SYNTHESIS OF *N*-CONTAINING DRIMANE SESQUITERPENOIDS FROM 11-DIHOMODRIMAN-8α-OL-12-ONE

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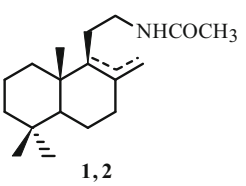
Beckmann reaction products of 11-dihomodriman-8α-ol-12-one oxime with Ac_2O in pyridine, 86% H_3PO_4, p-*TsCl in pyridine, and PCl_5 in ether were investigated. It has been found that the major product from treatment of the oxime with Ac_2O is the oxime acetate. Reaction of the oxime with 86% H_3PO_4 gave (1*S,*2*S,*4a*S,*8a*S)-2,5,5,8a-tetramethyldecahydro-1*H-*naphtho[1,2][5,6]-3-methyl-4,5-dihydro[1,2,6]oxazine; with* p-*TsCl, (1*S,*2*S,*4a*S,*8a*S)-2,5,5,8a-tetramethyldecahydro-1*H-*naphtho[1,2][5,6]-2-methyl-4,5-dihydro[1,3,6]oxazine; with PCl_5, a mixture of products containing 11-acetylamino- and 11-methylamino-oxodrimenes that were isomeric at the double bond, norambreinolide, and a 1,3,6-oxazine.*

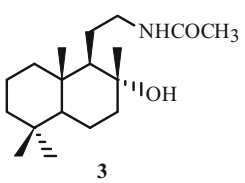
Keywords: Beckmann rearrangement, synthesis, drimane sesquiterpenoids, 11-dihomodriman-8α-ol-12-one, oxazine.

Nitrogen-containing drimanes and their biological activity represent a poorly studied area of terpenoid chemistry. Therefore, the synthesis of such compounds is of scientific interest.

The preparation of amides **1**–**4** via Beckmann rearrangement of the *Z*- and *E*-isomers of oxime **5** of 14,15-dinorlabd-8(17)-en-13-one (**6**) was reported earlier [1]. A multi-step synthesis of amide **7** from (-)-sclareol that uses the natural sesquiterpene drim-9,11-en-8α-ol (**8**) as an intermediate in the synthesis was described [2].



1, 2
1: $\Delta^{8,9}$; **2:** $\Delta^{8,17}$



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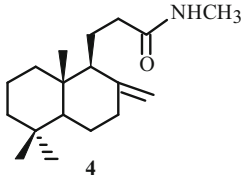

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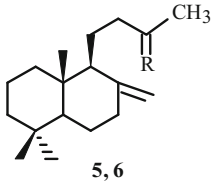
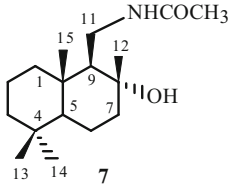


5, 6
5: R = NOH; **6:** R = O



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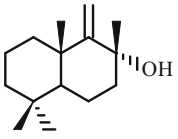

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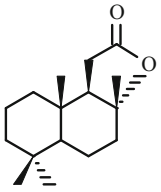

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Our goal was to study the synthesis of **7** via Beckmann rearrangement of oxime **9** of 11-dihomodriman-8α-ol-12-one (**10**). Hydroxyketone **10** is readily available and can be obtained from norambreinolide (**11**) by the method described by us [3]. Oxime **9** was prepared from **10** by reaction with $NH_2OH{\cdot}HCl$ in a mixture of EtOH and Py. It was a mixture of the *Z*- and *E*-isomers according to TLC and ^1H, ^{13}C, and ^{15}N NMR spectra. Because the *Z*-isomer can be easily converted to the *E*-isomer and the latter is energetically more favorable [1, 4], we used **9** for the reactions as a mixture of its *Z*- and *E*-isomers. The Beckmann rearrangement is known to occur stereospecifically as a result of anti-migration of the bulkier radical. Therefore, it was expected that the major product of the Beckmann rearrangement of **9** would be amide **7**.

