HETEROCYCLES, Vol. 64, 2004, pp. 241 - 248
Received, 9th July, 2004, Accepted, 16th August, 2004, Published online, 17th August, 2004

PREPARATION OF 2',3'-OXIRANE-FUSED CARBOCYCLIC NUCLEOSIDES BASED ON *N*-SUBSTITUTED 2-AZABICYCLO[2.2.1]-HEPT-5-EN-3-ONES

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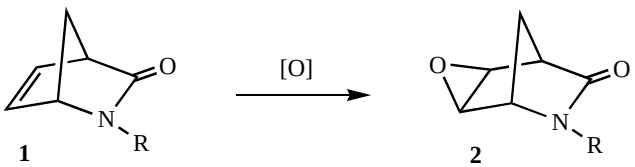
Abstract – The epoxidation of *N*-substituted 2-azabicyclo[2.2.1]hept-5-en-3-ones (**1**) led to the *exo*-selective formation of epoxides (**2**), and the use of **2** for the preparation of 2',3'-oxirane-fused carbocyclic nucleosides (**10**) was attempted.

2-Azabicyclo[2.2.1]hept-5-en-3-one (ABH) (**1a**) is a class of bicyclic lactam with greater strain energy, and we devoted attention to the development of its synthetic potential.[1] We have previously reported that cycloaddition of diazomethane[2] and azides[3] to *N*-substituted ABH (**1**) stereoselectively led to cyclopropane- and aziridine-fused ABHs, which were valuable for the preparation of 2',3'-methano- and 2',3'-epimino-carbocyclic nucleoside derivatives. In due course, we have also become interested in the preparation of 2',3'-oxirane-fused carbocyclic nucleosides,[4] for which the conversion of epoxide (**2**), available by the epoxidation of **1**, should serve as a concise approach. There are only a few reports[5] of the epoxidation of **1a** using oxone under pH-controlled conditions and *m*-CPBA, but the detailed descriptions have not been given. Thus, we initially targeted the epoxidation of *N*-substituted ABHs (**1**).



1

a: R=H
b: R=Boc
c: R=Cbz
d: R=Bn
e: R=TBDMS

2

a: R=H
b: R=Boc
c: R=Cbz
d: R=Bn
e: R=TBDMS

Scheme 1

This paper is dedicated to Dr. Pierre Potier on the occasion of his 70th birthday.

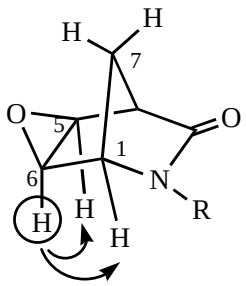
We first investigated the epoxidation of **1** using *m*-CPBA. Attempted epoxidation of **1a** using *m*-CPBA (2 equiv.) in CH_2Cl_2 at room temperature for 48 h resulted in very poor yield of **2a**, in contrast to the availability of **2a** from **1a** using *m*-CPBA.[5b] The epoxidation of **1b-e** with *m*-CPBA produced epoxides (**2b**-**e**) as seen in Table, and a significant increase in the susceptibility to epoxidation was observed when an electron-donating group was present at the nitrogen as **1d**,**e**. We reasoned that the electron-rich nature of **1d**,**e** by the neighboring participation[6] between the nitrogen and the double bond might allow for such susceptibility. Moreover, dimethyldioxorane (DMDO)[7] appeared to be highly effective for the epoxidation of **1**.

Table Epoxidation of **1**

1	Conditions	Yields (%) of **2**
1a	*m*-CPBA / CH_2Cl_2 / 48 h	5 (70)[a]
	DMDO[b] / CH_2Cl_2 / 36 h	80
1b	*m*-CPBA / CH_2Cl_2 / 48 h	66
	DMDO[b] / CH_2Cl_2 / 36 h	80
	H_2O_2 / CH_3CN / 48 h	-- (77)[a]
	UHP[c] / CH_2Cl_2 / 36 h	-- (40)[a]
1c	*m*-CPBA / CH_2Cl_2 / 48 h	62
	DMDO[b] / CH_2Cl_2 / 36 h	80
1d	*m*-CPBA / CH_2Cl_2 / 48 h	63
	DMDO[b] / CH_2Cl_2 / 36 h	80
	H_2O_2 / CH_3CN / 48 h	4 (80)[a]
	UHP[c] / CH_2Cl_2 / 36 h	37 (45)[a]
1e	*m*-CPBA / CH_2Cl_2 / 48 h	67
	DMDO[b] / CH_2Cl_2 / 36 h	85
	H_2O_2 / CH_3CN / 48 h	6 (74)[a]
	UHP[c] / CH_2Cl_2 / 36 h	47 (25)[a]

