Synthesis and Cytostatic Activities of New 6-Substituted Purinylcarbonucleosides Derived from Indan[1]

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Abstract: A new series of 6-substituted purinylcarbonucleosides derivatives of indan, **8a**–**g** and **10a**–**d**, was synthesized from (±)-*cis*-1,3-indandimethanol acetate (**5**), which was prepared in three steps from benzonorbornadiene. 6-Chloropurine was introduced both by Mitsunobu reaction with **5** and by substitution of the mesylate **6**. Suzuki–Miyaura reactions of the protected 6-chloropurine derivative **7** with substituted phenylboronic acids afforded **9a**–**d** (protected purine derivatives with substituted phenyl rings at position 6); deprotection of the latter yielded the new series of purinylcarbonucleoside indan derivatives **10a**–**d**. Treatment of compound **7** with R′H/NaOH afforded a parallel series **8a**–**g**, with alkoxy or amino groups R′ at position 6 instead of substituted phenyl rings.

Key words: synthesis, antineoplastic agent, indan carbocyclic nucleoside, Mitsunobu reaction, Suzuki–Miyaura cross-coupling reaction

Purine bases and their nucleosides constitute an important class of antineoplastic and antileukaemic agents.[2] Efforts to improve their performance in these roles have resulted in the introduction of a variety of structural modifications in both the base and the sugar moiety. In most cases an oxo or amino group has been retained at purine position 6 because this group is essential for the formation of the hydrogen bonds through which the base gets subjected to the action of key enzymes involved in nucleic acid metabolism; but cytostatic activity has also been displayed by arabinosides derived from 6-methoxypurine[3] and by 6-alkyl derivatives of mercaptopurines,[4] and a number of 6-arylpurine ribonucleosides have recently been reported to be cytotoxic for certain cell lines.[5] In view of these results, we decided to investigate the effects of 6-substituents other than OH and NH_2 on the properties of purine-based members of the indan carbonucleoside family, whose antineoplastic and antiviral activities are being explored by us in recent years.[6] We describe here the synthesis of two series of 6-substituted purinylcarbonucleoside indan derivatives, **8a**–**g** and **10a**–**d** (Scheme), and report their cytostatic activities against a number of cell lines.

The central step of the synthesis was the condensation of 6-chloropurine with (±)-*cis*-indandimethanol acetate (**5**), which was prepared from benzonorbornadiene (**2**). The classical Wittig method[7] for the preparation of benzonorbornadiene consists in the [4+2] cycloaddition of benzyne, generated in situ from 1-bromo-2-fluorobenzene (**1**), to cyclopentadiene in THF. In this work we achieved a considerably improved yield of 66%, by using diethyl ether instead of THF and carrying out the reaction in an ultrasound bath. Treatment of **2** with ozone and quenching with dimethyl sulphide afforded dialdehyde **3**, which upon treatment, without prior isolation, with lithium aluminum hydride, gave the diol **4** in 71% yield. Two methods were then compared for protection of the left-hand hydroxyl of **4**: reaction with acetic anhydride and pyridine, and transesterification with vinyl acetate catalysed by Novozym® 435. Both gave mixtures of **4** and **5** and the diacetylated product containing almost the same amount of **5** (around 55%), but with the enzymatic process, work-up was easier and the recovery of **4** was greater (Scheme).

6-Chloropurine was first condensed with **5** by a standard Mitsunobu reaction[8] in the presence of triphenylphosphine and diethyl azodicarboxylate, but with this method we were unable to achieve yields greater than 40%. More satisfactory was an indirect route via mesylate **6** (obtained from **5** in 93% yield by treatment at 0 °C with methanesulfonyl chloride, triethylamine and DMAP). Reaction of crude **6** with 6-chloropurine in DMF in the presence of NaH and 18-crown-6 ether[9] gave the condensation product **7** in 65% yield (60% from **5**, i.e. 1.5 times the yield obtained by the direct Mitsunobu route). Purinylcarbonucleosides **8a**–**g**, in which the purine 6-substituent is an NHR′ or OR′ group, were obtained directly from **7** in 45–75% yield by treatment with the corresponding nucleophiles NH_2R' or R′OH (Scheme).

Following the observation of cytostatic activity for compounds **8** (see below), synthesis of the 6-arylpurinyl carbonucleosides **10a**–**d** was prompted by reports of significant antineoplastic activity being displayed by 6-arylpurine bases and nucleosides[5] and acyclic nucleoside analogues[10] that have recently been prepared by Suzuki–Miyaura cross-coupling of 6-halopurines with boronic acids.[11] Treatment of **7** with boronic acids under Suzuki conditions[12] using potassium carbonate as base, tetrakis(triphenylphosphine)palladium as catalyst and toluene as solvent, afforded **9a**–**d** in 63–87% yield, whose

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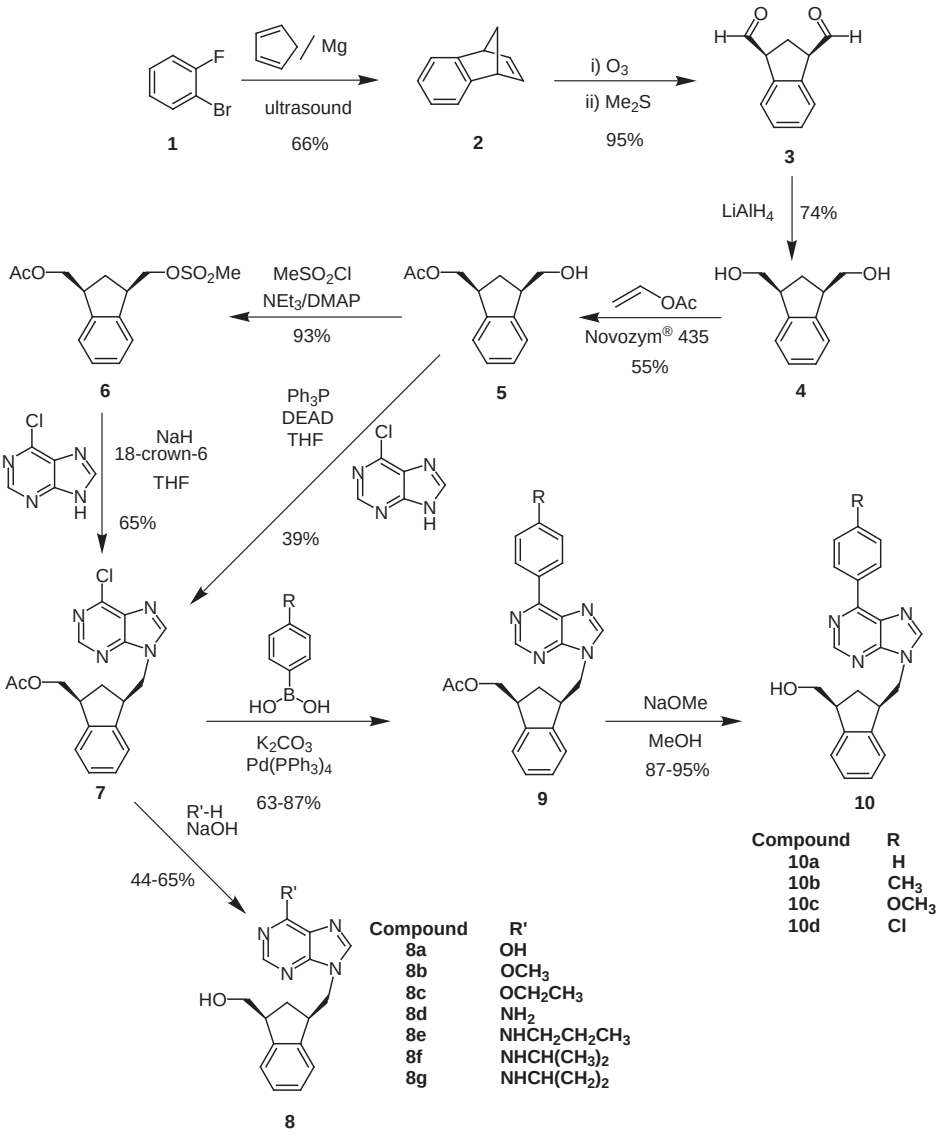

