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Anionic ring opening of norbornenes fused to heterocycles

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Dedicated to Professor José L. Soto, on the occasion of his retirement

Abstract—The 2-hydroxy and 2-oxo derivatives of 1,2,3,4-tetrahydro-1,4-methanophenazine were prepared and found to evolve in basic media through the opening of their bicyclo[2.2.1]heptene moiety, affording 2,3-dihydro-1*H*-cyclopenta[*b*]quinoxaline derivatives with two-carbon 1-substituents that depend on the starting compound. In the case of 2-hydroxy starting compounds, ring-opening occurs regardless of the orientation of the hydroxyl group, and in methanolic solution is spontaneous, though slow, even in the absence of added base (at least in the case of the *endo* derivative). It is presumably favoured by the steric strain of the heteroaryl-fused bicyclo[2.2.1]heptene moiety, and is hypothesized to involve the base-promoted formation of anionic intermediates that are stabilized by the π-deficient nature of the quinoxaline system.

1. Introduction

Though first reported over 40 years ago, molecules consisting of an aromatic heterocycle fused to norbornene or norbornadiene have only more recently attracted attention. Relatively simple derivatives of compounds of this kind have been proposed for storage of light energy,[1,2] while more complex derivatives have been developed as initiators of photochemical polymerization,[3,4] as components of holographic recording media,[5–8] as ligands forming part of models for the study of long-range electron transfer between chelated metal centres,[9,10] and as the monomers of self-assembling dimeric capsules[11,12] or of molecular cavities and ribbons.[13,14] In the pharmacological field, compounds of this type have been prepared in pursuit of virucidal or virustatic agents,[15] antiulcer agents,[16] brain acetylcholinesterase inhibitors,[17–19] serotonin antagonists,[20] central nervous system stimulants,[21–23] dihydrofolate reductase inhibitors,[24] and mGluR1 antagonists.[25]

Although much of the relevant literature, especially the older papers, merely describes their preparation (sometimes incidental) and/or their spectroscopic properties,[26–42] there have also been studies of their chemistry, including work on electrophilic addition reactions;[43–46] aromatic substitution in the heterocyclic moiety;[47] the regiochemistry of their di-π-methane photorearrangement;[48,49] the relationship between their basicity and internal strain;[50] and their behaviour as dienophiles in Diels–Alder reactions.[51] Of particular interest is the participation of the heterocyclic moiety as neighbouring group in the solvolysis of diverse sulfonates,[52–54] in the acidic opening of an epoxide ring previously formed on the norbornene moiety[55] and in electrophilic additions,[43–46] and the influence of the electronic π-richness or π-deficiency of that moiety on π-facial selectivity in the latter reactions.[56,57]

If the heterocyclic moiety is π-deficient the norbornene moiety can behave quite differently from carbocyclic or non-condensed analogues. For example, subjecting diols **1** to the conditions of Swern's reaction does not afford the corresponding diketones **2**, but instead 63–75% yields of alcohols **3** as the only isolatable products.[58] Here we report that the norbornene moiety of **1a** and of other oxygenated 1,2,3,4-tetrahydro-1,4-methanophenazine derivatives (**4** and **5**) also opens very readily in basic media, a finding that as far as we know has no precedent in the literature except for a preliminary report of ours concerning **1a**.[59]

Keywords: Quinoxaline-fused norbornene; Ring opening; Anionic intermediates; Basic medium.
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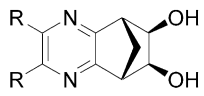

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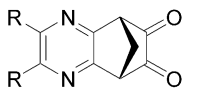
1b R = H



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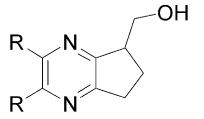

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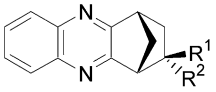
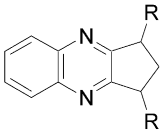
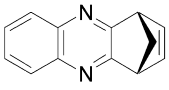
3b R = H



4a R^1 = H, R^2 = OH
4b R^1 = OH, R^2 = H
5 (R^1,R^2) = O



6 R = CO_2H
7 R = CH_2OH
8 R = CHO



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Our interest in **1a** originated from the wish to obtain diacid **6** and diol **7** for the synthesis of carbocyclic analogues of nucleosides with phthalazine-fused carbocycles; after several unsuccessful attempts to obtain **6** and **7** through oxidative cleavage of the double bond in **9**,[60] we hoped that mild treatment of **1a** (e.g., with periodic acid) would result in oxidative cleavage leading to dialdehyde **8**, which would then be oxidized to **6** or reduced to **7** in situ.[61] Since it was planned to use **1a** on more than one occasion in exploring its oxidative cleavage under diverse conditions, the finding that it tended to decompose when stored at rt led us to prepare compound **16** as a stable derivative that could presumably be easily converted to **1a** immediately before use. In the event, we found that the basic conditions used for conversion of **16** into **1a** caused the opening of its norbornene moiety.

2. Results and discussion

Compound **16** was obtained as shown in Scheme 1. A commercially available racemic mixture of *endo* and *exo* norbornenyl acetates (**10**) was dihydroxylated to **11**, and benzoylation followed by selective hydrolysis of the acetate afforded **13**. Since dihydroxylation of bicyclo[2.2.1]heptenes occurs almost exclusively at the *exo* face,[62] **11**–**13** were virtually monoepimeric at positions 2 and 3, and oxidation of both 5-epimers of **13** took place easily to afford monoketone **14**, which upon treatment with selenium dioxide gave the α-diketone **15**. Finally, condensation of **15** with *ortho*-phenylenediamine yielded the dibenzoate **16**.

Because of the likelihood of rearrangements of Wagner–Meerwein type due to its norbornene moiety, the conversion of **16** to **1a** was attempted by basic rather than acid hydrolysis. Initial attempts gave only intractable mixtures or unaltered starting material, but the mildest conditions compatible with effective saponification of the benzoate groups (0.9 M KOH in $MeOH/H_2O$, rt, 12 h) afforded a crude product that upon flash chromatography on silica gel gave a 66% yield of a dark green solid. This product underwent alteration when left standing in solution, but IR, MS and ^1H and ^{13}C NMR data obtained immediately after purification were compatible with its being the enediol **17**. This identification was confirmed by single-crystal X-ray crystallography of the stable diacetylated derivative **18** (Fig. 1),[63] which was obtained by acetylation of **17** with Ac_2O/pyridine.

