Indian Journal of Chemistry
Vol. 36B, January 1997, pp. 14-16

Phosphite deoxygenation of steroidal[3,4-*c*] and [16,17-*c*] furazan N-oxides

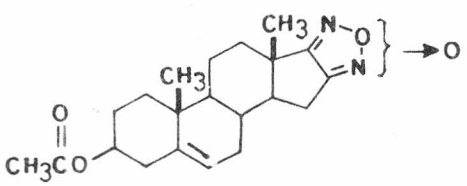
Dharam Paul Jindal*, Ranju Gupta, Inder Bir Singh, J S R A Sharma & M R Yadav
University Institute of Pharmaceutical Sciences†, Panjab University, Chandigarh

Received 19 March 1996; revised 4 July 1996

3β-Acetoxy-5-androsteno[16,17-*c*]-1′,2′,5′-oxadiazole N-oxide (**1**), 3-methoxy-1,3-5(10)-estratrieno[16,17-*c*]-1′,2′,5′-oxadiazole N-oxide (**2**), [16,17-*c*]furoxano-5α-androstano[3,4-*c*]furazan (**3**) and 17β-acetoxy-5α-androstano[3,4-*c*]-1′,2′,5′-oxadiazole N-oxide (**4**) have been synthesised to investigate the reactions with triethyl phosphite. The products obtained have been identified. Furazan N-oxide fused to D-ring gives dinitriles **5,6** and **7** whereas furoxan at 3,4-position yield furazan **8**.

It is well known that amine oxides[1], azoxy benzene and substituted nitroso benzenes[2] are deoxygenated by means of trialkyl phosphite. There are also reports that ethylene oxides[3], phthalic anhydride[4] and pyridine-1 oxide[5] can also be deoxygenated employing *tert*-phosphites. Trialkyl phosphites are also known to deoxygenate non-steroidal furoxans[6-8].

We thought it worthwhile to study the behaviour of triethyl phosphite with steroidal furazan N-oxides **1,2,3** and **4** which we report in this paper. The furoxan (**1**) was prepared by treating 3β-hydroxy-5-androsteno[16, 17-*c*]-1′,2′,5′-oxadiazole N-oxide[9] with acetic anhydride in pyridine at 100°. The compound **1** showed IR bands at 1735, 1655, 1250 and 1035 cm^{-1} and UV maximum was at 261 nm. In the ^1H NMR spectrum there appeared singlet at δ 2.03 (3H, $-OCOCH_3$). Compound **1** was refluxed with triethyl phosphite under nitrogen atmosphere to give a dinitrile derivative **5** which showed prominent IR bands at 2240 cm^{-1}. Its ^1H NMR spectrum showed singlets at δ 1.05 and 1.42 for 19-methyl and 18-methyl, respectively. A singlet appeared at δ 2.05 for acetoxy function. The α-configuration of the tertiary nitrile at Carbon-13 was assigned on the basis of earlier reports[10,11].



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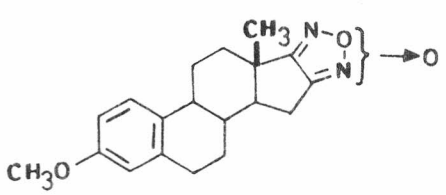

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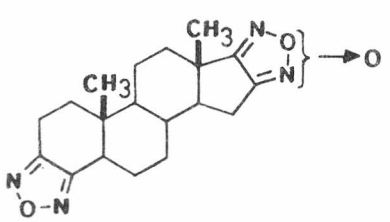

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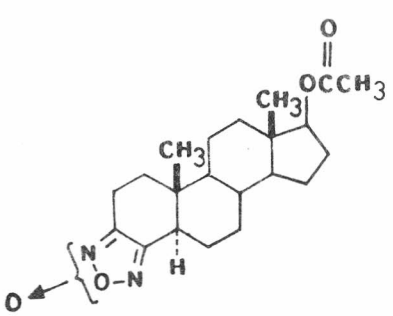

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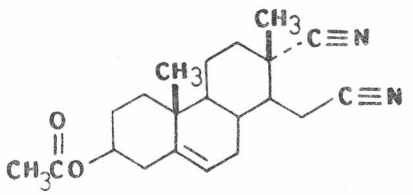
†Formerly Department of Pharmaceutical Sciences.



