Carbohydrate α-oxoketene N,O-ketals in the synthesis of dihydroquinolines

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The carbohydrate nitro enone **1** was found to react with amines to give α-ketene ketals; the formation of carbohydrate azo derivatives could be suppressed by addition of an electron-rich aniline quenching agent. Upon reaction with benzaldehyde in the presence of trifluoroacetic acid, the α-oxoketene ketals afforded dihydroquinolines in a cyclization reaction forming two new carbon–carbon bonds. For the dihydroquinoline **18** the newly formed stereocenter was ascertained by X-ray crystallography. The two-step reaction could be carried out as one multicomponent reaction. Electron-poor anilines led to Hantzsch-type products incorporating two enaminone molecules; the crystal structure of representative **30** is reported.

Introduction

Multicomponent reactions[1–3] represent an ideal method to construct compound libraries.[4–7] The variation of two or more components of the reaction can make available a large number of compounds and increase chemical diversity. We describe here a multicomponent reaction employing a carbohydrate α-oxoketene acetal as an intermediate. α-Oxoketene ketals are versatile precursors known to undergo regio-, stereo-, and chemoselective C–C bond-forming reactions due to their polarized double bond.[8,9] In particular, ketene S,S-, N,S-, S,O-, and N,N-ketals have found widespread use in organic synthesis.[10,11] α-Oxoketene O,O-[12] and N,O-ketals were used to a lesser extent.[13–16] Various representatives of this class, such as amino-substituted chromones, have been found to be of interest in a pharmaceutical context.[17,18] Carbohydrate α-oxoketene N,O-ketals have not been reported yet with the exception of the mention of a furanose derivative (1-amino-1-deoxy-L-*threo*-hex-1-enofuranos-3-ulose) which was not described in detail.[19] Related pyranose α-oxoketene S,S- and S,O-ketals with substituted ketene double bonds were published by the Peseke group.[20–22]

Results and discussion

As our key starting material we chose the alkoxy nitro enone **1**, which was synthesized from the known[23] nitro sugar **2** by Swern oxidation (Scheme 1). The synthesis was carried out on a multigram scale to have sufficient material for preliminary experiments and automated synthesis. We first studied the reactivity of alkoxy nitro enone **1**. Reaction with aniline in toluene resulted in imine **3** according to mass spectrometry; this compound was, however, not isolated. In contrast, the same reaction in the more polar solvent dichloromethane led to substitution of the nitro group and afforded the α-oxoketene N,O-ketal **4** in excellent yield (Scheme 1). The nitro-substitution of an alkoxy nitro enone with an amine represents a new approach to α-oxoketene N,O-ketals.

The reaction could be carried out also with other amines as summarized in Table 1. More polar solvents, chosen for solubility reasons, were compatible with the reaction (entries 3–5). While these results were obtained with short reaction times, longer reaction times and electron-rich anilines gave rise to azo derivatives **13** and **14** (Scheme 2, entries 6 and 7 in Table 1). This side reaction can be understood as an electrophilic attack of an intermediate diazonium salt resulting from nitrosation of the
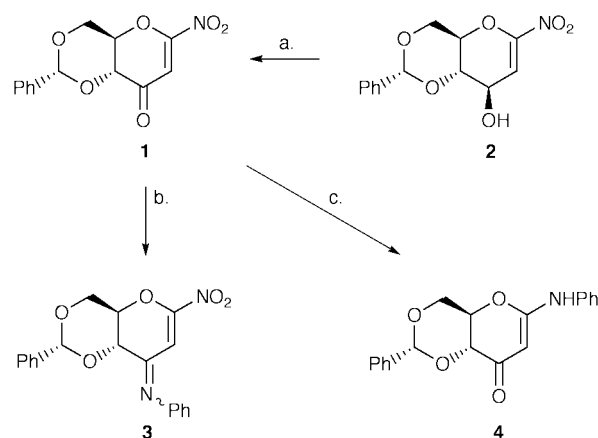
Scheme 1 *Reagents and conditions (and yields)*: (a) DMSO, CH$_2$Cl$_2$, (COCl)$_2$, DIPEA, −40 °C, 2.5 h (75%); (b) PhNH$_2$, toluene, rt, 5 min; (c) PhNH$_2$, CH$_2$Cl$_2$, rt, 5 min (97%).
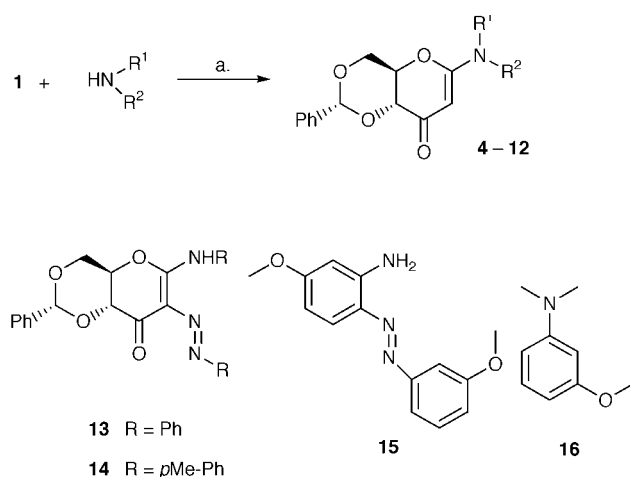
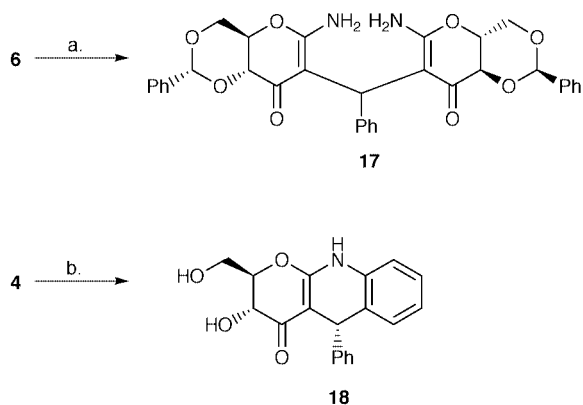**Scheme 2** *Reagents and conditions (and yields)*: see Table 1.

aniline by *in situ*-generated nitrosonium derivatives. Reaction of **1** with *m*-methoxyaniline furnished the α-oxoketene N,O-ketal **10** in good yield; in addition a small amount of azo derivative **15** was isolated. This observation signalled that the electron-rich aniline was more readily attacked than the enone double bond (entry 8).

Table 1 Reactions of **1** with amines R^{1}NHR^2 (see Scheme 2)

Entry	R^1	R^2	Solvent	Additive	T/°C	Time	Products (yield/%)
1	H	Ph	CH$_2$Cl$_2$		rt	5 min	**4** (97)
2	H	Bn	CH$_2$Cl$_2$		0	30 min	**5** (80)
3	H	H	THF		0	20 min	**6** (70)
4	-(CH$_2$)$_5$		EtOH–THF		0	1 h	**7** (94)
5	H	α-naphthyl	CH$_2$Cl$_2$–THF		0	4 min	**8** (76)
6	H	Ph	CH$_2$Cl$_2$		rt	2 d	**4** (20) + **13** (24)
7	H	4-MeC$_6$H$_4$	CH$_2$Cl$_2$		rt	4 h	**9** (33) + **14** (56)
8	H	3-(MeO)C$_6$H$_4$	CH$_2$Cl$_2$		rt	30 min	**10** (80) + **15** (5)
9	H	Ph	CH$_2$Cl$_2$	16	0–rt	2 h	**4** (72)
10	H	4-MeC$_6$H$_4$	CH$_2$Cl$_2$	16	0–rt	2 h	**9** (85)
11	H	β-naphthyl	CH$_2$Cl$_2$	16	0–rt	2 h	**11** (55)
12	H	3-(PhO)C$_6$H$_4$	CH$_2$Cl$_2$	16	0–rt	2 h	**12** (74)

For the application of this reaction in a multicomponent condensation it was desirable to have a greater range of reaction times and temperatures available. Therefore, *m*-methoxy-*N,N*-dimethylaniline **16** was used in the following reactions to quench any diazonium salts. A comparative experiment with aniline demonstrated that in the presence of quenching agent **16** the α-oxoketene N,O-ketal **4** could be obtained in reasonable yield upon prolonged reaction time (entry 9); no carbohydrate azo derivative was detected; instead azo derivatives of **16** such as 3-methoxy-*N,N*-dimethyl-4-(phenylazo)aniline[24] could be isolated (details not shown). Also the reaction of **1** with 4-methylaniline afforded a good yield of **9** in the presence of additive **16** (entry 10). As further shown with β-naphthylamine and 3-phenoxyaniline, the use of quenching agent **16** allowed the reaction of **1** with electron-rich anilines. In all cases, the addition of **16** avoided the formation of carbohydrate azo derivatives. Thus, anilines are one suitable component in the multicomponent reaction of alkoxy nitro enone **1**. As a second component we looked at aldehydes. Reaction of hemiketal **6** with benzaldehyde in the presence of zinc chloride–diethyl ether as Lewis acid furnished the C_2-symmetrical toluene derivative **17** in 85% yield, reflecting the good reactivity of C-2 of the oxoketene ketal. Compound **17** is a representative of a new class of carbohydrate mimetics[25] in which two saccharide units are linked *via* C-2 of the pyranose rings. The *m*-methoxyaniline derivative **10** was less reactive than **6** under similar reaction conditions and, under prolonged reaction time, led to a mixture of reaction products including a benzaldehyde hemiacetal and a partially debenzylidenated product (data not shown).

Under different conditions the course of the reaction changed. Reaction of **4** with benzaldehyde in the presence of trifluoroacetic acid (TFA) gave the sugar-anellated dihydroquinoline **18** (Scheme 3). In this reaction two new carbon–carbon bonds were formed, and the benzylidene protecting group was cleaved. Only one diastereomer was isolated after
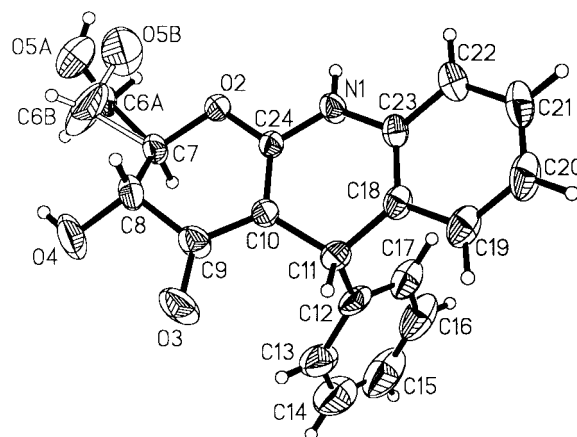

Fig. 1 Monoview of the X-ray structure of compound **18**. Atoms are drawn with anisotropic displacement parameters at 30% probability level with arbitrary numbering of the non-hydrogen atoms. The side chain at C-7 (arbitrary numbering) is disordered and was refined in two main conformations.

the reaction; a minor, unidentified compound, less than 10% of **18**, was removed by chromatography. Product **18** could be crystallized and was subjected to X-ray crystallography; the structure is depicted in Fig. 1. The stereocenters in the pyranose ring were not affected during the reaction, and the newly formed stereocenter could be classified as having 5S-configuration. One characteristic feature of the structure of **18** is the *quasi*-axial orientation of the phenyl group attached to C-5. A very similar conformation has been observed in numerous related 1,4-dihydropyridines[26] as well as dihydroquinolines[27] and dihydropyridones,[28] structures that have been studied by X-ray crystallography due to their interesting pharmacological properties as calcium-channel modulators.

Reaction of the *p*-methyl-substituted **9** with benzaldehyde–TFA gave a mixture of diastereomers **19**, with the 5S-isomer **19S** prevailing (Scheme 4). Tentative assignments of absolute configuration at C-5 were made according to NMR spectra based on the shifts of 2-H of the pyranose ring; in the 5R isomer 2-H resonated at lower field in deuterated DMSO than in the 5S isomer (for 5S: δ(2-H) 3.70–4.25 ppm). In addition, the shifts of H-3 and of the OH- and NH-signals in deuterated DMSO followed a similar pattern (for 5S: δ(1′-OH) ≤ 5.04, δ′(3-OH) ≤ 5.44 ppm). Oxidation of the dihydroquinolines with cerium(IV) ammonium nitrate (CAN) furnished the sugar-anellated quinoline derivative **22** in good yield (Table 2). CAN had been stated to cleanly oxidize 1,4-dihydropyridine-3,5-dicarboxylates,[29] but a variety of other reagents have also been used for this purpose.[30] The isolation of a single oxidation product further supported the suggestion that the diastereomers **19** were epimeric at C-5. Next we investigated the reaction of α-naphthyl derivative **8** with benzaldehyde–TFA: two diastereomers **20R/S** were found, with a slight excess of the 5S-

17

18

Scheme 3 *Reagents and conditions (and yields):* (a) PhCHO, THF, ZnCl$_2$·Et$_2$O, CH$_2$Cl$_2$, rt, 3 days (85%); (b) PhCHO, TFA, rt, 1 day (36%).

