Supplementary Information

Enzymatic cyclizations using laccases: Multiple bond formation between dihydroxybenzoic acid derivates and aromatic amines

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Additional Information to Experimental Section

General Methods. The products were characterized by mass spectrometry (MS) using electro spray ionization under atmospheric conditions (API-ES) (dry and nebulizer gas: nitrogen) on a Bruker-Daltoniks micrOTOF instrument (Bremen, Germany; software: HyStar). The nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 600 instrument (Rheinstetten, Germany) at 600 MHz. Solvent used was DMSO-d_6. Chemical shifts are expressed in δ (ppm) calibrated on the resonances of the residual nondeuterated solvent. *J* values are given in Hz.

For routine analysis, the reaction mixtures were analyzed using an HPLC system LC-10AT VP (Shimadzu, Germany) consisting of a FCV-10AL VP pump, SPD-M10A VP diode array detector, and a SCL-10A VP control unit controlled by Class-VP version 6.12 SP5. The separation of the substances was achieved on an endcapped, 5-µm, LiChroCART® 125-4 RP18 column (Merck, Darmstadt, Germany) at a flow rate of 1 mL/min. A solvent system consisting of methanol (eluent A) and 0.1% phosphoric acid (eluent B), starting from an initial ratio of 10% A and 90% B and reaching 100% methanol within 14 min, was used.

Chemicals were purchased from commercial suppliers. All chemicals were used as received.

All reaction mixtures for product isolation were performed with laccase of *Pycnoporus cinnabarinus* (final activity 0.5 U) in SAB. Isolation steps were performed by solid-phase extraction with a RP18 silicagel column (60 mL, 10 g adsorbent material, phenomenex, Strata, Germany). The reactants, molarity of the reaction partners, incubation time before isolation, volume of the complete reaction mixture and volume of the reaction mixture per purification run as well as the purification steps are described in Table 1.

Table 1. Synthesis and purification scheme

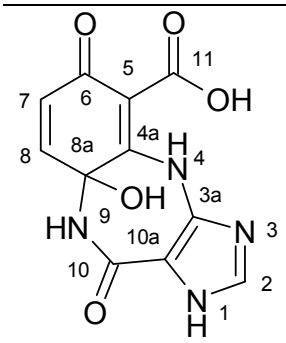
Product	Reactants	Molarity of the reaction partners (compound 1: compound 2)	Incu-bation time before isola-tion	Volume of the complete reaction mixture	Volume of the reaction mixture per puri-fication run	Washing steps (part of methanol in distilled water)	Elution
3a	**1a, 2a**	2:2 mM	2 h	340 mL	10 mL	100 mL 10 %	30 mL 40 %
3b	**1b, 2a**	2:2 mM	2 h	144 mL	8 mL	100 mL 10 %	20 mL 100 %
3c	**1a, 2b**	1:1 mM	2 h	360 mL	40 mL	15 mL 0 % 30 mL 10 %	20 mL 30 %
3d	**1b, 2b**	1:1 mM	2 h	120 mL	40 mL	20 mL 0 % 30 mL 10 %	30 mL 30 %
3e	**1b, 2c**	1:1 mM	2 h	120 mL	40 mL	10 mL 0 % 50 mL 10 % 40 mL 20 %	40 mL 30 %
3f	**1c, 2c**	1:1 mM	2 h	120 mL	40 mL	40 mL 0 % 20 mL 30 %	20 mL 50 %
3g	**1d, 2c**	1:1 mM	2 h	200 mL	40 mL	20 mL 0 % 30 mL 30 % 10 mL 50 %	20 mL 50 %
3h	**1b, 2d**	1:1 mM	2 h	200 mL	40 mL	40 mL 0 % 40 mL 10 %	30 mL 30 %
3i	**1c, 2d**	1:1 mM	2 h	120 mL	40 mL	20 mL 0 % 20 mL 10 % 40 mL 50 %	30 mL 100 %
3k and 5a	**1a, 2c**	1:1 mM	20 min	400 mL	40 mL	50 mL 0 % 20 mL 10 %	30 mL 30 %
3l and 5b	**1a, 2d**	1:1 mM	1 h	200 mL	40 mL	35 mL 0 % 70 mL 10 % 20 mL 20 %	30 mL 30 %
4a,b	**1c, 2a**	2:2 mM	24 h	460 mL	20 mL	80 mL 5 %; 10 ml 50 %	10 ml 50 %
4a,b	**1d, 2a**	2:2 mM	24 h	240 mL	20 mL	80 mL 5 %; 10 ml 50 %	10 ml 50 %
4c-f	**1c, 2b**	1:1 mM	2 h	120 mL	40 mL	40 mL 0 %	60 mL 10 %
4c-f	**1d, 2b**	1:1 mM	2 h	120 mL	40 mL	40 mL 0 %	60 mL 10 %
4c-f	**1a, 2b**	1:1 mM	2 h	360 mL	40 mL	20 mL 0 %	30 mL 10 %
6a	**1b, 2e**	1:1 mM	2 h	120 mL	40 mL	30 mL 0 % 20 mL 30 % 20 mL 50 %	30 mL 100 %
6b	**1c, 2e**	1:1 mM	2 h	120 mL	40 mL	30 mL 0 % 20 mL 30 % 20 mL 50 %	30 mL 100 %
6c	**1d, 2e**	1:1 mM	2 h	120 mL	40 mL	30 mL 0 % 20 mL 30 % 20 mL 50 %	30 mL 100 %

6d	**1a, 2f**	1:1 mM	2 h	200 mL	40 mL	40 mL 10 % 10 mL 50 %	30 mL 100 %
6e	**1c, 2f**	1:1 mM	2 h	200 mL	40 mL	20 mL 0 % 20 mL 10 % 30 mL 50 %	20 mL 100 %
7a	**1a, 2g**	1:1 mM	2 h	320 mL	40 mL	30 mL 0 % 10 mL 10 %	30 mL 30 %
7b and 8a	**1b, 2g**	1:1 mM	2 h	120 mL	40 mL	30 mL 0 % 40 mL 10 %	20 mL 50 %
7c and 8b	**1c, 2g**	1:1 mM	20 min	120 mL	40 mL	30 mL 0 % 40 mL 10 %	15 mL 50 %
9a and 10a	**1a, 2g**	1:1 mM	2 h	320 mL	40 mL	30 mL 0 % 10 mL 10 % 20 mL 50 % 30 mL 30 %	10 mL 100 %
9b	**1b, 2g**	1:2 mM	24 h	120 mL	40 mL	40 mL 0 % 40 mL 10 % 20 mL 50 %	40 mL 100 %
9c	**1c, 2g**	1:2 mM	24 h	120 mL	40 mL	40 mL 0 % 40 mL 10 % 20 mL 50 %	40 mL 100 %

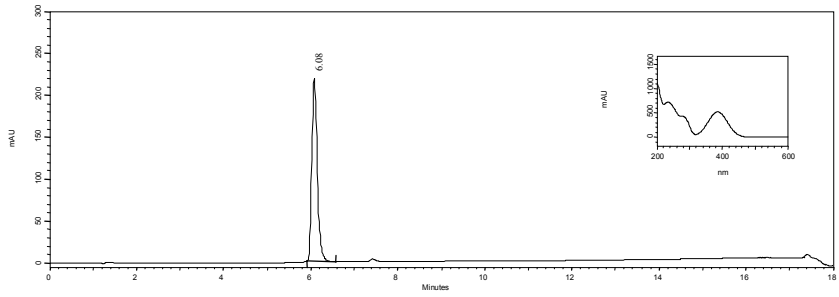
Structural Data of All Compounds

3a: product resulted from **1a** and **2a**

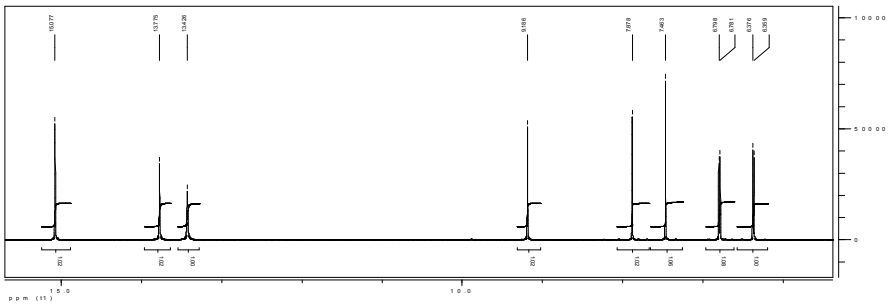
3a	**8a-Hydroxy-6,10-dioxo-1,4,6,8a,9,10-hexahydro-1,3,4,9-tetraaza-benzo[f]azulene-5-carboxylic acid**



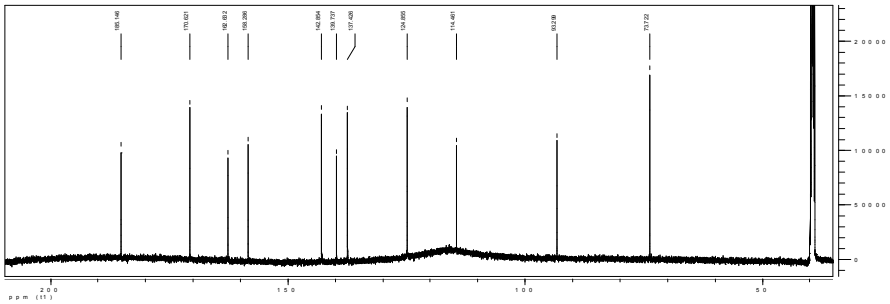
HPLC chromatogram and UV-vis spectrum



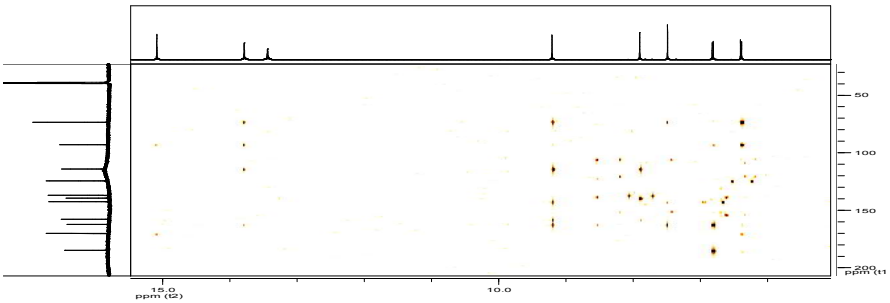
^{1}H NMR



^{13}C NMR



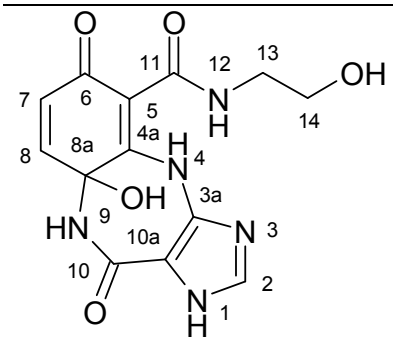
HMBC



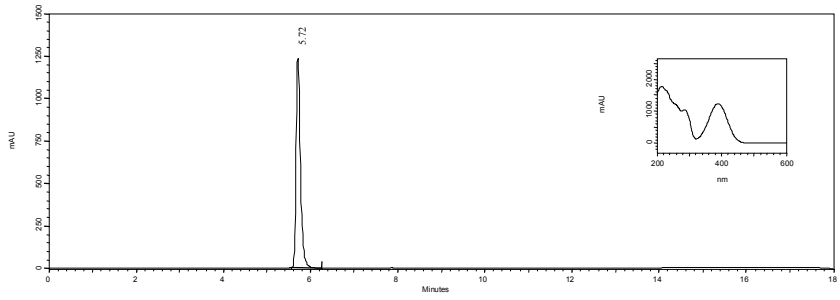
Synthesis and isolation as described above. Yellow green solid. Yield 27.82 % (51.9 mg): mp (decomposition) 168-170 °C. ^{1}H NMR: δ 6.36 (d, *J* = 10.1, 1H, H-7), 6.79 (d, *J* = 10.1, 1H, H-8), 7.46 (s, 1H, OH, on C-8a), 7.88 (s, 1H, H-2), 9.19 (s, 1H, NH, H-9), 13.43 (s, 1H, NH, H-1), 13.78 (s, 1H, NH, H-4), 15.08 (s, 1H, OH, on C-11). ^{13}C NMR: δ 73.8 (C-8a), 93.2 (C-5), 114.9 (C-10a), 124.7 (C-7), 137.3 (C-2), 139.5 (C-3a), 142.7 (C-8), 158.3 (C-10), 162.7 (C-4a), 170.6 (C-11), 185.5 (C-6). HMBC correlations: H-2 (C-3a, C-10, C-10a), H-4 (C-4a, C-5, C-8a, C-10a), H-7 (C-4a, C-5, C-6, C-8a, C-11), H-8 (C-4a, C-5, C-6, C-7, C-8a), H-9 (C-4a, C-5, C-8, C-8a, C-10, C-10a), OH on C-8a (C-4a, C-8, C-8a), OH on C-11 (C-5, C-11). R_f (HPLC) 6.1 min, UV-vis (MeOH) λ_{max} 204, 234, 387 nm. MS *m/z* AP-ESI: pos. ion mode $[M+H]^+$ 277.0610 (calculated 277.0567), $[2M+H]^+$ 553.1167 (calculated 553.1062); AP-ESI: neg. ion mode $[M-H]^-$ 275.0414 (calculated 275.0422), $[2M-H]^-$ 551.0892 (calculated 551.0917), $[3M-H]^-$ 827.1346 (calculated 827.1411).

3b: product resulted from **1b** and **2a**

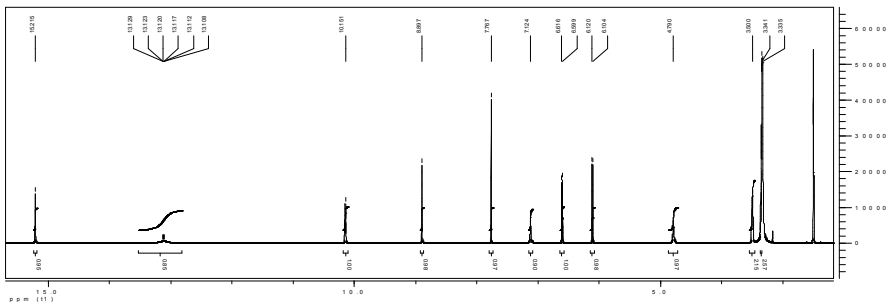
3b	**8a-Hydroxy-6,10-dioxo-2,4,6,8a,9,10-hexahydro-2,3,4,9-tetraaza-benzo[f]azulene-5-carboxylic acid**



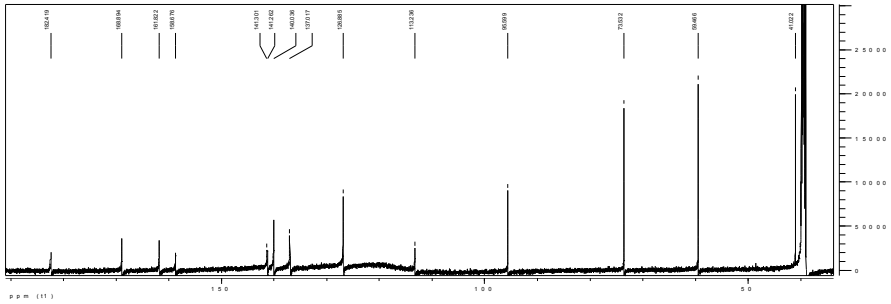
HPLC chromatogram and UV-vis spectrum



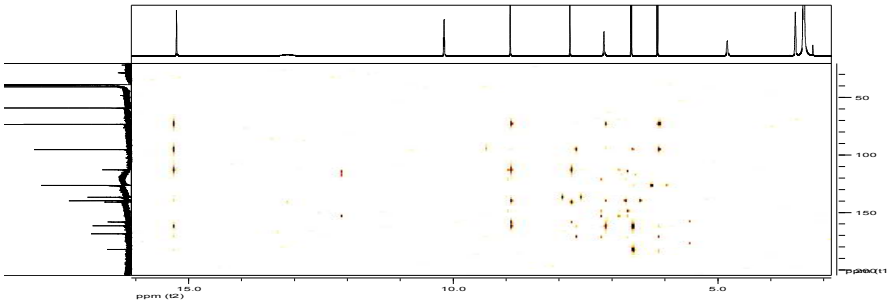
^{1}H NMR



^{13}C NMR



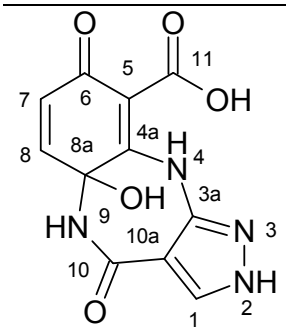
HMBC



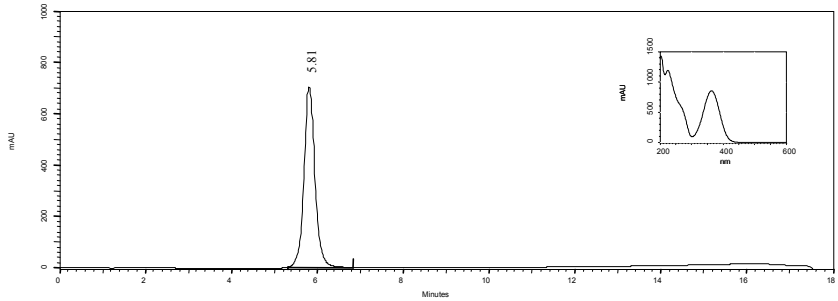
Synthesis and isolation as described above. Brown green solid. Yield 70.73 % (54.4 mg): mp (decomposition) 175-177 °C. ^{1}H NMR: δ 3.35 (m, *J* = 5.6, 2H, H-13), 3.50 (m, *J* = 5.6, 2H, H-14), 4.79 (s (broad), 1H, OH, on C-14), 6.11 (d, *J* = 10.1, 1H, H-7), 6.60 (d, *J* = 10.0, 1H, H-8), 7.12 (s, 1H, OH, on C-8a), 7.77 (s, 1H, H-2), 8.90 (s, 1H, NH, H-9), 10.15 (t, *J* = 5.5, 1H, NH, H-12), 13.12 (s (broad), 1H, NH, H-1), 15.21 (s, 1H, NH, H-4). ^{13}C NMR: δ 41.0 (C-13), 49.5 (C-14), 73.5 (C-8a), 95.6 (C-5), 113.2 (C-10a), 126.9 (C-7), 137.0 (C-2), 140.0 (C-8), 141.3 (C-3a), 158.7 (C-10), 161.8 (C-4a), 168.9 (C-11), 182.4 (C-6). HMBC correlations: H-2 (C-3a, C-10, C-10a), H-4 (C-4a, C-5, C-6, C-8, C-8a, C-10a, C-11), H-7 (C-4a, C-5, C-6, C-8, C-8a, C-11), H-8 (C-4a, C-5, C-6, C-7, C-8a), H-9 (C-4a, C-5, C-8, C-8a, C-10, C-10a), H-12 (C-5, C-11, C-13, C-14), H-13 (C5, C-11, C-15), H-14 (C-13), OH on C-8a (C-4a, C-8, C-8a), OH on C-14 (C-13, C-14). R_f (HPLC) 5.7 min, UV-vis λ_{max} 230, 387 nm. MS *m/z* AP-ESI: neg. mode $[M+H]^+$ 318.0838 (calculated 318.0844).

