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ONE-STEP SYNTHESIS OF THE VICINAL DINITROGUAIANOLIDES ACHILLIN AND GROSSMISIN

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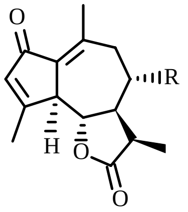
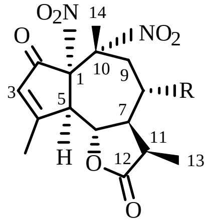
1,10-Dihydro-1α,10α-dinitrogrossmisin was synthesized by bubbling gaseous nitrosyl chloride through a chloroform solution of the guaianolide grossmisin. The molecular structure was determined by X-ray. It was found that the formation of similar dinitrates is accelerated by using NOCl containing nitrogen dioxide.

Key words: sesquiterpenoids, guaianolides, grossmisin, achillin, nitrosochlorination, nitro compounds.

Passage of gaseous NOCl through a $CHCl_3$ solution of achillin (**1**) very slowly (2 d) forms only one product, the structure of which (**2**) was established by X-ray structure analysis [1].



1: R = H;
3: R = OH



2: R = H
4: R = OH

Our research showed that the reaction also occurs with 8α-hydroxyachillin (grossmisin) (**3**). The dinitro product **4** forms analogously although in slightly lower yield. It structure was also proved by X-ray (Fig. 1).

The pentenone ring of **4** is planar within ±0.055(3) Å. The seven-membered ring has the distorted chair conformation [C(10)–C(1)–C(5)–C(6) torsion angle = -17.3(5)°]. The conformation of the lactone ring is close to an envelope with atom C(7) deviating from the plane by 0.565(6) Å. The conformations of the rings are the same in **2** [1] (the discrepancy of the torsion angles is less than 5°). The orientations of the nitro groups are practically identical in **2** and **4**. This is indicative of weak packing effects on their orientations. Thus, the O(5)–N(1)–C(1)–C(2) and O(8)–N(2)–C(10)–C(15) torsion angles in **2** and **4** are -17.1(3) and 22.3(3) and -10.0(5) and 14.7(5)°, respectively.

The unit cell of **4** also includes one water and one acetone of solvation. H-bonds in **4** form an infinite chain oriented along the *a* axis and involve the solvates: ...ROH...$OC(CH_3)_2$...H_2O...ROH... The H-bond parameters are: O(4)–H...O(1A) [H...O, 2.03; O...O, 2.822(6) Å, O–H...O, 162°], O(1A)...O(1W) 2.878(8) Å, and O(1W)...O(4), 2.933(8) Å.

Signals in the PMR and ^{13}C NMR spectra of **4** were interpreted by comparison with those of **2** [1] (Table 1).

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TABLE 1. Chemical Shifts (δ, ppm) and Spin—Spin Coupling Constants (J/Hz) of ^{13}C NMR and PMR Signals of **4**

Atom (i)	C_i	H_i*
1	91.56s	-
2	192.82s	-
3	130.95d	6.32 (m)
4	180.29s	-
5	60.04d	3.93(dq, J = 10.0; 1.5)
6	76.77d	5.10 (dd, J = 10.0; 11.0)
7	49.96d	3.25 (dt, J = 11.0; 7.5)
8	64.86d	4.10 (tdd, J = 11.0; 7.5; 5.0)
9	46.07t	H(9A): 2.36 (dd, J = 13.0; 5.0)
		H(9B): 3.38 (ddd, J = 13.0; 11.0; 0.5)
10	94.81s	-
11	38.98d	2.85 (quintet, J = 7.5)
12	177.82s	-
13	10.34q	1.40 (3H, d, J = 7.5)
14	19.62q	1.62 (3H, d, $J_{9B,14}$ = 0.5)
15	21.94q	2.33 (3H, dd, $J_{3,15} = J_{5,15}$ = 1.5)

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*The doublet for $\underline{H}$O–C(8) that is observed at 4.64 ppm ($J_{O\underline{H},7}$ = 6.0) disappears upon adding drops of D_2O to the tube.