Table 2 Formation of dihydroquinolines and quinolines (see Scheme 4)

Entry	R^1	R^2	R^3	R^4	Dihydroquinoline (yield/%)	[$R:S$]	Quinoline (yield/%)
1	H	H	CH₃	H	**19** (63)	1:5	**22** (83)
2	o-phenylene		H	H	**20** (85)	1:1.75	**23** (78)
3	H	o-phenylene		H	**21** (87)	1.8:1	**24** (74)
4	H	OPh	H	H			**25** (68)
					3 diastereomers (65)		
	H	H	H	OPh			+**26** (20)

**9, 8, 11, 12**

a.

19 – 21

b.

22 – 26
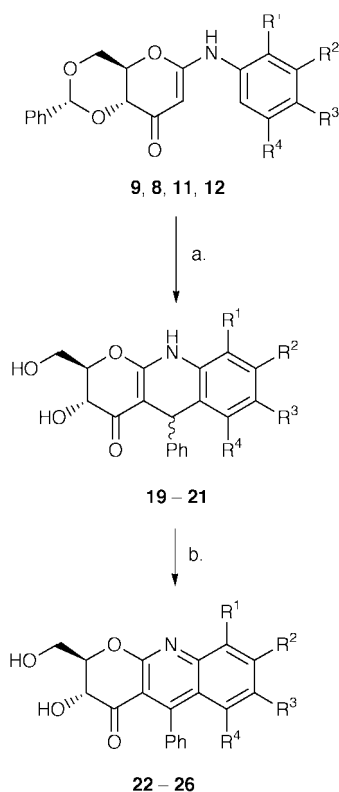
Scheme 4 *Reagents and conditions (and yields)*: see Table 2 for R^1–R^4 and yields. (a) PhCHO, TFA, rt, 1 day; (b) Ce(NH₄)₂(NO₃)₆, DMF, rt, 30 min.

stereoisomer. From the mixture, the minor component **20R** could be crystallized from ethanol. Again, oxidation of the dihydroquinolines **20R/S** furnished one quinoline derivative **23** in good yield (entry 2). The β-naphthyl ketene N,O-ketal **11** also afforded one regioisomer **21R/S**, formed by attack of a β-naphthyl position; this time, however, the 5R-stereoisomer was the major product. The mixture of **21R/S** was oxidized to furnish quinoline derivative **24** (entry 3). When the *meta*-substituted aniline derivative **12** was treated with benzaldehyde–TFA a mixture of three regio- and stereoisomers could be observed. These were not separated but oxidized directly to give the regioisomers **25** and **26** (entry 4). The major compound **25** with the phenoxy substituent at C-8 is obviously favoured over **26** with steric interaction of the substituents at C-5 and C-6.

Then the transformation of **1** to an α-oxoketene N,O-ketal, followed by cyclization with benzaldehyde, was investigated as a one-pot reaction. This is an important step, as it enables the reaction to be run in an automated fashion.[31] An aniline and the additive **16** were added to nitro enone **1** in dichloromethane or acetonitrile; after two hours, the aldehyde and TFA were added directly to the reaction mixture. These modified reaction conditions were reflected in a slightly different outcome of the reactions. With α-naphthylamine, a yield of 40% of **20R/S** ($R:S$ 1:4) was obtained; although the proportion of the 5S-isomer was higher than in the sequential synthesis, the yield was 20% lower. Cortéz *et al.* have reported an analogous cyclization

using dimedone, α-naphthylamine and benzaldehyde; in contrast to our results with N,O-ketal **8**, the respective enaminone formed from dimedone and α-naphthylamine in the presence of benzaldehyde and ethanol did not cyclize.[32] Similarly, a condensation of tetronic acid with anilines and benzaldehydes did not proceed well in a stepwise procedure, and the dihydroquinoline analogous to the system described here could not be obtained.[33]

In a one-pot reaction of **1** with β-naphthylamine, a similar yield of **21R/S** (40%; $R:S$ 1:4) to those in the sequential reactions was achieved, and the $R:S$-ratio changed from more 5R to the favour of the 5S-isomer. Even more selective was the one-pot reaction of **1** with 3-phenoxyaniline; only one product **27** with 5S-configuration was obtained instead of different regio- and stereoisomers as in the sequential reaction. Similarly, one-pot reactions of **1** with *m*-anisidine and 3-aminophenol gave single products **28** and **29** in yields of 52% and 43%, respectively.

27 R = Ph
28 R = Me
29 R = H

30 R = Me
31 R = H
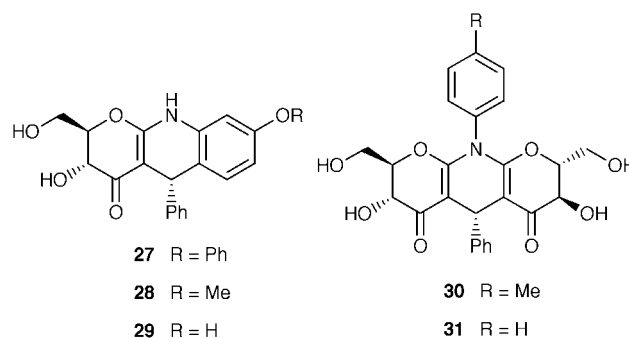
The one-pot reaction of nitro enone **1** with *p*-toluidine afforded the diastereomer **19S** nearly exclusively, but the aniline, less electron rich compared with the previous examples, furnished a low yield of only 14%. Instead, the bis-pyranosulose **30** was isolated in 25% yield. This experiment marks the transition into a different reaction path that is well known in the chemistry of enaminones: in a variation of the Hantzsch synthesis, enaminones upon reaction with aldehydes lead to symmetrical tetrahydropyridines or, in the case of cyclic enaminones, to acridinone derivatives.[34,35] Despite the known course of the reaction, our departure from alkoxy nitro enone **1** has led to a yet unexplored class of heterocycles, no decahydro-1,8-dioxa-9-azaanthracene-4,5-diones have been described, and only one analogous pyridine derivative (12*H*,14*H*-bis[1]benzo-pyrano[2,3-*b*:3′,2′-*e*]pyridine-12,14-dione) is known.[36,37] The structure of bis-pyranosulose **30** was ascertained by X-ray crystallography (Fig. 2). As in the structure of dihydroquino-line, the *C*-phenyl is found in a *quasi*-axial orientation. It should be noted that in this molecule C-5 is not a new stereocenter due to the two-fold rotation symmetry of the structure.

Consequently, the one-pot reaction of nitro enone **1** with aniline itself afforded only the 'classical' symmetrical product **31**. In summary, these results demonstrate that the one-pot transformations of **1** into dihydroquinoline derivatives, under the reaction conditions chosen, proceed only with electron-rich anilines. In all cases, the one-pot reaction was more selective than the respective two-step syntheses; the 5S-isomer was the favoured stereoisomer throughout.
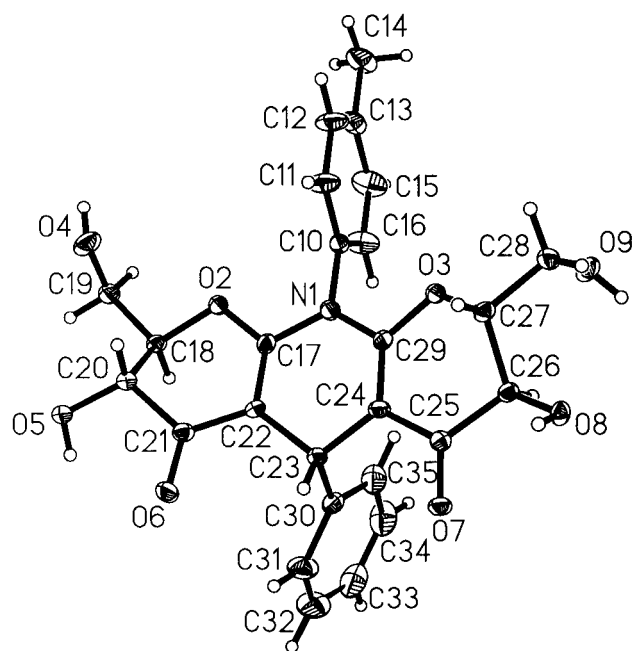
Fig. 2 Monoview of the X-ray structure of compound **30**. Atoms are drawn with anisotropic displacement parameters at 30% probability level with arbitrary numbering of the non-hydrogen atoms.

Experimental

Mps were recorded on a Büchi 510 melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 polarimeter, and $[a]_D^{20}$-values are given in 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed on a Vario EL elemental analyser. IR spectra were recorded on a Nicolet 860 or 20 SXB secrophotometer; some spectra were measured with the microscope technique (MIR) using neat substance. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC 250 or AMX 400 spectrometer. Chemical shifts δ are given in ppm relative to SiMe$_4$, and J-values in Hz. Mass spectra were obtained on a Finnigan MAT SSQ 7000 (EI) or a Perkin-Elmer Sciex API 300 (ISP). High-resolution mass spectra were obtained using a Finnigan MAT 95 spectrometer using electrospray ionization in the positive mode. Chromatography was performed using E. Merck silica gel 60 (230–400 mesh), and medium-pressure chromatography was carried out on an E. Merck Lobar B column (LiChroprep Si 60, 43–60 µm). THF was dried by passage through a column packed with activated alumina. All reactions were conducted under a positive pressure of argon.

4,6-*O*-(*R*)-Benzylidene-1,2-dideoxy-1-nitro-D-*erythro*-hex-1-enopyranos-3-ulose 1

A solution of DMSO (5.0 cm^3, 70.5 mmol) in dry dichloromethane (5 cm^3) was added over 20 min to a solution of oxalyl dichloride (5.3 cm^3, 61.8 mmol) in dry dichloromethane (100 cm^3) with stirring at -70 °C under argon. The solution was stirred for 15 min at the same temperature, then warmed to -40 °C and treated over 45 min with a solution of the nitrosugar **1**[23] (13.3 g, 47.6 mmol) in a mixture of DMSO (2.5 cm^3) and dry dichloromethane (250 cm^3). The suspension was stirred for 10 min at -40 °C, then treated over 20 min with a solution of *N*,*N*-diisopropylethylamine (24.3 cm^3, 141.9 mmol) in dry dichloromethane (25 cm^3) and allowed to react for 135 min under the same conditions. A thick precipitate appeared during the addition of the amine but dissolved thereafter leaving a clear yellow solution. The cool solution was poured into a mixture of acetic acid (120 cm^3), water (400 cm^3), crushed ice (250 g), and *tert*-butyl methyl ether (750 cm^3). The organic layer was separated, and the aqueous phase was extracted with a further

portion of *tert*-butyl methyl ether (500 cm^3). The combined organic phases were successively washed with water (2 × 500 cm^3), then with 0.1 M phosphate buffer (pH 6.5), and dried over sodium sulfate. The mixture was treated with charcoal (4.0 g) and filtered. The filtrate was evaporated to dryness at 45 °C under reduced pressure. The crude product (13.9 g) was purified by crystallization from dichloromethane–hexane to yield, after drying (45 °C, 4 mbar, 1 h), *enone* **1** (10.0 g, 75%) as yellow crystals; $[a]_D^{20}$ +98.1 (*c* 0.76 in CHCl$_3$) (Found: C, 54.18; H, 4.03; N, 4.60. C$_{13}$H$_{11}$NO$_6$ requires C, 54.35; H, 3.92; N, 4.82%); ν_{max} (Nujol)/cm^{-1} 2923, 2854, 1711 (C=O), 1637, 1558, 1461, 1377, 1336, 1275, 1141, 970, 756 and 701; δ_H (400 MHz; CDCl$_3$) 4.18–4.24 (1H, m, 6-H^b), 4.56 (1H, ≈d, 4-H), 4.66–4.76 (2H, m, 5-H and 6-H^a), 5.63 (1H, s, PhC*H*), 6.50 (1H, s, 2-H), 7.38–7.40 (3H, m, Ph) and 7.50–7.52 (2H, m, Ph); *m/z* (EI) 277 (M$^+$, 7%), 171 (8), 141 (11), 131 (33), 105 (100) and 77 (22).

