An Efficient Synthesis of 4-Heterofunction-Substituted 3-(1-Hydroxy)ethylazetidin-2-ones from 3-(1-Hydroxy)ethyl-4-phenylsulfinylazetidin-2-one by Reaction with Silylated Heteronucleophiles

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3-(1-*tert*-Butyldimethylsiloxy)ethyl-4-sulfinylazetidin-2-one was reacted with silylated N-, S-, O-, and P-nucleophiles in the presence of a catalytic amount of ZnI_2 to give the corresponding *trans*-4-heterofunction-substituted azetidin-2-ones in high yeilds.

Keywords 4-sulfinylazetidin-2-one; silylated heteronucleophile; 3-(1-hydroxy)ethylazetidin-2-one; substitution

The chemistry of β-lactam antibiotics is continuously developing and great efforts have been made to create novel nuclei, such as that of the carbapenem antibiotic, thienamycin (**1**)[1] or 1β-methylthienamycin (**2**).[2] In particular, the 6α-(1-hydroxy)ethyl side chain of these antibiotics is unusual, since this substituent is generally an amide moiety in the naturally occurring penicillin and cephalosporin. Therefore, the biological activity of the corresponding penem (**3**),[3] azapenem (**4**),[4] cephem (**5**),[5] and oxacephem (**6**)[6] bearing the α-(1-hydroxy)ethyl side chain instead of the amide side chain has become of interest in recent years. Recently, we have observed that treatment of 3-(1-*tert*-butyldimethylsiloxy)ethyl-4-phenylsulfinylazetidin-2-ones (**8**) with silyl ketene acetals (**7**) in the presence of a catalytic amount of ZnI_2 results in a facile silyl-transfer substitution reaction[7] to give *trans*-3-(1-*tert*-butyldimethylsiloxy)ethylazetidin-2-one esters (**9**), leading to the antibiotic, (+)-thienamycin (**1**).[8] In connection with this study, we have briefly communicated[9] an efficient synthesis of 4-heterofunction-substituted *trans*-3-(1-*tert*-butyldimethylsiloxy)ethylazetidin-2-ones (**10**) by the reaction of **8** with silylated heteronucleophiles (**11**), some of which are key intermediates of a new class of β-lactam antibiotics bearing the α-(1-hydroxy)ethyl side chain. We now give a full account of this work and another novel substitution reaction with a silylated phosphorus nucleophile.

In the first place, reaction of **8**[10] with trimethylsilyl azide (**11a**) was examined under various conditions (Table I). In the absence of catalyst, the reaction did not occur at room temperature but occurred at above 60 °C to give *trans*-4-azido-3-(1-*tert*-butyldimethylsiloxy)ethylazetidin-2-one (**10a**) in 89% yield (runs 7 and 8) *via* a reactive acyliminium intermediate (A). In the presence of a catalyst such as ZnI_2, trimethylsilyl trifluoromethane sulfonate (TMSOTf), or $TiCl_4$, the substitution reaction occurred at room temperature (runs 1—6). The best result was obtained in the presence of a catalytic amount of ZnI_2 in dry acetonitrile at room temperature. Only **10a** was obtained as a single product in a quantitative yield.

Other silylated aza-, thia-, and oxa-nucleophiles (**11b—m**)[11] were similarly reacted with **8** to give the corresponding 4-heterofunction-substituted azetidin-2-ones (**10b—m**). In every case, 3,4-*trans*-azetidin-2-ones were produced in high yields under mild conditions *via* the acyliminium intermediate (A) (Table II).

The 4-acyloxyazetidin-2-one (**10m**) has already been converted to the corresponding oxacephem antibiotic[6] bearing the α-(1-hydroxy)ethyl side chain. We were next interested in the preparation of 4-phosphorus-substituted azetidin-2-one, since a phosphorus-containing β-lactam can exhibit interesting biological activity.[12] Treatment of

