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Sodium Borohydride in an Acetonitrile Medium: an Efficient Reagent for Reductive Beckmann Type Fragmentation of α-Amino Oximes

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Abstract: When treated with sodium borohydride in boiling acetonitrile, α-amino oximes are transformed to the corresponding ω-amino nitriles in 31-87% yield. Easily available α-amino oximes with cyclohexane, methylcyclohexene, *p*-menthane, carane, pinane, and caryophyllane carbon skeletons are tested. The reaction was found to proceed only in an aliphatic nitrile medium; the specific role of a nitrile is discussed. Beckmann synchronous mechanism was confirmed for the fragmentation stage followed by reduction of the intermediate immonium salt.

Trying to convert a number of terpenic α-amino oximes to the corresponding 1,2-diamino derivatives, we have found that on treatment with sodium borohydride in an acetonitrile medium certain oximes of this type undergo reductive fragmentation resulting in formation of ω-amino nitriles[2]. Because the reaction results in the carbon-carbon bond cleavage and transformation of the oxime to the nitrile group, it may be formally classified as a variant of the Beckmann fragmentation. In this paper we wish to report the results of an extended study of the behavior of a variety of α-substituted oximes and the discussion of some peculiar features and possible mechanism of the reaction.

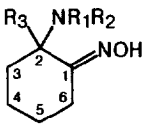
On the one hand, α-amino oximes, as well as α-hydroxy, α-methoxy and α-mercapto oximes, are known to undergo Beckmann fragmentation to give aldo and keto nitriles.[3,4] Compounds such as TsCl, $SOCl_2$, PCl_5, which transform the hydroxyl of the oxime group to a ready leaving group, are conventional reagents for the fragmentation of the oximes having an electron donor substituent adjacent to the α-position of the oxime group. The fragmentation of this type proceeds under mild conditions; more drastic conditions are required in the absence of readily leaving groups.[5] On the other hand, reductive transformations of the oxime group have been studied extensively. Reduction of aldo and keto oximes is known to be a general method for preparing primary amines.[6] Different reagents are used for this purpose: alkali metals in alcohols,[7] Zn-NH_4OAc,[8] $SnCl_2$-HCl,[9] $LiAlH_4$,[10] $NaAlH_4$,[11] BH_3,[12] AlH_3,[13] $(CH_3OCH_2CH_2O)_2AlH$.[14] Generally sodium borohydride does not reduce oximes.[6,15] At the same time, some mixed reagents containing sodium borohydride as one of the components, or certain sodium borohydride derivatives, such as $NaBH_4$-LiBr,[16] $NaBH_4$-$AlCl_3$,[17] $NaBH_2S_3$,[18] are used for transformations of oximes to the corresponding primary amines. Hydrogenation over Renay nickel either at high (60-100 atm) or at low hydrogen pressure[19] as well as the reduction over platinum metals[20,21] has been widely employed. Reduction of oximes with titanium(III) salts, being formally expressed as hydrolysis, has become an excellent method for regeneration of carbonyl compounds from the corresponding oximes.[22] Certain oximes may be transformed to rearranged secondary amines when treated with $LiAlH_4$[23] or $(i\text{-}Bu)_2AlH$.[24] Formation of aziridines in the reduction of aromatic oximes with $LiAlH_4$ is also reported.[25]

Hydroxylamino derivatives may be prepared in good yields by reduction of oximes with $NaBH_3CN$,[26] pyridine-borane,[27] Et_3SiH-CF_3COOH.[28] In some specific cases such reducing agents as $LiAlH_4$, $Na(CH_3OCH_2CH_2O)_2AlH_2$, Alk_3Al induce Beckmann rearrangement of oximes.[29] Finally, Beckmann fragmentation is possible when oximes are treated with reducing agents (R_3Al) in the presence of Lewis acids ($ZnCl_2$).[30] Thus, the literature on different aspects of reductive transformations of oxime group is extensive and diverse, but oximes have not been reported to undergo Beckmann fragmentation under the action of sodium borohydride or other reducing agents without assistance of Lewis acids.

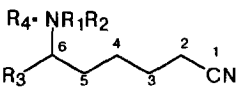
The resulting ω-amino nitriles are of special interest and may possess biological activity since a number of the simplest ω-amino nitriles are known to be acetylcholine esterase inhibitors.[31,32,33] Absence of simple synthetic methods for the ω-amino nitriles preparation stimulated our further investigation in this field because the reaction may be used as the basis for the general method for syntheses of different ω-amino nitriles.

RESULTS

The reaction of α-amino oximes of cyclohexene **1a**, methylcyclohexene **2a**, (+)-3-carene **3a-7a**, limonene **8a-10a**, α-terpinene **11a**, α-pinene **12a-13a** and caryophyllene **16a** types having distinct substituents at the amine nitrogen along with 3-methoxy oxime **14a** and 3-mercapto oxime **15a** with sodium borohydride was studied.[34] The reaction was carried out as follows. A suspension of an α-substituted oxime and sodium borohydride in acetonitrile was heated to boiling point (H_2 evolution was being observed during the first few minutes of the reaction) and was stirred at reflux until the disappearance of the starting material (TLC). This period was described as the reaction time (see **Table 1** in the **EXPERIMENTAL**). The desired ω-amino nitriles **19** and the corresponding amino borane complexes **20** were the main reaction products (**Scheme 1**). The total yields of the reaction products (**19** + **20**) were between 31% (for compound **1a**) and 87% (for compound **12a**). As it was shown in our preliminary experiments, such treatment of the reaction mixture in the case of the caryophyllene type amino oxime **16a** resulted in poor yield of the desired products because of hydroborating of the carbon-carbon double bond (^1H and ^{13}C NMR). The hydroboration could be avoided if adding HCl. It was this pattern of decomposition of the borohydride excess that was used in the transformations of compounds **8a**, **9a**, **11a**, **16a**. Amino boranes **2c** and **3c** were isolated and their structure was proved by mass-spectra, IR-spectroscopy (ν_{B-H} = 2220-2500 cm^{-1} and δ_{B-H} = 1165 cm^{-1}) and ^1H NMR spectra [δ_H for H_3B–$NR(C\underline{H}_3)_2$ are 2.42 and 2.50 ppm]. When treated with trifluoroacetic acid the borane-ω-amino nitrile complexes are easily transformed to the corresponding ω-amino nitriles in good yields. Such regeneration of amines from the corresponding borane-amine complexes is known for the simplest derivatives.[35] Elimination of dialkylamino group with the formation of the corresponding α,β-unsaturated oximes **17** was the main side reaction in the case of the α-amino oximes having tertiary amino group. As an example, (1*S*,6*R*)-2-carene-4-one (E)-oxime[36] was isolated and identified in the case of 3-carene derivatives **3a** and **7a**. It is interesting that the cleavage of the α-amino oximes by sodium borohydride takes place only in the presence of aliphatic nitriles (boiling CH_3CN; hexanenitrile, 80°C; 10% H_2O in CH_3CN at 80°C). In all other solvents tested (DMF, 80°C and under reflux; H_2O, 80°C; boiling Et_2O; 1,4 dioxane, 80°C; HMPA, 45°C and 80°C; PhCN, 80°C; nitroethane, 70°C; benzene, 80°C; 2-PrOH, 40°C and 70°C; diglyme, 40°C and 80°C) no ω-amino nitriles was found, mainly unsaturated oximes appeared even on long standing of amino oximes in the presence of sodium borohydride.

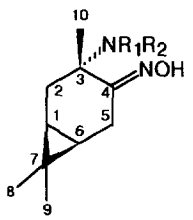


1a-2a

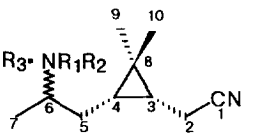


1b-2b,2c

	R_1	R_2	R_3	R_4
1a,1b	CH_3	CH_3	H	-
2a,2b	CH_3	CH_3	CH_3	-
2c	CH_3	CH_3	CH_3	BH_3

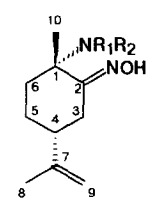


3a-7a

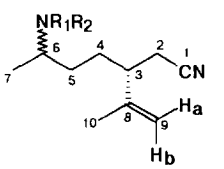


3b-6b,3c

	R_1	R_2	R_3
3a,3b	CH_3	CH_3	-
3c	CH_3	CH_3	BH_3
4a,4b	H	H	-
5a,5b	H	Ph	-
6a,6b	H	CH_2Ph	-
7a	N-morpholino		-

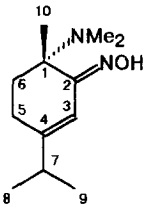


8a-10a

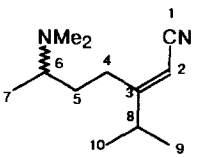


8b-9b

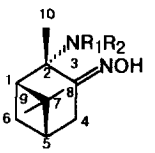
	R_1	R_2
8a,8b	CH_3	CH_3
9a,9b	H	CH_2Ph
10a	N-morpholino	



