Synthesis of new Schiff Bases Derived from 3-Acetylindol

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ABSTRACT

Schiff bases were prepared envolving the reaction of 3-acetylindol with bromine to give α-bromo acetylindol.The reaction of the later with urea,acetamide and thiourea afforded substituted oxazole and thiozole respectively. The reaction of substituted thiozole with different aldehydes gave new derivatives of Schiff bases (imines)

INTRODUCTION

In recent years there has been an increased interest in the chemistry of heterocyclic molecules because of their biological significance[1].Some heterocyclic molecules such as indole nucleus are known to possess antituberculesis activity[2]. Several thiazole derivatives and Schiff bases are reported to act as lipoxygenase inhibiters affecting inflammation[3]and anticancer activity[4]. Furthermore, Schiff bases can be used in industrial chemistry and inorganic chemistry field[5,6]. There are many methods found in the literatures to prepare Schiff bases, specially through the condensation of aldehydes or ketones with primary amines[7].Also reduction of nitriles compounds were carried out either by Lithium Aluminum Hydride ($LiAlH_4$) or addition of grinard reagent afforded the imines[8,9] .Finally, the synthesis of Schiff bases of amminothiazolyl was carried out by microwave-induced[10].

We In this paper reported a new method to synthesis Schiff bases derived from 3-acetylindol. .

EXPERIMENTAL

Melting points (M.P) were measured on "Electrothermal ,9300 ,Digital, series(1998) apparatus" and were uncorrected.Infrared spectra (FT.IR) were recorded on a"Tensor 27 Bruker Co.Germany 2003" spectrophotometer, using KBr disc as a sampling method.Ultra violet-visible spectrometer type "Shimadzu U.V (U.V-160) spectrophotometer.

Synthesis of α-Bromoacetylindol[11] (2).

Bromine (1.4gm,0.0088 mole) in chloroform (5ml) was added dropwise to a solution of 3-Acetylindol (1.4 gm,0.0088 mole) in chloroform (20 ml),with stirring,after the addition was completed the reaction mixture was refluxed for (2hrs),until the colour was disappeared.The solvent was evaporated. The crude was washed with saturated sodium bicarbonate, followed by water. Recrystalization from ethanol gave a yellow product m.p.(202-204 C)

Synthesis of substituted oxazole(3,4) and thiazole[11] (5).

To a α-Bromoacetylindol (2) (0.7 gm,0.003 mole) in methanol (15 ml) and the appropriately amides(urea ,thiourea and acetamide) (0.005 mole) was added in several portions through

mixing between addition. Refluxed for 24hrs, the solution was normally allowed to cool at room temp. Crude products were filtered, the filtrated was washed with sodium bicarbonate (40%) followed by washing with water. Purification was done by recrystalization from ethanol afforded the required oxazole and thiozole (3,4,5).For physical and spectra data see table (I).

Synthesis of Schiff bases (imines)[12] (5_{a-h}).

