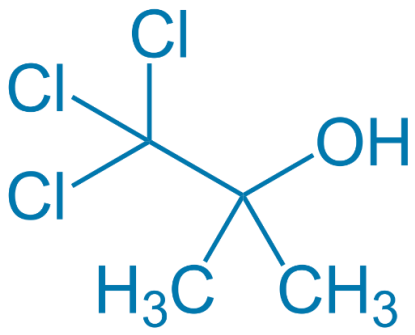
Study of the Official Compounds

Chlorbutol (Chlorobutanol)

Chemical Structure & Formula

- **IUPAC Name**: 1,1,1-Trichloro-2-methyl-2-propanol
- **Chemical Formula**: C4H7Cl3O
- **Molecular Weight**: 177.46 g/mol
- **Structure**:
  - Central carbon is bonded to:
    - Three chlorine atoms
    - One hydroxyl group (–OH)
    - One methyl group (–CH3)
- It is a tertiary alcohol and a chlorinated derivative of butanol.



Preparation

- Chlorbutol is synthesized by the reaction of chloroform with acetone in the presence of potassium or sodium hydroxide (a base).

Reaction:

$$(CH_3)_2CO + CHCl_3 + NaOH \rightarrow C(CH_3)(OH)(Cl)_3 + NaCl + H_2O$$

Steps:

1. **Reactants:**
   - Chloroform (CHCl3)
   - Acetone (CH3COCH3)
   - Sodium hydroxide (NaOH)
2. **Reaction Conditions:**
   - Low temperature (below 20°C)
   - Stirring and cooling

- Slow addition of NaOH to control the exothermic nature of the reaction

3. **Mechanism:**
   - Base catalyzes haloform reaction between chloroform and acetone
   - Trichloromethyl carbanion attacks acetone
   - Hydroxylation yields chlorbutol

Test for Purity

- **Melting Point**: Pure chlorbutol has a melting point of 95–97°C.
- **Infrared spectroscopy (IR)**: Peaks corresponding to –OH group (~3300 cm^{-1}) and C–Cl stretches.
- **Thin Layer Chromatography (TLC)**: Single spot indicates purity.
- **Loss on Drying**: Should be minimal to ensure absence of moisture.
- **Color of solution in alcohol**: Should remain clear without turbidity.

Assay

- **Method**: Non-aqueous titration using perchloric acid in glacial acetic acid.
- **Procedure**:
  1. Dissolve a known quantity in glacial acetic acid.
  2. Titrate with 0.1 N perchloric acid.
  3. Use crystal violet as an indicator (end-point: color change).
- **Calculation**: Based on volume used and normality.
- **Alternative:** UV/IR spectroscopy for precise quantitative analysis.

Medicinal Uses

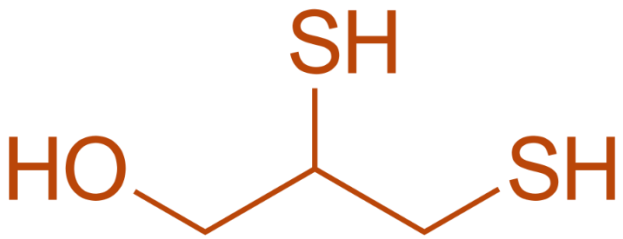
- **Preservative**: In eye drops, ear drops, and injectable solutions (low toxicity at low concentrations).
- **Sedative & Hypnotic**: Has mild CNS depressant properties.
- **Antibacterial/Antifungal**: Used topically or in formulations to maintain sterility.

Dimercaprol (British Anti-Lewisite, BAL)

Chemical Structure & Formula

- **IUPAC Name**: 2,3-Dimercaptopropanol
- **Chemical Formula**: C3H8OS2
- **Molecular Weight**: 124.22 g/mol

- **Structure**:
  - A propane backbone
  - Two adjacent thiol (–SH) groups at carbon 2 and 3
  - One hydroxyl (–OH) group at carbon 1



Preparation

- Dimercaprol was originally developed as an antidote to arsenic-based chemical warfare agents.

Synthesis:

1. **Starting materials**: Allyl alcohol (CH2=CH–CH2OH)
2. **Step 1**: React with elemental sulfur or hydrogen sulfide under reducing conditions.
3. **Step 2**: Catalytic hydrogenation of allyl alcohol to introduce –SH groups.

- **Modern processes may involve:**
  - **Thioacetate intermediates** (e.g., reaction of epichlorohydrin with sodium thioacetate followed by hydrolysis).
- **Note**: The product is unstable in presence of oxygen and must be stabilized in oil-based formulations (usually peanut oil).

