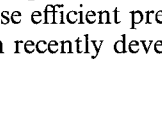
Enantioselective Synthesis of the Cyclopentene Segment of Queuosine

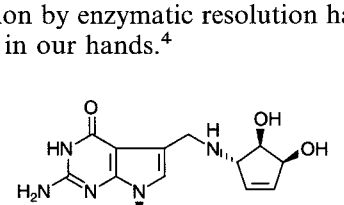
Keigo Tanaka, Kunio Ogasawara*
Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980-77, Japan
Fax +81(22)2176845; E-mail c21799@cctu.cc.tohoku.ac.jp
Received 16 June 1995

(3*S*,4*R*,5*S*)-3-Amino-4,5-dihydroxycyclopentene, the cyclopentene segment of queuosine found in the first position of the anticodon of +RNA,^{Tyr} +RNA,^{His} +RNA,^{Asn} and +RNA,^{Asp} has been synthesized in a stereoselective manner from (−)-3-*endo*-hydroxydicyclopentadiene.

(3*S*,4*R*,5*S*)-3-Amino-4,5-dihydroxycyclopentene **(1)** is the structural component of queuosine **(2)** which is a hypermodified nucleoside located at the first position of the anticodon of +RNA,^{Tyr} +RNA,^{His} +RNA,^{Asn} and +RNA^{Asp} in most prokaryotic and eukaryotic cells.[1] Since **1** is known to play the most decisive role in exhibiting the physiological activity of queuosine[2,3] **(2)**, we investigated its enantioselective synthesis utilizing optically pure (−)-3-*endo*-hydroxydicyclopentadiene **(3)** whose efficient preparation by enzymatic resolution has been recently developed in our hands.[4]



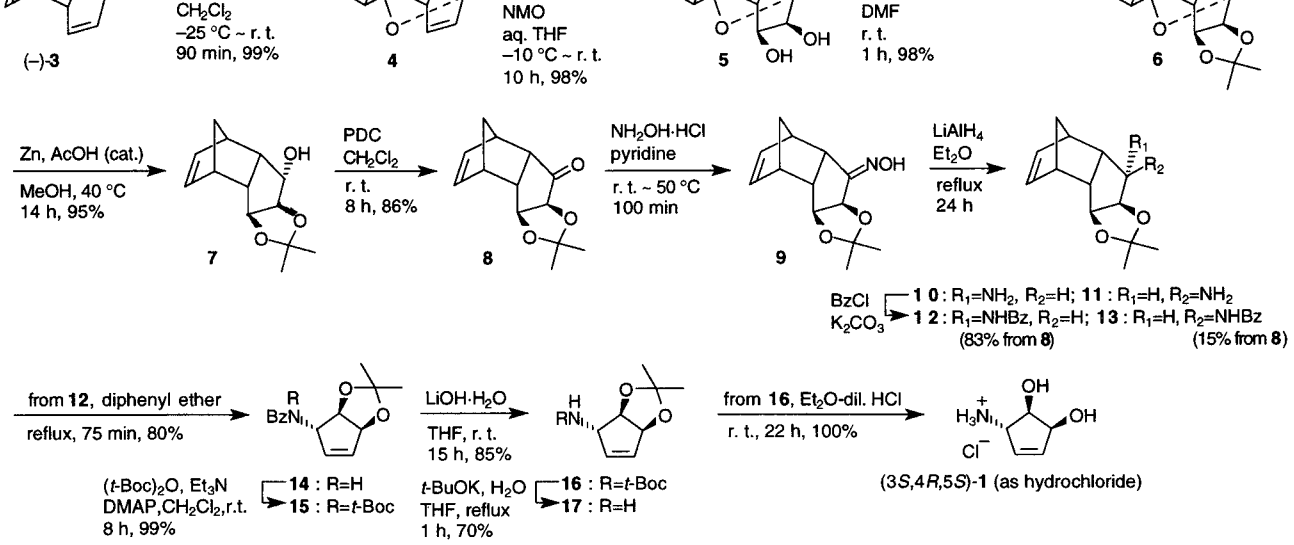
(3*S*,4*R*,5*S*)-3-amino-4,5-dihydrocyclopentene (**1**)



queuosine (**2**)

