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SYNTHESIS OF NITROGEN-CONTAINING DRIMANE SESQUITERPENOIDS FROM 11-DIHOMODRIM-8(9)-EN-12-ONE

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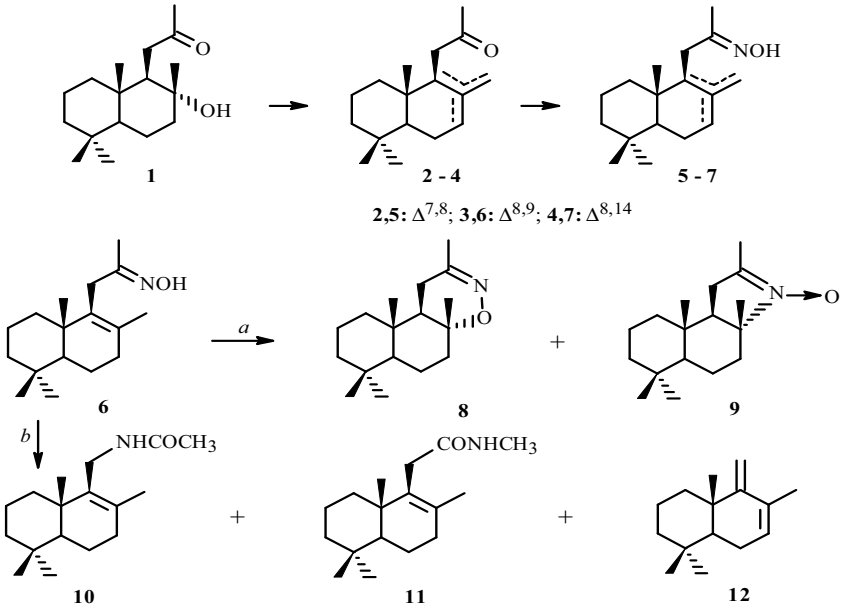
Products from the reaction of 11-dihomodriman-8α-ol-12-one with several reagents such as $MeSO_3SiMe_3$, $CF_3SO_3SiMe_3$, $Sc(CF_3SO_3)_3$, conc. H_2SO_4 in EtOH (30% solution), and Amberlist-15 ion-exchange resin were studied. 11-Dihomodrim-8(9)-en-12-one and its oxime were synthesized. The reaction of its oxime with H_3PO_4 (86%) or CF_3CO_2H produced (1S,2S,4aS,8aS)-2,5,5,8a-tetramethyldecahydro-1H-naphtho [1,2-e]-3-methyl-4,5-dihydro-[1,2,6]-oxazine; with p-TsCl in Py, (1S,2S,4aS,8aS)-2,5,5,8a-tetramethyldecahydro-1H-naphtho[1,2-d]-2-methylpyrroline-N-oxide; and with PCl_5 in Et_2O, 11-acetylaminodrim-8(9)-ene and 11-methylaminooxodrim-8(9)-ene.

Keywords: synthesis, drimane sesquiterpenoids, 11-dihomodrim-8(9)-en-12-one, oxime, *N*-oxide.

Many drimane sesquiterpenoids exhibit various types of biological activity [1, 2]. However, little has been published on the synthesis and biological activity of drimanes containing nitrogen [3–5]. In continuation of our research on the synthesis of N-containing drimane derivatives in order to test their biological activity [6, 7], we studied the products from reaction of oxime **6** of 11-dihomodrim-8(9)-en-12-one **3** with several reagents such as H_3PO_4 (86%), CF_3CO_2H, FSO_3H, conc. H_2SO_4, *p*-TsCl in Py, and PCl_5 in Et_2O. The starting material for preparing **3** was hydroxyketone **1**, the synthesis of which from norambreinolide we published earlier [8].



a. A: H_3PO_4, B: CF_3CO_2H; *b*. A: *p*-TsCl/Py, B: PCl_5

Scheme 1

†Deceased

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TABLE 1. Preparative Methods for Unsaturated Ketones **2**–**4**

