60. Derivatives of (2*R*)-*N*-Glyoxylbornane-10,2-sultam and Their Use as Auxiliaries in the Diastereoselective Spirocyclization of 2-Substituted Tryptamines[1])

by **Ralf Freund**[a])[b]), **Christos Allagiannis**[a]), **Peter Schönholzer**[c]), and **Karl Bernauer**[a])[c])[2])*

[a]) Organisch-Chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH–8057 Zürich
[b]) Chemisches Institut der Tierärztlichen Hochschule Hannover, Bischofsholer Damm 15, D–30173 Hannover
[c]) Pharmaforschung der *F. Hoffmann-La Roche AG*, CH–4002 Basel

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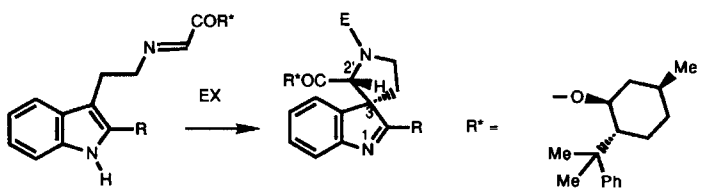
A crude hydrate **6** and a crystalline hemiacetal **7** of glyoxylamide **4** were prepared from crotonamide **5** (*Scheme 2*). Particularly hemiacetal **7**, but also **6** and the 'dimer' **8** (obtained from **7**) may serve as homochiral auxiliaries. The structure of **8** was determined by X-ray analysis. By arenesulfonyl halides, tryptimines **12**–**14** of **4** were diastereoselectively transformed into spirotricycles **15**–**17** and **19**.

1. Introduction. – Tryptimines of type **1** are transformed by various acid halogenides EX mainly into (2′*R**,3*S**)-tricycles of type **2** (*Scheme 1*) [1–3]. The remarkably high preference of this relative configuration prompted us to postulate a transition state of type **22**/**23** [2] (see below). Homochiral compounds **2** may be obtained, if R* is an appropriate homochiral auxiliary group. Of such groups, (–)-8-phenylmenth-3-yloxy (**A**), which was originally developed to steer *Diels-Alder*-type reactions [4], stood out for high directing ability [1] [2]. A mechanistic explanation of the observed absolute configuration appeared, however, questionable.

In recent years, the camphor-derived (2*R*)-bornane-10,2-sultam **B**-H (*Scheme 2*), introduced by *Oppolzer* and coworkers [5] as chiral auxiliary, was successfully applied in

Scheme 1



1 **2** **A**

(relative configuration)

R = Me, 3,4-Dimethoxyphenyl

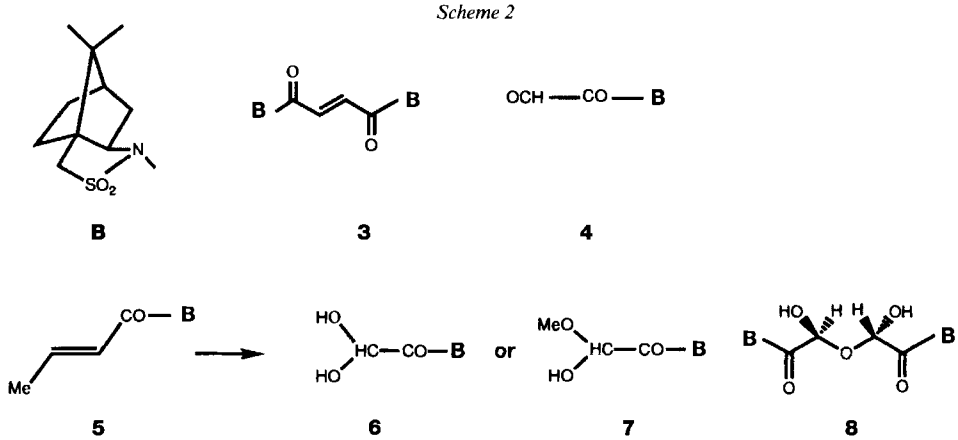
[1]) 7th Communication on 'Indoles, Indolenines, and Indolines'; 6th communication: [1].
[2]) Retired. Private address: Wartenbergstrasse 30, CH–4104 Oberwil.

various types of asymmetric reactions [6]. Concerning inducing power, **B** compares favourably with **A**. Because of its rigidity, it might facilitate mechanistic reasoning with regard to absolute product configuration.