[a] Recovery of **1** (%) [b] Dimethyldioxorane [c] Urea-hydrogen peroxide[8]

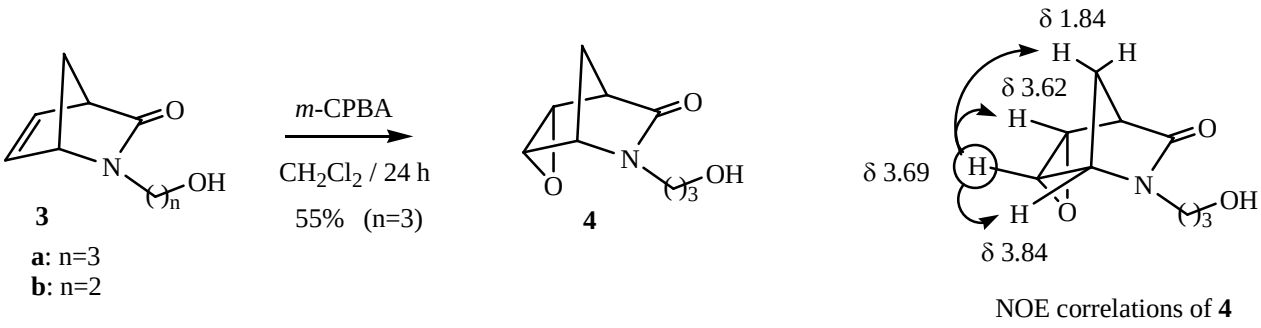
The proof of the stereoselective formation of epoxides (**2**) was obtained by NOE experiments, where no NOE between H-6 and H-7 was observed.



NOE correlatios of **2**

	C_6-H	C_5-H	C_1-H
2a	δ 3.67	δ 3.58	δ 3.90
2b	δ 3.75	δ 3.59	δ 4.59
2c	δ 3.78	δ 3.61	δ 4.70
2d	δ 3.52	δ 3.25	δ 3.75
2e	δ 3.54	δ 3.54	δ 3.86

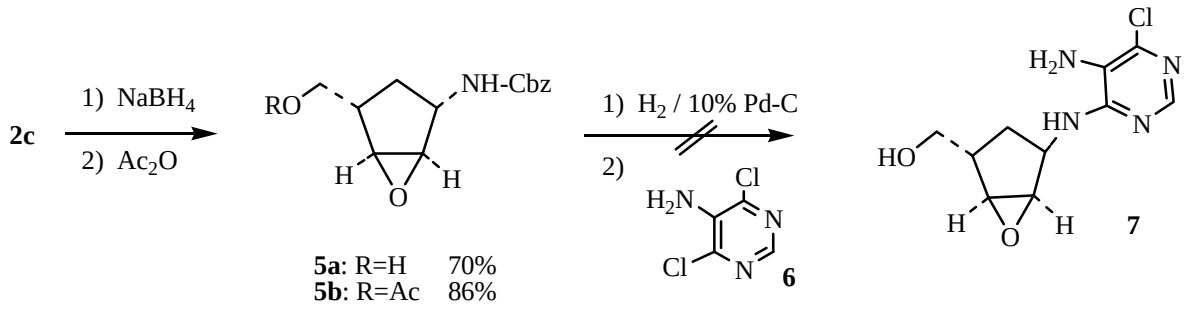
Next, as a study to examine the feasibility of the epoxidation taking place from the endo-side, the epoxidation of **3**, whose hydroxyl group might play a stereodirecting role, was run (Scheme 2). No reaction occurred when we attempted to oxidize **3b** using Sharpless' method, and **3b** was recovered unchanged. On the other hand, with the failure of the epoxidation of **3b**, treatment of **3a** with *m*-CPBA in CH_2Cl_2 for 24 h produced *endo*-epoxide (**4**) in 55% yield. The structure of **4** was determined on the basis of NOE experiments with the observation of NOE between H-6 and H-7.



