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Diastereoselectivity in the hetero [4+2] cycloaddition of cyclopentadiene to *N*-benzyliminoacetyl derivatives of (2*R*)-bornane-10,2-sultam and other chiral secondary alcohols

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Abstract—Various protonated chiral glyoxyloyl-α-imino-*N*-benzyl hetero-dienophiles have been examined in the diastereoselective *exo*-cycloaddition to cyclopentadiene at −78°C promoted by $CF_3CO_2^-BF_3$, a dissociated non-nucleophilic counter ion. The best π-facial selectivities were observed with (2*R*)-bornane-10,2-sultam (76% d.e.) and (2*R*)-10-dicyclohexylsulfonamoyl-isoborneol (80% d.e.) as chiral auxiliaries. These conditions were found to be superior in terms of yields and selectivities as compared to analogous aza-dienophiles treated with simple Lewis acids or under thermal conditions. Absolute configurations were assigned on the basis of an X-ray analysis of the major cycloadduct (3′*S*)-**3a** as well as by chiroptical comparison with the corresponding new amino alcohol (−)-(3*S*)-**4a**. Plausible transition states are briefly discussed on the basis of PM3 conformational calculations.

1. Introduction

The hetero-Diels–Alder reaction of electron deficient reactive imines with 1,3-dienes is a potent tool for the synthesis of six-membered ring alkaloids,[1] carbocyclic stable ribofuranosylamines analogues[2] or prostaglandin H_1 and thromboxane A_2 antagonists.[3] This methodology, using specifically glyoxyloyl derived imines, has been further extended to the asymmetric version[4] by means of chiral catalysts,[5] chiral dienes[6] or cyclic[7]/acyclic chiral heterodienophiles.[8] In this latter case, the chiral auxiliary is usually connected either directly to the nitrogen atom, using either a chiral amino acid[9] or amine,[10] or by connection to the acyl moiety.[11] Finally, double diastereoselection combining both options was also exploited.[12] The resulting cycloadducts have utility in the preparation of unnatural amino acids[13] or chiral ligands for asymmetric reduction,[14] the transfer hydrogenation of ketones,[15] in the Kharasch–Sosnovsky reaction,[16] the addition of dialkylzinc to aldehydes and imines[17] and the rearrangement of *meso*-epoxides.[18]

When the chiral auxiliary is connected directly to the nitrogen atom, its removal is often performed by hydrogenation with sacrifice of the inducing stereogenic center and concomitant reduction of unprotected unsaturated linkages. For this reason, we recently opted for the alternative acyl substitution.[11e] Thus, when the *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam **1a**[19] was treated with tosyl isocyanate, followed by cyclopentadiene in toluene, a selectivity of 60% d.e. was observed when the cycloaddition was catalyzed by $TiCl_4$ at −78°C. The diastereoselectivity decreased to 28% d.e. of the opposite (3′*S*) diastereoisomer when the reaction was conducted at 20°C in the absence of Lewis acid. More recently, reduction with $LiAlH_4$ to the optically pure new amino alcohol (−)-(3*S*)-**4b**,[20] regenerated the (2*R*)-bornane-10,2-sultam in 95% yield.

We now wish to report the analogous reaction performed with an *N*-benzyl substituent under Stella's 1:1 mixed Brønsted/Lewis acids conditions,[10a] with comparison of several chiral auxiliaries.

2. Results

The *N*-glyoxyloyl-(2*R*)-bornane-10,2-sultam **1a** (readily obtained by ozonolysis of the corresponding *N*,*N*′-bis-fumaroyl[21] or *N*-crotonoyl[22] derivatives), was treated with benzylamine in the presence of 3 Å molecular sieves in CH_2Cl_2 at 20°C for 30 min, prior to addition of trifluoroacetic acid (1.0 mol. equiv.) and boron tri-

