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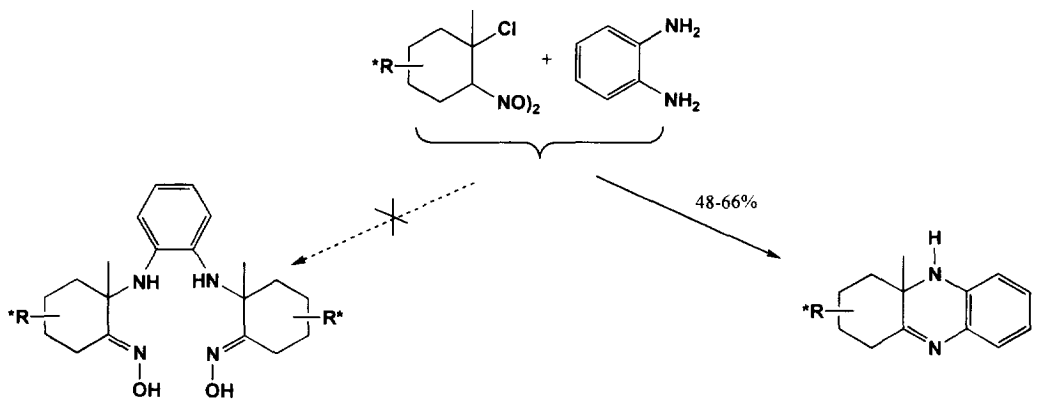
Synthesis of Chiral Hexahydrophenazines by Treatment of Dimeric Nitrosochlorides with 1,2-Diaminoarenes.

Pavel A. Petukhov and Alexey V. Tkachev*

Novosibirsk Institute of Organic Chemistry, Novosibirsk 630090, Russia

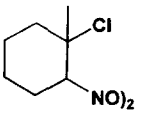
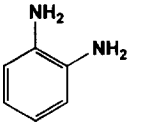
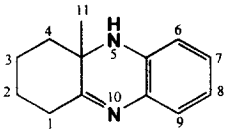
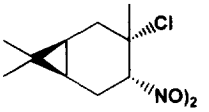
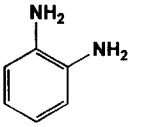
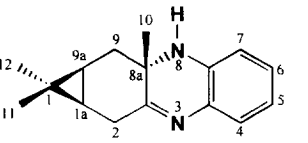
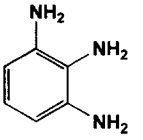
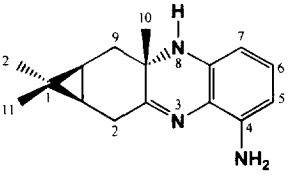
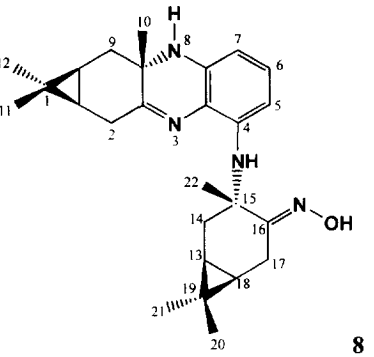
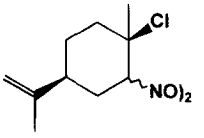
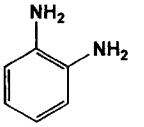
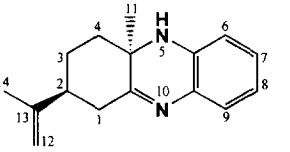
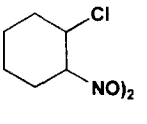
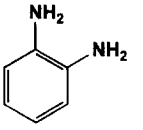
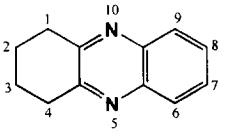
Abstract: Treatment of dimeric nitrosochlorides derived from unsaturated hydrocarbons 1-methylcyclohexene, (+)-3-carene and limonene with 1,2-phenylenediamine results in the formation of hexahydrophenazine derivatives in good yields (48-66%). Treatment of cyclohexene nitrosochloride under the same reaction conditions leads to tetrahydrophenazine. Stereochemistry of the phenazine derivatives and possible reaction pathway are discussed. © 1997 Elsevier Science Ltd.

In trying to synthesize precursors for macrocyclic polyfunctional compounds by reaction of dimeric nitrosochlorides with 1,2-diamines, we have found that in case of certain aromatic 1,2-diamines the reaction results in stereoselective heterocyclisation and formation of partially hydrogenated phenazine derivatives.



