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Multicomponent Reactions of Dapsone Derivatives: Synthesis, Study of Potentially Active Antimicrobial Bis 4*H*- Pyran and Bis 1,4- Dihydropyridine Derivatives.

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Abstract: The creation of 4*H*-pyran derivatives 4a and 4b was achieved through multi-component reactions involving dapsone derivative 2, aromatic aldehydes, and malononitrile (3), with triethylamine serving as the catalyst. Under analogous conditions, the same reaction pathway also yielded 1,4-dihydropyridine analogues 5a and 5b using ammonium acetate instead. Furthermore, the substitution of malononitrile with cyanoacetamide 6 under triethylamine catalysis afforded the 4*H*-pyran derivative 7. The compounds that were synthesized, were practiced in vitro, to test their efficacy against various microorganisms, this included testing against Gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*, Gram-negative bacteria like *Escherichia coli*, as well as fungal species including *Candida albicans* and *Aspergillus niger*. Among these, compounds 4b and 7 exhibited significant antimicrobial efficacy, with inhibition profiles comparable to those of the standard agents gentamycin and ketoconazole.

keywords: Dapsone, 4*H*-pyran, 1, 4-dihydropyridine, Antimicrobial.

1.Introduction

Methods where in three or more reactants are transformed in a one reaction pot concurrently are termed as Multicomponent reactions (MCRs), facilitating the efficient synthesis of complex molecular structures, have emerged as a powerful tool in modern synthetic chemistry. [1] Their high atom economy, operational simplicity, and convergent design make them an attractive alternative to

traditional stepwise approaches. Despite their advantages, the pursuit of innovative and broadly applicable MCR strategies continues to pose a significant challenge within both academic and industrial research environments. [2, 3]

The vast array of biological activity exhibited by 4*H*-pyran derivatives has attracted considerable scientific interest among the several classes of heterocyclic frameworks,[4] including antiphlogistic,[5] painkilling,[6] antioxidant,[7] tuberculosis inhibitor,[8] antidepressant,[9] tranquillizing,[10] and orally bioavailable pain-relieving properties [11] Since the pioneering contributions of Dömling and Ugi, who introduced enhanced four-component reactions (4CRs) [12] and the well-known Ugi reaction, multicomponent reactions (MCRs) have become a prominent focus in synthetic chemistry [13-15] particularly those employing isonitrile-based methodologies.[16-18] Nevertheless, many reported MCR protocols still remain largely confined to isonitrile chemistry, limiting their structural and mechanistic diversity.

The escalating threat of antimicrobial resistance underscores the urgent demand for new pharmacological agents capable of mitigating bacterial infections.[19] Heterocyclic compounds continue to serve as privileged scaffolds in medicinal chemistry, [20, 21] largely due to their structural diversity and potential for bioactivity modulation.[22] Originally synthesized in 1908, dapsone is a well-known antimicrobial agent that acts by disrupting the biosynthesis of dihydrofolic acid, ultimately inhibiting bacterial growth. [23] Although it has been employed in clinical settings for decades,

the precise redox pathways involved in its activity and the molecular basis of its associated toxicity remain incompletely understood.

In light of the documented antimicrobial potential of 2-amino-4*H*-pyran derivatives **(Figure 1)** and the therapeutic relevance of 1,4-dihydropyridine moieties **(Figure 2)**, The goal of this research is to create a set of unique hybrid chemicals incorporating both structural motifs, with the objective of enhancing antimicrobial efficacy and broadening the scope of active biological agents.

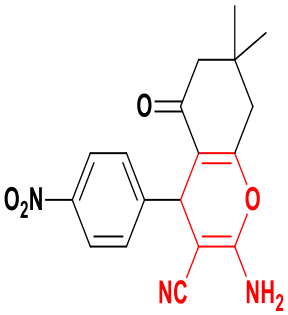


Figure 1.The structure of 2-amino-4*H*-Pyran compound with antimicrobial activity

