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SYNTHESIS OF *O*-VINYL ETHERS OF PENTACYCLIC TRITERPENE ALCOHOLS AND LUPANE-TYPE OXIMES

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*Vinylation by acetylene of lupane-type pentacyclic triterpene C-28- and C-3*β*-alcohols and C-20-oximes in superbase solutions synthesized the corresponding C-28- and C-3*β*-O-vinyl ethers and C-20-O-vinyloximes. The reaction of 3*β*,28-dimethoxy-29-norlupan-20-one with acetylene in superbase KOH–DMSO produced a derivative with an N-vinylpyrrole ring in the C-19 side chain.*

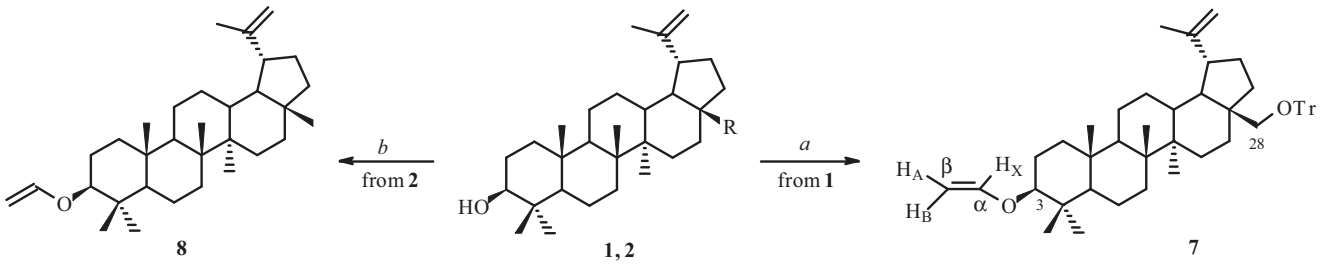
Keywords: betulin, lupeol, 3*β*,28-dimethoxy-29-norlupan-20-one oxime, acetylene, superbase solution, *O*-vinyl ethers.

Vinyl ethers of alcohols and oximes [1–3] are valuable intermediates in the synthesis of polymers [4] and various classes of heterocyclic compounds [1, 5]. The development of methods to prepare vinyl ethers of oxygenated compounds has recently become very significant because they can resolve design issues for biodegradable polymers [6].

Direct vinylation by acetylene of hydroxyl-containing compounds in superbase solutions is a rational method for preparing vinyl ethers [1–3]. The method is successfully used in the laboratory and industry, allows available reagents and simple apparatuses to be used, and is environmentally benign.

Previously, vinylation by acetylene of betulin and allobetulin in KOH–DMSO superbase solution was used by us to prepare betulin 28-*O*-vinyl and 3*β*,28-*O*,*O*-divinyl ethers [7] and allobetulin 3*β*-*O*-vinyl ether [8].

Herein, several lupane-type pentacyclic triterpenes (**1**–**3**) with C-3 or C-28 hydroxyls and 3*β*,28-dihydroxy- and 3*β*,28-dimethoxy-29-norlupan-20-ones (**4** and **5**) were used as examples to demonstrate the synthesis of new *O*-vinyl ethers of triterpene alcohols and the first *O*-vinylketoximes, which are of interest as monomers for polymerization and starting compounds for synthesizing heterocyclic derivatives.



8 **1, 2** **7**

1: R = CH_2OTr; **2:** R = CH_3

a. C_2H_2, KOH–DMSO, 130°C, 2 h; *b*. C_2H_2, NaOH–CsF–DMSO, 130°C, 2.5 h

Compound **1** was prepared by the literature method [9]. Lupeol (**2**) was isolated from birch bark as before [10]. Alcohol **3** was synthesized by treating 28-acetoxybetulin (**6**) with TsCl in Py first at room temperature and then under reflux to give 28-acetoxylupa-2,20(29)-diene, which was hydrolyzed without isolation by KOH in MeOH. Vinylation of the C-28-OH in betulin and 3*β*-OH in allobetulin to form the corresponding vinyl ethers was shown in our previous work to occur readily in KOH–DMSO superbase solution at 80 and 110°C with triterpenoid–DMSO ratios of 1:100 (for betulin 28-*O*-vinyl ether) and 1:40 ratios (for allobetulin 3*β*-*O*-vinyl ether) [7, 8]. Attempts to produce ethers **7**–**9** under analogous conditions did not give the desired results. Vinylation of the 3*β*-OH of C-28-*O*-trityl-substituted betulin derivative **1** formed ether **7** in KOH–DMSO

