Reaction of nitroso chlorides of the adamantane series with nucleophiles

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Reactions of nitroso chlorides of 2-alkylydene adamantanes with O- and N-nucleophiles resulted in α-substituted oximes of the adamantane series. Reaction involved 1,4-nucleophilic addition of the nucleophiles to the generated *in situ* nitroso alkenes acting as the Michael acceptors. Reduction of the precursors of nitroso alkenes with sodium cyanoborohydride gave 2-substituted adamantylated oximes.

Key words: adamantane, nitroso chlorides, nitroso alkenes, the Michael reaction.

Vinyl nitroso compounds are known for a long time; however being highly reactive and unstable they are of little significance for the synthesis compared to other Michael acceptors and heterodienes.[1—7] They are mainly applied in the synthesis of 5,6-dihydro-1,2-oxazines *via* intra- or intermolecular [4+2] cycloaddition to olefins.[8,9] Conjugated nitroso alkenes can be easily generated *in situ* from α-halooximes by treatment with bases.[10] Note that conjugated nitroso alkenes could be isolated pure only in few cases: in the presence of bulky substituents, halogen atoms, and aryl groups at the double bond.[3,11—14] Typically, they can be detected only in solutions; their presence is often evidenced by the blue color of the solution ($\lambda_{max} \approx$ ≈ 700 nm).[4]

In continuation of our research on chemical properties of sterically hindered nitroso alkenes,[15—18] in the present work we describe reactions of dimeric nitroso chlorides of 2-alkylydeneadamantanes **1a—c** and chloro oxime **1d** with O- and N-nucleophiles and reduction of nitroso alkenes generated from compounds **1a—d**.

Conjugated nitroso alkenes **A** are available by treatment of dimeric nitroso chlorides of 2-alkylydeneadamantanes **1a—c** or (*E*)-1-(2-chloroadamant-2-yl)-*N*-hydroxy-1-phenylmethaneimine (**1d**). Compounds **1a—d** are capable of nucleophilic conjugate addition to give the corresponding 2,2-disubstituted adamantane derivatives (Scheme 1).

Nitroso alkenes generated by treating the staring compounds with base (Na_2CO_3) in alcoholic medium (methanol or propargyl alcohol) produce alkoxy oximes **2a—e** in the yields of 76—93%. IR spectra of compounds **2a—e** exhibit wide absorption bands at 3400—3200 cm^{-1} characteristic of the hydroxy group vibrations of the oxime moiety. Mass spectra of methoxy oximes **2a—e** reveal the fragment ion peaks resulted from the loss of the hydroxy and methoxy ions. ^{1}H NMR spectra of oximes **2a—e** show a singlet signals at δ 3.05—3.13 attributed to the methoxy group protons. ^{1}H NMR spectrum of 2-(propyn-2-yl-1-oxy)adamantane-2-carbaldehyde (**2e**) contains triplet at δ 2.34 of the C≡CH group proton and doublet at δ 3.92 of the CH_2O group protons with long range spin-spin coupling constants ^4J = 2.3 Hz.

Refluxing precursors of nitroso alkenes **2a,d** with sodium azide in methanol in the presence of 15-crown-5 afforded selectively α-azido oximes **3** in the yields above 90%. Apparent competitive 1,4-addition of methanol was not detected. In IR spectra of compounds **3a,b**, the azido group vibrations appear as the intense bands at 2087 and 2091 cm^{-1}.

Reactions of dimeric nitroso chlorides **1a—c** with liquid amines (morpholine, piperidine, and benzylamine) and 1,1-dimethylhydrazine were performed in the corresponding amine or hydrazine as a solvent. In some cases, the addition of amines to nitroso chlorides **1a—c** at room temperature causes blue-green color of the reaction solution due to the presence of unsaturated nitroso compound; the color gradually fades during the reaction. This fact excludes the possibility of the reaction to occur *via* the S_N1 mechanism and formation of 2-adamantyl carbocation.

Amino oximes **4a—i** are unstable in acidic medium and at heating (they melt with decomposition). For instance, acid-mediated decomposition of compound **4a** gives adamantanone (Scheme 2).

Instability of such oximes can be explained in terms of a Beckmann rearrangement of the second type (Werner rearrangement), which can be regarded as a particular case of the Grob fragmentation.[19,20]

α-Chloro oxime **1d** reacts with aqueous ammonia in dichloromethane to give α-amino oxime in 95% yield. Compound **4i** also melts with decomposition producing adamantanone, benzonitrile, and ammonia.

Reduction of dimers **1a,c** and chloro oxime **1d** with sodium cyanoborohydride in DMF leads to oximes **5a—c**. Compounds **5** can resulted from the nucleophilic addition of an anion complex hydride to the conjugated system of nitroso alkene acting as the Michael acceptor. ^{1}H NMR spectra of

