

LABORATORY SERVICES BUREAU

Document: Controlled Substances Analysis Manual

Policy Number:
1497

Revision:
4

Subject: CS-SOP-19 Benzodiazepines

Approved:
Bell, Erica

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19. BENZODIAZEPINES

- A. Formula: Benzodiazepine structures most commonly consist of a ring system, with various substituents attached to the rings, depending on the specific benzodiazepine. The general structure of the ring system is shown in figure 1 (diazepam). Fusion of heterocyclic rings at position 1 and 2 to the 1,4-benzodiazepine ring system results in the general structure for midazolam, triazolam and alprazolam, as shown in figure 2 (alprazolam).
- B. Structure, Empirical Formula, Molecular Weight

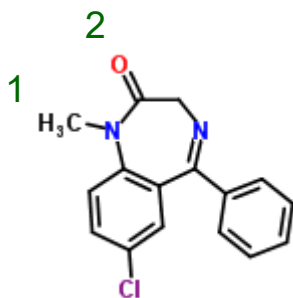


Figure 1: Diazepam
 $C_{16}H_{13}ClN_2O$
MW 284.7

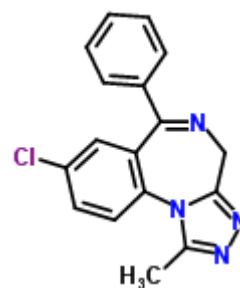


Figure 2: Alprazolam
 $C_{17}H_{13}ClN_4$
MW 308.7

- C. Synonyms: Vals, (Valium®), Libs, (Librium®), Rohypnol, ruffies, date rape drug
- D. Trade Names: Xanax®, Librium®, Klonopin®, Tranxene®, Valium®, ProSom™, Ativan®, Versed®, Serax®, Restoril®, Halcion®, Rohypnol®, etc.
- E. Drug Action: CNS depressant
- F. Common pharmaceutical/street forms: Tablets, capsules, and injectable solutions. Chlordiazepoxide may be combined with amitriptyline. Rohypnol, (flunitrazepam), has no medicinal use in the U. S. A., but is available from Mexico and the tablets are usually marked "Roche 1" and "Roche 2" for 1 and 2 mg tablets, respectively.
- G. Solubility:
- (1) Free 1,4-benzodiazepines: Chloroform, diethyl ether, slightly soluble in methanol, ethanol, insoluble in water
 - (2) Hydrochloride and dipotassium salts: Water, ethanol, methanol, insoluble in chloroform and diethyl ether

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H. Extraction:

(1) Dry extraction

- (a) Dissolve in C15 methanol.
- (b) Filter to remove any insoluble material if necessary.

Note: Chlordiazepoxide, lorazepam, oxazepam, and triazolam are more soluble in ethanol than methanol and can be extracted with ethanol. Methanol with C15 can then be added for GC/MS analysis.

Alprazolam and clonazepam can be extracted with chloroform. The chloroform is then evaporated and the residue reconstituted in methanol.

(2) Extraction for liquids

- (a) Add 1 drop of liquid to methanol.
- (b) Filter to remove any insoluble material if necessary.

Note: Liquid may require concentration or extraction with an organic solvent prior to addition to methanol.

I. Chemical indicator tests:

- (1) Marquis: Orange
- (2) Liebermann's: Light yellow

J. TLC:

(1) Mobile Phase:

- (a) System 1: Methanol:conc. ammonium hydroxide (100:1.5)
- (b) System 2: Chloroform:methanol (90:10)
- (c) System 3: Chloroform:acetone (80:20)
- (d) System 4: Ethyl acetate:methanol:conc. ammonium hydroxide (85:10:5)
- (e) System 5: Ethyl acetate

(2) Locator: Acidified iodoplatinate, Dragendorff reagent, Marquis reagent

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K. GC/MS: Analyze using "Drugs 1" program for all benzodiazepines except Alprazolam and Clonazepam, which should be analyzed using a longer program such as "Drugs 2". Due to low dosages associated with preparations of benzodiazepines, "Drugs 3" program can be used in lieu of other programs.

L. Comments: Benzodiazepines are used as anticonvulsants, sedatives, muscle relaxants, pre-anesthetic and anti-anxiety medication.

M. Report as: See ARS Title 13 for list of specific controlled benzodiazepines.

Example: Diazepam, a dangerous drug.

N. References:

- (1) Analytical Profiles of the Benzodiazepines, CND Analytical, Inc., Auburn, AL, 1989.
- (2) Rucker, C. L., Chemical Screening and Identification Techniques for Flunitrazepam, Drug Enforcement Administration, Western Laboratory, San Francisco, CA.
- (3) Chociay, J., Szarka, J., Procedure for the Identification of Flunitrazepam Tablets (Rohypnol), Microgram, Vol. XXXII, No. 2, Feb. 1999, pp. 75-82.
- (4) Inaba, D.S., Cohen, W. E., Holstein, M.E., Uppers, Downers, All Arounders, 3rd ed., CNS Publications, Inc., Ashland, OR, 1997, pp. 160 and 164-167.