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ULTRASOUND INDUCED BICYCLO HETEROCYCLES OF FURAN

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Abstract:
3-Benzoyl propionic acid was converted into 5-phenyl furan-2-one by treating it with Ac_2O in presence of H_2SO_4. 5H-3-amino–4-cyano-5-(substituted) phenyl-8–phenyl–2,9–dioxa [4.2.0] bicyclo–1(6),3,7-triene was obtained by reacting 5-phenyl furan-2-one with aromatic aldehyde and malanonitrile using sonication which promoted reduction in time and gave excellent yield. Structures of newly synthesized compounds were confirmed by spectral techniques. All synthesized compounds were screened for their anti microbial activity.

Key words: Furan, aromatic aldehyde, malanonitrile, amino pyrans and sonication.

Introduction:

The 4H-Pyran nucleus has proven itself to be a fertile source of biologically important molecules possessing a wide spectrum of biological and pharmacological activities, such as antimicrobial[i], antiviral[ii], mutagenicity[iii], antiproliferative[iv], sex pheromone[v], antitumor[vi], cancer therapy[vii] and central nervous system activity[viii]. Some of these molecules are widely used as cosmetics and pigments and as potential biodegradable agrochemicals[ix].

Sonication was used for carrying out the reaction since it is eco-friendly and time saving as well as it given excellent yield. Amino pyrans are already known for their active anti tubercular[x], antitumor[xi], antiviral[xii] and antifungal[xiii] activities. Due to the biological and pharmacological effects these molecules were chosen for synthesis.

Materials and Methods

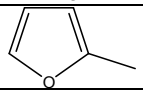
Melting points of all synthesized compounds were determined in open capillary tubes on an electro thermal apparatus and are uncorrected. The purity of the compounds was monitored by thin layer chromatography on silica gel coated aluminum plates (Merck) as adsorbent and UV light as visualizing agent. ^{1}H NMR spectra were recorded on Varian 500 MHz NMR spectrophotometer using $CDCl_3$/DMSO-d_6 as solvent and TMS as an internal standard (chemical shifts in δ ppm). C, H, N estimation was recorded on Carlo Erba 1108 (CHN) Elemental Analyzer

General Procedure:

Preparation of 5-phenyl furan-2-one (2)
A mixture of β-Benzoyl propanoic acid **(1)** (8.1gms, 0.05 mole) & acetic anhydride (10ml) in presence of concentrated sulfuric acid (2-3 drops) was stirred for 5 mins. Then, mixture was dumped on to crushed ice, solid thus separates out was filtered and washed with cold water, recrystallized form ethanol to yield 5-phenyl-furan-2(3H)-one **(2)**, melting point 91-92°C, yield 92%.

Synthesis of 5H-3-amino–4-cyano-5, 8–diphenyl–2, 9–dioxa [4.2.0] bicyclo–1(6),3,7-triene (5a) (Conventional)
An Equimolar solution of **(2)** (0.01 mole, 1.6g), Benzaldehyde (0.01 mole, 1.06 g) **(3)**, and malanonitrile (0.01 mole, 0.66g) **(4)** in methanol (10ml) and catalytic amount of piperidine were allowed to stir at room temperature. The reaction was monitored by TLC. Upon completion the reaction mass was quenched into crushed ice. The solid thus obtained, was filtered, washed with cold water and recrystallised from alcohol to afford compound **5a**. By adopting similar procedure **5b-f** were prepared and are listed in **Table I**

Synthesis of 5H-3-amino–4-cyano-5, 8–diphenyl–2,9–dioxa [4.2.0] bicyclo–1(6),3,7-triene (5a) (Sonication)
An Equimolar solution of **(2)** (0.01 mole, 1.6g), Benzaldehyde (0.01 mole, 1.06g) **(3)**, and malanonitrile (0.01 mole, 0.66g) **(4)** in methanol (10ml) and catalytic amount of piperidine were subjected to sonication. The reaction was monitored by TLC. The further step was carried forward as per above procedure.
Physical Charactersation table – Table 1

Compounds (5)	R′	M.F.	Molecular Weight(g)	m.p. (^{0}C)	Time(sec)		Yield (%)	
					C	S	C	S
a	H	$C_{20}H_{14}O_2N_2$	314	80	600	15	65	80
b	4- Cl	$C_{20}H_{13}O_2N_2Cl$	348.5	99	570	14	72	87
c	4- OCH_3	$C_{21}H_{16}O_3N_2$	344	120	500	10	75	87
d	4- OH	$C_{20}H_{14}O_3N_2$	330	85	550	13	73	88
e	4- OH-3- OCH_3	$C_{21}H_{16}O_4N_2$	360	135	570	14	74	86
f		$C_{17}H_{12}O_3N_2$	292	142	525	12	68	82

***C= Conventional, S= Sonication**
Spectral Interpretation:
5H-3-amino–4-cyano-5, 8–diphenyl–2,9–dioxa [4.2.0] bicyclo–1(6),3,7-triene (5a)
Anal.Calcd for $C_{20}H_{14}O_2N_2$: C: 76.43; H: 4.46; N: 8.92; O: 10.19%. Found C: 76.38; H: 4.41; N: 8.84; O: 10.25%. IR (cm^{-1}): 2225 (CN), 3210(NH_2), ^{1}H NMR (DMSO-d6, δ/ ppm):4.12 (s, 2H, NH_2), 4.75 (s, 1H, CH), 7.0-8.0 (m, 11H, Ar -H), ^{13}C NMR (DMSO-d6, δ/ ppm): 37.19 (CH), 116.92 (CN), 120.08- 152.48 (Ar-C & C=C)