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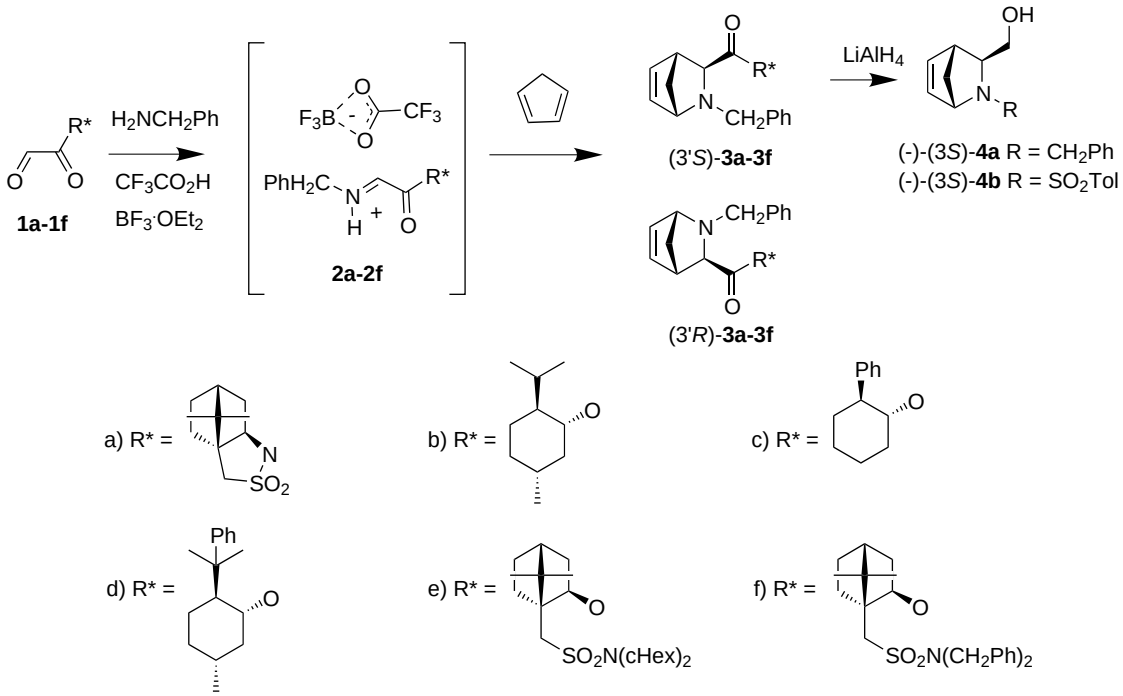


fluoride etherate (1.0 mol. equiv.) at −78°C. Subsequent addition of cyclopentadiene (1.0 mol. equiv.) to the crude heterodienophile **2a**, afforded after 5 h at −78°C a 12:88 diastereoisomeric mixture of (3′*R*)/(3′*S*)-*exo*-**3a** (76% d.e.), easily separated and isolated in 80% yield by chromatography (Table 1, entry 1).

The main cycloadduct (3′*S*)-*exo*-**3a** (Fig. 1), was recrystallized from hexane/ethyl acetate and submitted to X-ray analysis for determination of the absolute and relative (3′*S*)-*exo* configuration, prior to further $LiAlH_4$ reduction to the new optically pure amino alcohol (−)-(3*S*)-**4a**.[23] It is noteworthy that, under these conditions, the diastereoselectivity, which is not modified in toluene, is higher but opposite to that observed with $TiCl_4$.[11e]

When the known (1*R*)-menthyl glyoxylate **1b**[24] was treated under identical conditions, the π-facial selectivity only reached 42% d.e. in favor of the (3′*S*) cycloadduct **3b** as shown, after reduction, by chiroptical comparison of the corresponding alcohol (3*S*)-**4a** (entry 2). This was nevertheless encouraging with respect to the 12% d.e. reported under uncatalyzed conditions with the (−)-menthyl *N*-tosyl analogue.[11b] Replacement of the shielding *iso*-propyl moiety by a sterically more demanding phenyl substituent on the prosthetic group, by means of the known glyoxylate **1c**,[25] resulted in a slight increase in the diastereoselectivity to 53% d.e. (entry 3), while 70% d.e. was obtained when the known and more efficient (1*R*)-8-phenylmenthyl glyoxylate **1d**[26] generated the aza-dienophile **2d** (entry 4). This last result is to be compared with the 76% d.e. observed under analogous Stella's conditions by Garcia-Mera et al.,[11f] as well as the 20% d.e. reported under uncatalyzed addition for the (−)-8-phenylmenthyl *N*-tosyl analogue.[11b]