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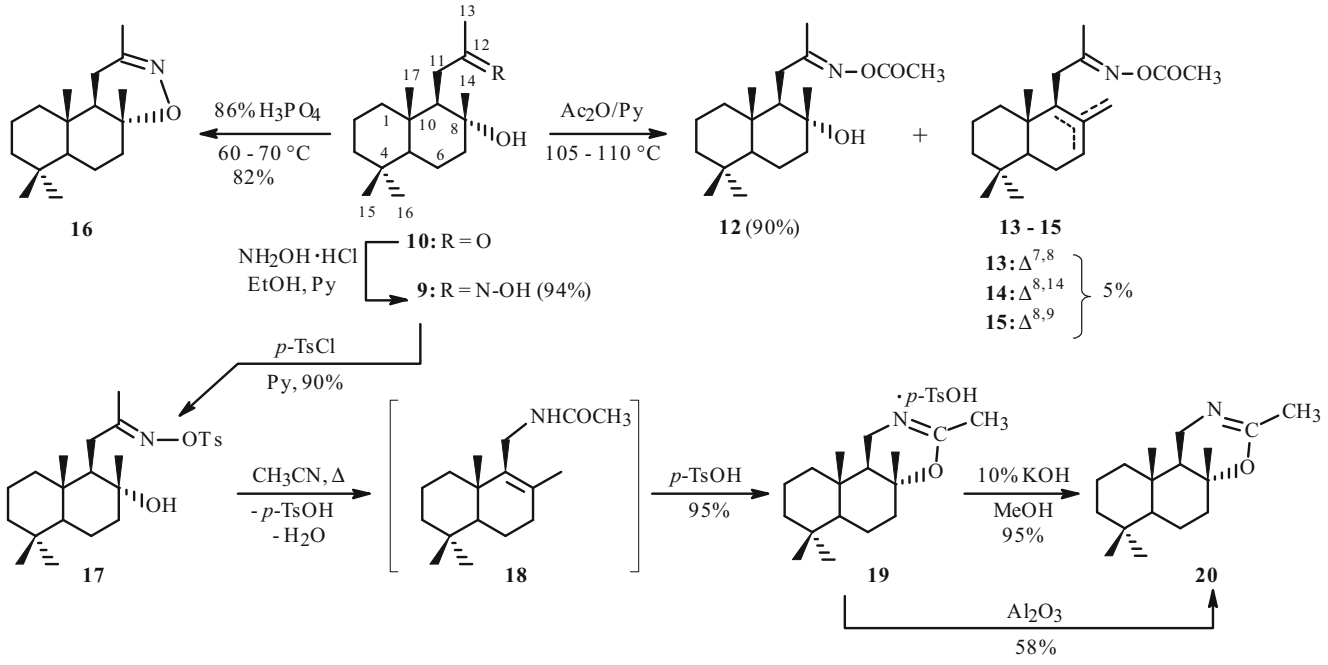


Scheme 1

We reacted **9** with Ac_2O in Py, 86% H_3PO_4, *p*-TsCl in Py, and PCl_5 in Et_2O in order to achieve our goal. A study of the products showed that treatment of **9** with Ac_2O in Py at 105–110°C did not cause rearrangement but gave oxime acetate **12** as the major product (90% yield) and a small amount of a mixture of three isomers of dehydrated oxime acetate **13–15** in a 50:39:11 ratio (5% yield) (Scheme 1).

