A CONVENIENT, ONE-POT SYNTHESIS OF TROPOCORONANDS AND TROPOPODANDS BY USE OF THE HETEROCYCLE-EXCHANGE REACTION OF BENZO[*b*]CYCLOHEPTA[*e*][1,4]OXAZINE[1]

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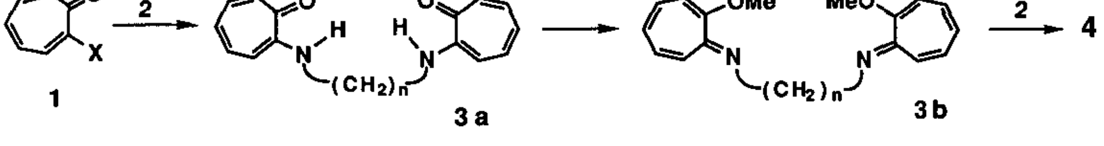
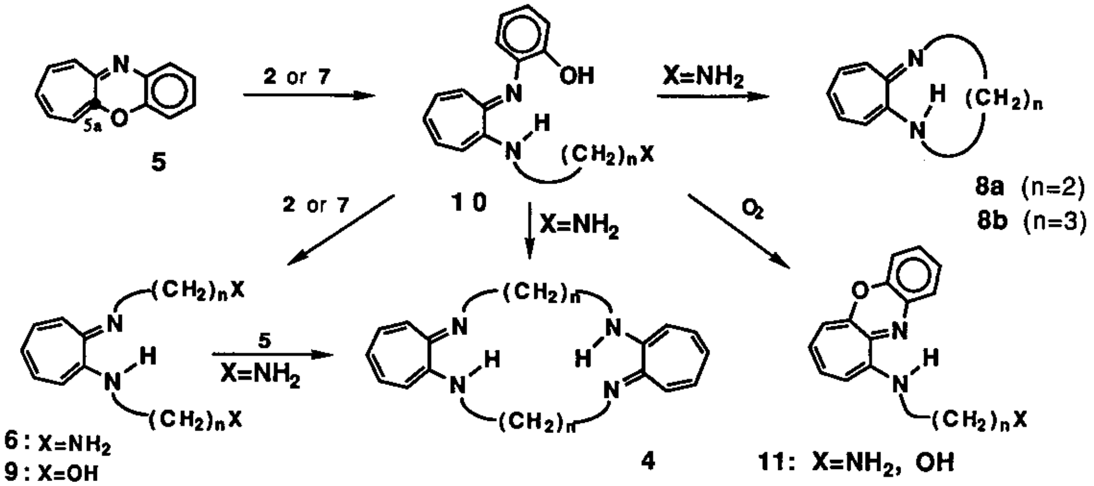
Abstract - Treatment of benzo[*b*]cyclohepta[*e*][1,4]oxazine (**5**) with 1.2 equiv. of α,ω-diaminoalkanes (**2**, n=4-12) in ethanol at 80 °C gave tropocoronands (**4**, n=4-12) in one step in high yields, while the reaction of **5** with an excess of **2** afforded tropopodands (**6**, n=4-6). The reactions of **5** with **2** (n=2,3) yielded bicyclic pyrazino or diazepino compounds in high yields. Coronands [**14** (instead of **4a**) and **4b** (n=3)] were, however, obtained by the reaction of **5** with *N*-acetyldiaminoalkanes. The reaction of **5** with α,ω-amino alcohol afforded the corresponding podands.

One of authors (T.N.) and his co-workers reported the synthesis of tropocoronands (**4**, n=2-6) and some related compounds having hetero atoms in the linker chain by the sequence of a reactive troponoid (**1**, X=OMe, OTs), bistropone (**3a**) and the methyl ether (**3b**).[2] The overall yields of **4** (from **1**) were in 12-23% (n=3-6) and <1% (n=2). We later found that the oxazine ring of benzo[*b*]cyclohepta[*e*][1,4]oxazine (**5**) was easily exchanged by *o*-aminophenol or other related compounds having 1,2-difunctional nucleophiles.[3,4] We wish to report here a very convenient, one-pot synthesis of **4** by the reaction of **5** with **2** through an intermolecular heterocycle exchange reaction.





