Supporting Information

Palladium-Indium Iodide-Mediated Allylation and Propargylation of Glyoxylic Oxime Ether and Hydrazone: The Role of Water in Directing The Diastereoselective Allylation

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X-ray analysis and rationalized stereochemical feature

The absolute configuration at the newly-formed stereocenter of **7** was determined by X-ray analysis. (FIGURE 1). The stereochemical feature of this reaction can be rationalized in terms of steric control in the conformationally restricted sultam derivative **4** (FIGURE 1). The rotamer of **4** having the carbonyl group anti to the sulfonyl group would be favored to minimize dipole-dipole interactions between these groups. Additionally, the sterically more stable *s-cis* planar conformation between the carbonyl group and the oxime ether group would be favored. Therefore, the reaction proceeds at the *si* face via the chelated transition state proposed by Marshall et al,⁴ presumably due to steric interactions with the axial oxygen of sulfonyl group, which effectively prevents addition to *re* face.

FIGURE 1. X-Ray crystal structure of **7** and possible cyclic transition state.

Cross-over experiment

To investigate the equilibration hypotheses, we provided a simple cross-over experiment (SCHEME 1). At first, the reaction of **1A** (1 equiv) with allyl acetate **2a** (0.9 equiv) in the presence of Pd(PPh₃)₄ (0.05 equiv) and indium(I) iodide (1 equiv) in THF proceeded smoothly to give the allylated adduct **A** after being stirred for 1 h under argon atmosphere. To the reaction vessel was added oxime ether **4** (1 equiv) in THF to afford allylated products **5** and **3A**, accompanied with starting materials **1A** and **4** after being stirred for 20 h.

SCHEME 1

General General. ¹H and ¹³C NMR spectra were recorded at 500 MHz and at 125 MHz, respectively. Mass spectra were obtained by EI or FAB method. Preparative TLC separations were carried out on precoated silica gel plates (E. Merck 60F₂₅₄). The diastereoselectivities of products were determined by ¹H NMR analysis of diastereomeric mixture obtained after rough purification of chromatography (hexane:AcOEt=2:1).

General procedure for allylation in THF. A mixture of **1A-D**, or **4** (0.125 mmol), allylic reagents **2a-f** (0.25 or 0.15 mmol), Pd(PPh₃)₄ (7.3 mg, 0.0063 mmol), and indium iodide (60 mg, 0.25 mmol) in THF (1.0 mL) was stirred under argon atmosphere at 20 °C. The reaction mixture was diluted with saturated aqueous potassium sodium (+)-tartrate and then extracted with AcOEt. The organic phase was dried over MgSO₄ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane:AcOEt=4:1, 2-fold development) afforded the products **3A**, **3C**, or (*S*)-**5** and (*R*)-**5**.

General procedure for allylation in THF-H₂O. A mixture of **4** (47.1 mg, 0.125 mmol), allylic

reagents **2a-f** (0.25 or 0.15 mmol), Pd(PPh₃)₄ (7.3 mg, 0.0063 mmol), and indium iodide (60 mg, 0.25 mmol) in H₂O-THF (1:10, v/v, 1.1 mL) was stirred under argon atmosphere at 20 °C. The reaction mixture was diluted with saturated aqueous potassium sodium (+)-tartrate and then extracted with AcOEt. The organic phase was dried over MgSO₄ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane:AcOEt=4:1, 2-fold development) afforded the products (*S*)-**5** and (*R*)-**5**.

2-(Phenylmethoxyamino)-4-pentenoic acid methyl ester (3A). A colorless oil. IR (CHCl₃) 1738, 1496 cm⁻¹. ¹H NMR (CDCl₃) δ 7.34-7.25 (5H, m), 5.96 (1H, br s), 5.72 (1H, ddt, *J* = 17.0, 10.2, 6.9 Hz), 5.12-5.03 (2H, m), 4.70 (2H, s), 3.74 (3H, s), 3.69 (1H, t, *J* = 6.9 Hz), 2.34 (1H, t, *J* = 6.9 Hz). ¹³C NMR (CDCl₃) δ 173.6, 137.6, 133.0, 128.4, 128.3, 127.8, 118.1, 76.2, 63.2, 51.9, 33.8. HRMS (EI⁺): calcd for C₁₃H₁₇NO₃ (M⁺): 235.1208, Found: 235.1205.

