding intermolecular transformations. We therefore prepared the sulfinimine **26**,

Figure 3. Pressure dependence of the diastereoselectivity of the cycloaddition of **11** and **14**

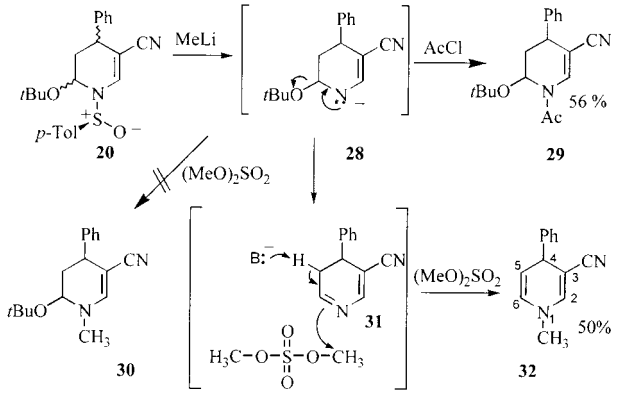


bearing a cyano group at C-3, starting from aldehyde **24**. The hetero Diels-Alder reaction of **26** was performed under high pressure at room temperature in dichloromethane, to give the cycloadducts **27a**–**d** in almost quantitative yield as a mixture of the four possible diastereomers in a ratio of 8.8:2.3:4.4:1.0. The mixture could be separated by column chromatography into two fractions containing **27a/27b** and **27c/27d**, respectively. The cycloadducts **27a** and **27b** are the two *endo* products, while **27c** and **27d** are the two *exo* products. Thus, upon analysis of the ^{1}H-NMR spectra of **27a** and **27b**, 4a-H shows only a diaxial coupling with 5-H^a, whereas in **27c** and **27d** this proton shows diaxial couplings with both 5-H^a and 10b-H. A differentiation of the two *endo* and two *exo* products on the basis of the spectroscopic data was not possible. Thus, the assignment stems from the assumption that, in analogy to the cycloaddition of **11**, the attack *anti* to the tolyl group should be preferred. The main product should therefore be **27a**. Interestingly, in the intramolecular reaction of **26**, the induced diastereoselectivity is higher, while the *endo*/*exo* selectivity is lower, compared to the intermolecular Diels-Alder reaction of **11**.

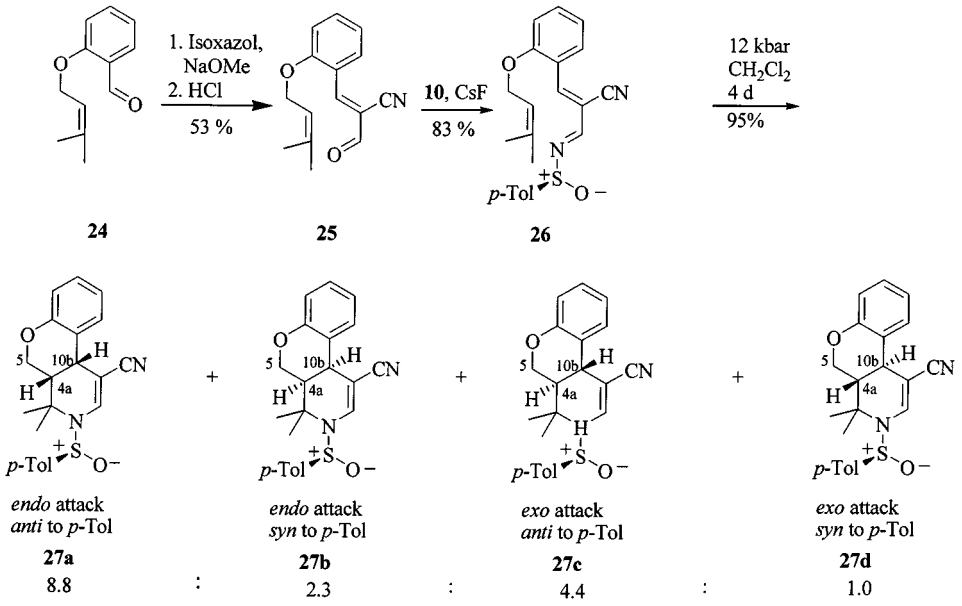
Cleavage of the Sulfininyl Group

Attempts to reductively cleave the sulfinyl group in **20** with $LiAlH_4$ or Raney Ni were unsuccessful, leading only to decomposition. However, the sulfinyl group could smoothly be removed by a nucleophilic substitution with MeLi at −78 °C, giving the enamide ion **28** and methyl toluyl sulfoxide. **28** was quenched with acetyl chloride to furnish **29**. In contrast, dimethyl sulfate was found to be insufficiently reactive to allow a methylation of **28** at −78 °C. At room temperature, however, the methylation does take place, although it is accompanied by elimination of the *tert*-butoxide. Thus, as the final product, the dihydropyridine **32** was isolated.

Scheme 6

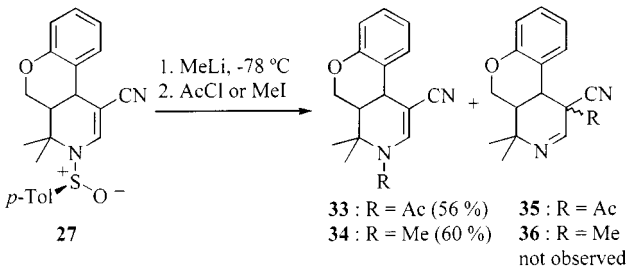


Scheme 5



The cleavage of the sulfinyl group in **27** could be performed in a similar manner as described for **20**. Reaction of **27** with MeLi led to the corresponding enamide ion, which was quenched with acetyl chloride or methyl iodide to give the tetrahydropyridines **33** and **34**, respectively, by attack at the nitrogen atom. Using the mixture of **27a**−**d**, two diastereomers were obtained in each case in a ratio corresponding to the *endo*/*exo* selectivity. The isomers **35** and **36**, which might have been formed by reaction at C-3 in **27**, were not observed.

