Synthesis and Biological Activity of Some 2,3-Diphenylindole Derivatives (Part II)

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Abstract: 5-Bromo-2,3-diphenylindole upon nitration followed by reduction afforded 6-amino derivative which were converted to new 2,3-diphenylindole derivatives: imidazole, benzoxazipine and quinoline derivatives. Investigation of the biological activity of some of these derivatives revealed that some of them have a higher antibacterial activity.

Keywords: 2,3-Diphenylindole; Biological activity; Synthesis; Reactions

I. INTRODUCTION

Compounds involving the indole nucleus have gained much attention due to their rich biological activity like hallucinogenic, hypnotic, sedative and antidepressant have been found to be associated with the indole derivatives. On the other hand, the importance of the indole nucleus is well documented in the field of pharmaceutical chemistry as well as plant and animal biochemistry. Based on these findings and in continuation to our work directed towards the synthesis of new indole heterocycles of potential biological activities, it was of interest to synthesize new indole derivatives by incorporating these biogenic moieties with a hope of increasing the drug action.

Schiff bases are long known to possess diverse biological activities, so some new Schiff bases from 6-amino 2,3-diphenyl-5-bromo-1-H-indole were synthesized. The reaction of primary aromatic amine with different aromatic or heterocyclic aldehydes seemed to be unique route for the synthesis of several new Schiff bases, which are highly promising for further chemical transformations. In light of the high biological activity of Schiff bases, it was considered to be an adaptable starting material for the synthesis of indole derivatives that include the moiety in its structure with the hope that the products would possess interesting pharmacological activities. Thus the aminoindole derivative (II) reacted with 5-Bromo-6-formyl2,3-diphenylindole (I) to form the Corresponding Schiff’s base (III).

Reaction of amino indole derivative (II) with phenyl isothiocyanate in THF afforded the desired compound (IV), in quantitative yield the IR spectrum of it exhibited three peaks due to NH at 3330, 3237 and 3159 cm\(^{-1}\) while the H-NMR spectrum (250 MHZ, DMSO) displayed three NH signals at \(\delta\) 9.7, 9.9 and 11.6 ppm in addition to a multiple at \(\delta\) 7.0-7.8 ppm for 17H, Ar-H) Compound (IV) was easily cyclized with NaH in dry DMF to give (V), the IR spectra of this product revealed absorption bands 3393 (br.), 1619 and 1274 cm\(^{-1}\) for NH, C=C, and C=S groups.

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Condensation of (II) with salicyldehyde in dry benzene furnished benzoazipenyl derivative (VI). The IR spectra showed absorption band 1618 cm\(^{-1}\) (C=N).

Imidazole derivative (VII) prepared by the reaction of (II) with acetonitrile in the presence of sodium hydride in DMF solvent.
Beside the correct elemental analysis, compounds (VII) revealed absorption bands at 3440(NH), 1618 cm (C=N), respectively. The H1-NMR spectrum (250MHz,DMSO) of (VII), showed signals at, δ 3.65ppm (s,3H, N=C-CH3), two NH signals at δ9.7 and 11.6 ppm in addition to a multiplet at δ 7.0-7.8 ppm for 12H Ar –H)

Condensation of (II) with penta -2,4-dione in the presence of anhydrous calcium sulfate yielded isquinoline derivative (VIII). The latter compounds revealed absorption bands at 1618 cm (C=N), The H- NMR spectrum (250MHz, DMSO) of (VIII) revealed signals at, δ 3.6 ppm (s, 3H, N =C-CH3), and at, δ 3.42 ppm (s, 3H, =C -CH3)

Experimental
Melting points (uncorrected) were determined on Stuart Scientific capillary melting point apparatus and are uncorrected. Elemental analyses were performed on a Perkin-Elmer analyzer. 1H NMR spectra were obtained on a Varian EM-390 instrument (200 MHz) with TMS as an internal standard. IR spectra were recorded on a Perkin-Elmer spectrophotometer. Elemental analyses were performed on a Perkin-Elmer analyzer.

1-Phenyl-2-mercapto-1,5-dihydro-imidazo[4,5-f]2,3-diphenylindole (V) :

To a solution of (II) (0.01mole ; 3.63gm) in THF (12ml ) , phenyl isocyanate (2mole) was added drop wise at room temperature with stirring for 2hrs and he reaction mixture was left for 3 days .The product (IV) was filtered off , dissolved in anhyd. DMF and sodium hydride (1gm) was added . The reaction mixture was refluxed for 1hr , left to cool , treated with ice / H2O, filtered off and washed with water. Compound (V) obtained as white crystals yield 82% m.p. above 300 °C

Elemental analysis: Calculated: C = 77.69% , H = 4.55% ,N= 10.31%

Found: C = 77.70% , H = 4.59% ,N= 10.06%

Benzoxazipenyl derivative(VI)

To a solution of (II) (1.089gm ,3mmole ) in anhyd. benzene (25 ml ) , salicyldehode (1ml , 8mmole ) was added , the reaction mixture was refluxed for 4hrs on water bath , sodium hydride (1gm) was added. The reaction mixture was refluxed for 1hr , left to cool , poured into ice / H2O and the precipitate was filtered off .Yield 72%, m.p. 289 °C
Elemental analysis: Calculated: C = 83.39% , H = 4.66% , N=  7.25%

Found: C = 83.91% , H = 4.69% , N=  7.24%

2-Methylimidazo[4,5-f]2,3-diphenylindole (VII):

To a solution of (II) 3.36gm 0.01mole) in anhyd. DMF (50 ml ), acetonitrile (30ml) was added the reaction mixture was refluxed for 1hr and left to cool , sodium hydride (1gm ) was added and the reaction mixture was poured into ice / H2O .The precipitated product was filtered off affording a white crystals .yield 78% , m.p. above 300 0C.

Elemental analysis: Calculated: C = 85.43% , H = 5.50% , N=  9.06%

Found: C = 85.45% , H = 5.54% , N=  9.05%

2,3-Diphenyl-3H-pyrrolo[3,2-f]-8-bromoquinoline(VIII):

To a mixture of amine (II) (1gm, 0.00275mole) and penta- 2.4-dione (2.6gm, 0.0025mole) 2gm of anhydrous calcium sulfate was added and the reaction mixture was refluxed on boiling water bath for 1hr with occasional shaking. The reaction mixture was shackled with ether (4x10 ml), the combined organic phase was dried with anhydrous sodium sulfate and the solvent was removed under reduced pressure. To the enamine produced, 3 ml of conc. sulfuric acid (d, 1.84) was added and heated on water bath 60-70°C for30min. The reaction mixture was cooled to room temperature, and was poured slowly to 25ml of ice-water then solid sodium carbonate

was added with stirring and the solid product was filtered off and washed with water, yield 65%, m.p above 300 °C

Elemental analysis: Calculated: C = 86.20%, H = 5.74%, N= 8.04%

Found: C = 86.25%, H = 5.79%, N= 8.15%

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