New Strategy for the Synthesis of Iminoglycitols from Amino Acids†

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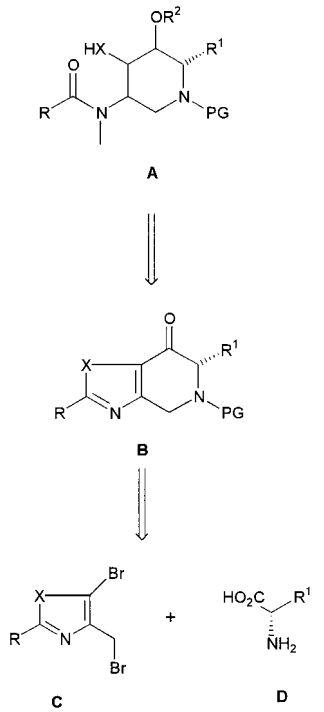
Received July 2, 2001

A novel strategy for the enantioselective synthesis of polyhydroxypiperidines, which can be considered as iminoglycitols or 2,6-dideoxyazasugars, was developed. α-Benzolsulfonylamino esters served as a C_2N building block while 2-bromo-3-(bromomethyl)oxazoles and -thiazoles contributed a C3-unit to the final piperidine ring. At first a dihydropyridine ring was established via alkylation and bromine−lithium exchange. The keto group of the resulting 5,6-dihydro[1,3]oxazolo- and 5,6-dihydro[1,3]thiazolo[4,5-*c*]pyridin-7(4*H*)-ones was reduced and, after alkylation reactions, the azole ring was cleaved, thus providing heteroatom substituents for the target piperdines. Protected 5-amino-3,4-dihydroxy and 5-amino-3-hydroxy-4-thiohydroxypiperdines were obtained in the *talose* series while Mitsunobu reaction of the intermiediates provided access to the *altrose* series.

Polyhydroxylated chiral piperidines widely occur as azasugars and alkaloids. Deoxynojirimycin, swainsonine, and castanospermine derivatives are prominent examples in this area.[1] Since a number of these products exhibit interesting pharmaceutical properties such as glycidase inhibition, [2,3] many syntheses have been developed in order to get access to new analogues of this type of structure. A number of these approaches start with chiral pool precursors, which incorporate the requisite chirality centers;[4] others establish new stereogenic centers by asymmetric synthesis, e.g., starting with amino acids.[5,6] We recently published a first example where a member of the hitherto unknown (L)-2,5-diamino-1,6-dideoxytalose series could be synthesized from (L)-alanine following a novel strategy,[7] exploiting a synthesis of annulated dihydropyridin-3-ones developed in our laboratories.[8] According to the retrosynthetic scheme (Scheme 1), the

Scheme 1



piperidine ring was established from 5-bromo-4-(bromomethyl)-2-phenyl-1,3-oxazole **1** (see **C**) as the C_3 building block and an amino acid, contributing two carbons and one ring nitrogen atom via N-alkylation and a Barbier-type cyclization. The oxazole ring of the resulting **B** served as a precursor for the substituents at positions 4 and 5 of the piperidine ring. In this synthetic sequence three new stereogenic centers were established in a highly stereoselective manner. Here, we give full report on this synthesis including new examples as well as the extension of this approach to the altrose series and to 5-amino-4-thiohydroxypiperidine derivatives **A** (X = S), revealing this method as a versatile way to iminoglycitols.

N-Benzosulfonated amino esters **2** ($R^1 = SO_2Ph$) turned out to be appropriate for the establishment of the 5,6-

† Dedicated to Professor Dr. Horst Hartmann on the occasion of his 65th birthday.

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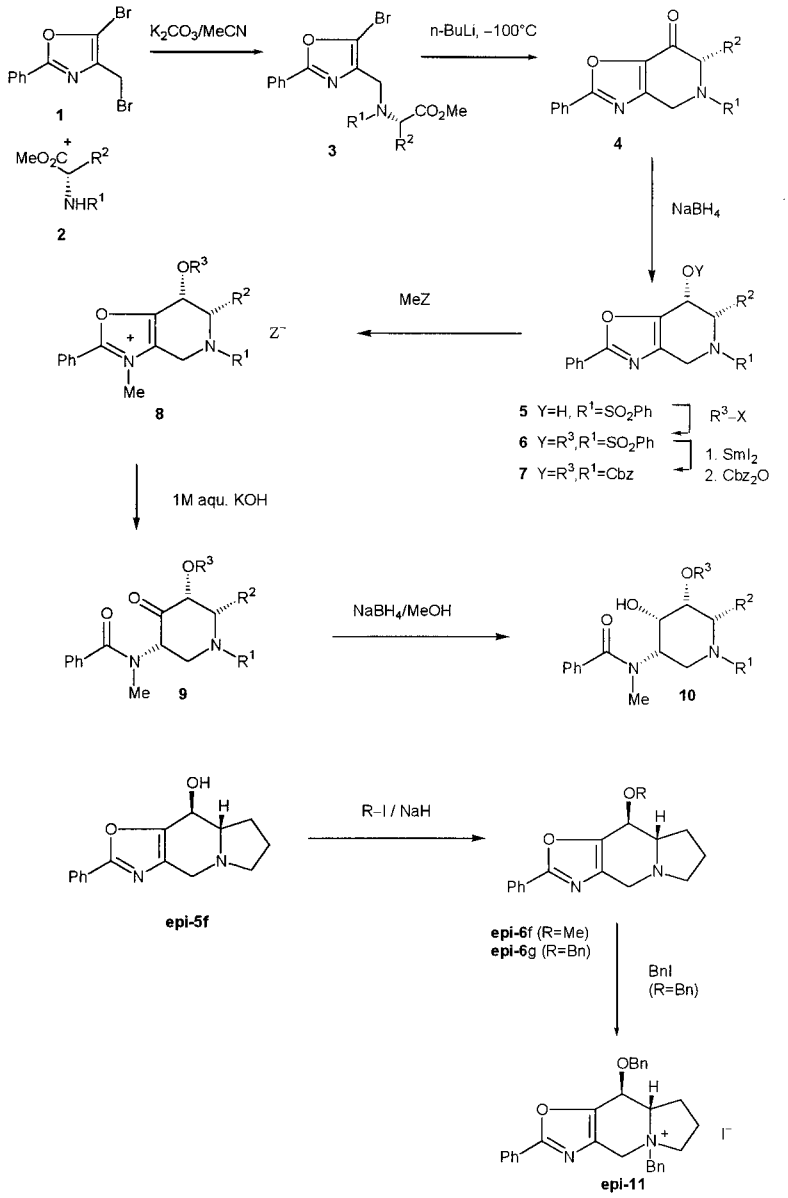
10.1021/jo010665z CCC: $22.00
Published on Web 04/17/2002

Scheme 2



	R¹	R²	product (% yield) 3	4	5/epi5
a	$PhSO_2$	Me	90	63	93
c		CH_2O TBDMS	53[a]	60	72
d		CH_2OH	63		
e	Cbz	Me	76[b]	33	
f		$(CH_2)_3$	82	76	96[c]

[a] by alkylation of **3d** [b] obtained by treatment of unprotected **3** (R^1 = H) with dibenzyl dicarbonate
[c] 20% **5e** + 76% **epi-5e**

	R¹	R²	R³	product (% yield) 6/epi-6	7	8	9	10
a	$PhSO_2$	Me	Me	97		86[a]	63	75
b			Bn	87		76[a]	52	70
c		CH_2O TBDMS	Bn	95				
d		CH_2OH				87[b]	46	51
e	Cbz	Me	Me		66[c]		74	54
f		$(CH_2)_3$	Me	76[d]				
g			Bn	92[d]				

[a] Z=OTf [b] Z=$MeSO_4$
[c] starting from **6a** by deprotection/protection [d] **epi-6**

dihydro[1,3]oxazolo[4,5-*c*]pyridin-7(4*H*)-ones **4**, while other protective groups such as Cbz or allyl or unprotected amino esters gave low yields or failed to give the desired products. While N-alkylation to **3** was routine, the subsequent cyclization via bromine−lithium exchange needed careful control of the reaction temperature (−100 °C). Otherwise, side reactions or racemization occurred. Reduction of the 5,6-dihydro[1,3]oxazolo[4,5-*c*]pyridin-7(4*H*)-ones **4** with sodium borohydride was completely stereoselective. Since several methods were reported in the literature for the reductive cleavage of oxazole rings,[9,10] the resulting *cis*-7-hydroxy-4,5,6,7-tetrahydro[1,3]oxazolo-

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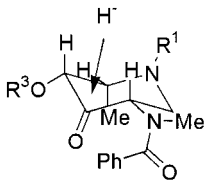


Figure 1. Stereochemical mode of reduction of **9**.

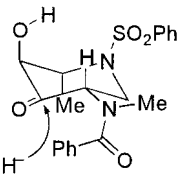
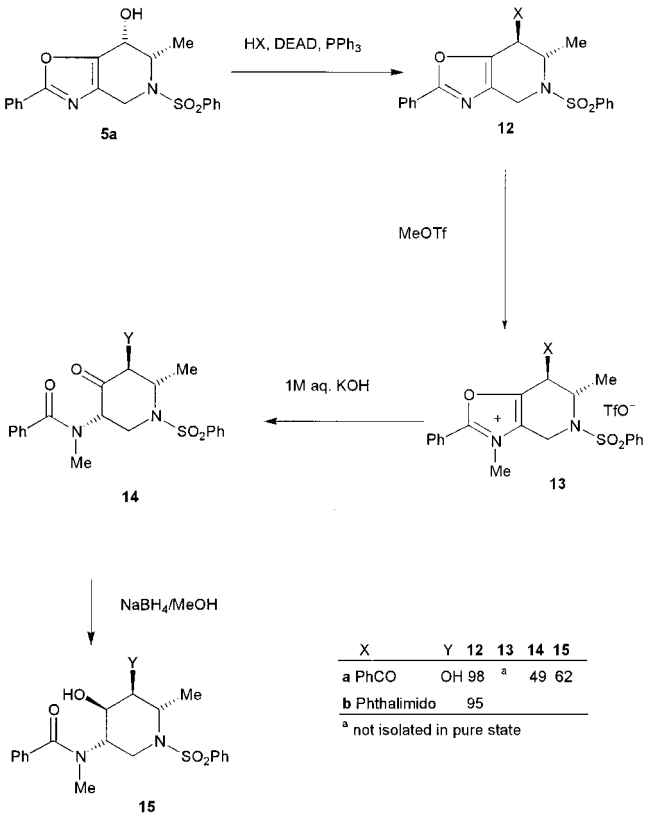


Figure 2. Stereochemical mode of reduction of **15**.

[4,5-*c*]pyridines **5** were submitted to more forcing reduction conditions in order to get access to ring-opened piperidines similar to **10** (R^3 = H). However, the oxazolopyridine ring turned out to be resisitant to all these approaches including treatment with sodium in boiling ethanol, with lithium alanate in THF, or ether and sodium borohydride in acetic acid. Thus, activation of the oxazole ring by N-alkylation was envisaged. As far as the yields are concerned, a two-step procedure turned out to be advantageous, alkylating first the hydroxy group in the presence of sodium hydride (formation of **6**) followed by quaternization of the ring nitrogen atom under forcing conditions (neat methyl triflate or dimethyl sulfate) to afford the oxazolium salts **8**. As in nonalkylated 4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridines **5**, all attempts to cleave the oxazole ring of the 4,5,6,7-tetrahydro[1,3]-oxazolo[4,5-*c*]pyridin-3-ium salts **8** by reduction failed too. Hydrolytic cleavage was thus attempted. Treatment with 1 M aqueous potassium hydroxide afforded 5-(benzoylamino)-3-alkoxypiperidin-4-ones **9**, which could further be reduced to the desired *talo*-5-amino-3,4-dihydroxypiperidine derivatives **10** by sodium borohydride. The whole sequence comprised eight synthetic steps with an overall maximum yield of 21%. All reactions occurred with high levels of diastereoselectivity. No diastereomers of **5**−**10** could be deduced by NMR (de > 90%). HPLC analysis of final product **10a** revealed an ee > 99%. The configuration of the products could be proved by the X-ray analysis of **10a** (see ref 7 and Supporting Information) which revealed an all-cis relationship consistent with the ^{1}H NMR spectra in the series of **10**. As far as the stereochemical course of the synthesis is concerned, the reduction of the 5,6-dihydro[1,3]oxazolo[4,5-*c*]pyridin-7(4*H*)-ones **4** occurred anti with respect to the substituent R^2, thus affording cis products **5**. The stereoselective ring opening of **8** to the piperidinones **9** is likely to be caused by the formation of the thermodynamically more stable stereoisomer after protonation of an intermediate enolate. The final reduction of the piperidones **9** might be governed by 1,3-shielding by the substituent R^2 during the attack of sodium borohydride at the most stable chair conformation (see Figure 1). Remarkably, the reduction of the tricyclic proline derivate **4f** showed the opposite facial selectivity, i.e., the *trans*-product *epi*-**5f** was formed as major product (Scheme 2) as proved by NOE experiments of *epi*-**5f** and X-ray crystal analysis of the minor isomer **5f** (see Supporting Information). Similar selectivities were observed in the reduction of benzoanelated benzoindolizidinones.[11] The epimers **5f** and *epi*-**5f** could be separated. O-Alkylation to *epi*-**6** was achieved in the presence of sodium hydride but subsequent N-alkylation affected the piperidine nitrogen atom rather than the

Scheme 3



X	Y	12	13	14	15
a PhCO	OH	98	[a]	49	62
b Phthalimido		95			

[a] not isolated in pure state

oxazole N-atom, thus leading to a 56:44 mixture of epimeric indolizidinium salts *epi*-**11**. All attempts to achieve a further N-alkylation of the oxazole N-atom failed. Thus, the envisaged opening of the oxazole ring of *epi*-**11** in order to get access to aminohydroxyindolizidines analogous to swainsonine or castanospermine could not be followed up.

