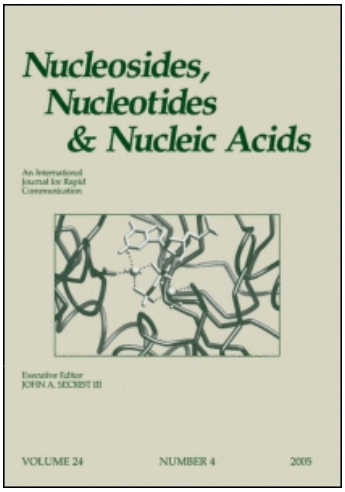

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Synthesis of a Potent A_1 Selective Adenosine Agonist: N^6-[1-R-[(3-Chloro-2-thienyl)methyl]propyl]adenosine, RG 14718(-)

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SYNTHESIS OF A POTENT A_1 SELECTIVE ADENOSINE AGONIST: N^6-[1-R-[(3-CHLORO-2-THIENYL)METHYL]PROPYL]ADENOSINE, RG 14718(-)

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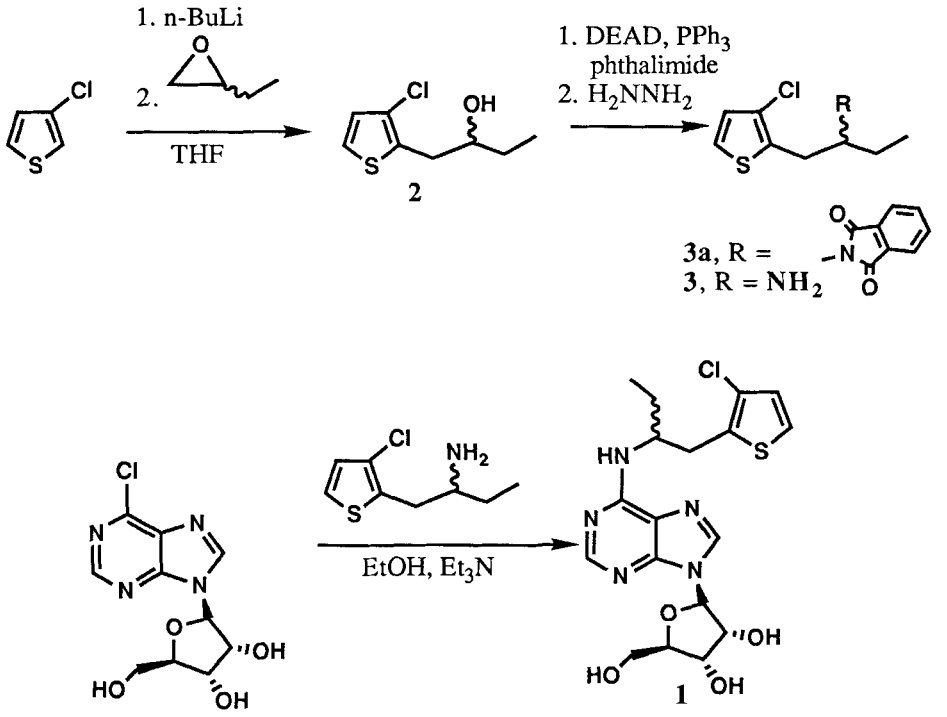
Abstract. This report describes the preparation of (R)-(3-chloro-2-thienyl)-2-butylamine and its conversion to the titled N^6-substituted adenosine agonist, RG 14718(-). RG 14718(-) was found to have exceptional affinity and selectivity for the adenosine A_1 receptor, IC_{50} = 5.7 +/- 1.6 pM.