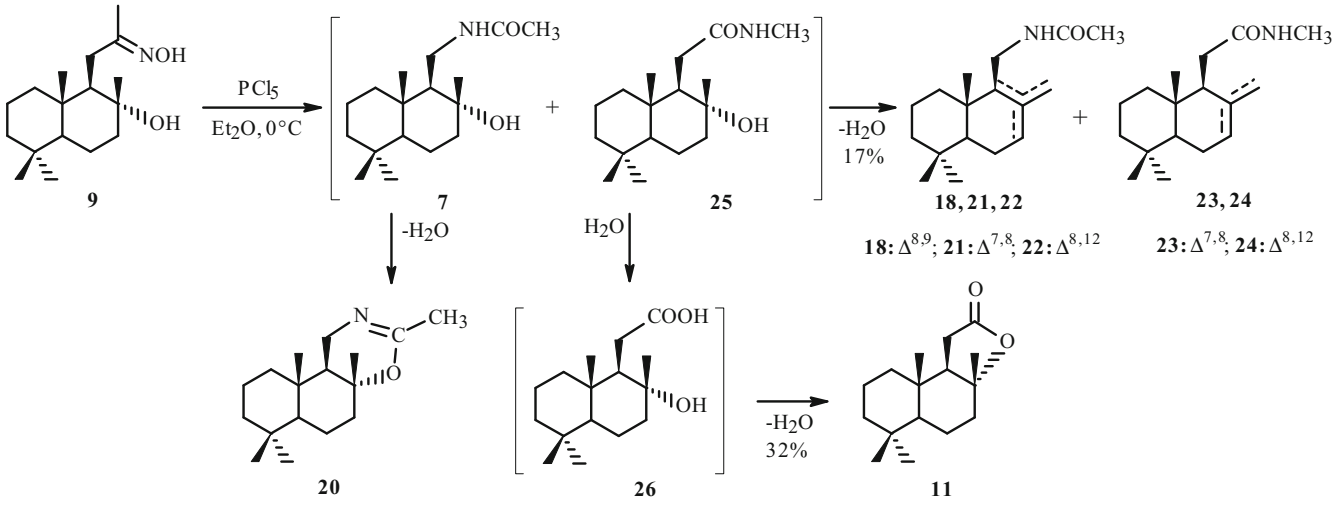
Oxime acetate **12** was a mixture of the *Z*- and *E*-isomers in a 1:4.9 ratio. One of the isomers with the smaller R_f value (TLC) was isolated as pure crystals. It was proven earlier [1] using the oxime of 14,15-dinorlabd-8(17)-en-13-one (**5**) as an example that the isomer with the greater *Rf* value has the *E*-configuration; with the smaller value, the *Z*-configuration. Therefore, by analogy the crystalline isomer of **12** can be assigned the *Z*-configuration. Heating a solution of **9** in 86% H_3PO_4 also did not cause a Beckmann rearrangement but dehydration and cyclization gave (1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyldecahydro-1*H*-naphtho[1,2][5,6]-3-methyl-4,5-dihydro[1,2,6]oxazine (**16**) (Scheme 1).

Reaction of **9** with *p*-TsCl in Py at room temperature gave the oxime tosylate **17**, which underwent Beckmann rearrangement upon brief refluxing in CH_3CN with subsequent loss of water and *p*-toluenesulfonic acid to form amide **18** as an intermediate. Then, this amide, probably due to *p*-TsOH, cyclized and formed the salt of (1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-tetramethyldecahydro-1*H*-naphtho[1,2][5,6]-2-methyl-4,5-dihydro[1,3,6]oxazine with *p*-TsOH (**19**), treatment of which with KOH solution (10%) in MeOH at 20°C or filtration of a solution of the salt in CH_2Cl_2 through a column of Al_2O_3 produced 1,3,6-oxazine **20**, the structure of which was confirmed by elemental analysis and spectral data. Oxazine **20** was also characterized by preparing its picrate and hydrochloride.

Reaction of **9** with PCl_5 in Et_2O at 0°C produced a multi-component mixture of products, column chromatography of which over silica gel isolated and identified pure crystalline norambreinolide (**11**) (32% yield). A mixture of compounds that according to ^1H, ^{13}C, and ^{15}N NMR spectra most likely contained 11-acetylaminodrimenes **18**, **21**, and **22** that are isomeric at the double bond and 11-methylaminooxodrimenes **23** and **24** also eluted from the column.

Also, a mixture of compounds containing two *N*-containing compounds according to ^{15}N NMR spectra eluted from the column. One of these compounds was a 1,3,6-oxazine (**20**); another, apparently hydroxyamide **25** based on spectral data (Scheme 2).

The observation of **18**, **20**, **21**-**24**, and **11** among the products of the reaction of **9** with PCl_5 can be explained by assuming that the Beckmann rearrangement under these conditions occurred with both anti-migration of the bulkier radical to form **7** and migration of the C_{13} methyl to form **25** as intermediates. Hydroxyamides **7** and **25** under the reaction conditions underwent further conversion. Their dehydration resulted in the formation of **18** and **21**-**24**. Loss of water and subsequent cyclization produced 1,3,6-oxazine **20** from **7**. Hydroxyamide **25** was hydrolyzed and converted into **26** that formed lactone norambreinolide **11**.



Scheme 2

Unfortunately, not all products from reaction of **9** with PCl_5 could be isolated pure and convincingly identified.

