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The reaction of tanshinones with diamines

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The reactions of cryptotanshinone and tanshinone IIA with diamines, including putrescine and cadaverine are carried out. Eleven new compounds, containing tetrahydrophenanthroimidazole and tetrahydrophenanthrooxazole rings, are synthesized and the possible reaction mechanism is proposed.

Keywords: cryptotanshinone, tanshinone IIA, diamine, putrescine, cadaverine

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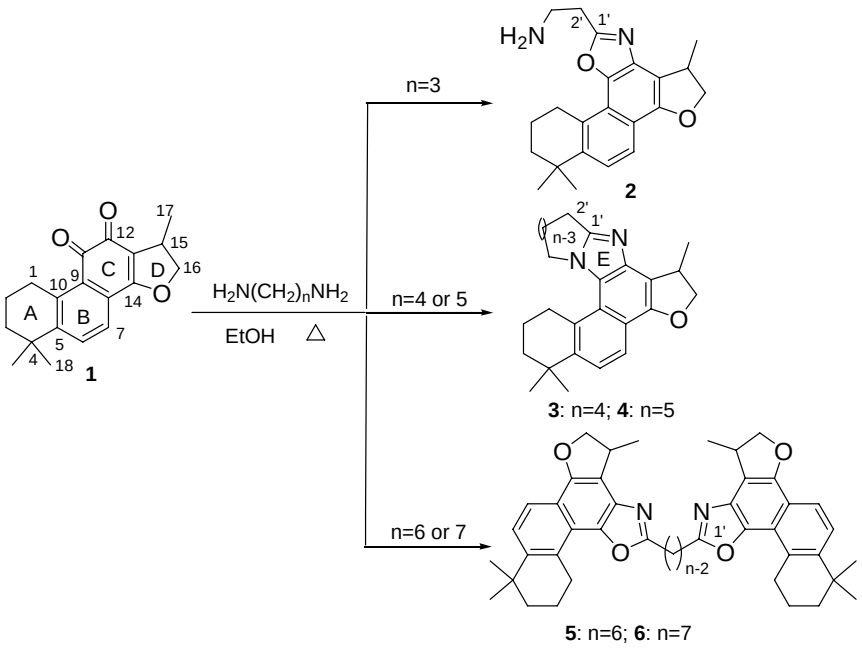
Tanshinones are naturally occurring diterpenoids isolated from *Salvia miltiorrhiza* Bunge[1-2]. These compounds have shown comprehensive pharmacological activities[3-7]. In our previous work we have investigated the possible relationship between pharmacological activities of tanshinones and their chemical properties with biogenic monoamines[8]. To investigate the chemical properties of tanshinones with biogenic diamines such as putrescine and cadaverine, which are involved in the process of cell multiplication and regulation[9-10], the reaction of tanshinones, including cryptotanshinone **1** and tanshinone IIA **7** with 1,3-diamino propane, putrescine, cadaverine, 1,6-diamino hexane and 1,7-diamino heptane are studied.

Results and Discussion

Cryptotanshinone has reacted with diamines under 50 °C in ethanol as shown in **Scheme I**.

The reaction of **1** with putrescine or cadaverine gave major products as light yellow needle crystals **3** or **4**, respectively. FAB-MS and elemental analysis of product **4** suggested a formula of $C_{24}H_{28}N_2O$. ^{13}C NMR (**Table I**) and IR data indicated that **4** had no *o*-quinone carbon, and also there was no absorption signal of quinone functional group in the UV absorption, indicating that the *o*-quinone moiety was changed during reaction. The ^1H NMR data showed that the product contained three methyl groups, eight methylene groups and three methenyl groups. An additional aromatic quaternary carbon signal (δ 152.0) appeared at lower field that could be assigned to C-1'. Two protons with an ABX type splitting at δ 4.38 and 4.87 could be assigned to CH_2-16, which was made diastereotopic by the chirality of CH-15. Signals of aromatic protons (CH-6 and CH-7) of **4** appeared at δ 7.46 and 7.91 as a sharp AB-quartet. The ^1H-^1H COSY spectrum showed that **4** contained a $-CH_2CH_2CH_2CH_2-$ moiety which was not found in compound **1**, indicating that the fragment was derived from cadaverine. In NOE spectrum, irradiating the protons of CH_3-17 (δ 1.53) resulted in the enhancement of CH-15 and CH_2-16, and irradiating one proton of CH_2-1 (δ 3.20) resulted in the enhancement of CH-5' (δ 4.41), indicating that CH_2-1 and CH_2-5' were spatially neighboring protons. The CH_2-1 protons were anisochronic and their ^1H NMR signals appeared at δ 3.18-3.23 and 3.27-3.32 as multiple peaks. The signals differ from those of compound **1**, which were triplet peaks (δ 3.22, J = 7 Hz)[8]. Similarly, the two proton signals of CH_2-5' appeared at δ 4.30-4.34 and 4.39-4.44 as multiple peaks, respectively. According to all of the spectral data, product **4** could be assigned as 2,7,7-trimethyl-2,3,7,8,9,10,11,12,13,14-decahydro[furo[2,3-*d*]phenanthro][1,2-*d*]pyrido[1,2-*a*] imidazole.

