Synthesis of Some New Spiropyranoquinolines and Evaluation of Their Free Radical Scavenging Activity

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The preparation of some new spiro-substituted 4-hydroxypyranoquinolinones and their corresponding dihydropyrano *cis*-diols is described. The free radical scavenging activity of the compounds was determined by means of their interaction with the stable free radical 1,1-diphenyl-2-picrylhydrazyl (DPPH) and the superoxide anions generated by the enzymic xanthine–xanthine oxidase system. The spiroadamatylpyranoquinolinone analogue proved to be the most efficient free radical scavenger.

Key words quinoline; spiropyranoquinoline; radical scavenging activity; antioxidant activity

Drugs with antioxidant mechanisms are being widely proposed as starting point for the development of new therapeutic interventions in several pathological disorders associated with oxidative damage, caused by reactive oxygen species (ROS), including hydrogen peroxide, superoxide anion and hydroxyl radical, under conditions of 'oxidative stress.'[1,2] This term refers to an imbalance between ROS production and detoxification, in favour of the former, and it is characterized by excessive production of ROS and/or reduction in the responsible for their metabolism antioxidant defences.[3,4]

The quinoline ring system is often found in natural alkaloids and in many synthetic derivatives exhibiting antibacterial, immunomodulatory, anti-inflammatory and antioxidant properties.[5—11] Among these compounds, the novel quinolinone derivative TA 270 (4-hydroxy-1-methyl-3-octyloxy-7-sinapinoylamino-2(1*H*)-quinolinone, Fig. 1), was initially designed as ROS scavenger and further pharmacological results suggest its therapeutic use in bronchial asthma.[12] Also, the antiulcer drug rebamipide, (2-(4-chlorobenzoylamino)-3-[2-(1*H*)-quinolinon-4-yl]propionic acid, Fig. 1) developed in Japan, inhibits lipid peroxidation and has a suppressive effect on oxygen derived free radical production in gastric mucosa. Rebamipide has been selected from a series of over 500 synthesized quinolinone derivatives tested for gastroprotective action and was found to possess anti-inflammatory properties, by stimulating endogenous prostaglandin and mucus glycoprotein synthesis and inhibiting inflammatory cytokines and chemokines.[13,14] It has been shown by the EPR (electron paramagnetic resonance) spin trapping method that rebamipide scavenges hydroxyl radicals and inhibits superoxide production.[15] Structure–activity studies revealed that the 3,4-double bond and the 2-oxo functionality of the quinolinone moiety are important determinants of the hydroxyl radical scavenging properties of this class of compounds and a reaction pathway was thus proposed, in which one molecule of the drug traps two hydroxyl radicals to form an unstable diol that readily decomposes to yield 3-hydroxylated rebamipide, as the major reaction product.[16]

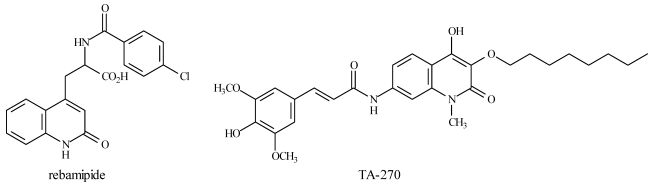
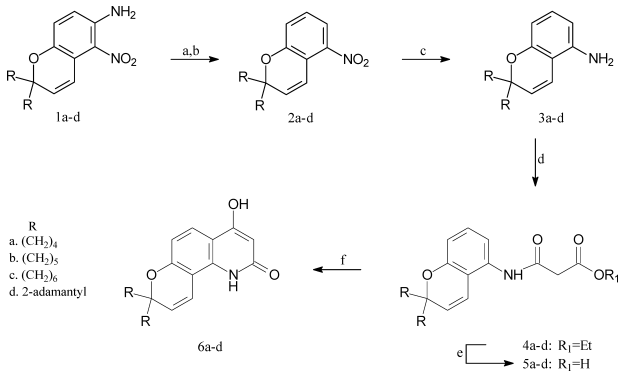


Fig. 1. Structures of Rebamipide and TA-270

Prompted by the interesting activity of several quinoline derivatives and in continuation of our efforts towards the study of structure–activity relationships of spiropyranoquinolinones as well as of spiropyranocoumarin derivatives,[17—19] we report the synthesis of some new lipophilic 4-hydroxypyrano quinolinones and the corresponding dihydropyrano *cis*-diols bearing spiro-substituents of various sizes on the pyran moiety. The antioxidant potential of these new compounds was also evaluated *in vitro* by means of their interaction with the stable 2,2-diphenyl-1-picrylhydrazyl radical (DPPH) and the quenching of superoxide anions generated by the enzymic xanthine–xanthine oxidase system.

Results and Discussion

Chemistry For the synthesis of the target pyranoquinolinones **6a**—**d** (Chart 1) we have used as starting material the 2-spirocyclical chromenes **1a**—**d**, which have been previously prepared by us[17] in seven steps from 2-hydroxyacetophenone upon annulation of the spiropyran moiety and suitable manipulation of the substituents. Diazotization of compounds **1a**—**d** and reduction of the intermediate diazonium salt provided the nitrochromenes **2a**—**d**. The nitro



Reagents and conditions: a) $NaNO_2$, H_2SO_4 98%–H_2O, 1 h, rt; b) EtOH, $CuSO_4$, 30 min, reflux; c) $SnCl_2 \cdot 2H_2O$, acetone, 12 h, reflux; d) diethyl malonate, 15 h, 190 °C; e) NaOH, EtOH, 2 h, rt; f) $(CF_3CO)_2O$, CH_2Cl_2 anh., 24 h, rt.

Chart 1

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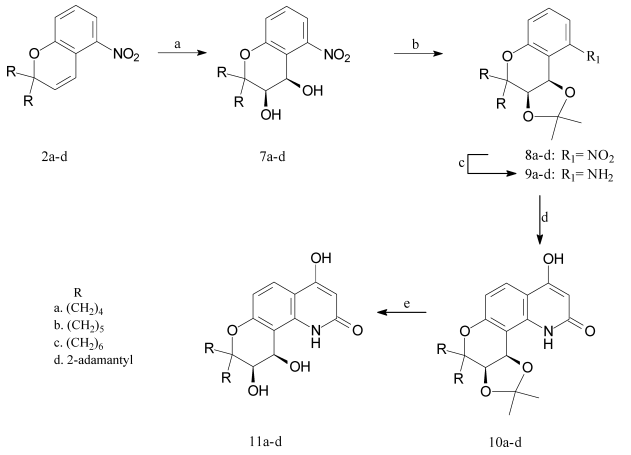

Reagents: a) 1) 2.5% OsO_4 in *tert*-butanol, *N*-methylmorpholine-*N*-oxide, *tert*-butanol/THF/H_2O, 3 d, rt, 2) sat. aq. $NaHSO_3$, 2 h, rt; b) acetone, H_2SO_4 98%, 2 h, reflux; c) H_2, 10% Pd/C, EtOH, 5 h, rt; d) diethyl malonate, 15 h, 190 °C; e) CF_3COOH, MeOH, 24 h, rt.

Chart 2

group was then reduced upon reaction with tin(II) chloride in refluxing acetone to result in the anilines **3a**—**d**, which were treated with diethylmalonate to yield the intermediate amidoesters **4a**—**d**. Saponification of compounds **4a**—**d** followed by cyclization of the resulting acids **5a**—**d** by treatment with trifluoracetic anhydride resulted into the spiropyranoquinolinones **6a**—**d**.

The preparation of the corresponding *cis*-diols **11a**—**d** is outlined in Chart 2 and was accomplished through initial catalytic *syn*-hydroxylation of the chromenes **2a**—**d** with osmium tetroxide and *N*-methylmorpholine-*N*-oxide as the oxidizing agent to provide the nitro diols **7a**—**d**. The abovementioned diols were converted to the corresponding acetonides **8a**—**d** and the nitro group of these derivatives was reduced to yield the anilines **9a**—**d**. Heating of these anilines with diethylmalonate provided, in one step, the pyranoquinolinones **10a**—**d**. The target *cis*-diols **11a**—**d** were obtained from compounds **10a**—**d** upon mild deprotection in acidic media.

Antioxidant Activity The new compounds were tested for their ability to interact with DPPH. The stable free radical 2,2-diphenyl-1-picrylhydrazyl (DPPH), is a useful reagent to investigate the free radical scavenging activity of compounds.[20] Experiments were performed at different concentrations and different reaction times starting from 20 min and exceeding 60 min. Percentage interaction of the majority of the tested compounds with DPPH was concentration dependent among the examined compounds the spiroadamatylpyranoquinolinone **6d** (Table 1) showed a strong interactive ability with DPPH which was concentration dependent only at the range of 1—5 μM (data not shown). This compound expressed an IC_{50} value of 20.65 μM, lower than that of ascorbic acid (43.9 mM), which was used as control. It should be noted that the previously prepared spiroadamantyl analogue which lack the 4-hydroxy-functionality[17] presented only weak interaction with DPPH, consequently our present finding could suggest that both the extended conjugation of the fused ring system and the free 4-hydroxy group are important determinants for the free radical scavenging activity.