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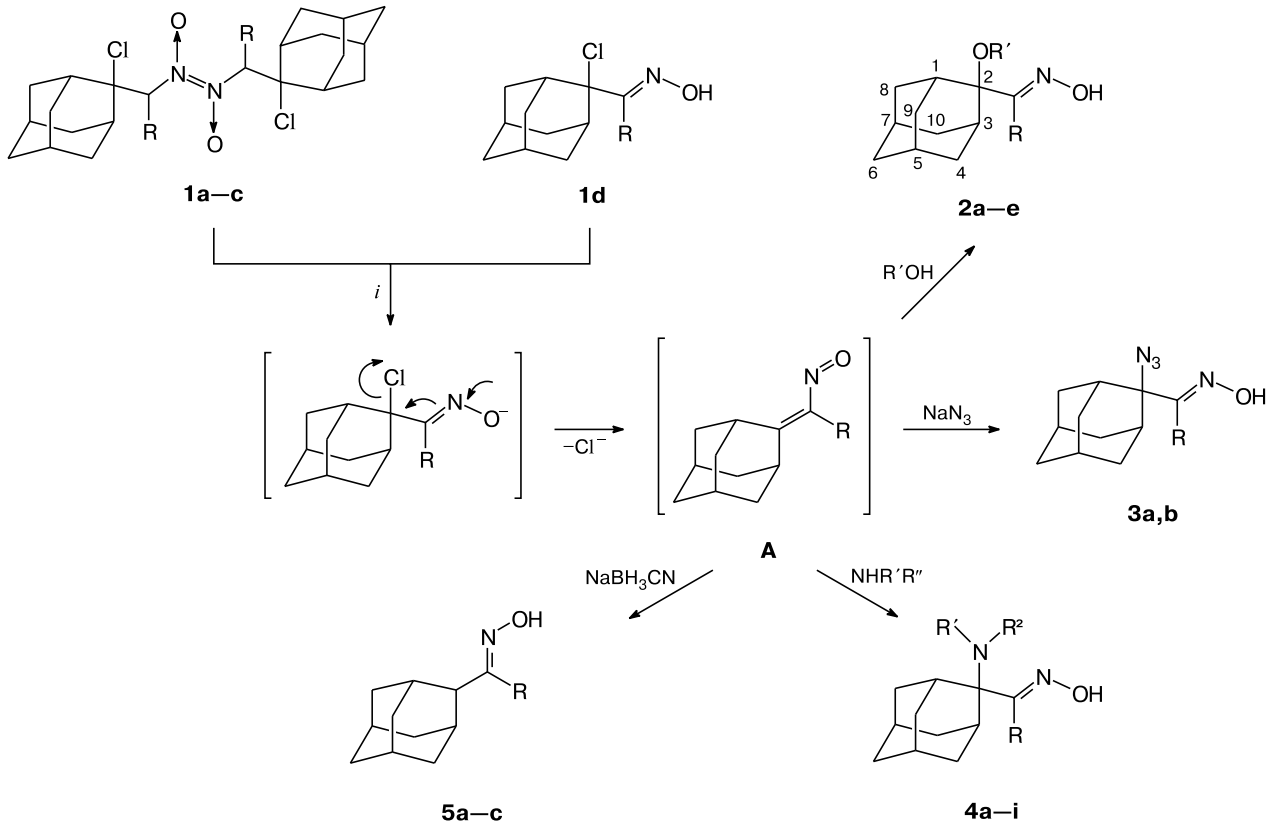
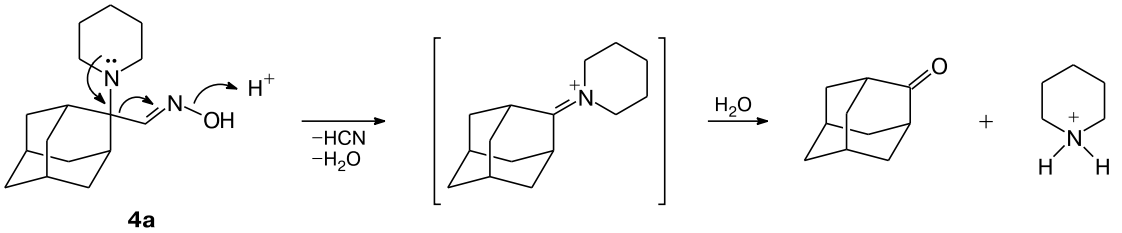
Scheme 1



i. Na_2CO_3 or an excess of nucleophile.

Compound	R	R′O	Compound	R	NR′R″
1a	H	—	**4a**	H	$N(CH_2)_5$
1b	Me	—	**4b**	Me	$N(CH_2)_5$
1c	Et	—	**4c**	H	$N(CH_2CH_2)_2O$
1d	Ph	—	**4d**	Me	$N(CH_2CH_2)_2O$
2a	H	MeO	**4e**	Et	$N(CH_2CH_2)_2O$
2b	Me	MeO	**4f**	H	$NHCH_2Ph$
2c	Et	MeO	**4g**	H	$NHNMe_2$
2d	Ph	MeO	**4h**	H	$NHNHCONH_2$
2e	H	$HC{\equiv}C{-}CH_2O$	**4i**	Ph	NH_2
3a	H	—	**5a**	H	—
3b	Ph	—	**5b**	Et	—
			5c	Ph	—

Scheme 2



compounds **5a—c** contain the broadened singlets at the range of δ 2.48—2.84 ascribed to the C(2)H proton of the adamantane framework. In the ^{13}C NMR spectra ($CDCl_3$), the C(2) atoms resonate in the range of δ 44.8—49.8.

^{13}C NMR spectra of the adamantane frameworks of compounds **2—5** comprise seven signals. Note that the C(2) atom of 2,2-disubstituted adamantane skeleton is strongly deshielded and resonates at δ 60.3—82.1; while, the oxime carbons are even more deshielded and appear at δ 151.4—163.9. ^{1}H NMR spectra contain singlets of the hydroxy group protons at the range of δ 7.76—8.81. The protons of the CH=N moieties of 2,2-disubstituted adamantane-2-carbaldehydes resonate in the ^{1}H NMR spectra at δ 6.95—8.06.