NOE correlations of **4**

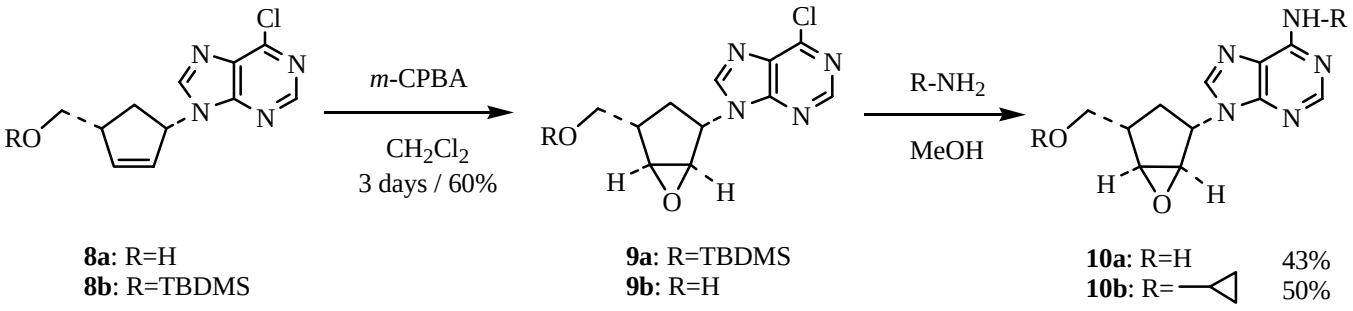
Scheme 2

With these results in hand, we attempted to use epoxide (**2c**) for the construction of 2',3'-oxirane-fused carbocyclic nucleoside derivatives (**10**) according to the previously reported methods.[2,3] Reduction of **2c** with $NaBH_4$ produced **5a**, and subsequent acetylation of **5a** with Ac_2O gave **5b**. According to the conventional method,[2,3] removal of the *N*-Cbz group in **5a**, followed by its subjection to the reaction with pyrimidine (**6**) resulted in complex mixtures without the formation of **7** (Scheme 3). The use of **5b**, various solvents, lower temperature, and longer reaction time did not improve the reaction, and no further optimization was attempted. The complicated situation seems to stem from higher lability of the epoxide in **5** under the reaction conditions.

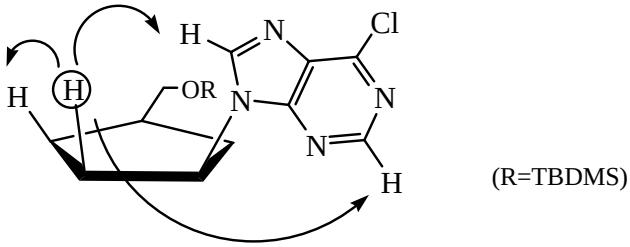


Scheme 3

Alternatively, the preparation of 2',3'-oxirane-fused carbocyclic nucleosides (**10**) began with the epoxidation of **8b**, derived from TBDMSCl and the known **8a**,[9,10] as shown in Scheme 4. Treatment of **8b** with *m*-CPBA in CH_2Cl_2 afforded epoxide (**9a**), most likely explicable by the attack of *m*-CPBA on **8b** from the less hindered side. The structure of **9a** was confirmed based on NOE experiments. Then, removal of the *N*-TBDMS group in **9a** with *n*-Bu_4NF afforded **9b**, followed by treatment of **9b** with ammonia and cyclopropylamine, leading to **10**a and **10b**, respectively.



Scheme 4



NOE Correlations of **9a**

In summary, we have shown that the epoxidation of *N*-substituted ABH (**1**) using *m*-CPBA and DMDO afforded epoxides (**2**) in an *exo*-selective manner. Although we encountered a lack of success in the

direct transformation of **2** to 2',3'-oxirane-fused carbocyclic nucleosides (**10**), an alternative route involving the epoxidation of **8b** yielded **10**.

EXPERIMENTAL

Melting points were recorded on a Yamato MP21 and are uncorrected. MS and HRMS spectra were recorded on a Micromass AutoSpec 3100 mass spectrometer. IR spectra were measured on a Hitachi Model 270-30 spectrophotometer. The NMR experiments were performed with a JEOL JNM-LA300 or JNM-ECA500 spectrometer, and chemical shifts are expressed in ppm (δ) with TMS as an internal reference. Medium pressure liquid column chromatography (MPLC) and flash column chromatography were performed on silica gel (Silica gel 60N, Kanto Chemical Co., Inc.). Dehydrated solvents were purchased from Kanto Chemical Co. Inc.

