An easy and convenient approach to NOVEL DIARYLPYRROLE-2-CARBALDEHYDES

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Un enfoque fácil y conveniente para el nuevo diarilpirrol-2-carbaldehídos

Un enfocament fàcil i convenient dels nous diarilpirrol-2-carbaldehids

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ABSTRACT

The ring modification of arylfuran-2-carbaldehydes with anilines in the presence of an acid yielded a variety of diarylpyrrole-2-carbaldehydes. Elemental analyses and spectroscopic methods (FTIR, 1H NMR, 13C-NMR, and MS) were used to characterize the produced compounds.

Keywords:Diarylpyrrole aldehydes, Ring transformation, Arylfuran-2-carbaldehydes, Meerwein arylation.

RESUMEN

La modificación del anillo de arilfuran-2-carbaldehídos con anilinas en presencia de un ácido produjo una variedad de diarilpirrol-2-carbaldehídos. Se utilizaron análisis elementales y métodos espectroscópicos (FTIR, 1H NMR, 13C-NMR y MS) para caracterizar los compuestos producidos.

Palabras claves: Aldehídos de diarilpirrol, Transformación de anillo, Arilfuran-2-carbaldehídos, Arilación de Meerwein.

RESUM:

La modificació de l'anell d'arilfuran-2-carbaldehids amb anilines en presència d'un àcid va produir una varietat de diarilpirrol-2-carbaldehids. Es van utilitzar anàlisis elementals i mètodes espectroscòpics (FTIR, 1H RMN, 13C-NMR i MS) per caracteritzar els compostos produïts.

Paraules clau: Aldehids de diarilpirrol, transformació en anell, arilfuran-2-carbaldehids, arilació de Meerwein.

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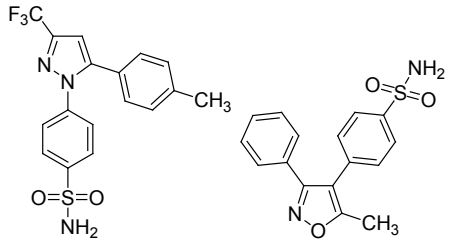
INTRODUCTION

Pyrrole, the simplest azole, is an important ring system.Many of its derivatives is abundant and have been isolated and identified from plant and animal source [1-5]. Various pyrrole derivatives have been synthesized for their biological activity [6].

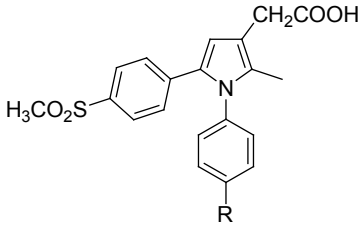
Because of its importance, pyrroles have been synthesized using various synthetic techniques [7-11], but the most popular is the Paal-Knorr synthesis employing 1,4-dicarbonyl compounds and appropriate amines [12].

Many vicinal diarylazoles/heterocycles function ascycloxygenase(COX) inhibitors Celecoxib **(1)** and Valdecoxib **(2)** may be cited [13, 14], which were in clinicaluse but have recently been withdrawn from the market due to their adverse side effects [15, 16]. Diarylpyrroles appear to be attracting a lot of attention in the research for better agents.



Celecoxib (1) *Valdecoxib (2)*

The synthesis of some 4,5-diarylpyrroles and their anti-inflammatory activity was reported by Wilkerson *et al.* [17], Biava *et al.*[18-20].There have also been reports of 1,5-diarylpyrroles (**3**) as possible antimycobacterial drugs [21, 22].

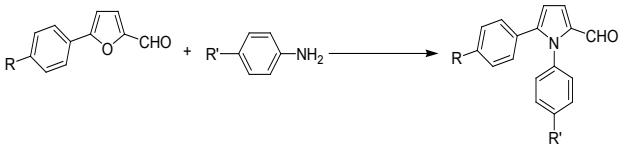


1, 5-diarylpyrrole-1H-3-acetic acid (3)

Earlier, the synthesis of many 1,5-diarylpyrroles from 1,4-substituted ketones was reported by A.Hall*et al.*, and these acted as EP1 receptor antagonists [23, 24]. Dialkoxytetrahydrofurans are "masked" or cyclic acetals of 1,4-dialdehydes, which either under acid catalysis [25] or microwave irradiation in the presence of iodine [26] react with aromatic amines affording *N*-aryl pyrroles. A ring transformation of furan-2-carbaldehyde to 1-aryl pyrrole-2-carbaldehyde occurs in the presence of an arylamine and an acid catalyst [27, 28].This process has been investigated for the production of 5-arylfuran-2-carbaldehydes. Here we would like to report a synthesis of various 1,5-diarylpyrrole-2-carbaldehydes from 5-arylfuran-2-carbaldehydes by this ring-opening ring-closing method.

RESULTS AND DISCUSSION

Various aryl furfurals(4-8) were prepared in 40-70% yield (Table 1)by the catalytic arylation of furfural with arene diazonium salts according to the Meerwein method [29]. These were treated with appropriate anilines at reflux in ethanol in the presence of a catalytic amount of hydrochloric acid to provide, in good yields, the respective 1,5-diarylpyrrole-2-carbaldehydes (9-22) by a ring transformation reaction(Scheme 1). The method was like that used to make 1-aryl pyrrole-2-carbaldehydes from furfural and anilines [27, 28]. Lewis and Mulquiney [30-32] have extensively studied the reaction of arylamines and furan-2-carbaldehyde and have identified the formation of the intermediate "Stenhouse salt" (A). (Scheme 2).This results in the synthesis of 1-aryl-3-hydroxy pyridine (B) and 1-aryl pyrrole-2-carbaldehydes under acid or basic conditions.



