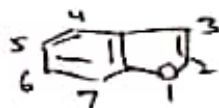




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Topic: Benzofuran

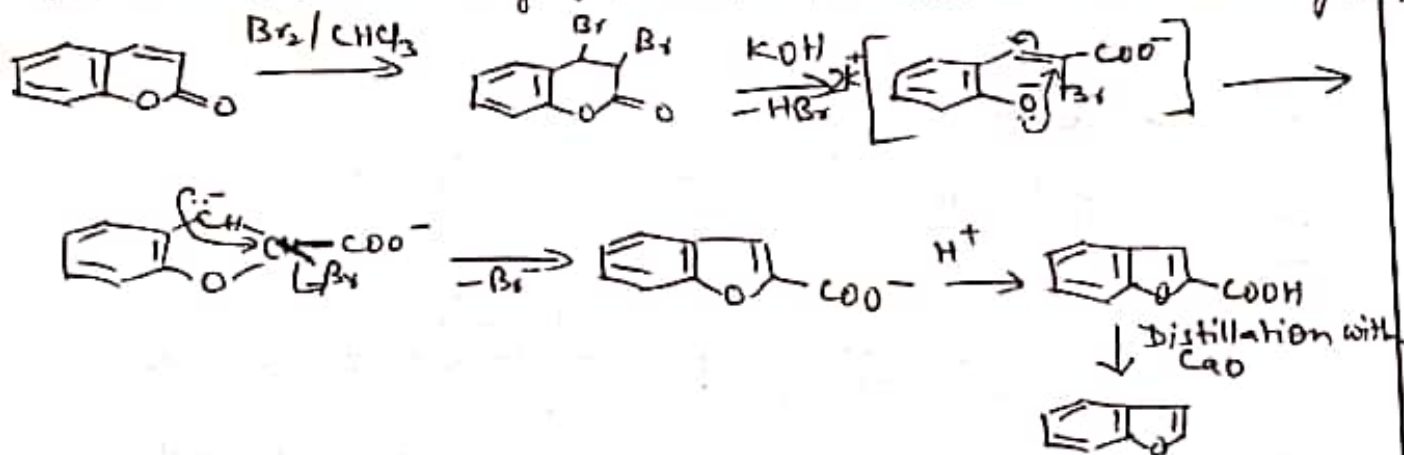
Benzofuran

Benzene ring condensed at 2,3 position of furan is Benzofuran. It was earlier known as Coumarone and was discovered in coal-tar by Kraemer and Spikler. This is also designated as benzob[2]furan. It is numbered as

