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Tetrahedron Letters 49 (2008) 2902–2906
Tetrahedron Letters

Synthesis of optically enriched 1,2-aminoalcohols by [2,3]-Wittig rearrangements of 3-aza-allylic alcohol derivatives

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Received 15 January 2008; revised 5 March 2008; accepted 5 March 2008
Available online 8 March 2008

Abstract

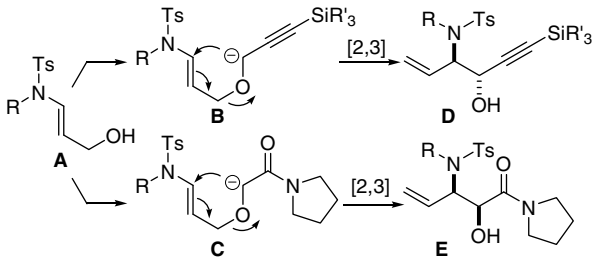
[2,3]-Wittig rearrangements of (*E*)-3-aza-allylic alcohol derivatives can provide access to *syn* or *anti* optically enriched 1,2-aminoalcohols by using a chirality transfer or a chiral auxiliary.

Keywords: 1,2-Aminoalcohols; Enamides; [2,3]-Wittig rearrangement; Diastereoselectivity; Chirality transfer

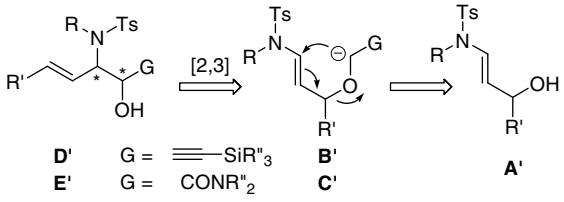
The [2,3]-Wittig sigmatropic rearrangement is a useful tool in organic synthesis that offers many opportunities for stereochemical control.[1,2] We have recently reported that propargylic ethers of type **B** or amides of type **C**, derived from the readily available (*E*)-3-aza-allylic alcohols **A**, underwent diastereoselective [2,3]-Wittig rearrangements that led to functionalized *anti* or *syn* 1,2-aminoalcohols of types **D** and **E**, respectively (Scheme 1).[3]

Optically active 1,2-aminoalcohols constitute a widespread structural feature in natural products and/or biologically active compounds and are often used as key building blocks for the preparation of chiral catalysts.[4,5] Therefore, the control of the absolute configuration of the two newly heterosubstituted stereocenters, created during the [2,3]-Wittig rearrangement of 3-aza-allylic alcohol derivatives, appeared to be an interesting issue to consider. To achieve this goal, it was first planned to synthesize 1,2-amino-alcohols of general formula **D′** or **E′**, by [2,3]-Wittig rearrangement of the propargylic ethers **B′** or amides **C′**, respectively, derived from secondary 3-aza-allylic alcohols of type **A′**. Indeed, a chirality transfer may enable to control the absolute configuration of the adjacent stereocenters in 1,2-aminoalcohols **D′** or **E′**, while creating at the same time a disubstituted alkene (Scheme 2).

Secondary (*E*)-3-aza-allylic alcohols of type **A′** are readily accessible according to a stereoselective route previously developed.[3] Thus, the protection of but-3-yn-2-ol (**1**) as a



Scheme 1. [2,3]-Wittig rearrangement of derivatives of (*E*)-3-aza-allylic alcohols **A**.



Scheme 2. [2,3]-Wittig rearrangement with chirality transfer from secondary (*E*)-3-aza-allylic alcohols of type **A′**.