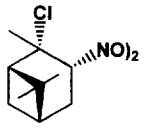
Phenazine type derivatives are of interest from the viewpoint of their biological activity as well as starting compounds for the synthesis of chiral auxiliaries. Syntheses of these compounds from easily available phenazines are questionable because reduction of phenazines and tetrahydrophenazines usually leads to over hydrogenated products.[1] Direct synthetic methods to hydrophenazines are also unknown. We have found that the phenazine derivatives are formed in good yield in the reaction of dimeric nitrosochlorides derived from 1-methylcyclohexene (**1**), (+)-3-carene (**2**) and (+)-limonene (**3**) with 1,2-phenylenediamine and 1,2,3-triaminobenzene. Chemical structures of the compounds synthesized as well as their yields and starting molecules are listed in the Table 1. Hexahydrophenazine derivatives **5-9** are colored solids with different tints of red, that are quite stable in crystalline state but unstable in solutions, especially in the open air. They have characteristic mass spectra with very intensive peaks of the molecular ions. ^{14}N NMR specroscopy shows two different nitrogens at δ –69 ppm ($W_{1/2}$=1000 Hz, imine) and –282 ppm ($W_{1/2}$=1800 Hz, amine).

Table 1. Reaction of nitrosochlorides with 1,2-diaminoarenes: structures and yields.

	Starting compounds		Reaction products[a]	Yields
1			 **5**	66%[b] (94%)[c]
2			 **6**	66%[b] (92%)[c]
			 **7**	21%[d]
			 **8**	26%[d]
3	 *cis*- or *trans*-		 **9**	48%[b] (98%)[c]
4			 **10**	66%[b]

[a]The numbering scheme for some of the molecules does not coincide with the numbering of the system according to IUPAC and is given for NMR interpretation only. [b]Yield of the product after crystallisation. [c]Yield of the raw material. [d]Yield after column chromatography.

Nitrosochloride of cyclohexene **4** is transformed to tetrahydrophenazine **10** under the same reaction conditions, probably, due to *in situ* oxidation of the intermediate hexahydrophenazine by atmospheric oxygen. Nitrosochloride of pinane type **11** does not form heterocyclic compounds and is transformed to the unsaturated oxime (pinocarvone oxime, **12**) due to simple dehydrochlorination. Dehydrochlorination also takes place in case of less nucleophilic diamines such as 3,4-diaminofurazan (**13**) and 4,5-diaminobenzofurazan (**14**) which cause transformation of nitrosochloride **2** to unsaturated oxime **15**.



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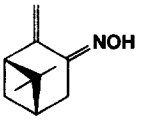

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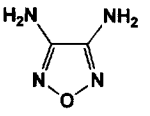

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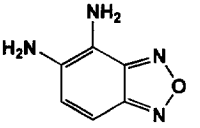
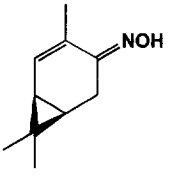


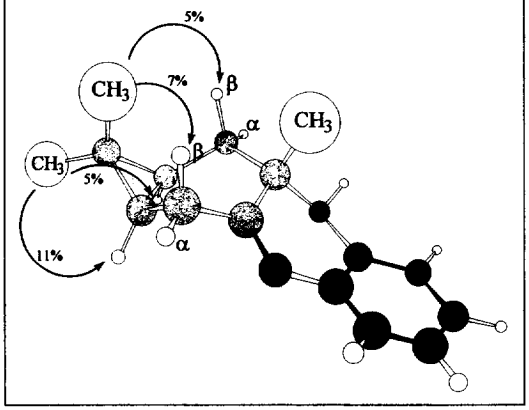
14



15

In the case of (+)-3-carene and limonene derivatives, one could expect the formation of pair of epimers, but only one diastereomer of the hexahydrophenazine was found in both cases. Signal assignments in the NMR spectra of the hydrophenazine derivatives and stereochemistry of the compounds were determined by NMR (^{1}H-^{1}H Nuclear Overhauser Effect, analysis of ^{13}C-^{1}H and ^{1}H-^{1}H couplings) in combination with conformational analysis using molecular mechanics (MM2) and semi-empirical quantum chemical calculations (PM3). NMR parameters of the carane derivative **6** (as well as **7** and **8**) show that the six-membered ring fused to the dihydroquinoxaline moiety is distorted as compared to the simple α-amino oximes[2] and has boat-like conformation that was determined for the transition metal complexes of the α-amino oximes.[3] Conformation of the carane derivative **6** according to the PM3 calculations and selected NOE are shown below. β-Alignment of the C-10 atom (*cis*- to cyclopropane) is obvious from the vicinal carbon-proton coupling: the value $J_{C10\text{-}C8a\text{-}C9\text{-}H9}$ = 3.6 Hz corresponds to synclinal alignment of the methyl and H-9β (ϕ=18°) in **6** (shown on the picture at the left) rather than to anticlinal alignment (ϕ=176°) in the epimer with the methyl *trans*- to cyclopropane.[4]

Space structure of compound **6** according to PM3 calculations and selected NOE in ^{1}H NMR.



