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Acid-promoted reactions in 1-hydroxy, 1-dimethylaminomethyl and 1-methylene-4-arylmethyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]-quinazoline-3,6-diones

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Abstract—The 1-dimethylaminomethyl or 1-methylene group of the title compounds was introduced through a Mannich or a tandem of Mannich–Hofmann reactions as the final step of a protocol that is shorter than other previously described for these precursors of *N*-acyliminium species. In these compounds, the acid-promoted intramolecular cyclizations of Pictet–Spengler-type were restricted to the N(2)-unsubstituted compounds, while their N(2)-methyl substituted analogues gave instead dimerization products. The cyclization was effective with 1-hydroxy-1,2-disubstituted compounds, which were obtained through addition of a Grignard reagent to 2*H*,4*H*-pyrazino[2,1-*b*]-quinazoline-1,3,6-triones. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

Several fungal metabolites such as glyantripine,[1] fumiquinazolines F and G,[2,3] fiscalin B,[4,5] *N*-acetylardeemin,[6,7] and some spiro compounds such as fumiquinazoline C,[2,3] spiroquinazoline[8] and alantrypinone[9] (Fig. 1), contain a pyrazino[2,1-*b*]quinazoline-3,6-dione moiety and an indole ring. With the exception of *N*-acetylardeemin, the N(2)-nitrogen atom in all these natural products is unsubstituted, this circunstance being relevant for their synthetic approaches.

(+)-Dehydrofumiquinazoline G, which is the 1-methylene derivative of (+)-glyantrypine, was first prepared by Snider in a thirteen-step protocol, in which the methylene group was originated in a preliminar step by acid-promoted cyclization of *N*-pyruvyl-*N′*-dimethoxybenzyl-2,3-dihydro-*N*-trifluoroacetyl-L-tryptophanamide.[10]

Dehydrofumiquinazoline G and other 1-methylene analogues (**A**, Scheme 1), were also obtained following a simpler protocol in which the methylene group was elaborated by elimination of an HXR portion in 1-RX–CH_2-substituted pyrazino[2,1-*b*]quinazoline-3,6-diones. These compounds were obtained through a Mazurkiewicz–Ganesan cyclyzation[11–14] of 'tripeptides' having tryptophan (or the adequate indole modified derivative), anthranilic acid, and *N*-Fmoc protected dehydroalanine precursors

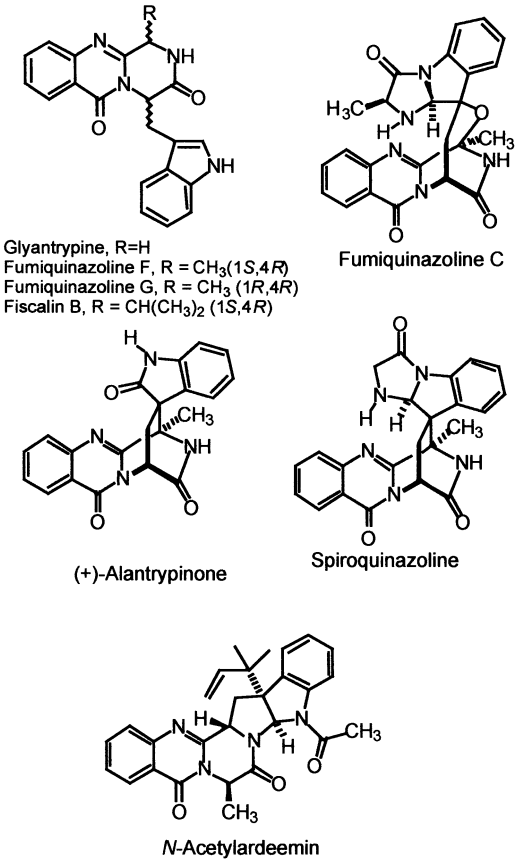

Figure 1.

Keywords: *N*-acyliminium; Pictet–Spengler-type reaction; dehydrofumiquinazoline; alantrypinone.

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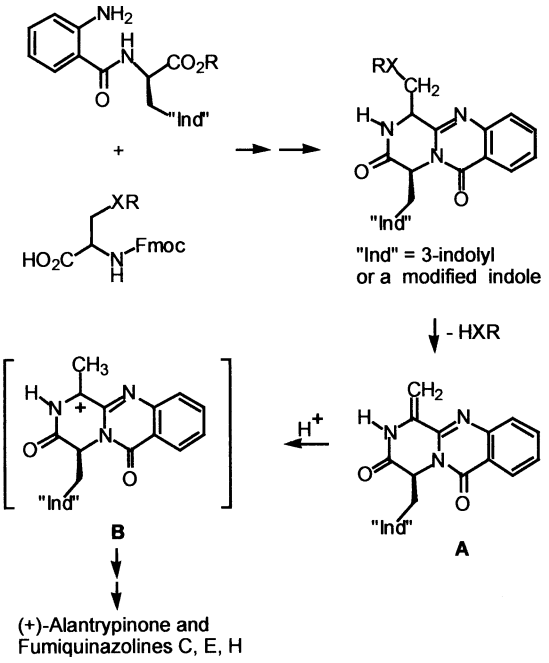
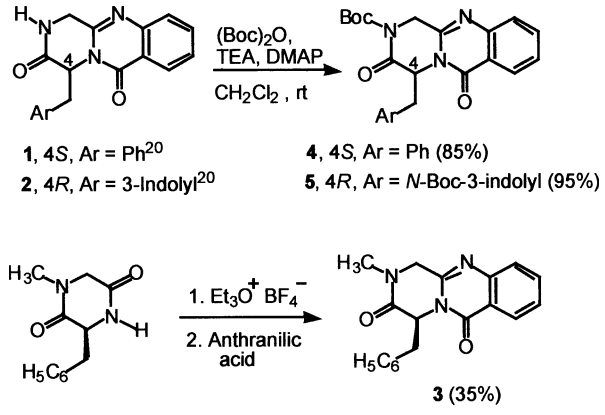


Scheme 1.



Scheme 2.

(*O*-acetyl or *O*-tosylserine, *S*-methylcysteine and phenylselenylalanine), as the first, second and N-terminal residues, respectively. The electrophilic species generated by protonation of the double bond (**B**) were trapped by a nucleophilic position of the 'indole' substituent or by methanol to give precursors of (+)-alantrypinone and fumiquinazolines C, E and H (Scheme 1).[15,16]

We have previously described that 2,4-disubstituted pyrazino[2,1-*b*]quinazoline-3,6-diones behave as nucleophilic glycine templates in which a 1-dimethyl-aminomethyl or 1-methylene group can be introduced through a Mannich or a tandem of Mannich–Hofmann reactions, respectively.[17,18] Attempts to use these compounds as precursors of *N*-acyliminium species (*N*-alkyl substituted **B**), by protonation and elimination of dimethylamine or by direct protonation, to be trapped by the *ortho*-position of a 2-phenethyl substituent failed. However, this acid promoted Pictet–Spengler cyclization worked for 1-substituted 1-hydroxy-2-phenethylpyrazino-[2,1-*b*]quinazoline-3,6-diones, which were obtained from oxidation at C(1) and subsequent addition of organometallics.[19]