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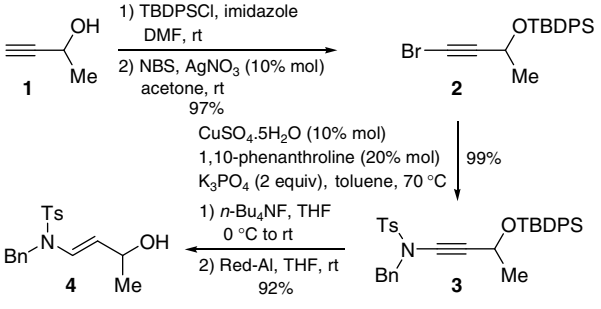
0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.03.023

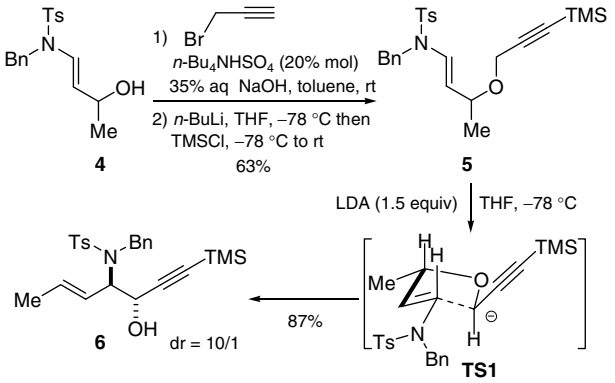
silyl ether (TBDPSCl, imidazole, DMF) and bromination of the terminal alkyne (NBS, cat. $AgNO_3$, acetone) led to the acetylenic bromide **2** (97%, 2 steps from **1**). The latter compound underwent a copper-catalyzed cross-coupling with *N*-benzylsulfonamide ($CuSO_4{\cdot}5H_2O$ (10% mol), 1,10-phenanthroline (20% mol), K_3PO_4 (2 equiv), toluene, 70 °C) to produce the disubstituted ynamide **3** (99%).[6] Subsequent deprotection of the alcohol (*n*-Bu_4NF, THF) and hydroalumination (Red-Al, THF) afforded alcohol **4** (92%, 2 steps from **3**) (Scheme 3).

The stereoselectivity of the [2,3]-Wittig rearrangement of the secondary propargylic ether **5** prepared in two steps from alcohol **4** ($HC{\equiv}CCH_2Br$, cat. *n*-Bu_4NHSO_4, 35% aq NaOH, toluene; *n*-BuLi, THF, −78 °C then TMSCl, 63%) was first examined. Upon treatment with LDA (1.5 equiv, THF, −78 °C), compound **5** underwent a diastereoselective [2,3]-Wittig rearrangement and the *anti*-1,2-aminoalcohol **6** was isolated in 87% yield (dr = 10/1). The configuration of the disubstituted alkene in **6** was readily assigned to (*E*) by ^1H NMR, and the *anti* relationship between the amino and the hydroxyl groups was confirmed by a chemical correlation.[7] The stereochemical outcome could be rationalized by considering a five-membered ring transition state of envelope conformation **TS1** in which the trimethylsilylethynyl group occupies an *exo* position whereas the methyl group preferentially adopts a pseudo-equatorial (*endo*) position (Scheme 4).[8]

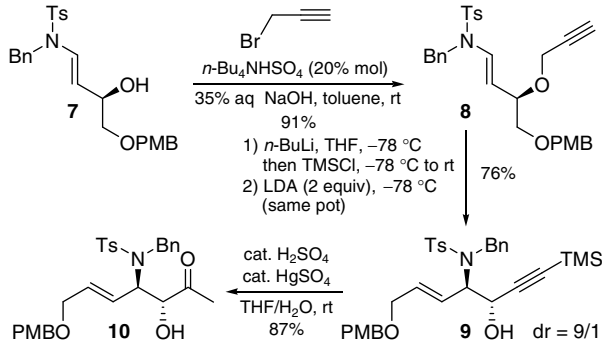
As the [2,3]-Wittig rearrangements of propargylic ethers of type **B′** proceed with a satisfactory level of diastereoselectivity, the stage was set to evaluate absolute chirality transfer. The optically active secondary alcohol **7** (ee ⩾ 98%)[9] was converted to propargylic ether **8** by alkylation with propargyl bromide (91%). However, after silylation of the terminal alkyne (*n*-BuLi, THF then TMSCl, −78 °C to rt), the resulting propargylic ether turned out to be unstable. To avoid isolation of this compound, the [2,3]-Wittig rearrangement was carried out in the same pot by the addition of LDA. A satisfactory level of diastereoselection (dr = 9/1) was observed and 1,2-aminoalcohol **9** was isolated in 76% yield (2 steps from **8**). The enantiomeric purity of **9** was determined to be >95%.[10] Moreover, the alkyne in compound **9** underwent hydration (cat. H_2SO_4, cat. $HgSO_4$, THF/H_2O)[11] to afford methyl ketone **10** (87%) without epimerization (Scheme 5).