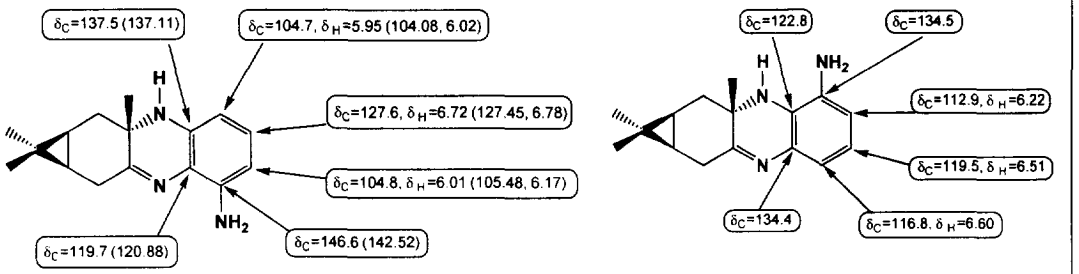
Non-aromatic parts of ^{1}H and ^{13}C NMR spectra of compounds **7** and **8** are practically the same as compared to the molecule **6**, so the derivatives of 1,2,3-triaminobenzene have the same stereochemistry.

In the case of the limonene derivative **9**, equatorial character of the H-2 atom (δ=2.59 ppm, $W_{1/2}$ = 12 Hz) demonstrates the axial alignment of the isopropenyl group. Vicinal carbon-proton couplings of the C-11 atom ($J_{C11\text{-}C4a\text{-}C4\text{-}H4\alpha,\beta}$ = 4.9 and 4.9 Hz) correspond to the equatorial (or pseudoequatorial) methyl group. These are possible only when the C-11 methyl group is *trans*- to the isopropenyl group. Stereochemistry of

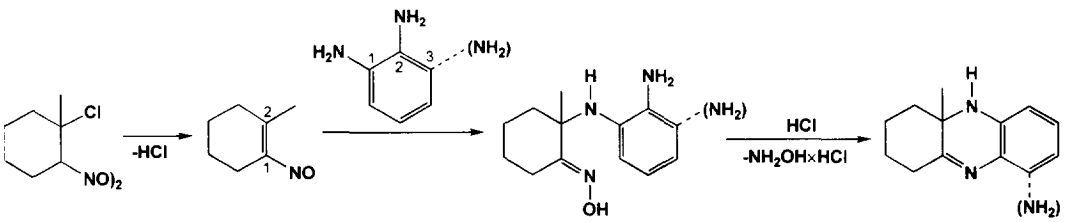
the phenazine derivatives **6-9** concides with that of the corresponding diastereomeric α-amino oximes of the carane- and *p*-menthane-types.

Only one positional isomer is formed in the reaction of nitrosochloride **2** with 1,2,3-triaminobenzene. Position of the free amino group in the aromatic ring of compound **7** was established by comparing calculated and experimental proton and carbon chemical shifts. Compound **8** has the same position of the substituted amino group because aromatic parts of the NMR spectra of this derivative and compound **7** are similar.

Calculated carbon and proton chemical shifts of the aromatic moiety (based on molecule **6** and increments of NH_2-group[5]) and experimental ones (given in parenthesis) for compound **7** and its positional isomer:



Reaction of dimeric nitrosochlorides with simple primary and secondary amines is the well known process and results in the formation of α-amino oximes.[6,7,8,9,10] The reaction seems to proceed *via* the intermediate nitroso olefin[11] followed by addition of the amine molecule from the least-hindered side of the carbon-carbon double bond.[2] In the case of the reaction of the nitrosochlorides with 1,2-diaminoarenes, the formation of the phenazine type compounds may be explained by a three-step process:



The formation of the products **6-9** having just the same stereochemistry as in the case of simple α-amino oximes and transformation of both *cis*- and *trans*-limonene nitrosochlorides to one and the same stereoisomer of compound **9** indicate that kinetically-controlled addition of the amine to the intermediate nitroso olefin takes place in the reaction of nitroso chlorides with 1,2-diaminoarenes. In the case of 1,2,3-triaminobenzene, due to steric reasons there is no addition of the C-2 amino group of the reagent to the C-2 atom of the nitroso olefin because (i) the formation of the other positional isomer does not occur at all and (ii) the model compound - 2,6-dimethylaniline - reacts with the nitrosochlorides under the same reaction conditions to give only α,β-unsaturated oximes. The intramolecular exchange of the nitrogen-containing groups on the last stage of the reaction demands an acidic catalyst, hydrogen chloride from the starting compound being the species promoting the exchange. Exchange of this type is known in the chemistry of

substituted oximes: the intermolecular exchange in the simplest α-amino oximes results in the formation of pyrazine-type derivatives.[12]

EXPERIMENTAL

See ref.[13] for *General Experimental*. ^{1}H, ^{13}C and ^{14}N NMR spectra were recorded at +25°C using a **Bruker AM-400** instrument (^{1}H 400.13 MHz, ^{13}C 100.61 MHz, ^{14}N 28.91 MHz) locked to the deuterium resonance of the solvent using standard Bruker NMR Software System. Carbon and proton chemical shifts were calculated relative to the solvent signal using as the internal standard: $CDCl_3$ (δ_H 7.24 ppm and δ_C 76.90 ppm) and C_6D_6 (δ_H 7.15 ppm and δ_C 128.5 ppm). Nitrogen chemical shifts were measured relative to 9M HNO_3 using as the external standard with δ_N −14.4 ppm (relative to CH_3NO_2). Optical rotations were measured for chloroformic solutions at 578 nm. Nitrosochlorides were prepared from the corresponding unsaturated hydrocarbons by standard procedure.[13]

Reaction of nitrosochlorides with 1,2-phenylenediamine.

A mixture of a nitrosochloride (4.96 mmol) and 1,2-phenylenediamine (7.40 mmol) in CH_3OH (10 mL) was heated at 40-50° for 1h under inert atmosphere (Ar). Then solvent was removed at reduced pressure and the residue was stirred with 20% HCl (10 mL) and H_2O (20 mL). The aqueous layer was washed with benzene (3×7 mL), treated with concentrated aqueous ammonia (15 mL) and extracted with benzene (2×10 mL). The combined organic extracts were washed with water (3×10 mL), brine (10 mL), dried (Na_2SO_4) and evaporated at reduced pressure to give crude heterocycle as red-yellow solid. The crude product was then purified according to the following procedure. A portion of the crude material was dissolved in a minimum of benzene or toluene at 40-45°C, pentane was then added over the resulting solution and the mixture was allowed to stay at room temperature for 3 h and then at −10°C for 1 h. Crystalline product was isolated by filtration.

4a-Methyl-1,2,3,4,4a,5-hexahydrophenazine (**5**). Reddish-brown powder with m.p. 127-129°C (pentane-benzene 1:10, v/v); IR ($CHCl_3$): ν_{max} = 3400, 1625, 1600, 1475, 1460, 1445, 1420, 1370, 1315, 1300, 1245, 1185, 1175, 1150, 1138, 1105, 1090, 1070, 1025, 1005, 980, 925, 875 cm^{-1}; UV (EtOH): λ_{max} = 234 nm (lgε = 4.46), 280 nm (lgε = 3.38), 355 nm (lgε = 3.39), 470 nm (lgε = 2.08); MS, *m/z* (%): 200.1295 (M^+, 42, calc. for $C_{13}H_{16}N_2$ 200.1313), 76(4), 77(10), 85(5), 91(5), 117(5), 143(5), 144(5), 157(9), 158(9), 159(21), 169(6), 171(19), 172(8), 183(5), 185(100), 186(14), 199(5), 200(42), 201(8); ^{1}H NMR ($CDCl_3$:C_6D_6:CCl_4=2:1:5): 1.24 (3H, *s*, H^{11}), 1.50-1.60 (2H, *m*, H^2 or H^3 or H^4), 1.73-1.79 (2H, *m*, H^2 or H^3 or H^4), 1.85-1.93 (2H, *m*, H^2 or H^3 or H^4), 2.45 (1H, *ddd*, ***J*** = 15.5, 13.0 and 5.5 Hz, H^{1ax}), 2.50 (1H, *dddd*, ***J*** = 15.5, 4.5, 3.5 and 2.0 Hz, H^{1eq}), 6.31 (1H, *dd*, ***J*** = 7.8 and 1.3 Hz, H^6), 6.59 (1H, *ddd*, ***J*** = 7.8, 7.8 and 1.3 Hz, H^8), 6.65 (1H, *ddd*, ***J*** = 7.8, 7.8 and 1.6 Hz, H^7), 6.84 (1H, *dd*, ***J*** = 7.8 and 1.6 Hz, H^9); ^{13}C NMR ($CDCl_3$: C_6D_6:CCl_4=2:1:5): 22.08 (C^2 or C^3), 23.94 (C^{11}), 25.27 (C^3 or C^2), 34.10 (C^1), 41.25 (C^4), 53.29 (C^{4a}), 112.72 d (C^6), 117.88 d (C^8), 126.45 d (C^7), 127.57 d (C^9), 131.44 s (C^{9a}), 136.63 s (C^{5a}), 168.96 (C^{10a}).