Adenosine is an endogenous mediator of a variety of physiological functions. Among these are its well known effects on the cardiovascular system. Adenosine is a potent vasodilator, and causes transient negative chronotropic and dromotropic effects on the heart. Most of its effects are mediated through specific membrane-bound receptors. Extracellular adenosine receptors have been divided into two subclasses, A_1 and A_2. These two receptor subtypes can be differentiated based on their opposing effects on adenylate cyclase, as well as in differences in their regional populations. [1,2]

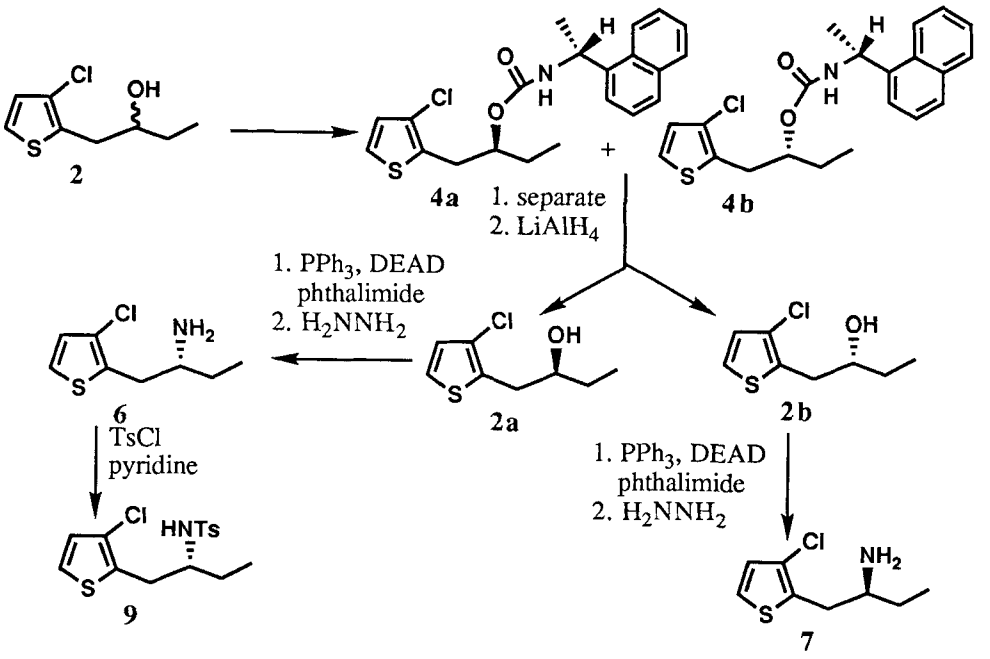
During the course of our efforts towards the development of an adenosine agonist for the treatment of hypertension we synthesized a number of substituted N^6-(thien-2-yl)ethyl adenosine analogues. The synthesis and biological activities of these analogues will be discussed in separate communications.[3] Of the compounds prepared, the 1-(3-chloro-2-thienyl)-2-butylamino analogue, RG 14718, **1** was of particular interest. It was found to be a potent ligand for both the adenosine A_1 and A_2 receptors (IC_{50}: A_1 = 0.026nM, A_2 = 12nM). The synthesis of the racemic amine **3** and RG 14718, are shown in Scheme 1. Deprotonation of 3-chlorothiophene with n-butyl



SCHEME 1

lithium at 0°C, followed by the dropwise addition of butylene oxide gave the racemic alcohol **2** in 69% yield. Treatment of this alcohol with triphenylphosphine, phthalimide and diethylazodicarboxylate afforded phthalimide **3a** which when refluxed with hydrazine hydrate, in ethanol yielded amine **3** in 45% overall yield. Condensation of amine **3** with 6-chloropurine riboside in the presence of triethylamine then provides RG 14718, **1** in 85% yield after chromatographic purification.