The best π-facial selectivity, reaching 80% d.e., was obtained with the known glyoxylate **1e**,[27] prepared from the commercially available isoborneol-derived dicyclohexyl sulfonamide[28] (entry 5). Comparatively, the sterically and conformationally less constrained dibenzyl analogue, developed by Yamamoto,[29] was slightly less efficient and afforded (3′*S*)-**3f** in 85% isolated yield with 72% d.e. (entry 6).

Table 1.

Entry	Dienophile	Isolated yield (%)	(3′*R*)-**3a**–**3f**/(3′*S*)-**3a**–**3f**
1	**2a**	80	12:88
2	**2b**	75	29:71
3	**2c**	78	23:77
4	**2d**	80	15:85
5	**2e**	82	10:90
6	**2f**	85	14:86

3. Discussion

The very high *exo*-selectivity resulting from this type of aza-Diels–Alder reaction was earlier explained on the basis of minimized hydrophobic interactions in aqueous or wet solvents[9,30] or greater second order orbital electronic requirements of the *N*-withdrawing group.[2b] With respect to the hetero-dienophile **2a**, all attempts to calculate the different concerted transition states at the PM3 level were unsuccessful.[31] This suggests either a highly asynchronous mechanism[32] or a different mechanistic pathway, such as, for example, a stepwise Mannich type reaction.[33] Thus, these reversible steps could partially account for a thermodynamic control of the more stable *exo*-stereoisomers. In view of this ambiguity, we restrained our calculations to the conformational stability and reactivity of (2*R*)-**2a** (Table 2).

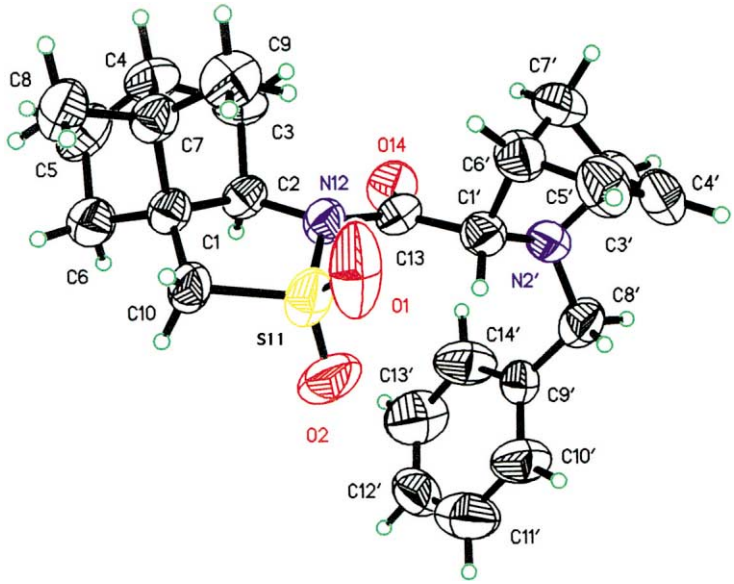


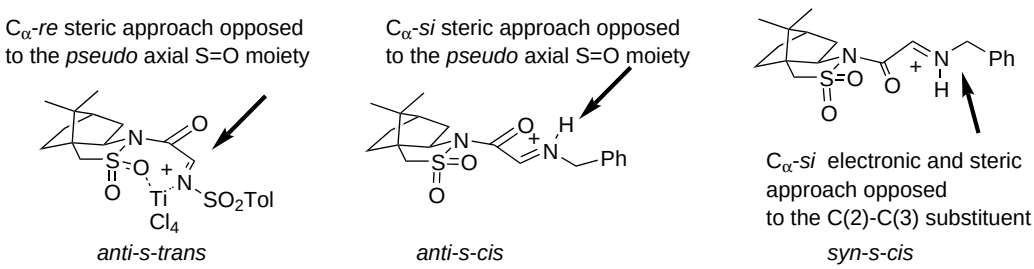
Figure 1. ORTEP diagram of (3′*S*)-*exo*-**3a** with arbitrary atom numbering. Ellipsoids are represented at the 40% probability level.