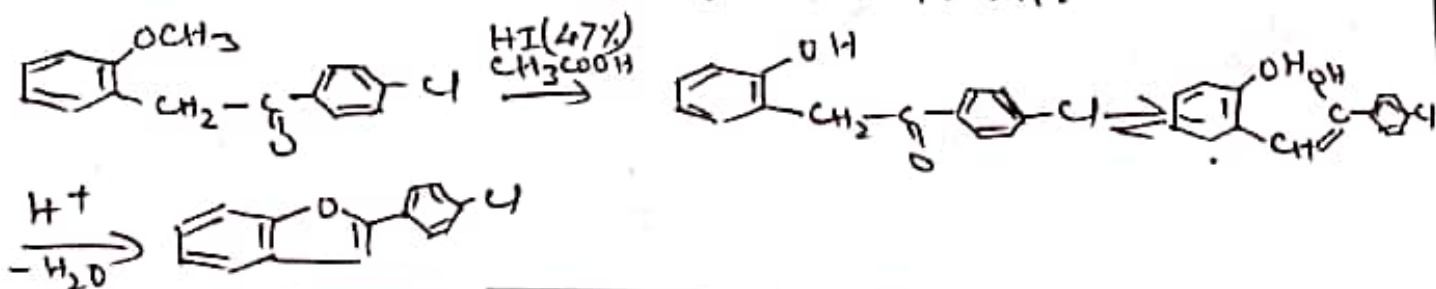


Synthesis

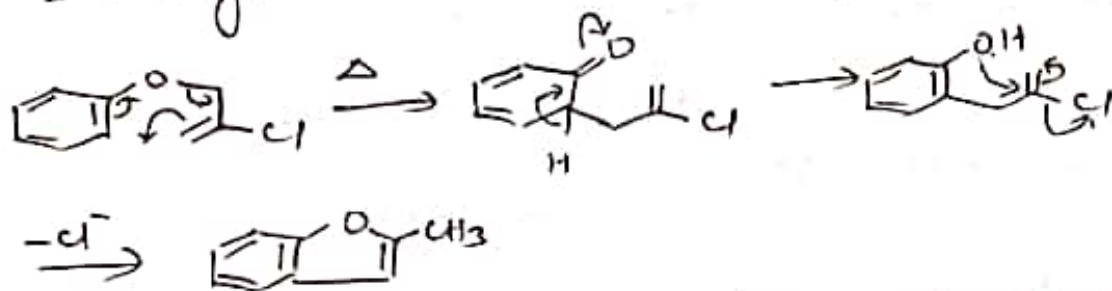
1. From Coumarin: Coumarin initially involves bromination to give 3,4-dibromocoumarin which is further treated with alkali to get Coumarillic acid. The acid finally decarboxylates to benzofuran. The base induced ring contraction is known as Perkin rearrangement.



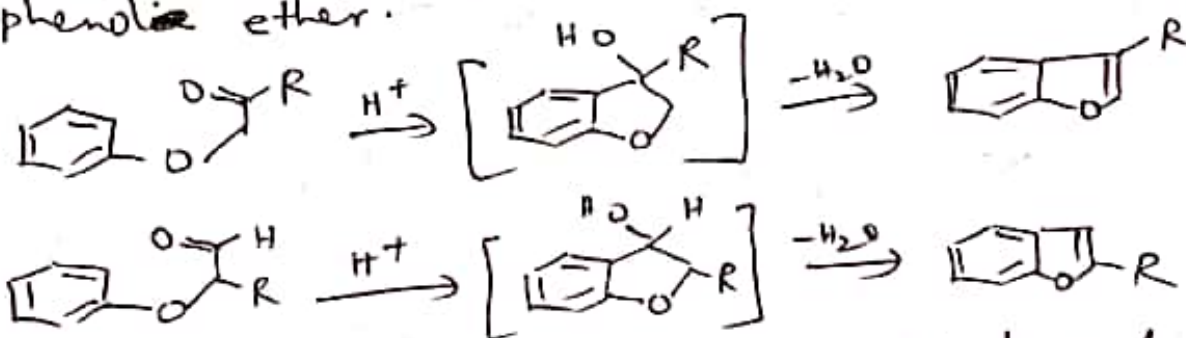
2. From 2-methoxyphenylmethyl-4-chlorophenylketone - It is first treated with HI(47%)/CH₃COOH to bring about an ether cleavage and subsequent cyclisation of intermediate leads to benzofuran.