Compounds (**1a**,[11] **1b**,[9] and **1d**[12]) were known, and compounds (**1c** and **1e**) were prepared by the treatment of **1a** with (*tert*-butyl)dimethylsilylchloride and benzyl chloridocarbonate, respectively, according to the literature.[9]

Benzyl 2-Azabicyclo[2.2.1]hept-5-en-3-one-2-carboxylate (1c):

mp 46-47 °C (hexane-AcOEt). IR ($CHCl_3$): 1700 cm^{-1}. ^{1}H-NMR ($CHCl_3$) δ: 2.15 (dd, 1H, *J*=1.4, 5.4 Hz), 2.33 (dd, 1H, *J*=1.4, 6.8 Hz), 3.39 (s, 1H), 5.00 (s, 1H), 5.21 (s, 2H), 6.63-6.65 (m, 1H), 6.86-6.88 (m, 1H), 7.26-7.41 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 54.1, 54.9, 62.5, 67.8, 127.9, 128.2, 128.5, 138.2, 140.0, 175.7. MS *m/z*: 243 (M^+). *Anal*. Calcd for $C_{14}H_{13}NO_3$: C, 69.13; H, 5.34; N, 5.76. Found: C, 69.18; H, 5.53; N, 5.78.

2-[*tert*-Butyl(dimethyl)silyl]-2-azabicyclo[2.2.1]hept-5-en-3-one (1e):

bp 121 °C/ 1 mmHg. IR (neat): 1700 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.18 (s, 3H), 0.19 (s, 3H), 0.88 (s, 9H), 2.12 (dt, 1H, *J*=1.1, 7.4 Hz), 2.30 (dt, 1H, *J*=1.7, 8.0 Hz), 3.21 (s, 1H), 4.35 (dd, 1H, *J*=1.7, 3.4 Hz), 6.62-6.66 (m, 1H), 6.74 (dd, 1H, *J*=2.3, 5.7 Hz). ^{13}C-NMR ($CDCl_3$) δ: -5.6, -5.5, 19.0, 26.2, 54.0, 60.7, 63.5, 138.4, 140.7, 187.2. MS *m/z*: 223 (M^+). *Anal*. Calcd for $C_{12}H_{21}NOSi$: C, 64.52; H, 9.48; N, 6.27. Found: C, 64.35; H, 9.56; N, 6.11.

Epoxidation of 1 with *m*-CPBA: General procedure:

A mixture of **1** and *m*-CPBA (2 equiv.) in CH_2Cl_2 was stirred at rt for the time shown in Table. Then the mixture was diluted with AcOEt, washed with aqueous $NaHCO_3$ and brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with hexane-AcOEt as an eluent to give **2**.

Epoxidation of 1 with DMDO: General procedure:

A mixture of **1** and an excess amount of DMDO[7] in acetone was stirred at rt for 36 h. Then the mixture was dilute with AcOEt, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with hexane-AcOEt as an eluent to give **2**.

***rel*-(1*R*,2*S*,4*R*,5*S*)-3-Oxa-6-azatricyclo[3.2.1.0^{2,4}]octan-7-one (2a):**

mp 122-124 °C (AcOEt-hexane) (lit.,[5b] mp 120-121 °C; lit.,[5a] 146 °C). IR ($CHCl_3$): 3448, 3212, 3000, 1724 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.68 (d, 1H, *J*=9.1 Hz), 1.85 (d, 1H, *J*=9.1 Hz), 2.89 (s, 1H), 3.58 (d, 1H, *J*=3.4 Hz), 3.67 (d, 1H, *J*=3.4 Hz), 3.90 (s, 1H), 6.48 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 31.2, 46.9, 51.5, 55.7, 180.7. MS *m/z*: 125 (M^+).

***rel*-(1*R*,2*S*,4*R*,5*S*)-*tert*-Butyl 7-Oxo-3-oxa-6-azatricyclo[3.2.1.0^{2,4}]octane-6-carboxylate (2b):**

mp 118-119 °C (hexane-AcOEt) (lit.,[5b] 115-116 °C). IR ($CHCl_3$): 1786, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.50 (s, 9H), 1.61 (d, 1H, *J*=10.3 Hz), 1.79 (d, 1H, *J*=10.3 Hz), 3.04 (s, 1H), 3.59 (d, 1H, *J*=2.8 Hz), 3.75 (d, 1H, *J*=2.8 Hz), 4.59 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 27.1, 28.1, 48.4, 50.0, 53.2, 59.0, 83.4, 149.8, 173.5. MS *m/z*: 225 (M^+).