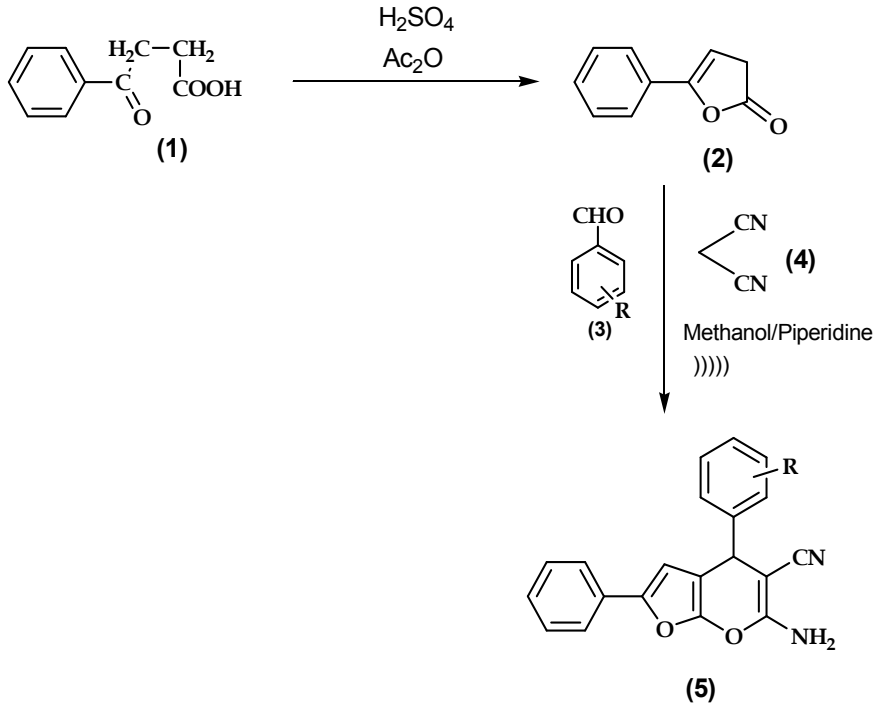
5H-3-amino–4-cyano-5-(4′-chloro) phenyl- 8–phenyl–2,9–dioxa [4.2.0] bicyclo–1(6),3,7-triene (5b)

Anal.Calcd for $C_{20}H_{13}O_2N_2Cl$: C: 68.87; H: 3.73; N: 8.03; O: 9.18%. Found C : 68.08 ; H: 3.81;
N: 8.11; O: 9.20%. IR (cm^{-1}): 2235 (CN), 3220(NH_2), ^{1}H NMR (DMSO-d6, δ/ ppm):4.32 (s, 2H, NH_2), 4.75 (s, 1H, CH), 7.0-8.0 (m, 10H, Ar -H), ^{13}C NMR (DMSO-d6, δ/ ppm): 38.19 (CH), 117.42 (CN), 120.08- 152.48 (Ar-C & C=C)

5H-3-amino–4-cyano-5-(4′-methoxy) phenyl- 8–phenyl–2,9–dioxa [4.2.0] bicyclo–1(6),3,7-triene (5c)

Anal.Calcd for $C_{21}H_{16}O_3N_2$: C: 73.26; H: 4.65; N: 8.14; O: 13.95%. Found C : 73.08; H: 4.41;
N: 8.24; O: 13.74%. IR (cm^{-1}): 1115 (C-O), 2222 (CN), 3215(NH_2), ^{1}H NMR (DMSO-d6, δ/ ppm):3.76(s, 3H, OCH_3), 4.12 (s, 2H, NH_2), 4.75 (s, 1H, CH), 7.0-8.0 (m, 10H, Ar -H), ^{13}C NMR (DMSO-d6, δ/ ppm): 37.19 (CH), 55.49 (OCH_3), 116.98 (CN), 120.08- 152.48 (Ar-C & C=C)

Reaction scheme:



Results and Conclusions:

Antimicrobial and antifungal activities

All the newly synthesized compounds were evaluated for their antibacterial activities against Gram-negative and Gram-positive bacteria using disc diffusion method. The zone of inhibition was measured in mm and the activities were compared with standard drug. The activities of representative compounds are reported in **Table II**

Table II

Antibacterial Activity of compound 5 & 6				
Compounds (5)	**Zone of inhibition (in mm)**			
	Gram Positive		**Gram negative**	
	S.aureus	***C.diphtheria***	***P.aeruginosa***	***E.coli***
a	21	23	18	19
b	17	25	16	13
c	22	19	20	15
d	18	17	19	12
e	23	20	18	17
f	20	18	22	19
Amphicilin trihydrate	26	28	24	21
DMSO	0	0	0	0

* Diameter of the disc was 6mm;
Concentration of the compounds taken was about 100 µg/Ml

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