Xanthine oxidase is an oxidative enzyme responsible for

Table 1. Effect of the Examined Compounds on Their Interaction with DPPH at 60 min of Incubation (200 μM)

Compound	Percentage of interaction with DPPH				
	[DPPH] μM[a]				
	5	25	50	100	200
6a	4	5	7	13	16
6b	5	6	7	12	16
6c	2	5	6	11	17
6d	47	51	55	63	76
11a	9	10	12	19	22
11b	5	9	9	12	38
11c	10	11	12	15	17
11d	5	8	10	12	16
Ascorbic acid	1	14	73	97	98

a) Based on absorbance values of samples with the tested compounds, against control containing equal volume of the solvent. Standard deviation of absorbance values was less than ±10%, n=3.

the oxidation of xanthine to uric acid. It is considered to be an important biological source of superoxide radicals, which, together with other reactive oxygen species, contribute to the oxidative stress in an organism and are involved in many pathological processes.[21] The superoxide radical scavenging activities of the new compounds were also investigated by using the xanthine–xanthine oxidase system, but no significant activity pattern was obtained from this experiment. However, the spiroadamantyl analogue **6d** was found again to possess significant inhibitory effect on superoxide radical at 0.5 mM concentration and we have recorded inhibition rates 45% for **6d**, which is comparable to that of allopurinol (42.3%).

In conclusion, we have developed a synthetic methodology for the preparation of 4-hydroxyspiropyranoquinolines and their corresponding dihydropyrano *cis*-diols. The free radical scavenging activity of the new compounds was evaluated by means of two different tests, the interaction with DPPH free radical and the quenching of superoxide anions generated by the xanthine–xanthine oxidase system. The spiroadamatyl derivative **6d** proved to be a potent radical scavenger presenting high activity in both assays.

Experimental

All chemicals were purchased from Aldrich Chemical Co. Melting points were determined on a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Spectrum RX I spectrophotometer. ^{1}H-NMR spectra and 2D spectra were recorded on a Bruker Avanche 400 instrument, whereas ^{13}C-NMR specra were recorded on a Bruker AC 200 spectrometer in deuterated solvents and were referenced to TMS (δ scale). The signals of ^{1}H and ^{13}C spectra were unambiguously assigned by using 2D NMR techniques: ^{1}H–^{1}H COSY, NOESY HMQC and HMBC. Flash chromatography was performed on Merck silica gel 60 (0.040—0.063 mm). Analytical thin layer chromatography (TLC) was carried out on precoated (0.25 mm) Merck silica gel F-254 plates. Elemental analyses were performed at the Microanalytical Sections of the National Hellenic Research Foundation on a Perkin-Elmer PE 240C Elemental Analyzer (Norwalk, CT) and are within±0.4% of the theoretical values.

5-Nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cyclopentane] (2a) Compound **1a** (1.8 g, 7.32 mmol)[17] was dissolved in a mixture of concentrated sulfuric acid (9 ml) and water (22 ml) with warming and then was cooled to 0 °C. A solution of sodium nitrite (565 mg, 8.19 mmol) in water (*ca.* 2 ml) was added dropwise, the mixture was stirred at room temperature for 1 h and the resulting solution was added to a suspension of $CuSO_4$ (15 mg, 0.094 mmol) in ethanol (40 ml). The resulting mixture was stirred at 60 °C for 30 min, and then the solvent was removed under reduced pressure. The remaining oil was partitioned between CH_2Cl_2 and water. The organic layer was separated,

dried (Na_2SO_4), filtered and evaporated to dryness. Flash chromatography on silica gel using cyclohexane/EtOAc (98/2, v/v) as the eluent, provided compound **2a** (1.32 g, 78%) as an oil. IR (film) ν (NO_2) 1526 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.5—2.2 (8H, m, H cyclopentyl), 5.90 (1H, d, J=10.2 Hz, H-3), 6.95 (1H, d, J=10.2 Hz, H-4), 6.99 (1H, d, J=8.0 Hz, H-8), 7.15 (1H, t, J=8.0 Hz, H-7), 7.49 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 23.57 and 39.12 (C cyclopentyl), 87.00 (C-2), 116.84 (C-4a), 117.03 (C-6), 118.32 (C-4), 121.83 (C-8), 128.06 (C-7), 133.66 (C-3), 145.98 (C-5), 154.17 (C-8a). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.33; H, 5.78; N, 6.24.

5-Nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cyclohexane] (2b) This compound was prepared by an analogous procedure as described for the preparation of **2a**, starting from **1b**. Yield: 76%. Oil. IR (film) ν (NO_2) 1531 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.2—2.0 (10H, m, H cyclohexyl), 5.88 (1H, d, J=10.2 Hz, H-3), 6.92 (1H, d, J=10.2 Hz, H-4), 7.06 (1H, d, J=8.0 Hz, H-8), 7.16 (1H, t, J=8.0 Hz, H-7), 7.49 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 21.23, 25.03 and 35.52 (C cyclohexyl), 76.80 (C-2), 116.95 (C-4a and C-6), 117.92 (C-4), 121.89 (C-8), 128.12 (C-7), 134.26 (C-3), 145.93 (C-5), 154.03 (C-8a). *Anal.* Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.62; H, 6.40; N, 5.54.

5-Nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cycloheptane] (2c) This compound was prepared by an analogous procedure as described for the preparation of **2a**, starting from **1c**. Yield: 66%. Oil. IR (film) ν (NO_2) 1522 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.4—2.1 (12H, m, H cycloheptyl), 5.89 (1H, d, J=10.2 Hz, H-3), 6.88 (1H, d, J=10.2 Hz, H-4), 7.03 (1H, d, J=8.0 Hz, H-8), 7.15 (1H, t, J=8.0 Hz, H-7), 7.47 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 21.51, 29.38 and 38.93 (C cycloheptyl), 80.79 (C-2), 114.36 (C-4a), 116.43 and 116.85 (C-4 and C-6), 121.97 (C-8), 128.04 (C-7), 135.17 (C-3), 145.88 (C-5), 154.01 (C-8a). *Anal.* Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.25; H, 6.91; N, 5.47.

5-Nitrospiro[2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decane] (2d) This compound was prepared by an analogous procedure as described for the preparation of **2a**, starting from **1d**. Yield: 71%. IR (Nujol) ν (NO_2) 1528 cm^{-1}. mp 110 °C (*n*-hexane–Et_2O). ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.5—2.4 (14H, m, H adamantyl), 6.36 (1H, d, J=10.3 Hz, H-3), 6.99 (1H, d, J=10.3 Hz, H-4), 7.14 (1H, d, J=8.0 Hz, H-8), 7.18 (1H, t, J=8.0 Hz, H-7), 7.54 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 26.66, 27.07, 32.38, 33.49, 35.55 and 37.65 (C adamantyl), 79.99 (C-2), 116.32 (C-6), 117.09 (C-4a), 118.61 (C-4), 122.18 (C-8), 128.16 (C-7), 132.84 (C-3), 145.79 (C-5), 153.90 (C-8a). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.84; H, 6.60; N, 4.51.

Spiro[2*H*-benzo[*b*]pyrano-2,1′-cyclopentan]-5-amine (3a) A suspension of **2a** (1 g, 4.05 mmol) and $SnCl_2 \cdot 2H_2O$ (3.66 g, 16.20 mmol) in acetone was heated at reflux for 6 h. Upon cooling, the mixture was partially concentrated *in vacuo* and poured into crushed ice, basified with sodium bicarbonate and extracted with dichloromethane (3×100 ml). The combined organic phase was washed with water, followed by brine, dried (Na_2SO_4) and evaporated to dryness, to afford compound **3a** as an oil (724 mg, 89%). IR (film) ν (NH_2) 3466, 3377 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.5—2.2 (8H, m, H cyclopentyl), 3.64 (2H, br s, D_2O exchang., NH_2), 5.64 (1H, d, J=9.9 Hz, H-3), 6.21 (1H, d, J=8.0 Hz, H-6), 6.25 (1H, d, J=8.0 Hz, H-8), 6.38 (1H, d, J=9.9 Hz, H-4), 6.88 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 23.57 and 38.81 (C cyclopentyl), 86.14 (C-2), 107.63 and 108.64 (C-6 and C-8), 109.12 (C-4a), 117.55 (C-4), 128.25 (C-3), 129.15 (C-7), 142.19 (C-5), 153.79 (C-8a). *Anal.* Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.45; H, 7.73; N, 7.12.

