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Research Article

Synthesis and Characterization of Bis-heteroyclic Derivatives of 1-(3-Chlorophenyl)-Pyrrolidine-2, 5-Dione

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ABSTRACT

Succinic acid was converted to 1-(3-chlorophenyl)-pyrrolidine-2, 5-dione **1**. This cyclic imide on condensation with p-hydroxy benzaldehyde in acetic acid furnished 1-(3-chlorophenyl)-3, 4-bis-(4-hydroxy-benzylidene)-pyrrolidine-2,5 dione **2**. This pyrrolidine-2, 5-dione undergo cyclisation with hydrazine hydrate, hydroxylamine hydrochloride, semicarbazide, furnish pyrazole, isoxazole, pyrazole acetamideand benzodiazodizepine compound $\mathbf{3_{a-c}}$ respectively. Similarly the pyrrolidine-2, 5-dione on treatment with substituted aromatic aldehydes, malononitrile in presence of piperidine in ethanol underwent ring closer and furnished azo-flurorene derivatives $\mathbf{4_{a-d}}$ and with acetaldehyde, malononitrile in presence of piperidine in ethanol pyrrolidine-2, 5-dione afforded azo-flurorene **5**.

Keywords: Cyclic imide, pyrrolidine-2, 5-dione, pyrazole, isoxazole, pyrazole acetamide, azo-flurorene.

INTRODUCTION

In recent years the study of the chemistry of imides has been given particular impacts, because of their pharmacological and other industrial uses. For examples, derivatives of imides have proved to be important medicinal agent and have been suggested for use in the treatment of arthritis[1], tuberculosis[2], convulsions and epilepsy[3]. A number of imides can be used to stimulate the growth of plants and seedlings during the early stage of germination. For examples 2, 4-dichlorophenyl succinimide stimulates the growth of wheat and radish seedlings[4]. Conversely other imide derivatives have been used as fungicides and as herbicides[5]. The surface active properties of some imides assist their insecticidal and fungicidal properties. Aromatic imides are used successfully as brightening agent in the laundry and allied industries[6].

In the recent years, attention has been increasingly paid to the synthesis of bis-heterocyclic compounds which exhibit various biological activity[7-10].

RESULT AND DISCUSSION

1-(3-chlorophenyl)-pyrrolidine-2,5 dione **1**, required for the synthesis of title compound was prepared from succinyl chloride by heating a mixture of succinic acid and thionyl chloride followed by conversion of the intermediate succinyl chloride to the title compound by refluxing with m-chloro aniline in presence of benzene[11]. I.R. Spectra of this compound showed doublet at around 1711 and 1680 cm^{-1} indicating the presence of cyclic imide. The PMR ($CDCl_3$) spectrum showed the characteristic slitting pattern of four succinimide proton as a singlet around δ 2.77. The other precursor 1-(3-chlorophenyl)-3, 4-bis-(4-hydroxy-benzylidene)-pyrrolidine-2,5 dione **2** was prepared by condensation of cyclic imides **1** with p-hydroxy benzaldehyde in acetic acid as shown in Scheme-I. the title compounds were then prepared by condensation of 1-(3-chlorophenyl)-3, 4-bis-(4-hydroxy-benzylidene)-pyrrolidine-2,5 dione with hydrazine hydrate, hydroxylamine hydrochloride, semicarbazide in ethanol in presence of piperidine Scheme-II.

On the other hand the 1-(3-chlorophenyl)-pyrrolidine-2, 5-dione on treatment with substituted aromatic aldehyde, malononitrile in presence of piperidine in ethanol underwent ring closure furnished azo-flurorene $\mathbf{4_{a-d}}$ Scheme-III. Similarly with acetaldehyde, malononitrile in presence of piperidine in ethanol 2, 5-dione afforded azo-flurorene **5** Scheme-IV.

Experimental Section

All the melting points were determined by open capillary method and are uncorrected. The purity of compound was monitored by TLC on silica gel coating aluminium plate using U.V. light as visualizing agent. The I.R. spectra (KBr in cm^{-1}) were recorded on Perkin-Elmer Spectrophotometer in the range of 4000-400 cm^{-1}. The ^1H NMR

Spectra were recorded on Varion 500 MHz NMR Spectrophotometer using DMSO-d6 as a solvent and TMS as an internal standard (chemical shift in δ ppm). C, H, N determinations were run on CarloErba 1108 (CHNS) Elemental analyzer.