An exchange of the benzosulfonyl protective group with other protective groups, which are easier to remove, was feasible at the stage of the 7-alkoxy-4,5,6,7-tetrahydro-[1,3]oxazolo[4,5-*c*]pyridine **6** (Scheme 2). Thus **6a** was treated with samarium(II) iodide in THF/1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone (DMPU).[12] Since the resulting N-unprotected compound **6** (H instead of SO_2Ph) could not be separated from the DMPU, it was further converted to the Cbz derivative **7a**. Further transformations into the end product **10e** occurred in a similar fashion as with the benzosulfonyl-protected compounds, affording the *talo* compound **10e**.

To extend the scope of the synthesis of azasugars according to the retrosynthetic Scheme 1, further attempts were made to obtain analogues with other configurations or other substituents. Mitsunobu reaction[13,14]

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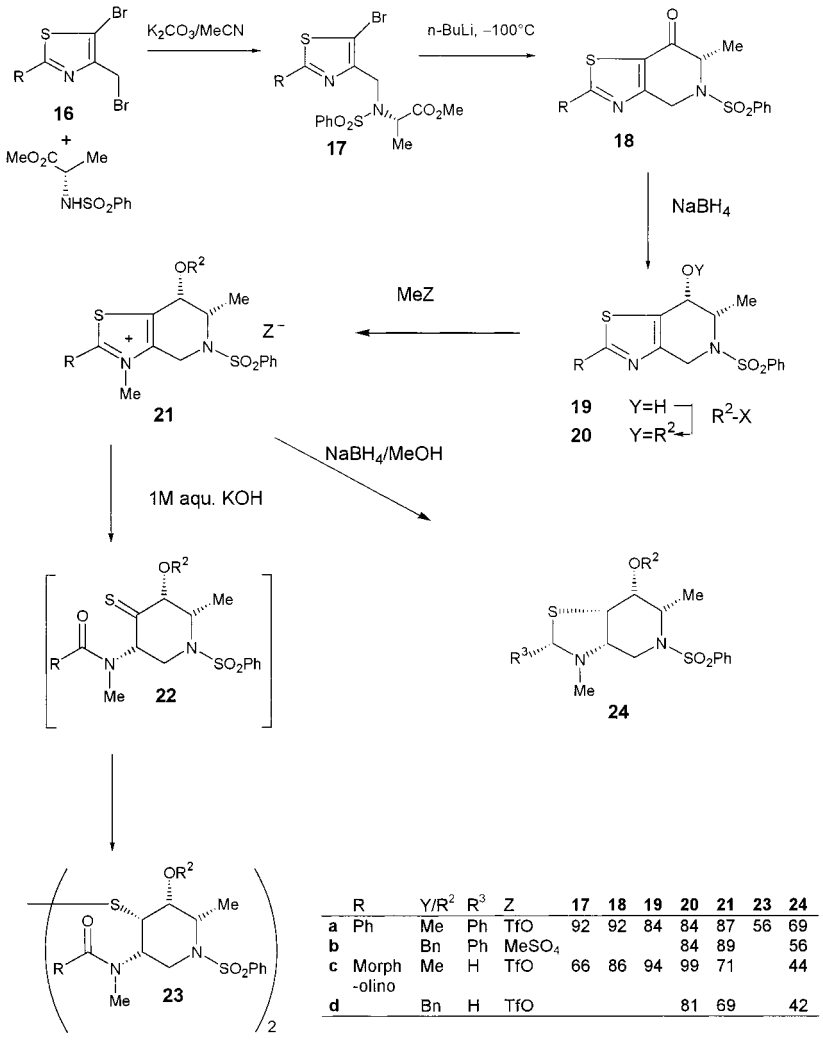
Scheme 4



	R	Y/R^2	R^3	Z	17	18	19	20	21	23	24
a	Ph	Me	Ph	TfO	92	92	84	84	87	56	69
b		Bn	Ph	$MeSO_4$				84	89		56
c	Morph-olino	Me	H	TfO	66	86	94	99	71		44
d		Bn	H	TfO				81	69		42

of the 7-hydroxy-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine **5a** turned out to be a useful tool to invert the configuration at position 7. Benzoate or phthalimide was introduced in this manner (Scheme 3). The substitution products **12** were submitted to the same protocol as the 7-alkoxyproducts **6**, i.e., *N*-methylation and hydrolytic opening of the oxazole ring. As could be clearly deduced by the vicinal coupling constants in the ^{1}H NMR spectra, the resulting aminohydroxypiperidines **15** differed in the configurations at positions 3 and 4 (*trans*−*cis*−*trans* relation) and thus belong to the *altro* series. Obviously, protonation after basic hydrolysis of **13** occurred in the same stereochemical manner as with **8** while the final reduction of the keto group of **14** gave the opposite stereochemical outcome. A likely transition state of the latter reaction is shown in Figure 2. Presumably, the axial 3-hydroxy group, after deprotonation, directs the attack of the hydride toward the opposite side.

As a further extension of the azasugar strategy according to Scheme 1, 5-bromo-4-(bromomethyl)-1,3-thiazoles **16** were used as starting materials, and the corresponding 5,6-dihydro-1,3-thiazolo[4,5-*c*]pyridin-7(4*H*)-ones **18** could be obtained in excellent yields and were reduced to corresponding alcohols **19** (Scheme 4). In contrast to reductive cleavages of 1,3-thiazoles reported in the literature,[15] all efforts to reduce the hydroxythiazolopyridines **19** failed. Thus, O-alkylation and quaternization was employed to activate the thiazole ring. Unlike the corresponding oxazolium salts **8**, the 4,5,6,7-tetrahydro-1,3-thiazolo[4,5-*c*]pyridin-3-ium salts **21** could be reduced by sodium borohydride in methanol. The resulting perhydro-1,3-thiazolo[4,5-*c*]pyridines **24** represent novel, suitably protected *talo*-5-amino-3-hydroxy-4-thiohydroxypiperidines. It is worth mentioning that the morpholino group was lost during the reduction of **20c** or **20d**. Obviously the corresponding morpholino products **24** (R^3 = morpholino) originally formed suffered the elimination of morpholine, and further reduction afforded the 2-unsubstituted final products **24** (R^3 = H). The structure of the aminothiohydroxypiperidine derivatives **24** was deduced from the NMR spectra. The all-cis relationship of substituents in the piperidine ring is in agreement with the small coupling constants. The configuration at position 2, i.e., the orientation of substituent R^3 could be proved by NOE. In addition, an X-ray crystal analysis could be provided for the thiazolopyridinium salt

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21c. An alternative manipulation of the thiazole ring of 4,5,6,7-tetrahydro-1,3-thiazolo[4,5-*c*]pyridin-3-ium salts **21** by hydrolytic ring opening gave disulfides **23** rather than the expected piperidinethiones **22** due to oxidation of the alkaline solution by air. This reaction was not further followed up since the transformation of **21** into the **24** turned out to be a more feasible way to orthogonal-protected thioiminoglycitols derivatives.

In summary a novel straightforward strategy for amino- and aminothiohydroxy-1,6-dideoxyazasugars was developed based on 5-bromo-4-(bromomethyl)azoles and N-protected α-amino esters. The starting azole ring served as the source for three carbon ring atoms and two heteroatom substituents as well as for a suitable protective group, i.e., an economic conservation of atoms was achieved. Three new stereogenic centers were established in a highly stereoselective way. By inclusion of an additional Mitsunobu step in the synthetic sequence, additional heteroatom substituents could be introduced, and the configurations were manipulated. The method allows synthesis of new compounds, whose configuration can be governed by the configuration of the starting amino acid and the eventual involvement of Mitsunobu steps. Biological activities of the new products need to be investigated.

Experimental Section

All reactions were carried out under argon in oven-dried glassware. Solvents were dried and deoxygenated by standard procedures. Starting materials were purchased from Aldrich and Merck. Compounds **1**,[16] **16a**, and **16c**[17] were synthesized according to literature procedures. TLC analysis was performed on Merck silica gel $60F_{254}$ plates and visualized with UV illumination and charring with phosphomolybdic acid in EtOH (5%, v/v) or 0.3% ninhydrin in EtOH. Column chromatography was conducted with Merck silica gel 60 (400−639 mesh). Melting points were determined on a Boetius hot-stage apparatus and are reported uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 and 75.5 MHz, respectively, on a Bruker AC-300 in $CDCl_3$ with TMS as internal standard. Mass spectra were measured at 70 eV. Optical rotations were determined with a Perkin-Elmer polarimeter 241 (d = 2 mm). Enantiomeric purity was proved by analytical HPLC on cellulose carbamate (Chiral PAK AD).

General Procedure for the Preparation of Compounds 3 and 17. A mixture of **1** (10 mmol), or **16** (10 mmmol), K_2CO_3 (2.07 g, 15.0 mmol), and **2** (20 mmol) in MeCN (30 mL) was stirred under reflux for 2 h. The resulting suspensions were cooled and filtered, and the filtrates were concentrated. The crude materials were chromatographed on silica gel, affording the pure products.

Methyl (2*S*)-2-[[(5-Bromo-2-phenyl-1,3-oxazol-4-yl)methyl](phenylsulfonyl)amino]propanoate (3a). The product **3a** (4.3 g, 90% yield) had the following data: R_f = 0.50 (CH_2Cl_2:acetone = 97:3); light yellow oil; $[\alpha]^{20}_D$ = −19.7 (*c* 1.3 $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.60 (d, *J* = 7.29 Hz, 3H), 3.56 (s, 3H), 4.37, 4.56 (d, *J* = 16.31 Hz, 2H), 4.77 (q, *J* = 7.29 Hz, 1H), 7.43 (m, 2H), 7.45 (m, 2H), 7.46 (m, 2H), 7.86 (m, 2H), 7.87 (m, 1H), 7.90 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 17.0, 40.5, 52.6, 55.7, 120.4, 126.5, 126.8, 127.8, 129.1, 129.2, 131.2, 132.9, 136.2, 140.5, 162.6, 172.3. Anal. Calcd for $C_{20}H_{19}BrN_2O_5S$: C 50.20, H 4.01, N 5.86, S 6.69, Br 16.50. Found: C 49.96, H 3.89, N 6.01, S 6.84, Br 16.76.

Methyl (2*S*)-2-[[(5-Bromo-2-phenyl-1,3-oxazol-4-yl)methyl](phenylsulfonyl)amino]-3-{[*tert*-butyl(dimethyl)silyl]oxy}propanoate (3c). The product **3c** (84.4% yield, see also Supporting Information) had the following data; R_f = 0.5 (pentane:EtOAc:CH_2Cl_2 = 10.5:1.5:3.5); light yellow oil; $[\alpha]^{20}_D$ = +1.0 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): −0.37, 0.00 (s, 6H), 0.7 (s, 9H), 3.55 (s, 3H), 4.2, 4.41 (d, *J* = 5.21 Hz, 2H), 4.5, 4.7 (d, *J* = 17.0 Hz, 2H), 4.8 (m, 1H), 7.37 (m, 2H), 7.38 (m, 1H), 7.40 (m, 2H), 7.80 (m, 2H), 7.82 (m, 1H), 7.84 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): −5.8, −5.7, 18.0, 25.6, 41.2, 52.0, 61.3, 63.1, 119.3, 126.0, 126.6, 127.4, 128.6, 128.7,130.6, 132.5, 136.4, 140.0, 161.9, 169.8.