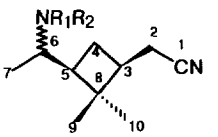
11a



11b

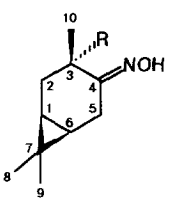


12a,13a

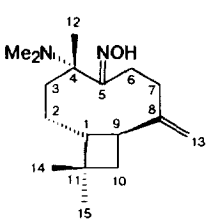


12b

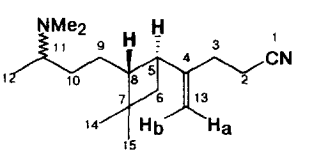
	R_1	R_2
12a,12b	H	CH_2Ph
13a	N-morpholino	



14a R = OCH_2
15a R = SH



16a



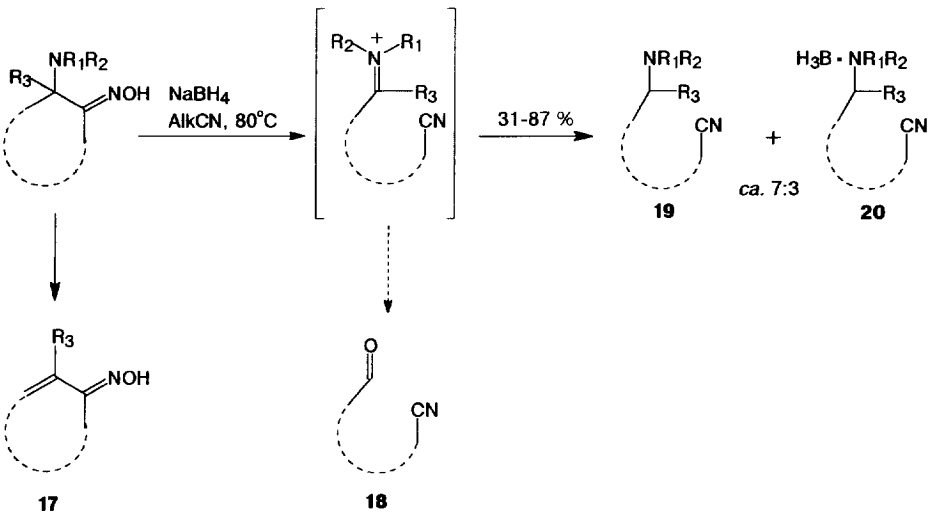
16b

The numbering of the C-atoms is given for NMR interpretation only and in some cases it does not coincide with the numbering of the system according to IUPAC.

DISCUSSION

Hypothetical scheme of the ω-amino nitrile formation from the corresponding α-amino oxime provides for the reduction of intermediate immonium salt, whose formation is typical for the usual Beckmann fragmentation leading to the corresponding carbonyl compound **18** due to the hydrolysis of this intermediate (Scheme 1):

Scheme 1

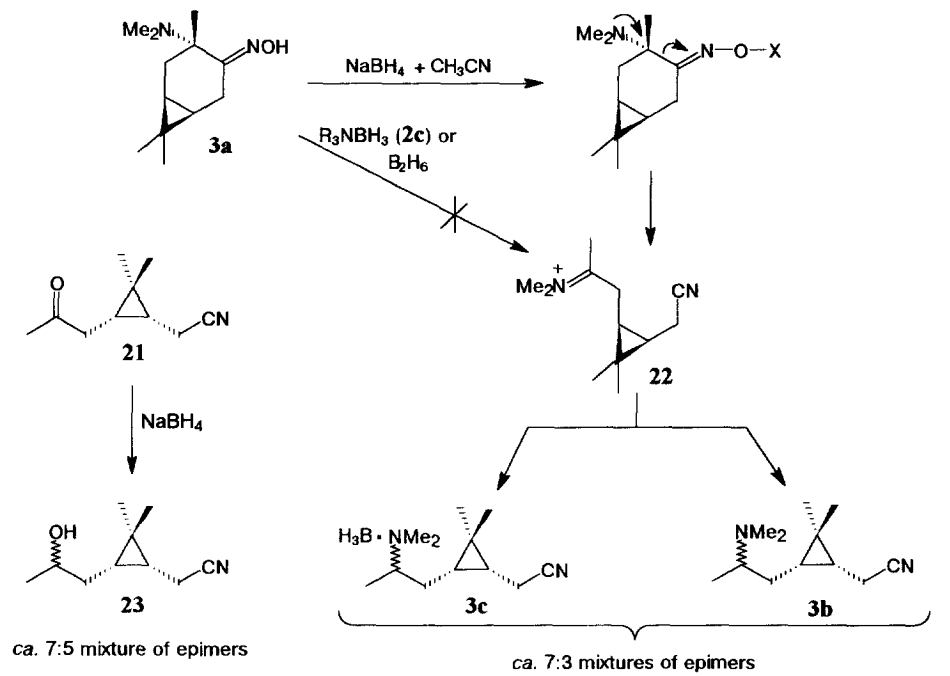


The mechanism and the reaction conditions of the Beckmann fragmentation are rather thoroughly studied.[37] Beckmann fragmentation is known to include the formation of the intermediate onium compound. In the case of the α-amino oximes fragmentation, the immonium salt has to be the intermediate species, and hydrolysis of this intermediate just leads to keto or aldo nitriles **18**.[3] Thus it should be clarified whether the reaction studied actually proceeds according to synchronous Beckmann mechanism with the reduction of the intermediate onium compounds, or another mechanism takes place.

One of the products of an α-amino oxime and sodium borohydride reaction is ω-amino borane complex, which might result from the reaction of ω-amino nitrile with diborane (borane). Additionally, borane-amine complexes were detected in the reaction mixture prior to hydrolysis (TLC). Although the ratio *amino nitrile/borane-amine complex* was dependent on the method of the $NaBH_4$ excess decomposition (see **EXPERIMENTAL**), the ratio 7:3 borane-amine complex/amine was found to be a result of the reaction itself - that is amino borane arises along with amino nitrile.

Our attempts to use solvents other than alkylnitriles have not been successful. We also tried to carry out the reaction under the action of diborane and amino borane **2c** (see **EXPERIMENTAL** and Scheme 2), but there were no changes in the reaction mixture even after 5 h. Immonium salt **22** formed may be reduced with sodium borohydride[38] to give free ω-amino nitrile **3b** or ω-amino borane **3c**. At the same time immonium salt **22** may be reduced with amino borane as well[39] forming free amino nitrile **3b**. Reduction of immonium salt by sodium borohydride is the most reasonable way of borane complex formation (Scheme 2).

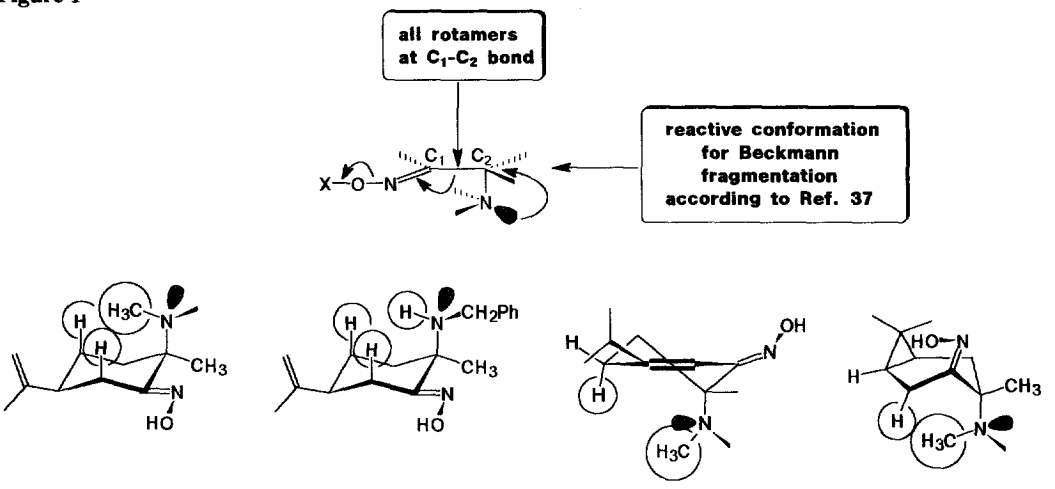
Scheme 2



In the case of starting compound **3a** mixtures of the ω-amino nitrile diastereomers **3b** in the ratio *ca.* 7:3 and ω-amino borane diastereomers **3c** in the ratio *ca.* 7:3 are formed (Scheme 2). Much the same ratio was previously found for epimeric alcohols **23** arising on keto nitrile **21** reduction by sodium borohydride.[40] Thus the mechanism of nucleophilic assistance to fragmentation has to be eliminated from the consideration as only one (or predominantly one) of the diastereoisomers would be formed in that case.

Immonium salt **22** is therefore the intermediate product of the reaction studied. As the data of Table 1 indicate that in general the reaction time increases as the stability of intermediate immonium salt decreases (or what is the same, as basicity of substituents in α-position to oxime function decreases). For the (+)-3-carene derivatives relative rates of the reaction coincide with the sequence of the immonium salt stability: NHPh<NH_2<$NHCH_2Ph$<NMe_2. In this case the reaction is under the control of electronic factors (the stability of intermediate immonium salt). For the limonene derivatives the reaction time for dimehtylamino derivative **8a** is longer than for benzylamino derivative **9a**. This is easily explained in the event that the fragmentation reaction proceeds synchronously. The synchronous process makes specific demands on the reactive conformation (the stereoelectronic reaction control, Figure 1).[37] Thus, antiperiplanar orientation of both the hydroxyl group of the oxime moiety and the lone pair of the nitrogen atom of the amino group with respect to the C1-C2 bond are required for performing the reaction (therewith rotamers of C1-C2 bond can participate in the reaction as well). Dimethylamino oxime of the limonene series **8a** is bound to have an extremely unfavorable reactive conformation because of non-bonded interaction of two axial hydrogens in 6-membered ring with one of the methyls of dimethylamine substituents (Figure 1).