3c: product resulted from **1a** and **2b**

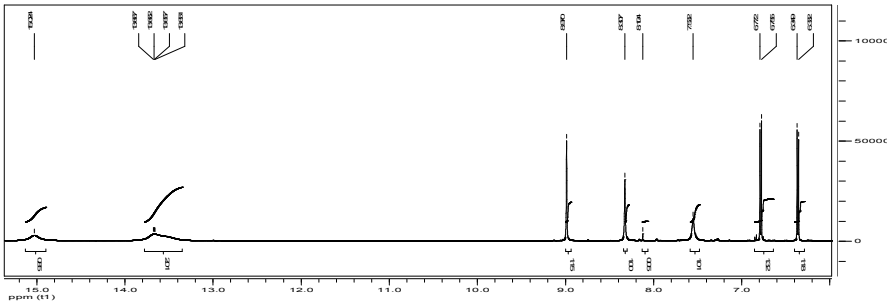
3c	**8a-Hydroxy-6,10-dioxo-2,4,6,8a,9,10-hexahydro-2,3,4,9-tetraaza-benzo[f]azulene-5-carboxylic acid**



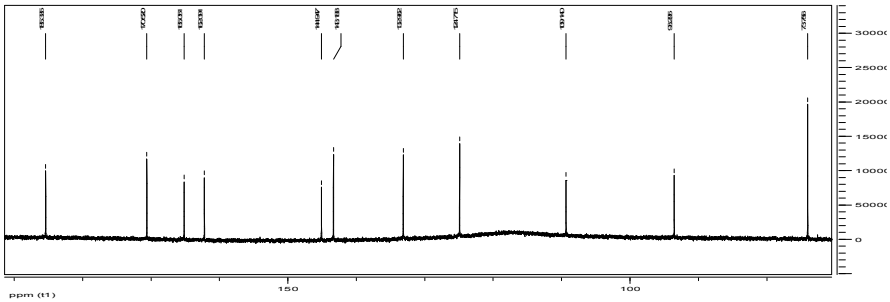
HPLC chromatogram and UV-vis spectrum



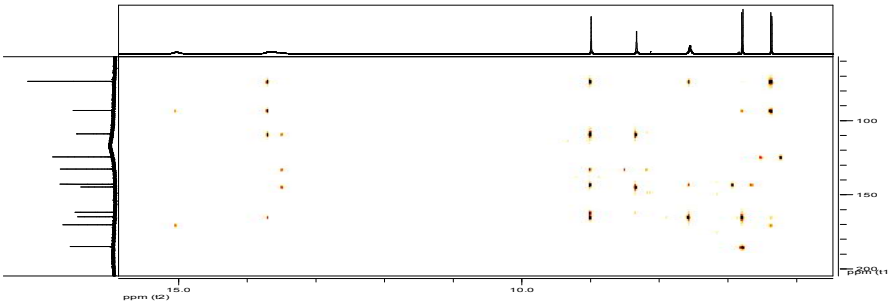
^{1}H NMR



^{13}C NMR

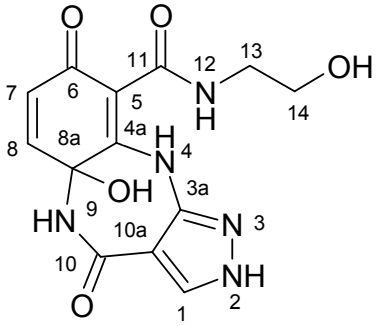
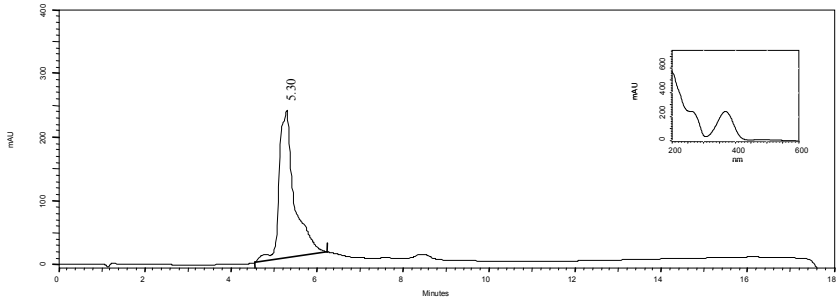
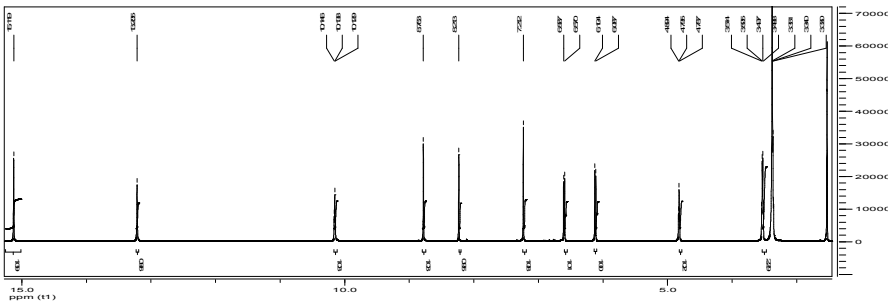


HMBC

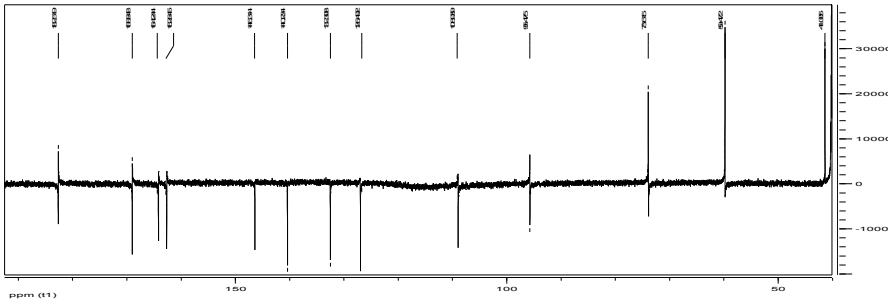


Synthesis and isolation as described above. Yellow brown solid. Yield 44.08 % (17.1 mg): mp (decomposition) 176-178 °C. ^{1}H NMR: δ 6.40 (d, *J* = 10.1, 1H, H-7), 6.76 (d, *J* = 10.1, 1H, H-8), 7.53 (s, 1H, OH, on C-8a), 8.31 (s, 1H, H-1), 8.97 (s, 1H, NH, H-9), 13.53 (s, 1H, NH, H-2), 13.66 (s (broad), 1H, NH, H-4), 15.02 (s (broad), 1H, OH, on C-11). ^{13}C NMR: δ 73.8 (C-8a), 93.3 (C-5), 109.1 (C-10a), 124.7 (C-7), 133.0 (C-1), 143.2 (C-8), 144.9 (C-3a), 162.1 (C-10), 165.1 (C-4a), 170.5 (C-11), 185.3 (C-6). HMBC correlations: H-1 (C-3a, C-10, C-10a), H-2 (C-1, C-3a, C-10a), H-4 (C-4a, C-5, C-8a, C-10a), H-7 (C-4a, C-5, C-6, C-8a, C-11), H-8 (C-4a, C-5, C-6, C-7, C-8a), H-9 (C-1, C-4a, C-5, C-8, C-8a, C-10, C-10a), OH on C-8a (C-4a, C-5, C-8, C-8a), OH on C-11 (C-5, C-11). R_f (HPLC) 5.8 min, UV-vis (MeOH) λ_{max} 224, 364 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 275.0396 (calculated 275.0416). AP-ESI: pos. mode $[M+H]^+$ 277.0591 (calculated 277.0573).

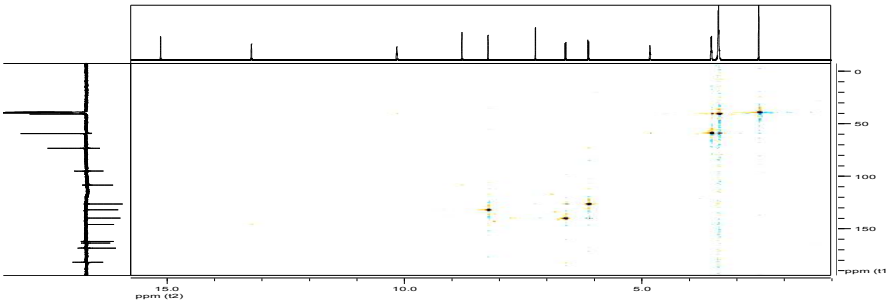
3d: product resulted from **1b** and **2b**

3d	**8a-Hydroxy-6,10-dioxo-2,4,6,8a,9,10-hexahydro-2,3,4,9-tetraaza-benzo[f]azulene-5-carboxylic acid (2-hydroxy-ethyl)-amide**
	HPLC chromatogram and UV-vis spectrum  ^{1}H NMR 

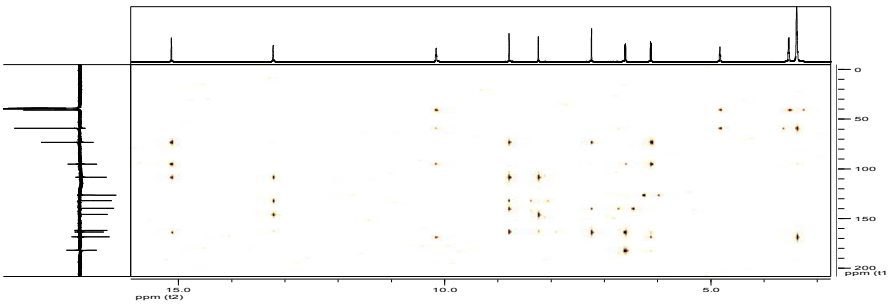
^{13}C NMR



HSQC



HMBC

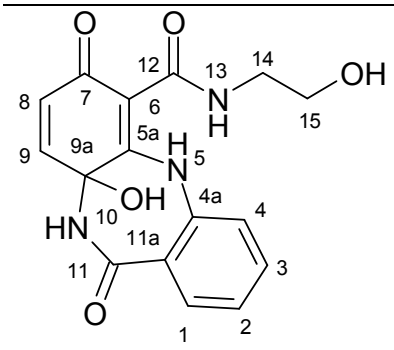


Synthesis and isolation as described above. Yellow brown solid. Yield 26.37 % (26.6 mg): mp (decomposition) 177-179 °C. ^{1}H NMR: δ 3.34 (m, *J* = 5.5, 2H, H-13), 3.50 (m, *J* = 5.3, 2H, H-14), 4.79 (t, *J* = 5.0, 1H, OH, on C-14), 6.09 (d, *J* = 10.0, 1H, H-7), 6.58 (d, *J* = 10.0, 1H, H-8), 7.21 (s, 1H, OH, on C-8a), 8.21 (s, 1H, H-1), 8.76 (s, 1H, NH, H-9), 10.14 (t, *J* = 5.4, 1H, NH, H-12), 13.21 (s, 1H, NH, H-2), 15.12 (s, 1H, NH, H-4). ^{13}C NMR: δ 40.8 (C-13), 59.3 (C-14), 73.5 (C-8a), 95.5 (C-5), 108.7 (C-10a), 126.6 (C-7), 132.1 (C-1), 140.0 C-8, 146.2 (C-3a), 163.8 (C-10), 164.2 (C-4a), 168.8 (C-11), 182.7 (C-6). HMBC correlations: H-1 (C-3a, C-10, C-10a), H-2 (C-1, C-3a, C-10, C-10a), H-4 (C-4a, C-5, C-8, C-8a, C-10a), H-7 (C-4a, C-5, C-6, C-8a, C-11), H-8 (C-4a, C-5, C-6, C-7), H-9 (C-1, C-4a, C-5, C-8,

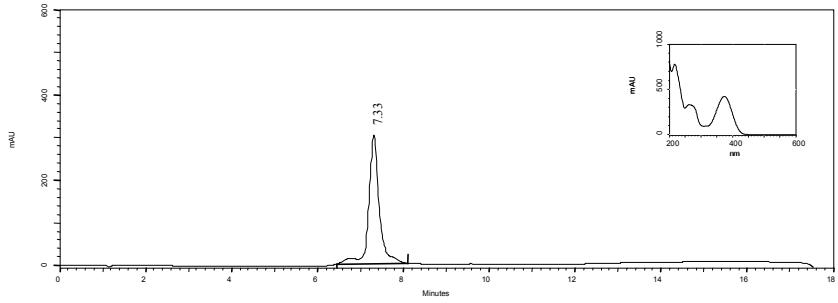
C-8a, C-10, C-10a), H-12 (C-5, C-11, C-13, C-14), H-13 (C-11, C-14), H-14 (C-13), OH on C-8a (C-4a, C-8, C-8a), OH on C-14 (C-13, C-14). R_f (HPLC) 5.3 min, UV-Vis (MeOH) λ_{max} 206, 370 nm. MS *m/z* AP-ESI: neg. $[M-H]^-$ 318.0829 (calculated 318.0838). AP-ESI: pos. mode $[M+H]^+$ 320.1031 (calculated 320.0995).

3e: product resulted from **1b** and **2c**

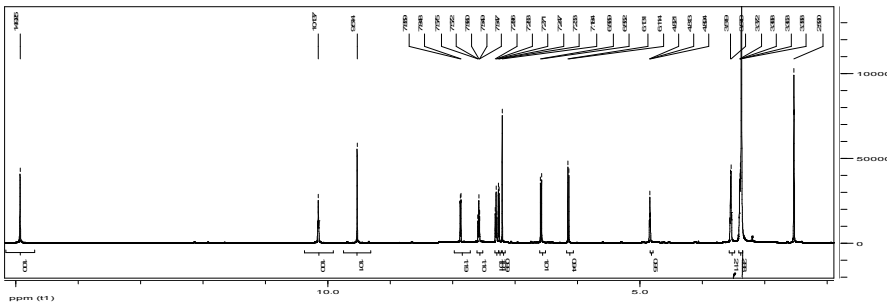
3e	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-dibenzo[b,e][1,4]diazepine-6-carboxylic acid (2-hydroxy-ethyl)-amide**



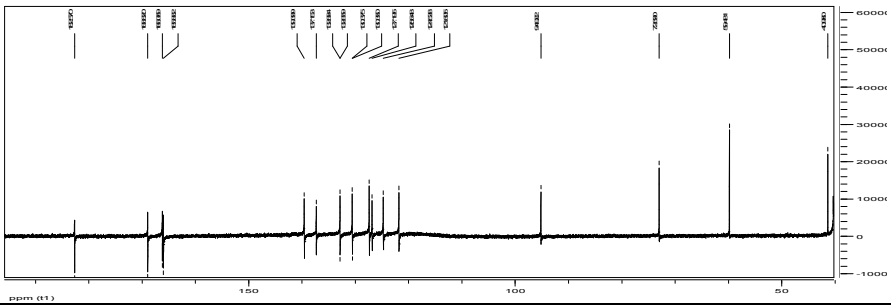
HPLC chromatogram and UV-vis spectrum



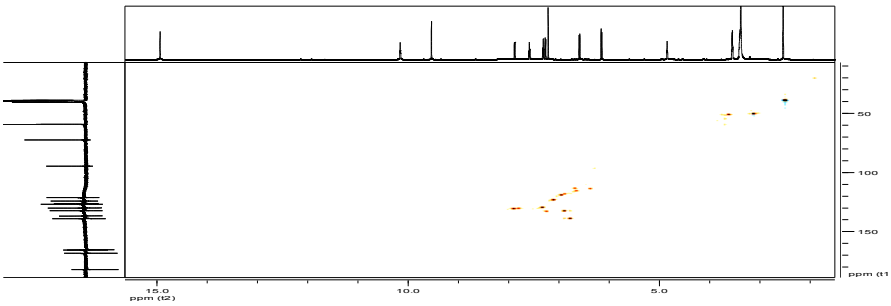
^{1}H NMR



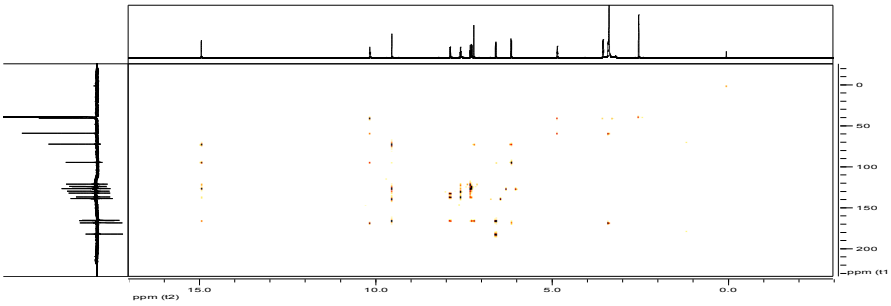
^{13}C NMR



HSQC



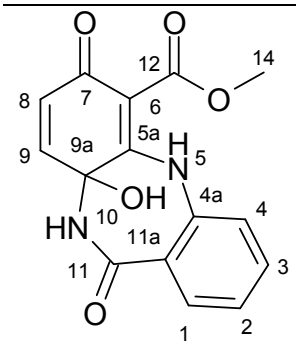
HMBC



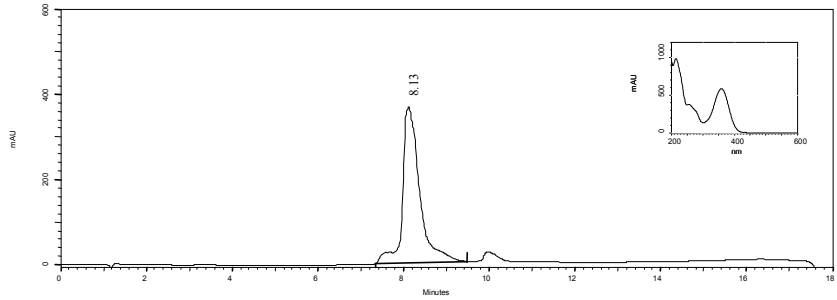
Synthesis and isolation as described above. Yellow solid. Yield 38.25 % (15.3 mg): mp (decomposition) 158-162 °C, mp 204-208 °C. ^{1}H NMR: δ 3.36 (m, *J* = 5.4, *J* = 2.4, 2H, H-14), 3.51 (m, *J* = 5.3, 2H, H-15), 4.81 (t, *J* = 5.0, 1H, OH, on C-15), 6.12 (d, *J* = 10.0, 1H, H-8), 6.56 (d, *J* = 10.0, 1H, H-9), 7.18 (s, 1H, OH, on C-9a), 7.24 (d, *J* = 8.0, 1H, H-4), 7.28 (dd, *J* = 7.9, *J* = 7.7, 1H, H-2), 7.56 (m, *J* = 7.9, *J* = 7.4, *J* = 1.4, 1H, H-3), 7.85 (d, *J* = 7.8, *J* = 1.2, 1H, H-1), 9.51 (s, 1H, NH, H-10), 10.14 (t, *J* = 5.4, 1H, NH, H-13), 14.92 (s, 1H, NH, H-5). ^{13}C NMR: δ 40.9 (C-14), 59.5 (C-15), 72.7 (C-9a), 94.9 (C-6), 121.6 (C-4), 124.5 (C-2), 126.6 (C-11a), 127.2 (C-8), 130.4 (C-1), 132.7 (C-3), 137.1 (C-4a), 139.4 (C-9), 165.9 (C-11), 166.1 (C-5a), 182.6 (C-7). HMBC correlations: H-1 (C-3, C-4, C-4a, C-11), H-2 (C-1, C-3a, C-4, C-4a, C-11a), H-3 (C-1, C-4, C-4a, C-11a), H-4 (C-2, C-4a, C-5, C-11a), H-5 (C-4, C-4a, C-5a, C-6, C-7, C-9a, C-11a), H-8 (C-6, C-7, C-9a, C-12), H-9 (C-5a, C-6, C-7, C-8), H-10 (C-5a, C-9, C-9a, C-11, C-11a), H-13 (C-6, C-12, C-14, C-15), H-14 (C-12, C-15), H-15 (C-14), OH on C-9a (C-5a, C-9, C-9a), OH on C-15 (C-14, C-15). R_f (HPLC) 7.3 min, UV-vis (MeOH) λ_{max} 224, 262, 374 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 328.0928 (calculated 328.0933). AP-ESI: pos. mode $[M+H]^+$ 330.1129 (calculated 330.1090).