Chapuis, *Jurczak*, and coworkers [7] synthesized the glyoxylamide **4** of **B**-H by ozonization of the fumaric-acid derivative **3** and studied its reaction with 1-methoxybuta-1,3-diene. We prepared independently on a similar route the (crude) hydrate and a crystalline hemiacetal of **4** and applied them as auxiliaries in the synthesis of homochiral 3-spiroindole derivatives. A crystalline dimeric hydrate, obtained from the hemiacetal, may serve the same purpose. We report in the following on some of our pertinent results.

2. Auxiliaries. – Ozonization of crotonamide **5** [8] in CH_2Cl_2/MeOH at −78°, subsequent reduction of the ozonide with Me_2S, and aqueous workup afforded hydrate **6** as a partially crystallized solid which, however, could not be recrystallized and, therefore, was used as crude product. If, on the other hand, the aqueous workup was omitted after the reduction and the mixture instead partially evaporated and treated with Et_2O, the crystalline hemiacetal **7** was obtained in 90% yield (*Scheme 2*). Its structure follows mainly from ^{1}H-NMR data (MeO of **7** at 3.44 ppm ($CDCl_3$), of added MeOH at 3.40 ppm). Compound **7** is stable, if kept in the ice box. It cannot be dried without decomposition under reduced pressure and/or at temperatures essentially higher than room temperature.

Scheme 2



Attempts to recrystallize **6** from CH_2Cl_2/Et_2O afforded compound **8**, a derivative of 2,2′-oxybis(2-hydroxyacetic acid). Its structure was established by X-ray analysis (*Chapt. 6, Fig. 3*). Closely related structures were described before [9].

3. Tryptimines of 4 and Spirocyclization. – From amine **9** [3] and crude **6**, tryptimine **12** was formed in CH_2Cl_2 in the presence of molecular sieves and cyclized by TsCl *in situ* at −20°[3]) after addition of 2,4,6-trimethylpyridine to (2′*S*,3*R*)-tricycle **15** (25.2%), a diastereoisomer was not observed.

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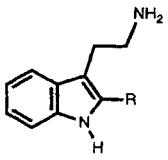
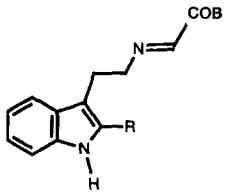
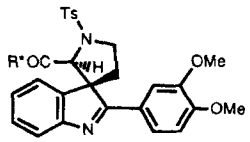
[3]) Spirocyclization of tryptimines of **4** at −78° (*cf.* [1] [2]) is an extremely slow reaction.



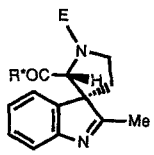
9 R = 3,4 $(MeO)_2C_6H_3$
10 R = Me
11 R = $CH_2COO(i\text{-}Pr)$



12 R = 3,4 $(MeO)_2C_6H_3$
13 R = Me
14 R = $CH_2COO(i\text{-}Pr)$

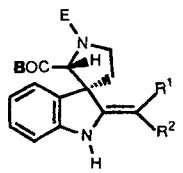


15 R* = **B**
20 R* = **A**



16 R* = **B**, E = Ts
17 R* = **B**, E = 4-Methoxy-2,3,6-trimethylphenylsulfonyl
21 R* = **A**, E = Ts

18



19a R^1 = H, R^2 = COO(i-Pr), E = 4-Methoxy-2,3,6-trimethylphenylsulfonyl
b R^1 = COO(i-Pr), R^2 = H, E = 4-Methoxy-2,3,6-trimethylphenylsulfonyl