Spiro[2*H*-benzo[*b*]pyrano-2,1′-cyclohexan]-5-amine (3b) This compound was prepared by an analogous procedure as described for the preparation of **3a**, starting from **2b**. Yield: 81%. Oil. IR (film) ν (NH_2) 3472, 3338 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.3—2.0 (10H, m, H cyclohexyl), 3.63 (2H, br s, D_2O exchang., NH_2), 5.61 (1H, d, J=9.9 Hz, H-3), 6.21 (1H, d, J=8.0 Hz, H-6), 6.25 (1H, d, J=8.0 Hz, H-8), 6.36 (1H, d, J=9.9 Hz, H-4), 6.89 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 21.21, 25.21 and 35.28 (C cyclohexyl), 75.53 (C-2), 107.17 and 108.28 (C-6 and C-8), 109.22 (C-4a), 116.99 (C-4), 128.49 (C-3), 129.01 (C-7), 142.16 (C-5), 153.34 (C-8a). *Anal.* Calcd for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 77.91; H, 7.76; N, 6.12.

Spiro[2*H*-benzo[*b*]pyrano-2,1′-cycloheptan]-5-amine (3c) This compound was prepared by an analogous procedure as described for the preparation of **3a**, starting from **2c**. Yield: 73%. Oil. IR (film) ν (NH_2) 3508, 3346 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$,) δ: 1.3—2.2 (12H, m, H cycloheptyl H), 3.63 (2H, br s, D_2O exchang., NH_2), 5.63 (1H, d, J=9.9 Hz, H-3), 6.20 (1H, d, J=8.0 Hz, H-6), 6.26 (1H, d, J=8.0 Hz, H-8), 6.30 (1H, d, J=9.9 Hz, H-4), 6.88 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 21.57, 29.50 and 38.84 (C cycloheptyl), 79.72 (C-2), 107.66 and 108.39 (C-6 and C-8), 111.70 (C-4a), 115.74 (C-4), 129.12 (C-3), 129.86 (C-7), 142.06 (C-5), 153.53 (C-8a). *Anal.* Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.98. Found: C, 78.34; H, 8.59; N, 7.17.

Spiro[2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decan]-5-amine (3d) This compound was prepared by an analogous procedure as described for the preparation of **3a**, starting from **2d**. Yield: 95%. mp 87 °C (EtOH). IR (Nujol) ν (NH_2) 3514, 3360 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.4—2.4 (14H, m, H adamantyl), 3.66 (2H, br s, D_2O exchang., NH_2), 6.08 (1H, d, J=9.9 Hz, H-3), 6.22 (1H, d, J=8.0 Hz, H-6), 6.36 (1H, d, J=8.0 Hz, H-8), 6.41 (1H, d, J=9.9 Hz, H-4), 6.91 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 26.78, 27.16, 32.31, 33.59, 35.32 and 37.78 (C adamantyl), 79.54 (C-2), 112.02 and 112.39 (C-6 and C-8), 113.55 (C-4a), 117.10 (C-4), 129.32 and 129.39 (C-3 and C-7), 134.35 (C-5), 153.45 (C-8a). *Anal.* Calcd for $C_{18}H_{21}NO$: C, 80.86; H, 7.92; N, 5.24. Found: C, 80.64; H, 8.15; N, 5.47.

2-Ethoxycarbonyl-*N*-[spiro(2*H*-benzo[*b*]pyrano-2,1′-cyclopentan-5-yl)]acetamide (4a) A mixture of **3a** (700 mg, 3.483 mmol) in diethyl malonate (53 ml, 348.3 mmol) was heated at 160 °C for 15 h. After completion of the reaction, the mixture was vacuum-evaporated and the residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate 5/1) to furnish compound **4a** (630 mg, 57%). mp 81—82 °C (EtOAc). IR (Nujol) ν (NH) 3239 cm^{-1}, ν (COOEt) 1725 cm^{-1}, ν (CONH) 1681 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.26 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.5—2.2 (8H, m, H cyclopentyl), 3.43 (2H, s, $COCH_2CO$), 4.20 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 5.70 (1H, d, J=9.9 Hz, H-3), 6.47 (1H, d, J=9.9 Hz, H-4), 6.54 (1H, d, J=8.0 Hz, H-8), 7.00 (1H, t, J=8.0 Hz, H-7), 7.31 (1H, d, J=8.0 Hz, H-6), 9.28 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz $CDCl_3$) δ: 13.88 ($CH_2\underline{C}H_3$), 23.36, 38.70 (C cyclopentyl), 41.11 ($CO\underline{C}H_2CO$), 61.76 ($\underline{C}H_2CH_3$), 86.19 (C-2), 113.62 (C-8), 114.54 (C-4a), 115.46 (C-6), 117.30 (C-4), 128.53 (C-7), 130.38 (C-3), 132.24 (C-5), 153.13 (C-8a), 163.19 (NHCO), 170.06 ($\underline{C}OCH_2CH_3$). *Anal.* Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.73; H, 6.68; N, 4.20.

2-Ethoxycarbonyl-*N*-[spiro(2*H*-benzo[*b*]pyrano-2,1′-cyclohexan-5-yl)]acetamide (4b) This compound was prepared by an analogous procedure as described for the preparation of **4a**, starting from **3b**. Yield: 63%. mp 98 °C (EtOAc). IR (Nujol) ν (NH) 3254 cm^{-1}, ν (COOEt) 1720 cm^{-1}, ν (CONH) 1677 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.28 (3H, t, J=7 Hz, $CH_2C\underline{H}_3$), 1.4—2.0 (10H, m, H cyclohexyl), 3.45 (2H, s, $COCH_2CO$), 4.22 (2H, q, J=7 Hz, $C\underline{H}_2CH_3$), 5.70 (1H, d, J=9.9 Hz, H-3), 6.48 (1H, d, J=9.9 Hz, H-4), 6.64 (1H, d, J=8.0 Hz, H-8), 7.04 (1H, t, J=8.0 Hz, H-7), 7.35 (1H, d, J=8.0 Hz, H-6), 9.30 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 14.03 ($CH_2\underline{C}H_3$), 21.31, 25.24 and 35.46 (C cyclohexyl), 41.01 ($CO\underline{C}H_2CO$), 62.00 ($\underline{C}H_2CH_3$), 77.18 (C-2), 113.72 (C-8), 114.42 (C-4a), 115.23 (C-6), 116.88 (C-4), 128.94 (C-7), 131.36 (C-3), 132.47 (C-5), 153.12 (C-8a), 162.94 (NHCO), 170.58 ($\underline{C}OCH_2CH_3$). *Anal.* Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 68.98; H, 7.22; N, 4.15.

2-Ethoxycarbonyl-*N*-[spiro(2*H*-benzo[*b*]pyrano-2,1′-cycloheptan-5-yl)]acetamide (4c) This compound was prepared by an analogous procedure as described for the preparation of **4a**, starting from **3c**. Yield: 60%. mp 104 °C (CH_2Cl_2–Et_2O). IR (Nujol) ν (NH) 3258 cm^{-1}, ν (COOEt) 1737 cm^{-1}, ν (CONH) 1658 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.30 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 1.5—2.2 (12H, m, H cycloheptyl), 3.46 (2H, s, $COCH_2CO$), 4.24 (2H, q, J=7.0 Hz, $C\underline{H}_2CH_3$), 5.74 (1H, d, J=9.9 Hz, H-3), 6.44 (1H, d, J=9.9 Hz, H-4), 6.62 (1H, d, J=8.0 Hz, H-8), 7.03 (1H, t, J=8.0 Hz, H-7), 7.36 (1H, d, J=8.0 Hz, H-6), 9.31 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 14.00 ($CH_2\underline{C}H_3$), 21.52, 29.44 and 38.83 (C cycloheptyl), 41.07 ($CO\underline{C}H_2CO$), 61.93 ($\underline{C}H_2CH_3$), 80.03 (C-2), 113.86 (C-8), 114.27 (C-4a), 115.28 (C-6), 115.57 (C-4), 128.78 (C-7), 132.22 (C-3), 132.31 (C-5), 153.10 (C-8a), 163.06 (NHCO), 170.41 ($\underline{C}OCH_2CH_3$). *Anal.* Calcd for $C_{20}H_{25}NO_4$: C, 69.95; H, 7.34; N, 4.08. Found: C, 70.17; H, 7.01; N, 4.30.