Methyl (2*S*)-2-[[(5-Bromo-2-phenyl-1,3-oxazol-4-yl)methyl](phenylsulfonyl)amino]-3-hydroxypropanoate (3d). The product **3d** (3.1 g, 63% yield) had the following data: R_f = 0.32 (CH_2Cl_2:acetone = 97:3); pale yellow wax; $[\alpha]^{20}_D$ = −2.36 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 3.48 (s, 3H), 3.83 (m, 1H), 3.95, 4.6 (d, *J* = 17.10, 2H), 4.8, 5.8 (d, *J* = 5.14 Hz, 2H), 7.08 (m, 2H), 7.12 (m, 1H), 7.22 (m, 2H), 7.27 (m, 2H), 7.5 (m, 1H), 7.56 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 39.5, 52.4, 60.4, 63.5, 119.7, 126.0, 127.1, 129.0, 131.5, 132.5, 135.9, 139.7, 162.7, 169; HRMS calcd for $C_{20}H_{19}BrN_2O_6S$: 494.0148. Found: 494.0148.

Methyl (2*S*)-1-[(5-Bromo-2-phenyl-1,3-oxazol-4-yl)methyl]-2-pyrrolidinecarboxylate (3f). The product **3f** (2.99 g, 82% yield) had the following data: R_f = 0.23 ($CHCl_3$:MeOH = 95:5); pale yellow oil; $[\alpha]^{20}_D$ = −51.4 (*c* = 1.35, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.86 (m, 2H), 2.0 (m, 2), 2.57 (m, 2H), 3.35 (m, 1H), 3.60 (s, 3H), 3.71 (d, *J* = 5.4 Hz, 2H), 7.33 (m, 3H), 7.91 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 23.0, 29.4, 47.4, 51.7, 53.1, 64.0, 120.1, 126.1, 126.6, 128.6, 130.5, 136.7, 162.2, 174.1; HRMS Calcd for $C_{16}H_{17}BrN_2O_3$: 364.0423. Found: 364.0425.

Methyl (2*S*)-2-[[(5-Bromo-2-phenyl-1,3-thiazol-4-yl)methyl](phenylsulfonyl)amino] propanoate (17a). The product **17a** (4.5 g, 92% yield) had the following data: R_f = 0.42 (hexane:EtOAc = 2:1); brown oil; $[\alpha]^{20}_D$ = −31.0 (*c* 1,-$CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.42 (d, *J* = 7.3 Hz, 3H), 3.36 (s, 3H), 4.4, 4.6 (d, *J* = 16.18 Hz, 2H), 4.65 (m, 1H), 7.18 (m, 2H), 7.20 (m, 2H), 7.23 (m, 1H), 7.48 (m, 1H), 7.5 (m, 2H), 7.7 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 16.9, 43.1, 52.7, 55.8, 107.0, 126.5, 126.6, 127.0, 129.0, 129.4, 130.9, 132.8, 133.2, 140.7, 151.1, 167.8, 172.3; HRMS Calcd for $C_{20}H_{19}BrN_2O_4S_2$: 493.9971. Found: 493.9973.

Methyl (2*S*)-2-[{[5-Bromo-2-(4-morpholino)-1,3-thiazol-4-yl]methyl}(phenylsulfonyl)amino]propanoate (17c). The product **17c** (3.3 g, 66% yield, starting from **16** with R = morpholino) had the following data: R_f = 0.36 (pentane:EtOAc:CH_2Cl_2 = 10:1.5:3.5); pale yellow oil; $[\alpha]^{20}_D$ = −13.6 (*c* 5.35, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1. 24 (d, *J* = 7.31 Hz, 3H), 2.94 (t, *J* = 5.31 Hz, 4H), 3.32 (s, 3H), 3.44(t, *J* = 4.88 Hz, 4H), 4.0, 4.27 (d, *J* = 15.93 Hz, 2H), 4.43 (q, *J* = 7.31 Hz, 1H), 7.2 (m, 2H), 7.24 (m, 1H), 7.54 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 16.4, 42.9, 47.8, 52.2, 55.5, 65.8, 93.5, 127.0, 129.0, 132.7, 140.7, 146.1, 169.3, 171.9; HRMS Calcd for $C_{18}H_{22}BrN_3O_5S_2$: 503.0186. Found: 503.0188.

General Procedure for the Preparation of Compounds 4 and 18. To a solution of **3** or **17** (1.80 mmol) in THF (30 mL) under argon atmosphere n-BuLi (1.25 mL, 2.00 mmol, 1.60 M solution in hexane) was added dropwise at −100 °C. The solution was quenched by saturated aqueous NH_4Cl solution after stirring for 4−5 h at −100 °C (−115 °C in the case of **4f**). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude materials were chromatographed on silica gel affording pure products.

(6*S*)-6-Methyl-2-phenyl-5-(phenylsulfonyl)-5,6-dihydro-[1,3]oxazolo[4,5-*c*]pyridin-7(4*H*)-one (4a). The product **4a** (490 mg, 74% yield) had the following data: R_f = 0.35 (pentane:EtOAc = 2:1); colorless crystals; mp 160−162 °C (EtOH), $[\alpha]^{20}_D$ = +31.0 (*c* 0.3, EtOH); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.51 (d, *J* = 7.3 Hz, 3H), 4.63, 5.18 (d, *J* = 18.72 Hz, 2H), 4.82 (q, *J* = 7.3 Hz, 1H), 7.42 (m, 1H), 7.46 (m, 1H), 7.55 (m, 2H), 7.62 (m, 1H) 8.1 (m, 2H), 7.8 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$), 16.6, 40.7, 59.6, 125.7, 127.2, 129.1, 130.7, 133.1, 133.6, 139.2, 141.3, 152.3, 166.4, 183.3; MS, *m*/*z* (%), 368.05 (M, 4.5), 227.06 (M − $PhSO_2$, 40.7), 157.1 (23), 129 (100), 104.1 (66), 51 (28).

(16) Gompper, R.; Rühle, H. *Liebigs Ann. Chem*. **1959**, *626*, 83.
(17) Asinger, F.; Thiel, M.; Gewald, K. *Liebigs Ann. Chem*. **1961**, *639*, 133.

Anal. Calcd for $C_{19}H_{16}N_2O_4S$: C 62.0, H 4.38, N 7.61, S, 8.68. Found: C 61.98, H 4.42, N 7.77, S 8.93.

(6*S*)-6-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2-phenyl-5-(phenylsulfonyl)-5,6-dihydro[1,3]oxazolo[4,5-*c*]pyridin-7(4*H*)-one (4c). The product **4c** (804 mg, 60% yield) had the following data: R_f = 0.26 (pentane:EtOAc:CH_2Cl_2 = 11:1:3); yellow oil; $[\alpha]^{20}_D$ = −10.1 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): −0.94, 0.00 (s, 6H), 0.70 (s, 9H), 4.19 (m, 2H), 4.75 (m, 1H), 4.9, 5.2 (d, *J* = 16.0, 2H), 7.47 (m, 2H), 7.51 (m, 2H), 7.55 (m, 1H), 7.59 (m, 2H) 8.1 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$), −6.1, −5.9, 17.7, 25.7, 44.1, 64.7, 66.7, 125.7, 126.7, 127.9, 129.1, 129.4, 132.7, 139.1, 142.6, 153.6, 165.7 180.9; MS, *m*/*z* (%): 441.1 (M − 57, 3.1), 299 (12), 148.95 (7), 105 (20), 89 (54), 77 (83), 57 (37), 41 (29). Anal. Calcd for $C_{25}H_{30}N_2O_5SSi$: C 59.97, H 6.44, N 5.66, S 6.38. Found: C 59.61, H 6.52, N 5.72, S 6.18.

Benzyl (6*S*)-6-Methyl-7-oxo-2-phenyl-6,7-dihydro[1,3]-oxazolo[4,5-*c*]pyridine-5(4*H*)-carboxylate (4e). The product **4e** (155 mg, 33% yield) had the following data: R_f = 0.53 (CH_2Cl_2:acetone = 95:5); pale yellow oil; $[\alpha]^{20}_D$ = −1.4 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.31(d, *J* = 7.21 Hz, 3H), 4.38 (m, 1H), 5.05−5.14 (d, *J* = 15.52, 2H), 5.01, 5.20 (d, *J* = 12.26, 2H), 7.21 (m, 2H), 7.24 (m, 2H), 7.33 (m, 1H), 7.35 (m, 2H), 7.41 (m, 1H), 8.0 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 16.0, 39.9, 58.2, 68.4, 129.0, 26.4, 126.5, 128.5, 128.8, 129.0, 129.5, 133.0, 136.3, 142.0, 155.0, 166.6, 184.0; MS, *m*/*z* (%), 363.2 (M + 1, 2), 227 (M − Cbz, 4.2), 129 (12), 91.1 (100), 76.9 (11), 65 (17), 56 (12), 42 (5); HRMS Calcd for $C_{21}H_{18}N_2O_4$: 262.1267. Found: 262.1269.

(8a*S*)-2-Phenyl-6,7,8,8a-tetrahydro[1,3]oxazolo[4,5-*f*]-indolizin-9(4*H*)-one (4f). The product **4f** (347 mg, 76% yield) had the following data: R_f = 0.41 ($CHCl_3$:MeOH = 9:1); light yellow crystals; mp 89−90 °C (EtOH), $[\alpha]^{20}_D$ = −10.0 (*c* 1.1, EtOH); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.83 (m, 2H), 2.58 (m, 1H), 3.04−3.2 (d, *J* = 18.59 Hz, 2H), 3.67−4.15 (d, *J* = 16.49, 2H), 7.41 (m, 2H), 7.47 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$), 21.8, 24.5, 48.8, 52.9, 125.9, 127.6, 128.9, 132.1, 155.5, 165.1, 185.1; MS, *m*/*z* (%), 254.1 (M, 70), 226.1 (20), 183 (10), 145 (10), 123.1 (100), 70.1 (100); HRMS Calcd for $C_{15}H_{14}N_2O_4$: 254.1056. Found, 254.1053.

(6*S*)-6-Methyl-2-phenyl-5-(phenylsulfonyl)-5,6-dihydro-[1,3]thiazolo[4,5-*c*]pyridin-7(4*H*)-one (18a). The product **18a** (580 mg, 84% yield) had the following data: R_f = 0.46 (CH_2Cl_2:acetone = 98:2); pale yellow crystals; mp 163−165 °C (EtOH), $[\alpha]^{20}_D$ = −31.4 (*c* 1,$CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.31 (d, *J* = 7.35 Hz, 3H), 4.72, 5.2 (d, *J* = 18.63, 2H), 5.18 (q, *J* = 5.49 Hz, 1H), 7.17 (m, 2H), 7.28 (m, 2H), 7.33 (m, 1H), 7.38 (m, 2H, 7.54 (m, 2H), 7.77 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 16.0, 42.7, 58.6, 127.2, 127.6, 129.6, 129.7, 132.5, 132.6, 133.5, 139.1, 176.4, 189.2. Anal. Calcd for $C_{19}H_{16}N_2O_3S_2$: C 59.21, H 4.19, N 7.29, S 16.64. Found C 58.69, H 4.45, N 7.31, S 16.60.

(6*S*)-6-Methyl-2-(4-morpholino)-5-phenylsulfonyl-5,6-dihydro[1,3]thiazolo[4,5-*c*] pyridin-7(4*H*)-one (18c). The product **18c** (610 mg, 86% yield) had the following data:, R_f = 0.52 (CH_2Cl_2:acetone = 97:3); light yellow crystals; mp 48 °C (with $[\alpha]^{20}_D$ = −33.67 (*c* 1.2, $CHCl_3$); ^{1}H NMR (δ/ppm, $CDCl_3$): 1.30 (d, *J* = 7.23 Hz, 3H), 3.49 (t, *J* = 4.80 Hz, 4H), 3.69 (t, *J* = 5.01 Hz, 4H), 4.32, 4.90 (d, *J* = 18.59 Hz, 2H), 4.50 (q, *J* = 7.20 Hz, 1H), 7.34 (m, 2H), 7.41 (m, 1H), 7.61 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 15.9, 42.1, 48.5, 57.8, 65.8, 116.6, 138.9, 162.2, 175.6, 187.0; MS, *m*/*z* (%): 393.08 (M, 11.62), 252 (100), 211 (69), 171.2 (13), 142.05 (14), 113.1 (27), 77 8 (39), 57 (19), 45 8 (19). Anal. Calcd for $C_{17}H_{19}N_3O_4S_2$: C 51.90, H 4.87, N 10.69, S 16.27. Found C 52.3, H 5.10, N 10.70, S 16.05.