***rel*-(1*R*,2*S*,4*R*,5*S*)-Benzyl 7-Oxo-3-oxa-6-azatricyclo[3.2.1.0^{2,4}]octane-6-carboxylate (2c):**

mp 105-106 °C (hexane-AcOEt). IR ($CHCl_3$): 1794, 1768, 1718 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.65 (d, 1H, *J*=10.2 Hz), 1.84 (dd, 1H, *J*=1.5, 10.2 Hz), 3.09 (t, 1H, *J*=1.5 Hz), 3.61 (dd, 1H, *J*=1.5, 3.4 Hz), 3.78 (dd, 1H, *J*=1.5, 3.4 Hz), 4.70 (t, 1H, *J*=1.5 Hz), 5.26 (s, 2H), 7.31-7.44 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 27.1, 48.1, 49.7, 52.9, 59.1, 68.3, 128.2, 128.5, 128.7, 135.1, 151.1, 172.9. MS *m/z*: 259 (M^+). *Anal*. Calcd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.05; N, 5.40. Found: C, 65.11; H, 5.12; N, 5.30.

***rel*-(1*R*,2*S*,4*R*,5*S*)-6-Benzyl-3-oxa-6-azatricyclo[3.2.1.0^{2,4}]octan-7-one (2d):**

Oil. IR (neat): 1704 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (d, 1H, *J*=9.7 Hz), 1.77 (d, 1H, *J*=9.7 Hz), 2.98 (s, 1H), 3.25 (d, 1H, J=2.8 Hz), 3.52 (d, 1H, J=2.8 Hz), 3.75 (s, 1H), 4.32 (d, 1H, J=14.9 Hz), 4.42 (d, 1H, *J*=14.9 Hz), 7.72-7.33 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 30.3, 46.1, 47.3, 51.8, 55.4, 59.7, 128.0, 128.3, 128.4, 128.9, 129.0, 137.4, 177.1. HRMS *m/z*: Calcd for $C_{13}H_{13}NO_2$: 215.0946. Found: 215.0939.

***rel*-(1*R*,2*S*,4*R*,5*S*)-6-[*tert*-Butyl(dimethyl)silyl]-3-oxa-6-azatricyclo[3.2.1.0^{2,4}]octan-7-one (2e):**

Oil. IR (neat): 1710, 1696 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.19 (s, 3H), 0.28 (s, 3H), 0.90 (s, 9H), 1.56 (d, 1H, *J*=9.8 Hz), 1.78 (d, 1H, *J*=9.8 Hz), 2.87 (s, 1H), 3.54 (br s, 2H), 3.86 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: -5.2, -4.8, 18.8, 26.3, 51.5, 48.3, 51.0, 55.1, 59.4, 183.4. HRMS *m/z*: Calcd for $C_{12}H_{21}NO_2Si$: 239.1341. Found: 239.1328.

***rel*-(1*R*,4*R*)-2-(3-Hydroxypropyl)-2-azabicyclo[2.2.1]hept-5-en-3-one (3a):**

After a mixture of **1a** (1.09 g, 10 mmol) and 60% NaH (400 mg, 15 mmol) was stirred in THF (50 mL) under ice-cooling for 30 min, 2-(3-bromopropoxy)tetrahydro-2*H*-pyran (3.3 g, 15 mmol) was added to the mixture, and, then, the whole was stirred at rt overnight. Excess NaH was decomposed by the addition of 20% NH_4Cl to the mixture under ice-cooling, and the mixture was extracted with AcOEt (200 mL). The extract was washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and MeOH (30 mL) and a catalytic amount of TsOH were added to the residue. The whole was stirred at rt for 1 h, and the mixture was extracted with ether. The extract was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with hexane-AcOEt (5:1) as an eluent to give 1.8 g of **3a** (70%).

Oil. IR ($CHCl_3$): 3450, 1684 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.50-1.65 (m, 2H), 2.15 (d, 1H, *J*=8.0 Hz), 2.32 (d, 1H, *J*=8.0 Hz), 3.15-3.30 (m, 3H), 3.34 (s, 1H), 3.35-3.45 (m, 1H), 3.46-3.55 (m, 1H), 4.17 (s, 1H), 6.67 (dd, 1H, *J*=1.7, 5.2 Hz), 6.84 (dd, 1H, *J*=1.8, 5.2 Hz). ^{13}C-NMR ($CDCl_3$) δ: 30.5, 39.9, 53.8, 58.9, 59.9, 64.4, 138.6, 139.9, 182.1. HRMS *m/z*: Calcd for $C_9H_{13}NO_2$ 167.0946. Found: 167.0953.