3f: product resulted from **1c** and **2c**

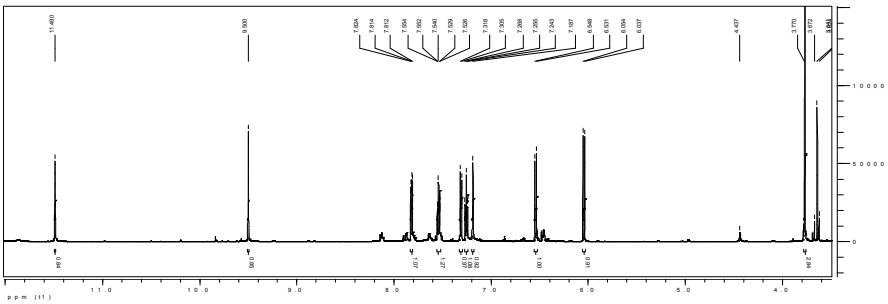
3f	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-dibenzo[b,e][1,4]diazepine-6-carboxylic acid methyl ester**



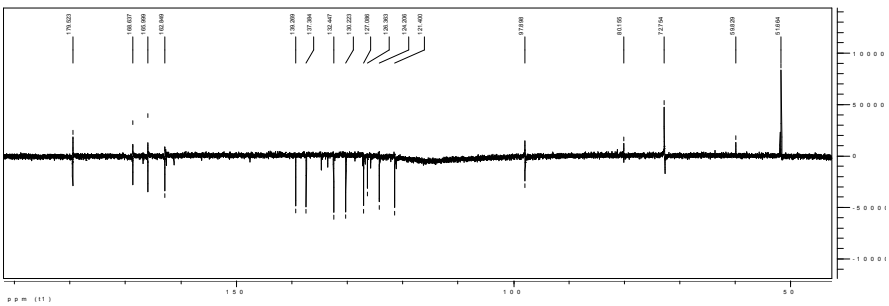
HPLC chromatogram and UV-vis spectrum



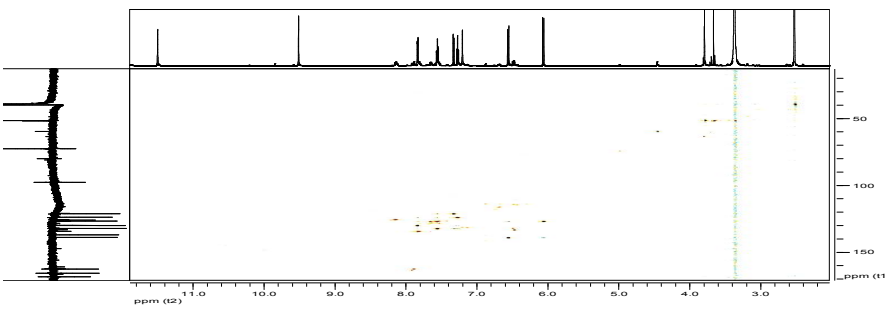
^{1}H NMR



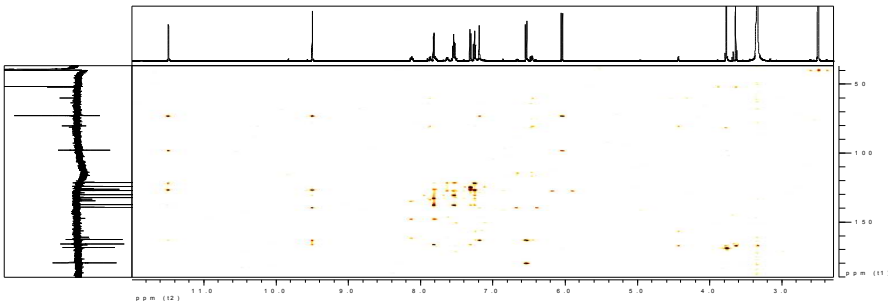
^{13}C NMR



HSQC



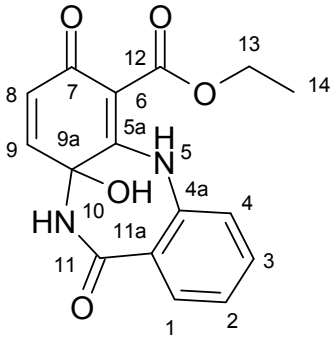
HMBC



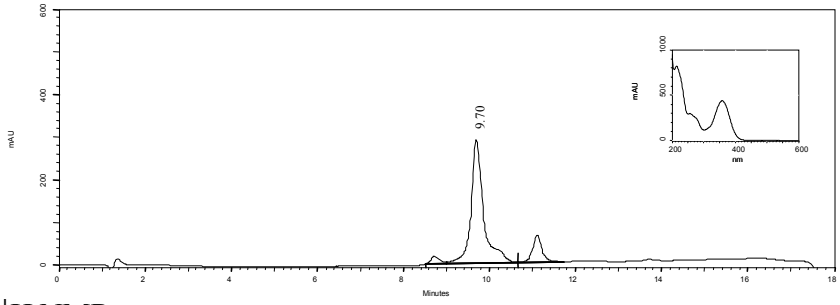
Synthesis and isolation as described above. Yellow solid. Yield 29.30 % (10.7 mg): mp (decomposition) 135-139 °C, mp 181-185 °C. ^{1}H NMR: δ 3.77 (s, 3H, H-14), 6.04 (d, *J* = 10.0, 1H, H-8), 6.54 (d, *J* = 10.0, 1H, H-9), 7.19 (s, 1H, OH, on C-9a), 7.26 (m, *J* = 7.9, *J* = 0.6, H-2), 7.31 (d, *J* = 7.9, 1H, H-4), 7.54 (m, *J* = 8.0, *J* = 1.4, 1H, H-3), 7.81 (d, *J* = 7.8, *J* = 1.3, 1H, H-1), 9.50 (s, 1H, NH, H-10), 11.49 (s, 1H, NH, H-5). ^{13}C NMR: δ 51.7 (C-14), 121.4 (C-2), 124.2 (C-2), 127.1 (C-8), 130.2 (C-1), 132.4 (C-3), 139.3 (C-9). HMBC correlations: H-1 (C-3, C-4a, C-11), H-2 (C-1, C-3, C-4, C-4a, C-11a), H-3 (C-1, C-4a), H-4 (C-2, C-4a, C-11, C-11a), H-5 (C-4, C-4a, C-5a, C-6, C-9a, C-11a), H-8 (C-6, C-9a, C-12), H-9 (C-5a, C-7), H-10 (C-5a, C-9, C-9a, C-11, C-11a), H-14 (C-6, C-12), OH on C-9a (C-5a, C-9, C-9a). R_f (HPLC) 8.1 min, UV-vis (MeOH) λ_{max} 214, 256, 359 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 299.0655 (calculated 299.0668). AP-ESI: pos. mode $[M+H]^+$ 301.0464 (calculated 301.0824).

3g: product resulted from **1d** and **2c**

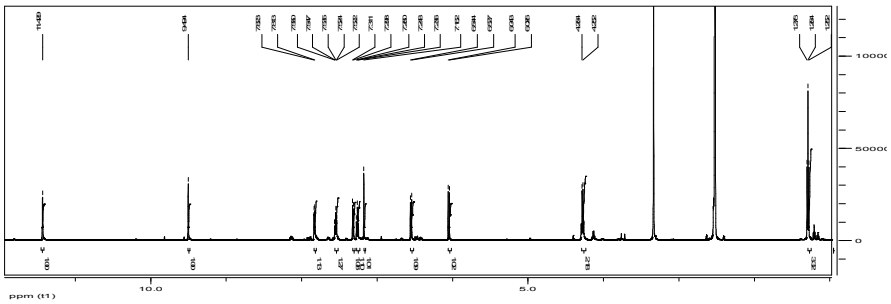
3g	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-dibenzo[b,e][1,4]diazepine-6-carboxylic acid ethyl ester**



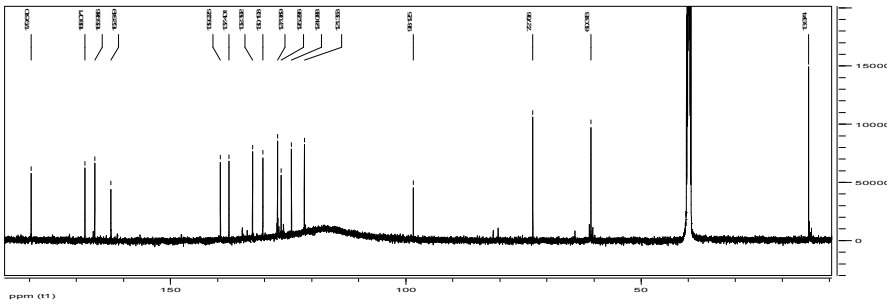
HPLC chromatogram and UV-vis spectrum



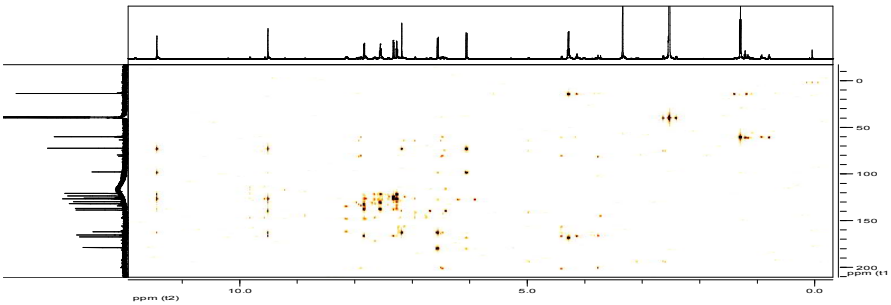
^{1}H NMR



^{13}C NMR

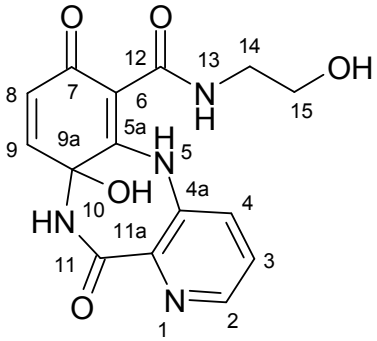
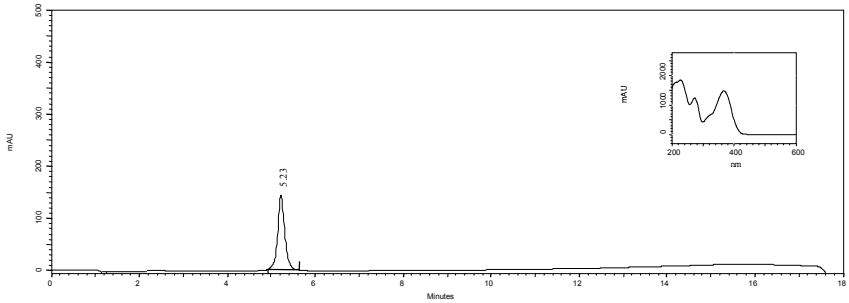


HMBC

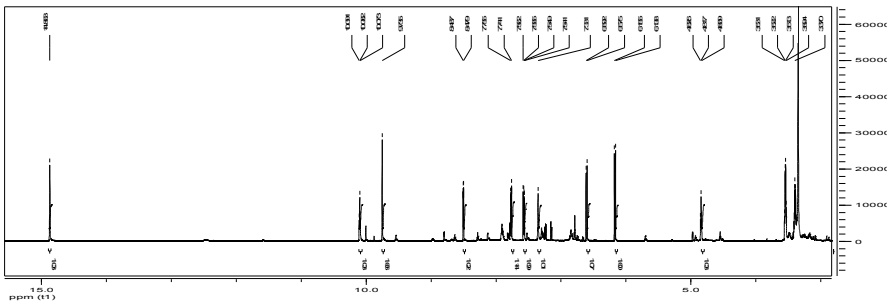


Synthesis and isolation as described above. Yellow solid. Yield 11.47 % (7.3 mg): mp (decomposition) 126-130 °C, mp 169-173 °C. ^{1}H NMR: δ 1.26 (t, *J* = 7.1, 3H, H-14), 4.26 (m, *J* = 7.0, 2H, H-13), 6.03 (d, *J* = 10.1, 1H, H-8), 6.56 (d, *J* = 10.1, 1H, H-9), 7.16 (s, 1H, OH, on C-9a), 7.25 (m, *J* = 7.6, *J* = 0.5, 1H, H-2), 7.30 (d, *J* = 7.9, 1H, H-4), 7.54 (m, *J* = 8.0, *J* = 1.5, 1H, H-3), 7.80 (d, *J* = 7.8, *J* = 1.3, 1H, H-1), 9.49 (s, 1H, NH, H-10), 11.43 (s, 1H, NH, H-5). ^{13}C NMR: δ 14.0 (C-14), 60.3 (C-13), 72.7 (C-9a), 98.1 (C-6), 121.4 (C-4), 124.1 (C-2), 126.3 (C-11a), 127.1 (C-8), 130.2 (C-1), 132.4 (C-3), 137.4 (C-4a), 139.2 (C-9), 162.6 (C-5a), 166.0 (C-10), 168.1 (C-12), 179.5 (C-7). HMBC correlations: H-1 (C-3, C-4a, C-10, C-11a), H-2 (C-1, C-4, C-4a, C-11a), H-3 (C-1, C-4, C-4a), H-4 (C-2, C-4a, C-10, C-11a), H-5 (C-4, C-4a, C-5a, C-6, C-9a, C-11a), H-8 (C-5a, C-6, C-7, C-9a, C-12), H-9 (C-5a, C-6, C-7, C-8), H-10 (C-5a, C-9, C-9a, C-10, C-11a), H-13 (C-12, C-13), H-14 (C-13), OH on C-9a (C-5a, C-9, C-9a). R_f (HPLC) 9.7 min, UV-vis (MeOH) λ_{max} 214, 256, 359 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 312.8888 (calculated 313.0824).

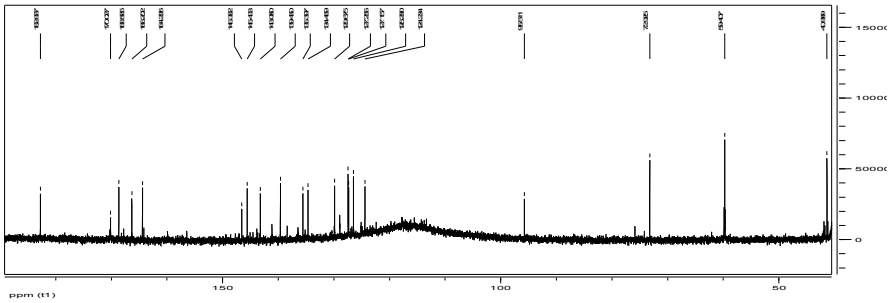
3h: product resulted from **1b** and **2d**

3h	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-1,5,10-triaza-dibenzo[a,d]cycloheptene-6-carboxylic acid (2-hydroxy-ethyl)-amide**
	HPLC chromatogram and UV-vis spectrum 

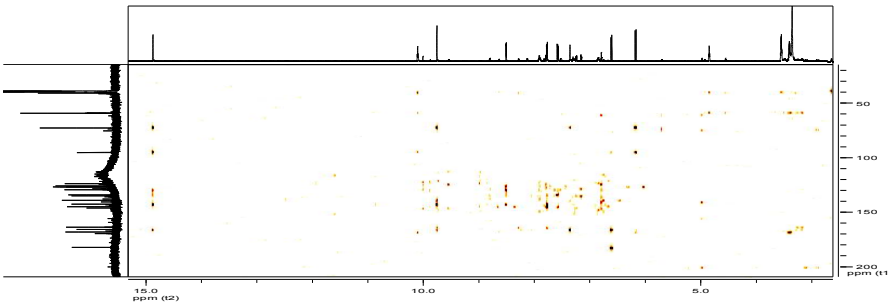
^{1}H NMR



^{13}C NMR



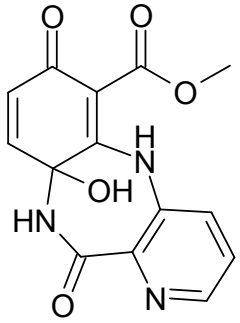
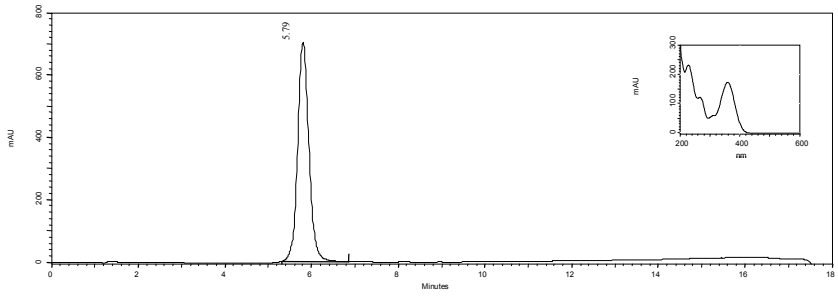
HMBC



Synthesis and isolation as described above. Yellow solid. Yield 15.55 % (10.4 mg). ^{1}H NMR: δ 3.37 (m, *J* = 5.6, 2H, H-14), 3.52 (m, *J* = 5.4, 2H, H-15), 4.82 (t, *J* = 5.1, 1H, OH, on C-15), 6.15 (d, *J* = 10.0, 1H, H-8), 6.58 (d, *J* = 10.0, 1H, H-9), 7.33 (s, 1H, OH, on C-9a), 7.55 (d, *J* = 8.2, *J* = 4.5, 1H, H-3), 7.75 (d, *J* = 8.2, *J* = 1.2, 1H, H-4), 8.48 (d, *J* = 4.5, *J* = 1.2, 1H, H-2), 9.74 (s, 1H, NH, H-10), 10.08 (t, *J* = 5.4, 1H, NH, H-13), 14.86 (s, 1H, NH, H-5). ^{13}C NMR: δ 41.0 (C-14), 59.4 (C-15), 72.9 (C-9a), 95.5 (C-6), 126.3 (C-3), 127.3 (C-8), 129.7 (C-4), 134.5 (C-4a), 139.4 (C-9), 143.1 (C-11a), 145.4 (C-2), 164.3 (C-11), 166.2 (C-5a), 168.6 (C-12), 182.7 (C-7). HMBC correlations: H-2 (C-3, C-4, C-4a, C-11a), H-3 (C-2, C-4, C-4a), H-4 (C-2, C-4a, C-11, C-11a), H-5 (C-4, C-4a, C-5a, C-6, C-9a, C-11a), H-8

(C-6, C-9a, C-12), H-9 (C-5a, C-6, C-7), H-10 (C-5a, C-9, C-9a, C-11, C-11a), H-13 (C-6, C-12, C-15), H-14 (C-12, C-15), H-15 (C-14), OH on C-9a (C-5a, C-9, C-9a), OH on C-15 (C-14, C-15). R_f (HPLC) 5.2 min, UV-vis (MeOH) λ_{max} 227, 273, 368 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 329.0868 (calculated 329.0891).

3i: product resulted from **1c** and **2d**

3i	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-1,5,10-triaza-dibenzo[a,d]cycloheptene-6-carboxylic acid methyl ester**
	HPLC chromatogram and UV-vis spectrum 

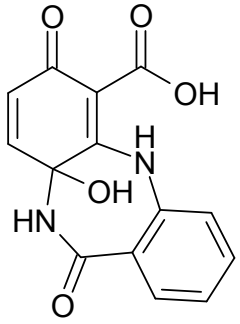
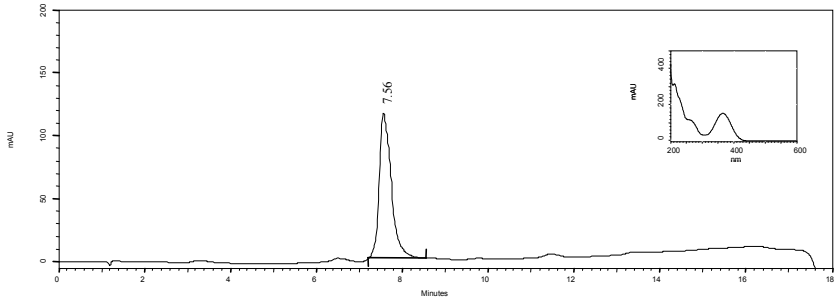
Synthesis and isolation as described above. Yellow solid. Yield 1.36 % (0.5 mg): mp (decomposition) 182-186 °C. R_f (HPLC) 5.8 min, UV-vis (MeOH) λ_{max} 227, 273, 368 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 300.0575 (calculated 300.0625).

3j: product resulted from **1d** and **2d**

R_f (HPLC) 6.5 min, UV-vis (MeOH) λ_{max} 214, 256, 359 nm received only from HPLC elution profile of the reaction mixture.

3k: product resulted from **1a** and **2c**

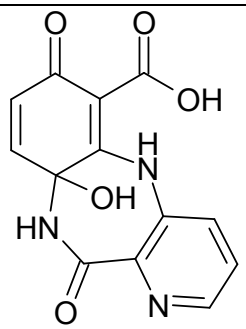
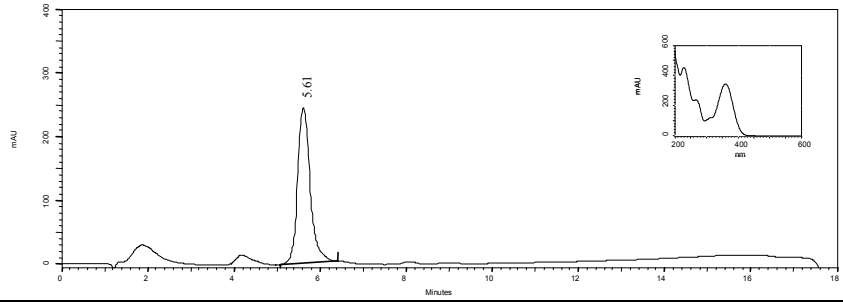
3k reacted to **5a**

3k	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-dibenzo[b,e][1,4]diazepine-6-carboxylic acid**
	HPLC chromatogram and UV-vis spectrum 

Synthesis and isolation as described above. Yellow solid. Yield 26.99 % (31.3 mg): mp (decomposition) 130-134 °C, mp 156-160 °C. R_f (HPLC) 7.6 min, UV-vis (MeOH) λ_{max} 213, 366 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 285.0499 (calculated 285.0517).

3l: product resulted from **1a** and **2d**

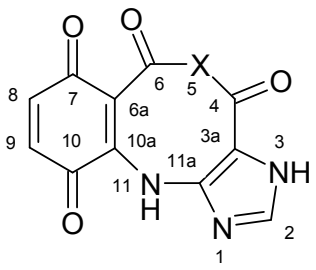
3l reacted to **5b**

3l	**9a-Hydroxy-7,11-dioxo-7,9a,10,11-tetrahydro-5H-1,5,10-triaza-dibenzo[a,d]cycloheptene-6-carboxylic acid**
	HPLC chromatogram and UV-vis spectrum 

Synthesis and isolation as described above. Yellow solid. Yield 26.44 % (15.4 mg): mp (decomposition) 134-138 °C. R_f (HPLC) 5.6 min, UV-vis (MeOH) λ_{max} 229, 267, 360 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 288.0590 (calculated 288.0626).