Similarly, the product **3** could be assigned as 2,7,7-trimethyl-2,3,7,8,9,10,11,12,13-enneahydro [furo[2,3-*d*]phenanthro][1,2-*d*]pyrrolo[1,2-*a*]imidazole according to its spectral data. The difference of the structures of compounds **3** and **4** was appeared in the F ring. The pyrrolidine moiety of **3** was formed from the



Scheme I

reaction of **1** with putrescine, and the piperidine moiety of **4** was from the reaction with cadaverine. Simulating model showed that the spatial distance between the CH_2-1 and CH_2-4' of **3** was longer than that between the CH_2-1 and CH_2-5' of **4**, which in turn resulted in less sterically hindrance comparing to **4**. Consequently, the ^{1}H NMR signals of CH_2-1 of product **3** appeared at δ 3.31 as multiple peaks, and those of CH_2-4' appeared at δ 4.66.

The reaction of **1** with 1,3-diamino propane, 1,6-diamino hexane or 1,7-diamino heptane gave a tetrahydrophenanthro oxazole derivative product, respectively. The reaction type was similar to the reaction with biogenic monoamines[8].

Like cryptotanshinone, the reaction of tanshinone IIA with diamines gave a similar major product, respectively, as shown in **Scheme II**. But the reaction needed under higher temperature, refluxing for 36 hr. Two major products, **9** and **10** (NMR data in **Table II**), were obtained from the reaction of **7** with putrescine at the same time. Compounds **11** and **12** were the major products of the reaction with cadaverine.

It was noticeable that most reaction of tanshinones with diamines gave tetrahydrophenanthrooxazole product. Their possible formation pathway was discussed already in the previous paper[8]. However, there was a tetrahydrophenanthroimidazole product obtained from the reaction of tanshinones with putrescine or cadaverine, respectively. The possible reaction mechanism was proposed in **Scheme III**.

A nucleophilic reaction took place between tanshinone and amino groups. Firstly, one of the amino groups in diamine attacked one *o*-quinone carbonyl group, and a quinone-imine intermediate was formed while one equivalent H_2O was eliminated. After that, the remained amino group of the diamine attacked another carbonyl group of the tanshinone. The rearrangement of intermediate **14** to the aromatic Schiff base might be spontaneous because of the stability of the latter[11]. Intramolecular additional reactions took place in the Schiff base intermediate, and resulted in intermediate **15**, which, in the presence of an oxidant such as tanshinone or air[8], underwent aromatization to give the imidazole product[12].

