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Nitration of N-Acetyl Enamines with Acetyl Nitrate

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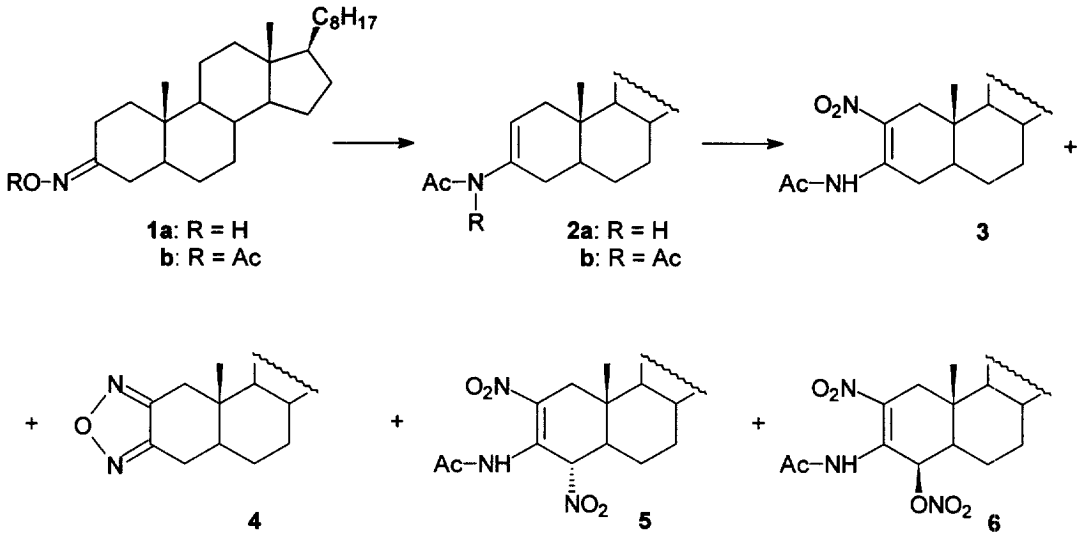
Abstract: N-acetyl enamines undergo nitration at the double bond. Products of further nitration and oxidation in an allylic position are also formed. Sterically unhindered enamide, N-acetyl-cholest-2-en-3-amine, yields oxadiazole, as one of the reaction products. © 1997 Elsevier Science Ltd.

Since the pioneering work of G. Stork,[1,2] who showed the great potential of enamines for electrophilic substitution, interest in their chemistry has been stimulated. In comparison with enamines, the chemistry of enamides has been studied less intensively, presumably due to shortage of synthetic methods to them.[3] However, many efficient methods have been recently elaborated[4,5] and, in consequence, the synthetic application of enamides as reactive intermediates increases.[6]

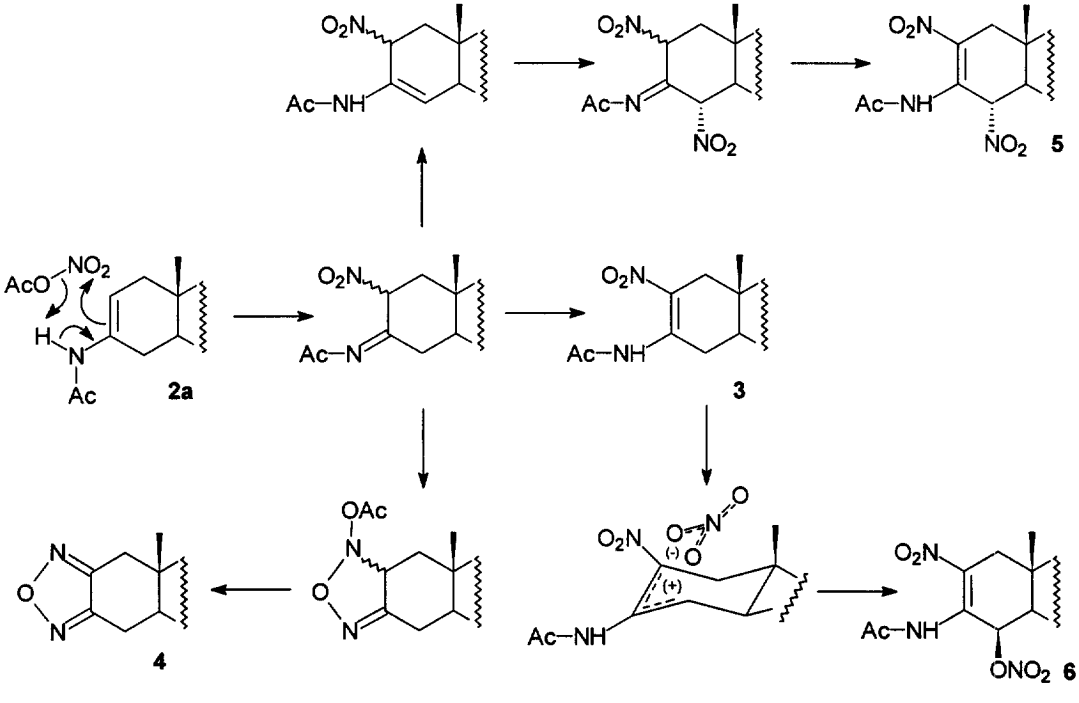
The preferred site of an electrophilic attack in enamides, likewise in enamines, is the terminal vinyl carbon atom. We have recently described the reactions of cyclic enamides with acetyl nitrate.[7,8] In all cases studied so far the electrophilic attack took place on the terminal carbon atom and the corresponding substitution products (nitro enamides) were formed. Alternatively, an acetate ion may be attached to the initial cation, thus yielding the $AcONO_2$ addition products (nitroacetates). Apart from these dominating reactions, many side reactions (such as an allylic oxidation, a Nef type reaction, and others) were also observed.