***rel*-(1*R*,2*R*,4*S*,5*S*)-6-(3-Hydroxypropyl)-3-oxa-6-azatricyclo[3.2.1.0^{2,4}]octan-7-one (4):**

A mixture of **3a** (167 mg, 1 mmol) and *m*-CPBA (344 mg, 2 mmol) was stirred at rt for 24 h. The mixture was then diluted with AcOEt, washed with aqueous $NaHCO_3$ and brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with hexane-AcOEt (5:1) as an eluent to give 100 mg (55%) of **4**.

Oil. IR ($CHCl_3$): 3428, 1692 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.58-1.71 (m, 3H), 1.84 (d, 1H, *J*=9.7 Hz), 2.97 (s, 1H), 3.12 (br s, 1H), 3.36 (t, 2H, *J*=6.3 Hz), 3.55 (d, 2H, *J*=5.1 Hz), 3.62 (d, 1H, *J*=3.4 Hz), 3.69 (d, 1H, *J*=3.4 Hz), 3.84 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: 31.0, 31.9, 38.8, 47.4, 51.9, 55.5, 58.7, 61.0, 178.8. HRMS *m/z*: Calcd for $C_9H_{13}NO_3$: 183.0895. Found: 183.0897.

Benzyl *rel*-[(1*R*,2*S*,4*S*,5*S*)-4-Hydroxymethyl-6-oxabicyclo[3.1.0]hex-2-yl]carbamate (5a):

Reduction of **2c** (155 mg, 0.6 mmol) with $NaBH_4$ (45 mg, 12 mmol) in MeOH (30 mL) was carried out according to the literature[2,3] to give 110 mg (70%) of **5a**.

mp 69-70 °C (AcOEt-hexane). IR ($CHCl_3$): 3624, 3444, 1706 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.43 (dt, 1H, *J*=13.7, 4.0 Hz), 1.54 (br s, 1H), 2.49 (dt, 1H, *J*=13.7, 8.6 Hz), 2.83 (br s, 1H), 3.56 (dd, 1H, *J*=4.6, 10.3 Hz), 3.65 (dd, 1H, *J*=4.0, 10.3 Hz), 4.75 (br s, 1H), 5.07 (s, 2H), 5.14 (br s, 1H), 5.72-5.78 (m, 1H), 5.81 (br s, 1H), 7.25-7.36 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 32.9, 40.2, 50.3, 59.3, 59.7, 63.1, 66.7, 128.1, 128.5, 136.6, 156.6. MS *m/z*: 263 (M^+). *Anal*. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.67; H, 6.67; N, 5.22.

[*rel*-(1*R*,2*R*,4*R*,5*S*)-4-Benzyloxycarbonylamino-6-oxabicyclo[3.1.0]hex-2-yl]methyl Acetate (5b):
A mixture of **5a** (263 mg, 1 mmol), Ac_2O (153 mg, 1.5 mmol) and Et_3N (202 mg, 2 mmol) in CH_2Cl_2 (50 mL) was stirred at rt overnight. The mixture was diluted with AcOEt, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane (10:1) as an eluent to give 262 mg (86%) of **5b**.
mp 68 °C (hexane-AcOEt). IR ($CHCl_3$): 3420, 1720 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.38 (d, 1H, *J*=14.9 Hz), 2.11 (s, 3H), 2.10-2.20 (m, 1H), 2.55-2.61 (m, 1H), 3.41 (s, 1H), 3.51 (s, 1H), 3.94 (dd, 1H, *J*=5.2, 11.5 Hz), 4.25-4.32 (m, 2H), 5.10 (s, 2H), 5.30 (br s, 1H), 7.32-7.35 (m, 5H). ^{13}C-NMR ($CDCl_3$) δ: 21.2, 32.3, 38.5, 50.8, 58.5, 65.2, 67.3, 128.1, 128.2, 129.0, 136.3, 155.6, 170.5. MS *m/z*: 305 (M^+). *Anal*. Calcd for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27; N, 4.59. Found: .C, 62.96; H, 6.28; N, 4.78.