(1aR,8aS,9aS)-1,1,8a-Trimethyl-1a,2,8,8a,9,9a-hexahydro-1H-3,8-diazacyclopropa[b]anthracene (**6**). Fawn crystalls with m.p. 135.0-136.5°C (toluene:pentane 1:3, v/v); $[\alpha]^{20}$ +26.8 (*c* 4.78). IR ($CHCl_3$): ν_{max} = 3390, 1625, 1600, 1480, 1470, 1445, 1400, 1365, 1300, 1287, 1250, 1150, 1100, 1075, 1025, 925, 890, 875

cm^{-1}; UV (EtOH): λ_{max} = 230 nm (lgε = 4.54), 280 nm (lgε = 3.38), 340 nm (lgε = 3.46); MS, *m/z* (%): 240.16275 (M^+, 84, calc. for $C_{16}H_{20}N_2$ 240.1626), 77(7), 91(6), 105(5), 117(5), 157(11), 158(100), 159(41), 169(5), 171(13), 181(12), 182(6), 183(6), 225(35), 226(6), 240(84), 241(17); ^{1}H NMR ($CDCl_3$): 0.79 (1H, *ddd*, ***J*** = 10.0, 9.5 and 7.5 Hz, H^{9a}), 0.93 (3H, *s*, H^{10}), 0.97 (1H, *ddd*, J = 9.5, 9.0 and 7.5 Hz, H^{1a}), 1.05 (3H, *s*, H^{12}), 1.11 (3H, *s*, H^{11}), 1.41 (1H, *dd*, ***J*** = 15.5 and 9.5 Hz, $H^{9\beta}$), 1.86 (1H, *dd*, ***J*** = 15.5 and 7.5 Hz, $H^{9\alpha}$), 1.86 (1H, *dd* ***J*** = 14.0 and 9.5 Hz, $H^{2\beta}$), 2.62 (1H, *dd*, ***J*** = 14.0 and 7.5 Hz, $H^{2\alpha}$), 3.66 (1H, *s*, NH), 6.60 (1H, *dd*, ***J*** = 7.8 and 1.3 Hz, H^7), 6.76 (1H, *ddd*, ***J*** = 7.8, 7.8 and 1.3 Hz, H^5), 6.97 (1H, *ddd*, ***J*** = 7.8, 7.8 and 1.5 Hz, H^6), 7.25 (1H, *dd*, ***J*** = 7.8 and 1.5 Hz, H^4); ^{13}C NMR ($CDCl_3$, $J_{C\text{-}H}$ ±0.2 Hz): 14.56 *qq* (C^{12}; ***J*** = 125.0, 4.5 Hz), 19.32 *qm* (C^{9a}; ***J*** = 164.9 Hz), 21.57 *m* (C^1), 22.20 *qd* (C^{10}; ***J*** = 127.2, 3.6 Hz), 24.49 *dm* (C^{1a}; ***J*** = 162.8 Hz), 27.87 *qq* (C^{11}; ***J*** = 125.7, 5.1 Hz), 29.64 *dd* (C^2; ***J*** = 135.2, 126.1 Hz), 34.49 *td* (C^9; ***J*** = 126.1, 5.8 Hz), 50.94 *m* (C^{8a}), 114.29 *dd* (C^7; ***J*** = 156.2, 8.0 Hz), 118.92 *ddd* (C^5; ***J*** = 159.1, 8.0, 2.2 Hz), 126.35 *dd* (C^4; ***J*** = 158.4, 8.7 Hz), 126.95 *ddd* (C^6; ***J*** = 157.0, 8.7, 2.9 Hz), 133.77 *dd* (C^{3a}; ***J*** = 8.0, 6.5 Hz), 136.88 *t* (C^{7a}; ***J*** = 8.0 Hz), 169.25 *m* (C^{2a}).