In this paper we report the results of our studies on reactions of N-acetyl enamines with acetyl nitrate. Two model N-acetyl derivatives of cyclic enamines with and without steric hindrance were chosen. The latter compound was a readily available N-acetyl-cholest-2-en-3-amine (**2a**) described by Barton.[9] 11-Acetamino-spirost-11-en-3β-ol acetate (**8a**) served as an example of a compound with a heavily hindered N-acetyl enamide moiety.

Compound **2a** (Scheme 1) was obtained from cholestan-3-one oxime (**1a**) by prolonged heating in an acetic anhydride - pyridine mixture followed by slow chromatography of the resulting imide **2b** over neutral alumina.[9] N-acetyl-cholest-2-en-3-amine (**2a**) was treated with acetyl nitrate prepared from acetic anhydride and nitric acid. The major reaction product, nitro enamide **3**, was accompanied by a number of by-products. They were isolated by a careful silica gel chromatography and identified as an oxadiazole derivative **4**,



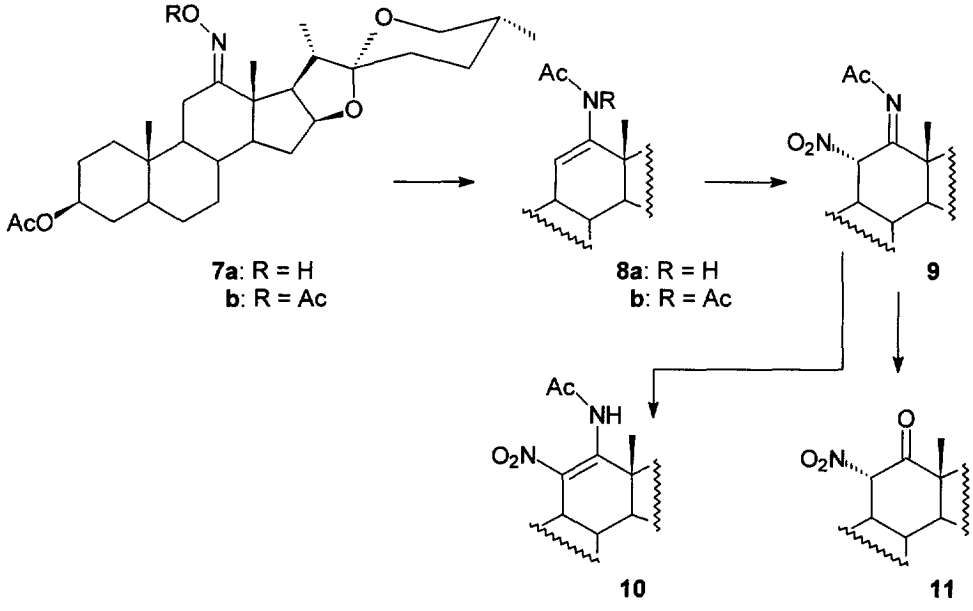
Scheme 1



Scheme 2

2,4α-dinitro compound **5** and nitrate **6**. A similar nitration reaction of compound **2b** afforded the same set of products. It is very likely that **2b** undergoes rapid deacetylation under the reaction conditions. The tentative mechanism of reaction with acetyl nitrate is depicted in Scheme 2. It seems that the initial product of nitration is N-acetylimine presumably formed *via* the six-membered transition state. The unstable N-acetylimine is probably the key intermediate, which either loses a molecule of acetic acid affording a heterocyclic compound **4**, or isomerizes to the more stable enamide tautomers (Δ^2 or Δ^3). The nitro enamide **3** is the major reaction product, whereas its Δ^3-isomer undergoes further nitration with acetyl nitrate at C-4, thus yielding the dinitro product **5**. Compound **3** is partially further oxidized in an allylic position to afford the nitrate **6**.