Test for Purity

- **Odor**: Strong sulfurous odor due to thiol groups.
- **Melting point**: Should conform to standard limits (~23°C).
- **GC-MS**: For identification and purity.
- **TLC or HPLC**: Used for quantification and impurity profiling.

Assay

- **Method**: Iodometric titration
- **Principle**: The thiol groups in dimercaprol reduce iodine to iodide.
- **Procedure**:
  1. Dissolve sample in water and acetic acid.
  2. Add excess iodine solution.

3. Back titrate unreacted iodine with sodium thiosulfate using starch as an indicator.

Alternate Methods:

- High-Performance Liquid Chromatography (HPLC) with UV detection.
- Spectrophotometry based on reaction with Ellman's reagent (DTNB).

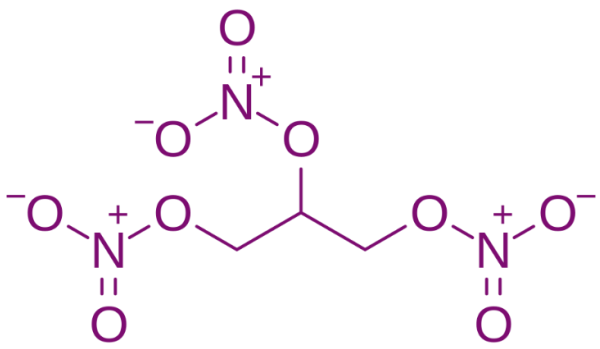
Medicinal Uses

- **Antidote for heavy metal poisoning**:
  - Arsenic, mercury, lead, and gold.
- **Chelating Agent**:
  - Binds to heavy metals through –SH groups forming stable, excretable complexes.
- **Usually administered**: Intramuscularly in peanut oil due to instability in aqueous media.
- **Cautions**: Narrow therapeutic index; causes nausea, hypertension, pain at injection site.

Glyceryl Trinitrate (Nitroglycerin)

Chemical Structure & Formula

- **IUPAC Name**: 1,2,3-Propanetriol trinitrate
- **Chemical Formula**: C3H5N3O9
- **Molecular Weight**: 227.09 g/mol
- **Structure**:
  - Glycerol molecule where all three –OH groups are esterified with nitric acid (–ONO2).
  - Three nitrate esters on a propane backbone.
- **Highly explosive** due to nitrate groups; also a powerful vasodilator.



Preparation

- **Process**: Nitration of glycerol using a nitrating mixture (Nitric acid + Sulfuric acid)
- **Reaction**:

$$C_3H_5(OH)_3 + 3\ HNO_3 \rightarrow C_3H_5(ONO_2)_3 + 3\ H_2O$$

Steps:

1. **Cooling**: Reaction must be done at 0–5°C to control exothermic reaction.
2. Add glycerol slowly into the nitrating mixture (not vice versa).
3. Stirring and temperature control are critical to avoid explosion.
4. After reaction, mixture is poured into cold water to precipitate product.
5. Product is washed and stored in alcohol or diluted for medical use.

Test for Purity

- **Appearance**: Colorless or pale yellow liquid.
- **IR Spectroscopy**: Strong absorption bands for nitrate esters (~1630–1650 cm^{-1}).
- **Stability Tests**: As it is volatile and sensitive, tested under stress for decomposition.
- **Limit tests**: For acidic impurities and residual sulfuric/nitric acid.

Assay

- **UV Spectrophotometry**: Nitroglycerin absorbs UV light (typically around 210–230 nm).
- **Chromatographic Methods**: HPLC is the preferred assay method.
    - Mobile Phase: Acetonitrile/water
    - Detection: UV
- **Standardization**: Compared with reference standards.

Alternative:

- Titration with sodium hydroxide after alkaline hydrolysis (liberates nitric acid equivalents).

Medicinal Uses

- **Anti-anginal agent**: Relieves chest pain by dilating coronary arteries.
- **Mechanism**:
    - Converts to nitric oxide (NO) in the body.
    - NO activates guanylate cyclase → increases cGMP → smooth muscle relaxation.
- **Dosage Forms**:
    - Sublingual tablets (fast action)
    - Ointments
    - Patches
    - Sprays
- **Used in**: Angina pectoris, heart failure, and hypertension emergencies.
- **Caution**: May cause headache, hypotension, and tolerance on prolonged use.

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