Scheme

deprotection with NaOMe/MeOH gave compounds **10a**–**d** in 87–95% yield.

Compounds **8a**–**g** and **10a**–**d** were evaluated for cytostatic activity using murine leukaemia cells (L1210/0) and human T-lymphocytes (Molt4/C8 and CEM/0).[13] Compounds **8a**–**g** all showed moderate activity, while compounds **10a**–**d** showed much greater activity, especially **10d**, which had IC_{50} values of 0.81 μg/mL for Molt4/C8 and 0.63 μg/mL for CEM/0, and **10b** (IC_{50} = 1.6 μg/mL for Molt4/C8, 1.4 μg/mL for CEM/0).

Mps were determined in a Reichert Kofler Thermopan or in capillary tubes in a Büchi 510 apparatus, and are uncorrected. IR spectra were recorded in a Perkin-Elmer 1640-FT spectrometer. ^{1}H NMR spectra (300 MHz) and ^{13}C NMR spectra (75.47 MHz) were recorded in a Bruker AMX spectrometer using TMS as internal standard [chemical shifts (δ) in ppm, *J* in Hz]. Elemental analyses were obtained on a Perkin-Elmer 240B microanalyser by the Microanalysis Service of the University of Santiago de Compostela. Flash chromatography was performed on silica gel (Merck 60, 230–240 mesh) and analytical TLC on pre-coated silica gel plates (Merck 60 F254, 0.25 mm).

1,4-Dihydro-1,4-methanenaphthalene (Benzonorbornadiene, 2)

A solution of **1** (13 g, 75 mmol) and cyclopentadiene (4.9 g, 75 mmol) in Et_2O (100 mL) was added over 45 min, under argon and at r.t., to a stirred suspension of Mg (2 g, 83 mmol) in Et_2O (50 mL) placed in an ultrasound bath. After stirring for 3 h in the ultrasound bath, the solvent was distilled off under reduced pressure and the residue was treated with aq sat. NH_4Cl solution (70 mL), Et_2O (3 × 150 mL) and brine (100 mL). The organic layer was drawn off and dried (Na_2SO_4), and the solvent was removed at reduced pressure. The resulting oil was distilled in a Kugelrohr distillation apparatus (80–85 °C/13–15 mm Hg) to afford **2** (10.68 g, 66%) as a colourless oil.

IR (film): 3066, 2983, 2934, 2866, 1565, 1508, 1455, 1303, 1110, 830 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 2.29–2.32 (d, 1 H, *J* = 7.08 Hz, 9-H), 2.37–2.39 (dt, 1 H, $J_{(d)}$ = 7.04 Hz, $J_{(t)}$ = 3.07 Hz, 9-H), 3.94 (t, 2 H,

J = 1.76 Hz, 1-H and 4-H), 6.85 (t, 2 H, J = 1.80 Hz, 2-H and 3-H), 6.98–7.00 (m, 2 H, ArH), 7.27–7.30 (m, 2 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 51.00 (CH), 70.81 (CH_2), 122.21 (CH), 124.88 (CH), 143.63 (CH), 152.39 (C).

Anal. Calcd for $C_{11}H_{10}$: C, 92.91; H, 7.09. Found: C, 93.04; H, 6.95.

cis-1,3-Indandimethanol (4)

Using a Fischer 503 ozone generator, ozone was bubbled for 30 min at a rate of 6 g/h (60 L/h O_2; according to the operating instructions of the apparatus) through a vigorously stirred solution of **2** (10.68 g, 75 mmol) in MeOH–$CHCl_3$ (1:1, 100 mL) at –78 °C. After the addition of Me_2S (11.70 mL, 9.89 g, 85.16 mmol), the reaction mixture was stirred for 12 h while returning to r.t. Concentration to dryness then afforded **3** (12.47 g, 95.33%) as a colourless oil.

3

IR (film): 3420, 2822, 2725, 1718, 1477, 1457, 1388, 1160, 1059, 755 cm^{-1}.

The crude **3** (12.47 g, 71.58 mmol) was then added dropwise to a solution of $LiAlH_4$ (8.5 g, 225 mmol) in anhyd THF (150 mL), and after standing for 48 h at 0 °C, this mixture was poured over ice, and left until all $LiAlH_4$ had been destroyed. After the removal of organic solvents in a rotary evaporator, aluminum hydroxides were filtered out, the filtrate was extracted with EtOAc (5 × 100 mL), and the pooled organic layers were dried (Na_2SO_4) and concentrated to dryness. Chromatography of the resulting white solid on silica gel (250 g) using EtOAc–hexane (1:1) as eluent afforded an eluate, from the middle fractions of which **4** was isolated as a white solid (6.32 g, 74.5%); mp 99–100 °C.

IR (KBr): 3276, 2918, 2864, 1474, 1456, 1091, 779, 745 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.75–1.84 (dt, 1 H, $J_{(d)}$ = 13.59 Hz, $J_{(t)}$ = 7.70 Hz, 2β-H), 2.03 (s, 2 H, exchang. with D_2O, OH), 2.43–2.53 (dt, 1 H, $J_{(d)}$ = 13.37 Hz, $J_{(t)}$ = 8.96 Hz, 2α-H), 3.35–3.45 (m, 2 H, 1β-H and 3β-H), 3.87–3.89 (m, 4 H, CH_2OH), 7.21–7.30 (m, 4 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 31.66 (CH_2), 46.52 (CH), 66.63 (CH_2), 124.53 (CH), 127.57 (CH), 144.92 (C).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.02; H, 7.79.

(±)-_cis_-1,3-Indandimethanol Acetate (5)

Novozym® 435 (8.18 g) was added to a solution of **4** (14.62 g, 82.1 mmol) in THF (200 mL), and after dropwise addition of vinyl acetate (4.2 mL, 45.15 mmol), the mixture was stirred for 20 h at r.t. The lipase was filtered out on a bed of Celite, the filtrate was concentrated to dryness, and the resulting oily residue was chromatographed on silica gel (350 g) using hexane–EtOAc (1:1.5) as eluent. The early-eluting fractions afforded 3 g of a solid identified as (±)-_cis_-1,3-indandimethanol diacetate, the middle fractions 9.94 g (55%) of an oil that crystallized spontaneously was identified as **5**, and the final fractions 3.74 g of a white solid was identified as the starting diol **4**; mp 101–103 °C.