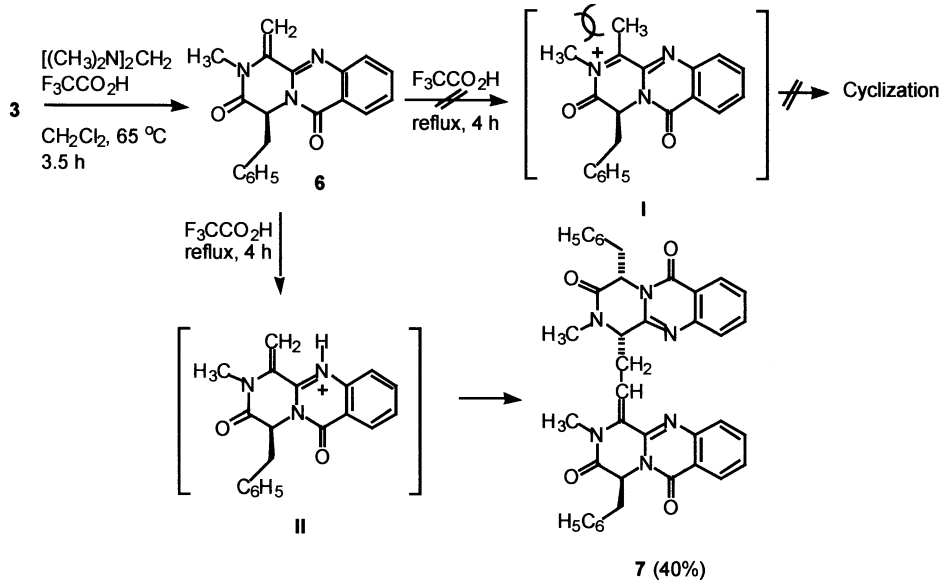
Here, we extend this study to the 4-arylmethyl compounds (**1**–**5**).

2. Results and discussion

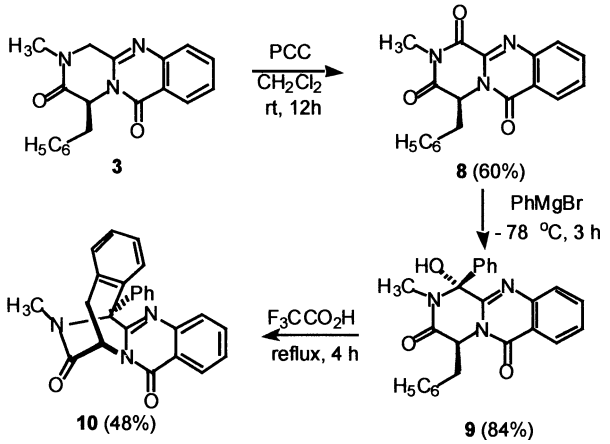
Compounds **1**–**5** were prepared following standard methods[20,21] (Scheme 2).

Compound **3** gave, as expected, the corresponding 1-methylene derivative **6**, but this compound dimerized in TFA to give **7** instead of a cyclization product arising from a Pictet–Spengler-type reaction.

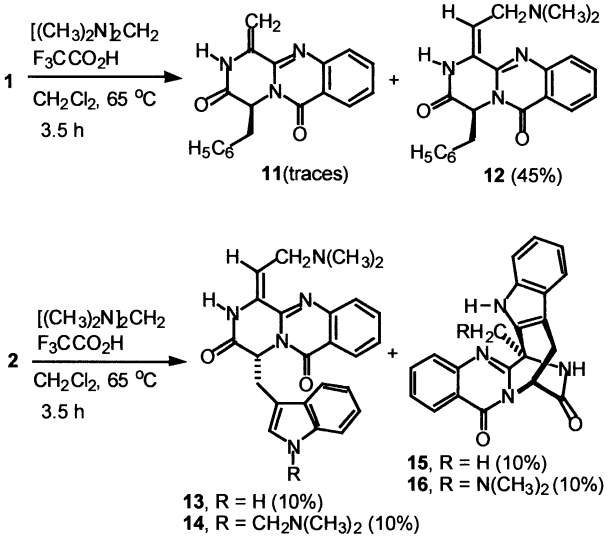
This result can be explained by assuming that the steric constraints imposed by the N(2)-substituent prevent the stabilization of the carbocation **I** formed by protonation of



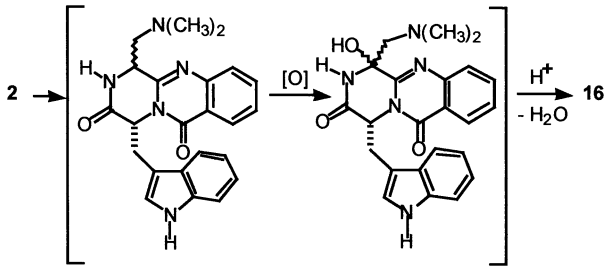
Scheme 3.



Scheme 4.



Scheme 5.



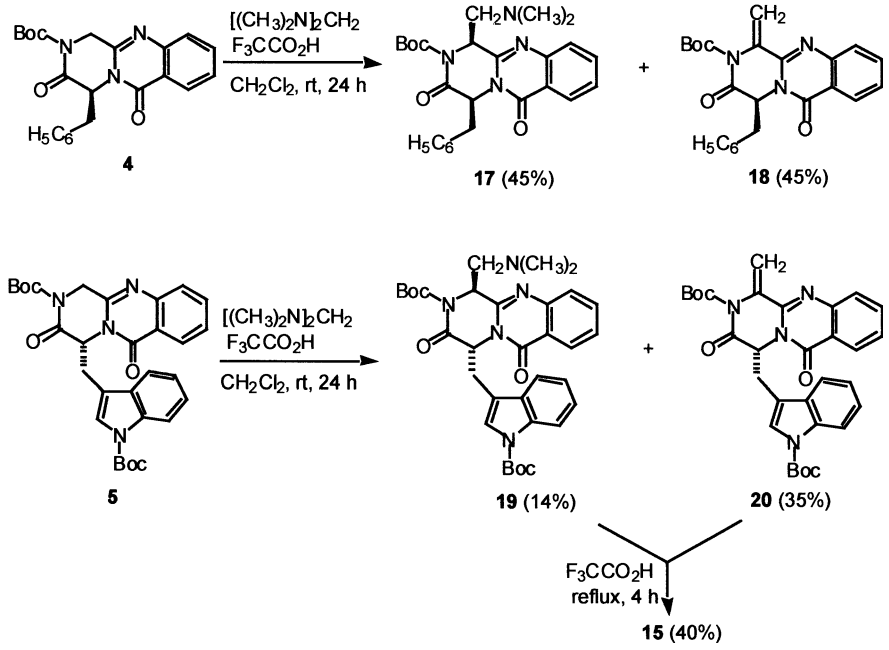
Scheme 6.

the exocyclic double bond, giving instead protonated species at N(11) (**II**, Scheme 3).[17,18]

In order to obtain alternative precursors of the desired *N*-acyliminium species, compound **3** was treated with PCC to give **8** which, after organometallic addition to the more electrophilic C(1)-carbonyl group, gave **9**. Its 1*R*,4*S*-stereochemistry was unequivocally established by NOE experiments, and was in accordance to the expected *syn* addition.[19] This compound was cyclized in TFA to give the Pictet–Spengler reaction product **10** (Scheme 4).