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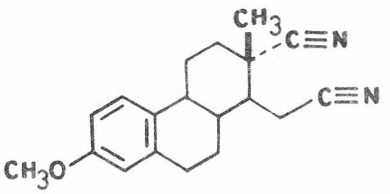

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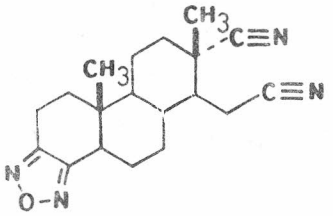
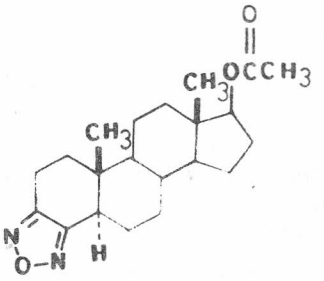


(7)



(8)

The behaviour of triethyl phosphite was further studied in estrone series. Deoxygenation of furoxan derivative **2**[9] with triethyl phosphite under the above mentioned experimental conditions gave **6**. IR spectrum showed vibrational bands at 2250 and 2228 cm^{-1} and ^1H NMR spectrum exhibited three-proton singlets at δ 1.47 (18-CH_3) and 3.70 ($-OCH_3$). Similarly refluxing **3**[12] with triethyl phosphite under nitrogen atmosphere gave **7**. It showed characteristic absorption bands at 2250 cm^{-1} (C≡N) in the IR spectrum. ^1H NMR showed peaks at δ 0.80 (s, 3H, 19-CH_3), 1.53 (s, 3H, 18-CH_3) and 2.77 (m, 2H, 15-CH_2).

It is interesting to note the deoxygenation with triethyl phosphite of furazan N-oxide **4**[13] fused to six membered ring, which on heating under reflux under similar conditions with triethyl phosphite gave a furazan **8**[13]. ^1H NMR spectrum exhibited singlets at δ 0.77 (s, 3H, 18-CH_3), 0.82 (s, 3H, 19-CH_3) and 2.05 (s, 3H, $OCOCH_3$)[13].

These observations lead us to confirm the suggested mechanism for the deoxygenation with triethyl phosphite under forcing conditions [refluxing with $(C_2H_5O)_3P$][14].

It is observed in this study that furazan fused to another five membered ring D is under strain[14] and there is ring opening giving dinitriles, whereas furazan fused to six membered ring A of steroid skeleton has the greater thermodynamic stability and does not result in the formation of dinitriles. We made unsuccessful attempts to prepare the steroidal[16,17-*c*]-1′,2′,5′-oxadiazole through this route from [16,17-*c*]-1′,2′,5′-oxadiazole N-oxide or refluxing 16,17-dioximino-5-androsten-3β-ol with potassium hydroxide and ethylene glycol.

Experimental Section

Melting points reported are uncorrected. ^1H NMR spectra (90 MHz) were recorded in $CDCl_3$ containing TMS as internal reference (chemical shifts in δ, ppm), IR spectra in KBr (ν_{max} in cm^{-1}) and UV spectra in methanol (λ_{max} in nm, figures within parentheses refer to log ε values). Mass spectra were recorded on Vg-11-250J 70S model. Elemental analyses were carried out on Perkin-Elmer-2400 model.

17β-Acetoxy-5α-androstano[3, 4-*c*]-1′, 2′, 5′-oxadiazole N-oxide (4). 3,4-Dioximino-5ξ-androstan-17β-ol[15] (1g) was dissolved in a mixture of ethanol (10 mL) and aq. NaOH (20%, 3 mL) and chilled. Freshly prepared sodium hypochlorite solution (8 mL) was added to the above chilled and stirred solution. The reaction mixture was kept at 0° for 24 hr, poured into ice-cold water, filtered, washed and dried. The residue so obtained was crystallised from ethanol to yield 17β-hydroxy-5α-androstano[3,4-*c*]-1′,2′,5′-oxadiazole N-oxide (0.65 g, 65.4%), m.p. 208-10°; UV (MeOH): 261 (3.92); IR: 1635, 1475, 1175, 1075; ^1H NMR: 0.78 (s, 6H, 18-CH_3 and 19-CH_3), 3.67 (t, 1H, 17α-H) (Found: C, 68.40; H, 8.44; N, 8.19. $C_{19}H_{28}N_2O_3$ requires C, 68.64; H, 8.48; N, 8.42%).