(±)-(2S,4aS*)-2-Isopropenyl-4a-methyl-1,2,3,4,4a,5-hexahydrophenazine* [(±)-(**9**)]. Ochre-colored powder with m.p. 53.0-54.0°C (pentane-benzene 5:2, v/v); IR ($CHCl_3$): ν_{max} = 3400, 1645, 1620, 1600, 1500, 1485, 1475, 1450, 1415, 1370, 1300, 1275, 1250, 1160, 1110, 1090, 1070, 1050, 1030, 925, 900, 870, 845 cm^{-1}; UV (EtOH): λ_{max} = 231 nm (lgε = 4.38), 280 nm (lgε = 3.40), 355 nm (lgε = 3.29); MS, *m/z* (%): 240.16275 (M^+, 93, calc. for $C_{16}H_{20}N_2$ 240.1626), 77(10), 80(8), 91(8), 98(6), 105(5), 107(7), 108(14), 131(5), 158(17), 159(22), 168(5), 169(11), 170(5), 171(12), 172(7), 180(7), 181(26), 182(31), 183(25), 184(7), 185(16), 196(7), 197(25), 209(6), 210(5), 211(7), 225(100), 226(17), 240(93), 241(18); ^{1}H NMR ($CDCl_3$): 1.22 (3H, *s*, H^{11}), 1.56 (1H, *dddd*, ***J*** = 12.7, 4.6, 2.0, and 0.5 Hz, H^{4eq}), 1.73 (3H, *s*, H^{14}), 1.7-2.1 (3H, *m*, H^{3ax}, H^{3eq} and H^{4ax}), 2.59 (1H, *m*, H^2), 2.72 (1H, *dd*, ***J*** = 15.9 and 6.1 Hz, H^{1ax}), 2.78 (1H, *dd*, ***J*** = 15.9, 2.7 and 2.0 Hz, H^{1eq}), 3.2-3.7 (1H, *m*, NH), 4.90 (2H, *d*, ***J*** = 8Hz, H^{12}), 6.46 (1H, *dd*, ***J*** = 7.8. and 1.2 Hz, H^6), 6.69 (1H, *ddd*, ***J*** = 7.8, 7.8 and 1.2 Hz, H^8), 6.94 (1H, *ddd*, ***J*** = 7.8, 7.8 and 1.4 Hz, H^7), 7.18 (1H, *dd*, ***J*** = 7.8 and 1.4 Hz, H^9); ^{13}C NMR ($CDCl_3$, $J_{C\text{-}H}$ ±0.1 Hz): 21.75 *qddd* (C^{14}; ***J*** = 125.7, 9.8, 7.0, 2.8 Hz), 23.17 *qdd* (C^{11}; ***J*** = 127.3, 4.9, 4.9 Hz), 23.93 *tm* (C^3; ***J*** = 126.5 Hz), 35.31 *tm* (C^4; ***J*** = 127.9 Hz), 37.02 *ddddd* (C^1; ***J*** = 132.1, 125.1, 5.5, 5.5, 1.5 Hz), 39.53 *dm* (C^2; ***J*** = 128.5 Hz), 52.54 *m* (C^{5a}), 112.64 *tqd* (C^{12}; ***J*** = 155.3, 5.5 and 5.5 Hz), 113.21 *dddd* (C^6; ***J*** = 156.3, 8.2, 1.5, 1.5 Hz), 118.11 *ddd* (C^8; ***J*** = 160.2, 8.2, 1.8 Hz), 126.21 *dddd* (C^9; 157.8, 7.9, 1.2, 1.2 Hz), 127.35 *ddd* (C^7; ***J*** = 157.5, 8.6, 2.1 Hz), 132.19 *m* (C^{9a}), 136.55 *ddd* (C^{5a}; ***J*** = 8.5, 6.7, 1.2 Hz), 145.86 *m* (C^{13}), 168.70 *m* (C^{10a}).

(–)-(2S,4aS)-2-Isopropenyl-4a-methyl-1,2,3,4,4a,5-hexahydrophenazine [(–)-(**9**)]. Red solid with $[\alpha]^{20}$ –29.5 (*c* 2.17). NMR spectra are identical with those of *(±)-(2S*,4aS*)-2-isopropenyl-4a-methyl-1,2,3,4,4a,5-hexahydrophenazine* [(±)-(**9**)].