Scheme 7

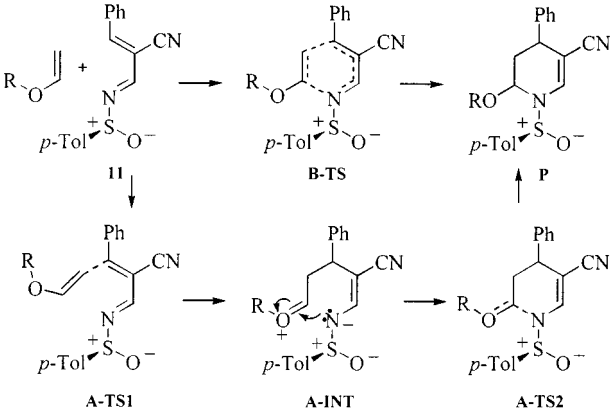


Conclusion

The asymmetric induction associated with the cycloaddition of enantiopure α,β-unsaturated sulfinimines to enol ethers is rather low. This is in contrast to calculations, which show a strong stabilization of a conformation with a C=N−S−O dihedral angle of about 0°, which is in agreement with an X-ray structure. It could be argued that the sulfinimines are conformationally less rigid than calculated. However, ground-state calculations are usually quite accurate nowadays. Therefore, another aspect must be discussed, namely the mechanism of the cycloaddition. The α,β-unsaturated sulfinimine can cyclize either in a concerted manner via B-TS (Figure 4), or by a stepwise mechanism in which the C−C bond is formed before the C−N bond. For the model reaction of 1-aza-1,3-butadiene with ethene, UHF/6-31+G* calculations have shown that the stepwise mechanism is favoured.[17] Following the concerted reaction path, one would expect a high asymmetric induction since bond formation with the generation of a stereogenic centre occurs in close proximity to the chiral sulfinyl group. In contrast, following the stepwise reaction path, the new stereogenic centre is generated far away from the inducing stereogenic centre, resulting in a low asymmetric induction. On the other hand, a strong acceleration of the reaction with increasing pressure is usually interpreted as an indication of a concerted reaction.[18] We therefore think that the described cycloadditions are concerted, but highly asynchronous.

Though the induced diastereoselectivity has to be improved, the described aza Diels-Alder reactions of sulfinimines represent a very efficient approach to chiral tetrahydro- and dihydropyridines in only three steps, starting from commercially available substrates. The reactions proceed under mild conditions and give high yields and excellent *endo* selectivities in most cases.

Figure 4. Proposed mechanism for the cycloaddition of **11** and dienophiles



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Experimental Section

Computational Methods: The PM3 calculations using MOPAC[11] were performed with a PC. The density functional calculations and NBO analysis with GAUSSIAN94[19] were performed with an IBM RS6000 Work Station and an SGI PowerChallenge. All starting geometries were pre-optimized with the MMX force field within PC-MODEL.[20]

General: All reactions were carried out under a positive pressure of nitrogen or argon in dried solvents. Unless stated otherwise, column chromatography was performed with mixtures of *t*BuOMe/petroleum ether as eluent on silica gel with mesh 0.032−0.063 mm from Macherey-Nagel. Reactions under high pressure were carried out in sealed Teflon tubes using a high-pressure cell built by the Institute of Physical Chemistry of the Polish Academy of Sciences. Sulfinimine **3** was prepared according to the procedure of Davis.[4] Aldehydes **8** and **24**, as well as the thioketene acetal **15**, were prepared according to the literature.[13][21][22] − IR: Bruker IFS. − NMR: Varian XL200, VXR 200, UNITY 300, INOVA 500, and Bruker AMX-300; solvent $CDCl_3$ with TMS as internal standard. − MS: Varian MAT 311A and MAT 731. The X-ray structures of **3** and **20b** have been deposited with the CCDC under the depository number 101157.

Aldehyde **25**: To a solution of sodium methoxide (2.53 ml of a 5.4 M solution in methanol, 14 mmol) in methanol (2.4 ml) at −10°C, isoxazole (0.94 g, 14 mmol) was added dropwise, followed, after stirring for 1 h, by aldehyde **24** (2.6 g, 14 mmol). The mixture was stirred for 4 d at 0°C, then poured into iced water (15 ml), and neutralized with 20% HCl. The resulting mixture was extracted with CH_2Cl_2 (3 × 50 ml), and the combined organic phases were washed with brine, dried with Na_2SO_4, and the solvent was removed in vacuo at 20°C. Chromatographic purification furnished 1.80 g (53%) of **25** as the main product, and 0.59 g (35%) of the intramolecular cycloadduct of **25** as a by-product. − IR (film): ν = 3110 cm^{-1}, 2830 (C−H), 2220 (CN), 1694 (CHO), 1594. − UV (CH_3CN): λ_{max} (lg ε) = 216.5 (4.06), 300.5 (4.11), 366.0 (4.03). − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.77 [d, *J* = 1.2 Hz, 3 H, prenyl-(*Z*)-CH_3], 1.83 [d, *J* = 1.2 Hz, 3 H, prenyl-(*E*)-CH_3], 4.65 (d, *J* =

6.8 Hz, 2 H, prenyl-CH_2), 5.49 (ddt, J = 6.8, 1.2, 1.2 Hz, 1 H, prenyl-CH), 7.00 (d, J = 7.8 Hz, 1 H, 3′-H), 7.08 (dd, J = 8.0, 7.8 Hz, 1 H, 5′-H), 7.56 (ddd, J = 7.8, 7.8, 1.2 Hz, 1 H, 4′-H), 8.40 (dd, J = 8.0, 1.2 Hz, 1 H, 6′-H), 8.48 (s, 1 H, 3-H), 9.56 (s, 1 H, 1-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.28 [prenyl-(*Z*)-CH_3], 25.78 [prenyl-(*E*)-CH_3], 65.78 (prenyl-CH_2), 111.49 (C-2), 112.59 (C-3′), 114.44 (CN), 118.55 (C-5′), 120.62 (C-1′), 121.05 (prenyl-CH), 129.62 (C-6′), 136.17 (C-4′), 139.14 [prenyl-*C*$(CH_3)_2$], 153.74 (C-3), 158.79 (C-2′), 187.63 (CHO). − MS (70 eV, FD); *m*/*z* (%): 241.2 (8) [M^+], 198.2 (16), 145.2 (26) [$M^+ - CN - C_5H_9$], 69.1 (100) [$C_5H_9^+$]. − $C_{15}H_{15}NO_2$ (241.28): calcd. C 74.67, H 6.27; found C 74.89, H 6.35.

Synthesis of Sulfinimines. − General Procedure: To a stirred solution of menthyl sulfinate **9** in THF (60 ml/mmol), LiHMDS (1.5 equiv. of a 1 M solution) was slowly added at −78°C and stirring was continued at room temp. for 1 h. The solution was then cooled to −78°C once more and HOAc (1.5 equiv.) was added from a microlitre syringe. After warming to 0°C, the aldehyde (1 equiv.) and CsF (2.0 equiv.) were added, and stirring was continued until completion of the transformation (TLC control, ca. 14 h). The reaction was then quenched by the addition of water (a quarter of the reaction volume) and the mixture was extracted with Et_2O (3 × 30 ml). The combined organic phases were washed with brine and dried with Na_2SO_4, the solvent was removed in vacuo, and the residue was purified by chromatography or crystallization.