It may be assumed that the first step in the conversion of **16** to **17** is the desired hydrolysis to **1a**; this is supported by the fact that a sample of **1a** prepared by an independent route,[58] was transformed into **17** in very similar yield when subjected to the same basic conditions as **16**. A plausible account of subsequent steps is shown in Scheme 2. Under the basic working conditions, diol **1a** will be in equilibrium with its monoalkoxide, which because of the stress in the bridged ring system must be highly susceptible to ring

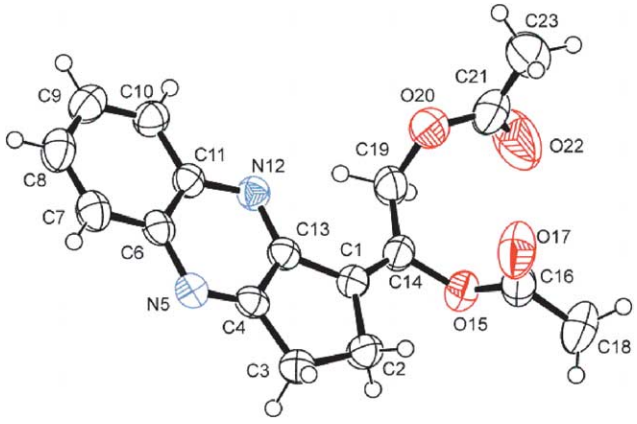
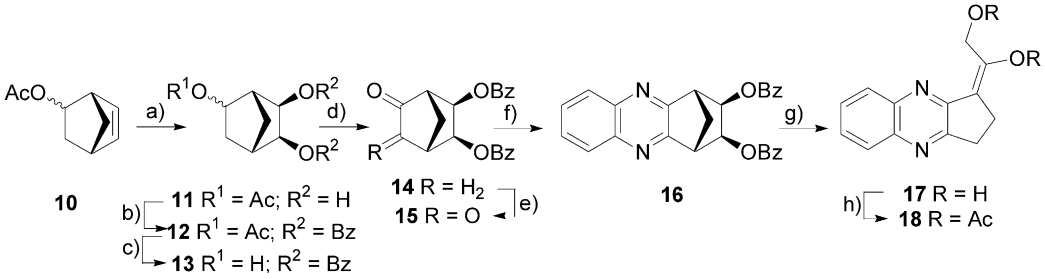
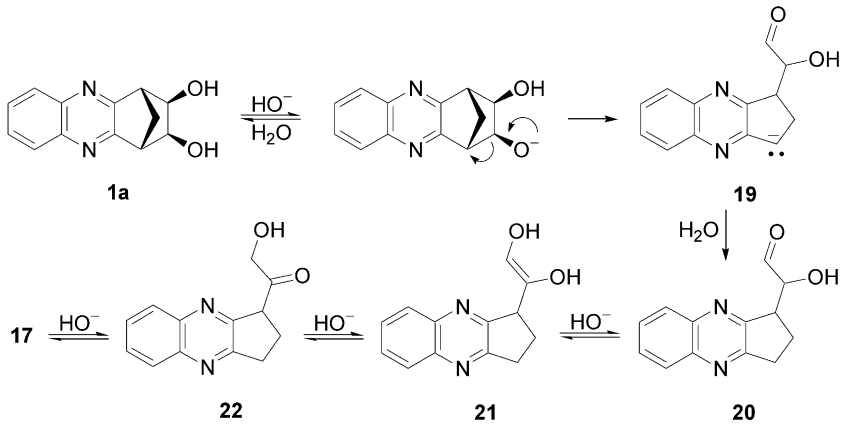


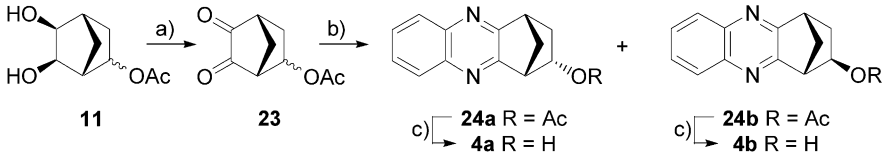
Figure 1. ORTEP plot of the molecular structure of **18** in the solid state.



Scheme 1. Reagents and conditions: (a) $OsO_4/NMNO/Me_2CO–H_2O$, 40 °C, 18 h; (b) BzCl/Py, rt, 24 h; (c) K_2CO_3/MeOH, rt, 30 min; (d) $CrO_3 \cdot Py$/DCM, rt, 6 h; (e) SeO_2/xylene, 140 °C, 24 h; (f) *o*-$(C_6H_4)(NH_2)_2/ZnCl_2$/THF, 66 °C, 18 h; (g) 0.9 M KOH/$MeOH–H_2O$, rt, 12 h; (h) Ac_2O/Py, rt, 14 h.



Scheme 2. Suggested mechanism for the formation of **17** from **1a**.



Scheme 3. Reagents and conditions: (a) DMSO-TFAA/DCM/TEA, −78 °C, 3 h; (b) *o*-$(C_6H_4)(NH_2)_2$/$ZnCl_2$/THF, 66 °C, 4.5 h; (c) 0.7 M Na_2CO_3/MeOH, rt, 2 h.

opening. The resulting carbanion **19** will be stabilized by its charge being formally located on the carbon α to position 3 of the π-deficient quinoxaline system, and following protonation of this carbon the resulting α-hydroxyaldehyde **20** will be susceptible to base-catalyzed isomerization to the α-hydroxyketone **22** via the enediol **21** (a well-known conversion in sugar chemistry). Finally, isomerization of **22** to the enediol **17** will be favoured by the exocyclic C═C bond of the latter being conjugated with the aromatic quinoxaline system.

As there appear to be no published precedents for the above anionically driven ring-opening of a bicyclo[2.2.1]heptene derivative, we began to explore its scope using the structurally simpler monoalcohols **4a** (*endo*) and **4b** (*exo*), which were prepared as shown in Scheme 3 by Swern oxidation of **11** to the mixture of epimeric diketones **23**, followed by condensation of **23** with *ortho*-phenylenediamine, chromatographic separation of the resulting mixture of diastereomeric methanophenazines **24**, and mild hydrolysis of **24a** and **24b** (0.7 M Na_2CO_3 in methanol, rt, 2 h). The identity of **24a** (the major isomer) was confirmed by X-ray crystallographic analysis of a single crystal (Fig. 2).[63]

Hydrolysis of **24a** or **24b** under more severe conditions (longer reaction times, or use of 1 M KOH instead of 0.7 M Na_2CO_3) afforded a mixture including a product with spectroscopic data compatible with its being aldehyde **25** (in particular, a substituted cycloalkyl acetaldehyde was indicated by a strong IR band at 1722 cm^{-1}, ^1H NMR signal at 9.88 ppm, and ^{13}C NMR signals at 201.03 and 47.52 ppm). Starting from **24a**, the greatest yield of **25** was obtained by simply maintaining the conditions used to obtain **4a** for 6 h instead of 2 h (Scheme 4); this gave an approximately 71% yield of a product shown by ^1H NMR data to be **25**, in a sample enriched to a 90% content, as

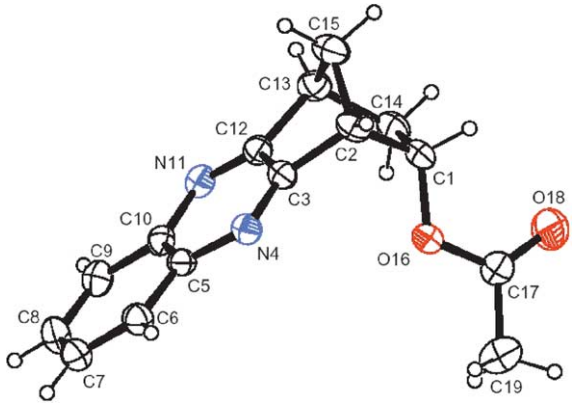
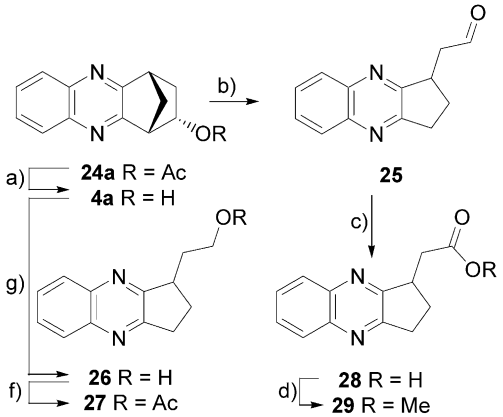


Figure 2. ORTEP plot of the molecular structure of **24a** in the solid state.