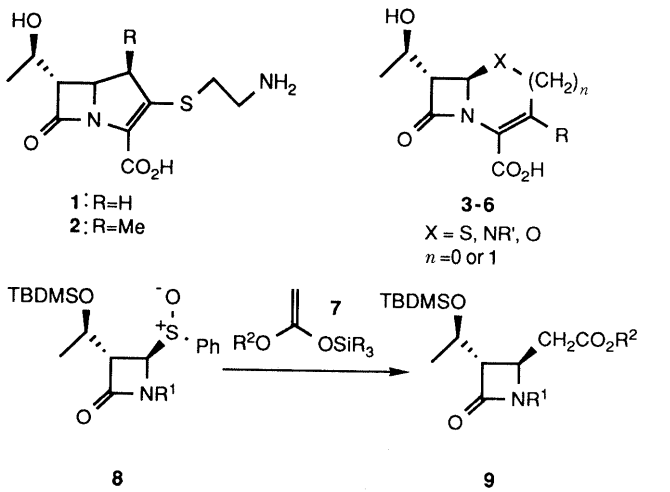
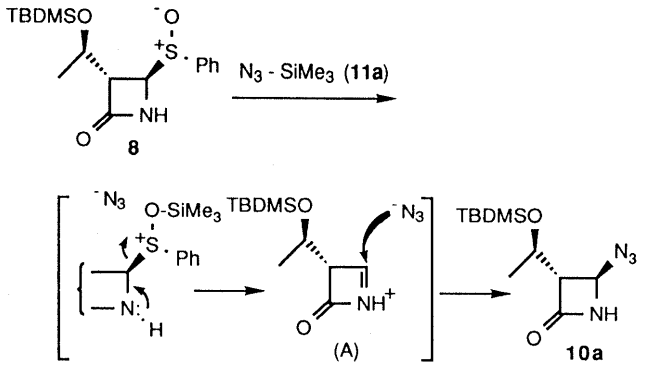


Fig. 1

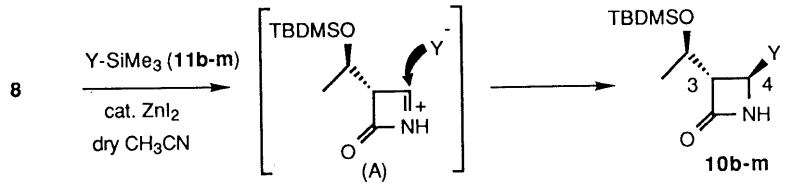
TABLE I. Substitution Reaction of 4-Sulfinylazetidin-2-one (**8**) with Trimethylsilyl Azide (**11a**)

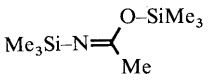
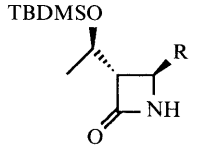
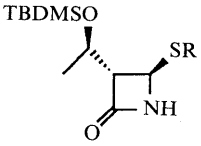
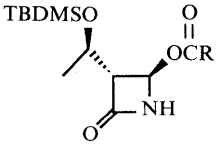
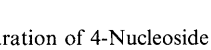


Run	Catalyst[a]	Solvent	Temperature	Time	Yield (%)
1	ZnI_2	CH_3CN	r.t.	4 h	100
2	ZnI_2	CH_2Cl_2	r.t.	12 h	91
3	ZnI_2	THF	r.t.	9 h	86
4	TMSOTf	CH_3CN	0 °C	1 h	87
5	$TiCl_4$	CH_3CN	r.t.	5 h	[b]
6	$TiCl_4$ (1 eq)	CH_3CN	r.t.	5 h	99
7	No catalyst	CH_3CN	r.t.	1 d	0
8	No catalyst	CH_3CN	60 °C	8 h	89

a) 0.1 molar eq of the reagent was used unless otherwise noted. *b*) Less than 5% of **10a** was obtained.

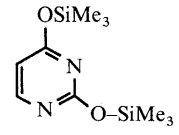
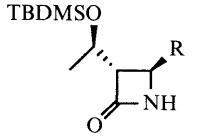
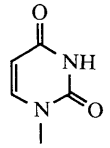
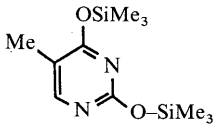
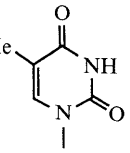
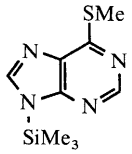
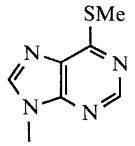
TABLE II. Substitution Reaction of 4-Sulfinylazetidin-2-one (**8**) with Silylated Heteronucleophiles (**11b—m**)