1,2,3,4-Tetrahydrophenazine (**10**). Yellowish crystalls with m.p. 93-95°C (pentane-benzene 10:1, v/v), lit.[14] 93-94°C (undefined solvent). IR (KBr): ν_{max} = 3025, 2925, 2860, 1476 (CN), 1424, 1384, 1348, 1334, 1296, 1234, 1208, 1164, 1125, 1070, 1008, 975, 940, 884, 875, 825, 800, 775, 766 cm^{-1} (the spectrum is identical to that reported in ref.[15]); UV (EtOH): λ_{max} = 240 nm (lgε = 4.21), 310 nm (lgε = 3.92), 320 nm (lgε = 4.05), 332 nm (lgε = 3.87); MS, *m/z* (%): 184.0991 (M^+, 100, Calc. for $C_{12}H_{12}N_2$ 184.1000), 76(9), 77(9), 102(9), 103(5), 129(6), 155(7), 156(10), 168(6), 169(22), 183(50), 184(100), 185(14); ^{1}H NMR (C_6D_6-CCl_4

1:5, v/v): 1.79 (2H, *m*, H^2), 2.94 (2H, *m*, H^1), 7.43 (1H, *m*, H^7), 7.84 (1H, *m*, H^8); ^{13}C NMR (C_6D_6-CCl_4 1:5, v/v): 22.69 (C^2), 32.75 (C^1), 127.96 (C^6 or C^7), 128.38 (C^7 or C^6), 141.20 (C^{5a}), 153.11 (C^{4a}).

Reaction of nitrosochloride 2 with 1,2,3-triaminbenzene.

A suspention of powdered Na_2CO_3 (1.50 g, 14.2 mmol) and dimeric nitrosochloride **2** (0.50 g, 1.25 mmol) in a solution of 1,2,3-triaminobenzene dihydrochloride (1.39 g, 7.09 mmol) in MeOH (15 mL) was stirred at reflux for 1 h under inert atmosphere (Ar). The solvent was distilled off and the residue was treated with water (15 mL) and 0.5 M aqueous N_2CO_3 followed by extraction with toluene (2×15 mL). The combined organic expracts were washed with water (2×20 mL), dried (Na_2SO_4) and concentrated at reduced pressure to leave dark brown solid that was percolated through Al_2O_3 to give 0.50 g of the crude product as brown solid (**7**:**8**=2:1 according to ^1H NMR). Compounds **7** and **8** were separated by column chromatography on Al_2O_3 (hexane-EtOAc).

(1aR, 8aS, 9aS) 1,1,8a-Trimethyl-1a,2,8,8a,9,9a-hexahydro-1H-3,8-diazacyclopropa[b]anthracene-4-ylamine (**7**). Red-brown solid with $[\alpha]^{18}$ –26.1 (*c* 2.38); IR ($CHCl_3$): ν_{max} = 3700, 3625, 3450, 3400, 1610, 1150, 1050, 925 cm^{-1}; UV (EtOH): λ_{max} = 216 nm (lgε = 4.30), 245 nm (lgε = 4.29), 305 nm (lgε = 3.75), 356 nm (lgε = 3.28); MS, *m/z* (%): 255.17430 (M^+, 24, calc. for $C_{16}H_{21}N_3$ 255.17354), 91(4), 172(6), 173(100), 174(19), 196(5), 240(14), 255(24), 256(4); ^1H NMR ($CDCl_3$): 0.77 (1H, *ddd*, *J* = 9.4, 9.0 and 7.8 Hz, H^{9a}), 0.93 (3H, *s*, H^{10}), 0.94 (1H, *ddd*, J = 9.0, 9.0 and 7.5 Hz, H^{1a}), 1.05 (3H, *s*, H^{12}), 1.16 (3H, *s*, H^{11}), 1.39 (1H, *dd*, *J* = 15.9 and 9.4 Hz, $H^{9\beta}$), 1.85 (1H, *dd*, *J* = 13.5 and 9.0 Hz, $H^{2\beta}$), 1.86 (1H, *dd*, *J* = 15.9 and 7.8 Hz, $H^{9\alpha}$), 2.63 (1H, *dd*, *J* = 13.5 and 7.5 Hz, $H^{2\alpha}$), 3.58 (1H, *br.s*, $W_{1/2}$ = 56 Hz, NH), 4.29 (2H, *br.s*, $W_{1/2}$ = 92 Hz, NH_2), 6.02 (1H, *dd*, *J* = 7.8 and 1.2 Hz, H^7), 6.17 (1H, *dd*, *J* = 7.8 and 1.2 Hz, H^5), 6.78 (1H, *dd*, *J* = 7.8 and 7.8 Hz, H^6); ^{13}C NMR ($CDCl_3$): 14.59 *q* (C^{12}), 19.21 *q* (C^{9a}), 21.50 *s* (C^1), 21.82 *q* (C^{10}), 24.48 *d* (C^{1a}), 27.91 *q* (C^{11}), 29.33 *dd* (C^2), 34.35 *dd* (C^9), 50.57 *s* (C^{8a}), 104.08 *d* (C^7), 105.48 *d* (C^5), 120.88 *s* (C^{3a}), 127.45 *d* (C^6), 137.11 *s* (C^{7a}), 142.52 *s* (C^4), 165.76 *s* (C^{2a}).