Thus, we synthesized new *N*-containing drimane sesquiterpenoids including those with 1,2,6- and 1,3,6-oxazine rings.

EXPERIMENTAL

Melting points were determined on a Boetius heating stage. IR spectra were recorded on Perkin–Elmer Spectrum 100FT-IR or Specord 74 spectrophotometers. PMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AC-E 400 (400 and 100 MHz) spectrometer. Chemical shifts are given on the δ-scale in ppm relative to $CHCl_3$ resonances as an internal standard (resonances at δ 7.24 and 77.00 ppm, respectively). Resonances in ^{13}C NMR spectra were assigned using the DEPT program and comparison with spectra of known related compounds [5, 6].

The course of reactions was monitored by TLC on Silufol plates with detection by I_2 vapor. Column chromatography used silica gel L 100/400 μm. Ether extracts were dried over anhydrous $MgSO_4$.

Preparation of Oxime 9. A. A solution of 11-dihomodriman-8α-ol-12-one (**10**, 1 g, 3.75 mmol) in EtOH (5 mL) and Py (5 mL) was treated with $NH_2OH{\cdot}HCl$ (0.29 g, 4.17 mmol), stirred, left at 18–20°C for 24 h, and treated with H_2O (100 mL). The resulting white oily solid crystallized upon standing. The precipitate was filtered off, washed with water, dried in air, and recrystallized from hexane to afford crystals (0.99 g, 94%) with mp 117–118°C.

The product was a mixture of the *Z*- and *E*-isomers of **9** according to TLC and spectral data. TLC: benzene:ether (1:2), R_f 0.33 and 0.56, $C_{17}H_{31}NO_2$.

IR spectrum (KBr, ν, cm^{-1}): 3500 (OH), 3340 (br.), 1660 (C=N), 1115, 940 (N–O).

PMR spectrum (ppm, J/Hz): (characteristic resonances) 0.79 (3H, s, CH_3-17), 0.80 (3H, s, CH_3-15), 0.87 (3H, s, CH_3-16), 1.20 (3H, s, CH_3-14), 1.92 (3H, s, CH_3-13), 2.19 (1H, dd, J = 3.6, 15.6), 2.42 (1H, dd, J = 6.8, 16) [$C_{11}(H_2)$], 8.64 (br.s, OH). Resonances in the ^{13}C NMR spectrum of one of the isomers, which was probably the energetically more favorable *E*-isomer, were about twice as strong as those of the other.

^{13}C NMR spectrum (ppm): (major isomer of **9**) 14.65 (C-17), 15.27 (C-13), 18.54 (C-2), 20.27 (C-6), 21.54 (C-15), 24.22 (C-14), 31.57 (C-11), 33.33 (C-4), 33.43 (C-16), 38.81 (C-10), 39.76 (C-1), 41.79 (C-3), 43.95 (C-7), 56.03 (C-5), 56.85 (C-9), 73.77 (C-8), 161.13 (C-12).

^{13}C NMR spectrum (ppm): (minor isomer of **9**) 15.16 (C-17), 18.63 (C-2), 20.06 (C-6), 20.19 (C-13), 21.52 (C-15), 24.07 (C-11), 24.43 (C-14), 33.33 (C-4), 33.43 (C-16), 38.94 (C-10), 39.88 (C-1), 41.83 (C-3), 42.87 (C-7), 56.16 (C-5), 58.40 (C-9), 73.54 (C-8), 161.21 (C-12).

^{15}N NMR spectrum (ppm): 335.8 and 338.51 (=N–OH of *Z*- and *E*-isomers).

B. A solution of hydroxyketone **10** (100 mg, 0.37 mmol) in EtOH (0.5 mL) and Py (0.5 mL) was treated with $NH_2OH·HCl$ (42 mg, 0.60 mmol), heated at 95–105°C for 1 h, cooled, treated with water (10 mL) and HCl solution (5 mL, 5%), and extracted with ether (3 × 10 mL). The extracts were washed with HCl (5%, 3 × 3 mL), $NaHCO_3$ solution (3 × 3 mL), and water (3 × 3 mL) and dried. The ether was distilled off. The solid was recrystallized from hexane to afford a mixture of the *Z*- and *E*-isomers of **9** (89 mg, 84%) with mp 118–119°C.