Optically pure (−)-3-*endo*-hydroxydicyclopentadiene **(3)**, obtained by lipase-mediated transesterification reaction,[4] was first treated with *N*-bromosuccinimide to give the cyclic bromo ether[5] **4** in an excellent yield. This was treated with a catalytic amount of osmium tetroxide in the presence of *N*-methylmorpholine 1-oxide (NMO)[6] to carry out stereoselective dioxylation from the convex face to give rise to a single dihydroxylation product **5**. Having discriminated two double bonds in the molecule, the glycol **5** was first protected by ketalization and the resulting acetonide **6** was treated with zinc in the presence of acetic acid to liberate the masked double bond to afford the enol **7** in a satisfactory overall yield. Oxidation of **7** with pyridinium dichromate (PDC) gave the ketone **8** without difficulty. The ketone **8** was transformed into the oxime **9** which was immediately reduced with lithium aluminum hydride to give a diastereomeric mixture of the *endo*- and the *exo*-amines **10** and **11**, respectively. Although the mixture was not separable at this stage, it furnished the readily separable benzamides on benzoylation. Thus, the *endo*-amide **12** and the *exo*-amide **13** were obtained in diastereomerically pure states in overall yields of 83 and 15% from the ketone **8** after separation by column chromatography.

Retro-Diels–Alder cleavage[7] of the *endo*-amide **12** proceeded facilely in refluxing diphenyl ether[8] within two hours to furnish the expected cyclopentene **14** in good yield with extrusion of cyclopentadiene. Optical purity was confirmed at this point by HPLC using a chiral column which did not show any detectable amount of the enantiomer (*ent*-**14**) in the product. The direct removal of the benzoyl group from **14** was unexpectedly difficult; however, it was accomplished by first transforming **14** into the imide **15** by application of the Grieco condi-



Scheme 1

tions.[9] Thus, the imide **15**, obtained quantitatively from **14** by reaction with di-*tert*-butyl dicarbonate, was next treated with lithium hydroxide in THF to furnish the carbamate **16** in good yield. This compound was then hydrolyzed under basic conditions to cleave the carbamate group to afford the primary amine[2] **17** in 70% yield. On the other hand, the carbamate **16**, on exposure to diluted hydrochloric acid, furnished (3*S*,4*R*,5*S*)-3-amino-4,5-dihydroxycyclopentene **(1)** in an excellent yield as its hydrochloride by concomitant removal of the amino and the glycol protecting groups.

Since the starting optically pure *endo*-alcohol **3** has also been obtained by stereoselective reduction of the keto precursor,[5] the present procedure can also utilize the *exo*-hydroxy isomer of **3** which has been obtained by a variety of procedures[5,10,11] and is readily convertible into the ketone.[12]

In conclusion, we have established an efficient, enantiocontrolled route to the most critical structural component of a physiologically interesting hypermodified nucleoside queuosine **(2)** using optically pure (−)-3-*endo*-hydroxydicyclopentadiene **(1)** as a starting material.

Melting points are uncorrected. IR spectra were recorded on a JASCO-IR-700 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-3000 (300 MHz). Mass spectra were obtained on a JEOL JMS-DX303 instrument. Optical purities were determined on a Gilson Model-307 instrument equipped with a chiral column. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter.

Satisfactory C, H, N analyses were obtained for all products (± 0.4%).

6-Bromo-3,5-epoxy-3a,4,5,6,7,7a-hexahydro-4,7-methano-1*H*-indene (4):
To a stirred solution of the alcohol **3** (6.13 g, 41.4 mmol) in CH_2Cl_2 (100 mL) was added NBS (8.47 g, 47.6 mmol) portionwise at −25 °C and stirring was continued for 90 min at r.t. The mixture was diluted with CH_2Cl_2 (150 mL) and the solution was washed successively with 10% $Na_2S_2O_3$ (40 mL), 5% NaHCO, (10 mL), brine (10 mL), and dried ($MgSO_4$). The mixture, after evaporation under reduced pressure, was chromatographed on silica gel (200 g, eluent: Et_2O–hexane, 1:20) to give the bromo ether as colorless needles; yield: 9.34 g (99%), mp 48.5–49.5 °C, $[\alpha]_D^{26}$ −115.2 (c = 1.02, $CHCl_3$).

