A Review on Synthesis and Biological Activity of some Indole Derivative

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ABSTRACT

Indole is a fused aromatic heterocyclic ring, consisting of a six-membered benzene ring fused to a five membered nitrogen containing pyrrole ring, indole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities like:- antimicrobial, anti-vira, antibercular, anti-inflammatory, anticancer, antidiabetic, anticonvulsant, antimicrobial, antioxidant, antidepressant activities.

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INTRODUCTION

The small and simple Indole nucleus is present in compounds involved in research aimed at evaluating new products that possess interesting biological activities like antimicrobial, anti-viral, antitubercular, anti-inflammatory, anticancer, antidiabetic, anticonvulsant, antimicrobial, antioxidant, antidepressant activities. Indole is used primarily in industry and research. Being an aromatic fused heterocyclic compound consisting of a six-membered benzene ring fused to five-membered nitrogen -containing pyrrole ring, indole finds use in research as a starting bioactive structures.

Chemistry of Indole:
Molecular formula:-C8H7N, Molar mass:-117.15 g/mol, Density:-1.1747 g/cm3,

[Figure no 1] General properties:
Indole is a solid at room temperature. It occurs naturally in human feces and has an intense fecal odor. At very low concentrations, however, it has a flowery smell, and is a constituent of many flower scents (such as orange blossoms) and perfumes. It also occurs in coal tar. Indole undergoes electrophilic substitution, mainly at position 3. Substituted indoles are structural elements of (and for some compounds the synthetic precursors for) the tryptophan-derived tryptamine alkaloids like the neurotransmitter serotonin, and melation. Other indolic compounds include the plant hormone Auxin (indole-3-acetic acid, IAA), the anti-inflammatory drug indomethacin, the betablocker pindolol, and the
Solid, Melting point:-52–54°C, Appearance:- White solid, Boiling point:-253– 254°C (526 K), Acidity (pKa):- 16.2, Basicity (pKb):- 17.6 words indigo dye and oleum, since indole was first isolated by treatment of the indigo dye with oleum.

Basicity:
Unlike most amines, indole is not basic; the bonding situation is completely analogous to that in pyrrole. Very strong acids such as hydrochloric acid are required to protonate indole. The protonated form has a pKa of −3.6. The sensitivity of many indolic compounds (e.g. tryptamine) under acidic conditions is caused by this protonation.

Methodology:
The main industrial routes start from aniline Illustrative of such large-scale syntheses; indole (and substituted derivatives) form via vapor-phase reaction of aniline with ethylene glycol in the presence of catalysts

In general, reactions are conducted between 200 and 500 °C. Yields can be as high as

Reactions:
Electrophilic Substitution of Indole: The electron density of carbons in heterocyclic ring of indole is higher due to contribution from nitrogen as in case of pyrrole. Therefore, the heterocyclic ring of indole is more reactive towards electrophiles compared to its benzene ring. The electrophilic substitution in indole takes place at C-3 and not at C-2 as in pyrrole. This can be explained from the following observations. Electrophilic attack at naturally occurring hallucinogen dimethyltryptamine (N,N-DMT). The name indole is a portmanteau of the 60%. Other precursors to indole include formyltoluidine, 2-ethylaniline, and 2-(2-nitrophenyl) ethanol, all of which undergo cyclizations. Many other methods have been developed that are applicable.

Fischer-Indole Synthesis: The most important synthesis of indole is the Fischer-indole Synthesis which has been investigated very widely. The Fischer-indole synthesis is carried out by heating phenyl hydrazone or substituted phenyl hydrazone of an aldehyde or ketone. The reaction is catalyzed by zinc chloride, polyphosphoric acid, sulphuric acid or boron trifluoride and proceeds with elimination of a molecule of ammonia

The most acceptable mechanism is given in [Fig. No 2]

C-2 and C-3 gives different intermediates as shown below,
The carbocation resulting from electrophilic attack at C-2 is less favourable than the carbocation resulting from electrophilic attack at C-3 because though the former has more resonance structures, in the latter intermediate, the positive charge resides on heterocyclic ring carbon or the nitrogen atom without affecting the benzene ring.

**Pharmacological importance of Indole:**
Indole possess the following activities that is shown in fig.3, out of these activities some research on Pharmacological activity of Indole Derivatives can be done by following, Scientist Popp and Pajouhesht et.al. Synthesized 3-o- nitrophenyl hydrazones of isatin by condensation of isatin with o-nitrophenyl hydrazine. These compounds were found to be active intramuscularly against Walker carcinoma-256 and inactive against L-1210 lymphoid leukemia.

Radwanet.et.al synthesized and evaluated the analgesic activity of 3, 4substituted indole derivatives. He prepare various derivatives of indole with various substituent at 3rd and 4th position from all this compounds, Tholidine-4-one derivative was found to exhibit more analgesic activity than other substituents.

**Conclusion:** The Indole Heterocyclic moiety has great biological and medicinal importance. A vast literature has been accumulated over the years and the chemistry of Indole continues to be a blossoming field. The versatile synthetic applicability and biological activities of these heterocyclic will help the medicinal chemists to plan, organize and implement new approaches towards discovery of Novel Drugs.

**References:**
Figures

![Indole](image1)

Fig. 1. Indole

![Chemical Reaction](image2)

Fig. 2

![Chemical Properties](image3)

Fig. 3