Run	Y-SiMe$_3$ (**11**)[a]		Conditions	Product (**10**)		Yield (%)
1		**11b**	−20 °C, 8 h		**10b** : R=NHCOMe	67
2		**11c**	60 °C, 6 h		**10c** : R= 	99
3	MeS–SiMe$_3$	**11d**	0 °C, 3 h		**10d** : R=Me	98
4	PhS–SiMe$_3$	**11e**	r.t., 1 d		**10e** : R=Ph	79
5	PhCH$_2$S–SiMe$_3$	**11f**	0 °C, 1 d		**10f** : R=CH$_2$Ph	80
6	PhCOS–SiMe$_3$	**11g**	r.t., 2 h		**10g** : R=COPh	59
7	MeCO$_2$CH$_2$COS–SiMe$_3$	**11h**	60 °C, 1 d		**10h** : R=COCH$_2$OCOMe	73
8	AcO–SiMe$_3$	**11i**	r.t., 2 d		**10i** : R=Me	52
9	PhCO$_2$–SiMe$_3$	**11j**	r.t., 2 d		**10j** : R=Ph	51
10	PhCH(Et)CO$_2$–SiMe$_3$	**11k**	r.t., 2 d		**10k** : R=CH(Et)Ph	66[b]
11	MeCO$_2$CH$_2$CO$_2$–SiMe$_3$	**11l**	50 °C, 6 h		**10l** : R=CH$_2$OCOMe	66
12		**11m**	r.t., 2 d		**10m**: R=CH=CHMe (*E*)	79

a) Excess (3—5 molar eq) of **11** was used. *b*) A mixture (1 : 1) of diastereomers was obtained.

TABLE III. Preparation of 4-Nucleoside Analogues

Run	Y-SiMe$_3$ (**14**)[a]		Conditions	Product (**15**)		Yield (%)
1		**14a**	r.t., 1 d		**15a** : R= 	89
2		**14b**	70 °C, 4 h		**15b** : R= 	83
3		**14c**	70 °C, 5 h		**15c** : R= 	57

a) Excess (3—5 molar eq) of **14** was used.

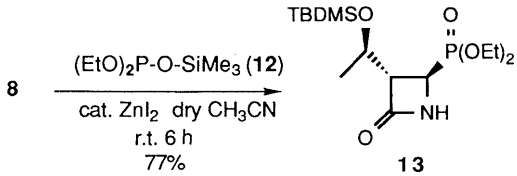


Chart 1

8 with silylated phosphite (**12**) in the presence of ZnI_2 at room temperature for 6 h gave the 4-phosphorus-substituted azetidin-2-one (**13**) in 77% yield.

Finally, 4-nucleoside-base substituted azetidin-2-ones (**15a—c**) were prepared in good yields by the reaction of **8** with nucleoside bases (**14a—c**) under similar conditions (Table III).

Although many methods have appeared for the nucleophilic substitution reaction at the C-4 position of azetidin-2-one, most of the methods start from the 4-acetoxy- and the 4-chloroazetidin-2-ones and usually involve strongly basic conditions. The present substitution reaction using the readily obtainable[13] 4-phenylsulfinylazetidin-2-ones (**8**) occurs under mild conditions (nearly neutral) and provides high yields of various types of

4-heterofunction substituted azetidin-2-ones (**10a—m**, **13**, and **15a—c**).

Experimental

All melting and boiling points are uncorrected. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a Hitachi R-22 (90 MHz), Hitachi R-250 (250 MHz), JEOL JNM-EX 270 (270 MHz) or a JEOL JNM-GX 500 (500 MHz) spectrometer with $CDCl_3$ as a solvent (with tetramethylsilane as an internal standard unless otherwise noted). Infrared (IR) absorption spectra were recorded in $CHCl_3$ on a JASCO HPIR-102 spectrophotometer. Low- and high-resolution (HR) mass spectra (MS) were obtained with a JEOL JMSD-300 instrument, with a direct inlet system at 70 eV. For column chromatography, E. Merck silica gel (70—230 mesh ASTM) was used. For preparative thin layer chromatography (TLC), E. Merck TLC plates pre-coated with Silica gel 60 F_{254} (0.5 mm) were used.