IR (Nujol): ν = 1037, 1024 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.99 (dd, 1 H, J = 10.4, 1.3 Hz), 2.41 (br s, 1 H), 2.45 (d, 1 H, J = 10.6 Hz), 2.72 (br s, 1 H), 3.03–3.05 (m, 2 H), 4.04 (d, 1 H, J = 2.2 Hz), 4.61 (d, 1 H, J = 5.1 Hz), 4.67 (dd, 1 H, J = 5.5, 2.6 Hz), 5.74–5.76 (m, 1 H), 6.02 (dd, 1 H, J = 5.5, 2.2 Hz).

MS: m/z = 228 and 226 (M^+), 66 (100%).

HRMS: m/z = calc. for $C_{10}H_{11}OBr^{79}$ 225.9994, found 225.9980; calc. for $C_{10}H_{11}OBr^{81}$ 227.9974, found 227.9978.

6-Bromo-3,5-epoxy-1,2,3a,4,5,6,7,7a-octahydro-1,2-dihydroxy-4,7-methano-1*H*-indene (5):
To a stirred solution of the bromo ether **4** (9.20 g, 40.5 mmol) in THF–H_2O (3:1, 140 mL) was added NMO (5.20 g, 43.0 mmol) and 0.1 M OsO_4 in THF (2.5 mL, 0.25 mmol) at −10 °C and stirring was continued for 10 h at r.t. The mixture was treated with Na_2SO_3 (0.4 g) and filtered through a Celite pad. The filtrate was diluted with EtOAc (150 mL) and washed with 5% $NaHCO_3$ (15 mL), brine (15 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was chromatographed on silica gel (200 g, eluent: EtOAc–hexane, 1:3) to give the glycol **5** as colorless needles; yield: 10.33 g (98%), mp 92–93 °C, $[\alpha]_D^{29}$ −97.9 (c = 0.64, $CHCl_3$).

IR (Nujol): ν = 3246 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.83 (d, 1 H, J = 10.6 Hz), 2.34 (d, 1 H, J = 10.3 Hz), 2.54–2.61 (m, 3 H), 2.79–2.82 (m, 1 H), 2.86 (br s, 1 H), 3.07–3.14 (m, 1 H), 3.88 (d, 1 H, J = 2.2 Hz), 4.21–4.25 (m, 2 H), 4.30 (br s, 1 H), 4.53 (d, 1 H, J = 5.1 Hz).

MS: m/z = 244 and 242 (M^+ − 18), 163 (100%).

HRMS: m/z = calc. for $C_{10}H_{11}O_2Br^{79}$ 241.9942, found 241.9926; calc. for $C_{10}H_{11}O_2Br^{81}$ 243.9922, found 243.9893.

6-Bromo-3,5-epoxy-1,2,3a,4,5,6,7,7a-octahydro-1,2-isopropylidenedioxy-4,7-methano-1*H*-indene (6):
A mixture of the glycol **5** (8.63 g, 33.1 mmol), *p*-toluenesulfonic acid (0.3 g, 1.7 mmol), and 2,2-dimethoxypropane (5.40 mL, 43.0 mmol) in DMF (100 mL) was stirred at r.t. for 1 h. After concentration of the solvent under vacuum, the mixture was chromatographed on silica gel (300 g, eluent: EtOAc–hexane, 1:15) to give the acetonide **6** as colorless scales; yield: 9.77 g (98%), mp 62.5–63.0 °C, $[\alpha]_D^{29}$ −77.5 (c = 0.97, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.27 (s, 3 H), 1.42 (s, 3 H), 1.75 (dd, 1 H, J = 11.0, 1.5 Hz), 2.24 (d, 1 H, J = 11.0 Hz), 2.51 (d, 1 H, J = 4.4 Hz), 2.73 (dd, 1 H, J = 10.1, 5.0 Hz), 2.80–2.83 (m, 1 H), 3.10 (dt, 1 H, J = 9.9, 5.1 Hz), 3.54 (d, 1 H, J = 2.2 Hz), 4.39 (d, 1 H, J = 5.1 Hz), 4.53 (d, 1 H, J = 5.1 Hz), 4.59 (d, 1 H, J = 5.5 Hz), 4.63 (d, 1 H, J = 5.1 Hz).