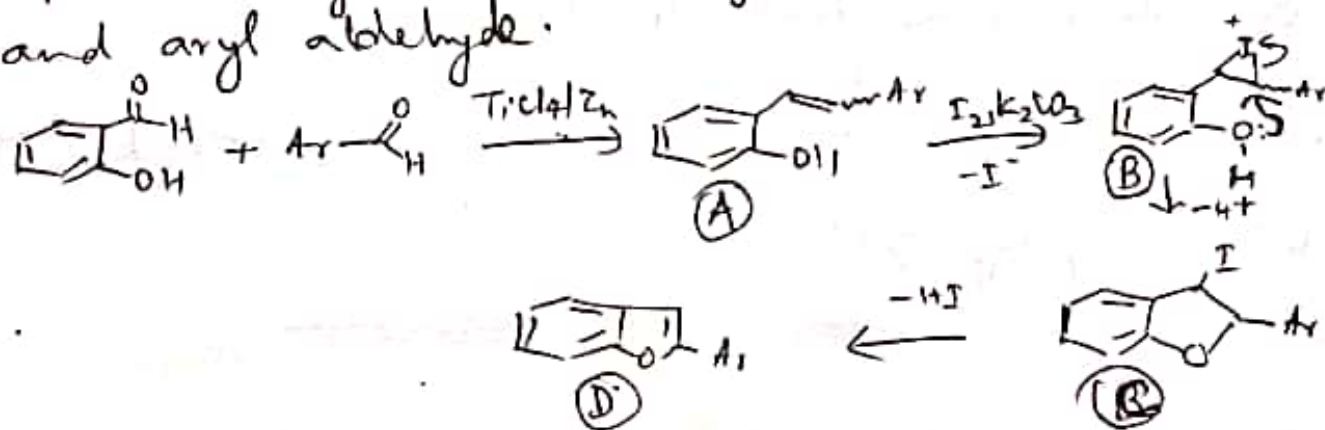
3. Through Claisen Rearrangement: Aryl-2-chloroprop-2-en ethers undergoes Claisen rearrangement to give 2-methylbenzofuran.



4. From 2-phenoxyalkanol or from 2-phenoxyalkanal: It is an acid catalyzed intramolecular hydroxyalkylation/elimination sequence (SE_{Ar}) reaction from 2-phenoxyalkanol or 2-phenoxyalkanal carrying a carbonyl moiety in the β-position of a phenolic ether.

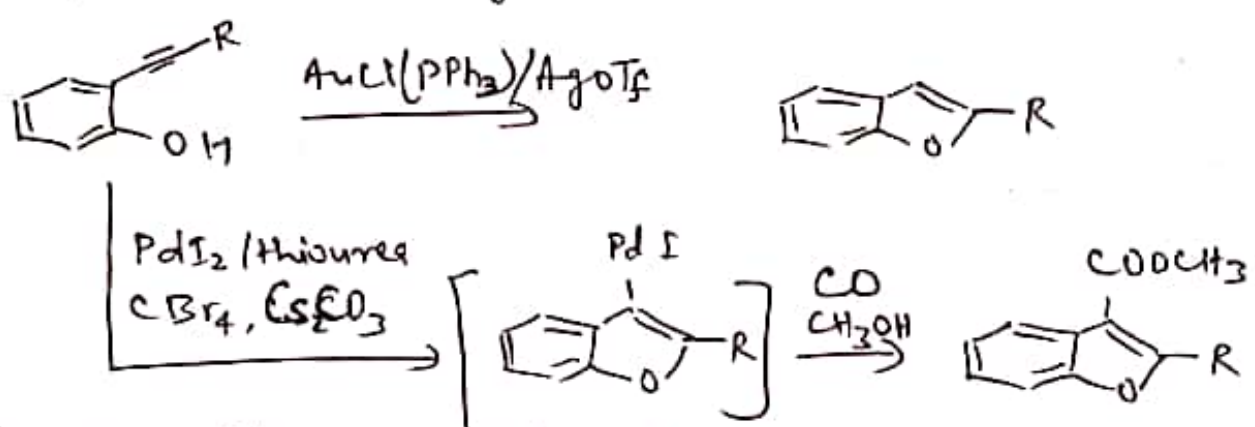


5. By cross coupling of salicylic aldehyde and aryl aldehydes: 2-Arylbenzofuran is obtained by iodine mediated cyclization of o-hydroxy stilbene prepared by cross coupling of salicylic aldehyde and aryl aldehyde.