Scheme 3.

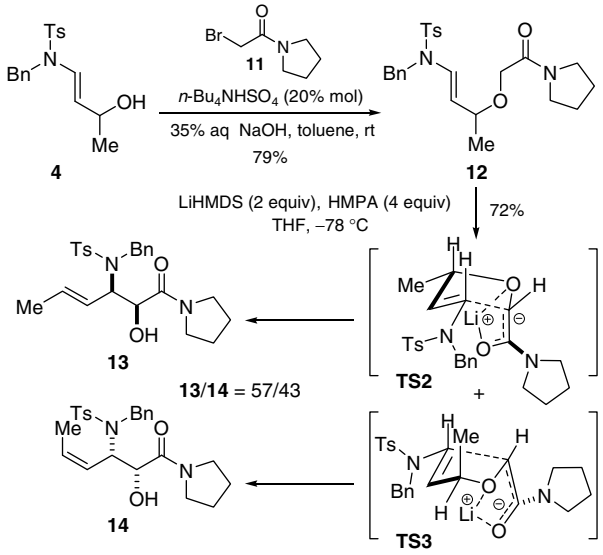


Scheme 4.



Scheme 5.

The behavior of amides of type **C′** was next examined. Compound **4** was alkylated with *N*-(bromoacetyl)-pyrrolidine (**11**) to afford amide **12** (79%). The latter compound smoothly underwent [2,3]-Wittig rearrangement by treatment with LiHMDS (2 equiv) in the presence of HMPA (4 equiv) as an additive (THF, −78 °C).[3] Unfortunately, the reaction led to a mixture of the diastereomeric α-hydroxy-β-aminoamides **13** and **14** in an almost stereorandom fashion (**13**/**14** = 57/43, 72%). The configuration of the double bond in compounds **13** and **14** was assigned to (*E*) and (*Z*), respectively, by ^1H NMR and a chemical correlation established the *syn* relative orientation of the amino and hydroxyl groups in both compounds.[12] The high *syn* diastereoselectivity of the Wittig rearrangement of amides of type **C** has been explained by the more favorable *endo* orientation of the π-acceptor carboxamide moiety in the envelope-like five-membered ring transition state, due to secondary orbital overlap or electrostatic interactions with the negatively charged olefinic moiety.[8] Whereas transition state **TS2** leading to **13**, having the allylic methyl group in an *endo* position, is destabilized by steric interactions with the *endo* carboxamide group (further enhanced by lithium chelation), the alternative transition state **TS3** leading to **14**, wherein the methyl group lies in the *exo* position, is destabilized due to interaction between the methyl group and the vinylic hydrogen close in space.[8] Thus, no net stereochemical preference is

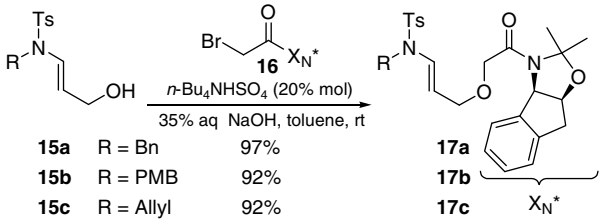


Scheme 6.

observed during the [2,3]-Wittig rearrangement of amide **12** and the α-hydroxy-β-amino-amides **13** and **14**, resulting from opposite π-facial selectivities, are obtained. Therefore, an efficient diastereoselective chirality transfer could not be achieved for such substrates (Scheme 6).

In order to control the absolute configuration of the two newly created heterosubstituted stereocenters in the [2,3]-Wittig rearrangement of amides derived from 3-aza-allylic alcohols of type **A**, a covalently bond chiral auxiliary could be used. Thus, the primary 3-aza-allylic alcohols **15a**–**c**[3] were alkylated under phase-transfer catalysis conditions, in the presence of the *N*-(bromoacetyl)amide **16**, derived from optically active (1*R*,2*S*)-1-aminoindan-2-ol[13,14] to afford amides **17a**–**c** (92–97%) (Scheme 7).