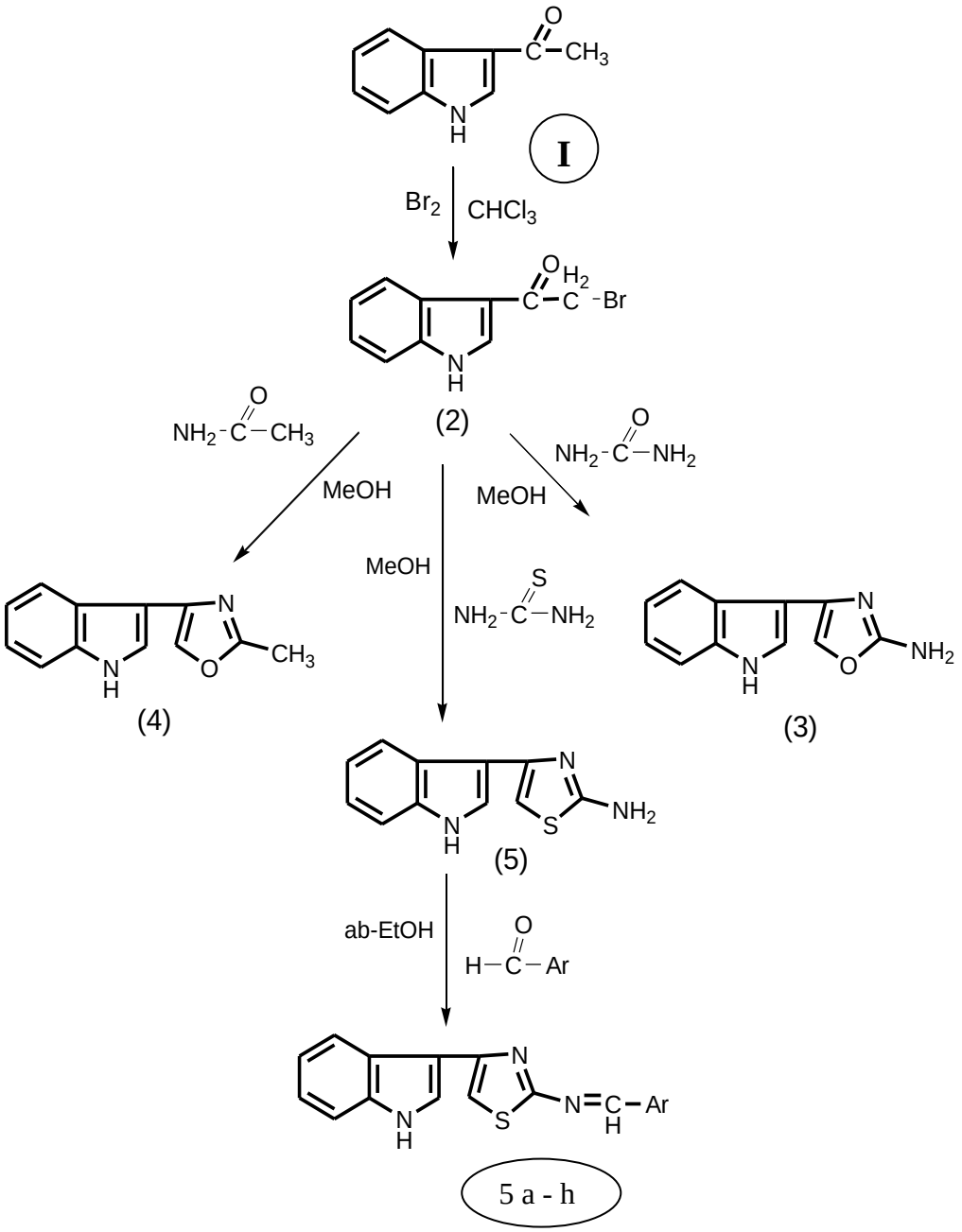
General procedure

A compound (5) (0.4 gm,0.002 mole) was dissolved in absolute ethanol (15 ml), aldehyde (0.002 mole) was added. Refluxed for 3hrs,allowed to cool, the precipitate was formed. Recrystalization from ethanol gave (5_{a-h}).

For physical and spectra data see table (II).

RESULT AND DISCUTION

α-Bromoacetylindol in this study was synthesed by refluxing bromine in chloroform with 3-acetylindol.The reaction of the general method proved very effective for obtaining mostly good yield of high purity material as shown in scheme (I).

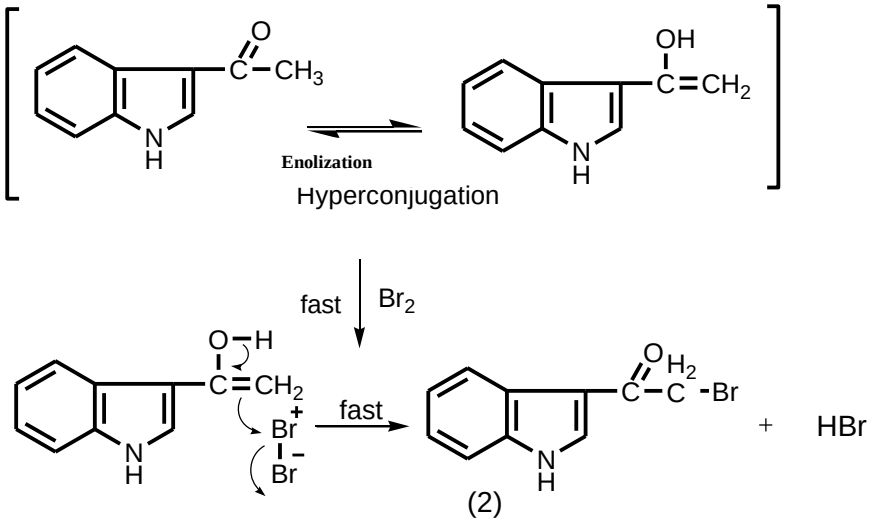


Scheme (I)

The structure of α-bromoacetylindol was elucidated using classification test for alkyl bromide,when (2) treated with alchoholic silver nitrate a white precipitate was formed,that's means the substitution took place on the acetyl group rather than indole ring. The IR spectrum of the α-bromo acetylindole showed an absorption band at 1440 cm^{-1} due to $-CH_2$ in substituted keton at α position,and absorption band at around 1691 cm^{-1} due to C=O group.The U.V Spectrum gave λmax at 297 nm.

