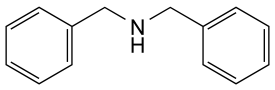
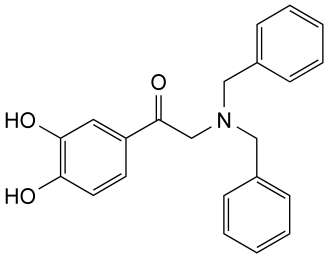


F. *N*-benzyl-1-phenylmethanamine,

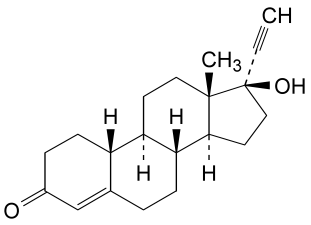


G. 2-(dibenzylamino)-1-(3,4-dihydroxyphenyl)ethanone.

01/2008:0234
corrected 6.0

NORETHISTERONE

Norethisteronum



$C_{20}H_{26}O_2$ M_r 298.4
[68-22-4]

DEFINITION

17-Hydroxy-19-nor-17α-pregn-4-en-20-yn-3-one.

Content: 98.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or yellowish-white, crystalline powder.

Solubility: practically insoluble in water, soluble in methylene chloride, sparingly soluble in acetone and in anhydrous ethanol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *norethisterone CRS*.

TESTS

Specific optical rotation (*2.2.7*): – 32.0 to – 37.0 (dried substance).

Dissolve 0.250 g in *acetone R* and dilute to 25.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25.0 mg of the substance to be examined in a mixture of 40 volumes of *water R* and 60 volumes of *acetonitrile R1* and dilute to 10.0 ml with the same mixture of solvents.

Reference solution (a). Dissolve 5 mg of *norethisterone for system suitability CRS* (containing impurities A, B, C, D, E, F, G and H) in a mixture of 40 volumes of *water R* and 60 volumes of *acetonitrile R1* and dilute to 2.0 ml with the same mixture of solvents.

Reference solution (b). Dilute 1.0 ml of the test solution to 100.0 ml with a mixture of 40 volumes of *water R* and 60 volumes of *acetonitrile R1*. Dilute 1.0 ml of this solution to 10.0 ml with a mixture of 40 volumes of *water R* and 60 volumes of *acetonitrile R1*.

Column:

– *size*: *l* = 0.15 m, Ø = 4.6 mm,

– *stationary phase*: spherical *end-capped octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase:

– *mobile phase A*: *water R*;

– *mobile phase B*: *acetonitrile R1*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 20	63	37
20 - 25	63 → 20	37 → 80
25 - 35	20	80
35 - 36	20 → 63	80 → 37
36 - 50	63	37

Flow rate: 1.0 ml/min.

Detection: variable wavelength spectrophotometer capable of operating at 254 nm and at 210 nm.

Injection: 20 µl.

Identification of impurities: use the chromatogram obtained with reference solution (a) and the chromatogram supplied with *norethisterone for system suitability CRS* to identify the peaks due to the impurities A, B, C, D, E, F, G and H.

Relative retention at 254 nm with reference to norethisterone (retention time = about 10 min): impurity H = about 0.3; impurity A = about 0.8; impurity B = about 0.9; impurity G = about 1.5; impurity C (at 210 nm) = about 1.6; impurity D (at 210 nm) = about 1.7; impurity E = about 2.3; impurity F = about 2.4.

System suitability: reference solution (a) at 254 nm:

– *resolution*: baseline separation between the peaks due to impurity B and norethisterone;

– *peak-to-valley ratio*: minimum 1.2, where H_p = height above the baseline of the peak due to impurity A and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity B.