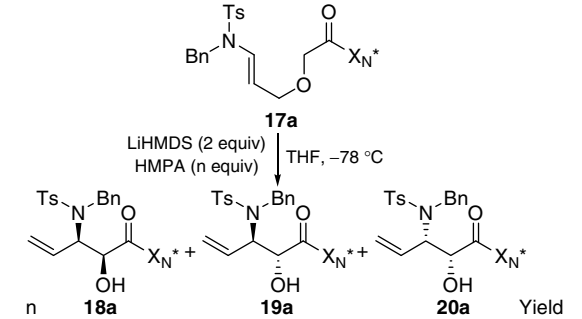
Optimization of the reaction conditions for the [2,3]-Wittig rearrangement was first carried out with substrate **17a**. Under our standard conditions (LiHMDS (2 equiv), HMPA (4 equiv), THF, −78 °C),[3] a mixture of the diastereomeric amides **18a**, **19a**, and **20a** was generated in a 79/17/4 ratio (69%). The structure of **18a** was unambiguously fully established by chemical correlations, and the relative orientation of the hydroxyl and amino groups was found to be *anti* in the first minor diastereomer **19a**.[15,16] Assuming that the π-facial bias exerted by the chiral auxiliary was responsible for the formation of both diastereomers **18a** and **19a**, the problem was to improve the 1,2-*syn* diastereoselectivity. As we had previously observed that



Scheme 7.

the presence of HMPA dramatically improved the *syn* diastereoselectivity of [2,3]-Wittig rearrangements of amides of type **C**,[3] the effect of the quantity of this additive was investigated. In the absence of HMPA, the reaction has to be run at a higher temperature (−40 °C to 0 °C) and we confirmed that a poor *syn*/*anti* ratio was observed (**18a**/**19a**/**20a** = 42/54/4) while the *anti* diastereomer **19a** was predominantly obtained. Gratifyingly, raising the quantity of HMPA from 4 to 10 equiv substantially reduced the amount of the *anti* diastereomer **19a** (**18a**/**19a**/**20a** = 88/6/6) whereas the use of a larger amount (30 equiv) again had a slightly beneficial influence and the ratio of **18a**/(**19a**+**20a**) finally reached 90/10 (Scheme 8).

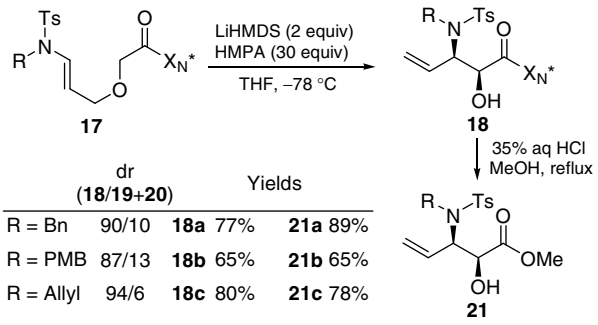
Under these optimized conditions, the major diastereomer **18a** (dr ⩾ 95/5) could be isolated in 77% yield. Similarly, the other amides **17b** and **17c** underwent [2,3]-Wittig rearrangement with satisfactory levels of diastereoselection (dr = 87/13 and 94/6) and the *syn* α-hydroxy-β-amino-amides **18b** and **18c** (dr ⩾ 95/5) were isolated in 65% and 80% yields, respectively. Subsequent cleavage of the chiral auxiliary was achieved by acidic methanolysis (35% aq HCl/MeOH, reflux)[14] and led to the methyl esters **21a**–**c** in good yields (65–89%), without alteration of the diastereomeric purity, whereas 1-aminoindan-2-ol could be recovered (70–80%) (Scheme 9).



n	18a	19a	20a	Yield
0*	42	54	4	66%
4	79	17	4	69%
10	88	6	6	89%
30	90	5	5	83%

* The reaction was run from –40 °C to 0 °C

Scheme 8.



	dr (18/19+20)		Yields		
R = Bn	90/10	**18a**	77%	**21a**	89%
R = PMB	87/13	**18b**	65%	**21b**	65%
R = Allyl	94/6	**18c**	80%	**21c**	78%

Scheme 9.