4,6-*O*-(*R*)-Benzylidene-1,2-dideoxy-1-phenylamino-D-*erythro*-hex-1-enopyranos-3-ulose 4 and 4,6-*O*-(*R*)-benzylidene-1,2-dideoxy-1-phenylamino-2-phenylazo-D-*erythro*-hex-1-enopyranos-3-ulose 13

(*a*) To a solution of nitro enone **1** (30 mg, 0.108 mmol) in CH$_2$Cl$_2$ (0.5 cm^3) at rt was added aniline (19.7 mm^3, 0.216 mmol). After stirring for 5 min, the suspension was diluted with CH$_2$Cl$_2$ and a few drops of MeOH, and immediately applied to a silica gel column conditioned with CH$_2$Cl$_2$. Elution with CH$_2$Cl$_2$–MeOH 30:1 yielded N,O-ketal **4** as a light yellow solid (34 mg, 97%).

(*b*) To a solution of nitro enone **1** (30 mg, 0.108 mmol) in CH$_2$Cl$_2$ (1.0 cm^3) at 0 °C was added aniline (19.7 mm^3, 0.216 mmol). After 25 min at 0 °C, the white suspension was stirred at rt for 44 h. The resulting dark yellow solution was purified by chromatography (CH$_2$Cl$_2$–MeOH 20:1). A first fraction (30 mg) was rechromatographed (hexane–ethyl acetate 3:1) to give azo derivative **13** as a red solid (11 mg, 24%); a second fraction gave **4** (7 mg, 20%).

(*c*) To a solution of nitro enone **1** (160 mg, 0.58 mmol) in CH$_2$Cl$_2$ (2.4 cm^3) at 0 °C were added 3-(dimethylamino)anisole **16** (85 mm^3, 0.58 mmol) followed by aniline (106 mm^3, 1.16 mmol). The suspension was stirred for 1 h at 0 °C and for 1 h at rt. After addition of DMSO (2 cm^3) the suspension was evaporated under reduced pressure, and the dark red syrup was purified by chromatography (toluene–acetone 3:1, then toluene–acetone 2:1) to give **4** as a *light yellow solid* (134 mg, 72%); $[a]_D^{20}$ +397 (*c* 0.53 in DMSO) (Found: C, 70.31; H, 5.32; N, 4.38. C$_{19}$H$_{17}$NO$_4$ requires C, 70.58; H, 5.30; N, 4.33%); ν_{max} (Nujol)/cm^{-1} 3240, 3200, 2923, 2854, 1631, 1600, 1547, 1450, 1376, 1104, 753 and 698; δ_H (250 MHz; d$_6$-DMSO) 4.05–4.14 (1H, m, 6-H^b), 4.40–4.55 (3H, m, 4-H, 5-H and 6-H^a), 4.71 (1H, s, 2-H), 5.72 (1H, s, PhC*H*), 7.10–7.17 (1H, m, Ph), 7.21–7.24 (2H, m, Ph), 7.33–7.49 (7H, m, Ph) and 9.78 (1H, s, NH); *m/z* (EI) 323 (M$^+$, 13%), 162 (47), 105 (PhCO$^+$, 100), 93 (39) and 77 (22).

For compound **13**: $[a]_D^{20}$ −218 (*c* 0.23 in CHCl$_3$); ν_{max} (MIR)/cm^{-1} 1695, 1610, 1578, 1399, 1227, 1112, 1066, 969, 758 and 688; δ_H (250 MHz; d$_6$-DMSO) 3.98 (1H, dd ≈ t, $J_{6b,6a}$ 10.1 and $J_{6b,5}$ 10.1, 6-H^b), 4.42 (1H, dd, $J_{6a,6b}$ 10.1 and $J_{6a,5}$ 5.1, 6-H^a), 4.72 (1H, ddd, $J_{5,4}$ 11.2, $J_{5,6b}$ 10.1 and $J_{5,6a}$ 5.1, 5-H), 4.97 (1H, d, $J_{5,4}$ 11.2, 4-H), 5.78 (1H, s, PhC*H*), 7.18–7.58 (15H, m, Ph) and 15.31 (1H, s, NH); *m/z* (ISP) 450 (MNa$^+$, 13%), 428 (MH$^+$, 100) and 322 (16).

1-Benzylamino-4,6-*O*-(*R*)-benzylidene-1,2-dideoxy-D-*erythro*-hex-1-enopyranos-3-ulose 5

To a solution of nitro enone **1** (100 mg, 0.36 mmol) in CH$_2$Cl$_2$ (1.5 cm^3) at 0 °C was added benzylamine (79 mm^3, 0.72 mmol). After stirring at 0 °C for 30 min, the solution was applied to a silica gel column and eluted with toluene–acetone 2:1 to give *N,O-ketal* **5** as a colourless solid (97 mg, 80%); $[a]_D^{20}$ +279 (*c* 0.31

in DMSO) (Found: C, 71.15; H, 5.67; N, 4.09. $C_{20}H_{19}NO_4$ requires C, 71.20; H, 5.68; N, 4.15%); ν_{max} (MIR)/cm^{-1} 3286, 3074, 2879, 1633, 1542, 1353, 1272, 1197, 1134, 1090, 752 and 692; δ_H (250 MHz; d$_6$-DMSO) 4.02 (1H, dd ≈ t, $J_{6b,5}$ 9.8 and $J_{6b,6a}$ 9.8, 6-H^b), 4.19–4.43 (6H, m, 2-H, 4-H, 5-H, 6-H^a and PhCH_2), 5.68 (1H, s, PhCH), 7.24–7.45 (10H, m, Ph) and 8.25 (1H, br s, NH); m/z (EI) 337 (M$^+$, 9%), 176 (59), 162 (30), 146 (22), 105 (PhCO$^+$, 100) and 91 (53, Bn$^+$).

1-Amino-4,6-*O*-(*R*)-benzylidene-1,2-dideoxy-D-*erythro*-hex-1-enopyranos-3-ulose 6

To a solution of nitro enone **1** (300 mg, 1.08 mmol) in THF (5 cm^3) at 0 °C was added ammonium hydroxide (25% in water; 1 cm^3, 13 mmol). After stirring for 20 min, the suspension was evaporated under reduced pressure and coevaporated with MeOH. The residue was purified by chromatography on silica gel (CH$_2$Cl$_2$–MeOH 10:1) to give *N,O-ketal* **6** as a colourless solid (188 mg, 70%); [a]$_D^{20}$ +306 (*c* 0.52 in DMSO) (Found: C, 63.05; H, 5.35; N, 5.64. $C_{13}H_{13}NO_4$ requires C, 63.15; H, 5.30; N, 5.67%); ν_{max} (MIR)/cm^{-1} 3300, 3122, 2880, 1658, 1545, 1457, 1274, 1135, 1088, 961, 770 and 692; δ_H (250 MHz; d$_6$-DMSO) 4.00 (1H, dd ≈ t, $J_{6b,6a}$ 9.5 and $J_{6b,5}$ 9.5, 6-H^b), 4.23 (1H, dd, $J_{6a,6b}$ 9.5 and $J_{6a,5}$ 4.8, 6-H^a), 4.28–4.39 (3H, m, 2-, 4- and 5-H), 5.68 (1H, s, PhCH) and 7.32–7.45 (7H, m, NH$_2$ and Ph); m/z (EI) 247 (M$^+$, 4%), 162 ($C_{10}H_2O_2^+$, 66) and 105 (PhCO$^+$, 100).

4,6-*O*-(*R*)-Benzylidene-1,2-dideoxy-1-piperidino-D-*erythro*-hex-1-enopyranos-3-ulose 7

To a solution of nitro enone **1** (30 mg, 0.108 mmol) in THF (0.5 cm^3) and EtOH (0.5 cm^3) at 0 °C was added piperidine (21.3 mm^3, 0.216 mmol). After stirring for 1 h at 0 °C, the solution was evaporated under reduced pressure, and the residue was purified by chromatography on silica gel (CH$_2$Cl$_2$–MeOH 30:1) to give N,O-acetal **7** as a colourless solid (32 mg, 94%); [a]$_D^{20}$ +358 (*c* 0.20 in DMSO); ν_{max} (MIR)/cm^{-1} 2933, 2855, 1641, 1562, 1432, 1233, 1132, 1095, 1012, 962, 859, 769 and 694; δ_H (250 MHz; d$_6$-DMSO) 1.44–1.62 (6H, m, CH_2CH_2CH_2), 3.30–3.37 (4H, m, CH_2NCH_2), 4.01 (1H, dd ≈ t, $J_{6b,6a}$ 9.8 and $J_{6b,5}$ 9.8, 6-H^b), 4.22 (1H, ddd, $J_{5,4}$ 11.5, $J_{5,6b}$ 9.8 and $J_{5,6a}$ 4.8, 5-H), 4.35 (1H, d, $J_{4,5}$ 11.5, 4-H), 4.41 (1H, dd, $J_{6a,6b}$ 9.8 and $J_{6a,5}$ 4.8, 6-H^a), 4.65 (1H, s, 2-H), 5.68 (1H, s, PhCH) and 7.37–7.47 (5H, m, Ph); m/z (EI) 315 (M$^+$, 5%), 162 (9), 154 (M$^+$ − $C_{10}H_9O_2$, 44) and 105 (PhCO$^+$, 100); m/z 316.1550 (M + H$^+$. $C_{18}H_{22}NO_4$ requires m/z, 316.1549).

4,6-*O*-(*R*)-Benzylidene-1,2-dideoxy-1-(α-naphthylamino)-D-*erythro*-hex-1-enopyranos-3-ulose 8

To a solution of nitro enone **1** (200 mg, 0.721 mmol) in a mixture of CH$_2$Cl$_2$ (2.5 cm^3) and EtOH (0.5 cm^3) at 0 °C was added 1-naphthylamine (206 mg, 1.44 mmol). After stirring for 4 min at 0 °C the solution was chromatographed on silica gel (CH$_2$Cl$_2$–MeOH 20:1) to give *N,O-ketal* **8** as a light brown solid (204 mg, 76%); [a]$_D^{20}$ +357 (*c* 0.36 in DMSO); ν_{max} (MIR)/cm^{-1} 2980, 1632, 1590, 1541, 1273, 1135, 1100, 779 and 697; δ_H (250 MHz; d$_6$-DMSO) 4.04–4.13 (1H, m, 6-H^b), 4.40 (1H, d, $J_{4,5}$ 11.5, 4-H), 4.48–4.61 (2H, m, 5-H and 6-H^a), 4.70 (1H, s, 2-H), 5.62 (1H, s, PhCH), 6.55 (1H, s, NH), 7.26 (1H, ≈s, ArH), 7.34–7.37 (3H, m, Ph), 7.43–7.58 (6H, m, Ph and ArH) and 7.80–7.93 (3H, m, ArH); m/z (ISP) 396 (MNa$^+$, 17%), 374 (MH$^+$, 100) and 344 (14); m/z 374.1387 (M + H$^+$. $C_{23}H_{20}NO_4$ requires m/z, 374.1392).

4,6-*O*-(*R*)-Benzylidene-1,2-dideoxy-1-(*p*-tolylamino)-D-*erythro*-hex-1-enopyranos-3-ulose 9 and 4,6-*O*-(*R*)-benzylidene-1,2-dideoxy-1-(*p*-tolylamino)-2-(*p*-tolylazo)-D-*erythro*-hex-1-enopyranos-3-ulose 14

(*a*) To a solution of nitro enone **1** (50 mg, 0.180 mmol) in CH$_2$Cl$_2$ (1 cm^3) at rt was added *p*-toluidine (38.6 mg, 0.360

mmol). After stirring for 4 h at rt, the suspension was applied to a silica gel column and eluted with CH$_2$Cl$_2$–MeOH 20:1. The first fraction (61 mg) was a black solid. The second fraction (23 mg) was a light yellow solid, which was rechromatographed using CH$_2$Cl$_2$–MeOH 30:1 as eluent to give N,O-ketal **9** as a beige solid (20 mg, 33%). The first fraction was suspended in DMSO–toluene and rechromatographed using ethyl acetate followed by CH$_2$Cl$_2$–MeOH 10:1 as eluents to give a syrup. By addition of ethyl acetate and MeOH at rt, yellow crystals separated, which were washed successively with ethyl acetate and diethyl ether to give azo derivative **14** (29 mg, 35%). The mother liquid was purified by chromatography (CH$_2$Cl$_2$–MeOH 30:1) to give more azo derivative **14** as a yellow solid (17 mg, 21%).