Scheme 1

Treatment of a solution of **5** with **2** (n=4-12) (1: 1.2 ratio) in absolute ethanol at 80 °C for 20-30 h under an inert atmosphere yielded orange crystals, which showed similar uv absorption maxima to the previously known compounds (**4**; n=2-6) at *ca.* 270, 350, 360, and 400-500 nm and were identified as tropocoronands (**4**; n=4-12) on the basis of nmr and mass spectra (Scheme 1). Properties and yields of **4** obtained by this one-pot method are shown in Table 1.

Table 1. Synthesis of Tropocoronands (**4**) by the Reaction of **5** with **2**

Reagents	Products	Yield / %[b]	mp / °C	Color - Shape
2a (n=2)	**4a**[a]	0		
2b (n=3)	**4b**[a]	3	214-229	Orange crystals
2c (n=4)	**4c**[a]	70	197-202	Orange crystals
2d (n=5)	**4d**[a]	67	199-207	Orange crystals
2e (n=6)	**4e**[a]	76	199-200	Orange crystals
2f (n=7)	**4f**[6]	86	32-38	Orange crystals
2g (n=8)	**4g**	81	75-77	Orange crystals
2h (n=9)	**4h**[7]	72	162-164	Orange crystals
2i (n=10)	**4i**	85	65-67	Orange crystals
2j (n=11)	**4j**	79	40-45	Orange crystals
2k (n=12)	**4k**	84	71-73	Orange crystals

a. Known compound, see ref. 2. b. Yield of the crystals that precipitated.

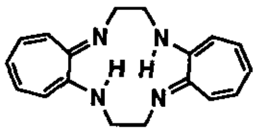
A similar reaction of **5** with **2a,b** (n=2-3) as above afforded 2,3-dihydro-1*H*-cyclohepta[*b*]pyrazine (**8a**)[5] and 1,2,3,4-tetrahydrocyclohepta[*b*]diazepine (**8b**)[8] and gave no tropocoronand (**4a**) under these reaction conditions. The reaction of **5** with an excess of **2** (n=4-6) or α,ω-amino alcohols (**7**, $NH_2(CH_2)_nOH$, n=2-6) gave podands (**6**; n=4-6) and (**9**; n=2-6) (Table 2). In contrast, the reaction of **5** with **2c** (n=4) (1:1.2 ratio) at 20 °C gave a readily crystallized intermediate compound (**10c**[11]; X=NH_2, n=4) in 84% yield, which was

Table 2. Synthesis of Tropopodands (**6**) and (**8**) by the Reactions of **5** with **2** or **7**