Reaction time	Total yield of unsaturated ketones **2**–**4**, %	Ratio of unsaturated ketones **2**–**4**, %
	a) $MeSO_3SiMe_3$ (1.5 eq), CH_3CN	
5 min	91	20:80:0
25 min	89	22:78:0
2 h	90	25:75:0
	b) $CF_3SO_3SiMe_3$	
25 min	45	34:66:0
	c) $Sc(OTf)_3$ (1.1 eq), CH_3CN	
3 h	90	27:73:0
	d) conc. H_2SO_4 in EtOH (30% solution)	
2 h	80	55:24:21
24 h	92	53:33:14
	e) Amberlist-15 (1:1), CH_2Cl_2	
1.5 h	98	29:66:5
5 h	96	28:72:0
20 h	97	25:75:0

Hydroxyketone **1** was reacted with trimethylsilylmethanesulfonate ($MeSO_3SiMe_3$) (method a), trimethylsilyltrifluoromethanesulfonate ($CF_3SO_3SiMe_3$) (method b), scandium trifluoromethanesulfonate [$Sc(CF_3SO_3)_3$] (method c), conc. H_2SO_4 in EtOH (30% solution) (method d), and ion-exchanger Amberlist-15 (method e) in a search for an effective method of regioselective dehydration of **1** (Scheme 1).

All reactions were carried out at 18–20°C and different reaction times. Mixtures of unsaturated ketones **2** and **3** with a significant predominance of 11-dihomodrim-8(9)-en-12-one (**3**) were produced using methods a, b, and c. Ketones **2** and **3** were also produced in method e if the reaction was carried out for 5–20 h. Ketone **4**, which was formed in a detectable amount only using method d, was observed in addition to **2** and **3** if the reaction time was decreased (1.5 h). Increasing the reaction time caused its content in the mixture to decrease, obviously as a result of the isomerization into ketone **3**. Ketone **2** predominated in the mixture obtained using method d. The yield of the mixture of unsaturated ketones was high (83–98%) except for the reaction with $CF_3SO_3SiMe_3$, for which the yield was 45% because of the formation of side products. The ratios of unsaturated ketones were determined by PMR spectroscopy. Table 1 presents these ratios, the total yield of ketones **2**–**4**, the reagents and reaction conditions, and the reaction time.

Two routes were used to prepare pure oxime **6**. Reaction of a mixture of ketones **2** and **3** with $NH_2OH{\cdot}HCl$ in a mixture of EtOH and Py produced a mixture of oximes **5** and **6**, from which **6** was isolated by recrystallization. In the other version, ketone **3** was isolated from the mixture of **2** and **3** using column chromatography over silica gel impregnated with $AgNO_3$. Then, the oxime of **3** was prepared (Scheme 1). TLC, PMR, and ^{13}C and ^{15}N NMR spectra suggested that the oxime **6** was a mixture of the *Z*- and *E*-isomers in an approximately 1:1 ratio. Column chromatography of this mixture over silica gel isolated and characterized both pure isomers. In determining the stereochemistry of these isomers, we held to the principle that the oxime with the smaller R_f value had the *Z*-configuration; with the larger value, the *E*-configuration, as was established previously using the oxime of 14,15-dinorlabd-8(17)-en-13-one as an example [3]. Considering that the *E*-isomer was energetically more favorable and that the *Z*-isomer could convert easily into the *E*-isomer [3, 9], we used oxime **6** as the mixture of its *Z*- and *E*-isomers to carry out the reactions.

A study of the reaction products of oxime **6** found that heating it at 70–80°C in H_3PO_4 (86%) caused intramolecular cyclization to form (1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyldecahydro-1*H*-naphtho[1,2-*e*]-3-methyl-4,5-dihydro-[1,2,6]-oxazine (**8**), which we synthesized previously from 11-dihomodriman-8α-ol-12-one (**1**) [7], and (1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyldecahydro-1*H*-naphtho[1,2-*d*]-2-methylpyrroline-*N*-oxide (**9**) (Scheme 1). The structures of these compounds were confirmed by IR, ^1H NMR, and ^{13}C and ^{15}N spectral data and elemental analysis.

The structure and stereochemistry of *N*-oxide **9** was established by an x-ray structure analysis (XSA). The compound crystallized in the acentric monoclinic space group $P2_1$. The asymmetric unit of the unit cell contained two similar molecules of **9** with the same configuration and similar geometric parameters in addition to two water molecules. Thus, the crystals were the monohydrate $\mathbf{9}{\cdot}H_2O$.