Scheme 4. Reagents and conditions: (a) 0.7 M Na_2CO_3/MeOH, rt, 2 h; (b) 0.7 M Na_2CO_3/MeOH, rt, 6 h; (c) $AgNO_3$/NH_4OH, rt, 3 h; (d) MeOH/TsOH, 65 °C, 3.5 h; (e) $NaBH_4$/EtOH, rt, 15 h; (f) Ac_2O/Py, rt, 18 h; (g) 0.5 M Na_2CO_3/$NaBH_4$/EtOH, rt, 18 h.

estimated by ^{1}H NMR. Since this product tended to undergo alteration during work-up,[64] it was converted to more stable forms by Tollens oxidation to acid **28** and $NaBH_4$ reduction to alcohol **26**, which were then further converted into the methyl ester **29** and the acetate **27**, respectively (Scheme 4). Compounds **26–29** all had spectra in keeping with the proposed structures, and that of **26** was confirmed by X-ray crystallography of a single crystal (Fig. 3).[63] If both Na_2CO_3 and $NaBH_4$ are included in the reaction medium, **4a** is transformed into **25** and **25** into **26** in a tandem process with an overall yield of 63%, as against an estimated 54% if **25** is first isolated.

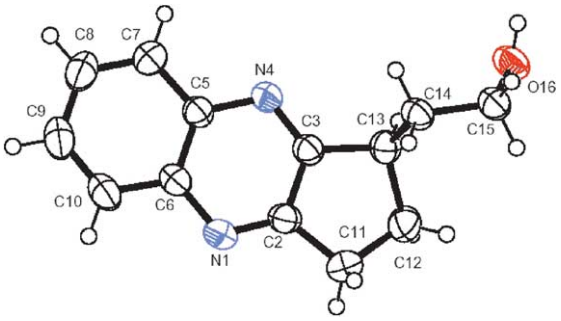
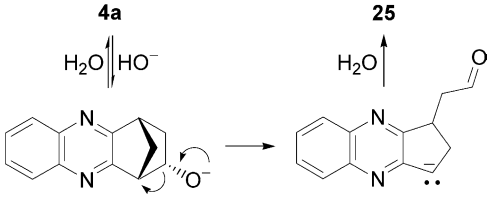


Figure 3. ORTEP plot of the molecular structure of **26** in the solid state.

The formation of **25** from **4a** (or, similarly, from **4b**) may be attributed to the mechanism shown in Scheme 5, which is exactly analogous to the first part of that shown in Scheme 2 for the conversion of **1a** into **17**. At rt it occurs even in methanol without added base (being detectable by ^{1}H NMR after 48 h), possibly being autocatalysed by the basic centres of the tetrahydrophenazine alcohol (although solid **4a** can be stored at 5 °C for several weeks without any alteration detectable by ^{1}H NMR). The acetylated precursors **24** are perfectly stable in methanol at rt.

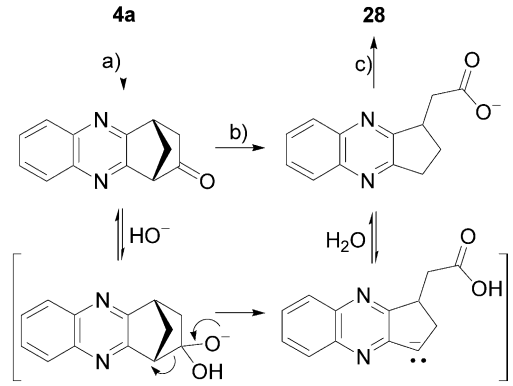


Scheme 5. Suggested mechanism for the formation of **25** from **4a**.

Finally, we also performed the ring-opening reaction on ketone **5**, which was easily obtained by oxidation of **4a** with CrO_3. In basic medium, **5** was converted to the acid **28** by a mechanism hypothesized as starting by the nucleophilic attack of the base to the carbonyl carbon and otherwise being analogous to those proposed above (Scheme 6). Under appropriate conditions, the reaction could be used preparatively, though spontaneous partial transformation of **5** into **28** in chloroform-*d* $CDCl_3$/methanol-d_3 CD_3OD solution was also observed (^{1}H NMR) after 3 days at rt.

3. Conclusion

Basic media promote the opening of the bicyclo[2.2.1]heptene moiety of 2-hydroxy and 2-oxo derivatives of 1,2,3,4-tetrahydro-1,4-methanophenazine, affording 2,3-dihydro-1*H*-cyclopenta[*b*]quinoxaline derivatives with two-carbon 1-substituents that depend on the starting compound. Ring-opening occurs regardless of the orientation of the hydroxyl group in the case of 2-hydroxy starting compounds, and in methanolic solution is spontaneous, though slow, even in the absence of added base (at least in the case of the 2-*endo*-hydroxy or 2-oxo derivatives). It is presumably favoured by the steric strain of the heteroaryl-fused bicyclo[2.2.1]heptene moiety, and may involve the base-promoted formation of anionic intermediates that are stabilized by the π-deficient nature of the quinoxaline system. Although there have been several reports of Wagner–Meerwein and ring-opening processes involving cationic intermediates which are undergone by benzene-fused[65–69] or heteroarene-fused[44–46,54,55] bicyclo[2.2.1]heptenes, the reactions described here are as far as we know the first examples of base-promoted ring-opening involving a carbanion intermediate.



Scheme 6. Preparation of **5** from **4a** and suggested mechanism for the rearrangement of **5** to **26** in basic media. Reagents and conditions: (a) CrO_3·Py/DCM, 0 °C, 6 h; (b) 1 M NaOH/H_2O, rt, 14 h; (c) H_3O^+/pH 4.

4. Experimental

4.1. General

Melting points are uncorrected and were determined in a Reichert Kofler Thermopan or in capillary tubes in a Büchi apparatus. ^{1}H NMR spectra (300 MHz) and ^{13}C NMR spectra (75 MHz) were recorded using TMS as internal reference (chemical shifts in δ values, J in Hz). Microanalyses were performed by the Microanalysis Service of the University of Santiago. Crystallographic data were obtained with a MACH3 Enraf Nonius diffractometer. Flash chromatography was performed on silica gel (230–240 mesh) and analytical TLC on pre-coated silica gel plates (F254, 0.25 mm) and spots were examined with UV light and sulfuric acid/anisaldehyde spray.