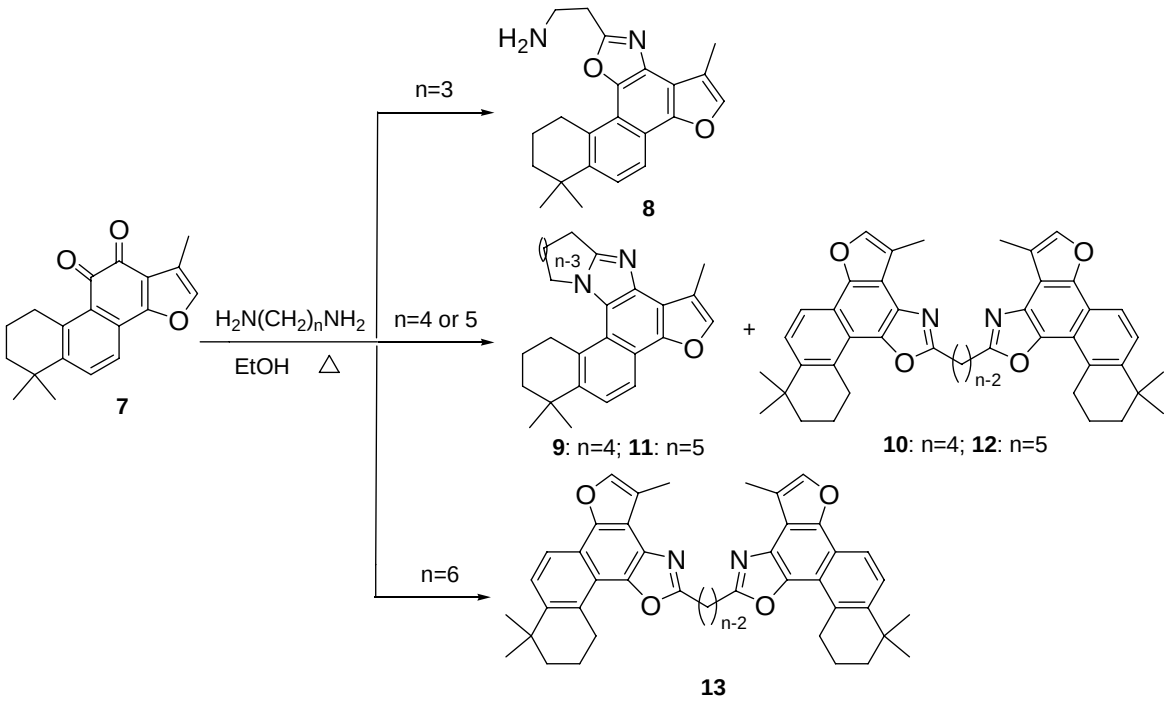
In the reaction of tanshinones with 1,3-diamino propane, only one of the amino groups reacted with quinone group of tanshinones, while all of two amino groups would react in the reaction of tanshinones with other diamines such as putrescine, cadaverine, 1,6-diamino hexane and 1,7-diamino heptane. It was possible because of the spatial effects that hindered the second amino group to react after the first amino group reacted with tanshinone.

Compared with that of cryptotanshinone, the conjugation structure of tanshinone IIA was more stable, so that tanshinone IIA was more difficult to

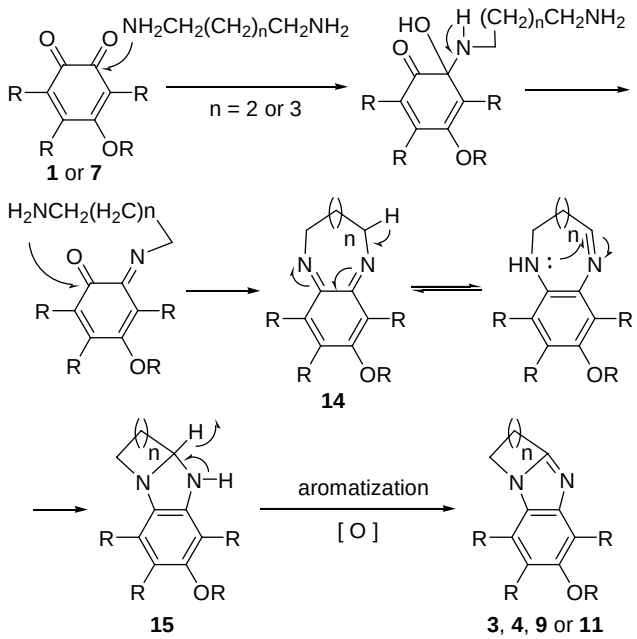
Table I — NMR data of compounds **2-6** ($CDCl_3$, 500 Hz)