Earlier,[15] existence of oximes in the most energetically favorable *E*-configuration was suggested. Effects of both the bulky adamantane skeleton and the substituent at the bridgehead positions will favor the *E*-isomer formation. The NMR and IR spectroscopy data obtained in the present work for 2,2-disubsituted adamantanes clearly indicate formation of only one geometrical isomer of oximes, which in all cases was attributed to *E*-isomer.

Experimental

IR spectra were recorded with a Shimadzu IRAffinity-1 spectrophotometer in the KBr pellets. Mass spectrometry was performed on a Thermo Finnigan Trace DSQ instrument using direct inlet injection into the ion source; ionizing electron energy was 70 eV. ^{1}H and ^{13}C NMR spectra (working frequencies of 400 and 100 MHz, respectively) were recorded with a JEOL JNM-ECX400 spectrometer, the chemical shifts are given in the δ scale relative to $SiMe_4$ (inner standard). Elemental analysis was performed with a Euro Vector EA-3000 CHNS analyzer. Melting points were measured in capillaries using PTP-M apparatus. Thin layer chromatography was performed with Silufol UV-254 plates, the spots were visualized by UV light and iodine vapors. Dimeric nitroso chlorides **1a—c** and chloro oxime **1d** were synthesized by the known procedures.[18,21]

Synthesis of α-alkoxy oximes 2a—e (general procedure). To a suspension of sodium carbonate (5 g) in MeOH (50 mL) or propargyl alcohol (for **2e**), dimeric nitroso chloride **1a—c** (5 mmol) or 1-(2-chloroadamant-2-yl)-*N*-hydroxy-1-phenylmethane imine **1d** was added portionwise over 5 min at 55—65 °C. The mixture was heated for 30 min, cooled, and poured into cold water (300 mL) with stirring. The precipitate formed was collected by filtration, washed with water, and recrystallized from MeOH.

2-Methoxyadamantane-2-carbaldehyde (*E*)-oxime (2a). Yield 91%, m.p. 105—107 °C. IR, ν/cm^{-1}: 3400—3200 (OH); 2905, 2851 (CH_{Ad}); 1450, 1423, 1354, 1300, 1080, 1045, 984, 941, 906, 833, 748. ^{1}H NMR ($CDCl_3$), δ: 1.51—1.56 (m, 2 H, H_{Ad}); 1.67—1.80 (m, 8 H, H_{Ad}); 2.10 (br.s, 4 H, H_{Ad}); 3.13 (s, 3 H, CH_3O); 7.08 (s, 1 H, CH=N); 8.81 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.1, 27.5, 32.2, 32.9, 34.2, 37.7, 48.9 (CH_3O), 78.8 (C_{Ad}(2)), 152.9 (C=N). MS, *m/z* (I_{rel} (%)): 192 (100) $[M - OH]^+$, 179 (30), 177 (34), 165 (42) $[M - CH_2NO]^+$, 160 (41), 133 (15), 105 (16), 91 (54) $[C_7H_7]^+$. Found (%): C, 68.71; H, 9.00; N, 6.55. $C_{12}H_{19}NO_2$. Calculated (%): C, 68.87; H, 9.15; N, 6.69.

1-(2-Methoxyadamant-2-yl)ethanone (*E*)-oxime (2b). Yield 82%, m.p. 148—150 °C. IR, ν/cm^{-1}: 3400—3200 (OH); 2905, 2851 (CH_{Ad}); 1450, 1362, 1080, 1049, 984, 941, 895, 737. ^{1}H NMR ($CDCl_3$), δ: 1.54 (d, 2 H, H_{Ad}, J = 12.1 Hz); 1.66—1.72 (m, 4 H, H_{Ad}); 1.81 (br.s, 7 H, 4 H_{Ad}, CH_3); 2.11 (d, 2 H, H_{Ad}, J = 12.1 Hz); 2.23 (br.s, 2 H, H_{Ad}); 3.05 (s, 3 H, CH_3O); 8.85 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 8.6 (CH_3); 27.1, 27.5, 31.7, 32.5, 34.4, 37.7, 48.7 (CH_3O); 81.5 (C_{Ad}(2)); 157.6 (C=N). Found (%): C, 69.82; H, 9.30; N, 6.11. $C_{13}H_{21}NO_2$. Calculated (%): C, 69.92; H, 9.48; N, 6.27.

1-(2-Methoxyadamant-2-yl)propan-1-one (*E*)-oxime (2c). Yield 86%, m.p. 121—123 °C. IR, ν/cm^{-1}: 3400—3200 (OH), 2908, 2851 (CH_{Ad}), 1447, 1084, 964, 937, 887, 841, 721. ^{1}H NMR ($CDCl_3$), δ: 1.12 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.6 Hz); 1.54 (d, 2 H, H_{Ad}, J = 11.7 Hz); 1.66—1.72 (m, 4 H, H_{Ad}); 1.81—1.88 (m, 4 H, H_{Ad}); 2.13 (d, 2 H, H_{Ad}, J = 12.1 Hz); 2.24 (br.s, 2 H, H_{Ad}); 2.31 (q, 2 H, $C\underline{H}_2CH_3$, J = 7.6 Hz); 3.05 (s, 3 H, CH_3O); 8.76 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 10.8 ($\underline{C}H_3CH_2$); 17.5 ($CH_3\underline{C}H_2$); 27.0, 27.7, 31.7, 32.6, 34.6, 37.8, 48.7 (CH_3O); 82.0 (C_{Ad}(2)); 161.2 (C=N). MS, *m/z* (I_{rel} (%)): 220 $[M - OH]^+$ (8), 205 $[M - CH_3OH]^+$ (51), 188 (8), 165 (100) $[C_{11}H_{17}O]^+$, 150 $[C_{10}H_{14}O]^+$ (7), 149 (9), 133 (6), 105 (6), 91 (16) $[C_7H_7]^+$. Found (%): C, 70.73; H, 9.65; N, 5.60. $C_{14}H_{23}NO_2$. Calculated (%): C, 70.85; H, 9.77; N, 5.90.