4.1.1. (±)-(5-*exo*,6-*exo*)-5,6-Dihydroxybicyclo[2.2.1]-hept-2-yl acetate (mixture of 2-*endo* and 2-*exo*) (11). A solution of commercial (±)-5-norbornen-2-yl acetate (10.0 g, 65.8 mmol) in 4:1 acetone/water (140 mL) was heated to 40 °C, *N*-methylmorpholine *N*-oxide (8.50 g, 72.5 mmol) was added, and 5 min later this mixture was treated with 2 mL of a commercial solution of OsO_4 (4 wt% in water), which caused it to turn brown almost

immediately. The stirred, heated mixture was monitored by TLC, and after 18 h the reaction was deemed complete. The acetone was removed under reduced pressure, the remaining aqueous solution was extracted with AcOEt, the resulting organic extract was dried (Na_2SO_4), the solvent was removed, and the crude residue was purified by column chromatography with 1:1 (v/v) hexane/EtOAc as eluent, affording a yellowish oil composed of a mixture of diols **11** (11.6 g, 95%) in approximate *endo*/*exo* ratio 78:22 (as determined by ^{1}H NMR). This oil solidified spontaneously. IR (KBr) ν: 3385 (OH), 1731 (CO), 1377, 1248, 1147, 942 cm^{-1}. EIMS *m*/*z* (%): 168 (4), 126 (79), 79 (100), 70 (79), 67 (55), 58 (81). ^{1}H NMR and ^{13}C NMR for the major isomer (2-*endo*) were in accordance with the literature.[70]

4.1.2. (±)-(5-*exo*,6-*exo*)-5,6-Dibenzoyloxybicyclo[2.2.1]-hept-2-yl acetate (mixture of 2-*endo* and 2-*exo*) (12). Benzoyl chloride (8 mL, 68 mmol) was slowly added to a solution of **11** (5.00 g, 26.8 mmol) in dry pyridine (37 mL) at 0 °C, and the mixture was stirred at rt for 24 h and then placed in an ice-bath, brought to pH 8 with 2 N NaOH, and extracted with EtOAc (2×150 mL). The pooled organic extracts were washed several times with water and dried (Na_2SO_4), the solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography using 5:1 (v/v) hexane/EtOAc as eluent, which afforded the ester mixture **12** as a low melting solid (8.05 g, 76%) in approximate *endo*/*exo* ratio 4:1 (as determined by ^{1}H NMR). IR (KBr) ν: 1738, 1719, 1708, 1651, 1615, 1558, 1540, 1456, 1239, 1026, 712 cm^{-1}. EIMS *m*/*z* (%): 394 (M^+, 1), 335 (7), 289 (11), 272 (4), 186 (6), 106 (7), 105 (100), 78 (3), 77 (42), 76 (2), 51 (9). Major isomer (2-*endo*): ^{1}H NMR ($CDCl_3$) δ: 7.89–7.81 [4H, m, 2×(2′,6′-H_2)], 7.51–7.43 [2H, m, 2×(4′-H)], 7.31–7.21 [4H, m, 2×(3′,5prime;-H_2)], 5.64 (1H, dd, J=5.9, 1.4 Hz, 6-H), 5.26 (1H, dd, J=5.9, 1.3 Hz, 5-H), 5.12–5.08 (1H, m, 2-*exo*-H), 2.81 (1H, d, J=3.4 Hz, 1-H), 2.52 (1H, d, J=4.7 Hz, 4-H), 2.25–2.17 (2H, m, 3-*exo*-H+7-*H*H), 2.13 (3H, s, CH_3), 2.07–2.03 (1H, m, 7-H*H*), 1.28–1.21 (1H, m, 3-*endo*-H). ^{13}C NMR and DEPT ($CDCl_3$) δ: 171.4 (CO), 165.9 (CO), 133.3 (CH), 130.2 (C), 129.98 (CH), 129.97 (C), 128.6 (CH), 128.5 (CH), 76.6 (CH), 72.3 (CH), 72.1 (CH), 45.8 (CH), 42.0 (CH), 33.4 (CH_2), 33.0 (CH_2), 21.5 (CH_3). HRMS calcd for $C_{23}H_{22}O_6$: 394.1416. Found: 394.1409.

4.1.3. (±)-(5-*exo*,6-*exo*)-5,6-Dibenzoyloxybicyclo[2.2.1]-heptan-2-ol (mixture of 2-*endo* and 2-*exo*) (13). Solid K_2CO_3 (1.43 g, 10.3 mmol) was added to a solution of **12** (8.16 g, 20.7 mmol) in MeOH (120 mL), and the mixture was successively stirred at rt for 30 min, diluted with EtOAc (500 mL), washed with saturated NH_4Cl solution followed by water, and dried (Na_2SO_4). The organic solvents were removed under reduced pressure, and the residue was purified by silica gel column chromatography using 1:1 (v/v) hexane/EtOAc as eluent, which afforded the alcohol mixture **13** (6.71 g, 92%) as a waxy solid in approximate *endo*/*exo* ratio 4:1, as determined by ^{1}H NMR. IR (KBr) ν: 3505 (OH), 1720 (CO), 1651, 1540, 1455, 1286, 1123, 1025, 707 cm^{-1}. EIMS *m*/*z* (%): 352 (0.5, M^+), 335 (7), 289 (11), 247 (2), 230 (9), 186 (5), 136 (4), 125 (11), 108 (4), 106 (7), 105 (100), 77 (42), 51 (9). Major isomer (2-*endo*): ^{1}H NMR ($CDCl_3$) δ: 7.89–7.84 [4H, m, 2×(2′,6′-H_2)], 7.49–7.44 [2H, m, 2×(4′-H)], 7.29–7.23 [4H, m, 2×(3′,5′-H_2)], 5.79 (1H, d, J=6.0 Hz, 6-H), 5.27 (1H, d, J=6.0 Hz, 5-H), 4.39 (1H, dt, J=10.3, 4.1 Hz, 2-*exo*-H), 2.62 (1H, d, J=3.4 Hz, 1-H), 2.49 (1H, d, J=4.1 Hz, 4-H), 2.25–2.12 (2H, m, 3-*exo*-H+7-*H*H), 1.71 (1H, b s, D_2O exchang., OH), 1.47 (1H, d, J=10.8 Hz, 7-H*H*), 1.46 (1H, dt, J=13.8, 3.4 Hz, 3-*endo*-H). ^{13}C NMR and DEPT ($CDCl_3$) δ: 166.1 (CO), 166.0 (CO), 133.2 (CH), 130.4 (C), 130.0 (CH), 125.6 (CH), 77.1 (CH), 72.3 (CH), 70.3 (CH), 48.2 (CH), 42.6 (CH), 35.1 (CH_2), 33.7 (CH_2). HRMS calcd for $C_{21}H_{20}O_5$: 352.1311. Found: 352.1304.

4.1.4. (±)-(*exo*,*exo*)-5,6-Dibenzoyloxybicyclo[2.2.1]heptan-2-one (14). A solution of **13** (3.86 g, 11.0 mmol) in CH_2Cl_2 (100 mL) was added during 15 min to a stirred mixture of pyridine (11 mL), CH_2Cl_2 (110 mL) and CrO_3 (6.63 g, 66.3 mmol) kept at 0 °C, and stirring was continued for 6 h. The mixture was then filtered through celite and evaporated to dryness under reduced pressure. Purification of the resulting residue by silica gel column chromatography with 7:3 (v/v) hexane/EtOAc as eluent afforded **14** (2.99 g, 78%) as a white solid. An analytical sample was obtained by recrystallization from cyclohexane. Mp 141–142 °C. IR (KBr) ν: 1751 (CO), 1726 (CO), 1651, 1600, 1558, 1548, 1508, 1315, 1287, 708 cm^{-1}. EIMS *m*/*z* (%): 350 (M^+, 0.5), 323 (3), 322 (14), 228 (3), 186 (14), 106 (8), 105 (100), 79 (4), 78 (4), 77 (60), 76 (3), 51 (13). ^{1}H NMR ($CDCl_3$) δ: 7.90–7.82 [4H, m, 2×(2′,6′-H_2)], 7.55–7.45 [2H, m, 2×(4′-H)], 7.33–7.22 [4H, m, 2×(3′,5′-H_2)], 5.37 (2H, virtual s, 5-H+6-H), 3.01 (1H, d, J=3.8 Hz, 4-H), 2.96 (1H, s, 1-H), 2.58 (1H, d, J=11.1 Hz, 7-*H*H), 2.30 (1H, dd, J=18.6, 5.3 Hz, 3-*exo*-H), 2.16 (1H, dd, J=18.6, 4.2 Hz, 3-*endo*-H), 1.95 (1H,d, J=11.1 Hz, 7-H*H*). ^{13}C NMR and DEPT ($CDCl_3$) δ: 212.4 (CO), 165.8 (CO), 165.5 (CO), 133.62 (CH), 133.56 (CH), 130.1 (CH), 130.0 (CH), 129.8 (C), 129.7 (C), 128.7 (CH), 128.6 (CH), 75.6 (CH), 71.6 (CH), 56.3 (CH), 41.7 (CH_2), 41.2 (CH), 34.0 (CH_2). Anal. Calcd for $C_{21}H_{18}O_5$ (350.36): C, 71.99; H, 5.18. Found: C, 71.72; H, 5.28.