MS: m/z = 287 and 285 (M^+ − 15, 100%).

HRMS: m/z = calc. for $C_{12}H_{14}O_3Br^{79}$ 285.0127, found 285.0116; calc. for $C_{12}H_{14}O_3Br^{81}$ 287.0106, found 287.0078.

***endo*-1,2,3a,4,7,7a-Hexahydro-3-hydroxy-1,2-isopropylidenehydroxy-4,7-methano-1*H*-indene (7):**
A solution of the bromo ether **6** (9.77 g, 32.5 mmol) in MeOH (100 mL) containing AcOH (0.37 mL, 6.5 mmol) was stirred at 40 °C with activated zinc dust (6.37 g, 97.4 matom) for 14 h. After cooling the mixture was filtered through a Celite pad and the filtrate was evaporated under reduced pressure. The residue was diluted with CH_2Cl_2 (150 mL) and washed with 5% $NaHCO_3$ (2 × 20 mL), brine (20 mL), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was chromatographed on silica gel (200 g, eluent: EtOAc–hexane, 1:10) to give the enol **7** as colorless needles; yield: 6.86 g (95%), mp 131–131.5 °C $[\alpha]_D^{29}$ +45.3 (c = 0.56, $CHCl_3$).

IR (Nujol): ν = 3244 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (s, 3 H), 1.31 (d, 1 H, J = 8.4 Hz), 1.45 (s, 3 H), 1.46 (d, 1 H, J = 8.4 Hz), 1.82 (d, 1 H, J = 4.4 Hz), 2.87 (dd, 1 H, J = 8.1, 4.4 Hz), 2.97 (br s, 2 H), 3.08 (dt, 1 H, J = 13.6, 4.2 Hz), 4.06 (s, 1 H), 4.07 (dd, 1 H, J = 10.4, 5.7 Hz), 4.04–4.09 (m, 1 H), 6.12 (dd, 1 H, J = 5.9, 2.9 Hz), 6.27 (dd, 1 H, J = 5.5, 2.9 Hz).

MS: m/z = 222 (M^+), 66 (100%).

HRMS: m/z = calc. for $C_{13}H_{18}O_3$ 222.1256, found 222.1242.

1,2,3a,4,7,7a-Hexahydro-1,2-isopropylidenedioxy-4,7-methano-1*H*-inden-3-one (8):
A mixture of the alcohol **7** (4.00 g, 18.0 mmol), and PDC (8.30 g, 21.6 mmol) in CH_2Cl_2 (150 mL) was stirred at r.t. for 8 h. Silica gel (20 g) was added to the mixture and stirring continued for 30 min. The mixture after filtration through a Celite pad was chromatographed on silica gel (110 g, eluent: Et_2O–hexane, 1:4) to give the enone **8** as colorless needles; yield: 3.41 g (86%), mp 95–95.5 °C $[\alpha]_D^{26}$ +276.9 (c = 0.79, $CHCl_3$).

IR (Nujol): ν = 1745 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 3 H), 1.36 (s, 3 H), 1.47 (d, 1 H, J = 8.4 Hz), 1.58 (d, 1 H, J = 8.4 Hz), 3.08–3.09 (m, 2 H), 3.21 (br s, 1 H), 3.25 (br s, 1 H), 3.93 (d, 1 H, J = 5.5 Hz), 4.30 (d, 1 H, J = 5.5 Hz), 6.14 (dd, 1 H, J = 5.7, 2.8 Hz), 6.21 (dd, 1 H, J = 5.5, 2.9 Hz).

MS: m/z = 220 (M^+), 66 (100%).

HRMS: m/z = calc. for $C_{13}H_{16}O_3$ 220.1099, found 220.1098.