The auxiliary **7** was reacted with the amines **10** [10] [11] and **11** [11] to the imines **13** and **14**, respectively, under the conditions mentioned for **12**, and the imines were cyclized *in situ*, *i.e.* without removing the MeOH which is released from **7**. From **13** and TsCl at −21°, the (2′*R*,3*S*)-tricycle **16** was obtained as main product (53%; 66% de), and from **13** and 4-methoxy-2,3,6-trimethylbenzenesulfonyl chloride (**18**), after 92 h at −21°, the analogous compound **17** (7.5%; 94.5% de). Reaction at 20° for 115 h gave a 39% yield of **17**, but with a de of only 81%. Imine **14** was transformed by arenesulfonyl chloride **18** at −10° into a 4:3 mixture of the two diastereoisomeric (2′*R*,3*S*)-tricycles **19a** and **19b** (together 58%), besides very small ammounts of unidentified isomers. Chromatography (silica gel) allowed a partial separation of the main components, which, however, could not be isolated in pure form.

In a preliminary experiment, compound **8** was reacted in $CHCl_3$ at room temperature with amine **10** in the presence of molecular sieves. The resulting imine afforded, with arenesulfonyl chloride **18** ($CHCl_3$, 2,4,6-trimethylpyridine, 96 h, room temperature), **17**. This means that also **8** could serve as homochiral auxiliary.

4. Structure of the Cyclization Products. – The UV-, IR-, and ^{1}H-NMR spectra of the cyclization products are in agreement with the given structures (see *Exper. Part*).

The (3*R*)-configuration of **15** follows from CD comparison with compound **20** [2] (pos. maxima at 366, 276, and 211 nm, neg. maxima at 329 and 234 nm). The (*S*)-configuration at C(2′) (analogous to **20**) is not strictly proved. The CD spectra of the 2-methyl compounds **16** and **17** correspond to that of **21** [2], establishing the (2′*R*,3*S*)-configuration for both.

The two tricycles obtained from **14** and **18** must be the (*E*)- and (*Z*)-isomers **19a** and **19b**, respectively[4]), for the following reasons: CD comparison of the mixture with (−)-tabersonine[5]) points to (3*S*)-configuration for both components. On refluxing of the mixture with $HCl/H_2O/EtOH$, the 2-methyl compound **17** (41.5%) was formed (besides *ca.* 45% of the sultam **B**-H) as the only spirotricyclic product. Furthermore, we could show that a 1.9:1 mixture of the components (chromatographic top fraction), on treatment with $AcOH/CF_3COOH$ for 230 h, was transformed in a 1:2.6 mixture. It is reasonable to attribute structure **19a** to the component enriched in the top fraction (lower polarity due to H-bond formation: N(1)–H···O=C–O(i-Pr)).

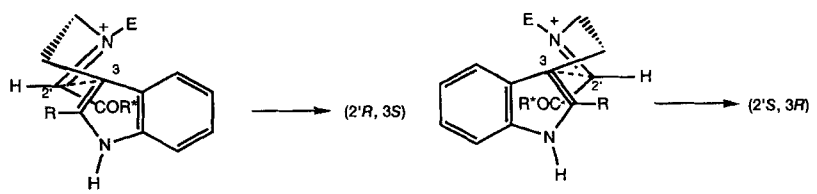
5. Discussion. – The above presented results show that the easily prepared hemiacetal **7** is a useful equivalent of aldehyde **4** if tryptimines of the latter are to be formed. The tricycles obtained as main products from these imines possess (2′*R**,3*S**)-configuration. Taking into account the analogous steric outcome in formerly discussed cases [1] [2], it can be concluded that the previously formulated transition state of type **22**/**23** (*Scheme 3*) explains correctly the relative steric course of the main reaction.

As to the tryptimine **14**, it is of interest that – in contrast to the corresponding (−)-8-phenylmenth-3-yl derivative[6]) – (2′*R**,3*R**)-tricycles are not formed (at least not to an extent which would allow isolation and identification). (*E*,*Z*)-Isomerisation and/or cyclization of the (*Z*)-isomer must be relatively slow in this case.

Apart from that, the residue **B** is, with respect to absolute configuration and enantiomeric excess, comparable to the 8-phenylmenthyloxy group **A**. A drawback is, however, the relatively low reaction rate.

