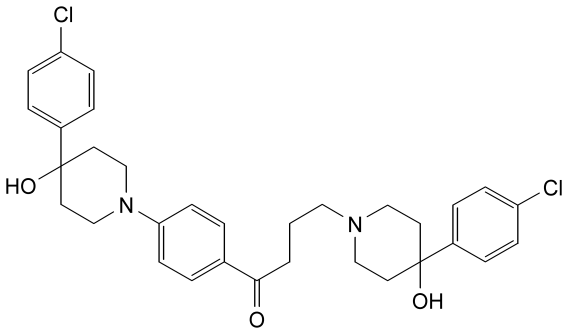
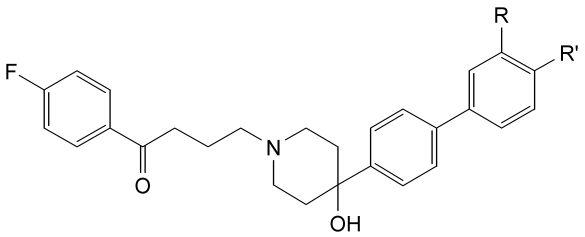


D. 4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-1-[4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]phenyl]butan-1-one,



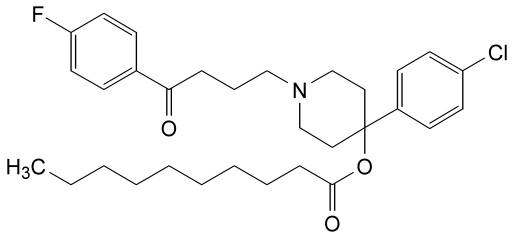
E. R = H, R′ = Cl: 4-[4-(4′-chlorobiphenyl-4-yl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one,

F. R = Cl, R′ = H: 4-[4-(3′-chlorobiphenyl-4-yl)-4-hydroxypiperidin-1-yl]-1-(4-fluorophenyl)butan-1-one.

01/2008:1431

HALOPERIDOL DECANOATE

Haloperidoli decanoas



$C_{31}H_{41}ClFNO_3$ M_r 530.1
[74050-97-8]

DEFINITION

4-(4-Chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate.

Content: 98.5 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water, very soluble in ethanol (96 per cent), in methanol and in methylene chloride.

mp: about 42 °C.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Preparation: mulls in *liquid paraffin R*.
Comparison: *haloperidol decanoate CRS*.

B. To 0.1 g in a porcelain crucible add 0.5 g of *anhydrous sodium carbonate R*. Heat over an open flame for 10 min. Allow to cool. Take up the residue with 5 ml of *dilute nitric acid R* and filter. To 1 ml of the filtrate add 1 ml of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution B_5 (*2.2.2, Method II*).

Dissolve 2.0 g in *methylene chloride R* and dilute to 20 ml with the same solvent.

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use and protect from light.*

Test solution. Dissolve 0.100 g of the substance to be examined in *methanol R* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dissolve 2.5 mg of *bromperidol decanoate CRS* and 2.5 mg of *haloperidol decanoate CRS* in *methanol R*, then dilute to 50.0 ml with the same solvent.

Reference solution (b). Dilute 5.0 ml of the test solution to 100.0 ml with *methanol R*. Dilute 1.0 ml of this solution to 10.0 ml with *methanol R*.

Column:

– *size*: *l* = 0.1 m, Ø = 4.0 mm;
– *stationary phase*: *base-deactivated octadecylsilyl silica gel for chromatography R* (3 µm).

Mobile phase:

– *mobile phase A*: 27 g/l solution of *tetrabutylammonium hydrogen sulphate R*;
– *mobile phase B*: *acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	80 → 40	20 → 60
30 - 35	40	60
35 - 40	40 → 80	60 → 20

Flow rate: 1.5 ml/min.

Detection: spectrophotometer at 230 nm.

Equilibration: with *acetonitrile R* for at least 30 min and then with the mobile phase at the initial composition for at least 5 min.

Injection: 10 µl; inject *methanol R* as a blank.

Retention time: haloperidol decanoate = about 24 min; bromperidol decanoate = about 24.5 min.

System suitability: reference solution (a):

– *resolution*: minimum 1.5 between the peaks due to haloperidol decanoate and bromperidol decanoate; if necessary, adjust the gradient or the time programme for the linear gradient elution.

Limits:

– *impurities A, B, C, D, E, F, G, H, I, J, K*: for each impurity, not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);
– *total*: not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent);

– *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying *in vacuo* at 30 °C.