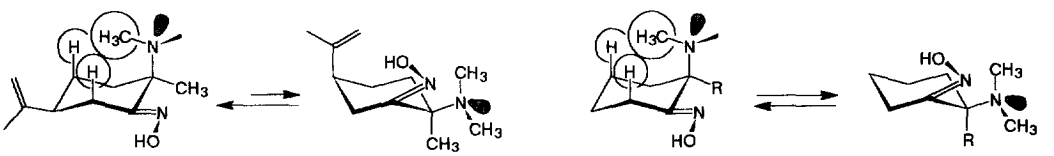
Figure 1



8a **9a** **11a** **3a**

In the case of α-amino oximes derived from cyclohexene and methylcyclohexene (**1a** and **2a** respectively), cycle inversion brings about no additional destabilizing interaction. So, despite of the substituted amino group occupying an axial position in these compounds (according to ^{1}H and ^{13}C NMR spectroscopy) the reaction can proceed (partially or completely) *via* the inverted conformation having equatorial amino group. This proposal is indirectly supported by shorter reaction time of amino oxime **1a** (6 h) as compared with the corresponding methyl derivative **2a** (6 h 50 min). The additional methyl group makes less favorable reactive conformation with an equatorial amino group in the case of compound **2a**.

Scheme 3



8a **1a R=H** **2a R=Me**

Thus, there is strong reason to assume that the reaction described is under stereoelectronic and electronic controls.

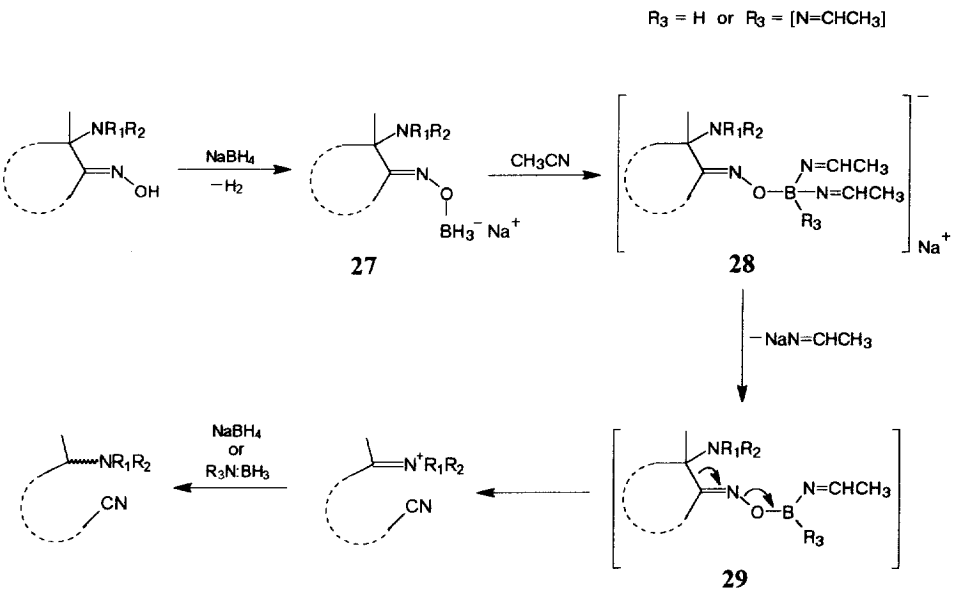
Our attempts to employ the reductive fragmentation for α-methoxy oxime **14a** and α-mercapto oxime **15a** derived from (+)-3-carene have not been successful. α-Methoxy oxime **14a** was unaffected when treated with $NaBH_4$ in boiling acetonitrile: fragmentation is likely to take place too slowly due to insufficient stability of the oxonium ion. On the contrary α-mercapto oxime **15a** was converted rapidly (1h), but the main product was unsaturated oxime - (1*S*,6*R*)-2-carene-4-on (E)-oxime.[36] The rate of the sulfur-containing group elimination is most likely to exceed considerably the rate of all other reactions including the fragmentation.

Although aliphatic nitriles are to be inert toward the action of sodium borohydride[41] we have found that it is not quite so. We prepared a solution of $NaBH_4$ in acetonitrile (a suspension of $NaBH_4$ in acetonitrile was

stirred at reflux for 1 h and undissolved solid was removed by filtration) and studied its ^{1}H NMR spectra. Besides the signals of the solvent (δ 1.73 *s*) and $NaBH_4$ (δ −0.55 *q*, $^1J_{H-^{11}B}$ = 81 Hz; according to lit.[42] $^1J_{H-^{11}B}$ = 82 Hz) there was a set of signals (δ 1.03 *t*, *J* = 7 Hz; δ 2.59 *tq*, *J* = 7 and 7 Hz; δ 3.60 *br.*, $W_{1/2}$ = 65 Hz) that may be assigned to ethylamino borane complex $CH_3CH_2NH_2BH_3$. This complex was previously studied and found to be very unstable one.[43] So the following pathway of the reaction is suggested (Scheme 4).

Because H_2 evolution occurs at the initial period of the reaction, the first intermediate product must be drawn as oxime ether **27**. The complexes $(RO)BH_3Na$ are more strongly reducing compared with $NaBH_4$,[44] so complex **27** may take part in the reduction of the acetonitrile to give adduct **28** (two or three hydrogen atoms may be replaced by the group -N=CHCH$_3$). Elimination of sodium salt of acetaldimine from the molecule **28** gives rise to adduct **29** having the readily leaving group with trivalent boron atom.

Scheme 4



Thus the reaction found is the general method for the preparation of ω-amino nitriles and may be used as the final step in the reaction sequence leading from unsaturated hydrocarbons (certain terpenes and less complex molecules) *via* nitrosochlorides and α-amino oximes[4] to the corresponding α,ω-functionalized *seco*-derivatives.

EXPERIMENTAL

General experimental.

Petroleum ether refers to that fraction which boils in the range 70-100°C. Diethyl ether was freshly distilled. Other reagent quality solvents were used without further purification. Analytical TLC plates were **"Silufol"®** (SILPEARL on aluminum foil, Czechoslovakia). Silica gel "KSK" (Russia, 100-200 mech., air dried and activated at 140°C for 5 h) was used for column chromatography. IR spectra were obtained for 1% solutions unless otherwise stated using a ***Specord M-80*** infrared spectrometer. IR spectrum for compound **15a** was obtained using a ***Bruker* IFS-66** infrared spectrometer. UV spectra (1×10^{-4} M solutions in EtOH) were

obtained on a ***Specord UV VIS*** spectrometer. A ***Polamat A*** polarimeter was used to measure optical rotation at 578 nm. Melting points were obtained using a ***Kofler*** melting point apparatus. Microanalyses were obtained using a ***Hewlett Packard 185*** analyzer and a ***Carlo Erba 1106*** analyzer. For some of the new compounds, precise mass determinations for the molecular ion of a pure sample were obtained instead of combustion analyses. Mass spectra were recorded on a ***Finnigan MAT-8200*** instrument using Electron Impact Ionization Technique (70 eV). ^{1}H and ^{13}C NMR spectra were recorded using a ***Bruker AC-200*** spectrometer (^{1}H 200.13 MHz, ^{13}C 50.32 MHz) locked to deuterium resonance of the solvent ($CDCl_3$). The chemical shifts were calculated relative to the solvent signal using as internal standard: δ_H 7.24 ppm, δ_C 76.90 ppm.

Starting amino oximes.

Starting α-amino oximes were synthesized from the corresponding hydrocarbons *via* crystalline dimeric nitrosochlorides.[45,46] The following α-amino oximes were identical with those published earlier: (1*S*,3*S*,6*R*)-3-dimethylaminocaran-4-one (E)-oxime **(3a)**,[45,47] (1*S*,3*S*,6*R*)-3-N-phenylaminocaran-4-one (E)-oxime **(5a)**,[45,47] (1*S*,3*S*,6*R*)-3-morpholinocaran-4-one (E)-oxime **(7a)**,[4,45] (±)-(1*S**,4*R**)-1-dimethylamino-*p*-menth-7-en-2-one (E)-oxime **(8a)**,[4] (±)-(1*S**,4*R**)-1-benzylamino-*p*-menth-7-en-2-one (E)-oxime **(9a)**,[46,47] (±)-(1*S**,4*R**)-1-morpholino-*p*-menth-7-en-2-one (E)-oxime **(10a)**,[46,47] (±)-(1*S**,2*S**,5*S**)-2-benzylaminopinocamphone (E)-oxime **(12a)**,[46,47] (±)-(1*S**,2*S**,5*S**)-2-morpholinopinocamphone (E)-oxime **(13a)**,[46,47] (1*S*,9*S*,)-4-dimethylamino-4,5-dihydrocaryophyllen-5-one (E)-oxime **(16a)** (mixture of C-4 epimers).[4]

(±)-2-Dimethylaminocyclohexanone (E)-oxime **(1a):** m.p. 121-123°C (CCl_4) (lit.[3] 119-120°C from CH_3OH); IR ($CHCl_3$): ν = 3600, 3300 (O-H), 1630 (C=N), 940 cm^{-1} (N-O); NMR ^{1}H ($CDCl_3$): δ = 2.15 *s* (NMe_2), 2.58 *dd* ***J*** = 3.5 and 3.5 Hz (H^2), 2.99 *ddd* ***J*** = 14.0, 3.5 and 3.5 Hz ($H^{6\beta}$), 9.71 *br.s* $W_{1/2}$ = 24 Hz (NOH); NMR ^{13}C ($CDCl_3$): δ = 20.18 (C^4), 21.36 (C^6), 25.99 (C^5), 30.38 (C^3), 43.00 (NMe_2), 66.74 (C^2), 161.42 (C^1).