Sulfinimine **11**: Reaction of **9** (1.00 g, 3.3 mmol) and **8** (0.53 g, 3.3 mmol) gave **11** (0.74 g, 76%) after purification by column filtration and crystallization from *t*BuOMe/CH_2Cl_2, m.p. 133°C (decomp.). − $[\alpha]_D^{20}$ = +343 (*c* = 1, $CHCl_3$). − IR (film): ν = 3060 cm^{-1} (Ar−H), 3032, 2918, 2228, 2208 (CN), 1598, 1590 (C=N), 1070 (S−O), 544. − UV (CH_3CN): λ_{max} (lg ε) = 192.0 (4.84), 226.5 (1.50), 315.5 (2.43). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, Tol-CH_3), 7.33 (d, J = 7.9 Hz, 2 H, *m*-Tol-H), 7.50−7.53 (m, 3 H, *o*,*p*-Ph-H), 7.61 (s, 1 H, 3-H), 7.64 (d, J = 7.9 Hz, 2 H, *o*-Tol-H), 7.95−8.00 (m, 2 H, *m*-Ph-H), 8.45 (s, 1 H, 1-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 21.42 (Tol-CH_3), 109.32 (C-2), 114.58 (CN), 124.75, 129.33, 129.52, 130.7, 131.87, 133.19, 140.70, 142.03 (aryl-C), 154.96 (C-3), 158.01 (C-1). − MS (70 eV, FD); *m*/*z* (%): 294.3 (5) [M^+], 155.1 (14) [M^+ − TolSO], 139.1 (100) [$TolSO^+$], 91.1 (6) [Tol^+], 77.1 (4) [Ph^+]. − $C_{17}H_{14}N_2OS$ (294.37): calcd. C 69.36, H 4.79; found C 69.14, H 4.83.

Sulfinimine **26**: Reaction of **9** (1.00 g, 3.3 mmol) with **25** (0.84 g, 3.3 mmol) gave **26** (1.04 g, 83%) as a yellow solid after chromatographic purification. − $[\alpha]_D^{20}$ = +596 (*c* = 0.5, $CHCl_3$). − IR (film): ν = 3036 cm^{-1} (Ar−H), 2972, 2224 (CN), 1592, 1590 (C=N), 1070, 1046 (S−O). − UV (CH_3CN): λ_{max} (lg ε) = 233.5 (3.01), 306.0 (3.05), 367.5 (3.03). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.76 [s, 3 H, prenyl-(*Z*)-CH_3], 1.84 [s, 3 H, prenyl-(*E*)-CH_3], 2.41 (s, 3 H, Tol-CH_3), 4.59 (d, J = 6.6 Hz, 2 H, prenyl-CH_2), 5.49 (t, J = 6.6 Hz, 1 H, prenyl-CH), 6.96 (d, J = 8.3 Hz, 1 H, 3′-H), 7.05 (dd, J = 8.0, 7.6 Hz, 1 H, 5′-H), 7.32 (d, J = 8.5 Hz, 2 H, *m*-Tol−H), 7.49 (ddd, J = 8.3, 7.6, 1.2 Hz, 1 H, 4′-H), 7.64 (d, J = 8.5 Hz, 2 H, *o*-Tol-H), 8.24 (s, 1 H, 3-H), 8.35 (dd, J = 8.0, 1.2 Hz, 1 H, 6′-H), 8.49 (s, 1 H, 1-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 18.27 [prenyl-(*Z*)-CH_3], 21.42 (Tol-CH_3), 25.84 [prenyl-(*E*)-CH_3], 65.54 (prenyl-CH_2), 108.15 (C-2), 112.23 (C-3′), 114.99 (CN), 118.60 (C-5′), 120.86 (prenyl-CH), 121.21 (C-1′), 124.80, 129.03, 129.88, 134.94 (aryl-C), 139.21 [prenyl-*C*$(CH_3)_2^*$], 140.98, 141.92 (aryl-C), 149.96 (C-3), 158.40 (C-2′), 158.98 (C-1). − MS (70 eV, FD); *m*/*z* (%): 378.7 (3) [M^+], 278.4 (37), 239.4 (21) [M^+ − TolSO], 171.2 (23) [M^+ − TolSO − prenyl], 139.1 (100) [$TolSO^+$], 91.1 (6) [Tol^+], 69.1 (4) [$prenyl^+$]. − $C_{22}H_{22}N_2O_2S$ (378.48): calcd. C 69.81, H 5.86; found C 69.87, H 5.90.

Diels-Alder Reactions Under High Pressure. − General Procedure: Cycloadditions of the sulfinimines **11** (0.2 mmol) to the dienophiles **12**−**16** (1.0 mmol) and of **26** (0.2 mmol) were performed in CH_2Cl_2 (1 ml) at 11 kbar, with reaction times of 2 d. Evaporation of the solvent and excess dienophile in vacuo or chromatographic separation gave the cycloadducts **18**−**22** and **27**, respectively.

Tetrahydropyridine **18**: Reaction of sulfinimine **11** (58 mg, 0.2 mmol) with ethyl vinyl ether (**12**) (72 mg, 1.0 mmol) gave the cycloadducts **18a** and **18b** (70 mg, 96%) as a 1.7:1 mixture in the form of a yellow oil. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.64 (t, J = 7.0 Hz, 3 H, Et-CH_3, II), 0.84 (t, J = 7.0 Hz, 3 H, Et-CH_3, I), 1.10−1.40 (m, 1 H, 5-H^a, I and II), 1.94 (ddd, J = 14.0, 7.5, 3.0 Hz, 1 H, 5-H^b, I), 2.06 (ddd, J = 14.0, 7.4, 2.7 Hz, 1 H, 5-H^b, II), 2.43 (s, 3 H, Tol-CH_3, II), 2.47 (s, 3 H, Tol-CH_3, I), 2.90 (dq, J = 15.5, 7.0 Hz, 1 H, Et-CH_2^a, II), 3.00−3.20 (m, 1 H, Et-CH_2^b, I and II), 3.45 (dq, J = 16.0, 7.0 Hz, 1 H, Et-CH_2^a, I), 4.65−3.75 (m, 1 H, 4-H, I and II), 4.97 (dd, J = 3.0, 2.7 Hz, 1 H, 6-H, I), 5.03 (dd, J = 2.6, 2.3 Hz, 1 H, 6-H, II), 7.11 (s, 1 H, 2-H, I), 7.17 (s, 1 H, 2-H, II), 7.18−7.38 (m, 5 H, Ph-H, I and II), 7.35 (d, J = 8.3 Hz, 2 H, Tol-*m*-H, II), 7.40 (d, J = 8.0 Hz, 2 H, Tol-*m*-H, I), 7.53 (d, J = 8.3 Hz, 2 H, Tol-*o*-H, II), 7.59 (d, J = 8.0 Hz, 2 H, I). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 14.17 (Et-CH_3, II), 14.47 (Et-CH_3, I), 21.41 (Tol-CH_3, II), 21.45 (Tol-CH_3, I), 33.97 (C-5, II), 34.04 (C-5, I), 36.80 (C-4, I), 36.88 (C-4, II), 63.04 (Et-CH_2, II), 63.15 (Et-CH_2, I), 82.02 (C-6, II), 82.93 (C-6, I), 91.40 (C-3, I), 91.48 (C-3, II), 119.18 (CN, I and II), 125.32, 125.36, 126.58, 126.67, 127.72, 127.83, 128.00, 128.04, 130.00, 130.23, 138.60, 138.66, 138.93, 139.06, 140.50, 140.66, 142.95, 143.05 (aryl-C and C-2).