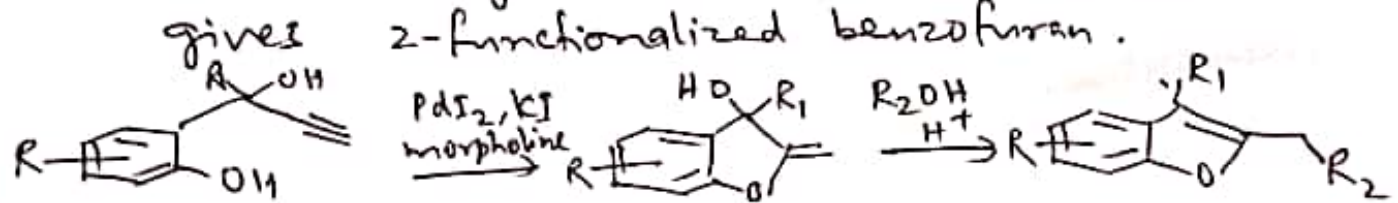


The iodine induced cyclisation $A \rightarrow D$ can be understood via formation of the iodonium ion (B), its intramolecular opening by attack of phenolate $B \rightarrow C$ and base induced HI elimination $C \rightarrow D$.

6. From 2-ethynylphenol: It involves transition metal mediated cyclization. Use of an Au(I)/Ag(I) or Rh/BINAP catalyst system gives 2-substituted benzofuran directly while application of a PdI₂/thiourea/CBr₄ cocatalyst system followed by carbonylation of the Pd-intermediate in methanol yields benzofuran-3-carboxylate.

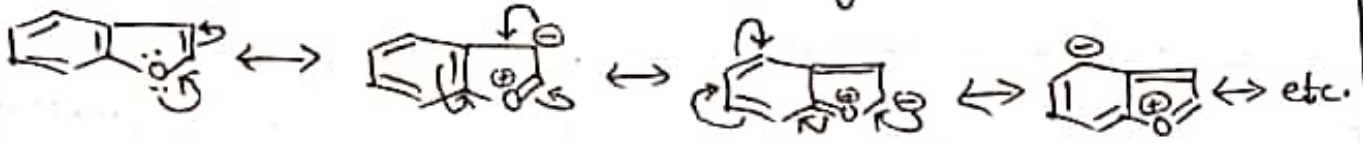


7. By Pd-catalysed cyclodimerization of (o-hydroxyphenyl)-substituted propargyl alcohol leading to enol ether followed by acid catalyzed allylic ~~rearrangement~~ rearrangement with solvent incorporation



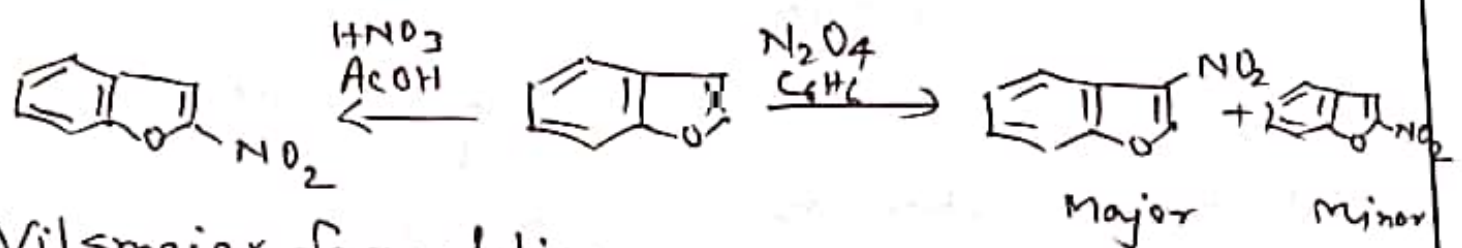
Properties.

Benzofuran is a colourless liquid having B. Pt. 173°C. A number of derivatives of benzofuran are present in plant products and have pharmacological applications. Benzofuran is highly aromatic and is a resonance hybrid of the following resonance structures

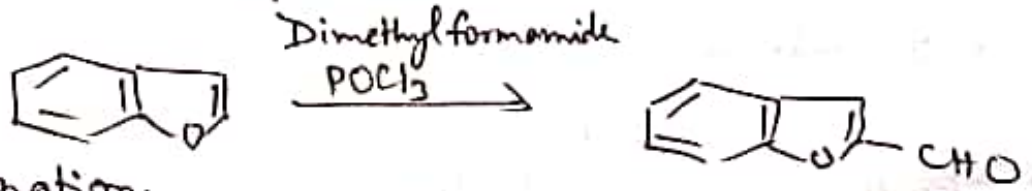


The electrophilic reactants attack on benzofuran under mild conditions and in contrast to Pyrrole the attack takes place at the 2 and 3-positions, but preferentially at the 2-position, due to the high electronegativity of oxygen atom.