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

Scheme 1

4. R= 4-NO_2, **5**. R= 4-Cl, **6.** R= 4-Br, **7**. R= 4-COOH, **8**. R= 4-$COOCH_3$

9.R= 4-NO_2, R'= 4-$COOCH_3$, **10.** R= 4-NO_2, R'= 4-SO_2NH_2, **11.** R= 4-Cl, R'= 4-$COOCH_3$

12. R= 4-Cl, R'= 4-SO_2NH_2, **13.** R= 4-Br, R'= 4-$COOCH_3$, **14.** R= 4-Br, R'= 4-SO_2NH_2

15. R= 4-COOH, R'= 4-$COOCH_3$, **16.** R= 4-COOH, R'= 4-SO_2NH_2, **17.** R= 4-$COOCH_3$, R'= 4-NO_2, **18.** R= 4-$COOCH_3$, R'= 4-Cl **19.** R= 4-$COOCH_3$, R'= 4-Br **20.** R= 4-$COOCH_3$, R'= 4-COOH **21.** R= 4-$COOCH_3$, R'= 4-$COOCH_3$, **22.** R= 4-$COOCH_3$, R'= 4-SO_2NH_2,

FTIR analysis

Assignment of selected characteristic IR absorption bands provides significant indication for the formation of 1,5-diaryl pyrrole-2-carbaldehydes. The aldehydic group (C=O) and (C-H) absorbed in the expected regions; (C=O) in the 1610-1681cm^{-1}, (C-H) stretch of aldehydes shows a weak absorption band around 2846-2863cm^{-1}, while NO_2 group present in some compounds (**9,10,17**) shows characteristics strong absorption bands in the 1298-1341 and at 1584-1600 cm^{-1} region and are given in **table 2**.

^{1}H-NMR analysis

The ^{1}H-NMR spectra (300 MHz, $CDCl_3$) of the starting aryl furfurals and 1,5-diaryl pyrrole-2-carbaldehydes show characteristic signals between 9.439-9.860ppm for aldehydic proton and two doublets at 6.78-6.98ppm and 7.29-7.96ppm for the pyrrole ring hydrogens.

^{13}C-NMR analysis

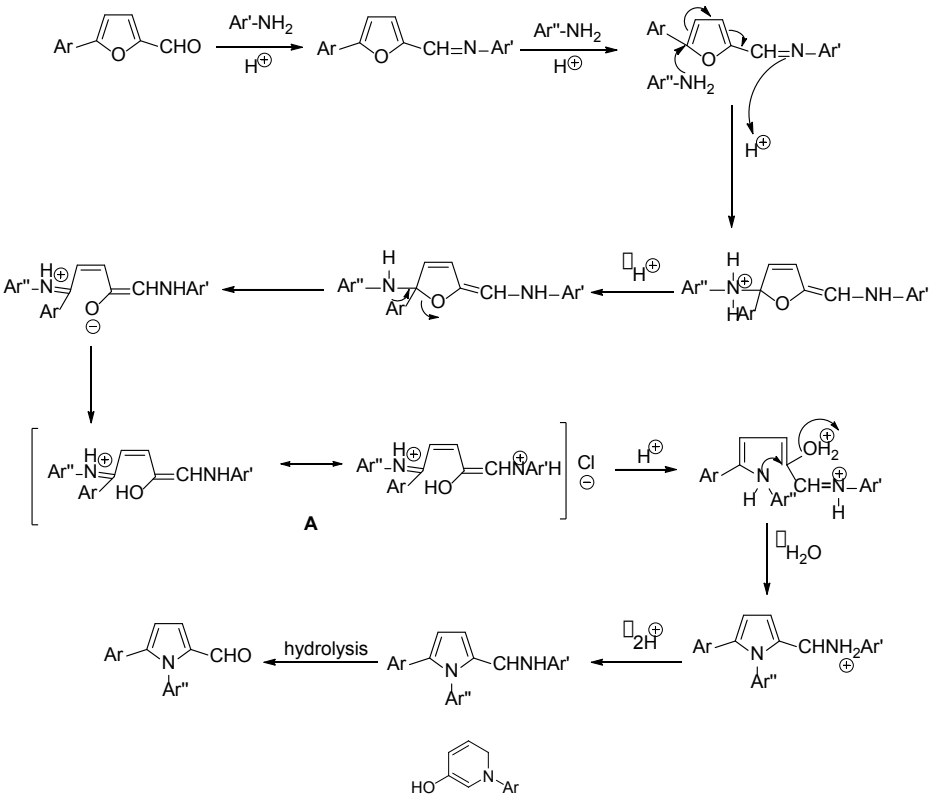
Finally, ^{13}C-NMR (75MHz $CDCl_3$) spectra of all compounds were recorded, and spectral signals are

in good agreement with the structures and are given in **table 2**. The carbon of C=O displayed signals at 177.2-177.7ppm in the arylfuran-2-carbaldehydes and their corresponding 1, 5-diarylpyrrole-2-carbaldehydes while the pyrrole ring carbons show signals for their characteristic positions.

Mass spectra

Mass spectra of all the compounds were recorded, and their values are given in the experimental section and also in **table 2**. These also help characterize the formation of arylfuran-2-carbaldehydes and 1,5-diarylpyrrole-2-carbaldehydes as starting materials. The molecular ion peaks in all the new compounds were as predicted.