Table 2.

(2*R*)-**2a**	ΔH_{form} (kcal mol^{-1})	LUMO (eV)	S–N–C=O (°)	C_α-*re* at coef	N_β-*re* at coef	C_α-*si* at coef	N_β-*si* at coef
syn-s-trans	105.73	−5.89	−48.0	0.35	−0.36	−0.33	0.38
syn-s-cis	94.95	−5.94	−11.5	−0.31	0.36	0.33	−0.35
anti-s-cis	90.12	−5.80	163.0	0.35	−0.40	−0.34	0.39
anti-s-trans	88.60	−5.51	140.5	−0.33	0.35	0.34	−0.32

The *anti-s-trans* conformer **2a** is thermodynamically the most stable conformer as a consequence of an intramolecular H-bond between the H–N$^+$ atom and the *pseudo* equatorial S=O group. It follows that the π-system of the reactive O=C–C=N moiety is not fully aligned with the SO_2–N lone pair as shown by the strong deviation of the S–N–C=O dihedral angle (140.5°).[34] This results in a lower reactivity as shown by both the highest LUMO level (−5.51 eV) and the smallest global sum of the square of the C_α–N_β atomic coefficients,[34] as compared to the three other considered coplanar conformations. In contrast, the *syn-s-trans* conformer is (by far) too high in energy to statistically enter into consideration. As a consequence, the most reactive coplanar species are the *syn-s-cis* conformer **2a**, as expressed by its low LUMO level, as well as the thermodynamically more stable *anti-s-cis* conformer, which possesses the greatest global sum of the square of the C_α–N_β atomic coefficients. Independently from a concerted/non-concerted mechanism, we thus rationalize the main (3′*S*)-**3a** formation, either by a steric approach on the C_α-*si* face of the *anti-s-cis* conformer[35] and/or by a cumulative steric and electronic approach on the C_α-*si* face of the *syn-s-cis* conformer.[34] Indeed, as expressed by the sum of the square of the specific C_α–N_β atomic π-facial coefficients, the preferred electronic approach is opposite to the steric one in the case of the *anti-s-cis* conformer, as already earlier observed for analogous homo-[34] and hetero-dienophiles.[36]

In the case of the secondary alcohols **2b**–**2f** as cycloaddition control elements, Oppolzer earlier proposed,[37] supported by a recent X-ray analysis,[11f] that the most favorable conformation is reached when the alkoxy C–H bond is *syn*-periplanar with the C=O moiety of the ester. As a consequence, all these prosthetic groups possess an identical sterically induced C_α-*si* topicity, when the (*E*) C=N$^+$ bond is *s-cis* with that of the C=O. PM3 calculations confirmed the thermodynamic stability and higher reactivity of the *s-cis* over the *s-trans*



conformers (Table 3). Despite the fact that the N^+–H and C=O bonds are parallel, an intramolecular weak hydrogen bond character with the carbonyl moiety is not excluded and could partially account for this conformational stability/reactivity.

4. Conclusion

The [4+2]-cycloadditions of chiral glyoxyloyl derived α-imino-dienophiles to cyclopentadiene promoted by Stella's 1:1 $CF_3CO_2H/BF_3{\cdot}Et_2O$ conditions are superior in terms of diastereoselectivity and chemical yield when compared to the corresponding Lewis acids or thermal conditions reported for analogous aza-Diels–Alder reactions. The resulting cycloadducts are of considerable interest in medicinal chemistry as valuable starting materials for the straightforward synthesis of aristeromycin,[11b] amidomycin,[38] carbovir NCS614846[39] and are prone to further specific chemical/skeletal transformations.[40] Acyclic dienes may also open access to MQPA thrombin inhibitor,[41] streptolutin[42] or carpamic acid.[43] Finally, both antipodes of the most efficient cyclic or acyclic camphor derived sulfonamide auxiliaries are commercially available and readily recovered.