(2-Methoxyadamant-2-yl)(phenyl)methanone (*E*)-oxime (2d). Yield 93%, m.p. 184—186 °C. IR, ν/cm^{-1}: 3400—3300 (OH), 2910, 2854 (CH_{Ad}), 1493, 1447, 1400, 1358, 1231, 1196, 1099, 1076, 972, 941, 883, 833, 764, 741, 721, 702. ^{1}H NMR ($CDCl_3$), δ: 1.48 (d, 2 H, H_{Ad}, J = 12.2 Hz); 1.62—1.65 (m, 4 H, H_{Ad}); 1.80—1.93 (m, 4 H, H_{Ad}); 2.08—2.11 (m, 4 H, H_{Ad}); 3.30 (s, 3 H, CH_3O); 7.35—7.45 (m, 5 H, Ph); 8.25 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.0 (CH); 27.5 (CH); 31.7 (CH); 32.4 (CH_2); 34.3 (CH_2); 37.6 (CH_2); 48.4 (CH_3O); 82.1 (C_{Ad}(2)); 128.0 and 128.5 (5 CH_{Ph}); 131.4 (C_{Ph}); 157.0 (C=N). MS, *m/z* (I_{rel} (%)): 285 $[M]^+$ (8), 268 $[M - OH]^+$ (13), 253 $[M - CH_3OH]^+$ (6), 236 (8), 165 $[C_{11}H_{17}O]^+$ (100), 150 $[C_{10}H_{14}O]^+$ (4), 133 (6), 129 (7), 105 (9), 103 (12), 91 (28) $[C_7H_7]^+$. Found (%): C, 75.58; H, 8.01; N, 4.81. $C_{18}H_{23}NO_2$. Calculated (%): C, 75.76; H, 8.12; N, 4.91.

2-(Propyn-2-yl-1-oxy)adamantane-2-carbaldehyde (*E*)-oxime (2e). Yield 76%, m.p. 124—126 °C. IR, ν/cm^{-1}: 3310, 3271 (OH); 2908, 2862 (CH_{Ad}); 2125 (C≡C); 1458, 1450, 1377, 1103, 1083, 1072, 1053, 933, 922, 887, 748, 663. ^{1}H NMR (CD_3CN), δ: 1.50 (d, 2 H, H_{Ad}, J = 11.9 Hz); 1.66—1.80 (m, 8 H, H_{Ad}); 2.04 (br.s, 2 H, H_{Ad}); 2.13 (d, 2 H, H_{Ad}, J = 12.4 Hz); 2.34 (t, 1 H, C≡CH, ^4J = 2.3 Hz); 3.92 (d, 2 H, CH_2O, ^4J = 2.3 Hz); 6.95 (s, 1 H, CH=N); 8.49 (br.s, 1 H, OH). ^{13}C NMR (CD_3CN), δ: 27.2 and 27.4 ($C(5)H_{Ad}$, $C(7)H_{Ad}$); 32.2 (2 $(CH_2)_{Ad}$); 33.1 (2 $(CH_2)_{Ad}$); 34.2 ($C(1)H_{Ad}$, $C(3)H_{Ad}$); 37.7 ($H_2C(6)_{Ad}$); 49.5 (CH_2O); 75.5 (C≡$\underline{C}$H); 79.5 (C_{Ad}(2)); 81.1 ($\underline{C}$≡CH); 151.4 (CH=N). Found (%): C, 71.83; H, 8.10; N, 5.80. $C_{14}H_{19}NO_2$. Calculated (%): C, 72.07; H, 8.21; N, 6.00.

Synthesis of α-azido oximes 3a,b (general procedure). To a suspension of sodium azide (0.65 g, 10 mmol) in MeOH (10 mL), 15-crown-5 (0.1 g) was added followed by portionwise addition of 1-(2-chloroadamant-2-yl)-*N*-hydroxy-1-phenylmethane imine (**1d**) (1.45 g, 5 mmol) or dimeric 2-chloro-2-(nitrosomethyl)adamantane (**1a**) (1.07 g, 2.5 mmol) at 65 °C. The solution was stirred for 20 min, cooled, and poured into cold water (100 mL). The precipitate formed was collected by filtration, washed with water, and recrystallized from MeOH.

2-Azidoadamantane-2-carbaldehyde (*E*)-oxime (3a). Yield 91%, m.p. 180—182 °C (decomp.). IR, ν/cm^{-1}: 3400—3100 (OH); 2905, 2858 (CH_{Ad}); 2087 (N_3); 1454, 1234, 1065, 957, 933, 756, 706. ^{1}H NMR ($CDCl_3$), δ: 1.64 (d, 2 H, H_{Ad}, J = = 12.1 Hz); 1.70—1.90 (m, 8 H, H_{Ad}); 2.12—2.21 (m, 4 H, H_{Ad}); 7.38 (s, 1 H, CH=N); 8.05 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.0, 27.1, 32.7, 33.5, 33.9, 37.5, 68.1 (C_{Ad}(2));

152.3 (C=N). MS, m/z (I_{rel} (%)): 178 $[M - N_3]^+$ (100), 177 $[M - HN_3]^+$ (26), 175 (17), 129 (11), 91 (24) $[C_7H_7]^+$, 79 (49). Found (%): C, 59.80; H, 7.20; N, 25.31. $C_{11}H_{16}N_4O$. Calculated (%): C, 59.98; H, 7.32; N, 25.44.