Mechanism:



Scheme 2

Table:1-*Physical data of Diarylpyrrole-2-carbaldehydes*

Compound no	R	'R	Yield(%)	M.P (°C)	Mol. wt	M.F	Elemental analysis %Calc, (found)		
							C	H	N
9	4-NO_2	4-$COOCH_3$	60%	202	350	$C_{19}H_{14}N_2O_5$	65.14(64.78)	4.00(3.67)	8.00(7.59)
10	4-NO_2	4-SO_2NH_2	65%	218	371	$C_{17}H_{13}N_3O_5S$	54.98(54.68)	3.50(3.87)	11.32(11.19)
11	4-Cl	4-$COOCH_3$	70%	188	339.5	$C_{19}H_{14}ClNO_3$	67.25(66.87)	4.12(3.75)	4.12(3.85)
12	4-Cl	4-SO_2NH_2	55 %	212	360.5	$C_{17}H_{13}ClN_2O_3S$	56.66(56.85)	3.61(3.28)	7.77(7.43)
13	4-Br	4-$COOCH_3$	62%	188	385	$C_{19}H_{14}BrNO_3$	59.53(59.15)	3.65(3.28)	3.65(3.19)
14	4-Br	4-SO_2NH_2	65%	218	406	$C_{17}H_{13}BrN_2O_3S$	50.49(50.15)	3.21(2.90)	6.93(6.57)
15	4-COOH	4-$COOCH_3$	70%	128-130	349	$C_{20}H_{15}NO_5$	68.76(68.28)	4.29(3.98)	4.01(3.68)
16	4-COOH	4-SO_2NH_2	72%	84-86	305	$C_{19}H_{15}NO_3$	74.75(74.39)	4.91(4.68)	4.59(4.35)
17	4-$COOCH_3$	4-NO_2	64%	66-68	350	$C_{19}H_{14}N_2O_5$	65.14(64.84)	4.00(3.95)	8.00(7.78)
18	4-$COOCH_3$	4-Cl	68%	98-100	339.5	$C_{19}H_{14}ClNO_3$	67.25(67.13)	4.12(3.98)	4.12(3.69)
19	4-$COOCH_3$	4-Br	70%	134-136	385	$C_{19}H_{14}BrNO_3$	59.53(59.27)	3.65(3.17)	3.65(3.42)
20	4-$COOCH_3$	4-COOH	72%	138-140	349	$C_{20}H_{15}NO_5$	68.76(68.45)	4.29(4.08)	4.01(3.75)
21	4-$COOCH_3$	4-$COOCH_3$	60%	166-168	363	$C_{21}H_{17}NO_5$	69.42(69.15)	4.68(4.28)	3.85(3.44)
22	4-$COOCH_3$	4-SO_2NH_2	63%	120-122	384	$C_{19}H_{16}N_2O_5S$	59.37(59.11)	4.16(3.67)	7.29(7.09)