N-Acetyl enamine **8a** (Scheme 3) was prepared from the hecogenine acetate oxime **7a** using a procedure similar to that of Barton et al.[9] The highly encumbered spirostan-11-one oxime derivative required refluxing for several days in the acetic anhydride-pyridine mixture to afford imide **8b**. One of its acetyl groups was removed by adsorbing the compound on an alumina column. Enamide **8a** was eluted from the column after



Scheme 3

a period of 16 hours. It was then subjected to the reaction with acetyl nitrate. The spirostane acetal moiety is sensitive to acids and could be destroyed during the reaction. However the reaction with $AcONO_2$ proved to be very fast (5 minutes) and therefore the decomposition of the spirostane system was negligible. The main reaction product, nitro N-acetylimine **9**, was isolated by flash silica gel chromatography. The chromatography over alumina or florisil led to the immediate isomerization of **9** to the more stable nitro enamide **10** by sigmatropic shift [1,3] of a proton. Thermic isomerization is also possible although it requires 1 hour refluxing in toluene. Molecular mechanics calculations[10] show relatively low difference (about 0.5 kcal/mol) in the steric energy between the tautomers in this case. However, there is no equilibration in the absence of catalyst due to

an activation barrier. Alumina decreases the barrier by coordinating the steroid ligands **9** or **10** and as a base catalyses the tautomeric transformation. It is interesting to note that the nitro group plane in **10** is nearly perpendicular to the plane of the ring C due to steric reasons. Nitro enamides (such as **3**, **5** and **6**) usually show a strong intramolecular hydrogen bond and their amide proton resonance is observed at a very low field (δ 11.86, 10.68, and 10.90, respectively). Contrary to that, the arrangement of the nitro group in **10** is not suitable for an intramolecular hydrogen bond formation with the amide proton and therefore its chemical shift is only about 6.4 ppm (δ varies slightly with concentration).

N-Acetylimine **9** appeared to be sensitive to moisture and slowly hydrolyses to the nitro ketone **11**. When allowed to stand (neat or in a chloroform solution) at room temperature for about 4 days, the compound **9** undergoes almost quantitative transformation into **11**. The functional group manipulation in **11** (for example, reduction of its nitro group to NH_2) can lead to the biologically active 11-substituted steroids (analogs of corticosteroids).

Further studies, aiming mainly at the improvement of yield of the pharmaceutically important oxadiazole system (such as **4**) in the nitration of N-acetyl enamines, are in progress.

EXPERIMENTAL

Melting points were determined on a Köffler apparatus of the Boetius type and were uncorrected. NMR spectra were taken with a Bruker AC 200F spectrometer using $CDCl_3$ solutions with TMS as the internal standard. Infrared spectra were recorded on a Nicolet series II Magna-IR 550 FT-IR spectrometer as chloroform solutions unless otherwise stated. Mass spectra were obtained at 70 eV with an AMD-604 spectrometer. Elemental analyses were performed in the Institute of Organic Chemistry, Polish Academy of Sciences. The reaction products were isolated by column chromatography performed on 70-230 or 230-400 mesh silica gel (Merck). Thin-layer chromatograms were developed on aluminum TLC sheets precoated with silica gel F_{254} and visualized with 50% sulfuric acid after heating. All solvents were dried and freshly distilled prior to use. N-Acetyl-cholest-2-en-3-amine (**2a**) was prepared by prolonged heating of cholestan-3-one oxime (**1a**) with acetic anhydride/pyridine followed by deacetylation according to the known procedure.[9]

Nitration of 3-Acetylaminocholest-2-en (2a) with acetyl nitrate

Acetyl nitrate was prepared by dropwise addition of a concentrated nitric acid (1 mL) to acetic anhydride (5 mL) with stirring. The mixture was maintained 15 minutes at room temperature and then N-acetyl enamine **2a** (1 g; 2.34 mmol) was added. The stirring was continued for 40 minutes, the reaction mixture was quenched by pouring into saturated sodium bicarbonate solution and extracted with chloroform. In order to fully hydrolyse acetic anhydride, the mixture was stirred for 1 hour before extraction. The solvent was removed *in vacuo* from the dried ($MgSO_4$) extract and the residue was subjected to the careful column chromatography over silica gel. An oxadiazole steroid **4** (77 mg; 8%) was eluted with petroleum ether - ethyl acetate (96:4). A mixture of petroleum ether - ethyl acetate (92:8) eluted nitro enamide **3** (431 mg; 39%), followed by nitrate **6** (14.5 mg; 1.2%) and the dinitro derivative **5** (206 mg; 17%).