General Procedure for the Reaction of 4-Phenylsulfinylazetidin-2-ones (8) with Y-SiMe$_3$ (11a—m, 12, 14a—c) Zinc iodide (0.01 mmol) was added to a stirred solution of 4-phenylsulfinylazetidin-2-one (**8**, 0.10 mmol) and Y-SiMe$_3$ (**11a—m**, **12**, **14a—c**, 0.3—0.5 mmol) in dry CH_3CN (2 ml). The mixture was stirred for the period indicated in Tables I, II, and III, then the reaction was quenched with saturated aqueous $NaHCO_3$ solution (20 ml) and the mixture was diluted with CH_2Cl_2 (50 ml). The whole was partitioned between CH_2Cl_2 and water. The aqueous layer was separated and extracted with CH_2Cl_2 (50 ml). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by preparative TLC on silica gel to give the 4-hetero substituted azetidin-2-one.

(3*S*,4*R*)-4-Azido-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)ethyl]azetidin-2-one (10a) This (41.5 mg, quant.) was prepared from **8** (53.1 mg, 0.15 mmol), **11a** (104 mg, 0.903 mmol), and ZnI_2 (4.80 mg, 0.0150 mmol) in CH_3CN (2 ml) as colorless crystals, mp 67—69 °C (petroleum ether). IR: 3400, 2100, 1780 cm^{-1}. ^{1}H-NMR δ: 0.067, 0.084 (total 6H, each s, $SiMe_2$), 0.87 (9H, s, Si *tert*-Bu), 1.26 (3H, d, J=6.5 Hz, MeCH<), 3.18 (1H, dd, J=2.0, 3.7 Hz, 3-H), 4.23 (1H, dq, J=3.7, 6.5 Hz, >CHMe), 5.02 (1H, d, J=2.0 Hz, 4-H), 6.43 (1H, br s, NH). *Anal.* Calcd for $C_{11}H_{22}N_4O_2Si$: C, 48.86; H, 8.20; N, 20.71. Found: C, 48.96; H, 8.25; N, 20.64.

(3*S*,4*S*)-4-Acetamido-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)ethyl]azetidin-2-one (10b) This (50.0 mg, 67%) was prepared from **8** (93.7 mg, 0.265 mmol), **11b** (162 mg, 0.796 mmol), and ZnI_2 (8.60 mg, 0.0265 mmol) in CH_3CN (3.5 ml) as colorless crystals, mp 125—127 °C (petroleum ether). IR: 3450, 3400, 1760, 1670 cm^{-1}. ^{1}H-NMR δ; 0.09 (6H, s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 1.23 (3H, d, J=6.7 Hz, MeCH<), 2.03 (3H, s, MeCO), 2.98 (1H, dd, J=2.0, 4.0 Hz, 3-H), 4.18 (1H, m, >CHMe), 5.52 (1H, dd, J=2.0, 8.5 Hz, 4-H), 6.56 (1H, br s, NH), 6.72 (1H, br d, J=8.5 Hz, NH). HRMS Calcd for $C_{13}H_{26}N_2O_3Si$ (M^+): 229.1006. Found: 229.1001.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-imidazoylazetidin-2-one (10c) This (26.7 mg, 99%) was prepared from **8** (32.3 mg, 0.0915 mmol), **11c** (25.6 mg, 0.183 mmol), and ZnI_2 (2.90 mg, 0.00915 mmol) in CH_3CN (1 ml) as colorless crystals, mp 82—83 °C (petroleum ether). IR: 3420, 1780 cm^{-1}. ^{1}H-NMR δ: 0.099, 0.11 (total 6H, each s, $SiMe_2$), 0.89 (9H, s, Si *tert*-Bu), 1.23 (3H, d, J=6.1 Hz, MeCH<), 3.30 (1H, dd, J=1.8, 3.1 Hz, 3-H), 4.30 (1H, qd, J=6.1, 3.1 Hz, >CHMe), 5.79 (1H, d, J=1.8 Hz, 4-H), 6.79 (1H, br s, NH), 7.15 (2H, br s, CH=CH), 7.70 (1H, br s, N=CH). HRMS Calcd for $C_{10}H_{16}N_3O_2Si$ (M^+ − *tert*-Bu): 238.1010. Found: 238.1010; *Anal.* Calcd for $C_{14}H_{25}N_3O_2Si \cdot 1/3H_2O$: C, 55.77; H, 8.60; N, 13.94. Found: C, 55.59; H, 8.59; N, 13.75.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-methylthioazetidin-2-one (10d) This (38.3 mg, 98%) was prepared from **8** (50.0 mg, 0.142 mmol), **11d** (35.7 mg, 0.283 mmol), and ZnI_2 (4.50 mg, 0.0142 mmol) in CH_3CN (2 ml) as colorless crystals, mp 78—79 °C (petroleum ether) (lit.[14] no data). IR: 3400, 1760 cm^{-1}. ^{1}H-NMR δ: 0.057 (6H, s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 1.22 (3H, d, J=6.3 Hz, MeCH<), 2.14 (3H, s, SMe), 3.10 (1H, ddd, J=0.9, 2.3, 3.8 Hz, 3-H), 4.23 (1H, qd, J=6.3, 3.8 Hz, >CHMe), 4.78 (1H, d, J=2.3 Hz, 4-H), 6.30 (1H, br s, NH). HRMS Calcd for $C_8H_{16}NO_2SSi$ (M^+ − *tert*-Bu): 218.0672. Found: 218.0679.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-phenylthioazetidin-2-one (10e) This (38.2 mg, 79%) was prepared from **8** (50.4 mg, 0.143 mmol), **11e** (78.0 mg, 0.428 mmol), and ZnI_2 (4.50 mg, 0.0143 mmol) in CH_3CN (2 ml) as colorless crystals, mp 119—120 °C (petroleum ether) (lit.[13] no data). IR: 3400, 1765 cm^{-1}. ^{1}H-NMR δ: 0.051, 0.066 (total 6H, each s, $SiMe_2$), 0.87 (9H, s, Si *tert*-Bu), 1.20 (3H, d, J=6.4 Hz, MeCH<), 3.03 (1H, ddd, J=0.7, 2.2, 3.5 Hz, 3-H), 4.22 (1H, qd, J=6.4, 3.5 Hz, >CHMe), 5.07 (1H, dd, J=0.4, 2.2 Hz, 4-H), 6.15 (1H, br s, NH), 7.34—7.50 (5H, m, Ph). MS (m/z): 280 (M^+ − *tert*-Bu).