Table:2-Spectral Data of Diarylpyrrole-2-carbaldehydes

Com-pound no	R	'R	IR	Mass spectra	H-NMR	C-NMR
9	4-NO_2	4-$COOCH_3$	2365 (Aromatic ring), 1730 (C=O ester) 1678 (C=O aldehyde), 1580 and 1348 (Asym and sym -NO_2),	[M^+] (19), 217 [M^+-$PhCOOCH_3$] (100), 75 [Ph] (11),	9.6 (s, 1H), 8.3-7.3 (m, 8H), 6.8 (d, 1H, *J*= 4.5 Hz), 6.6 (d, 1H, *J*= 4.5 Hz), 4.5 (s, 3H),	177.5 (C=O aldehydes), 156.3 (C=O ester) 153.1, 134.5, 131.5, 125.7, 124.5, 124.4, 124.3, 123.8, 122.7, 110.6 (Ar-C)52.3 (CH_3ester),
10	4-NO_2	4-SO_2NH_2	2365 (Aromatic ring), 1635 (C=O aldehyde), 1590 and 1316 (Asym and sym -NO_2),	371[M^+] (1), 216 [M^+- Ph-SO_2NH_2] (5), 156 [Ph-SO_2NH_2] (5), 80 [SO_2NH_2] (32), 65 [pyrrole] (80),	9.7 (s, 1H), 7.6 (d, 2H, *J*= 3.30 Hz), 7.5 (d, 2H, *J*= 3.3 Hz),7.5 (d, 2H, *J*= 5.8 Hz), 7.3 (d, 2H, = 5.8 Hz) 6.9 (d, 1H, *J*= 6.3 Hz), 6.7 (d, 1H, *J*= 6.3 Hz), 1.90 (s, 2H)	178.5 (C=O aldehyde), 149.8, 143.9, 137.6, 133.6, 129.9, 128.6, 126.6, 122.8, 121.3, 119.9, 109.8 (Ar-C),
11	4-Cl	4-$COOCH_3$	2365.43 (Aromatic ring), 1735.12 (C=O ester), 1665.89(C=O aldehyde), 1071.88 (C-Cl bond),	341 [M^++2] (100), 339 [M^+] (35), 279 [M^+- $COOCH_3$] (28), 251 [M^+- $COOCH_3$-CHO] (6), 75 [Ph] (7) 308 [M^+- CHO] (27), 204 [M^+-$PhCOOCH_3$] (1),	9.6 (s, 1H), 8.3-7.2 (m, 8H), 6.8 (d, 1H, *J*= 4.60 Hz), 6.6 (d, 1H, *J*= 4.60 Hz), 3.9 (s, 3H),	177.2 (C=O aldehyde), 165.9 (C=O ester) 152.1, 135.7, 131.6, 131.1, 129.2, 127.47, 126.5, 123.4, 120.7, 113.8, 107.9 (Ar-C)52.1 (CH_3 ester),
12	4-Cl	4-SO_2NH_2	2364 (Aromatic ring), 1657 (C=O aldehyde), 1093 (C-Cl bond),	362 [M^++2] (100), 360 [M^+] (35), 279 [M^+- SO_2NH_2] (31), 251 [M^+- SO_2NH_2-Cl] (17),	9.8 (s, 1H), 7.7 (d, 2H, *J*= 4.3 Hz), 7.5 (d, 2H, *J*= 4.3 Hz),7.3 (d, 1H, J= 3.9 Hz), 7.3 (d, 1H, *J*= 3.9 Hz) 6.9 (d, 1H, *J*= 5.80 Hz), 6.6 (d, 1H, *J*= 5.80 Hz), 1.7 (s, 2H)	178.9 (C=O aldehyde), 149.8, 145.6, 137.5, 134.9, 133.9, 130.7, 129.6, 126.5, 121.9, 119.6, 109.3(Ar-C),
13	4-Br	4-$COOCH_3$	2365 (Aromatic ring), 1725 (C=O ester), 1610 (C=O aldehyde), 1025 (C-Br bond),	385 [M^++ 2] (100), 383 [M^+] (82), 354 [M^+-CHO] (24), 249 [M^+- $PhCOOCH_3$-CHO] (18), 249 [M^+- $PhCOOCH_3$] (24), 155 [PhBr]	9.6 (s, 1H), 7.6-7.2 (m, 8H), 6.8 (d, 1H, *J*= 4.7 Hz), 6.6 (d, 1H, *J*= 4.7 Hz), 4.4 (s, 3H)	177.4 (C=O aldehyde), 165.9 (C=O ester) 142.7, 132.3, 132.2, 131.8, 131.6, 131.1, 130.9, 126.71, 125.2, 113.9, 108.0 (Ar-C)52.23 (CH_3 ester)
14	4-Br	4-SO_2NH_2	2345 (Aromatic ring), 1649 (C=O aldehyde), 1021 (C-Br bond), 3240 (-NH)	406 [M^++2] (17), 404 [M^+] (15), 378 [M^++2-CHO] (2), 325 [M^+- Br] (4), 245 [M^+-Br-SO_2NH_2] (3), 156 [PhBr] (90), 80 [SO_2NH] (16),	): 9.7 (s, 1H), 7.5 (d, 2H, *J*= 3.5 Hz), 7.4 (d, 2H, *J*= 3.5 Hz),7.3 (d, 2H, *J*= 5.8 Hz), 7.1 (d, 2H, *J*= 5.8 Hz) 6.9 (d, 1H, *J*= 5.5 Hz), 6.7 (d, 1H, *J*= 5.5 Hz), 2.1 (s, 2H)	179.8 (C=O aldehyde), 149.3, 146.8, 137.8, 133.4, 130.8, 130.4, 129.7, 126.4, 121.9, 119.8, 109.4 (Ar-C),
15	4-COOH	4-$COOCH_3$	2365 (Aromatic ring), 1715 (C=O ester), 1690 (C=O acid), 1638 (C=O aldehyde), 3298 (-OH)	349 [M^+] (100), 290 [M^+- COOCH3] (10), 320 [M^+- CHO] (4), 262 [M^+- $COOCH_3$-CHO] (3), 218 [M^+- COOCH3-CHO-COOH] (3), 65 [pyrrole] (9)	9.4 (s, 1H), 8.0-7.4 (m, 8H), 7.4 (d, 1H, *J*= 4.6 Hz), 6.6 (d, 1H, *J*= 4.6 Hz)	178.9 (C=O aldehyde), 140.4, 131.6, 130.9, 130.2, 128.9, 127.6, 125.0, 113.8, 109.3, 106.6 (Ar-C),
16	4-COOH	4-SO_2NH_2	2363 (Aromatic ring), 1715 (C=O ester), 1628 (C=O aldehyde),	306 [M^+] 40, 218 [M^+-$COOCH_3$-CHO] 17, 278 [M^+- CHO] (3)	9.7 (s, 1H), 7.9-7.0 (m, 8H), 7.0 (d, 1H, *J*= 6.5 Hz), 6.9 (d, 1H, *J*= 6.5 Hz)	177.4 (C=O aldehyde), 166.6 (C=O ester) 155.8, 152.4, 147.6, 134.9, 133.5, 130.2, 129.6, 129.2, 125.1, 124.4, 123.1, 121.3, 110.7, 108.1 (Ar-C)52.3 (CH_3 ester),
17	4-$COOCH_3$	4-NO_2	2348 (Aromatic ring), 1728 (C=O ester), 1649 (C=O aldehyde), 1578 and 1318 (Asym and sym -NO_2),	350 [M^+] 100, 215 [M^+- $PhCOOCH_3$] 17, 320 [M^+- CHO] 26, 135 [$PhCOOCH_3$] 3, 76 [Ph] 18,	9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H, *J*= 3.1 Hz), 6.6 (d, 1H, *J*= 3.1 Hz), 3.9 (s, 1H)	177.5 (C=O aldehyde), 164.6 (C=O ester) 152.4, 149.4, 130.2, 126.3, 125.1, 125.1, 124.7, 123.1, 121.5, 113.4, 109.4 (Ar-C), 52.3 (CH_3 ester),
18	4-$COOCH_3$	4-Cl	2345 (Aromatic ring), 1718 (C=O ester), 1645 (C=O aldehyde), 1091 (C-Cl bond),	341 [M^++2] (100), 339 [M^+] (40), 229 [M^+- PhCl] 21, 310 [M^+- CHO] 5, 135 [$PhCOOCH_3$] 2, 76 [Ph] 55,	9.6 (s, 1H), 8.2-7.3 (m, 8H), 7.1 (d, 1H, *J*= 3.3 Hz), 6.9 (d, 1H, *J*= 3.3 Hz), 3.9 (s, 1H)	177.5 (C=O aldehyde), 166.5 (C=O ester) 157.9, 152.6, 147.2, 132.8, 130.7, 130.2, 129.4, 125.1, 124.7, 123.5, 122.9, 122.3, 110.0, 109.7 (Ar-C), **52.30** (CH_3 ester),
19	4-$COOCH_3$	4-Br	2365 (Aromatic ring), 1715 (C=O ester), 1645 (C=O aldehyde), 1021 (C-Br bond),	385 [M^++2] (38), 383 [M^+] (11), 64 [pyrrole] (37),	9.6 (s, 1H), 8.8-7.3 (m, 8H), 7.1 (d, 1H, *J*= 5.2 Hz), 6.6 (d, 1H, *J*= 5.2 Hz), 4.4 (s, 1H)	177.7 (C=O aldehyde) 165.9 (C=O ester) 131.6, 130.3, 130.2, 128.9, 125.1, 109.3 (Ar-C)52.3 (CH_3 ester),