Compound **4**: mp 95-97°C (hexane); IR, ν_{max} 1494, 1468, 1005, 876 cm^{-1}; ^1H NMR, δ 3.09 (d, J = 16.8 Hz, 1H, 1β-H), 2.91 (dd, J = 17.7 Hz, 5.0 Hz, 1H, 4α-H), 2.42 (dd, J = 17.7 Hz, 12.1 Hz, 1H, 4β-H), 2.27 (d, J = 16.8 Hz, 1H, 1α-H), 2.06 (m, 1H, 5α-H), 0.92 (d, J = 6.5 Hz, 3H, 21-H), 0.88 (d, J = 6.6 Hz, 6H, 26-H and 27-H), 0.75 (s, 3H, 19-H), 0.69 (s, 3H, 18-H); ^{13}C NMR, δ 152.0 (C), 150.9 (C), 56.2 (CH), 56.1 (CH), 53.4 (CH), 42.3 (C), 41.6 (CH), 39.7 (CH_2), 39.5 (CH_2), 36.5 (C), 36.1 (CH_2), 35.8 (CH), 35.5 (CH), 33.7 (CH_2), 31.3 (CH_2), 28.9 (CH_2), 28.2 (CH_2), 28.0 (CH), 24.2 (CH_2), 23.9 (CH_2), 23.8 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 21.1 (CH_2), 18.6 (CH_3), 11.9 (CH_3), 11.8 (CH_3); MS, m/z 412 (M^+,36), 397 (4), 257 (100); exact mass calcd for $C_{27}H_{44}N_2O$: 412.3454; found: 412.3466.

Compound **3**: mp 164-166°C (hexane); IR, ν_{max} 3255, 1723, 1610, 1418, 1188, 1122 cm^{-1}; ^1H NMR, δ 11.86 (s, 1H, N–H), 3.24 (dd, J = 19.9 Hz, 4.2 Hz, 1H, 1β-H), 2.5-2.9 (m, 2H, 1α-H and 4α-H), 2.22 (s, 3H, Ac-N), 0.91 (d, J = 6.5 Hz, 3H, 21-H), 0.86 (d, J = 6.5 Hz, 6H, 26-H and 27-H), 0.76 (s, 3H, 19-H), 0.66 (s, 3H, 18-H); ^{13}C NMR, δ 169.1 (C), 148.2 (C), 126.9 (C), 56.19 (CH), 56.16 (CH), 53.6 (CH), 42.4 (C), 40.2 (CH), 39.7 (CH_2), 39.6 (CH_2), 39.5 (CH_2), 36.1 (CH_2), 35.7 (CH), 35.0 (CH), 34.2 (C), 32.4 (CH_2), 31.3 (CH_2), 28.2 (CH_2), 28.0 (CH), 27.6 (CH_2), 26.0 (CH_3), 24.1 (CH_2), 23.8 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 21.0 (CH_2), 18.7 (CH_3), 12.0 (CH_3), 11.8 (CH_3); MS, m/z 454 (100), 439 (25), 426 (98), 397 (26), 383 (62); anal. calcd for $C_{29}H_{48}N_2O_3$: C, 73.69; H, 10.23; N, 5.93; found: C, 73.56; H, 10.30; N, 5.89.

Compound **6**: mp 165-167°C (hexane); IR, ν_{max} (CCl_4) 3292, 1731, 1658, 1631, 1277 cm^{-1}; ^1H NMR, δ 10.91 (s, 1H, N–H), 7.00 (d, J = 3.6 Hz, 1H, 4α-H), 2.76 (d, J = 17.4 Hz, 1H, 1β-H), 2.27 (d, J = 17.4 Hz, 1H, 1α-H), 2.20 (s, 3H, Ac-N), 1.25 (s, 3H, 19-H), 0.93 (d, J = 6.5 Hz, 3H, 21-H), 0.86 (d, J = 6.6 Hz, 6H, 26-H and 27-H), 0.65 (s, 3H, 18-H); ^{13}C NMR, δ 168.9 (C), 137.2 (C), 132.2 (C), 76.7 (CH), 56.1 (CH), 56.0 (CH), 54.0 (CH), 46.7 (CH), 42.3 (C), 39.8 (CH_2), 39.5 (CH_2), 39.1 (CH_2), 35.7 (CH), 34.6 (CH), 33.9 (C), 31.2 (CH_2), 29.7 (CH_2), 28.1 (CH_2), 28.0 (CH), 25.5 (CH_3), 24.1 (CH_2), 23.8 (CH_2), 22.8 (CH_3), 22.6 (CH_2), 22.5 (CH_3), 20.8 (CH_2), 18.6 (CH_3), 13.6 (CH_3), 11.9 (CH_3); MS, m/z 487 (19), 471 (6), 454 (23), 440 (100), 426 (40), 125 (52); anal. calcd for $C_{29}H_{47}N_3O_6$: C, 65.25; H, 8.88; N, 7.88; found: C, 65.35; H, 9.07; N, 7.91.