9-[*rel*-(1*R*,4*S*)-4-(*tert*-Butyldimethylsilyloxymethyl)cyclopent-2-en-1-yl]-6-chloro-9*H*-purine (8b):
A mixture of **8a**[9,10] (250 mg, 1 mmol), TBDMSCl (225 mg, 1.5 mmol), Et_3N (202 mg, 2 mmol) and DMAP (12 mg, 0.1 mmol) in CH_2Cl_2 (50 mL) was stirred at rt overnight. The mixture was diluted with AcOEt, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by MPLC with AcOEt-hexane (1:2) as an eluent to give 262 mg (86%) of **8b**.
mp 77°C (hexane-AcOEt). IR ($CHCl_3$): 1595, 1565 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 0.05 (s, 6H), 0.86 (s, 9H), 1.71 (dt, 1H, *J*=13.8, 6.8 Hz), 2.80 (dt, 1H, *J*=13.8, 8.6 Hz), 3.02-3.11 (m, 1H), 3.63 (dd, 1H, *J*=5.1, 9.7 Hz), 3.74 (dd, 1H, *J*=5.1, 9.7 Hz), 5.80-5.90 (m, 2H), 6.21 (dt, 1H, *J*=5.8, 2.0 Hz), 8.23 (s, 1H), 8.74 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: -5.2, 18.5, 26.0, 34.6, 47.9, 60.1, 65.3, 128.8, 131.9, 140.1, 143.8, 150.8, 151.5, 151.8. MS *m/z*: 307, 309 (M^+-C_4H_9). *Anal*. Calcd for $C_{17}H_{25}N_4OClSi$: C, 55.95; H, 6.90; N, 15.35. Found: .C, 55.69; H, 6.81; N, 15.43.

9-[*rel*-(1*R*,2*S*,4*S*,5*S*)-4-(*tert*-Butyldimethylsilyloxymethyl)-6-oxabicyclo[3.1.0]hex-2-yl]-6-chloro-9*H*-purine (9a):
Epoxidation of **8b** (364 mg, 1 mmol) with *m*-CPBA (344 mg, 2 mmol) was carried out for 3 days according to the procedure described for **1**, producing 228 mg (60%) of **9a**.
mp 108-109 °C (hexane-AcOEt). IR ($CHCl_3$): 1592, 1566 cm^{-1}. ^{1}H-NMR (pyridine-d_5) δ: 0.12 (s, 3H), 0.13 (s, 3H), 0.95 (s, 9H), 1.43 (dt, 1H, *J*=12.1, 9.7 Hz), 2.32 (dt, 1H, *J*=15.5, 8.6 Hz), 3.74 (dd, 1H, *J*=6.3, 9.7 Hz), 3.78-3.84 (m, 3H), 3.99 (s, 1H), 5.27 (t, 1H, *J*=9.2 Hz), 8.92 (s, 1H), 8.93 (s, 1H). ^{13}C-NMR ($CDCl_3$) δ: -5.3, 18.5, 25.9, 29.2, 42.0, 55.0, 56.9, 57.3, 62.7, 143.7, 152.0. MS *m/z*: 365, 367 (M^+-CH_3). *Anal*. Calcd for $C_{17}H_{25}N_4O_2ClSi$: C, 53.60, H, 6.61; N, 14.71. Found: .C, 54.35; H, 6.66; N, 14.66.

[*rel*-(1*R*,2*R*,4*R*,5*S*)-4-(6-Chloro-9*H*-purin-9-yl)-6-oxabicyclo[3.1.0]hex-2-yl]methanol (9b):
A mixture of **9a** (190 mg, 0.5 mmol) and *n*-Bu_4NF (1M solution in THF, 1 mmol) in THF (50 mL) was stirred at rt under an argon atmosphere for 30 min. The mixture was diluted with AcOEt, washed with brine, and dried over anhydrous $MgSO_4$. The solvent was removed, and the residue was separated by flash chromatography with hexane-AcOEt (1:1) as an eluent to give 120 mg (90%) of **9b**.
mp 174-175 °C (hexane-AcOEt). IR (nujol): 3632 cm^{-1}. ^{1}H-NMR (MeOH-d_4) δ: 1.35 (dt, 1H, *J*=12.6, 9.7 Hz), 2.36 (dt, 1H, *J*=12.6, 8.0 Hz), 2.49 (dt, 1H, *J*=15.4, 8.0 Hz), 3.69 (dd, 1H, *J*=6.3, 10.9 Hz), 3.74 (dd, 1H, *J*=8.0, 10.9 Hz), 3.78 (dd, 1H, *J*=1.1, 2.9 Hz), 3.94 (dd, 1H, *J*=1.1, 2.9 Hz), 5.10 (t, 1H, *J*=9.0 Hz), 8.66 (s, 1H), 8.74 (s, 1H). ^{13}C-NMR (MeOH-d_4) δ: 28.4, 41.6, 55.7, 56.8, 56.9, 61.4, 130.9, 144.8, 150.1, 151.7, 151.9. MS *m/z*: 266, 268 (M^+). *Anal*. Calcd for $C_{11}H_{11}N_4O_2Cl$: C, 49.54; H, 4.16; N, 21.01. Found: C, 49.46; H, 4.23; N, 20.92.