2-Ethoxycarbonyl-*N*-[spiro(2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decan-5-yl)]acetamide (4d) This compound was prepared by an analogous procedure as described for the preparation of **4a**, starting from **3d**. Yield: 64%. mp 190 °C (EtOAc). IR (Nujol) ν (NH) 3245 cm^{-1}, ν (COOEt) 1728 cm^{-1}, ν (CONH) 1679 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.30 (3H, t, J=7.0 Hz, $CH_2C\underline{H}_3$), 1.4—2.4 (14H, m, H adamantyl), 3.47 (2H, s, $COCH_2CO$), 4.24 (2H, q, J=7.0 Hz, $C\underline{H}_2CH_3$), 6.20 (1H, d, J=10.2 Hz, H-3), 6.55 (1H, d, J=10.2 Hz, H-4), 6.71 (1H, d, J=8.0 Hz, H-8), 7.09 (1H, t, J=8.0 Hz, H-7), 7.46 (1H, d, J=8.0 Hz, H-6), 9.38 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 13.99 ($CH_2\underline{C}H_3$), 26.72, 27.09, 32.29, 33.54, 35.17 and 37.69 (C adamantyl), 41.09 ($CO\underline{C}H_2CO$), 61.93 ($\underline{C}H_2CH_3$), 79.13 (C-2), 113.66 (C-8), 115.04 (C-6 and C-4a), 117.24 (C-4), 128.88 (C-7), 129.80 (C-3), 132.53 (C-5), 152.75 (C-8a), 162.97 (CO), 170.39 (CO).

Anal. Calcd for $C_{2327}NO_4$: C, 72.42; H, 7.13; N, 3.67. Found: C, 72.57; H, 7.00; N, 3.86.

***N*-[Spiro(2*H*-benzo[*b*]pyrano-2,1′-cyclopentan-5-yl)]malonamide (5a)** To a solution of **4a** (550 mg, 1.746 mmol) in ethanol (5 ml) at room temperature, was added dropwise a cold 1 N NaOH solution (10 ml) in a period of 20 min. The mixture was stirred for 2 h at room temperature and then poured into water and acidified (pH *ca.* 3) with a 18% HCl solution. The ethanol was removed under reduced pressure and the residue was partitioned between dichloromethane and brine. The organic layer was dried over Na_2SO_4, filtered and concentrated to dryness, to afford 460 mg (92%) of acid **5a**. mp 150—151 °C (EtOH). IR (Nujol) ν (OH, NH) 2910—3495 cm^{-1}, ν (COOH) 1710 cm^{-1}, ν (CONH) 1656 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.4—2.1 (8H, m, H cyclopentyl), 3.42 (2H, s, $COCH_2CO$), 5.85 (1H, d, J=10.2 Hz, H-3), 6.56 (2H, m, H-4 and H-8), 7.10 (2H, m, H-6 and H-7), 9.81 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 23.14 and 38.25 (C cyclopentyl), 43.25 ($CO\underline{C}H_2CO$), 86.07 (C-2), 113.19 (C-8), 115.73 (C-4a), 117.12 (C-6), 118.70 (C-4), 128.30 (C-7), 129.51 (C-3), 133.37 (C-5), 152.77 (C-8a), 164.98 (CO), 169.50 (CO). *Anal.* Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found: C, 66.55; H, 6.26; N, 4.65.

***N*-[Spiro(2*H*-benzo[*b*]pyrano-2,1′-cyclohexan-5-yl)]malonamide (5b)** This compound was prepared by an analogous procedure as described for the preparation of **5a**, starting from **4b**. Yield: 88%. mp 159 °C (EtOH). IR (Nujol) ν (OH, NH) 2975—3550 cm^{-1}, ν (COOH) 1711 cm^{-1}, ν (CONH) 1656 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.4—2.1 (10H, m, H cyclohexyl), 3.40 (2H, s, $COCH_2CO$), 5.83 (1H, d, J=10.0 Hz, H-3), 6.58 (1H, d, J=10.0 Hz, H-4), 6.63 (1H, d, J=8.0 Hz, H-8), 7.06 (2H, m, H-6 and H-7), 9.79 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 20.94, 24.76 and 35.00 (C cyclohexyl), 43.34 ($CO\underline{C}H_2CO$), 75.71 (C-2), 113.14 (C-6), 115.79 (C-4a), 116.97 (C-8), 118.48 (C-4), 128.49 (C-7), 130.14 (C-3), 133.54 (C-5), 152.64 (C-8a), 165.10 (CO), 169.70 (CO). *Anal.* Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 68.01; H, 6.22; N, 4.88.

***N*-[Spiro(2*H*-benzo[*b*]pyrano-2,1′-cycloheptan-5-yl)]malonamide (5c)** This compound was prepared by an analogous procedure as described for the preparation of **5a**, starting from **4c**. Yield: 94%. mp 161 °C (EtOH). IR (Nujol) ν (OH, NH) 3050—3498 cm^{-1}, ν (COOH) 1710 cm^{-1}, ν (CONH) 1654 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.4—2.3 (12H, m, H cycloheptyl), 3.36 (2H, s, $COCH_2CO$), 5.82 (1H, d, J=10.2 Hz, H-3), 6.52 (1H, d, J=10.2 Hz, H-4), 6.59 (1H, d, J=7.8 Hz, H-8), 7.04 (2H, m, H-6 and H-7), 9.76 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 21.03, 28.82 and 38.27 (C cycloheptyl), 43.27 ($CO\underline{C}H_2CO$), 79.58 (C-2), 113.21 (C-6), 115.50 (C-4a), 116.89 (C-8), 117.04 (C-4), 128.36 (C-7), 131.12 (C-3), 133.39 (C-5), 152.62 (C-8a), 165.01 (CO), 169.57 (CO). *Anal.* Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.93; H, 6.34; N, 4.17.

***N*-[Spiro(2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decan)-5-yl)]malonamide (5d)** This compound was prepared by an analogous procedure as described for the preparation of **5a**, starting from **4d**. Yield: 87%. mp 162 °C (EtOH). IR (Nujol) ν (OH, NH) 3100—3630 cm^{-1}, ν (COOH) 1709 cm^{-1}, ν (CONH) 1653 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$+DMSO-d_6) δ: 1.4—2.4 (14H, m, H adamantyl), 3.43 (2H, s, $COCH_2CO$), 6.17 (1H, d, J=10.2 Hz, H-3), 6.52 (1H, d, J=10.2 Hz, H-4), 6.71 (1H, d, J=8.2 Hz, H-8), 7.07 (1H, t, J=8.2 Hz, H-7), 7.29 (1H, d, J=8.2 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$+DMSO-d_6) δ: 26.57, 26.94, 32.12, 33.37 and 35.06 (C adamantyl), 37.53 ($CO\underline{C}H_2CO$), 79.17 (C-2), 113.94 (C-8), 115.03 (C-4a), 115.70 (C-8), 117.46 (C-4), 128.64 (C-7), 129.56 (C-3), 132.06 (C-5), 152.64 (C-8a), 162.84 (CO), 171.34 (CO). *Anal.* Calcd for $C_{21}H_{23}NO_4$: C, 71.37; H, 6.56; N, 3.96. Found: C, 71.12; H, 6.22; N, 4.13.

4′-Hydroxyspiro[cyclopentane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (6a) Trifluoacetic anhydride (2.27 ml, 16.0 mmol) was added under argon to a solution of acid **5a** (1.15 g, 4.0 mmol) in dry dichloromethane (30 ml) and the resulting solution was stirred at room temperature for 24 h. The reaction mixture was concentrated *in vacuo* and the residue was partitioned between ethyl acetate and water. The organic phase was separated, washed with saturated $NaHCO_3$ solution, dried (Na_2SO_4) and concentrated to dryness to afford compound **6a** (947 mg, 88%). mp >250 °C (EtOH). IR (Nujol) ν (OH) 3500—3160 cm^{-1}, ν (NH) 3178 cm^{-1}, ν (CONH) 1659 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.5—2.1 (8H, m, H cyclopentyl), 5.61 (1H, s, H-3), 5.84 (1H, d, J=10.0 Hz, H-9), 6.59 (1H, d, J=8.8 Hz, H-6), 7.21 (1H, d, J=10.0 Hz, H-10), 7.57 (1H, d, J=8.8 Hz, H-5), 10.76 (1H, br s, D_2O exchang., OH), 11.35 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 23.14 and 38.42 (C cyclopentyl), 86.82 (C-8), 95.77 (C-3), 107.02 (C-10a), 109.50 (C-4a), 111.12 (C-6), 116.98 (C-10), 123.56 (C-5), 128.66 (C-9), 135.44 (C-10b), 154.61 (C-6a), 162.75 (C-4), 164.30 (C-2). *Anal.* Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.27; H, 5.31; N, 5.33.