Compound **5**: mp 188-190°C (hexane); IR, ν_{max} 3291, 1722, 1630, 1558 cm^{-1}; ^1H NMR, δ 10.69 (s, 1H, N–H), 6.07 (d, J = 11.7 Hz, 1H, 4β-H), 3.03 (d, J = 17.5 Hz, 1H, 1β-H), 2.30 (dd, J = 17.5 Hz, 2.2 Hz, 1H, 1α-H), 2.18 (s, 3H, Ac-N), 1.26 (s, 3H, 19-H), 0.97 (d, J = 6.5 Hz, 3H, 21-H), 0.87 (d, J = 6.6 Hz, 6H, 26-H and 27-H), 0.68 (s, 3H, 18-H); ^{13}C NMR, δ 169.1 (C), 134.9 (C), 134.4 (C), 88.2 (CH), 56.1 (CH), 55.8 (CH), 53.2 (CH), 47.8 (CH), 42.4 (C), 39.5 (CH_2), 39.4 (CH_2), 38.8 (CH_2), 36.11 (C), 36.07 (CH_2), 35.7 (CH), 34.6 (CH), 30.4 (CH_2), 29.7 (CH_2), 28.1 (CH_2), 28.0 (CH), 25.1 (CH_2), 24.9 (CH_3), 24.0 (CH_2), 23.8 (CH_2), 22.8 (CH_3), 22.5 (CH_3), 20.8 (CH_2), 18.6 (CH_3), 12.4 (CH_3), 12.0 (CH_3); MS, m/z 471 (97), 454 (69), 439 (44), 426 (92), 411 (100), 397 (36), 383 (45); anal. calcd for $C_{29}H_{47}N_3O_5$: C, 67.28; H, 9.15; N, 8.12; found: C, 67.36; H, 9.30; N, 8.00.

An analogous reaction of 3-diacetylaminocholest-2-en (**2b**) afforded nitro enamide **3** (40%) and oxadiazole **4** (9%).

*Preparation of 12-diacetylaminospirost-11-en-3β-ol acetate (**8b**) from the hecogenine acetate oxime (**7a**)*

Hecogenine acetate oxime (**7a**; 1.3 g; 2.67 mmol)[11] was dissolved in a mixture of acetic anhydride (60 mL) and anhydrous pyridine (90 mL), and heated under reflux for 5 days. The reaction mixture was then

poured into iced water, extracted with chloroform and evaporated to dryness. Flash silica gel chromatography of the crude product (elution with petroleum ether - ethyl acetate 8:2) yielded 325 mg (23%) of oxime acetate (**7b**), followed by 944 mg (64%) of enimide **8b**.

Compound **7b**: mp 184-187°C (hexane); IR, ν_{max} 1754, 1725, 1631, 1252, 1243, 981, 899 cm^{-1}; ^1H NMR, δ 4.67 (m, 1H, 3α-H), 4.40 (m, 1H, 16α-H), 3.25-3.55 (2 x m, 2H, 26-H), 3.15 (dd, J = 14.9 Hz, 4.6 Hz, 1H, 11α-H), 2.60 (dd, J = 8.5 Hz, 6.2 Hz, 1H, 17α-H), 2.19 (s, 3H, Ac-N), 2.01 (s, 3H, Ac-O), 1.12 (d, J = 7.0 Hz, 3H, 21-H), 1.02 (s, 3H, 18-H), 0.90 (s, 3H, 19-H), 0.78 (d, J = 6.2 Hz, 3H, 27-H).