(*b*) To a solution of nitro enone **1** (60 mg, 0.216 mmol) in CH$_2$Cl$_2$ (2 cm^3) at 0 °C was added 3-(dimethylamino)anisole **16** (31.7 mm^3, 0.216 mmol) followed by *p*-toluidine (46.4 mg, 0.433 mmol). After stirring of the mixture for 1 h, cooling was stopped, and the orange suspension was stirred at rt for 1 h. Addition of DMSO (2.5 cm^3) and evaporation under reduced pressure gave a syrup, which was purified by chromatography (toluene–acetone 3:1, then 2:1) to yield compound **9** (62 mg, 85%); [a]$_D^{20}$ +390 (*c* 0.42 in DMSO) (Found: C, 70.89; H, 5.69; N, 4.19. $C_{20}H_{19}NO_4$ requires C, 71.20; H, 5.68; N, 4.15%); ν_{max} (MIR)/cm^{-1} 3220, 3020, 1620, 1537, 1373, 1205, 1100, 736 and 693; δ_H (250 MHz; d$_6$-DMSO) 2.27 (3H, s, CH$_3$), 4.02–4.12 (1H, m, 6-H^b), 4.25–4.47 (2H, m, 5-H and 6-H^a), 4.50 (1H, d, 4-H), 4.64 (1H, s, 2-H), 5.71 (1H, s, PhCH), 7.09–7.19 (4H, m, ArH), 7.38–7.48 (5H, m, ArH) and 9.68 (1H, s, NH); m/z (EI) 337 (M$^+$, 18%), 175 (M$^+$ − $C_{10}H_{10}O_2$, 66) and 105 (PhCO$^+$, 100).

For *compound* **14**: [a]$_D^{20}$ −180 (*c* 0.11 in DMSO) (Found: C, 71.42; H, 5.33; N, 9.28. $C_{27}H_{25}N_3O_4$ requires C, 71.19; H, 5.53; N, 9.23%); ν_{max} (MIR)/cm^{-1} 1710, 1627, 1405, 1238, 1120, 817, 762 and 708; δ_H (250 MHz; d$_6$-DMSO) 2.33 (6H, s, 2 × CH$_3$), 4.00 (1H, dd ≈ t, $J_{6b,6a}$ 10.0 and $J_{6b,5}$ 10.0, 6-H^b), 4.43 (1H, dd, $J_{6a,6b}$ 10.0 and $J_{6a,5}$ 5.0, 6-H^a), 4.69 (1H, ddd, $J_{5,4}$ 11.3, $J_{5,6b}$ 10.0 and $J_{5,6a}$ 5.0, 5-H), 4.93 (1H, d, $J_{4,5}$ 11.3, 4-H), 5.77 (1H, s, PhCH), 7.19–7.33 (6H, m, ArH), 7.40–7.48 (7H, m, ArH) and 15.37 (1H, s, NH); m/z (ISP) 494 (MK$^+$, 36%), 478 (MNa$^+$, 16) and 456 (MH$^+$, 100).

4,6-*O*-(*R*)-Benzylidene-1,2-dideoxy-1-(3-methoxyphenylamino)-D-*erythro*-hex-1-enopyranos-3-ulose 10 and 5-methoxy-2-(3-methoxyphenylazo)aniline 15

To a solution of nitro enone **1** (200 mg, 0.72 mmol) in CH$_2$Cl$_2$ (4 cm^3) at rt was added *m*-anisidine (161 mm^3, 1.44 mmol). The red suspension was stirred for 30 min, MeOH (0.5 cm^3), DMF (0.5 cm^3) and DMSO (1 cm^3) were added, and the mixture was evaporated under reduced pressure. The syrup was chromatographed twice on silica gel using CH$_2$Cl$_2$–MeOH 40:1 and toluene–acetone 1:1. Product fractions were evaporated, partly dissolved in CH$_2$Cl$_2$ (35 cm^3) and precipitated by addition of diethyl ether (7 cm^3) and pentane (20 cm^3). The precipitate was washed with diethyl ether to give *N,O-ketal* **10** as a beige solid (178 mg, 70%). The mother liquid was purified by chromatography (toluene–acetone 3:1) to yield more **10** (27 mg, 10%). The first main fraction gave a red oil (30 mg), which was rechromatographed (hexane–ethyl acetate 1:1) to give azo dye **15** as a red solid (10 mg, 5%).

Compound **10**: [a]$_D^{20}$ +392 (*c* 0.53 in DMSO) (Found: C, 67.93; H, 5.31; N, 3.99. $C_{20}H_{19}NO_5$ requires C, 67.98; H, 5.31; N, 3.96%); ν_{max} (Nujol)/cm^{-1} 3330, 2924, 2854, 1660, 1619, 1584, 1460, 1377, 1230, 1099, 762 and 700; δ_H (250 MHz; d$_6$-DMSO) 3.74 (3H, s, CH$_3$), 4.05–4.14 (1H, m, 6-H^b), 4.41–4.54 (3H, m, 4-H, 5-H and 6-H^a), 4.72 (1H, s, 2-H), 5.72 (1H, s, PhCH), 6.68–6.73 (1H, m, ArH), 6.78–6.84 (2H, m, ArH), 7.25 (1H, dd, ArH), 7.38–7.48 (5H, m, Ph) and 9.76 (1H, s, NH); m/z (ISP) 376 (MNa$^+$, 19%) and 354 (MH$^+$, 100).

For compound **15**: ν_{max} (MIR)/cm^{-1} 3480, 3352, 3010, 2840,

1614, 1592, 1473, 1318, 1252, 1206, 1109, 1018, 827, 790 and 685; δ_H (400 MHz; CDCl$_3$) 3.88 (3H, s, CH$_3$), 3.98 (3H, s, CH$_3$), 4.09 (2H, br s, NH$_2$), 6.29 (1H, dd, $J_{4,3}$ 8.5 and $J_{4,6}$ 2.3, 4-H), 6.31 (1H, d, $J_{6,4}$ 2.3, 6-H), 6.94 (1H, ddd, $J_{6',5'}$ 8.8, $J_{6',2'}$ 2.5 and $J_{6',4'}$ 0.9, 6'-H), 7.36 (1H, dd ≈ t, $J_{5',6'}$ 8.8 and $J_{5',4'}$ 7.8, 5'-H), 7.37 (1H, dd ≈ d, $J_{2',6'}$ 2.5 and $J_{2',4'}$ ≈ 0.3, 2'-H), 7.45 (1H, ddd ≈ dd, $J_{4',5'}$ 7.8, $J_{4',6'}$ 0.9 and $J_{4',2'}$ ≈ 0.3, 4'-H) and 7.70 (1H, d, $J_{3,4}$ 8.5, 3-H); m/z (ISP) 248 (MH$^+$, 100%) and 135 (8); m/z 258.1241 (M + H$^+$. C$_{14}$H$_{16}$N$_3$O$_2$ requires m/z, 258.1243).

4,6-O-(R)-Benzylidene-1,2-dideoxy-1-(β-naphthylamino)-D-erythro-hex-1-enopyranos-3-ulose 11

To a solution of nitro enone **1** (200 mg, 0.72 mmol) in CH$_2$Cl$_2$ (3 cm^3) were added, at 0 °C, 3-(dimethylamino)anisole **16** (106 mm^3, 0.72 mmol) followed by 2-naphthylamine (206 mg, 1.44 mmol). The dark red suspension was stirred for 1 h at 0 °C and for 1 h at rt. After addition of DMSO (3 cm^3) the suspension was evaporated under reduced pressure, and the dark syrup was purified by chromatography (toluene–acetone 2:1, then toluene–acetone 1:1) to give N,O-ketal **11** as a light brown solid (147 mg, 55%); $[a]_D^{20}$ +424 (c 0.40 in DMSO); ν_{max} (MIR)/cm^{-1} 3260, 3060, 1635, 1600, 1547, 1375, 1273, 1210, 1137, 1012, 822, 737 and 697; δ_H (250 MHz; d$_6$-DMSO) 4.08–4.17 (1H, m, 6-H^b), 4.45–4.58 (3H, m, 4-H, 5-H and 6-H^a), 4.83 (1H, s, 2-H), 5.75 (1H, s, PhCH), 7.38–7.54 (8H, m, ArH), 7.71 (1H, br s, ArH), 7.86–7.92 (3H, m, ArH) and 9.99 (1H, s, NH); m/z (EI) 373 (M$^+$, 17%), 211 (42), 183 (48), 143 (61), 115 (28) and 105 (PhCO$^+$, 100); m/z 374.1396 (M + H$^+$. C$_{23}$H$_{20}$NO$_4$ requires m/z, 374.1392).

4,6-O-(R)-Benzylidene-1,2-dideoxy-1-(3-phenoxyphenylamino)-D-erythro-hex-1-enopyranos-3-ulose 12

To a solution of nitro enone **1** (50 mg, 0.180 mmol) in CH$_2$Cl$_2$ (1.3 cm^3) at 0 °C were added 3-(dimethylamino)anisole **16** (26.4 mm^3, 0.180 mmol) and 3-phenoxyaniline (66.7 mg, 0.36 mmol). The red solution was stirred for 1 h at 0 °C and for 1 h at rt. After addition of a few drops of MeOH and dilution with CH$_2$Cl$_2$–MeOH 40:1, the solution was chromatographed using CH$_2$Cl$_2$–MeOH 40:1 as eluent to give N,O-ketal **12** as a beige solid (55 mg, 74%); $[a]_D^{20}$ +334 (c 0.32 in DMSO); ν_{max} (Nujol)/cm^{-1} 3448, 2954, 2854, 1649, 1616, 1598, 1578, 1486, 1228, 1100, 980, 757 and 695; δ_H (250 MHz; d$_6$-DMSO) 4.01 (1H, dd ≈ t, $J_{6b,6a}$ 9.2 and $J_{6b,5}$ 9.2, 6-H^b), 4.33 (1H, ddd, $J_{5,4}$ 11.2, $J_{5,6b}$ 9.2 and $J_{5,6a}$ 4.5, 5-H), 4.44 (1H, dd, $J_{6a,6b}$ 9.2 and $J_{6a,5}$ 4.5, 6-H^a), 4.50 (1H, d, $J_{4,5}$ 11.2, 4-H), 4.72 (1H, s, 2-H), 5.70 (1H, s, PhCH), 6.74–6.77 (1H, m, ArH), 6.81–6.82 (1H, m, ArH), 6.96–7.00 (1H, m, ArH), 7.05–7.08 (2H, m, ArH), 7.19–7.23 (1H, m, ArH), 7.31–7.48 (8H, m, Ph and ArH) and 9.84 (1H, s, NH); m/z (ISP) 479 (MNa$^+$ + CH$_3$CN, 29%), 454 (MK$^+$, 16), 438 (MNa$^+$, 7) and 416 (MH$^+$, 100); m/z 416.1495 (M + H$^+$. C$_{25}$H$_{22}$NO$_5$ requires m/z, 416.1498).