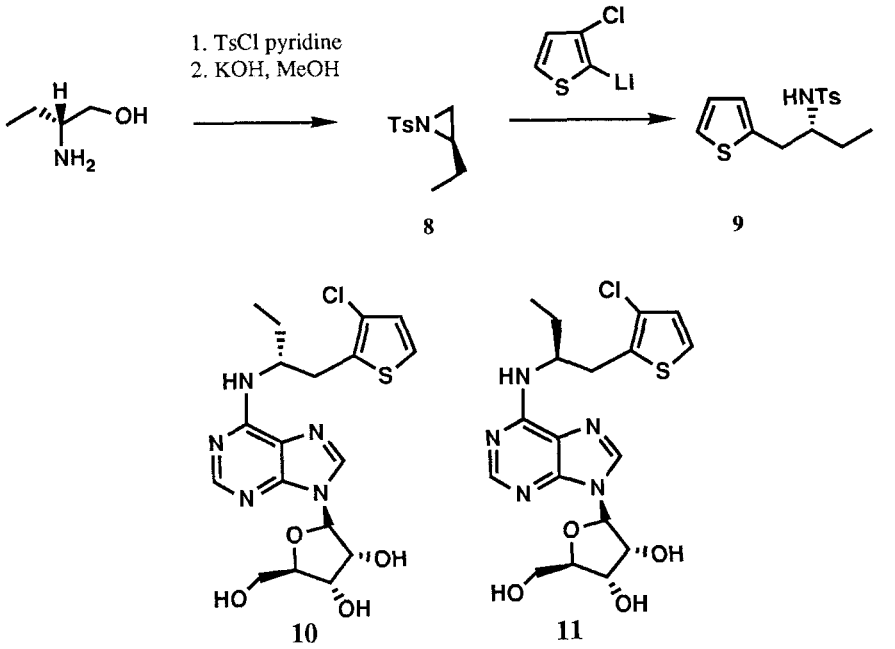
It is well precedented that the binding affinity of adenosine derivatives is greatly influenced by the nature and absolute stereochemistry of substituents appended to the N^6-position.[4] Thus, we expected that the diastereomers obtained, shown in Scheme 1, would have quite different binding affinity for the adenosine receptors. Unfortunately, attempts to separate these diastereomers by conventional methods proved unsuccessful. We resorted to an independent



SCHEME 2

synthesis of each optically pure diastereomer. The enantiomerically pure amines required for these syntheses were prepared as shown in Scheme 2. Treatment of racemic alcohol **2** with (R)-(-)-1-(1-napthyl)ethyl isocyanate afforded the diastereomeric carbamates **4a** and **4b** in 25% and 29% yield respectively. These compounds were separable by flash chromatography and the calculated diastereomeric excess for each carbamate was >95%(**4a**) and 90%(**4b**).[5] Reduction of the separated carbamates with lithium aluminum hydride in tetrahydrofuran gave the enantiomerically pure alcohols **2a** and **2b** in 66%(e. e.>95%) and 70%(e. e. = 90%) yield respectively. Mitsunobu reaction of the alcohols with triphenylphosphine, diethylazodicarboxylate and phthalimide gave the enantiomerically pure phthalimides which, following treatment with hydrazine hydrate afforded amines **6** and **7** in 56% and 55% overall yield from the alcohols.[6] These amines exhibited optical rotations of -11.96° (MeOH, c = 15, 22°C) and +10.33° (MeOH, c = 15, 22°C).

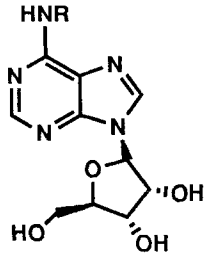
The absolute configuration of the amine enantiomers was firmly established through an unambiguous synthesis of the R-amine enantiomer by the route detailed in Scheme 3. Treatment of (R)-2-amino-1-butanol with



SCHEME 3

p-toluenesulfonyl chloride followed by methanolic potassium hydroxide afforded p-toluenesulfonylaziridine **8** in 54% yield. [7] The aziridine **8**, was then treated with 2-lithio-3-chlorothiophene to afford p-toluenesulfonamide **9** in 67% yield. The optical rotation of **9** was determined to be -23.5° (MeOH, c= 6, 22°C), which compares well with the tosylate prepared from amine **6** (optical rotation = -22.80°), and thus confirmed the absolute configuration of **6** as (R). Thus, replacing racemic amine **3** with enantiomerically pure amines **6** and **7** afforded the corresponding diastereomerically pure adenosine analogues **10** and **11** in 42% and 73% yield respectively. Compound **10**, possessing the R-stereoconfiguration at the ethyl center was found to be a very potent and selective ligand for the adenosine A_1 receptor. The binding affinities of these N^6-substituted adenosine analogues are listed in Table 1.