C	**2**		**3** in $(CD_3)_2CO$			**4**			**5**			**6**	
No [a]	δ_H [b]	δ_C	HMQC δ_H	HMBC[c] δ_C	δ_C	HMQC δ_H	HMBC δ_C	δ_C	HMQC δ_H	HMBC δ_C	δ_C	δ_H	δ_C
1	3.42 (t, *J* =6.5Hz, 2H)	29.3t	3.32-3.37 (m, 2H)	40.0; 142.9	34.1t	3.18-3.23 (m, 1H); 3.29-3.32 (m, 1H)	40.1; 142.9	34.3t	3.35 (t, *J* =6Hz, 4H)	38.5; 119.6; 143.7	29.2t	3.43 (t, *J* =6.5Hz, 4H)	29.7t
2	1.92-1.97 (m, 2H)	19.5t	1.83-1.90 (m, 2H)	35.5; 129.8	21.0t	1.70-1.75 (m, 2H)		21.4t	1.85-1.90 (m, 4H)	34.3; 129.3	19.5t	1.63-1.69 (m, 4H)	19.5t
3	1.72-1.76 (m, 2H)	38.6t	1.79-1.82 (m, 2H)	34.1; 142.9	40.0t	1.81-1.84 (m, 2H)	32.7; 34.3	40.1t	1.68-1.70 (m, 4H)	31.6; 143.7	38.5t	1.73-1.75 (m, 4H)	38.6t
4		34.3s			35.5s			35.2s			34.3s		34.3s
5		143.8s			142.9s			142.9s			143.7s		143.7s
6	7.48 (d, *J* =9Hz, 1H)	124.2d	7.45 (d, *J* =8.8Hz, 1H)	35.5; 117.6; 129.8	123.5d	7.46(d, *J* =8.8Hz, 1H)	35.2; 117.4	123.6d	7.46 (d, *J* =9Hz, 2H)	34.3; 116.9; 129.3	124.2d	7.48 (d, *J* =7.5Hz, 2H)	124.1d
7	7.83 (d, *J* =9Hz, 1H)	119.8d	7.85 (d, *J* =8.8Hz, 1H)	125.0; 142.9; 152.3	121.2d	7.91 (d, *J* =8.8Hz, 1H)	142.9; 151.9	120.4d	7.82 (d, *J* =9Hz, 2H)	119.6; 143.7; 153.1	119.8d	7.84 (d, *J* =7.5Hz, 2H)	119.8d
8		116.9s			117.6s			117.4s			116.9s		116.9s
9		119.6s			125.0s			122.9s			119.6s		119.6s
10		129.3s			129.8s			129.5s			129.3s		129.3s
11		142.9s			121.3s			126.6s			142.9s		142.8s
12		135.4s			145.3s			138.9s			135.5s		135.5s
13		115.2s			116.8s			115.2s			115.3s		115.3s
14		153.1s			152.3s			151.9s			153.1s		153.0s
15	4.00-4.07 (m, 1H)	36.8d	3.98-4.04 (m, 1H)	152.3	38.2d	4.05-4.11 (m, 1H)	138.9; 151.9	36.9d	3.98-4.06 (m, 2H)	135.5; 153.1	36.8d	3.98-4.05 (m, 2H)	36.8d
16	4.90 (t, *J* =9Hz, 1H); 4.37 (dd, *J*=6,9Hz,1H)	79.4t	4.87 (t, *J* =8.8Hz, 1H); 4.30(dd, *J*=6.3,8.8Hz,1H)	19.8; 116.8; 152.3	79.5t	4.87 (t, *J* =8.5Hz, 1H); 4.38(dd, *J*=5.3,8.5Hz,1H)	20.0; 115.2; 151.9	79.3t	4.89 (t, *J* =9Hz, 2H); 4.37(dd, *J* =6,9Hz,2H)	19.8; 115.3; 153.1	79.4t	4.89 (t, *J* =8.5Hz, 2H); 4.37(dd, *J*=6, 8.5Hz, 2H)	79.4t
17	1.53 (d, *J* =7Hz, 3H)	19.8q	1.53(d, *J* =6.5Hz, 3H)	79.5; 116.8	19.8q	1.53 (d, *J* =7Hz, 3H)	79.3; 115.2	20.0q	1.51(d, *J* =7Hz, 6H)	115.3	19.8q	1.52(d, *J* =7.5Hz,6H)	19.8q
18	1.37 (s, 6H)	31.5q; 31.6q	1.36 (s, 3H); 1.38 (s, 3H)	40.0; 142.9	32.6q	1.37 (s, 3H); 1.42 (s, 3H)	142.9	32.7q	1.33 (s, 6H); 1.34 (s, 6H)	143.7	31.5q; 31.6q	1.37 (s, 6H); 1.39 (m, 6H)	31.6q; 31.7q
1'		164.4s			161.6s			152.0s			165.7s		166.1s
2'	3.16 (t, *J* =6.5Hz, 2H)	32.7t	2.99-3.05 (m, 2H)	161.6	24.0t	3.28 (t, *J* =7Hz, 2H)	24.7; 152.0	25.6t	3.13 (t, *J* =7Hz, 4H)	26.6; 165.7	28.6t	3.07 (t, *J* =8 Hz, 4H)	29.3t
3'	3.31 (t, *J* =6.5Hz, 2H)	39.6t	2.60-2.70 (m, 2H)	24.0	27.3t	2.07-2.13 (m, 2H)	51.3; 152.0	20.0t	2.11-2.14 (m, 4H)	165.7	26.6t	1.96 (m, 4H)	28.2t
4'			4.61-4.71 (m, 2H)	24.0; 161.6	52.6t	1.91-1.96 (m, 2H)		24.7t				2.04(p, *J* =7.5Hz, 2H)	26.8t
5'						4.30-4.34 (m, 1H); 4.41-4.44 (m, 1H)	20.0	51.3t					

