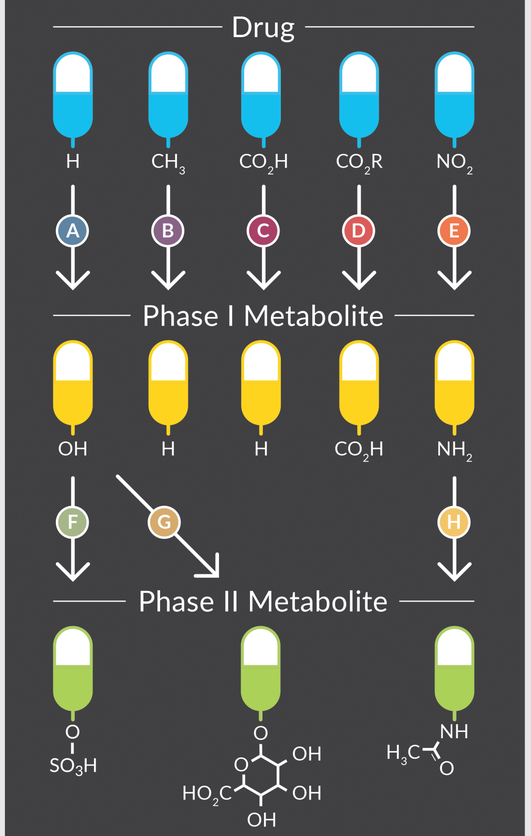
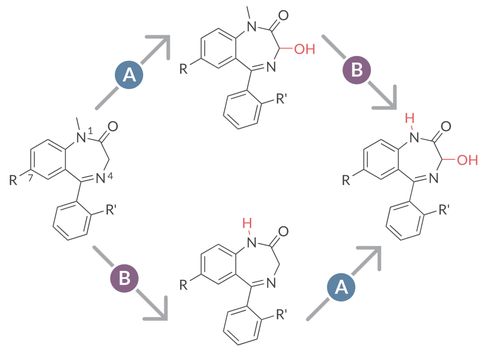
BENZODIAZEPINE METABOLISM LAB GUIDE

Biotransformation Pathway

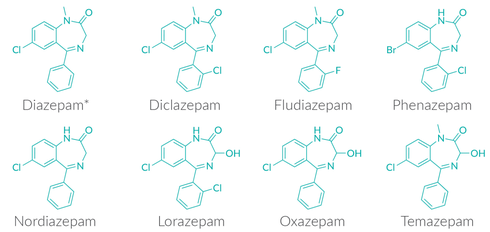


- A Hydroxylation (MW plus 16)
- B Demethylation (MW minus 14)
- C Decarboxylation (MW minus 44)
- D Hydrolysis
- E Reduction (MW minus 30)
- F Sulfation (MW plus 80)
- G Glucuronidation (MW plus 176)
- H Acetylation (MW plus 42)

7-Halogenated-1,4-Benzodiazepines

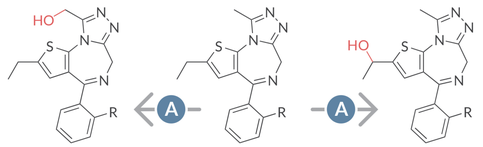


Examples

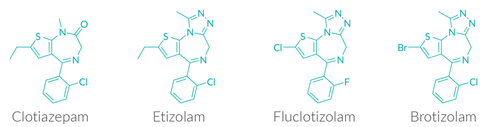


*The primary metabolite of diazepam is nordiazepam *via* phase I demethylation.

Thienodiazepines

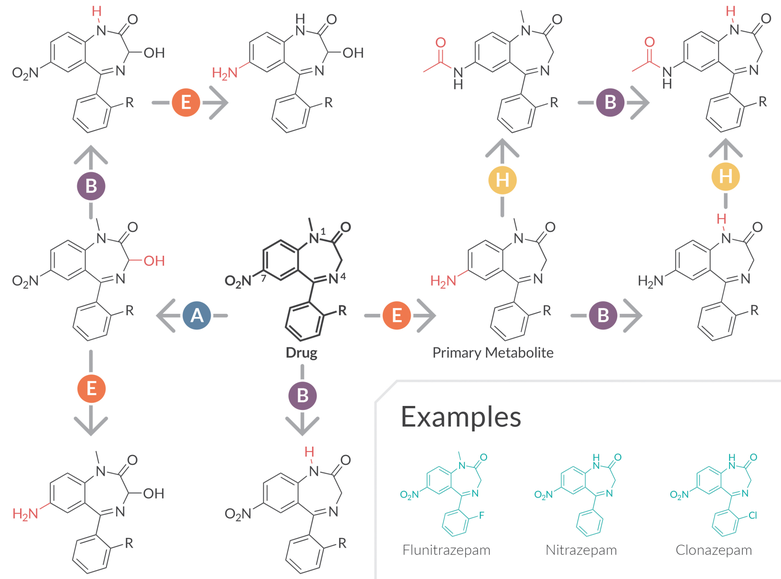


Examples



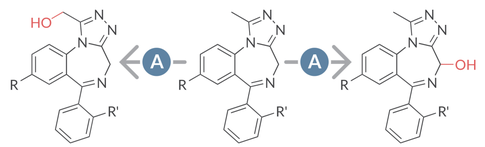
Thienodiazepines contain a thiophene ring in place of the benzene ring of a standard benzodiazepine but exhibit similar activity and pharmacological effects.