Attempts to explain the observed *absolute* steric courses of the reactions **12** → **15** and **13** → **16** by means of *Dreiding* models remained unsuccessful, in spite of the fact that **B** possesses much less degrees of freedom than **A**[6]). The model inspection allows, however, to preclude a purely steric explanation of the remarkable fact that identical groups R* steer the reaction in the 2-methyl and the 2-(3,4-dimethoxyphenyl) series to inversely configurated spirotricycles: In neither of the two series, the 2-substituent interferes sterically with any other part of the corresponding molecule (*cf.* **22**/**23**, *Scheme 3*). It appears, however, plausible that the transition state in the former (**22**) is educt-like,

Scheme 3



22 R = Me, R* = **B**, E = $ArSO_2$

23 R = 3,4 $(MeO)_2C_6H_3$, R* = **B**, E = $ArSO_2$

[4]) (*E*/*Z*)-Equilibria were observed also with comparable simpler indole derivatives [12].
[5]) *Cf.* Fig. 3 in [2].
[6]) *Cf.* Discussion in [2].

whereas it is product-like in the latter (**23**) because of the strong electron-donating character of 3,4-dimethoxyphenyl, which effects a relatively high electron density at C(3) of the indole moiety. This difference may be the reason for the stereochemical divergence.

6. X-Ray Structure Analysis. – The stereoscopic drawing of the structure of **8** is given in the *Figure*[7]).

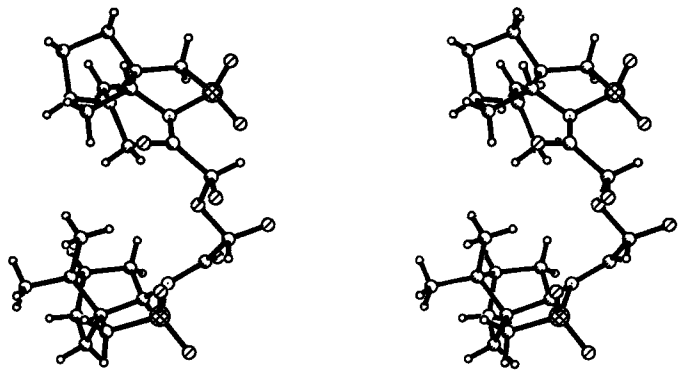


Figure. *Stereoscopic drawing of* **8**

Data were collected on a *Nicolet-R3m* four-circle diffractometer fitted with a *LT1* cooling apparatus. Temp. 190 K; wavelength 0.71069 Å; scan mode $\theta/2\theta$; scan speed 0.52°/min minimum speed; strong reflections measured up to 14.65°/min; scan width 1.0°; 2θ range, θ–56 peak to background ratio 5:1; total data measured 1809 excluding standards; total observed 1568; rejection criterion $I > 2.5\sigma(I)$; number of parameters 191; weights $w = 1/\sigma^2(F) + 0.001|F|^2$. The structure was determined by direct methods using the SHELXTL PLUS (VAX II) system. The refinement converged at $R = 0.065$ with anisotropic refinement of all non-H-atoms. Space group: orthorhombic, $P2_12_12$; cell dimensions: $a = 7.028(3)$, $b = 20.544(6)$, $c = 8.845(3)$ Å; $D = 1.453$ Mg/m^3, $Z = 2$; $\mu(\text{Mo}K_\alpha) = 0.253$ mm^{-1}.

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Experimental Part

General. See [11] [2].

1. *(3a*S*,6*R*,7a*R*)-1-(Dihydroxyacetyl)-hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**6**). A soln. of **5** [13] (1.98 g, 7 mmol) in CH_2Cl_2 (20 ml) and MeOH (15 ml) was ozonized at −78°. After removal of excess O_3 by flushing with N_2, Me_2S (0.77 ml, 10.5 mmol) was added and the mixture kept at −78° overnight and then evaporated at r.t. The soln. of the residue in CH_2Cl_2 (25 ml) was washed with brine (4 × 5 ml), dried with molecular sieves, and evaporated. The residue (1.77 g; colourless, partially crystalline solid) contained *ca.* 40% of **6** besides structurally related unknown compounds. ^{1}H-NMR (250 MHz, (D_6)DMSO, characteristic signals of **6** only): 0.94 (*s*, Me); 1.04 (*s*, Me); 1.18–1.34 (*m*); 1.40–1.58 (*m*); 1.68–2.08 (*m*); 3.66 (*d*, J = 15); 3.86 (*d*, J = 15); 3.95 (*dd*, J = 12.5, 5); 4.63 (br. *s*).