17β-hydroxy-5α-androstano[3,4-*c*]-1′,2′,5′-oxadiazole N-oxide (1 g), was dissolved in acetic anhydride (2 mL) and pyridine (5 mL) and heated on

water bath for 1 hr. After cooling, the reaction mixture was poured into crushed ice. The precipitate was filtered, washed off free from pyridine and dried. The product was crystallised from methanol to yield **4** (0.8 g, 71%), m.p. 221-22°; UV (MeOH): 261 (3.79); IR: 1725, 1630, 1460, 1240, 1035; ^{1}H NMR: 0.78 (s, 3H, 19-CH_3), 0.82 (s, 3H, 18-CH_3), 2.05 (s, 3H, $-OCOCH_3$), 4.70 (m, 1H, 17α-H) (Found: C, 67.59; H, 8.30; N, 7.44. $C_{21}H_{30}N_2O_4$ requires C, 67.35; H, 8.07; N, 7.48%).

3β-Acetoxy-16,17-seco-5-androsten-16, 17-dinitrile (5). 3β-Acetoxy-5-androsteno[16,17-*c*]-1′,2′,5′-oxadiazole N-oxide (**1**) (0.5 g) was refluxed in triethyl phosphite (10 mL) for 15 min under nitrogen atmosphere. The reaction mixture was poured into ice-cold water and made acidic with dil. H_2SO_4. The precipitated material was filtered, washed and dried. The product was crystallised from methanol to yield **5** (0.35 g, 76.6%), m.p. 175-76°; IR: 2240, 2260, 1710, 1360, 1260, 1040, 1030; ^{1}H NMR: 1.05 (s, 3H, 19-CH_3), 1.42 (s, 3H, 18-CH_3), 2.05 (s, 3H, $-OCOCH_3$), 2.72 (d, 2H, 15-CH_2), 4.60 (m, 1H, 3-CH), 5.40 (m, 1H, 6-CH) (Found: C, 73.68; H, 8.35; N, 7.78. $C_{21}H_{28}N_2O_2$ requires C, 74.08; H, 8.29; N, 8.23%).

3-Methoxy-16, 17-seco-1, 3, 5(10)-estratriene-16,17-dinitrile (6). 3-Methoxy-1,3,5(10)-estratrieno[16,17-*c*]-1′,2′,5′-oxadiazole N-oxide (**2**)[9] (0.3 g) was treated as above to give **6** (0.2 g, 74.1%) m.p. 142-44°; UV: 230 (3.69), 277 (3.28), 285.6 (3.24); IR: 2945, 2250, 2228, 1613, 1574, 1501, 1460, 1432, 1283, 1140, 1045; ^{1}H NMR: 1.47 (s, 3H, 18-CH_3), 3.70 (s, 3H, $-OCH_3$), 6.60 (s, 1H, 4-CH), 6.70 (d, 1H, 2-CH), 7.06 (d, 1H, 1-CH); MS: m/z 294 (M^+) (Found: C, 77.21; H, 7.76; N, 9.33. $C_{19}H_{22}N_2O$ requires C, 77.52; H, 7.53; N, 9.52%).

16, 17-Seco-5α-androstano[3, 4-*c*]-1′,2′,5′-oxadiazole-16,17-dinitrile (7). [16,17-*c*]Furoxano-5α-androstano[3,4-*c*]furazan (**3**)[12] (0.1 g) was treated as above to afford **7** (0.055 g, 50%), m.p. 206-07°; UV: 212 (3.65); IR: 2250, 1490, 1425, 1395, 1025, 945; ^{1}H NMR: 0.80 (s, 3H, 19-CH_3), 1.53 (s, 3H, 18-CH_3), 2.77 (m, 2H, 15-CH_2) (Found: C, 67.13; H, 6.44; N, 16.24. $C_{19}H_{24}N_4O.H_2O$ requires C, 66.64; H, 7.65; N, 16.36%).

17β-Acetoxy-5α-androstano [3,4-*c*]-1′,2′,5′-oxadiazole (8). 17β-Acetoxy-5α-androstano[3,4-*c*]-1′,2′,5′-oxadiazole N-oxide (**4**) (0.2 g) was treated as above to yield **8**[13] (0.11 g, 57.5%), m.p. 177.78° (lit. 174-76°); UV: 222 (3.61); IR: 1730, 1445, 1390, 1255, 1055, 1040, 875; ^{1}H NMR: 0.77 (s, 3H, 18-CH_3), 0.82 (s, 3H, 19-CH_3), 2.05 (s, 3H, $-OCOCH_3$), 4.70 (m, 1H, 17-CH); MS: m/z 358 (M^+) (Found: C, 70.52; H, 8.86; N, 7.73. $C_{21}H_{30}N_2O_3$ requires C, 70.35; H, 8.43; N, 7.82%).

Acknowledgement

We are grateful to CIPLA, Bombay for supplying DHA acetate, to M/s Schering Aktiengesell Schaft, Berlin, Germany for the generous supply of estrone methyl ether and to the Panjab University and UGC for financial assistance.

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