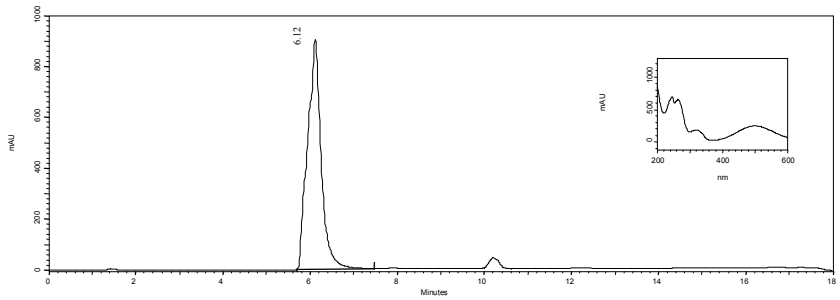
4a,b: products resulted from **1c** and **2a**

4a	**3,11-Dihydro-1,3,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4b	**3,11-Dihydro-5-oxa-1,3,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**

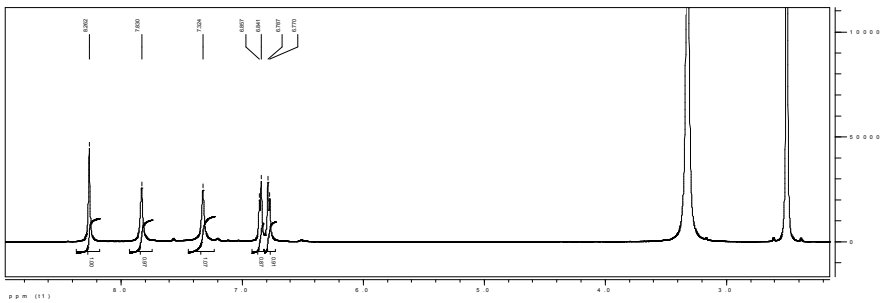


4a X = NH
4b X = O

HPLC chromatogram and UV-vis spectrum



^{1}H NMR



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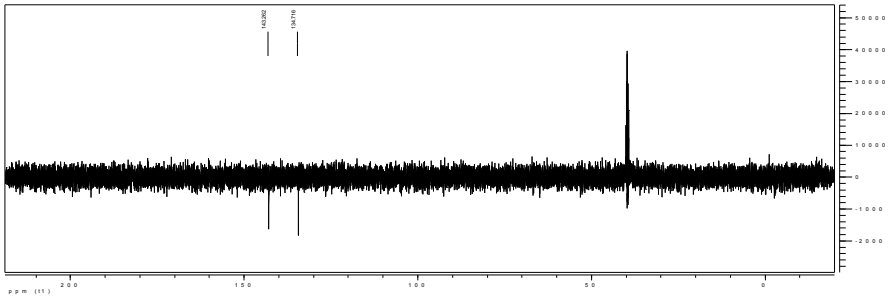
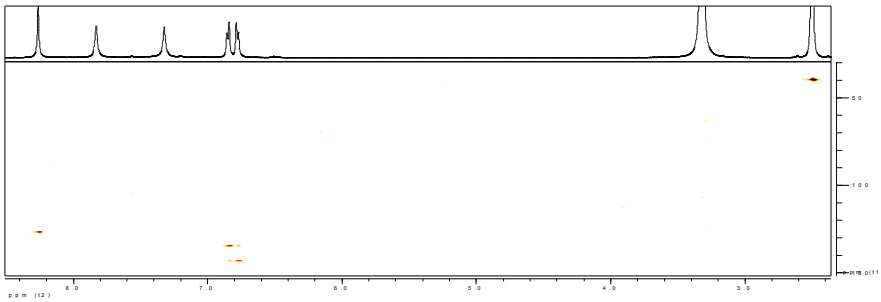
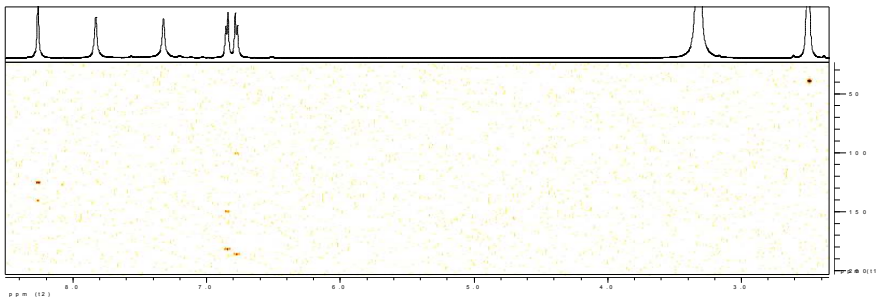


HSQC



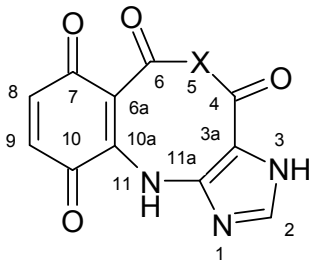
HMBC



Synthesis and isolation as described above. Dark violet solid. Yield 47.70 % (90.6 mg): mp (decomposition) 149-153 °C. ^{1}H NMR: δ 6.78 (d, *J* = 9.7, 1H, H-8), 6.85 (d, *J* = 9.7, 1H, H-9), 7.32 (s, 1H, NH), 7.83 (s, 1H, NH), 8.26 (s, 1H, H-2). ^{13}C NMR: δ 100.2 (C-6a), 125.0 (C-3a), 126.3 (C-2), 134.1 (C-9), 140.0 (C-11a), 142.5 (C-8), 149.1 (C-10a), 153.8 (C-6), 164.2 (C-4), 181.0 (C-7), 185.1 (C-10). HMBC correlations: H-2 (C-3a, C-11a), H-8 (C-6a, C-10), H-9 (C-7, C-10a), NH (C-3a). R_f (HPLC) 6.1 min, UV-vis (MeOH) λ_{max} 246, 265, 323, 503 nm. (**4a**) MS *m/z* AP-ESI: pos. mode $[M+H]^+$ 259.0513 (calculated 259.0462). (**4b**) MS *m/z* AP-ESI: pos. mode $[M+H]^+$ 260.0368 (calculated 260.0302).

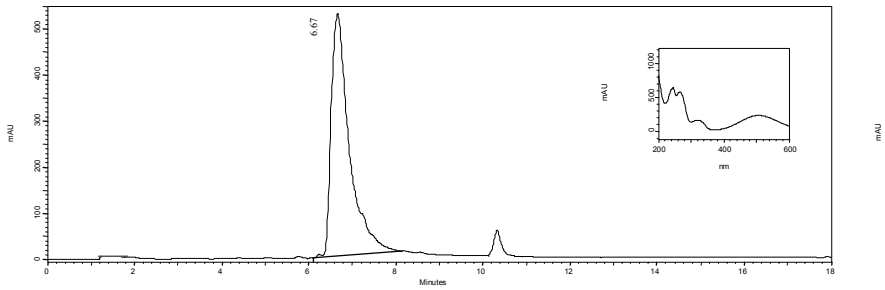
4a,b: products resulted from **1d** and **2a**

4a	**3,11-Dihydro-1,3,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4b	**3,11-Dihydro-5-oxa-1,3,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**

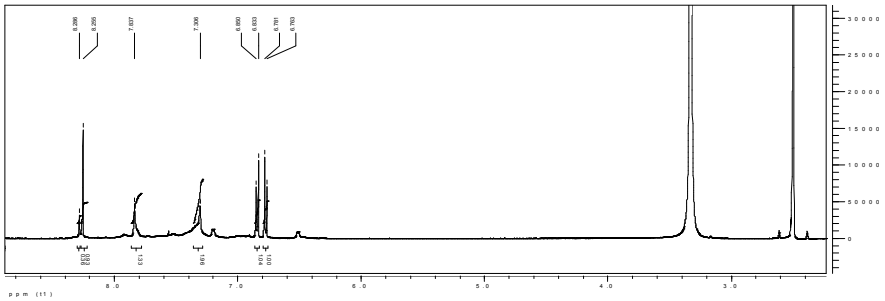


4a X = NH
4b X = O

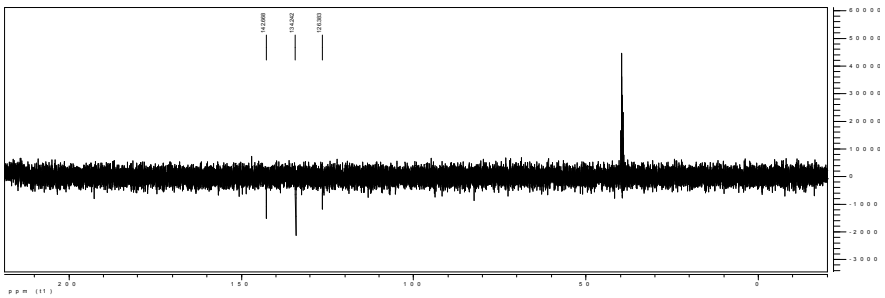
HPLC chromatogram and UV-vis spectrum



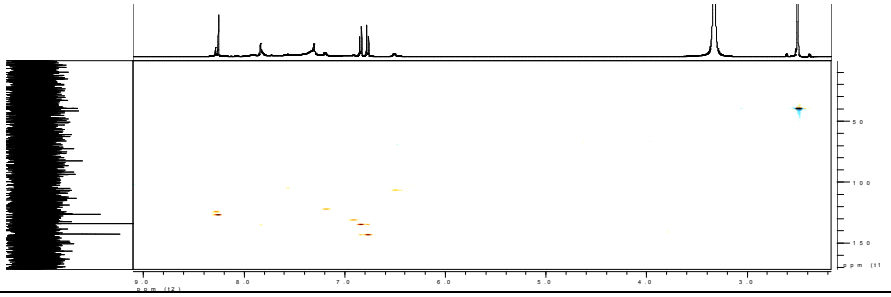
^{1}H NMR



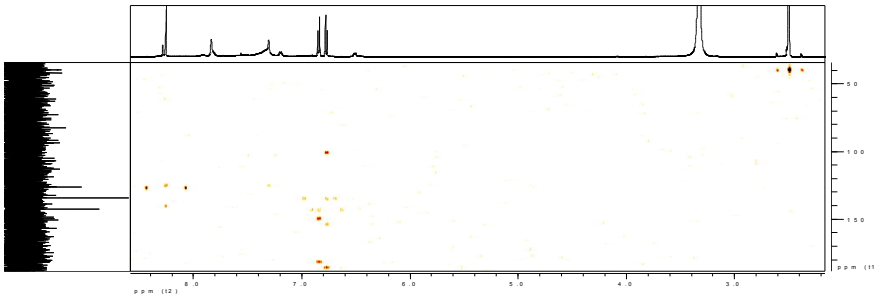
DEPT



HSQC



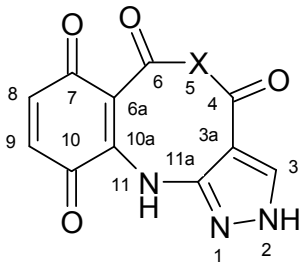
HMBC



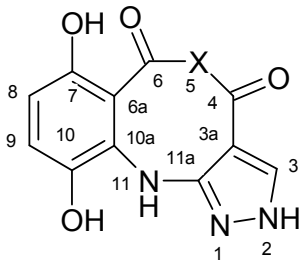
Synthesis and isolation as described above. Dark violet solid. Yield 63.4 % (78.9 mg): mp (decomposition) 148-150 °C. ^{1}H NMR: δ 6.77 (d, *J* = 10.3, 1H, H-8), 6.84 (d, *J* = 10.3, 1H, H-9), 7.31 (s, 1H, NH), 7.84 (s, 1H, NH), 8.26 (s, 1H, H-2). ^{13}C NMR: δ 100.2 (C-6a), 124.5 (C-3a), 126.4 (C-2), 134.2 (C-9), 139.8 (C-11a), 142.6 (C-8), 148.8 (C-10a), 153.1 (C-6), 163.8 (C-4), 180.8 (C-7), 184.8 (C-10). HMBC correlations: H-2 (C-3a, C-11a), H-8 (C-6, C-6a, C-9, C-10), H-9 (C-7, C-8, C-10a), NH (C-3a). R_f (HPLC) 6.7 min, UV-vis (MeOH) λ_{max} 246, 265, 323, 503 nm. (**4a**) MS *m/z* AP-ESI: pos. mode $[M+H]^+$ 259.0539 (calculated 259.0463). (**4b**) MS *m/z* AP-ESI: pos. mode $[M+H]^+$ 260.0396 (calculated 260.0302).

4c-f: products resulted from **1c** and **2b**

4c	**2,11-Dihydro-1,2,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4d	**2,11-Dihydro-5-oxa-1,2,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4e	**7,10-Dihydroxy-2,11-dihydro-1,2,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6-dione**
4f	**7,10-Dihydroxy-2,11-dihydro-5-oxa-1,2,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6-dione**

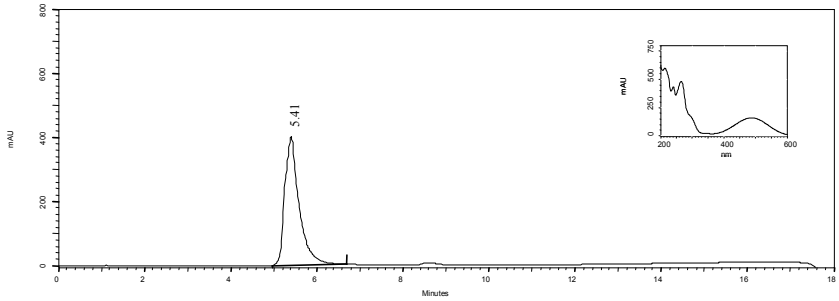


4c X = NH
4d X = O

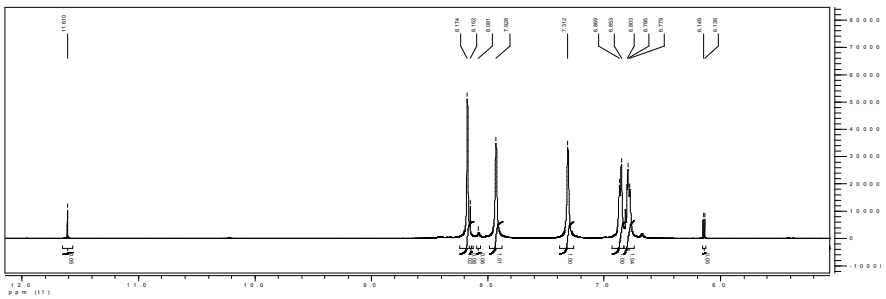


4e X = NH
4f X = O

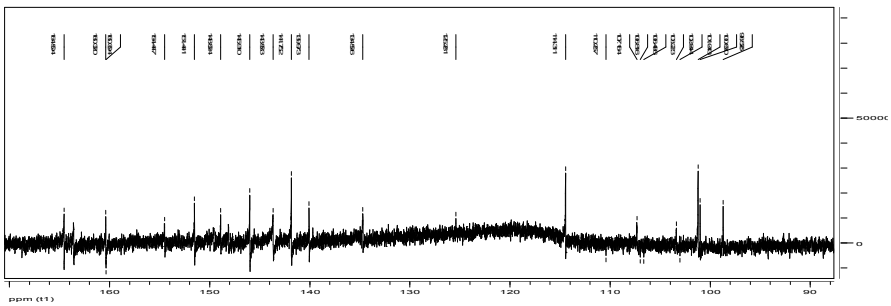
HPLC chromatogram and UV-vis spectrum



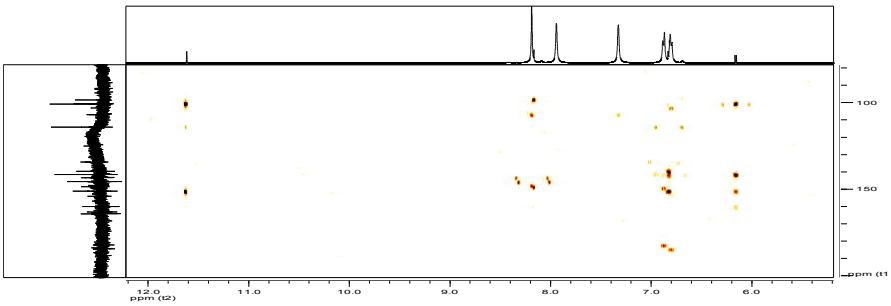
^{1}H NMR



^{13}C NMR



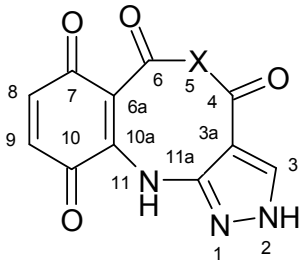
HMBC



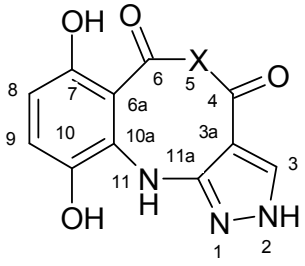
Synthesis and isolation as described above. Red solid. Yield 56.64 % (20 mg): mp (decomposition) 141-143 °C. R_f (HPLC) 5.4 min, UV-vis (MeOH) λ_{max} 214, 241, 265, 487 nm. NMR data of quinonoid and hydroquinonoid products are available from one ^{1}H NMR, one ^{13}C NMR, one HSQC, and one HMBC spectrum. (**4c,d**) ^{1}H NMR: δ 6.78 (d, *J* = 9.7, 1H, H-8), 6.86 (d, *J* = 9.8, 1H, H-9), 7.31 (s, 1H, NH), 7.93 (s, 1H, NH), 8.17 (s, 1H, H-3). ^{13}C NMR: δ 100.2 (C-6a), 124.5 (C-3a), 126.4 (C-2), 134.2 (C-9), 139.8 (C-11a), 142.6 (C-8), 148.8 (C-10a), 153.1 (C-6), 163.8 (C-4), 180.8 (C-7), 184.8 (C-10). HMBC correlations: H-2 (C-3a, C-11a), H-8 (C-6, C-6a, C-9, C-10), H-9 (C-7, C-8, C-10a), NH (C-3a). (**4e,f**) ^{1}H NMR: δ 6.14 (d, *J* = 8.1, 1H, H-8), 6.80 (d, *J* = 8.2, 1H, H-9), 8.15 (s, 1H, H-3), 11.61 (s, 1H, OH). ^{13}C NMR: δ 98.4 (C-3a), 100.1 (C-8), 100.8 (C-6), 101.1 (C-8), 114.2 (C-9), 139.9 (C-10a), 141.7 (C-10), 145.7 (C-3), 149.1 (C-11a), 151.3 (C-7), 160.4 (C-6/C-4). HMBC correlations: H-3 (C-3a, C-4, C-11a), H-8 (C-6, C-6a, C-7, C-10), H-9 (C-7, C-10, C-10a), OH (C-6a, C-7). (**4c**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 257.0293 (calculated 257.03163). (**4d**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 258.0323 (calculated 258.0206). (**4e**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 259.0449 (calculated 259.0473). (**4f**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 260.0482 (calculated 260.0313).

4c-f: products resulted from **1d** and **2b**

4c	**2,11-Dihydro-1,2,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4d	**2,11-Dihydro-5-oxa-1,2,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4e	**7,10-Dihydroxy-2,11-dihydro-1,2,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6-dione**
4f	**7,10-Dihydroxy-2,11-dihydro-5-oxa-1,2,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6-dione**

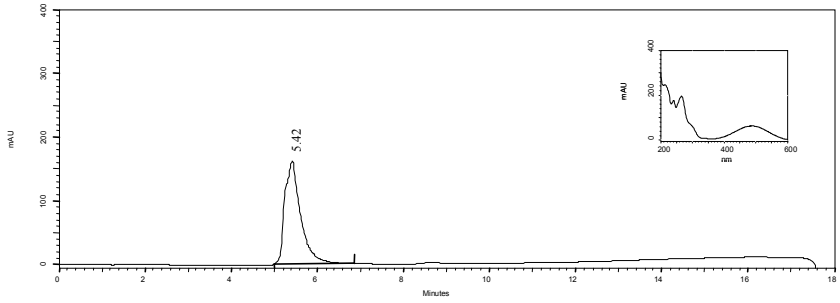


4c X = NH
4d X = O

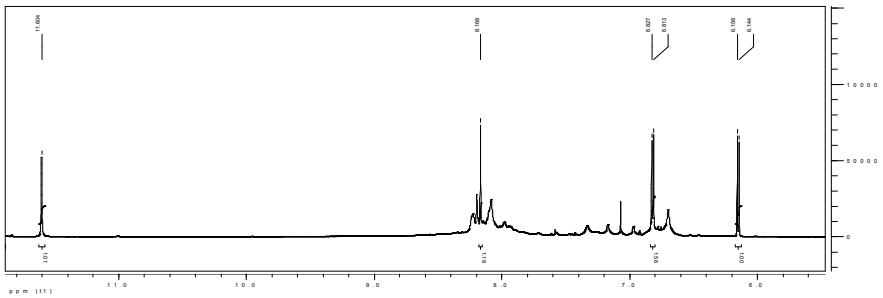


4e X = NH
4f X = O

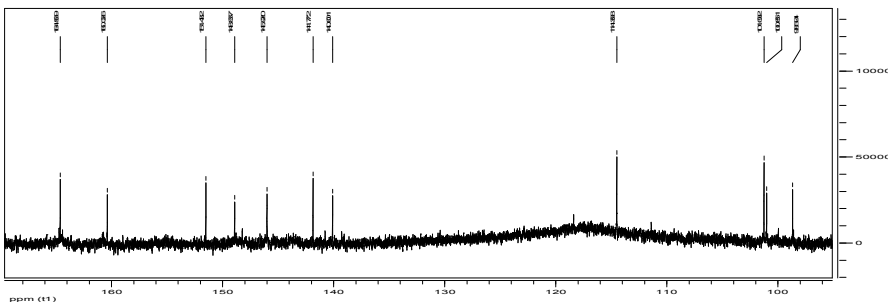
HPLC chromatogram and UV-vis spectrum



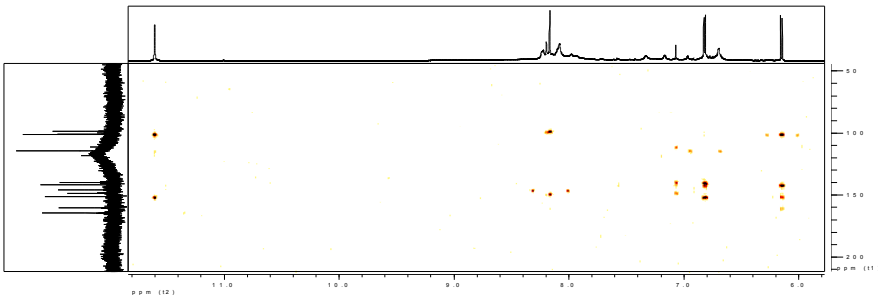
^{1}H NMR



^{13}C NMR



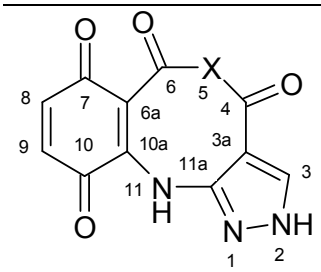
HMBC



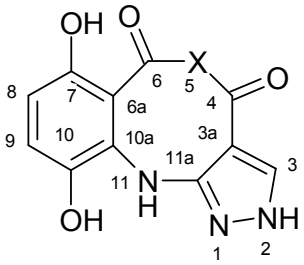
Synthesis and isolation as described above. Red solid. Yield 56.76 % (21 mg). R_f (HPLC) 5.4 min, UV-vis (MeOH) λ_{max} 214, 240, 265, 488 nm. (**4e,f**) ^{1}H NMR: δ 6.15 (d, *J* = 8.1, 1H, H-8), 6.82 (d, *J* = 8.1, 1H, H-9), 8.17 (s, 1H, H-3), 11.60 (s, 1H, OH). ^{13}C NMR: δ 98.4 (C-3a), 100.8 (C-6a), 101.1 (C-8), 114.4 (C-9), 140.0 (C-10a), 141.7 (C-10), 145.7 (C-3), 149.1 (C-11a), 151.4 (C-7), 160.3 (C-6), 160.4 (C-4). HMBC correlations: H-3 (C-3a, C-4, C-11a), H-8 (C-6, C-6a, C-7, C-10), H-9 (C-7, C-10, C-10a), OH (C-6a, C7). (**4c**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 257.0298 (calculated 257.03163). (**4d**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 258.0329 (calculated 258.0206). (**4e**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 259.0454 (calculated 259.0473). (**4f**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 260.0485 (calculated 260.0313).

