Supporting Information
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Diastereoselective One-pot Tandem Synthesis of Chromeno-pyrido-diazepinones via 1,4- and 1,6-Aza-conjugate additions/heterocyclisations

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Supplementary Material

Table of Contents:

General procedure for the synthesis of chromeno-pyrido-diazepinones 2a-c  

Figure 1. \textsuperscript{1}H NMR spectrum of compound 2a (300.13 MHz)  

Figure 2. \textsuperscript{13}C NMR spectrum of compound 2a (75.47 MHz)  

Figure 3. HMBC NMR spectrum of compound 2a  

Figure 4. Partial HMBC NMR spectrum of compound 2a  

Figure 5. \textsuperscript{1}H NMR spectrum of compound 2b (300.13 MHz)  

Figure 6. \textsuperscript{13}C NMR spectrum of compound 2b (75.47 MHz)  

Figure 7. HMBC NMR spectrum of compound 2b  

Figure 8. Partial HMBC NMR spectrum of compound 2b  

Figure 9. \textsuperscript{1}H NMR spectrum of compound 2c (300.13 MHz)  

Figure 10. \textsuperscript{13}C NMR spectrum of compound 2c (75.47 MHz)  

Figure 11. HMBC NMR spectrum of compound 2c  

Figure 12. Partial HMBC NMR spectrum of compound 2c  

Single-Crystal X-ray Diffraction Studies for compounds 2a and 2c  

References
General procedure for the synthesis of chromeno-pyrido-diazepinones 2a-c:
Ethylenediamine (10 mmol) is added to a THF (20 mL) stirred solution of (E,E)-3-[3-(2-
hydroxyphenyl)-3-oxoprop-1-en-1-yl]-2- styrylchromones 1a-c1 (1 mmol). The reaction
mixture was stirred for 2 h at room temperature. After solvent removal under reduced pressure, the
obtained resinous material was subjected to short-plug silica-gel column chromatography. The
product was recrystallized from a mixture of hexane–dichloromethane (1:1) by slow
evaporation at 6 °C to afford bright yellow crystals of compounds 2a-c. Good-quality single-
crystals suitable for X-ray analysis could only be obtained for 2a and 2c.

2-(2-Hydroxyphenyl)-7-(4-methoxyphenyl)-1,4,5,7,8,14b-hexahydro-14H-
chremeno[3′,2′:3,4]pyrido[1,2-d][1,4]diazepin-14-one (2a): C36H28N8O4 (Yellow crystals,
MW 466.54 g/mol, 0.34 g, 73% yield, mp 241-242 °C). 1H NMR (300.13 MHz, CDCl3): δ 2.84-
3.13 (m, 4H, H-4, H-5), 3.30 (dd, J 15.3, 9.5 Hz, 1H, H-1), 3.50 (dd, J 15.0, 4.7 Hz, 1H, H-8),
3.59 (d, J 15.3 Hz, 1H, H-1), 3.84 (s, 3H, 4″-OCH3), 4.00 (dd, J 15.0, 9.0 Hz, 1H, H-8), 4.49
(dd, J 9.0, 4.7 Hz, 1H, H-7), 4.61 (d, J 9.5 Hz, 1H, H-14b), 6.83-6.99 (m, 4H, H-5′, H-3′, H-
3″, 5″), 7.28-7.37 (m, 3H, H-4′, H-2″, 6″), 7.39-7.44 (m, 2H, H-10, H-12), 7.67 (ddd, J 8.8, 7.2,
1.7 Hz, 1H, H-11), 8.08 (dd, J 8.1, 1.4 Hz, 1H, H-6′), 8.30 (dd, J 9.0, 1.7 Hz, 1H, H-13), 16.43
(br s, 1H, 2′-OH) ppm. 13C NMR (75.47 MHz, CDCl3): δ 31.0 (C-1), 45.1 (C-8), 37.3 and 50.1
(C-4, C-5), 52.1 (C-14b), 55.3 (4″-OCH3), 55.9 (C-7), 114.5 (C-3″, 5″), 117.3 (C-5′), 117.8
(C-10), 118.8 (C-1′, C-3′), 119.7 (C-14a), 123.5 (C-13a), 124.9 (C-12), 126.0 (C-13), 129.49 and
129.52 (C-2″, 6″, C-6′), 131.4 (C-1′′), 133.1 (C-4′), 133.5 (C-11), 155.8 (C-9a), 159.5 (C-4″),
162.2 (C-8a), 165.0 (C-2′), 175.6 (C-14), 177.1 (C-2) ppm. HRMS-ESI+: m/z calcd for