2-(2-Benzoylhydrazino)-4-pentenoic acid methyl ester (3C). A colorless oil. IR (CHCl₃) 1737, 1661, 1457 cm⁻¹. ¹H NMR (CDCl₃) δ 8.24 (1H, br m), 7.76 (2H, d, *J* = 7.0 Hz), 7.51 (1H, br t, *J* = 7.4 Hz), 7.43 (2H, br t, *J* = 7.6 Hz), 5.87 (1H, m), 5.23-5.12 (2H, m), 3.87 (1H, br m), 3.75 (3H, s), 2.62 (1H, m), 2.49 (1H, m). ¹³C NMR (CDCl₃) δ 173.1, 167.1, 132.8, 132.5, 131.9, 128.6, 127.0, 118.9, 62.1, 52.0, 35.1. HRMS (EI⁺): calcd for C₁₃H₁₆N₂O₃ (M⁺): 248.1161, Found: 248.1154.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (major isomer (S)-5). A colorless crystal. mp 106-108 °C (AcOEt/hexane). [α]_D³² -107.4 (c 0.99, CHCl₃). IR (CHCl₃) 2964, 1693 cm⁻¹. ¹H NMR (CDCl₃) δ 7.37-7.26 (5H, m), 6.16 (1H, br d, *J*=11.0 Hz), 5.78-5.70 (1H, m), 5.09-5.02 (2H, m), 4.76, 4.72 (2H, AB q, *J*=12.0 Hz), 4.49-4.44 (1H, br m), 3.97 (1H, br t, *J*=6.0 Hz), 3.50, 3.47 (2H, AB q, *J*=14.0 Hz), 2.41-2.29 (2H, m), 2.10-2.04 (2H, m), 1.92-1.86 (3H, m), 1.44-1.33 (2H, m), 1.14, 0.97 (each 3H, s). ¹³C NMR (CDCl₃) δ 173.0, 137.8, 132.7, 128.6, 128.2, 127.6, 118.3, 75.9, 65.1, 62.4, 53.0, 48.6, 47.8, 44.6, 38.3, 34.8, 32.8, 26.4, 20.8, 19.9. HRMS (FAB⁺): calcd for C₂₂H₃₁N₂O₄S (M + H⁺):

419.2004, Found: 419.1996. Anal. Calcd for C₂₂H₃₀N₂O₄S: C, 63.13; H, 7.22; N, 6.69; S, 7.66. Found: C, 63.12; H, 7.26; N, 6.60; S, 7.74.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-1-oxo-2-[(phenylmethoxy)amino]-4-pentenyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (minor isomer (*R*)-9). A white solid. $[\alpha]_D^{22} -35.2$ (c 1.23, CHCl₃). IR (CHCl₃) 2963, 1690 cm⁻¹. ¹H NMR (CDCl₃) δ 7.44-7.11 (5H, m), 6.21 (1H, br d, *J*=9.5 Hz), 5.81 (1H, m), 5.18-4.99 (2H, m), 4.72-4.60 (2H, m), 4.35 (1H, br m), 3.97 (1H, m), 3.52, 3.43 (2H, AB q, *J*=13.7 Hz), 2.50 (1H, m), 2.31 (1H, m), 2.13 (1H, m), 2.05 (1H, m), 1.91-1.81 (3H, m), 1.42-1.25 (2H, m), 1.07, 0.95 (each 3H, s). ¹³C NMR (CDCl₃) δ 173.0, 137.4, 133.6, 128.6, 128.1, 127.7, 117.7, 76.2, 65.2, 62.2, 53.0, 48.7, 47.7, 44.5, 38.1, 32.9, 32.7, 26.3, 20.6, 19.8. HRMS (FAB⁺): calcd for C₂₂H₃₁N₂O₄S (M + H⁺): 419.2004, Found: 419.2010.