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Dissolve 0.425 g in 50 ml of a mixture of 1 volume of *anhydrous acetic acid R* and 7 volumes of *methyl ethyl ketone R*. Titrate with *0.1 M perchloric acid* using 0.2 ml of *naphtholbenzein solution R* as indicator.

1 ml of *0.1 M perchloric acid* is equivalent to 53.01 mg of $C_{31}H_{41}ClFNO_3$.

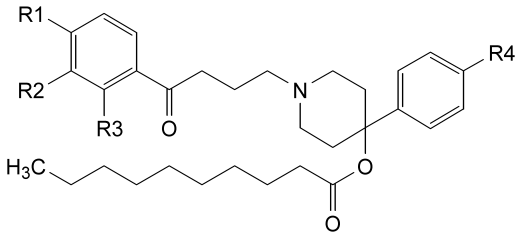
STORAGE

Protected from light, at a temperature below 25 °C.

IMPURITIES

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

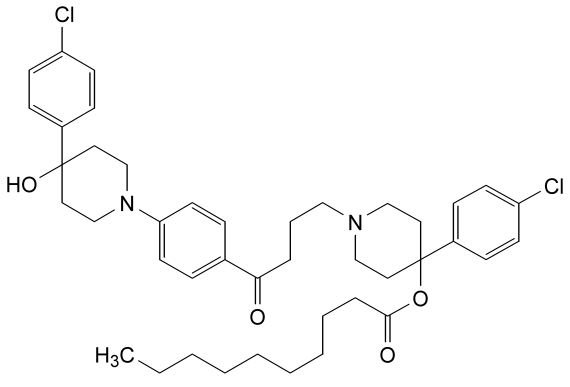
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *L.*



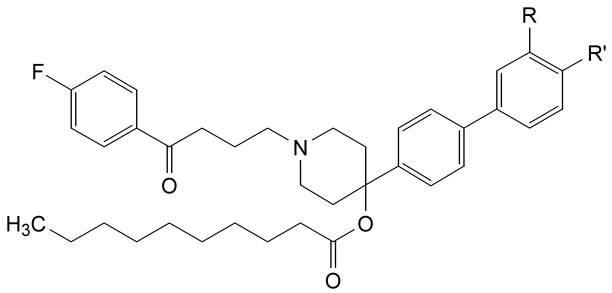
A. R1 = F, R2 = R3 = R4 = H: 1-[4-(4-fluorophenyl)-4-oxobutyl]-4-phenylpiperidin-4-yl decanoate,

B. R1 = R2 = H, R3 = F, R4 = Cl: 4-(4-chlorophenyl)-1-[4-(2-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate,

C. R1 = F, R2 = C_2H_5, R3 = H, R4 = Cl: 4-(4-chlorophenyl)-1-[4-(3-ethyl-4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate,



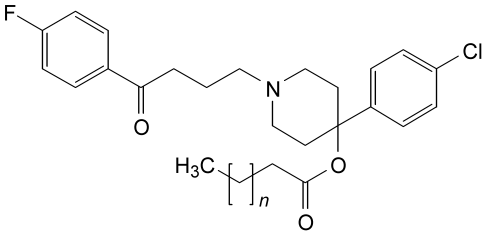
D. 4-(4-chlorophenyl)-1-[4-[4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]phenyl]-4-oxobutyl]piperidin-4-yl decanoate,



E. R = H, R′ = Cl: 4-(4′-chlorobiphenyl-4-yl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate,

F. R = Cl, R′ = H: 4-(3′-chlorobiphenyl-4-yl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl decanoate,

G. haloperidol,

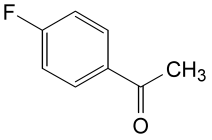


H. *n* = 5: 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl octanoate,

I. *n* = 6: 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl nonanoate,

J. *n* = 8: 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl undecanoate,

K. *n* = 9: 4-(4-chlorophenyl)-1-[4-(4-fluorophenyl)-4-oxobutyl]piperidin-4-yl dodecanoate,

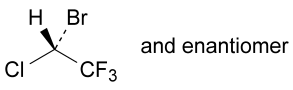


L. 1-(4-fluorophenyl)ethanone.

01/2008:0393

HALOTHANE

Halothanum



$C_2HBrClF_3$ M_r 197.4
[151-67-7]

DEFINITION

(*RS*)-2-Bromo-2-chloro-1,1,1-trifluoroethane to which 0.01 per cent *m/m* of thymol has been added.

CHARACTERS

Appearance: clear, colourless, mobile, heavy, non-flammable liquid.

Solubility: slightly soluble in water, miscible with anhydrous ethanol and with trichloroethylene.