4.1.5. (*exo*,*exo*)-5,6-Dibenzoyloxybicyclo[2.2.1]heptane-2,3-dione (15). A mixture of **14** (1.95 g, 5.56 mmol), SeO_2 (0.61 g, 5.56 mmol) and xylenes (6 mL) was refluxed for 24 h, vacuum-filtered through celite, and condensed to dryness under reduced pressure. Purification of the resulting residue by silica gel column chromatography with 4:1 (v/v) hexane/EtOAc as eluent afforded **15**·H_2O as a white solid (1.59 g, 74%). An analytical sample was obtained by recrystallization from EtOAc–hexane. Mp 109–110 °C. IR (KBr) ν: 3423, 1777, 1723, 1600, 1450, 1279, 1114, 713 cm^{-1}. Anal. Calcd for $C_{21}H_{16}O_6 \cdot H_2O$ (382.36): C, 65.96; H, 4.74. Found: C, 66.21; H, 4.57.

4.1.6. (*exo*,*exo*)-1,2,3,4-Tetrahydro-1,4-methanophenazine-2,3-diyl dibenzoate (16). A mixture of **15**·H_2O (1.45 g, 3.79 mmol), *o*-phenylenediamine (1.10 g, 10.5 mmol) and the zinc catalyst $ZnCl_2[C_6H_5CH(NH_2)-CH_3]_2$ (10 mg) in dry THF (33 mL) was refluxed for 18 h. The solvent was then evaporated off, and chromatographic purification of the resulting crude product with 7:3 (v/v) hexane/EtOAc as eluent afforded **16** (1.31 g, 79%) as a white solid. An analytical sample was obtained by recrystallization from EtOAc–hexane. Mp 194–195 °C. IR

(KBr) ν: 1731, 1716, 1600, 1276, 1120, 1072, 971, 760, 708 cm^{-1}. EIMS *m/z* (%): 437 (14, M+1), 436 (47, M^+), 331 (16), 209 (11), 181 (8), 169 (11), 105 (100), 77 (24). ^1H NMR ($CDCl_3$) δ: 8.06 (2H, dd, $J=6.3$, 3.3 Hz, 6-H+9-H), 7.90 [4H, d, $J=8.0$ Hz, 2×(2′,6′-H_2)], 7.73 (2H, dd, $J=6.2$, 3.5 Hz, 7-H+8-H), 7.50 [2H, t, $J=7.3$ Hz, 2×(4′-H)], 7.28 [4H, t, $J=7.7$ Hz, 2×(3′,5′-H_2)], 5.48 (2H, s, 2-H+3-H), 3.87 (2H,s, 1-H+4-H), 2.96 (1H, d, $J=10.3$ Hz, 7-*H*H), 2.44 (1H, d, $J=10.3$ Hz, 7-H*H*). ^{13}C NMR and DEPT ($CDCl_3$) δ: 165.6 (CO), 159.9 (C), 142.4 (C), 133.6 (CH), 130.1 (CH), 129.9 (CH), 129.8 (C), 129.6 (CH), 128.7 (CH), 73.3 (CH), 50.1 (CH), 42.0 (CH_2). Anal. Calcd for $C_{27}H_{20}N_2O_4$ (436.47): C, 74.30; H, 4.62; N, 6.42. Found: C, 74.11; H, 4.71; N 6.29.

4.1.7. *E*-1-(2,3-Dihydro-1*H*-cyclopenta[*b*]quinoxalin-1-ylidene)-1,2-ethanediol (17). 1 N KOH (20 mL) was added to a solution of **16** (1.25 g, 2.86 mmol) in MeOH (3 mL), and the mixture was stirred at rt for 12 h, brought to pH 8 with 1 N HCl, concentrated under reduced pressure, and extracted with CH_2Cl_2 (2×20 mL). The pooled extracts were washed with saturated NaCl solution and dried (Na_2SO_4), and the solvent was removed under reduced pressure. The purification of the resulting residue by flash chromatography with 10:1 (v/v) EtOAc/MeOH as eluent afforded **17** as a deep green solid (0.43 g, 66%), solutions of which changed with time from fluorescent green to black. The best samples were obtained by rapid recrystallization from EtOAc–hexane. The product obtained by chromatography was used directly to obtain its diacetylated derivative. IR (KBr) ν: 3434, 3318, 1644, 1610, 1580, 1558, 1232, 1068, 901, 770, 600 cm^{-1}. EIMS *m/z* (%): 228 (32, M^+), 197 (71), 170 (41), 169 (61), 168 (26), 58 (100), 52 (2). ^1H NMR ($CDCl_3$) δ: 10.32 (1H, b s, D_2O exchang., 1-OH), 7.55 (1H, dt, $J=7.9$, 1.2 Hz), 7.32 (1H, dt, $J=7.7$, 1.3 Hz), 7.18 (1H, dt, $J=7.7$, 1.3 Hz), 7.04 (1H, dt, $J=7.9$, 1.2 Hz), 4.34 (2H, s, CH_2O), 3.49 (1H, b s, D_2O exchang., 2-OH), 3.06–3.02 (2H, m), 2.81–2.77 (2H, m). ^{13}C NMR and DEPT ($CDCl_3$) δ: 194.6 (C), 171.1 (C), 143.3 (C), 136.5 (C), 129.6 (CH), 129.3 (C), 128.6 (CH), 124.7 (CH), 115.8 (CH), 105.9 (C), 65.7 (CH_2), 30.2 (CH_2), 22.7 (CH_2).

4.1.8. *E*-1-(2,3-Dihydro-1*H*-cyclopenta[*b*]quinoxalin-1-ylidene)ethane-1,2-diyl diacetate (18). Acetic anhydride (5 mL) was slowly added to a solution of **17** (0.30 g, 1.31 mmol) in dry pyridine (5 mL), and the mixture was stirred at rt for 14 h. The solvent and excess reagent were removed under reduced pressure, and purification of the residue by silica gel column chromatography with 1:1 (v/v) EtOAc/hexane as eluent afforded **18** as a white solid (0.35 g, 85%). An analytical sample was obtained by recrystallization from EtOAc–hexane. Mp 136–137 °C. IR (KBr) ν: 1758, 1736, 1437, 1375, 1230, 1170, 1102, 1017, 803 cm^{-1}. EIMS *m/z* (%): 312 (7, M^+), 253 (35), 213 (23), 211 (29), 195 (12), 61 (100), 59 (12), 43 (82), 42 (82), 42 (29), 41 (39), 33 (17), 28 (87), 19 (49), 17 (76). ^1H NMR ($CDCl_3$) δ: 8.07–8.03 (1H, m), 8.00–7.97 (1H, m), 7.73–7.67 (2H, m), 5.76 (2H, s, CH_2O), 3.27–3.22 (2H, m), 2.96–2.90 (2H, m), 2.27 (3H, s, CH_3), 2.11 (3H, s, CH_3). ^{13}C NMR and DEPT ($CDCl_3$) δ: 171.2 (CO), 168.5 (CO), 162.5 (C), 152.6 (C), 145.2 (C), 142.1 (C), 142.0 (C), 131.0 (C), 130.3 (CH), 130.2 (CH), 129.7 (CH), 128.9 (CH), 60.7 (CH_2), 29.3 (CH_2), 24.6 (CH_2), 21.3 (CH_3), 21.1 (CH_3). Anal. Calcd for $C_{17}H_{16}N_2O_4$ (312.33): C, 65.38; H, 5.16; N, 8.97. Found: C, 65.17; H, 5.23; N 8.84.