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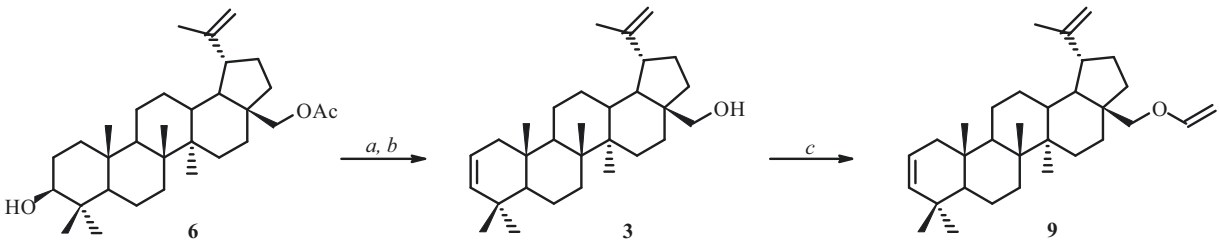
superbase solution at 130°C for 2 h (**1**–DMSO, 1:40). Vinylation of lupeol (**2**) occurred at 130°C in the presence of NaOH–CsF–DMSO (**2**–DMSO, 1:40, 2.5 h). Vinylation of C-28-alcohol **3** went smoothly in 20 min in KOH–DMSO superbase solution at 130°C (**3**–DMSO, 1:100). The yields of **7**, **8**, and **9** after isolation of them by column chromatography (CC) over silica gel or Al_2O_3 were 52, 76, and 50%, respectively.



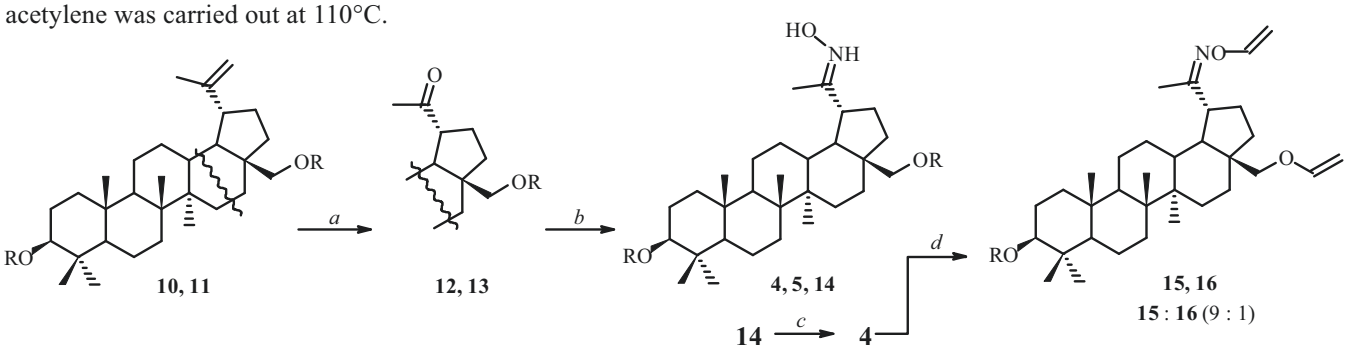
a. TsCl, Py, 25°C, 8 h, then reflux 16 h; *b.* KOH, MeOH, 3 h; *c.* C_2H_2, KOH–DMSO, 130°C, 20 min

The reaction of acetylene in superbase solution with ketoximes without an α-methylene was a general method for synthesizing *O*-vinylketoximes, which were key intermediates in the Trofimov pyrrole synthesis [1, 2].

This method has been used in the scientific literature to synthesize *O*-vinylketoximes of various structural types. In particular, steroidal Δ^5-pregnen-3β-ol-20-one oxime was reacted with acetylene in KOH–DMSO to form Δ^5-pregnen-3β-ol-20-one *O*-vinyloxime (10% yield) [11]. *O*-Vinyl derivatives of pentacyclic triterpenoid ketoximes have not been reported.

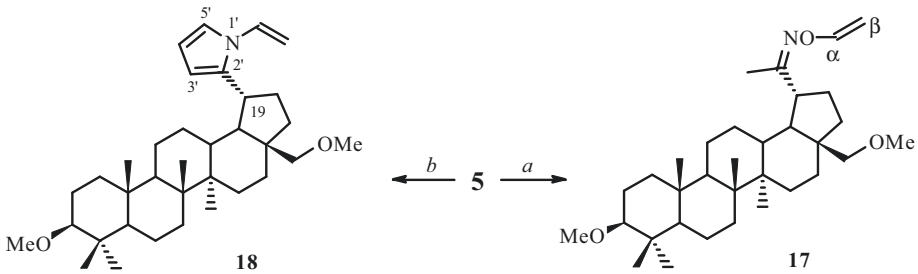
Triterpenoids **4** and **5** with free and protected C-3 and C-28 hydroxyls were used as examples to study reactions of triterpene ketoximes with acetylene in superbase solution.