Bis[1-amino-4,6-O-(R)-benzylidene-1,2-dideoxy-D-erythro-hex-1-enopyranos-3-ulose-2-yl](phenyl)methane 17

To a solution of **6** (30 mg, 0.121 mmol) and benzaldehyde (12.1 mm^3, 0.121 mmol) in dry THF (0.7 cm^3) at rt was added ZnCl$_2$·Et$_2$O (2.2 M in CH$_2$Cl$_2$; 55 mm^3, 0.12 mmol). After stirring of the mixture at rt for 72 h, triethylamine (50 mm^3, 0.36 mmol), THF (4 cm^3) and DMSO (0.6 cm^3) were added, and the solution was evaporated under reduced pressure. The residue was chromatographed twice using CH$_2$Cl$_2$–MeOH 9:1 and toluene–acetone 4:1 as eluents to afford **17** as a colourless solid (30 mg, 85%); $[a]_D^{20}$ +122 (c 0.15 in DMSO) (Found: C, 67.48; H, 5.06; N, 4.55. C$_{33}$H$_{30}$N$_2$O$_4$ requires C, 68.03; H, 5.19; N, 4.81%); ν_{max} (MIR)/cm^{-1} 3321, 3085, 2868, 1689, 1654, 1567, 1528, 1450, 1271, 1107, 1068, 958, 759 and 693; δ_H (400 MHz; d$_6$-DMSO) 4.04 (2H, dd ≈ t, 6-H$_A^b$ and 6-H$_B^b$), 4.41–4.61 (6H, m, 4-H$_A$, 4-H$_B$, 5-H$_A$, 5-H$_B$, 6-H$_A^a$ and 6-H$_B^b$), 5.25 (1H, s, PhCH), 5.70

(1H, s, PhCH), 5.72 (1H, s, PhCH), 7.09–7.13 (1H, m, Ph), 7.21–7.25 (2H, m, Ph), 7.28–7.32 (2H, m, Ph), 7.38–7.46 (10H, m, Ph), 7.81 (1H, br s, NH), 7.93 (1H, br s, NH), 8.50 (1H, br s, NH) and 8.89 (1H, br s, NH); δ_C (100.6 MHz; d$_6$-DMSO, extract of data) 34.35 (PhCH), 67.87 (6$_A$- and 6$_B$-C), 71.05, 71.30, 75.83 and 75.95 (4$_A$-, 4$_B$-, 5$_A$- and 5$_B$-C), 93.08 and 93.65 (2$_A$- and 2$_B$-C), 101.62 (PhCH), 101.80 (PhCH), 168.4 and 170.80 (3$_A$- and 3$_B$-C), 184.86 and 185.57 (1$_A$- and 1$_B$-C); m/z (ISP) 605 (MNa$^+$, 49%), 583 (MH$^+$, 100) and 336 (36); m/z 583.2082 (MH$^+$. C$_{33}$H$_{31}$N$_2$O$_8$ requires m/z, 583.2080).

(2R,3R,5S)-2,3,5,10-Tetrahydro-3-hydroxy-2-hydroxymethyl-5-phenylpyrano[2,3-b]quinolin-4-one 18

To N,O-ketal **4** (85 mg, 0.263 mmol) and benzaldehyde (26.6 mm^3, 0.263 mmol) was added TFA (1 cm^3) at rt, and the solution was stirred for 24 h and concentrated at rt under reduced pressure. Pyridine (0.15 cm^3) was added to the syrup and removed by evaporation under reduced pressure. The residue was chromatographed twice (toluene–EtOH 9:1 and CH$_2$Cl$_2$–MeOH 12:1) to give pyranoquinolinone **18** as a colourless solid (31 mg, 36%). The solid was dissolved in boiling ethyl acetate–CH$_2$Cl$_2$–MeOH 4:1:1, and the solution was slightly concentrated. Crystallization took place overnight at rt; mp 254 °C (from ethyl acetate–CH$_2$Cl$_2$–MeOH); $[a]_D^{20}$ +379 (c 0.36 in DMSO) (Found: C, 70.22; H, 5.21; N, 4.19. C$_{19}$H$_{17}$NO$_4$ requires C, 70.58; H, 5.30; N, 4.30%); ν_{max} (MIR)/cm^{-1} 3250, 2935, 1600, 1569, 1521, 1479, 1452, 1240, 1038, 865, 745 and 696; δ_H (400 MHz; d$_6$-DMSO) 3.74 (1H, ddd, $J_{1'b,1'a}$ 12.4, $J_{1'b,OH}$ 6.0, $J_{1'b,2}$ 5.5, 1'-H^b), 3.88 (1H, ddd, $J_{1'a,1'b}$ 12.4, $J_{1'a,OH}$ 4.5 and $J_{1'a,2}$ 2.0, 1'-H^a), 4.02 (1H, dd, $J_{3,2}$ 12.2 and $J_{3,OH}$ 4.4, 3-H), 4.14 (1H, ddd, $J_{2,3}$ 12.2, $J_{2,1'b}$ 5.1 and $J_{2,1'a}$ 2.0, 2-H), 4.97 (1H, dd, $J_{OH,1'a}$ 4.5 and $J_{OH,1'b}$ 6.0, OH), 5.10 (1H, s, 5-H), 5.44 (1H, d, $J_{OH,3}$ 4.4, OH), 6.91–6.95 (1H, m, ArH), 6.98–7.00 (1H, m, ArH), 7.08–7.13 (2H, m, ArH), 7.18–7.36 (5H, m, Ph) and 10.40 (1H, s, NH); m/z (ISP) 324 (MH$^+$, 100%); m/z 324.1232 (M + H$^+$. C$_{19}$H$_{18}$NO$_4$ requires m/z, 324.1236).

(2R,3R,5S)-2,3,5,10-Tetrahydro-3-hydroxy-2-hydroxymethyl-7-methyl-5-phenylpyrano[2,3-b]quinolin-4-one 19S and (2R,3R,5R)-2,3,5,10-tetrahydro-3-hydroxy-2-hydroxymethyl-7-methyl-5-phenylpyrano[2,3-b]quinolin-4-one 19R

(a) To N,O-ketal **9** (152 mg, 0.451 mmol) and benzaldehyde (46 mm^3, 0.45 mmol) was added TFA (1.5 cm^3) at rt. The solution was stirred for 24 h and evaporated at rt under reduced pressure. Pyridine (0.5 cm^3) was added to the residue and evaporated at rt. The residue was purified by chromatography on silica gel (toluene–EtOH 10:1) to give pyranoquinolinones **19R/S** as a colourless solid (95 mg, 63%, R:S 1:5).

(b) **19S** was obtained as a by-product in the preparation of **30** (see below).

19R/S: ν_{max} (MIR)/cm^{-1} 3380, 3220, 1622, 1606, 1571, 1524, 1490, 1153, 1038, 901, 812, 720 and 700; δ_H (250 MHz; d$_6$-DMSO) 2.13 (0.5 H, R-CH$_3$), 2.16 (2.5H, s, S-CH$_3$), 3.66–3.91 (2H, m, 1'-H$_2$), 3.99 (1H, dd, 3-H), 4.11 (0.83H, ddd, 2$_S$-H), 4.30 (0.17H, ddd, 2$_R$-H), 4.97 (0.83H, dd, J 6.0, J 5.5, OH$_S$), 5.04 (1H, s, PhCH), 5.07 (0.17H, dd, OH$_R$), 5.20 (0.83H, d, J 4.4, OH$_S$), 5.44 (0.17H, d, J 4.8, OH$_R$), 6.83–6.96 (2H, m, ArH), 6.99 (1H, s, ArH), 7.04–7.12 (1H, m, Ph), 7.18–7.21 (4H, m, Ph), 10.10 (0.17H, s, NH$_R$) and 10.33 (0.83H, s, NH$_S$); m/z (ISP) 401 (MNa$^+$ + CH$_3$CN, 16%) and 338 (MH$^+$, 100); m/z 338.1386 (M + H$^+$. C$_{20}$H$_{20}$NO$_4$ requires m/z, 338.1392).

Compound **19S**: $[a]_D^{20}$ +281 (c 0.20 in DMSO); ν_{max} (MIR)/cm^{-1} 3400, 3280, 2960, 1622, 1606, 1568, 1486, 1163, 1031, 901, 809, 720 and 693; δ_H (250 MHz; d$_6$-DMSO) 2.16 (3H, s, CH$_3$), 3.71 (1H, ddd, $J_{1'b,1'a}$ 12.1, $J_{1'b,OH}$ 6.0 and $J_{1'b,2}$ 4.9, 1'-H^b), 3.86 (1H, ddd, $J_{1'a,1'b}$ 12.1, $J_{1'a,OH}$ 5.7 and $J_{1'a,2}$ 1.9, 1'-H^a), 4.00 (1H, dd, $J_{3,2}$ 11.2 and $J_{3,OH}$ 4.4, 3-H), 4.11 (1H, ddd, $J_{2,3}$ 11.2, $J_{2,1'b}$ 4.9 and $J_{2,1'a}$ 1.9, 2-H), 4.97 (1H, dd, $J_{OH,1'b}$ 6.0 and $J_{OH,1'a}$ 5.7,

OH), 5.04 (1H, s, PhC*H*), 5.20 (1H, d, $J_{OH,3}$ 4.4, OH), 6.87–6.96 (2H, m, ArH), 6.99 (1H, s, ArH), 7.05–7.14 (1H, m, Ph), 7.16–7.22 (4H, m, Ph) and 10.33 (1H, s, NH); *m/z* (ISP) 360 (MNa⁺, 13%) and 338 (MH⁺, 100); *m/z* 338.1393 (M + H⁺. $C_{20}H_{20}NO_4$ requires *m/z*, 338.1392).

(2*R*,3*R*)-2,3-Dihydro-3-hydroxy-2-hydroxymethyl-7-methyl-5-phenylpyrano[2,3-*b*]quinolin-4-one 22

To solution of **19*S/R*** (*R*:*S* 1:5; 46 mg, 0.136 mmol) in DMF (0.6 cm³) at rt was added cerium(IV) ammonium nitrate (149 mg, 0.272 mmol). After stirring for 30 min, the solution was chromatographed with toluene–acetone 2:1 as eluent to give pyranoquinolinone **22** as a colourless solid (38 mg, 83%); $[a]_D^{20}$ +93.9 (*c* 0.30 in DMSO); ν_{max} (MIR)/cm⁻¹ 3300, 3160, 2860, 1717, 1573, 1555, 1369, 1121, 1040, 837, 731 and 695; δ_H (250 MHz; d₆-DMSO) 2.31 (3H, s, CH₃), 3.80 (1H, ddd, $J_{1'b,1'a}$ 11.9, $J_{1'b,OH}$ 6.2 and $J_{1'b,2}$ 4.0, 1′-Hᵇ), 3.93 (1H, ddd, $J_{1'a,1'b}$ 11.9, $J_{1'a,OH}$ 5.5 and $J_{1'a,2}$ 2.0, 1′-Hᵃ), 4.40 (1H, ddd, $J_{2,3}$ 10.3, $J_{2,1'b}$ 4.0 and $J_{2,1'a}$ 2.0, 2-H), 4.54 (1H, dd, $J_{3,2}$ 10.3 and $J_{3,OH}$ 4.8, 3-H), 5.17 (1H, dd, $J_{OH,1'b}$ 6.2 and $J_{OH,1'a}$ 5.5, OH), 5.73 (1H, d, $J_{OH,2}$ 4.8, OH), 7.02 (1H, s, ArH), 7.13–7.18 (1H, m, ArH), 7.32–7.35 (1H, m, ArH), 7.44–7.58 (3H, m, ArH) and 7.62–7.75 (2H, m, ArH); *m/z* (EI) 335 (M⁺, 25%), 262 (M⁺ − C₃H₅O₂, 100), 233 (74) and 190 (41); *m/z* 336.1239 (M + H⁺. $C_{20}H_{18}NO_4$ requires *m/z*, 336.1236).

(7*S*,9*R*,10*R*)-7,9,10,12-Tetrahydro-9-hydroxy-10-hydroxymethyl-7-phenylbenzo[*h*]pyrano[2,3-*b*]quinolin-8-one 20*S* and (7*R*,9*R*,10*R*)-7,9,10,12-tetrahydro-9-hydroxy-10-hydroxymethyl-7-phenylbenzo[*h*]pyrano[2,3-*b*]quinolin-8-one 20*R*

(*a*) To N,O-ketal **8** (200 mg, 0.536 mmol) and benzaldehyde (54.1 mm³, 0.54 mmol) was added TFA (1.5 cm³) at rt. After stirring of the mixture for 15 h, TFA was evaporated under reduced pressure at rt. Pyridine (0.2 cm³) was added, and evaporated under reduced pressure. The residue was purified by chromatography (toluene–EtOH 10:1) to give quinolinones **20*R/S*** as a colourless solid (*R*:*S* 1:1.75; 170 mg, 85%). The mixture was dissolved in refluxing EtOH (10 cm³), and **20*R*** (20 mg) crystallized at 0 °C.