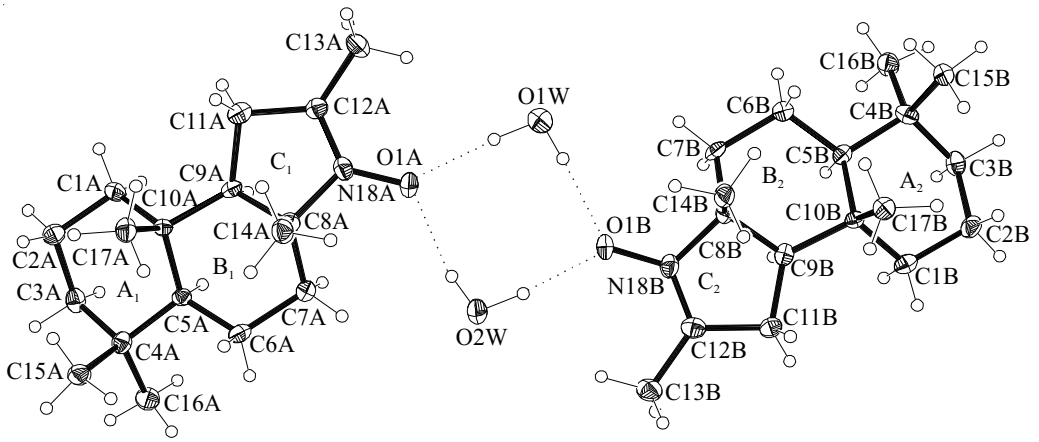

Fig. 1. Molecular structure and packing diagram of dimers in the x-ray structure of **9**·H_2O. Thermal vibration ellipsoids are shown at the 50% probability level.

The symmetrically independent water molecules acted as bridges and combined molecules of **9** into dimer through four O(H_2O) –H···O(1) H-bonds: O1W–H···O1A = 2.854(5) Å, O1W–H = 0.97(6) Å, H···O1A = 1.89(6) Å, <O1W–H···O1A = 173(5)°; O1W–H···O1B = 2.830(5) Å, O1W–H = 0.87(6) Å, H···O1B = 1.97(6) Å, <O1W–H···O1B = 173(5)°; O2W–H···O1A = 2.810(5) Å, O2W–H = 0.85(6) Å, H···O1A = 1.98(6) Å, <O2W–H···O1A = 166(6)°; O2W–H···O1B = 2.819(4) Å, O2W–H = 0.97(6) Å, H···O1B = 1.86(6) Å, <O2W–H···O1B = 171(5)° (Fig. 1).

The conformations of the rings were estimated quantitatively by calculating the puckering parameters [10]: ring A_1 (puckering amplitude Q = 0.5627 Å, θ = 1.57°, φ = 316.02°); ring A_2 (Q = 0.5587 Å, θ = 3.14°, φ = 328.11°); ring B_1 (Q = 0.6014 Å, θ = 2.46°, φ = 222.81°); ring B_2 (Q = 0.6005 Å, θ = 3.46°, φ = 234.47°). The resulting parameters were similar for the two symmetrically independent molecules and indicated that the cyclohexane moieties of A and B had the chair conformation. The five-membered rings also had similar puckering parameters: for ring C_1, Q_2 = 0.3926 Å, φ_2 = 244.01°; for C_2, Q_2 = 0.3855 Å, φ_2 = 242.99°. These corresponded to conformations intermediate between an envelope and twisted half-chair. The bond lengths and angles in the two molecules were practically the same. The mean-square deviations in the distances and angles upon superimposing the molecules were 0.0081 Å and 0.499°, respectively. The maximum differences of 0.016 Å and 1.0° were observed for bonds C3A–C4A = 1.558(6) Å and C3B–C4B = 1.542(6) Å and C7A–C8A–C14A 110.8(4)° and C7B–C8B–C14B 111.8(4)°. The average C–C distance in the six-membered rings was 1.540 Å; the average C–CH_3 distance, 1.537 Å. The length of the O1–N18 polar bond in the five-membered rings was 1.325(5) and 1.321(5) Å; of the N18–C12 double bond, 1.296(6) and 1.295(6) Å; and of the N18–C8 single bond, 1.505(6) and 1.501(6) Å in molecules A and B, respectively. The distances C9–C11, C11–C12, and C12–C13 were 1.532(6) and 1.530(6), 1.508(6) and 1.499(6), and 1.479(6) and 1.492(6) Å, respectively.

