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Research Article

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Synthesis of Novel Diarylpyrrole-2- Aldehydes, their Antiurease and Antioxidant Activities

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ABSTRACT

Various diarylpyrrole-2-carbaldehydes were prepared in good to excellent yields by a ring transformation of arylfurfuran-2-carbaldehydes with anilines in the presence of an acid catalyst. All the synthesized compounds were duly characterized through their elemental analyses and by spectroscopic techniques (FTIR, ^{1}HNMR, ^{13}CMR, and mass). These were screened for their antibacterial and antioxidant activities.

Keywords: Diarylpyrrole aldehydes; Ring transformation; Arylfuran-2-carbaldehydes; Meerwein arylation; Antibacterial activity; Antioxidant activity

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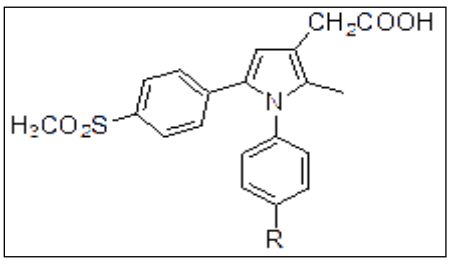
INTRODUCTION

Pyrrole a five membered heterocycle is one of the most important heterocyclic ring system abundantly found in the vegetable and animal kingdom [1]. Many diarylpyrroles (I) have recently been reported with interesting biological properties including anti-inflammatory among others [2].This prompts us to report our ongoing work with the chemistry of arylpyrroles.



(I)

EXPERIMENTAL SECTION

General

All reagents and solvents were used as obtained from the supplier or recrystallized or redistilled as were found necessary. Thin Layer chromatography was performed using aluminium sheets (Merck) coated with silica gel 60 F_{254}. IR spectra were recorded by using an IR Perkin-Elmer Spectrum 1 FTIR spectrophotometer and peaks are reported max (neat)/cm^{-1} which refer to the min wave numbers. Proton magnetic resonance spectra were

recorded in Deuteriochloroform with Bruker AM 300 spectrometers (Rheinstetten–Forchheim, Germany) operating at 300 MHz, respectively. The ^{13}C NMR spectra were recorded in Deuteriochloroform with Bruker AM 100 spectrometer operating at 100 MHz. Tetramethyl-silane was used as an internal standard. Elemental analysis for C, H and N were recorded with Perkin-Elmer 2400 Series II CHN Analyzer. Melting points were recorded on a GallenKamp apparatus and are uncorrected.

General procedure for the synthesis of 5-arylfuran-2-carbaldehydes

Substituted aniline (0.01mol) is dissolved in a mixture of conc. hydrochloric acid and 20mL of water under stirring and cooled in an ice bath at -5°C. A solution of sodium nitrite (2g in 10mL of water) is added portion wise, keeping the temperature below 7-8°C. The reaction mixture is left for an hour for the completion of diazotization, filtered with the help of glass wool (in case there is any turbidity observed). The filtered diazonium solution is added dropwise to a solution of furfural (2 mL in 10 mL of acetone and water) followed by a solution of copper chloride (2g in 10mL of water). The temperature is raised to 30°C by heating (if necessary), and stirred for 4-6 hours then left for 24 hours at room temperature. Precipitates obtained are filtered, dried, and recrystallized from ethanol.

Following 5-arylfuran-2-carbaldehydes are prepared in this manner:

5-(4'-Nitrophenyl) furan-2-carbaldehyde (4): yellow crystals, mp 196°C (EtOH) (mp 192°C (EtOH) [3]

5-(4'-Chlorophenyl) furan-2-carbaldehyde (5): light yellow crystals, mp 118°C (EtOH) (mp 118°C (EtOH) [4]

5-(4'-Bromophenyl) furan-2-carbaldehyde (6): off white crystals, mp 150 °C (EtOH) (mp 150 °C (EtOH) [4]

4-(5'-Formylfuran-2'-yl) benzoic acid (7): light brown crystals, mp 296°C (EtOH)[4]

5-(4'-Methyl benzoate) furan-2-carbaldehyde (8) light brown crystals, 242°C (EtOH) [4]

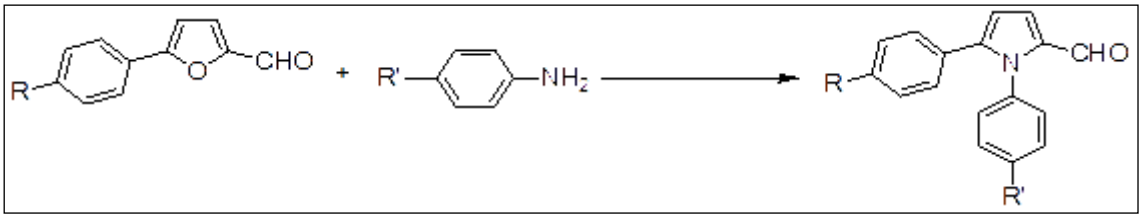
General method for the ring transformation reaction of 5-arylfuran-2-carbaldehydes

Equimolar quantities (0.01mole) of a 5-arylfuran-2-carbaldehyde and an aniline are refluxed in 20 mL ethanol for 6 hours in the presence of conc. hydrochloric acid (0.5mL) as a catalyst, and then poured the reaction mixture over crushed ice, the precipitates are filtered, dried and recrystallized from ethanol.