The N(2)-unsubstituted compounds **1** and **2** could not be conveniently derived to their 1-dimethylaminomethyl or 1-methylene analogues because they over-react with bis(dimethylamino) methane in anhydrous trifluoroacetic acid. In the case of **1**, only traces of **11** were obtained,[22] being **12** the main reaction product. This compound may be formed by addition of the Mannich reagent to the enamide **11**. Compound **2** gave in the same reaction conditions a mixture of compounds **13**, its *N*-alkyl derivative **14**, and the cyclized products **15** (precursor of (−)-alantrypinone) and **16** (Scheme 5).

A possible rationalization to explain formation of compound **16** is shown in Scheme 6.



Scheme 7.

To diminish the unexpected reactivity towards the Mannich reagent of the *N*-unsubstituted enamides, the *N*-Boc protected compounds **4** and **5** were used as starting materials, giving mixtures of dimethylaminomethyl compounds **17** and **19** and 1-methylene derivatives **18** and **20**. One-pot treatment of the mixture of compounds **19** and **20** with trifluoroacetic acid produced the *N*-Boc-deprotection and the cyclization of **20** to give **15** in 40% yield. In these conditions compound **19** must give **20** through a Hofmann elimination (Scheme 7).

In conclusion, we have developed an alternative protocol to prepare 1-dimethylaminomethyl, 1-mehylene and 1-hydroxy-4-arylmethylpyrazino[2,1-*b*]quinazoline-3,6-diones and have shown their ability to give Pictet–Spengler-type cyclizations through *N*-acyliminium species.

3. Experimental

3.1. General

All reagents were of commercial quality (Aldrich, Fluka, SDS, Probus) and were used as received. Solvents (SDS, Scharlau) were dried and purified using standard techniques. Reactions were monitored by thin layer chromatography, on aluminium plates coated with silica gel or aluminium oxide with fluorescent indicator (Merck 60 F_{254}). Separations by flash chromatography were performed on silica gel (Merck 60, 230–400 mesh) or aluminium oxide (Merck 90, 70–230 mesh). Melting points were uncorrected and were determined either using recrystallized samples or samples which crystallized during concentration of the chromatography eluents. Infrared spectra were recorded with solid compounds compressed into KBr pellets. NMR spectra were obtained at 250 or 300 MHz for ^{1}H and at 63 or 75 MHz for ^{13}C (Servicio de Resonancia Magnética Nuclear, Universidad Complutense). When necessary, assignments were aided by DEPT, COSY and ^{13}C–^{1}H correlation experiments. Mass spectra were carried out by the Servicio de Espectroscopía, Universidad Complutense. Elemental analyses were determined by the Servicio de Microanálisis Elemental, UCM. Optical rotations were measured at 25°C on a 1 mL cell in $CHCl_3$ or MeOH at 589 nm, concentrations being given in g/100 mL.

3.1.1. (+)-(4*S*)-4-Benzyl-2-*t*-butyloxycarbonyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (4). To a solution of **1** (100 mg, 0.3 mmol) in dry CH_2Cl_2 (10 mL) was added, under nitrogen, a solution of DMAP (60 mg, 0.49 mmol) and di-*t*-butyldicarbonate (107 mg, 0.49 mmol) in dry CH_2Cl_2 (5 mL). The resulting solution was stirred for 3 h at room temperature, quenched with 5% HCl and extracted with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Chromatography separation (EtOAc/hexane 1:2, silica gel) gave **4** as a white solid (114 mg, 85%) [found: C, 68.11; H, 5.69; N, 10.26. $C_{23}H_{23}N_3O_4$ requires: C, 68.13; H, 5.71; N, 10.36]; mp 158–59°C; $[\alpha]_D^{25}=+19$ (*c* 0.145, $CHCl_3$); ν_{max} (KBr) 1784, 1732, 1683 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.31 (dd, 1H, *J*=8.0 and 1.5 Hz), 7.79 (ddd, 1H, *J*=7.7, 7.6 and 1.5 Hz), 7.61 (d, 1H, *J*=7.7 Hz), 7.53 (ddd, 1H, *J*=8.0, 7.6 and 1.1 Hz), 7.31–7.16 (m, 3H), 6.93 (dd, 2H, *J*=7.5 and 1.0 Hz), 5.72 (t, 1H, *J*=4.6 Hz), 4.56 (d, 1H, *J*=17.1 Hz), 3.48 (dd, 1H, *J*=4.9 and 4.6 Hz), 2.78 (d, 1H, *J*=17.1 Hz), 1.52 (s, 9H); δ_C (63 MHz, $CDCl_3$) 166.8, 160.4, 150.2, 148.5, 147.5, 135.4, 135.1, 129.9, 129.5, 128.6, 127.7, 127.5, 127.4, 120.5, 85.3, 59.0, 47.5, 38.1, 28.3.

3.1.2. (−)-(4*R*)-2,1′-Bis(*t*-butyloxycarbonyl)-4-(3′indolylmethyl)-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (5). To a solution of glyantrypine [(4*R*)-**2**] (100 mg, 0.3 mmol) in dry CH_2Cl_2 (5 mL) was added, under nitrogen, a solution of DMAP (74 mg, 0.6 mmol), Et_3N (0.08 mL) and di-*t*-butyldicarbonate (197 mg, 0.9 mmol) in dry CH_2Cl_2 (5 mL). The resulting solution was stirred for 3 h at room temperature, quenched with 5% HCl and extracted with CH_2Cl_2. The organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Chromatography separation (EtOAc/hexane 1:2, silica gel) gave compound **5** as a white solid (155 mg, 95%) [found: C, 65.90; H, 6.04; N, 10.40. $C_{30}H_{32}N_4O_6$ requires: C, 66.16; H, 5.92; N, 10.28]; mp 170–71°C; $[\alpha]_D^{25}=-31$ (*c* 0.33, $CHCl_3$); ν_{max} (KBr) 1732, 1686 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.30 (dd, 1H, *J*=8.0 and 1.5 Hz), 8.05 (d, 1H, *J*=8.3 Hz), 7.77 (ddd, 1H, *J*=7.6, 7.4 and 1.5 Hz), 7.56 (d, 1H, *J*=7.4 Hz), 7.52 (ddd, 1H, *J*=8.0, 7.6 and 1.1 Hz), 7.30 (d, 1H, *J*=7.8 Hz), 7.24 (dt, 1H, *J*=8.2 and 1.1 Hz), 7.10 (s, 1H), 7.03 (dt, 1H, *J*=7.6 and 0.9 Hz), 5.75 (dd, 1H, *J*=5.7 and 3.8 Hz), 4.58 (d, 1H, *J*=17.2 Hz), 3.61 (dd, 1H, *J*=14.8 and 3.8 Hz), 3.53 (dd, 1H, *J*=14.8 and 5.7 Hz), 3.30 (d, 1H, *J*=17.2 Hz), 1.51 (s, 9H), 1.44 (s, 9H); δ_C (63 MHz, $CDCl_3$) 166.7, 160.2, 149.6, 149.3, 147.9, 147.3, 135.5, 135.2, 129.6, 127.5, 127.1, 127.0, 125.2, 125.1, 123.2, 120.3, 118.6, 115.5, 113.8, 85.0, 84.9, 57.7, 47.6, 28.2, 27.9, 27.6.