Compound **8b**: mp 162-165°C (hexane); IR, ν_{max} 1716 (shoulder), 1702, 1252, 1239, 981, 899 cm^{-1}; ^1H NMR, δ 5.50 (d, J = 1.9 Hz, 1H, 11-H), 4.69 (m, 1H, 3α-H), 4.41 (m, 1H, 16α-H), 3.25-3.55 (2 x m, 2H, 26-H), 2.41 (s, 3H, Ac-N), 2.33 (s, 3H, Ac-N), 2.02 (s, 3H, Ac-O), 0.95 (s, 3H, 18-H), 0.88 (d, J =6.6 Hz, 3H, 21-H), 0.87 (s, 3H, 19-H), 0.77 (d, J = 6.1 Hz, 3H, 27-H); ^{13}C NMR, δ 173.8 (C), 173.2 (C), 170.6 (C), 144.9 (C), 130.3 (CH), 109.2 (C), 80.3 (CH), 73.2 (CH), 66.8 (CH_2), 56.9 (CH), 56.0 (CH), 54.0 (CH), 47.9 (C), 44.3 (CH), 41.8 (CH), 36.2 (C), 35.8 (CH_2), 33.7 (CH_2), 36.1 (CH_2), 33.2 (CH), 31.2 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.1 (CH), 28.9 (CH_2), 28.7 (CH_2), 27.1 (CH_2), 27.0 (CH_3), 26.7 (CH_3), 21.3 (CH_3), 21.1 (CH_3), 17.0 (CH_3), 13.48 (CH_3), 13.45 (CH_3); MS, m/z 555 (M^+,33), 512 (99), 495 (20), 453 (23), 139 (100); exact mass calcd for $C_{33}H_{49}NO_6$: 555.3560; found: 555.3560.

*12-Acetylaminospirost-11-en-3β-ol acetate (**8a**) by deacetylation of **8b***

Compound **8b** (930 mg; 1.66 mmol) was introduced on the alumina (activity stage 1 according to Brockmann) column and allowed to stand overnight. The steroid material was eluted from the column with a mixture of petroleum ether - ethyl acetate 6:4. The product **8a** was slightly contaminated with hecogenine acetate and therefore subjected to rechromatography over silica gel. After removal of the non-polar contaminants, the enamide **8a** was collected. Yield - 714 mg (83%), mp 222-225 °C (hexane - methylene chloride); IR, ν_{max} (CCl_4) 3455, 1733, 1695, 1504, 1244, 1052, 984, 901 cm^{-1}; ^1H NMR, δ 6.20 (bs, 1H, 11-H), 6.10 (bs, 1H, N-H), 4.71 (m, 1H, 3α-H), 4.49 (m, 1H, 16α-H), 3.25-3.55 (2 x m, 2H, 26-H), 2.04 (s, 3H, Ac-N), 2.02 (s, 3H, Ac-O), 1.12 (d, J = 6.7 Hz, 3H, 21-H), 0.96 (s, 3H, 18-H), 0.83 (s, 3H, 19-H), 0.80 (d, J = 6.2 Hz, 3H, 27-H); ^{13}C NMR, δ 170.5 (C), 168.2 (C), 140.5 (C), 112.2 (CH), 109.1 (C), 81.0 (CH), 73.5 (CH), 66.8 (CH_2), 57.5 (CH), 56.0 (CH), 53.1 (CH), 45.5 (C), 44.3 (CH), 41.6 (CH), 36.1 (C), 35.8 (CH_2), 33.8 (CH_2), 33.2 (CH), 31.4 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.1 (CH), 28.8 (CH_2), 28.6 (CH_2), 27.1 (CH_2), 24.6 (CH_3), 21.3 (CH_3), 19.4 (CH_3), 17.0 (CH_3), 14.6 (CH_3), 12.7 (CH_3); MS, m/z 513 (M^+,100), 470 (12), 453 (56), 438 (22), 139 (62); exact mass calcd for $C_{31}H_{47}NO_5$: 513.3454; found: 513.3456.

*Nitration of 12-Acetylaminospirost-11-en-3β-ol acetate (**8a**) with acetyl nitrate*

Acetyl nitrate was prepared by dropwise addition of a concentrated nitric acid (1 mL) to acetic anhydride (5 mL) with stirring. The above mixture was maintained at room temperature 15 minutes. N-Acetyl enamine **8a** (150 mg; 0.29 mmol) was treated with 2 mL of the freshly prepared acetyl nitrate for 5 minutes with stirring. The reaction was then quenched by pouring into saturated sodium bicarbonate solution. In order to decompose unreacted acetic anhydride the mixture was stirred for 1 hour before extraction with chloroform. The solvent