(2-Azidoadamant-2-yl)(phenyl)methanone (*E*)-oxime (3b). Yield 95%, m.p. 167—169 °C (decomp.). IR, ν/cm^{-1}: 3400—3200 (OH); 2924, 2854 (CH_{Ad}); 2091 (N_3); 1470, 1447, 1242, 1099, 980, 941, 879, 833, 764, 714. ^{1}H NMR ($CDCl_3$), δ: 1.59—1.69 (m, 6 H, H_{Ad}); 1.86—1.95 (m, 4 H, H_{Ad}); 2.12—2.15 (m, 4 H, H_{Ad}); 7.37—7.46 (m, 5 H, Ph); 7.95 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 26.8, 27.0, 32.1, 33.0, 34.0, 37.5, 71.9 (C_{Ad}(2)); 128.1 (2 CH_{Ph}); 128.6 (2 CH_{Ph}); 128.9 (CH_{Ph}); 130.8 (C_{Ph}); 158.1 (C=N). MS, m/z (I_{rel} (%)): 296 $[M]^+$, 267 (22), 254 $[M - N_3]^+$ (45), 251 $[M - OH - N_2]^+$ (82), 236 (43), 223 (34), 148 $[C_{10}H_{14}N]^+$ (100), 131 (26), 121 (31), 104 (55), 91 $[C_7H_7]^+$ (60), 79 $[C_6H_7]^+$ (81), 77 $[C_6H_5]^+$ (73). Found (%): C, 68.75; H, 6.68; N, 18.01. $C_{17}H_{20}N_4O$. Calculated (%): C, 68.89; H, 6.80; N, 18.90.

Synthesis of α-amino oximes 4a—g (general procedure). To dimeric nitroso chloride **1a—c** (2.5 mmol), the corresponding amine or 1,1-dimethylhydrazine (5 mL) was added. The resulting suspension was heated with stirring at 80—90 °C for 10 min until complete dissolution of the starting dimer and disappearance of blue color of the solution. The reaction mixture was poured into cold water (100 mL). The precipitate formed was collected by filtration, washed with water, and recrystallized from MeOH.

2-(Piperidin-1-yl)adamantane-2-carbaldehyde (*E*)-oxime (4a). Yield 86%, m.p. 179—181 °C (decomp.). IR, ν/cm^{-1}: 3400—3200 (OH); 2970, 2910, 2849, 2802, 1468, 1447, 1354, 1298, 1285, 1204, 1153, 1101, 993, 939, 743. ^{1}H NMR ($CDCl_3$), δ: 1.38—1.45 and 1.59—1.81 (both m, 16 H, 14 H_{Ad}, 2 H_{pyp})*; 1.99 (t, 2 H, H_{pyp}, J = 11.2 Hz); 2.25 (br.s, 4 H, H_{pyp}); 3.01 (d, 2 H, H_{pyp}, J = 10.1 Hz); 7.21 (s, 1 H, CH=N); 7.76 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 25.4, 27.2, 27.3, 27.6, 31.2, 31.4, 34.0, 38.0, 45.1, 62.6 (C_{Ad}(2)); 154.6 (C=N). MS, m/z (I_{rel} (%)): 262 $[M]^+$ (3), 245 $[M - OH]^+$ (48), 243 (8), 230 (5), 218 $[M - CH_2NO]^+$ (100), 162 (15), 91 $[C_7H_7]^+$ (9), 84 $[C_5H_{10}N]^+$ (65), 79 $[C_6H_7]^+$ (8). Found (%): C, 73.11; H, 9.93; N, 10.52. $C_{16}H_{26}N_2O$. Calculated (%): C, 73.24; H, 9.99; N, 10.68.

1-[2-(Piperidin-1-yl)adamant-2-yl]ethanone (*E*)-oxime (4b). Yield 89%, m.p. 200—202 °C (decomp.). IR, ν/cm^{-1}: 3400—3100 (OH); 2951, 2901, 2847, 2808, 1447, 1366, 1223, 1099, 980, 949, 930, 903, 860, 729. ^{1}H NMR ($CDCl_3$), δ: 1.38—1.44 and 1.59—1.81 (both m, 21 H, 14 H_{Ad}, 4 H_{pyp}, CH_3); 2.24 (d, 2 H, H_{pyp}, J = 11.7 Hz); 2.39 (br.s, 2 H, H_{pyp}); 2.98 (d, 2 H, H_{pyp}, J = = 10.3 Hz); 8.55 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 12.3 (CH_3); 25.6, 27.1, 27.4, 27.6, 30.4, 32.1, 34.3, 38.0, 46.0, 66.1 (C_{Ad}(2)); 157.1 (C=N). Found (%): C, 73.75; H, 10.10; N, 10.03. $C_{17}H_{28}N_2O$. Calculated (%): C, 73.87; H, 10.21; N, 10.13.

