

Novel Synthesis of 2-[2-Hydroxy-5-(2-Substitutedimino-4-Ethyl- Imino-1,3,5-Dithiazin-6-Yl)]Aminophenylindoles

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Abstract

One pot synthesis of 2-[2-hydroxy-5-(2-substitutedimino-4-ethylimino-1,3,5-dithiazin-6-yl)]aminophenylindoles (IIIa-e) was carried out by interactions of 2-[2-hydroxy-5-(2,4-ethylthiobiureto)]phenylindole(I) and substitutedisocyanochlorides(IIa-e) in ethanol medium. This method is easier, convenient, cheaper and less time consumable method to isolate products in good yields and maintain purity of products.

KEYWORDS: 2-[2-Hydroxy-5-(2-substitutedimino-4-ethylimino-1,3,5-dithiazin-6-yl)]amino- phenylindoles, Substitutedisocyanochlorides and Ethanol.

Introduction

In organic and synthetic chemistry dithiazinoindolenucleus containing heterocycles created their special and important applications in pharmaceutical, agricultural (Antre et al 2011), industrial Betircan et al.(2006), biological fields Choudhari et al. (2013). Sulphur itself acts as an antibiotic and increases potency of a molecule for biological activities Shie et al. (2007), considering this; researchers(Kodapeet al2013) work out on sulphur molecules. 1,3,5-Dithiazino nucleus containing molecules showed anti-corrosive property against copper(Alesandroet al 2005) and lubrication of oil(Dafaliet al 2002). Recently in this laboratory various novelseries of 1,3,5- dithiazino based molecules were successfully synthesised (Kale et al 2016)and their antimicrobial Tayadeet al.(2016), biological Tayade et al.(2016)studies have been investigated by our research group, hence this research scheme was designed.

Materials and Method

AR grade Merck and Sigma-Aldrich chemicals were used for synthesis.

Follow-up of reactions and checking homogeneity of compounds were made by TLC on silica Gel-protected glass plates and spots were detected by exposure to UV-lamp at 200to400 nm. Unless otherwise noted. Carbon and hydrogen analysis was carried out on Carlo-Ebra-1106 analyser.

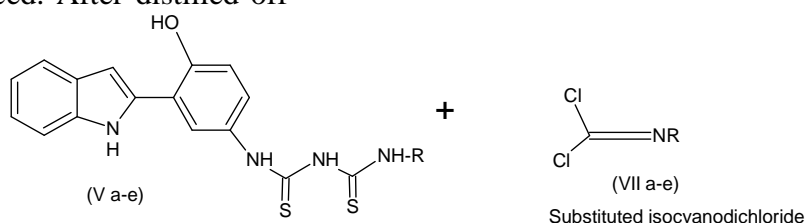
Nitrogen estimations were carried out on Colman-N-analyser-29, while sulphur estimations were carried out by Carius method. Melting points of all compounds were determined in open glass capillaries with a SGW X-4 digital apparatus and were uncorrected. IR spectra were recorded on Perkin-Elmer spectrometer in range of 4000-400 cm^{-1} in KBr pellets. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker ARX-400-4000 Hz spectrometers with tetramethylsilane (TMS) as an internal standard and DMSO-d_6 , CDCl_3 as a solvent (Chemical shifts in ppm). LC-MS were recorded by Waters Micro mass Q-TOF premier Mass Spectrometer.

General procedure for the synthesis of 2-[2-hydroxy-5-(2-substitutedimino-4-

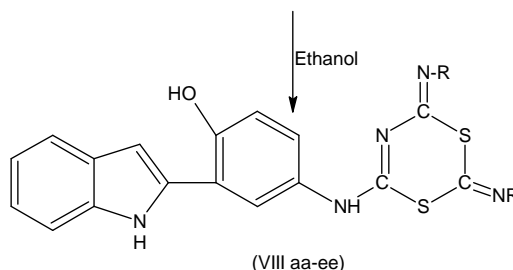
substitutedimino-1,3,5-dithiazin-6-yl)]aminophenylindoles (IIIa-e):