20	4-$COOCH_3$	4-COOH	2359 (Aromatic ring), 1725 (C=O ester), 1698 (C=O acid), 1610 (C=O aldehyde),3267 (-OH)	349 [M^+] (100), 321 [M^+-CHO] (50), 304 [M^+-COOH] (11) ,64 [pyrrole] (14),	9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H, *J*= 5.5 Hz) 6.8 (d, 1H, *J*= 5.5 Hz), 4.4 (s, 1H), 10.9 (s, 1H)	178.4 (C=O aldehyde), 166.4 (COOH), 165.9 (C=O ester) 147.9, 142.6, 132.9, 130.8, 130.3, 130.2, 125.1, 125.1, 122.9, 109.4 (Ar-C)52.3 (CH_3 ester),
21	4-$COOCH_3$	4-$COOCH_3$	2365 (Aromatic ring), 1715 (C=O ester), 1649 (C=O aldehyde),	363 [M^+] 100, 304 [M^+- $COOCH_3$] 17, 332 [M^+- CHO] 29, 135 [$PhCOOCH_3$] 6, 76 [Ph] 13	9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H, *J*= 3.50 Hz), 6.8 (d, 1H, *J*= 3.50 Hz), 4.0 (s, 1H)	177.5 (C=O aldehyde) 1654.5 (C=O ester) 131.6, 130.3, 125.1, 109.4 (Ar-C),52.3 (CH_3 ester),
22	4-$COOCH_3$	4-SO_2NH_2	2345 (Aromatic ring), 1725 (C=O ester), 1610 (C=O aldehyde), 3240 (-NH),	384 [M^+] (75), 356 [M^+-CHO] (100), 325 [M^+-$COOCH_3$] (45), 304 [M^+-SO_2NH_2] (11),	9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H, *J*= 6.3 Hz), 6.9 (d, 1H, *J*= 6.3 Hz), 4.4 (s, 1H), 1.5 (s, 2H)	177.3 (C=O aldehyde), 166.4 (C=O ester) 157.95, 152.6, 132.9, 130.8, 130.3, 130.2, 125.1, 122.9 (Ar-C)52.3 (CH_3 ester),

CONCLUSIONS

This work describes a simple and effective technique for producing 1,5-diarylpyrrole-2-carbaldehydes **(9-22)** by ring transformation of arylfuran-2-carbaldehydes **(4-8)** in acidic environments. A variety of 1,5-diarylpyrrole-2-carbaldehyde derivatives can be made from them. Other 1, 5-diarylpyrrole-5-carbaldehydes and their derivatives are currently being prepared.

EXPERIMENTAL:

General

All reagents and solvents were used as obtained from the supplier and recrystallized or redistilled when necessary. Thin-layer chromatography was performed using aluminum sheets (Merck) coated with silica gel 60 F_{254}. IR spectra were recorded using an IR Perkin-Elmer Spectrum 1 FTIR spectrophotometer, and peaks are reportedmax(neat)/cm^{-1}, which refers to the min wave numbers. Proton magnetic resonance spectra were recorded in Deuterochloroform with Bruker AM 300 spectrometers (Rheinstetten–Forchheim, Germany) operating at 300 MHz, respectively. The ^{13}C NMR spectra were recorded in Deuterochloroform with Bruker AM 100spectrometer operating at 100 MHz.Tetramethylsilanewas used as an internal standard. Elemental analysis for C, H, and N recorded with Perkin-Elmer 2400 Series II CHN Analyzer.Melting points were measured using a Gallen Kamp instrument and are unadjusted. Shimadzu MAT 312 mass spectrometers were used to record the low-resolution EI-MS.

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

Substituted aniline (0.01 mol) 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 sodium nitrite solution (2g in 10mL of water) is added portion-wise, keeping the temperature below 7-8°C. The reaction mixture is allowed to diazotize for an hour before being filtered with glass wool (if there is any turbidity observed). A solution of furfural (2 mL in 10 mL of acetone and water) is added dropwise to the filtered diazonium solution, followed by a solution of copper chloride (2g in 10mL of water). The temperature is raised to 30°C (if necessary) and stirred for 4-6 hours before being left at room temperature for 24 hours.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) (lit mp 192°C (EtOH) [33]
5-(4'-Chlorophenyl) furan-2-carbaldehyde (5): light yellow crystals, mp 118°C (EtOH) (lit mp 118°C (EtOH) [33]
5-(4'-Bromophenyl) furan-2-carbaldehyde (6): off white crystals, mp 150 °C (EtOH) (lit mp150 °C (EtOH) [33]
4-(5'-Formylfuran-2'-yl) benzoic acid (7): light brown crystals, mp 296°C (EtOH) [33]
5-(4'-Methyl benzoate) furan-2-carbaldehyde (8) light brown crystals, 242°C (EtOH) [34]

General Method for the ring transformation reaction of 5-Arylfuran-2-carbaldehydes:

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

Methyl 4-(2-formyl-5-(4-nitrophenyl)-1H-pyrrol-1-yl) benzoate (9)

Yellow, mp 202°C (EtOH)FTIR (KBr) (ν, cm^{-1}):2365 (Aromatic ring), 1730 (C=O ester) 1678 (C=O aldehyde), 1580 and 1348 (Asym and sym -NO_2), Mass spectrum (EI, 70 eV, (I_{rel}%):350 [M^+] (19), 217 [M^+- $PhCOOCH_3$] (100), 75 [Ph] (11), ^1H NMR (300MHz, $CDCl_3$,), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.3-7.3 (m, 8H), 6.8 (d, 1H, *J*= 4.5 Hz), 6.6 (d, 1H, *J*= 4.5 Hz), 4.5 (s, 3H),^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.5 (C=O aldehydes), 156.3 (C=O ester) 153.1, 134.5, 131.5, 125.7, 124.5, 124.4, 124.3, 123.8, 122.7, 110.6 (Ar-C)52.3 (CH_3 ester),Anal. Calcd.for $C_{19}H_{14}N_2O_5$: C 65.14; H 4.00; N 8.00 **Found** C 64.78; H 3.67; N 7.59

4-(2-formyl-5-(4-nitrophenyl)-1H-pyrrol-1-yl) benzenesulfonamide (10)

Yellow, mp 218°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2365 (Aromatic ring), 1635 (C=O aldehyde), 1590 and 1316 (Asym and sym -NO_2), Mass spectrum (EI, 70 eV, (I_{rel}%): 371[M^+] (1), 216 [M^+- $PhSO_2NH_2$] (5), 156 [Ph-SO_2NH_2] (5), 80 [SO_2NH_2] (32), 65 [pyrrole] (80), ^{1}H NMR (300MHz, $CDCl_3$,), δ ppm(*J,* Hz): 9.7 (s, 1H), 7.6 (d, 2H, *J*= 3.30 Hz), 7.5 (d, 2H, *J*= 3.3 Hz),7.5 (d, 2H,*J*= 5.8 Hz), 7.3 (d, 2H, = 5.8 Hz) 6.9 (d, 1H, *J*= 6.3 Hz), 6.7 (d, 1H,*J*= 6.3 Hz), 1.90 (s, 2H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 178.5 (C=O aldehyde), 149.8, 143.9, 137.6, 133.6, 129.9, 128.6, 126.6, 122.8, 121.3, 119.9, 109.8 (Ar-C),Anal.Calcd.for $C_{17}H_{13}N_3O_5S$: C 54.98; H 3.50; N 11.32 **Found** C 54.68; H 3.87; N 11.19

Methyl 4-(2-formyl-5-(4-chlorophenyl)-1H-pyrrol-1-yl) benzoate (11)

Yellow, mp 188°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2365.43 (Aromatic ring), 1735.12 (C=O ester), 1665.89(C=O aldehyde), 1071.88 (C-Cl bond), Mass spectrum (EI, 70 eV, (I_{rel}%): 341 [M^++2] (100), 339 [M^+] (35), 279 [M^+-$COOCH_3$] (28), 251 [M^+- $COOCH_3$-CHO] (6), 75 [Ph] (7) 308 [M^+- CHO] (27), 204 [M^+- $PhCOOCH_3$] (1), ^{1}H NMR (300MHz, $CDCl_3$,), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.3-7.2 (m, 8H), 6.8 (d, 1H, *J*= 4.60 Hz), 6.6 (d, 1H, *J*= 4.60 Hz), 3.9 (s, 3H), ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.2 (C=O aldehyde), 165.9 (C=O ester) 152.1, 135.7, 131.6, 131.1, 129.2, 127.47, 126.5, 123.4, 120.7, 113.8, 107.9 (Ar-C)52.1 (CH_3 ester), Anal. Calcd.for $C_{19}H_{14}ClNO_3$:C 67.25; H 4.12; N 4.12 **Found** C 66.87; H 3.75; N 3.85

4-(2-formyl-5-(4-chlorophenyl)-1H-pyrrol-1-yl) benzenesulfonamide (12)

Yellow, mp 212°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2364 (Aromatic ring), 1657 (C=O aldehyde), 1093 (C-Cl bond), Mass spectrum (EI, 70 eV, (I_{rel}%): 362 [M^++2] (100), 360 [M^+] (35), 279 [M^+- SO_2NH_2] (31), 251 [M^+-SO_2NH_2-Cl] (17), ^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.8 (s, 1H), 7.7 (d, 2H,*J*= 4.3 Hz), 7.5 (d, 2H, *J*= 4.3 Hz),7.3 (d, 1H, J= 3.9 Hz), 7.3 (d, 1H,*J*= 3.9 Hz) 6.9 (d, 1H,*J*= 5.80 Hz), 6.6 (d, 1H,*J*= 5.80 Hz), 1.7 (s, 2H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 178.9 (C=O aldehyde), 149.8, 145.6, 137.5, 134.9, 133.9, 130.7, 129.6, 126.5, 121.9, 119.6, 109.3(Ar-C),Anal.Calcd. for $C_{17}H_{13}ClN_2O_3S$: C 56.66; H 3.61; N 7.77 **Found** C 56.45; H 3.28; N 7.43

Methyl 4-(2-formyl-5-(4-bromophenyl)-1H-pyrrol-1-yl) benzoate (13)