We have shown that the [2,3]-Wittig rearrangement of substituted 3-aza-allylic alcohol derivatives can provide access to functionalized enantiomerically enriched 1,2-aminoalcohols either by a chirality transfer[17] or by using a chiral auxiliary.[18–20] Applications of this methodology to natural and/or biologically active compounds will be examined.

Acknowledgments

Financial support from Glaxo-Smithkline and the CNRS (BDI grant to M.B.) is gratefully acknowledged.

References and notes

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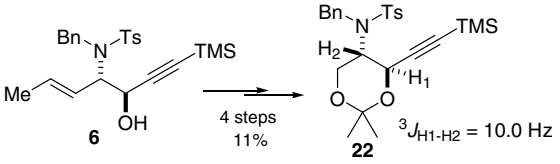
7. Compound **6** was converted to acetonide **22** and the coupling constant value between H1 and H2 ($^3J_{H1-H2} = 10.0$ Hz) was used to assign the relative configuration.



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9. Alcohol **7** was synthesized according to the sequence depicted in Scheme 3 (5 steps, 79% overall yield) from the corresponding propargylic alcohol (ee ⩾ 98%). For the preparation of the latter alcohol, see: Yadav, J. S.; Chander, M. C.; Joshi, B. V. *Tetrahedron Lett.* **1988**, *29*, 2737–2740.
10. The enantiomeric purity and absolute configuration of **9** were determined by analysis of the ^{1}H NMR spectra of the corresponding crude diastereomeric (*R*)- and (*S*)-*O*-methyl-mandelates, see: Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370–2374.
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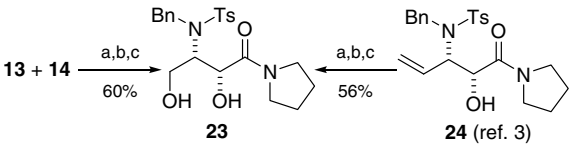
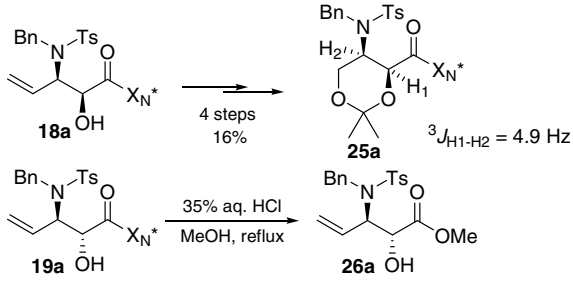
12. The mixture of **13**+**14** and the *syn*-2-amino-1,3-diol **24** was independently converted to the same *syn*-α-hydroxy-β-aminoamide **23**[3] by the same sequence.

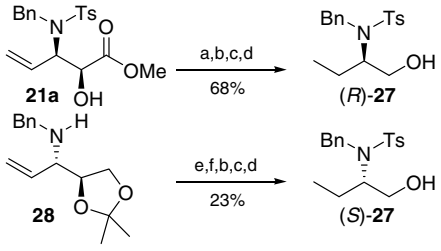


Reagents and conditions: (a) O_3, MeOH/CH_2Cl_2, –78 °C; (b) PPh_3, –78 °C to rt; (c) $NaBH_4$, MeOH, rt.

13. Amide **16** was prepared from (1*R*,2*S*)-1-aminoindan-2-ol (86%) by acylation with bromoacetyl bromide (Et_3N, THF, 45 °C) and ketalization (2-methoxypropene, MsOH, 50 °C), see: Song, Z. J.; Zhao, M.; Desmond, R.; Devine, P.; Tschaen, D. M.; Tillyer, R.; Frey, L.; Heid, R.; Xu, F.; Foster, B.; Li, J.; Reamer, R.; Volante, R.; Grabowski, E. J. J.; Dolling, U. H.; Reider, P. J.; Okada, S.; Kato, Y.; Mano, E. *J. Org. Chem.* **1999**, *64*, 9658–9667.
14. Kress, M. H.; Yang, C.; Yasuda, N.; Grabowski, E. J. J. *Tetrahedron Lett.* **1997**, *38*, 2633–2636.
15. Amide **18a** was converted to acetonide **25a** and the coupling constant value between H1 and H2 ($^3J_{H1-H2} = 4.9$ Hz) was used to assign the relative configuration. Acidic methanolysis of **19a** afforded the methyl ester **26a**, a diastereomer of **21a**.