IR (KBr): 3420, 2948, 2871, 1654, 1479, 1457, 1385, 1365, 1244, 1035, 759 cm^{-1}.

^{1}H NMR (acetone-d_6): δ = 1.59–1.69 (dt, 1 H, $J_{(d)}$ = 13.19 Hz, $J_{(t)}$ = 7.53 Hz, 2β-H), 2.03 (s, 3 H, $OCOCH_3$), 2.40–2.49 (dt, 1 H, $J_{(d)}$ = 13.09 Hz, $J_{(t)}$ = 8.30 Hz, 2α-H), 3.30 (m, 1 H, 3β-H), 3.44 (m, 1 H, 1β-H), 3.70 (m, 1 H, OH, exchange with D_2O), 3.84 (m, 2 H, CH_2OH), 4.17–4.20 (part A of an ABM system, 1 H, J_{AB} = 10.74 Hz, J_{AM} = 7.36 Hz, CHHOAc), 4.28–4.35 (part B of an ABM system, 1 H, J_{BA} = 10.74 Hz, J_{BM} = 6.26 Hz, CHHOAc), 7.17–7.38 (m, 4 H, ArH).

^{13}C NMR (acetone-d_6): δ = 21.24 (CH_3), 33.84 (CH_2), 44.16 (CH), 47.75 (CH), 66.97 (CH_2), 68.80 (CH_2), 125.26 and 125.61 (CH), 127.95 and 128.17 (CH), 145.39 and 146.65 (C), 171.50 (COOR).

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.66; H, 7.19.

(±)-_cis_-3-(Methylsulfonyloxymethyl)indanylmethyl Acetate (6)

Mesyl chloride (8.5 mL, 110 mmol) was added dropwise to a solution of **5** (7.54 g, 36.6 mmol), Et_3N (15 mL) and a catalyitic amount of DMAP in $CHCl_3$ (150 mL) at 0 °C. The mixture was refluxed for 12 h, then washed with H_2O, and the organic layer was separated, washed with 1 M aq NaOH (100 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated to dryness in a rotary evaporator. The residue (10 g) was chromatographed on a column of silica gel (300 g) with hexane–EtOAc (3:1) as eluent; light brown solid (9.65 g, 93%); mp 40–43 °C.

IR (KBr): 3450, 3025, 2975, 1733, 1466, 1296, 1285, 1250, 1170, 1045, 977, 954, 869, 825, 755 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.62–1.72 (dt, 1 H, $J_{(d)}$ = 13.38 Hz, $J_{(t)}$ = 7.59 Hz, 2β-H), 2.15 (s, 3 H, $OCOCH_3$), 2.62–2.72 (dt, 1 H, $J_{(d)}$ = 13.35 Hz, $J_{(t)}$ = 8.36 Hz, 2α-H), 3.07 (s, 3 H, OSO_2CH_3), 3.49 (m, 1 H, 1β-H), 3.62 (m, 1 H, 3β-H), 4.27–4.34 (part A of an ABM system, 1 H, J_{AB} = 10.93 Hz, J_{AM} = 6.95 Hz, CHHOAc), 4.40–4.46 (part B of an ABM system, 1 H, J_{BA} = 10.95 Hz, J_{BM} = 5.90 Hz, CHHOAc), 4.39–4.45 (part A of an ABM system, 1 H, J_{AB} = 9.61 Hz, J_{AM} = 7.23 Hz, CHHOSO$_2$CH$_3$), 4.54-4.61 (part B of an ABM system, 1H, J_{BA} = 9.70 Hz, J_{BM} = 5.93 Hz, CHHOSO$_2$CH$_3$), 7.30–7.39 (m, 4 H, ArH).

^{13}C NMR ($CDCl_3$): δ = 21.35 (CH_3), 32.91 (CH_2), 37.86 (OSO_2CH_3), 43.21 (CH), 43.63 (CH), 67.77 (CH_2), 72.72 (CH_2), 124.59 and 124.81 (CH), 127.95 and 128.23 (CH), 142.54 and 144.09 (C), 171.50 (COOR).

Anal. Calcd for $C_{14}H_{18}O_5S$: C, 56.36; H, 6.08. Found: C, 56.54; H, 5.88.

(±)-_cis_-3-(6-Chloro-9_H_-purin-9-ylmethyl)indanylmethyl Acetate (7)

Method A: Diethyl azodicarboxylate (1.32 mL, 8.40 mmol) was added to a suspension of Ph_3P (2.08 g, 7.94 mmol) and 6-chloropurine (1.26 g; 8.15 mmol) in THF (55 mL) and the mixture was stirred for 1 h. Following the slow addition of a solution of **5** (1.47 g, 6.68 mmol) in THF (20 mL), the stirring was continued for 36 h at r.t. and 24 h at 40 °C. Removal of the solvent under reduced pressure gave a residue that was chromatographed on silica gel (100 g) with hexane–EtOAc (3:2) as eluent; yellow solid (0.93 g, 39%).

Method B: A solution of 6-chloropurine (1.18 g, 7.53 mmol), NaH (0.30 g, 7.53 mmol) and 18-crown-6 ether (1.35 g, 5.10 mmol) in DMF (50 mL) was stirred at 55 °C for 30 min. A solution of **6** (1.50 g, 5.02 mmol) in DMF (25 mL) was slowly added and the stirring was continued at the same temperature for a further 24 h. The solvent was then removed under reduced pressure and the resulting residue was chromatographed on silica gel (210 g) using hexane–EtOAc (3:2); yellow solid (1.53 g, 65%); mp 112–114 °C (Et_2O).

IR (KBr): 3245, 3068, 2990, 1741, 1594, 1336, 1247, 1034, 772, 758 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.54–1.63 (dt, 1 H, $J_{(d)}$ = 13.47 Hz, $J_{(t)}$ = 7.30 Hz, 2β-H), 2.04 (s, 3 H, $OCOCH_3$), 2.34–2.44 (dt, 1 H, $J_{(d)}$ = 13.30 Hz, $J_{(t)}$ = 8.30 Hz, 2α-H), 3.47 (m, 1 H, 1β-H), 3.88 (m, 1 H, 3β-H), 4.16–4.22 (part A of an ABM system, 1 H, J_{AB} = 10.98 Hz, J_{AM} = 7.23 Hz, CHHOAc), 4.24–4.32 (part B of an ABM system, 1 H, J_{BA} = 10.98 Hz, J_{BM} = 7.09 Hz, CHHOAc), 4.38–4.45 (part A of an ABM system, 1 H, J_{AB} = 13.92 Hz, J_{AM} = 8.30 Hz, CHHN), 4.71–4.77 (part B of an ABM system, 1 H, J_{BA} = 13.92 Hz,

J_{BM} = 6.87 Hz, CH*H*N), 7.07–7.32 (m, 4 H, ArH), 8.05 (s, 1 H, 2′-H), 8.77 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 21.32 (CH_3), 33.77 (CH_2), 43.25 (CH), 44.10 (CH), 49.36 (CH_2), 67.50 (CH_2), 124.26, 125.09, 128.14 and 128.46 (CH), 131.95 (C), 142.99 (C), 143.91 (C), 145.70 (CH), 152.48 (CH), 171.49 [C(O)OR].