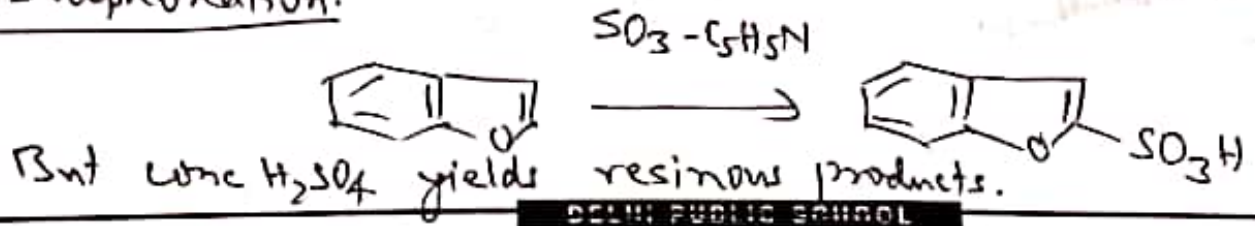
Nitration - With HNO₃ in acetic acid yields 2-nitrobenzofuran while N₂O₄ in benzene leads to 4:1 mixture of 3 and 2 substituted products



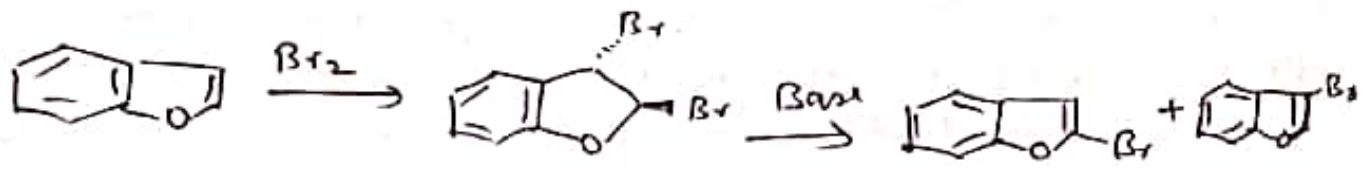
Vilsmeier formylation



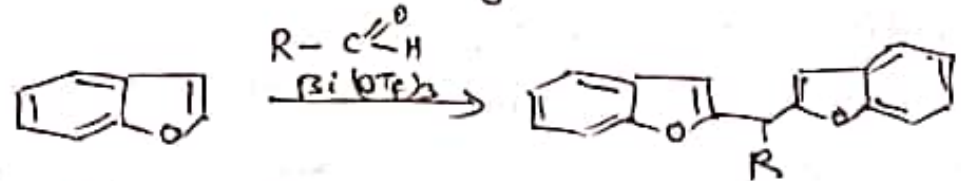
Sulphonation.



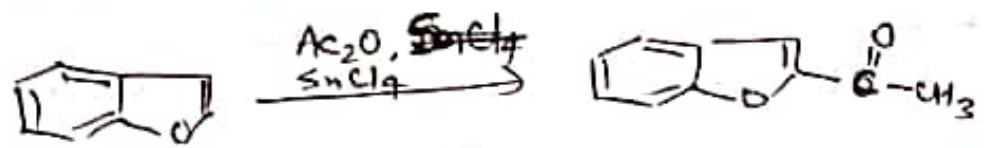
Benzofuran reacts with bromine to give the addition product with trans configuration. which on dehydrobromination with base gives rise to a mixture of 2- and 3-bromobenzofuran.