2-(Morpholin-4-yl)adamantane-2-carbaldehyde (*E*)-oxime (4c). Yield 80%, m.p. 142—144 °C (decomp.). IR, ν/cm^{-1}: 3400—3100 (OH); 2957, 2912, 2885, 2845, 2814, 1450, 1310, 1286, 1269, 1117, 1001, 935, 868, 746. ^{1}H NMR ($CDCl_3$), δ: 1.42 (d, 2 H, H_{Ad}, J = 11.9 Hz); 1.66—1.84 (m, 8 H, H_{Ad}); 2.18 (br.s, 2 H, H_{Ad}); 2.23 (d, 2 H, H_{Ad}, J = 11.9 Hz); 2.30—2.45 (m, 2 H, H_{morph})*; 2.67—2.78 (m, 2 H, H_{morph}); 3.47—3.60 (m, 2 H, H_{morph}); 3.76—3.88 (m, 2 H, H_{morph}); 7.21 (s, 1 H, CH=N); 8.06 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.2, 27.4, 30.8, 31.3, 33.8, 37.9, 44.6 (2 CH_2N); 62.2 (C_{Ad}(2)); 68.0 (2 CH_2O); 153.7 (C=N). MS, m/z (I_{rel} (%)): 264 $[M]^+$ (3), 247 $[M - OH]^+$ (48), 220 $[M - CH_2NO]^+$ (100), 179 (18); 162 (34), 91 $[C_7H_7]^+$ (15), 86 $[C_4H_8NO]^+$ (48). Found (%): C, 69.92; H, 9.00; N, 10.43. $C_{15}H_{24}N_2O_2$. Calculated (%): C, 68.15; H, 9.15; N, 10.60.

1-[2-(Morpholin-4-yl)adamant-2-yl]ethanone (*E*)-oxime (4d). Yield 79%, m.p. 173—175 °C (decomp.). IR, ν/cm^{-1}: 3400—3100 (OH); 2935, 2908, 2851, 2816, 1450, 1358, 1288, 1273, 1242, 1119, 995, 980, 933, 903, 868, 733. ^{1}H NMR ($CDCl_3$), δ: 1.46 (d, 2 H, H_{Ad}, J = 11.5 Hz); 1.65—1.85 (m, 11 H, 8 H_{Ad}, CH_3); 2.16—2.24 (m, 4 H, H_{Ad}); 2.35 (br.s, 2 H, H_{morph}); 2.71 (d, 2 H, H_{morph}, J = 10.8 Hz); 3.51—3.56 (m, 2 H, H_{morph}); 3.79 (d, 2 H, H_{morph}, J = 10.6 Hz); 8.69 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 12.5 (CH_3); 27.0, 27.2, 29.9, 31.9, 34.1, 37.9, 45.5 (2 CH_2N); 65.7 (C_{Ad}(2)); 68.3 (2CH_2O); 156.4 (C=N). Found (%): C, 68.93; H, 9.36; N, 9.97. $C_{16}H_{26}N_2O_2$. Calculated (%): C, 69.03; H, 9.41; N, 10.06.

1-[2-(Morpholin-4-yl)adamant-2-yl]propan-1-one (*E*)-oxime (4e). Yield 85%, m.p. 169—171 °C (decomp.). IR, ν/cm^{-1}: 3400—3100 (OH); 2932, 2851, 2812, 1447, 1358, 1269, 1122, 1072, 995, 933, 89, 872, 833, 806, 744. ^{1}H NMR ($CDCl_3$), δ: 1.24 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.3 Hz); 1.46 (d, 2 H, H_{Ad}, J = 11.9 Hz); 1.60—1.83 (m, 8 H, H_{Ad}); 2.16—2.27 (m, 6 H, 4 H_{Ad}, $C\underline{H}_2CH_3$); 2.35 (br.s, 2 H, H_{morph}); 2.71 (d, 2 H, H_{morph}, J = 10.5 Hz); 3.52—3.55 (m, 2 H, H_{morph}); 3.78 (d, 2 H, H_{morph}, J = 10.6 Hz); 8.27 (s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 10.8 ($\underline{C}H_3CH_2$); 20.6 ($CH_3\underline{C}H_2$); 27.3 (2 C); 30.1, 32.2, 34.3, 38.0, 45.6 (2 CH_2N); 66.5 (C_{Ad}(2)); 68.3 (2 CH_2O); 160.9 (C=N). MS, m/z (I_{rel} (%)): 292 (1) $[M]^+$, 275 $[M - OH]^+$ (22), 220 $[M - CH_2NO]^+$ (100), 207 (36), 206 (22), 190 (33), 150 $[C_{10}H_{14}O]^+$ (10), 91 (12) $[C_7H_7]^+$, 86 $[C_4H_8NO]^+$ (13). Found (%): C, 69.66; H, 9.57; N, 9.45. $C_{17}H_{28}N_2O_2$. Calculated (%): C, 69.83; H, 9.65; N, 9.58.

2-(Benzylamino)adamantane-2-carbaldehyde (*E*)-oxime (4f). Yield 95%, m.p. 128—130 °C (decomp.). IR, ν/cm^{-1}: 3300—3100 (OH); 2935, 2889, 2851 (CH_{Ad}); 1605, 1497, 1466, 1447, 1354, 1296, 1219, 1115, 926, 887, 752. ^{1}H NMR ($CDCl_3$), δ: 1.27 (br.s, 1 H, NH); 1.59 (d, 2 H, H_{Ad}, J = 12.1 Hz); 1.71—1.77 (m, 4 H, H_{Ad}); 1.88—2.00 (m, 6 H, H_{Ad}); 2.35 (d, 2 H, H_{Ad}, J = = 12.1 Hz); 3.63 (s, 2 H, CH_2N); 7.20 (s, 1 H, CH=N); 7.25—7.40 (m, 5 H, Ph); 8.51 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.5, 27.9, 32.0, 33.6, 34.0, 38.2, 45.3 (CH_2N); 60.3 (C_{Ad}(2)); 126.9 and 128.4 (5 CH_{Ph}); 141.1 (C_{Ph}); 155.3 (C=N). MS, m/z (I_{rel} (%)): 267 $[M - OH]^+$ (53), 240 $[M - CH_2NO]^+$ (36), 239 (19), 238 (17), 193 (5), 162 (20), 106 $[C_7H_8N]^+$ (46), 91 $[C_7H_7]^+$ (100). Found (%): C, 75.84; H, 8.37; N, 9.71. $C_{18}H_{24}N_2O$. Calculated (%): C, 76.02; H, 8.51; N, 9.85.