Apossible pathway accounting for the formation of (2) was firstly the ketone perform the enol,secondly the acidic hydrogen atom in acetyl group was easly substituted by halogen.since the substitution of halogen through the mechanism of formation of enol or

enolate ion which is more active[13].As shown in scheme (II).

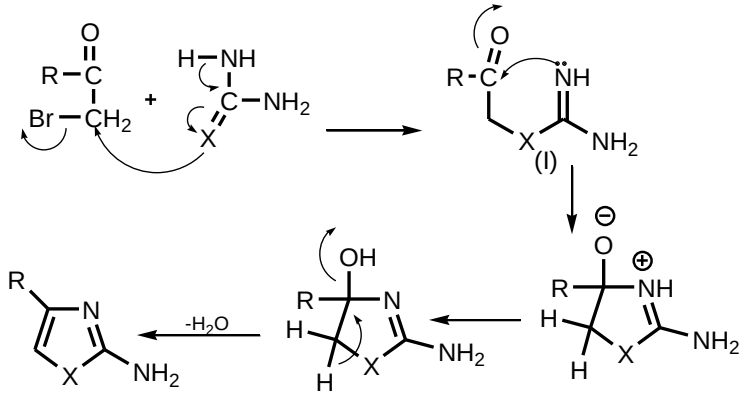


Scheme (II)

Synthesis of substituted oxazole (3 and 4) and thiazole (5).

The preparation of oxazole 3,4 and thiazole (5) was carried out by the reaction of α-bromoacetylindole (2) with urea or acetamide to give the oxazole (3 and 4) and with thiourea afforded the thiazole (5).The structure of (3-5) was elucidated by physical chemical and spectral evidences. The IR Spectra showed that absorption bands at around 1625-1636 cm^{-1} ,at around 1598-1605 cm^{-1} and at around 3142-3414 cm^{-1} due to C=C,C=N and N-H respectively,also an absorption band at around 1117-1125 cm^{-1} and 1236-1242 cm^{-1} for C-O-C.The U.V spectra gave λmax (227-268 nm).

In addition to the absence of carbonyl group was proved by a negative test with 2,4 dinitro phenyl hydrazine while gave a positive test for sulpher by the element test for compound (5).The mechanism of the reaction is probably as follows, nucleophilic attacked (S_N^2) of the heterogeneous atom in amides on the methylene carbon bearing halogen to form the intermediate (I), which cyclized by attacked of unshair pair of electron for the nitrogen to the carbon atom of carbonyl group through nucleophilic addition mechanism. Finally the lost of water molecular from the intermediate to give the product[14] as shown in scheme (III).

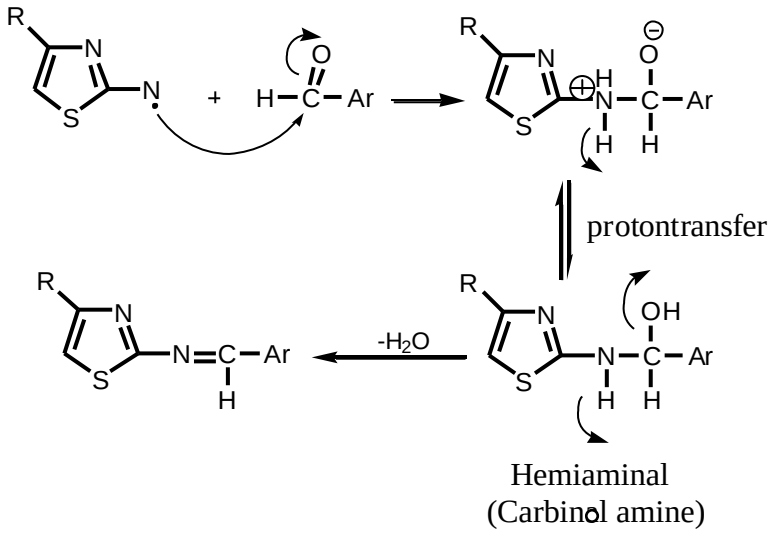


Scheme(III)

Synthesis of Schiff bases (imines) (5_{a-h}).