[a]: Compounds are numbered for convenience. [b]: Chemical shift is in ppm from TMS. [c]: H to C.



Scheme II



Scheme III

react with diamines. The product from the reaction of **7** was more stable than corresponding product that from **1**. Product **4** could be dehydrogenated to slowly transform into 15,16-dedihydro derivative, product **11**, after exposed to air for a long time.

In conclusion, the reaction of tanshinones with diamines revealed a possible mechanism of the effect of tanshinones on the cell multiplication and regulation. The reaction offers a potential strategy for the preparation of imidazole derivatives. Optimization of the reaction conditions to get higher yields is currently underway.

Experimental Section

Melting points were uncorrected and were determined using a XT-4 apparatus. ^{1}H NMR, ^{13}C NMR, DEPT, 2D NMR and NOE spectra were measured on a Varian UNITY INOVA 500 MHz spectrometer using TMS as an internal standard. FAB-MS was measured on a VG ZAB-HS analytical spectrometer. Elementary analysis was recorded on an Elementar Vario EL elementary analysis device. IR absorption was recorded on a Bruker EQUINOX-55 spectrophotometer. UV-Vis absorption was recorded on a Shimadzu UV-2501 PC spectrophotometer.

Cryptotanshinone and tanshinone IIA were isolated from the Chinese medicinal herb, *Salvia miltiorrhiza* Bunge[8]. 1,3-Diamino propane, 1,6-diamino hexane and 1,7-diamino heptane were purchased from Acros Organics. Putrescine and cadaverine were purchased from Sigma Chemical Co. All chemicals were analytical reagents and not refined before usage.

Table II—NMR data of compounds **8-13** ($CDCl_3$, 500 Hz)

