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NOTE

Synthesis of 3-Ethyl Indole

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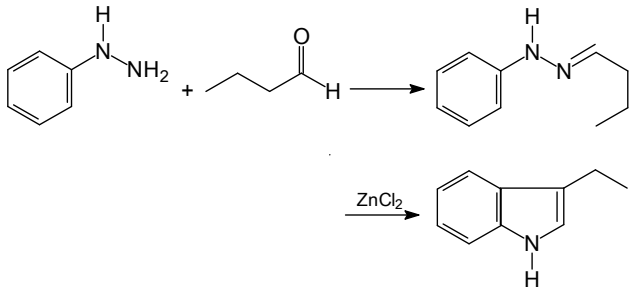
In this study, it is planned to synthesize intermediates to get β-carboline alkaloids having effective bioligical activities. In this way, we tried to synthesize 3-ethyl indole as an intermediate from simple and cheap compounds to obtain the β-carboline structure. This synthesis was carried out with a suitable method called the Fisher indole synthesis to synthese substitued indoles. That synthesis was tried for different acids and methods for acid catalyzed cyclization of buthenal phenylhydrazone to give 3-ethyl indole. FTIR, GSMS and NMR spectra were taken to determine the structural anaylsis of synthesized compounds.

Key Words: Alkaloid, β-Carboline, Synthesis of indole.

Pharmaceutics and natural compounds contained in the variety of indole groups. Thus the synthesis of indole compounds have become more important because of their importance in pharmaceutics field[1]. Melatonin is a hormone that organize the biological rhythm of human and tirptofan is a non-produced essential amino acid by the human body is an indole derivative. β-Carboline alkaloids are a class of alkaloids that they have great interest coz of their antibiotic, antiviral, antitumor, antidepressant, *etc*., effects on living creatures[2]. β-Carboline alkaloids are class of indole alkaloids and structurally similar to L-tryptophane[3]. Harmala alkaloids have the type of planar tricyclic molecular structure which contains indole and pyrrole ring is known as β-carboline structure (9*H*-pyrid-[3,4-b]-indole). β-Carbolines have similar molecular structure to brain metabolites serotonin, melatonin and monoamine oxidase inhibitors so they are very effective on the human nervous system. Many of them are used as anti-depressants. Also considered as illicit substances such as heroin, morphine, opium *etc*. and very pleasant drug substances have the β-carboline structure.

The easiest way to transition to the structure of β-carboline is the synthesis over the intermediate products of indoles[4,5]. Indole have two tautomers. Different alkaloids can be obtained by adding different heterosiclic and aromatic compounds to indole ring[6].

In this study, we have synthesized 3-ethyl indole which is a derivative of tryptophan and an important intermediate for the synthesis of the tryptophan derivative alkaloids and other β-carboline compounds. This synthesis was carried out with one step from simple starting materials by Fisher indole synthesis (**Scheme-I**).



Scheme-I

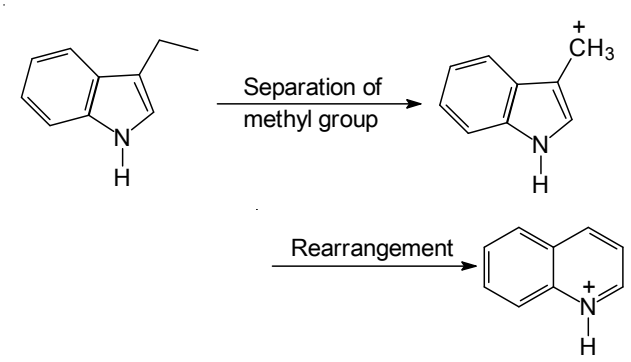
Phenyl hydrazone: 49.15 mL of phenyl hydrazone; (0.5 mol, 54.07 g), 45.06 mL of (0.5 mol, 36.055 g) butanal and acetic acid (25 mL) added to 250 mL toluene and refluxed for 3 h. At the end of the reaction solvent, acetic acid and unreacted butanal was removed under vacuum. The remaining orange coloured part was used for the next stage without being subjected to a purification process to obtain 3-ethyl indole.

Synthesis of 3-ethyl indole: 34.095 g (0.25 mol) anhydrous zinc chloride was added the orange-coloured portion obtained from the synthesis of phenyl hydrazone. This mixture is boiled for 3 h under reflux. At the end of the reaction a black-coloured gel was obtained. This gel was extracted by adding water and

dichloromethane and dichloromethane phase was removed by evaporation. The remaining portion was treated with 75 % hexane, 25 % dichloromethane mixture (v/v) on the silica gel column chromatography. Finally transparent yellowish 3-ethyl indole was obtained as pure.

On the GC chromatogram of the synthesized product there is a total 100 % single peak over 15 min retention time (14.775 min).

The mass spectrum of the product maximum m/e of peak value is 145. This corresponds to 3-ethyl indoles molecular ion peak (M^+). Main peak observed in the spectrum is a separation of methyl group and then re-arrangement of the ion forms a quinolinium ion ($[C_9H_8N]^+$) the peak has 130 m/e value (**Scheme-II**).



Scheme-II

This rearrangement is a normal status in mass spectroscopy if a cation occurs on benzilic structure. Peaks observed at 103, 77 and 51 m/e values are the consist of quinolinium ion. These peaks are due to $[C_8H_7]^+$, $[C_6H_5]^+$ and $[C_4H_3]^+$ ions occurs from the separation peaks from quinolinium ion, respectively HCN, C_2H_2 and C_2H_2 molecules. All of these peaks are evidence which for the formation of 3-ethyl indole.

IR spectrum of the compound have the expected bands from 3-ethyl indole. There are stretching band at 3414 cm^{-1} ovned to N-H bond and aromatic CH stretching bands are observed at 3054 cm^{-1}. Bands observed at 2961, 2931 and 2873 cm^{-1} are bands of aliphatic C-H groups. Band at 1616 cm^{-1} are correspounds to CN stretching bands on aromatic structures and band at 1456 cm^{-1} correspounds to CC stretching bands on aromatic structures. Band observed at 738 cm^{-1} owned to 1,2-disubstituted aromatic ring out of plane flexion of C-H bonds.

From the ^1H NMR spectrum of the compound δ (ppm) = 1,2-1,3'-triplet CH_3 protons which split to 3 by the ethyl group at δ (ppm) = 2.68-2.75' quartet CH_2 protons which split to 4 by CH_3 protons. Peaks observed at δ (ppm) = 6.85-7.55 belongs to aromatic ring. Also peaks at δ (ppm) = 7.7-7.82 belongs the proton which located on the indole rings nitrogen atom. All these peaks supports that our structure is 3-ethyl indole structure.

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