(±)-2-Methyl-2-Dimethylaminocyclohexanone (E)-oxime **(2a):** m.p. 98-101°C (CH_3CN) (lit.[3] 99-101°C from CH_3OH); IR ($CHCl_3$): ν = 3600, 3300 (O-H), 1630 (C=N), 940 cm^{-1} (N-O); NMR ^{1}H ($CDCl_3$:CCl_4 = 1:1): δ = 2.12 *s* (NMe_2), 3.17 *dddd* ***J*** = 13.5, 2.5, 2.5 and 2.0 Hz ($H^{6\beta}$), 9.53 *s* $W_{1/2}$ = 8 Hz (NOH); NMR ^{13}C ($CDCl_3$:CCl_4 = 1:1): δ = 12.35 (C^7), 20.25 (C^4), 20.63 (C^6), 26.37 (C^5), 37.55 (NMe_2), 38.76 (C^3), 61.15 (C^2), 164.65 (C^1).

(1S,3S,6R)-3-Aminocaran-4-one (E) oxime **(4a)**. M.p. 78-80°C (CH_3CN), $[\alpha]^{25}$ +141 (*c* = 8.88, $CHCl_3$). Found: C 65.5, H 9.9, N 15.3. Calclulated for $C_{10}H_{18}N_2O$: C 65.90, H 9.95, N 15.37. IR (CCl_4): ν = 3580, 3300 (OH), 930 cm^{-1} (N-O); NMR ^{1}H (C_6D_6:CCl_4 = 1:5 v/v): δ = 0.72 *m* (H^1), 0.77 *s* (H^8), 0.80 *m* (H^6), 0.99 *s* (H^9), 1.18 *s* (H^{10}), 1.24 *dd* ***J*** = 14.5 and 5.0 Hz ($H^{2\beta}$), 1.99 *dd* ***J*** = 14.5 and 9.0 Hz ($H^{2\alpha}$), 2.44 *dd* ***J*** = 19.0 and 8.5 Hz ($H^{5\alpha}$), 2.78 *dd* ***J*** = 19.0 and 1.5 Hz ($H^{5\beta}$); NMR ^{13}C ($CDCl_3$:CCl_4 = 1:1 v/v): δ = 14.39 (C^8), 16.91 (C^1 or C^6), 17.21 (C^5), 18.19 (C^6 or C^1), 18.52 (C^7), 25.35 (C^{10}), 27.90 (C^9), 34.12 (C^2), 50.84 (C^4), 162.72 (C^4).

(1S,3S,6R)-3-Benzylaminocaran-4-one (E)-oxime **(6a):** viscous oil; $[\alpha]^{20}$ +221 (*c* = 1.27, $CHCl_3$); IR ($CHCl_3$): ν = 3600, 3300 (O-H), 900 cm^{-1} (N-O); NMR ^{1}H (CCl_4:$CDCl_3$ = 2:1, v/v): δ = 0.85 *s* (H^9), 1.03 *s* (H^8), 1.25 *s* (H^{10}), 1.42 *dd* ***J*** = 14.5 and 5.0 Hz ($H^{2\beta}$), 2.24 *dd* ***J*** = 14.5 and 9.0 Hz ($H^{2\alpha}$), 2.30 *dd* ***J*** = 19.0 and 8.5 Hz ($H^{5\alpha}$), 2.97 *dd* ***J*** = 19.0 and 1.0 Hz ($H^{5\beta}$), 3.46 *d* ***J*** = 12.5 Hz and 3.72 *d* ***J*** = 13.0 Hz ($\underline{CH_2}$Ph), 7.25 *m* (<u>H</u>-Ph); NMR ^{13}C (CCl_4:$CDCl_3$ = 2:1, v/v): δ = 14.60 (C^8), 16.65 (C^1), 17.91 (C^5) , 19.01 (C^7), 19.16 (C^6), 21.95 (C^{10}), 28.10 (C^9), 34.82 (C^2), 47.55 ($\underline{CH_2}$Ph), 55.00 (C^3), 160.98 (C^4); 126.81 (*meta*-C), 128.30 (*ortho*-C), 128.33 (*para*-C), 140.63 (*ipso*-C). ***(1S,3S,6R)-3-Benzylaminocaran-4-one (E)-oxime hydrochloride*** was

obtained from oxime **6a** and gaseous HCl in an ethereal solution; m.p. 103-105°C. Found: C 66.0, H 8.4, Cl 11.2, N 9.1. Calc. for $C_{17}H_{25}ClN_2O$: C 66.11, H 8.16, Cl 11.48, N 9.07.

(1S)-1-Dimethylamino-p-menth-3-en-2-one (E)-oxime **(11a).** Sulfuric acid (96 %, 36 mL) was added dropwise to a stirred solution of amino oxime **3a** (6 g, 28.6 mmol) in CH_2Cl_2 (30 mL) at 0°C. The reaction mixture was heated to 40°C and kept at this temperature for 15 min. The reaction mixture was poured into ice-cooled water (100 mL), extracted with Et_2O (3×100 mL). The aqueous layer was treated with aq NH_3 (pH 14), extracted with Et_2O (3×70 mL). The combined etheral extracts were washed with water (70 mL), brine (70 mL), dried ($MgSO_4$) and evaporated at reduced pressure to give the title compounds as dark brown crystals: yield 2.5 g (42%). Recrystallization of the crude product from acetonitrile gave an analytical sample as white crystals. R_f = 0.3 (CH_3OH:$CHCl_3$ = 2:8 v/v); m.p. 111-113°C (CH_3CN) (lit.[48] for racemate 160-161° C from ethanol); $[\alpha]^{19}$ +246 (*c* = 1.75, $CHCl_3$). Found: C 68.1, H 11.0, N 13.0. Calc. for $C_{12}H_{22}N_2O$: C 68.53, H 10.54, N 13.32. IR (CCl_4): ν = 3600 (O-H), 1630 (C=N), 937 cm^{-1} (N-O); UV: λ_{max} = 239 nm ($lg\varepsilon$ = 4.16); NMR ^1H ($CDCl_3$:CCl_4 = 1:1): δ = 1.02 *d* ***J*** = 7.0 Hz and 1.04 *d* ***J*** = 7.0 Hz (H^9 and H^8), 1.05 *s* (H^{10}), 2.18 *s* (NMe_2), 6.42 *br. s* $W_{1/2}$ = 4.5 Hz (H^3), 10.3 *br.* (NOH); NMR ^{13}C ($CDCl_3$:CCl_4 = 1:1): δ = 13.93 (C^{10}), 21.01 (C^9 or C^8), 21.10 (C^8 or C^9), 24.14 (C^5), 33.86 (C^6), 35.01 (C^7), 38.40 (NMe_2), 57.85 (C^1), 109.06 (C^3), 155.60 (C^2), 156.08 (C^4); MS: *m/z* (%) = 210.1738 [(M)+,5; calc. for $C_{12}H_{22}N_2O$, 210.1732], 209 (4), 195 (7), 194 (30), 178 (7), 177 (15), 168 (6), 167 (44), 166 (6), 164 (33), 152 (9), 150 (15), 124 (16), 123 (36), 122 (9), 108 (10), 107 (12), 106 (15), 91 (12), 85 (100), 70 (45), 56 (38), 46 (36).

(1S,3S,6R)-3-Methoxycaran-4-one (E)-oxime **(14a)**. M.p. 102-103°C (EtOAc); $[\alpha]^{21}$ +128 (*c* 4.22, $CHCl_3$). Found: C 67.2, H 10.0, N 6.9. Calc. for $C_{11}H_{19}NO_2$: C 66.97, H 9.71, N 7.10. IR ($CHCl_3$): ν = 3300, 3600 (O-H), 960 cm^{-1} (N-O); NMR ^1H ($CDCl_3$): δ = 0.74 *s* (H^9), 0.74 *ddd* ***J*** = 10.0, 10.0 and 5.0 Hz (H^1), 0.91 *ddd* ***J*** = 10.0, 9.0 and 1.0 Hz (H^6), 0.96 *s* (H^8), 1.35 *dd* ***J*** = 16.0 and 5.0 Hz ($H^{2\beta}$), 1.96 *s* (H^{10}), 2.22 *dd* ***J*** = 18.0 and 9.0 Hz ($H^{5\alpha}$), 2.24 *dd* ***J*** = 16.0 and 10.0 Hz ($H^{2\alpha}$), 2.97 *dd* ***J*** = 18.0 and 1.0 Hz ($H^{5\beta}$), 3.09 *s* (OCH_3); NMR ^{13}C ($CDCl_3$): δ = 14.31 (C^8), 16.77 (C^1), 18.16 (C^5), 18.26 (C^7), 19.52 (C^9), 19.82 (C^6), 27.87 (C^{10}), 34.64 (C^2), 50.41 (OCH_3), 74.23 (C^3), 160.91 (C^4).