Refluxing oxime **6** in CF_3CO_2H also produced **8** and **9**. However, **6** did not react at room temperature in CH_2Cl_2 with an equimolar amount of CF_3CO_2H or FSO_3H. Reaction of **6** with an excess of conc. H_2SO_4 at 20°C formed a mixture of many products.

Reaction of **6** with *p*-TsCl in Py at 20°C produced 11-acetylaminodrim-8(9)-ene (**10**) and its isomer 11-methylaminooxodrim-8(9)-ene (**11**) in overall yield 40%. Drim-7(8),9(11)-diene (**12**) was also isolated (13% yield) from the product mixture (Scheme 1).

Reaction of **6** and PCl_5 in Et_2O at 0°C for 30 min produced amides **10** and **11** in overall yield 30%; diene **12**, 13%. About 20% of the starting oxime did not react. Increasing the duration of the reaction at 0°C or carrying out the reaction at 20°C increased significantly the yield of diene **12** and formed other side products.

Thus, the new N-containing drimane compound **9** with an unusual pyrroline *N*-oxide ring structure in addition to 11-acetylaminodrim-8(9)-ene (**10**) and 11-methylaminooxodrim-8(9)-ene (**11**) were synthesized from 11-dihomodriman-8α-ol-12-one (**1**).

EXPERIMENTAL

Melting points were determined on a Boetius heating stage. IR spectra were recorded on a Perkin–Elmer Spectrum 100 FT-IR spectrophotometer. PMR, ^{13}C, and ^{15}N NMR spectra were recorded in $CDCl_3$ on an Avance III Bruker 400 spectrometer (400 and 100 MHz). Chemical shifts are given on the δ scale in ppm relative to $CHCl_3$ resonances as an internal

standard (δ 7.24 and 77.00 ppm for H and C, respectively) and TMS for ^{15}N spectra. Resonances in ^{13}C NMR spectra were assigned using DEPT, ^{1}H–^{1}H COSY-45, and ^{1}H–^{13}C HMQC and HMBC programs and in ^{15}N NMR spectra, a ^{1}H–^{15}N HMBC program. The course of reactions was monitored by TLC on Silufol plates with detection by I_2 vapor. Column chromatography used L 100/400 μm silica gel and petroleum ether (bp 30–60°C). Ether extracts were dried over anhydrous $MgSO_4$. Reagents trimethylsilylmethanesulfonate ($MeSO_3SiMe_3$), trimethylsilyltriflate (Me_3SiOTf), and scandium triflate [$Sc(OTf)_3$] were purchased (Aldrich). Starting 11-dihomodriman-8α-ol-12-one was synthesized by the literature method [8].

X-ray Structure Analysis (XSA). Experimental data for crystals of **9**·H_2O were obtained at 100 K on a Nonius Kappa CCD diffractometer (Mo K_α-radiation, λ = 0.71073 Å, graphite monochromator). Integration of intensities of x-ray reflections, their adjustment, and refinement of unit-cell constants were performed using the programs Denzo and Scalepack [11]. The monoclinic unit-cell constants were refined using 4948 reflections measured in the range $1.00° < \theta < 30.03°$: a = 6.3936(2) Å, b = 38.3441(16) Å, c = 7.2435(3) Å, β = 116.009(2)°, V = 1595.95(11) Å^3, space group $P2_1$, Z = 4, $C_{17}H_{31}NO_2$, ρ_{calc} = 1.171 g/cm^3, μ = 0.075 mm^{-1}. The structure was solved by direct methods and refined by full-matrix least-squares methods over F^2 using the SHELX-97 programs [12]. Nonhydrogen atoms were refined anisotropically. Hydrogen atoms bonded to C atoms were placed in the calculated positions and refined isotropically using a solid-state model. The positions of the water H atoms were determined in a difference electron-density synthesis and refined isotropically. The structure (383 parameters) was refined over 2758 [R(int) = 0.0330] independent reflections to $R1$ = 0.0516, $wR2$ = 0.1121 for 2486 reflections with $I > 2\sigma(I)$, S = 1.001, and maximum and minimum residual electron density in the difference synthesis of 0.250 and –0.216 e·Å^{-3}. The ring puckering parameters were calculated using the PLATON program [13]. Crystallographic data were deposited as CIF-files in the Cambridge Crystallographic Data Centre (CCDC 781759).