4.1.9. (±)-5,6-Dioxobicyclo[2.2.1]hept-2-yl acetate (mixture of *endo* and *exo*) (23). Dry DMSO (7 mL) was added very slowly to a solution of dry trifluoroacetic anhydride (12.3 mL, 88.1 mmol) in dry CH_2Cl_2 (52 mL) at −78 °C (internal temperature), and the mixture was stirred for 10 min, treated with a solution of the acetate mixture **11** (5.75 g, 30.9 mmol) in CH_2Cl_2 (15 mL), stirred at −78 °C for 2.5 h, treated with Et_3N (23 mL), stirred at −78 °C for a further 3 h, allowed to reach 0 °C, transferred to an ice-bath, acidified with 3 M HCl, and extracted with CH_2Cl_2 (2× 120 mL). The pooled extracts were washed with brine and dried (Na_2SO_4), and the solvent was removed under reduced pressure, leaving the acetate mixture **23** as a dark, viscous oil (4.03 g). Crude product was used directly in the next synthetic step. A small sample (0.53 g) was resolved by silica gel column chromatography with 7:1 (v/v) hexane/EtOAc as eluent into the two epimers of **23**, isolated as clear oils.

Compound endo-**23**. IR (NaCl) ν: 1747 (CO), 1407, 1244, 1046 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 5.39 (1H, ddd, $J=9.5$, 5.5, 3.5 Hz, 2-*exo*-H), 3.37 (1H, dd, $J=5.1$, 1.2 Hz, m, 1-H), 3.06 (1H, d, $J=5.1$ Hz, 4-H), 2.65 (1H ddd, $J=14.7$, 9.9, 5.1 Hz, 3-*exo*-H), 2.30–1.98 (2H, m, 7-H_2), 1.97 (3H, s, CH_3), 1.72 (1H, dt, $J=14.7$, 3.0 Hz, 3-*endo*-H).

Compound exo-**23**. IR (NaCl) ν: 1740 (CO), 1376, 1230, 1057 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 4.87 (1H, d, $J=6.9$ Hz, 2-*endo*-H), 2.79–2.76 (1H, m, 1-H), 2.09–1.99 (1H, m, 4-H), 2.03 (3H, s, CH_3), 1.89–1.70 (2H, m, 7-H_2), 1.14–1.04 (1H, m, 3-*exo*-H), 0.89–0.82 (1H, m, 3-*endo*-H).

4.1.10. (±)-*endo*- and (±)-*exo*-1,2,3,4-Tetrahydro-1,4-methanophenazin-2-yl acetates (24a and 24b). *o*-Phenylenediamine (2.70 g, 25.0 mmol) and the zinc catalyst $ZnCl_2[C_6H_5CH(NH_2)CH_3]_2$ (10 mg) were added to a solution of the crude product of the previous reaction (3.50 g) in dry THF (80 mL), and the mixture was refluxed for 4.5 h. The solvent was then removed under reduced pressure, and fractionation of the residue by column chromatography, first with 7:3 (v/v) hexane/EtOAc as eluent which afforded the minor isomer **24b** (0.37 g) and then with 4:6 (v/v) hexane/EtOAc to isolate the major isomer, **24a** (1.47 g) (joint yield from mixture **11**, 27%). Analytical samples of both isomers were obtained by recrystallization from EtOAc/hexane.

Compound **24a**. White solid, mp 131–132 °C. IR (KBr) ν: 1730 (CO), −339, 1114, 769 cm^{-1}. EIMS *m/z* (%): 254 (47, M^+), 212 (64), 184 (76), 183 (100), 181 (29), 169 (31), 168 (69), 76 (9). ^1H NMR ($CDCl_3$) δ: 8.07–8.01 (2H, m, 6-H+9-H), 7.71–7.68 (2H, m, 7-H+8-H), 5.62 (1H, ddd, $J=9.4$, 4.5, 3.1 Hz, 2-*exo*-H), 3.86 (1H, dd, $J=4.5$, 1.4 Hz, 1-H), 3.58 (1H, d, $J=3.3$ Hz, 4-H), 2.71 (1H, ddd, $J=13.6$, 9.5, 4.5 Hz, 3-*exo*-H), 2.16 (1H, dm, $J=10.5$ Hz, 11-*H*H), 2.06 (1H, dm, $J=10.5$ Hz, 11-H*H*), 1.82 (3H, s, CH_3), 1.43 (1H, dt, $J=13.6$, 3.2 Hz, 3-*endo*-H). ^{13}C NMR and DEPT ($CDCl_3$) δ: 171.2 (CO), 163.4 (C), 159.8 (C), 142.1 (C), 142.0 (C), 129.4 (CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 73.2 (CH), 48.6 (CH), 44.4 (CH_2), 43.9 (CH), 35.2 (CH_2),

21.2 (CH_3). Anal. Calcd for $C_{15}H_{14}N_2O_2$ (254.29): C, 70.85; H, 5.55; N, 11.02. Found: C, 70.68; H, 5.63; N 10.84.

Compound **24b**. White solid, mp 83–84 °C. IR (KBr) ν: 1731 (CO), 1460, 1033, 762 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.77–7.71 (2H, m, 6-H+9-H), 7.41–7.38 (2H, m, 7-H+8-H), 4.74–4.76 (1H, m, 2-*endo*-H), 3.46 (1H, s, 1-H), 3.37 (1H, d, J=2.8 Hz, 4-H), 2.12 (1H, d, J=10.0 Hz, 11-*H*H), 1.97 (1H, d, J=10.0 Hz, 11-H*H*), 1.88 (3H, s, CH_3), 1.91–1.80 (2H, m, 3-H_2). ^{13}C NMR and DEPT ($CDCl_3$) δ: 170.2 (CO), 163.8 (C), 159.7 (C), 141.4 (C), 141.3 (C), 129.1 (CH), 129.0 (CH), 128.9 (CH), 128.7 (CH), 73.8 (CH), 50.1 (CH), 43.5 (CH), 42.8 (CH_2), 36.5 (CH_2), 21.2 (CH_3). Anal. Calcd for $C_{15}H_{14}N_2O_2$ (254.29): C, 70.85; H, 5.55; N, 11.02. Found: C, 70.74; H, 5.62; N, 10.87.