7-Nitro-1,4-Benzodiazepines

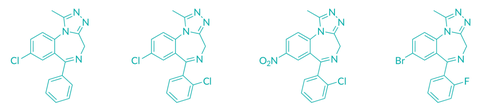


Examples

Triazolobenzodiazepines



Examples



8-Nitrotriazolobenzodiazepines can also undergo reduction to 8-aminotriazolobenzodiazepines.

View a complete list of parent compounds, metabolites, and labeled standards at **www.caymanchem.com**

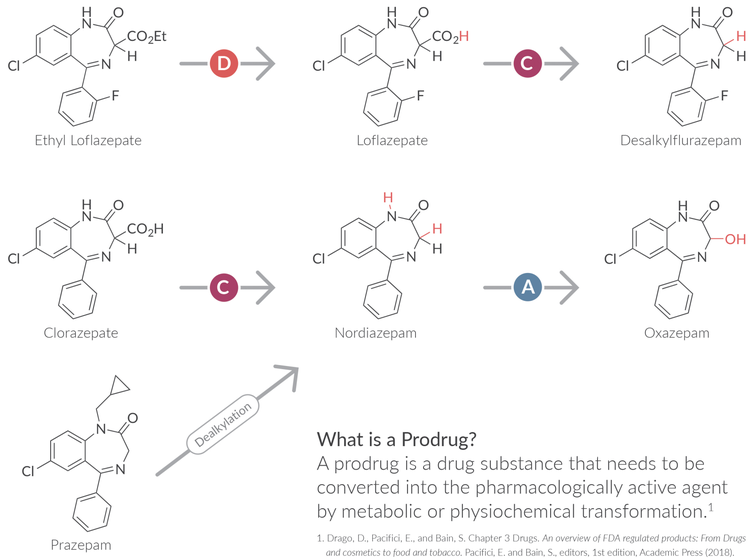
Half-Life of Common Benzodiazepines

Drug (Brand Name)	Half-Life (h)*	Primary Metabolite (half-life, h)*
Long Half-Life (effective >24 h)		
Diazepam (Valium)	20-100	Nordiazepam (36-200)
Chlordiazepoxide (Librium)	5-30	Nordiazepam (36-200)
Clorazepate (Tranxene)	*	Nordiazepam (36-200)
Prazepam (Centrax)	*	Nordiazepam (36-200)
Flurazepam (Dalmane)	*	Desalkylflurazepam (40-250)
Intermediate to Short Half-Life (effective 5-24 h)		
Nitrazepam (Alodorm)	15-38	7-Aminonitrazepam
Flunitrazepam (Rohypnol)	20-30	7-Aminoflunitrazepam
Temazepam (Restoril)	8-22	Oxazepam (4-15)
Bromazepam (Lectopam)	10-20	3-hydroxy Bromazepam
Lorazepam (Ativan)	10-20	Lorazepam Glucuronide
Alprazolam (Xanax)	6-20	α-hydroxy Alprazolam
Oxazepam (Serax)	4-15	Oxazepam Glucuronide
Etizolam (Etizest)	3.4-7.1	α-hydroxy Etizolam
Ultra-Short Half-Life (effective <5 h)		
Midazolam (Versed)	<5	α-hydroxy Midazolam
Triazolam (Halcion)	<5	α-hydroxy Triazolam

*Approximate half-life data adapted from Greenblatt, D.J., Shader, R.I., Divoll, M., *et al. Br. J. Clin. Pharmacol.* **11 (Suppl 1)**, 11S-16S (1981) and Manchester, K.R., Lomas, E.C., Waters, L., *et al. Drug Test Anal.* **10(1)**, 37-53 (2018).

*Indicates prodrugs or drug precursors that do not reach the systemic circulation in clinically important amounts.

Benzodiazepine Prodrugs



What is a Prodrug?

A prodrug is a drug substance that needs to be converted into the pharmacologically active agent by metabolic or physiochemical transformation.[1]

1. Drago, D., Pacifici, E., and Bain, S. Chapter 3 Drugs. *An overview of FDA regulated products: From Drugs and cosmetics to food and tobacco.* Pacifici, E. and Bain, S., editors, 1st edition, Academic Press (2018).