TABLE 1



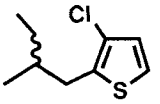
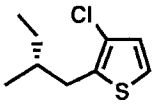
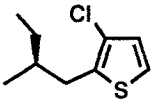
R	$IC_{50}A_1$nM	$IC_{50}A_2$nM	A_2/A_1
	0.026 +/- 0.006	12.1 +/- 1.1	465
	0.0057 +/- 0.0016	13.1 +/- 2.6	2298
	2.99 +/- 0.18	190 +/- 37	63

TABLE 2

COMPOUND	$IC_{50}A_1$nM
14718(-)	0.0057 +/- 0.006
14718(+)	2.99 +/- 0.18
CPA	0.72 +/- 0.15
R-PIA	2.41 +/- 0.60
S-ENBA	0.28 +/- 0.05

In comparision to other standard adenosine A_1 receptor agonists, for example, CPA, R-PIA and S-ENBA, RG 14718(-) has improved A_1 receptor affinity, as shown in Table 2. RG 14718(-) is approximately 47 times more potent for the adenosine A_1 receptor over S-ENBA, which was previously reported to be the most potent adenosine A_1 receptor ligand.[8]

Experimental Section

Materials and Methods

All reagents and solvents were purchased from commercial sources and were used without further purification. CPA, R-PIA and S-ENBA were purchased from Research Biochemicals Incorporated, Natick, MA. Synthetic manipulations were carried out routinely under an argon atmosphere. ^{1}H NMR spectra were recorded on Varian EM390 and Bruker AC-F 300 MHz spectrometers in deuteriochloroform or deuteriodimethylsulfoxide using tetramethylsilane as the internal standard; chemical shifts are expressed in ppm. Infrared spectra were recorded on the Nicolet 740 FT-IR spectrometer. Mass spectra were recorded on a Finnigan 4500MS spectrometer at 70eV. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 20°C. Melting points were determined on a Thomas Hoover apparatus and are uncorrected. Microanalyses were performed on a Perkin-Elmer 2400CHN Elemental Analyzer.

Receptor Binding Assay

Membrane preparations and receptors assays were done according to the method of Jarvis.[9] A_1 Membranes: Frozen rat brains were obtained from Pel-Freez (Rogers, AK). After removal of the brainstem and cerebellum the brains were homogenized using a Polytron (setting 6 for 30 seconds) in 10 volumes of ice cold 50nM Tris-HCl buffer (pH 7.7). The homogenate was centrifuged at 47,800 x g for 10 minutes. The supernatant was discarded and the homogenization step repeated once with the pellet. The final pellet was suspended in 50nM Tris-HCl (pH 7.7) at a final concentration of 1 g /5 mL, aliquoted and stored at -80°C. A_2 Membranes: Rat brain striatum was homogenized using a Polytron in 15 volumes of ice cold 50mM Tris-HCl (pH 7.7), 10mM $MgCl_2$. The homogenate was centrifuged at 47,800 x g for 10 minutes at 4°C. The supernatant was discarded and the pellet resuspended at a concentration of 20 mg /mL (original tissue weight) in 50 mM Tris-HCl (pH 7.7), 10 mM $MgCl_2$, containing 2 units / mL adenosine deaminase. The homogenate was incubated for 30 minutes at 37°C and centrifuged as before. The pellet was resuspended in 50mM Tris-HCl, 10mM $MgCl_2$, (pH 7.7), alliquoted and stored at -80°C. The protein concentration was determined

using the Bio-Rad Micro Assay according to the manufacturer's instructions using bovine serum albumin as a standard.

The assay conditions were as follows: A_1-Assay: (final assay volume = 2 mL); 50 mM Tris-HCl (pH 7.7), 1% DMSO, 1nM [^{3}H] cyclohexyladenosine, 0.050 units/mL adenosine deminase, 20mg whole rat brain homogenate. A_2-Assay: (final assay volume = 1 mL); 50 mM Tris-HCl (pH 7.4), 10 mM $MgCl_2$, 5nM [^{3}H]CGS 21680, 0.3 mg/mL of rat brain striatal membranes.