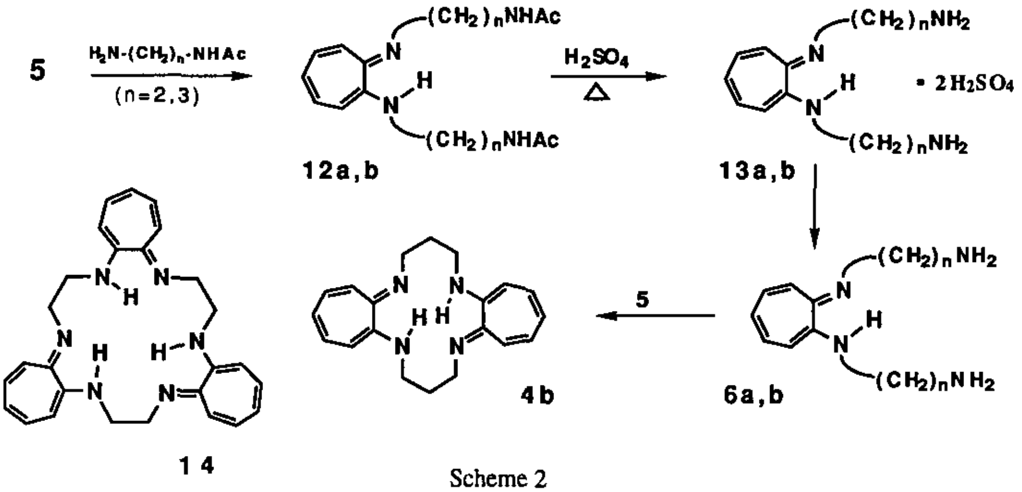
Reagents	Products	Yield / %	mp / °C	Color - Shape
2a (n=2)	**6a**	trace	110-112	Orange crystals
2b (n=3)	**6b**	trace	···	Orange oil
2c (n=4)	**6c**[2]	62	>300	Orange crystals
2d (n=5)	**6d**[9]	68	···	Orange oil
2e (n=6)	**6e**	81	72-75	Orange crystals
7a (n=2)	**9a**	58	77-79	Orange crystals
7b (n=3)	**9b**[10]	72	59-65	Orange crystals
7c (n=4)	**9c**	68	···	Orange oil
7d (n=5)	**9d**	90	64-69	Orange crystals
7e (n=6)	**9e**	79	40-43	Orange crystals

at 20 °C gave a readily crystallized intermediate compound (**10c**[11]; X=NH_2, n=4) in 84% yield, which was converted on heating into **4c** in high yield. Compound (**10c**) gave oxidation product (**11c**[12]; X=NH_2, n=4) under atmosphere condition.

Compounds (**6a,b**[13]; n=2,3) were prepared from **5** and *N*-monoacetyl derivatives of **2a,b** via **12a,b** and **13a,b** as shown in Scheme 2. Compound (**4b**) having three methylene chains was then obtained by the reaction of **6b** with another molecule of **5** in 16% yield, while coronand (**14**)[14] having three seven-menberd rings was obtained insteated of **4a** by the reaction of **6a** with **5**.



4a



Scheme 2

We thank Prof. Hiroshi Yamamoto (Okayama Univ.) for his helpful discussion .

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6 **4f:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 1.43 (12H, m, CH_2), 1.72 (8H, m, CH_2), 3.27 (8H, t, J=7 Hz, CH_2), 6.11 (2H, t, J=10 Hz, H-5), 6.25 (4H, d, J=10 Hz, H-3,7), 6.72 (4H, t, J=10 Hz, H-4,6); ^{13}C nmr (67.8 MHz, $CDCl_3$) δ 27.55 (t, CH_2), 29.31 (t, CH_2), 29.99 (t, CH_2), 46.30 (t, CH_2), 109.99 (d, C-3,7), 117.45 (d, C-5), 132.86 (d, C-4,6), 152.88 (s, C-1,2); M^+ m/z 432.

7 **4h:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 1.34 (12H, m, CH_2), 1.43 (8H, m, CH_2), 1.72 (8H, m, J=7 Hz, CH_2), 3.29 (8H, m, J=7 Hz, CH_2), 6.10 (2H, t, J=10 Hz, H-5), 6.25 (4H, d, J=10 Hz, H-3,7), 6.72 (4H, t, J=10 Hz, H-4,6); ^{13}C nmr (67.8 MHz, $CDCl_3$) δ 27.59 (t, CH_2), 29.48 (t, CH_2), 29.66 (t, CH_2), 30.05 (t, CH_2), 46.32 (t, CH_2), 109.97 (d, C-3,7), 117.42 (d, C-5), 132.84 (d, C-4,6), 152.90 (s, C-1,2); M^+ m/z 488.

8 **8b:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 1.83 (2H, m, J=6 Hz),3.64 (4H, t, J=6 Hz, CH_2), 4.48 (1H, br, NH), 7.35 (3H, m, H-3,5,7), 7.64 (2H, m, H-4,6); M^+ m/z 160.