Tetrahydropyridine **19**: Reaction of sulfinimine **11** (58 mg, 0.2 mmol) with phenyl vinyl sulfide (**13**) (54 mg, 0.4 mmol) gave cycloadduct **19** (86 mg, 80%) as a 1.9:1 mixture of the *endo* diastereomers I and II. The product was obtained as a yellow oil, which was found to contain residual **13**. The diastereomer ratio was determined from the C-4, C-5, C-6 signals in the ^{13}C-NMR spectrum. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.30−2.55 (m, 2 H, 5-H, I and II), 2.36 (s, 3 H, Tol-CH_3, I), 2.41 (s, 3 H, Tol-CH_3, II), 3.67 (dd, J = 5.7, 5.7 Hz, 1 H, 4-H, I), 3.73 (dd, J = 5.8, 5.8 Hz, 1 H, 4-H, II), 5.00 (dd, J = 6.0, 3.8 Hz, 1 H, 6-H, I), 5.35 (dd, J = 5.3, 4.6 Hz, 6-H, II), 6.89 (d, J = 0.9 Hz, 1 H, 2-H, II), 7.10 (d, J = 1.7 Hz, 1 H, 2-H, I), 7.10−7.55 (m, 14 H, aryl-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.42 (Tol-CH_3, I and II), 36.79 (C-5, I), 37.37 (C-5, II), 38.27 (C-4, II), 38.76 (C-4, I), 62.80 (C-6, I), 64.67 (C-6, II), 92.39 (C-3, I), 92.89 (C-3, II), 118.75 (CN, II), 118.83 (CN, I), 124.99, 125.72, 126.97, 127.28, 127.97, 128.03, 128.44, 128.50, 128.79, 129.06, 129.17, 130.09, 130.22, 130.30, 132.00, 132.28, 133.30, 133.42, 139.02, 139.11, 137.81, 138.64, 139.76, 139.81, 143.17 (aryl-C).

Tetrahydropyridine **20**: The reaction of sulfinimine **11** (135 mg, 0.5 mmol) with *tert*-butyl vinyl ether (**15**) (163 mg, 1.6 mmol) gave cycloadduct **20** (181 mg, 99%) as a white solid consisting of a mixture of *endo* I/*endo* II/*exo* I/*exo* II in a ratio of 2.3:1.0:0.2:0.3. The ratio was determined from the *p*-Tol-CH_3 and *t*BuO signals in the ^{1}H-NMR spectrum. By means of column chromatography with *t*BuOMe/petroleum ether (3:7) as eluent, the *endo* I (41 mg) and *endo* II (28 mg) diastereomers could be obtained in a pure form, and *exo* I and *exo* II as a mixture (12 mg). − IR (film): ν = 3056 cm^{-1} (C−H), 2206 (CN), 1626 (enamine), 1098, 1040 (S−O). − UV (CH_3CN): λ_{max} (lg ε) = 258.5 (4.25). − MS (70 eV, FD); *m*/*z* (%): 394.4 (12) [M^+], 338.3 (7) [$M^+ - C_4H_8$], 139.1 (100) [$TolSO^+$], 91.1 (10) [Tol^+], 57.1 (52) [$C_4H_9^+$]. − $C_{23}H_{26}N_2O_2S$ (394.53): calcd. C 70.02, H 6.64; found C 70.28, H 6.91.

endo I. − *Tetrahydropyridine* **20a**: $[\alpha]_D^{20}$ = +178.0 (*c* = 0.5, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (s, 9 H, *t*BuO), 2.13 (ddd, *J* = 13.6, 6.8, 2.6 Hz, 1 H, 5-H^a), 2.25 (ddd, *J* = 13.6, 4.9, 4.9 Hz, 1 H, 5-H^b), 2.39 (s, 3 H, Tol-CH_3), 3.64 (ddd, *J* = 6.8, 4.9, 1.0 Hz, 1 H, 4-H), 5.26 (dd, *J* = 4.9, 2.6 Hz, 1 H, 6-H), 6.87 (d, *J* = 1.0 Hz, 1 H, 2-H), 7.1−7.3 (m, 5 H, Ph-H), 7.21 (d, *J* = 7.9 Hz, 2 H, *m*-Tol-H), 7.43 (d, *J* = 7.9 Hz, 2 H, *o*-Tol-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.39 (Tol-CH_3), 27.90 (*t*Bu-CH_3), 37.89 (C-4), 38.18 (C-5), 75.80 [*t*Bu-*C*$(CH_3)_3$], 79.48 (C-6), 92.74 (C-3), 119.12 (CN), 125.42, 126.74, 127.90, 128.20, 130.26, 138.85, 139.25, 140.58, 142.75 (aromatic and C-2).

endo II. − *Tetrahydropyridine* **20b**: $[\alpha]_D^{20}$ = −12.4 (*c* = 0.5, $CHCl_3$). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99 (s, 9 H, *t*BuO), 2.20 (dd, *J* = 6.4, 3.4 Hz, 1 H, 5-H^a), 2.21 (dd, *J* = 4.9, 4.1 Hz, 1 H, 5-H^b), 2.42 (s, 3 H, Tol-CH_3), 3.69 (dd, *J* = 6.4, 4.9 Hz, 1 H, 4-H), 5.35 (dd, *J* = 4.1, 3.4 Hz, 1 H, 6-H), 6.84 (s, 1 H, 2-H), 7.1−7.25 (m, 5 H, Ph-H), 7.36 (d, *J* = 7.9 Hz, 2 H, *m*-Tol-H), 7.56 (d, *J* = 7.9 Hz, 2 H, *o*-Tol-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.47 (Tol-CH_3), 28.25 (*t*Bu-CH_3), 37.57 (C-4), 38.53 (C-5), 75.69 [*t*Bu-*C*$(CH_3)_3$], 79.06 (C-6), 91.69 (C-3), 119.16 (CN), 125.94, 126.80, 127.70, 128.70, 130.31, 138.81, 139.35, 140.65, 142.87 (aryl-C and C-2).