7-(3,4-Dimethoxyphenyl)-2-(2-hydroxyphenyl)-1,4,5,7,8,14b-hexahydro-14H-
chremeno[3′,2′:3,4]pyrido[1,2-d][1,4]diazepin-14-one (2b): C36H28N8O5 (Yellow crystals,
MW 496.56 g/mol, 0.26 g, yield 52%, mp 253-254 °C). 1H NMR (300.13 MHz, CDCl3): δ 2.84-
3.18 (m, 4H, H-4, H-5), 3.32 (dd, J 15.3, 9.5 Hz, 1H, H-1), 3.50 (dd, J 15.0, 4.7 Hz, 1H, H-8),
3.56 (d, J 15.3 Hz, 1H, H-1), 3.90 and 3.92 (2s, 6H, 3″- and 4″-OCH3), 4.02 (dd, J 15.0, 9.0
Hz, 1H, H-8), 4.49 (dd, J 9.0, 4.7 Hz, 1H, H-7), 4.65 (d, J 9.5 Hz, 1H, H-14b), 6.84-7.01 (m,
(m, 1H, H-11), 8.07 (d, J 7.8 Hz, 1H, H-6′), 8.30 (dd, J 8.1, 1.4 Hz, 1H, H-13), 16.38 (br s, 1H,
2′-OH) ppm. 13C NMR (75.47 MHz, CDCl3): δ 30.9 (C-1), 45.0 (C-8), 37.2 and 50.0 (C-4, C-5),
52.1 (C-14b), 55.89 (C-7), 55.99 and 56.0 (4″-OCH3), 110.4 (C-6″), 111.0 (C-5″), 117.3 (C-5″),
117.7 (C-10), 118.7 and 118.8 (C-3′, C-1′), 119.6 (C-14a), 120.9 (C-2″), 123.5 (C-13a), 124.9
(C-12), 126.0 (C-13), 129.4 (C-6″), 131.8 (C-1″), 133.0 (C-4″), 133.5 (C-11), 149.0 and 149.7
(C-3″, C-4″), 155.8 (C-9a), 161.9 (C-8a), 164.8 (C-2″), 175.5 (C-14), 176.9 (C-2) ppm. HRMS-
ESI+: m/z calcd for [C36H28N8O5+H]+ 497.2076; found 497.2181.
2-(2-Hydroxyphenyl)-7-phenyl-1,4,5,7,8,14b-hexahydro-14H-chromeno[3′,2′:3,4]pyrido[1,2-d][1,4]diazepin-14-one (2c): C_{28}H_{24}N_{2}O_{3} (Yellow crystals, MW 436.51 g/mol, 0.27 g, yield 62%, mp 238-239 °C). \textsuperscript{1}H NMR (300.13 MHz, CDCl\textsubscript{3}): δ 2.85-3.18 (m, 4H, H-4, H-5), 3.31 (dd, J 15.3, 9.5 Hz, 1H, H-1), 3.51 (dd, J 15.0, 4.7 Hz, 1H, H-8), 3.60 (d, J 15.3 Hz, 1H, H-1), 3.99 (dd, J 15.0, 9.0 Hz, 1H, H-8), 4.53 (dd, J 9.0, 4.7 Hz, 1H, H-7), 4.63 (d, J 9.5 Hz, 1H, H-14b), 6.85-6.97 (m, 2H, H-5', H-3'), 7.28-7.36 (m, 1H, H-4'), 7.36-7.48 (m, 7H, H-10, H-12, H-4'', H-2'', H-3'', H-6'), 8.08 (dd, J 8.1, 1.2 Hz, 1H, H-6'), 8.30 (dd, J 8.2, 1.7 Hz, 1H, H-13), 16.41 (br s, 1H, 2''-OH) ppm. \textsuperscript{13}C NMR (75.47 MHz, CDCl\textsubscript{3}): δ 31.0 (C-1), 45.1 (C-8), 37.3 and 50.1 (C-4, C-5), 52.1 (C-14b), 55.3 (4''-OCH\textsubscript{3}), 55.9 (C-7), 114.5 (C-3'', 5''), 117.3 (C-5''), 117.8 (C-10), 118.8 (C-1', C-3''), 119.7 (C-14a), 123.5 (C-13a), 124.9 (C-12), 126.0 (C-13), 129.49 and 129.52 (C-2'', 6'', C-6''), 131.4 (C-1''), 133.1 (C-4''), 133.5 (C-11), 155.8 (C-9a), 159.5 (C-4''), 162.2 (C-8a), 165.0 (C-2'), 175.6 (C-14), 177.1 (C-2) ppm. HRMS-ESI\textsuperscript{+}: m/z calcd for [C\textsubscript{28}H\textsubscript{24}N\textsubscript{2}O\textsubscript{3}+Na\textsuperscript{+} 459.1685; found 459.1668.