16. A chemical correlation was used to assign the absolute configuration of **21a** involving its conversion to the optically active sulfonamide (*R*)-**27**. In parallel, the known amine **28** was transformed to sulfonamide (*S*)-**27**. For the preparation of **28** from D-glyceraldehyde acetonide, see: Badorrey, R.; Cativiela, C.; Díaz-de-Villegas, M. D.; Gálvez, J. A. *Synthesis* **1997**, 747–749.



Reagents and conditions: (a) DIBAL-H, CH_2Cl_2, –78 °C; (b) H_2, cat. Pd/C, EtOH, rt; (c) $NaIO_4$, THF/H_2O, rt; (d) $NaBH_4$, MeOH, rt; e) TsCl, Pyr, rt; f) 80% aq AcOH, 80 °C.

17. *N-Benzyl-N-[(E)-(R)-1-((S)-1-hydroxy-3-trimethylsilanyl-prop-2-ynyl)-4-(4-methoxybenzyloxy)but-2-enyl]-4-methylbenzenesulfonamide* (**9**). To a solution of propargylic ether **8** (419 mg, 0.829 mmol) in THF (10 mL) at −78 °C was added dropwise *n*-BuLi (500 μL, 2.5 M in hexanes, 1.25 mmol, 1.5 equiv). After 20 min at −78 °C, TMSCl (180 μL, 1.41 mmol, 1.7 equiv) was added dropwise and the reaction mixture was warmed to rt. After 1 h at rt, the reaction mixture was cooled to −78 °C and LDA (1.7 mL, from a 1 M freshly prepared stock solution in THF/hexanes, 1.7 mmol, 2 equiv) was added dropwise. After 10 min at −78 °C, the reaction mixture was poured into a saturated aqueous solution of NH_4Cl, acidified (pH 3) by the addition of 1 M hydrochloric acid and extracted with EtOAc. The combined organic extracts were washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Analysis of the crude material by ^{1}H NMR

indicated the formation of two diastereomers in a 9/1 ratio (*anti*/*syn* = 9/1). Purification by flash chromatography (petroleum ether/EtOAc gradient: 90:10 to 70:30) afforded 114 mg (24%) of a 9/1 mixture of *anti*/*syn* diastereomers and 251 mg of pure **9** (52%) as viscous yellow oils (76% combined yield); $[\alpha]_D$ −10.5 (*c* 0.97, $CHCl_3$); IR 3487, 2176, 1613, 1513, 1340, 1249, 1159, 1092, 1033, 844, 817 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, $J = 8.3$ Hz, 2H), 7.34–7.31 (m, 2H), 7.29–7.21 (m, 7H), 6.88 (br d, $J = 8.3$ Hz, 2H), 5.77 (ddt, $J = 15.6$, 8.3, 1.3 Hz, 1H), 5.57 (ddd, apparent dt, $J = 15.6$, 5.3 Hz, 1H), 4.58 (d, AB syst, $J = 15.8$ Hz, 1H), 4.56 (dd, apparent t, $J = 5.6$ Hz, 1H), 4.38 (dd, $J = 8.3$, 6.0 Hz, 1H), 4.35 (s, 2H), 4.34 (d, AB syst, $J = 15.8$ Hz, 1H), 3.90 (br d, $J = 5.3$ Hz, 2H), 3.81 (s, 3H), 2.39 (s, 3H), 2.06 (d, $J = 5.5$ Hz, 1H, OH), 0.13 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2 (s), 143.4 (s), 137.3 (s), 137.1 (s), 134.2 (d), 130.1 (s), 129.5 (d, 2C), 129.3 (d, 2C), 128.45 (d, 2C), 128.37 (d, 2C), 127.62 (d), 127.55 (d, 2C), 125.2 (d), 113.8 (d, 2C), 103.7 (s), 92.0 (s), 71.7 (t), 69.3 (t), 65.1 (d), 64.5 (d), 55.3 (q), 50.1 (t), 21.5 (q), −0.3 (q, 3C); Anal. Calcd for $C_{32}H_{39}NO_5SSi$: C, 66.52; H, 6.80; N, 2.42. Found: C, 66.27; H, 6.92; N, 2.43.