Preparation of 1-(3-chlorophenyl)-pyrrolidine-2,5-dione (1)

A mixture of succinic acid (11.8 gm, 0.1mole) and thionyl chloride (26.18 gm, 2.2mole) was refluxed for 30 minutes. M-chloro aniline (0.1mole) was dissolved in 5 ml benzene. The solution of aromatic amine was added slowly in above reaction mixture. The reaction mixture was then refluxed till complete HCl gas was evolved. The product was cooled and recrystallise from ethanol. Yield 76.38 %, m.p.116-118 ^{0}C, IR (KBr) : 1711(C=O), 2937, 1503, 802 cm^{-1}, ^{1}H-NMR (DMSO-d_6) : δ 2.7 (s,2H,CH_2), 7.2-7.6 (m, 4H,Ar-H), Anal calculated for $C_{10}H_8NO_2$: C,57.30; H,3.85; N,6.68 Found: C,57.21; H,3.73; N,6.54.

General procedure for preparation of 1-(3-chlorophenyl)-3,4-bis-(4-hydroxy-benzylidene)-pyrrolidine-2,5-dione (2)

A mixture of 1 (0.01mole) and p-hydroxy benzaldehyde (0.02mole) in glacial acetic acid (15ml) was taken into a beaker. The reaction mixture was heated on sand bath form15 minutes and left overnight at room temperature. The compound **2** was separated as colored crystals. Filtered dried and recrystalise from benzene. Yield 78 %, m. p. 82 ^{0}C.

7-(3-chlorophenyl)-3,4-bis-(4-hydroxyphenol)-3,3a,3b,4,5,7-hexahydro-2*H*-pyrrolo[2,3-c,5,4-c] dipyrazole (3_a)

To a solution of 2 (0.01mole) and hydrazine hydrate (0.02mole) in ethanol (50ml) two drops of piperidine was added and refluxed on water bath for 16-18 hrs. The reaction mixture was concentrated cooled and poured into ice cold water. The Solid thus separated was filtered washed and recrystalise from alcohol. Yield 72 %, m. p. 140-142 ^{0}C, IR (KBr): 3450 (OH), 1590(C=N), 3275 (N-H), ^{1}H-NMR(DMSO-d_6): δ 10.7 (s,1H,OH), 2.1 (s,1H,CH, pyrrole), Anal calculated for $C_{24}H_{20}ClN_5O_2$: C,64.65; H,4.52; N,15.71 Found: C,64.52; H,4.38; N,15.69.

7-(3-chlorophenyl)-3,4-bis-(4-hydroxyphenol)-3,3a,3b,4,-tetrahydro-7*H*-2,5-dioxa-1,6,7-triazo-cyclopenta[a]pentalene (3_b)

To a solution of 2 (0.01mole) and hydroxyl amine hydrochloride (0.02mole) in ethanol (50ml), KOH (0.04mole) was added and refluxed on water bath for 16-18 hrs. The reaction mixture was concentrated cooled and poured into ice cold water. The Solid thus separated was filtered washed and recrystalise from alcohol. Yield 54 %, m. p. 94 ^{0}C, IR (KBr): 3420 (OH), 1595(C=N), 1120 (C-O), ^{1}H-NMR(DMSO-d_6): δ 11.6 (s,1H,OH), 6.97-8.58 (m,12H, Ar), 3.26 (s,1H,CH, isoxazole), 2.58 (s,1H,CH, pyrrole), Anal calculated for $C_{24}H_{18}ClN_3O_4$: C,64.36; H,4.05; N,9.38 Found: C,64.25; H,3.94; N,9.28.

2-[5-carbamoylmethyl-7-(3-chlorophenyl)-3,4-bis-(4-hydroxyphenyl)-3,3a,3b,4,5,7-hexahydropyrrol [2,3-c,5,4-c] dipyrazol-2-yl]-acetamide (3_c)

A mixture of chalcone 2 (0.01mole) and semicarbazide hydrochloride (0.02mole) in ethanol (50ml) was refluxed on water bath for 16-18 hrs. It was cooled and poured into ice water. The product thus separated was filtered, washed with water dried and recrystalise from ethanol. Yield 82 %,m.p.-208-210 ^{0}C, IR (KBr): 3450 (OH), 1601(C=N), 1675 (C=O), ^{1}H-NMR(DMSO-d_6): δ 10.62 (s,1H,OH), 5.43 (s,2H,NH_2), 6.99-8.61 (m,12H, Ar), 3.20 (s,1H,CH, pyrazole), 2.4 (s,1H,CH, pyrrole).