C	**8** in DMSO-d_6		**9**		**10**		**11**		**12** in DMSO-d_6		**13**	
No [a]	δ_H [b]	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
1	3.47 (t, *J* =6Hz, 2H)	37.9t	3.25 (t, *J* =5.5Hz, 2H)	33.8t	3.17 (t, *J* =6.3Hz, 4H)	29.7t	3.27 (t, *J* =5.8Hz, 2H)	34.1t	3.44 (t, *J* =6.5Hz, 4H)	29.3t	3.40 (t, *J* =6.5Hz, 4H)	29.3t
2	1.94-1.96 (m, 2H)	18.9t	1.74-1.80 (m, 4H)	20.6t	1.60-1.64 (m, 4H)	19.2t	1.67-1.73 (m, 2H)	20.2t	1.91-1.96 (m, 4H)	19.5t	1.67-1.70 (m, 4H)	19.5t
3	1.73-1.75 (m, 2H)	28.7t		39.3t	1.55-1.57 (m, 4H)	38.4t	1.78-1.81 (m, 2H)	40.2t	1.70-1.73 (m, 4H)	38.5t	1.84-1.86 (m, 4H)	38.5t
4		34.0s		35.0s		34.3s		35.1s		34.4s		34.3s
5		143.1s		142.3s		143.1s		142.4s		143.1s		143.1s
6	7.71 (d, *J* =9Hz, 1H)	125.3d	7.49 (d, *J* =8.8Hz, 1H)	124.4d	7.54 (d, *J* =8.5Hz, 2H)	125.1d	7.55 (d, *J* =8.3Hz, 1H)	124.4d	7.55 (d, *J* =8.8Hz, 2H)	125.1d	7.56 (d, *J* =8.5Hz, 2H)	124.9d
7	8.12 (d, *J* =9Hz, 1H)	117.9d	8.16 (d, *J* =8.8Hz, 1H)	119.2d	8.13 (d, *J* =8.5Hz, 2H)	118.3d	8.21 (d, *J* =8.3Hz, 1H)	119.0d	8.04 (d, *J* =8.8Hz, 2H)	118.3d	8.14 (d, *J* =8.5Hz, 2H)	118.3d
8		116.9s		118.0s		117.5s		118.5s		117.8s		117.8s
9		116.8s		120.4s		118.0s		120.7s		117.3s		117.5s
10		129.6s		129.3s		130.1s		130.2s		130.0s		130.0s
11		143.6s		127.3s		144.6s		127.5s		144.1s		144.3s
12		132.1s		124.7s		132.7s		124.0s		132.0s		132.8s
13		115.8s		116.7s		116.4s		116.7s		116.2s		116.4s
14		148.4s		149.3s		149.6s		149.2s		149.4s		149.5s
15		115.6s		116.2s		116.1s		116.2s		115.4s		116.2s
16	7.96 (s, 1H)	142.2d	7.44 (q, *J* =1Hz, 1H)	140.6d	7.56 (q, *J* =1Hz, 2H)	141.1d	7.50 (q, *J* =1.5Hz, 1H)	140.6d	7.40 (q, *J* =1Hz, 2H)	140.9d	7.54 (q, *J* =1.5Hz, 2H)	141.0d
17	2.51 (s, 3H)	8.9q	2.57 (d, *J* =1Hz, 3H)	9.9q	2.58 (d, *J* =1Hz, 6H)	9.4q	2.64 (d, *J* =1.5Hz, 3H)	9.9q	2.35 (d, *J* =1Hz, 6H)	9.1q	2.55 (d, *J* =1.5Hz, 6H)	9.4q
18	1.36 (s, 6H)	31.4q	1.34 (s, 6H)	32.5q	1.31 (s, 12H)	31.7q	1.41 (s, 6H)	32.8q	1.37 (s, 12H)	31.8q	1.36(s, 6H); 1.37(s, 6H)	31.7q
1'		163.2s		159.4s		163.8s		151.4s		164.8s		165.4s
2'	3.33-3.37 (m, 4H)	28.4t	3.17 (t, *J* =7.8Hz, 2H)	23.9t	3.76 (s, 4H)	26.9t	3.35 (t, *J* =7Hz, 2H)	25.4t	3.37 (t, *J* =7 Hz, 4H)	28.2t	3.20 (m, 4H)	28.6t
3'		37.4t	2.59-2.63 (m, 2H)	27.1t			2.08-2.14 (m, 2H)	21.5t	2.71 (p, *J* =7Hz, 2H)	25.0t	2.16-2.18 (m, 4H)	26.7t
4'	3.26 (s, br, 2H, NH_2)		4.58 (t, *J* =7Hz, 2H)	52.4t			1.82-1.85 (m, 2H)	24.7t				
5'							4.38 (t, *J* =5.5Hz, 2H)	51.3t				

[a]: Compounds are numbered for convenience. [b]: Chemical shift is in ppm from TMS.

General procedure 1. To the solution of cryptotanshinone (50.0 mg, 0.17 mmole) in ethanol (8 mL), the diamine (0.18 mmole) was added. The mixture was stirred for 24 hr under 50 °C. The solution was concentrated in vacuum. The residue was separated by silica gel chromatography to obtain the main product and unreacted cryptotanshinone.

General procedure 2. To the solution of tanshinone IIA (50.0 mg, 0.17 mmole) in ethanol (8 mL), the diamine (0.18 mmole) was added. The mixture was refluxed for 36 hr. After that, the solvent was removed in vacuum. The residue was separated by silica gel chromatography to obtain the main product and unreacted tanshinone IIA.