5. Experimental

5.1. General

See Ref. 44

5.2. X-Ray structure determination of (3′*S*)-3a

Suitable crystals were grown from a hexane/AcOEt soln. The measurements were run on a Nonius MACH3 diffractometer using Express softpress software, without absorption corrections. Table 4 shows details of the data collection and refinement and Table 5 shows selected bond lengths and angles. In the final steps of the least-squares procedure, all but Me group H-atoms were kept fixed at their calculated positions. The structures were solved by the SHELXS-86[45] and refined with the SHELXL-93[46] programs. The known configuration of the asymmetric centers of the sultam unit has been confirmed by the Flack parameter refinement.[47] Lists of the fractional atomic coordinates, isotropic thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre as supplementary material (3′*S*)-**3a** reg. no CCDC 164399.

5.3. General procedure for the cycloaddition reactions

Benzylamine (321 mg, 0.33 mL, 3.0 mmol) was added at 0°C to a suspension of glyoxyloyl derivative **1** (3.0 mmol) and molecular sieves (3 Å, 0.6 g) in CH_2Cl_2 (6 mL). After 30 min the flask was cooled to −78°C and CF_3CO_2H (342 mg, 0.23 mL, 3.0 mmol) and $BF_3{\cdot}OEt_2$ (426 mg, 0.38 mL, 3.0 mmol) were added dropwise, followed by a solution of cyclopentadiene in CH_2Cl_2 (1 M, 3.0 mL, 3.0 mmol). After 5 h at −78°C, the reaction was quenched by addition of satd aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2, washed to

Table 4. Crystal data and structure refinement for (3′*S*)-**3a**

Identification code	(3′*S*)-**3a**
Empirical formula	$C_{24}H_{30}N_2O_3S$
Formula weight	426.56
Temperature (K)	293(2)
Wavelength (Å)	1.54178
Crystal system, space group	Monoclinic, C_2
Unit cell dimensions	
a (Å)	22.882(5)
b (Å)	8.237 (2), 125.80(3) (°)
c (Å)	14.002(3)
Volume (Å^3)	2140.5(8)
Z, Calculated density (Mg/m^3)	4, 1.324
Absorption coefficient (mm^{-1})	1.571
F(000)	912
Crystal size (mm)	$0.14\times0.21\times0.54$
θ-Range for data collection (°)	3.89–78.94
Index ranges	$-23\le h\le28$, $0\le k\le10$, $-17\le l\le0$
Reflections collected/unique	1595/1530 [$R_{int}=0.0394$]
Refinement method	Full-matrix least-squares on F_2
Data/restraints/parameters	1530/1/272
Goodness-of-fit on F_2	1.051
Final *R* indices [$I>2\sigma(I)$]	$R_1=0.0576$, $wR_2=0.1352$
R indices (all data)	$R_1=0.0666$, $wR_2=0.1436$
Absolute structure parameter	0.00(5)
Extinction coefficient	0.0033(5)
Largest diff. peak and hole (e Å^{-3})	0.337 and −0.212

Table 5. Selected bond lengths (Å) and angles (°)

S(11)–O(1)	1.424(7)
S(11)–O(2)	1.381(7)
S(11)–N(12)	1.665(6)
O(2)–S(11)–O(1)	117.3(5)
C(2)–N(12)–S(11)	111.1(5)
C(2)–N(12)–C(13)	117.9(6)
C(13)–N(12)–S(11)	124.3(5)
S(11)–N(12)–C(13)–O(14)	151.9(6)
Δ*h*N(12)	0.225(5)

Table 3.