General procedure for preparation of azo-flurorene (4_{a-f}) and (5)

A mixture of 1-(3-chlorophenyl)-pyrrolidine-2, 5-dione (0.01mole), malononitrile (0.02mole), substituted benzaldehyde, acetaldehyde (0.02mole) and piperidine (1ml) in ethanol (40ml) was refluxed 4-5 hrs. After completion of reaction the mixture was cooled and the resulting solid was crystalised from ethanol.

2,7-diamino-9-(3-chlorophenyl)-4,5-bis-(4-hydroxyphenol)-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (4_a)

Yield 65 %, m. p. 124-126 ^{0}C, IR (KBr): 3450 (OH), 2220 (CN), 3231-3322 (NH_2), ^{1}H-NMR(DMSO-d_6): δ 10.70 (s,1H,OH), 8.62 (s,2H, NH_2), 6.15-7.70 (m,12H, Ar), 4.73 (s,1H,CH), Anal calculated for $C_{30}H_{20}ClN_5O_4$: C,70.03; H,3.92; N,13.61 Found: C,69.93; H,3.80; N,13.54.

2,7-diamino-9-(3-chlorophenyl)-4,5-bis-(4-dimethylaminophenyl)-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (4_b) :

Yield 72 %, m. p. 114-116 ^{0}C, IR (KBr): 3215-3305 (NH_2), 2210(CN) ^{1}H-NMR(DMSO-d_6): δ 8.72 (s,2H, NH_2), 6.40-7.68 (m,12H, Ar), 4.68 (s,1H,CH), 2.85 (s, 3H, N-CH_3) Anal calculated for $C_{34}H_{30}ClN_7O_2$: C,67.60; H,5.01; N,16.23 Found: C,67.48; H,4.95; N,16.27.

2,7-diamino-9-(3-chlorophenyl)-4,5-bis-(3-nitrophenyl)-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (4_c)

Yield 65 %, m. p. 120-122 ^{0}C, IR (KBr): 3231-3322 (NH_2), 2210(CN), 1484 (NO_2), ^{1}H-NMR(DMSO-d_6): δ 8.70 (s,2H, NH_2), 7.12-8.00 (m,12H, Ar), 5.22 (s,1H,CH), Anal calculated for

$C_{30}H_{18}ClN_7O_6$: C,59.27; H,2.98; N,16.13 Found: C,59.30; H,2.91; N,16.05.

2,7-diamino-9-(3-chlorophenyl)-4,5-bis-(3-chlorophenyl)-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (4_d)

Yield 58 %, m. p. 120-122 ^{0}C, IR (KBr): 3225-3331 (NH_2), 2210(CN) ^{1}H-NMR(DMSO-d_6): δ 8.88 (s,2H, NH_2), 7.12-7.55 (m,12H, Ar), 5.68 (s,1H,CH), Anal calculated for $C_{30}H_{18}Cl3N_5O_2$: C,61.40; H,3.09; N,11.93 Found: C,61.31; H,3.00; N,11.84.

2,7-diamino-9-(3-chlorophenyl)-4,5-bis-(2-chlorophenyl)-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (4_e)

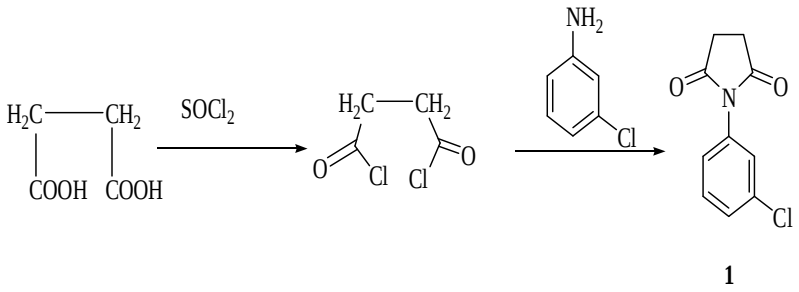
Yield 61 %, m. p. 90-92 ^{0}C.

2,7-diamino-9-(3-chlorophenyl)-4,5-diphenyl-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (4_f)

Yield 71 %, m. p. 124-126 ^{0}C, IR (KBr): 3270-3341 (NH_2), 2215(CN) ^{1}H-NMR(DMSO-d_6): δ 8.71 (s,2H, NH_2), 7.13-7.50 (m,14H, Ar), 5.12 (s,1H,CH), Anal calculated for $C_{30}H_{20}ClN_5O_2$: C,69.59; H,3.89; N,13.52 Found: C,69.65; H,3.81; N,13.60.

