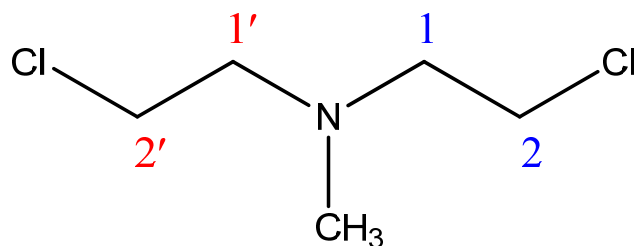


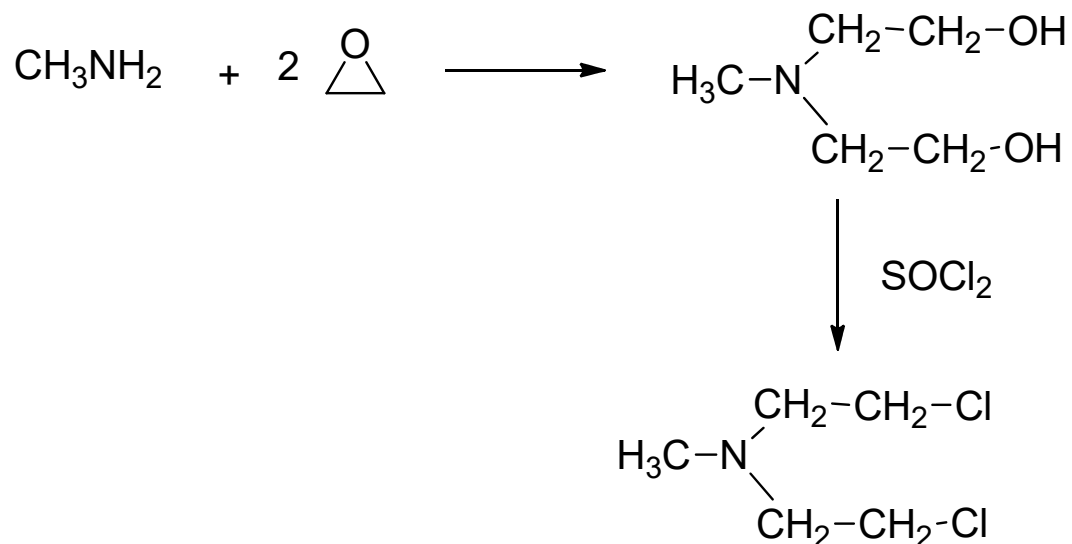
# Alkylating agents

## Meclorothamine



IUPAC: 2,2'-dichloro-N-methyldiethylamine

## Synthesis

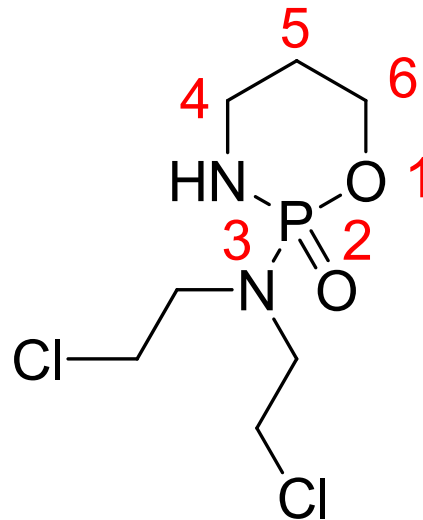


## MOA

- ❖ It produces highly reactive carbonium ion intermediates which transfer alkyl groups to cellular macromolecules by forming covalent bonds.
- ❖ Alkylation results in cross-linking/ abnormal base pairing/ scission of DNA.
- ❖ cross-links (bonds between atoms in the DNA) prevent DNA from being separated for synthesis or transcription.
- ❖ The induction of mispairing of the nucleotides leads to mutations.

Uses: For the palliative treatment of Hodgkin's disease (Stages III and IV), lymphosarcoma, chronic myelocytic or chronic lymphocytic leukemia and bronchogenic carcinoma.