4.1.11. (±)-*endo*-1,2,3,4-Tetrahydro-1,4-methanophenazin-2-ol (4a). Na_2CO_3 (2.00 g, 18.86 mmol) was added to a solution of **24a** (1.00 g, 3.93 mmol) in MeOH (25 mL), and the mixture was stirred vigorously for 2 h. The MeOH was then removed under reduced pressure, and the residue was taken into water (50 mL) and extracted with EtOAc (2× 100 mL). The pooled organic extracts were dried (Na_2SO_4), the solvent was removed under reduced pressure, and purification of the solid residue by silica gel column chromatography with 10:1 (v/v) EtOAc/hexane as eluent afforded **4a** as a white solid (0.77 g, 92%). An analytical sample was obtained by recrystallization from EtOAc/hexane. Mp 171–172 °C. IR (KBr) ν: 3208 (OH), 1510, 1465, 1367, 1343, 1309, 1288, 1235, 1202, 1183, 1134, 1118, 1076, 1054, 941, 767 cm^{-1}. EIMS *m/z* (%): 212 (41, M^+), 183 (100), 169 (32), 167 (49), 102 (16), 76 (10), 50 (11). ^1H NMR ($CDCl_3$) δ: 8.03–7.99 (2H, m, 6-H+9-H), 7.70–7.63 (2H, m, 7-H+8-H), 5.00 (1H, ddd, J=9.4, 4.3, 3.4 Hz, 2-*exo*-H), 3.96 (1H, b s, D_2O exchang., OH), 3.62–3.54 (2H, m, 1-H+4-H), 2.67 (1H, ddd, J=13.3, 9.2, 4.4 Hz, 3-*exo*-H), 2.09 (1H, dm, J=10.3 Hz, 11-*H*H), 2.00 (1H, d, J=10.3 Hz, 11-H*H*), 1.37 (1H, dt, J=13.3, 3.1 Hz, 3-*endo*-H). ^{13}C NMR and DEPT ($CDCl_3$) δ: 164.2 (C), 160.6 (C), 142.1 (C), 141.5 (C), 129.4 (CH), 129.1 (CH), 129.0 (CH), 128.8 (CH), 71.3 (CH), 51.3 (CH), 44.5 (CH_2), 44.4 (CH), 37.1 (CH_2). Anal. Calcd for $C_{13}H_{12}N_2O$ (212.25): C, 73.56; H, 5.70; N, 13.20. Found: C, 73.38; H, 5.77; N 13.04.

4.1.12. (±)-*exo*-1,2,3,4-Tetrahydro-1,4-methanophenazin-2-ol (4b). Compound **4b** was obtained from **24b** in the same way as **4a** from **24a**. Yield 93%. Mp 154–155 °C. IR (KBr) ν: 3262, 1541, 1512, 1452, 1440, 1401, 1360, 1329, 1307, 1283, 1241, 1227, 1196, 1166, 1154, 1125, 1082, 1053, 1019, 972, 959, 916, 902, 839, 772, 717, 677 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 7.99–7.96 (2H, m, 6-H+9-H), 7.69–7.65 (2H, m, 7-H+8-H), 4.34 (1H, d, J=4.9 Hz, 2-*endo*-H), 3.60–3.57 (2H, m, 1-H+4-H), 2.52 (1H, d, J=10.0 Hz, 11-*H*H), 2.20 (1H, d, J=10.0 Hz, 11-H*H*), 2.14–2.00 (2H, m, 3-H_2). Anal. Calcd for $C_{13}H_{12}N_2O$ (212.25): C, 73.56; H, 5.70; N, 13.20. Found: C, 73.31; H, 5.83; N 13.12.

4.1.13. 2-(2,3-Dihydro-1*H*-cyclopenta[*b*]quinoxalin-1-yl)ethanol (26). (a) $NaBH_4$ (17 mg, 0.45 mmol) was added to a solution of **25** (77 mg of the chromatographed material) in EtOH (4 mL), and the mixture was successively stirred at rt for 14 h, treated with 1 N HCl (1 mL), brought to about pH 8 with saturated $NaHCO_3$ solution, and extracted with EtOAc (2×10 mL). The pooled organic extracts were dried (Na_2SO_4), the solvent was removed under reduced pressure, and purification of the residue by silica gel column chromatography with 7:3 (v/v) EtOAc/hexane as eluent afforded **26** as a clear oil that subsequently crystallized (50 mg; overall yield with regard to **24a**, 51%). An analytical sample was obtained by recrystallization from EtOAc/hexane. Mp 80–81 °C. IR (KBr) ν: 3284 (OH), 1375, 1323, 1145, 1057, 774 cm^{-1}. EIMS *m/z* (%): 214 (13, M^+), 184 (23), 183 (38), 182 (17), 181 (29), 168 (100), 102 (27), 89 (15), 77 (29), 76 (29), 75 (23), 63 (15), 51 (17), 50 (21), 39 (13), 31 (22). ^1H NMR ($CDCl_3$) δ: 8.04–8.00 (2H, m, 5-H+8-H), 7.72–7.68 (2H, m, 6-H+7-H), 5.12 (1H, b s, D_2O exchang., OH), 3.99 (2H, t, J=6.8 Hz, CH_2O), 3.49–3.43 (1H, m, 1-H), 3.22–3.17 (2H, m, 3-H_2), 2.61–2.54 (1H, m, 1-C*H*H), 2.10–1.90 (3H, m, 1-CH*H*+2-H_2). ^{13}C NMR and DEPT ($CDCl_3$) δ: 162.4 (C), 161.2 (C), 142.1 (C), 140.8 (C), 129.6 (CH), 129.5 (CH), 129.1 (CH), 128.8 (CH), 62.7 (CH_2), 44.6 (CH), 36.5 (CH_2), 31.8 (CH_2), 30.1 (CH_2). Anal. Calcd for $C_{13}H_{14}N_2O$ (214.27): C, 72.87; H, 6.59; N, 13.07. Found: C, 72.69; H, 6.70; N 13.00.

(b) Alternatively, a solution of alcohol **4a** (100 mg, 0.47 mmol), Na_2CO_3 (98 mg, 0.92 mmol) and $NaBH_4$ (35 mg, 0.92 mmol) in EtOH (2 mL) was stirred at rt for 18 h, diluted with water (5 mL) and extracted with EtOAc (2×10 mL). Work-up and purification as in method (a) afforded a product (64 mg, 63%) with characteristics identical to those of **26** prepared as above.

4.1.14. 2-(2,3-Dihydro-1*H*-cyclopenta[*b*]quinoxalin-1-yl)ethyl acetate (27). Alcohol **26** (25 mg, 0.12 mmol) was dissolved in a mixture of dry pyridine (1 mL) and Ac_2O (1 mL), and this solution was stirred at rt for 18 h, poured over crushed ice (5 g), stirred for 1 h more, and extracted with EtOAc (2×5 mL). The pooled extracts were washed successively with 2 N HCl (5 mL) and brine, and dried (Na_2SO_4). Removal of the solvent under reduced pressure then left **27** as a colourless oil (23 mg, 77%). IR (NaCl) ν: 1736 (CO), 1653, 1497, 1459, 1366, 1241, 1120, 764 cm^{-1}. EIMS *m/z* (%): 256 (19, M^+), 213 (14), 196 (99), 186 (23), 185 (20), 184 (22), 183 (79), 181 (48), 168 (100), 142 (14), 129 (21), 115 (19), 103 (18), 102 (47), 90 (14), 89 (33), 78 (14), 77 (37), 76 (37), 75 (31), 63 (17), 51 (16), 50 (21), 43 (21), 42 (60), 41 (19), 39 (17). ^1H NMR ($CDCl_3$) δ: 8.01–7.95 (2H, m, 5-H+8-H), 7.66–7.61 (2H, m, 6-H+7-H), 4.35 (2H, t, J=6.6 Hz, CH_2O), 3.40–3.31 (1H, m, 1-H), 3.17–3.08 (2H, m, 3-H_2), 2.59–2.43 (2H, m, 1-CH_2), 2.02 (3H, s, CH_3), 1.97–1.84 (2H, m, 2-H_2). ^{13}C NMR and DEPT ($CDCl_3$) δ: 171. 5 (CO), 162.3 (C), 160.6 (C), 142.1 (C), 142.1 (C), 129.4 (CH), 129.3 (CH), 129.14 (CH), 129.10 (CH), 63.0 (CH_2), 41.1 (CH), 32.7 (CH_2), 31.4 (CH_2), 29.0 (CH_2), 21.4 (CH_3). HRMS calcd for $C_{15}H_{16}N_2O_2$: 256.1212. Found: 256.1218.