Ozonolysis of betulin diacetate **10** and 3β,28-dimethoxylup-20(29)-ene **11** produced the corresponding C-20-ketones **12** and **13**, subsequent reaction of which with $NH_2OH{\cdot}HCl$ synthesized oximes **14** and **5**. Hydrolysis of the acetates in **14** by $Ca(OH)_2$ in MeOH–$CHCl_3$ gave 3β,28-dihydroxy-29-norlupan-20-one **4**, *O*-vinylation of which by acetylene in KOH–DMSO superbase solution under conditions analogous to those for preparing betulin 28-*O*-vinyl ether formed an unidentified product mixture. A mixture of divinyl- (**15**) and trivinyloxy-derivatives (**16**) in a 9:1 ratio (according to PMR data) was isolated in overall yield ~20% if the reaction was performed at 80°C under high-dilution conditions (oxime–DMSO, 1:330). However, the reaction of 3β,28-*O*,*O*-dimethyl-substituted ketoxime **5** with acetylene in KOH–DMSO at 80°C with a **5**–DMSO ratio of 1:100 gave after 15 min C-20-*O*-vinylketoxime **17** in 66% yield (after CC over Al_2O_3). A difficultly identified mixture of compounds including **18** (4% yield) with an *N*-vinylpyrrole ring in the C-19 side chain formed if the reaction of **5** with acetylene was carried out at 110°C.



4, 15: R = H; **5, 11, 13:** R = Me; **10, 12, 14:** R = Ac; **16:** R = $CH{=}CH_2$

a. O_3, CH_2Cl_2, –60°C, Me_2S; *b.* $NH_2OH{\cdot}HCl$, Py, MeOH, reflux, 6 h; *c.* $Ca(OH)_2$, 70 h, 50°C; *d.* C_2H_2, KOH–DMSO, 80°C, 75 min



a. C_2H_2, KOH–DMSO, 80°C, 15 min; *b.* C_2H_2, KOH–DMSO, 110°C, 40 min

The structures of the obtained compounds were established by NMR spectroscopy and mass spectrometry. PMR and ^{13}C NMR resonances for **5**, **8**, **15**, **17**, and **18** were fully assigned using 2D experiments on Bruker Avance III or Bruker AM-300 instruments.

Thus, direct vinylation by acetylene in superbase solution of lupane-type pentacyclic triterpene alcohols and C-20-ketoximes produced new *O*-vinyl triterpene alcohols and the first triterpene *O*-vinylketoximes.

EXPERIMENTAL

PMR and ^{13}C NMR spectra were obtained on a Bruker Avance III pulsed spectrometer (Germany) at operating frequency 500.13 MHz for ^{1}H and 125.47 MHz for ^{13}C or on a Bruker AM-300 spectrometer (Germany) at operating frequency 300.13 and 75.47 MHz, respectively. Chemical shifts in PMR and ^{13}C NMR spectra were given in ppm vs. solvent resonances ($CDCl_3$ and CD_3OD) or TMS internal standard. SSCC (^{1}H–^{1}H) were given in Hz. 2D spectra were recorded in standard modes using multi-pulse sequences embedded in Bruker Avance III or Bruker AM-300 instrument software. Electron-impact mass spectra were measured using direct sample introduction into the ion source of a Thermo Finnigan MAT95XP mass spectrometer (temperature programmed from 50 to 270°C, ionizing potential 70 eV). Column chromatography used SiO_2 (L grade, 100/160 mesh, Russia) and Al_2O_3 (L grade, 40/250 mesh, Czechoslovakia). TLC used Sorbfil plates (PTSKh-AF-A, Imid Ltd., Krasnodar, Russia) with detection of chromatograms by anisaldehyde. Melting points were determined on a Kofler apparatus.

Lupa-2,20(29)-dien-28-ol (3). A solution of **6** (2.0 g, 4.126 mmol) [12] and TsCl (7.55 g, 39.610 mmol) in anhydrous Py (48 mL) was stirred for 8 h at room temperature, refluxed for 16 h, cooled, treated with HCl solution (10%) to pH ~2, and extracted with $CHCl_3$. The organic layer was separated, washed with H_2O, dried over Na_2SO_4, and evaporated. The resulting solid was dissolved in MeOH (250 mL), treated with KOH (10.10 g, 0.18 mol), stirred for 3 h, treated with HCl solution (5%), and filtered. The filtrate was concentrated and extracted with $CHCl_3$. The organic layer was separated, washed with H_2O, dried over Na_2SO_4, and evaporated. The solid was chromatographed over SiO_2 (eluents hexane and hexane–EtOAc, 5:1) to afford **3** (1.12 g, 75%). Amorphous compound. ^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.86, 0.87, 0.94, 0.99, 1.05, 1.67 (3H each, s, CH_3-25, 24, 23, 27, 26, 30), 2.41 (1H, m, H-19), 3.34, 3.81 (1H each, d, J = 11.0, H-28), 4.59, 4.69 (1H each, s, H-29), 5.36 (1H, d, J = 10.0, H-3), 5.40 (1H, dd, J = 10.0, 5.0, H-2). ^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 14.70 (CH_3-27), 15.64 (CH_3-26), 16.36 (CH_3-25), 19.10 (CH_3-30), 19.35 (C-6), 21.20 (C-11), 22.53 (CH_3-24), 25.33 (C-12), 27.00 (C-15), 29.87 (C-16, 21), 31.72 (C-23), 33.29 (C-7), 34.67 (C-4), 34.72 (C-22), 36.35 (C-10), 37.39 (C-13), 40.95 (C-8), 41.17 (C-1), 42.69 (C-14), 47.06 (C-17), 47.80 (C-19), 48.80 (C-18), 48.93 (C-9), 52.04 (C-5), 60.54 (C-28), 109.44 (C-29), 121.58 (C-2), 137.94 (C-3), 150.70 (C-20).