18. *N-Allyl-N-{(E)-3-[2-((3aR,8aS)-2,2-dimethyl-8,8a-dihydro-3aH-indeno[1,2-d]oxazol-3-yl)-2-oxoethoxy]propenyl}-4-methylbenzenesulfonamide (***17c***)*. $[\alpha]_D$ −84 (*c* 1.21, $CHCl_3$); IR 1655, 1425, 1358, 1309, 1244, 1165, 1090, 937, 904, 814, 748, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, $J = 8.3$ Hz, 2H), 7.32–7.21 (m, 6H), 7.00 (d, $J = 14.2$ Hz, 1H), 5.60 (ddt, $J = 17.2$, 10.4, 5.3 Hz, 1H), 5.37 (d, $J = 4.4$ Hz, 1H), 5.16 (dd, $J = 17.2$, 0.9 Hz, 1H), 5.10 (dd, $J = 10.4$, 0.9 Hz, 1H), 4.96 (dt, $J = 14.2$, 7.1 Hz, 1H), 4.88 (dt, $J = 4.4$, 2.0 Hz, 1H), 4.38 (d, AB syst, $J = 13.8$ Hz, 1H), 4.34 (d, AB syst, $J = 13.8$ Hz, 1H), 4.18 (dd, $J = 7.1$, 0.8 Hz, 2H), 4.01 (br d, $J = 5.3$ Hz, 2H), 3.13 (apparent d, $J = 2.0$ Hz, 2H), 2.41 (s, 3H), 1.65 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (s), 144.0 (s), 140.8 (s), 140.6 (s), 136.1 (s), 131.1 (d), 130.7 (d), 129.8 (d, 2C), 128.5 (d), 127.3 (d), 126.9 (d, 2C), 125.9 (d), 124.4 (d), 118.0 (t), 105.1 (d), 96.9 (s), 79.3 (d), 70.5 (t), 69.3 (t), 64.8 (d), 48.1 (t), 36.3 (t), 26.5 (q), 24.1 (q), 21.5 (q); HRMS (FAB) Calcd for $C_{27}H_{32}O_5N_2NaS$ ($M+Na^+$): 519.19241. Found: 519.19179.