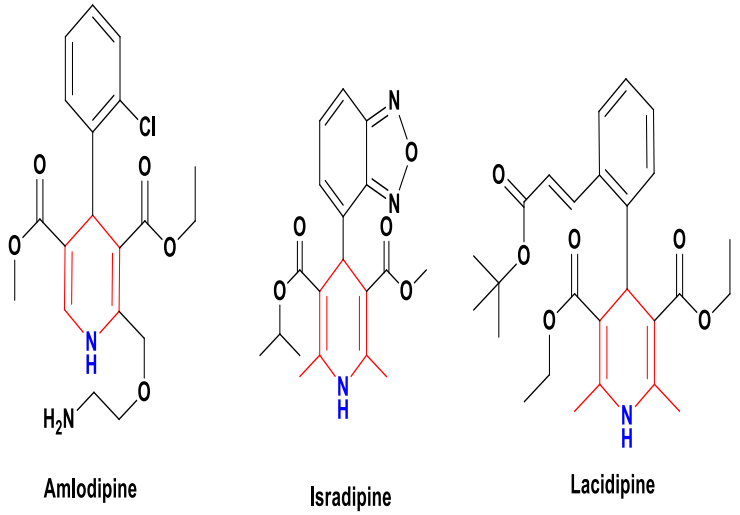


Figure 2. Some commertial available drugs containing 1,4- dihydropyridine moities

In light of this, the current study outlines a one-pot synthesis method for the efficient manufacture of 4*H*-pyran and 1,4-dihydropyridine derivatives through multi-component reactions involving dapsone derivative **2**, aromatic aldehydes and cyanomethylene-containing compounds. The synthesized derivatives were structurally described using infrared (IR), (^{1}H NMR), and mass spectroscopic techniques. Furthermore,The compounds that were synthesized were confirmed in vitro, to test their efficacy against various microorganisms, this included testing against Gram-positive bacteria such as *Staphylococcus aureus* and *Bacillus subtilis*, Gram-negative bacteria like *Escherichia coli*, as well as fungal species including *Candida albicans* and *Aspergillus nig*er.

2. Materials and methods

Instruments

The Gallenkamp device was used to record the melting points. Using the FT-IR 6300 equipment, the spectra were recorded onto KBr disk. A ^{1}H NMR spectrum was acquired with a 500 MHz Jeol instrument in DMSO-d_6 solvent.

Chemical shifts are given in δ. Mass spectrophotometry was investigated using Termoscientifc EI (70 eV). Electron impact (EI) mass spectra at 70 eV were collected at Al-Azhar University's Mycology and Biotechnology Center using Thermo Scientific Focus/DSQII equipment (Waltham, MA, USA).

N, N'-(Sulfonylbis(4,1-phenylene))bis(3-oxobutanamide)(2).

Dapsone (1) (0.24 g, 1 mmol) was reacted with

ethyl acetoacetate (0.26 mL, 2 mmol) under

reflux for 15 hours. Upon completion, the ethanol generated during the reaction was removed by

heating the resulting blackish liquid in a water

bath. The mixture was permitted to equilibrate to

room temperature, then the resultant solid was

obtained after filtering. The obtained product was further purified by stirring in

diethyl ether for 20 minutes, followed by filtration and thorough

drying. Final purification was achieved via recrystallization from ethanol, affording the target compound as a yellow powder; Mol. Formula: $C_{20}H_{20}N_2O_6S$; M.Wt:416.45.

Property	Details
Yield	0.35 g (85%)
Melting Point (m.p.)	155–157 °C
IR (ν/cm⁻¹)	3357 (NH), 2982 (CH-aliphatic), 1720, 1634 (C=O)
^{1}H NMR (DMSO-d_6, 500 MHz, δ ppm)	2.19(s, 6H, 2CH3), 3.58(s, 4H, 2CH2), 7.50(d, 1H, J= 5 Hz , Ar-H), 7.51(d, 1H, J= 5Hz , Ar-H), 7.73 (d,1H, J= 5Hz , Ar-H), 7.75(d, 1H, J= 5Hz , Ar-H), 7.81(d, 3H, J= 5Hz, Ar-H), 7.85 (d, 1H, J= 5Hz, Ar-H), 10.11(s, 2H, 2NH).

General procedure for the synthesis of 4-aryl-

4*H* pyran-3-carboxylic acid arylamide derivatives (4a, b).

A solution furfural (0.2 g, 0.002 mol) and/or 4-chlorobenzaldehyde (0.29 g, 0.002 mol) in 15 mL of 100% ethanol was introduced to a pre-prepared solution of dapsone derivative 2 (0.416 g, 0.001

mol) in 40 mL of 1,4-dioxane. Malononitrile

(0.13 g, 0.002 mol) was introduced to the mixture, accompanied by one or two drops of triethylamine.