Yellow, mp 188°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2365 (Aromatic ring), 1725 (C=O ester), 1610 (C=O aldehyde), 1025 (C-Br bond), Mass spectrum (EI, 70 eV, (I_{rel}%):385 [M^++ 2] (100)**,** 383 [M^+] (82), 354 [M^+-CHO] (24), 249 [M^+- $PhCOOCH_3$-CHO] (18), 249 [M^+- $PhCOOCH_3$] (24), 155 [PhBr] (19)^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.6 (s, 1H), 7.6-7.2 (m, 8H), 6.8 (d, 1H, *J*= 4.7 Hz), 6.6 (d, 1H, *J*= 4.7 Hz), 4.4 (s, 3H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.4 (C=O aldehyde), 165.9 (C=O ester) 142.7, 132.3, 132.2, 131.8, 131.6, 131.1, 130.9, 126.71, 125.2, 113.9, 108.0 (Ar-C)52.23 (CH_3 ester),Anal.Calcd.for $C_{19}H_{14}BrNO_3$**:** C 59.53; H 3.65; N 3.65 Found C 59.15; H 3.28; N 3.19

4-(2-fomyl-5-(4-bromophenyl)-1H-pyrrol-1-yl) benzenesulfonamide (14)

Yellow, mp 218°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2345 (Aromatic ring), 1649 (C=O aldehyde), 1021 (C-Br bond), 3240 (-NH)Mass spectrum (EI, 70 eV, (I_{rel}%):406 [M^++2] (17), 404 [M^+] (15), 378 [M^++2-CHO] (2), 325 [M^+- Br] (4), 245 [M^+- Br-SO_2NH_2] (3), 156 [PhBr] (90), 80 [SO_2NH] (16),^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.7 (s, 1H), 7.5 (d, 2H,*J*= 3.5 Hz), 7.4 (d, 2H,*J*= 3.5 Hz),7.3 (d, 2H,*J*= 5.8 Hz), 7.1 (d, 2H,*J*= 5.8 Hz) 6.9 (d, 1H,*J*= 5.5 Hz), 6.7 (d, 1H,*J*= 5.5 Hz), 2.1 (s, 2H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 179.8 (C=O aldehyde), 149.3, 146.8, 137.8, 133.4, 130.8, 130.4, 129.7, 126.4, 121.9, 119.8, 109.4 (Ar-C),Anal.Calcd.for $C_{17}H_{13}BrN_2O_3S$: C 50.49; H 3.21; N 6.93 Found C 50.14; H 2.90; N 6.57

4-(5-formyl-1-(4-(methoxycarbonyl) **phenyl)-1H-pyrrol-2-yl) benzoic acid (15)**

Yellow, mp 128-130 °C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2365 (Aromatic ring), 1715 (C=O ester), 1690 (C=O acid), 1638 (C=O aldehyde), 3298 (-OH)Mass spectrum (EI, 70 eV, (I_{rel}%):349 [M^+] (100), 290 [M^+- COOCH3] (10), 320 [M^+- CHO] (4), 262 [M^+- $COOCH_3$-CHO] (3), 218 [M^+- COOCH3-CHO-COOH] (3), 65 [pyrrole] (9) ,^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.4 (s, 1H), 8.0-7.4 (m, 8H), 7.4 (d, 1H,*J*= 4.6 Hz), 6.6 (d, 1H,*J*= 4.6 Hz)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 178.9 (C=O aldehyde), 140.4, 131.6, 130.9, 130.2, 128.9, 127.6, 125.0, 113.8, 109.3, 106.6 (Ar-C), Anal.Calcd.for $C_{20}H_{15}NO_5$: C 68.76; H 4.29; N 4.01 Found C 68.28; H 3.98; N 3.68

Methyl 4-(5-formyl-1-phenyl-1H-pyrrol-2-yl) benzoate (16)

Yellow, mp 84-86°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2363 (Aromatic ring), 1715 (C=O ester), 1628 (C=O aldehyde), Mass spectrum (EI, 70 eV, (I_{rel}%):306 [M^+] 40, 218 [M^+- $COOCH_3$-CHO] 17, 278 [M^+- CHO] (3),^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.7 (s, 1H), 7.9-7.0 (m, 8H), 7.0 (d, 1H,*J*= 6.5 Hz), 6.9 (d, 1H, *J*= 6.5 Hz)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.4 (C=O aldehyde), 166.6 (C=O ester) 155.8, 152.4, 147.6, 134.9, 133.5, 130.2, 129.6, 129.2, 125.1, 124.4, 123.1, 121.3, 110.7, 108.1 (Ar-C)52.3 (CH_3 ester), Anal.Calcd. for $C_{19}H_{15}NO_3$: C 74.75; H 4.91; N 4.59 **Found** C 74.39; H 4.68; N 4.35

Methyl 4-(5-formyl-1-(4-nitrophenyl)-1H-pyrrol-2-yl) benzoate (17)

Yellow, mp 66-68°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2348 (Aromatic ring), 1728 (C=O ester), 1649 (C=O aldehyde), 1578 and 1318 (Asym and sym -NO_2), Mass spectrum (EI, 70 eV, (I_{rel}%):350 [M^+] 100, 215 [M^+- $PhCOOCH_3$] 17, 320 [M^+- CHO] 26, 135 [$PhCOOCH_3$] 3, 76 [Ph] 18, ^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H,*J*= 3.1 Hz), 6.6 (d, 1H, *J*= 3.1 Hz), 3.9 (s, 1H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.5 (C=O aldehyde), 164.6 (C=O ester) 152.4, 149.4, 130.2, 126.3, 125.1, 125.1, 124.7, 123.1, 121.5, 113.4, 109.4 (Ar-C), 52.3 (CH_3 ester), Anal.Calcd.for $C_{19}H_{14}N_2O_5$: C 65.14; H 4.00; N 8.00 **Found** C 64.84; H 3.95; N 7.78

Methyl 4-(5-formyl-1-(4-chlorophenyl)-1H-pyrrol-2-yl) benzoate (18)