4c-f: products resulted from **1a** and **2b**

4c	**2,11-Dihydro-1,2,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4d	**2,11-Dihydro-5-oxa-1,2,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6,7,10-tetraone**
4e	**7,10-Dihydroxy-2,11-dihydro-1,2,5,11-tetraaza-benzo[a]cyclopenta[d]cyclooctene-4,6-dione**
4f	**7,10-Dihydroxy-2,11-dihydro-5-oxa-1,2,11-triaza-benzo[a]cyclopenta[d]cyclooctene-4,6-dione**

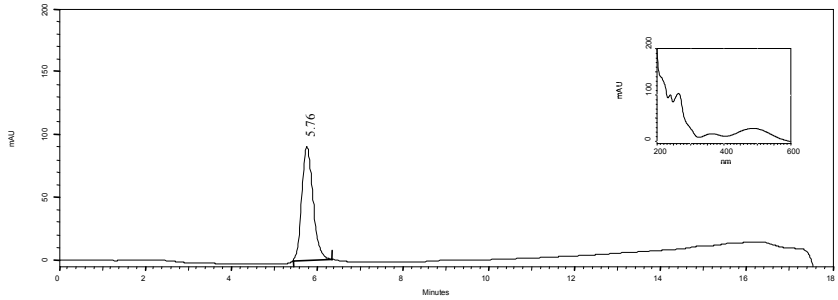


4c X = NH
4d X = O

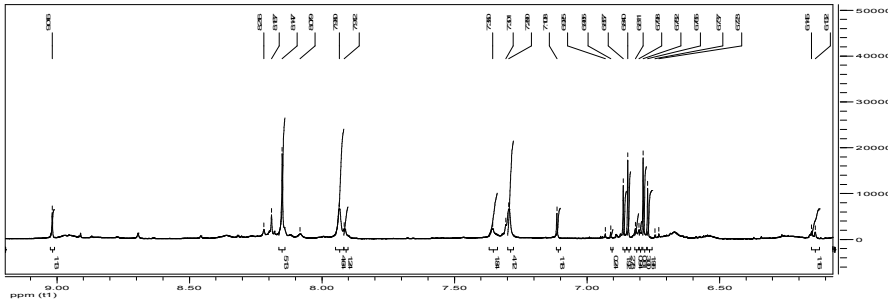


4e X = NH
4f X = O

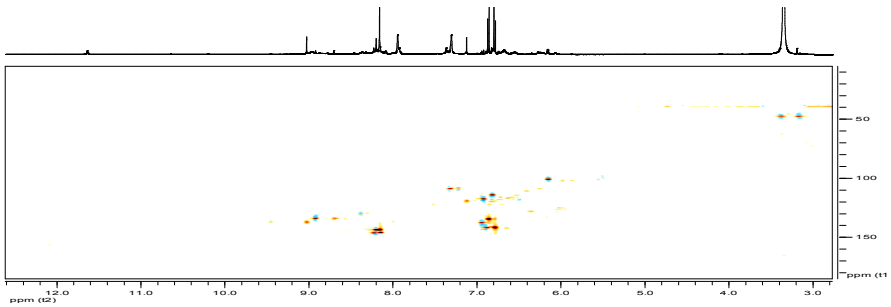
HPLC chromatogram and UV-vis spectrum



^{1}H NMR

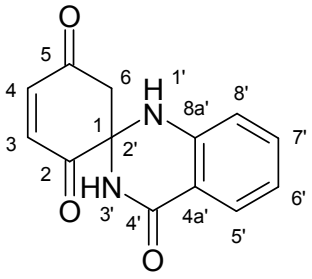
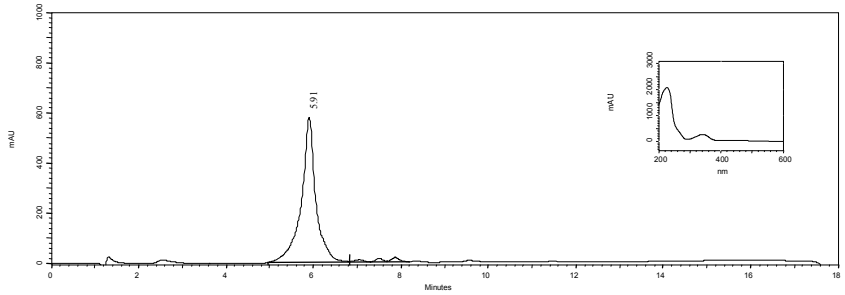


HSQC

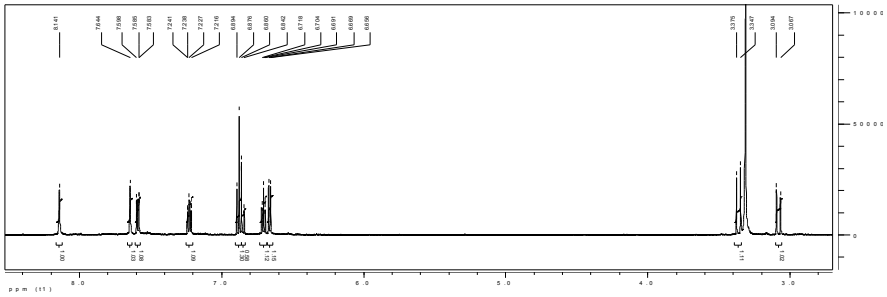


Synthesis and isolation as described above. Red solid. Yield 10.01 % (10.1 mg). R_f (HPLC) 5.5 min, UV-vis (MeOH) λ_{max} 210, 240, 265, 487 nm. NMR data of quinonoid and hydroquinonoid products are available from one ^{1}H NMR and one HSQC spectrum. (**4c,d**) ^{1}H NMR: δ 6.77 (d, *J* = 10.3, 1H, H-8), 6.85 (d, *J* = 10.3, 1H, H-9), 7.29 (s, 1H, NH), 7.93 (s, 1H, NH), 8.15 (s, 1H, H-3). ^{13}C NMR: δ 134.3 (C-9), 141.3 (C-8), 143.3 (C-3). HMBC correlations: HMBC was not measured. (**4e,f**) ^{1}H NMR: δ 6.14 (d, *J* = 8.1, 1H, H-8), 6.80 (d, *J* = 8.2, 1H, H-9), 8.14 (s, 1H, H-3), 11.63 (s, 1H, NH or OH). ^{13}C NMR: δ 100.7 (C-8), 114.0 (C-9), 145.5 (C-3). HMBC correlations: HMBC was not measured. (**4c**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 257.0305 (calculated 257.0316). AP-ESI: pos. mode $[M+H]^+$ 259.0495 (calculated 259.0462). (**4d**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 258.0333 (calculated 258.0206). (**4e**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 259.0457 (calculated 259.0473). (**4f**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 260.0489 (calculated 260.0313).

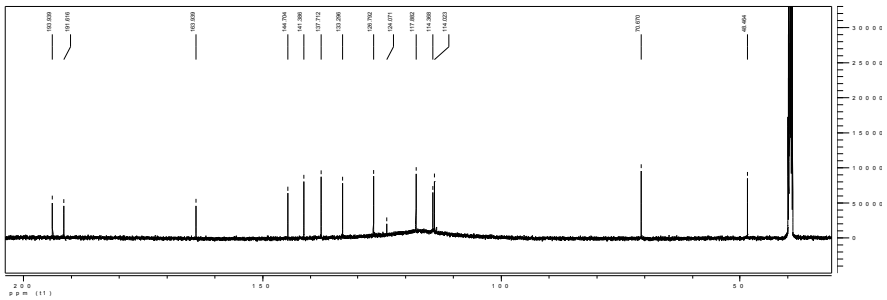
5a: product resulted from conversion of **3k**

5a	**1'H,2H,3'H,5H-spiro[cyclohex-3-ene-1,2'-quinazoline]-2,4',5-trione**
	HPLC chromatogram and UV-vis spectrum 

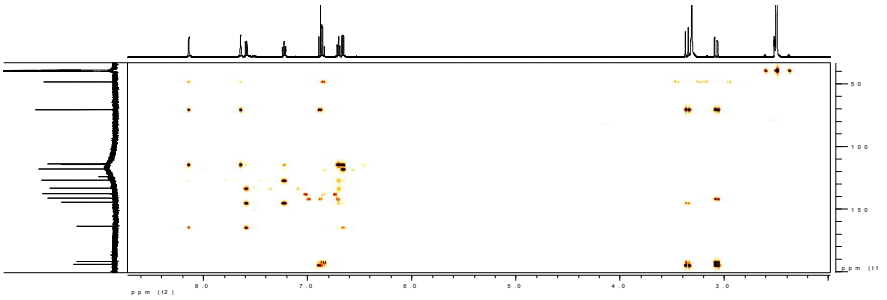
^{1}H NMR



^{13}C NMR



HMBC

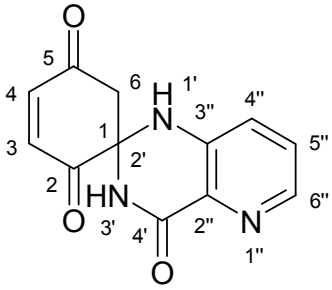


^{1}H NMR: δ 3.08 (d, *J* = 17.1, *J* = 0.9, 1H, H-6), 3.36 (d, 1H, H-6), 6.66 (d, *J* = 7.8, 1H, H-8'), 6.70 (m, *J* = 7.8, *J* = 7.2, *J* = 0.9, 1H, H-9), 6.85 (m, *J* = 10.3, *J* = 0.9, *J* = 0.7, 1H, H-4), 6.88 (d, *J* = 10.3, 1H, H-3), 7.23 (m, *J* = 7.9, *J* = 7.3, *J* = 1.6, 1H, H-7'), 7.59 (m, *J* = 7.7, *J* = 1.4, 1H, H-5') 7.64 (s (broad), 1H, NH, H-1'), 8.14 (s (broad), 1H, NH, H-3'). ^{13}C NMR: δ 48.5 (C-6), 70.7 (C-1), 114.0 (C-8'), 114.4 (C-4a'), 117.9 (C-6'), 126.8 (C-5'), 133.3 (C-7'), 137.7 (C-3), 141.4 (C-4), 144.7 (C-8a'), 164.0 (C-11), 191.6 (C-2), 194.0 (C-5). HMBC correlations: H-1' (C-1, C-4a', C-6), H-3 (C-1, C-2, C-4, C-5), H-3' (C-1, C-4', C-4a', C-5', C-6), H-4 (C-2, C-5, C-6, C-6'), H-5' (C-4', C-4a', C-7', C-8a'), H-6 (C-1, C-2, C-4, C-5), H-6' (C-4', C-4a', C-5', C-7', C-8', C-8a'), H-7' (C-5', C-6', C-8', C-8a'), H-8'

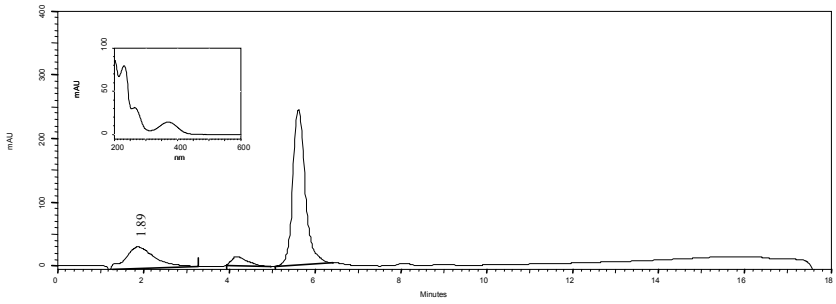
(C-4', C-4a', C-5', C-6', C-8a'). R_f (HPLC) 5.9 min, UV-vis (MeOH) λ_{max} 213, 366 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 241.0614 (calculated 241.0619). AP-ESI: pos. mode $[M+H]^+$ 243.0734 (calculated 243.0764).

5b: product resulted from conversion of **3l**

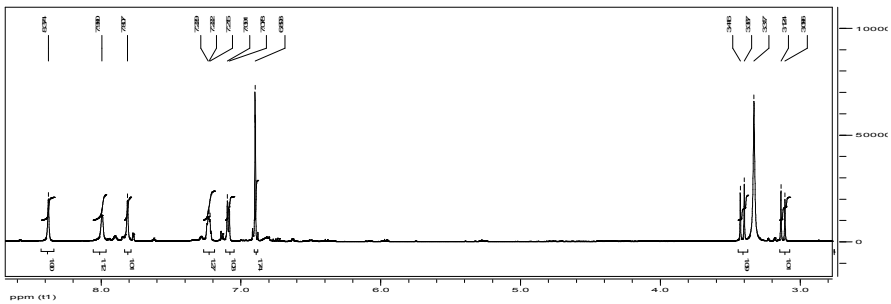
5b	**1'H,2H,3H',5H-spiro[cyclohex-3-ene-1,2'-pyrido[3'',2''-d]pyrimidine-2,4',5-trione**



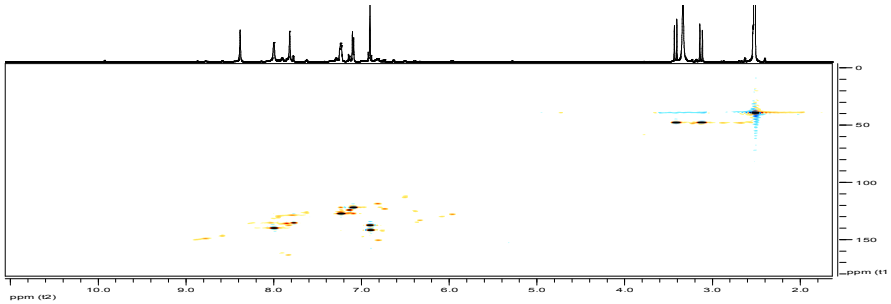
HPLC chromatogram and UV-vis spectrum



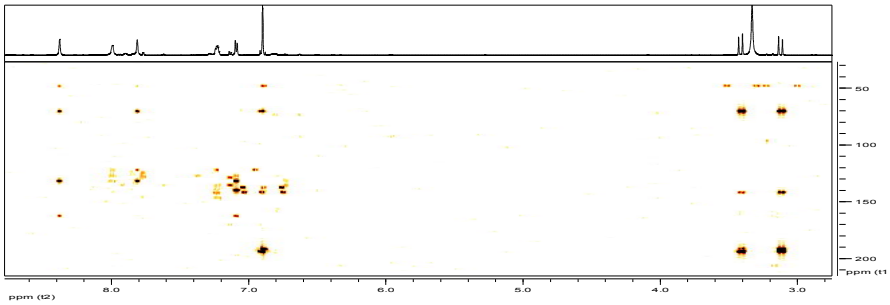
^{1}H NMR



HSQC



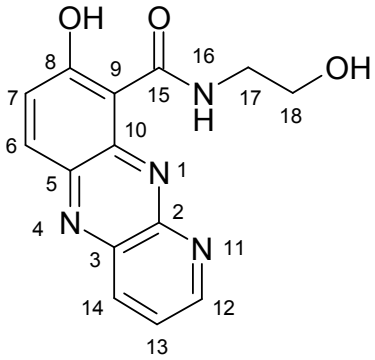
HMBC



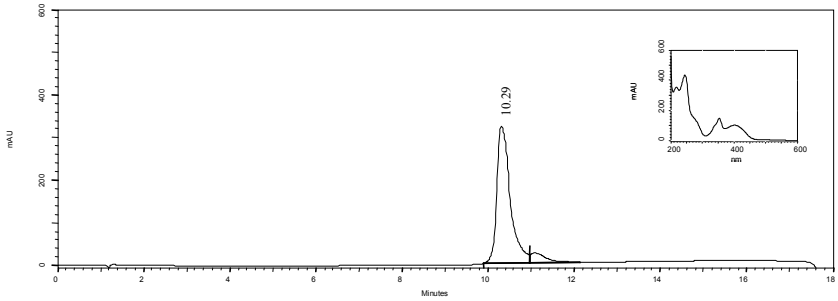
^{1}H NMR: δ 3.11 (d, *J* = 17.0, 1H, H-6), 3.40 (d, *J* = 17.1, 1H, H-6), 6.88 (d, *J* = 10.9, 1H, H-4), 6.90 (d, *J* = 10.4, 1H, H-3), 7.08 (d, *J* = 8.2, 1H, H-4''), 7.22 (m, *J* = 8.5, *J* = 4.4, 1H, H-5''), 7.81 (s, 1H, NH, H-1'), 7.99 (s (broad), 1H, H-6''), 8.37 (s, 1H, NH, H-3'). ^{13}C NMR: δ 48.1 (C-6), 70.5 (C-1), 121.8 (C-4''), 127.3 (C-5''), 131.9 (C-2''), 137.3 (C-3), 139.7 (C-6''), 141.6 (C-4), 142.0 (C-3''), 162.5 (C-4'), 191.5 (C-2), 193.5 (C-5). HMBC correlations: H-1 (C-1, C-2'', C-4', C-4'', C-6), H-3 (C-1, C-4, C-5), H-3' (C-1, C-2'', C-4', C-6), H-4 (C-2, C-3, C-6), H-4'' (C-2'', C-4', C-5'', C-6''), H-5'' (C-3'', C-6''), H-6 (C-1, C-2, C-4, C-5), H-6'' (C-2'', C-4'', C-5''). R_f (HPLC) 1.9 min, UV-vis (MeOH) λ_{max} 230, 254, 370 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 242.0535 (calculated 242.0571).