Preparation of the Mixture of Unsaturated Ketones 2-4 from 11-Dihomodriman-8α-ol-12-one (1). ***Method (a).*** A solution of **1** (100 mg, 0.375 mmol) in CH_3CN (1 mL) was treated with $MeSO_3SiMe_3$ (0.087 mL, 95 mg, 0.56 mmol), stirred for 5 min at 20°C, and treated with H_2O (5 mL) and Et_2O (15 mL). The mixture was transferred to a separatory funnel and shaken. The aqueous layer was separated. The Et_2O layer was washed with $NaHCO_3$ solution (3 × 2 mL) and H_2O (3 × 2 mL) and dried. The Et_2O was vacuum distilled to afford a viscous liquid (92 mg) that was chromatographed over a column of silica gel (1.84 g) with elution by petroleum ether:Et_2O (49:1) to afford the mixture of **2** and **3** (85 mg, 91%) in a 20:80 ratio. The PMR spectrum (ppm) showed characteristic resonances at 1.43 and 1.49 ppm (two s, $2CH_3$–C=C), 2.15 and 2.18 (two s, $2CH_3$–C=O), 3.13 [s, $C_{11}(H_2)$], 5.4 [br.s, $C_7(H)$].

Method (e). A solution of **1** (1 g, 3.75 mmol) in CH_2Cl_2 (20 mL) was treated with Amberlist-15 (1 g), stirred at 20°C for 5 h, filtered, and washed with CH_2Cl_2 (30 mL). The filtrate was evaporated to afford the mixture of **2** and **3** (0.89 g, 96%) in a 28:72 ratio.

Analogously **1** (1 g) with stirring for 20 h afforded the mixture of **2** and **3** (0.9 g, 97%) in a 25:75 ratio that was chromatographed over a column of silica gel impregnated with $AgNO_3$ (45 g) with elution by petroleum ether to afford the mixture of **2** and **3** (0.23 g, 25%) in approximately a 1:1 ratio (PMR spectral data) and then **3** (0.51 g, 55%), the structure of which was confirmed by IR, PMR, and ^{13}C NMR spectra.

IR spectrum (ν, cm^{-1}): 1719 (C=O). PMR spectrum (δ, ppm): 0.83 (3H, s, CH_3-16), 0.89 (3H, s, CH_3-15), 0.91 (3H, s, CH_3-17), 1.50 (3H, s, CH_3-14), 2.15 (3H, s, CH_3-13), 3.13 [2H, s, $C_{11}(H_2)$]. ^{13}C NMR spectrum (δ, ppm): 18.89 (C-2), 18.92 (C-6), 19.86 (C-17), 20.22 (C-14), 21.62 (C-16), 29.21 (C-13), 33.12 (C-15), 33.26 (C-4), 33.48 (C-7), 36.49 (C-1), 38.46 (C-10), 41.50 (C-3), 43.33 (C-11), 51.36 (C-5), 129.66 (C-8), 134.61 (C-9), 207.78 (C-12).

Preparation of 11-Dihomodrim-8(9)-en-12-one Oxime (6). A. A solution of **3** (0.48 g, 1.93 mmol) in EtOH (2.5 mL) and Py (2.5 mL) was treated with NH_2OH·HCl (0.16 g, 2.3 mmol), stirred at 20°C for 20 h, treated with H_2O (60 mL), and extracted with Et_2O (3 × 50 mL). The extract was washed with HCl (5%, 5 × 10 mL), $NaHCO_3$ solution (3 × 10 mL), and H_2O (3 × 10 mL), and dried. The Et_2O was evaporated. The solid was recrystallized from pentane to afford crystals (0.5 g, 98%), mp 93–105°C. According to TLC and spectral data, the product was a mixture of the *Z*- and *E*-isomers of **6** in approximately a 1:1 ratio (PMR and ^{15}N NMR spectral data). TLC (benzene:Et_2O, 3:1) R_f 0.46 and 0.68. IR spectrum (ν, cm^{-1}): 3221 (OH), 1591 (C=N), 1552, 947 (N–O).