The reaction was terminated by rapid filtration through 2.4 cm GF/B filters using a Brandel Cell Harverster. The test tubes were washed three times with cold 50 mM Tris-HCl (pH 7.7 or 7.4 for the A_1 and A_2 assay respectively); filtration was completed within 15 seconds. The damp filter circles were placed into glass scintillation vials filled with 10 mL of Aquasol II. Vials were allowed to shake overnight on a rotary shaker and were placed into a liquid scintillation analyzer for two minute counts.

1-(3-Chloro-2-thienyl)-2-butanol 2

To a stirred solution of 3-chlorothiophene (8.50 g, 71.7 mmol) in anhydrous tetrahydrofuran (100 mL) at 0°C was added n-butyllithium (1.6 M solution in hexanes, 44.8 mL, 71.7 mmol). The solution was stirred for 1.5 hours at 0°C and then butylene oxide (5.68 g, 78.9 mmol) was added dropwise. The mixture was stirred at 0°C for 4 hours and then quenched with a saturated ammonium chloride solution (5 mL). Brine (50 mL) was added and the layers were separated. The organic phase was dried over magnesium sulfate, filtered and the solvent was removed *in vacuo* to yield 9.40 g (69%) of a light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) 1.00 (t, 3H), 1.56 (m, 2H), 2.88 (dd, 1H), 3.00 (dd, 1H), 3.80 (m, 1H), 6.88 (d, 1H), 7.15 (d, 1H); IR (neat) 3570, 3373, 2964, 2936, 2880, 1355, 1107, 979, 701 cm^{-1}; MS (EI) m/e 190 (26.62), 173 (14.71), 134 (57.47), 131 (80.43), 97 (100.00), 59 (92.45), 45 (38.56), 41 (33.01).

1H-Isoindole-1,3(2H)-dione, 2-[1-[(3-chloro-2-thienyl)methyl]propyl]- 3a To a stirred solution of the alcohol **2** (6.54 g, 34.4 mmol) in anhydrous tetrahydrofuran (100 mL) at room temperature was added triphenylphosphine (9.01 g, 34.4 mmol) and phthalimide (5.07 g, 34.4 mmol). To this solution was added dropwise diethylazodicarboxylate (5.44 mL, 34.4 mmol). The mixture was stirred for 16 hours, and then the solvent was removed to give an orange oil. The oil was purified by flash chromatography (SiO_2: 3 : 7; hexanes / methylene chloride) to give 8.12 g (74%) of a light yellow

oil. The oil was crystallized from methanol. m.p. 54-55°; ^{1}H NMR (300 MHz, $CDCl_3$) 0.92 (t, 3H), 1.92 (sept, 1H), 2.19 (m, 1H), 3.29 (dd, 1H), 3.54 (dd, 1H), 4.41 (sept, 1H), 6.78 (d, 1H), 7.01 (d, 1H), 7.69 (dd, 2H), 7.80 (dd, 2H); IR (KBr) 3118, 3082, 2970, 2934, 1764, 1704, 1468, 1397, 1369, 1070, 882, 715 cm^{-1}; MS (EI) m/e 321 (0.32), 319 (1.24), 189 (11.48), 188 (100.00), 172 (6.86), 160 (14.24), 130 (26.95), 76 (13.77), 41 (22.21); Analysis calc'd for $C_{16}H_{14}SNO_2Cl$: C, 60.09; H, 4.41; N, 4.38; found: C, 60.07; H, 4.47; N, 4.40.

1-(3-Chloro-2-thienyl)-2-butylamine 3

To a stirred solution of the phthalimide **3a** (8.12 g, 25.5 mmol) in ethanol (75 mL) was added hydrazine hydrate (2 mL). The mixture was heated to reflux for 1 hour and then allowed to cool to room temperature. The solid precipitate was removed by filtration, and the solvent was removed *in vacuo* to give a yellow oil. The oil was dissolved in ethyl acetate (150 mL) and water (50 mL). The layers were separated, and the organic phase was extracted with 5N HCl (2 x 50 mL). The aqueous phase was basified to pH 11 with 10% sodium hydroxide solution and then extracted into ethyl acetate (3 x 75 mL). The combined organic layers were washed with brine, dried over magnesium sulfate, filtered and concentrated to afford 2.95 g (61%) of a light yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) 0.98 (t, 3H), 1.44 (m, 3H), 2.71 (dd, 1H), 2.93 (dd, 1H), 6.88 (d, 1H), 7.13 (d, 1H); IR (neat) 3310, 3202, 3072, 2961, 2921, 2874, 1627, 1524, 1450, 1349, 858, 699 cm^{-1}; MS (EI) m/e 192 (4.42), 190 (13.11), 131 (7.27), 80 (2.93), 58 (100.00), 41 (26.10).