The mixture was subsequently refluxed for 4–5 hours. Upon completion, The concoction

was let to cool until it reached ambient temperature before being transferred into ice-cold water while stirring vigorously. In order to obtain the target compound, the filtrate was composed, washed extensively with H_2O, and then recrystallized from EtOH.

***N, N*'-(Sulfonylbis(4,1-phenylene))bis(6-amino-**

5-cyano-4-(furan-2-yl)-2-methyl-4*H*-pyran-3-carboxamide)(4a).

Pale brown powder; Mol. Formula:

$C_{36}H_{28}N_6O_8S$; M.Wt: 704.71.

Property	Details
Yield	0.6 g (85%)
Melting Point (m.p.)	200–202 °C
IR (ν/cm⁻¹)	3452, 3287, 3107 (NH_2 and NH), 2223 (C≡N), 1646 (C=O)
^{1}H NMR (DMSO-d_6, 500 MHz, δ ppm)	2.10(s, 6H, $2CH_3$), 4.13(s, 2H, CH,4*H*-pyran), 6.14(s, 4H, Ar-H), 6.59(d, 4H, *J*= 5 Hz, Ar-H), 7.32(s, 2H, Ar-H), 7.50(s, 4H, $2NH_2$), 7.75- 7.86(m, 4H, Ar-H), 10.37(s, 1H, NH), 10.56(s, 1H, NH).
MS (EI) m/z (% relative intensity)	704.50 (M^+, 38.73), 693.51 (14.62), 642.06 (54.77), 477.03 (53.45), 441.09 (49.35), 386.59 (80.07), 272.32 (92.41), 210.21 (62.76), 147.64 (100), 141.47 (60.99), 127.98 (32.42), 111.42 (54.29)

N, N'-(Sulfonylbis(4,1-phenylene))bis(6-amino-

4-(4-chlorophenyl)-5-cyano-2-methyl-4H-pyran-3-carboxamide)(4b).

Black powder; Mol. Formula:

$C_{40}H_{30}C_{l2}N_6O_6S$; M.Wt: 793.67.

Property	Details
Yield	0.7 g (89%)
Melting Point (m.p.)	270–272 °C
IR (ν/cm⁻¹)	3492, 3452, 3420, 3387, 3356 (NH_2 and NH), 2200 (C≡N), 1663 (C=O)
^{1}H NMR (DMSO-d_6, 500 MHz, δ ppm)	2.18(s, 6H, $2CH_3$), 4.21(s, 2H, CH, 4*H*-pyran), 6.59(d, 2H, *J*= 10 Hz, Ar-H), 7.50 (d, 4H, *J*= 10 Hz, Ar-H), 7.74(br. s, 2H, Ar-H), 7.76 (br. s, 2H, Ar-H), 7.77 (br. s, 2H, Ar-H), 7.81(d, 2H, *J*= 10 Hz, Ar-H), 7.86 (d, 2H, *J*= 5 Hz, Ar-H), 7.93(s, 4H, $2NH_2$), 10.49(s, 2H, 2NH).
MS (EI) m/z (% relative intensity)	793.84 (M^+, 12.25), 793.10 (45.93), 765.85 (30.69), 660.25 (44.30), 604.91 (100), 511.17 (87.41), 487.22 (85.31), 479.40 (42.88), 290.06 (48.73), 179.00 (49.66), 99.25 (79.90)

General procedure for the synthesis of 4-aryl-1, 4- dihydro-pyridine-3-carboxylic acid arylamide (5a, b).

Combine 0.2 g of furfural or 0.29 g of 4-chlorobenzaldehyde with 15 mL of pure ethanol

and 40 mL of 1,4-dioxane to get dapsone

derivative **2**. Ammonium acetate (0.15 g, 0.002 mol) and malononitrile (0.13 g, 0.002 mol) were put into the final mixture, after three hrs of reflux heating, the reaction mixture was cooled, then the cooled mixture was then placed in icy water, and the precipitate was filtered and washed with H_2O. The target was refined by recrystallizing with ethyl alcohol.

***N, N'*-(Sulfonylbis(4,1-phenylene))bis(6-amino-5-cyano-4-(furan-2-yl)-2-methyl-1,4-dihydropyridine-3-carboxamide)(5a).**

Black powder; Mol. Formula: $C_{36}H_{30}N_8O_6S$; M.Wt: 702.74.