2-(4,9,9-Trimethyl-4,5,9,10,11,12-hexahydro-1,6-dioxa-3-aza-dicyclopenta[*a, c*]phenanthren-2-yl) ethylamine 2. This product was synthesized according to general procedure 1, from the reaction of compound **1** with 1,3-diamino propane, white solid **2** (23.3 mg, 39.2%) was obtained; m.p. 97-99.5ºC; UV-Vis (EtOH): 348.0, 333.0, 318.0, 254.0, 230.0 nm; IR (KBr): 3064, 2957, 2928, 1562, 1456, 1402 cm^{-1}; FAB-MS *m/z* (%):351 $[M+1]^+$ (100).

Imidazole derivative 3. This product was synthesized according to general procedure 1, from the reaction of compound **1** with putrescine, light yellow needle crystals **3** (8.8 mg, 15.0%) were obtained; m.p. 227-30ºC; UV-Vis (EtOH): 348.0, 333.0, 258.0, 233.0 nm; IR (KBr): 3060, 2957, 2928, 2868, 1543, 1513, 1455, 1397, 1295 cm^{-1}; FAB-MS *m/z* (%): 347 $[M+1]^+$ (95), 346 $[M]^+$ (100); Anal Calcd for $C_{23}H_{26}N_2O$: C, 79.73; H, 7.56; N, 8.09; O, 4.62. Found: C, 79.69; H, 7.60; N, 8.02.

Imidazole derivative 4. This product was synthesized according to general procedure 1, from the reaction of compound **1** with cadaverine, light yellow needle crystals **4** (7.3 mg, 11.9%) were obtained; m.p. 103-104.5ºC; UV-Vis (EtOH): 352.0, 263.0, 236.0, 203.0 nm; IR (KBr): 3067, 2927, 2859, 1461, 1402, 1118, 824 cm^{-1}; FAB-MS *m/z* (%): 361 $[M+1]^+$ (100); Anal. Calcd for $C_{24}H_{28}N_2O$: C, 79.96; H, 7.83; N, 7.77; O, 4.44. Found: C, 79.91; H, 7.85; N, 7.70.

1,4-Di(4,9,9-Trimethyl-4,5,9,10,11,12-hexahydro-1,6-dioxa-3-aza-dicyclopenta[*a,c*]phenanthren-2-yl) butane 5. This product was synthesized according to general procedure 1, from the reaction of compound **1** with 1,6-diamino hexane, light yellow solid **5** (10.8 mg, 19.0%) was obtained; m.p. 161.5-63.5ºC; UV-Vis (EtOH): 348.0, 332.0, 253.0, 230.0 nm; IR (KBr): 3061, 1562, 1523, 1457, 1403, 1124 cm^{-1}; FAB-MS *m/z* (%): 668 $[M]^+$ (25), 57 (100); Anal. Calcd for $C_{44}H_{48}N_2O_4$: C, 79.01; H, 7.23; N, 4.19; O, 9.57. Found: C, 78.93; H, 7.27; N, 4.13.

1,3-Di(4,9,9-Trimethyl-9,10,11,12-tetrahydro-1,6-dioxa-3-aza-dicyclopenta[*a,c*]phenanthren-2-yl)propane 6. This product was synthesized according to general procedure 1, from the reaction of compound **1** with 1,7-diamino heptane, white solid **6** (9.9 mg, 17.1%) was obtained; m.p. 101-04ºC; UV-Vis (EtOH): 348.0, 332.0, 317.0, 253.0, 230.0 nm; IR (KBr): 3065, 2927, 2866, 1562, 1457, 1402, 1124 cm^{-1}; FAB-MS *m/z* (%): 683 $[M+1]^+$ (10), 69 (100); Anal. Calcd for $C_{45}H_{50}N_2O_4$: C, 79.15; H, 7.38; N, 4.10; O, 9.37. Found: C, 79.18; H, 7.44; N, 4.03.