Anal. Calcd for $C_{18}H_{17}ClN_4O_2$: C, 60.59; H, 4.80; N, 15.70. Found: C, 60.44; H, 4.63; N, 15.55.

(±)-*cis*-3-(6-Hydroxy-9*H*-purin-9-ylmethyl)indanylmethanol (8a)

A solution of **7** (0.39 g, 1.09 mmol) in 0.25 N aq NaOH (25 mL) was refluxed for 5 h. Removal of the solvent under reduced pressure using an azeotropic mixture with toluene afforded a brown solid. This was chromatographed on silica gel (30 g) with EtOAc as eluent to give **8a** as a light brown solid (0.23 g 71%); mp 222–225 °C.

IR (KBr): 3450, 2861, 1699, 1587, 1549, 1475, 1414, 1342, 1201, 1128, 1030, 905, 790, 759 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.70–1.74 (dt, 1 H, $J_{(d)}$ = 13.53 Hz, $J_{(t)}$ = 7.79 Hz, 2β-H), 2.26–2.37 (dt, 1 H, $J_{(d)}$ = 13.52 Hz, $J_{(t)}$ = 8.74 Hz, 2α-H), 3.36–3.40 (m, 1 H, 1β-H), 3.83–3.88 (m, 1 H, 3β-H), 3.87–3.88 (d, 2 H, J = 4.77 Hz, CH_2OH), 4.43–4.50 (part A of an ABM system, 1 H, J_{AB} = 13.93 Hz, J_{AM} = 8.95 Hz, C*H*HN), 4.65-4.71 (part B of an ABM system, 1 H, J_{BA} = 13.92 Hz, J_{BM} = 7.90 Hz, CH*H*N), 7.02–7.04 (d, 1 H, J = 7.35 Hz, ArH), 7.18–7.32 (m, 4 H, ArH), 8.10 (s, 1 H, 2′-H), 8.75 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 32.63 (CH_2), 43.06 (CH), 45.54 (CH), 47.62 (CH_2), 64.39 (CH_2), 123.22, 123.56, 126.77 and 126.67 (CH), 124.06 (C), 140.05 (C), 144.93 (CH), 145.14 and 145.22 (C), 148.23 (CH), 156.33 (C).

Anal. Calcd for $C_{22}H_{20}N_4O_2$: C, 70.95; H, 5.41; N, 15.04. Found: C, 70.73; H, 5.60; N, 15.19.

(±)-*cis*-3-(6-Methoxy-9*H*-purin-9-ylmethyl)indanylmethanol (8b)

A solution of **7** (0.30 g, 0.84 mmol) in MeOH (9 mL) was stirred at r.t. for 24 h and then extracted with EtOAc (100 mL) and brine (100 mL). The pooled organic layers were dried (Na_2SO_4) and concentrated to dryness under reduced pressure to afford **8b** as a pale yellow solid (0.17 g, 65%); mp 140–142 °C (hexane–Et_2O).

IR (KBr): 3300, 2852, 1700, 1598, 1575, 1480, 1342, 1311, 1223, 1102, 799, 759 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.70–1.78 (dt, 1 H, $J_{(d)}$ = 13.61 Hz, $J_{(t)}$ = 5.14 Hz, 2β-H), 2.28–2.38 (dt, 1 H, $J_{(d)}$ = 13.89 Hz, $J_{(t)}$ = 8.69 Hz, 2α-H), 2.98 (s, 1 H, OH exchang. with D_2O), 3.33–3.38 (m, 1 H, 1β-H), 3.76–3.84 (m, 1 H, 3β-H), 3.88 (s, 2 H, CH_2OH), 4.40–4.48 (part A of an ABM system, 1 H, J_{AB} = 13.96 Hz, J_{AM} = 9.32 Hz, C*H*HN), 4.53–4.59 (part B of an ABM system, 1 H, J_{BA} = 14.01 Hz, J_{BM} = 6.17 Hz, CH*H*N), 7.04–7.06 (d, 1 H, J = 7.41 Hz, ArH), 7.17–7.32 (m, 3 H, ArH), 7.90 (s, 1 H, 2′-H), 8.53 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 34.77 (CH), 47.62 (CH), 49.39 (CH), 51.71 (CH_2), 57.25 (CH_3), 68.51 (CH_2), 127.06, 127.50, 130.23 y 130.83 (CH), 146.36 (C), 147.31 (C), 145.45 (CH), 155.00 (CH), 164.37 (C).

Anal. Calcd for $C_{23}H_{22}N_4O_2$: C, 71.48; H, 5.74; N, 14.50. Found: C, 71.33; H, 5.52; N, 14.72.

(±)-*cis*-3-(6-Ethoxy-9*H*-purin-9-ylmethyl)indanylmethanol (8c)

A solution of **7** (0.33 g, 0.92 mmol) in EtOH (10 mL) was stirred at r.t. for 24 h and then extracted with EtOAc (150 mL) and brine (100 mL). The pooled organic layers were dried (Na_2SO_4) and concentrated to dryness under reduced pressure. The solid obtained was recrystallized from Et_2O to afford **8c** as a light brown solid (0.22 g, 73%); mp 127–129 °C (Et_2O).

IR (KBr): 3314, 2903, 1654, 1609, 1575, 1474, 1381, 1341, 1319, 1239, 1111, 797, 741 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.48–1.53 (t, 3 H, J = 7.02 Hz, OCH_2CH_3), 1.69–1.77 (dt, 1 H, $J_{(d)}$ = 13.59 Hz, $J_{(t)}$ = 5.13 Hz, 2β-H), 2.26–2.37 (dt, 1 H, $J_{(d)}$ = 13.72 Hz, $J_{(t)}$ = 8.89 Hz, 2α-H), 3.32–3.36 (m, 1 H, 1β-H), 3.78–3.83 (m, 1 H, 3β-H), 3.85–3.91 (m, 2 H, CH_2OH), 4.40–4.48 (part A of an ABM system, 1 H, J_{AB} = 13.96 Hz, J_{AM} = 9.46 Hz, C*H*HN), 4.51–4.58 (part B of an ABM system, 1 H, J_{BA} = 13.94 Hz, J_{BM} = 6.10 Hz, CH*H*N), 4.62–4.69 (q, 2 H, J = 7.02 Hz, OCH_2CH$_3$), 7.02–7.05 (d, 1 H, J = 7.23 Hz, ArH), 7.15–7.30 (m, 3 H, ArH), 7.90 (s, 1 H, 2′-H), 8.50 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 19.73 (CH_3), 31.98 (CH_2), 41.29 (CH), 42.37 (CH), 46.44 (CH_2), 60.23 (CH_2), 65.82 (CH_2), 118.12 (C) 122.96, 1123.29, 126.23 and 126.35 (CH), 146.36 (C), 139.80 (CH), 142.79 (C), 151.22 (CH), 154.66 (C), 169.50 (C).

Anal. Calcd for $C_{24}H_{24}N_4O_2$: C, 71.98; H, 6.04; N, 13.99. Found: C, 72.15; H, 5.86; N, 14.09.