Yellow, mp 98-100°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2345 (Aromatic ring), 1718 (C=O ester), 1645 (C=O aldehyde), 1091 (C-Cl bond), Mass spectrum (EI, 70 eV, (I_{rel}%): 341 [M^++2] (100), 339 [M^+] (40), 229 [M^+-PhCl] 21, 310 [M^+- CHO] 5, 135 [$PhCOOCH_3$] 2, 76 [Ph] 55,^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.2-7.3 (m, 8H), 7.1 (d, 1H,*J*= 3.3 Hz), 6.9 (d, 1H, *J*= 3.3 Hz), 3.9 (s, 1H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.5 (C=O aldehyde), 166.5 (C=O ester) 157.9, 152.6, 147.2, 132.8, 130.7, 130.2, 129.4, 125.1, 124.7, 123.5, 122.9, 122.3, 110.0, 109.7 (Ar-C), **52.30** (CH_3 ester), Anal.Calcd.for $C_{19}H_{14}ClNO_3$:C 67.25; H 4.12; N 4.12 **Found** C 67.13; H 3.98; N 3.69

Methyl 4-(5-formyl-1-(4-bromophenyl)-1H-pyrrol-2-yl) benzoate (19)

Yellow, mp 134-136°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2365 (Aromatic ring), 1715 (C=O ester), 1645 (C=O aldehyde), 1021 (C-Br bond), Mass spectrum (EI, 70 eV, (I_{rel}%):385 [M^++2] (38), 383 [M^+] (11), 64 [pyrrole] (37), ^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.8-7.3 (m, 8H), 7.1 (d, 1H,*J*= 5.2 Hz), 6.6 (d, 1H, *J*= 5.2 Hz), 4.4 (s, 1H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.7 (C=O aldehyde) 165.9 (C=O ester) 131.6, 130.3, 130.2, 128.9, 125.1, 109.3 (Ar-C)52.3 (CH_3 ester), Anal.Calcd.for $C_{19}H_{14}BrNO_3$: C 59.53; H 3.65; N 3.65 Found C 59.27; H 3.17; N 3.42

4-(2-formyl-5-(4-(methoxycarbonyl) phenyl)-1H-pyrrol-1-yl) benzoic acid (20)

Yellow, mp 138-140°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2359 (Aromatic ring), 1725(C=O ester), 1698 (C=O acid), 1610 (C=O aldehyde),3267 (-OH)Mass spectrum (EI, 70 eV, (I_{rel}%):349 [M^+] (100), 321 [M^+-CHO] (50), 304 [M^+-COOH] (11) ,64 [pyrrole] (14),^{1}H NMR (300MHz , $CDCl_3$), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H,*J*= 5.5 Hz) 6.8 (d, 1H,*J*= 5.5 Hz), 4.4 (s, 1H), 10.9 (s, 1H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 178.4 (C=O aldehyde), 166.4 (COOH), 165.9 (C=O ester) 147.9, 142.6, 132.9, 130.8, 130.3, 130.2, 125.1, 125.1, 122.9, 109.4 (Ar-C)52.3 (CH_3 ester), Anal. Calcd.for $C_{20}H_{15}NO_5$: C 68.76; H 4.29; N 4.01 Found C 68.45; H 4.08; N 3.75

Methyl 4-(2-formyl-5-(4-(methoxycarbonyl) phenyl)-1H-pyrrol-1-yl) benzoate (21)

Yellow, mp 166-168°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2365 (Aromatic ring), 1715 (C=O ester), 1649 (C=O aldehyde), Mass spectrum (EI, 70 eV, (I_{rel}%):363 [M^+] 100, 304 [M^+- $COOCH_3$] 17, 332 [M^+- CHO] 29, 135 [$PhCOOCH_3$] 6, 76 [Ph] 13,^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.6(s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H,*J*= 3.50 Hz), 6.8 (d, 1H,*J*= 3.50 Hz), 4.0 (s, 1H)^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.5 (C=O aldehyde) 1654.5 (C=O ester) 131.6, 130.3, 125.1, 109.4 (Ar-C),52.3 (CH_3 ester), Anal.Calcd.for $C_{21}H_{17}NO_5$: C 69.42; H 4.68; N 3.85 Found C 69.15; H 4.28; N 3.44

4-(2-formyl-5-(4-(methoxycarbonyl) phenyl)-1H-pyrrol-1-yl) benzenesulfonamide (22)

Yellow, mp 120-122°C (EtOH)**,** FTIR (KBr) (ν, cm^{-1}): 2345 (Aromatic ring), 1725 (C=O ester), 1610 (C=O aldehyde), 3240 (-NH), Mass spectrum (EI, 70 eV, (I_{rel}%):384 [M^+] (75), 356 [M^+-CHO] (100), 325 [M^+-$COOCH_3$] (45), 304 [M^+-SO_2NH_2] (11), ^{1}H NMR (300MHz, $CDCl_3$), δ ppm(*J,* Hz): 9.6 (s, 1H), 8.1-7.3 (m, 8H), 6.9 (d, 1H,*J*= 6.3 Hz), 6.9 (d, 1H,*J*= 6.3 Hz), 4.4 (s, 1H), 1.5 (s, 2H) ^{13}C NMR spectrum ($CDCl_3$, 75 MHz) δ ppm: 177.3 (C=O aldehyde), 166.4 (C=O ester) 157.95, 152.6, 132.9, 130.8, 130.3, 130.2, 125.1, 122.9 (Ar-C)52.3 (CH_3 ester), Anal. Calcd.for $C_{19}H_{16}N_2O_5S$: C 59.37; H 4.16; N 7.29 Found C 59.11; H 3.67; N 7.09

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