(*b*) To a solution of nitro enone **1** (150 mg, 0.541 mmol) in CH₂Cl₂ (1.5 cm³) at 0 °C were added 3-(dimethylamino)anisole **16** (79 mm³, 0.54 mmol) and 1-naphthylamine (155 mg, 1.08 mmol). After stirring for 1 h, ice-cooling was removed, and the dark solution was stirred at rt for 1 h. After the addition of, first, benzaldehyde (55 mm³, 0.54 mmol) and then TFA (1.5 cm³) the solution was stirred at rt for 20 h and then evaporated at rt under reduced pressure. Pyridine (0.5 cm³) was added to the residue and evaporated at rt. The residue was chromatographed with toluene–EtOH 12:1 and CH₂Cl₂–MeOH 40:1 to give quinolinones **20*R/S*** as a solid (*R*:*S* 1:4, 80 mg, 40%); **20*R***: mp 257 °C (from EtOH); $[a]_D^{20}$ −172 (*c* 0.16 in DMSO) (Found: C, 73.84; H, 5.06; N, 3.78. $C_{23}H_{19}NO_4$ requires C, 73.98; H, 5.13; N, 3.75%); ν_{max} (MIR)/cm⁻¹ 3255, 1633, 1589, 1512, 1394, 1265, 1008, 919, 803, 698 and 661; δ_H (250 MHz; d₆-DMSO) 3.75 (2H, dd ≈ t, $J_{1',OH}$ 5.1 and $J_{1',10}$ 5.0, 1′-H₂), 3.92 (1H, dd, $J_{9,10}$ 7.6 and $J_{9,OH}$ 4.8, 9-H), 4.41 (1H, ddd ≈ dt, $J_{10,9}$ 7.6 and $J_{10,1'}$ 5.0, 10-H), 5.15 (1H, t, $J_{OH,1'}$ 5.1, OH), 5.24 (1H, s, 7-H), 5.60 (1H, d, $J_{9,OH}$ 4.8, OH), 7.05–7.11 (1H, m, Ph), 7.19–7.30 (5H, m, Ph and ArH), 7.46–7.57 (3H, m, ArH), 7.80–7.84 (1H, m, ArH), 8.50–8.54 (1H, m, ArH) and 10.13 (1H, s, NH); *m/z* (ISP) 396 (MNa⁺, 10%), 374 (MH⁺, 100) and 296 (8).

Mixture **20*R/S*** (*R*:*S* 1:1.75); ν_{max} (MIR)/cm⁻¹ 3257, 2930, 1640, 1586, 1569, 1490, 1392, 1259, 1036, 1001, 804, 724 and 696; *m/z* (ISP) 412 (MK⁺, 5%), 396 (MNa⁺, 18), 374 (MH⁺, 100) and 296 (21).

Compound **20*S***: δ_H (250 MHz; d₆-DMSO) 3.80 (1H, ddd, $J_{1'b,1'a}$ 12.3, $J_{1'b,OH}$ 5.9 and $J_{1'b,10}$ 4.6, 1′-Hᵇ), 3.95 (1H, ddd, $J_{1'a,1'b}$ 12.3, $J_{1'a,OH}$ 5.4 and $J_{1'a,10}$ 1.8, 1′-Hᵃ), 4.11 (1H, dd, $J_{9,10}$ 12.2 and $J_{9,OH}$ 4.4, 9-H), 4.21 (1H, ddd, $J_{10,9}$ 12.2, $J_{10,1'b}$ 4.6 and

$J_{10,1'a}$ 1.8, 10-H), 5.04 (1H, dd, $J_{OH,1'b}$ 5.9 and $J_{OH,1'a}$ 5.4, OH), 5.23 (1H, s, PhC*H*), 5.32 (1H, d, $J_{OH,9}$ 4.6, OH), 7.05–7.11 (1H, m, Ph), 7.19–7.29 (4H, m, Ph), 7.34 (1H, ≈d, ArH), 7.46–7.57 (3H, m, ArH), 7.80–7.84 (1H, m, ArH), 8.50–8.54 (1H, m, Ph) and 10.39 (1H, s, NH).

(9*R*,10*R*)-9,10-Dihydro-9-hydroxy-10-hydroxymethyl-7-phenylbenzo[*h*]pyrano[2,3-*b*]quinolin-8-one 23

To a solution of quinolinones **20*R/S*** (*R*:*S* 1:1.75; 50 mg, 0.136 mmol) in DMF (0.7 cm³) was added cerium(IV) ammonium nitrate (148 mg, 0.270 mmol) at rt. After stirring for 30 min, the solution was chromatographed with toluene–acetone 3:1 to give pyranoquinolinone **23** as a *light yellow solid* (39 mg, 78%); mp 185 °C (from CH₂Cl₂–hexane); $[a]_D^{20}$ +103 (*c* 0.20 in DMSO) (Found: C, 74.45; H, 4.63; N, 3.77. $C_{23}H_{17}NO_4$ requires C, 74.38; H, 4.61; N, 3.77%); ν_{max} (MIR)/cm⁻¹ 3360, 3060, 1702, 1622, 1556, 1480, 1360, 1220, 1053, 731 and 696; δ_H (250 MHz; d₆-DMSO) 3.79 (1H, ddd, $J_{1'b,1'a}$ 12.2, $J_{1'b,OH}$ 6.0 and $J_{1'b,10}$ 3.8, 1′-Hᵇ), 3.94 (1H, ddd, $J_{1'a,1'b}$ 12.2, $J_{1'a,OH}$ 5.8 and $J_{1'a,10}$ 2.0, 1′-Hᵃ), 4.43 (1H, ddd, $J_{10,9}$ 10.8, $J_{10,1'b}$ 3.8 and $J_{2,1'a}$ 2.0, 10-H), 4.55 (1H, dd, $J_{9,10}$ 10.8 and $J_{9,OH}$ 4.4, 9-H), 5.19 (1H, dd ≈ t, $J_{OH,1'b}$ 6.0 and $J_{OH,1'a}$ 5.8, OH), 5.71 (1H, d, $J_{OH,9}$ 4.4, OH), 7.13–7.25 (2H, m, ArH), 7.36–7.40 (1H, ≈d, ArH), 7.47–7.60 (3H, m, ArH), 7.71–7.84 (3H, m, ArH), 7.96–8.01 (1H, m, ArH) and 9.03–9.09 (1H, m, ArH); *m/z* (EI) 371 (M⁺, 61%), 298 (M⁺ − C₃H₅O₂, 90), 269 (100) and 240 (64); *m/z* 372.1233 (M + H⁺. $C_{23}H_{18}NO_4$ requires *m/z*, 372.1236).

(2*R*,3*R*,5*S*)-2,3,5,12-Tetrahydro-3-hydroxy-2-hydroxymethyl-5-phenylbenzo[*g*]pyrano[2,3-*b*]quinolin-4-one 21*S* and (2*R*,3*R*,5*R*)-2,3,5,12-tetrahydro-3-hydroxy-2-hydroxymethyl-5-phenyl-benzo[*g*]pyrano[2,3-*b*]quinolin-4-one 21*R*

(*a*) To N,O-ketal **11** (99 mg, 0.265 mmol) and benzaldehyde (26.8 mm³, 0.265 mmol) was added TFA (1.5 cm³) at rt. After stirring of the mixture for 15 h, TFA was evaporated under reduced pressure at rt. Pyridine (0.3 cm³) was added, and evaporated under reduced pressure. The residue was dissolved in EtOH (8 cm³) and purified by chromatography (toluene–EtOH 12:1) to give pyranoquinolinones **21*R/S*** as a colourless solid (*R*:*S* 1.8:1; 86 mg, 87%). Crystallization from ethanol yielded pyranoquinolinones **21*R/S*** (40 mg) as a mixture of diastereomers (*R*:*S* 1:1).

(*b*) To a solution of nitro enone **1** (150 mg, 0.541 mmol) in CH₂Cl₂ (1.5 cm³) at 0 °C were added 3-(dimethylamino)anisole **16** (79 mm³, 0.54 mmol) and 2-naphthylamine (155 mg, 1.08 mmol). After stirring for 1 h, ice-cooling was removed, and the dark orange solution was stirred at rt for 1 h. After the addition of benzaldehyde (55 mm³, 0.54 mmol) and TFA (1.5 cm³) the solution was stirred at rt for 20 h and evaporated at rt under reduced pressure. Pyridine (0.5 cm³) was added to the residue and evaporated at rt. The residue was purified by chromatography (toluene–EtOH 12:1) to give pyranoquinolinones **21*R/S*** as a *solid* (*R*:*S* 1:1.5; 80 mg, 40%) (Found: C, 73.29; H, 5.20; N, 3.57. $C_{23}H_{19}NO_4$ requires C, 73.71; H, 5.32; N, 3.70%); ν_{max} (MIR)/cm⁻¹ 3220, 1670, 1620, 1590, 1572, 1519, 1501, 1467, 1395, 1300, 1233, 1037, 960, 812, 717 and 694; δ_H (400 MHz; d₆-DMSO; *R*:*S* 1:1) 3.58–3.66 (1H, m, 1′$_R$-H₂), 3.70–3.76 (0.5H, m, 2$_S$-H), 3.81 (0.5H, dd, $J_{3,2}$ 7.8 and $J_{3,OH}$ 4.9, 3$_R$-H), 3.87 (0.5H, dd, $J_{3,2}$ 12.0 and $J_{3,OH}$ 4.8, 3$_S$-H), 4.00–4.07 (1H, m, 1′$_S$-H₂), 4.33 (0.5H, ddd, $J_{2,3}$ 7.8, $J_{2,1'b}$ 4.9 and $J_{2,1'a}$ 4.4, 2$_R$-H), 4.96 (0.5H, dd ≈ t, $J_{OH,1'b}$ 5.9 and $J_{OH,1'a}$ 5.9, OH$_S$), 5.04 (0.5H, dd ≈ t, $J_{OH,1'b}$ 5.6 and $J_{OH,1'a}$ 5.6, OH$_R$), 5.31 (0.5H, ≈d, OH$_S$), 5.56 (0.5H, d, $J_{OH,3}$ 4.9, OH$_R$), 5.76 (0.5H, s, 5$_S$-H), 5.78 (0.5H, s, 5$_R$-H), 6.99–7.05 (1H, m, Ph), 7.12–7.17 (2H, m, Ph), 7.23–7.24 (2H, m, Ph), 7.29–7.36 (2H, m, ArH), 7.39–7.44 (1H, m, ArH), 7.79–7.83 (2H, m, ArH), 7.90–7.92 (1H, m, ArH), 10.44 (0.5H, s, NH$_R$) and 10.68 (0.5H, s, NH$_S$); *m/z* (ISP) 396 (MNa⁺, 11%), 374 (MH⁺, 100) and 296 (15); *m/z* 374.1387 (M + H⁺. $C_{23}H_{20}NO_4$ requires *m/z*, 374.1392).

(2*R*,3*R*)-2,3-Dihydro-3-hydroxy-2-hydroxymethyl-5-phenyl-benzo[*g*]pyrano[2,3-*b*]quinolin-4-one 24

To a solution of pyranoquinolines **21***R*/***S*** (*R*:*S* 1:1.5; 46 mg, 0.123 mmol) in DMF (0.4 cm³) was added cerium(IV) ammonium nitrate (135 mg, 0.246 mmol) at rt. After stirring of the mixture for 30 min, additional DMF (0.4 cm³) was added to the suspension. The mixture was chromatographed twice using CH_2Cl_2–MeOH 30:1 and CH_2Cl_2–MeOH 20:1 as eluents to give pyranoquinolinone **24** as a yellow solid (34 mg, 74%); $[a]_D^{20}$ +149 (*c* 0.24 in DMSO); v_{max} (MIR)/cm⁻¹ 3105, 3025, 2840, 1710, 1565, 1542, 1278, 1130, 1030, 750, 720 and 690; δ_H (250 MHz; d₆-DMSO) 3.81 (1H, ddd, $J_{1'b,1'a}$ 12.2, $J_{1'b,OH}$ 6.0 and $J_{1'b,2}$ 3.8, 1'-H^b), 3.94 (1H, ddd, $J_{1'a,1'b}$ 12.2, $J_{1'a,OH}$ 5.8 and $J_{1'a,2}$ 1.9, 1'-H^a), 4.43 (1H, ddd, $J_{2,3}$ 10.5, $J_{2,1'b}$ 3.8 and $J_{2,1'a}$ 1.9, 2-H), 4.54 (1H, dd, $J_{3,2}$ 10.5 and $J_{3,OH}$ 4.4, 3-H), 5.20 (1H, dd ≈ t, $J_{OH,1'a}$ 5.8 and $J_{OH,1'b}$ 6.0, OH), 5.73 (1H, d, $J_{OH,3}$ 4.4, OH), 6.98–7.11 (2H, m, ArH), 7.21 (1H, d, ArH), 7.39–7.61 (5H, m, ArH), 7.73 (1H, d, *J* 9.0, ArH), 7.98 (1H, d, ArH) and 8.18 (1H, d, *J* 9.0, ArH); *m/z* (EI) 371 (M⁺, 18%), 298 (M⁺ − $C_3H_4O_2$, 100), 269 (30) and 240 (32); *m/z* 372.1234 (M + H⁺. $C_{23}H_{18}NO_4$ requires *m/z*, 372.1236).