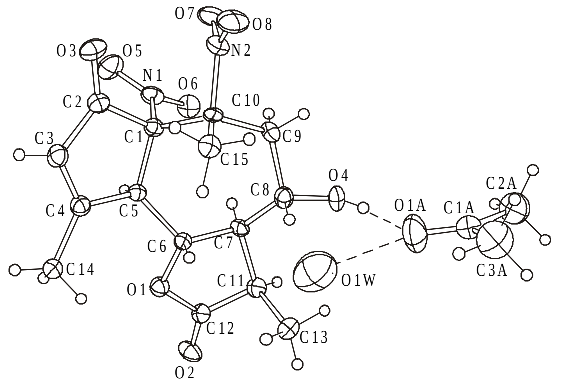

Fig. 1. Structure of **4**.

Thus, the presence of a hydroxyl on C(8) of the reacting molecule has no effect on the formation of the *cis*-1,10-dinitro derivative. Apparently this reaction is also typical of other available guaianolides similar to achillin such as leucomisin (11-epiachillin) and matricarin (8-acetoxyleucomisin). The slowness of the reaction indicates that NOCl is not the principal reactant. Therefore, the dinitro derivative is apparently formed by a microimpurity of N_2O_4 [2]. In fact, we used the described method of purifying gaseous NOCl that includes passage of the purified gas through three sequential columns packed with $NaNO_2$, moistened KCl, and $CaCl_2$ [2]. The first of these (with $NaNO_2$) captures HCl; the second, N_2O_4; the third, water (drying). Removing the N_2O_4 purification step results in formation of **2** from **1** in 2.5 h (TLC monitoring) instead of 2 d. The yield of **2** was 80%.

We also conducted an experiment on the reaction of **1** with N_2O_4 in $CHCl_3$ solution at -10°C. A mixture of the starting compound and two products were formed. One of the products is **2** according to PMR; the second, the nitrosonitrate according to our hypothesis [3].

TABLE 2. Coordinates ($Å^2 \times 10^4$) and Equivalent Thermal Factors ($Å^2 \times 10^3$) of Nonhydrogen Atoms in **4**

Atom	x/a	y/b	z/c	U_{eq}
O1	8035(4)	7377(2)	4412(1)	38(1)
N1	11739(4)	7902(3)	2795(2)	41(1)
C1	9532(5)	8151(3)	2814(2)	32(1)
O2	8435(5)	7321(2)	5403(1)	57(1)
N2	10043(6)	9656(3)	2179(2)	49(1)
C2	8554(6)	7631(3)	2255(2)	39(1)
O3	8882(5)	7848(3)	1739(1)	59(1)
C3	7152(6)	6923(3)	2492(2)	42(1)
O4	10299(5)	10616(2)	4241(1)	52(1)
C4	7158(6)	6902(3)	3090(2)	35(1)
C5	8731(5)	7563(3)	3367(2)	30(1)
O5	12276(5)	7275(3)	2434(2)	68(1)
C6	8071(5)	8126(2)	3933(2)	29(1)
O6	12793(4)	8269(3)	3175(2)	55(1)
C7	9440(6)	8913(3)	4182(2)	33(1)
O7	11778(5)	9452(3)	2099(2)	67(1)
O8	9091(6)	10176(3)	1844(2)	72(1)
C8	9196(6)	9911(3)	3888(2)	39(1)
C9	10011(6)	9970(3)	3251(2)	40(1)
C10	9090(6)	9272(3)	2778(2)	35(1)
C11	8955(6)	8876(3)	4862(2)	40(1)
C12	8495(6)	7802(3)	4949(2)	39(1)
C13	7178(8)	9482(4)	5070(2)	60(1)
C14	5819(7)	6296(3)	3480(2)	45(1)
C15	6869(6)	9444(3)	2724(2)	41(1)
O1A	7363(8)	12089(3)	4263(2)	108(2)
C1A	7171(9)	12962(4)	4278(2)	62(1)
C2A	8709(11)	13644(5)	4491(3)	89(2)
C3A	5312(10)	13445(6)	4079(4)	107(2)
O1W	4407(9)	10733(5)	3840(3)	146(2)

EXPERIMENTAL

Melting points were determined on a Boetius stage. IR spectra were obtained on a Vector 22 instrument in KBr; UV spectra (in EtOH), on a Specord UV-VIZ instrument. NMR spectra were recorded on a Bruker DRX-500 spectrometer (working frequency 500.13 MHz for ^{1}H, 125.76 MHz for ^{13}C, δ-scale). Optical rotations were measured (at 580 nm) on a Polamat A polarimeter.