Limits: spectrophotometer at 254 nm:

– *correction factors*: for the calculation of content, multiply the peak areas of the following impurities by the corresponding correction factor: impurity A = 2.5; impurity E = 0.7; impurity F = 1.4; impurity H = 1.7;

– *impurities E, G, H*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent);

– *impurities A, B, F*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent);

– *unspecified impurities*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent);

– *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent);

– *disregard limit*: 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Limits: spectrophotometer at 210 nm:

– *impurities C, D*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

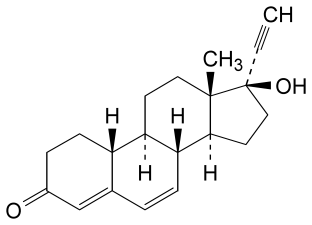
ASSAY

Dissolve 0.200 g in 40 ml of *tetrahydrofuran R*. Add 10 ml of a 100 g/l solution of *silver nitrate R* and titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Rinse the electrode with *acetone R* after each titration.

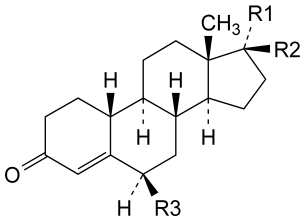
1 ml of *0.1 M sodium hydroxide* is equivalent to 29.84 mg of $C_{20}H_{26}O_2$.

IMPURITIES

Specified impurities: *A, B, C, D, E, F, G, H.*



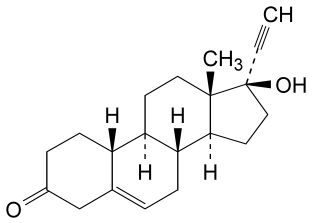
A. 17-hydroxy-19-nor-17α-pregna-4,6-dien-20-yn-3-one,



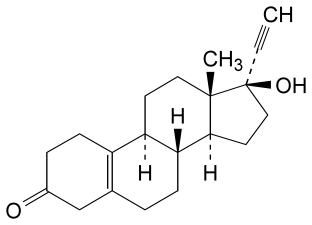
B. R1 + R2 = O, R3 = H: estr-4-ene-3,17-dione (norandrostenedione),

G. R1 = OH, R2 = C≡CH, R3 = H: 17-hydroxy-19-norpregn-4-en-20-yn-3-one (17-*epi*-norethisterone),

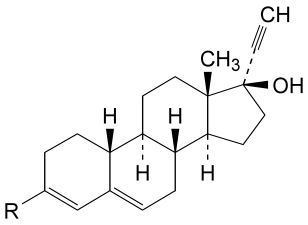
H. R1 = C≡CH, R2 = R3 = OH: 6β,17-dihydroxy-19-nor-17α-pregn-4-en-20-yn-3-one (6β-hydroxynorethisterone),



C. 17-hydroxy-19-nor-17α-pregn-5-en-20-yn-3-one,



D. 17-hydroxy-19-nor-17α-pregn-5(10)-en-20-yn-3-one,



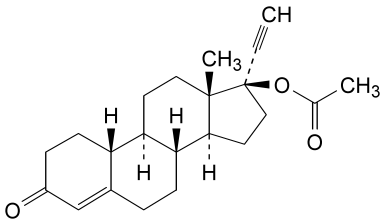
E. R = C≡CH: 3-ethynyl-19-nor-17α-pregna-3,5-dien-20-yn-17-ol,

F. R = O-C_2H_5: 3-ethoxy-19-nor-17α-pregna-3,5-dien-20-yn-17-ol.

01/2008:0850
corrected 6.0

NORETHISTERONE ACETATE

Norethisteroni acetas



$C_{22}H_{28}O_3$ M_r 340.5
[51-98-9]

DEFINITION

3-Oxo-19-nor-17α-pregn-4-en-20-yn-17-yl acetate.

Content: 98.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or yellowish-white, crystalline powder.

Solubility: practically insoluble in water, freely soluble in methylene chloride, soluble in alcohol.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *norethisterone acetate CRS*.

If the spectra show differences, dissolve the substance to be examined and the reference substance separately in *methylene chloride R*, evaporate to dryness on a water-bath and record new spectra using the residues.

TESTS

Specific optical rotation (*2.2.7*) – 30 to – 35 (dried substance).

Dissolve 0.500 g in *ethanol R* and dilute to 25.0 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 25.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (a). Dissolve 2 mg of *desoxycortone acetate CRS* and 2 mg of *norethisterone acetate CRS* in the mobile phase and dilute to 50.0 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of the test solution to 100.0 ml with the mobile phase.