General procedure for propargylation. A mixture of **4** (47.1 mg, 0.125 mmol), propargylic reagents **6a**, or **8** (0.25 mmol), additive (0.25 mmol), Pd(PPh₃)₄ (7.3 mg, 0.0063 mmol), and indium iodide (60 mg, 0.25 mmol) in THF (1.0 mL) was stirred under argon atmosphere at 20 °C. The reaction mixture was diluted with saturated aqueous potassium sodium (+)-tartrate and then extracted with AcOEt. The organic phase was dried over MgSO₄ and concentrated at reduced pressure. Purification of the residue by preparative TLC (hexane:AcOEt=4:1, 2-fold development) afforded the products **7**, **9**, and **10**.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*,3*R*)-1-oxo-3-methyl-2-[(phenylmethoxy)amino]-4-pentynyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (7**).** A colorless crystal. mp 129-131 °C (AcOEt/hexane). $[\alpha]_D^{22} -89.0$ (c 0.85, CHCl₃). IR (CHCl₃) 2962, 1700, 1456 cm⁻¹. ¹H NMR (CDCl₃) δ 7.37 (2H, d, *J*=7.0 Hz), 7.34-7.23 (3H, m), 6.54 (1H, d, *J*=11.0 Hz), 4.68 (2H, s), 4.11 (1H, dd, *J*=11.0, 7.3 Hz), 3.97 (1H, br t, *J*=6.5 Hz), 3.48, 3.46 (2H, AB q, *J*=13.8 Hz), 2.98 (1H, m), 2.14-2.05 (3H, m), 1.95-1.80 (3H, m), 1.47-1.30 (2H, m), 1.26 (3H, d, *J*=7.0 Hz), 1.12, 0.97 (each 3H, s). ¹³C NMR (CDCl₃) δ 171.3, 137.7, 128.9, 128.1, 127.7, 82.3, 76.0, 71.6, 66.1, 64.9, 53.0, 48.8, 47.8, 44.4, 38.1, 32.6, 27.7, 26.4,

20.5, 19.8, 18.7. HRMS (FAB⁺): calcd for C₂₃H₃₁N₂O₄S (M + H⁺): 431.2004, Found: 431.1999. Anal. Calcd for C₂₃H₃₀N₂O₄S: C, 64.16; H, 7.02; N, 6.51; S, 7.45. Found: C, 64.28; H, 6.94; N, 6.40; S, 7.54.

Crystal data of **7**: C₂₃H₃₀N₂O₄S, space group P2₁2₁2₁ with *a*=00000(00), *b*=00000(00), *c*=00000(00) Å, *V*=00000(00) Å³, final *R* value 0.000 for 00000 reflections.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-1-oxo-2-[(phenylmethoxy)amino]-4-hexynyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (9).

A colorless crystal. mp 136-140 °C (AcOEt/hexane). [α]_D²³ -96.8 (c 1.06, CHCl₃). IR (CHCl₃) 2962, 1699, 1455 cm⁻¹. ¹H NMR (CDCl₃) δ 7.40-7.25 (5H, m), 6.32 (1H, d, *J*=10.4 Hz), 4.72, 4.69 (2H, AB q, *J*=11.6 Hz), 4.41 (1H, br m), 3.96 (1H, br m), 3.49, 3.46 (2H, AB q, *J*=13.7 Hz), 2.60 (2H, br m), 2.21-2.03 (2H, br m), 1.92-1.60 (3H, br m), 1.72 (3H, s), 1.46-1.30 (2H, m), 1.15, 0.97 (each 3H, s). ¹³C NMR (CDCl₃) δ 171.2, 137.7, 128.6, 128.2, 127.7, 79.2, 76.0, 72.6, 64.9, 61.5, 52.9, 48.6, 47.8, 44.5, 38.1, 32.6, 26.4, 20.8, 20.5, 19.8, 3.5. HRMS (FAB⁺): calcd for C₂₃H₃₁N₂O₄S (M + H⁺): 431.2004, Found: 431.1994. Anal. Calcd for C₂₃H₃₀N₂O₄S: C, 64.16; H, 7.02; N, 6.51; S, 7.45. Found: C, 64.20; H, 7.06; N, 6.47; S, 7.46.

(3a*S*,6*R*,7a*R*)-1,4,5,6,7,7a-Hexahydro-8,8-dimethyl-1-[(2*S*)-1-oxo-3-methyl-2-[(phenylmethoxy)amino]-3,4-pentadienyl]-3*H*-3a,6-methano-2,1-benzisothiazole 2,2-dioxide (10).

A colorless crystal. mp 127-129 °C (AcOEt/hexane). [α]_D²³ -61.9 (c 1.22, CHCl₃). IR (CHCl₃) 2961, 1698, 1455 cm⁻¹. ¹H NMR (CDCl₃) δ 7.38 (2H, d, *J*=7.0 Hz), 7.34-7.25 (3H, m), 6.25 (1H, d, *J*=11.3 Hz), 4.72, 4.69 (2H, AB q, *J*=11.6 Hz), 4.75-4.65 (2H, m), 4.59 (1H, br d, *J*=11.0 Hz), 3.96 (1H, t, *J*=6.5 Hz), 3.47, 3.45 (2H, AB q, *J*=13.7 Hz), 2.07 (2H, m), 1.94-1.72 (3H, br m), 1.76 (3H, t, *J*=3.0 Hz), 1.46-1.32 (2H, m), 1.12, 0.96 (each 3H, s). ¹³C NMR (CDCl₃) δ 207.0, 170.3, 137.9, 128.9, 128.3, 127.8, 95.1, 77.7, 76.0, 65.7, 65.0, 53.0, 48.7, 47.8, 44.7, 38.4, 32.8, 26.5, 20.6, 20.0, 17.7. HRMS (FAB⁺): calcd for C₂₃H₃₁N₂O₄S (M + H⁺): 431.2004, Found: 431.2009. Anal. Calcd for C₂₃H₃₀N₂O₄S: C, 64.16; H, 7.02; N, 6.51; S, 7.45. Found: C, 64.12; H, 7.05; N, 6.45; S, 7.35.