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-(phenylmethylthio)azetidin-2-one (10f) This (39.6 mg, 80%) was prepared from **8** (50.0 mg, 0.142 mmol), **11f** (55.5 mg, 0.284 mmol), and ZnI_2 (4.50 mg, 0.0142 mmol) in CH_3CN (2 ml) as colorless crystals, mp 66—67 °C (petroleum ether). IR: 3410, 1760 cm^{-1}. ^{1}H-NMR δ: 0.019, 0.041 (total 6H, each s, $SiMe_2$), 0.85 (9H, s, Si *tert*-Bu), 1.15 (3H, d, J=6.4 Hz, MeCH<), 3.03 (1H, dd, J=2.6, 3.5 Hz, 3-H), 3.85 (2H, s, CH_2Ph), 4.18 (1H, qd, J=6.4, 3.5 Hz, >CHMe), 4.75 (1H, d, J=2.6 Hz, 4-H), 5.68 (1H, br s, NH), 7.31 (5H, m, Ph). *Anal.* Calcd for $C_{18}H_{29}NO_2SSi$: C, 61.54; H, 8.26; N, 3.99; S, 9.12. Found: C, 61.31; H, 8.17; N, 4.15; S, 9.02.

(3*S*,4*R*)-4-Benzoylthio-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)ethyl]-azetidin-2-one (10g) This (29.1 mg, 59%) was prepared from **8** (48.0 mg, 0.136 mmol), **11g** (106 mg, 0.544 mmol), and ZnI_2 (4.50 mg, 0.0142 mmol) in CH_3CN (2 ml) as colorless crystals, mp 111—114 °C (petroleum ether). IR: 3450, 1775, 1665 cm^{-1}. ^{1}H-NMR δ: 0.098 (6H, s, $SiMe_2$) 0.90 (9H, s, Si *tert*-Bu), 1.25 (3H, d, J=6.3 Hz, MeCH<), 3.28 (1H, dd, J=2.5, 3.8 Hz, 3-H), 4.30 (1H, qd, J=6.3, 3.8 Hz, >CHMe), 5.47 (1H, d, J=2.5 Hz, 4-H), 6.51 (1H, br s, NH), 7.4—8.0 (5H, m, Ph). *Anal.* Calcd for $C_{18}H_{27}NO_3SSi$: C, 59.17; H, 7.40; N, 3.84; S, 8.78. Found: C, 58.90; H, 7.59; N, 3.59; S, 8.48.