3.1.3. (+)-(4*S*)-4-Benzyl-2-methyl-2,4-dihydro-1*H*-pyrazino-[2,1-*b*]quinazoline-3,6-dione (3). To a stirred solution of 3 g (11.3 mmol) of *N*-Boc-(L)-phenylalanine in 50 mL dry CH_2Cl_2, under argon, methyl *N*-(methyl)glycinate (2 g, 14.7 mmol) and EDC [1-ethyl-3-(3′-(dimethylamino) propyl] carbodiimide] (2.4 g, 13.56 mmol) were added and stirring was continued overnight. The solution was washed with 1N aqueous HCl (15 mL) and 1N aqueous $NaHCO_3$ (15 mL), dried over Na_2SO_4 and evaporated to yield (+)-Methyl-*N*′-(*t*-butyloxycarbonyl)-L-phenylalanyl-*N*-methylglycinate as a syropous residue (3 g, 75%) [found: C, 61.38; H, 7.15; N, 7.82. $C_{18}H_{26}N_2O_5$ requires: C, 61.69; H, 7.47; N, 7.99]; $[\alpha]_D^{25}=+14$ (*c* 0.13, $CHCl_3$); ν_{max} (KBr) 2977, 1751, 1710 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.19–7.07 (m, 5H), 5.45 (d, 1H, *J*=8.6 Hz), 4.79 (dd, 1H, *J*=15.2 and 7.0 Hz), 4.02 (m, 2H), 3.59 (s, 3H), 2.94 (dd, 1H, *J*=13.4 and 7.0 Hz), 2.83 (dd, 1H, *J*=13.4 and 6.5 Hz), 1.29 (s, 9H); δ_C (63 MHz, $CDCl_3$) 172.2, 169.1, 154.9, 136.2, 129.4, 128.2, 126.6, 79.3, 51.9, 51.3, 49.3, 39.3, 36.0, 28.1.

The above Boc-protected dipeptide (3 g, 8.56 mmol) was heated at 200°C under a stream of argon for 3–4 h. After cooling, the residue was washed with ethyl acetate and the precipitate formed was removed by filtration yielding (−)-(3*S*)-3-benzyl-1-methyl-2,5-piperazinedione as a white solid (1.5 g, 80%) [found: C, 65.83; H, 6.52; N, 12.51. $C_{12}H_{14}N_2O_2$ requires: C, 66.04; H, 6.46; N, 12.84]; mp 169–70°C; $[\alpha]_D^{25}=-32$ (*c* 0.13, $CHCl_3$); ν_{max} (KBr) 3250, 1683, 1665 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.29–7.25 (m, 3H), 7.18–7.14 (m, 2H), 4.26 (m, 1H), 3.46 (d, 1H,

J=17.6 Hz), 3.19 (dd, 1H, J=13.6 and 5.4 Hz), 3.05 (dd, 1H, J=13.6 and 4.1 Hz), 2.81 (d, 1H, J=17.6 Hz), 2.78 (s, 3H); δ_C (63 MHz, $CDCl_3$) 166.3, 165.5, 135.1, 129.9, 128.6, 127.5, 56.3, 50.7, 40.7, 33.4.

A solution of the above described piperazinedione (220 mg, 1.01 mmol), triethyloxonium tetrafluoroborate (250 mg, 1.31 mmol) and anhydrous Na_2CO_3 (154 mg, 1.1 mmol) in 3 mL of dry CH_2Cl_2 was stirred overnight, under argon at rt, poured on ice water, extracted with CH_2Cl_2, dried (Na_2SO_4) and evaporated. Column chromatography (EtOAc, aluminium oxide) of the residue afforded *(+)-(3S)-3-benzyl-5-ethoxy-1-methyl-3,6-dihidro-1H-2-pirazinone* (150 mg, 60%) as a colorless oil [found: C, 67.99; H, 7.51; N, 11.25. $C_{14}H_{18}N_2O_2$ requires: C, 68.27; H, 7.37; N, 11.37.]; $[\alpha]_D^{25}$=+55 (*c* 0.19, $CHCl_3$); ν_{max} (KBr) 1696, 1657 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 7.17–7.10 (m, 3H), 7.04–6.99 (m, 2H), 4.39 (m, 1H), 4.11 (m, 2H), 3.26 (d, 1H, J=16.5 Hz), 3.25 (d, 1H, J=16.5 Hz), 2.96 (dd, 1H, J=13.5 and 4.3 Hz), 2.66 (s, 3H), 2.44 (dd, 1H, J=13.5 and 2.1 Hz), 1.21 (t, 3H, J=7.1 Hz); δ_C (63 MHz, $CDCl_3$) 168.5, 157.6, 136.4, 130.0, 127.7, 126.6, 61.3, 60.1, 47.7, 40.2, 32.8, 14.1.

A mixture of the above described iminoether (115 mg, 0.47 mmol) and anthranilic acid (90 mg, 0.66 mmol) was melted at 120°C under a stream of argon and kept at this temperature for 3 h. The cooled melt was triturated with 3N ammonium hydroxide, and the mixture was extracted with CH_2Cl_2 (5×5 mL). The combined organic layers were dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica gel eluting with EtOAc affording compound **3** (145 mg, 97%) [found: C, 71.69; H, 5.11; N, 13.34. $C_{19}H_{17}N_3O_2$ requires: C, 71.46; H, 5.36; N, 13.16]; mp 56–57°C; $[\alpha]_D^{25}$=+267 (*c* 0.33, $CHCl_3$); ν_{max} (KBr) 1673, 1603 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.33 (dd, 1H, J=7.9 and 1.5 Hz), 7.77 (ddd, 1H, J=7.4, 7.0 and 1.5 Hz), 7.56 (d, 1H, J=7.4 Hz), 7.51 (ddd, 1H, J=7.9, 7.6 and 1.1 Hz), 7.30–7.14 (m, 3H), 6.87 (dd, 2H, J=7.6 and 1.5 Hz), 5.60 (t, 1H, J=4.0 Hz), 3.74 (d, 1H, J=17.0 Hz), 3.62 (dd, 1H, J=14.0 and 3.5 Hz), 3.41 (dd, 1H, J=14.0 and 4.5 Hz), 2.86 (s, 3H), 2.59 (d, 1H, J=17.0 Hz); δ_C (63 MHz, $CDCl_3$) 165.9, 160.2, 148.1, 147.1, 134.9, 134.8, 129.6, 128.7, 127.9, 127.0, 126.9, 126.8, 120.0, 56.9, 51.0, 37.5, 33.3.

3.2. General procedure for the Mannich reactions

Method A. To a stirred and cooled (ice-salt bath) anhydrous trifluoroacetic acid (0.348 mL, 4.5 mmol), bis(dimethylamino)methane (0.12 mL, 0.905 mmol) was added slowly. The temperature of the resulting solution was kept below −15°C and the substituted pyrazino quinazolinedione (0.905 mmol) disolved in dry CH_2Cl_2 (6 mL) was then added. The cooling bath was removed and the solution was heated at 65°C for 3.5 h. To the cooled solution H_2O (5 mL) was added, neutralized with saturated solution of $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, filtered and concentrated. Flash column chromatography (silica gel) afforded pure products.