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[7]) Coordinates and geometrical data were deposited with the *Cambridge Crystallographic Data Centre*, University Chemical Lab, Cambridge CB2 1EZ, UK.

2. *(3aS,6R,7aR)-Hexahydro-1-[(ζ)-(hydroxy)(methoxy)acetyl]-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**7**). As described for **6**, with **5** [13] (6.44 g, 22.7 mmol), CH_2Cl_2 (54 ml), MeOH (34 ml), and Me_2S (8.3 ml, 113.2 mmol; –20° instead of –78°). $MgSO_4$ was added, the mixture warmed to r.t., filtered, and evaporated. From a soln. of the residue in CH_2Cl_2 (*ca.* 10 ml) and Et_2O (*ca.* 25 ml) at 4°, **7** (3.99 g) crystallized as colourless needles which were washed with Et_2O and dried at r.t. After addition of MeOH (10 ml), the mother liquor was poured into H_2O (100 ml). The mixture was extracted with CH_2Cl_2 (2 × 50 ml) and Et_2O (50 ml) and the combined org. phase partially evaporated. On treatment with Et_2O, a further crop of **7** (2.21 g) crystallized. Total yield 6.2 g (89.9%). M.p. 170° (dec.). IR ($CHCl_3$): 1699, 1345, 1312, 1299, 1291, 1154, 1141, 1098, 1066. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.92 (*s*, 3 H); 1.10 (*s*, 3 H); 1.18–1.42 (*m*, 2 H); 1.78–2.16 (*m*, 5 H); 3.34–3.48 (*m*, 2 H); 3.44 (*s*, 3 H); 3.86 (*dd*, *J* = 7.7, 5.1, 1 H); 5.23 (*d*, *J* = 10, 1 H); on addition of MeOH, its Me signal appears at 3.40 and the *d* at 5.23 is transformed into a sharp *s*. CI-MS: 320 (15), 304 (7, $[M + 1]^+$), 286 (21), 272 (100), 135 (46). HR-MS: 272.0966 ($C_{12}H_{18}NO_4S^+$, $[M - OMe]^+$, calc. 272.0957).

3. *1,1′-[Oxybis[(*S*)-2-hydroxy-1-oxoethane-2,1-diyl]bis[(3aS,6R,7aR)-hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole] 2,2,2′,2′-Tetraoxide* (**8**). To a soln. of **7** (179 mg, 0.59 mmol) in CH_2Cl_2 (*ca.* 5 ml), Et_2O (5 ml) was added. After 10 days at 4°, pure **8** (26.5 mg, 16%) was isolated by filtration. M.p. 183° (dec.). IR (KBr): 3486, 2961, 1702, 1457, 1413, 1395, 1341, 1242, 1170, 1142, 1115, 1065, 1035, 847, 826, 770, 616, 535, 490. ^{1}H-NMR (300 MHz, (D_6)DMSO): 0.92 (*s*, 6 H); 1.05 (*s*, 6 H); 1.28–1.35 (*m*, 2 H); 1.43–1.51 (*m*, 2 H); 1.70–1.87 (*m*, 6 H); 2.00–2.15 (*m*, 4 H); 3.58 (*d*, *J* = 14.1, 2 H); 3.77 (*d*, *J* = 14.1, 2 H); 3.97 (*dd*, *J* = 4.5, 4.5, 2 H); 5.40 (*d*, *J* = 9, 2 H); 7.31 (*d*, *J* = 9, 2 H). MS: 272 (3), 242 (16), 136 (16), 135 (100), 132 (10), 107 (32).