(±)-*cis*-3-(6-Amino-9*H*-purin-9-ylmethyl)indanylmethanol (8d)

A solution of **7** (0.35 g, 0.98 mmol) in MeOH (4 mL) and liquid NH_3 (3 mL) was heated in a bomb at 75 °C for 60 h. Once the reaction mixture had cooled to r.t., the solvent was evaporated under reduced pressure and **8d** was isolated as a white solid (0.18 g, 55%); mp 226–228 °C (Et_2O).

IR (KBr): 3353, 1653, 1558, 1418, 1318, 1237, 1072, 796, 775 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 1.48–1.57 (dt, 1 H, $J_{(d)}$ = 13.14 Hz, $J_{(t)}$ = 7.56 Hz, 2β-H), 2.07–2.17 (dt, 1 H, $J_{(d)}$ = 13.05 Hz, $J_{(t)}$ = 8.22 Hz, 2α-H), 3.15 (m, 1 H, 1β-H), 3.48 (m, 1 H, 3β-H), 3.64–3.81 (m, 2 H, CH_2OH), 4.09–4.21 (part A of an ABM system, 1 H, J_{AB} = 13.55 Hz, J_{AM} = 8.95 Hz, C*H*HN), 4.55–4.68 (part B of an ABM system, 1 H, J_{BA} = 13.59 Hz, J_{BM} = 5.91 Hz, CH*H*N), 4.75 (s, 1 H, OH exchange with D_2O), 7.03–7.33 (m, 4 H, ArH), 7.22 (s, 2 H, NH_2 exchange with D_2O), 8.10 (s, 1 H, 2′-H), 8.15 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 33.46 (CH_2), 43.54 (CH), 46.16 (CH), 48.01 (CH_2), 65.01 (CH_2), 123.96, 124.74, 127.01 and 127.37 (CH), 141.45 (C), 144.09 and 145.61 (C), 150.02 (CH), 152.81 (CH), 156.12 (C).

Anal. Calcd for $C_{22}H_{21}N_5O$: C, 71.14; H, 5.70; N, 18.85. Found: C, 71.27; H, 5.48; N, 18.73.

(±)-*cis*-3-(6-*N*-propylamino-9*H*-purin-9-ylmethyl)indanylmethanol (8e)

A solution of **7** (0.30 g, 0.84 mmol) and propylamine (4 mL) in MeOH (9 mL) was heated in a bomb at 75 °C for 60 h. Once the reaction mixture had cooled to r.t., the solvent was evaporated under reduced pressure, leaving a brown oil. This was chromatographed on silica gel (15 g) using AcOH–MeOH (10:1) as eluent to afford **8e** as a white solid (0.17 g, 60%); mp 116–118 °C (acetone–Et_2O).

IR (KBr): 3273, 2952, 2862, 1618, 1577, 1540, 1476, 1339, 1248, 1224, 1082, 794, 758 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 0.96–1.01 (t, 3 H, J = 7.66 Hz, CH_3CH$_2$CH$_2$N), 1.61–1.69 (sext, 2 H, J = 14.59, 7.44, 7.15 Hz, CH$_3$CH_2CH$_2$N), 1.71–1.77 (m, 1 H, 2β-H), 2.24–2.34 (dt, 1 H, $J_{(d)}$ = 13.66 Hz, $J_{(t)}$ = 8.90 Hz, 2α-H), 3.28–3.34 (m, 1 H, 1β-H), 3.49–3.61 (m, 2 H, CH_2OH), 3.71–3.79 (m, 1 H, 3β-H), 3.81–3.92 (m, 2 H, CH$_3$CH$_2$CH_2N), 4.26–4.34 (part A of an ABM system, 1 H, J_{AB} = 13.90 Hz, J_{AM} = 9.70 Hz, C*H*HN), 4.43–4.50 (part B of an ABM system, 1 H, J_{BA} = 13.90 Hz, J_{BM} = 6.22 Hz, CH*H*N), 4.70 (br s, 1 H, OH exchange with D_2O), 6.21 (br s, 1 H, NH exchange with

D_2O), 6.97–6.99 (d, 1 H, J = 6.96 Hz, ArH), 7.13–7.28 (m, 3 H, ArH), 7.44 (s, 1 H, 2′-H), 8.34 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 14.33 (CH_3), 24.91 (CH_2), 34.78 (CH_2), 44.85 (CH_2), 47.65 (CH), 49.61 (CH), 51.49 (CH_2), 68.32 (CH_2), 127.06, 127.52, 130.04 and 130.69 (CH), 142.60 (CH), 146.58 (C), 147.55 (C), 156.12 (CH), 158.45 (C).

Anal. Calcd for $C_{25}H_{27}N_5O$: C, 72.61; H, 6.58; N, 16.94. Found: C, 72.83; H, 6.41; N, 16.71.

(±)-*cis*-3-(6-*N*-isopropylamino-9*H*-purin-9-ylmethyl)indanylmethanol (8f)

A solution of **7** (0.10 g, 0.28 mmol) and isopropylamine (1 mL) in MeOH (3 mL) was heated in a bomb at 75 °C for 60 h. Once the reaction mixture had cooled to r.t., the solvent was evaporated under reduced pressure leaving a brown oil. This was purified by chromatography on silica gel (4 g) using AcOH–MeOH (10:1) as eluent to furnish **8f** as a light brown solid (0.045 g, 52%); mp 170–71 °C (acetone).

IR (KBr): 3260, 2951, 2857, 1684, 1653, 1576, 1474, 1337, 1225, 1082, 793, 758 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.30–1.31 (d, 6 H, $J_{(d)}$ = 2.5 Hz, 2 CH_3), 1.72–1.80 (dt, 1 H, $J_{(d)}$ = 9.44 Hz, $J_{(t)}$ = 4.72 Hz, 2β-H), 2.26–2.36 (dt, 1 H, $J_{(d)}$ = 13.53 Hz, $J_{(t)}$ = 8.81 Hz, 2α-H), 3.35 (m, 1 H, 1β-H), 3.75 (m, 1 H, 3β-H), 3.80–3.90 (m, 2 H, CH_2OH), 4.30–4.38 (part A of an ABM system, 1 H, J_{AB} = 14.05 Hz, J_{AM} = 9.76 Hz, C*H*HN), 4.43–4.50 (part B of an ABM system, 1 H, J_{BA} = 14.05 Hz, J_{BM} = 6.30 Hz, CH*H*N), 4.60 (s, 1 H, OH, exchang. with D_2O), 6.00 (s, 1 H, NH exchang. with D_2O), 7.02–7.05 (d, 1 H, ArH), 7.18–7.31 (m, 3 H, ArH), 7.55 (s, 1 H, 2′-H), 8.36 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 20.79 (CH_3), 27.12 (CH), 29.58 (CH_2), 42.83 (CH), 44.60 (CH), 46.43 (CH_2), 63.35 (CH_2), 122.04, 122.50, 125.02 y 125.69 (CH), 137.55 (C), 141.51 y 142.49 (C), 151.09 (CH), 154.04 (C).

Anal. Calcd for $C_{25}H_{27}N_5O$: C, 72.61; H, 6.58; N, 16.94. Found: C, 72.78; H, 6.69; N, 16.75.