General Procedure for the Preparation of 5 and 19. To a solution of **4** and **18** (1.36 mmol) in THF/EtOH (1:1, 20 mL) was added $NaBH_4$ (2.72 mmol), and the mixture was stirred for 2 h at room temperature. The resulting solution was concentrated, and the crude product was partitioned between CH_2Cl_2 (20 mL) and saturated aqueous $NaHCO_3$ (20 mL). The organic layer was dried (Na_2SO_4) and the solvent evaporated. The crude materials were chromatographed on silica gel affording pure products.

(6*S*,7*R*)-6-Methyl-2-phenyl-5-(phenylsulfonyl)oxazolo-[4,5-*c*]pyridin-7-ol (5a). The product **5a** (467 mg, 93% yield) had the following data: R_f = 0.42 (CH_2Cl_2:acetone = 94:6); white crystals; mp 155−156 °C (EtOH), $[\alpha]^{20}_D$ = −64.3 (*c* 1, acetone); ^{1}H NMR (δ/ppm, *J*/Hz, CD_3COCD_3): 0.77 (d, *J* = 6.87 Hz, 3H), 3.92, 4.46 (d, *J* = 14.11, 2H), 4.34 (q, *J* = 6.81, 1H), 4.78 (m, 1H), 4.93 (d, *J* = 5.91 Hz, 1H), 7.28 (2H$_r$), 7.30 (1H), 7.34 (2H), 7.40 (2H), 7.48 (1H), 7.76 (2H); ^{13}C NMR (δ/ppm, CD_3COCD_3): 11.5, 41.5, 55.1, 66.2, 128.2, 129.2, 129.4, 131.2, 131.6, 132.7, 135.1, 135.2, 143.2, 149.0, 167.1; MS, *m*/*z* (%), 370.1 (M, 0.97), 229.05(4.6), 187 (100), 158 (20), 141 (27), 104 (69), 76.95 (71), 55 (24), 43 (13.91); HRMS Calcd for $C_{19}H_{18}N_2O_4S$: 370.0984. Found: 370.0990.

(6*S*,7*R*)-6-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo-[4,5-*c*]pyridin-7-ol (5c). The product **5c** (489 mg, 72% yield) had the following data: R_f = 0.30 (CH_2Cl_2:acetone); white wax; mp 166−167 °C (EtOH), $[\alpha]^{20}_D$ = −14.55 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): −0.31, 0.00 (s, 6H), 0.77 (s, 9H), 3.93−4.1 (dd, 2H), 3.96 (br, 1H), 4.2, 4.7 (d, *J* = 14.0, 2H), 4.6 (m, 1H), 5.0 (m, 1H), 7.42 (m, 2H), 7.47 (m, 2H), 7.52 (m, 1H), 7.81 (m, 1H) 7.99 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): −5.78, 17.9, 25.6, 41.1, 55.5, 61.8, 64.2, 126.3, 126.9, 127.1, 128.8, 129.3, 130.6, 132.4, 133.2, 140.1, 145.6, 161.9; MS, *m*/*z* (%): $C_{25}H_{32}N_2O_5SSi$ (500), 443.25 (M − 57, 3.50), 301.0 (3), 256 (14), 197 (69), 187 (30), 173 (30), 158 (15), 116 (30), 103 (58), 76 (100), 56.9 (78).

(8a*S*,9*S*)-2-Phenyl-4,6,7,8,8a,9-hexahydro[1,3]oxazolo-[4,5-*f*]indolizin-9-ol (*epi*-5f). The product *epi*-**5f** (265 mg, 76% yield) had the following data: R_f = 0.33 ($CHCl_3$:MeOH = 9:1); white crystals; mp 190−191 °C (EtOH), $[\alpha]_D^{20}$ = +120.4 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.67 (m, 2H), 1.85 (m, 1H), 2.38 (br, 1H), 2.40 (m, 2H), 3.12 (q, *J* = 16.0 Hz, 1H), 3.20, 3.88 (d, *J* = 14.0 Hz, 2H), 4.58 (d, *J* = 7.25 Hz, 1H), 7.34 (m, 2H), 7.91 (m, 1H), 7.93 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 22.8, 28.6, 49.6, 54.0, 68.8, 69.3, 126.5, 127.6, 128.9, 130.5, 133.1, 147.5, 162.0; MS, *m*/*z* (%): 256.1 (M, 20), 187.1 (30), 104.0 (40), 70 (100), 55 (15); HRMS calcd for $C_{15}H_{14}N_2O_4$: 256.1213. Found: 256.1215.

(8a*S*,9*R*)-2-Phenyl-4,6,7,8,8a,9-hexahydro[1,3]oxazolo-[4,5-*f*]indolizin-9-ol (5f). The product **5f** (69.7 mg**,** 20% yield) had the following data: R_f = 0.46 ($CHCl_3$:MeOH = 9:1); white crystals; mp 181−182 °C, (EtOH), $[\alpha]^{20}_D$ = −17.3 (*c* 1.1, CH_3Cl); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.76 (m, 2H), 1.79 (m, 1H), 2.1 (m, 2H), 2.6 (br, 1H), 3.12, 3.85 (d, *J* = 14.5 Hz, 2H), 3.14 (q, *J* = 16.0 Hz, 1H), 4.50 (d, *J* = 1.89 Hz, 1H), 7.34 (m, 2H,), 7.90 (m, 1H), 7.92 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 22.6, 23.3, 49.8, 53.8, 62.1, 66.4, 126.3, 127.4, 128.7, 137.23, 130.3, 147.9, 162.1. Anal. Calcd for $C_{15}H_{16}N_2O_2$: C 70.29, H 6.52, N 10.92. Found: C 70.18, H 6.39, N 10.73.

(6*S*,7*R*)-6-Methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridin-7-ol (19a). The product **19a** (439 mg, 84% yield) had the following data: mp 92−93 °C (EtOAc:hexane = 1.5:1); pale yellow crystals; $[\alpha]^{20}_D$ = −7.1 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.85 (d, *J* = 6.76 Hz, 3H), 3.02 (br, 1H), 4.05,4.82 (d, *J* = 16.01 Hz, 2H), 4.65 (m, 1H), 5.03 (m, 1H), 7.33 (2H), 7.41 (2H$_r$), 7.43 (1H), 7.46 (2H), 7.50 (2H), 7.79 (1H); ^{13}C NMR (δ/ppm, CD_3COCD_3): 9.6, 42.3, 52.6, 67.2, 126.7, 127.4, 129.4, 129.7, 130.7, 131.8, 133.7, 147.3, 168.8; MS, *m*/*z* (%): 386.05 (M, 1.15), 217.10 (39.3), 203 (100), 184.05 (26), 141.0 (24), 121.00 (12), 104.1 (67), 100 (20.6), 77.1 (77), 45 (32); HRMS Calcd for $C_{19}H_{18}N_2O_3S_2$: 386.0760. Found: 386.0756.

(6*S*,7*R*)-6-Methyl-2-(4-morpholino)-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridin-7-ol (19c). The product **19c** (505 mg, 94% yield) had the following data: R_f = 0.46 (CH_2Cl_2:acetone = 95:5); colorless crystals; mp 165−166 °C, $[\alpha]_D^{20}$= −16.7 (*c* 1.05, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.83 (d, *J* = 6.80 Hz, 3H), 3.3 (t, *J* = 4.0, 4H), 3.6 (t, *J* = 5.0 Hz, 4H), 3.7, 4.5 (d, *J* = 14.42 Hz, 2H), 4.3 (m, 1H), 4.85 (m, 1H), 7.17 (m, 1H), 7.45 (m, 2H), 7.7 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 9.2 (CH_3), 41.7, 48.3, 52.2, 65.8, 66.3, 118.9, 127.1, 129.2, 132.8, 139.8, 142.7, 171.2; MS, *m*/*z* (%): 395.1 (M, 15), 254.1 (30), 212 (100), 155.0 (14), 77 (30), 51.0 (11); HRMS Calcd for $C_{17}H_{21}N_3O_4S_2$: 395.0975. Found: 395.0975.

General Procedure for the Preparation of Compounds 6a, ***epi*-6f or 20a**, **20c). Method A.** A solution of **5**(**a**,**f**) (1.7 mmol) or **19**(**a**,**c**) in a mixture of DMSO (10 mL) and DMF (10 mL) was added to barium oxide (2.25 g, 14.7 mmol) and barium hydroxide octahydrate (1.23 g, 3.90 mmol) at 0 °C. Subsequently dimethyl sulfate (3.31 mL, 350 mmol) was added dropwise at 0 °C under argon. After stirring for 18 h at ambient temperature under argon, concentrated aqueous ammonia solution (3.3 mL) was added dropwise over 0.25 h and subsequently 4 N hydrochloric acid (3.5 mL) at 0 °C over 0.25 h. The mixture was poured in water and extracted with ethyl acetate (3 × 50 mL). The organic layer was washed with water and brine and was dried. Evaporation of the solvent in vacuo gave crude products, which were purified by column chromatography to afford the final methyl ethers in pure form.

Method B. Compound **5**(**a**,**f**) or **19**(**a**,**c**) (10.2 mmol) was added to a cooled suspension of NaH (270 mg, 11.25 mmol of a 60% dispersion in oil) in THF (30 mL) at 0 °C under argon. The reaction mixture was stirred at room temperature for 30 min, and MeI (4.34 g, 1.90 mL 30.6 mmol) was then added in one portion. After 2 h the reaction was quenched by addition of saturated aqueous NH_4Cl (10 mL), and CH_2Cl_2 (100 mL) was added. The organic layer was washed with water and brine and dried with $MgSO_4$. The solvent was removed in vacuo to give crude materials that were chromatographed to obtain pure products.

(6*S*,7*R*)-7-Methoxy-6-methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine (6a) (Method B). The product **6a** (3.81 g, 97% yield) had the following data: R_f = 0.45 (CH_2Cl_2:acetone = 98:2); yellow oil; $[\alpha]^{20}_D = -12.1$ (*c* 1 EtOH); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.79 (d, *J* = 6.83 Hz, 3H), 3.44 (s, 3H), 3.87 (m, 1H), 4.58(m, 1H), 4.10, 4.63 (d, *J* = 13.33 Hz, 2H), 7.27 (m, 2H), 7.35 (m, 2H), 7.41 (m,1H), 7.72 (m, 2H), 7.82 (m, 2H), 7.86 (m,1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 10.3, 39.9, 50.8, 58.4, 73.5, 126.6, 127.3, 127.4: 133.2, 133.3, 140.1, 144.9, 162.3. Anal. Calcd for $C_{20}H_{20}N_2O_4S$: C 62.48, H 5.25, N 7.29, S 8.32. Found: C 62.33, H 5.18, N 7.22, S 8.45.

(8a*S*,9*S*)-9-Methoxy-2-phenyl-4,6,7,8,8a,9-hexahydro-[1,3]oxazolo[4,5-*f*]indolizine (*epi*-6f) (Method B). The product *epi*-**6f** (2.09 g, 76% yield) had the following data: R_f = 0.43 ($CHCl_3$:MeOH = 95:5); pale yellow wax; $[\alpha]^{20}_D = +20.0$ (*c* 1.2, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.89 (m, 2H), 1.98 (m, 1H), 2.48 (m, 2H), 3.26 (q, *J* = 6.68 Hz, 1H, CHN), 3.35, 4.3 (d, *J* = 14.02 Hz, 2H), 3.74 (s, 3H), 4.39 (d, 1H, *J* = 6.25 Hz), 7.48 (m, 2H), 8.07 (m, 1H), 8.11 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$), 22.6, 29.1, 49.3 (CH_2N), 53.5, 66.3, 76.7, 126.2, 127.5, 128.6, 130.1, 137.5, 146.9, 161.5; HRMS Calcd for $C_{16}H_{18}N_2O_2$: 270.1369. Found. 270.1372.