[*rel*-(1*R*,2*R*,4*R*,5*S*)-4-(6-Amino-9*H*-purin-9-yl)-6-oxabicyclo[3.1.0]hex-2-yl]methanol (10a):
A mixture of **9b** (100 mg) and MeOH (10 mL) saturated with NH_3 was heated in a sealed tube at 60 °C overnight. The mixture was concentrated under reduced pressure, and the residue was separated by flash chromatography with AcOEt as an eluent to give 40 mg (43%) of **10a**.
mp 183-184 °C (MeOH). IR (nujol): 3300, 3325 cm^{-1}. ^{1}H-NMR (MeOH-d_4) δ: 1.25 (dt, 1H, *J*=12.6, 9.7

Hz), 2.30 (dt, 1H, *J*=12.6, 8.0 Hz), 2.45 (dt, 1H, *J*= 16.0, 8.0 Hz), 3.67 (dd, 1H, *J*=10.3, 5.7 Hz), 3.72 (dd, 1H, *J*=10.3, 8.0 Hz), 3.75 (dd, 1H, *J*=2.9, 1.1 Hz), 3.87 (dd, 1H, *J*=2.9, 1.1 Hz), 5.10 (t, 1H, *J*=9.0 Hz), 8.20 (s, 1H), 8.25 (s, 1H). ^{13}C-NMR (MeOH-d_4) δ: 28.5, 41.6, 54.9, 56.5, 57.1, 61.5, 118.5, 139.1, 149.3, 152.5, 155.9. MS *m/z*: 247 (M^+). *Anal*. Calcd for $C_{11}H_{13}N_5O_2$: C, 53.43; H, 5.30; N, 28.32. Found: C,53.38; H, 5.54; N, 28.08.

***rel*-[(1*R*,2*R*,4*R*,5*S*)-4-(6-Cyclopropylamino-9*H*-purin-9-yl)-6-oxabicyclo[3.1.0]hex-2-yl]methanol (10b):**

A mixture of **9b** (133 mg, 0.5 mmol), cyclopropylamine (114 mg, 2 mmol) and MeOH (10 mL) in a sealed tube was heated at 60 °C overnight. The mixture was concentrated under reduced pressure, and the residue was separated by flash chromatography with AcOEt as an eluent to give 71 mg (50%) of **10b**.

mp 161-162 °C (MeOH). IR (nujol): 3292 cm^{-1}. ^{1}H-NMR (MeOH-d_4) δ: 0.61-0.65(m, 2H), 0.84-0.92 (m, 2H), 1.24 (dt, 1H, *J*=12.6, 9.7 Hz), 2.29 (dt, 1H, *J*=16.0, 7.5 Hz), 2.45 (dt, 1H, *J*=16.0, 7.5 Hz), 2.95 (br s, 1H), 3.66 (dd, 1H, *J*=6.0, 10.5 Hz), 3.71 (dd, 1H, *J*=8.1, 10.5 Hz), 3.74 (d, 1H, *J*=2.9 Hz), 3.86 (s, 1H), 5.08 (t, 1H, *J*=8.6 Hz), 8.20 (s, 1H), 8.29 (s, 1H). ^{13}C-NMR (MeOH-d_4) δ: 7.5, 24.3, 29.6, 42.6, 55.8, 57.6, 58.2, 62.5, 120.1, 139.8, 149.6, 153.5, 156.8. MS *m/z*: 287 (M^+). *Anal*. Calcd for $C_{14}H_{17}N_5O_2$: C, 58.52; H, 5.96; N, 24.37. Found: C, 58.69; H, 6.08; N, 24.25.

ACKNOWLEDGEMENTS

The authors thank Kuraray Co., Ltd. for providing the ABH.

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