(±)-*cis*-3-(6-*N*-cyclopropylamino-9*H*-purin-9-ylmethyl)indanylmethanol (8g)

A solution of **7** (0.30 g, 0.84 mmol) and cyclopropylamine (3 mL) in MeOH (9 mL) was heated in a bomb at 75 °C for 60 h. Once the reaction mixture had cooled to r.t., the solvent was evaporated under reduced pressure leaving a brown oil. Chromatography of this oil on silica gel (15 g) using AcOH–MeOH (8:1) as eluent afforded **8g** as a light brown solid (0.125 g, 44%); mp 167–170 °C (acetone).

IR (KBr): 3319, 2920, 1717, 1615, 1578, 1477, 1356, 1285, 1235, 1075, 797, 759 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.59 (m, 2 H, cyclopropyl CH_2) 0.86 (m, 2 H, cyclopropyl CH_2), 1.64–1.74 (dt, 1 H, $J_{(d)}$ = 9.60 Hz, $J_{(t)}$ = 4.80 Hz, 2β-H), 2.19–2.31 (dt, 1 H, $J_{(d)}$ = 13.63 Hz, $J_{(t)}$ = 8.98 Hz, 2α-H), 2.96–2.98 (d, 1 H, J = 2.87 Hz, cyclopropyl CH), 3.26–3.31 (m, 1 H, 1β-H), 3.66–3.77 (m, 1 H, 3β-H), 3.84 (s, 2 H, CH_2OH), 4.25–4.34 (part A of an ABM system, 1 H, J_{AB} = 13.90 Hz, J_{AM} = 9.70 Hz, C*H*HN), 4.39–4.47 (part B of an ABM system, 1 H, J_{BA} = 13.90 Hz, J_{BM} = 6.32 Hz, CH*H*N), 4.70 (s, 1 H, OH exchang. with D_2O), 6.30 (s, 1 H, NH exchang. with D_2O), 6.95–6.98 (d, 1 H, J = 7.06 Hz, ArH), 7.10–7.25 (m, 3 H, ArH), 7.49 (s, 1 H, 2′-H), 8.40 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 7.72 (CH_2), 23.91 (CH), 32.28 (CH_2), 45.15 (CH), 47.13 (CH), 49.01 (CH_2), 66.01 (CH_2), 124.55, 125.02, 127.58, 128.23 (CH), 140.46 (CH), 144.04 (C), 144.99 (C), 153.69 (CH), 156.22 (C).

Anal. Calcd for $C_{25}H_{25}N_5O$: C, 72.97; H, 6.12; N, 17.02. Found: C, 73.15; H, 5.98; N, 16.93.

Suzuki–Miyaura Coupling of 7 with Substituted Arylboronic Acids; General Procedure

A mixture of **7** (220 mg, 0.61 mmol), the appropriate arylboronic acid (0.92 mmol), $Pd(PPh_3)_4$ (33.3 mg, 0.029 mmol) and K_2CO_3 (127.6 mg, 0.92 mmol) in toluene (30 mL) was stirred under argon at 100 °C until the starting material had disappeared (TLC monitoring). Once at r.t., the solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (60 g) using hexane–EtOAc (3:1) as eluent, affording fractions from which the corresponding 6-arylpurine derivative **9** was isolated by evaporation of the solvent and drying.

(±)-*cis*-3-(6-Phenyl-9*H*-purin-9-ylmethyl)indanylmethyl Acetate (9a)

Yield: 73%; mp 96–99 °C.

IR (KBr): 2888, 1731, 1580, 1567, 1502, 1457, 1397, 1324, 1241, 1027, 928, 764 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.49–1.60 (dt, 1 H, $J_{(d)}$ = 13.20 Hz, $J_{(t)}$ = 7.38 Hz, 2β-H), 1.95 (s, H, CH_3CO), 2.28–2.39 (dt, 1 H, $J_{(d)}$ = 13.20 Hz, $J_{(t)}$ = 8.34 Hz, 2α-H), 3.33–3.45 (m, 1 H, 1β-H), 3.79–3.90 (m, 1 H, 3β-H), 4.07–4.14 (part A of an ABM system, 1 H, J_{AB} = 11.01 Hz, J_{AM} = 7.04 Hz, C*H*HOAc), 4.19–4.26 (part B of an ABM system, 1 H, J_{BA} = 11.01 Hz, J_{BM} = 5.83 Hz, CH*H*OAc), 4.30–4.39 (part A of an ABM system, 1 H, J_{AB} = 13.98 Hz, J_{AM} = 8.21 Hz, C*H*HN), 4.64–4.72 (part B of an ABM system, 1 H, J_{BA} = 13.98 Hz, J_{BM} = 5.97 Hz, CH*H*N), 7.00–7.24 (m, 4 H, ArH), 7.44–7.53 (m, 3 H, ArH), 7.96 (s, 1 H, 2′-H), 8.70–8.74 (m, 2 H, ArH), 8.96 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 21.32 (CH_3), 33.88 (CH_2), 43.25 (CH), 44.08 (CH_3), 48.87 (CH_2), 67.61 (CH_2), 124.36, 125.01, 128.07 and 128.30 (CH), 129.10 (C), 130.19 (CH), 131.40 and 131.46 (CH), 136.00 (C), 143.42 (C), 143.99 (C), 144.89 (CH), 152.88 (CH), 153.14 (C), 155.36 (C), 171.43 (COO).

Anal. Calcd for $C_{24}H_{22}N_4O_2$: C, 72.34; H, 5.57; N, 14.06. Found: C, 72.09; H, 5.71; N, 14.20.

(±)-*cis*-3-[6-(4′-Methyl)phenyl-9*H*-purin-9-ylmethyl]indanylmethyl Acetate (9b)

Yield: 64%; mp 136–140 °C.

IR (KBr): 2889, 1733, 1579, 1560, 1514, 1455, 1325, 1304, 1231, 1204, 1179, 1025, 930, 799, 649 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.48–1.56 (dt, 1 H, $J_{(d)}$ = 13.36 Hz, $J_{(t)}$ = 7.15 Hz, 2β-H), 1.95 (s, H, CH_3CO), 2.29–2.37 (dt, 1 H, $J_{(d)}$ = 13.36 Hz, $J_{(t)}$ = 8.25 Hz, 2α-H), 2.36 (s, 3 H, CH_3), 3.30–3.40 (m, 1 H, 1β-H), 3.75–3.85 (m, 1 H, 3β-H), 4.05–4.13 (part A of an ABM system, 1 H, J_{AB} = 10.98 Hz, J_{AM} = 7.14 Hz, C*H*HOAc), 4.18–4.25 (part B of an ABM system, 1 H, J_{BA} = 10.98 Hz, J_{BM} = 5.85 Hz, CH*H*OAc), 4.26–4.35 (part A of an ABM system, 1 H, J_{AB} = 13.89 Hz, J_{AM} = 8.15 Hz, C*H*HN), 4.61–4.69 (part B of an ABM system, 1 H, J_{BA} = 13.89 Hz, J_{BM} = 5.97 Hz, CH*H*N), 7.00–7.19 (m, 4 H, ArH), 7.27–7.30 (d, 2 H, $J_{(d)}$ = 8.12 Hz, 3″-H and 5″-H), 7.92 (s, 1 H, 2′-H), 8.61–8.64 (d, 2 H, $J_{(d)}$ = 8.26 Hz, 2″-H and 6″-H), 8.92 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 21.31 (CH_3), 22.02 (CH_3), 33.88 (CH_2), 43.23 (CH), 44.06 (CH), 48.78 (CH_2), 67.70 (CH_2), 124.35, 124.97, 128.04 and 128.25 (CH), 129.84 and 130.14 (CH), 131.16 (C), 133.30 (C), 141.87 (C), 143.46 and 143.99 (C), 144.63 (CH), 152.84 (CH), 153.00 (C), 155.35 (C), 171.42 (COO).