Property	Details
Yield	0.65 g (92%)
Melting Point (m.p.)	230–232 °C
IR (ν/cm⁻¹)	3480, 3345, 3103 (NH_2, NH), 2195 (CN), 1664 (C=O)
^{1}H NMR (DMSO-d_6, 500 MHz, δ ppm)	2.05 (s, 6H, $2CH_3$), 4.09 (s, 2H, CH, 4H-pyridine), 6.59 (d, 4H, J = 10 Hz, Ar-H), 6.65 (br. s, 2H, Ar-H), 7.52 (s, 4H, $2NH_2$), 7.72 (br. s, 2H, Ar-H), 7.74–7.76 (m, 2H, Ar-H), 7.82 (br. s, 2H, Ar-H), 7.84–7.87 (m, 4H, Ar-H), 10.38 (s, 2H, 2NH), 13.05 (s, 2H, 2NH)
MS (EI, m/z %)	702.11 (M^+, 14.51), 692.71 (12.02), 529.58 (25.37), 504.65 (16.54), 334.92 (100), 334.12 (66.78), 323.21 (19.95), 264.00 (24.35), 215.28 (46.30).

***N, N'*-(Sulfonylbis(4,1-phenylene))bis(6-amino-4-(4-chlorophenyl)-5-cyano-2-methyl-1,4-dihydropyridine-3-carboxamide)(5b).**

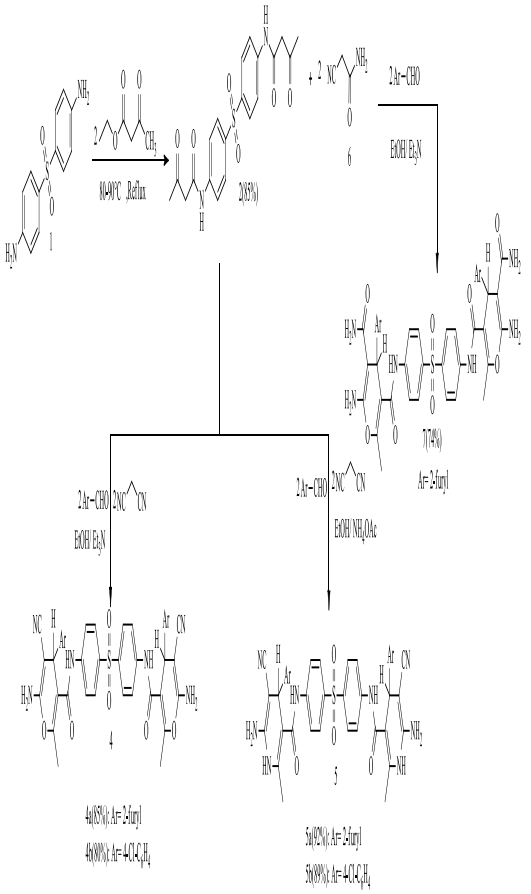
Brown powder; Mol. Formula: $C_{40}H_{32}Cl_2N_8O_4S$; M.Wt:791.70 .

Synthesis of N^3, $N^{3'}$-(sulfonylbis(4,1-phenylene))bis(6-amino-4-(furan-2-yl)-2-methyl-4*H*-pyran-3,5-dicarboxamide)(7).

A solution of dapsone derivative **2** (0.416, 0.001 mol) and furfural (0.2 g, 0.001 mol) in pure ethanol (15 mL) was treated with cyano-acetamide (6) (0.17 g, 0.002 mol) and Et_3N (0.50 mL) as a catalyst. Reflux heating the reaction mixture for five hours was followed by cooling it to room temperature. After cooling, the liquid was gradually added to ice-cold water while continually stirring. After filtering, the precipitate was rinsed with water, and refined via recrystallization from ethyl alcohol, producing the crude product as a reddish brown powder; Mol. Formula: $C_{36}H_{32}N_6O_{10}S$; M.Wt: 740.74.

Property	Details
Yield	0.71 g (89%)
Melting Point (m.p.)	263–265 °C
IR (ν/cm⁻¹)	3453, 3368, 3239 (NH_2, NH), 2054 (CN), 1693 (C=O)
^{1}H NMR (DMSO-d_6, 500 MHz, δ ppm)	2.05 (s, 6H, $2CH_3$), 4.12 (s, 2H, CH, 4H-pyridine), 6.63 (br. s, 6H, Ar-H), 7.53 (s, 4H, $2NH_2$), 7.76–7.92 (m, 10H, Ar-H), 10.39 (s, 2H, 2NH), 13.07 (s, 2H, 2NH)
MS (EI, m/z %)	791.03 (M^+, 21.59), 788.18 (29.24), 699.56 (47.82), 441.68 (54.64), 403.23 (100), 257.08 (50.86), 200.95 (51.66), 183.81 (67.51), 173.14 (57.16), 170.43 (52.33)