(2*R*,3*R*)-2,3-Dihydro-3-hydroxy-2-hydroxymethyl-8-phenoxy-5-phenylpyrano[2,3-*b*]quinolin-4-one 25 and (2*R*,3*R*)-2,3-dihydro-3-hydroxy-2-hydroxymethyl-6-phenoxy-5-phenylpyrano[2,3-*b*]-quinolin-4-one 26

To N,O-ketal **12** (161 mg, 0.388 mmol) and benzaldehyde (39 mm³, 0.39 mmol) was added TFA (1.5 cm³) at rt. After stirring of the mixture for 6 h, TFA was evaporated under reduced pressure at rt. Pyridine (0.3 cm³) was added, and evaporated under reduced pressure. The residue was purified by chromatography (toluene–EtOH 9:1) to give a mixture of three compounds as a solid (104 mg, 65%; 4:3:3); *m/z* (ISP) 479 (MNa⁺ + CH_3CN, 8%), 454 (MK⁺, 7), 438 (MNa⁺, 3), 416 (MH⁺, 100). A part of the solid (99 mg, 0.238 mmol) was dissolved in DMF (0.8 cm³) and cerium(IV) ammonium nitrate (270 mg, 0.49 mmol) was added at rt. After stirring for 30 min, the solution was chromatographed with toluene–acetone 2:1 to give a fraction of pure *pyranoquinolinone* **25** as a foam (47 mg, 48%) followed by a mixture of isomers **25** and **26** (41 mg), which were separated by medium-pressure chromatography (toluene–acetone 3:1) to give more **25** (20 mg, 20%) and pyranoquinolinone **26** as a light yellow solid (20 mg, 20%).

For **25**: $[a]_D^{20}$ + 78.3 (*c* 0.44 in DMSO) (Found: C, 72.36; H, 4.67; N, 3.39. $C_{25}H_{19}NO_5$ requires C, 72.63; H, 4.63; N, 3.39%); v_{max} (MIR)/cm⁻¹ 3280, 3060, 2930, 1712, 1574, 1551, 1487, 1239, 1118, 1070, 724 and 686; δ_H (250 MHz; d₆-DMSO) 3.78 (1H, ddd, $J_{1'b,1'a}$ 12.2, $J_{1'b,OH}$ 5.8 and $J_{1'b,2}$ 3.2, 1'-H^b), 3.90 (1H, ddd, $J_{1'a,1'b}$ 12.2, $J_{1'a,OH}$ 5.8 and $J_{1'a,2}$ 1.8, 1'-H^a), 4.38 (1H, ddd, 2-H), 4.51 (1H, dd, $J_{3,2}$ 10.6 and $J_{3,OH}$ 4.7, 3-H), 5.14 (1H, dd ≈ t, $J_{OH,1'a}$ 5.8 and $J_{OH,1'b}$ 5.8, OH), 5.74 (1H, d, $J_{OH,3}$ 4.7, OH), 7.04 (1H, ≈d, ArH), 7.15–7.22 (4H, m, ArH), 7.26–7.39 (3H, m, ArH) and 7.46–7.53 (5H, m, ArH); *m/z* (EI) 413 (M⁺, 8%), 340 (M⁺ − $C_3H_4O_2$, 100), 311 (26) and 190 (35); *m/z* 414.1342 (M + H⁺. $C_{25}H_{20}NO_5$ requires *m/z*, 414.1341).

Compound **26**: $[a]_D^{20}$ + 85.8 (*c* 0.13 in DMSO); v_{max} (MIR)/cm⁻¹ 3280, 3060, 2930, 1712, 1574, 1551, 1487, 1239, 1116, 1024, 841, 724 and 686; δ_H (250 MHz; d₆-DMSO) 3.78 (1H, ddd, $J_{1'b,1'a}$ 12.2, $J_{1'b,OH}$ 5.8 and $J_{1'b,2}$ 3.9, 1'-H^b), 3.91 (1H, ddd, $J_{1'a,1'b}$ 12.2, $J_{1'a,OH}$ 5.8 and $J_{1'a,2}$ 2.0, 1'-H^a), 4.39 (1H, ddd, $J_{2,3}$ 11.0, $J_{2,1'b}$ 3.9 and $J_{2,1'a}$ 2.0, 2-H), 4.50 (1H, dd, $J_{3,2}$ 11.0 and $J_{3,OH}$ 4.5, 3-H), 5.18 (1H, dd ≈ t, $J_{OH,1'a}$ 5.8 and $J_{OH,1'b}$ 5.8, OH), 5.71 (1H, d, $J_{OH,3}$ 4.5, OH), 6.45–6.48 (2H, m, ArH), 6.75 (1H, ≈d, ArH), 6.98–7.26 (8H, m, ArH), 7.59 (1H, ≈d, ArH) and 7.73 (1H, dd ≈ t, ArH); *m/z* (ISP) 436 (MNa⁺, 10%), 414 (MH⁺, 100) and 340 (18); *m/z* 414.1342 (M + H⁺. $C_{25}H_{20}NO_5$ requires *m/z*, 414.1341).

(2*R*,3*R*,5*S*)-2,3,5,10-Tetrahydro-3-hydroxy-2-hydroxymethyl-8-phenoxy-5-phenylpyrano[2,3-*b*]quinolin-4-one 27

To a solution of nitro enone **1** (200 mg, 0.72 mmol) in CH_2Cl_2 (2.0 cm³) were added 3-(dimethylamino)anisole **16** (106 mm³, 0.72 mmol) followed by 3-phenoxyaniline (267 mg, 1.44 mmol) at 0 °C. The suspension was stirred for 1 h at 0 °C and for 1 h at rt. Benzaldehyde (73 mm³, 0.72 mmol) and then TFA (2.0 cm³) were added, and the dark solution was stirred for 5 h at rt. The solution was evaporated at rt under reduced pressure. Pyridine (0.5 cm³) was added to the residue and then evaporated at rt. The residue was chromatographed twice using toluene–EtOH 12:1 and toluene–EtOH 14:1 as eluents and afforded pyranoquinolinone **27** as a light yellow solid (109 mg, 36%); $[a]_D^{20}$ +219 (*c* 0.23 in DMSO); v_{max} (MIR)/cm⁻¹ 3250, 3100, 1630, 1593, 1566, 1527, 1476, 1211, 1126, 993, 725 and 691; δ_H (250 MHz; d₆-DMSO) 3.73 (1H, ddd, $J_{1'b,1'a}$ 12.2, $J_{1'b,OH}$ 6.0 and $J_{1'b,2}$ 4.8, 1'-H^b), 3.87 (1H, ddd, $J_{1'a,1'b}$ 12.2, $J_{1'a,OH}$ 5.5 and $J_{1'a,2}$ 1.9, 1'-H^a), 4.02 (1H, dd, $J_{3,2}$ 11.8 and $J_{3,OH}$ 4.6, 3-H), 4.14 (1H, ddd, $J_{2,3}$ 11.8, $J_{2,1'b}$ 4.8 and $J_{2,1'a}$ 1.9, 2-H), 4.98 (1H, dd, $J_{OH,1'b}$ 6.0 and $J_{OH,1'a}$ 5.5, OH), 5.07 (1H, s, 5-H), 5.28 (1H, d, $J_{OH,3}$ 4.6, OH), 6.56–6.59 (1H, m, ArH), 6.62–6.63 (1H, m, ArH), 6.98–7.01 (2H, m, ArH), 7.14–7.23 (7H, m, Ph), 7.35–7.41 (2H, m, Ph) and 10.36 (1H, s, NH); *m/z* (EI) 415 (M⁺, 13%), 338 (M⁺ − C_6H_5, 100) and 264 (56); *m/z* 416.1498 (M + H⁺. $C_{25}H_{22}NO_5$ requires *m/z*, 416.1498).

(2*R*,3*R*,5*S*)-2,3,5,10-Tetrahydro-3-hydroxy-2-hydroxymethyl-8-methoxy-5-phenylpyrano[2,3-*b*]quinolin-4-one 28

To a solution of nitro enone **1** (100 mg, 0.360 mmol) in CH_2Cl_2 (1.0 cm³) were added 3-(dimethylamino)anisole **16** (53 mm³, 0.36 mmol) and *m*-anisidine (81 mm³, 0.72 mmol) at 0 °C. The orange suspension was stirred for 1 h at 0 °C and for 1 h at rt. Benzaldehyde (37 mm³, 0.36 mmol) and TFA (1.0 cm³) were added, and the dark solution was stirred at rt for 5 h. The solution was evaporated at rt under reduced pressure. Pyridine (0.3 cm³) was added to the residue and then evaporated at rt. The residue was chromatographed twice using toluene–EtOH (10:1 and toluene–EtOH 12:1 as eluents to afford pyrano-quinolinone **28** as a light yellow solid (67 mg, 52%); $[a]_D^{20}$ +265 (*c* 0.41 in DMSO); v_{max} (Nujol)/cm⁻¹ 3250, 2954, 2854, 1626, 1603, 1575, 1530, 1490, 1340, 1205, 1040 and 730; δ_H (400 MHz; d₆-DMSO) 3.68 (3H, s, CH_3), 3.73 (1H, ddd, $J_{1'b,1'a}$ 12.0, $J_{1'b,OH}$ 6.0 and $J_{1'b,2}$ 5.6, 1'-H^b), 3.87 (1H, ddd, $J_{1'a,1'b}$ 12.0, $J_{1'a,OH}$ 5.5 and $J_{1'a,2}$ 1.9, 1'-H^a), 4.01 (1H, dd, $J_{3,2}$ 11.5 and $J_{3,OH}$ 4.5, 3-H), 4.12 (1H, ddd, $J_{2,3}$ 11.5, $J_{2,1'b}$ 5.6 and $J_{2,1'a}$ 1.9, 2-H), 4.97 (1H, dd, $J_{OH,1'b}$ 6.0 and $J_{OH,1'a}$ 5.5, OH), 5.02 (1H, s, 5-H), 5.21 (1H, d, $J_{OH,3}$ 4.5, OH), 6.51–6.55 (2H, m, ArH), 7.05–7.10 (2H, m, ArH), 7.14–7.22 (4H, m, Ph) and 10.50 (1H, s, NH); *m/z* (EI) 353 (M⁺, 16%), 276 (M⁺ − C_6H_5, 100) and 202 (55); *m/z* 354.1339 (M + H⁺. $C_{20}H_{20}NO_5$ requires *m/z*, 354.1341).