(1S,3S,6R)-3-Mercaptocaran-4-one (E)-oxime **(15a)**. A stirred suspension of carene nitrosochloride (5 g, 26.7 mmol) and $Na_2S{\times}9H_2O$ (25 g, 0.104 mol) in methanol (200 mL) was heated to boiling point and allowed to reflux for 45 min. The reaction mixture was cooled to room temperature and an excess of $Na_2S{\times}9H_2O$ was separated by filtration. Methanol was evaporated and the residue was treated with H_2O (50 mL). The mixture was extracted with Et_2O (3×50 mL), organic layer was separated and the aqueous phase was treated with 5N aq HCl (50 mL), extracted with Et_2O (3×50 mL). The combined etheral extracts were washed with water (40 mL), brine (40 mL), dried ($MgSO_4$) and evaporated at reduced pressure to give the crude product as yellow crystals; yield 1.18 g (22%). Recrystallization of the crude product from CH_3CN gave an analytical sample (white crystals). R_f = 0.7 (Et_2O:petroleum ether = 4:6 v/v); m.p. 67-69°C (CH_3CN), $[\alpha]^{30}$ +213 (*c* = 3.08, $CHCl_3$). Found: C 58.2, H 8.7, N 6.7, S 18.3. Calc. for $C_{10}H_{17}NOS$: C 60.26, H 8.60, N 7.03, S 16.09. IR (1% in CCl_4): ν = 3599 (O-H), 2583 (*S*-H), 950 cm^{-1} (N-O); ^1H NMR ($CDCl_3$): δ = 0.73 *s* (H^8), 0.86 *ddd* ***J*** = 9.5, 9.5 and 5.5 Hz (H^1), 0.94 *ddd* ***J*** = 9.5, 9.5 and 3.0 Hz (H^6), 1.01 *s* (H^9), 1.50 *s* (H^{10}), 1.41 *dd* ***J*** = 15.0 and 5.5 Hz, $W_{1/2}$ = 3 Hz ($H^{2\beta}$), 2.20 *dd* ***J*** = 15.0 and 9.5 ($H^{2\alpha}$), 2.66 *dd* ***J*** = 19.0 and 7.5 ($H^{5\alpha}$), 2.80 *dd* ***J*** = 19.0 and 2.5 ($H^{5\beta}$), 9.55 *s* (NOH), 2.21 *s* (SH); ^{13}C NMR ($CDCl_3$): δ = 14.58 (C^8), 17.75 (C^5), 17.89 (C^1), 18.44 (C^6), 18.82 (C^7), 27.67 (C^9), 28.11 (C^{10}), 36.29 (C^2), 45.53 (C^3), 163.16 (C^4).

ω-Amino nitriles and corresponding amino borane complexes. General procedures.

Method A. A stirring suspension of an α-amino oxime (1 mmol) and sodium borohydride (0.2 g, 6 mmol) in CH_3CN (5 mL) was heated to boiling point and allowed to reflux for a certain period of time (see Table 1) up to the disappearance of the starting material (TLC). The mixture was cooled to room temperature and 9N aq HCl (4 mL) was added dropwise. The resultant mixture was extracted with Et_2O (2×8 mL). The combined etheral extracts were washed with water (5 mL), brine (5 mL), dried ($MgSO_4$) and evaporated at reduced pressure to give corresponding amino borane as yellow oil. R_f = 0.5-0.7 (Et_2O:petroleum ether = 4:6 v/v). The aqueous phase was treated with concentrated aq. ammonia (6 mL, pH 11) and extracted with Et_2O (2×10 mL). The combined etheral extracts were washed with water (5 mL), brine (5 mL), dried ($MgSO_4$) and evaporated at reduced pressure to give corresponding amino nitrile as yellowish oil, R_f = 0.2-0.4 (CH_3OH:$CHCl_3$ = 2:8 v/v). The crude amino borane was chromatographed on a silica gel column (Et_2O:petroleum ether = 2:10 v/v) to give an analytical sample of the amino borane as colorless oil. The crude amino nitrile was chromatographed on a silica gel column ($CHCl_3$:CH_3OH = 20:1 v/v), followed by vacuum sublimation to give an analytical sample of the amino nitrile as colorless oil.

Method B. A stirring suspension of an α-amino oxime (1 mmol) and $NaBH_4$ (6 mmol, 0.22 g) in acetonitrile (5 mL) was heated to boiling point and allowed to reflux for a certain period of time (Table 1) up to the disappearance of the starting material (TLC). The mixture was cooled to 0°C and 1N aq HCl (36 mL) was added dropwise at the same temperature. Further treatments were the same as in the case of ***Method A***.

Table 1.

Conversion times of α-amino oximes and yields of the corresponding fragmentation products.

Starting compound	Method	Reaction time	Total yiled (%) of the fragmentation products (amino nitrile + amino borane complex)[a]	Isolated products (yield, %)[b]
1a	A	6 h	45	**1b** (31)
2a	A	6 h 50 min	70	**2b** (49), **2c** (21)
3a	A	30 min	60	**3b** (40), **3c** (20)
4a	A	1 h 50 min	52	**4b** (36)
5a	A	15 h 30 min	80	**5b** (55)
6a	A	1 h 30 min	45	**6b** (32)
8a	B	11 h	71	**8b** (50)
9a	B	1 h	75	**9b** (53)
11a	B	2 h 30 min	33	**11b** (20)
12a	A	2 h 40 min	87	$\mathbf{12b}_{min}$ (21), $\mathbf{12b}_{maj}$ (28)
16a	B	2 h	71	**16b** (50)

[a] amino nitrile/amino borane complex = 7/3; [b] as an example, amino borane complexes were isolated in the cases of fragmentation of oximes **2a** and **3a**.

Borane-amine/amine ratio. A stirring suspension of α-amino oxime **2a** (1 mmol, 0.15 g) and sodium borohydride (6 mmol, 0.22 g) in CH_3CN (5 mL) was heated to boiling point and allowed to reflux for 6 h 30 min. The mixture was cooled to room temperature and the excess of $NaBH_4$ was decomposed using one of the methods listed below. The following values of **2b/2c** ratio were found:

(a) addition of 1N aq. HCl (spontaneous boiling) – 34:66;

(b) addition of 1N aq. HCl at 0°C – 32:68;

(c) addition of the reaction mixture to conc. aq. HCl (spontaneous boiling) – 35:65;

(d) addition of conc. aq. HCl (spontaneous boiling) – 31:65;

(e) addition of conc. H_2SO_4 (spontaneous boiling) – 7:93;

(f) addition of H_2O at 20°C – 25:75.

6-Dimethylaminohexanenitrile **(1b)**. IR ($CHCl_3$): ν_{max} = 2250 cm^{-1}; MS, *m/z*: 140.1316 (M^+, Calc. for $C_8H_{16}N_2$ 140.1313); ^1H NMR ($CDCl_3$): 1.40-1.80 *m* (H^3, H^4, H^5), 2.20-2.40 *m* (H^6), 2.22 *s* (NMe_2), 2.32 *t* ***J*** = 7.5 Hz (H^2); ^{13}C NMR ($CDCl_3$): 16.98 (C^2), 25.21 (C^3, C^4 or C^5), 26.38 (C^3, C^4 or C^5), 26.6 (C^3, C^4 or C^5), 45.18 (NMe_2), 59.0 (C^6), 119.48 (C^1).

6-Dimethylaminoheptanenitrile **(2b)**. IR ($CHCl_3$): ν_{max} = 2250 cm^{-1}; MS, *m/z*: 154.1461 (M^+, Calc. for $C_9H_{18}N_2$ 154.1470); ^1H NMR ($CDCl_3$): 0.93 *d* ***J*** = 6.5 Hz (H^7), 1.15-1.75 *m* (H^3, H^4, H^5), 2.20 *s* (NMe_2), 2.31 *t* ***J*** = 7.0 Hz (H^2), 2.52 *qt* ***J*** = 5.0 and 5.0 Hz (H^6); ^{13}C NMR ($CDCl_3$): 12.94 (C^7), 25.40 (C^3, C^4 or C^5), 25.69 (C^3, C^4 or C^5), 32.56 (C^3, C^4 or C^5), 40.14 (NMe_2), 58.73 (C^6), 119.53 (C^1), 166.94 (C^2).