The mixture of *Z*- and *E*-isomers of **6** (100 mg) was chromatographed over a column of silica gel (3 g) with elution by petroleum ether:Et_2O (9:1) to afford the *E*-isomer (48 mg); by petroleum ether:Et_2O (85:15), a mixture of the *Z*- and *E*-isomers (5 mg); and by petroleum ether:Et_2O (4:1), the *Z*-isomer (43 mg) of **6**.

Z-isomer of **6**, mp 93–95°C (pentane), R_f 0.46.

PMR spectrum (δ, ppm, J/Hz): 0.86 (3H, s, CH_3-16), 0.91 (3H, s ,CH_3-15), 0.98 (3H, s, CH_3-17), 1.57 (3H, s, CH_3-14), 1.80 (3H, s, CH_3-13), 3.01 (1H, d, J = 17.2), 3.36 [1H, d, J = 17.2, $C_{11}(H_2)$], 8.60 (br.s, OH).

^{13}C NMR spectrum (δ, ppm): 18.92 (C-2), 18.98 (C-6), 19.06 (C-13), 20.17 (C-17), 20.34 (C-14), 21.69 (C-16), 26.07 (C-11), 33.27 (C-15), 33.34 (C-4), 33.61 (C-7), 36.10 (C-1), 39.07 (C-10), 41.77 (C-3), 51.82 (C-5), 129.15 (C-8), 135.76 (C-9), 159.80 (C-12).

^{15}N NMR spectrum (δ, ppm): 336 (=N–OH).

E-isomer of **6**, mp 104–105°C (pentane), R_f 0.68.

PMR spectrum (δ, ppm, J/Hz): 0.84 (3H, s, CH_3-16), 0.91 (3H, s ,CH_3-15), 0.95 (3H, s, CH_3-17), 1.57 (3H, s, CH_3-14), 1.86 (3H, s, CH_3-13), 2.86 (1H, d, J = 16.8), 3.01 [1H, d, J = 16.8, $C_{11}(H_2)$], 8.60 (br.s, OH).

^{13}C NMR spectrum (δ, ppm): 13.60 (C-13), 18.85 (C-2), 18.99 (C-6), 20.11 (C-17), 20.18 (C-14), 21.68 (C-16), 33.01 (C-4), 33.28 (C-15), 33.50 (C-7), 34.15 (C-11), 36.37 (C-1), 38.71 (C-10), 41.68 (C-3), 51.18 (C-5), 129.25 (C-8), 135.36 (C-9), 157.98 (C-12).

^{15}N NMR spectrum (δ, ppm): 342 (=N–OH).

B. A solution of the mixture of **2** and **3** (0.84 g, 3.38 mmol, 28:72 ratio) in EtOH (4.5 mL) and Py (4.5 mL) was treated with $NH_2OH{\cdot}HCl$ (0.28 g, 4.03 mmol), stirred, left at 20°C for 20 h, diluted with H_2O (100 mL), and extracted with Et_2O (4 × 50 mL). The extract was washed with HCl (5%, 5 × 20 mL), $NaHCO_3$ solution (3 × 20 mL), and H_2O (3 × 20 mL), and dried. The Et_2O was distilled off. The resulting crystalline solid (0.88 g, 99%) was recrystallized from pentane to afford the mixture of *Z*- and *E*-isomers of **6**, mp 95–105°C.

Products from the Reaction of 6 with H_3PO_4 (86%). Oxime **6** (100 mg, 0.38 mmol) was treated with H_3PO_4 (86%, 1 mL), heated at 70–75°C for 15 min until the oxime dissolved completely, heated at the same temperature for another hour, cooled in an ice bath, and treated dropwise with H_2O (20 mL). The resulting white crystalline precipitate was filtered off, washed with H_2O, dried in air, and recrystallized from hexane to afford a product (36 mg, 36%), mp 146–147°C, that had the same melting point and spectral characteristics as 1,2,6-oxazine (**8**) [7]. TLC used benzene:Et_2O (1:2), R_f 0.60.