6a: product resulted from **1b** and **2e**

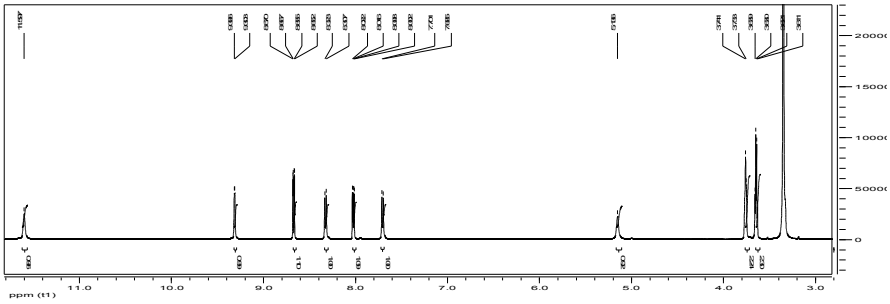
6a	**8-Hydroxy-pyrido[2,3-b]quinoxaline-9-carboxylic acid (2-hydroxy-ethyl)-amide**



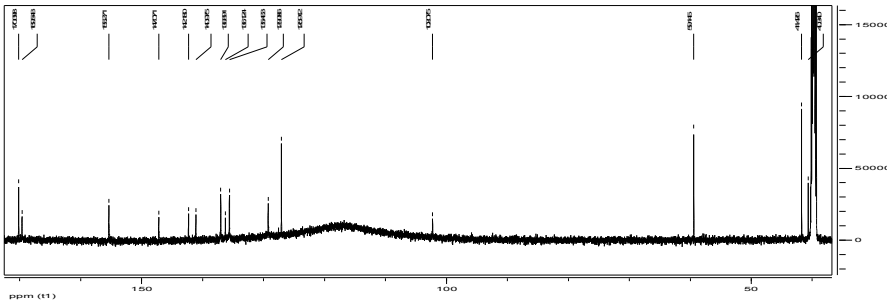
HPLC chromatogram and UV-vis spectrum



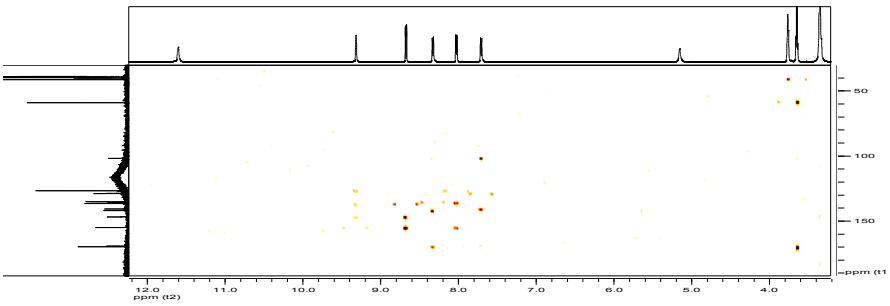
^{1}H NMR



^{13}C NMR



HMBC

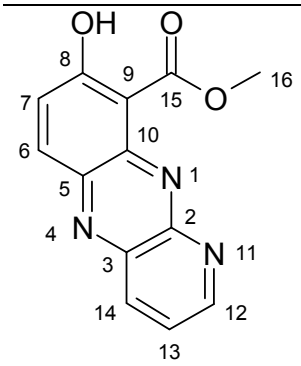


Synthesis and isolation as described above. Yellow solid. Yield 48.15 % (17.7 mg): mp (decomposition) 220-223 °C. ^{1}H NMR: δ 3.62 (m, *J* = 5.5, 2H, H-17), 3.74 (d, *J* = 5.0, 2H, H-18), 5.14 (s (broad), 1H, OH), 7.69 (d, *J* = 9.5, 1H, H-7), 8.01 (dd, *J* = 8.5, *J* = 3.9, 1H, H-13), 8.31 (d, *J* = 9.5, 1H, H-6), 8.66 (dd, *J* = 8.5, *J* = 1.8, 1H, H-14), 9.30 (dd, *J* = 1.7, 1H, H-12), 11.6 (s (broad), 1H, NH). ^{13}C NMR: δ 41.4 (C-17), 59.1 (C-18), 102.1 (C-9), 126.9 (C-13), 129.1 (C-7), 135.5 (C-6), 136.1 (C-3), 136.7 (C-14), 141.0 (C-5), 142.2 (C-10), 147.1 (C-2), 155.3 (C-12), 169.6 (C-8), 170.1 (C-15). HMBC correlations: H-6 (C-8, C-10), H-7 (C-5, C-9), H-12 (C-2, C-13, C-14), H-13 (C-3, C-12), H-14 (C-2, C-12), H-17 (C-15, C-18), H-18 (C-17). R_f (HPLC) 10.3 min, UV-vis (MeOH) λ_{max} 218, 245, 354, 402

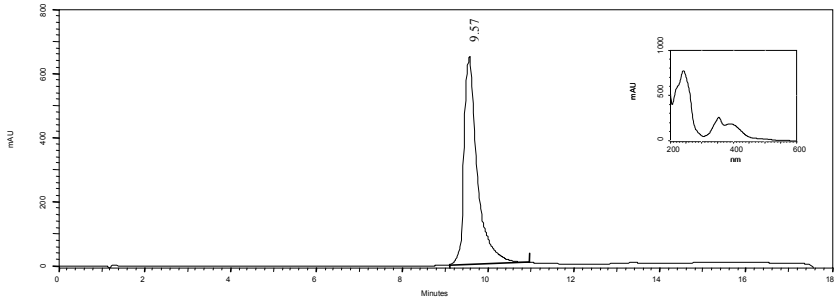
nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 283.0818 (calculated 283.0831). AP-ESI: pos. mode $[M+H]^+$ 285.1012 (calculated 285.0988).

6b: product resulted from **1c** and **2e**

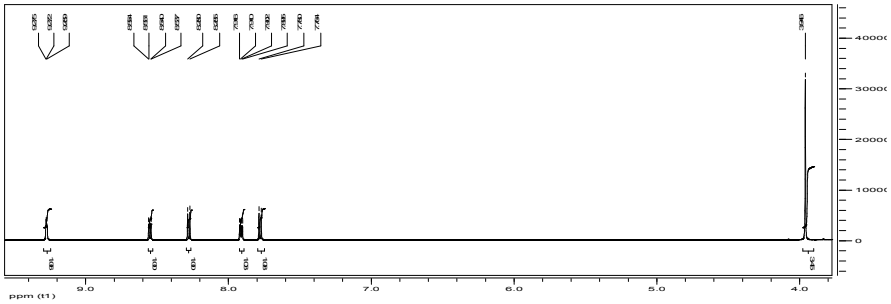
6b	**8-Hydroxy-pyrido[2,3-b]quinoxaline-9-carboxylic acid methyl ester**



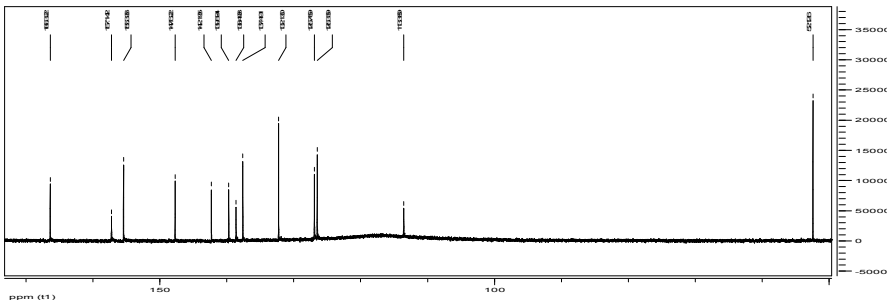
HPLC chromatogram and UV-vis spectrum



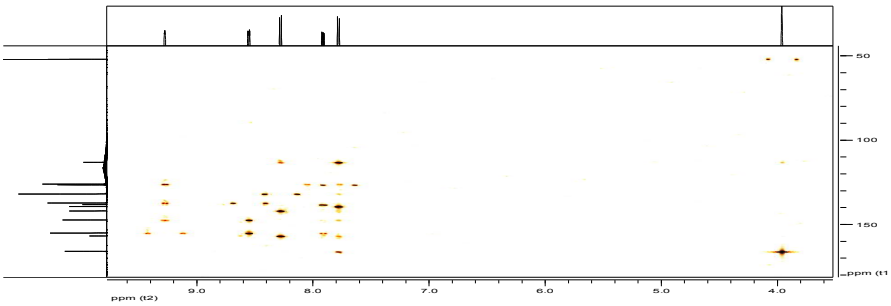
^{1}H NMR



^{13}C NMR



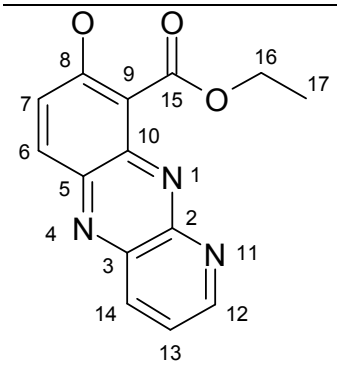
HMBC



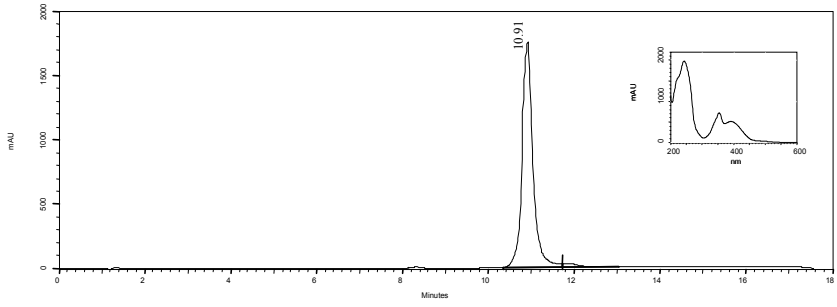
Synthesis and isolation as described above. Yellow orange solid. Yield 25.25 % (8.4 mg): mp (decomposition) 188-191 °C. ^{1}H NMR: δ 3.95 (s, 3H, H-16), 7.77 (d, *J* = 9.5, 1H, H-7), 7.91 (dd, *J* = 8.6, *J* = 3.8, 1H, H-13), 8.27 (d, *J* = 9.5, 1H, H-6), 8.55 (dd, *J* = 8.6, *J* = 1.8, 1H, H-14), 9.27 (dd, *J* = 1.7, J = 3.6, 1H, H-12). ^{13}C NMR: δ 52.1 (C-16), 113.4 (C-9), 126.4 (C-13), 126.8 (C-7), 132.1 (C-6), 137.5 (C-14), 138.5 (C-3), 139.6 (C-5), 142.2 (C-10), 147.6 (C-2), 155.3 (C-12), 157.1 (C-8), 166.3 (C-15). HMBC correlations: H-6 (C-8, C-9, C-10), H-7 (C-5, C-6, C-8, C-9, C-15), H-12 (C-2, C-13, C-14), H-13 (C-2, C-3, C-12), H-14 (C-2, C-12), H-16 (C-9, C-15). R_f (HPLC) 9.6 min, UV-vis (MeOH) λ_{max} 243, 354, 390 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 254.0560 (calculated 254.0566). AP-ESI: pos. mode $[M+H]^+$ 256.0747 (calculated 256.0722).

6c: product resulted from **1d** and **2e**

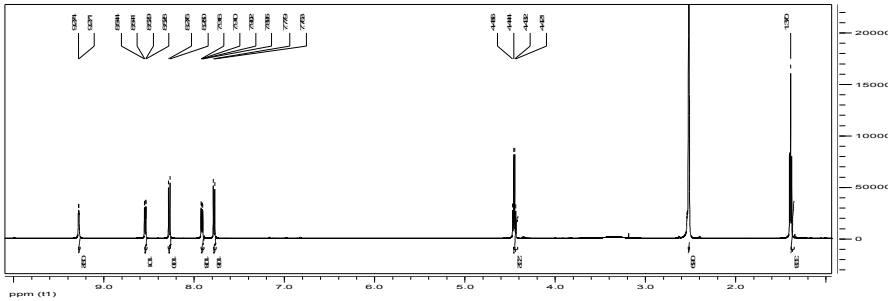
6c	**8-Hydroxy-pyrido[2,3-b]quinoxaline-9-carboxylic acid methyl ester**



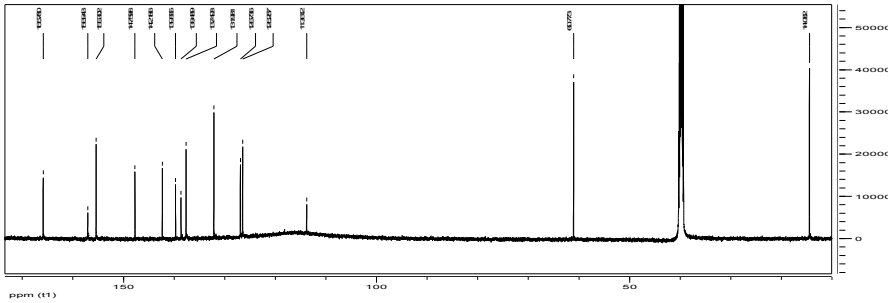
HPLC chromatogram and UV-vis spectrum



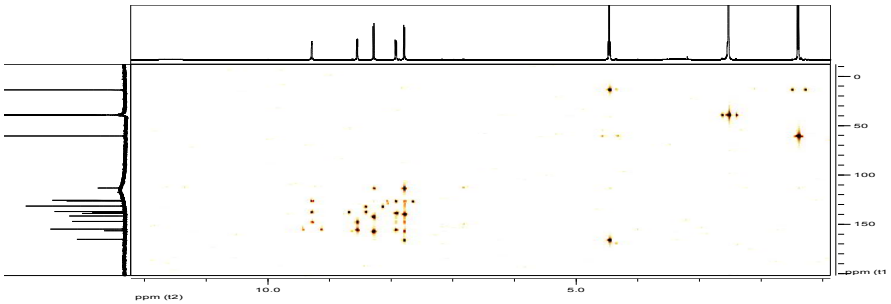
^{1}H NMR



^{13}C NMR



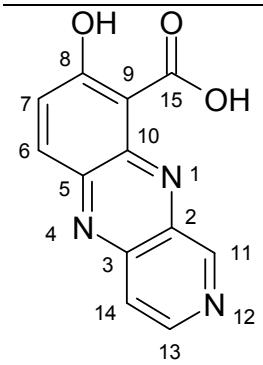
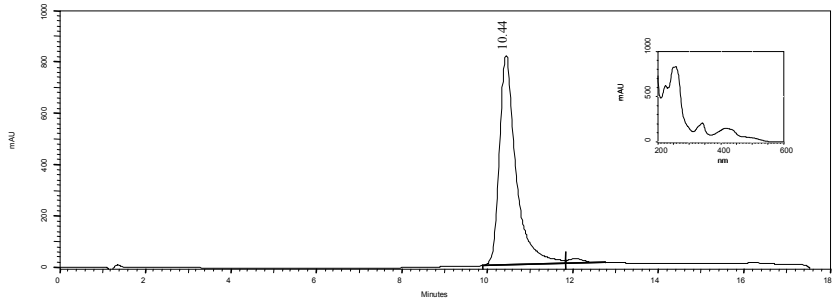
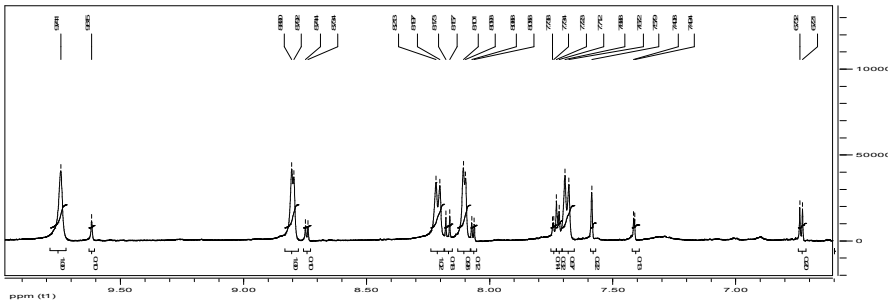
HMBC



Synthesis and isolation as described above. Dark yellow solid. Yield 40.05 % (14 mg): mp (decomposition) 180-182 °C. ^{1}H NMR: δ 1.37 (t, *J* = 7.1, 3H, H-17), 4.44 (q, *J* = 7.1, 2H, H-16), 7.77 (d, *J* = 9.5, 1H, H-7), 7.91 (dd, *J* = 8.6, *J* = 3.8, 1H, H-13), 8.27 (d, *J* = 9.5, 1H, H-6), 8.53 (dd, *J* = 8.6, *J* = 1.8, 1H, H-14), 9.27 (dd, *J* = 1.7, *J* = 3.6, 1H, H-12). ^{13}C NMR: δ 14.1 (C-17), 60.8 (C-16), 113.6 (C-9), 126.3 (C-13), 126.7 (C-7), 132.0 (C-6), 137.5 (C-14), 138.5 (C-3), 139.6 (C-5), 142.2 (C-10), 147.6 (C-2), 156.9 (C-8), 165.8 (C-15). HMBC correlations: H-6 (C-8, C-9, C-10), H-7 (C-5, C-8, C-9, C-15), H-12 (C-2, C-13, C-14), H-13 (C-3, C-12), H-14 (C-2, C-12), H-16 (C-9, C-15, C-17), H-17 (C-

16). R_f (HPLC) 10.9 min, UV-vis (MeOH) λ_{max} 243, 355, 392 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 268.0717 (calculated 268.0728). AP-ESI: pos. mode $[M+H]^+$ 270.0862 (calculated 270.0873).

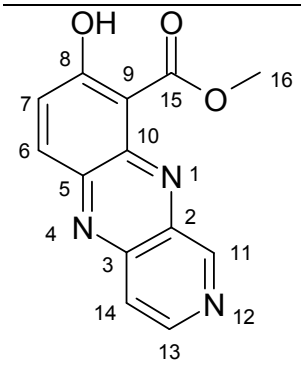
6d: product resulted from **1a** and **2f**

6d	**8-Hydroxy-pyridol[3,4-b]quinoxaline-9-carboxylic acid**
	HPLC chromatogram and UV-vis spectrum  ^{1}H NMR 

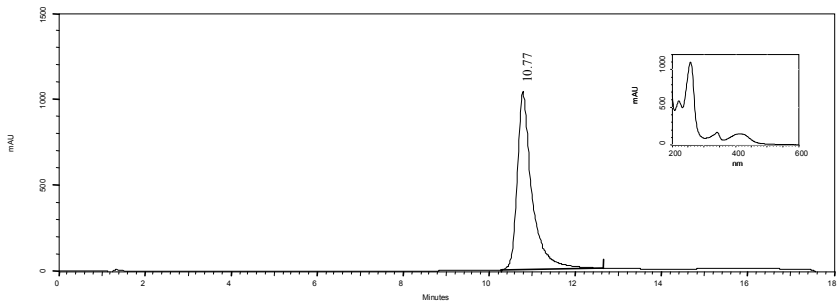
Synthesis and isolation as described above. Dark red solid. Yield 20.32 % (10.7 mg): mp (decomposition) 196-198 °C. ^{1}H NMR: δ 7.68 (d, J = 9.5, 1H, H-7), 8.10 (d, J = 5.2, 1H, H-14), 8.20 (d, J = 9.4, 1H, H-6), 8.80 (d, J = 5.3, 1H, H-13), 9.74 (s, 1H, H-11). R_f (HPLC) 10.4 min, UV-vis (MeOH) λ_{max} 224, 255, 342, 416 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 240.0375 (calculated 240.0415).

6e: product resulted from **1c** and **2f**

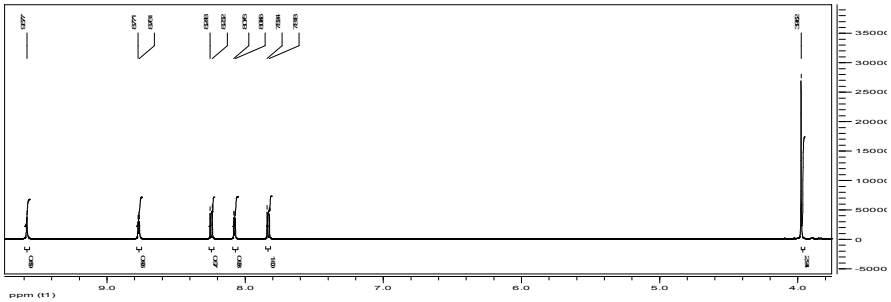
6e	**8-Hydroxy-pyrido[2,3-b]quinoxaline-9-carboxylic acid methyl ester**



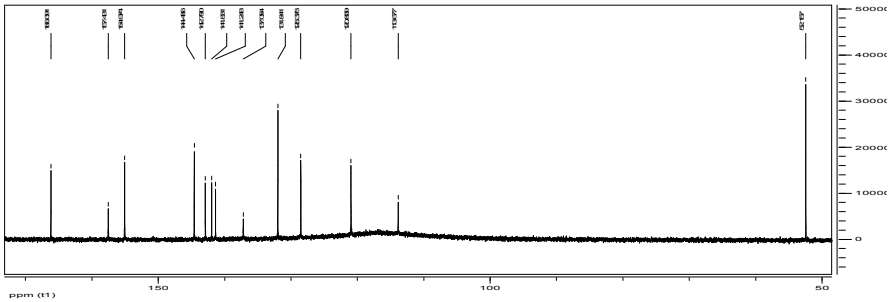
HPLC chromatogram and UV-vis spectrum



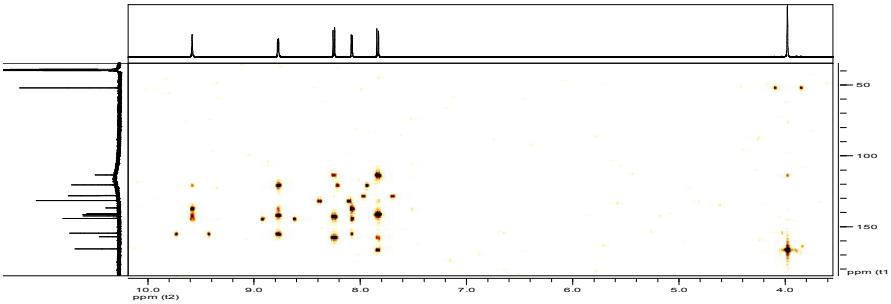
^{1}H NMR



^{13}C NMR

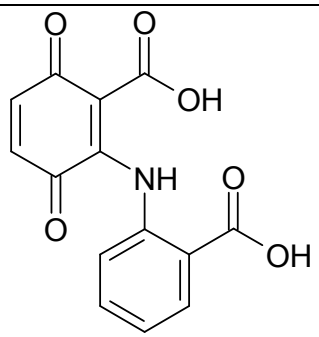
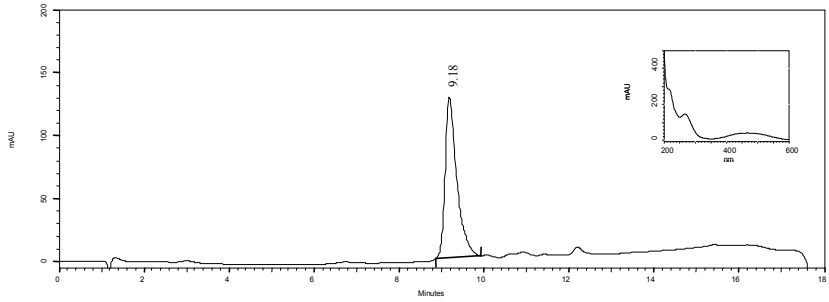


HMBC



Synthesis and isolation as described above.Yellow solid. Yield 26.51 % (14.7 mg): mp (decomposition) 187-189 °C. ^{1}H NMR: δ 3.96 (s, 3H, H-16), 7.82 (d, *J* = 9.5, 1H, H-7), 8.07 (dd, *J* = 6.0, 1H, H-14), 8.24 (d, *J* = 9.5, 1H, H-6), 8.77 (d, *J* = 6.0, 1H, H-13), 9.58 (s, 1H, H-11). ^{13}C NMR: δ 52.2 (C-16), 113.7 (C-9), 120.8 (C-14), 128.4 (C-7), 131.8 (C-6), 137.1 (C-2), 141.3 (C-5), 141.8 (C-3), 142.8 (C-10), 144.5 (C-13), 155.0 (C-11), 157.4 (C-8), 166.1 (C-15). HMBC correlations: H-6 (C-8, C-9, C-10), H-7 (C-5, C-6, C-8, C-9, C-15), H-11 (C-2, C-3, C-14), H-13 (C-2, C-3, C-11, C-14), H-14 (C-2, C-11, C-13), H-16 (C-9, C-15). R_f (HPLC) 10.8 min, UV-vis (MeOH) λ_{max} 221, 258, 342, 414 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 254.0543 (calculated 254.0571).