4. *(3aS,6R,7aR)-1-{{(2′S,3R)-2-(3,4-Dimethoxyphenyl)-1′-(4-tolylsulfonyl)spiro[3*H*-indole-3,3′-pyrrolidin]-2′-yl}carbonyl}-hexahydro-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**15**). A mixture of crude **6** (320 mg, 1.1 mmol), CH_2Cl_2 (5 ml), and molecular sieves was stirred at r.t. overnight. Then, a soln. of **9** (1 mmol) in CH_2Cl_2 (10 ml) was added dropwise at 0° within 1 h. After additional 2 h at 0° and 2 h at r.t., the soln. was separated from the molecular sieves and cooled to –20°. First 2,4,6-trimethylpyridine (0.2 ml) and then a soln. of TsCl (198.9 mg, 1.04 mmol) in CH_2Cl_2 (3 ml) were added by syringe. After stirring at –20° for 24 h, the mixture was shaken with 2N Na_2CO_3 (5 ml), the aq. phase extracted twice CH_2Cl_2, the combined org. layer washed with 0.5M citric acid and evaporated, and the residue chromatographed (hexane/$CHCl_3$/AcOEt 2:2:1, silica gel (80 g)): **15** (179.6 mg, 25.2%). Colorless foam. UV (MeOH): 230 (4.43), 336 (4.13). CD (EtOH, 1.0 mM): 366 (1.44), 329 (–1.26), 276 (1.34), 234 (–14.5), 211 (20.95). ^{1}H-NMR ($CDCl_3$, 250 MHz): 0.07 (*s*, 3 H); 0.72 (*s*, 3 H); 1.03–1.38 (*m*, 4 H); 1.64–1.80 (*m*, 3 H); 1.90–2.03 (*m*, 1 H); 2.50 (*s*, 3 H); 2.62–2.79 (*m*, 1 H); 3.16 (*d*, *J* = 14, 1 H); 3.27 (*d*, *J* = 14, 1 H); 3.67 (*dd*, *J* = 8, 4, 1 H); 3.92 (*s*, 3 H); 4.01 (*s*, 3 H); 4.04–4.20 (*m*, 2 H); 5.71 (*s*, 1 H); 6.53 (*d*, *J* = 10, 1 arom. H); 7.08–7.93 (*m*, *ca.* 10 arom. H).

5. *(3aS,6R,7aR)-Hexahydro-8,8-dimethyl-1-{{(2′R,3S)-2-methyl-1′-(4-tolylsulfonyl)spiro[3*H*-indole-3,3′-pyrrolidin]-2′-yl}carbonyl}-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**16**). To a stirred mixture of **7** (334 mg, 1.1 mmol), CH_2Cl_2 (14 ml), and molecular sieves at –78°, a soln. of crude **10** [11] (198 mg, 1.14 mmol) in CH_2Cl_2 (15 ml) was added by syringe. After 14 h at –5°, the mixture was cooled to –78°. A soln. of TsCl (315 mg, 1.65 mmol) and 2,4,6-trimethylpyridine (0.44 ml, 3.32 mmol) in CH_2Cl_2 (1.4 ml) was added dropwise. The mixture was stirred at –21° for 70 h and then poured on 0.5M aq. citric acid (40 ml). The aq. phase was extracted with CH_2Cl_2 (2 × 40 ml), the combined org. layer evaporated, and the residue submitted to FC (silica gel, Et_2O/CH_2Cl_2 7:1): colorless foam (339 mg, 53%), consisting of **16** and a diastereoisomer (66.2% de). On twofold crystallisation from CH_2Cl_2/Et_2O, a mixture of **16** and its diastereoisomer (73.5% de) was obtained. M.p. 137° (dec.). UV (EtOH): 201.7 (4.49), 215 (4.40), 221 (4.42), 227 (sh, 4.39), 263 (sh, 3.64). CD (EtOH, 2.1 mM): 264 (–6.45), 251 (0.60), 227 (–74.19), 207 (66.51). IR ($CHCl_3$): 1710, 1593, 1582, 1508, 1340, 1274, 1168, 1138. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.13 (*s*, 3 H); 0.75 (*s*, 3 H); 0.88–1.74 (*m*, *ca.* 7 H); 1.77 (*s*, 0.6 H); 1.83 (*s*, 2.4 H); 1.86–2.19 (*m*, *ca.* 2 H); 2.42 (*s*, 0.6 H); 2.47 (*s*, 2.4 H); 3.22 (*d*, *J* = 14, 1 H); 3.33 (*d*, *J* = 14, 1 H); 3.76–3.85 (*m*, *ca.* 2 H); 3.9–4.1 (*m*, 1 H); 4.49 (*s*, *ca.* 0.2 H); 5.02 (*s*, *ca.* 0.8 H); 7.05–7.75 (*m*, *ca.* 6 arom. H); 7.97 (*d*, *J* = 8.2, 2 arom. H). MS: 581 (8, $M^{+\cdot}$), 431 (10), 426 (14), 339 (57), 183 (100). HR-MS: 581.2023 ($C_{30}H_{35}N_3O_5S_2^+$, calc. 581.2018).