(6*S*,7*R*)-7-Methoxy-6-methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridine (20a) (Method A). The product **20a** (571 mg, 84% yield) had the following data: R_f = 0.38 (CH_2Cl_2:acetone = 95:5); yellow oil; $[\alpha]^{20}_D = -5.5$ (*c* 1 $CHCl_3$); ^{1}H NMR (δ/ppm, J/Hz, $CDCl_3$): 0.71 (d, *J* = 6.79 Hz, 3H), 3.4 (s, 3H), 4.0−4.8 (dd, 2H), 4.48 (m, 1H), 4.67 (m, 1H), 4.63(m, 2H, 7.27 (m, 2H), 7.35 (m, 2H), 7.29 (m, 2H), 7.42 (m, 2H), 7.44 (m,1H), 7.74 (m,1H), 7.77 (m, 2H), 7.94 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 9.3, 42.4, 49.6, 57.7, 76, 126.6, 126.7, 127.4, 129.3, 129.7, 130.3: 130.6, 133.4, 140.1, 147.0, 168.7. Anal. Calcd for $C_{20}H_{20}N_2O_3S_2$: C 59.99, H 5.04, N 7.00, S 15.98. Found: C 59.72, H 5.09, N 7.12, S 15.82.

(6*S*,7*R*)-7-Methoxy-6-methyl-2-(4-morpholino)-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridine (20c) (Method B). The product **20c** (4.17 g, 100% yield) had the following data; R_f = 0.35 (CH_2Cl_2:acetone = 95:5); pale yellow oil; $[\alpha]^{20}_D = -13.7$ (*c* 1.3, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.73 (d, *J* = 6.76 Hz, 3H), 3.31 (t, *J* = 3.75 Hz, 4H), 3.34 (s, 3H), 3.64 (t, *J* = 4.92 Hz, 4H), 3.8, 4.5 (d, *J* = 15.88 Hz, 2H), 4.48 (m, 1H), 4.6 (m, 1H), 7.45 (m, 2H), 7.74 (m, 2H), 7.77 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 8.8, 41.8, 48.3, 49.3, 56.9, 75.2, 117.2, 127.1, 129.2, 132.8, 142.3, 171; HRMS Calcd for $C_{18}H_{23}N_3O_4S_2$: 409.1132. Found: 409.1136.

General Procedure for the Preparation of Compounds 6b, **6c**, **6g and 20b**, **20d.** Sodium hydride (9.29 mmol of a 60% dispersion in oil) was added portionally to a cooled solution (0 °C) of **5b**, **5c**, **5f**) or **19b**, **19c** (2.16 mmol) in DMF (15 mL) followed immediately with dropwise addition of benzyl bromide (0.59 mL, 4.97 mmol), respectively. The reaction mixture was stirred for 2 h when TLC (CH_2Cl_2:acetone = 97:3) showed a major fast moving product. The solution was poured into ice-cold water. The product was extracted with CH_2Cl_2 (3 × 40 mL), and the combined organic layers were washed with water and brine and were dried with Na_2SO_4 and concentrated. The resulting syrup was purified by passage through a column of silica gel affording pure product.

(6*S*,7*R*)-7-(Benzyloxy)-6-methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine (6b). The product **6b** (865 mg, 87% yield) had the following data: R_f = 0.48 (CH_2Cl_2:acetone = 99:1); yellow oil; $[\alpha]^{20}_D = +26.0$ (*c* 1.15 $CHCl_3$); ^{1}H NMR (δ/ppm, J/Hz, $CDCl_3$): 0.90 (d, *J* = 6.34 Hz, 3H), 3.9, 3.97 (d, *J* = 15.74 Hz, 2H,), 4.55 (m, 1H), 4.60 (m, 1H), 4.65, 4.74 (d, *J* = 6.16 Hz, 2H), 7.21 (m, 2H), 7.23 (m, 2H), 7.41 (m, 1H), 7.29 (m, 2H), 7.31 (m, 1), 7.35 (m, 1H), 7.67 (m, 2H), 7.84 (m, 2H), 7.86 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 10.6, 39.5, 50.9, 70.7, 72.5, 126.3, 126.9, 127.1, 127.8, 128.1, 128.6, 128.8, 129.3, 130.6, 132.9, 133.2, 137.3, 139.9, 144.6, 162.3. Anal. Calcd for $C_{26}H_{24}N_2O_4S$: C 67.80, H 5.26, N 6.09, S 6.95. Found: C 67.62, H 5.20, N 6.21, S 7.11.

(6*S*,7*R*)-7-(Benzyloxy)-6-({[*tert*-butyl(dimethyl)silyl]-oxy}methyl)-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine (6c). The product **6c** (1.21 g, 95% yield) had the following data: R_f = 0.46 (pentane: CH_2Cl_2:EtOAc = 10: 3 0.5:1.5); yellow oil; $[\alpha]^{20}_D = +2.0$ (*c* 1. $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): −0.41, 0.00 (s, 6H), 0.83 (s, 9H), 3.8, 4.2 (d, *J* = 8.42 Hz, 2H), 4.7, 4.85 (d, *J* = 11.86 Hz, 2H), 4.7 (m, 1), 4.8 (m,1H), 7.4 (m, 2H), 7.44 (m, 2H), 7.47 (m, 1H), 7.48 (m, 2H), 7.51 (m,1H), 7.84 (m, 2H), 7.87 (m, 1H), 8.01 (m, 2H), 8.02 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): −5.6, −5.5, 18.2, 25.8, 40.6, 56.5, 59.1, 69.7, 73.1, 126.3, 127.1, 127.9, 128.6, 129.0, 130.6, 132.6, 134.0: 137.3, 140.6, 144.7, 161.6; MS, *m*/*z* (%): $C_{32}H_{38}N_2O_5SSi$, 533.2 (M − 57, 1.4), 277.1 (6), 105 (11), 77 (22), 57 (10), 45 (14).

(8a*S*,9*S*)-9-(Benzyloxy)-2-phenyl-4,6,7,8,8a,9-hexahydro-[1,3]oxazolo[4,5-*f*]indolizine (*epi*-6g). The product **6g** (688 mg, 92% yield) had the following data: R_f = 0.49 ($CHCl_3$: MeOH = 95:5); pale yellow wax; sweet smell; mp 37 °C (with decomposition), $[\alpha]^{20}_D = -22.7$ (*c* 1.3, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.74 (m, 2H,), 1.96 (m, 1H), 2.42, 2.74 (q, *J* = 8.86 Hz, 2H), 3.24 (q, *J* = 6.53 Hz, 1H), 3.42, 3.9 (d, *J* = 15.58 Hz, 2H,), 3.99 (d, *J* = 13.98 Hz, 1H), 4.89, 5.10 (d, *J* = 11.70 Hz, 2H), 7.36 (m, 2H), 7.42 (m, 2H), 7.47 (m, 1H), 7.52 (m, 1H), 8.13 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 22.7, 29.4, 49.5, 53.6, 66.5, 72.1, 126.2, 127.6, 127.7, 127.7, 130.2, 137.6, 138.1, 147.1, 161.5; MS, *m*/*z* (%): 346.2 (M, 49%), 277.1 (16), 255.1 (100), 186 (40), 91.1 (100), 77 (20); HRMS Calcd for $C_{22}H_{22}N_2O_2$: 346.1682. Found: 346.1685.

(6*S*,7*R*)-7-(Benzyloxy)-6-methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridine (20b). The product **20b** (864 mg, 84% yield) had the following data: R_f = 0.39 (CH_2Cl_2:acetone = 97:3); yellow oil; ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.82 (d, *J* = 6.52 Hz, 3H), 4.0, 4.84 (d, *J* = 14.79 Hz, 2H), 4.55 (m, 2H), 4.62 (m, 1H), 4.67 (m, 1H), 7.29 (m, 2H), 7.37 (m, 2H), 7.39 (m, 2H), 7.43 (m, 1H), 7.46 (m, 1H), 7.74 (m, 1H), 7.75 (m, 2H), 7.77 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 9.5, 42.0, 49.6, 71.6, 73.1, 126.3, 126.4, 127.0, 127.8, 128.2, 128.7, 128.8, 129.3, 129.8, 130.2, 132.9, 132.9, 133.4, 137.2, 139.7, 146.8, 168.2; MS, *m*/*z* (%): 476 (M, 1), 386.05 (1), 293 (3), 91 (100), 77 (31), 65 (15), 43 (8). Anal. Calcd for $C_{26}H_{24}N_2O_3S_2$: C 65.53, H 5.08, N 5.88, S 13.43. Found: C 65.36, H 5.01, N 5.70, S 13.69.

(6*S*,7*R*)-7-(Benzyloxy)-6-methyl-2-(4-morpholino)-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridine (20d). The product **20d** (849 mg, 81% yield) had the following data: R_f = 0.58 (CH_2Cl_2:acetone = 98:2); pale yellow wax; $[\alpha]^{20}_D = -4.35$ (*c* 2.3, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.95 (d, *J* = 6.38 Hz, 3H), 3.43 (t, *J* = 2.48 Hz, 4H), 3.78 (t, *J* = 4.9 Hz, 4H), 3.93−4.59 (dd, 2H), 4.66 (m, 1H), 4.69 (s, 3H), 7.39 (1H), 7.40 (2H), 7.46 (m, 2H), 7.5 (m, 2H), 7.58 (m, 1H), 7.8 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 9.5 (CH_3), 41.8, 48.3, 49.6, 66.1, 71.2, 72.8, 117.4, 127.0, 128.0, 128.6, 129.2, 132.8, 137.4,

139.8, 142.4, 171.5; HMRS Calcd for $C_{24}H_{27}N_3O_4S_2$: 485.1445. Found: 485.1443.

Benzyl (6*S*,7*R*)-7-Methoxy-6-methyl-2-phenyl-6,7-dihydro[1,3]oxazolo[4,5-*c*]pyridine-5(4*H*)-carboxylate (7e). To the N_2-purged solution of 0.1 M SmI_2 in THF (10 mL) was added a solution of **6a** (665 mg, 1.73 mmol in 5 mL of THF) followed by DMPU (10 mL). The mixture was refluxed under N_2 for 5 h while the violet color completely faded. The solution was then cooled and quenched with saturated aqueous NH_4-Cl (100 mL). Subsequently it was extracted with CH_2Cl_2 (2 × 100 mL). The organic layer was washed with water (2 × 100 mL), 5% $Na_2S_2O_3$ (2 × 100 mL), and brine (2 × 100 mL) and dried with $MgSO_4$, and finally the solvent was evaporated. To a chilled solution of the crude product 430 mg, 1.70 mmol) and dibenzyl dicarbonate (650 mg, 2.20 mmol) in THF (10 mL) was added Et_3N (350 mg, 40.0 mmol) dropwise. The reaction mixture was stirred at ambient temperature for 24 h. The resulting solution was concentrated in a vacuum to an oily residue. The crude product was purified by column chromatography on SiO_2 (CH_2Cl_2:acetone = 95:5) to afford **7** (433 mg, (66.1% yield $R_f = 0.62$) as a pale yellow oil: $[\alpha]^{20}_D = -24.8$ (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.24 (d, $J = 6.63$ Hz, 3H), 3.69 (s, 3H), 4.2,4.96 (d, $J = 16.63$ Hz, 2H), 4.6, 5.2 (d, $J = 10.82$ Hz, 2H), 5.2 (m, 1H), 5.26 (m, 1H), 7.4 (m, 2H), 7.43 (m, 4H), 7.48 (m, 2H), 8.1 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 12.0 (CH_3), 38.7, 49.0, 58.0 (OCH_3), 67.7, 72.6, 126.3, 127.2 (CH_{ar}), 127.9, 128.4, 130.5, 132.2,), 137.1, 145.3, 155.3, 162.8. Anal. Calcd for $C_{22}H_{22}N_2O_4$: C 69.83, H 5.86, N 7.40. Found: C 69.77, H 5.76, N 7.29.

General Procedure for the Preparation of Compounds 12. To a solution of Ph_3P (1.02 g, 2.90 mmol) in THF (10 mL) was added DEAD (0.60 mL, 3.9 mmol) dropwise at 0 °C. After 5 min stirring, benzoic acid (480 mg, 3.90 mmol) or phthalimide (570 mg, 3.90 mmol) in THF (1 mL) and compound **5a** (362 mg, 1.0 mmol) in THF (2 mL) were successively added dropwise. The reaction mixture was stirred for 15 h at 0 °C for **12a** or overnight at room temperature for **12b**. If the reaction was not complete (monitoring by TLC), 1 equiv or more of each reagent was added. The reaction mixture was then concentrated under vacuum. The residue dissolved in EtOAc was filtered through a silica pad, concentrated under vacuum, and the crude materials were chromatographed on silica gel, affording pure products.