Products from Reaction of 9 with Ac_2O in Py. A solution of **9** (100 mg, 0.35 mmol) in Py (0.5 mL) and Ac_2O (0.17 mL, 184 mg, 1.80 mmol) was heated at 105–115°C for 1 h, cooled in an ice bath, treated with several pieces of ice and dropwise with H_2SO_4 (5 mL, 10%), and extracted with ether (3 × 10 mL). The extracts were washed with $NaHCO_3$ solution (3 × 3 mL) and water (3 × 3 mL) and dried. The ether was distilled off. The solid was chromatographed over a column of silica gel (3.4 g) with elution by hexane:ether (9:1) to afford dehydrated oxime acetate (5 mg, 5%) as a mixture of isomers **13–15** in a 50:39:11 ratio [PMR spectra had characteristic resonances (ppm) at 1.26 (s, CH_3–C=C), 1.89, 1.90, and 1.93 (3s, 3 CH_3–C=N–), 2.15, 2.17, and 2.19 (3s, 3 OAc), 4.72 and 4.82 (both 1H s, >C=CH_2), 5.43-5.44 (m, >C=CH)]. The amounts of **13–15** were determined in two ways. The amounts of **13** and **14** and their sum were determined by integrating the resonances of OAc and (>C=CH) and (>C=CH_2) groups for the three isomers. The content of the isomer with the tetrasubstituted double bond (**15**) was determined by difference.

IR spectrum (film, ν, cm^{-1}): 3100 (>C=CH_2), 1750 (OAc), 1640 (C=N), 1200, 930 (N–O), 880, 830 (>C=CH).

Elution by hexane:ether (2:3) afforded a mixture (104 mg, 90%) of the *Z*- and *E*-isomers of **12**. TLC: benzene:ether (1:2), R_f 0.31 and 0.48, $C_{19}H_{33}NO_3$.

IR spectrum (film, ν, cm^{-1}): 940 (N–O), 1200, 1750 (OAc), 1640 (C=N), 1115, 3470 (OH).

^{15}N NMR spectrum (ppm): 347.33 and 349.92 (2 × =N–OAc of the *Z*- and *E*-isomers). The ratio of the *Z*- and *E*-isomers in the mixture was 1:4.9 (PMR spectrum). This ratio was determined by integrating resonances of methyls with characteristic resonances (ppm) at 1.24 and 1.26 (2 CH_3–C–OH), 2.00 and 2.10 (2 CH_3–C=N), 2.14 and 2.18 (2 OAc). The product was partially crystalline. Crystals were filtered off and washed with hexane to afford the *Z*-isomer of **12** (7 mg), R_f 0.31, mp 105–107°C.

IR spectrum (KBr, ν, cm^{-1}): 3450 (OH), 1750 (OAc), 1640 (C=N), 1210, 1180, 980 (N–O).

PMR spectrum (ppm, J/Hz): 0.79 (3H, s, CH_3-17), 0.86 (3H, s, CH_3-16), 0.89 (3H, s, CH_3-15), 1.24 (3H, s, CH_3-14), 2.10 (3H, s, CH_3-13), 2.18 (3H, s, CH_3-19), 2.48 (1H, dd, J = 4.8, 14), 2.57 [1H, dd, J = 7.6, 14, $C_{11}(H_2)$].

^{13}C NMR spectrum (ppm): 15.16 (C-17), 18.54 (C-2), 19.86 (C-19), 20.31 (C-6), 20.41 (C-13), 21.56 (C-15), 24.09 (C-14), 26.26 (C-11), 33.36 (C-4), 33.48 (C-16), 39.04 (C-10), 39.63 (C-1), 41.71 (C-3), 44.55 (C-7), 56.22 (C-5), 58.11 (C-9), 73.58 (C-8), 168.79 (C-12), 169.42 (C-18).

^{15}N NMR spectrum (ppm): 347.41 (=N–OAc).

The *E*-isomer of **12** was a viscous liquid.

PMR spectrum (ppm, J/Hz): 0.80 (3H, s, CH_3-17), 0.84 (3H, s, CH_3-16), 0.88 (3H, s, CH_3-15), 1.26 (3H, s, CH_3-14), 2.00 (3H, s, CH_3-13), 2.14 (3H, s, CH_3-19), 2.35 (1H, dd, J = 4.4, 14.8), 2.58 [1H, dd, J = 8.0, 15.2, $C_{11}(H_2)$].