exo I and exo II. − *Tetrahydropyridine* **20c** *and* **20d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 9 H, *t*BuO, *exo* I), 1.35 (s, 9 H, *t*BuO, *exo* II), 1.67−1.76 (m, 1 H, 5-H^a, *exo* I), 1.81 (ddd, *J* = 13.2, 6.4, 3.4 Hz, 1 H, 5-H^a, *exo* II), 2.09−2.16 (m, 1 H, 5-H^b, *exo* I and *exo* II), 2.39 (s, 3 H, Tol-CH_3, *exo* II), 2.46 (s, 3 H, Tol-CH_3, *exo* I), 3.72 (ddd, *J* = 12, 6.4, 4.9 Hz, 1 H, 4-H, exo II), 3.80−3.85 (m, 1 H, 4-H, *exo* I), 5.36 (dd, *J* = 2.6, 1.9 Hz, 1 H, 6-H, *exo* I), 5.41 (dd, *J* = 2.6, 2.2 Hz, 1 H, 6-H, *exo* II), 6.70 (d, *J* = 1.9 Hz, 1 H, 2-H, *exo* II), 6.92 (d, *J* = 1.9 Hz, 1 H, 2-H, *exo* I), 7.10−7.35 (m, 5 H, Ph-H, *exo* I and *exo* II), 7.34 (d, *J* = 8.3 Hz, 2 H, *m*-Tol-H, *exo* I), 7.38 (d, *J* = 8.3 Hz, 2 H, *m*-Tol-H, *exo* II), 7.50 (d, *J* = 8.3 Hz, 2 H, *o*-Tol-H, *exo* I), 7.50 (d, *J* = 8.3 Hz, 2 H, *o*-Tol-H, *exo* II). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.35 (Tol-CH_3, I), 26.95 (Tol-CH_3, II), 29.88 (*t*Bu-CH_3, I), 31.18 (*t*Bu-CH_3, II), 39.56 (C-4, I and II), 49.44 (C-5, I and II), 76.47 [*t*Bu-*C*$(CH_3)_3$, I and II], 82.60 (C-6, I and II), 100.80 (C-3, I), 109.60 (C-3, II), 115.30 (CN, II), 115.33 (CN, I), 124.81, 125.26, 125.91, 127.57, 127.57, 128.44, 129.15, 129.33, 129.44, 129.57, 134.28, 134.74, 136.47, 141.11, 142.04, 143.59 (aryl-C and C-2).

Tetrahydropyridine **21**: Reaction of sulfinimine **11** (88 mg, 0.3 mmol) with the thioketene acetal **15** (54 mg, 0.5 mmol) gave the cycloadduct **21** (93 mg, 76%) as a white solid consisting of a mixture of the two diastereomers I and II in a ratio of 1.8:1. The ratio was determined from the SCH_3 and 2-H signals in the ^{1}H-NMR spectrum. − IR (film): ν = 3442 cm^{-1}, 2920 (C−H), 2208 (CN), 1612 (enamine), 1254, 1238, 1102 (S−O), 702. − UV (CH_3CN): λ_{max} (lg ε) = 258.0 (4.20), 254.4 (4.20), 264.5 (4.18). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.10−2.30 (m, 1 H, 5-H^a, I and II), 2.25 (s, 3 H, MeS^a, I), 2.28 (s, 3 H, MeS^a, II), 2.35 (s, 3 H, MeS^b, II), 2.39 (s, 3 H, MeS^b, I), 2.46 (s, 3 H, Tol-CH_3, II), 2.49 (s, 3 H, Tol-CH_3, I), 2.40−2.50 (m, 1 H, 5-H^b, II), 2.58 (dd, *J* = 14.0 Hz, 5.6 Hz, 5-H^b, I), 3.80−4.00 (m, 1 H, 4-H, I and II), 6.74 (d, *J* = 2.2 Hz, 1 H, 2-H, II), 6.87 (d, *J* = 1.8 Hz, 1 H, 2-H), 7.16 (d, *J* = 8.3 Hz, 2 H, Tol-*m*-H, I), 7.23 (d, *J* = 8.3 Hz, 2 H, Tol-*m*-H, II), 7.20−7.48 (m, 5-H, Ph-H, I and II), 7.63 (d, *J* = 8.3 Hz, 2 H, Tol-*o*-H, II), 7.64 (d, *J* = 8.3 Hz, 2 H, Tol-*o*-H, I). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.30 (MeS^a, II), 13.52 (MeS^a, II), 14.8 (MeS^b, I and II), 21.52 (Tol-CH_3, I and II), 38.62 (C-4, II), 39.25 (C-4, I), 40.95 (C-5, II), 43.95 (C-5, I), 77.97 (C-6, I and II), 92.60 (C-3, II), 93.85 (C-3, I), 118.15 (CN, II), 118.19 (CN, I), 125.72, 127.80, 127.90, 127.98, 129.06, 130.43, 130.57, 137.54, 137.80, 138.89, 138.98, 139.31, 140.15, 143.09, 149.13 (aryl-C and C-2). − MS (70 eV, FD); *m/z* (%): 389.1 (12) [M^+ − CN], 352.2 (13) [M^+ − MeS − Me], 350.2 (100) [M^+ − MeS − Me − H_2], 273.1 (67) [M^+ − TolSO − H_2], 139.1 (30) [$TolSO^+$], 77.1 (6) [Ph^+]. − $C_{21}H_{22}N_2OS_3$ (414.40): calcd. C 60.86, H 5.35; found C 61.04, H 5.63.

Tetrahydropyridine **22**: Reaction of sulfinimine **11** (29 mg, 0.1 mmol) with the enol ether **16** (20 mg, 0.5 mmol) gave cycloadduct **22** (26 mg, 98%) as a yellow oil consisting of a mixture of four diastereomers I−IV in a ratio of 1.1:1.0:0.4:0.3. The ratio was determined from the MeO and C-5 signals in the ^{13}C-NMR spectrum. − IR (film): ν = 3030 cm^{-1}, 2976 (C−H), 2208 (CN), 1618 (enamine), 1072 (S−O). − UV (CH_3CN): λ_{max} (lg ε) = 257.5 (4.08). − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.69 (s, 3 H, 6-Me, II), 1.81 (s, 3 H, 6-Me, I), 1.82 (s, 3 H, 6-Me, III), 1.91 (s, 3 H, 6-Me, IV), 2.00−2.50 (m, 1 H, 5-H^a, I−IV), 2.43 (s, 3 H, Tol-CH_3, III and IV), 2.47 (s, 3 H, Tol-CH_3, II), 2.49 (s, 3 H, Tol-CH_3, I), 2.80−3.40 (m, 1 H, 5-H^b, I−IV), 3.31 (s, 3 H, MeO, I), 3.36 (s, 3 H, MeO, II), 3.40 (s, 3 H, MeO, III), 3.47 (s, 3 H, MeO, IV), 3.60 (ddd, *J* = 9.6, 5.8, 1.8 Hz, 1 H, 4-H, II), 3.70 (ddd, *J* = 10.5, 5.7, 1.7 Hz, 1 H, 4-H, I), 3.84 (ddd, *J* = 12.1, 6.3, 2.1 Hz, 1 H, 4-H, III), 4.09 (s, *J* = 16.2, 10.0, 2.3 Hz, 1 H, 4-H, IV), 6.73 (d, *J* = 2.3 Hz, 1 H, 2-H, IV), 6.82 (d, *J* = 2.1 Hz, 1 H, 2-H, III), 6.87 (d, *J* = 1.8 Hz, 1 H, 2-H, II), 6.89 (d, *J* = 1.7 Hz, 1 H, 2-H, I), 7.10−7.62 (m, 9 H, aryl-H, I−IV). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.47 (Tol-CH_3, II), 21.51 (Tol-CH_3, I and III), 21.98 (Tol-CH_3, IV), 22.77 (6-CH_3, IV), 23.92 (6-CH_3, III), 25.44 (6-CH_3, I), 26.72 (6-CH_3, II), 26.88 (C-4, III), 37.58 (C-4, IV), 39.12 (C-4, II), 40.10 (C-4, II), 40.48 (C-5, II), 40.77 (C-5, I), 43.37 (C-5, III), 45.05 (C-5, IV), 49.85 (MeO, IV), 50.13 (MeO, II), 50.62 (MeO, III), 50.93 (MeO, I), 88.04 (C-3, IV), 88.23 (C-3, III), 89.65 (C-3, II), 90.04 (C-3, I), 91.13 (C-6, II), 92.77 (C-6, I), 95.34 (C-6, IV), 95.64 (C-6, III), 116.83, 118.56, 118.83, 125.09, 125.17, 125.39, 125.47, 125.86, 125.90, 127.11, 127.16, 127.49, 127.53, 127.60, 127.74, 128.86, 128.95, 130.16, 130.36, 130.55, 130.59, 137.02, 137.98, 138.36, 139.05, 139.42, 139.62, 139.81, 139.86, 140.00, 140.27, 142.89, 142.99, 143.02, 143.18 (CN, aryl-C and C-2). − MS (70 eV, FD); *m/z* (%): 366.5 (4) [M^+], 278.4 (39), 227.4 (13) [M^+ − TolSO], 194.3, 139.2 (100) [$TolSO^+$]. − $C_{21}H_{22}N_2O_2S$ (366.47): calcd. 366.1402; found 366.1402 (MS).