(2*R*,3*R*,5*S*)-2,3,5,10-Tetrahydro-3,8-dihydroxy-2-hydroxymethyl-5-phenylpyrano[2,3-*b*]quinolin-4-one 29

To a solution of nitro enone **1** (200 mg, 0.721 mmol) in CH_3CN (1.0 cm³) were added 3-(dimethylamino)anisole **16** (106 mm³, 0.72 mmol) and a solution of 3-aminophenol (157 mg, 1.44 mmol) in CH_3CN (1.0 cm³) at 0 °C. The orange suspension was stirred for 1 h at 0 °C and for 1 h at rt. Benzaldehyde (73 mm³, 0.72 mmol) and TFA (1.5 cm³) were added, and the dark solution was stirred at rt for 5 h. The solution was evaporated at rt under reduced pressure. Pyridine (0.5 cm³) was added to the residue and then evaporated at rt. The residue was chromatographed twice using toluene–EtOH 7:1 as eluent to afford pyranoquino-linone **29** as a brownish solid (106 mg, 43%); $[a]_D^{20}$ +221 (*c* 0.28 in DMSO); v_{max} (MIR)/cm⁻¹ 3240, 2940, 1672, 1607, 1567, 1532, 1484, 1129, 1034, 994, 799 and 695; δ_H (250 MHz; d₆-DMSO) 3.73 (1H, ddd, $J_{1'b,1'a}$ 11.8, $J_{1'b,OH}$ 5.8 and $J_{1'b,2}$ 5.0, 1'-H^b), 3.87 (1H, ddd, $J_{1'a,1'b}$ 11.8, $J_{1'a,OH}$ 4.8 and $J_{1'a,2}$ 1.8, 1'-H^a),

4.00 (1H, dd, $J_{3,2}$ 12.2 and $J_{3,OH}$ 4.4, 3-H), 4.10 (1H, ddd, $J_{2,3}$ 12.2, $J_{2,1'b}$ 5.0 and $J_{2,1'a}$ 1.8, 2-H), 4.96 (1H, s, 5-H), 4.98 (1H, dd, OH), 5.21 (1H, d, $J_{OH,3}$ 4.4, OH), 6.34 (1H, dd, ArH), 6.44 (1H, d, ArH), 6.94 (1H, d, J 8.4, ArH), 7.03–7.11 (1H, m, Ph), 7.15–7.22 (4H, m, Ph), 9.36 (1H, s, OH) and 10.25 (1H, s, NH; m/z (ISP) 362 (MNa$^+$, 47%) and 340 (MH$^+$, 100); m/z 340.1186 (M + H$^+$. $C_{19}H_{18}NO_5$ requires m/z, 340.1185).

(2R,3R,7R,8R)-2,3,5,7,8,10-Hexahydro-3,7-dihydroxy-2,8-bis-(hydroxymethyl)-5-phenyl-10-(p-tolyl)dipyrano[2,3-b:3,2-e]-pyridine-4,6-dione 30

To a solution of nitro enone **1** (150 mg, 0.541 mmol) in CH_2Cl_2 (1.5 cm^3) were added 3-(dimethylamino)anisole **16** (79 mm^3, 0.54 mmol) and *p*-toluidine (116 mg, 1.08 mmol) at 0 °C. The orange suspension was stirred for 1 h at 0 °C and for 1 h at rt. Benzaldehyde (55 mm^3, 0.54 mmol) and TFA (1.5 cm^3) were added, and the dark solution was stirred at rt for 20 h and evaporated at rt under reduced pressure. Pyridine (0.5 cm^3) was added to the residue and evaporated at rt. The residue was purified by chromatography (toluene–EtOH 6:1). The first fraction (44 mg) was rechromatographed (CH_2Cl_2–MeOH 30:1) to give pyranoquinolinone **19S** (**19R** < 5%; 25 mg, 14%). The second fraction was an orange solid, which was rechromatographed (CH_2Cl_2–MeOH 9:1) to furnish the dihydropyridine **30** as a beige solid (32 mg, 25%). Dissolution in CH_2Cl_2 ($\approx$1.0 cm^3) and addition of 3 drops of hexane at rt led to crystallization after 2 days at 0 °C to give the pyridine **30** as colourless crystals; mp 150 °C (change), 246 °C (melting) (from CH_2Cl_2–hexane); $[a]_D^{20}$ + 177.8 (c 0.10 in DMSO); v_{max} (MIR)/cm^{-1} 3260, 1622, 1508, 1369, 1216, 821 and 708; δ_H (400 MHz; d$_6$-DMSO) 2.38 (3H, s, CH$_3$), 3.41 (1H, ddd, $J_{1'b,1'a}$ 11.9, $J_{1'b,8}$ 6.0 and $J_{1'b,OH}$ 4.9, 1''-H^b), 3.46 (1H, ddd, $J_{1'a,1'b}$ 11.9, $J_{1'a,8}$ 6.0 and $J_{1'a,OH}$ 5.7, 1''-H^a), 3.52 (1H, ddd, $J_{1'b,1'a}$ 12.6, $J_{1'b,OH}$ 5.2 and $J_{1'b,2}$ 2.2, 1'-H^b), 3.56 (1H, ddd, $J_{1'a,1'b}$ 12.6, $J_{1'a,OH}$ 5.8 and $J_{1'a,2}$ 3.5, 1'-H^a), 3.83 (1H, dd, $J_{7,8}$ 6.1 and $J_{7,OH}$ 5.3, 7-H), 4.02 (1H, ddd, 2-H), 4.10 (1H, dd, $J_{3,2}$ 12.2 and $J_{3,OH}$ 5.3, 3-H), 4.34 (1H, ddd, 8-H), 4.73 (1H, dd, $J_{OH,1'a}$ 5.7 and $J_{OH,1'b}$ 4.9, OH), 4.87 (1H, s, 5-H), 4.90 (1H, dd, $J_{OH,1'a}$ 5.8 and $J_{OH,1'b}$ 5.2, OH), 5.51 (1H, d, J 5.3, OH), 5.82 (1H, d, J 5.3, OH), 7.14 (1H, dd, Ph), 7.24–7.28 (6H, m, Ph and 2Arh), 7.34–7.36 (2H, m, ArH); δ_H (400 MHz; CDCl$_3$) 1.47 (1H, dd $\approx$ t, J 7.2, OH), 1.49 (1H, dd $\approx$ t, J 6.8, OH), 2.45 (3H, s, CH$_3$), 3.49 (1H, d, J 1.4, OH), 3.56 (1H, d, J 1.4, OH), 3.75–3.89 (4H, m, 1' and 1''-H$_2$), 4.07 (1H, dd, $J_{7,8}$ 12.6 and $J_{7,OH}$ 1.4, 7-H), 4.11 (1H, ddd, $J_{2,3}$ 12.6, $J_{2,1'b}$ 4.6, and $J_{2,1'a}$ 2.8, 2-H), 4.17 (1H, dd, $J_{3,2}$ 12.6 and $J_{3,OH}$ 1.4, 3-H), 4.28 (1H, ddd, $J_{8,7}$ 12.6, $J_{8,1'b}$ 5.0 and $J_{8,1'a}$ 2.8, 8-H), 5.16 (1H, s, 5-H), 7.17–7.21 (3H, m, Ph and 2ArH), 7.26–7.32 (4H, m, Ph) and 7.41–7.44 (2H, m, ArH); δ_C 100.6 MHz; d$_6$-DMSO; extract of data) 20.74 (CH$_3$), 32.05 (PhCH), 58.61 (1''-C), 59.16 (1'-C), 66.47 (3-C), 67.00 (7-C), 83.56 (2-C), 85.25 (8-C), 188.65 and 190.48 (2 × C=O); m/z (ISP) 480 (MH$^+$, 100%) and 402 (M$^+$ − C$_6$H$_5$, 24); m/z 480.1658 (M + H$^+$. $C_{26}H_{26}NO_8$ requires m/z, 480.1658).

(2R,3R,7R,8R)-2,3,5,7,8,10-Hexahydro-3,7-dihydroxy-2,8-bis(hydroxymethyl)-5,10-diphenyldipyrano[2,3-b:3,2-e]pyridine-4,6-dione 31

To a solution of nitro enone **1** (150 mg, 0.541 mmol) in CH_2Cl_2 (1.5 cm^3) were added 3-(dimethylamino)anisole **16** (79 mm^3, 0.54 mmol) and aniline (99 mm^3, 1.08 mmol) at 0 °C. The orange suspension was stirred for 1 h at 0 °C and for 1 h at rt. Benzaldehyde (55 mm^3, 0.54 mmol) and TFA (1.5 cm^3) were added, and the dark solution was stirred at rt for 20 h and evaporated at rt under reduced pressure. Pyridine (0.5 cm^3) was added to the residue and evaporated at rt. The residue was chromatographed twice (toluene–EtOH 6:1 and CH_2Cl_2–MeOH 9:1) to give the dihydropyridine **31** as a light yellow foam (31 mg, 25%); $[a]_D^{20}$ +182 (c 0.20 in DMSO); v_{max} (MIR)/cm^{-1} 3348, 2920, 1620, 1590, 1368, 1214, 1115, 901, 750 and

699; δ_H (250 MHz; d$_6$-DMSO) 3.37–3.60 (4H, m, 1'- and 1''-H$_2$), 3.83 (1H, dd, $J_{7,8}$ 6.2 and $J_{7,OH}$ 5.2, 7-H), 4.02 (1H, ddd, 2-H), 4.11 (1H, dd, $J_{3,2}$ 12.0 and $J_{3,OH}$ 5.0, 3-H), 4.35 (1H, ddd, 8-H), 4.74 (1H, dd $\approx$ t, J 5.2 and 5.2, OH), 4.88 (1H, s, 5-H), 4.91 (1H, dd $\approx$ t, J 5.0 and 5.0, OH), 5.55 (1H d, $J_{OH,3}$ 5.0, OH), 5.85 (1H, d, $J_{OH,7}$ 5.2, OH), 7.13–7.19 (1H, m, Ph), 7.25–7.31 (2H, m, Ph) and 7.36–7.54 (7H, m, Ph); δ_H (400 MHz; CDCl$_3$) 1.59 (2H, br s, 2 × OH), 3.56 (2H, br s, 2 × OH), 3.76–3.88 (4H, m, 1'- and 1''-H$_2$), 4.08 (1H, d, $J_{7,8}$ 12.5, 7-H), 4.11 (1H, ddd, $J_{2,3}$ 12.5, $J_{2,1'b}$ 4.3 and $J_{2,1'a}$ 3.0, 2-H), 4.19 (1H, d, $J_{3,2}$ 12.5, 3-H), 4.29 (1H, ddd, $J_{8,7}$ 12.5, $J_{8,1'b}$ 4.8 and $J_{8,1'a}$ 2.9, 8-H), 5.16 (1H, s, 5-H), 7.18–7.22 (1H, m, Ph), 7.26–7.33 (7H, m, Ph) and 7.42–7.44 (2H, m, Ph); m/z (ISP) 488 (MNa$^+$, 13%), 466 (MH$^+$, 100) and 388 (19); m/z 466.1499 (M + H$^+$. $C_{25}H_{24}NO_8$ requires m/z, 466.1502).

Crystal structure determination†

Single crystals of (2R,3R,5S)-2,3,5,10-tetrahydro-3-hydroxy-2-hydroxymethyl-5-phenylpyrano[2,3-b]quinolin-4-one **18** were crystallized from a mixture of dichloromethane, methanol and ethyl acetate and mounted in a glass capillary for X-ray diffraction at room temperature.

Crystal data for compound 18. $C_{19}H_{17}NO_4$, $M = 323.34$, orthorhombic, $a = 7.0460(10)$, $b = 7.2040(10)$, $c = 31.591(4)$ Å, $V = 1603.5(4)$ Å^3, $T = 293$ K, space group $P2_12_12_1$ (no. 19), $Z = 4$, μ(Cu-Kα) = 0.775 mm^{-1}, 2169 reflections measured, 1979 unique ($R_{int} = 0.0173$) which were used in all calculations. The final R-factor was 0.0570 and wR-factor 0.1529 (all data). Full crystallographic details have been deposited at the Cambridge Crystallographic Data Centre, deposition number CCDC 125068.[31]

Single crystals of compound **30** were crystallised from a mixture of dichloromethane, and hexane, mounted in a cryo-loop and transferred to a cold N$_2$-gas stream for X-ray diffraction at 193 K.

Crystal data of compound 30. $C_{26}H_{25}NO_8 + 2 \times CH_2Cl_2$, $M = 649.35$, monoclinic, $a = 23.144(2)$, $b = 11.273(2)$, $c = 12.3570(10)$ Å, $V = 2925.2(6)$ Å^3, $T = 193$ K, space group $C2$ (no. 5), $Z = 4$, μ(Cu-Kα) = 4.116 mm^{-1}, 2784 reflections measured, 2549 unique ($R_{int} = 0.0231$) which were used in all calculations. The final R-factor was 0.0603 and wR-factor 0.1627 (all data).

Data collection. Data were measured on a Siemens P4 diffractometer with graphite-monochromated Cu-Kα radiation from an M18XHF rotating anode. The data were corrected Lorentz and polarization factors.

Structure solution and refinement. The structure was solved by direct methods and expanded using Fourier techniques and the program SHELX-97.[38] All non-hydrogen atoms were refined anisotropically using full matrix least-squares refinement without restraints.

† CCDC reference number 207/384. See http://www.rsc.org/suppdata/p1/a9/a908806g for crystallographic files in .cif format.

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