Preparation of *O*-Vinyl Ethers 7, 9, and 17 and *N*-Vinylpyrrole 18. A mixture of **1**, **3**, or **5** (0.52 g, 0.759 mmol) and $KOH \cdot 0.5H_2O$ (0.25 g, 3.91 mmol) in DMSO [ratios of alcohol or oxime (g) to DMSO (mL), 1:40 for **7**, 1:100 for **9**, **17**, and **18**] was heated and purged with acetylene until the starting compound disappeared according to TLC (130°C and 2 h for **7**, 130°C and 20 min for **9**, 80°C and 15 min for **17**, 110°C and 40 min for **18**). The mixture was cooled, diluted with ice H_2O, and extracted with methyl-*t*-butyl ether (MTBE). The organic layer was separated, washed with H_2O, dried over Na_2SO_4, and evaporated. The resulting solid was stirred with pentane. The insoluble part was filtered off. The filtrate was evaporated. The solid was chromatographed. Compounds **7** and **9** were isolated over SiO_2 and worked up with Et_3N [hexane eluent and hexane–EtOAc (10:1 and 5:1) for **7**; hexane and hexane–EtOAc (9:1) for **9**]. Compounds **17** and **18** were chromatographed over Al_2O_3 (eluent benzene for **17**; hexane for **18**).

28-Triphenylmethoxylup-20(29)-en-3β-ol *O*-Vinyl Ether (7). Yield 52%, Amorphous compound. ^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.50 (3H, s, CH_3-25), 0.64 (1H, d, J = 10.0, H-5), 0.76, 0.79, 0.88, 0.91, 1.64 (3H each, s, CH_3-27, 24, 26, 23, 30), 2.15 (3H, m, H_a-16, 22, H-19), 2.90, 3.21 (1H each, d, J = 8.8, H -28), 3.23 (1H, dd, J = 11.2, 4.0, H-3), 3.90 (1H, dd, J = 6.5, 1.2, vinyl: H_A), 4.25 (1H, dd, J = 14.1, 1.2, vinyl: H_B), 4.50, 4.57 (1H each, d, J = 1.5, H-29), 6.30 (1H, dd, J = 14.1, 6.5, vinyl: H_X), 7.10–7.40 (9H, m, Ph), 7.50 (6H, d, J = 7.2, Ph). ^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 14.81 (C-26), 15.95 (C-25), 16.18 (C-27), 16.43 (C-24), 19.22 (C-6, 30), 20.82 (C-11), 23.70 (C-12), 25.23 (C-15), 26.98 (C-2), 28.05 (C-23), 29.97 (C-21), 30.23 (C-16), 35.33 (C-7, 22), 37.31 (C-10, 13), 38.69 (C-1, 4), 40.70 (C-8), 42.55 (C-14), 47.65 (C-17), 47.82 (C-19), 48.96 (C-18), 50.34 (C-9), 55.73 (C-5), 59.57 (C-28), 85.90 (O$\underline{C}$$Ph_3$), 87.23 (C-β), 87.42 (C-3), 109.50 (C-29), 126.90, 127.80, 128.84, 144.54 (Ph), 150.83 (C-20), 152.32 (C-α).

Lup-20(29)-en-3β-ol *O*-Vinyl Ether (8). A mixture of lupeol (**2**, 1.84 g, 4.312 mmol), NaOH (0.86 g, 21.560 mmol), and CsF (3.28 g, 21.560 mmol) in DMSO (74 mL) at atmospheric pressure and 130°C was purged with acetylene for 2.5 h (TLC monitoring), cooled, diluted with ice H_2O (50 mL), and extracted with MTBE (5 × 30 mL). The combined organic extracts were washed with H_2O, dried over Na_2SO_4, and evaporated. The solid was chromatographed over SiO_2 and worked up with Et_3N (eluents hexane and hexane–EtOAc, 30:1) to afford **2** (0.33 g) and **8** (1.48 g) (76% yield, 81% conversion of **2**). Amorphous compound. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.71 (1H, d, J = 9.1, H-5), 0.79, 0.82, 0.85, 0.94, 0.95 (3H each, s, CH_3-28, 24, 25, 23, 27), 0.88 (1H, td, J = 13.7, 4.1, H_a-1), 1.03 (4H, s, H_a-15, CH_3-26), 1.06 (1H, m, H_a-12), 1.20 (1H, m, H_a-22), 1.26 (2H, m, H-9, H_a-11), 1.29 (1H, m, H_a-21), 1.36 (2H, m, H_a-16, H-18), 1.39 (5H, m, H_a-6, H-7, H_b-11, 22), 1.48 (1H, m, H_b-16), 1.52 (1H, m, H_b-6), 1.58 (1H, m, H_a-2), 1.66 (1H, m, H_b-1), 1.68 (4H, m, H_b-2, 12, 15, H-13; 3H, s, CH_3-30), 1.92 (1H, tt, J = 11.0, 10.3, H_b-21), 2.39 (1H, td, J = 11.0, 5.2, H-19), 3.48 (1H, dd, J = 11.8, 4.1, H-3), 3.92 (1H, d, J = 6.3, vinyl: H_A), 4.02 (1H, d, J = 14.0, vinyl: H_B), 4.57, 4.69 (1H each, s, H-29), 6.03 (1H, dd, J = 14.0, 6.3, vinyl: H_X). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 14.51 (C-27), 15.96 (C-24), 16.12 (C-26), 16.32 (C-25), 17.98 (C-28), 18.15 (C-6), 19.30 (C-30), 20.94 (C-11), 23.57 (C-2), 25.10 (C-12), 27.41 (C-15), 27.95 (C-23), 29.84 (C-21), 34.24 (C-7), 35.56 (C-16), 37.13 (C-10), 38.00 (C-13), 38.46 (C-1), 38.60 (C-4), 39.98 (C-22), 40.84 (C-8), 42.80 (C-14), 42.98 (C-17), 47.95 (C-19), 48.27 (C-18), 50.40 (C-9), 55.69 (C-5), 87.10 (C-β), 87.39 (C-3), 109.34 (C-29), 150.90 (C-20), 152.28 (C-α).