5 (minor isomer)

[illegible]

17 Dec 2002

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Sweep Width (Hz)	10000.00	Temperature (degree C)	0.000

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2	-0.03	-0.153	0.0162	21	1.36	681.2	0.1023	41	2.09	1045.3	0.1866	61	4.11	2053.9	0.9343
3	-0.03	-0.153	0.0162	22	1.36	685.5	0.0725	42	2.10	1057.1	0.2004	62	4.11	2053.9	0.9343
4	-0.03	-0.153	0.0162	23	1.36	685.5	0.0725	43	2.10	1057.1	0.2004	63	4.11	2053.9	0.9343
5	0.07	0.454	0.0255	24	1.40	699.2	0.0378	44	2.15	1079.1	0.0111	64	4.13	2064.9	0.9689
6	0.07	0.454	0.0255	25	1.42	718.5	0.1177	45	2.18	1079.1	0.0111	65	4.13	2064.9	0.9689
7	0.07	0.454	0.0255	26	1.42	718.5	0.1177	46	2.18	1079.1	0.0111	66	4.13	2064.9	0.9689
8	0.94	467.8	0.0484	27	4.5	228.5	0.9553	47	2.97	1484.5	0.0340	67	4.11	2053.9	0.9343
9	0.94	467.8	0.0484	28	4.5	228.5	0.9553	48	2.98	1491.1	0.0364	68	4.59	3764.9	1.1379
10	0.99	495.9	0.0324	29	4.66	239.2	0.9776	49	2.99	1484.5	0.0371	69	4.55	3725.5	1.1279
11	1.00	498.6	0.0242	30	4.66	239.2	0.9776	50	2.99	1484.5	0.0369	70	4.55	3725.5	1.1279
12	1.09	544.1	0.0536	31	4.87	835.9	0.9174	51	3.01	1504.3	0.0178	71	4.72	3632.0	0.9816
13	1.12	559.7	0.0675	32	4.88	938.4	0.9152	52	3.01	1504.3	0.0178	72	4.72	3632.0	0.9816
14	1.15	575.9	0.0318	33	4.86	940.1	0.928	53	3.04	1520.8	0.0314	73	4.72	3632.0	0.9816
15	1.23	613.4	0.0376	34	5.00	951.3	0.9513	54	3.04	1520.8	0.0314	74	4.72	3632.0	0.9816
16	1.23	613.4	0.0376	35	5.00	951.3	0.9513	55	3.04	1520.8	0.0314	75	4.72	3632.0	0.9816
17	1.23	613.4	0.0376	36	5.00	951.3	0.9513	56	3.04	1520.8	0.0314	76	4.72	3632.0	0.9816
18	1.23	613.4	0.0376	37	5.00	951.3	0.9513	57	3.04	1520.8	0.0314	77	4.72	3632.0	0.9816
19	1.23	613.4	0.0376	38	5.00	951.3	0.9513	58	3.04	1520.8	0.0314	78	4.72	3632.0	0.9816
20	1.23	613.4	0.0376	39	5.00	951.3	0.9513	59	3.04	1520.8	0.0314	79	4.72	3632.0	0.9816
21	1.23	613.4	0.0376	40	5.00	951.3	0.9513	60	3.04	1520.8	0.0314	80	4.72	3632.0	0.9816
22	1.23	613.4	0.0376	41	5.00	951.3	0.9513	61	3.04	1520.8	0.0314	81	4.72	3632.0	0.9816
23	1.23	613.4	0.0376	42	5.00	951.3	0.9513	62	3.04	1520.8	0.0314	82	4.72	3632.0	0.9816
24	1.23	613.4	0.0376	43	5.00	951.3	0.9513	63	3.04	1520.8	0.0314	83	4.72	3632.0	0.9816
25	1.23	613.4	0.0376	44	5.00	951.3	0.9513	64	3.04	1520.8	0.0314	84	4.72	3632.0	0.9816
26	1.23	613.4	0.0376	45	5.00	951.3	0.9513	65	3.04	1520.8	0.0314	85	4.72	3632.0	0.9816
27	1.23	613.4	0.0376	46	5.00	951.3	0.9513	66	3.04	1520.8	0.0314	86	4.72	3632.0	0.9816
28	1.23	613.4	0.0376	47	5.00	951.3	0.9513	67	3.04	1520.8	0.0314	87	4.72	3632.0	0.9816
29	1.23	613.4	0.0376	48	5.00	951.3	0.9513	68	3.04	1520.8	0.0314	88	4.72	3632.0	0.9816
30	1.23	613.4	0.0376	49	5.00	951.3	0.9513	69	3.04	1520.8	0.0314	89	4.72	3632.0	0.9816
31	1.23	613.4	0.0376	50	5.00	951.3	0.9513	70	3.04	1520.8	0.0314	90	4.72	3632.0	0.9816
32	1.23	613.4	0.0376	51	5.00	951.3	0.9513	71	3.04	1520.8	0.0314	91	4.72	3632.0	0.9816
33	1.23	613.4	0.0376	52	5.00	951.3	0.9513	72	3.04	1520.8	0.0314	92	4.72	3632.0	0.9816
34	1.23	613.4	0.0376	53	5.00	951.3	0.9513	73	3.04	1520.8	0.0314	93	4.72	3632.0	0.9816
35	1.23	613.4	0.0376	54	5.00	951.3	0.9513	74	3.04	1520.8	0.0314	94	4.72	3632.0	0.9816
36	1.23	613.4	0.0376	55	5.00	951.3	0.9513	75	3.04	1520.8	0.0314	95	4.72	3632.0	0.9816
37	1.23	613.4	0.0376	56	5.00	951.3	0.9513	76	3.04	1520.8	0.0314	96	4.72	3632.0	0.9816
38	1.23	613.4	0.0376	57	5.00	951.3	0.9513	77	3.04	1520.8	0.0314	97	4.72	3632.0	0.9816
39	1.23	613.4	0.0376	58	5.00	951.3	0.9513	78	3.04	1520.8	0.0314	98	4.72	3632.0	0.9816
40	1.23	613.4	0.0376	59	5.00	951.3	0.9513	79	3.04	1520.8	0.0314	99	4.72	3632.0	0.9816
41	1.23	613.4	0.0376	60	5.00	951.3	0.9513	80	3.04	1520.8	0.0314	100	4.72	3632.0	0.9816