(3*S*,4*R*)-4-(Acyloxyacetylthio)-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)-ethyl]azetidin-2-one (10h) This (76.5 mg, 73%) was prepared from **8** (103 mg, 0.292 mmol), **11h** [prepared from butyryloxythioacetic acid (78.3 mg, 0.584 mmol) and 1-methoxy-1-(trimethylsiloxy)propene (187 mg, 1.17 mmol) in CH_3CN (2 ml)], and ZnI_2 (9.60 mg, 0.030 mmol) in CH_3CN (2 ml); as colorless crystals, mp 52—54 °C (petroleum ether). IR: 3400, 1765, 1690 cm^{-1}. ^{1}H-NMR δ: 0.053, 0.063 (total 6H, each s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 1.19 (3H, d, J=6.5 Hz, MeCH<), 2.18 (3H, s, OAc), 3.18 (1H, dd, J=2.4, 3.7 Hz, 3-H), 4.25 (1H, qd, J=6.5, 3.7 Hz, >CHMe), 4.73 (2H, s, OCH_2CO), 5.33 (1H, d, J=2.4 Hz, 4-H), 6.47 (1H, br s, NH). HRMS Calcd for $C_{11}H_{18}NO_5SSi$ (M^+ − *tert*-Bu): 304.0673. Found: 304.0665.

(3*R*,4*R*)-4-Acetoxy-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)ethyl]azetidin-2-one (10i) This (20.0 mg, 52%) was prepared from **8** (47.2 mg, 0.134 mmol), **11i** (35.2 mg, 0.267 mmol), and ZnI_2 (4.30 mg, 0.0134 mmol) in CH_3CN (1 ml) as colorless crystals, mp 103—105 °C (petroleum ether) (lit.[15] 104—106 °C). IR: 3400, 1760 cm^{-1}. ^{1}H NMR δ: 0.06 (6H, s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 1.25 (3H, d, J=6.3 Hz, MeCH<), 2.10 (3H, s, OAc), 3.17 (1H, dd, J=1.2, 3.5 Hz, 3-H), 4.22 (1H, m, >CHMe), 5.83 (1H, d, J=1.2 Hz, 4-H), 6.56 (1H, br s, NH). MS (m/z): 230 (M^+ − *tert*-Bu).

(3*R*,4*R*)-4-Benzoyloxy-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)ethyl]-azetidin-2-one (10j) This (11.2 mg, 51%) was prepared from **8** (22.2 mg, 0.0629 mmol), **11j** (24.4 mg, 0.126 mmol), and ZnI_2 (2.00 mg, 0.00629 mmol) in CH_3CN (1 ml) as colorless crystals, mp 103—105 °C (petroleum ether) (lit.[16] 100—102 °C). IR: 3450, 1790, 1720 cm^{-1}. ^{1}H-NMR δ: 0.10 (6H, s, $SiMe_2$), 0.85 (9H, s, Si *tert*-Bu), 1.31 (3H, d, J=6.0 Hz, MeCH<), 3.34 (1H, dd, J=1.0, 3.5 Hz, 3-H), 4.26 (1H, qd, J=6.0, 3.5 Hz, >CHMe), 6.08 (1H, d, J=1.0 Hz, 4-H), 6.65 (1H, br s, NH), 7.3—8.2 (5H, m, Ph). MS (m/z): 292 (M^+ − *tert*-Bu).

(3*R*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-(2-phenylbutyroyloxy)azetidin-2-one (10k) This (36.3 mg, 66%) was prepared from **8** (50.0 mg, 0.142 mmol), **11k** (66.9 mg, 0.284 mmol), and ZnI_2 (4.50 mg, 0.0142 mmol) in CH_3CN (1 ml) as a yellow oil. IR: 3420, 1780, 1735 cm^{-1}. ^{1}H-NMR δ: −0.010, 0.027, 0.034, 0.054 (total 6H, each s, $SiMe_2$), 0.81, 0.84 (total 9H, each s, Si *tert*-Bu), 0.90 (3H, t, J=7.3 Hz, $MeCH_2$), 1.16, 1.24 (total 3H, each d, J=6.3 Hz, MeCH<), 1.81, 2.09 (total 2H, each m, $MeCH_2$), 3.10 (0.5H, dd, J=1.3, 4.4 Hz, 3-H), 3.13 (0.5H, dd, J=1.3, 3.8 Hz, 3-H), 3.46 (1H, dd, J=7.6 Hz, OCOCH), 4.15 (1H, m, >CHMe), 5.79, 5.85 (total 1H, each d, J=1.3 Hz, 4-H), 6.39, 6.50 (total 1H, each br s, NH), 7.27 (5H, m, Ph). HRMS Calcd for $C_{17}H_{24}NO_4Si$ (M^+ − *tert*-Bu): 334.1474. Found: 334.1494.