N^6-[1-[(3-Chloro-2-thienyl)methyl]propyl]adenosine 1

To a solution of 6-chloropurine riboside (1.07 g, 3.8 mmol) in ethanol (50 mL) was added triethylamine (2 mL) and the amine **3** (0.71 g, 3.8 mmol). The mixture was heated to reflux for 16 hours, cooled and then the solvent was removed to give a tan foam. Purification by flash chromatography (SiO_2: 1 : 9; methanol / methylene chloride) gave 1.40 g (85%) of a white solid.
m.p. 137-139°; ^{1}H NMR (300 MHz, DMSO-d_6) 0.89 (t, 3H), 1.61 (m, 2H), 3.07 (m, 2H), 3.53 (m, 1H), 3.63 (m, 1H), 3.95 (d, 1H), 4.13 (d, 1H), 4.49 (m, 1H), 4.61 (m, 1H), 5.18 (d, 1H), 5.44 (m, 2H), 5.86 (d, 1H), 6.96 (d, 1H), 7.37 (d, 1H), 7.88 (d, 1H), 8.14 (s, 1H), 8.36 (s, 1H); IR (KBr) 3260, 2928, 1618, 1477, 1337, 1294, 1076, 865 cm^{-1}; MS

(EI) m/e 439 (0.32), 350 (2.38), 308 (39.23), 176 (100.00), 135 (5.27), 131 (3.46), 45 (2.11), 41 (4.99); Analysis calc'd for $C_{18}H_{22}N_5SO_4Cl$: C, 49.15; H, 5.04; N, 15.92; found: C, 49.08; H, 4.88; N, 15.66.

(S) and (R)-Carbamic acid, [R-1-(1-Naphthalenyl)ethyl]-1-[(3-chloro-2-thienyl)methyl]propyl ester 4a and 4b

To a stirred solution of the alcohol **2** (5.79 g, 30.5 mmol) in anhydrous tetrahydrofuran (80 mL) under argon was added diazabicyclo[5.4.0]undec-7-ene (0.20 mL). To this solution was added dropwise (R)-(-)-1-(1-napthyl)ethyl isocyanate (6.00 g, 30.5 mmol). The mixture was heated at reflux for 16 hours, cooled and the solvent was removed *in vacuo* to give a brown oil. The residue was purified by flash chromatography (SiO_2: 1 : 9; ethyl acetate / hexanes) to give 3.00 g of **4a** (25%) and 3.40 g of **4b** (29%).[10] **4a**. m.p. 84-85°; ^1H NMR (300 MHz, $CDCl_3$) 0.93 (t, 3H), 1.59 (m, 2H), 1.65 (d, 3H), 3.04 (dd, 1H), 3.10 (dd, 1H), 4.95 (m, 2H), 5.65 (m, 1H), 6.89 (d, 1H), 7.17 (d, 1H), 7.49 (m, 4H), 7.80 (d, 1H), 7.88 (d, 1H), 8.13 (d, 1H); IR (KBr) 3322, 3077, 2971, 1682, 1551, 1282, 1106, 1058, 773 cm^{-1}; MS (EI) m/e 403 (0.01), 401 (0.01), 216 (16.17), 215 (43.78), 200 (38.55), 174 (36.13), 172 (88.40), 156 (27.11), 155 (100.00), 131 (37.82), 129 (16.03), 88 (6.30), 45 (6.26); Analysis calc'd for $C_{21}H_{22}NO_2ClS$: C, 65.02; H, 5.72; N, 3.61; found: C, 64.99; H, 5.31; N, 3.43. **4b**. m.p. 95°; ^1H NMR (300 MHz, $CDCl_3$) 0.97 (t, 3H), 1.56 (m, 2H), 1.64 (d, 3H), 2.99 (dd, 1H), 3.04 (dd, 1H), 4.90 (m, 2H), 5.61 (m, 1H), 6.80 (d, 1H), 7.04 (d, 1H), 7.49 (m, 4H), 7.77 (d, 1H), 7.86 (d, 1H), 8.08 (d, 1H); IR (KBr) 3314, 2966, 1688, 1552, 1267, 1108, 1059, 767 cm^{-1}; Analysis calc'd for $C_{21}H_{22}NO_2ClS$: C, 65.02; H, 5.72; N, 3.61; found: C, 65.27; H, 5.39; N, 3.40.