Borane-(6-dimethylaminoheptanenitrile) complex **(2c)**. IR (neat): ν_{max} = 2220-2500, 1165 cm^{-1}; MS, *m/z*: 167.1715 (M^+, Calc. for $C_9H_{21}N_2B$ 167.1834); ^1H NMR ($CDCl_3$): 1.19 *d* ***J*** = 7.0 Hz (H^7), 1.20-1.75 m (H^3, H^4, H^5), 2.34 *t* (H^2), 2.42s 2.50 *s* (NMe_2), 2.7 *m* (H^6); ^{13}C NMR ($CDCl_3$): 13.92 (C^7), 16.75 (C^2), 24.91 (C^3, C^4 or C^5), 26.32 (C^3, C^4 or C^5), 30.25 (C^3, C^4 or C^5), 46.95 and 49.61 (NMe_2), 65.84 (C^6), 119.16 (C^1).

(1R,3S)-2,2-Dimethyl-3-(2-dimethylaminopropyl)-cyclopropaneacetonitrile **(3b)** (7:5 mixture of epimers, NMR). $[\alpha]^{24}$ +8.5 (*c* 6.59). IR ($CHCl_3$): ν_{max} = 2245 cm^{-1}; MS, *m/z*: 194.1780 (M^+, Calc. for $C_{12}H_{22}N_2$ 194.1783). ***Major component*** **($3b_{maj}$)**. ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.50-0.90 *m* (H^3, H^4), 0.69 *s* (H^8), 0.875 *d* ***J*** = 7.0 Hz (H^7), 0.878 *s* (H^9), 1.0-1.6 *m* (H^5), 1.003 *s* (H^{10}), 2.13 *s* (NMe_2), 2.0-2.4 *m* (H^2), 2.4 *m* (H^6); ^{13}C NMR ($CDCl_3$:CCl_4=1:1):13.08 (C^2), 13.18 (C^9), 14.31 (C^7), 17.39 (C^8), 21.49 (C^3), 23.91 (C^4), 27.10 (C^5), 28.09 (C^{10}), 40.40 (NMe_2), 59.44 (C^6), 119.46 (C^1). ***Minor component*** **($3b_{min}$)**. ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.50-0.90 *m* (H^3, H^4), 0.69 *s* (H^8), 0.885 *s* (H^9), 0.895 *d* ***J*** = 7.0 Hz (H^7), 1.0-1.6 *m* (H^5), 1.003 *s* (H^{10}), 2.13 *s* (NMe_2), 2.0-2.4 *m* (H^2), 2.4 *m* (H^6); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.03 (C^2), 13.34 (C^9), 14.16 (C^7), 17.27 (C^8), 21.72 (C^3), 23.30 (C^4), 27.17 (C^5), 28.09 (C^{10}), 40.40 (NMe_2), 59.07 (C^6), 119.46 (C^1).

Borane-[(1R,3S)-2,2-dimethyl-3-(2-dimethylaminopropyl)-cyclopropaneacetonitrile] complex **(3c)** (7:5 mixture of epimers, NMR). $[\alpha]^{24}$ +12.9 (*c* 4.95). Found C 68.8, H 12.6, N 13.4. Calc. for $C_{12}H_{25}N_2B$: C 69.24, H 12.11 N 13.46, B 5.19. IR (neat): ν_{max} = 2230-2480, 1165 cm^{-1}. ***Major component*** **($3c_{maj}$)**. ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.45-1.0 *m* (H^3, H^4), 0.98 *s* (H^9), 1.2-1.5 *m* (H^5), 1.06 *s* (H^{10}), 1.22 *d* ***J*** = 6.5 Hz (H^7), 2.53 *s* and 2.40 *s* (NMe_2), 2.0-2.4 *m* (H^2), 2.8 *m* (H^6); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.31 (C^9), 13.37 (C^2), 14.56 (C^7), 17.91 (C^8), 21.92 (C^3), 24.33 (C^4), 25.87 (C^5), 28.23 (C^{10}), 45.96 and 50.58 (NMe_2), 66.33 (C^6), 119.21 (C^1). ***Minor component*** **($3c_{min}$)**. ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.45-1.0 *m* (H^3, H^4), 1.24 *d* ***J*** = 6.5 Hz (H^7), 1.03 *s* (H^9), 1.06 *s* (H^{10}), 1.2-1.5 *m* (H^5), 2.0-2.4 *m* (H^2), 2.52 *s* and 2.41 *s* (NMe_2), 2.8 *m* (H^6); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.23 (C^2), 13.51 (C^9), 14.56 (C^7), 17.84 (C^8), 22.22 (C^3), 24.01 (C^4), 25.64 (C^5), 28.37 (C^{10}), 46.28 and 50.15 (NMe_2), 66.13 (C^6), 118.91 (C^1);

(1R,3S)-3-(2-Aminopropyl)-2,2-dimethylcyclopropaneacetonitrile **(4b)** (7:5 mixture of epimers, NMR). $[\alpha]^{24}$ +3.1 (*c* 0.66). Found C 71.5, H 11.1, N 15.5. Calc. for $C_{19}H_{18}N_2$: C 72.24, H 10.91, N 16.85. IR

($CHCl_3$): ν_{max} = 3520, 3380, 2250 cm^{-1}. ***Major component*** (**4b**$_{maj}$). ^1H NMR ($CDCl_3$): 0.55-1.0 *m* (H^3, H^4), 1.07 *d* ***J*** = 6.5 Hz (H^6), 0.95 *s* (H^8), 1.03 *s* (H^9), 1.25-1.45 *m* (H^5), 2.15-2.30 *m* (H^2), 2.19 *d* ***J*** = 7.5 Hz (H^1), 2.33 *s* $W_{1/2}$ = 7.5 Hz (Ph), 2.85-3.05 *m* (H^6); ^{13}C NMR ($CDCl_3$): 13.23 (C^1), 14.48 (C^8), 17.44 (C^7), 21.78 (C^6), 23.09 (C^2), 23.40 (C^3), 28.18 (C^9), 33.48 (C^4), 47.45 (C^5), 119.53 (C^1). ***Minor component*** (**4b**$_{min}$). ^1H NMR ($CDCl_3$): 0.55-1.0 *m* (H^3, H^4), 0.94 *s* (H^9), 1.03 *s* (H^{10}), 1.06 *d* ***J*** = 6.5 Hz (H^7), 1.25-1.45 *m* (H^5), 2.15-2.30 *m* (H^2), 2.20 *d* ***J*** = 7.5 Hz (H^2), 2.33 *s* $W_{1/2}$ = 7.5(NH_2), 2.85-3.05 *m* (H^6); ^{13}C NMR ($CDCl_3$): 13.30 (C^2), 14.47 (C^9), 17.44 (C^8), 21.78 (C^7), 22.93 (C^3), 23.60 (C^4), 28.18 (C^{10}), 33.48 (C^5), 47.15 (C^6), 119.53 (C^1).

(1R,3S)-2,2-Dimethyl-3-(2-phenylaminopropyl)-cyclopropaneacetonitrile (**5b**) (7:5 mixture of epimers, NMR). $[\alpha]^{24}$ +10.2 (*c* 2.95). IR (in $CHCl_3$): ν_{max} = 2250 cm^{-1}; MS, *m/z*: 242.1790 (M^+, Calc. for $C_{16}H_{22}N_2$ 242.1783). ***Major component*** (**5b**$_{maj}$). ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.55-1.0 *m* (H^3, H^4), 0.97 *s* (H^9), 1.092 *s* (H^{10}), 1.20-1.70 *m* (H^5), 1.22 *d* ***J*** = 6.5 Hz (H^7), 2.19 *d* ***J*** = 7.5 Hz (H^2), 3.52 *tq* ***J*** = 6.5 and 6.5 Hz (H^6), 6.47 *m*, 7.10 *m* and 6.62 *m* (Ph); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.45 (C^2), 14.75 (C^9), 17.79 (C^8), 20.95 (C^7), 22.05 (C^3), 23.54 (C^4), 28.43 (C^{10}), 31.42 (C^5), 48.92 (C^6), 119.14 (C^1), 147.15 *s* and 129.30 *d* and 117.26 *d* and 113.13 *d* (Ph). ***Minor component*** (**5b**$_{min}$). ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.55-1.0 *m* (H^3, H^4), 1.02 *s* (H^9), 1.090 *s* (H^{10}), 1.20-1.70 *m* (H^5), 1.23 *d* ***J*** = 6.5 Hz (H^7), 2.20 *d* ***J*** = 7.5 Hz (H^2), 3.54 *tq* ***J*** = 6.5 and 6.5 Hz (H^6), 6.47 *m*, 7.10 *m* and 6.62 *m* (Ph); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.37 (C^2), 14.70 (C^9), 17.78 (C^8), 20.89 (C^7), 21.93 (C^3), 23.22 (C^4), 28.43 (C^{10}), 31.20 (C^5), 48.55 (C^6), 119.14 (C^1), 147.15 *s* 129.30 *d* 117.26 *d* 113.08 *d* (Ph).