4′-Hydroxyspiro[cyclohexane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (6b) This compound was prepared by an analogous procedure as described for the preparation of **6a**, starting from **5b**. Yield: 82%. mp >250 °C (EtOH). IR (Nujol) ν (OH) 3628—3145 cm^{-1}, ν (NH) 3188 cm^{-1}, ν (CONH) 1662 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.2—1.9 (10H, m, H cyclohexyl), 5.67 (1H, s, H-3), 5.85 (1H, d, J=10.0 Hz, H-9), 6.72 (1H, d, J=8.8 Hz, H-6), 7.25 (1H, d, J=10.0 Hz, H-10), 7.59 (1H, d, J=8.8 Hz, H-5). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 20.88, 24.74 and 35.11 (C cyclohexyl), 76.61 (C-8), 95.72 (C-3), 107.21 (C-10a), 109.58 (C-4a), 111.27 (C-6), 116.69 (C-10), 123.77 (C-5), 129.41 (C-9), 135.53 (C-10b), 154.57 (C-6a), 162.99 (C-4), 164.48 (C-2). *Anal.* Calcd for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 71.70; H, 5.93; N, 4.93.

4′-Hydroxyspiro[cycloheptane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (6c) This compound was prepared by an analogous procedure as described for the preparation of **6a**, starting from **5c**. Yield: 80%. mp >250 °C (EtOH). IR (Nujol) ν (OH) 3618—2970 cm^{-1}, ν (NH) 3150 cm^{-1}, ν (CONH) 1660 cm^{-1}. ^{1}H-NMR (50 MHz, DMSO-d_6) δ: 1.4—2.0 (12H, m, H cycloheptyl), 5.59 (1H, s, H-3), 5.82 (1H, d, J=9.9 Hz, H-9), 6.62 (1H, d, J=8.4 Hz, H-6), 7.14 (1H, d, J=9.9 Hz, H-10), 7.57 (1H, d, J=8.4 Hz, H-5), 10.72 (1H, br s, D_2O exchang., OH), 11.21 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 20.99, 28.88 and 38.27 (C cycloheptyl), 80.45 (C-8), 95.76 (C-3), 106.80 (C-10a), 109.40 (C-4a), 111.18 (C-6), 115.26 (C-10), 123.62 (C-5), 130.39 (C-9), 135.46 (C-10b), 154.46 (C-6a), 162.73 (C-4), 164.26 (C-2). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.96; H, 6.22; N, 4.48.

4-Hydroxyspiro[8*H*-pyrano[2,3-*h*]quinolin-8,2′-tricyclo[3.3.1.1^{3,7}]decan-2(1*H*)-one] (6d) This compound was prepared by an analogous procedure as described for the preparation of **6a**, starting from **5d**. Yield: 76%. mp >250 °C (EtOH). IR (Nujol) ν (OH) 3629—2990 cm^{-1}, ν (NH) 3180 cm^{-1}, ν (CONH) 1662 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.5—2.3 (14H, m, H adamantyl), 5.58 (1H, s, H-3), 6.17 (1H, d, J=10.2 Hz, H-9), 6.83 (1H, d, J=8.8 Hz, H-6), 7.25 (1H, d, J=10.2 Hz, H-10), 7.64 (1H, d, J=8.8 Hz, H-5), 10.73 (1H, br s, D_2O exchang., OH), 11.21 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 26.25, 26.60, 31.87, 32.87, 34.98 and 37.20 (C adamantyl), 79.53 (C-8), 95.83 (C-3), 108.07 (C-10a), 109.62 (C-4a), 111.25 (C-6), 117.39 (C-10), 123.80 (C-5), 127.77 (C-9), 135.55 (C-10b), 154.18 (C-6a), 162.84 (C-2), 164.33 (C-4). *Anal.* Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 75.33; H, 6.19; N, 4.25.

(±)*cis*-3,4-Dihydro-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cyclopentane]-3,4-diol (7a) To a solution of osmium tetroxide (2.5% in isopropanol) (0.12 ml, 0.373 mmol) and *N*-methylmorpholine-*N*-oxide (600 mg, 5.18 mmol) in a mixture of *tert*-butanol/THF/water (10/3/1.5 ml) was added compound **2a** (863 mg, 3.73 mmol) and the resulting mixture was stirred at room temperature for 3 d. A saturated $NaHSO_3$ solution (5 ml) was then added and the mixture was stirred for an additional 2 h. The bulk of THF was removed under reduced pressure and the residue was partitioned between dichloromethane and brine. The organic layer was dried (Na_2SO_4), filtered and concentrated to dryness. The crude product was purified by column chromatography (silica gel), using a mixture of cyclohexane/ethyl acetate (3/2, v/v) as the eluent (751 mg, 76%). Yield: 76%. Oil. IR (film) ν (OH) 3640—2870 cm^{-1}, ν (NO_2) 1462 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.5—2.2 (8H, m, H cyclopentyl), 3.89 (1H, d, J=4.8 Hz, H-3), 5.20 (1H, d, J=4.8 Hz, H-4), 7.07 (1H, d, J=8.0 Hz, H-8), 7.33 (1H, t, J=8.0 Hz, H-7), 7.47 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 24.82, 24.18, 34.29 and 34.55 (C cyclopentyl), 63.07 (C-4), 69.80 (C-3), 90.30 (C-2), 117.50 (C-6), 117.84 (C-4a), 123.05 (C-8), 129.30 (C-7), 150.65 (C-5), 153.41 (C-8a). *Anal.* Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 59.07; H, 5.50; N, 4.93.

(±)*cis*-3,4-Dihydro-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cyclohexane]-3,4-diol (7b) This compound was prepared by an analogous procedure as described for the preparation of **7a**, starting from **2b**. Yield: 82%. Oil. IR (film) ν (OH) 3665—2900 cm^{-1}, ν (NO_2) 1466 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.4—1.8 (9H, m, H cyclohexyl), 2.13 (1H, d, J=4.8 Hz, H cyclohexyl), 2.84 (1H, br s, D_2O exchang., OH), 3.52 (1H, br s, D_2O exchang., OH), 3.77 (1H, d, J=4.8 Hz, H-3), 5.23 (1H, d, J=4.8 Hz, H-4), 7.10 (1H, d, J=8.0 Hz, H-8), 7.28 (1H, t, J=8.0 Hz, H-7), 7.39 (1H, d, J=8.0 Hz, *H*-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 20.90, 25.24, 30.64 and 31.07 (C cyclohexyl), 62.50 (C-4), 70.29 (C-3), 78.96 (C-2), 117.21 (C-6), 117.85 (C-4a), 122.50 (C-8), 129.24 (C-7), 150.73 (C-5), 153.33 (C-8a). *Anal.* Calcd for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.14; N, 5.01. Found: C, 60.41; H, 6.22; N, 4.88.

(±)*cis*-3,4-Dihydro-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cycloheptane]-3,4-diol (7c) This compound was prepared by an analogous procedure as described for the preparation of **7a**, starting from **2c**. Yield: 85%. Oil. IR (film) ν (OH) 3645—2920 cm^{-1}, ν (NO_2) 1463 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.3—2.3 (12H, m, H cycloheptyl), 3.84 (1H, d, J=4.8 Hz, H-3), 5.27 (1H, d, J=4.8 Hz, H-4), 7.06 (1H, d, J=8.1 Hz, H-8), 7.28 (1H, t, J=8.1 Hz, H-7), 7.37 (1H, d, J=8.1 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 21.75, 29.94, 33.73 and 34.27 (C cycloheptyl), 62.60 (C-4), 69.78 (C-3), 83.52 (C-2), 117.01 (C-6), 117.64 (C-4a), 122.43 (C-8), 129.11 (C-7), 150.88 (C-5), 153.47 (C-8a). *Anal.* Calcd for $C_{15}H_{19}NO_5$: C, 61.42; H, 6.53; N, 4.78. Found: C, 61.67; H, 6.33; N, 4.47.

(±)*cis*-3,4-Dihydro-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decane]-3,4-diol (7d) This compound was prepared by an analogous procedure as described for the preparation of **7a**, starting from **2d**. Yield: 82%. mp 124 °C (EtOH). IR (Nujol) ν (OH) 3649—2915 cm^{-1}, ν (NO_2) 1470 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.4—2.3 (14H, m, H adamantyl), 4.47 (1H, d, J=4.8 Hz, H-3), 5.23 (1H, d, J=4.8 Hz, H-4), 7.09 (1H, d, J=7.9 Hz, H-8), 7.27 (1H, t, J=7.9 Hz, H-7), 7.30 (1H, d, J=7.9 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 26.87, 26.95, 30.47, 31.09, 31.84, 31.91, 32.33, 33.43, 33.53 and 37.70 (C adamantyl), 62.17 (C-4), 62.21 (C-3), 83.38 (C-2), 116.91 (C-6), 118.13 (C-4a), 121.58 (C-8), 128.95 (C-7), 151.24 (C-5), 152.78 (C-8a). *Anal.* Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.51; H, 6.56; N, 4.02.