The reaction of primary amines with carbonyl compounds in neutral or weak acidic media gave the required Schiff bases.The synthesis of (5_{a-h}) was carried out by the reaction of amino compound (5) with different Aldehydes. The structure of (5_{a-h}) was elucidated using spectral data and chemical interconvertion.The physical and spectral data were showed in table (II).In addition the test of phenolic OH gave a positive test with ferric chloride.the IR for (5_{a-h}) gave an absorption band about 1595-1610 cm^{-1} due to C=N,and around 3427-3310 cm^{1} for (OH) group of ($5_{c\ and\ e}$),also around 1090-1136 cm^{-1} and 1217-1229 cm^{-1} for C-O-C of ($5_{d,e\ and\ g}$).The U.V spectra for (5_{a-h}) showed that λmax 288-322 nm which due to electronic transfer ($n \longrightarrow \pi^*$) in the active group C=N for these compounds.It is worth notice that increasing in the value of λmax for (5_{a-h}) due to conjugation which reduce the influence and cause the bathochromic Schiff.

Apossible pathway accounting for the formation of compound (5_{a-h}) through nucleophilic addition mechanism tetrahedral form which gave the intermediate called hemiaminal or carbinol amine followed by lost one molecule of water to give the imine[13]as shown in scheme(IV).



Scheme(IV)

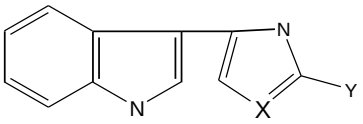


Table (I): Physical and spectroscopic data of compounds (3,4 and 5).

Comp .No	Molecular formula	m.p. C	Yield %	X,Y	F T I.R. cm^{-1} (KBr)				U.V λ_{max}nm (EtOH)
					$\nu_{C=N}$	$\nu_{C=C}$	ν_{N-H} asy. Sym.	ν_{C-O-C} asy. Sym.	

3	$C_{11}H_8N_3O$	174-176	68	O,NH_2	1603	1638	3319 3157	1242 1125	242
4	$C_{12}H_9N_3O$	156-159	71	O,CH_3	1605	1632	–	1236 1117	227
5	$C_{11}H_8N_3S$	217-219	79	S,NH_2	1598	1625	3414 3142	–	268

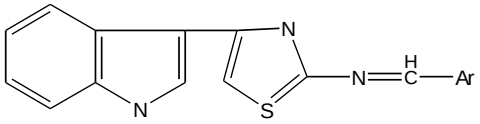


Table (II): Physical and spectroscopic data of imines (5_{a-h})

Comp (5)	Ar	Molecular formula	m.p. C	Yield %	F T I.R. cm^{-1} (KBr)			U.V λ_{max}nm (EtOH)
					$\nu_{C=N}$	ν_{O-H}	ν_{C-O-C} asy. Sym.	
a	C_6H_5	$C_{18}H_{12}N_3S$	160-162	43	1602	–	–	288
b	m-$NO_2C_6H_4$	$C_{18}H_{12}N_4O_2S$	132 (dec)	72	1606	–	_	302
c	p-OHC_6H_4	$C_{18}H_{12}N_3OS$	171-173	63	1595	3427	–	295
d	m,p-OCH_3 C_6H_3	$C_{20}H_{16}N_3O_2S$	113-115	61	1600	–	1229 1108	291
e	p-OH-m-$OCH_3C_6H_3$	$C_{19}H_{14}N_3O_2S$	122-125	57	1610	3310	1217 1136	305
f	Indol-3-Carbaldehyde	$C_{20}H_{12}N_4S$	212-214	86	1609	–	–	322
g	2-Furfaldehyde	$C_{16}H_{10}N_3OS$	182-184	65	1597	–	1223 1090	317
h	o-ClC_6H_4	$C_{18}H_{11}ClN_3S$	166-168	82	1602	–	–	309

تحضير قواعد شيف جديدة مشتقة من ٣-اسيتايل أندول

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الملخص:-

تم تحضير عدد من قواعد شيف الجديدة من خلال مفاعله ٣-اسيتايل أندول مع محلول البروم ليعطي -بروموا سيتايل أندول والذي يتفاعل مع اليوريا،الاسيتاميد،والثايويوريا ليعطي معوضات الاوكسازول والثايازول على التوالي.مفاعله معوض الثايازول مع مختلف الالديهايدات ليعطي مشتقات قواعد شيف (الايمينات) الجديدة.

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