6. *(3aS,6R,7aR)-Hexahydro-1-{{(2′R,3S)-1′-(4-methoxy-2,3,6-trimethylphenylsulfonyl)-2-methylspiro[3*H*-indole-3,3′-pyrrolidin]-2′-yl}carbonyl}-8,8-dimethyl-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-Dioxide* (**17**). To a stirred mixture of **10** [11] (555 mg, 3.2 mmol), CH_2Cl_2 (42 ml), and molecular sieves at –78°, a soln. of **7** (938 mg, 3.1 mmol) in CH_2Cl_2 (39 ml) was added by syringe. After 15 h at –5°, the mixture was cooled to –78°. Then, a soln. of 4-methoxy-2,3,6-trimethylbenzenesulfonyl chloride (**18**; 884 mg, 3.6 mmol) and 2,4,6-trimethylpyridine (1 ml, 7.5 mmol) in CH_2Cl_2 (3 ml) was added dropwise. After further stirring at –21° for 92 h, the mixture was poured on 0.5M aq. citric acid (80 ml). The aq. phase was extracted with CH_2Cl_2 (2 × 80 ml), the combined org. layer evaporated, and the residue submitted to FC (silica gel, Et_2O/petroleum ether (low boiling) 10:1, then Et_2O): **17** as

colourless foam (149 mg, 8%; 94.5% de). CD (EtOH, 1.68 mM): 264 (−3.99), 240 (5.55), 220 (−6.94), 207 (23.16). IR ($CHCl_3$): 1700, 1585, 1562, 1468, 1378, 1345, 1310, 1274, 1180, 1142. ^{1}H-NMR (200 MHz, $CDCl_3$): 0.06 (*s*, 3 H); 0.71 (*s*, 3 H); 1.05–1.30 (*m*, 2 H); 1.51 (*s*, 1 H); 1.60–1.84 (*m*, *ca.* 3 H); 2.17 (*s*, 3 H); 2.35–2.75 (*m*, 2 H); 2.55 (*s*, 3 H); 2.66 (*s*, 3 H); 2.75 (*s*, 3 H); 3.13–3.27 (*m*, 2 H); 3.47–3.57 (*m*, 1 H); 3.64–3.80 (*m*, 1 H); 3.86 (*s*, 3 H); 3.93–4.04 (*m*, 2 H); 5.59 (*s*, 1 H); 6.59 (*s*, 1 arom. H); 7.05–7.50 (*m*, *ca.* 4 arom. H). MS: 639 (2.8, M^+), 426 (11.6), 397 (100), 213 (92), 157 (49), 149 (100), 134 (41), 119 (68). Anal. calc. for $C_{33}H_{41}N_3O_6S_2$ (639.83): C 61.95, H 6.49, N 6.57; found: C 61.62, H 6.46, N 6.65.