Cycloadducts **27**: Reaction of **26** (21 mg, 0.06 mmol) in CH_2Cl_2 at 11 kbar for a period of 4 d gave **27** (20 mg, 95%) as a yellow solid consisting of a mixture of diastereomers *endo* I/*endo* II/*exo* I/*exo* II in the ratio 8.5:2.3:4.9:1.0. The ratio was determined from the methyl signals in the ^{1}H-NMR spectrum of the crude product. By means of column chromatography, the *exo* and the *endo* diastereomers could be separated in amounts suitable for recording ^{1}H-NMR spectra. − IR (film): ν = 3626 cm^{-1}, 2978 (C−H), 2206 (CN), 1608 (enamine), 1490, 1454, 1286 (aryl ether), 1100, 1072 (S−O). − UV (CH_3CN): λ_{max} (lg ε) = 195.0 (4.79), 262.0 (4.26). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.33 (Tol-CH_3, *endo* I and *exo* I), 21.40 (Tol-CH_3, *endo* II and *exo* II), 24.72 (4-CH_3^a, *exo* I), 24.91 (4-CH_3^b, *exo* I and *exo* II), 25.88 (4-CH_3^a, *endo* II), 26.40 (4-CH_3^a, *exo* II), 26.88 (4-CH_3^a, *endo* I), 28.09 (4-CH_3^b, *endo* II), 29.08 (4-CH_3^b, *endo* I), 31.63 (C-10b, *endo* I), 31.69 (C-10b, *exo* I), 31.75 (C-10b, *endo* II), 31.86 (C-10b, *exo* II), 39.30 (C-4a, *endo* I), 40.80 (C-4a, *exo* II), 45.89 (C-4a, *exo* I), 49.36 (C-4a, *endo* I), 58.27 (C-4, *endo* II), 58.36 (C-4, *endo* I), 60.43 (C-4, *exo* I), 62.50 (C-5, *endo* I), 62.61 (C-5, *endo* II), 62.24 (C-5, *exo* I), 72.69 (C-5, *exo* II), 89.75 (C-1, *exo* I), 91.36 (C-1, *endo* I), 92.66 (C-1, *endo* II), 116.41 (C-7, *endo* II), 116.52 (C-7, *endo* I), 116.97 (C-7, *exo* II), 117.10 (C-7, *exo* I), 118.96, 119.00, 120.48, 120.66 (CN), 120.75, 121.0, 121.09 (C-9), 125.29, 125.43, 125.79, 127.11, 128.21, 128.41, 129.00,

130.40, 130.46, 121.36, 131.43, 138.51, 138.97, 139.40, 141.28, 141.41, 142.88, 142.97, 143.09 (Tol-C and C-10), 153.64 (C-6a, *endo* I and *endo* II), 154.12 (C-6a, *exo* I and *exo* II). − MS (70 eV, FD); *m/z* (%): 378.1 (13) [M^+], 278.0 (37), 240.1 (29) [M^+ − TolSO], 139.1 (100) [$TolSO^+$], 91.1 (30) [Tol^+]. − $C_{22}H_{22}N_2O_2S$ (378.48): calcd. C 69.81, H 5.86; found C 69.56, H 6.04.

endo I and endo II. − **27a and 27b**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.48 (s, 3 H, 4-CH_{3a}, I), 1.63 (s, 3 H, 4-CH_{3a}, II), 1.82 (s, 3 H, 4-CH_3^b, II), 1.83 (s, 3 H, 4-CH_3^b, I), 2.14 (ddd, *J* = 11.2, 5.5, 3.6 Hz, 1 H, 4a-H, I), 2.18 (ddd, *J* = 11.2, 4.9, 3.5 Hz, 1 H, 4a-H, II), 2.43 (s, 3 H, Tol-CH_3, II), 2.47 (s, 3 H, Tol-CH_3, I), 3.54 (dd, *J* = 11.2, 11.0 Hz, 1 H, 5-H^{ax}, II), 3.60 (d, *J* = 6.0 Hz, 1 H, 10b-H, I), 3.68 (d, *J* = 5.3 Hz, 1 H, 10b-H, II), 3.70 (dd, *J* = 11.2, 11.2 Hz, 1 H, 5-H^{ax}, I), 4.36 (ddd, *J* = 11.2, 3.7, 1.9 Hz, 1 H, 5-H_{eq}, I), 4.43 (ddd, *J* = 11.0, 3.1, 1.6 Hz, 5-H^{eq}, II), 6.66 (d, *J* = 2.0 Hz, 1 H, 2-H, I), 6.68 (d, *J* = 2.0 Hz, 1 H, 2-H, II), 6.81 (d, *J* = 8.3 Hz, 1 H, 7-H, II), 6.83 (d, *J* = 8.3 Hz, 1 H, 7-H, I), 6.94 (dd, *J* = 7.6, 7.4 Hz, 1 H, 9-H, I), 6.65 (dd, *J* = 7.6, 7.0 Hz, 1 H, 9-H, II), 7.16−7.20 (m, 1 H, 8-H, I and II), 7.32 (d, *J* = 7.6 Hz, 2 H, Tol-*m*-H, II), 7.35−7.40 (m, 1 H, 10-H, I and II), 7.39 (d, *J* = 8.4 Hz, 2 H, Tol-*m*-H, I), 7.44 (d, *J* = 7.6 Hz, 2 H, Tol-*o*-H, II), 7.49 (d, *J* = 8.4 Hz, 2 H, Tol-*o*-H, I).