(1R,3S)-3-(2-Benzylaminopropyl)-2,2-dimethylcyclopropaneacetonitrile (**6b**) (7:5 mixture of epimers, NMR). $[\alpha]^{24}$ +11.4 (*c* 5.28). Found C 79.8, H 9.2, N 10.1. Calc. for $C_{17}H_{24}N_2$ C 79.64, H 9.44, N 10.93. IR ($CHCl_3$): ν_{max} = 2250 cm^{-1}. ***Major component*** (**6b**$_{maj}$) ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.60-1.10 *m* (H^3, H^4), 0.96 *s* (H^9), 1.08 *s* (H^{10}), 1.10 *d* ***J*** = 6.5 Hz (H^7), 1.20-1.55 *m* (H^5), 2.10-2.25 *m* (H^2), 2.57-2.77 *m* (H^6), 3.80 *dd* ***J*** = 13.0 and 1.5 Hz, 3.70 *dd* ***J*** = 13.0 and 2.5 Hz (CH_2Ph), 7.1-7.4 (Ph); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.11 (C^2), 14.42 (C^9), 17.34 (C^8), 20.10 (C^7), 21.73 (C^3), 23.17 (C^4), 28.20 (C^{10}), 31.00 (C^5), 51.25 (CH_2Ph), 52.49 (C^6), 118.95 (C^1), 140.53 and 128.05 and 127.72 and 126.57 (Ph). ***Minor component*** (**6b**$_{min}$) ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.60-1.10 *m* (H^3, H^4), 0.96 *s* (H^9), 1.08 *s* (H^{10}), 1.09 *d* ***J*** = 6.5 Hz (H^7), 1.20-1.55 *m* (H^5), 2.10-2.25 *m* (H^2), 2.57-2.77 *m* (H^6), 3.80 *dd* ***J*** = 13.0 and 1.5 Hz and 3.70 *dd* ***J*** = 13.0 and 2.5 Hz (CH_2Ph), 7.1-7.4(Ph); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.11 (C^2), 14.42 (C^9), 17.34 (C^8), 20.05 (C^7), 21.73 (C^3), 23.46 (C^4), 28.20 (C^{10}), 31.21 (C^5), 51.29 (CH_2Ph), 52.64 (C^6), 140.53 and 128.05 and 127.72 and 126.57 (Ph).

(±)-3-(1-Methyl-1-ethenyl)-6-dimethylaminoheptanenitrile (**8b**) (3:2 mixture of diastereomers, NMR). IR (neat): ν_{max} = 2245 cm^{-1}; MS, *m/z*: 194.1784 (M^+, Calc. for $C_{12}H_{22}N$ 194.1783). ***Major component*** (**8b**$_{maj}$). ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.88 *d* ***J*** = 6.5 Hz (H^7), 1.10-1.60 *m* (H^4, H^5), 1.66 $W_{1/2}$=3.5 Hz (H^{10}), 1.90-2.30 *m* (H^2, H^3), 2.16 *s* (NMe_2), 2.30-2.55 *m* (H^6), 4.88 *dd* ***J*** = 2.5 and 1.5 Hz (H^{9a}) and 4.82 *m* $W_{1/2}$ = 3.2 Hz (H^{9b}); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 12.80 (C^7), 18.70 (C^{10}), 22.26 (C^2), 29.31 (C^4), 31.41 (C^5), 40.28 (NMe_2), 43.73 (C^3), 58.63 (C^6), 113.64 (C^9), 117.98 (C^1), 144.10 (C^8). ***Minor component*** (**8b**$_{min}$). ^1H NMR ($CDCl_3$:CCl_4=1:1): 0.90 *d* ***J*** = 6.5 Hz (H^7), 1.10-1.60 *m* (H^4, H^5), 1.73 *m* $W_{1/2}$=3.0 Hz (H^{10}), 1.90-2.30 *m* (H^2, H^3), 2.15 *s* (NMe_2), 2.30-2.55 *m* (H^6), 4.89 *dd* ***J*** = 2.5 and 1.5 Hz (H^{9a}) and 4.82 *m* $W_{1/2}$ = 3.2 Hz (H^{9b}); ^{13}C NMR ($CDCl_3$:CCl_4=1:1): 13.14 (C^7), 18.77 (C^{10}), 22.25 (C^2), 29.39 (C^4), 31.12 (C^5), 40.40 (NMe_2), 43.73 (C^3), 58.82 (C^6), 109.17 (C^9), 117.98 (C^1), 144.10 (C^8).

(±)-6-Benzylamino-3-(1-methyl-1-ethenyl)-heptanenitrile **(9b)** (3:2 mixture of diastereomers, NMR). IR ($CHCl_3$): ν_{max} = 2230, 3320 cm^{-1}; MS, *m/z*: 256.1933 (M^+, Calc. for $C_{17}H_{24}N$ 256.1939). ***Major component*** **($9b_{maj}$)**. ^1H NMR ($CDCl_3$): 1.06 *d J* = 6.5 Hz (H^7), 1.20-1.60 *m* (H^4, H^5), 1.65 *m* $W_{1/2}$ = 3.0 Hz (H^{10}), 2.30-2.40 *m* (H^2, H^3), 2.55-2.75 *m* (H^6), 3.72 *dd J* = 13.5 1.5 Hz and 3.77 *dd J* = 13.5 2.5 Hz (CH_2Ph), 4.98 *dd J* = 2.5, 1.5 Hz (H^{9a}) and 4.81 *m* $W_{1/2}$ = 5.0 Hz (H^{9b}), 7.17-7.31 *m* (Ph); ^{13}C NMR ($CDCl_3$): 18.48 (C^{10}), 20.04 (C^7), 22.07 (C^2), 28.34 (C^4), 34.09 (C^5), 34.09 (CH_2Ph), 43.53 (C^3), 51.98 (C^6), 113.56 (C^9), 118.39 (C^1), 140.63 128.19 127.87 126.67 (Ph), 143.85 (C^8). ***Minor component*** **($9b_{min}$)**. ^1H NMR ($CDCl_3$): 1.06 *d J* = 6.5 Hz (H^7), 1.20-1.60 *m* (H^4, H^5), 1.65 *m* $W_{1/2}$ = 3.0 Hz (H^{10}), 2.30-2.40 *m* (H^2, H^3), 2.55-2.75 *m* (H^6), 3.72 *dd J* = 13.5 1.5 Hz and 3.77 *dd J* = 13.5 2.5 Hz (CH_2Ph), 4.98 *dd J* = 2.5 1.5 (H^{9a}) and 4.81 $W_{1/2}$=5.0(H^{9b}), 7.17-7.31(Ph); ^{13}C NMR ($CDCl_3$): 18.56 (C^{10}), 20.24 (C^7), 22.02 (C^2), 28.26 (C^4), 34.09 (C^5), 34.09 (CH_2Ph), 43.42 (C^3), 51.89 (C^6), 113.50 (C^9), 118.39 (C^1), 140.63 128.19 127.91 126.67 (Ph), 143.85 (C^8).

(±)-(2Z)-6-Dimethylamino-3-(1-methyl-1-ethenyl)-hept-2-enenitrile **(11b)**. $[\alpha]^{24}$ 0.00. Found C 74.5, H 11.0, N 13.3. Calc. for $C_{12}H_{22}N$ C 74.17, H 11.41, N 14.42. IR ($CHCl_3$): ν_{max} = 2210, 1620, 1725 cm^{-1}; ^1H NMR ($CDCl_3$): 0.93 *d J* = 6.5 Hz (H^7), 1.04 *d J* = 7.0 Hz (H^9), 1.04 *d J* = 7.0 Hz (H^{10}), 1.30-1.75 *m* (H^5), 2.17 *s* (NMe_2), 2.20-2.60 *m* (H^4, H^6, H^8), 5.04 *d J* = 1.2 Hz (H^2); ^{13}C NMR ($CDCl_3$): 12.62 (C^7), 21.19 (C^9), 21.19 (C^{10}), 31.12 (C^4), 33.01 (C^5), 34.41 (C^8), 40.24 (NMe_2), 58.83 (C^6), 93.29 (C^2), 117.23 (C^1), 174.91 (C^3).

(±)-(1S*,3S*)-3-(1-Benzylaminoethyl)-2,2-dimethylcyclobutaneacetonitrile **(12b)**. ***Major component*** **($12b_{min}$)**. $[\alpha]^{24}$ –44.8 (*c* 0.85). IR ($CHCl_3$): ν_{max} = 2245, 3320 cm^{-1};MS, *m/z*: 256.1948 (M^+, Calc. for $C_{17}H_{24}N_2$ 256.1939); ^1H NMR ($CDCl_3$): 0.95 *s* (H^9), 1.01 *d J* = 6.5 Hz (H^7), 1.14 *s* (H^{10}), 1.76 *ddd J* = 10.0, 8.0 and 7.0 Hz and 1.29 *ddd J* = 10.0, 10.0 and 10.0 Hz (H^4), 2.00-2.25 *m* (H^2), 2.58 *dq J* = 10.5 and 6.5 Hz (H^6), 3.82 *d J* = 13.0 Hz and 3.62 *d J* = 13.0 Hz (CH_2Ph), 7.15-7.35 *m* (Ph); ^{13}C NMR ($CDCl_3$): 15.69 (C^9), 16.79 (C^7), 17.12 (C^2), 27.23 (C^4), 30.72 (C^{10}), 37.53 (C^3), 39.95 (C^8), 48.80 (C^5), 50.74 (CH_2Ph), 53.53 (C^6), 118.69 (C^1), 140.58 *s* 128.12 *d* 127.96 *d* 126.65 *d* (Ph). ***Minor component*** **($12b_{maj}$)**. $[\alpha]^{24}$ +49.7 (*c* 0.60). IR (*c* 1% in $CHCl_3$): ν_{max} = 2245, 3320 cm^{-1};MS, *m/z* (%): 256.1946 (Calc. for $C_{17}H_{24}N_2$ 256.1939); ^1H NMR ($CDCl_3$): 0.93 *s* (H^9), 0.94 *d J* = 6.5 Hz (H^7), 1.18 *s* (H^{10}), 1.74 *ddd J* = 10.0, 8.0 and 7.0 Hz, 1.2-1.35 *m* (H^4), 2.00-2.25 *m* (H^2), 2.58 *dq J* = 10.5 and 6.5 Hz (H^6), 3.83 *d J* = 13.0 Hz and 3.57 *d J* = 13.0 Hz (CH_2Ph), 7.15-7.35 m (Ph); ^{13}C NMR ($CDCl_3$): 15.96 (C^9), 17.21 (C^2), 19.27 (C^7), 27.97 (C^4), 30.19 (C^{10}), 38.17 (C^3), 40.07 (C^8), 49.28 (C^5), 50.74 (CH_2Ph), 53.59 (C^6), 118.65 (C^1), 140.69 *s* 128.25 *d* 127.90 *d* 126.75 *d* (Ph).