Lupa-2,20(29)-dien-28-ol *O*-Vinyl Ether (9). Yield 50%, Amorphous compound. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.81, 0.86, 0.93, 0.98, 1.04, 1.68 (3H each, s, CH_3-25, 24, 23, 27, 26, 30), 1.95 (3H, m, H_b-16, 21, 22), 2.43 (1H, td, J = 11.0, 5.0, H-19), 3.37, 3.82 (1H each, d, J = 9.2, H-28), 3.96 (1H, dd, J = 6.7, 1.8, vinyl: H_A), 4.20 (1H, d, J = 14.3, 1.8, vinyl: H_B), 4.59, 4.69 (1H each, s, H-29), 5.36 (1H, dd, J = 10.0, 2.0, H-3), 5.40 (1H, ddd, J = 10.0, 5.5, 1.3, H-2), 6.54 (1H, dd, J = 14.3, 6.7, vinyl: H_X). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 14.77 (C-27), 15.67 (C-26), 16.38 (C-25), 19.13 (C-30), 19.48 (C-6), 21.22 (C-11), 22.62 (C-24), 25.30 (C-12), 27.12 (C-15), 29.79 (C-16, 21), 31.74 (C-23), 33.34 (C-7), 34.59 (C-22), 34.67 (C-4), 36.38 (C-10), 37.73 (C-13), 40.99 (C-8), 41.24 (C-1), 42.69 (C-14), 46.75 (C-17), 47.94 (C-19), 48.78 (C-18), 49.03 (C-9), 52.10 (C-5), 66.16 (C-28), 85.54 (C-β), 109.57 (C-29), 121.58 (C-2), 137.96 (C-3), 150.51 (C-20), 152.84 (C-α).

General Method for Preparing Ketones 12 and 13. A solution of **10** [12] or **11** [13] (1.90 mmol) in anhydrous CH_2Cl_2 (90 mL) at –60°C was purged with an O_3/O_2 mixture (ozonator output 45 mmol/min) until the solution became deep blue, purged with Ar, treated with Me_2S (6 mL), and stirred for 1 h at 10°C and for 12 h at room temperature. The solvent was evaporated. The solid was chromatographed over SiO_2 [eluents hexane and hexane–EtOAc (10:1 and 5:1) for **12**; dichloroethane for **13**].

3β,28-Diacetoxy-29-norlupan-20-one (12). Yield 86%, mp 187–188°C (lit.: 186.5–189.5°C [14], 185–187°C [15], 190–191°C [16]). ^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.80 (1H, d, J = 10.2, H-5), 0.83, 0.95, 1.02, 2.16 (3H each, s, CH_3-24, 25, 26, 30), 0.85 (6H, s, CH_3-23, 27), 2.03, 2.08 (3H each, s, 28, 3-OAc), 2.65 (1H, td, J = 11.3, 5.8, H-19), 3.79, 4.20 (1H each, d, J = 11.0, H-28), 4.48 (1H, dd, J = 10.6, 4.4, H-3). The ^{13}C NMR spectrum agreed with the literature [15, 16].