(6*S*,7*S*)-6-Methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridin-7-yl Benzoate (12a). The product **12a** (455 mg, 98% yield) had the following data: $R_f = 0.35$ (pentane:EtOAc:CH_2Cl_2 = 10:1.5:3.5); pale yellow wax: mp 113−115 °C, $[\alpha]^{20}_D = +77.5$ (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.12 (d, $J = 7.0$ Hz, 3H), 4.11, 4.73 (d, $J = 16.19$ Hz, 2H), 4.69 (q, $J = 7.15$ Hz, 1H), 5.8 (d, $J = 3.48$ Hz, 1H), 7.22 (2H), 7.25 (2H), 7.30 (1H), 7.34 (1H), 7.43 (2H), 7.47 (2H), 7.7 (1H) 7.8 (2H), 7.9 (2H);^{13}C NMR (δ/ppm, $CDCl_3$): 14.4, 39.1, 53.4, 67.2, 126.2, 126.3, 126.5, 128.4, 128.7 (2 × CH_{ar}), 128.8, 130.6, 132.0, 133.2, 136.1, 140.0, 140.8, 162.8, 165.6. Anal. Calcd for $C_{26}H_{22}N_2O_5S$: C 68.62, H 5.12, N 5.93, S 6.79. Found: C 68.59, H 5.09, N 5.88, S 6.68.

(6*S*,7*S*)-6-Methyl-2-phenyl-5-(phenylsulfonyl)-7-phthalimido-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine (12b). The product **12b** (465 mg, 95% yield) had the following data: $R_f = 0.22$ (CH_2Cl_2:acetone); pale yellow oil; $[\alpha]^{20}_D = +7.344$ (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 1.28(d, $J = 6.06$ Hz, 3H), 4.27, 4.98 (d, $J = 15.72$ Hz, 2H), 4.56 (d, $J = 6.47$ Hz, 1H), 5.09 (m, 1H), 7.25−8.0 (14H); ^{13}C NMR (δ/ppm, $CDCl_3$): 15.4, 39.7, 49.3, 123.4, 126.43, 126.7, 127.0, 128.8, 128.9, 130.7, 131.4, 132.4, 133.9, 135.9, 138.5, 139.8, 162.5, 167.1.

General Procedure for the Preparation of Compounds 8, 13, and 21. Method A: A neat mixture of **6**, **12**, or **20** (1 mmol) and dimethyl sulfate (252 mg, 0.190 mL, 2.00 mmol) or methyl tosylate (372 mg, 0.300 mL, 2.00 mmol) in the case of **6a** were heated at 100 °C for 3 h under argon atmosphere. The resulting viscous oil was washed several times with diethyl ether. NMR of the crude samples indicated the expected products with >95% purity. Solids could be recrystallized from ethanol and diethyl ether. **Method B**: A solution of **6** or **20** (1.2 mmol) in anhydrous CH_2Cl_2 (5 mL) was cooled to 0 °C, and methyl triflate (262 mg, 0.180 mL, 1.60 mmol) was added in one portion. The solution was left to stir until all starting material had been consumed. The reaction mixture was then concentrated and the residue washed severally with diethyl ether (3 × 15 mL). The crude products were further used without prior purification.

(6*S*,7*R*)-7-Methoxy-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine-3-ium Triflate 8a (Method B). The product **8a** (566 mg, 86% yield) had the following data: $R_f = 0.28$ ($CHCl_3$:MeOH = 9:1); pale yellow oil; ^{1}H NMR (δ/ppm, *J*/Hz, DMSO-d_6): 0.76 (d, $J = 6.43$ Hz, 3H), 3.54 (s, 3H), 4.00 (s, 3H), 4.16, 5.04 (d, $J = 14.25$ Hz, 2H), 4.74 (m, 1H), 4.79 (m, 1H), 7.67 (m, 2H), 7.74 (m, 2H), 7.83 (m,1H), 7.96 (m, 2H$_r$), 7.99 (m, 2H), 8.02 (m, 2H); ^{13}C NMR (δ/ppm, DMSO-d_6): 9.4, 35.5, 36.7, 50.3, 58.1, 71.9, 120.2, 127.3, 128.1), 130.2, 130.1, 130.2, 134.1, 135.3, 139.0 ($C_{q/ar}$), 146.6, 161.5.

(6*S*,7*R*)-7-(Benzyloxy)-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine-3-ium Triflate 8b (Method B). The product **8b** (570 mg, 76% yield) had the following data: $R_f = 0.28$ ($CHCl_3$:MeOH = 6:4); pale yellow oil; ^{1}H NMR (δ/ppm, *J*/Hz, DMSO-d_6): 0.74 (d, $J = 6.28$ Hz, 3H), 3.32 (m, 1H), 3.58 (m, 2H), 3.86 (s, 3H), 4.70 (m, 2H), 4.90 (m, 1H), 7.2−7.98 (15H).

(6*S*,7*R*)-7-(Benzyloxy)-6-(hydroxymethyl)-3-methyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo-[4,5-*c*]pyridine-3-ium Methyl Sulfate (8d) (Method A). The product **8d** (313 mg, 52% yield) had the following data: $R_f = 0.43$ ($CHCl_3$:MeOH = 8:2); pale yellow oil; ^{1}H NMR (δ/ppm, *J*/Hz, DMSO-d_6): 2.99 (br, 1H), 3.39 (d, $J = 6.95$ Hz, 2H), 3.44 (m, 2H), 3.69 (s, 3H), 3.74 (m, 1H), 3.99 (d, $J = 8.5$ Hz,), 4.35, 4.40 (dd, 2H), 7.29−7.99 (15H); ^{13}C NMR (δ/ppm, DMSO-d_6): 36.8, 56.1, 58.1, 61.3, 72.4, 119.9, 127.1, 128.1, 128.4 128.6, 129.3, 129.4, 12.9, 129.9, 133.3, 134.7, 137.1, 139.6, 146.3, 162.2.

(6*S*,7*R*)-7-(Benzoyloxy)-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]oxazolo[4,5-*c*]pyridine-3-ium Methyl Sulfate (13a) (Method A). The product **13a** (427 mg, 71% yield) had the following data: $R_f = 0.24$ ($CHCl_3$:MeOH = 6:4); brown crystals; mp 105−106 °C (EtOH/ether), ^{1}H NMR (δ/ppm, *J*/Hz, DMSO-d_6): 0.81 (d, $J = 6.95$ Hz, 3H), 3.19 (s, 3H), 3.80 (s, 3H), 4.11−5.0 (d, $J = 16.77$ Hz, 2H), 3.80 (s, 3H), 4.53 (m, 1H), 5.80 (m, 1H), 7.10 (m, 2H), 7.30 (m, 2H), 7.42 (m, 1H), 7.48 (m, 1H), 7.50 (m, 2H), 7.60 (m, 2H), 7.71(m, 1H), 7.73 (m, 2H), 7.78 (m, 2H), 7.79 (m, 2H); ^{13}C NMR (δ/ppm, DMSO-d_6): 13.1, 35.8, 37.0, 53.6, 66.4, 126.5, 127.0, 128.9, 129.5 (2xCH_{ar}), 129.7, 129.8, 120.2, 133.7, 134.1, 135.1, 139.4, 143.7, 162, 165.0.

(6*S*,7*R*)-7-Methoxy-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridine-3-ium Methyl Sulfate (21a) (Method A). The product **21a** (458 mg, 87% yield) had the following data: $R_f = 0.26$ ($CHCl_3$:MeOH = 9:1); white crystals; mp 158−161 °C (EtOH), ^{1}H NMR (δ/ppm, *J*/Hz, DMSO-d_6): 0.7 (d, $J = 6.61$ Hz, 3H), 3.55 (s, 3H), 3.72 (s, 3H), 3.9 (s, 3H), 4.23, 5.00 (d, $J = 16.52$ Hz, 2H,), 4.75 (m, 1H), 4.84 (m, 1H), 7.67 (m, 2H), 7.73 (m, 2H), 7.76 (m,1H), 7.97 (m,2H), 7.80 (m, 2H); ^{13}C NMR (δ/ppm, DMSO-d_6): 8.7, 38.8 39.2, 49.7, 57.6, 73.8, 125.2, 127.5, 130.1, 130.2, 130.4, 132.8, 133.8, 134.2, 139.1, 140.8, 169.9. Anal. Calcd for $C_{22}H_{26}N_2O_7S_3$: C 50.18, H 4.98, N 5.32, S 18.23. Found: C 50.31, H 5.07, N 5.37, S 18.32.

(6*S*,7*R*)-7-(Benzyloxy)-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]pyridine-3-ium Methyl Sulfate (21b) (Method A). The product **21b** (536 mg, 89% yield) had the following data: $R_f = 0.24$ ($CHCl_3$:MeOH = 6:4); pale yellow oil; ^{1}H NMR (δ/ppm, *J*/Hz, DMSO-d_6): 0.77 (d, $J = 6.34$ Hz, 3H), 3.97 (s, 3H), 4.3, 5.0 (d, $J = 15.67$ Hz, 2H), 4.75, 4.89 (d, $J = 6.43$ Hz, 2H), 4.82 (m, 1H), 7.36 (m, 2H), 7.40 (m, 2H), 7.54 (m, 1H), 7.67 (m, 2H), 7.68(m, 2H), 7.74 (m, 2H), 7.76 (m, 2H), 7.78 (m, 1H), 7.98 (m, 2H): ^{13}C NMR (δ/ppm, DMSO-d_6): 9.1, 38.7, 40.3, 49.2, 61.2, 71.5, 124.9, 127.1, 128.2, 128.6, 129.8, 129.9, 130.1, 132.7, 133.3, 133.7, 137.1, 140.6, 169.7;

(6*S*,7*R*)-7-Methoxy-3,6-dimethyl-2-(4-morpholino)-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]-

pyridine-3-ium Triflate (21c) (Method B). The product **21c** (130 mg, 71% yield) had the following data: white crystals; mp 34−36 °C (EtOH), $[\alpha]^{20}_D = -13.7$ (*c* 1.05, MeOH); ^{1}H NMR (*δ*/ppm, *J*/Hz, DMSO-d_6): 1.00 (d, *J* = 6.81 Hz, 3H), 3.70 (s, 3H), 3.80 (t, *J* = 4.91,4H), 3.97 (s, 3H), 4.10 (t, *J* = 4.81 Hz, 4H), 4.23, 5.00 (d, *J* = 13.93 Hz, 2H), 4.65 (m,1H), 4.97 (m, 1H), 7.85 (m, 2H), 7.9 (m, 2H), 8.2 (m,1H); ^{13}C NMR (*δ*/ppm, DMSO-d_6): 8.9, 37.8, 39.9, 50., 53.5 $(CH_2)_2$N), 57.9, 75.1, 122.7, 128.4, 130.9, 134.7, 135.9, 140.7, 175.2.

(6*S*,7*R*)-7-(Benzyloxy)-3,6-dimethyl-2-(4-morpholino)-5-(phenylsulfonyl)-4,5,6,7-tetrahydro[1,3]thiazolo[4,5-*c*]-pyridine-3-ium Triflate (21d) (Method B). The product **21d** (538 mg, 69% yield) had the following data: $R_f = 0.29$ ($CHCl_3$:MeOH = 6:4); pale yellow oil; ^{1}H NMR (*δ*/ppm, *J*/Hz, DMSO-d_6): 1.02 (d, *J* = 6.74 Hz, 3H,), 3.7 (t, *J* = 7.08 Hz, 4H), 3.9 (s, 3H), 4.0 (t, *J* = 4.9 Hz, 4H), 4.3, 5.11 (d, *J* = 16.47 Hz, 2H), 4.6 (m, 1H), 4.8 (m,1H), 4.99 (m, 1H), 7.54 (m, 2H), 7.76 (m, 1H), 7.79 (m, 1H), 7.81 (m, 2HH), 8.0 (m, 2H), 8.12 (m, 2H); ^{13}C NMR (*δ*/ppm, DMSO-d_6): 9.8 (CH_3), 35.6, 38.1, 48.5, 53.5, 66.5, 72.1, 73.0, 119.8, 128.3, 135.0,136.0, 138.0, 140.6, 174.7.

(8a*S*,9*R*)-5-Benzyl-9-(benzyloxy)-2-phenyl-4,6,7,8,8a,9-hexahydro[1,3]oxazolo[4,5-*f*] indolizine-5-ium Iodide (*epi*-11). A mixture of compound **6g** (550 mg, 1.61 mmol) and benzyl iodide (390 mg, 1.77 mmol) in ethanol was stirred at ambient temperature for 24 h. The resulting reaction mixture was then concentrated under reduced pressure. The crude product was recrystallized from absolute ethanol to afford *epi*-**11** (870 mg, 97% yield, R_f = 0.25 ($CHCl_3$:MeOH = 9:1) as needlelike crystals: cis:trans = 56:44, mp 103−105 °C, ^{1}H NMR (*δ*/ppm, *J*/Hz, DMSO-d_6): 2.44 (m, 2H), 2.53 (m, 2H,), 3.28(m, 2H), 3.3, 3.40 (d, *J* = 14.0 Hz, 2H), 4.25−4.37 (dd, 2H), 4.45 (m, 1H), 4.85−4.99 (dd, 2H), 5.23 (d, 1H, *J* = 6.09 Hz), 7.24−8.04 (15H); ^{13}C NMR (*δ*/ppm, DMSO-d_6): 19.8, 22.9, 49.1, 54.1, 59.3, 69.5, 72.5, 74.4, 126.3, 126.4, 127.3, 128.6, 128.2, 128.5, 128.6, 129.2, 129.4, 130.7, 131.6, 137.6, 141.5, 145.3, 163.2.