exo I and exo II. − **27c and 27d**: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.29 (s, 3 H, 4-CH_{3a}, I), 1.41 (s, 3 H, 4-CH_{3a}, II), 1.76 (s, 3 H, 4-CH_3^b, II), 1.82 (s, 3 H, 4-CH_3^b, I), 2.12 (ddd, *J* = 11.3, 11.2, 3.6 Hz, 1 H, 4a-H, II), 2.14 (ddd, *J* = 11.3, 11.3, 3.4 Hz, 1 H, 4a-H, I), 2.40 (s, 3 H, Tol-CH_3, II and I), 3.48 (dd, *J* = 11.5, 1.8 Hz, 1 H, 10b-H, II), 3.49 (dd, *J* = 11.5, 1.8 Hz, 1 H, 10b-H, 1 H, I), 3.69 (dd, *J* = 11.2, 11.2 Hz, 1 H, 5-H^{ax}, II), 3.81 (dd, *J* = 10.8, 10.8 Hz, 1 H, 5-H^{ax}, I), 4.29 (dd, *J* = 11.2, 3.6 Hz, 1 H, 5-H^{eq}, II), 4.31 (ddd, *J* = 10.8, 3.4 Hz, 5-H^{eq}, I), 6.59 (d, *J* = 1.8 Hz, 1 H, 2-H, I), 6.62 (d, *J* = 1.8 Hz, 1 H, II), 6.76 (d, *J* = 8.2 Hz, 1 H, 7-H, II), 6.80 (d, *J* = 8.3 Hz, 1 H, 7-H, I), 6.82−6.93 (m, 9-H, I and II), 7.16−7.20 (m, 1 H, 8-H, I), 7.12 (dd, *J* = 7.3, 1.8 Hz, 1 H, 10-H, I), 7.22−7.35 (m, 1 H, 8-H, II), 7.25 (dd, *J* = 7.7, 1.4 Hz, 1 H, 10-H, II), 7.32 (d, *J* = 8.3 Hz, 1 H, Tol-*m*-H, II), 7.37 (d, *J* = 8.3 Hz, 2 H, Tol-*m*-H, I), 7.41 (d, *J* = 8.3 Hz, 2 H, Tol-*o*-H, I), 7.75 (d, *J* = 8.3 Hz, 2 H, Tol-*o*-H, II).

Removal of the Sulfinyl Groups in **20** *and* **27**. − *General Procedure:* To a solution of the sulfinyl-substituted cycloadduct **20** or **27** (as a mixture of diastereomers) in THF (5 ml) at −78°C, 1.5 equiv. of methyllithium (as a 1.6 M solution in Et_2O) was added, and the mixture was stirred for 1 h at this temperature. Then, 1.5 equiv. of the electrophile [CH_3I or $(MeO)_2SO_2$ or AcCl] was added and stirring was continued for 1 h at −78°C, and, if the reaction was incomplete (TLC control), for a further 1 h at room temperature. The solution was then diluted with brine (2 ml) and extracted with Et_2O (3 × 5 ml). The combined organic phases were dried (Na_2SO_4), the solvent was removed in vacuo, and the residue was purified by column chromatography in order to remove the by-product methyl tolyl sulfoxide.

Tetrahydropyridine **29**: Cycloadduct **20** (78 mg, 0.2 mmol) was treated with MeLi and acetyl chloride to give **29** (34 mg, 56%) (*endo* configuration). − UV (CH_3CN): λ_{max} (lg ε) = 258.0 (3.38). − IR (film): ν = 2976 cm^{-1} (C−H), 2208 (CN), 1694 (CO−NR_2), 1624 (enamine). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.86 (s, 9 H, *t*BuO), 2.09 (ddd, *J* = 14.0, 7.6, 2.4 Hz, 1 H, 5-H^{ax}), 2.30 (s, 1 H, Ac), 2.38 (ddd, *J* = 14.0, 3.2, 1.2 Hz, 1 H, 5-H^{eq}), 3.75 (dd, *J* = 7.4, 1.2 Hz, 1 H, 4-H), 6.01 (m, 1 H, 6-H), 7.20−7.35 (m, 5 H, Ph-H), 7.59 (s, 1 H, 2-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.81 (Ac-CH_3), 28.01 (*t*Bu-CH_3), 36.07 (C-5), 36.87 (C-4), 74.99 [*t*Bu-*C*$(CH_3)_3$], 93.37 (C-3), 119.42 (CN), 126.45 (Ph-*m*-C), 128.05 (Ph-*o*-C and Ph-*p*-C), 138.78 (C-2), 141.42 (Ph-*ipso*-C), 167.40 (Ac-CO). − MS (70 eV, FD); *m/z* (%): 298.4 (12) [M^+], 242.3 (13) [M^+ − C_4H_8], 224.3 (47) [M^+ − C_4H_8O], 200.3 (100) [M^+ − C_4H_8 − C_2H_2O], 182.2 (56), 57.1 (67) [$C_4H_9^+$], 43.1 [Ac^+]. − $C_{18}H_{22}N_2O_2$ (298.38): calcd. 298.1681; found 298.1681 (MS).

Dihydropyridine **32**: Cycloadduct **20** (39 mg, 0.1 mmol) was treated with MeLi and $(MeO)_2SO_4$ to give **32** (9 mg, 50%). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.04 (s, 3 H, NMe), 4.32 (d, *J* = 3.9 Hz, 1 H, 4-H), 4.78 (dd, *J* = 8.0, 3.9 Hz, 1 H, 5-H), 5.86 (d, *J* = 8.0 Hz, 1 H, 6-H), 6.47 (s, 1 H, 2-H), 7.25−7.40 (m, 5 H, Ph-H). − ^{13}C NMR (125 MHz, $CDCl_3$): δ = 39.27 (N−CH_3), 41.01 (C-4), 82.77 (C-3), 105.81 (C-5), 120.99 (CN), 127.15 (C-6), 127.73 (Ph-*o*-C), 127.93 (Ph-*p*-C), 128.74 (Ph-*m*-C), 141.93 (C-2), 145.41 (Ph-*ipso*-C). − MS (70 eV, FD); *m/z* (%): 196.1 (19) [M^+], 119.1 (100) [M − Ph^+]. − $C_{13}H_{12}N_2$ (196.25).