3β,28-Dimethoxy-29-norlupan-20-one (13). Yield 40%, mp 171–173°C (Et_2O) (lit.: 170–173°C [13]). ^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.64 (1H, d, J = 9.0, H-5), 0.73, 0.81, 0.94, 0.98, 1.00, 2.14 (3H each, s, CH_3-24, 25, 27, 23, 26, 30), 2.63 (2H, m, H-3, 19), 2.97, 3.42 (1H each, d, J = 9.3, H-28), 3.34, 3.36 (3H each, s, 28, 3-OCH_3). ^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 14.72 (C-27), 15.95 (C-24), 16.05 (C-25), 16.14 (C-26), 18.19 (C-6), 20.89 (C-11), 22.21 (C-2), 27.29 (C-12, 15), 27.95 (C-21), 28.01 (C-23), 29.31 (C-30), 29.80 (C-16), 34.19 (C-7), 34.79 (C-22), 36.42 (C-13), 37.21 (C-10), 38.57 (C-1), 38.81 (C-4), 40.87 (C-8), 42.55 (C-14), 47.23 (C-17), 49.68 (C-18), 50.28 (C-9), 52.34 (C-19), 55.82 (C-5), 57.50 (3-OCH_3), 59.65 (28-OCH_3), 71.62 (C-28), 88.55 (C-3), 212.28 (C-20). EI-MS, *m/z* 472 $[M]^+$ (calcd for $C_{31}H_{52}O_3$ 472).

General Method for Preparing Ketoximes 5 and 14. A suspension of ketone **13** or **12** (1.10 mmol) and $NH_2OH{\cdot}HCl$ (10.99 mmol) in anhydrous MeOH (12 mL) and Py (4 mL) was refluxed for 6 h and evaporated to dryness. The resulting solid (**5**) was chromatographed over SiO_2 (eluent dichloroethane) or (**14**) over Al_2O_3 (eluents benzene and benzene–MTBE, 8:1).

3β,28-Dimethoxy-28-norlupan-20-one (*E*)-Oxime (5). Yield 63%, mp 143–144°C (lit.: 148–151°C [17]). ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.67 (1H, d, J = 9.3, H-5), 0.75 (3H, s, CH_3-24), 0.81 (1H, m, H_a-1), 0.82, 0.92, 0.95 (3H each, s, CH_3-25, 27, 23), 0.95 (1H, m, H_a-15), 1.01 (3H, s, CH_3-26), 1.05 (1H, m, H_a-12), 1.07 (1H, m, H_a-22), 1.20 (1H, m, H_a-16), 1.22 (1H, m, H_a-11), 1.25 (1H, m, H-9), 1.38 (3H, m, H_a-6, H-7), 1.42 (2H, m, H_a-2, H_b-11), 1.47 (1H, m, H_a-21), 1.50 (1H, m, H_b-6), 1.52 (1H, m, H_b-15), 1.57 (1H, m, H-18), 1.68 (2H, m, H_b-1, 12), 1.70 (1H, m, H-13), 1.78 (1H, m, H_b-2), 1.81 (3H, s, CH_3-30), 1.97 (3H, m, H_b-16, 21, 22), 2.60 (1H, td, J = 10.5, 6.3, H-19), 2.63 (1H, dd, J = 11.5, 4.0, H-3), 3.02, 3.45 (1H each, d, J = 9.0, H-28), 3.34, 3.35 (3H each, s, 28, 3-OCH_3), 9.04 (1H, br.s, NOH). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 10.59 (C-30), 14.50 (C-27), 16.05 (C-24), 16.06 (C-25), 16.07 (C-26), 18.09 (C-6), 20.65 (C-11),

22.13 (C-2), 25.20 (C-15), 26.97 (C-12), 27.50 (C-21), 27.92 (C-23), 29.83 (C-16), 34.09 (C-7), 34.71 (C-22), 36.70 (C-13), 37.09 (C-10), 38.52 (C-1), 38.72 (C-4), 40.81 (C-8), 42.48 (C-14), 45.34 (C-19), 46.91 (C-17), 49.30 (C-18), 50.15 (C-9), 55.78 (C-5), 57.60 (3-OCH_3), 59.73 (28-OCH_3), 71.19 (C-28), 88.57 (C-3), 162.81 (C-20). EI-MS, *m/z* 487 $[M]^+$ (calcd for $C_{31}H_{53}NO_3$ 487).

3*β*,28-Diacetoxy-29-norlupan-20-one (*E*)-Oxime (14). Yield 55%, mp 193–195°C (lit.: 197–198°C [17]). ^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.79 (1H, d, J = 9.0, H-5), 0.84, 0.95, 1.03, 1.82 (3H each, s, CH_3-24, 25, 26, 30), 0.85 (6H, s, CH_3-23, 27), 2.05, 2.07 (3H each, s, 28, 3-OAc), 2.60 (1H, td, J = 11.3, 5.8, H-19), 3.80, 4.28 (1H each, d, J = 11.0, H-28), 4.48 (1H, dd, J = 10.5, 4.5, H-3).