7. *1-Methylethyl {(2′R,3S,2Z)-2′-{[(3aS,6R,7aR)-Hexahydro-8,8-dimethyl-2,2-dioxo-3H-3a,6-methano-2λ⁶,1-benzisothiazol-1-yl]carbonyl}-1′-(4-methoxy-2,3,6-trimethylphenylsulfonyl)spiro[3H-indole-3,3′-pyrrolidin]-2(1H)-ylidene}acetate* (**19a**) *and (2′R,3S,2E)-Isomer* **19b**. To a stirred soln. of **7** (612 mg, 2.02 mmol) in CH_2Cl_2 (5 ml) at −10°, a soln. of freshly prepared **11** [11] (525.9 mg, 2.02 mmol) in CH_2Cl_2 (5 ml) was added by syringe (infusion pump) within 35 min. The syringe was flushed twice with CH_2Cl_2 (2.5 ml). After 18 h, the mixture was cooled to −78°. A mixture of CH_2Cl_2 (4 ml), **18** (611.3 mg, 2.5 mmol), and 2,4,6-trimethylpyridine (0.4 ml) was added dropwise by syringe. After warming to −10°, stirring was continued for 120 h. Then, the mixture was treated with 0.5N aq. citric acid (5 ml) and warmed to r.t. The aq. phase was extracted with CH_2Cl_2 (5 ml), the combined org. layer evaporated, and the residue chromatographed (silica gel (100 g), Et_2O/hexane 3:1): **19a**/**19b** (15 fractions, together 850.2 mg, 58%). Data of the combined fractions *6–12*: CD (EtOH, 1.45 mM): 366 (−0.46), 328 (9.28), 317 (7.14), 305 (3.80), 296 (2.31), 282 (−0.78), 280 (−1.12), 269 (−2.66), 250 (2.14), 240 (4.94), 219 (−5.42), 207 (2.04). ^{1}H-NMR (400 MHz, $CDCl_3$, clearly separated signals only): 0.26 (*s*, 1.8 H); 0.77 (*s*, 1.8 H); 2.17 (*s*, 1.2 H); 2.18 (*s*, 1.8 H); 2.22–2.33 (*m*, 1 H); 2.36–2.49 (*m*, 1 H); 2.64 (*s*, 1.2 H); 2.67 (*s*, 1.8 H); 2.74 (*s*, 1.2 H); 2.76 (*s*, 1.8 H); 3.18–3.35 (*m*, 2 H); 3.60–3.85 (*m*, *ca.* 2 H); 3.87 (*s*, 3 H); 4.86 (*s*, 0.4 H); 4.95–5.00 (*q*, 0.4 H); 5.01–5.07 (*q*, 0.6 H); 5.08 (*s*, 0.6 H); 5.28 (*s*, 0.4 H); 5.39 (*s*, 0.6 H); 6.59 (*s*, 0.4 arom. H); 6.60 (*s*, 0.6 arom. H); 6.69–7.42 (*ca.* 4 arom. H); 9.80 (br. *s*, 0.4 H); 9.89 (br. *s*, 0.6 H). MS: 726 (19, $[M + 1]^+$), 725 (14, M^+), 512 (34), 484 (32), 483 (27), 339 (44), 270 (29), 184 (30), 183 (100). HR-MS: 725.2808 ($C_{37}H_{47}N_3O_8S_2^+$, calc. 725.2805).

8. **17** from **19a**/**19b**. A mixture of **19a**/**19b** (50.8 mg, 0.07 mmol from the combined fractions *6–12*), EtOH (10 ml), and 25% aq. HCl soln. (5 ml) was refluxed for 2 h and then evaporated. The residue was treated with 2N Na_2CO_3 (5 ml) and CH_2Cl_2 (5 ml), the aq. phase extracted with CH_2Cl_2 (2 × 5 ml), the combined org. layer evaporated, and the residue separated by prep. TLC (silica gel (5 mm; *Merck*), hexane/$CHCl_3$/AcOEt 3:4:1; removal of products with CH_2Cl_2/AcOEt): first **B**-H (6.5 mg, 45%), then **17** (17.8 mg, 41.5%), identical with **17** described above.

9. *Acid-Catalyzed Equilibration of* **19a**/**19b**. A soln. of **19a**/**19b** 1.9:1 (16 mg, 0.022 mmol) in AcOH (20 drops) and CF_3COOH (25 drops) was kept at r.t. for 230 h and then evaporated: **19a**/**19b** 1:2.6 (by ^{1}H-NMR). ^{1}H-NMR (300 MHz, $CDCl_3$): 5.39 (H–C(2′) of **19a**); 5.28 (H–C(2′) of **19b**).

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