Anal. Calcd for $C_{25}H_{24}N_4O_2$: C, 72.79; H, 5.86; N, 13.58. Found: C, 72.95; H, 5.69; N, 13.44.

(±)-*cis*-3-[6-(4′-Methoxy)phenyl-9*H*-purin-9-ylmethyl]indanylmethyl Acetate (9c)
Yield: 63%; mp 105-109 °C.

IR (KBr): 2934, 1735, 1603, 1581, 1560, 1515, 1447, 1366, 1325, 1300, 1248, 1211, 1182, 1171, 1030, 927, 853, 806, 748 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.48–1.59 (m, 1 H, 2β-H), 1.96 (s, 3 H, CH_3CO), 2.28–2.36 (m, 1 H, 2α-H), 3.36–3.41 (m, 1 H, 1β-H), 3.76–3.86 (m, 1 H, 3β-H), 3.82 (s, 3 H, OCH_3), 4.07–4.28 (m, 2 H, CH_2OAc), 4.29–4.37 (part A of an ABM system, 1 H, J_{AB} = 13.51 Hz, J_{AM} = 7.86 Hz, C*H*HN), 4.63–4.71 (part B of an ABM system, 1 H, J_{BA} = 13.51 Hz, J_{BM} = 5.47 Hz, CH*H*N), 6.98–7.02 (d, 2 H, $J_{(d)}$ = 8.29 Hz, 3′′-H and 5′′-H), 7.02–7.19 (m, 4 H, ArH), 7.93 (s, 1 H, 2′-H), 8.73–8.76 (d, 2 H, $J_{(d)}$ = 8.29 Hz, 2′′-H and 6′′-H), 8.91 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 21.32 (CH_3), 33.89 (CH_2), 43.23 (CH), 44.06 (CH), 48.80 (CH_2), 55.80 (CH_3), 67.62 (CH_2), 114.50 (CH), 124.37, 124.98, 128.05 and 128.26 (CH), 128.66 (C), 130.05 (C), 131.95 (CH), 143.47 (CH), 143.99 and 144.40 (C), 152.82 (CH), 154.98 (C), 162.48 (C), 171.44 (COO).

Anal. Calcd for $C_{25}H_{24}N_4O_3$: C, 70.08; H, 5.65; N, 13.08. Found: C, 69.96; H, 5.49; N, 12.91.

(±)-*cis*-3-[6-(4′-Chloro)phenyl-9*H*-purin-9-ylmethyl]indanylmethyl Acetate (9d)
Yield: 87%; mp 127–130 °C.

IR (KBr): 2966, 1725, 1578, 1558, 1498, 1447, 1382, 1326, 1244, 1174, 1032, 927, 855, 804, 763 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.49–1.60 (dt, 1 H, $J_{(d)}$ = 13.27 Hz, $J_{(t)}$ = 7.11 Hz, 2β-H), 1.96 (s, 3 H, CH_3CO), 2.28–2.40 (dt, 1 H, $J_{(d)}$ = 13.27 Hz, $J_{(t)}$ = 8.20 Hz, 2α-H), 3.34–3.46 (m, 1 H, 1β-H), 3.79–3.91 (m, 3 H, 3β-H), 4.07–4.14 (part A of an ABM system, 1 H, J_{AB} = 11.00 Hz, J_{AM} = 7.19 Hz, C*H*HOAc), 4.19–4.25 (part B of an ABM system, 1 H, J_{BA} = 11.00 Hz, J_{BM} = 5.88 Hz, CH*H*OAc), 4.31–4.40 (part A of an ABM system, 1 H, J_{AB} = 13.82 Hz, J_{AM} = 8.16 Hz, C*H*HN), 4.65–4.73 (part B of an ABM system, 1 H, J_{BA} = 13.82 Hz, J_{BM} = 5.96 Hz, CH*H*N), 7.03–7.22 (d, 2 H, $J_{(d)}$ = 8.29 Hz, 3′′-H and 5′′-H), 7.44–7.47 (m, 4 H, ArH), 7.96 (s, 1 H, 2′-H), 8.71–8.75 (d, 2 H, $J_{(d)}$ = 8.71 Hz, 2′′-H and 6′′-H), 8.95 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 21.32 (CH_3), 33.83 (CH_2), 43.25 (CH), 44.09 (CH), 48.88 (CH_2), 67.60 (CH_2), 124.34, 125.04, 128.09 and 128.34 (CH), 129.33 and 131.51 (CH), 134.52 (C), 137.70 (C), 143.36 (C), 143.99 (C), 144.98 (CH), 152.85 (CH), 153.24 (C), 153.95 (C), 171.41 (COO).

Anal. Calcd for $C_{24}H_{21}ClN_4O_2$: C, 66.59; H, 4.89; N, 12.94. Found: C, 66.41; H, 4.68; N, 13.15.

Cleavage of the Acetyl Group from Compounds 9a–d; General Procedure
A 1 M solution of NaOMe (700 μL, 0.7 mmol) was added to a solution of **9** (0.350 mmol) in MeOH (10 mL) and dioxane (10 mL) and the mixture was stirred at r.t. overnight. Then the solution was neutralized by addition of Dowex 50 × 8 (H^+) (ca. 100 mg) and the resultant solution was stirred for 1 h. The ion-exchanger was filtered out and was washed with NH_4OH 30% (5 mL) and MeOH (10 mL). The combined filtrates were evaporated to dryness affording the compounds **10a**–**d**.

(±)-*cis*-3-(6-Phenyl-9*H*-purin-9-ylmethyl)indanylmethanol (10a)
Yield: 96%; mp 96–99 °C.

IR (KBr): 3365, 2919, 1684, 1654, 1581, 1476, 1399, 1325, 1259, 1209, 1029, 929, 802, 766, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.71–1.80 (dt, 1 H, $J_{(d)}$ = 13.60 Hz, $J_{(t)}$ = 5.40 Hz, 2β-H), 2.31–2.41 (dt, 1 H, $J_{(d)}$ = 13.60 Hz, $J_{(t)}$ = 8.88 Hz, 2α-H), 3.33–3.38 (m, 1 H, 1β-H), 3.81–3.90 (m, 3 H, 3β-H and CH_2OH), 4.43–4.51 (part A of an ABM system, 1 H, J_{AB} = 13.96 Hz, J_{AM} = 9.20 Hz, C*H*HN), 4.60–4.67 (part B of an ABM system, 1 H, J_{BA} = 13.96 Hz, J_{BM} = 6.04 Hz, CH*H*N), 7.06–7.32 (m, 4 H, ArH), 7.52–7.60 (m, 3 H, ArH), 8.08 (s, 1 H, 2′-H), 8.77–8.80 (m, 2 H, ArH), 9.01 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 32.52 (CH_2), 44.81 (CH), 46.83 (CH), 49.01 (CH_2), 66.10 (CH_2), 124.53, 124.99, 127.76 and 128.33 (CH), 129.11(C), 130.25 (CH), 131.45 (CH), 135.95 (C), 143.87 (C), 144.78 (C), 145.14 (CH), 152.70 (CH), 153.14 (C), 155.51 (C).