Tetrahydropyridine **33**: Cycloadduct **27** (38 mg, 0.1 mmol) was treated with MeLi and acetyl chloride to give **33** (28 mg, 98%) as a mixture of the *endo* and *exo* diastereomers in a ratio of 2:1. − IR (film): ν = 2934 cm^{-1} (C−H), 2204 (CN), 1704 (acetyl), 1618 (enamine), 1292 (aryl ether), 760. − UV (CH_3CN): λ_{max} (lg ε) = 194.5 (4.59), 264.0 (4.29). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.42 (s, 3 H, 4-CH_3^a, *exo*), 1.48 (s, 3 H, 4-CH_3^a, *endo*), 1.79 (s, 3 H, 4-CH_3^b, *endo*), 1.81 (s, 3 H, 4-CH_3^b, *exo*), 2.00−2.20 (m, 1 H, 4a-H, *endo* and *exo*), 2.27 (s, 3 H, Ac-CH_3, *endo*), 2.32 (s, 3 H, Ac-CH_3, *exo*), 3.60−3.75 (m, 1 H, 10b-H, *endo* and *exo*), 3.70 (d, *J* = 11.0, 11.0 Hz, 1 H, 5-$H^{ax\ endo}$), 3.81 (dd, *J* = 10.8, 10.5 Hz, 1 H, 5-H^{ax}, *exo*), 4.39 (dd, *J* = 10.8, 3.4 Hz, 1 H, 5-H^{eq}, *exo*), 4.40 (dd, *J* = 11.0, 3.4 Hz, 5-H^{eq}, *endo*), 6.84 (dd, *J* = 8.2, 1.2 Hz, 1 H, 7-H, *endo*), 6.90 (dd, *J* = 8.2, 1.3 Hz, 1 H, 7-H, *exo*), 6.98 (dd, *J* = 7.5, 7.5 Hz, 1 H, 9-H, *endo*), 7.03 (dd, *J* = 7.5, 7.5 Hz, 1 H, 9-H, *exo*), 7.05−7.30 (m, 2 H, 2-H and 8-H, *exo* and *endo*), 7.35 (d, *J* = 7.5 Hz, 1 H, 10-H, *endo*), 7.79 (d, *J* = 7.5 Hz, 1 H, 10-H, *exo*). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16.91 (Ac-CH_3, *exo*), 20.98 (Ac-CH_3, *endo*), 21.91 (4-CH_3^a, *exo*), 21.98 (4-CH_3^b, *exo*), 22.27 (4-CH_3^a, *endo*), 23.51 (4-CH_3^b, *endo*), 28.28 (C-10b, *exo*), 28.44 (C-10b, *endo*), 39.32 (C-4a, *endo*), 44.64 (C-4a, *exo*), 54.07 (C-4, *endo*), 57.23 (C-4, *exo*), 59.57 (C-5, *endo*), 63.02 (C-5, *exo*), 89.25 (C-1, *endo*), 90.29 (C-1, *exo*), 113.63 (C-7, *endo*), 114.23 (C-7, *exo*), 115.74 (CN, *exo*), 116.10 (CN and C-10a, *endo*), 116.66 (C-10a *exo*), 117.68 (C-9, *endo*), 118.19 (C-9, *exo*), 125.59 (C-8, *exo*), 126.07 (C-10, *exo*), 126.17 (C-8, *endo*), 128.27 (C-8, *exo*), 134.17 (C-2, *endo*), 139.19 (C-2, *exo*), 150.72 (C-6a, *endo*), 151.61 (C-6a, *exo*), 166.09 (Ac-CO, *endo*), 166.67 (Ac-CO, *exo*). − MS (70 eV, FD): *m/z* (%) = 282.2 (100) [M^+], 240.1 (68) [M^+ − C_2H_2O], 225.1 (55), 43.1 (37) [Ac^+]. − $C_{17}H_{18}N_2O_2$ (282.43): calcd. 283.1368; found 283.1368 (MS).

Tetrahydropyridine **34**: Cycloadduct **27** (19 mg, 0.05 mmol) was treated with MeLi and methyl iodide to give **34** (8 mg, 60%) as a mixture of the *endo* and *exo* diastereomers in a ratio of 2:1. The by-product methyl tolyl sulfoxide could not be completely removed in this case. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 (s, 3 H, 4-CH_3^a, *exo*), 1.20 (s, 3 H, 4-CH_3^b, *exo*), 1.28 (s, 3 H, 4-CH_3^a, *endo*), 1.40 (s, 3 H, 4-CH_3^b, *endo*), 2.00−2.20 (m, 1 H, 4a-H, *endo* and *exo*), 2.89 (s, 3 H, N−CH_3, *endo*), 2.95 (s, 3 H, N−CH_3, *exo*), 3.60−3.75 (m, 1 H, 10b-H, *endo* and *exo*), 3.76 (d, *J* = 11.3, 11.2 Hz, 1 H, 5-H^{ax}, *endo*), 3.84 (dd, *J* = 10.6, 10.6 Hz, 1 H, 5-H^{ax}, *exo*), 4.27 (ddd, *J* = 10.8, 3.4, 1.9 Hz, 1 H, 5-H^{eq}, *endo*), 4.37 (dd, *J* = 10.2, 3.4 Hz, 5-H^{eq}, *exo*), 6.57 (s, 1 H, 2-H, *endo* and *exo*), 6.81 (dd, *J* = 8.0, 1.9 Hz, 1 H, 7-H, *endo*), 6.84 (dd, *J* = 8.0, 1.9 Hz, 1 H, 7-H, *exo*), 6.94 (ddd, *J* = 8.5, 7.1, 1.9 Hz, 1 H, 9-H, *endo*), 6.98 (ddd, *J* = 8.5, 7.1, 1.9 Hz, 1 H, 9-H, *exo*), 7.16 (ddd, *J* = 8.0, 7.1, 1.9 Hz, 1 H, 8-H, *exo* and *endo*), 7.35 (dd, *J* = 7.5,

1.9 Hz, 1 H, 10-H, *endo*), 7.47 (d, J = 7.5 Hz, 1 H, 10-H, *exo*). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.52 (4-CH_3[a], *exo*), 22.69 (4-CH_3[b], *exo*), 24.15 (4-CH_3[a], *endo*), 24.42 (4-CH_3[b], *endo*), 31.00 (C-10b, *exo*), 31.15 (C-10b, *endo*), 36.64 (N−CH_3, *exo*), 36.88 (N−CH_3, *endo*), 39.99 (C-4a, *endo*), 44.68 (C-4a, *exo*), 54.25 (C-4, *exo*), 63.06 (C-4, *endo*), 66.97 (C-5, *exo* and *endo*), 78.30 (C-1, *exo* and *endo*), 116.26 (C-7, *endo*), 116.69 (C-7, *exo*), 120.39 (C-9, *endo*), 120.89 (C-9, *exo*), 121.04 (CN, *exo* and *endo*), 122.17 (C-10a, *endo*), 123.55 (C-10a, *exo*), 127.95 (C-8, *exo*), 128.46 (C-8, *endo*), 129.05 (C-8, *exo*), 131.46 (C-10, *exo*), 146.36 (C-2, *endo*), 150.69 (C-2, *exo*), 153.53 (C-6a, *endo*), 153.78 (C-6a, *exo*).

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