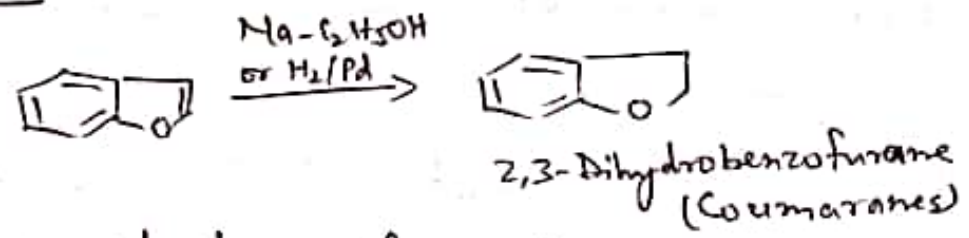
Condensation with aldehydes in the presence of $Bi(OTf)_3$ as catalyst leads to bis(2-benzofuryl)methane



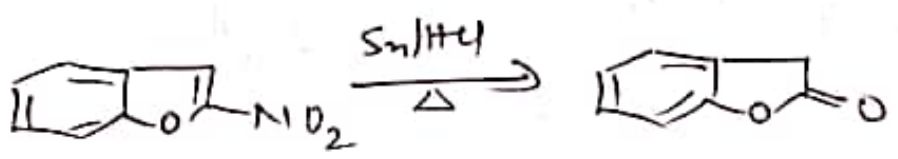
Friedel Crafts reaction:



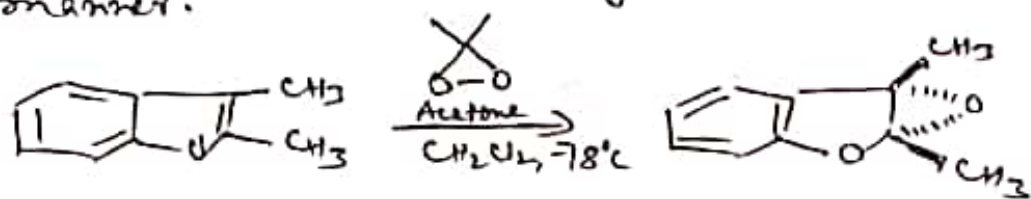
Reduction



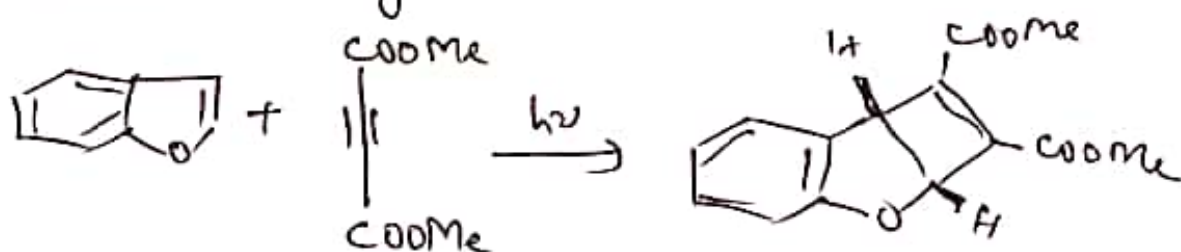
But the reduction of 2-nitrobenzofuran with Sn/HCl gives benzofuranone in stead of expected 2-aminobenzofuran.



Epoxidation: 2,3-Dimethylbenzofuran undergoes epoxidation with dimethyldioxirane in quantitative manner.



In contrast to furans, the benzene ring in benzofuran is dominant due to its large resonance energy to such an extent that (4+2) Cycloaddition (Diels-Alder Reaction) are not possible. However photochemical [2+2] cycloaddition with activated alkynes occurs readily on the C-2/C-3 double bond and leads to cyclobutene derivatives.



Photooxygenation of 2,3-dimethylbenzofuran at -78°C produces a dioxetane which isomerizes at room temperature to give 2-acetoxyacetophenone.