2-(2,2-Dimethylhydrazino)adamantane-2-carbaldehyde (*E*)-oxime (4g). Yield 75%, m.p. 139—141 °C (decomp.). IR, ν/cm^{-1}: 3240, 3175, 3094 (NH, OH); 2955, 2905, 2851 (CH_{Ad}); 1466, 1447, 1354, 1246, 1107, 995, 940, 868, 833, 748. ^{1}H NMR ($CDCl_3$), δ: 1.46 (d, 2 H, H_{Ad}, J = 12.1 Hz); 1.65—2.00 (m, 10 H, H_{Ad}); 2.31 (d, 2 H, H_{Ad}, J = 12.1 Hz); 2.42 (s, 6 H, 2 CH_3); 7.28 (s, 1 H, CH=N); 8.08 (br.s, 2 H, OH, NH). MS, m/z (I_{rel} (%)): 237 $[M]^+$ (3), 192 $[M - CH_3NO]^+$ (7), 178 (3), 91 $[C_7H_7]^+$ (7), 59 (100). Found (%): C, 65.60; H, 9.69; N, 17.63. $C_{13}H_{23}N_3O$. Calculated (%): C, 65.79; H, 9.77; N, 17.70.

2-{2-[(*E*)-(Hydroxyimino)methyl]adamant-2-yl}hydrazinecarboxamine (4h). To a solution of dimeric 2-chloro-2-(nitrosomethyl)adamantane **1a** (1.07 g, 2.5 mmol) in pyridine (10 mL), semicarbazide (0.45 g, 6 mmol) was added and the resulting mixture was heated with stirring at 80—90 °C (water bath) for 20 min. The reaction mixture was poured into cold water (100 mL). The precipitate formed was collected by filtra-

* H_{pyp} is $H_{piperidinyl}$.

* H_{morph} is $H_{morpholinyl}$.

tion, washed with water, and recrystallized from MeOH. Yield 1.15 g (91%), m.p. 243—245 °C (decomp.). IR, ν/cm^{-1}: 3491, 3329, 3236 (OH, NH); 2901, 2854 (CH_{Ad}); 1663 (C=O); 1566, 1466, 1408, 1308, 1246, 1107, 933, 906, 883, 833. ^{1}H NMR (DMSO-d_6), δ: 1.43 (d, 2 H, H_{Ad}, J = 11.6 Hz); 1.60—1.85 (m, 10 H, H_{Ad}); 2.29 (d, 2 H, H_{Ad}, J = 11.2 Hz); 4.74 (s, 1 H, NH); 5.85—6.10 (m, 3 H, NH, NH_2); 7.08 (s, 1 H, CH=N); 10.70 (br.s, 1 H, OH). MS, m/z (I_{rel} (%)): 252 $[M]^+$ (3), 234 $[M - H_2O]^+$ (2), 208 $[M - CH_2NO]^+$ (6), 207 (10), 206 (10), 191 (11), 189 (9), 178 $[M - CH_4N_3O]^+$ (100), 164 (46), 163 (45), 161 (36), 150 $[C_{10}H_{14}O]^+$ (15), 119 (19), 106 (27), 91 (43) $[C_7H_7]^+$. Found (%): C, 56.85; H, 7.85; N, 21.98. $C_{12}H_{20}N_4O_2$. Calculated (%): C, 57.12; H, 7.99; N, 22.21.

(2-Aminoadamant-2-yl)(phenyl)methanone (*E*)-oxime (4i). To 1-(2-chloroadamant-2-yl)-*N*-hydroxy-1-phenylmethane imine (**1d**) (1 g, 3.5 mmol), dichloromethane (10 mL) and 25% aqueous ammonia (5 mL) were added, and the mixture was stirred for 2 h at room temperature. The organic layer was separated, washed with water, dried with Na_2SO_4, and the volatiles were removed *in vacuo*. The residue was recrystallized from MeOH. Yield 0.78 g (83%), m.p. 174—176 °C (decomp.). IR, ν/cm^{-1}: 3402, 3321, 3294 (OH, NH_2); 3059, 2908, 2858 (CH_{Ad}); 1639, 1601, 1427, 1358, 945, 705. ^{1}H NMR (DMSO-d_6), δ: 1.39 (d, 2 H, H_{Ad}, J = = 12.6 Hz); 1.48 (d, 2 H, H_{Ad}, J = 12.4 Hz); 1.57, 1.70—1.79 (s, m, 8 H, 6 H_{Ad}, NH_2); 1.97 (d, 2 H, H_{Ad}, J = 11.9 Hz); 2.22 (d, 2 H, H_{Ad}, J = 11.9 Hz); 7.23—7.31 (m, 3 H, Ph); 7.41 (dd, 2 H, Ph, J = = 8.2 Hz, J = 1.6 Hz); 10.37 (s, 1 H, OH). ^{13}C NMR (DMSO-d_6), δ: 27.4 (C(5)H_{Ad}, C(7)H_{Ad}); 32.4 (2 $(CH_2)_{Ad}$); 34.7 (2 $(CH_2)_{Ad}$); 34.9 (C(1)H_{Ad}, C(3)H_{Ad}); 38.4 (CH_2(6)$_{Ad}$); 60.3 (C_{Ad}(2)); 127.7 (2 CH_{Ph}); 127.8 (CH_{Ph}); 129.5 (2 CH_{Ph}); 134.0 (C_{Ph}); 161.2 (C=N). MS, m/z (I_{rel} (%)): 269 $[M - 1]^+$ (1), 253 (21), 151 (19), 150 $[C_{10}H_{14}O]^+$ (100), 133 (10), 91 (13). Found (%): C, 75.39; H, 8.08; N, 10.28. $C_{17}H_{22}N_2O$. Calculated (%): C, 75.52; H, 8.20; N, 10.36.