O=C–C=N$^+$	**2b**	**2c**	**2d**	**2e**	**2f**
s-*trans* Δ*H* (kcal mol^{-1})	85.06	133.51	116.21	6.74	101.87
s-*trans* LUMO (ev)	−6.16	−6.10	−5.96	−5.31	−5.26
s-*cis* Δ*H* (kcal mol^{-1})	83.78	132.10	115.87	6.70	99.30
s-*cis* LUMO (eV)	−6.17	−6.12	−6.01	−5.37	−5.26

neutrality with brine, dried, evaporated and the residue purified by chromatography (see Table 1 for yields). The main cycloadducts were further purified by crystallization.

5.4. Cycloadduct (3′*S*)-3a

Mp 151–152°C; $[\alpha]_D$ −155.5 ($c=0.31$, $CHCl_3$); IR: 3447; 3096; 2992; 2964; 2917; 2864; 1698; 1483; 1442; 1406; 1328; 1274; 1248; 1213; 1127; 1103; 1057; 902; 892; 776; 754; 738. ^{1}H NMR: 0.96 (s 3H); 1.17 (s 1H); 1.26–1.39 (m 3H); 1.68 (s 1H); 1.85–2.07 (m 7H); 3.01 (s 1H); 3.12 (s 1H); 3.43 (d 2H); 3.50 (d 2H); 3.80–3.88 (m 2H); 6.27–6.31 (m 1H); 6.52–6.57 (m 1H); 7.21–7.39 (m 5H). ^{13}C NMR: 20.1; 20.4; 21.0; 26.6; 32.9; 38.6; 44.7; 45.5; 47.7; 50.9; 53.2; 58.6; 64.4; 65.4; 66.7; 74.2; 127.1; 128.3; 129.4; 134.4; 136.9; 163.2. LSIMS HR calculated for $C_{24}H_{30}N_2O_3S^+$: 426.1977, obtained 426.1977. Elem. anal. calculated: C, 67.61%; H, 7.04%; N, 6.57% obtained C, 67.01%; H, 7.25%; N, 6.42%.

5.5. Cycloadduct (3′*S*)-3b

IR: 3401; 3085; 3028; 2978; 2922; 2876; 1744; 1506; 1457; 1388; 1376; 1309; 1246; 1168; 1138; 1106; 1091; 1022; 984; 921; 875; 772; 752; 701. ^{1}H NMR: 0.62–0.94 (m 12H); 0.96–2.05 (m 7H); 2.28 (s 0.29H); 2.29 (s 0.71H); 3.04 (s 1H); 3.49 (qAB 0.29H); 3.52 (qAB 0.71H); 3.86 (d 0.29H); 3.90 (d 0.71H); 4.55–4.70 (m 1H); 4.83–4.96 (m 2H); 6.22–6.25 (m 1H); 6.45–6.49 (m 1H); 7.20–7.37 (m 5H). ^{13}C NMR: 16.2; 16.5;21.0; 22.2; 22.1; 23.3; 26.4; 34.3; 34.4; 40.8; 40.8; 41.0; 46.7; 47.1; 47.2; 48.9; 59.2; 64.6; 65.1; 74.3; 76.1; 127.1; 128.3; 128.3; 128.8; 129.1; 129.2; 133.8; 136.6; 154.8; 159.3. LSIMS HR calculated for $C_{24}H_{33}NO_2^+$: 367.2511, found 367.2518.

5.6. Cycloadduct (3′*S*)-3c

IR: 3449; 3063; 2986; 2937; 2857; 1739; 1708; 1601; 1493; 1447; 1380; 1324; 1235; 1191; 1170; 1112; 1025; 909; 856; 761; 740. ^{1}H NMR: 1.04–1.08 (d 1H); 1.11–1.63 (m 6H); 1.71–1.92 (m 4H); 2.01 (s 0.77H); 2.04 (s 0.23H); 2.20 (s 1H); 2.58 (dt 1H); 3.10–3.39 (qAB 0.23H); 3.21–3.53 (qAB 0.77H); 3.67 (d 0.23H); 3.73 (d 0.77H); 4.90–5.04 (dt 1H); 6.05–6.13 (m 1H); 6.23–6.33 (m 1H); 7.09–7.31 (m 10H). ^{13}C NMR: 24.9; 26.0; 32.2; 32.3; 34.2; 34.6; 46.3; 48.5; 48.9; 49.9; 50.2; 58.7; 58.8; 64.0; 64.3; 64.8; 65.6; 75.6; 76.1; 126.5; 127.0; 127.6; 127.7; 128.2; 128.2; 128.3; 129.1; 129.2; 133.2; 133.6; 136.6; 136.7; 139.3; 143.3; 173.1. LSIMS HR calculated for $C_{26}H_{29}NO_2^+$: 387.2193, obtained 387.2185.