7a: product resulted from **1a** and **2g**

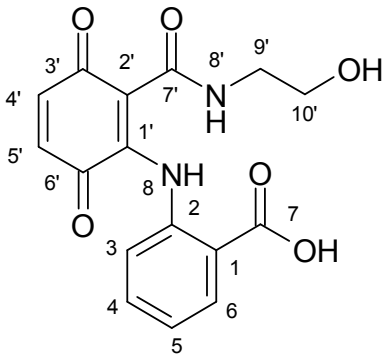
7a	**2-(2-Carboxy-3,6-dioxo-cyclohexa-1,4-dienylamino)-benzoic acid**
	HPLC chromatogram and UV-vis spectrum 

Synthesis and isolation as described above. Dark red solid. Yield 13.16 % (12.3 mg): mp (decomposition) 95-99 °C, mp 197 °C. R_f (HPLC) 9.2 min, UV-vis (MeOH) λ_{max} 215, 267, 466 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 286.0332 (calculated 286.0357).

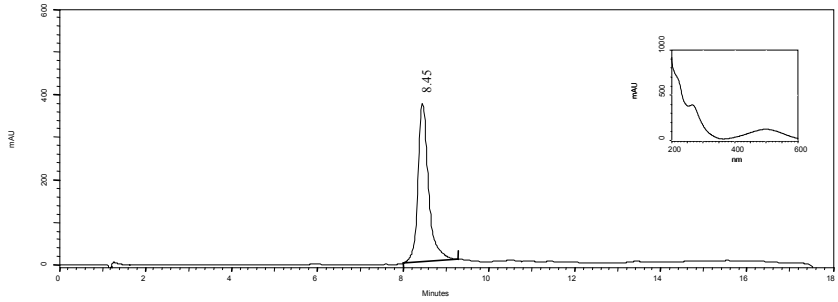
7b and **8a**: products resulted from **1b** and **2g**

7b	**2-[2-(2-Hydroxy-ethylcarbamoyl)-3,6-dioxo-cyclohexa-1,4-dienylamino]-benzoic acid**
8a	**2-[2-(2-Hydroxy-ethylcarbamoyl)-3,6-dioxo-cyclohexa-1,4-dienylamino]-benzoic acid radical**

7b

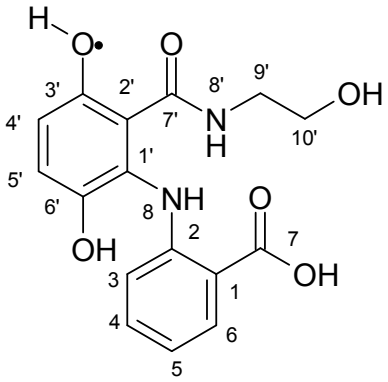


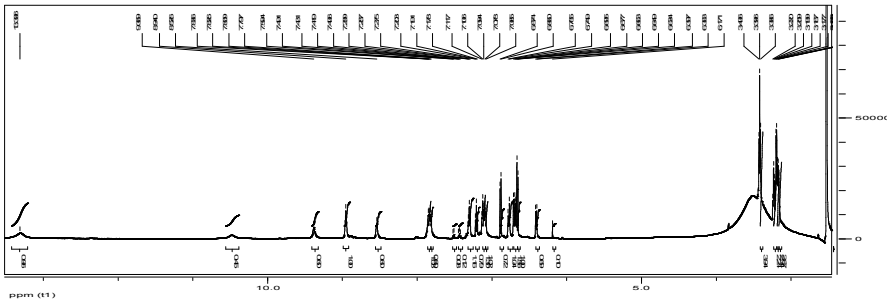
HPLC chromatogram and UV-vis spectrum



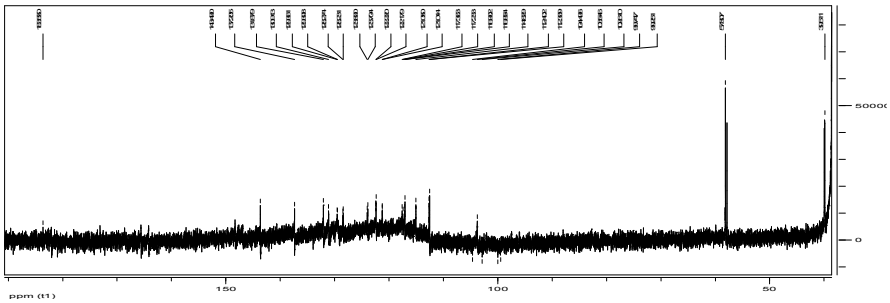
^{1}H NMR

8a

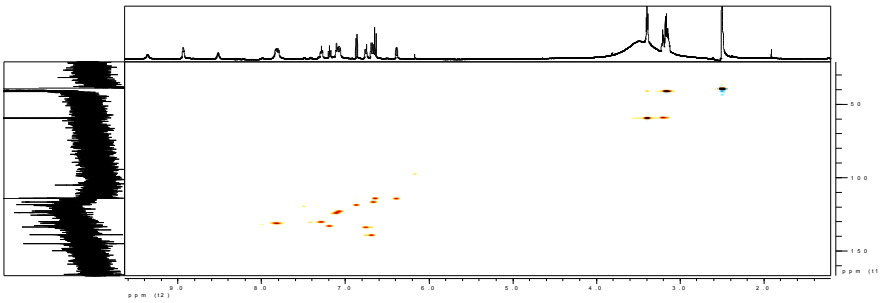




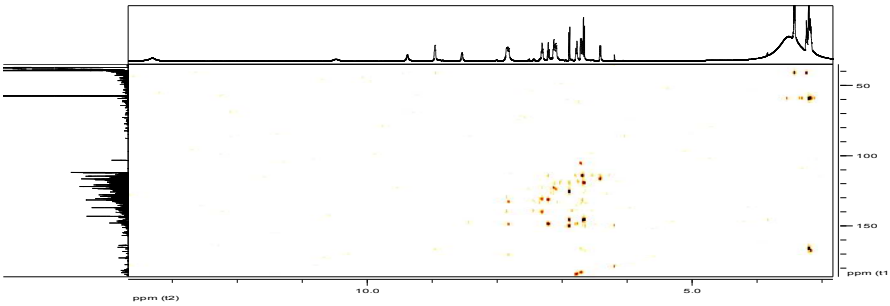
^{13}C NMR



HSQC



HMBC



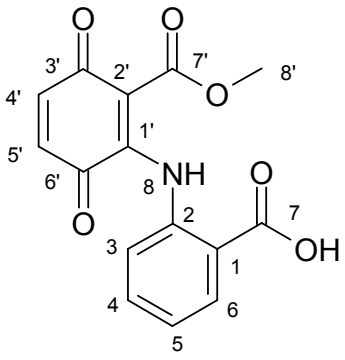
Synthesis and isolation as described above. Dark red solid. Yield 38.39 % (15.4 mg): mp (decomposition) 76-80 °C, mp 183 °C. R_f (HPLC) 8.5 min, UV-vis (MeOH) λ_{max} 211, 266, 499 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 329.0792 (calculated 329.0779). NMR data of quinonoid product and hydroquinonoid radical are available from one ^{1}H NMR, one ^{13}C NMR, one HSQC, and one HMBC spectrum. (**7b**) ^{1}H NMR: δ 3.17 (m, *J* = 5.7, 2H, H-9'), 3.39 (t, *J* = 5.8, 2H, H-10'), 6.68 (d, *J* = 10.0, 1H, H-4'), 6.76 (d, *J* = 10.0, 1H, H-5'), 7.07 (d, *J* = 7.9, 1H, H-3), 7.11 (dd, *J* = 7.3, *J* = 6.7, 1H, H-5), 7.29 (dd, *J* = 7.5, *J* = 7.4, 1H, H-4), 7.83 (d, *J* = 6.2, 1H, H-6), 8.94 (t, *J* = 5.6, 1H, H-8'), 13.32 (s (broad), 1H, NH). ^{13}C NMR: δ 41.2 (C-9'), 41.2 (C-9'), 105.2 (C-2'), 122.7 (C-3), 123.9 (C-5), 126.7 (C-1), 129.9 (C-4), 131.0 (C-6), 133.6 (C-5'), 138.9 (C-2), 138.9 (C-4'), 148.5 (C-1'), 165.7 (C-7'), 182.6 (C-6'), 183.6 (C-3'). HMBC correlations: H-3 (C-5), H-4 (C-2, C-3, C-6), H-4' (C-2', C-6', C-7'), H-5 (C-1, C-3), H-5' (C-1', C-3'), H-6 (C-2, C-4), H-8' (C-7', C-9'), H-9' (C-7', C-10'), H-10' (C-9'). (**8a**) ^{1}H NMR: δ 3.15 (m, *J* = 6.0, 2H, H-9'), 3.21 (t, *J* = 6.1, 2H, H-10'), 6.39 (d, *J* = 8.3, 1H, H-3), 6.64 (d, *J* = 8.8, 1H, H-4'), 6.66 (t, *J* = 8.1, 1H, H-5), 6.87 (d, *J* = 8.8, 1H, H-5'), 7.19 (t, *J* = 7.7, *J* = 7.3, 1H, H-4), 7.80 (d, *J* = 7.7, 1H, H-6), 8.53 (s, 1H, NH), 9.37 (s, 1H, NH). ^{13}C NMR: δ 41.3 (C-9'), 59.2 (C-

10’), 114.0 (C-4’), 114,1 (C-3), 116.5 (C-5), 118.5 (C-5’), 118.9 (C-2’), 125.4 (C-3’), 131.1 (C-6), 132.6 (C-4), 145.2 (C-6’), 148.5 (C-2), 149.8 (C-1’), 167.2 (C-7’), 169.9 (C-7). HMBC correlations: H-3 (C-5), H-4 (C-2, C-3, C-6), H-4’ (C-1’, C-2’, C-3’, C-6’, C-7’), H-5 (C-3, C-6), H-5’ (C-1’, C-2’, C-3’, C-6’), H-6 (C-2, C-4, C-7), H-9’ (C-7’, C-10’), H-10’ (C-9’).

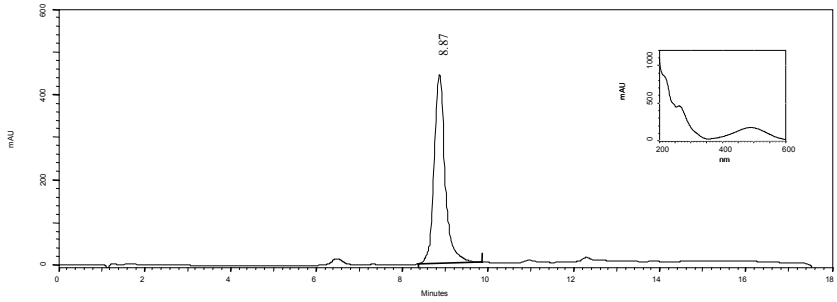
7c and **8b**: products resulted from **1c** and **2g**

7c	**2-(2-Methoxycarbonyl-3,6-dioxo-cyclohexa-1,4-dienylamino)-benzoic acid**
8b	**2-(2-Methoxycarbonyl-3,6-dioxo-cyclohexa-1,4-dienylamino)-benzoic acid radical**

7c

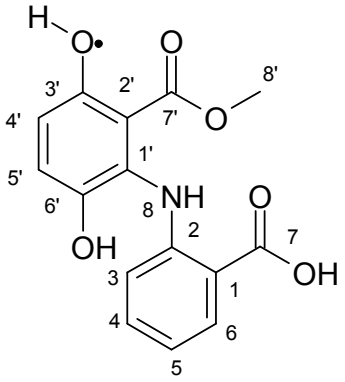


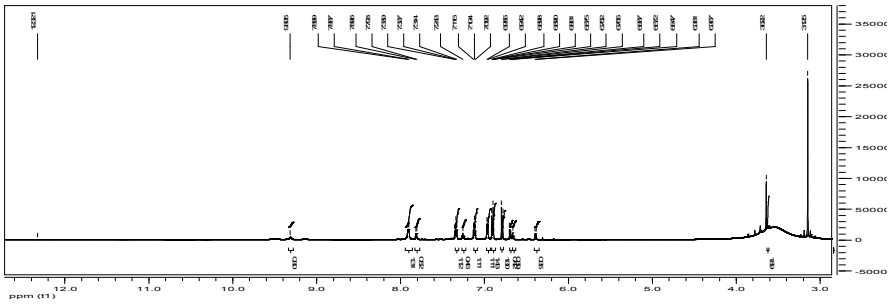
HPLC chromatogram and UV-vis spectrum



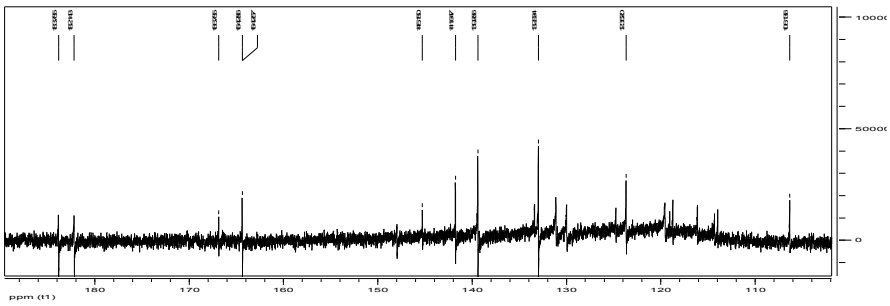
^{1}H NMR

8b

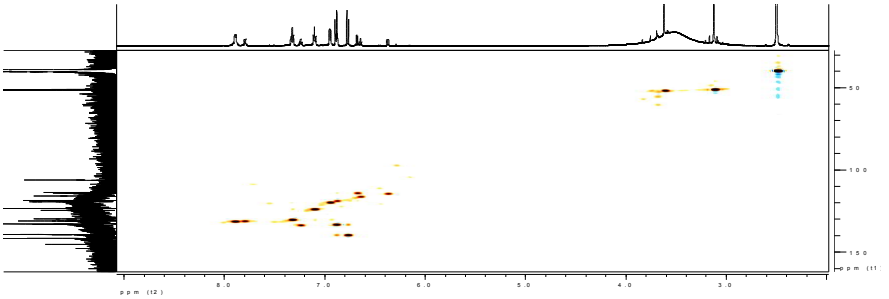




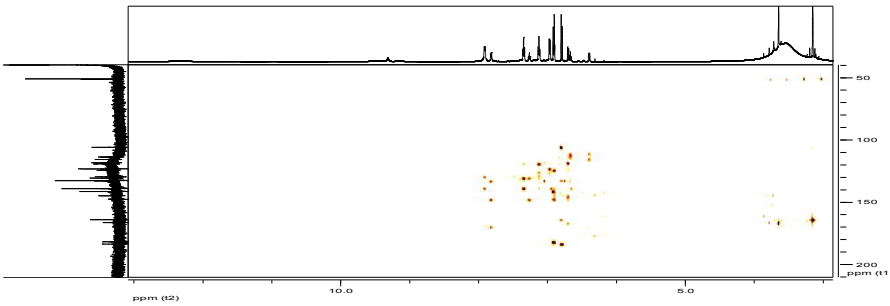
^{13}C NMR



HSQC



HMBC

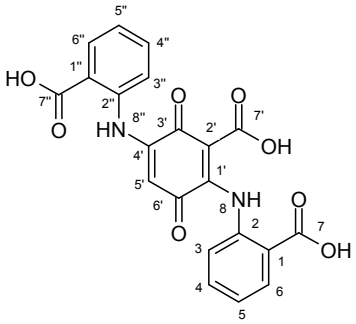


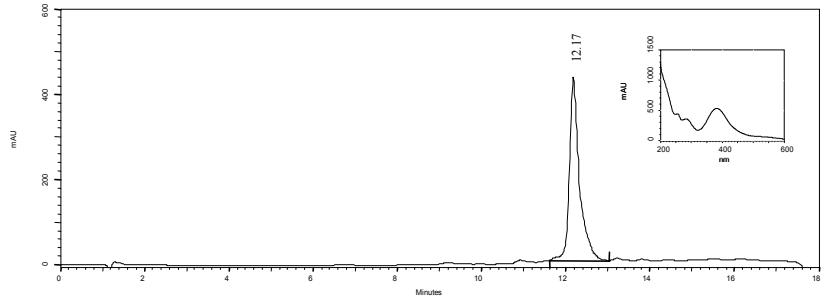
Synthesis and isolation as described above. Dark red solid. Yield 44.77 % (16.4 mg): mp (decomposition) 84-88 °C, mp 188 °C. R_f (HPLC) 8.9 min, UV-vis (MeOH) λ_{max} 210, 263, 487 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 302.0677 (calculated 302.0670). NMR data of quinonoid product and hydroquinonoid radical are available from one ^{1}H NMR, one ^{13}C NMR, one HSQC, and one HMBC spectrum. (**7c**) ^{1}H NMR: δ 3.12 (s, 3H, H-8'), 6.77 (d, *J* = 10.1, 1H, H-4'), 6.88 (t, *J* = 10.1, 1H, H-5'), 6.95 (d, *J* = 8.0, 1H, H-3), 7.10 (dd, *J* = 7.4, 1H, H-5), 7.33 (dd, *J* = 7.6, 1H, H-4), 7.89 (d, *J* = 7.2, 1H, H-6), 12.32 (s (broad), 1H, NH). ^{13}C NMR: δ 50.9 (C-8'), 106.1 (C-2'), 119.5 (C-3), 123.5 (C-5), 126.2 (C-1), 129.8 (C-4), 131.0 (C-6), 132.8 (C-5'), 139.3 (C-2), 139.3 (C-4'), 141.6 (C-1'), 164.3 (C-7'),

168.3 (C-7), 182.3 (C-3'), 183.8 (C-6'). HMBC correlations: H-3 (C-1, C-5), H-4 (C-2, C-3, C-6), H-4' (C-2', C-5', C-6', C-7'), H-5 (C-1, C-2, C-3), H-5' (C-1', C-3'), H-6 (C-2, C-4, C-7), H-8' (C-2', C-7'). (**8b**) ^{1}H NMR: δ 3.62 (s, 3H, H-8'), 6.37 (d, *J* = 8.4, 1H, H-3), 6.65 (t, *J* = 7.6, 1H, H-5), 6.68 (d, *J* = 8.8, 1H, H-4'), 6.87 (d, *J* = 8.8, 1H, H-5'), 7.24 (t, *J* = 7.7, *J* = 1.1, 1H, H-4), 7.80 (d, *J* = 7.6, 1H, H-6), 9.31 (s, 1H, NH). ^{13}C NMR: δ 51.6 (C-8'), 111.4 (C-1), 113.8 (C-4'), 114.1 (C-3), 115.9 (C-5), 118.5 (C-5'), 118.9 (C-2'), 124.6 (C-3'), 130.5 (C-6), 133.3 (C-4), 145.2 (C-6'), 147.8 (C-1'), 147.8 (C-2), 166.8 (C-7'), 170.1 (C-7). HMBC correlations: H-3 (C-1, C-5, C-7), H-4 (C-2, C-3, C-6), H-4' (C-2', C-6'), H-5 (C-1, C-3, C-4, C-6), H-5' (C-1', C-3', C-6'), H-6 (C-2, C-4, C-7), H-8' (C-7').