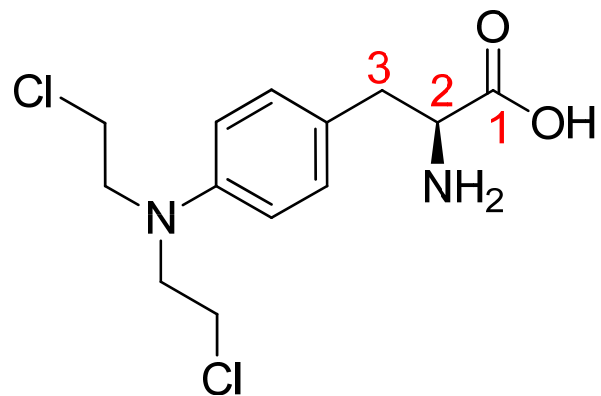
# Cyclophosphamide



IUPAC: 2-[Bis(2-chloroethylamino)]-tetrahydro-2H-1,3,2-oxazaphosphorine-2-oxide

MOA: Similar to meclorethamine

Uses: Cyclophosphamide is indicated for the treatment of malignant lymphomas, multiple myeloma, leukemias, neuroblastoma, adenocarcinoma of the ovary, retinoblastoma, and carcinoma of the breast.



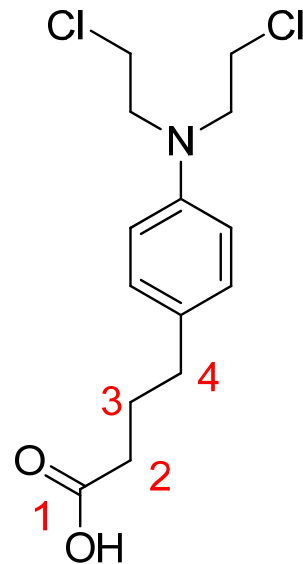
Melphalan

IUPAC: 3-(p-(Bis(2-chloroethyl) amino)phenyl)-L-alanine

MOA: Similar to meclorethamine

Uses: Has also been used alone or as part of various chemotherapeutic regimens as an adjunct to surgery in the treatment of breast cancer and carcinoma of the ovary.

# Chlorambucil

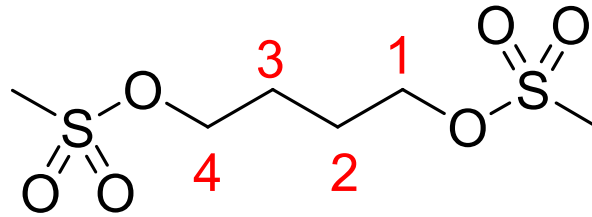


IUPAC: 4-(p-bis(beta-chloroethyl)aminophenyl)butyric acid

MOA: Similar to meclorethamine

Uses: For treatment of chronic lymphocytic leukemia, malignant lymphomas including lymphosarcoma, giant follicular lymphoma, Hodgkin's disease and non-Hodgkin's lymphomas.

## Busulfan

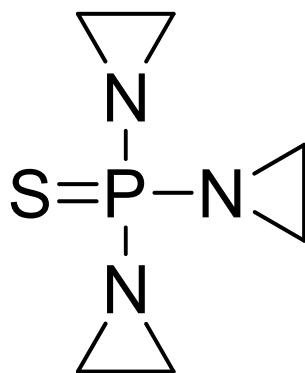


IUPAC: 1,4-Bis(methanesulfonyl)butane

MOA: Busulfan is an alkylating agent that contains 2 labile methanesulfonate groups attached to opposite ends of a 4-carbon alkyl chain. Once busulfan is hydrolyzed, the methanesulfonate groups are released and carbonium ions are produced. These carbonium ions alkylate DNA, which results in the interference of DNA replication and RNA transcription, ultimately leading to the disruption of nucleic acid function.

Uses: For use in combination with cyclophosphamide for chronic myelogenous leukemia.

## Thiotepa



IUPAC: *N,N',N''*-triethylenethiophosphoramidate

**MOA:** The alkyl group is attached to the guanine base of DNA, at the number 7 nitrogen atom of the imidazole ring. They stop tumor growth by crosslinking guanine nucleobases in DNA double-helix strands, directly attacking DNA. This makes the strands unable to uncoil and separate. As this is necessary in DNA replication, the cells can no longer divide.

**Uses:** ThioTEPA is used as a conditioning treatment prior to allogeneic or autologous haematopoietic progenitor cell transplantation (HPCT) in haematological diseases in adult and paediatric patients. It is also appropriate for the treatment of solid tumours in adult and paediatric patients.