5.7. Cycloadduct (3′*S*)-3d

IR: 3444; 3059; 2956; 2924; 2801; 1735; 1599; 1495; 1454; 1365; 1325; 1234; 1187; 1161; 1094; 999; 905; 863; 766; 736. ^{1}H NMR: 0.76–0.99 (m 6H); 1.08 (s 3H); 1.10 (s 3H); 1.17–1.62 (m 7H); 1.78–2.05 (m 3H); 2.79 (s 0.85H); 2.88 (s 0.15H); 3.28–3.63 (m 2H); 3.71 (d 0.15H); 3.87 (d 0.85H); 4.68–4.83 (m 1H); 6.14–6.23 (m 1H); 6.34–6.38 (m 1H); 7.13–7.42 (m 10H). ^{13}C NMR: 22.0; 26.3; 28.0; 31.4; 34.8; 39.9; 41.6; 46.4; 47.2; 49.0; 50.5; 59.2; 63.6; 64.7; 65.3; 74.5; 74.8; 125.2; 125.6; 127.2; 128.1; 128.4; 129.2; 129.3; 133.7; 133.9; 136.6; 151.8; 172.9; 177.4. LSIMS HR calculated for $C_{30}H_{38}NO_2H^+$: 444.2903, obtained 444.2867.

5.8. Cycloadduct (3′*S*)-3e

IR: 3443; 3062; 2936; 2857; 1731; 1494; 1453; 1393; 1324; 1235; 1167; 1144; 1109; 1050; 982; 894; 845; 774; 745. ^{1}H NMR: 0.79–0.82 (m 2H); 0.90 (s 3H); 1.05 (s 3H); 1.05–1.35 (m 8H); 1.53–2.06 (m 20H); 2.35 (s 0.10H); 2.38 (s 0.90H); 2.56–2.62 (d 0.10H); 2.65–2.71 (d 0.90H); 3.14–3.33 (m 4H); 3.69–3.76 (m 2H); 4.82–4.88 (dd 0.1H); 4.93–4.98 (dd 0.90H); 6.17–6.25 (m 1H); 6.45–6.49 (m 1H); 7.16–7.43 (m 5H). ^{13}C NMR: 20.5; 20.7; 25.4; 26.7; 27.2; 30.8; 32.8; 33.2; 40.0; 44.7; 46.9; 48.3; 49.4; 49.7; 54.1; 57.7; 58.7; 63.0; 66.3; 79.0; 127.1; 128.4; 129.2; 133.5; 136.7; 139.4; 170.7. LSIMS HR calculated for $C_{36}H_{52}N_2O_4S^+$: 608.3647, obtained 608.3666. Elem. anal. calculated: C, 71.05%; H, 8.55%; N, 4.61%; S, 5.26%; obtained C, 71.02%; H, 8.48%; N, 4.57%; S, 4.67%.