9 **6d:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 1.50 (6H, m, CH_2), 1.76 (4H, m, CH_2), 2.40 (4H, br, NH_2), 2.72 (4H, t, J=6.5 Hz, CH_2), 3.31 (4H, t, J=6.5 Hz, CH_2), 6.13 (1H, t, J=9 Hz, H-5), 6.27 (2H, d, J=11 Hz, H-3,7), 6.74 (2H, dd, J=11, 9 Hz, H-4,6); ^{13}C nmr (67.8 MHz, $CDCl_3$) δ 24.85 (t, CH_2), 29.87 (t, CH_2), 33.64 (t, CH_2), 42.18 (t, CH_2), 46.19 (t, CH_2), 110.05 (d, C-3,7), 117.56 (d, C-5), 132.90 (d, C-4,6), 152.93 (s, C-1,2); M^+ m/z 290.

10 **9b:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 1.97 (4H, m, J=6 Hz, CH_2), 3.44 (4H, t, J=6 Hz, CH_2), 3.80 (4H, t, J=6 Hz, CH_2), 4.98 (3H, br, NH, 2OH), 6.22 (1H, t, J=10 Hz, H-5), 6.32 (2H, d, J=10 Hz, H-3,7), 6.82 (2H, t, J=10 Hz, H-4,6); ^{13}C nmr (67.8 MHz, $CDCl_3$) δ 31.8 (t, CH_2), 44.5 (t, CH_2), 61.8 (t, CH_2), 110.9 (d, C-3,7), 118.5 (d, C-5), 133.8 (d, C-4,6), 153.5 (s, C-1,2); M^+ m/z 236.

11 **10c:** ^{1}H Nmr (270 MHz, DMSO-d_6) δ 1.82 (4H, br, CH_2), 3.34 (4H, br, CH_2), 3.44 (2H, br, NH_2), 6.22 (1H, t, J=9 Hz, H-5), 6.30 (1H, t, J=10 Hz, H-3), 6.43 (1H, d, J=12 Hz, H-7), 6.70 (1H, ddd, J=12, 9, 2 Hz, H-6), 6.76 (2H, m, H-3',5'), 6.85 (2H, m, H-4',6'), 6.89 (1H, ddd, J=10, 9, 2 Hz, H-4), 8.15 (1H, br, NH); M^+ m/z 283.

12 **11c:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 2.03 (2H, m, CH_2), 2.28 (2H, m, CH_2), 2.89 (2H, m, NCH_2), 3.20 (2H, m, NCH_2), 4.30 (2H, br, NH_2), 5.81 (1H, d, J=10 Hz, H-6), 5.88 (1H, t, J=10 Hz, H-8), 5.94 (1H, dd, J=10, 2 Hz, H-9), 6.22 (1H, td, J=10, 2 Hz, H-7), 6.36 (1H, m, H-4), 6.69 (2H, m, H-2,3), 6.79 (2H, m, H-1), 6.95 (1H, br, NH); M^+ m/z 281.

13 **6a:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 1.75 (4H, br, NH_2), 3.06 (4H, t, J=6 Hz, CH_2), 3.38 (4H, t, J=6 Hz, CH_2), 6.18 (1H, t, J=9.5 Hz, H-5), 6.33 (2H, d, J=11 Hz, H-3,7), 6.77 (2H, dd, J=11, 9.5 Hz, H-4,6); ^{13}C nmr (67.8 MHz, $CDCl_3$) δ 42.13 (t, CH_2), 49.30 (t, CH_2), 110.57 (d, C-3,7), 118.21 (d, C-5), 133.13 (d, C-4,6), 153.48 (s, C-1,2); M^+ m/z 206.

14 **14:** ^{1}H Nmr (270 MHz, $CDCl_3$) δ 3.63 (12H, s, CH_2), 6.14 (3H, t, J=9.0 Hz, H-5), 6.36 (6H, t, J=11 Hz, H-3,7), 6.78 (6H, dd, J=11, 9.0 Hz, H-4,6); M^+ m/z 438.

Received, 20th January, 1992