We used Silufol plates for TLC with development by spraying with vanillin (1%) in H_2SO_4 and aqueous $KMnO_4$ solution (1%).

Starting grossmisin (**3**), mp 145.5-146.5°C, from the aerial part of *Achillea micrantha* Willd [3].

Gaseous NOCl was prepared by the literature method [4] (method 1).

(1*S*,6*R*,7*S*,10*R*,11*S*)-2-Oxo-1,10-dinitroguai-3-en-6-ol-11,8-olide (4). NOCl was bubbled for 2 d through a solution of **3** (0.5 g) in freshly distilled cooled (from 0 to -10°C) $CHCl_3$ (20 mL, until the starting compound disappeared completely according to TLC). Ethanol (5 mL) was added. The resulting fine crystalline rhomboids were filtered off and recrystallized from acetone. Yield 0.25 g (37%) of **4**, mp 200-202°C (dec.), $[\alpha]_D^{20}$ +47° (*c* 1.92, acetone).

UV spectrum, λ/nm: 236 nm (ε 7509). IR spectrum (KBr, cm^{-1}): 3420 (OH), 1721 (C=O), 1557, 1384, 1344, 1313, 1194, 899, 868, 810, 643. ^1H and ^{13}C NMR data are given in Table 1.

The X-ray of **4** was performed on a Syntex $P2_1$ diffractometer (Cu Kα-radiation, graphite monochromator, 2Θ/Θ-scanning for 2Θ < 140°). A crystal of **4** of dimensions 0.80×0.17×0.1 mm^3 was selected for the analysis. Crystals of **4** are orthorhombic, a = 6.793(1), b = 13.539(2), c = 22.134(4) Å, V = 2035.7(6) $Å^3$, space group $P2_12_12_1$, $Z = 4$, $C_{15}H_{18}N_2O_8 + C_3H_6O + H_2O$, $d_{calc} = 1.398$ g/cm^3, $\mu = 0.986$ mm^{-1}. Intensities of 2232 independent reflections were measured. Absorption corrections were applied along the crystal faces (transmission 0.71-0.92). The structure was solved by direct methods using the SHELXS-97 program. Positions of H atoms were calculated geometrically. The H atoms of the water of solvation could not be found in difference syntheses. Structure factors were refined by full-matrix anisotropic least-squares methods using the SHELXL-97 program. The H atom parameters were calculated in each refinement cycle using the coordinates of the corresponding C atoms. The final structure was determined over all F^2 with $wR_2 = 0.1308$ and S = 1.013 for 272 parameters (R = 0.0484 for 1706 F > 4σ).

Reaction of 1 with NOCl Containing N_2O_4. NOCl that was passed only through columns packed with $NaNO_2$ and $CaCl_2$ was bubbled through a solution of **1** (0.10 g) in cooled (from 0 to -10°C) $CHCl_3$. The starting material disappeared after only 2.5 h according to TLC. The solution was treated with EtOH (5 mL). The resulting finely crystalline rhomboids were filtered off and recrystallized from acetone. Yield 0.11 g (80%) of **2**, mp 220°C (dec.).

Reaction of 1 with N_2O_4. A solution of **1** (0.10 g) in cooled (to -10°C) $CHCl_3$ (5 mL) was treated with N_2O_4 (0.10 g) in cooled (to -10°C) $CHCl_3$ (1 mL) and held at the same temperature for 3 h. The mixture was washed with water and extracted with $CHCl_3$ (20 mL). The PMR spectrum of the resulting mixture contained signals of starting **1**, **2**, and an unidentified compound in approximately equal amounts.

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