5.9. Cycloadduct (3′*S*)-3f

IR: 3442; 3062; 2953; 2881; 1721; 1604; 1495; 1455; 1335; 1247; 1148; 1052; 1028; 941; 894; 847; 790; 750; 700. ^{1}H NMR: 0.77–0.93 (m 2H); 0.80 (s 3H); 1.01 (s 3H); 1.04–1.31 (m 4H); 1.60–1.75 (m 5H); 1.90–2.05 (m 2H); 2.29 (s 1H); 2.51–2.57 (d 1H); 3.12 (s 0.28H); 3.19 (s 1.72H); 3.41–3.63 (qAB 2H); 3.42 (s 0.14); 3.43 (s 0.86H); 5.00–5.05 (dd 1H); 6.07–6.11 (dd 1H); 6.36–6.41 (m 1H); 2.19–2.34 (m 15H). ^{13}C NMR: 20.5; 27.3; 30.4; 39.7; 44.6; 46.8; 48.2; 49.4; 49.9; 51.2; 58.9; 63.0; 66.3; 78.7; 127.2; 128.1; 128.4; 128.8; 129.0; 129.4; 133.3; 133.6; 136.2; 136.8; 169.7. LSIMS HR calculated for $C_{38}H_{44}N_2O_4S^+$: 624.3021, obtained 624.3011. Elem. anal. calculated C, 73.08%; H, 7.05%; N, 4.49%, obtained C, 72.67%; H, 7.28%; N, 4.10%.

5.10. (1*S*)-2-Benzyl-2-aza-bicyclo[2.2.1]hept-5-en-(3*S*)-yl-methanol (3*S*)-4a

A solution of cycloadduct (3′*S*)-**3a** (213 mg, 0.5 mmol) in dry THF (2.5 mL) was added dropwise to a suspension of $LiAlH_4$ (17 mg, 0.5 mmol) in dry THF (2.5 mL). After 30 min at 20°C, the reaction was quenched with H_2O, the mixture was extracted with THF, dried and evaporated to afford after chromatographic purification both (3*S*)-**4a** and the (2*R*)-bornane-10,2-sultam in 95% respective yields. $[\alpha]_D^{20}$ −6.8 (*c* 1.02; $CHCl_3$). IR: 3369; 3061; 2985; 2871; 1673; 1604; 1565; 1495; 1454; 1368; 1324; 1264; 1189; 1078; 1029; 911; 834; 768; 747. ^{1}H NMR: 1.25–1.29 (d 1H); 1.67–1.72 (d 1H); 1.83 (t 1H); 2.18 (s 1H); 2.69 (d 1H); 3.31–3.45 (m 5H); 3.69 (d 1H); 6.10–6.14 (m 1H); 6.41–6.45 (m 1H); 2.16–2.28 (m 5H). ^{13}C NMR: 34.4; 46; 47.1; 59.1; 64.2; 64.6; 65.4; 73.2; 127.3; 128.6; 129.2; 132.6; 138.0; 140.0. LSIMS HR calculated for $C_{14}H_{18}NO^+$: 216.1383, obtained 216.1363.

5.11. (1*S*)-2-(Toluene-4-sulfonyl)-2-aza-bicyclo[2.2.1]-hept-5-en-(3*S*)-yl-methanol (3*S*)-4b

Obtained similarly to (3*S*)-**4a** from the corresponding cycloadduct[11e] in 95% yield. $[\alpha]_D^{20}$ −4.8 (*c* 1.02; $CHCl_3$).

IR: 3448; 3410; 3061; 2957; 2891; 1595; 1494; 1402; 1343; 1322; 1251; 1158; 1092; 1040; 1014; 892; 815; 755; 723. ^{1}H NMR: 1.40–1.45 (d 1H); 1.81–1.85 (d 1H); 2.42 (s 3H); 2.79 (t 1H); 2.99 (s 1H); 3.23–3.29 (dd 1H); 3.67–3.80 (m 1H); 3.92–4.032 (m 1H); 4.63 (d 1H); 5.73–5.77 (dd 1H); 6.01–6.06 (m 1H); 7.24–7.66 (dd 4H). ^{13}C NMR: 21.7; 46.4; 47.1; 60.2; 61.0; 65.6; 66.8; 71.2; 128.3; 129.7; 133.9; 135.3; 137.2; 143.9. LSIMS HR calculated for $C_{14}H_{17}NO_3SNa^+$: 302.0835, obtained 302.0821. Elem. anal. calculated C, 60.21%; H, 6.09%; N, 5.02%; S, 11.47%; obtained C, 60.04%; H, 6.33%; N, 4.82%; S, 11.21%.

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