[(1S,4R)-4-(3-Dimethylaminobutyl)-2,2-dimethylcyclobutyl]-pent-4-enenitrile **(16b)** (3:2 mixture of epimers, NMR). $[\alpha]^{24}$ +68.1 (*c* 8.45). IR ($CHCl_3$): ν_{max} = 2250, 890 cm^{-1}; MS, *m/z*: 262.2409 (M^+, Calc. for $C_{17}H_{30}N_2$ 262.2409). ***Major component*** **($16b_{maj}$)**. ^1H NMR ($CDCl_3$): 0.84 *d J* = 6.5 Hz (H^{12}), 0.98 *s* (H^{14}), 0.98 *s* (H^{15}), 1.00-1.50 *m* (H^{6a}, H^9, H^{10}), 1.60-1.85 *m* (H^{6b}, H^8), 2.10-2.50 *m* (H^2), 2.14 *s* (NMe_2), 4.81 *br.s* $W_{1/2}$ = 4.0 Hz (H^{13a}), 4.70 *br.s* $W_{1/2}$ = 4.2 Hz (H^{13b}); ^{13}C NMR ($CDCl_3$): 12.92 (C^{12}), 15.74 (C^2), 21.96 (C^{14}), 27.65 (C^9), 29.01 (C^3), 30.99 (C^{15}), 31.67 (C^{10}), 33.59 (C^7), 39.18 (C^6), 40.12 (NMe_2), 40.89 (C^5), 48.96 (C^8), 59.09 (C^{11}), 108.64 (C^{13}), 119.07 (C^1), 148.59*s* (C^4). ***Minor component*** **($16b_{min}$)**. ^1H NMR ($CDCl_3$): 0.87*d J* = 6.5 Hz (H^{12}), 0.96 *s* (H^{14}), 0.96 *s* (H^{15}),), 1.00-1.50 *m* (H^{6a}, H^9, H^{10}), 1.60-1.85 *m* (H^{6b}, H^8), 2.10-2.50 *m* (H^2), 2.13 *s* (NMe_2), 4.81 $W_{1/2}$ = 4.0 Hz (H^{13a}), 4.70 $W_{1/2}$ = 4.2 Hz (H^{13b}); ^{13}C NMR ($CDCl_3$): 13.40 (C^{12}), 15.74 (C^2), 21.96 (C^{14}), 27.65 (C^9), 29.01 (C^3), 30.99 (C^{15}), 31.40 (C^{10}), 33.59 (C^7), 39.18 (C^6), 40.27 (NMe_2), 40.89 (C^5), 48.85 (C^8), 59.25 (C^{11}), 108.64 (C^{13}), 119.07 (C^1), 148.59 (C^4).

Fragmentation of amino oxime 3a in different media.

Reaction with $NaBH_4$ in hexanenitrile. The reaction of **3a** in hexanenitrile was conducted as follows. A stirring suspension of an α-amino oxime **3a** (1 mmol) and sodium borohydride (0.2 g, 6 mmol) in hexanenitrile (5 mL) was heated to 80°C and allowed stirring for 18 h. Futher procedure was the same as in the ***Method A***. Yields of **3b** and **3c** were 15% and 10% respectively.

Reaction with $NaBH_4$ in aqueous acetonitrile. The reaction of **3a** in 10% H_2O in CH_3CN was conducted as in the previous example. Yields of **3b** and **3c** are 40% and 30% respectivelly.

Reaction with $NaBH_4$ in other solvents. Treatment of **3a** with $NaBH_4$ in other solvents (DMF at 80°C and at reflux; H_2O at 80°C; boiling Et_2O; 1,4 dioxane at 80°C; HMPA at 45°C and 80°C; PhCN at 80°C; nitroethane at 70°C; benzene at 80°C; *iso*-PrOH at 40°C and 70°C; diglyme at 40°C and 80°C) did not lead even to traces of **3b** and **3c** (TLC). At lower temperatures the starting compound was recovered, while at higher temperatures the amino oxime was transformed to the corresponding α,β-unsaturated oxime (TLC, NMR).

Reaction with $(BH_3)_2$. A mixture of CH_3COOH (2 mL, 0.87 mmol) and 1,4-dioxane (2 mL) was added dropwise to a stirring suspension of α-amino oxime **3a** (0.21 g, 0.95 mmol) and sodium borohydride (0.50 g, 13 mmol) in 1,4-dioxane (20 mL) at room temperature. The reaction mixture was heated to boiling point and allowed to reflux for 10 h. Neither amino borane **3c** nor amino nitrile **3b** was detected by TLC.

Reaction with borane-amine complex. A suspension of amino oxime **3a** (0.15 g, 0.71 mmol) and amino borane **2c** (0.12 g, 0.71 mmol) in acetonitrile (5 mL) was allowed to reflux for 5 h. Neither amino borane **3c** nor amino nitrile **3a** was detected by TLC.

Preparation of borane-aminonitrile complexes.

Boran-amine complex 3b. A stirring suspension of α-amino oxime **3a** (0.5 g, 2.5 mmol) and $NaBH_4$ (0.54 g, 14.3 mmol) in CH_3CN (12 mL) was heated to and allowed to reflux for 30 min. The solvent was removed under reduced pressure, replaced by Et_2O (20 mL) and followed by addition of CH_3COOH (3.0 g, 50 mmol) at vigorous stirring. The resultant mixture was allowed to stay at room temperature for 10 hours and then treated with H_2O (10 mL) and extracted with Et_2O (3×15 mL). The combined ethereal extracts were washed with 1M Na_2CO_3 (3×50 mL), brine (15 mL), dried (Na_2SO_4) and concentrated at reduced pressure to give amino borane **3c** (0.43 g, 87%) as colorless oil. The aqueous phase was treated with 30% NaOH (2 mL) and extracted with Et_2O (3×15 mL). The combined ethereal extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated at reduced pressure to give amino nitrile **3b** (30 mg, 7%).

Preparation of aminonitrile from amino oxime.

Dimethylamino nitrile 3b. A stirring suspension of an α-amino oxime **3a** (1.00 g, 4.8 mmol) and $NaBH_4$ (1.08 g, 28.6 mmol) in CH_3CN (24 mL) was heated to boiling point and allowed to reflux for 30 min. Then solvent was removed under reduced pressure and the residue was treated with concentrated HCl (4 mL, dropwise, vigorous stirring). The resultant mixture was then treated with H_2O (15 mL) and extracted with Et_2O (3×30 mL). The combined ethereal solutions were washed with H_2O (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated at reduced pressure to give amino borane (0.05 g, 5%).The aqueous phase was treated with concentrated aq NH_3 (5 mL, pH 11) and extracted with Et_2O (3×30 mL). The combined etheral extracts were washed with H_2O (20 mL), brine (20 mL), dried (Na_2SO_4) and concentrated at reduced pressure to give corresponding amino nitrile **3b** (0.61 g, 66%).

Preparation of amino nitrile from borane-aminonitrile complex.

Dimethylamino nitrile 2b. Heating of amino borane **2c** (5 mg) in CF_3COOH (1 mL) at 70°C for 12 h gave the salt of amino nitrile **2b** with CF_3COOH as the only product according to ^1H -NMR. And this salt was completely identical to the salt prepared from pure amino nitrile **2b** and CF_3COOH according to ^1H -NMR.

Dimethylamino nitrile 3b. Heating of amino borane **3c** (0.29 g, 1.4 mmol) in trifluoroacetic acid solution (amino borane:CF_3COOH = 1:10 w/v, 70-80°C) followed by evaporation the solvent gave white solid. The product was dissolved in H_2O (3 mL) and extracted with Et_2O (2×5 mL). The aqueous phase was treated with concentrated aq NH_3 (1 mL, pH 11) and extracted with Et_2O (2×10 mL). The ethereal extracts were washed with brine (3 mL), dried (Na_2SO_4) and concentrated at reduced pressure to give amino nitrile **3b** (0.23g, 1.2 mmol, 86%).

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