Property	Details
Yield	0.55 g (74%)
Melting Point (m.p.)	250–252 °C
IR (ν/cm⁻¹)	3454, 3364, 3102 (NH_2, NH), 1719, 1633 (C=O)
^{1}H NMR (DMSO-d_6, 500 MHz, δ ppm)	2.13 (br. s, 6H, $2CH_3$), 4.08 (s, 2H, CH, 4H-pyran), 6.10 (br. s, 2H, Ar-H), 6.55 (br. s, 2H, Ar-H), 7.46 (s, 4H, $2NH_2$), 7.58 (br. s, 5H, Ar-H), 7.69–7.76 (m, 5H, Ar-H), 7.98 (s, 4H, $2NH_2$), 9.56 (s, 2H, 2NH)
MS (EI, m/z %)	740.46 (M^+, 41.89), 713.73 (96.79), 553.83 (67.24), 517.06 (71.05), 475.45 (65.13), 404.91 (77.47), 229.25 (85.21), 215.29 (100), 112.72 (76.88)



Scheme 1. A brief schematic summary of all synthesized compounds.

Antimicrobial Assay:

In Cairo, Egypt, at the Bioscience Laboratory, researchers performed an antimicrobial activity

assay. They used the diffusion technique of agar

well to measure the antibacterial efficacy of the compounds they made. To do this, they inoculated agar plates with test organisms and aseptically punched 6 mm diameter wells into the agar. Each well

contained 100 µL of the test solution,

which had a concentration of 10 mg/Ml.

For bacterial and yeast strains, the plates were kept warm at 37°C for 24-48 hours. For filamentous fungus, the temperature was set at 28°C for 48 hours. Antimicrobial effectiveness was verified by measuring the width of the inhibition zones (millimeters). Dimethyl sulfoxide (DMSO) served as the solvent for the test substances and was also employed as the negative control; no inhibitory action was detected with DMSO, demonstrating its lack of effect on microbial evolution.

3. Results and Discussion

3.1. Chemistry

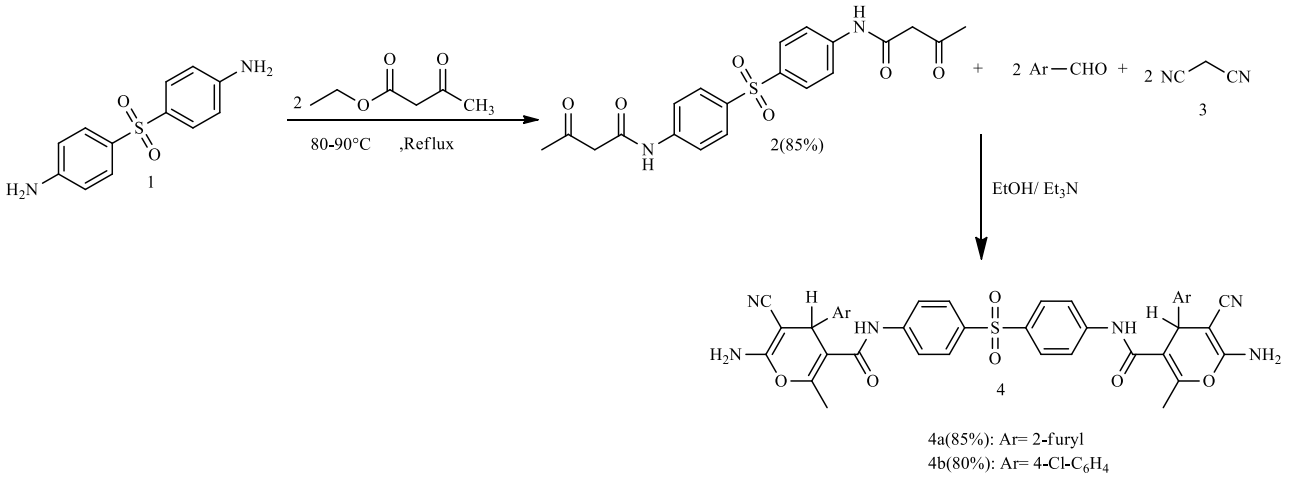
The condensation reaction between dapsone **1** and ethyl acetoacetate was performed at a temperature array of 80–90 °C, resulting in the formation of *N*, *N′*-(sulfonylbis(4,1-phenylene))bis(3-oxobutanamide) **(2)** [24] in an excellent yield of 85% **(Scheme 2)**. Infrared (IR) spectroscopy confirmed the transformation, as the characteristic absorption bands corresponding to the amino ($–NH_2$) groups of the starting material **1** disappeared, and a new absorption band performed at 1634 cm^{-1}, indicative of amide carbonyl stretching. This supports the successful formation of the amide bond through benzamine condensation. The ^{1}H NMR spectrum of chemical **2** displayed a singlet at δ 10.11 ppm, which corresponds to the amide NH proton. Additionally, methyl and methylene protons were observed at δ 2.19 and 3.58 ppm, respectively.