Reduction of nitroso chlorides with sodium cyanoborohydride (general procedure). To a stirred suspension of $NaBH_3CN$ (0.94 g, 15 mmol) in DMF (15 mL), nitroso compound **1a**,**c**,**d** (5 mmol) was added at 80 °C. After 20 min, the mixture was cooled to room temperature and poured into cold water (150 mL). The precipitate formed was collected by filtration, washed with water, and recrystallized from MeOH.

Adamantane-2-carbaldehyde (*E*)-oxime (5a). Yield 83%, m.p. 143—145 °C. IR, ν/cm^{-1}: 3257, 3163 (OH); 2901, 2891 (CH_{Ad}); 1448, 1306, 933, 723. ^{1}H NMR ($CDCl_3$), δ: 1.62 (d, 2 H, H_{Ad}, J = = 12.2 Hz); 1.74—2.03 (m, 12 H, H_{Ad}); 2.59 (br.s, 1 H, H_{Ad}(2)); 7.59 (d, 1 H, CH=N, J = 5.5 Hz); 7.97 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.7 and 27.8 (C(5)H_{Ad}, C(7)H_{Ad}); 31.2 (C(1)H_{Ad}, C(3)H_{Ad}); 32.5 (2 $(CH_2)_{Ad}$); 37.7 (H_2C(6)$_{Ad}$); 38.3 (2 $(CH_2)_{Ad}$); 44.8 (C(2)H_{Ad}); 155.6 (C=N). Found (%): C, 73.59; H, 9.50; N, 7.70. $C_{11}H_{17}NO$. Calculated (%): C, 73.70; H, 9.56; N, 7.81.

1-(2-Adamantyl)propan-1-one (*E*)-oxime (5b). Yield 89%, m.p. 153—155 °C. IR, ν/cm^{-1}: 3228 (OH); 2970 (CH_{Ad}); 1450, 1099, 953, 933, 752. ^{1}H NMR ($CDCl_3$), δ: 1.08 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.8 Hz); 1.56 (d, 2 H, H_{Ad}, J = 12.6 Hz); 1.72 (br.s, 1 H, H_{Ad}); 1.76—1.82 (m, 4 H, H_{Ad}); 1.88—1.91 (m, 3 H, H_{Ad}); 1.98 (d, 2 H, H_{Ad}, J = 12.2 Hz); 2.20 (br.s, 2 H, H_{Ad}); 2.34 (q, 2 H, $C\underline{H}_2CH_3$, J = 7.8 Hz); 2.48 (s, 1 H, H_{Ad}(2)); 8.74 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 10.8 ($\underline{C}H_3CH_2$); 20.0 ($CH_3\underline{C}H_2$); 28.0 and 28.1 (C(5)H_{Ad}, C(7)H_{Ad}); 29.5 (C(1)H_{Ad}, C(3)H_{Ad}); 32.7 (2 $(CH_2)_{Ad}$); 37.8 (H_2C(6)$_{Ad}$); 39.1 (2 $(CH_2)_{Ad}$); 49.0 (C(2)H_{Ad}); 163.9 (C=N). Found (%): C, 75.21; H, 10.11; N, 6.72. $C_{13}H_{21}NO$. Calculated (%): C, 75.32; H, 10.21; N, 6.76.

2-Adamantyl(phenyl)methanone (*Z*)-oxime (5c). Yield 79%, m.p. 218—220 °C. IR, ν/cm^{-1}: 3269 (OH); 2920, 2858 (CH_{Ad}); 1452, 1443, 1358, 1099, 972, 945, 883, 833, 764, 721, 698. ^{1}H NMR ($CDCl_3$), δ: 1.62 (d, 2 H, H_{Ad}, J = 12.2 Hz); 1.70—1.90 (m, 8 H, H_{Ad}); 2.02 (br.s, 2 H, H_{Ad}); 2.07 (d, 2 H, H_{Ad}, J = = 12.8 Hz); 2.84 (s, H, H_{Ad}(2)); 7.25—7.29 (m, 2 H, Ph); 7.33—7.43 (m, 3 H, Ph); 8.11 (br.s, 1 H, OH). ^{13}C NMR ($CDCl_3$), δ: 27.9 and 28.1 (C(5)H_{Ad}, C(7)H_{Ad}); 29.5 (C(1)H_{Ad}, C(3)H_{Ad}); 32.4 (2 $(CH_2)_{Ad}$); 37.8 (H_2C(6)$_{Ad}$); 38.8 (2 $(CH_2)_{Ad}$); 49.8 (C(2)H_{Ad}); 127.4 (2 CH_{Ph}); 128.3 (2 CH_{Ph}); 128.4 (CH_{Ph}); 134.0 (C_{Ph}); 161.2 (C=N). Found (%): C, 79.89; H, 8.20; N, 5.42. $C_{17}H_{21}NO$. Calculated (%): C, 79.96; H, 8.29; N, 5.49.

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