(3*R*,4*R*)-4-(Acyloxycarbonyloxy)-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)-ethyl]azetidin-2-one (10l) This (40.0 mg, 66%) was prepared from **8** (61.6 mg, 0.174 mmol), **11l** [prepared from acyloxycarboxylic acid (61.8 mg, 0.523 mmol), trimethylsilyl chloride (0.44 ml), and hexamethyldisilazane (4 ml)], and ZnI_2 (5.40 mg, 0.0170 mmol) in CH_3CN (4 ml) as colorless crystals, mp 69—70 °C (petroleum ether). IR: 3450, 1790, 1760 cm^{-1}. ^{1}H-NMR δ: 0.062, 0.067 (total 6H, each s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 1.25 (3H, d, J=6.7 Hz, MeCH<), 2.16 (3H, s, OAc), 3.21 (1H, dd, J=1.2, 3.1 Hz, 3-H), 4.22 (1H, qd, J=6.7, 3.1 Hz, >CHMe), 4.63 (2H, AB-q, J=15.9 Hz, OCH_2CO), 5.95 (1H, d, J=1.2 Hz, 4-H), 6.62 (1H, br s, NH). *Anal.* Calcd for $C_{15}H_{27}NO_6Si$: C, 52.17; H, 7.83; N, 4.06. Found: C, 51.93; H, 7.73; N, 4.11.