4.1.15. (2,3-Dihydro-1*H*-cyclopenta[*b*]quinoxalin-1-yl) acetic acid (28). Acetate **24a** (240 mg, 0.94 mmol) was treated and worked up as in the preparation of **4a** except that reaction was prolonged for 6 h. Chromatography of the crude product with 10:1 (v/v) EtOAc/hexane as eluent, afforded a dark slurry (159 mg) that consisted very predominantly of **25** (90% as determined by ^1H NMR;

estimated yield in **25**, 71%). This material was used directly in subsequent transformations.

Compound **25**. IR (KBr) ν: 1722 (CO) cm^{-1}. EIMS *m/z* (%): 212 (1, M^+), 184 (76), 183 (100, M−CHO), 169 (44), 168 (21), 102 (9), 76 (8), 58 (9). ^1H NMR ($CDCl_3$) δ: 9.88 (1H, s, CHO). ^{13}C NMR and DEPT ($CDCl_3$) δ: 201.0 (CHO), 161.3 (C), 160.3 (C), 141.93 (C), 141.86 (C), 129.4 (CH), 129.2 (CH), 129.1 (CH), 129.0 (CH), 47.5 (CH_2), 38.3 (CH), 31.3 (CH_2), 29.3 (CH_2).

Minor contaminant: EIMS *m/z* (%): 424 (7), 213 (44), 212 (23), 184 (33), 183 (100), 181 (32), 169 (100), 168 (47), 129 (7), 102 (10), 77 (11).

A solution of the above product (66 mg) in MeOH (2 mL) was treated with 3 drops of Tollens' reagent,[71] left for 3 h at rt (a silver mirror was formed on the wall of the flask), diluted with water (10 mL), extracted with $CHCl_3$ (5 mL), brought to pH 5 with formic acid, and finally extracted with EtOAc (2×5 mL). These last extracts were pooled and dried (Na_2SO_4), and the solvent was removed under reduced pressure, leaving **28** as a yellowish thick paste (40 mg; yield, 45% with regard to starting **24a**). IR (NaCl) ν: 3420, 2508, 1718, 1507, 1329, 1192, 770 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.05–8.00 (2H, m, 5-H+8-H), 7.70–7.67 (2H, m, 6-H+7-H), 3.82–3.71 (1H, m, 1-H), 3.27–3.17 (3H, m, 1-C*H*H+3-H_2), 2.77–2.63 (2H, m, 1-CH*H*+2-*H*H), 1.98 (1H, dd, J=12.9, 9.2 Hz, 2-H*H*).

4.1.16. Methyl (2,3-dihydro-1*H*-cyclopenta[*b*]quinoxalin-1-yl)acetate (29). *p*-Toluenesulfonic acid (5 mg) was added to a solution of **28** (35 mg, 0.15 mmol) in dry MeOH (3 mL), and the mixture was refluxed under argon for 3.5 h, mixed with saturated $NaHCO_3$ solution (5 mL), and extracted with EtOAc (2×5 mL). The pooled organic extracts were dried (Na_2SO_4) and the solvent was removed under reduced pressure, leaving **29** as a clear oil that solidified spontaneously (25 mg, 67%). An analytical sample was obtained by recrystallization from EtOAc/hexane. Mp 155 °C, dec.). IR (KBr) ν: 1732 (CO), 1560, 1501, 1436, 1369, 1325, 1263, 1196, 1171, 764 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 8.03–7.98 (2H, m, 5-H+8-H), 7.69–7.65 (2H, m, 6-H+7-H), 3.82–3.70 (1H, m, 1-H), 3.74 (3H, s, CH_3), 3.28–3.15 (3H, m, 1-C*H*H+3-H_2), 2.73–2.58 (2H, m, 1-CH*H*+2-*H*H), 1.95 (1H, m, J=12.9, 9.2 Hz, 2-H*H*). ^{13}C NMR and DEPT ($CDCl_3$) δ: 173.0 (CO), 161.3 (C), 160.5 (C), 142.1 (C), 142.0 (C), 129.4 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 52.2 (CH_3), 40.5 (CH), 37.8 (CH_2), 31.3 (CH_2), 29.2 (CH_2). Anal. Calcd for $C_{14}H_{14}N_2O_2$ (242.28): C, 69.41; H, 5.82; N, 11.56. Found: C, 69.28; H, 5.89; N 11.60.

4.1.17. 1,2,3,4-Tetrahydro-1,4-methanophenazin-2-one (5). To a solution of dry pyridine (0.67 mL, 8.4 mmol) in CH_2Cl_2 (7.5 mL) at 0 °C was added CrO_3 (0.42 g, 4.2 mmol) followed by a solution of **4a** (150 mg, 0.71 mmol) in CH_2Cl_2 (3.5 mL). The reaction mixture was left stirring overnight at rt, and was then filtered through celite. The celite was washed with EtOAc (10 mL), the pooled filtrates were dried (Na_2SO_4), and the solvents were removed under reduced pressure. Purification of the residue by silica gel column chromatography with 7:3 (v/v) EtOAc/hexane as eluent afforded **5** as a clear yellowish oil (99 mg, 67%). IR (NaCl) ν: 1751 (CO), 1578, 1510, 1463, 1410, 1361, 1303, 1274, 1254, 1216, 1200, 1158, 1111, 1086, 1059, 957, 834, 762, 732, 700 cm^{-1}. EIMS *m/z* (%): 210 (75, M^+), 181 (100), 168 (99), 140 (20), 129 (31), 128 (22), 103 (27), 102 (39), 91 (28), 78 (25), 77 (22), 76 (62), 75 (20), 74 (25), 64 (20), 63 (30), 53 (21), 52 (22), 51 (32), 50 (42), 39 (27). ^1H NMR ($CDCl_3$) δ: 7.91–7.86 (2H, m, 6-H+9-H), 7.62–7.56 (2H, m, 7-H+8-H), 3.85–3.82 (2H, m, 1-H+4-H), 2.66–2.54 (2H, m, 3-*exo*-H+11-*H*H), 2.46 (1H, dd, J=10.4, 1.2 Hz, 11-H*H*), 2.16 (1H, dd, J=17.8, 4.3 Hz, 3-*endo*-H). ^{13}C NMR and DEPT ($CDCl_3$) δ: 208.2 (CO), 163.1 (C), 156.3 (C), 142.1 (C), 141.6 (C), 129.9 (CH), 129.6 (CH), 129.5 (CH), 129.2 (CH), 59.9 (CH), 46.7 (CH_2), 42.6 (CH), 40.2 (CH_2). HRMS calcd for $C_{13}H_{10}N_2O$: 210.0793. Found: 210.0801.

^1H and ^{13}C NMR spectra obtained after **5** had been left in an NMR spectrometry tube for 3 days at rt showed signals of **5** and **28** in approximately 1:1 ratio.

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