2-(4,9,9-Trimethyl-9,10,11,12-tetrahydro-1,6-dioxa-3-aza-dicyclopenta[*a, c*]phenanthren-2-yl)ethyl amine 8. This product was synthesized according to general procedure 2, from the reaction of compound **7** with 1,3-diamino propane, light yellow solid **8** (28.4 mg, 48.0%) was obtained; m.p. 197.5-201ºC; UV-Vis (EtOH): 343.0, 326.0, 263.0, 256.0, 203.0 nm; IR (KBr): 3395 (br), 2926, 1564, 1457, 1425, 1381 cm^{-1}; FAB-MS *m/z* (%): 349 $[M+1]^+$ (40), 51 (100); Anal. Calcd for $C_{22}H_{24}N_2O_2$: C, 75.83; H, 6.94; N, 8.04; O, 9.18. Found: C, 75.71; H, 7.01; N, 7.96.

According to general procedure 2, two products, colourless needle crystals **9** and white solid **10**, were obtained from the reaction of **7** with putrescine.

2,7,7-Trimethyl-7,8,9,10,11,12,13-heptahydro[furo[2,3-*d*]phenanthro][1,2-*d*]pyrrolo[1,2-*a*] imidazole 9. Yield 14.2% (8.3 mg), m.p. 282-84ºC; UV-Vis (EtOH): 266.0, 203.0 nm; IR (KBr): 2925, 2854, 1543, 1513, 1458, 1375 cm^{-1}; FAB-MS *m/z* (%): 345 $[M+1]^+$ (100); Anal. Calcd for $C_{23}H_{24}N_2O$: C, 80.20; H, 7.02; N, 8.13; O, 4.64. Found: C, 80.15; H, 7.09; N, 8.07.

1,2-Di(4,9,9-trimethyl-9,10,11,12-tetrahydro-1,6-dioxa-3-aza-dicyclopenta[*a,c*]phenanthren-2-yl) ethane 10. Yield 12.9% (7.0 mg); UV-Vis (EtOH): 256.0, 203.0 nm; IR (KBr): 2924, 2854, 1563, 1459, 1379 cm^{-1}; FAB-MS *m/z* (%): 637 $[M+1]^+$ (10), 57 (100).

According to general procedure 2, two products, white solids **11** and **12**, were obtained from the reaction of **7** with cadaverine.

2,7,7-Trimethyl-7,8,9,10,11,12,13,14-octahydro [furo[2,3-*d*]phenanthro][1,2-*d*]pyrido[1,2-*a*] imidazole 11. 11.8 mg, yield 19.4%; m.p. 126-28ºC; UV-Vis (EtOH): 348.0, 332.0, 269.0, 205.0 nm; IR (KBr): 3061, 2929, 2860, 1607, 1499, 1457, 1329 cm^{-1}; FAB-MS *m/z* (%): 359 $[M+1]^+$ (20), 154 (100); Anal. Calcd for $C_{24}H_{26}N_2O$: C, 80.41; H, 7.31; N, 7.81; O, 4.46. Found: C, 80.43; H, 7.35; N, 7.76.

1,3-Di(4,9,9-trimethyl-9,10,11,12-tetrahydro-1,6-dioxa-3-aza-dicyclopenta[*a,c*]phenanthren-2-yl) propane 12. Yield 11.6% (6.4 mg); m.p. 233-34.5ºC; UV-Vis (EtOH): 345, 328, 263, 256, 203 nm; IR (KBr): 3062, 2945, 1562, 1453, 1426, 1382 cm^{-1}; FAB-MS *m/z* (%): 651 $[M+1]^+$ (20), 154 (100); Anal. Calcd for $C_{43}H_{42}N_2O_4$: C, 79.36; H, 6.50; N, 4.30; O, 9.84. Found: C, 79.33; H, 6.54; N, 4.26.

1,4-Di(4,9,9-trimethyl-9,10,11,12-tetrahydro-1,6-dioxa-3-aza-dicyclopenta[*a*, *c*]phenanthren-2-yl) butane 13. This product was synthesized according to general procedure 2, from the reaction of compound **2** with 1,6-diamino hexane, white solid **13** (9.2 mg, 16.3%) was obtained; m.p. 234-36ºC; UV-Vis (EtOH): 264.0, 256.0, 203.0 nm; FAB-MS *m/z* (%): 665 $[M+1]^+$ (10), 154 (100); Anal. Calcd for $C_{44}H_{44}N_2O_4$: C, 79.49; H, 6.67; N, 4.21; O, 9.63. Found: C, 79.42; H, 6.71; N, 4.16.

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