^{13}C NMR spectrum (ppm): 15.32 (C-17), 15.99 (C-13), 18.60 (C-2), 19.68 (C-19), 20.26 (C-6), 21.54 (C-15), 23.97 (C-14), 31.78 (C-11), 33.33 (C-4), 33.46 (C-16), 38.80 (C-10), 39.94 (C-1), 41.71 (C-3), 44.16 (C-7), 56.07 (C-5), 57.01 (C-9), 73.68 (C-8), 168.90 (C-12), 170.88 (C-18).

Preparation of (1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-Tetramethyldecahydro-1*H*-naphtho[1,2][5,6]-3-methyl-4,5-dihydro[1,2,6]oxazine (16). Oxime **9** (100 mg, 0.35 mmol) was treated with H_3PO_4 (86%, 1 mL), heated at 60–70°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 water (20 mL). The white crystalline precipitate was filtered off, washed with water, dried in air, and recrystallized from hexane to afford crystals (77 mg, 82%), mp 146–147°C. Elemental analysis and spectral data indicated that the product was 1,2,6-oxazine **16**, $C_{17}H_{29}NO$.

IR spectrum (KBr, ν, cm^{-1}): 1630 (C=N), 920 (N–O).

PMR spectrum (ppm): 0.79 (3H, s, CH_3-17), 0.82 (3H, s, CH_3-15), 0.88 (3H, s, CH_3-16), 1.11 (3H, s, CH_3-14), 1.92 (3H, s, CH_3-13).

^{13}C NMR spectrum (ppm): 14.36 (C-17), 18.33 (C-2), 19.42 (C-6), 19.67 (C-14), 21.48 (C-15), 22.00 (C-13), 23.29 (C-11), 33.14 (C-4), 33.27 (C-16), 35.93 (C-10), 38.65 (C-7), 38.90 (C-1), 41.81 (C-3), 49.29 (C-9), 56.06 (C-5), 75.28 (C-8), 155.11 (C-12).

^{15}N NMR spectrum (ppm): 349.96 (=N–O).

Products from Reaction of 9 with *p*-TsCl in Py. A solution of **9** (200 mg, 0.71 mmol) in Py (2 mL) was treated with *p*-TsCl (164 mg, 0.86 mmol), stirred, left at 20°C for 30 min, treated dropwise with HCl (16 mL, 5%), cooled in an ice bath, and extracted with ether (3 × 10 mL). The extracts were washed with HCl (5%, 3 × 3 mL), $NaHCO_3$ solution (3 × 3 mL), and water (3 × 3 mL) and dried. The ether was distilled off. The solid (280 mg, 90%) was partially crystalline. Crystals were flitered off and washed with hexane:ether (99:1) to afford the product (20 mg), mp 61–62°C, that was oxime tosylate **17**, $C_{24}H_{37}SNO_4$, according to spectral data and elemental analysis.

IR spectrum (KBr, ν, cm^{-1}):3580 (OH),3350, 3270, 1670 (C=N), 1640, 1600 (benzene ring), 1450, 1350 (O–SO_2–), 1280, 1180, 1170, 1080, 1030, 930 (N–O), 870, 780.

PMR spectrum (ppm, J/Hz): 0.75 (3H, s, CH_3-17), 0.80 (3H, s, CH_3-15), 0.85 (3H, s, CH_3-16), 1.07 (3H, s, CH_3-14), 1.98 (3H, s, CH_3-13), 2.22–2.38 (2H, m, H_2-11), 2.42 (3H, s, CH_3-C_6H_4), 7.30 (2H) and 7.83 (2H, J = 8.8, AA^1BB^1-system, C_6H_4).

The filtrate from the separated crystals of tosylate oxime **17** was evaporated. The solid (260 mg) was dissolved in CH_3CN (3 mL) and refluxed for 30 min. The CH_3CN was distilled off. The crystalline solid was washed with a small amount of ether to afford a crystalline product (240 mg), mp 138–139°C, that was the salt of a 1,3,6-oxazine with *p*-TsOH (**19**) according to IR and PMR spectral data.

IR spectrum (KBr, ν, cm^{-1}): 3250 (NH), 3130, 1730 (=CH_2), 1680, 1530, 1450, 1220, 1120, 1030, 1000, 805, 680, (*p*-TsOH).