2,7-diamino-9-(3-chlorophenyl)-4,5-dimethyl-5,9-dihydro-4*H*-1,8-dioxa-9-azo-fluorene-3,6-dicarbonitrite (5)

Yield 54 %, m. p. 90-92 ^{0}C, IR (KBr): 3250-3328 (NH_2), 2235(CN) ^{1}H-NMR(DMSO-d_6): δ 8.99 (s,2H, NH_2), 7.12-7.66 (m,12H, Ar), 2.85 (s, 3H, CH_3), 4.11 (s,1H,CH), Anal calculated for $C_{20}H_{16}ClN_5O_2$: C,60.99; H,4.09; N,17.78 Found: C,60.64; H,3.98; N,17.69.



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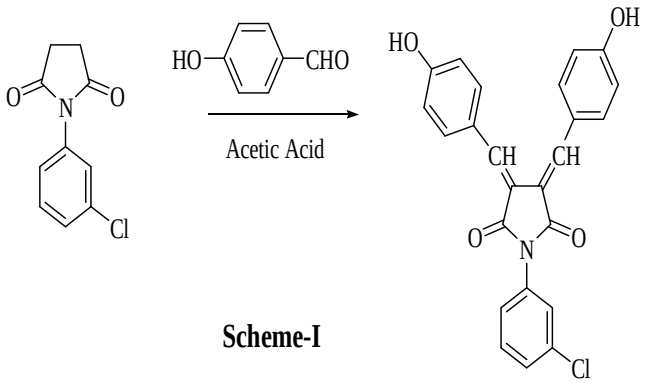
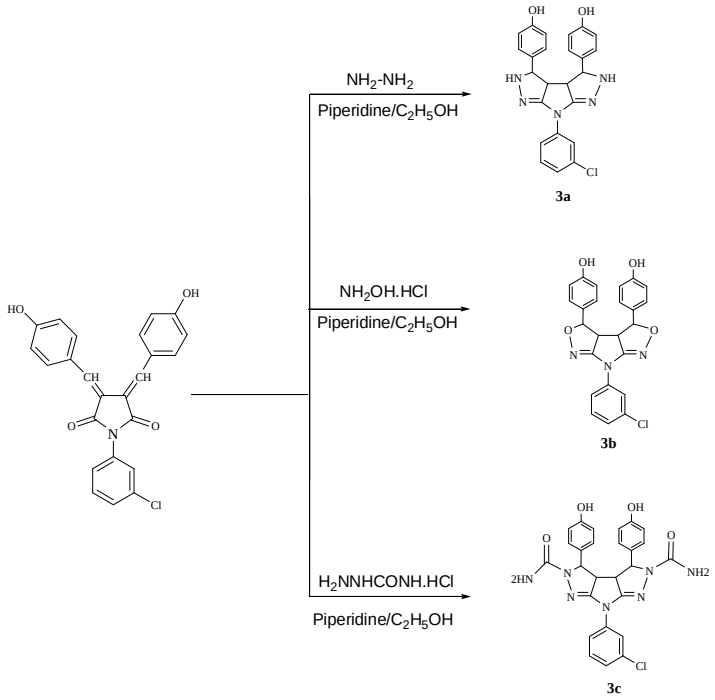
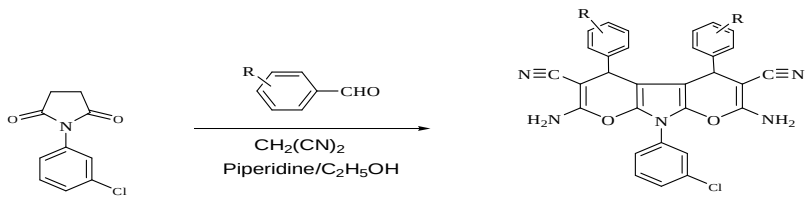


Scheme-I

2

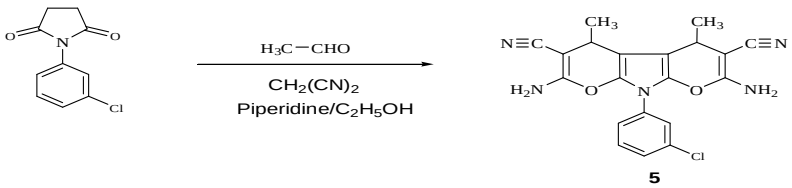


Scheme-II



R, a= 4OH, b= 4N(CH3)2, c= 3NO2, d= 4Cl, e= 2Cl, f= H

Scheme-III



Scheme-IV

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