A reaction mixture of 2-[2-hydroxy-5-(2-substituted-4-ethylthiobiureto)]-phenylindole,

substitutedisocyanodichloride and ethanol was refluxed for 1 hrs during reflux evolution of hydrochloride gas was clearly noticed. After distilled off



2-[2-Hydroxy-5-(2, 4-substituted-dithiobiureto)]phenylindoles



2-[2-Hydroxy-5-(2-substitutedimino-4-substitutedimino-1, 3, 5 dithiazin-6-yl)]-aminophenylindole

where, R = -t-butyl, -ethyl, -phenyl, *p*-Cl-phenyl, *o*-tolyl
(Scheme-I)

2-[2-Hydroxy-5-(2-ethylimino-4-ethylimino-1,3,5-dithiazin-6-yl)]aminophenylindole (IIIa):

Yellow solid, C₂₁H₂₁N₅O₁S₂, Yield-73%, M.P.-163°C, %Composition found(calculated): C-63.59 (59.57), H-5.8 (4.96), N-10.72 (16.54) and S-12.50 (15.13); FTIR (KBr) ν cm⁻¹-3362.2 (O-H stretching), 3412 (N-H stretching), 2972 Ar-CH stretching, S-C=N stretching, 2065 C=N stretching, 1281 C-N stretching; ¹H NMR (400 MHz CDCl₃ δ ppm) Indole -NH proton at δ 12.8694 ppm, -NH proton flanked between dithiazino and aromatic ring at δ 9.6147 ppm, Ar-H protons at δ 7.74944-6.8418 ppm, Ar-OH proton at δ 4.5664 ppm, -CH₂ protons at δ 2.8583-2.0821 ppm, -CH₃ 1.3405 ppm.; ¹³C NMR (400 MHz CDCl₃ δ ppm) C=S carbon at δ 180.21 ppm,

excess solvent yellow colour product was isolated, on basification with dilute ammonium hydroxide yellow crystalline product was obtained, washed several times with petroleum ether and recrystallized from aqueous ethanol (Scheme-I). Completion of reaction was examined by TLC.

Ar-C carbon at δ 154.16-124.28 ppm, -CH₃ carbon at δ 28.32 ppm, respectively; LC-MS (m/z) Mol. Wt.: 423, (M⁺) 423, 365.30, 340.2

[2-Hydroxy-5-(2-t-butylimino-4-ethylimino-1,3,5-dithiazin-6-yl)]aminophenylindole(IIIb):

Lemon yellow crystalline solid, C₂₃H₂₅N₅O₁S₂, yield-67%, m.p.178°C, % Composition found(calculated): C-61.03 (61.19), H-6.57 (5.54), N-11.33 (15.52) and S-13.52 (14.19);, FTIR (KBr) ν cm⁻¹-3420.2 (O-H stretching), 3356 (N-H stretching), 3131 Ar-CH stretching, 2060 S-C=N stretching, 1688 C=N stretching, 1197 C-N stretching; ¹H NMR (400 MHz CDCl₃ δ ppm) Indole -NH proton at δ 12.8215 ppm, -NH proton flanked between dithiazino and aromatic ring at δ 9.6412 ppm, Ar-H protons at δ 7.5210-6.8321 ppm, Ar-OH proton at δ 4.2321 ppm, -CH₂ protons at δ 2.377 ppm, -CH₃ protons at δ 1.3214 ppm. ¹³C NMR (400

MHz CDCl₃ δ ppm) C=S carbon at δ 184.21 ppm, Ar-C carbon at δ 162.16-135.28 ppm, -CH₃ carbon at δ 34.32 ppm, respectively; LC-MS (m/z) Mol. Wt.: 451, (M⁺) 451, 400.30, 375.