Preparation of the Benzamides 12 and 13 from the Enone 8:
To a stirred solution of the enone **8** (2.48 g, 11.3 mmol) in pyridine (16 mL) was added hydroxylamine hydrochloride (1.18 g,

16.9 mmol) and the stirring was continued for 30 min at r.t. and for 70 min at 50 °C. The mixture was diluted with water (40 mL) and acidified at 0 °C by addition of 10% HCl. The mixture was extracted with Et_2O (2 × 100 mL) and the ether solution was washed with brine (40 mL), dried ($MgSO_4$), and evaporated under reduced pressure to leave the crude oxime **9** which was used immediately for the next reaction. To a stirred solution of the crude oxime **9** in Et_2O (90 mL) was added $LiAlH_4$ (1.28 g, 33.8 mmol) dropwise at 0 °C and the solution was heated under reflux for 24 h. After cooling to 0 °C, to the solution were added successively water (2.24 mL, 124 mmol), K_2CO_3 (9.35 g, 67.7 mmol), and benzoyl chloride (1.57 mL, 13.5 mmol). After warming up to r.t., Celite (10 g) was added to this mixture and the stirring was continued for 30 min. The mixture after filtration was evaporated under reduced pressure. The residue was treated with 5% $NaHCO_3$ (20 mL) for 30 min, extracted with dichloromethane (2 × 100 mL), the combined extract was washed with brine (40 mL), and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure the residue was chromatographed on silica gel (300 g) to give the *endo*-amide **12** (EtOAc–hexane, 1:6) and the *exo*-amide **13** (EtOAc–hexane, 1:2).

12; yield: 3.03 g (83%), colorless crystals, mp 178–179 °C, $[\alpha]_D^{29}$ + 111.0 (c = 1.16, $CHCl_3$).

IR (Nujol): ν = 3306, 1633 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.30 (s, 3 H), 1.35 (d, 1 H, J = 8.1 Hz), 1.52 (d, 1 H, J = 8.4 Hz), 1.56 (s, 3 H), 2.86–2.90 (m, 1 H), 2.93–2.99 (m, 2 H), 3.18 (br s, 1 H), 3.96 (q, 1 H, J = 5.9 Hz), 4.15 (dd, 1 H, J = 5.1, 2.2 Hz), 4.43 (t, 1 H, J = 5.7 Hz), 6.24 (dd, 1 H, J = 5.7, 3.1 Hz), 6.45 (dd, 1 H, J = 5.5, 2.9 Hz), 6.84 (br d, 1 H, J = 5.9 Hz), 7.41–7.52 (m, 3 H), 7.79–7.82 (m, 2 H).

MS: m/z = 325 (M^+), 105 (100%).

HRMS: m/z = calc. for $C_{20}H_{23}NO_3$ 325.1678, found 325.1646.

13; yield: 566 mg (15%), colorless amorphous solid, $[\alpha]_D^{27}$ + 32.7 (c = 0.90, $CHCl_3$).

IR (film): ν = 3426, 3342, 1646 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.27 (s, 3 H), 1.38 (d, 1 H, J = 8.4 Hz), 1.46 (d, 1 H, J = 8.4 Hz), 1.51 (s, 3 H), 2.81 (br s, 1 H), 3.00–3.04 (m, 2 H), 3.49–3.56 (m, 1 H), 4.14–4.17 (m, 2 H), 4.33–4.39 (m, 1 H), 6.10 (br d, 1 H, J = 5.9 Hz), 6.23 (br s, 2 H), 7.41–7.54 (m, 3 H), 7.76–7.79 (m, 2 H).

MS: m/z = 325 (M^+), 105 (100%).

HRMS: m/z = calc. for $C_{20}H_{23}NO_3$ 325.1678, found 325.1641.

(3*S*,4*R*,5*S*)-3-Benzoylamino-4,5-isopropylidenedroxycyclopent-1-ene (14):
A solution of amide **12** (389 mg, 1.20 mmol) in diphenyl ether (4 mL) was heated under reflux for 75 min. After cooling, the mixture was directly chromatographed on silica gel (50 g, eluent: EtOAc–hexane, 1:4) to give the cyclopentenone **14** as colorless crystals, yield: 248 mg (80%), mp 124.5–125.5 °C, $[\alpha]_D^{28}$ + 224.3 c = 0.98, $CHCl_3$). Optical purity was determined as > 99% ee by HPLC using a chiral column (CHIRALCEL OD, elution: *i*-PrOH–hexane, 1:9).