PMR spectrum (ppm, J/Hz): 0.78 (3H, s, CH_3-15), 0.82 (3H, s, CH_3-13), 0.86 (3H, s, CH_3-14), 1.38 (3H, s, CH_3-12), 2.32 (3H, s, CH_3-17), 2.38 (3H, s, CH_3-C_6H_4), 3.02-3.57 (2H, m, H_2-11), 7.15 and 7.79 (2H, J = 8.06, 8.20, AA1BB1-system, C_6H_4), 13.09 (1H, br.s, SO_3H).

Preparation of (1*S*,2*S*,4a*S*,8a*S*)-2,5,5,8a-Tetramethyldecahydro-1*H*-naphtho[1,2][5,6]-2-methyl-4,5-dihydro[1,3,6]oxazine with *p*-TsOH (20). A. *p*-Toluenesulfonate **19** (220 mg) was treated with KOH solution (4.4 mL, 10%) in MeOH and stirred at 20°C for 1 h. The MeOH was vacuum distilled. The solid was treated with water (20 mL) and extracted with ether (5 × 10 mL). The extract was washed with water (3 × 5 mL) and dried. The ether was distilled off to afford a viscous liquid (127 mg, 95%) of **20**, the structure of which was confirmed by elemental analysis and spectral data, $C_{17}H_{29}NO$.

IR spectrum (CCl_4, ν, cm^{-1}): 1674 (C=N).

PMR spectrum (ppm, J/Hz): 0.81 (3H, s, CH_3-15), 0.83 (3H, s, CH_3-13), 0.88 (3H, s, CH_3-14), 1.24 (3H, s, CH_3-12), 1.85 (3H, s, CH_3-17), 3.13 (1H, ddd, J = 1.6, 12.4, 16), 3.29 (1H, dd, J = 4.8, 16) [$C_{11}(H_2)$].

^{13}C NMR spectrum (ppm): 15.37 (C-15), 18.38 (C-2), 19.59 (C-6), 21.45 (C-13), 21.68 (C-17), 22.08 (C-12), 33.15 (C-4), 33.34 (C-14), 36.12 (C-10), 38.99 (C-1), 40.37 (C-7), 40.76 (C-3), 41.83 (C-11), 52.05 (C-5), 56.28 (C-9), 76.72 (C-8), 156.85 (C-16).

^{15}N NMR spectrum (ppm): 212.3 (–N=C–O).

B. A solution of *p*-toluenesulfonate **19** (20 mg) in CH_2Cl_2 (1 mL) was filtered through a column of Al_2O_3 (Brockmann activity II, 0.4 g). The column was eluted with CH_2Cl_2 (2 mL) to afford 1,3,6-oxazine **20** (7 mg, 58%).

Preparation of 1,3,6-Oxazine 20 Picrate. A solution of 1,3,6-oxazine **20** (16 mg) in EtOH was treated with an aqueous solution of picric acid. The resulting yellow precipitate was filtered off, washed with water, dried in air, and recrystallized from EtOH to afford the picrate of **20** (10 mg), mp 150–151°C, $C_{17}H_{29}NO{\cdot}C_6H_3N_3O_7{\cdot}1/2C_2H_5OH$.

IR spectrum (KBr, ν, cm^{-1}): 1670 (C=N), 1630 (picric acid), 1600, 1520, 1420, 1340, 1300, 1270, 1070, 900, 730, 700.

Preparation of 1,3,6-Oxazine 20 Hydrochloride. A solution of 1,3,6-oxazine **20** (40 mg) in hexane (1 mL) was treated with a saturated ether solution of HCl until acidic. Solvents were evaporated to afford crystals (46 mg) of **20** hydrochloride, mp 156–157°C.

IR spectrum (KBr, ν, cm^{-1}): 2620 (C=NH), 1650.