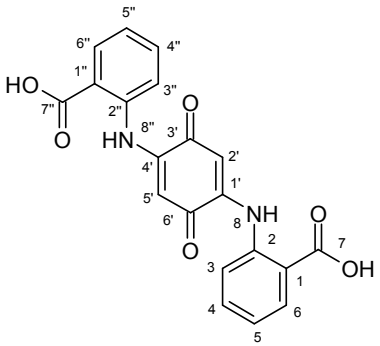
9a and **10a**: products resulted from **1a** and **2g**

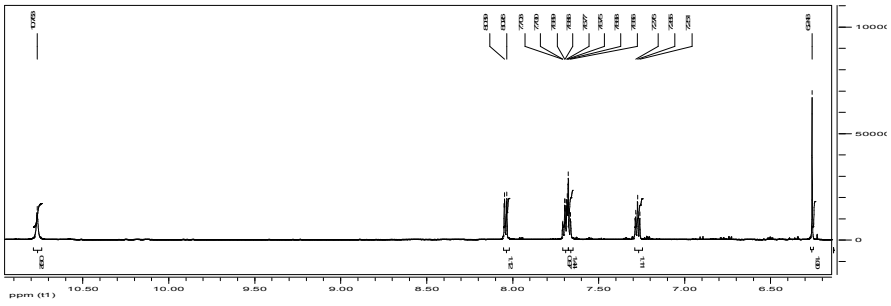
9a	**2-{4-[2-(Carboxyphenyl)amino]-2-carboxy-3,6-dioxocyclohexa-1,4-dienylamino}-benzoic acid**
10a	**2-{4-[2-(Carboxyphenyl)amino]-3,6-dioxocyclohexa-1,4-dienylamino}-benzoic acid**
9a	HPLC chromatogram and UV-vis spectrum



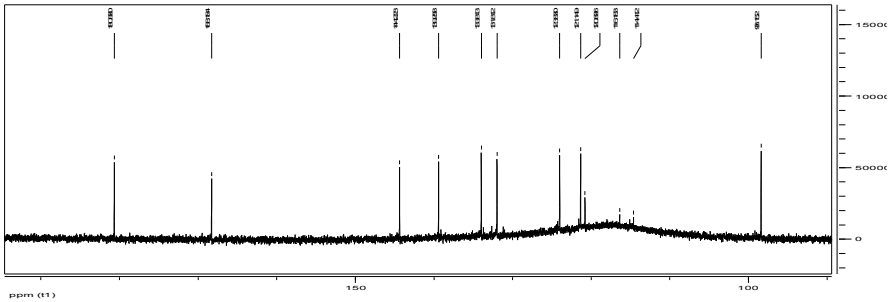


10a ^{1}H NMR

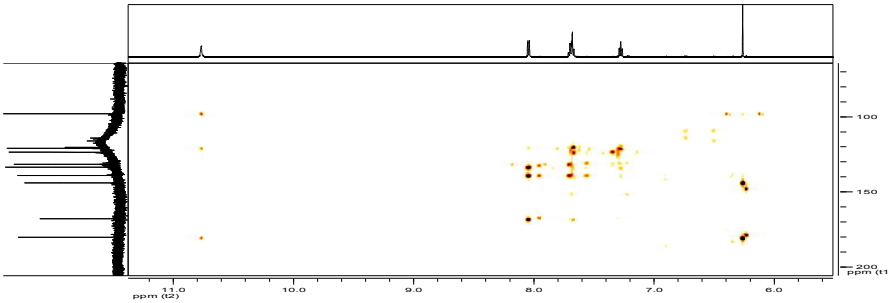




^{13}C NMR



HMBC

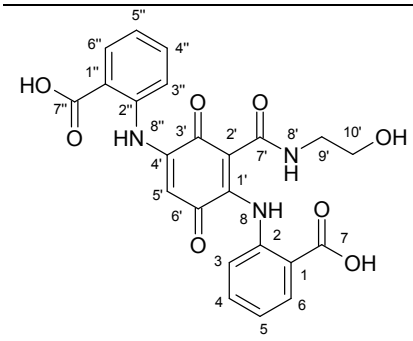


Synthesis and isolation as described above. Brown red solid. Yield 26.07 % (17.9 mg). R_f (HPLC) 12.2 min, UV-vis (MeOH) λ_{max} 255, 282, 382 nm. (**9a**) ^{1}H NMR: δ 6.22 (s, 1H, H-5'), 7.27 (m, *J* = 7.4, *J* = 1.4, 1H, H-5), 7.29 (d, 1H, H-3''), 7.33 (t, *J* = 7.6, 1H, H-5''), 7.55 (m, *J* = 8.3, *J* = 7.9, *J* = 1.4, 1H, H-4''), 7.67 (m, *J* = 8.1, *J* = 1.0, 2H, H-3), 7.68 (m, *J* = 8.2, *J* = 6.8, *J* = 1.5, 1H, H-4), 7.94 (m, *J* = 7.9, *J* = 1.4, 1H, H-6''), 8.02 (m, *J* = 7.8, *J* = 1.6, 1H, H-6). ^{13}C NMR: δ 98.9 (C-5'), 102.2 (C-2'), 120.6 (C-1), 121.1 (C-3), 122.8 (C-5), 123.3 (C-1''), 124.1 (C-3''), 125.7 (C-5''), 131.0 (C-6''), 131.8 (C-6), 132.5 (C-4''), 133,8 (C-4), 139.0 (C-2''), 139.3 (C-2), 148.0 (C-1'), 166.9 (C-7''), 168.2 (C-7), 178.3 (C3'). HMBC correlations: H-3 (C-1, C-5, C-7), H-3'' (C-1'', C-5''), H-4 (C-2, C-6), H-4'' (C-2'', C-3'', C-6''), H-5 (C-2, C-3, C-4, C-7), H-5' (C-1', C-2', C-3'), H-5'' (C-1'', C-6''), H-6 (C-1, C-2, C-4, C-7), H-6'' (C-2'', C-4'', C-7''). (**10a**) ^{1}H NMR: δ 6.25 (s, 2H, H-2'/H-5'), 7.27 (m, *J* = 7.4, *J* = 1.4, 2H, H-5/H-5''), 7.67 (m, *J* = 8.1, *J* = 1.0, 2H, H-3/H-3''), 7.68 (m, *J* = 8.2, *J* = 6.8, *J* = 1.5, 2H, H-4/H-4''), 8.03 (m, *J* = 7.8, *J* = 1.3, 2H, H-6/H-6''), 10.76 (s, 2H, NH, H-8/H-8''). ^{13}C NMR: δ 98.2 (C-2'/C-5'), 120.6 (C-1/C-1''), 121.1 (C-3/C-3''), 131.8 (C-6/C-6''), 133,8 (C-4/C-4''), 139.3 (C-2/C-2''), 144.2 (C-1'/C-4'), 168.2 (C-7/C-7''), 180.6 (C-3'/C-6'). HMBC correlations: H-2'/H-5' (C-1'/C-4', C-

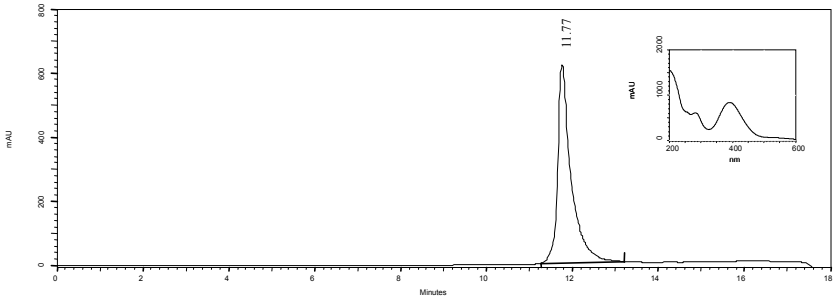
2’/C-5’, C-3’/C-6’), H-3/H-3’’ (C-1/C-1’’, C-5/C-5’’, C-7/C-7’’), H-4/H-4’’ (C-2/C-2’’, C-6/C-6’’), H-5/H-5’’ (C-2/C-2’’, C-3/C-3’’, C-4/C-4’’, C-7/C-7’’), H-6/H-s6’’ (C-1/C-1’’, C-2/C-2’’, C-4/C-4’’, C-7/C-7’’), H-8/H-8’’ (C-2’/C-5’), C-3/C-3’’, C-3’/C-6’). (**9a**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 421.0659 (calculated 421.0677). (**10a**) MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 377.0753 (calculated 377.0779).

9b: product resulted from **1b** and **2g**

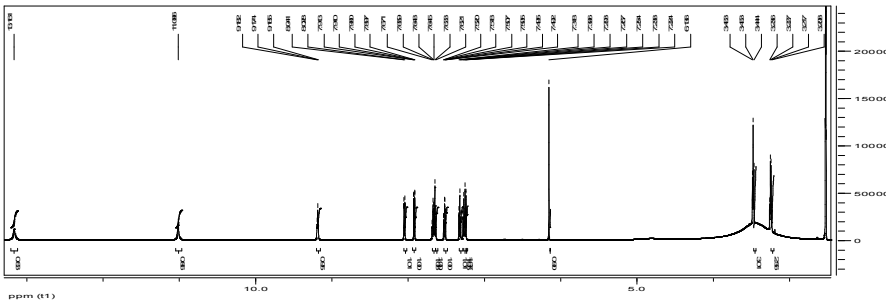
9b	**2-{4-[2-(Carboxyphenyl)amino]-2-(2-hydroxy-ethylcarbamoyl)-3,6-dioxocyclohexa-1,4-dienylamino}-benzoic acid**



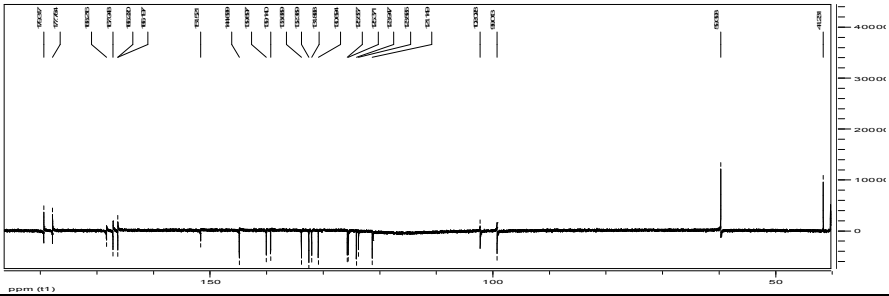
HPLC chromatogram and UV-vis spectrum



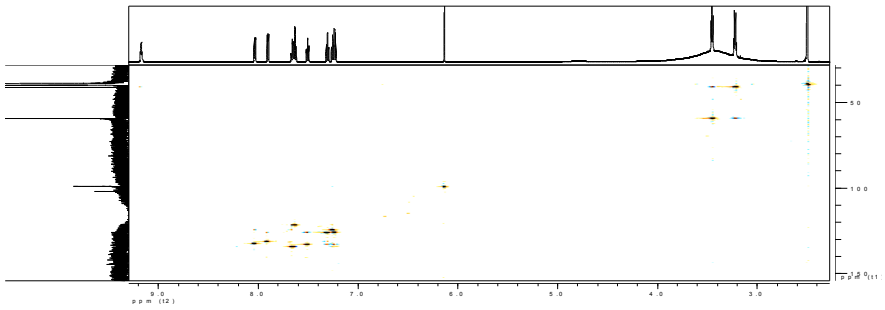
^{1}H NMR



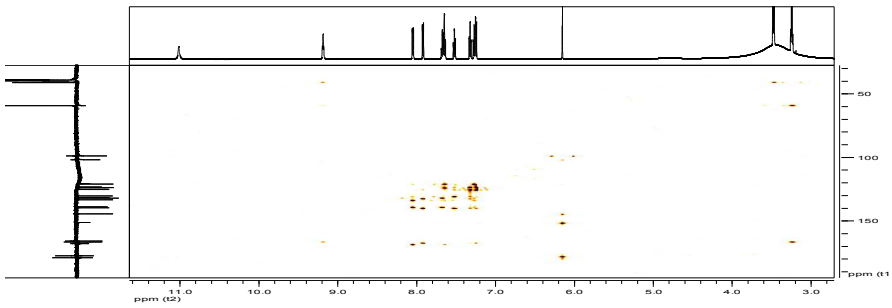
^{13}C NMR



HSQC



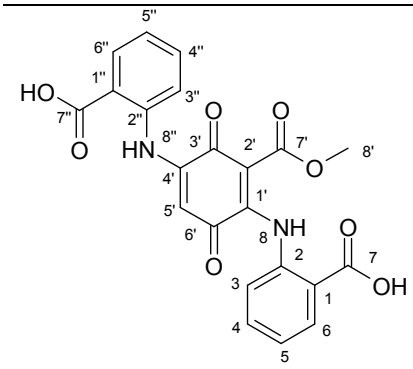
HMBC



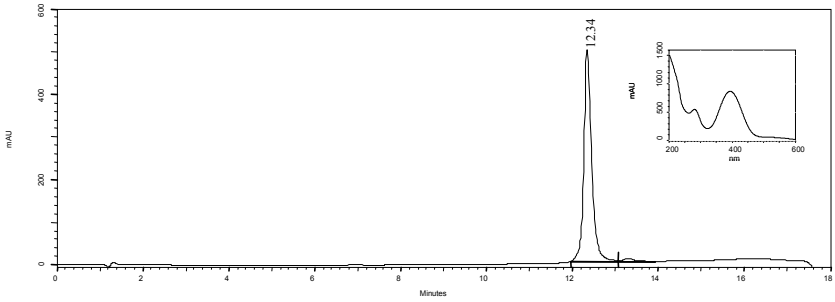
Synthesis and isolation as described above. Brown red solid. Yield 23.12 % (24.5 mg): mp 235 °C. ^{1}H NMR: δ 3.22 (q, *J* = 5.7, 2H, H-9'), 3.45 (t, *J* = 5.8, 2H, H-10'), 6.14 (s, 1H, H-5'), 7.23 (d, *J* = 8.1, 1H, H-3''), 7.25 (m, *J* = 7.5, *J* = 1.2, 1H, H-5), 7.31 (m, *J* = 7.3, *J* = 0.9, 1H, H-5''), 7.51 (m, *J* = 7.9, *J* = 1.5, 1H, H-4''), 7.63 (d, *J* = 7.4, 1H, H-3), 7.65 (m, *J* = 7.5, *J* = 8.1, *J* = 1.5, 1H, H-4), 7.91 (d, *J* = 7.9, *J* = 1.5, 1H, H-6''), 8.03 (d, *J* = 7.8, *J* = 1.3, 1H, H-6), 9.17 (t, *J* = 5.4, 1H, NH, H-8'), 11.01 (s, 1H, NH), 13.16 (s, 1H, NH). ^{13}C NMR: δ 41.2 (C-9'), 59.4 (C-10'), 99.0 (C-5'), 102.0 (C-2'), 121.0 (C-1), 121.1 (C-3), 123.6 (C-1''), 123.9 (C-5), 125.4 (C-3''), 125.6 (C-5''), 130.7 (C-6''), 131.9 (C-6), 132.4 (C-4''), 133.7 (C-4), 139.1 (C-2), 139.9 (C-2''), 144.7 (C-4'), 151.5 (C-1'), 166.2 (C-7'), 167.0 (C-7''), 168.2 (C-7), 177.8 (C-3'), 179.3 (C-6'). HMBC correlations: H-3 (C-1, C-4, C-5, C-7), H-3'' (C-1'', C-2'', C-5'', C-7''), H-4 (C-2, C-6), H-4'' (C-1'', C-2'', C-3'', C-6''), H-5 (C-2, C-3, C-4, C-6), H-5' (C-1', C-2', C-2'', C-3', C-4', C-6'), H-5'' (C-1'', C-2'', C-3'', C-4'', C-6'', C-7''), H-6 (C-1, C-2, C-4, C-7), H-6'' (C-2'', C-3'', C-4'', C-7''), H-8' (C-2', C-7', C-9', C-10'), H-9' (C-7', C-10'), H-10' (C-9'). R_f (HPLC) 11.8 min, UV-vis (MeOH) λ_{max} 280, 391 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 464.1125 (calculated 464.1094).

9c: product resulted from **1c** and **2g**

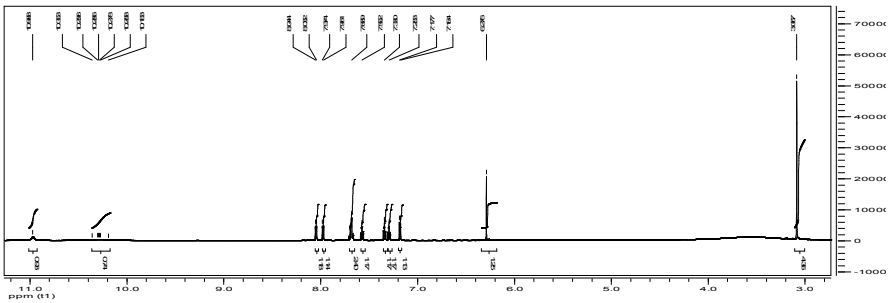
9c	**2-{4-[2-(Carboxyphenyl)amino]-2-methoxycarbonyl-3,6-dioxocyclohexa-1,4-dienylamino}-benzoic acid**



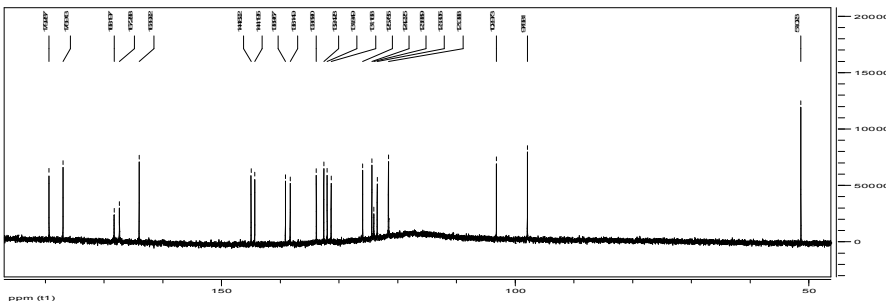
HPLC chromatogram and UV-vis spectrum



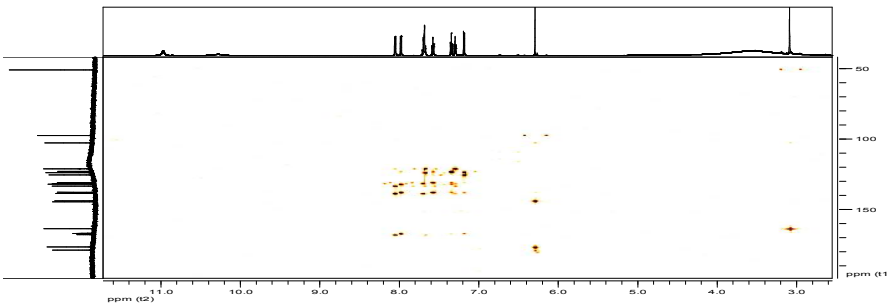
^{1}H NMR



^{13}C NMR



HMBC



Synthesis and isolation as described above. Brown red solid. Yield 25.86 % (26.5 mg): mp 246 °C. ^{1}H NMR: δ 3.07 (s, 3H, H-8'), 6.28 (s, 1H, H-5'), 7.17 (d, *J* = 7.7, *J* = 0.5, 1H, H-3''), 7.28 (m, *J* = 7.2, *J* = 1.7, 1H, H-5), 7.33 (m, *J* = 7.4, *J* = 7.7, *J* = 0.9, 1H, H-5''), 7.56 (m, *J* = 7.5, *J* = 1.5, 1H, H-4''), 7.66 (d, *J* = 7.5, *J* = 1.4, 1H, H-3), 7.68 (m, *J* = 8.2, *J* = 1.4, 1H, H-4), 7.97 (d, *J* = 7.9, *J* = 1.4, 1H, H-6''), 8.04 (d, *J* = 8.1, *J* = 1.3, 1H, H-6), 10.29 (s (broad), 1H, NH), 10.97 (s, 1H, NH). ^{13}C NMR: δ 51.0 (C-8'), 97.7 (C-5'), 103.0 (C-2'), 121.3 (C-1), 121.4 (C-3), 123.3 (C-3''), 123.9 (C-1''), 124.2 (C-5), 125.8 (C-5''), 131.2 (C-6''), 131.8 (C-6), 132.4 (C-4''), 133.7 (C-4), 138.1 (C-2''), 139.0 (C-2), 144.2 (C-1'), 144.8 (C-4'), 163.9 (C-7'), 167.3 (C-7''), 168.2 (C-7), 176.9 (C-3'), 179.3 (C-6'). HMBC correlations: H-3 (C-1, C-4, C-5, C-7), H-3'' (C-1'', C-2'', C-5'', C-6'', C-7''), H-4 (C-2, C-6), H-4'' (C-2'', C-3'', C-6''), H-5 (C-2, C-3, C-4, C-6), H-5' (C-1', C-2', C-2'', C-3', C-4', C-6'), H-5'' (C-2'', C-3'', C-4'', C-6'', C-7''), H-6 (C-2, C-3, C-4, C-7), H-6'' (C-2'', C-3'', C-4'', C-7''), H-8' (C-2', C-7'). R_f (HPLC) 12.3 min, UV-vis (MeOH) λ_{max} 281, 393 nm. MS *m/z* AP-ESI: neg. mode $[M-H]^-$ 435.0845 (calculated 435.0828).