19. *N-Allyl-N-{(R)-1-[(S)-2-((3aR,8aS)-2,2-dimethyl-8,8a-dihydro-3aH-indeno[1,2-d]oxazol-3-yl)-1-hydroxy-2-oxo-ethyl]allyl}-4-methylbenzenesulfonamide (***18c***)*. To a solution of amide **17c** (120 mg, 0.242 mmol) and HMPA (1.26 mL, 7.26 mmol, 30 equiv) in THF (5 mL) at −78 °C was added dropwise LiHMDS (480 μL, 1 M in THF, 0.480 mmol, 2 equiv). After 30 min at −78 °C, the reaction mixture was poured into a saturated aqueous solution of NH_4Cl and extracted with EtOAc. The combined organic extracts were washed successively with saturated aqueous solutions of NaCl and LiCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Analysis of the ^1H NMR spectrum of the crude material indicated a diastereomeric ratio **18c**/(**19c**+**20c**) > 94/6. Purification by flash chromatography (petroleum ether/EtOAc gradient: 80:20 to 70:30) afforded 96 mg (80%) of **18c** as a colorless oil; $[\alpha]_D$ −77.1 (*c* 1.04, $CHCl_3$); IR 3385, 1645, 1378, 1331, 1156, 1091, 1052, 930, 815, 749, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, $J = 8.3$ Hz, 2H), 7.41 (d, $J = 7.2$ Hz, 1H), 7.32–7.24 (m, 5H), 6.02 (ddd, $J = 17.0$, 10.3, 8.5 Hz, 1H), 5.85 (ddt, $J = 17.0$, 10.1, 6.4 Hz, 1H), 5.36 (d, $J = 4.4$ Hz, 1H), 5.26 (d, $J = 10.1$ Hz, 1H), 5.24 (d, $J = 17.0$ Hz, 1H), 5.15 (dq, $J = 17.0$, 1.3 Hz, 1H), 5.09 (dq, $J = 10.1$,1.3 Hz, 1H), 5.02 (dd, $J = 9.8$, 8.3 Hz, 1H), 4.89 (dd, apparent br t, $J = 4.0$ Hz, 1H), 4.44 (t, $J = 8.4$ Hz, 1H), 3.99 (dd, $J = 16.0$, 6.4 Hz, 1H), 3.87 (dd, $J = 16.0$, 6.4 Hz, 1H), 3.22 (d, $J = 9.8$ Hz, 1H, OH), 3.16–3.13 (m, 2H), 2.42 (s, 3H), 1.57 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5 (s), 143.4 (s), 140.6 (s), 139.9 (s), 137.5 (s), 135.1 (d), 131.6 (d), 129.5 (d, 2C), 128.8 (d), 127.6 (d), 127.5 (d, 2C), 125.9 (d), 124.1 (d), 121.3 (t), 118.0 (t), 97.1 (s), 79.1 (d), 71.3 (d), 66.0 (d), 65.3 (d), 49.8 (t), 36.5 (t), 26.5 (q), 23.7 (q), 21.5 (q); HRMS (ES^+) Calcd for $C_{27}H_{33}N_2O_5S$ ($M+H^+$): 497.2105. Found: 497.2093.

20. *Methyl (2S,3R)-3-[allyl(toluene-4-sulfonyl)amino]-2-hydroxypent-4-enoate (***21c***)*. To a solution of amide **18c** (80 mg, 0.16 mmol) in MeOH (3 mL) was added 35% hydrochloric acid (1 mL). After 5 h heating at reflux, the reaction mixture was cooled to rt, diluted with water (5 mL), and extracted with EtOAc. The combined organic extracts were washed with a saturated aqueous solution of NaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (petroleum ether/EtOAc gradient: 80:20 to 65:35) afforded 43 mg (78%) of **21c** as a colorless oil $[\alpha]_D$ −40.3 (*c* 2.08, $CHCl_3$); IR 3500, 1742, 1439, 1339, 1287, 1214, 1156, 1090, 1015, 930, 816, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, $J = 8.3$ Hz, 2H), 7.29 (d, $J = 8.3$ Hz, 2H), 5.89 (dddd, $J = 17.2$, 10.2, 7.0, 5.2 Hz, 1H), 5.63 (ddd, $J = 17.2$, 10.6, 6.8 Hz, 1H), 5.20 (dq, $J = 17.2$, 1.4 Hz, 1H), 5.18 (dt, $J = 10.6$, 1.0 Hz, 1H), 5.15 (dq, $J = 10.2$, 1.4 Hz, 1H), 5.09 (dt, $J = 17.2$, 1.0 Hz, 1H), 4.66 (ddt, $J = 7.0$, 5.2, 1.0 Hz, 1H), 4.41 (m, 1H), 3.89 (ddt, $J = 16.4$, 5.2, 1.4 Hz, 1H), 3.81 (s, 3H), 3.77 (ddt, $J = 16.4$, 7.0, 1.4 Hz, 1H), 3.19 (d, $J = 7.0$ Hz, 1H, OH), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6 (s), 143.6 (s), 136.8 (s), 135.9 (d), 131.6 (d), 129.6 (d, 2C), 127.5 (d, 2C), 120.6 (t), 117.3 (t), 73.1 (d), 62.2 (d), 52.6 (q), 48.7 (t), 21.5 (q); HRMS (FAB) Calcd for $C_{16}H_{21}NNaO_5S$ ($M+Na^+$): 362.10326. Found: 362.10277.