(±)*cis*-3,4-Dihydro-3,4-*O*-(isopropylidene)-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cyclopentane]-3,4-diol (8a) To a solution of *cis*-diol **7a** (760 mg, 2.87 mmol) in acetone (20 ml), was added concentrated H_2SO_4 (2 drops) and the resulting mixture was heated at reflux for 3 h. Upon cooling, the mixture was vacuum evaporated, extracted with dichloromethane–water, the organic layer was dried (Na_2SO_4) and evaporated to dryness, to afford compound **8a** (840 mg, 96%). mp 110 °C (Et_2O). IR (Nujol) ν (NO_2) 1531 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.00 (3H, s, CH_3), 1.36 (3H, s, CH_3), 1.5—2.2 (8H, m, H cyclopentyl), 4.17 (1H, d, J= 5.5 Hz, H-3), 5.75 (1H, d, J=5.5 Hz, H-4), 7.03 (1H, d, J=8.0 Hz, H-8), 7.26 (1H, t, J=8.0 Hz, H-7), 7.42 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 24.12 (C cyclopentyl), 26.61 (CH_3), 27.62 (CH_3), 34.32 and 36.49 (C cyclopentyl), 68.47 (C-4), 77.22 (C-3), 86.48 (C-2), 110.58 (<u>C</u>(CH_3)$_2$), 117.32 (C-4a and C-6), 122.50 (C-8), 129.04 (C-7), 150.51 (C-5), 153.38 (C-8a). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 62.94; H, 6.27; N, 4.59. Found: C, 63.21; H, 6.44; N, 4.78.

(±)*cis*-3,4-Dihydro-3,4-*O*-(isopropylidene)-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cyclohexane]-3,4-diol (8b) This compound was prepared by an analogous procedure as described for the preparation of **8a**, starting from **7b**. Yield: 95%. mp 118 °C (Et_2O). IR (Nujol) ν (NO_2) 1523 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.99 (3H, s, CH_3), 1.34 (3H, s, CH_3), 1.3—2.2 (10H, m, H cyclohexyl), 4.13 (1H, d, J=5.5 Hz, H-3), 5.73 (1H, d, J=5.5 Hz, H-4), 7.10 (1H, d, J=8.0 Hz, H-8), 7.28 (1H, t, J=8.0 Hz, H-7), 7.41 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 20.67, 20.91 and 25.28 (C cyclohexyl), 26.59 (CH_3), 27.58 (CH_3), 30.12, 33.20 (C cyclohexyl), 67.94 (C-4), 70.29 (C-3), 78.96 (C-2), 110.34 (<u>C</u>(CH_3)$_2$) 116.86 (C-4a), 117.23 (C-6), 122.27 (C-8), 129.18 (C-7), 150.40 (C-5), 152.56 (C-8a). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 63.94; H, 6.63; N, 4.39. Found: C, 64.15; H, 6.42; N, 4.58.

(±)*cis*-3,4-Dihydro-3,4-*O*-(isopropylidene)-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,1′-cycloheptane]-3,4-diol (8c) This compound was prepared by an analogous procedure as described for the preparation of **8a**, starting from **7c**. Yield: 95%. mp 115 °C (Et_2O). IR (Nujol) ν (NO_2) 1527 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.90 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.3—2.1 (12H, m, H cycloheptyl), 4.17 (1H, d, J=5.4 Hz, H-3), 5.67 (1H, d, J=5.4 Hz, H-4), 7.00 (1H, d, J=8.0 Hz, H-8), 7.23 (1H, t, J=8.0 Hz, H-7), 7.32 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 21.50 (C cycloheptyl), 26.26 (CH_3), 27.28 (CH_3), 29.39 and 35.48 (C cycloheptyl), 67.60 (C-4), 76.08 (C-3), 80.46 (C-2), 109.80 (<u>C</u>(CH_3)$_2$), 116.40 (C-4a), 116.66 (C-6), 121.96 (C-8), 128.88 (C-7), 150.16 (C-5), 152.44 (C-8a). *Anal.* Calcd for $C_{18}H_{19}NO_3$: C, 64.85; H, 6.95; N, 4.20. Found: C, 65.07; H, 6.74; N, 3.92.

(±)*cis*-3,4-Dihydro-3,4-*O*-(isopropylidene)-5-nitrospiro[2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decane]-3,4-diol (8d) This compound was prepared by an analogous procedure as described for the preparation of **8a**, starting from **7d**. Yield: 93%. mp 161—162 °C (EtOH). IR (Nujol) ν (NO_2) 1535 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 0.98 (3H, s, CH_3), 1.35 (3H, s, CH_3), 1.4—2.5 (12H, m, H adamantyl), 4.86 (1H, d, J= 5.5 Hz, H-3), 5.74 (1H, d, J=5.5 Hz, H-4), 7.13 (1H, d, J=8.0 Hz, H-8), 7.28 (1H, t, J=8.0 Hz, H-7), 7.43 (1H, d, J=8.0 Hz, H-6). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 26.61 (CH_3), 27.71 (CH_3), 27.03, 29.65, 31.49, 32.01, 32.43, 32.90, 33.48, 34.27 and 37.99 (C adamantyl), 67.59 (C-4), 72.47 (C-3), 80.50 (C-2), 110.15 (<u>C</u>(CH_3)$_2$), 117.29 (C-6), 118.60 (C-4a), 122.38 (C-8), 129.26 (C-7), 150.25 (C-5), 152.35 (C-8a). *Anal.* Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77; Found: C, 68.12; H, 6.61; N, 3.52.

(±)*cis*-5-Amino-3,4-dihydro-3,4-*O*-(isopropylidene)spiro[2*H*-benzo[*b*]pyrano-2,1′-cyclopentane]-3,4-diol (9a) A solution of the amine **8a** (440 mg, 1.443 mmol) in absolute ethanol (30 ml) was hydrogenated in the presence of 10% Pd/C (50 mg), under a pressure of 50 psi at room temperature for 5 h. The resulting mixture was filtered through a celite pad and the filtrate was evaporated to dryness to result in an oil corresponding to the 5-aminoderivative **9a**. Isolated yield: 360 mg (90%). mp 114 °C (EtOH). IR (Nujol) ν (NH_2) 3459, 3366 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.27 (3H, s, CH_3), 1.43 (3H, s, CH_3), 1.5—2.0 (8H, m, H cyclopentyl), 4.13 (2H, br s, D_2O exchang., NH_2), 4.22 (1H, d, J=6.2 Hz, H-3), 5.09 (1H, d, J=6.2 Hz, H-4), 6.25 (1H, d, J=8.0 Hz, H-6), 6.27 (1H, d, J=8.0 Hz, H-8), 6.95 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 23.89, 24.33 (C cyclopentyl), 26.57 (CH_3), 27.38 (CH_3), 34.88 and 34.99 (C cyclopentyl), 69.43 (C-4), 77.22 (C-3), 86.30 (C-2), 106.70 (C-4a), 107.91 and 108.31 (C-6 and C-8), 109.78 (<u>C</u>(CH_3)$_2$), 129.56 (C-7), 147.13 (C-5), 153.41 (C-8a). *Anal.* Calcd for $C_{16}H_{21}NO_3$. C, 69.79; H, 7.69; N, 5.09. Found (%): C, 69.90; H, 7.43; N, 5.33.

(±)*cis*-5-Amino-3,4-dihydro-3,4-*O*-(isopropylidene)spiro[2*H*-benzo[*b*]pyrano-2,1′-cyclohexane]-3,4-diol (9b) This compound was prepared by an analogous procedure as described for the preparation of **9a**, starting from **8b**. Yield: 88%. mp 125 °C (EtOH). IR (Nujol) ν (NH_2) 3465, 3373 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$) δ 1.25 (3H, s, CH_3), 1.41 (3H, s, CH_3), 1.3—1.8 (10H, m, H cyclohexyl), 4.08 (1H, d, J=6.0 Hz, H-3), 5.08 (1H, d, J=6.0 Hz, H-4), 6.26 (1H, d, J=8.0 Hz, H-8), 6.31(1H, d, J=8.0 Hz, H-6), 6.97 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ 20.50, 20.76 and 25.26 (C cyclohexyl), 26.31 (CH_3), 27.10 (CH_3), 31.26 and 31.38 (C cyclohexyl), 68.69 (C-4), 75.55 (C-3), 77.90 (C-2), 107.32 (C-4a), 107.88 and 108.12 (C-6 and C-8), 109.38 (<u>C</u>(CH_3)$_2$), 129.38 (C-7), 146.64 (C-5), 152.19 (C-8a). *Anal.* Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 71.23; H, 7.69; N, 4.58.