(3*R*,4*R*)-4-Butenoyloxy-3-[(1*R*)-(1-*tert*-butyldimethylsiloxy)ethyl]-azetidin-2-one (10m) This (23.2 mg, 79%) was prepared from **8** (33.0 mg, 0.0935 mmol), **11m** (44.3 mg, 0.280 mmol), and ZnI_2 (2.90 mg, 0.00940 mmol) in CH_3CN (1.5 ml) as colorless crystals, mp 72—75 °C (petroleum ether) (lit.[6] no data). IR: 3430, 1780, 1720, 1655 cm^{-1}. ^{1}H-NMR δ: 0.061, 0.066 (total 6H, each s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 1.26 (3H, d, J=6.3 Hz, MeCH), 1.91 (3H, dd, J=1.5, 6.7 Hz, MeC=), 3.20 (1H, dd, J=1.7, 5.0 Hz, 3-H), 4.23 (1H, qd, J=6.3, 3.0 Hz, >CHMe), 5.85 (1H, dd, J=1.5, 13.4 Hz, COCH=), 5.90 (1H, br s, 4-H), 6.49 (1H, br s, NH), 7.06 (1H, dq, J=6.7, 13.4 Hz, MeCH=). HRMS Calcd for $C_{11}H_{18}NO_4Si$ ($M^+ - tert$-Bu): 256.1005. Found: 256.1018.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-diethylphosphonyl-azetidin-2-one (13) This (40.0 mg, 77%) was prepared from **8** (50.0 mg, 0.141 mmol), **12** (127 mg, 0.706 mmol), and ZnI_2 (4.50 mg, 0.0142 mmol) in CH_3CN (1 ml) as a colorless oil. IR: 3400, 1780, 1250, 1140 cm^{-1}. ^{1}H-NMR δ: 0.059, 0.065 (total 6H, each s, $SiMe_2$), 0.86 (9H, s, Si *tert*-Bu), 0.88 (3H, d, J=6.3 Hz, MeCH), 1.34 (6H, t, J=7.0 Hz, $(MeCH_2O)_2$), 3.38 (1H, ddt, J=1.0, 9.8, 2.5 Hz, 3-H), 3.92 (1H, dd, J=2.5, 9.8 Hz, 4-H), 4.17 (4H, dq, J=1.0, 7.0 Hz, $(MeCH_2O)_2$), 4.23 (1H, qd, J=3.0, 6.3 Hz, >CHMe), 6.20 (1H, br s, NH). HRMS Calcd for $C_{15}H_{32}NO_5PSi$ (M^+): 365.1786. Found: 365.1781.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-[1-(2,4-dihydroxypyrimidinyl)]azetidin-2-one (15a) This (42.9 mg, 89%) was prepared from **8** (50.0 mg, 0.142 mmol), **14a** (109 mg, 0.425 mmol), and ZnI_2 (4.50 mg, 0.142 mmol) in CH_3CN (2.0 ml) as colorless crystals, mp 234—235 °C (petroleum ether). IR: 3400, 1780, 1710, 1690 cm^{-1}. ^{1}H-NMR δ: 0.087, 0.11 (total 6H, each s, $SiMe_2$), 0.88 (9H, s, Si *tert*-Bu), 1.29 (3H, d, J=6.1 Hz, MeCH), 3.19 (1H, dd, J=1.8, 3.7 Hz, 3-H), 4.29 (1H, qd, J=6.1, 3.7 Hz, >CHMe), 5.84, (1H, dd, J=1.8, 8.0 Hz, 4-H), 6.21 (1H, br s, =CHCO), 6.30 (1H, br s, NH), 7.49 (1H, d, J=8.0 Hz, >NCH=), 8.57 (1H, br s, NH). *Anal.* Calcd for $C_{15}H_{25}N_3O_4Si$: C, 53.07; H, 7.42; N, 12.38. Found: C, 52.97; H, 7.38; N, 12.37.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-[1-(2,4-dihydroxy-5-methylpyrimidinyl)]azetidin-2-one (15b) This (248 mg, 83%) was prepared from **8** (300 mg, 0.850 mmol), **14b** (1.10 g, 4.07 mmol), and ZnI_2 (45.0 mg, 0.141 mmol) in CH_3CN (10 ml) as colorless crystals, mp 213—214 °C (petroleum ether). IR: 3400, 1780, 1685 cm^{-1}. ^{1}H NMR δ: 0.080, 0.10 (total 6H, each s, $SiMe_2$), 0.87 (9H, s, Si *tert*-Bu), 1.27 (3H, d, J=6.0 Hz, MeCH), 1.96 (3H, d, J=1.3 Hz, COCMe=), 3.19 (1H, dd, J=1.8, 3.5 Hz, 3-H), 4.27 (1H, qd, J=6.0, 3.5 Hz, >CHMe), 6.22 (1H, d, J=1.8 Hz, 4-H), 6.35 (1H, br s, NH), 7.31 (1H, d, J=1.3 Hz, NCH=), 8.70 (1H, br s, NH). *Anal.* Calcd for $C_{16}H_{27}N_3O_4Si$: C, 54.01; H, 7.70; N, 11.89. Found: C, 53.82; H, 7.50; N, 11.76.

(3*S*,4*R*)-3-[(1*R*)-(1-*tert*-Butyldimethylsiloxy)ethyl]-4-[9-(6-methylthio)-adeninyl]azetidin-2-one (15c) This (49.9 mg, 57%) was prepared from **8** (78.8 mg, 0.223 mmol), **14c** [prepared from 6-(methylthio)adenine (112.6 mg, 0.677 mmol), trimethylsilyl chloride (0.6 ml), and hexamethyldisilazane (5.7 ml)], and ZnI_2 (7.00 mg, 0.022 mmol) in CH_3CN (4 ml) as colorless crystals, mp 162—163 °C (petroleum ether). IR: 3400, 1780, 1560 cm^{-1}. ^{1}H NMR δ: 0.11, 0.12 (total 6H, each s, $SiMe_2$), 0.89 (9H, s, Si *tert*-Bu), 1.26 (3H, d, J=6.3 Hz, MeCH), 2.71 (3H, s, SMe), 3.68 (1H, dd, J=1.8, 3.0 Hz, 3-H), 4.34 (1H, qd, J=6.3, 3.0 Hz, >CHMe), 6.26 (1H, d, J=1.8 Hz, 4-H), 6.88 (1H, br s, NH), 8.16, 8.72 (total 2H, each s, Ar-H). *Anal.* Calcd for $C_{17}H_{27}N_5O_4SSi$: C, 51.88; H, 6.91; N, 17.79; S, 8.15. Found: C, 51.65; H, 6.80; N, 17.95, S, 8.16.

References and Notes

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