Figure S1. \textsuperscript{1}H NMR spectrum of compound 2a (300.13 MHz)
Figure S2. $^{13}$C NMR spectrum of compound 2a (75.47 MHz)

Figure S3. HMBC NMR spectrum of compound 2a
Figure S4. Partial HMBC NMR spectrum of compound 2a

Figure S5. $^1$H NMR spectrum of compound 2b (300.13 MHz)
Figure S6. $^{13}$C NMR spectrum of compound 2b (75.47 MHz)

Figure S7. HMBC NMR spectrum of compound 2b
Figure S8. Partial HMBC NMR spectrum of compound 2b

Figure S9. $^1$H NMR spectrum of compound 2c (300.13 MHz)
Figure S10. $^{13}$C NMR spectrum of compound 2c (75.47 MHz)

Figure S11. HMBC NMR spectrum of compound 2c
Figure S12. Partial HMBC NMR spectrum of compound 2c

**Single-Crystal X-ray Diffraction Studies for compounds 2a and 2c**

Single crystals of compounds 2a and 2c were manually harvested from the crystallization vials and immersed in highly viscous FOMBLIN Y perfluoropolyether vacuum oil (LVAC 140/13, Sigma-Aldrich) to avoid degradation caused by the evaporation of the solvent. Crystals were mounted on Hampton Research CryoLoops with the help of a Stemi 2000 stereomicroscope equipped with Carl Zeiss lenses. X-ray diffraction data for 2a and 2c were collected on a Bruker D8 QUEST at 150(2) K equipped with Mo Kα sealed tube (λ = 0.71073 Å), a multilayer TRIUMPH X-ray mirror, a PHOTON 100 CMOS detector, and a Oxford Instruments Cryostrem 700+ Series low temperature device.

Diffraction images were processed using the software package SAINT+, and data were corrected for absorption by the multiscan semi-empirical method implemented in SADABS. Structures were solved using the algorithm implemented in SHELXT-2014, which allowed the immediate location of almost all of the heaviest atoms composing the molecular unit of the two compounds. The remaining missing and misplaced non-hydrogen atoms were located from difference Fourier maps calculated from successive full-matrix least-squares refinement cycles.
on $F^2$ using the latest SHELXL from the 2014 release.$^6$ All structural refinements were performed using the graphical interface ShelXle.$^7$

Hydrogen atoms bound to carbon were placed at their idealized positions using appropriate HFIX instructions in SHELXL: 43 (aromatic carbon atoms), 13 (tertiary carbon atoms), 23 (–CH$_2$– carbon atoms) or 137 (for the terminal methyl group). These hydrogen atoms were included in subsequent refinement cycles with isotropic thermal displacements parameters ($U_{iso}$) fixed at 1.2 (for the three former families of hydrogen atoms) or 1.5×$U_{eq}$ (solely for those associated with the methyl group) of the parent carbon atoms.

In 2a the hydrogen atom of the hydroxyl group could be were directly located from difference Fourier maps. This hydrogen atom was included in the final structural model with the O–H distance restrained to 0.95(1) Å. In 2c the hydrogen atom of the hydroxyl group was added geometrically using the HFIX147 instruction in SHELXL. In both cases the isotropic thermal displacements parameters ($U_{iso}$) of these hydrogen atoms were fixed at 1.5×$U_{eq}$ of the parent atoms.

The last difference Fourier map synthesis showed: for 2a, the highest peak (0.259 eÅ$^{-3}$) and the deepest hole (-0.242 eÅ$^{-3}$) located at 0.86 and 0.83 Å from C8 and C20, respectively; for 2c, the highest peak (0.922 eÅ$^{-3}$) and the deepest hole (-0.299 eÅ$^{-3}$) located at 0.97 and 0.68 Å from C12 and N1, respectively. Structural drawings have been created using the software package Crystal Impact Diamond.$^9$

Crystallographic data (including structure factors) for the crystal structure of both compounds were deposited with the Cambridge Crystallographic Data Centre as supplementary publication Nos CCDC-1584430 and -1584431. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 2EZ, U.K. FAX: (+44) 1223 336033. E-mail: deposit@ccdc.cam.ac.uk.

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