Products from Reaction of 9 with PCl_5 in Ether. A stirred suspension of PCl_5 (1.1 g, 5.28 mmol) in anhydrous ether (5 mL) was treated dropwise over 5 min with a solution of **9** (0.5 g, 1.78 mmol) in anhydrous ether (22 mL) with cooling in an ice bath, stirred at the same temperature for 30 min, treated with several pieces of ice, and extracted with ether (3 × 10 mL) (extract I). The extract was washed with water (3 × 5 mL) and dried. The ether was distilled off. The aqueous extracts were combined with the acidic aqueous layer, made basic with NH_4OH (24%, 15 mL), and extracted with ether (3 × 20 mL) (extract II). The extract was washed with water (3 × 5 mL) and dried. The ether was distilled off. The solid (0.4 g) after distillation of ether from extract I was dissolved in $CHCl_3$ (2 mL) and chromatographed over a column of silica gel

(12 g) with elution by $CHCl_3$ to afford a crystalline product (90 mg, 20%), mp 123–124°C, that corresponded to norambreinolide **11** according to mp and IR, PMR, and ^{13}C NMR spectral data [5]; lit. mp 123–124°C [7].

IR spectrum (KBr, ν, cm^{-1}): 1772 (lactone).

PMR spectrum (ppm, J/Hz): 0.84 (3H, s, CH_3-16), 0.89 (3H, s, CH_3-14), 0.91 (3H, s, CH_3-15), 1.34 (3H, s, CH_3-13), 2.23 (1H, dd, J = 6.4, 16), 2.39 (1H, dd, J = 14.8, 16.4) [$C_{11}(H_2)$].

^{13}C NMR spectrum (ppm): 15.03 (C-16), 18.05 (C-2), 20.52 (C-6), 20.88 (C-13), 21.53 (C-14), 28.68 (C-11), 33.08 (C-4), 33.13 (C-15), 36.01 (C-10), 38.67 (C-1), 39.46 (C-7), 42.13 (C-3), 56.61 (C-5), 59.08 (C-9), 86.35 (C-8), 176.85 (C-12).

A mixture of $CHCl_3$:CH_3OH (99:1) eluted a viscous liquid (76 mg, 17%) that was a mixture of 11-acetylaminodrimenes (**18**, **21**, **22**) isomeric at the double bond and 11-methylaminooxodrimenes **23** and **24**.

IR spectrum (CCl_4, ν, cm^{-1}): 3291 (NHCO), 3087, 1645, 1552, 1412 (=CH_2), 1280, 887, 845 (>C=CH), 813.

PMR spectrum (ppm, J/Hz): (characteristic resonances) 1.62, 1.68, 1.69 (3s, 3 CH_3 on double bond), 1.93, 1.95, 1.96 (3s, 3 $COCH_3$), 2.78 (d, J = 4.8) and 2.82 (d, J = 5.2) (2 $NHCH_3$), 4.50 and 4.53 (both 1H s, >C=CH_2 of the first isomer), 4.79 and 4.91 (both 1H s, >C=CH_2 of the second isomer), 5.11, 5.38, 5.42, 5.50, 5.53 (5 br.s, 5 NH), 5.54 and 5.55 (2 br.s, 2 × >C=CH).

^{13}C NMR spectrum (ppm): (characteristic resonances) 172.22, 173.59, 174.37 (3 NH<u>C</u>OCH_3), 169.61 and 169.93 (2 <u>C</u>ONHCH_3), 122.60 and 124.94 (2 × >C=<u>C</u>H), 106.52 and 106.93 (2 × >C=<u>C</u>H_2). The total number of resonances in the spectra corresponded to the presence of five isomers with 17 C atoms in each in the mixture.

^{15}N NMR spectrum (ppm): 100.95, 101.60, 118.09, 120.73, 123.39 (5 NHCO).

The solid (0.1 g) after distillation of ether from extract II was dissolved in hexane (3 mL) and chromatographed over a column of silica gel (3 g) with elution by $CHCl_3$ to afford a crystalline product (50 mg), mp 123–124°C, that was identical by TLC and spectral data to norambreinolide **11**. The overall yield of **11** was 140 mg (32%). A mixture of $CHCl_3$:CH_3OH (99:1) eluted a product (40 mg) that contained two *N*-containing compounds according to ^{15}N NMR. One of the components of this mixture was 1,3,6-oxazine **20** according to ^{1}H, ^{13}C, and ^{15}N NMR spectral data, which are given above. The second was most probably hydroxyamide **25**. However, these compounds could not be separated pure from the mixture and convincingly identified.

^{15}N NMR spectrum (ppm): 211.02 (–N=C–O), 102.05 ($NHCH_3$).

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