(±)*cis*-5-Amino-3,4-dihydro-3,4-*O*-(isopropylidene)spiro[2*H*-benzo[*b*]pyrano-2,1′-cycloheptane]-3,4-diol (9c) This compound was prepared by an analogous procedure as described for the preparation of **9a**, starting from **8c**. Yield: 91%. mp 120 °C (EtOH). IR (Nujol) ν (NH_2) 3461, 3375 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.22 (3H, s, CH_3), 1.41 (3H, s, CH_3), 1.3—2.0 (12H, m, H cycloheptyl), 4.15 (1H, d, J=5.9 Hz, H-3), 5.08 (1H, d, J=5.9 Hz, H-4), 6.24 (1H, d, J=8.0 Hz, H-8), 6.26 (1H, d, J=8.0 Hz, H-6), 6.95 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 22.00 (C cycloheptyl), 26.63 (CH_3), 27.47 (CH_3), 29.64, 29.80, 35.02 and 35.49 (C cycloheptyl), 69.10 (C-4), 78.13 (C-3), 80.00 (C-2), 107.75 and 108.16 (C-4a, C-6 and C-8), 109.68 (<u>C</u>(CH_3)$_2$), 129.58 (C-7), 146.94 (C-5), 152.37 (C-8a). *Anal.* Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 70.97; H, 8.62; N, 4.51.

(±)*cis*-5-Amino-3,4-dihydro-3,4-*O*-(isopropylidene)spiro[2*H*-benzo[*b*]pyrano-2,2′-tricyclo[3.3.1.1^{3,7}]decane]-3,4-diol (9d) This compound was prepared by an analogous procedure as described for the preparation of **9a**, starting from **8d**. Yield: 89%. mp 142 °C (EtOH). IR (Nujol) ν (NH_2) 3463, 3370 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 1.23 (3H, s, CH_3), 1.40 (3H, s, CH_3), 1.1—2.1 (14H, m, H adamantyl), 4.84 (1H, d, J=5.8 Hz, H-3), 5.12 (1H, d, J=5.8 Hz, H-4), 6.34 (1H, d, J=8.0 Hz, H-8), 6.37 (1H, d, J=8.0 Hz, H-6), 6.97 (1H, t, J=8.0 Hz, H-7). ^{13}C-NMR (50 MHz, $CDCl_3$) δ: 27.00 (CH_3), 27.23 (CH_3), 27.14, 28.05, 29.69, 30.31, 31.71, 32.52, 33.50, 34.47 and 38.18 (C adamantyl), 68.58 (C-4), 73.31 (C-3), 80.03 (C-2), 108.78 and 109.19 (C-6 and C-8), 107.95 (C-4a), 109.93 (<u>C</u>(CH_3)$_2$), 129.49 (C-7), 145.43 (C-5), 152.10 (C-8a). *Anal.* Calcd for $C_{21}H_{27}NO_3$: C, 73.87; H, 7.97; N, 4.10. Found: C, 74.09; H, 7.71; N, 4.32.

(±)*cis*-9′,10′-Dihydro-9′,10′-*O*-(isopropylidene)-4′,9′,10′-trihydroxyspiro[cyclopentane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (10a) A mixture of **9a** (770 mg, 2.8 mmol) in diethyl malonate (42 ml, 280.0 mmol) was heated at 160 °C for 15 h. After completion of the reaction, the mixture was vacuum-evaporated and the residue was purified by column chromatography (silica gel, cyclohexane/ethyl acetate 5/1) to furnish compound **10a** (413 mg, 43%). mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3651—2930 cm^{-1}, ν (CONH) 1673 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.17 (3H, s, CH_3), 1.46 (3H, s, CH_3), 1.5—2.2 (8H, m, H cyclopentyl), 4.31 (1H, d, J=5.7 Hz, H-9), 5.24 (1H, d, J=5.7 Hz, H-10), 5.58 (1H, s, H-3), 6.88 (1H, d, J=8.8 Hz, H-6), 8.05 (1H, d, J=8.8 Hz, H-5), 9.56 (1H, br s, D_2O exchang., OH), 12.59 (1H, br s, D_2O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 24.08 and 24.18 (C cyclopentyl), 26.43 (CH_3), 27.64 (CH_3), 35.47 and 35.80 (C cyclopentyl), 67.59 (C-10), 77.29 (C-9),

87.84 (C-8), 89.83 (C-3), 107.21 (C-4a and C-10a), 111.80 (C(CH$_3$)$_2$), 116.03 (C-6), 125.44 (C-5), 138.08 (C-10b), 157.23 (C-6a), 163.48 (C-4), 168.99 (C-2). *Anal.* Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.33; H, 6.02; N, 3.89.

(±)*cis*-9′,10′-Dihydro-9′,10′-*O*-(isopropylidene)-4′,9′,10′-trihydroxyspiro[cyclohexane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (10b) This compound was prepared by an analogous procedure as described for the preparation of **10a**, starting from **9b**. Yield: 48%. mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3628—3110 cm^{-1}, ν (CONH) 1684 cm^{-1}. ^{1}H-NMR (400 MHz, DMSO-d_6) δ: 1.14 (3H, s, CH$_3$), 1.44 (3H, s, CH$_3$), 1.4—2.2 (10H, m, H cyclohexyl), 4.25 (1H, d, J=5.7 Hz, H-9), 5.26 (1H, d, J=5.7 Hz, H-10), 5.56 (1H, s, H-3), 6.95 (1H, d, J=8.8 Hz, H-6), 8.06 (1H, d, J=8.8 Hz, H-5), 9.71 (1H, br s, D$_2$O exchang., OH), 12.60 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 20.51, 20.84 and 25.14 (C cyclohexyl), 26.39 (CH$_3$), 27.60 (CH$_3$), 31.35 and 32.31 (C cyclohexyl), 67.08 (C-10), 77.29 (C-9), 87.84 (C-8), 88.13 (C-3), 106.95 and 107.17 (C-4a and C-10a), 111.55 (C(CH$_3$)$_2$), 116.10 (C-6), 125.51 (C-5), 138.05 (C-10b), 156.53 (C-6a), 163.52 (C-4), 168.99 (C-2). *Anal.* Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.45; H, 6.20; N, 3.99.

(±)*cis*-9′,10′-Dihydro-9′,10′-*O*-(isopropylidene)-4′,9′,10′-trihydroxyspiro[cycloheptane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (10c) This compound was prepared by an analogous procedure as described for the preparation of **10a**, starting from **9c**. Yield: 42%. mp 234 °C (EtOH). IR (Nujol) ν (OH, NH) 3565—3140 cm^{-1}, ν (CONH) 1679 cm^{-1}. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.13 (3H, s, CH$_3$), 1.45 (3H, s, CH$_3$), 1.4—2.1 (12H, m, H cycloheptyl), 4.30 (1H, d, J=5.5 Hz, H-9), 5.23 (1H, d, J=5.5 Hz, H-10), 5.57 (1H, s, H-3), 6.91 (1H, d, J=8.8 Hz, H-6), 8.05 (1H, d, J=8.8 Hz, H-5), 9.58 (1H, br s, D$_2$O exchang., OH), 12.60 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, CDCl$_3$) δ: 21.91 (C cycloheptyl), 26.45 (CH$_3$), 27.66 (CH$_3$), 29.60, 35.30 and 35.57 (C cycloheptyl), 67.26 (C-10), 77.18 (C-9), 82.25 (C-8), 89.25 (C-3), 106.79 and 107.17 (C-10a and C-4a), 111.60 (C(CH$_3$)$_2$), 115.93 (C-6), 125.53 (C-5), 138.10 (C-10b), 156.78 (C-6a), 163.49 (C-4), 169.04 (C-2). *Anal.* Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78, N; 3.77. Found: C, 68.01; H, 6.66; N, 3.60.