1	1.26	628.6	0.6512	34	1.92	899.8	0.0799	55	3.47	1735.3	0.3516	74	2.30	3648.2	0.0629
4	1.26	628.6	0.6144	35	1.94	971.1	0.0800	56	3.47	1739.2	0.3481	75	2.31	3654.3	0.1944
15	1.27	629.6	0.6144	36	1.95	975.7	0.0820	57	3.51	1753.0	0.0547	76	7.32	3661.8	0.3212
18	1.29	845.8	0.0426	36	1.95	975.7	0.0820	58	3.57	1986.0	0.0946	77	7.34	3666.6	0.1763
17	1.29	647.3	0.0409	37	2.00	1019.9	0.0843	59	3.97	1980.1	0.1395	78	7.37	3666.6	0.3423
18	1.31	652.8	0.0350	38	2.05	1023.6	0.0293	58	3.97	1986.0	0.1395	78	7.34	3666.6	0.3423
19	1.34	667.7	0.0408	39	2.07	1035.8	0.2768	59	3.99	1992.8	0.0041	79	7.36	3691.5	0.1916
20	1.34	671.7	0.0547	40	2.08	1038.2	0.2821	60	4.01	2050.2	0.0933

9 Apr 2003
noe

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Solvent	CHLOROFORM-D	Number of Transients	1024
Points Count	32768	Date	Wed Apr 8 06:22:54 2003

No.	Chemical Shift (ppm)	Height	No.	Chemical Shift (ppm)	Height
1	17.69	2223.3	13	76.01	9550.9
2	19.95	2506.8	14	76.84	9654.3
3	20.61	2599.3	15	77.09	9686.4
4	26.50	3329.2	16	77.35	9718.5
5	32.79	4119.6	17	77.70	9763.0
6	38.43	4828.3	18	85.14	11954.1
7	44.69	5615.5	19	127.78	16056.0
8	47.77	6002.4	20	128.29	16119.1
9	48.71	6120.4	21	128.90	16196.7
10	53.03	6663.5	22	137.88	17325.3
11	65.02	8169.8	23	170.35	21404.5
12	65.71	8256.7	24	207.05	26015.4