3.2.1. (+)-(4*S*)-4-Benzyl-2-methyl-1-methylene-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (6). Compound **6** was obtained from **3** (EtOAc/hexane, 2:1) as a white solid; (194 mg, 65%) [found: C, 72.13; H, 4.98; N, 12.77. $C_{20}H_{17}N_3O_2$ requires: C, 72.49; H, 5.17; N, 12.68]; mp 54–55°C; $[\alpha]_D^{25}$=+242 (*c* 0.13, $CHCl_3$); ν_{max} (KBr) 1684, 1624 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.30 (dd, 1H, J=7.8 and 1.6 Hz), 7.76 (ddd 1H, J=7.9, 7.6 and 1.6 Hz), 7.63 (dd, 1H, J=7.9 and 1.3 Hz), 7.49 (ddd, 1H, J=7.8, 7.6 and 1.3 Hz), 7.17 (m, 1H), 7.05 (dt, 2H, J=6.2 and 1.2 Hz), 6.69 (dd, 2H, J=7.7 and 1.4 Hz), 5.76 (t, 1H, J=4.2 Hz), 5.50 (d, 1H, J=1.6 Hz), 4.40 (d, 1H, J=1.6 Hz), 3.34 (d, 2H, J=4.2 Hz), 3.06 (s, 3H); δ_C (63 MHz, $CDCl_3$) 164.4, 160.3, 147.4, 144.9, 136.8, 134.9, 134.0, 129.7, 128.7, 127.9, 127.8, 127.3, 126.9, 120.3, 101.3, 56.3, 38.3, 30.2.

3.2.2. (+)-(4*S*)-4-Benzyl-1-dimethylaminoethyliden-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (12). Compound **12** was obtained from **1** (EtOAc/CH_3OH; 95:5) as a white solid, (152 mg, 45%) [found: C, 70.65; H, 5.87; N, 14.78. $C_{22}H_{22}N_4O_2$ requires: C, 70.56; H, 5.92; N, 14.96]; mp 76–77°C; $[\alpha]_D^{25}$=+176 (*c* 0.09, $CHCl_3$); ν_{max} (KBr) 1683, 1581 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.33 (dd, 1H, J=8.0 and 1.4 Hz), 7.76 (dd 1H, J=7.7 and 1.4 Hz), 7.62 (d, 1H, J=7.7 Hz), 7.52 (dd, 1H, J=8.0 and 7.7 Hz), 7.17–7.06 (m, 3H), 6.83 (dd, 2H, J=7.5 and 1.5 Hz), 5.86 (dd, 1H, J=5.7 and 4.3 Hz), 5.71 (dd, 1H, J=4.8 and 3.7 Hz), 3.42 (d, 1H, J=4.8 Hz), 3.41 (d, 1H, J=3.7 Hz), 3.0 (dd, 1H, J=16.2 and 4.3 Hz), 2.85 (dd, 1H, J=16.2 and 5.7 Hz), 2.16 (s, 6H); δ_C (63 MHz, $CDCl_3$) 164.4, 161.0, 147.5, 144.0, 135.2, 134.6, 130.9, 130.3, 128.8, 127.8, 127.4, 127.3, 120.5, 109.9, 57.4, 56.8, 45.5, 38.1.

The same reaction conditions, but using **2** as starting material and EtOAc/methanol (3:2) as eluent for the silica gel chromatography gave compounds **13**–**16**. Compound **15** is described later.

3.2.3. (−)-(4*R*)-4-(3′-Indolylmethyl)-1-(2′-dimethylaminoethyliden)-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (13). Yellow solid, (12 mg, 10%) [found: C, 69.77; H, 5.58; N, 16.96. $C_{24}H_{23}N_5O_2$ requires: C, 69.72; H, 5.61; N, 16.94]; mp 128–129°C; $[\alpha]_D^{25}$=−230 (*c* 0.09, $CHCl_3$); ν_{max} (KBr) 3142, 1683 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.32 (dd, 1H, J=8.0 and 1.5 Hz), 7.98 (ws, 1H), 7.74 (ddd, 1H, J=8.0, 7.6 and 1.5 Hz), 7.63 (d, 1H, J=7.9 Hz), 7.57 (d, 1H, J=8.0 Hz), 7.47 (ddd, 1H, J=8.0, 7.6 and 1.1 Hz), 7.24 (d, 1H, J=8.0 Hz), 7.13 (dt, 1H, J=6.9 and 1.1 Hz), 7.01 (dt, 1H, J=7.9 and 1.1 Hz), 6.27 (d, 1H, J=2.3 Hz), 5.72 (dd, 1H, J=5.0 and 2.5 Hz), 5.50 (dd, 1H, J=6.2 and 3.6 Hz), 3.72 (dd, 1H, J=14.8 and 2.5 Hz), 3.45 (dd, 1H, J=14.8 and 5.0 Hz), 2.31 (dd, 1H, J=16.0 and 6.2 Hz), 1.89 (s, 6H), 1.77 (dd, 1H, J=16.0 and 3.6 Hz); δ_C (63 MHz, $CDCl_3$) 165.2, 160.6, 147.4, 144.7, 136.3, 134.8, 130.5, 128.0, 127.4, 127.1, 126.9, 124.2, 122.4, 120.2, 119.8, 119.5, 110.8, 108.8, 108.7, 56.1, 55.7, 44.8, 28.2.

3.2.4. (−)-(4*R*)-1-(2′-Dimethylaminoethyliden)-4-(1′-dimethyl-aminomethyl-3′-indolylmethyl)-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (14). Yellow solid, (14 mg, 10%) [found: C, 68.89; H, 6.44; N, 17.90. $C_{27}H_{30}N_6O_2$ requires: C, 68.92; H, 6.43; N, 17.86]; mp 80–81°C; $[\alpha]_D^{25}$=−195 (*c* 0.49, $CHCl_3$); ν_{max} (KBr)

3135, 1683 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.32 (dd, 1H, J=7.9 and 1.6 Hz), 7.73 (ddd, 1H, J=7.7, 6.9 and 1.6 Hz), 7.66 (d, 1H, J=7.8 Hz), 7.52 (d, 1H, J=6.9 Hz), 7.48 (ddd, 1H, J=7.9, 7.6 and 1.6 Hz), 7.30 (d, 1H, J=8.2 Hz), 7.15 (dt, 1H, J=7.0 and 1.0 Hz), 7.02 (dt, 1H, J=7.4 and 1.0 Hz), 6.20 (s, 1H), 5.72 (dd, 1H, J=5.2 and 2.4 Hz), 5.52 (dd, 1H, J=6.2 and 3.5 Hz), 4.63 (d, 1H, J=13.0 Hz), 4.36 (d, 1H, J=13.0 Hz), 3.72 (dd, 1H, J=14.8 and 2.4 Hz), 3.44 (dd, 1H, J=14.8 and 5.2 Hz), 2.32 (dd, 1H, J=16.0 and 6.2 Hz), 2.11 (s, 6H), 1.91 (s, 6H), 1.78 (dd, 1H, J=16.0 and 3.5 Hz); δ_C (63 MHz, $CDCl_3$) 164.9, 160.4, 147.1, 144.2, 137.5, 134.6, 130.4, 128.5, 128.4, 127.0, 126.9, 126.7, 121.9, 120.0, 119.4, 109.6, 108.9, 107.4, 62.3, 55.9, 55.5, 44.7, 42.2, 28.1.