Anal. Calcd for $C_{22}H_{20}N_4O$: C, 74.14; H, 5.66; N, 15.72. Found: C, 73.97; H, 5.81; N, 15.54.

(±)-*cis*-3-[6-(4′-Methyl)phenyl-9*H*-purin-9-ylmethyl]indanylmethanol (10b)
Yield: 95%; mp 184–186 °C.

IR (KBr): 3373, 2876, 1581, 1477, 1444, 1396, 1326, 1214, 1183, 1020, 929, 798, 752, 650 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.65–1.74 (dt, 1 H, $J_{(d)}$ = 13.64 Hz, $J_{(t)}$ = 5.18 Hz, 2β-H), 2.23–2.32 (dt, 1 H, $J_{(d)}$ = 13.62 Hz, $J_{(t)}$ = 8.91 Hz, 2α-H), 2.38 (s, 3 H, CH_3), 3.27–3.32 (m, 1 H, 1β-H), 3.73–3.82 (m, 3 H, 3β-H and CH_2OH), 4.38–4.47 (part A of an ABM system, 1 H, J_{AB} = 13.97 Hz, J_{AM} = 9.22 Hz, C*H*HN), 4.51–4.59 (part B of an ABM system, 1 H, J_{BA} = 13.97 Hz, J_{BM} = 6.13 Hz, CH*H*N), 7.02–7.27 (m, 4 H, ArH), 7.29–7.32 (d, 2 H, $J_{(d)}$ = 8.12 Hz, 3′′-H and 5′′-H), 8.02 (s, 1 H, 2′-H), 8.62–8.65 (d, 2 H, $J_{(d)}$ = 8.25 Hz, 2′′-H and 6′′-H), 8.92 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 22.06 (CH_3), 32.37 (CH_2), 45.01 (CH), 46.88 (CH), 48.97 (CH_2), 66.16 (CH_2), 124.56, 125.00, 127.78 and 128.36 (CH), 129.89 and 130.19 (CH), 131.25 (C), 133.21 (C), 142.01 (C), 143.89 (CH), 144.76 and 144.83 (C), 152.68 (CH), 153.04 (C), 155.60 (C).

Anal. Calcd for $C_{23}H_{22}N_4O$: C, 74.57; H, 5.99; N, 15.12. Found: C, 74.39; H, 5.73; N, 15.35.

(±)-*cis*-3-[6-(4′-Methoxy)phenyl-9*H*-purin-9-ylmethyl]indanylmethanol (10c)
Yield: 88%; mp 172-176 °C.

IR (KBr): 3346, 2962, 1606, 1579, 1517, 1438, 1328, 1251, 1183, 1104, 1031, 872, 843, 802, 746, 646 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.65–1.74 (dt, 1 H, $J_{(d)}$ = 13.65 Hz, $J_{(t)}$ = 5.10 Hz, 2β-H), 2.23–2.35 (dt, 1 H, $J_{(d)}$ = 13.65 Hz, $J_{(t)}$ = 8.92 Hz, 2α-H), 2.86 (br s, 1 H, OH, exchang. with D_2O), 3.25–3.34 (m, 1 H, 1β-H), 3.70–3.76 (m, 3 H, 3β-H and CH_2OH), 3.83 (s, 3 H, OCH_3), 4.37–4.47 (part A of an ABM system, 1 H, J_{AB} = 13.99 Hz, J_{AM} = 9.30 Hz, C*H*HN), 4.50–4.58 (part B of an ABM system, 1 H, J_{BA} = 13.99 Hz, J_{BM} = 6.18 Hz, CH*H*N), 6.99–7.26 (m, 6 H, ArH), 8.00 (s, 1 H, 2′-H), 8.73–8.77 (d, 2 H, $J_{(d)}$ = 8.91 Hz, 2′′-H and 6′′-H), 8.88 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 32.33 (CH_2), 45.05 (CH), 46.90 (CH), 48.95 (CH_2), 55.83 (CH_3), 66.17 (CH_2), 114.51 (CH), 124.57, 125.00, 127.77 and 128.36 (CH), 128.61 (C), 130.09 (C), 132.01 (CH), 143.90 (CH), 144.58 and 144.77 (C), 152.65 (CH), 152.91 (C), 155.13 (C), 162.81 (C).

Anal. Calcd for $C_{23}H_{22}N_4O_2$: C, 71.48; H, 5.74; N, 14.50. Found: C, 71.35; H, 5.87; N, 14.36.

(±)-*cis*-3-[6-(4′-Chloro)phenyl-9*H*-purin-9-ylmethyl]indanyl-methanol (10d)
Yield: 87%; mp 183–187 °C.

IR (KBr): 3376, 1654, 1583, 1559, 1506, 1447, 1328, 1213, 1015, 844, 801, 748, 644 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.72–1.80 (dt, 1 H, $J_{(d)}$ = 13.57 Hz, $J_{(t)}$ = 5.40 Hz, 2β-H), 2.32–2.43 (dt, 1 H, $J_{(d)}$ = 13.57 Hz, $J_{(t)}$ = 8.90 Hz, 2α-H), 2.58 (br s, 1 H, OH, exchang. with D_2O), 3.35–3.40 (m, 1 H, 1β-H), 3.82–3.89 (m, 3 H, 3β-H and C*H*$_2$OH), 4.46–4.54 (part A of an ABM system, 1 H, J_{AB} = 13.95 Hz, J_{AM} = 9.19 Hz, C*H*HN), 4.62–4.69 (part B of an ABM system, 1 H, J_{BA} = 13.95 Hz, J_{BM} = 6.01 Hz, CH*H*N), 7.08–7.33 (m, 4 H, ArH), 7.51–7.55 (d, 2 H, $J_{(d)}$ = 8.66 Hz, 3″-H and 5″-H), 8.10 (s, 1 H, 2′-H), 8.78–8.82 (d, 2 H, $J_{(d)}$ = 8.63 Hz, 2″-H and 6″-H), 9.00 (s, 1 H, 8′-H).

^{13}C NMR ($CDCl_3$): δ = 32.46 (CH_2), 44.88 (CH), 46.84 (CH), 49.03 (CH_2), 66.14 (CH_2), 124.53, 124.99, 127.82 and 128.41 (CH), 129.35 and 131.57 (CH), 134.70 (C), 137.80 (C), 143.82 (C), 144.68 (C), 145.19 (CH), 152.66 (CH), 153.21 (C), 154.08 (C).

Anal. Calcd for $C_{22}H_{19}ClN_4O$: C, 67.60; H, 4.90; N, 14.33. Found: C, 67.95; H, 4.70; N, 14.17.

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