IR (Nujol): ν = 3316, 1637 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.36 (s, 3 H), 1.46 (s, 3 H), 4.61 (d, 1 H, J = 5.9 Hz), 5.05–5.08 (m, 1 H), 5.29–5.31 (m, 1 H), 5.87–5.89 (m, 1 H), 6.08–6.10 (m, 2 H), 7.39–7.53 (m, 3 H), 7.74–7.77 (m, 2 H).

MS: m/z = 224 (M^+ − 15), 105 (100%).

HRMS: m/z = calc. for $C_{14}H_{14}NO_3$ 244.0973, found 244.0970.

(3*S*,4*R*,5*S*)-Benzoyl(*tert*-butoxycarbonyl)amino-4,5-isopropylidenedioxycyclopent-1-ene (15):
A mixture of the amide **14** (45.9 mg, 0.177 mmol), Et_3N (74 µl, 0.531 mmol), di-*tert*-butyl dicarbonate (162 µl, 0.705 mmol), and 4-*N*,*N*-dimethylaminopyridine (42.4 mg, 0.347 mmol) in CH_2Cl_2 (2 mL) was stirred at r.t. for 8 h. The mixture was diluted with CH_2Cl_2 (20 mL), washed with brine (2 mL × 2), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was chromatographed on silica gel (5 g, eluent: Et_2O–hexane, 1:4) to give the imide **15** as colorless crystals; yield: 63.2 mg (99%), mp 78.5–79.5 °C, $[\alpha]_D^{28}$ + 188.5 (c = 1.05, $CHCl_3$).

IR (Nujol): ν = 1733, 1680 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.10 (s, 9 H), 1.38 (s, 3 H), 1.45 (s, 3 H), 4.98 (d, 1 H, J = 5.9 Hz), 5.48–5.50 (m, 2 H), 5.69 (dd, 1 H, J = 4.8, 2.2 Hz), 6.08–6.11 (m, 1 H), 7.40 (t, 2 H, J = 7.3 Hz), 7.47–7.57 (m, 3 H).

MS: m/z = 359 (M^+), 105 (100%).

HRMS: m/z = calc. for $C_{20}H_{25}NO_5$ 359.1733, found 359.1752.

(3*S*,4*R*,5*S*)-3-*tert*-Butoxycarbonylamino-4,5-isopropylidenedioxycyclopent-1-ene (16):
To a stirred solution of the imide **15** (63.2 mg, 0.176 mmol) in THF (2 mL) was added $LiOH \cdot H_2O$ (37 mg, 0.881 mmol) at r.t. and stirring was continued for 15 h at the same temperature. The mixture was diluted with Et_2O (20 mL), washed with brine (2 mL × 2), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was chromatographed on silica gel (5 g, eluent: EtOAc–hexane, 1:4) to give the carbamate **16** as colorless crystals; yield: 38.2 mg (85%), mp 92–93 °C, $[\alpha]_D^{29}$ + 117.2 (c = 1.06, $CHCl_3$).

IR (Nujol): ν = 3372, 1688 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.34 (s, 3 H), 1.41 (s, 3 H), 1.46 (s, 9 H), 4.49 (d, 2 H, J = 5.5 Hz), 4.55 (br s, 1 H), 5.22 (d, 1 H, J = 5.5 Hz), 5.75–5.78 (m, 1 H), 5.98 (d, 1 H, J = 5.5 Hz).

MS: m/z = 240 (M^+ − 15), 57 (100%).

HRMS: m/z = calc. for $C_{12}H_{18}NO_4$ 240.1235, found 240.1259.

(3*S*,4*R*,5*S*)-3-Amino-4,5-isopropylidenedioxycyclopentene (17):
To a stirred solution of potassium *tert*-butoxide (63 mg, 0.56 mmol) in THF (1.5 mL) was added water (10µl, 0.56 mmol) at 0 °C. After 5 min at the same temperature, the carbamate **16** (28.5 mg, 0.112 mmol) was added and the mixture was heated under reflux for 1 h. After evaporation of the solvent under reduced pressure, the residue was chromatographed on silica gel (5 g, eluent: EtOAc–MeOH–30% NH_4OH, 100:1:0.3) to give the amine **17** as a colorless oil; yield: 12.1 mg (70%), $[\alpha]_D^{29}$: + 123.3 (c = 0.46, $CHCl_3$).