3.2.5. (−)-(1*R*,4*R*)-1,4-(2,3)-Indolmethane-1-dimethylaminomethyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (16). Yellow solid, (12 mg, 10%) [found: C, 69.22; H, 5.27; N, 17.55. $C_{23}H_{21}N_5O_2$ requires: C, 69.16; H, 5.30; N, 17.53]; mp 141–42°C; $[\alpha]_D^{25}$=−162 (c 0.18, $CHCl_3$); ν_{max} (KBr) 3194, 1684 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.24 (dd, 1H, J=7.9 and 1.5 Hz), 7.67 (dt, 1H, J=8.2 and 1.5 Hz), 7.56 (d, 1H, J=7.4 Hz), 7.46–7.38 (m, 2H), 7.29 (d, 1H, J=8.0 Hz), 7.16 (dt, 1H, J=6.9 and 1.2 Hz), 7.06 (dt, 1H, J=7.4 and 1.1 Hz), 6.03 (dd, 1H, J=4.7 and 2.6 Hz), 3.55 (dd, 1H, J=17.3 and 2.6 Hz), 3.39 (dd, 1H, J=17.3 and 4.7 Hz), 2.91–2.78 (m, 2H), 2.34 (s, 6H); δ_C (63 MHz, $CDCl_3$) 170.1, 160.2, 153.4, 146.8, 134.9, 134.4, 132.1, 127.7, 127.4, 127.1, 126.8, 123.0, 120.6, 120.1, 118.2, 111.3, 107.7, 58.6, 54.7, 54.2, 44.8, 25.7.

Method B. It was the same as Method A but starting by N-Boc protected compounds **4** (139 mg, 0.34 mmol) or **5** (100 mg, 0.18 mmol) and solution stirring at room temperature for 24 h. Flash column chromatography (silica gel) of the residue afforded pure compounds.

3.2.6. (+)-(4*S*)-4-Benzyl-1-dimethylaminomethyl-2-*t*-butyloxycarbonyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (17). Compound **17** was obtained from **4** (EtOAc/CH_3OH; 95:5) as a white solid, (71 mg, 45%) [found: C, 67.39; H, 6.46; N, 12.07. $C_{26}H_{30}N_4O_4$ requires: C, 67.51; H, 6.53; N, 12.11]; mp 62–63°C; $[\alpha]_D^{25}$=+95 (c 0.1, $CHCl_3$); ν_{max} (KBr) 2996, 1779, 1732, 1688 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.30 (dd, 1H, J=7.7 and 1.5 Hz), 7.80 (ddd, 1H, J=7.9, 7.6 and 1.5 Hz), 7.67 (dd, 1H, J=7.9 and 1.2 Hz), 7.52 (ddd, 1H, J=7.7, 7.6 and 1.2 Hz), 7.30–7.20 (m, 5H), 5.33 (dd, 1H, J=7.1 and 3.8 Hz), 5.27 (dd, 1H, J=7.7 and 4.3 Hz), 3.54 (dd, 1H, J=13.8 and 7.1 Hz), 3.41 (dd, 1H, J=13.8 and 3.8 Hz), 2.61 (dd, 1H, J=13.3 and 4.3 Hz), 2.09 (dd, 1H, J=13.3 and 7.7 Hz), 2.19 (s, 6H), 1.54 (s, 9H); δ_C (63 MHz, $CDCl_3$) 165.6, 160.9, 151.1, 149.9, 147.5, 136.7, 135.3, 130.4, 129.1, 127.7, 127.5, 127.4, 127.2, 120.5, 84.6, 64.7, 59.2, 58.9, 46.4, 39.5, 28.1.

3.2.7. (+)-(4*S*)-4-Benzyl-1-methylene-2-*t*-butyloxycarbonyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (18). Compound **18** was obtained from **4** (EtOAc/CH_3OH; 95:5) as a white solid, (64 mg, 45%) [found: C, 68.94; H, 5.36; N, 9.98. $C_{24}H_{23}N_3O_4$ requires: C, 69.05; H, 5.55; N, 10.06]; mp 64–65°C; $[\alpha]_D^{25}$=+105 (c 0.095, $CHCl_3$); ν_{max} (KBr) 1772, 1685, 1473 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.32 (dd, 1H, J=8.0 and 1.5 Hz), 7.80 (ddd, 1H, J=7.9, 7.6 and 1.5 Hz), 7.68 (dd, 1H, J=7.9 and 1.2 Hz), 7.53 (ddd, 1H, J=8.0, 7.6 and 1.2 Hz), 7.22–7.09 (m, 3H), 6.87 (dd, 2H, J=7.6 and 1.5 Hz), 5.81 (t, 1H, J=4.8 Hz), 5.64 (d, 1H, J= 1.8 Hz), 4.75 (d, 1H, J=1.8 Hz), 3.39 (d, 2H, J=4.8 Hz), 1.58 (s, 9H); δ_C (63 MHz, $CDCl_3$) 163.7, 160.4, 149.4, 147.6, 144.8, 135.3, 133.7, 132.9, 130.4, 129.1, 128.2, 128.1, 127.9, 127.3, 120.5, 105.2, 86.7, 57.0, 38.3, 27.9.

3.2.8. (−)-(1*S*,4*R*)-2,1′-Bis(*t*-butyloxycarbonyl)-4-(3′indolyl-methyl)-1-dimethylaminomethyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (19). Compound **19** was obtained from **5** ($HCCl_3$/EtOAc, 9:1) (15 mg, 14%) [found: C, 65.91; H, 6.50; N, 11.65. $C_{33}H_{39}N_5O_6$ requires: C, 65.87; H, 6.53; N, 11.64]; mp 89–90°C; $[\alpha]_D^{25}$=−20 (c 0.12, $CHCl_3$); ν_{max} (KBr) 1781, 1735, 1686 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.30 (dd, 1H, J=8.0 and 1.5 Hz), 8.05 (d, 1H, J=8.1 Hz), 7.78 (ddd, 1H, J=7.6, 7.5 and 1.5 Hz), 7.64 (d, 1H, J=7.6 Hz), 7.56 (d, 1H, J=7.8 Hz), 7.50 (ddd, 1H, J=8.0, 7.5 and 1.2 Hz), 7.28 (s, 1H), 7.27 (m, 1H), 7.1 (dt, 1H, J=7.5 and 1.9 Hz), 5.63 (dd, 1H, J=7.3 and 4.0 Hz), 5.25 (dd, 1H, J=8.0 and 4.1 Hz), 3.66 (dd, 1H, J=14.6 and 7.3 Hz), 3.50 (dd, 1H, J=14.6 and 4.0 Hz), 2.52 (d, 1H, J= 13.2 and 4.1 Hz), 2.05 (s, 6H), 2.02 (d, 1H, J=13.0 Hz), 1.62 (s, 9H), 1.49 (s, 9H); δ_C (63 MHz, $CDCl_3$) 164.8, 160.5, 150.6, 149.5, 149.4, 147.1, 135.1, 134.8, 130.3, 127.1, 126.9, 126.7, 124.7, 124.5, 122.7, 120.0, 119.2, 115.1, 115.0, 84.2, 83.5, 64.8, 57.7, 45.8, 28.5, 28.0, 27.6.