(S)-1-(3-Chloro-2-thienyl)-2-butanol 2a

To a stirred solution of carbamate **4a** (2.80 g, 6.97 mmol) in anhydrous tetrahydrofuran (60 mL) under argon was added dropwise lithium aluminum hydride (1.0 M solution in tetrahydrofuran, 6.97 mL, 6.97 mmol). The mixture was heated to 40°C for one hour, cooled and quenched slowly with 10% sodium hydroxide solution. The layers were separated, and the organic phase was washed with brine, dried over magnesium sulfate and the solvent was removed to yield a yellow oil. The oil was purified by flash chromatography

(SiO_2: methylene chloride) to afford 0.87 g (66%) of a clear oil. ^1H NMR (300 MHz, $CDCl_3$) 1.02 (t, 3H), 1.58 (m, 2H), 1.76 (m, 1H), 2.86 (dd, 1H), 3.02 (dd, 1H), 3.76 (m, 1H), 6.88 (d, 1H), 7.12 (d, 1H); $[\alpha]_D^{22}$ +14.63° (c=5, MeOH).

Benzenesulfonamide, N-[1-R-[(3-chloro-2-thienyl)methyl]propyl]-methyl- 9 To a stirred solution of amine **6** (0.30 g, 1.6 mmol) in pyridine under argon (10 mL) was added p-toluenesulfonyl chloride (0.30 g, 1.59 mmol). The mixture was stirred at room temperature for 16 hours and then the solvent was removed. The residue was purified by flash chromatography (SiO_2: 2 : 8; hexanes / methylene chloride) to give 0.35 g (64%) of a clear oil. The oil was crystallized from hexanes. m.p. 54-55°; ^1H NMR (300 MHz, $CDCl_3$) 0.84 (t, 3H), 1.42 (sept, 1H), 1.64 (sept, 1H), 2.41 (s, 3H), 2.87 (d, 2H), 3.45 (m, 1H), 4.58 (d, 1H), 6.77 (d, 1H), 7.07 (d, 1H), 7.24 (d, 2H), 7.69 (d, 2H); IR (KBr) 3356, 3281, 3105, 2978, 2943, 1598, 1411, 1346, 1157, 1088, 1007, 707 cm^{-1}; MS (EI) m/e 344 (34.42), 214 (21.50), 212 (100.00), 155 (49.92), 133 (15.56), 131 (40.79), 91.1 (69.98), 65.0 (16.86), 45 (7.89); $[\alpha]_D^{22}$ -23.5° (c=6, MeOH); Analysis calc'd for $C_{15}H_{18}ClNS_2O_2$: C, 52.39; H, 5.28; N, 4.07; found: C, 52.31; H, 5.37; N, 3.96.