IR (Nujol): ν = 3372 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.34 (s, 3 H), 1.41 (s, 3 H), 1.46 (br s, 2 H), 4.00 (br s, 1 H), 4.37 (d, 1 H, J = 5.9 Hz), 5.27 (d, 1 H, J = 5.5 Hz), 5.83–5.89 (m, 2 H).

MS: m/z = 156 (M^+ + 1), 97 (100%).

HRMS: m/z = calc. for $C_8H_{14}NO_2$ 156.1024, found 156.1060.

(3*S*,4*R*,5*S*)-3-Amino-4,5-dihydroxycyclopentene Hydrochloride (1 · HCl):
To a stirred solution of the carbamate **16** (113 mg, 0.444 mmol) in Et_2O (0.7 mL) was added water (3.4 mL) and 10% HCl (1.4 mL) at r.t. and stirring was continued for 22 h at the same temperature. The mixture was evaporated under reduced pressure at 0 °C and further evacuated under vacuum to leave the aminocyclopentene hydrochloride as a pale yellow hygroscopic foam; yield: 67.3 mg (100%), $[\alpha]_D^{28}$ + 194.9 (c = 0.42, MeOH).

IR (Nujol): ν = 3342, 2926, 1604 cm^{-1}.

^1H NMR (CD_3OD): δ = 4.03 (t, 1 H, J = 5.5 Hz), 4.08–4.10 (m, 1 H), 4.56–4.58 (m, 1 H), 5.93 (dd, 1 H, J = 6.2, 1.5 Hz), 6.19 (dt, 1 H, J = 6.2, 2.2 Hz).

MS: m/z = 97 (M^+ − 18), 36 (100%).

HRMS: m/z = calc. for C_5H_7NO 97.0528, found 97.0515.

(1) Nishimura, S. In: *Progress in Nucleic Acid Research and Molecular Biology*; Vol. 28, Cohen, W.E. Ed.; Academic: New York, 1983, pp. 49–73.
(2) Ohgi, T.; Kondo, T.; Goto, T. *J. Am. Chem. Soc.* **1979**, *101*, 3629.
(3) Akimoto, H.; Nomura, H.; Yoshida, M.; Shindo-Okada, N.; Hoshi, A.; Nishimura, N. *J. Med. Chem.* **1986**, *29*, 1749. Kuchino, Y.; Kimura, K.; Akimoto, H.; Nomura, H.; Akita, N.; Nishimura, S. *Proc. Japan Acad.* **1987**, *63*, Ser. B, 393.

(4) Tanaka, K.; Ogasawara, K. *Synthesis* **1995**, 1237.
(5) Takano, S.; Inomata, K.; Ogasawara, K. *Chem. Lett.* **1989**, 359.
(6) Rheenen, V. Van; Kelly, R.C.; Cha, D.Y. *Tetrahedron Lett.* **1976**, 1973.
(7) Ogasawara, K. *Pure Appl. Chem.* **1994**, *66*, 2119.
(8) Kamikubo, T.; Ogasawara, K. *Tetrahedron Lett.* **1995**, *36*, 1685.
(9) Flynn, D.L.; Zelle, R.E.; Grieco, P.A. *J. Org. Chem.* **1983**, *48*, 2424.
(10) Woodward, R.B.; Katz, T.T. *Tetrahedron* **1959**, *5*, 79.
Ito, T.; Okamoto, Y.; Matsumoto, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3631.
Klunder, A.J.H.; Huisinga, W.B.; Hulshof, A.; Zwanenburg, B. *Tetrahedron Lett.* **1986**, *27*, 2543.
Sato, M.; Hattori, H.; Murakami, M.; Kaneko, C. *Chem. Lett.* **1993**, 1919.
Liu, Z.-Y.; He, L.; Zheng, H. *Tetrahedron: Asymmetry* **1993**, *4*, 2277.
(11) Takano, S.; Inomata, K.; Ogasawara, K. *J. Chem. Soc., Chem. Commun.* **1989**, 271.
Takano, S.; Inomata, K.; Takahashi, M.; Ogasawara, K. *Synlett* **1991**, 636.
(12) Takano, S.; Moriya, M.; Tanaka, K.; Ogasawara, K. *Synthesis* **1994**, 687.