3.2.9. (−)-(4*R*)-2,1′-Bis(*t*-butyloxycarbonyl)-4-(3′indolylmethyl)-1-methylene-2,4-dihydro-1*H*-pyrazino[2,1-*b*]-quinazoline-3,6-dione (20). ($HCCl_3$/EtOAc, 9:1), (35 mg, 35%) [found: C, 66.93; H, 5.77; N, 10.03. $C_{31}H_{32}N_4O_6$ requires: C, 66.89; H, 5.79; N, 10.06]; mp 66–67°C; $[\alpha]_D^{25}$=−20 (c 0.12, $CHCl_3$); ν_{max} (KBr) 1772, 1734, 1684 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.30 (dd, 1H, J=7.9 and 1.5 Hz), 8.02 (d, 1H, J=8.3 Hz), 7.75 (ddd, 1H, J= 8.4, 7.7 and 1.5 Hz), 7.56 (d, 1H, J=8.4 Hz), 7.50 (ddd, 1H, J=7.9, 7.1 and 1.1 Hz), 7.19–7.12 (m, 2H), 7.08 (s, 1H), 6.87 (dt, 1H, J=7.5 and 0.9 Hz), 5.84 (dd, 1H, J=5.7 and 3.7 Hz), 5.51 (d, 1H, J=1.6 Hz), 4.65 (d, 1H, J= 1.6 Hz), 3.53 (dd, 1H, J=14.7 and 5.7 Hz), 3.44 (d, 1H, J=14.7 and 3.7 Hz), 1.55 (s, 9H), 1.50 (s, 9H); δ_C (63 MHz, $CDCl_3$) 163.5, 160.1, 149.2, 148.7, 147.1, 144.4, 135.2, 134.8, 133.0, 130.1, 127.6, 127.4, 126.7, 125.4, 124.4, 122.5, 120.4, 118.0, 114.8, 112.6, 105.2, 86.1, 83.9, 56.0, 27.9, 27.4, 27.2.

3.3. Oxidation at C-1 and subsequent Grignard addition

3.3.1. (+)-(4*S*)-4-Benzyl-2-methyl-2,4-dihydropyrazino-[2,1-*b*]quinazoline-1,3,6-trione (8). A mixture of **3** (262 mg, 0.82 mmol) and PCC (371 mg, 1.72 mmol) in dry CH_2Cl_2 (20 mL) was stirred under nitrogen at room temperature overnight. After evaporation in vacuo of the solvent, the crude was chromatographed in silica gel. (EtOAc/hexane, 2:1) as a white solid (164 mg, 60%) [found: C, 68.41; H, 4.79; N, 12.56. $C_{19}H_{15}N_3O_3$ requires: C, 68.46; H, 4.53; N, 12.61]; mp 163–64°C; $[\alpha]_D^{25}$=+390 (c 0.11, $CHCl_3$); ν_{max} (KBr) 1742, 1685, 1595 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.32 (dd, 1H, J=7.9 and 1.0 Hz), 7.91 (dd, 1H, J=7.8 and 0.8 Hz), 7.84 (m, 1H), 7.63 (m, 1H), 7.18 (m, 1H), 7.08 (t, 2H, J=7.5 Hz), 6.59 (dd, 2H, J=7.6

and 1.2 Hz), 5.84 (t, 1H, *J*=4.0 Hz), 3.46 (dd, 2H, *J*=14.0 and 4.7 Hz), 3.36 (dd, 1H, *J*=14.0 and 3.3 Hz), 3.07 (s, 3H); δ_C (63 MHz, $CDCl_3$) 167.5, 159.5, 156.3, 146.4, 139.3, 135.5, 132.7, 129.7, 129.2, 129.1, 128.7, 126.9, 121.4, 57.0, 38.8, 27.3.

3.3.2. (+)-(1*R*,4*S*)-4-Benzyl-1-hydroxy-2-methyl-1-phenyl-2,4-dihydro-(1*H*)-pyrazino [2,1-*b*]quinazoline-3,6-dione (9). To a solution of **8** (0.39 mmol) in dry THF (7 mL) was added, under nitrogen, a solution of PhMgBr (0.5 mmol) at −78°C. The resulting mixture was stirred for 3 h, quenched by the addition of saturated solution of NH_4Cl (1 mL), and allowed to warm to 20°C. Ethyl acetate was added (10 mL), the organic layer was separated, and the aqueous phase was extracted with EtOAc (3×10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. Flash column chromatography in silica gel (EtOAc/hexane, 1:2) afforded **9** as a white solid, (130 mg, 84%) [found: C, 73.07; H, 5.09; N, 10.15. $C_{25}H_{21}N_3O_3$ requires: C, 72.98; H, 5.26; N, 10.21]; mp 80–81°C; $[\alpha]_D^{25}$=+46 (*c* 0.17, $CHCl_3$); ν_{max} (KBr) 3372, 1669, 1607 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.18 (dd, 1H, *J*=7.9 and 1.5 Hz), 7.78 (ddd, 1H, *J*=8.2, 7.4 and 1.5 Hz), 7.73 (dd, 1H, *J*=8.2 and 1.6 Hz), 7.50 (ddd, 1H, *J*=7.9, 7.4 and 1.6 Hz), 7.42–7.28 (m, 5H), 7.23–7.18 (m, 3H), 7.08–7.03 (m, 2H), 6.13 (ws, 1H), 5.52 (dd, 1H, *J*=8.4 and 5.5 Hz), 3.18 (s, 3H), 2.93 (dd, 1H, *J*=13.6 and 8.4 Hz), 2.79 (dd, 1H, *J*=13.6 and 5.5 Hz); δ_C (63 MHz, $CDCl_3$) 165.2, 160.6, 152.8, 145.9, 140.8, 135.9, 135.1, 129.6, 129.1, 128.6, 128.1, 127.3, 127.2, 127.1, 126.4, 120.6, 85.1, 57.8, 37.6, 27.2.

3.4. Cyclization attempts. Synthesis of 7 and 10

A solution of compound **6** or **9** (0.82 mmol), in anhydrous TFA (5 mL) was refluxed with stirring for 4 h. After evaporation of the solvent, a small amount of EtOAc was added to the residue, basified with saturated $NaHCO_3$ solution and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and concentrated. The solid residue was chromatographed in silica gel to afford the pure products.