(1S,3S,6R)-3-N-{(1aR,8aS,9aS)-1,1,8a-trimethyl-1a,2,8,8a,9,9a-hexahydro-1H-3,8--diazacyclopropa[b]anthracen-4-yl}-aminocaran-4-one E-oxime (**8**). Red-brown solid with $[\alpha]^{22}$ +161.83 (*c* 0.72); IR ($CHCl_3$): ν_{max} = 3570, 3370, 1590 cm^{-1}; UV (EtOH): λ_{max} = 214 nm (lgε = 4.34), 252 nm (lgε = 4.33), 320 nm (lgε = 3.75), 345 nm (lgε = 3.70); MS, *m/z* (%): 420.2885 (M^+, 24, Calc. for $C_{26}H_{36}N_4O$ 420.28889), 77(6), 79(6), 91(10), 105(7), 123(6), 132(5), 148(6), 172(15), 173(100), 174(26), 184(10), 186(8), 196(7), 198(11), 224(6), 225(5), 240(19), 254(9), 255(29), 256(8), 281(5), 321(6), 338(28), 339(7), 351(5), 420(16); ^1H NMR ($CDCl_3$): 0.84 *s* (H^{20}), 0.92 (3H, *s*, H^{10}), 1.02 (3H, *s*, H^{21}), 1.05 (3H, *s*, H^{12}), 1.16 (3H, *s*, H^{11}), 1.49 (3H, *s*, H^{22}), 1.38 (1H, *dd*, *J* = 15.5 and 9.2 Hz, $H^{9\beta}$), 1.54 (1H, *dd*, *J* = 15.6 and 4.3 Hz, $H^{14\beta}$), 1.85 (1H, *dd*, *J* = 13.6 and 9.0 Hz, $H^{2\beta}$), 1.86 (1H, *dd*, *J* = 15.5 and 7.8 Hz, $H^{9\alpha}$), 1.90 (1H, *dd*, *J* = 17.0 and 8.2 Hz, $H^{17\alpha}$), 2.41 (1H, *dd*, *J* = 15.0 and 9.9 Hz, $H^{14\alpha}$), 2.60 (1H, *dd*, *J* = 13.6 and 7.5 Hz, $H^{2\alpha}$), 3.05 (1H, *d*, *J* = 17.0 Hz, $H^{17\beta}$), 5.96 (1H, *d*, *J* = 7.8 Hz, H^7), 6.24 (1H, *d*, *J* = 7.8 Hz, H^5), 6.74 (1H, *dd*, *J* = 7.8 and 7.8 Hz, H^6); ^{13}C NMR ($CDCl_3$): 14.16 *q* (C^{20}), 14.59 *q* (C^{12}), 16.61 *d* (C^{13}), 18.25 *dd* (C^{17}), 19.25 *q* (C^{9a}), 19.39 *s* (C^{19}), 21.47 *s* (C^1), 21.99 *d* (C^{18}), 22.11 *q* (C^{10}), 23.34 *q* (C^{22}), 24.53 *d* (C^{1a}), 27.88 *q* (C^{11}), 28.13 *q* (C^{21}), 29.54 *dd* (C^2), 34.30 *dd* (C^9), 37.70 *dd* (C^{14}), 50.26 *s* (C^{8a}), 54.42 *s* (C^{15}), 103.47 *d* (C^7), 104.07 *d* (C^5), 121.04 *s* (C^{3a}), 127.47 *d* (C^6), 136.17 *s* (C^{7a}), 142.41 *s* (or C^4), 164.26 *s* (C^{2a} or C^{16}), 164.63 *s* (C^{16} or C^{2a}).

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