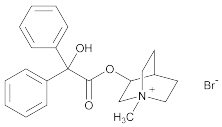
Clidinium Bromide



$C_{22}H_{26}BrNO_3$ 432.35

1-Azoniabicyclo[2.2.2]octane, 3-[(hydroxydiphenylacetyl)oxy]-1-methyl-, bromide, (±)-;
(±)-3-Hydroxy-1-methylquinuclidinium bromide benzilate [3485-62-9].

DEFINITION

Clidinium Bromide contains NLT 99.0% and NMT 100.5% of $C_{22}H_{26}BrNO_3$, calculated on the dried basis.

IDENTIFICATION

• **A. Infrared Absorption** ⟨197K⟩

Change to read:

• **B.** •The R_F value of the principal spot of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Organic Impurities*.• (RB 1-Oct-2010)

• **C. Bromide**

Sample solution: 50 mg/mL

Analysis: To 2 mL of the *Sample solution*, add a few drops of 2 N nitric acid and 1 mL of silver nitrate TS.

Acceptance criteria: A yellowish white precipitate is formed.

ASSAY

• **Procedure**

Sample: 1.2 g

Analysis: Dissolve the *Sample* in 80 mL of glacial acetic acid, warming if necessary to effect solution. Cool, and add 15 mL of mercuric acetate TS. Titrate with 0.1 N perchloric acid in dioxane VS, determining the endpoint potentiometrically. Perform a blank determination (see *Titrimetry* ⟨541⟩). Each mL of 0.1 N perchloric acid is equivalent to 43.24 mg of $C_{22}H_{26}BrNO_3$.

Acceptance criteria: 99.0%–100.5% on the dried basis

IMPURITIES

• **Residue on Ignition** ⟨281⟩

Acceptance criteria: NMT 0.1%

• **Heavy Metals** ⟨231⟩

Sample solution: 1 g in 25 mL of water

Acceptance criteria: NMT 20 ppm

Change to read:

• **Organic Impurities**

Standard solution: 100 mg/mL of USP Clidinium Bromide RS in 0.1 N methanolic hydrochloric acid

Sample solution: 100 mg/mL of Clidinium Bromide in 0.1 N methanolic hydrochloric acid

•**Reference solution:**• (RB 1-Oct-2010) Dissolve 100 mg of USP Clidinium Bromide RS in 1.0 mL of 0.1 N methanolic hydrochloric acid, and add 20 µL of a solution of 25.0 mg of USP Clidinium Bromide Related Compound A RS in 1.0 mL of 0.1 N methanolic hydrochloric acid.

Chromatographic system

(See *Chromatography* ⟨621⟩, *Thin-Layer Chromatography*.)

Adsorbent: 0.25-mm layer of chromatographic silica gel mixture

Application volume: 20 µL

Developing solvent system: Acetone, methanol, hydrochloric acid, and water (70:20:5:5)

Spray reagent: Dissolve 850 mg of bismuth subnitrate in a mixture of 10 mL of glacial acetic acid and 40 mL of water. In a separate container, dissolve 20 g of potassium iodide in 50 mL of water. Mix the two solutions, and dilute with dilute sulfuric acid (1 in 10) to 500 mL. Add 7.5 g ± 2.5 g of iodine, and mix until the solution is complete.

Chromatographic plates: Predevelop suitable thin-layer chromatographic plates by placing in a chromatographic chamber saturated with the *Developing solvent system*, and allow the *Developing solvent system* to move about 15 cm. Remove the plates from the chamber, dry at 105° for 15 min, and cool.

Analysis 1 (3-quinuclidinyl benzilate): Apply the *Standard solution* •• (RB 1-Oct-2010) and the *Sample solution* to a *Chromatographic plate*. Place the plate in an unsaturated chromatographic chamber containing freshly prepared *Developing solvent system*, and allow the solvent front to move 10 cm. Remove the plate, dry at 105° for 10 min, cool, and spray with potassium iodoplatinate TS.

Acceptance criteria 1: The •• (RB 1-Oct-2010) *Sample solution* shows no spot at an R_F value (about 0.8) corresponding to that of 3-quinuclidinyl benzilate.

Analysis 2 (limit of clidinium bromide related compound A): Apply the *Sample solution* and •*Reference solution* •(RB 1-Oct-2010) to a second *Chromatographic plate*. Place the plate in an unsaturated chromatographic chamber containing freshly prepared *Developing solvent system*, and allow the solvent front to move 15 cm. Remove the plate, dry at 105° for 10 min, cool, and spray with the *Spray reagent*.

Acceptance criteria 2: Any spot from the *Sample solution* at an R_F value of about 0.4 is not greater in size or intensity than the minor spot of the •*Reference solution:*• (RB 1-Oct-2010) NMT 0.5% of clidinium bromide related compound A is found.

SPECIFIC TESTS

• **Loss on Drying** ⟨731⟩

Analysis: Dry a sample at 105° for 3 h.

Acceptance criteria: The sample loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

Change to read:

• **USP Reference Standards** ⟨11⟩

USP Clidinium Bromide RS

USP Clidinium Bromide Related Compound A RS

•• (RB 1-Oct-2010)