2-[2-Hydroxy-5-(2-phenylimino-4-ethylimino-1,3,5-dithiazin-6-yl)]aminophenylindole(IIIc):

Ivory solid, C₂₅H₂₁N₅O₁S₂, yield-76%, m.p.172 °C, % Composition found(calculated): C-62.34 (63.69), H-5.84 (4.45), N-10.72 (14.86) and S-12.91 (13.58); FTIR (KBr) v cm⁻¹-3355.2 (O-H stretching), 3380 (N-H stretching), 3013 Ar-CH stretching, 2044 S-C=N stretching, 1595 C=N stretching, 1188 C-N stretching; ¹H NMR (400 MHz CDCl₃ δ ppm) Indole -NH proton at δ 12.8356 ppm, -NH proton flanked between dithiazino and aromatic ring at δ 9.6252 ppm, Ar-H protons at δ 7.5364-6.8362 ppm, Ar-OH proton at δ 4.2521 ppm, -CH₂ protons at δ 2.3687 ppm, -CH₃ protons at δ 1.3198 ppm. ¹³C NMR (400 MHz CDCl₃ δ ppm) C=S carbon at δ 180.21 ppm, Ar-C carbon at δ 158.16-128.28 ppm, -CH₃ carbon at δ 28.32 ppm, respectively; LC-MS (m/z) Mol. Wt.: 471, (M⁺) 471, 395.30, 365.

2-[2-Hydroxy-5-(2-p-chlorophenylimino-4-ethylimino-1,3,5-dithiazin-6-yl)]aminophenylindole(III d):

Yellow solid, C₂₅H₂₀N₅O₁S₂Cl₁, yield-70%, m.p.194°C, %Composition found(calculated): C-64.3 (59.34), H-5.11 (3.95), N-10.32 (13.84) and S-11.45 (12.66),Cl(7.02); FTIR (KBr) v cm⁻¹- 3440.2 (O-H stretching), 3339 (N-H stretching), 3043 Ar-CH stretching, 2045 S-C=N stretching, 1593 C=N stretching, 1164 C-N stretching; ¹H NMR (400 MHz CDCl₃ δ ppm) Indole -NH proton at δ12.8459 ppm, -NH proton flanked between dithiazino and aromatic ring at δ

9.6321 ppm, Ar-H protons at δ 7.5364-6.8409 ppm, Ar-OH proton at δ 4.2696 ppm, -CH₂ protons at δ 2.3785 ppm, -CH₃ protons at δ 1.3208 ppm. ¹³C NMR (400 MHz CDCl₃ δ ppm) C=S carbon at δ 180.21 ppm, Ar-C carbon at δ 150.16-120.28 ppm, -CH₃ carbon at δ 20.32 ppm, respectively; LC-MS (m/z) Mol. Wt.: 505, (M⁺) 505, 465.30 395.

2-[2-Hydroxy-5-(2-o-tolylimino-4-ethylimino-1,3,5-dithiazin-6-yl)]aminophenylindole(IIIe):

Faint yellow solid, C₂₆H₂₃N₅O₁S₂, yield-74%, m.p.182 °C, %Composition found(calculated): C-63.24 (64.30), H-4.20 (4.77), N-14.10 (14.42) and S-12.16 (13.21)FTIR (KBr) v cm⁻¹- 3364 (O-H stretching), 3256(N-H stretching), 2934Ar-CH stretching, 2050 S-C=N stretching, 1720 C=N stretching, 1072 C-N stretching; ¹H NMR (400 MHz CDCl₃ δ ppm) Indole -NH proton at δ 12.8512ppm, -NH proton flanked between dithiazino and aromatic ring at δ 9.5932 ppm, Ar-H protons at δ 7.5394-6.8374 ppm, Ar-OH proton at δ 4.3200 ppm, -CH₂ protons at δ 2.3854 ppm, -CH₃ protons at δ1.3380 ppm. ¹³C NMR (400 MHz CDCl₃ δ ppm) C=S carbon at δ 176.21 ppm, Ar-C carbon at δ 150.16-130.28 ppm, -CH₃ carbon at δ 26.32 ppm, respectively; LC-MS (m/z) Mol. Wt.: 486, (M⁺) 486, 400.30 375.

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