3*β*,28-Dihydroxy-29-norlupan-20-one (*E*)-Oxime (4). A suspension of **14** (0.44 g, 0.81 mmol) and $Ca(OH)_2$ (1.90 g, 25.67 mmol) in MeOH–$CHCl_3$ (15 mL, 1:1) was stirred vigorously for 70 h at 50°C. The precipitate was filtered off. The solvent was evaporated. The solid was chromatographed over Al_2O_3 (eluent hexane–MeOH, 5:1) to afford **4** (0.20 g, 54%), mp 178–179°C. ^{1}H NMR spectrum (300 MHz, CD_3OD, δ, ppm, J/Hz): 0.67 (1H, d, J = 9.2, H-5), 0.75, 0.81, 0.95, 0.96, 1.00, 1.80 (3H each, s, CH_3-24, 25, 27, 23, 26, 30), 1.95 (3H, m, H_b-16, 21, 22), 2.60 (1H, m, H-19), 3.18 (1H, dd, J = 11.0, 5.5, H-3), 3.30, 3.80 (1H each, d, J = 10.0, H-28). ^{13}C NMR spectrum (75 MHz, CD_3OD, δ, ppm): 10.86 (C-30), 15.18 (C-27), 16.16 (C-25), 16.52 (C-26), 16.73 (C-24), 19.43 (C-6), 21.86 (C-11), 26.47 (C-2), 28.00 (C-15, 21), 28.24 (C-12), 28.66 (C-23), 30.19 (C-16), 35.01 (C-7), 35.40 (C-22), 38.00 (C-13), 38.21 (C-10), 39.92 (C-4, 8), 40.01 (C-1), 42.05 (C-14), 43.70 (C-17), 46.45 (C-19), 50.26 (C-18), 51.64 (C-9), 56.76 (C-5), 60.29 (C-28), 79.54 (C-3), 163.49 (C-20).

Vinylation of Ketoxime 4. A mixture of **4** (0.10 g, 0.22 mmol) and $KOH{\cdot}0.5H_2O$ (0.07 g, 1.09 mmol) in DMSO (33 mL) was purged with acetylene at 80°C for 1 h 15 min (TLC monitoring), cooled, diluted with ice H_2O (50 mL), and extracted with EtOAc (5 × 20 mL). The organic layer was washed with H_2O, dried over Na_2SO_4, and evaporated. The solid was extracted with pentane. The solution was decanted and evaporated to afford a mixture (0.02 g) of **15** and **16** in a 9:1 ratio (PMR).

3*β*-Hydroxy-28-*O*-vinyl-29-norlupan-20-one (*E*)-*O*-Vinyloxime (15). ^{1}H NMR spectrum (300 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.70 (1H, d, J = 8.7, H-5), 0.74, 0.81, 0.95, 0.96, 1.00, 1.84 (3H each, s, CH_3-24, 25, 27, 23, 26, 30), 1.95 (3H, m, H_b-16, 21, 22), 2.63 (1H, m, H-19), 3.20 (1H, dd, J = 11.5, 4.8, H-3), 3.35, 3.77 (1H each, d, J = 9.5, H-28), 3.97 (1H, dd, J = 6.8, 2.0, vinyl: H_A), 4.07 (1H, dd, J = 6.8, 1.5, vinyloxime: H_A), 4.19 (1H, dd, J = 14.4, 2.0, vinyl: H_B), 4.55 (1H, dd, J = 14.3, 1.4, vinyloxime: H_B), 6.53 (1H, dd, J = 14.4, 6.8, vinyl: H_X), 6.87 (1H, dd, J = 14.3, 6.8, vinyloxime: H_X). ^{13}C NMR spectrum (75 MHz, $CDCl_3$, δ, ppm): 11.96 (C-30), 14.63 (C-27), 15.33 (C-24), 15.88 (C-26), 16.03 (C-25), 18.26 (C-6), 20.68 (C-11), 22.66 (C-2), 25.43 (C-15), 26.99 (C-12), 27.37 (C-21), 27.96 (C-23), 31.90 (C-16), 34.14 (C-7), 34.60 (C-22), 36.94 (C-13), 37.15 (C-10), 38.70 (C-1), 38.84 (C-4), 40.84 (C-8), 42.58 (C-14), 45.18 (C-19), 46.56 (C-17), 49.10 (C-18), 50.23 (C-9), 55.29 (C-5), 65.99 (C-28), 78.93 (C-3), 85.76 (vinyl: C-*β*), 87.11 (vinyloxime: C-*β*), 152.59 (vinyl, vinyloxime: C-*α*), 164.80 (C-20).

