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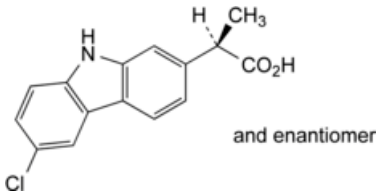
Edition: BP 2025 (Ph. Eur. 11.6 update)

Carprofen

General Notices

(Carprofen for Veterinary Use, Ph. Eur. monograph 2201)



$C_{15}H_{12}ClNO_2$ 273.7 *53716-49-7*

Action and use

Cyclo-oxygenase inhibitor; analgesic; anti-inflammatory.

Preparations

Carprofen Injection

Carprofen Tablets

Ph Eur

DEFINITION

(2*RS*)-2-(6-Chloro-9*H*-carbazol-2-yl)propanoic acid.

Content

98.5 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance

White or almost white, crystalline powder.

Solubility

Practically insoluble in water, freely soluble in acetone, soluble in methanol, slightly soluble in 2-propanol.

It shows polymorphism (*5.9*).

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison carprofen CRS.

If the spectra obtained in the solid state show differences, dissolve the substance to be examined and the reference substance separately in acetone R, evaporate to dryness and record new spectra using the residues.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution BY_3 (2.2.2, Method II).

Dissolve 1.0 g in methanol R and dilute to 25 mL with the same solvent.

Related substances

Liquid chromatography (2.2.29). *Carry out the test protected from light.*

Test solution Dissolve 50 mg of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a) Dissolve 2.5 mg of carprofen for system suitability CRS (containing impurity C) in the mobile phase and dilute to 10 mL with the mobile phase.

Reference solution (b) Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Column:

— *size*: *l* = 0.25 m, Ø = 4.6 mm;

— *stationary phase*: end-capped polar-embedded octadecylsilyl amorphous organosilica polymer R (5 µm).

Mobile phase Mix 30 volumes of a 1.36 g/L solution of potassium dihydrogen phosphate R adjusted to pH 3.0 with phosphoric acid R and 70 volumes of methanol R1.

Flow rate 1.3 mL/min.

Detection Spectrophotometer at 235 nm.

Injection 20 µL.

Run time 4 times the retention time of carprofen.

Identification of impurities Use the chromatogram supplied with carprofen for system suitability CRS and the chromatogram obtained with reference solution (a) to identify the peak due to impurity C.

Relative retention With reference to carprofen (retention time = about 10 min): impurity C = about 0.8.

System suitability Reference solution (a):

— resolution: minimum 1.5 between the peaks due to impurity C and carprofen.

Limits:

— *unspecified impurities*: for each impurity, not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.20 per cent);

— *total*: not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent);

— *disregard limit*: the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 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 2 h.

Sulfated ash (*2.4.14*)

Maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 50 mL of *ethanol (96 per cent) R*. Add 1.0 mL of *0.1 M hydrochloric acid*. Titrate with *0.1 M sodium hydroxide*, determining the end-point potentiometrically (*2.2.20*). Read the volume added between the 2 points of inflexion.

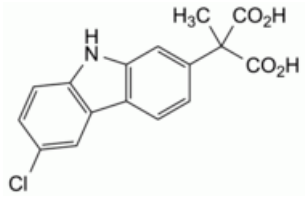
1 mL of *0.1 M sodium hydroxide* is equivalent to 27.37 mg of $C_{15}H_{12}ClNO_2$.

STORAGE

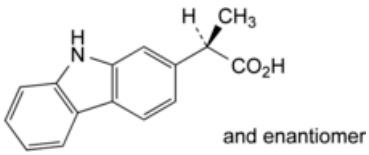
Protected from light.

IMPURITIES

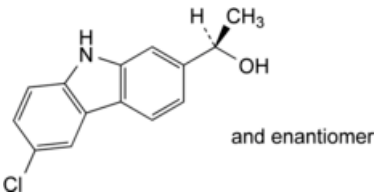
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph Substances for pharmaceutical 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) A, B, C, D, E, F, G, H.



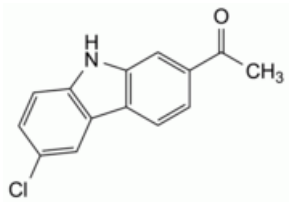
A. 2-(6-chloro-9*H*-carbazol-2-yl)-2-methylpropanedioic acid,



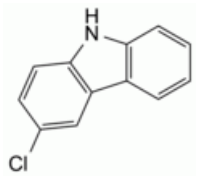
B. (2*RS*)-2-(9*H*-carbazol-2-yl)propanoic acid,



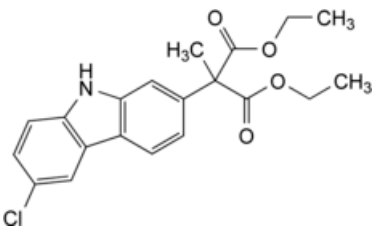
C. (1*RS*)-1-(6-chloro-9*H*-carbazol-2-yl)ethan-1-ol,



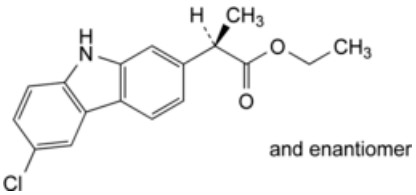
D. 1-(6-chloro-9*H*-carbazol-2-yl)ethan-1-one,



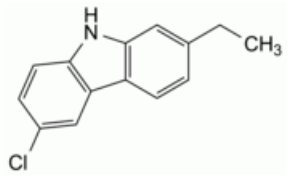
E. 3-chloro-9*H*-carbazole,



F. diethyl 2-(6-chloro-9*H*-carbazol-2-yl)-2-methylpropanedioate,



G. ethyl (2*RS*)-2-(6-chloro-9*H*-carbazol-2-yl)propanoate,



H. 6-chloro-2-ethyl-9*H*-carbazole.

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