The filtrate from separation of the solid was neutralized by KOH (50%) and extracted with Et_2O (3 × 10 mL). The extract was washed with H_2O (3 × 3 mL) and dried. The Et_2O was distilled off. The resulting crystalline solid was recrystallized from Et_2O to afford crystals (60 mg, 56%), mp 119–120°C. According to IR, ^{1}H NMR, ^{13}C, and ^{15}N spectral data, the product was the *N*-oxide **9**. The elemental analysis and XSA indicated that crystalline **9** was the hydrate **9**·H_2O.

TLC ($CHCl_3$:*i*-C_3H_7OH, 9:1), R_f 0.46, $C_{17}H_{29}NO{\cdot}H_2O$. IR spectrum (ν, cm^{-1}): 3467 (H_2O), 3409, 1657 (C=N), 1599, 1221 (N–O), 1201, 969.

PMR spectrum (δ, ppm, J/Hz): 0.84 (3H, s, CH_3-16), 0.87 (3H, s, CH_3-15), 0.97 (3H, s, CH_3-17), 1.29 (3H, s, CH_3-14), 2.02 (3H, s, CH_3-13), 2.28 (1H, dd, J = 5.8, 16), 2.42 [1H, dd, J = 1.6, 14, $C_{11}(H_2)$].

^{13}C NMR spectrum (δ, ppm): 13.23 (C-13), 16.28 (C-17), 18.08 (C-2), 18.65 (C-14), 19.86 (C-6), 20.89 (C-16), 30.05 (C-11), 33.11 (C-4), 33.31 (C-15), 35.18 (C-7), 36.40 (C-10), 38.91 (C-1), 42.41 (C-3), 57.23 (C-5), 57.83 (C-9), 74.49 (C-8), 142.78 (C-12).

^{15}N NMR spectrum (δ, ppm): 302 (=N–O).

Products from the Reaction of 6 with CF_3CO_2H. Oxime **6** (100 mg, 0.38 mmol) was treated with CF_3CO_2H (1 mL), refluxed for 3 h, cooled in an ice bath, treated dropwise with H_2O (20 mL), neutralized with dry $NaHCO_3$, and extracted with Et_2O (3 × 10 mL). The extract was washed with H_2O (3 × 3 mL) and dried. The Et_2O was distilled off. The solid (100 mg) was recrystallized from Et_2O to afford a product (35 mg), mp 119–120°C, that had a melting point, spectral characteristics, and TLC that were identical to those of *N*-oxide **9** obtained by reaction of **6** with H_3PO_4 (86%). The filtrate from separation of the crystals of *N*-oxide **9** was evaporated. The resulting precipitate (67 mg) was chromatographed over a column of silica gel (2 g).

Elution by $CHCl_3$:MeOH (99.5:0.5) gave a product (30 mg, 30%) that had a melting point, TLC, and spectral characteristics that corresponded to 1,2,6-oxazine **8**. Elution by $CHCl_3$:MeOH (98.5:1.5) isolated a product (17 mg) that had a melting point, TLC, and spectral properties that were identical to those of *N*-oxide **9**. The overall yield of *N*-oxide **9** was 52 mg (48%).

Products from the Reaction of 6 with *p*-TsCl in Py. A solution of **6** (100 mg, 0.38 mmol) in Py (1 mL) was treated with *p*-TsCl (87 mg, 0.46 mmol), stirred, left at 20°C for 1 h, treated dropwise with HCl (5%, 15 mL), cooled in an ice bath, and extracted with Et_2O (3 × 10 mL). The extract was washed with HCl (5%, 3 × 3 mL), $NaHCO_3$ solution (3 × 3 mL), and H_2O (2 × 3 mL), and dried. The Et_2O was distilled off. The resulting precipitate (114 mg) was chromatographed over a column of silica gel (3.5 g). Elution by petroleum ether gave a product (10 mg, 13%) that had PMR and ^{13}C NMR spectra that were consistent with the structure of diene **12** [14].

Elution by petroleum ether:Et_2O (1:1) gave a product (7 mg) with spectral data corresponding to the structure of **11**.

Elution by petroleum ether:Et_2O (2:3) gave a mixture (33 mg) of **10** and **11** in a 53:47 ratio (^1H NMR and ^{15}N spectral data). Overall yield of **10** and **11** was 40%.