was removed *in vacuo* from the dried ($MgSO_4$) extract and the crude product was subjected to the flash chromatography over silica gel. Elution with petroleum ether - ethyl acetate 85:15 yielded N-acetyl imine **9** (136 mg; 83%); IR, ν_{max} 1725, 1673, 1562, 1254, 1244, 981, 898 cm^{-1}; ^1H NMR, δ 5.51 (d, J = 10.3 Hz, 1H, 11β-H), 4.62 (m, 1H, 3α-H), 4.42 (m, 1H, 16α-H), 3.25-3.55 (2 x m, 2H, 26-H), 2.50 (m, 1H, 17α-H), 2.11 (s, 3H, Ac-N), 1.99 (s, 3H, Ac-O), 1.03 and 1.02 (2 x s, 6H, 18-H and 19-H), 0.95 (d, J = 6.9 Hz, 3H, 21-H), 0.77 (d, J = 6.2 Hz, 3H, 27-H); ^{13}C NMR, δ 176.0 (C), 170.4 (C), 160.1 (C), 109.0 (C), 86.6 (CH), 78.9 (CH), 72.1 (CH), 66.9 (CH_2), 57.7 (CH), 56.7 (CH), 52.1 (CH), 51.5 (C), 44.3 (CH), 42.4 (CH), 38.1 (C), 34.0 (CH), 33.9 (CH_2), 33.7 (CH_2), 31.6 (CH_2), 31.3 (2 x CH_2), 30.0 (CH), 28.6 (CH_2), 28.4 (CH_2), 27.0 (CH_2), 24.2 (CH_3), 21.2 (CH_3), 17.0 (CH_3), 16.5 (CH_3), 13.3 (CH_3), 11.8 (CH_3); MS, m/z 558 (M^+,0.6), 542 (0.8), 528 (2), 512 (53), 139 (100).

*Isomerization of N-acetyl imine **9** to 12-Acetylamino-11-nitrospirost-11-en-3β-ol acetate (**10**)*

The crude N-acetyl imine **9** (obtained from 75 mg of **8a** according to the above procedure) was slowly chromatographed over florisil. Elution with petroleum ether - ethyl acetate 1:1 yielded 37 mg (45%) of nitro enamide **10**, mp 171-174 °C (hexane - methylene chloride); IR (CCl_4) ν_{max} 3421, 3244, 1735, 1666, 1530, 1243 cm^{-1}; ^1H NMR, δ 6.52 (s, 1H, N-H), 4.62 (m, 1H, 3α-H), 4.43 (m, 1H, 16α-H), 3.25-3.55 (2 x m, 2H, 26-H), 2.66 (d, J = 11.3 Hz, 1H, 9α-H), 2.01 (s, 3H, Ac-N), 1.99 (s, 3H, Ac-O), 1.05 and 1.02 (2 x s, 2 x 3H, 18-H and 19-H), 0.94 (d, J = 6.8 Hz, 3H, 21-H), 0.77 (d, J = 6.1 Hz, 3H, 27-H); ^{13}C NMR, δ 170.5 (C), 169.1 (C), 149.8 (C), 140.0 (C), 109.1 (C), 80.0 (CH), 72.5 (CH), 66.9 (CH_2), 56.6 (CH), 56.4 (CH), 51.5 (CH), 47.0 (C), 44.5 (CH), 41.9 (CH), 38.9 (C), 34.2 (CH), 34.1 (CH_2), 33.2 (CH_2), 31.3 (CH_2), 30.5 (CH_2), 30.1 (CH), 29.7 (CH_2), 29.5 (CH_2), 28.6 (CH_2), 27.3 (CH_2), 21.3 (2 x CH_3), 18.7 (CH_3), 17.1 (CH_3), 13.9 (CH_3), 12.8 (CH_3); MS, m/z 558 (M^+, 1), 542 (1.5), 528 (4), 512 (100), 139 (68); exact mass calcd for $C_{31}H_{46}N_2O_7$: 558.3305; found: 558.3307.

An analogous isomerization of **9** to the nitro enamide **10** was also performed on an alumina (activity stage 1 according to Brockmann) column or by refluxing of a toluene solution of compound **9** for 1 hour.