3*β*,28-Dimethoxy-29-norlupan-20-one (*E*)-*O*-Vinyloxime (17). Yield 66%, **A**morphous compound. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.68 (1H, d, J = 9.5, H-5), 0.74, 0.82, 0.94, 0.95, 1.02 (3H each, s, CH_3-24, 25, 26, 23, 27), 1.05 (1H, m, H_a-12), 1.08 (1H, m, H_a-22), 1.20 (1H, m, H_a-16), 1.25 (2H, m, H-9, H_a-11), 1.38 (2H, m, H-7), 1.39 (1H, m, H_a-6), 1.40 (1H, m, H_a-2), 1.42 (1H, m, H_b-11), 1.47 (1H, m, H_a-21), 1.51 (1H, m, H_b-6), 1.52 (1H, m, H_a-15), 1.63 (1H, m, H-18), 1.67 (1H, m, H_b-12), 1.68 (1H, m, H_b-1), 1.72 (1H, m, H-13), 1.79 (1H, m, H_b-2), 1.82 (3H, s, CH_3-30), 1.92 (1H, m, H_b-15), 1.97 (3H, m, H_b-16, 21, 22), 2.63 (2H, m, H-3, 19), 3.05, 3.48 (1H each, d, J = 9.0, H-28), 3.34, 3.36 (3H each, s, 28, 3-OCH_3), 4.05 (1H, dd, J = 6.8, 1.5, vinyloxime: H_A), 4.52 (1H, dd, J = 14.2, 1.5, vinyloxime: H_B), 6.85 (1H, dd, J = 14.2, 6.8, vinyloxime: H_X). ^{13}C NMR spectrum (125 MHz, $CDCl_3$, δ, ppm): 11.89 (C-30), 14.56 (C-27), 15.89 (C-25), 15.90 (C-26), 16.10 (C-24), 18.12 (C-6), 20.69 (C-11), 22.13 (C-2), 25.38 (C-15), 27.03 (C-12), 27.71 (C-21), 27.96 (C-23), 29.98 (C-16), 34.11 (C-7), 34.73 (C-22), 36.74 (C-13), 37.12 (C-10), 38.52 (C-1), 38.74 (C-4), 40.83 (C-8), 42.51 (C-14), 45.09 (C-19), 46.98 (C-17), 49.14 (C-18), 50.18 (C-9), 55.76 (C-5), 57.43 (3-OCH_3), 59.69 (28-OCH_3), 71.25 (C-28), 86.97 (C-*β*), 88.51 (C-3), 152.54 (C-*α*), 165.03 (C-20). EI-MS, *m/z* 513 $[M]^+$ (calcd for $C_{33}H_{55}O_3N$ 513).

3*β*,28-Dimethoxy-19-(1-vinyl-1*H*-pyrrol-2-yl)-20,29,30-trinorlupane (18). Yield 4%, mp 89°C. ^{1}H NMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.62 (1H, d, J = 8.8, H-5), 0.73 (3H, s, CH_3-24), 0.75 (1H, m, H_a-1), 0.80 (3H, s, CH_3-25), 0.88 (1H, m, H_a-12), 0.95 (1H, m, H_a-15), 0.96, 1.01, 1.05 (3H each, s, CH_3-23, 27, 26), 1.07 (1H, m, H_b-12), 1.12 (1H, m, H_a-11), 1.20 (1H, m, H_a-9), 1.21 (1H, m, H_a-22), 1.25 (1H, m, H_a-16), 1.35 (1H, m, H_b-11), 1.40 (4H, m, H_a-2, 6, H-7), 1.46 (1H, m, H_a-21), 1.50 (1H, m, H_b-6), 1.65 (1H, m, H_b-1), 1.67 (1H, ddd, J = 11.5, 11.5, 4.5, H-13), 1.72 (2H, m, H_b-2, 15), 1.88 (1H, t, J = 12.0, H-18), 1.92 (1H, ddd, J = 11.0, 11.0, 3.5, H_b-22), 1.96 (1H, ddd, J = 10.5, 5.0, 2.0, H_b-16), 2.23 (1H, dq, J = 11.0, 7.0, H_b-21), 2.62 (1H, dd, J = 11.7, 4.4, H-3), 2.80 (1H, ddd, J = 11.0, 6.0, 5.0, H-19), 3.11, 3.53 (1H each, d, J = 9.0, H-28), 3.34, 3.38 (3H each, s, 28, 3-OCH_3), 4.62 (1H, d, J = 8.7, vinyl: H_A), 5.07 (1H, d, J = 15.6, vinyl: H_B), 5.87 (1H, dd, J = 3.2, 1.7, H-4′), 6.10 (1H, t, J = 3.2, H-3′), 6.85 (1H, dd, J = 3.2, 1.7, H-5′), 6.92 (1H, dd, J = 15.6, 8.7, vinyl: H_X). ^{13}C NMR

spectrum (125 MHz, $CDCl_3$, δ, ppm, J/Hz): 14.76 (C-27), 16.03 (C-25), 16.06 (C-26), 16.14 (C-24), 18.17 (C-6), 21.05 (C-11), 22.19 (C-2), 27.24 (C-12), 27.28 (C-21), 27.99 (C-23), 30.10 (C-16), 32.98 (C-15), 34.18 (C-22), 34.27 (C-7), 35.67 (C-18), 37.12 (C-13), 37.15 (C-10), 38.52 (C-1), 38.77 (C-4), 41.00 (C-8), 42.67 (C-14), 47.02 (C-17), 50.24 (C-9), 52.08 (C-19), 55.77 (C-5), 57.53 (3-OCH_3), 59.74 (28-OCH_3), 71.29 (C-28), 88.62 (C-3), 98.25 (C-β), 104.63 (C-4′), 108.97 (C-3′), 115.38 (C-5′), 130.54 (C-α), 140.02 (C-2′). EI-MS, *m/z* 521 $[M]^+$ (calcd for $C_{35}H_{55}O_2N$ 521).

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