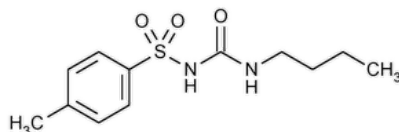


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Tolbutamide



$C_{12}H_{18}N_2O_3S$ 270.35

Benzenesulfonamide, *N*-[(butylamino)carbonyl]-4-methyl-

1-Butyl-3-(*p*-tolylsulfonyl)urea;

N-(Butylcarbamoyl)-4-methylbenzenesulfonamide CAS RN®: 64-77-7; UNII: 982XCM1FOI.

DEFINITION

Tolbutamide contains NLT 97.0% and NMT 103.0% of tolbutamide ($C_{12}H_{18}N_2O_3S$), calculated on the dried basis.

IDENTIFICATION

- **A.** [SPECTROSCOPIC IDENTIFICATION TESTS \(197\)](#), *Infrared Spectroscopy*: 197M, 197K, or 197A
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the Assay.

ASSAY

PROCEDURE

Buffer: 1.36 g/L of [potassium phosphate, monobasic](#) in [water](#). Adjust with [phosphoric acid](#) to a pH of 3.5.

Mobile phase: [Acetonitrile](#) and *Buffer* (35:65)

Diluent: [Acetonitrile](#) and *Buffer* (70:30)

System suitability solution: 1 mg/mL of [USP Tolbutamide RS](#) and 10 µg/mL of [USP Tolazamide RS](#) in *Diluent*

Standard solution: 0.1 mg/mL of [USP Tolbutamide RS](#) in *Diluent*

Sample solution: 0.1 mg/mL of Tolbutamide in *Diluent*

Chromatographic system

(See [Chromatography \(621\)](#), *System Suitability*.)

Mode: LC

Detector: UV 230 nm

Column: 4.6-mm x 25-cm; 5-µm packing [L1](#)

Autosampler temperature: 4°

Flow rate: 1.5 mL/min

Injection volume: 30 µL

Run time: NLT 1.5 times the retention time of tolbutamide

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between tolbutamide and tolazamide, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 0.73%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of tolbutamide ($C_{12}H_{18}N_2O_3S$) in the portion of Tolbutamide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of tolbutamide from the *Sample solution*

r_S = peak response of tolbutamide from the *Standard solution*

C_S = concentration of [USP Tolbutamide RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of tolbutamide in the *Sample solution* (mg/mL)

Acceptance criteria: 97.0%–103.0% on the dried basis

IMPURITIES

Change to read:

- [▲SELENIUM \(291\), Procedures, Procedure 1▲](#) (CN 1-JUN-2023)

Sample: Mix 100 mg of tolbutamide with 100 mg of [magnesium oxide](#).

Acceptance criteria: NMT 0.003%

• ORGANIC IMPURITIES

Buffer, Mobile phase, Diluent, System suitability solution, and Chromatographic system: Proceed as directed in Assay.

Standard solution: 0.001 mg/mL of [USP Tolbutamide RS](#) in *Diluent*

Sensitivity solution: 0.5 µg/mL of [USP Tolbutamide RS](#) in *Diluent* from the *Standard solution*

Sample solution: 1 mg/mL of Tolbutamide in *Diluent*

System suitability

Samples: *System suitability solution, Standard solution, and Sensitivity solution*

Suitability requirements

Resolution: NLT 2.0 between tolbutamide and tolazamide, *System suitability solution*

Tailing factor: NMT 2.0, *Standard solution*

Relative standard deviation: NMT 5.0%, *Standard solution*

Signal-to-noise ratio: NLT 10, *Sensitivity solution*

Analysis

Samples: *Standard solution and Sample solution*

Calculate the percentage of each impurity in the portion of Tolbutamide taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (1/F) \times 100$$

r_U = peak response of each impurity from the *Sample solution*

r_S = peak response of tolbutamide from the *Standard solution*

C_S = concentration of [USP Tolbutamide RS](#) in the *Standard solution* (mg/mL)

C_U = concentration of Tolbutamide in the *Sample solution* (mg/mL)

F = relative response factor (see [Table 1](#))

Acceptance criteria: See [Table 1](#). The reporting threshold is 0.05%.

Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Tosylurea ^a	0.21	1.3	0.1
Tosylamide ^b	0.26	1.3	0.1
Tolbutamide	1.00	—	—
Tolazamide	1.14	0.85	0.1