The mixture of amides **10** and **11** (33 mg) was chromatographed over a column of silica gel (1.7 g). Elution by petroleum ether:Et_2O (57:43) gave sequentially **11** (8 mg), a mixture of **10** and **11** (10 mg, 1:1 ratio), and **10** (11 mg). The yield of pure **11** was 15 mg (15%); **10**, 11 mg (11%).

11-Methylaminooxodrim-8(9)-ene (11), mp 104–105°C (pentane). TLC, benzene:Et_2O (1:3), R_f 0.30. IR spectrum (ν, cm^{-1}): 3306 (CONH), 3073, 1726 (CO), 1646, 1530, 1272.

PMR spectrum (δ, ppm, J/Hz): 0.86 (3H, s, CH_3-15), 0.92 (3H, s, CH_3-14), 0.96 (3H, s, CH_3-16), 1.60 (3H, s, CH_3-13), 2.82 (3H, d, J = 4.8, CH_3-17), 2.91 (1H, d, J = 17.2), 3.06 [1H, d, J = 17.6, $C_{11}(H_2)$], 5.84 (br.s, NH).

^{13}C NMR spectrum (δ, ppm): 18.78 (C-2), 18.85 (C-6), 19.89 (C-16), 20.10 (C-13), 21.62 (C-15), 26.38 (C-17), 33.22 (C-14), 33.35 (C-4), 33.57 (C-7), 35.99 (C-11), 36.12 (C-1), 38.90 (C-10), 41.63 (C-3), 52.14 (C-5), 131.14 (C-8), 136.22 (C-9), 172.12 (C-12).

^{15}N NMR spectrum (δ, ppm); 102 (CONH).

11-Acetylaminodrim-8(9)-ene (10), mp 144–145°C. TLC, benzene:Et_2O (1:3) R_f 0.20. IR spectrum (ν, cm^{-1}): 3298 (NH–CO), 3073, 1727 (CO), 1644, 1531, 1272.

PMR spectrum (δ, ppm, J/Hz): 0.84 (3H, s, CH_3-14), 0.89 (3H, s, CH_3-13), 0.95 (3H, s, CH_3-15), 1.62 (3H, s, CH_3-12), 1.96 (3H, s, CH_3-17), 3.76 (1H, dd, J = 4, 16), 3.82 [1H, dd, J = 4, 12, $C_{11}(H_2)$], 5.11 (br.s, NH).

^{13}C NMR spectrum (δ, ppm): 18.84 (C-6), 18.89 (C-2), 19.45 (C-12), 20.18 (C-15), 21.57 (C-14), 23.23 (C-17), 33.27 (C-4), 33.27 (C-13), 33.70 (C-7), 36.62 (C-1), 36.98 (C-11), 38.60 (C-10), 41.71 (C-3), 52.04 (C-5), 132.04 (C-8), 137.56 (C-9), 169.29 (C-16).

^{15}N NMR spectrum (δ, ppm): 124 (NHCO).

Products from the Reaction of 6 with PCl_5 in Et_2O. A solution of **6** (100 mg, 0.38 mmol) in anhydrous Et_2O (3.5 mL) was stirred, cooled in an ice bath, treated with PCl_5 (250 mg, 1.2 mmol), stirred for another 30 min. treated with pieces of ice (10 g), neutralized by dry $NaHCO_3$, and extracted with Et_2O (3 × 10 mL). The extract was washed with H_2O (2 × 3 mL) and dried. The Et_2O was distilled off. The resulting precipitate (94 g) was chromatographed over a column of silica gel (2.8 g). Elution by petroleum ether gave diene **12** (10 mg, 13%); by petroleum ether:Et_2O (9:1), the *E*-isomer of **6** (8 mg); by petroleum ether:Et_2O (85:15), a mixture of the *Z*- and *E*-isomers of **6** (5 mg); petroleum ether:Et_2O (4:1), the *Z*-isomer of **6** (7 mg). The overall yield of the *Z*- and *E*-isomers of **6** was 20 mg (20%). Then, elution by petroleum ether:Et_2O (1:1) isolated a mixture of **10** and **11** (30 mg, 30%), which was chromatographed again over a column of silica gel (1.5 g) as described above to afford **11** (9 mg), a mixture of **11** and **10** (9 mg), and **10** (8 mg).

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