RESULTS AND DISCUSSION

Generally the synthesis of pyrroles make use of the classical Paal-Knorr method [5] utilising an appropriately substituted 1,4-dicarbonyl compounds and amines. The pyrroles thus obtained can suffer desired reactions and transformations to produce the desired targets. We have explored the hitherto little employed ring transformation of furans to pyrroles involving the formation of the intermediate "Stenhouse Salt" [6].

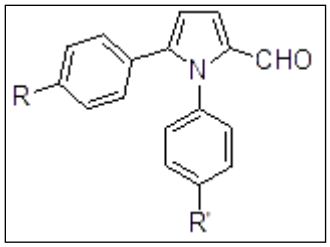
Reaction scheme



(4-8) **(9-22)**

Scheme 1

Thus a reaction of 5-arylfuran-2-carbaldehyde with an arylamine gives a 1,5-diarylpyrrole-2-carbaldehyde e.g (2) in good to excellent yields. This carbaldehyde has been successfully used as a scaffold to prepare a large number of pyrrole derivatives including a number of heterocyclic compounds.



(2)

Biological activitiesAntioxidant activity:

Garret nitric oxide (NO) scavenging method was used for the determination of antioxidant activity [7]. The method is based on the principle that nitrate present in the sample must be reduced to nitrite. This method involves the determination of nitrite, instead of nitrate in the presence of Griss reagent. The results are presented in Table 1.It is clear that most of the compounds showed significant antioxident activities. When the activities of the different diaryl pyrrole-2-aldehyde are compared, very interesting results are obtained. In compounds, on substitution of H with –Cl, -NO_2, COOH or –$COOCH_3$ at 4` position in the Diaryl pyrrole-2-aldehyde, the antioxident activity increased to significant extent. So, the presence of some group at the specified position causes an increase in the activity; this increase is greater in case of small sized group (-Cl) as compared to large ones. It can be concluded that the diaryl pyrrole-2-aldehyde having the electron withdrawing group (-NO_2) were the most active compound.

Antiurease activity:

Urease inhibition was determined by the combination of protocoal adopted by Pervez et al [8] and Weatherburn [9].Urease inhibition was determined by measuring the ammonia production using indophenol method and percentage inhibitions were calculated at each instance. Thiourea was employed as a standard (Table 2).

When the results of antiurease activity of diaryl pyrrole-2-aldehyde were compared, results were related to substituent present in the compounds. The compounds containing –NO_2, Cl or COOH group show significant antiurease activity.

Table 1: Antioxidant activity

Compound	R	R'	(Inhibition %) 10 µmol	(Inhibition %) 100 µmol
9	4-NO_2	H	4.56±0.099	6.47±0.012
10	4-NO_2	4-NO_2	17.36±0.134	24.35±0.234
11	4-NO_2	4-Cl	10.23±0.999	21.24±1.112
12	4-NO_2	4-Br	----	3.37±0.234
13	4-NO_2	4-COOH	----	------
14	4-NO_2	4-$COOCH_3$	6.56 ±0.023	14.73±0.012
15	4-NO_2	4-SO_2NH_2	12.67±0.412	36.01±0.012
16	4-Cl	4-H	3.35±0.958	14.77±1.001
17	4-Cl	4-NO_2	-----	------
18	4-Cl	4-Cl	-----	-----
19	4-Cl	4-Br	2.25±0.156	6.73±0.034
20	4-Cl	4-COOH	-----	4.40±0.357
21	4-Cl	4-$COOCH_3$	6.67±1.023	16.93±1.876
22	4-Cl	4-SO_2NH_2	5.98±0.256	16.01±0.623
23	4-Br	H	0.56±0.764	2.85±0.589
24	4-Br	4-NO_2	-----	------
25	4-Br	4-Cl	-----	------
26	4-Br	4-Br	-----	-----
27	4-Br	4-COOH	-----	------
28	4-Br	4-$COOCH_3$	8.56±0.243	20.99±0.223
29	4-Br	4-SO_2NH_2	0.87±1.901	4.15±1.128
30	4-COOH	H	-----	-----
31	4-COOH	4-NO_2	1.13±0.766	3.88±1.246
32	4-COOH	4-Cl	4.65±1.656	15.02±0.634
33	4-COOH	4-Br	2.97±0.526	8.29±0.507
34	4-COOH	4-COOH	4.45±0.861	6.99±0.786
35	4-COOH	4-$COOCH_3$	2.99±0.589	4.34±0.714
36	4-$COOCH_3$	H	2.95±0.523	5.72±0.367
37	4-$COOCH_3$	4-NO_2	7.45±0.146	20.36±0.056
38	4-$COOCH_3$	4-Cl	5.78±0.108	18.50±1.453
39	4-$COOCH_3$	4-Br	11.56±0.55	47.36±0.034
40	4-$COOCH_3$	4-COOH	3.11±1.237	12.12±0.877
41	4-$COOCH_3$	4-$COOCH_3$	4.53±0.256	15.1±0.564
42	4-$COOCH_3$	4-SO_2NH_2	1.11±0.543	6.40±0.357
Ascorbic acid			8.5±0.16	84.1±0.12