Benzenesulfonamide, N-[1-R-[(3-chloro-2-thienyl)methyl]propyl]-methyl- 9 To a stirred solution of 3-chlorothiophene (0.54 g, 4.5 mmol) in anhydrous tetrahydrofuran (20 mL) at 0°C was added n-butyllithium (1.6 M solution in hexanes, 2.8 mL, 4.5 mmol). The mixture was stirred for 1.5 hours and then cooled to -78°C. A solution of (R)-2-ethyl-N-toluenesulfonylaziridine (1.02 g, 4.5 mmol) in tetrahydrofuran (1 mL) was added dropwise. The mixture was then allowed to warm to 0°C and was stirred for 6 hours. The reaction mixture was quenched with a saturated ammonium chloride solution (5 mL). The organic phase was washed with brine, dried over magnesium sulfate and the solvent was removed to give a yellow oil. The residue was purified by flash chromatography (SiO_2: 2 : 8; hexanes / methylene chloride) and crystallized from hexanes to give 1.01 g (67%) of a white solid. m.p. 57°; ^1H NMR (300 MHz, $CDCl_3$) 0.85 (t, 3H), 1.42 (sept, 1H), 1.64 (sept, 1H), 2.41 (s, 3H), 2.87 (d, 2H), 3.45 (m, 1H), 4.58 (d, 1H), 6.77 (d, 1H), 7.07 (d, 1H), 7.24 (d, 2H), 7.69 (d, 2H); IR (KBr) 3356, 3281, 3105, 2978, 2943, 1598, 1411, 1346, 1157, 1088, 1007, 707 cm^{-1}; MS (EI) m/e 344 (34.42),

214 (21.50), 212 (100.00), 155 (49.92), 133 (15.56), 131 (40.79), 91.1 (69.98), 65.0 (16.86), 45 (7.89); $[\alpha]_D^{22}$ -22.80° (c=6, MeOH); Analysis calc'd for $C_{15}H_{18}ClNS_2O_2$: C, 52.39; H, 5.28; N, 4.07; found: C, 52.50; H, 5.44; N, 3.93.

N^6-[1-R-[(3-Chloro-2-thienyl)methyl]propyl]adenosine 10

Preparation is the same as for **1**. Collected 0.18 g (42%). m.p. 165-166°; ^1H NMR (300 MHz, DMSO-d_6) 0.89 (t, 3H), 1.64 (m, 2H), 3.09 (m, 2H), 3.59 (m, 2H), 3.96 (m, 1H), 4.13 (q, 1H), 4.48 (m, 1H), 4.62 (q, 1H), 5.19 (d, 1H), 5.40 (t, 1H), 5.45 (d, 1H), 5.87 (d, 1H), 6.94 (d, 1H), 7.39 (d, 1H), 7.88 (bd, 1H), 8.15 (s, 1H), 8.35 (s, 1H); IR (KBr) 3329, 3239, 2962, 2921, 1622, 1475, 1335, 1075, 860, 705 cm^{-1}; MS (EI) m/e 441 (0.14), 439 (0.26), 350 (2.26), 336 (2.18), 308 (29.23), 218 (2.66), 204 (1.42), 177 (10.48), 176 (100.00), 160 (3.23); $[\alpha]_D^{22}$ -114° (MeOH); Analysis calc'd for $C_{18}H_{22}N_5SO_4Cl$: C, 49.15; H, 5.04; N, 15.92; found: C, 49.07; H, 4.98; N, 15.99.

N^6-[1-S-[(3-Chloro-2-thienyl)methyl]propyl]adenosine 11

Preparation is the same as for **1**. Collected 0.19 g (73%). m.p. 89-90°; ^1H NMR (300 MHz, DMSO-d_6) 0.88 (t, 3H), 1.64 (m, 2H), 3.08 (m, 2H), 3.53 (d, 1H), 3.63 (d, 1H), 3.94 (m, 1H), 4.13 (m, 1H), 4.48 (m, 1H), 4.62 (m, 1H), 5.18 (d, 1H), 5.44 (m, 2H), 5.86 (d, 1H), 6.93 (d, 1H), 7.37 (d, 1H), 7.86 (bd, 1H), 8.14 (s, 1H), 8.34 (s, 1H); IR (KBr) 3323, 2921, 1612, 1473, 1333, 1291, 1221, 1120, 1078, 701 cm^{-1}; MS (EI) m/e 439 (0.54), 308 (41.70), 218 (2.65), 177 (10.25), 176 (100.00), 135 (6.19), 73 (2.22), 45 (4.50); Analysis calc'd for $C_{18}H_{22}N_5SO_4Cl$: C, 49.15; H, 5.04; N, 15.92; found: C, 48.91; H, 5.37; N, 15.24.

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