General Procedure for the Preparation of Compounds 9, 14, and 23: Method A. To an aqueous solution of **8** or **21** (1.0 mmol) was added a 1 M solution of potassium hydroxide until the mixture was slightly alkaline to test paper (pH 9−11). The solution was extracted with CH_2Cl_2 (3 × 20 mL) and the organic layer dried. The crude material was chromatographed on silica gel, affording pure product.

Method B. To a solution of **7** or the quaternary salts **8** or **13** (1.0 mmol) in CH_2Cl_2 was added a 1 M solution of potassium hydroxide until the pH of the organic phase was alkaline to test paper. The organic layer was separated and extracted with water and dried (Na_2SO_4). The solvent was evaporated and the residue chromatographed on silica column.

***N*-[(3*S*,5*R*,6*S*)-5-Methoxy-6-methyl-4-oxo-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (9a) (Method B).** The product **9a** (254 mg, 63% yield) had the following data: R_f = 0.35 (CH_2Cl_2:acetone = 95:5); colorless crystals; mp 225−227 °C, $[\alpha]^{20}_D = +54.1$ (*c* 1, MeOH); ^{1}H NMR (*δ*/ppm, *J*/Hz, $CDCl_3$): 0.94 (d, *J* = 6.82 Hz, 3H), 2.86 (s,3H), 3.39 (s, 3H), 3.62 (t, *J* = 11.85 Hz,1H), 3.85 (m, 1H), 4.24 (m, 1H), 4.57, 4.83 (d, *J* = 6.95 Hz, 2H), 7.24 (2H), 7.34 (2H), 7.36 (1H), 7.50 (2H), 7.58 (2H), 7.85 (1H); ^{13}CNMR (*δ*/ppm $CDCl_3$): 12.1, 37.2, 41.7, 53.7, 59.2, 61.5, 127.3, 127.6, 128.9, 130.0, 130.5, 133.7, 133.7, 135.7, 140.2, 175, 200.9; MS, *m*/*z* (%): 416.1 (M, 0.32), 275 (2), 222 (4), 175 (13), 112 (27), 105 (100), 77 (63), 56 (139), 42 (17). Anal. Calcd for $C_{20}H_{24}N_2O_5S$: C, 60.56, H, 5.81, N, 6.73, S, 7.68. Found: C, 60.50, H, 5.94, N, 6.91, S, 7.59.

***N*-[(3*S*,5*R*,6*S*)-5-(Benzyloxy)-6-methyl-4-oxo-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (9b) (Method B).** The product **9b** (256 mg, 52% yield) had the following data: R_f= 0.3 (CH_2Cl_2:acetone = 95:5); waxy substance; ^{1}H NMR (*δ*/ppm, *J*/Hz, $CDCl_3$): 1.03 (d, *J* = 6.83 Hz, 3H), 2.80 (s, 3H), 3.05 (m, 2H), 4.2 (m, 1H), 4.3 (t, *J* = 12.0 Hz, 1H), 4.4, 4.7 (d, *J* = 6.07 Hz, 2H), 4.53 (m, 1H), 7.43 (m, 2H), 7.17 (m, 2H), 7.25(m, 1H), 7.26 (m, 1H), 7.33 (m, 2H), 7.36 (m, 2H), 7.41 (m, 2H), 7.43 (m, 2H), 7.47 (m, 2H), 7.72 (m, 1H); ^{13}C NMR (*δ*/ppm, $CDCl_3$): 12.3, 36.6, 41.3, 53.9, 60.7, 72.3, 80.9, 126.8, 127.2, 127.8, 128.0, 128.5, 128.6, 129.6, 130.1, 135.2, 137.5, 140.1, 167.5, 200.8; HMRS Calcd for $C_{27}H_{28}N_2O_5S$: 492.1720. Found: 492.1723.

***N*-[(3*S*,5*R*,6*S*)-5-(Benzyloxy)-6-(hydroxymethyl)-4-oxo-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (9d) (Method A).** The product **9d** (234 mg, 46% yield) had the following data: R_f = 0.25 (CH_2Cl_2:acetone = 93:7); waxy substance; ^{1}H NMR (*δ*/ppm, *J*/Hz, $CDCl_3$): 2.1 (br, 1H), 3.10 (s, 3H),), 3.60, 3.83 (d, *J* = 14.43 Hz, 2H), 3.70(m**,** 1H), 4.0, 4.3 (d, *J* = 12.30 Hz, 2H), 4.4 (m, 2H), 4.8 (m, 1H), 5.2 (t, *J* = 1H,), 7.2 (m, 2H), 7.26 (m, 2H), 7.28 (m, 1H), 7.3 (m, 1H), 7.34 (m, 1H), 7.37 (m, 2H), 7.38 (m, 1H), 7.68 (m, 2H), 7.70 (m, 2H); ^{13}C NMR (*δ*/ppm, $CDCl_3$): 44.3, 57.4, 58.0, 59.1, 72.2, 72.8, 76.8, 126.2, 126.7, 127.1, 127.7, 128.6, 128.69, 129.4, 126.6, 129.9, 133.2, 135.4, 137.1, 139.9, 172.8, 199.6; HMRS Calcd for $C_{27}H_{28}N_2O_6S$: 508.1669. Found: 508.1672.

Benzyl (2*S*,3*R*,5*S*)-5-[Benzoyl(methyl)amino]-3-methoxy-2-methyl-4-oxo-1-piperidinecarboxylate (9e) (Method B). The product **9e** (304 mg, 74% yield) had the following data: R_f = 0.42 ($CHCl_3$:MeOH = 99:1); waxy substance; $[\alpha]^{20}_D = +28.1$ (*c* 1, $CHCl_3$); ^{1}H NMR (*δ*/ppm, *J*/Hz, $CDCl_3$) 1.21 (d, *J* = 6.78 Hz, 3H),), 3.18 (s, 3H), 3.32 (s, 3H), 3.5 (m, 1H), 3.7 (m, 1H), 3.8, 4.10 (d, *J* = 18.64 Hz, 2H), 4.1 (m, 1H), 5.2 (m, 2H), 7.29 (m, 1H,), 7.32 (m, 1H), 7.40 (m, 2H), 7.44 (m, 2H), 7.47 (m, 1H), 7.50 (m, 2H), 7.60(m, 1H); ^{13}C NMR (*δ*/ppm, $CDCl_3$): 12.6, 35.4, 40.5, 46.3, 57.0, 67.5, 73.1, 126.5, 126.7, 127.6, 128.5, 128.6, 129.9, 136.1, 147.5, 155.1, 172.6, 201.7; Calcd for $C_{23}H_{26}N_2O_5$: 410.1843. Found: 410.1840.

***N*-[(3*S*,5*S*,6*S*)-5-Hydroxy-6-methyl-4-oxo-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (14a) (Method B).** The product **14a** (197 mg, 49% yield) had the following data: R_f = 0.32 ($CHCl_3$:MeOH = 9:1); white wax; ^{1}H NMR (*δ*/ppm, *J*/Hz, $CDCl_3$), 1.22 (d, *J* = 6.33 Hz, 3H), 2.97 (s, 3H), 3.66 (m, 1H), 3.85, 3.99 (d, *J* = 7.83 Hz, 2H), 4.28 (m, 1H), 5.20 (m, 1H), 7.19−7.98 (10H); ^{13}C NMR (*δ*/ppm, $CDCl_3$): 14.3, 38.2, 41.4, 53.9, 76.7, 85.5, 126.2, 127.2, 128.4, 129.4, 132.8, 133.6, 135.2, 140.3, 172.3, 194.1; HRMS Calcd for $C_{20}H_{22}N_2O_5S$: 402.1251. Found: 402.1253.

***N*-[(5*S*,6*R*)-4-{[(2*S*,3*R*)-5-[Benzoyl(methyl)amino]-3-methoxy-2-methyl-1-(phenylsulfonyl)-1,2,3,6-tetrahydro-4-pyridinyl]disulfanyl}-5-methoxy-6-methyl-1-(phenylsulfonyl)-1,2,5,6-tetrahydro-3-pyridinyl]-*N*-methylbenzamide (23a) (Method A).** The product **23a** (486 mg, 56% yield) had the following data: R_f = 0.42 (hexane:EtOAc:CH_2Cl_2 = 7:3:5); pale yellow wax; ^{1}H NMR ((*δ*/ppm, *J*/Hz, $CHCl_3$): 0.782 (d, *J* = 6.69 Hz, 3H,), 3.03 (s, 3H), 3.27 (s, 3H), 3.44, 3.7 (d, *J* = 13.1 Hz, 2H), 3.61 (d, *J* = 2.34 Hz, 1H), 4.20 (m, 1H), 7.1−7.80 (m, 10H); ^{13}C NMR (*δ*/ppm, $CHCl_3$): 9.8, 30.1, 43.5, 50.2, 58.9, 78.6, 127.4−134.1, 132.3, 136.1, 172.2.

General Procedure for the Preparation of Compounds 10 and 15. A solution of **9** or **14** (1 mmol) in MeOH (5 mL) was cooled to 0 °C and treated with $NaBH_4$ (0.08 g, 2.2 mmol). After stirring at room temperature for 3 h, the solvent was evaporated and the residue was partitioned between CH_2Cl_2 (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The organic layer was dried and the solvent evaporated under reduced pressure. The crude materials was chromatographed on silica column affording pure product.

***N*-[(3*S*,4*S*,5*R*,6*S*)-4-Hydroxy-5-methoxy-6-methyl-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (10a).** The product **10a** (314 mg, 75% yield) had the following data: R_f = 0.36 (CH_2Cl_2:acetone = 94:6); colorless crystals; mp 142−143 °C (EtOAc:hexane = 2:1), $[\alpha]^{20}_D = -14.1$ (*c* 1, MeOH); ^{1}H NMR (*δ*/ppm, *J*/Hz, CD_3COCD_3): 1.18 (d, *J* = 7.02 Hz, 3H),), 2.89 (s, 3H), 3.10 (s, 3H), 3.32 (m, 1H), 3.69 (t, *J* = 12.26 Hz, 1H), 3.83 (m,1H), 3.88, 4.37, (d, *J* = 4.96 Hz, 2H), 4.30 (m, 1H), 7.43 (m, 2H), 7.45 (m, 2H), 7.64 (m, 1H), 7.66 (m, 2H), 7.73 (m, 1H), 7.88 (m, 2H); ^{13}C NMR (*δ*/ppm, CD_3OD): 13.6, 36, 38 1, 52.3, 54.1, 57.2, 72.1, 79.7, 128., 130.1, 131, 131.3, 134.4, 138.1, 144.3, 175.2; MS, *m*/*z* (%), 419.1 (M, 1.2), 277 (7), 142 (12), 104 (100), 76.9 (77), 71 (15), 55 (11), 41 (11). Anal. Calcd for $C_{21}H_{26}N_2O_5S$: C 60.27, H 6.26, N 6.57, S 7.65. Found: C 60.07, H 6.21, N 6.69, S 7.63.

***N*-[(3*S*,4*S*,5*R*,6*S*)-5-(Benzyloxy)-4-hydroxy-6-methyl-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (10b).** The product **10b** (314 mg, 70% yield) had the following data: R_f = 0.33 (CH_2Cl_2:acetone = 94:6); white crystals: mp 44−45 °C, $[\alpha]^{20}_D = -3.1$ (*c* 1, $CHCl_3$); ^{1}H NMR (*δ*/ppm, J/Hz, $CDCl_3$):

0.78 (d, J = 6.87 Hz, 3H), 2.05 (br, 1H), 2.96 (s, 3H), 3.56 (d, J = 11.50 Hz, 2H), 3.7 (m, 1H), m, 2H), 4.31 (m, 1H), 4.4 (m, 1H), 7.18 (m, 2H), 7.25 (m, 1H), 7.27 (m, 1H), 7.29 (m, 2H7.35 (m, 2H), 7.41 (m, 2H), 7.44(m, 2H), 7.46 (m, 2H), 7.68 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 12.97, 35.1, 36.7, 50.2, 52.5, 70.3, 71.2, 75.1, 126.7, 126.9, 127.7, 128.1, 128.5, 128.6, 129.3, 129.6, 132.2, 136.2, 137.2, 144.0, 172.0; MS, *m*/*z* (%): 494 (M, 2%), 493 (M − 1, 8%), 437 (205), 403 (52), 353 (30), 218 (50), 91 (100), 56.0 (15). Anal. Calcd for $C_{27}H_{30}N_2O_5S$: C 65.56, H 6.12, N 5.67, S 6.47. Found: C 65.41, H 6.18, N 5.59, S 6.56.