Table 2: Antiurease inhibition (% ± SD)

Compound	R	R'	(Inhibition %) 10 µmol	(Inhibition %) 100 µmol
9	4-NO_2	H	13.11± 0.890	21.23 ± 0.450
10	4-NO_2	4-NO_2	7.29 ± 1.360	16.34 ± 0.012
11	4-NO_2	4-Cl	-----	8.58 ± 0.469
12	4-NO_2	4-Br	14.23± 2.580	32.87 ± 0.354
13	4-NO_2	4-COOH	11.29 ± 0.524	24.50 ± 0.654
14	4-NO_2	4-$COOCH_3$	10.99 ± 0.015	25.18 ± 0.028
15	4-NO_2	4-SO_2NH_2	1.10 ± 0.890	9.92 ± 0.689
16	4-Cl	4-H	6.28 ± 0.894	17.97 ± 1.120
17	4-Cl	4-NO_2	7.94 ± 0.029	15.76 ± 0.657
18	4-Cl	4-Cl	9.94 ± 0.549	16.18 ± 0.028
19	4-Cl	4-Br	------	6.23 ± 1.649
20	4-Cl	4-COOH	11.23 ± 0.694	28.65 ± 1.234
21	4-Cl	4-$COOCH_3$	12.08 ± 0.268	27.84 ± 0.633
22	4-Cl	4-SO_2NH_2	10.54 ± 1.400	23.35 ± 0.254
23	4-Br	H	1.23 ± 1.239	8.94 ± 1.074
24	4-Br	4-NO_2	1.11 ± 0.698	8.21 ± 2.580
25	4-Br	4-Cl	2.11 ± 0.854	7.66 ± 0.698
26	4-Br	4-Br	2.22 ± 0.069	8.52 ± 1.700
27	4-Br	4-COOH	3.93 ± 0.863	12.53 ± 0.214
28	4-Br	4-$COOCH_3$	2.01 ± 1.600	10.04 ± 0.150
29	4-Br	4-SO_2NH_2	14.86 ± 0.296	30.15 ± 1.820
30	4-COOH	H	-----	8.52 ± 0.029
31	4-COOH	4-NO_2	12.17 ± 0.547	28.25 ± 0.063
32	4-COOH	4-Cl	10.33 ± 1.322	24.50 ± 1.247
33	4-COOH	4-Br	8.02 ± 1.074	21.51 ± 2.160
34	4-COOH	4-COOH	13.55 ± 0.080	42.05 ± 0.012
35	4-COOH	4-$COOCH_3$	15.69 ± 0.082	25.73 ± 2.660
36	4-$COOCH_3$	H	--------	11.19 ± 0.640
37	4-$COOCH_3$	4-NO_2	11.19 ± 0.467	34.78 ± 0.396
38	4-$COOCH_3$	4-Cl	6.02 ± 1.245	14.54 ± 0.095
39	4-$COOCH_3$	4-Br	3.25 ± 0.696	11.86 ± 0.249
40	4-$COOCH_3$	4-COOH	13.02 ± 0.547	22.53 ± 0.896
41	4-$COOCH_3$	4-$COOCH_3$	4.28 ± 0.066	17.46 ± 0.781
42	4-$COOCH_3$	4-SO_2NH_2	11.29 ± 0.450	24.84 ± 0.082
Thiourea			21.25±0.15	94.00±0.101

CONCLUSIONS

A good and efficient method for the preparation of diarylpyrrole-2-carbaldehydes by the ring transformation of Arylfuran-2-carbaldehydes in acidic media is presented in this paper. From these diaryl pyrrole-2-carbaldehydes, various other heterocyclic compounds can be synthesized. We have mentioned synthesis of compounds of this series in our previous paper [10]. Further work is in progress.

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