*Hydrolysis of N-acetyl imine **9** to 11α-nitrospirost-12-on-3β-ol acetate (**11**)*

N-Acetyl imine **9** (62 mg) was allowed to stand in an open flask at room temperature for 4 days. The resulting crystalline nitro ketone **11** was purified by filtration through a layer of a silica gel in petroleum ether - ethyl acetate 85:15. Yield of **11** - 50 mg (88%); mp 246-249°C (hexane - methylene chloride); IR, ν_{max} 1728, 1564, 1254, 1244, 980, 897 cm^{-1}; ^1H NMR, δ 5.47 (d, J = 11.0 Hz, 1H, 11β-H), 4.62 (m, 1H, 3α-H), 4.36 (m, 1H, 16α-H), 3.25-3.55 (2 x m, 2H, 26-H), 2.62 (dd, J = 8.7 Hz, 6.9 Hz, 1H, 17α-H), 2.00 (s, 3H, Ac-O), 1.08 and 1.05 (2 x s, 2 x 3H, 18-H and 19-H), 1.02 (d, J = 7.0 Hz, 3H, 21-H), 0.78 (d, J = 6.2 Hz, 3H, 27-H); ^{13}C NMR, δ 200.4 (C), 170.4 (C), 109.1 (C), 92.7 (CH), 78.6 (CH), 72.2 (CH), 66.9 (CH_2), 57.4 (CH), 54.4 (C), 54.0 (CH), 52.9 (CH), 44.0 (CH), 42.3 (CH), 38.0 (C), 34.00 (CH), 33.98 (CH_2), 33.9 (CH_2), 31.5 (CH_2), 31.3 (CH_2), 31.2 (CH_2), 30.0 (CH), 28.6 (CH_2), 28.3 (CH_2), 27.0 (CH_2), 21.3 (CH_3), 17.0 (CH_3), 14.6 (CH_3), 13.0 (CH_3), 11.9 (CH_3); MS, m/z 517 (M^+, 3), 489 (1), 471 (13), 445 (15), 139 (100); exact mass calcd for $C_{29}H_{43}NO_7$: 517.3039; found: 517.3036.

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REFERENCES AND NOTES

1. Stork, G.; Terrell, R.; Smuszkowicz, J. *J. Am. Chem. Soc.* **1954**, 76, 2029.
2. Stork, G.; Landesman, H. K. *J. Am. Chem. Soc.* **1956**, 78, 5128.
3. a. Campbell, A. L.; Lenz, G. R. *Synthesis* **1987**, 421.
   b. Speckamp, W. N.; Hiemstra, H. *Tetrahedron* **1985**, 41, 4367.
4. a. Paterson, I.; Cowden, C.; Watson, C. *Synlett* **1996**, 209.
   b. Baldwin, J. E.; Aldous, D. J.; O'Neil, I. A.; *Tetrahedron Lett.* **1990**, 31, 2051.
   c. Barton, D. H. R.; Bowles, T.; Husinec, S.; Forbes, J. E.; Llobera, A.; Porter, A. E. A.; Zard, S. Z. *Tetrahedron Lett.* **1988**, 29, 3343.
5. a. Palomo, C; Aizpurua, J. M.; Legido, M.; Picard, J. P.; Dunogues, J.; Constantieux, T. *Tetrahedron Lett.* **1992**, 33, 3903.
   b. Couture, A.; Deniau, E.; Grandclaudon, P. *Tetrahedron Lett.* **1993**, 34, 1479.
   c. Kondo, T.; Tanaka, A.; Kotachi, S.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 413.
   d. Jacobi, P. A.; Brielmann, H. L.; Hauck, S. I. *J. Org. Chem.* **1996**, 61, 5013.
   e. Laso, N. M.; Quiclet-Sire, B.; Zard, S. Z. *Tetrahedron Lett.* **1996**, 37, 1605.
6. a. Schultz, A. G.; Guzzo, P. R.; Nowak, D. M. *J. Org. Chem.* **1995**, 60, 8044.
   b. Rigby, J. H.; Qabar, M. N. *J. Org. Chem.* **1993**, 58, 4473.
   c. D'Annibale, A.; Resta, S.; Trogolo, C. *Tetrahedron Lett.* **1995**, 36, 9039.
   d. Murai, T.; Oda, T.; Kimura, F.; Onishi, H.; Kanda, T.; Kato, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2143.
7. Morzycki, J. W.; Wilczewska, A. Z.; Łotowski, Z. *Tetrahedron Lett.* **1996**, 37, 2079.
8. Morzycki, J. W.; Wilczewska, A. Z. *Tetrahedron* **1997**, 53, 10565.
9. a. Boar, R. B.; McGhie, J. F.; Robinson, M.; Barton, D. H. R.; Horwell, D. C.; Stick, R. V. *J. Chem. Soc., Perkin Trans. I* **1975**, 1237.
   b. Kasal, A.; Stárka, L; Hampl, R.; Kohout, L. *Collect. Czech. Chem. Commun.* **1983**, 48, 2040.
10. Molecular modeling was performed with HyperChem™ Release 4 from Hypercube, Inc.
11. Mazur, R. H. *J. Am. Chem. Soc.* **1959**, 81, 1454.

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