(±)*cis*-9,10-Dihydro-9,10-*O*-(isopropylidene)-4,9,10-trihydroxyspiro-[8*H*-pyrano[2,3-*h*]quinolino-8,2′-tricyclo[3.3.1.1^{3,7}]decan-2(1*H*)-one] (10d) This compound was prepared by an analogous procedure as described for the preparation of **10a**, starting from **9d**. Yield: 50%. mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3688—2990 cm^{-1}, ν (CONH) 1680 cm^{-1}. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.11 (3H, s, CH$_3$), 1.45 (3H, s, CH$_3$), 1.6—2.5 (14H, m, H adamantyl), 4.98 (1H, d, J=5.2 Hz, H-9), 5.21 (1H, d, J=5.2 Hz, H-10), 5.57 (1H, s, H-3), 6.97 (1H, d, J=9.0 Hz, H-6), 8.07 (1H, d, J=9.0 Hz, H-5), 9.39 (1H, br s, D$_2$O exchang., OH), 12.58 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, CDCl$_3$) δ: 26.26 (CH$_3$), 27.84 (CH$_3$), 27.30, 27.95, 29.99, 30.44, 31.16, 33.73, 34.00 and 38.33 (C adamantyl), 66.79 (C-10), 72.06 (C-9), 80.24 (C-8), 89.25 (C-3), 106.97 and 107.15 (C-10a and C-4a), 111.66 (C(CH$_3$)$_2$), 115.62 (C-6), 125.38 (C-5), 138.63 (C-10b), 156.48 (C-6a), 161.27 (C-4), 169.71 (C-2). *Anal.* Calcd for $C_{24}H_{27}NO_5$: C, 70.40; H, 6.65; N, 3.42. Found: C, 70.45; H, 6.47; N, 3.68.

(±)*cis*-9′,10′-Dihydro-4′,9′,10′-trihydroxyspiro[cyclopentane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (11a) A solution of **10a** (508 mg, 1.48 mmol) in a mixture of trifuoroacetic acid (9 ml) and dry methanol (3 ml) was stirred at room temperature for 24 h. After completion of the reaction, the mixture was concentrated *in vacuo* and the residue was recrystallized from ethanol to afford 368 mg of the title compound. Yield: 82%. mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3630—3150 cm^{-1}, ν (CONH) 1684 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.6—2.0 (8H, m, H cyclopentyl), 3.78 (1H, m, H-9), 5.13 (1H, m, H-10), 5.51 (1H, s, H-3), 5.54 (1H, d, J=5.7 Hz, D$_2$O exchang., 9-OH), 6.04 (1H, br s, D$_2$O exchang., 10-OH), 6.86 (1H, d, J=8.8 Hz, H-6), 7.84 (1H, d, J=8.8 Hz, H-5), 11.47 (1H, br s, D$_2$O exchang., 4-OH), 13.20 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 23.61, 23.86, 34.85 and 35.00 (C cyclopentyl), 63.85 (C-10), 69.11 (C-9), 91.08 (C-8), 88.40 (C-3), 106.04 (C-4a), 109.06 (C-10a), 115.76 (C-6), 123.76 (C-5), 139.19 (C-10b), 157.75 (C-6a), 162.79 (C-4), 169.14 (C-2). *Anal.* Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.44; H, 5.41; N, 4.72.

(±)*cis*-9′,10′-Dihydro-4′,9′,10′-trihydroxyspiro[cyclohexane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (11b) This compound was prepared by an analogous procedure as described for the preparation of **11a**, starting from **10b**. Yield: 85%. mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3641—3125 cm^{-1}, ν (CONH) 1680 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6) δ: 1.2—2.1 (10H, m, H cyclohexyl), 3.74 (1H, m, H-9), 5.17 (1H, m, H-10), 5.47 (d, J=5.3 Hz, 1H, D$_2$O exchang., 9-OH), 5.52 (s, 1H, H-3), 5.95 (1H, br s, D$_2$O exchang., 10-OH), 6.93 (1H, d, J=8.8 Hz, H-6), 7.88 (1H, d, J=8.8 Hz, H-5), 11.42 (1H, br s, D$_2$O exchang., 4-OH), 13.22 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, DMSO-d_6) δ: 20.78, 20.89, 24.89 and 31.21 (C cyclohexyl), 63.08 (C-10), 68.78 (C-9), 88.39 (C-3), 80.39 (C-8), 106.04 (C-4a), 108.80 (C-10a), 115.19 (C-6), 123.83 (C-5), 139.34 (C-10b), 157.50 (C-6a), 162.75 (C-4), 169.18 (C-2). *Anal.* Calcd for $C_{17}H_{19}NO_5$: C, 64.34; H, 6.03; N, 4.41. Found: C, 64.56; H, 6.14; N, 4.24.

(±)*cis*-9′,10′-Dihydro-4′,9′,10′-trihydroxyspiro[cycloheptane-1,8′-8′*H*-pyrano[2,3-*h*]quinolin-2′(1′*H*)-one] (11c) This compound was prepared by an analogous procedure as described for the preparation of **11a**, starting from **10c**. Yield: 87%. mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3590—2985 cm^{-1}, ν (CONH) 1677 cm^{-1}. ^{1}H-NMR (200 MHz, CDCl$_3$) δ: 1.3—2.3 (12H, m, H cycloheptyl), 3.77 (1H, br s, H-9), 5.17 (1H, br s, H-10), 5.53 (1H, s, H-3), 6.88 (1H, d, J=8.8 Hz, H-6), 7.86 (1H, d, J=8.8 Hz, H-5), 11.45 (1H, br s, D$_2$O exchang., 4-OH), 13.19 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, CDCl$_3$) δ: 21.32, 21.46, 29.60, 33.45 and 35.04 (C cycloheptyl), 63.31 (C-10), 68.32 (C-9), 85.14 (C-8), 88.33 (C-3), 105.96 (C-4a), 108.60 (C-10a), 115.34 (C-6), 123.73 (C-5), 139.27 (C-10b), 157.63 (C-6a), 160.78 (C-4), 169.09 (C-2). *Anal.* Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.50; H, 6.13; N, 4.41.

(±)*cis*-9,10-Dihydro-4,9,10-trihydroxyspiro[8*H*-pyrano[2,3-*h*]quinolino-8,2′-[tricyclo[3.3.1.1^{3,7}]decan]-2(1*H*)-one] (11d) This compound was prepared by an analogous procedure as described for the preparation of **11a**, starting from **10d**. Yield: 79%. mp >250 °C (EtOH). IR (Nujol) ν (OH, NH) 3635—3110 cm^{-1}, ν (CONH) 1683 cm^{-1}. ^{1}H-NMR (400 MHz, CDCl$_3$) δ: 1.3—2.3 (14H, m, H adamantyl), 4.36 (1H, m, H-9), 5.14 (1H, m, H-10), 5.44 (1H, br s, D$_2$O exchang., 9-OH), 5.49 (1H, s, H-3), 6.06 (1H, br s, D$_2$O exchang., 10-OH), 6.93 (1H, d, J=8.6 Hz, H-6), 7.85 (1H, d, J=8.6 Hz, H-5), 11.33 (1H, br s, D$_2$O exchang., 4-OH), 13.16 (1H, br s, D$_2$O exchang., NH). ^{13}C-NMR (50 MHz, CDCl$_3$) δ: 26.27, 26.52, 37.70, 32.52, 36.66 and 37.68 (C adamantyl), 63.54 (C-10), 65.16 (C-9), 87.84 (C-8), 88.63 (C-3), 106.53 (C-4a), 109.20 (C-10a), 115.22 (C-6), 124.07 (C-5), 139.86 (C-10b), 158.37 (C-6a), 161.12 (C-4), 169.35 (C-2). *Anal.* Calcd for $C_{21}H_{23}NO_5$: C, 68.28; H, 6.28; N, 3.79. Found: C, 67.99; H, 6.26; N, 3.47.

Measurement of DPPH Radical-Scavenging The method has been previously described in detail.[17] Briefly, to a solution of DPPH (final concentration 200 μM) in absolute ethanol, an equal volume of the compound dissolved in ethanol was added at various concentrations (5—200 μM). Ethanol was added to the control solution. Absorbance was recorded at 517 nm after 20, 30, 45 and 60 min of incubation at room temperature. Each experiment was performed at least in triplicate and the standard deviation in absorbance values was less than ±10%. IC_{50} values were determined by linear regression analysis[19] using at least five different concentrations in triplicate.

Quenching of the Superoxide Anion Radical The $O_2^{\cdot-}$ quenching capacity of the synthesized compounds was tested by estimation of the reduction product of nitro blue tetrazolium (NBT), as described previously.[18] The incubation system contained 200 μM xanthine, 600 μM NBT, in 0.1 M phosphate buffer (pH 7.4). The tested substances were dissolved in 0.1% DMF in buffer, and added to the reaction mixture (300 μl, final concentration 0.5 mM). An equal volume of the solvent system was added to the control mixture. The reaction was started with the addition of 0.07 units/ml of xanthine oxidase. After incubation (25 °C, 10 min), absorbance was recorded at 560 nm, against blank samples, which did not contain the enzyme. DMF was tested and found not to interfere with the assay at the concentration used (0.1% v/v). Each experiment was performed at least in triplicate and the deviation in absorbance values was less than ±10%.

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