***N*-[(3*S*,4*S*,5*R*,6*S*)-5-(Benzyloxy)-4-hydroxy-6-(hydroxymethyl)-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (10d).** The product **10d** (206 mg, 51% yield) had the following data: R_f = 0.52 (CH_2Cl_2:acetone = 2:1); wax substance; $[\alpha]^{20}_D$ = +2.3 (*c* 2, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$) 3.0 (s, 3H), 3.2 (br, 1H), 3.5 (m, 2H), 3.8 (m, 1H), 3.9 (m, 1H), 4.01 (m, 1H), 4.06 (d, J = 17.16 Hz, 2H), 4.22 (m, 1H), 4.40, 4.49 (d, J = 11.52 Hz, 2H), 7.26(m, 2H), 7.28 (m, 2H), 7.29 (m, 1H), 7.33 (m, 2H), 7.37 (m, 2H), 7.39 (m, 1H), 7.44 (m, 2H), 7.50 (m, 1H), 7.72 (m, 2H); ^{13}C NMR (δ/ppm, $CDCl_3$): 38.3, 52.1, 55.3, 59.8, 69.3, 71.2, 75.4, 77.2, 126.8, 127.8, 128.2, 128.5, 129.4, 129.7, 130.1, 133.2, 136.1, 137.2, 140.2, 172.4; HRMS Calcd for $C_{20}H_{24}N_2O_5S$: 404.1407. Found: 404.1408.

Benzyl (2*S*,3*R*,4*S*,5*S*)-5-[Benzoyl(methyl)amino]-4-hydroxy-3-methoxy-2-methyl-1-piperidinecarboxylate (10e). The product **10e** (214 mg, 54% yield) had the following data: R_f = 0.35 ($CHCl_3$:MeOH = 90:10); light yellow oil; $[\alpha]^{20}_D$ = +30.0 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.78 (d, J = 6.83 Hz, 3H), 1.17 (br, 1H), 3.06 (s, 3H), 3.23 (s, 3H), 3.3 (m, 1H), 3.62 (m, 2H), 3.9(m 1H), 4.07 (m, 1H), 4.5(m, 1H), 5.03(m, 2H), 7.0 (m, 1H), 7.03 (m, 2H), 7.10 (m, 2H), 7.20 (m, 1H), 7.26 (m, 2H), 7.35 (m, 1H), 7.4 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 11.2, 35.3, 40.5, 46.3, 57.2, 57.6, 67.2, 67.5, 73.1, 126.9, 127.8, 128.0, 128.6, 129.7, 129.9, 136.2, 147.5, 155.3, 171.9; HRMS Calcd for $C_{23}H_{28}N_2O_5$: 412.1999. Found: 412.1998.

***N*-[(3*S*,4*R*,5*S*,6*S*)-4,5-Dihydroxy-6-methyl-1-(phenylsulfonyl)piperidinyl]-*N*-methylbenzamide (15).** The product **15a** (250 mg, 62% yield) had the following data: R_f = 0.32 ($CHCl_3$:MeOH = 9:1); colorless wax; mp 74−75 °C (EtOH), $[\alpha]^{20}_D$ = +3.42 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz, $CDCl_3$): 0.79 (d, J = 6.95 Hz, 3H), 2.96 (s, 3H), 3.16 (m, 1H), 3.27 (dq, J = 24.24 Hz, 1H), 3.67 (t, J = 12.24, 1H), 3.78 (br, 1H), 4.00 (t, J = 7.14, 1H), 4.03 (m, 2H), 4.12 (m, 1H), 7.2 (2H), 7.3 (2H), 7.41 (2H), 7.67 (2H), 7.8; ^{13}C NMR (δ/ppm, $CDCl_3$): 14.2, 27.5, 29.7, 52.1, 54.6, 72.6, 77.1, 126.8, 127.1, 129.1, 131.4, 132.6, 140.7, 171.2; MS, *m*/*z* (%): 404 (M, 0.3), 296 (2), 212 (1), 112 (21), 105 (100), 77 (75), 56.1 (16), 42 (15.). Anal. Calcd for $C_{20}H_{24}N_2O_5S$: C 59.39, H 5.99, N 6.93, S 7.91. Found: C 59.23, H 6.07, N 7.06, S 7.98.

General Procedure for the Preparation of Thiazolidines 24. A solution of **21** (0.500 mmol) in MeOH (8 mL) was cooled to 0 °C and treated with $NaBH_4$ (60 mg, 1.6 mmol). The mixture was stirred for 10 min at room temperature, the solvent was evaporated, and the crude product obtained was partitioned between CH_2Cl_2 (10 mL) and saturated aqueous $NaHCO_3$ (10 mL). The organic layer was dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The crude products were chromatographed on a silica column.

(3a*S*,6*S*,7*R*,7a*S*)-7-Methoxy-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)octahydro[1,3]thiazolo[4,5-*c*]pyridine (24a). The product **24a** (144 mg, 69% yield) had the following data: R_f = 0.35 (hexane:EtOAc:CH_2Cl_2 = 10:1.5:3.5); pale yellow oil with an unpleasant smell; $[\alpha]^{20}_D$ = −10.54 (*c* 1, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz $CDCl_3$): 0.96 (d, J = 6.99 Hz, 3H), 2.07 (s, 3H), 2.64 (m, 1H), 3.17 (m, 1H), 3.23 (s, 3H), 3.44, 4.0 (d, J = 15.10 Hz), 3.48 (m, 1H), 4.23 (m, 1H), 4.43 (s, 1H), 7.23 (2H), 7.32 (2H), 7.47, 7.51 (2H), 7.77 (2H), 7.84; ^{13}C NMR (δ/ppm, CD_3COCD_3): 8.9, 37.2, 38.9, 46.6, 48.9, 57.9, 67.7, 73.9, 82.6, 126.9, 127.2, 127.5, 128.4, 129.2, 132.5, 140.4, 140.6; MS, *m*/*z* (%): 418 (M, 1), 277 (25), 220 (10), 217 (20), 149.0 (10), 126.0 (20), 77 (100), 69 (32), 42.0 (58); HRMS Calcd for $C_{21}H_{26}N_2O_3S_2$: 418.1351. Found: 418.1350.

(3a*S*,6*S*,7*R*,7a*S*)-7-(Benzyloxy)-3,6-dimethyl-2-phenyl-5-(phenylsulfonyl)octahydro[1,3]thiazolo[4,5-*c*]pyridine (24b). The product **24b** (138 mg, 56% yield) had the following data: R_f = 0.36 (hexane: EtOAc: CH_2Cl_2 = 10:1.5: 3.5); pale yellow oil; $[\alpha]^{20}_D$ = −15.16 (*c* 1, $CHCl_3$): ^{1}H NMR (δ/ppm, *J*/Hz $CDCl_3$): 1.07 (d, J = 6.95 Hz, 3H), 2.02 (s, 3H), 2.65 (m, 1H)), 3.22, 4.09, (d, J = 15.53 Hz, 2H), 3.24 (m, 1H), 3.68 (m, 1H), 4.13 (m, 2H), 4.34, 4.48 (d, J = 11.91 Hz, 2H), 4.39 (s, 1H), 7.08 (1H), 7.15 (2H), 7.20 ($2H_r$), 7.25 (2H), 7.31 (2H), 7.36 (1H), 7.44 ($2H_r$), 7.49 ($2H_r$), 7.7 (1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 9.5, 37.2, 38.7, 46.8, 48.2, 67.8, 71.9, 73.9, 79.5, 127.1, 127.3, 127.8, 128.2, 128.3, 128.7, 128.9, 129.1, 132.3, 137.1, 137.5, 140.4, 140.6; MS, *m*/*z* (%), $C_{27}H_{30}N_2O_3S_2$, 494.2 (M, 0.32), 353.1 (1.02), 245 (10.83), 148 (179, 90 (100), 76.9 (61.83), 57 (30.8), 42 (23.95); HRMS calcd for $C_{27}H_{30}N_2O_3S_2$: 494.1700. Found: 494.1704.

3a*S*,6*S*,7*R*,7a*S*)-7-Methoxy-3,6-dimethyl-5-(phenylsulfonyl)octahydro[1,3]thiazolo[4,5-*c*]pyridine (24c). The product **24c** (75.3 mg, 44% yield) had the following data: R_f = 0.43 (pentane:EtOAc:CH_2Cl_2 = 7:3:5); light yellow oil; $[\alpha]^{20}_D$ = −49.67 (*c* 1.2, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz $CDCl_3$): 0.86 (d, J = 6.96 Hz, 3H), 2.31 (s, 3H), 2.5 (m, 1H), 3.08, 3.88 (d, J = 6.83 Hz, 2H), 3.28 (s, 3H), 3.32 (m, 1H), 3.40, 4.00 (d, J = 6.83 Hz, 2H), 4.23 (m, 1H), 7.43 (m, 2H), 7.46 (m, 2H), 7.49 (m, 1H), 7.79 (m, 2H), 7.81 (m, 2H,); ^{13}C NMR (δ/ppm, $CDCl_3$): 8.9, 38.8, 39.6, 47.5, 49.7, 57.6, 57.8, 82.0, 126.6, 127.2 ($2XCH_{ar}$), 132.6, 140.2; MS, *m*/*z* (%): 342.1 (M, 0.5), 285 (5), 201 (90), 169 (100), 141 (30), 77 (40), 42 (25); HRMS cacld for $C_{15}H_{22}N_2O_3S_2$: 342.1074. Found: 342.1076.

(3a*S*,6*S*,7*R*,7a*S*)-7-(Benzyloxy)-3,6-dimethyl-5-(phenylsulfonyl)octahydro[1,3]thiazolo[4,5-*c*]pyridine (24d). The product **24d** (87.4 mg, 42% yield) had the following data: R_f = 0.35 (pentane:EtOAc:CH_2Cl_2 = 7:3:5); pale yellow oil; $[\alpha]^{20}_D$ = −95.2 (*c* 3, $CHCl_3$); ^{1}H NMR (δ/ppm, *J*/Hz $CDCl_3$): 0−90 (d, J = 6.96 Hz, 3H), 2.30 (s, 3H), 2.49 (m, 1H), 3.07 (m, 2H), 3.26 (m, 1H), 3.40−3.97 (d, J = 6.79 Hz, 2H), 3.58 (m, 1H), 4.14 (m, 1H), 4.46 (s, 2H), 7.18 (m, 2H), 7.23 (m, 1H), 7.39 (m, 2H), 7.42 (m, 2H,), 7.47 (m, 2H), 7.74 (m, 1H); ^{13}C NMR (δ/ppm, $CDCl_3$): 9.3, 38.7, 39.5, 47.7, 50.5, 57.7, 66.9 (*C*HNCH$_3$), 72.5, 127.2, 127.8, 127.8, 128.5, 129.1, 132.5, 137.9, 140.2; MS, *m*/*z* (%): 418 (M + 1, 50), 417 (M, 49), 277 (67), 327 (48), 169 (80), 91.1 (10), 77 (32), 42 (16); HRMS Calcd for $C_{21}H_{26}N_2S_2O_3$: 418.1387. Found: 418.1384.

Acknowledgment. We gratefully acknowledge financial support from DAAD and the Fonds der Chemischen Industrie. We thank Dr. Burkhard Ziemer, Humboldt-Universität Berlin, for providing X-ray crystal analyses and Degussa-Hüls AG for a generous donation of amino acids and Prof. Horst Hartmann for providing 2-morpholino-3-methyl-1,3-thiazole.

Supporting Information Available: X-ray crystal analysis of **5f**, **10a**, and **21c**. ^{1}H NMR data of **3c**, **3f**, **4e**, **4f**, **5a**, *epi*-**5f**, *epi*-**6f**, *epi*-**6g**, **9e**, **10e**, **17a**, **17c**, **19a**, **19c**, **20c**, **24a**, **24b**, **24c**, **24d**. Experimental procedure for **3c**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO010665Z