3.4.1. (+)-(1*S*,4*S*)-4-Benzyl-2-methyl-1-{2-[(4′*S*)-4′-benzyl-2′-methyl-3′6′-dioxo-2′,3′,4′,6′-tetrahydro-1′*H*-pyrazino-[2,1-*b*]quinazolinyliden]ethyl}-2,4-dihydro-1*H*-pyrazino-[2,1-*b*]quinazoline-3,6-dione (7). Compound **7** was obtained from **6** (EtOAc/hexane, 1:1) as a white solid, (109 mg, 40%) [found: C, 72.61; H, 4.99; N, 12.75. $C_{40}H_{34}N_6O_4$ requires: C, 72.49; H, 5.17; N, 12.68]; mp 114–115°C; $[\alpha]_D^{25}$=+182 (*c* 0.12, $CHCl_3$); ν_{max} (KBr) 1676 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.33 (dd, 1H, *J*=8.0 and 1.4 Hz), 8.32 (dd, 1H, *J*=8.3 and 1.3 Hz), 7.79 (dt, 1H, *J*=6.9 and 1.5 Hz), 7.76 (dt, 1H, *J*=6.8 and 1.5 Hz), 7.6 (d, 1H, *J*=8.1 Hz), 7.58 (d, 1H, *J*=7.5 Hz), 7.51 (t, 2H, *J*=7.5 Hz), 7.25–7.23 (m, 3H), 7.11–7.08 (m, 2H), 7.04–6.98 (m, 3H), 6.81–6.77 (m, 2H), 5.75 (t, 1H, *J*=5.0 Hz), 5.54 (t, 1H, *J*=5.5 Hz), 4.92 (dd, 1H, *J*=10.8 and 5.2 Hz), 4.81 (dd, 1H, *J*=9.8 and 7.3 Hz), 3.47 (d, 2H, *J*=5.5 Hz), 3.28 (d, 2H, *J*=5.0 Hz), 3.24 (s, 3H), 3.17 (m, 1H), 3.10 (s, 3H), 0.94 (m, 1H); δ_C (63 MHz, $CDCl_3$) 165.1, 164.9, 160.6, 159.9, 149.4, 146.9, 146.7, 145.1, 135.9, 135.1, 134.9, 134.6, 130.6, 129.9, 129.5, 128.6, 128.4, 127.7, 127.6, 127.5, 127.3, 127.2, 127.1, 120.2, 117.9, 62.1, 60.4, 57.3, 56.5, 37.9, 37.7, 32.9, 32.8, 31.2.

3.4.2. (+)-(1*R*,4*S*)-1-Phenyl-1,4(1,2)benzenemethane-2,4-dihydro-(1*H*)-pyrazino[2,1-*b*]quinazoline-3,6-dione (10). It was obtained from **9** (EtOAc/hexane, 1:3) as a white solid, (155 mg, 48%) [found: C, 76.29; H, 4.91; N, 10.65. $C_{25}H_{19}N_3O_2$ requires: C, 76.32; H, 4.87; N, 10.68]; mp 197–98°C; $[\alpha]_D^{25}$=+53 (*c* 0.12, $CHCl_3$); ν_{max} (KBr) 1668, 1608 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.31 (dd, 1H, *J*=8.3 and 1.6 Hz), 8.0 (dd, 1H, *J*=8.3 and 1.6 Hz), 7.89 (ddd, 1H, *J*=8.3, 5.3 and 3.4 Hz), 7.73 (ddd, 1H, *J*=8.3, 7.5 and 1.6 Hz), 7.54 (dd, 1H, *J*=6.4 and 3.4 Hz), 7.33 (dd, 1H, *J*=8.3 and 7.5 Hz), 7.19–7.13 (m, 2H), 6.89–6.81 (m, 5H), 5.58 (dd, 1H, *J*=5.3 and 3.9 Hz), 3.54 (s, 3H), 3.42 (dd, 1H, *J*=13.7 and 5.3 Hz), 3.31 (dd, 1H, *J*=13.7 and 3.9 Hz); δ_C (63 MHz, $CDCl_3$) 163.0, 157.1, 138.4, 135.0, 134.9, 130.1, 129.4, 128.9, 127.9, 127.1, 123.8, 122.5, 122.1, 120.9, 120.5, 117.3, 117.1, 114.6, 113.1, 100.4, 58.6, 37.6, 30.5.

3.4.3. (−)-(1*R*,4*R*)-1,4-(2,3)-Indolmethane-1-methyl-2,4-dihydro-1*H*-pyrazino[2,1-*b*]quinazoline-3,6-dione (15). A mixture of **19** (10 mg, 0.016 mmol) and **20** (30 mg, 0.05 mmol) in anhydrous TFA (2 mL) was treated as described for **10**. Compound **15** was obtained ($CHCl_3$/EtOAc, 3:1) as a white solid, (9.5 mg, 40%) [found: C, 70.71; H, 4.55; N, 15.69. $C_{21}H_{16}N_4O_2$ requires: C, 70.77; H, 4.52; N, 15.72]; mp 158–159°C; $[\alpha]_D^{25}$=−258 (*c* 0.243, EtOAc); ν_{max} (KBr) 3318, 1689 cm^{-1}; δ_H (250 MHz, $CDCl_3$) 8.24 (dd, 1H, *J*=7.9 and 1.2 Hz), 8.13 (ws, 1H), 7.75–7.72 (m, 2H), 7.59 (d, 1H, *J*=7.3 Hz), 7.45 (dd, 1H, *J*=7.5 and 1.2 Hz), 7.39 (dt, 1H, *J*=7.5 and 1.2 Hz), 7.30 (d, 1H, *J*=8.1 Hz), 7.18 (dt, 1H, *J*=7.1 and 1.1 Hz), 7.06 (dt, 1H, *J*=7.5 and 1.1 Hz), 6.06 (ws, 1H), 3.52 (dd, 2H, *J*=17.4 and 2.8 Hz), 3.40 (dd, 1H, *J*=17.4 and 4.6 Hz), 2.25 (s, 3H); δ_C (63 MHz, $CDCl_3$) 170.5, 160.1, 153.1, 146.9, 134.5, 134.4, 132.2, 127.7, 127.5, 127.3, 126.8, 123.4, 120.6, 120.5, 118.3, 111.2, 107.5, 54.6, 54.4, 25.8, 17.9. EIMS *m/z* (rel. intensity) 356 (M^+, 57), 341 (M^+-CH_3, 100).

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22. ^{1}H NMR (250 MHz, $CDCl_3$) δ 8.64 (ws, 1H), 8.34 (dd, 1H, J=7.9 and 1.4 Hz), 7.81 (ddd, 1H, J=8.2, 7.6 and 1.4 Hz), 7.68 (dd, 1H, J=8.2 and 1.3 Hz), 7.54 (ddd, 1H, J=7.9, 7.6 and 1.3 Hz), 7.22 (m, 1H), 7.16–7.10 (m, 2H), 6.84 (d, 2H, J=7.6 Hz), 5.76 (dd, 1H, J=5.0 and 3.8 Hz), 5.54 (d, 1H, J=1.2 Hz), 4.55 (d, 1H, J=1.2 Hz), 3.43 (d, 1H, J=5.0 Hz), 3.42 (d, 1H, J=3.8 Hz). ^{13}C NMR (63 MHz, $CDCl_3$) δ 166.1, 160.8, 147.4, 143.8, 135.3, 134.1, 133.0, 130.2, 129.0, 128.2, 127.8, 127.3, 120.6, 101.4, 57.3, 38.2. [found: C, 71.76; H, 4.68; N, 13.28. $C_{19}H_{15}N_3O_2$ requires: C, 71.91; H, 4.76; N, 13.24].