To explore the synthetic possibility of such a reaction for the preparation of 4*H*-pyran and 1,4-dihydropyridine derivatives, various catalysts were evaluated. A multicomponent reaction involving acetoacetanilide derivative **2**, malononitrile **(3)**, and either furfural or 4-chlorobenzaldehyde in absolute EtOH, with a

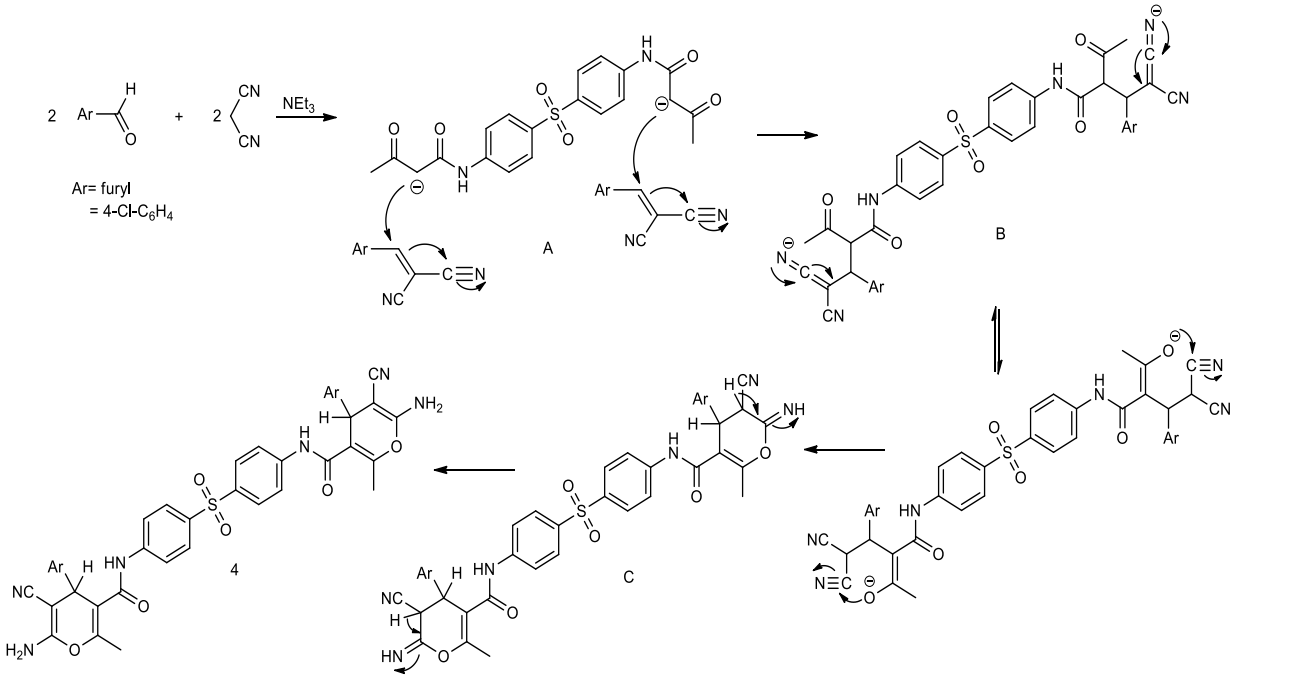
catalytic drops of triethylamine, led to the formation of 4*H*-pyran derivatives **4a** and **4b (Scheme 2)**. The formation of these products can be rationalized by a reasonable mechanism explained in Scheme **2A**. It is suggested that the reaction move forward via the first synthesis of acrylonitrile intermediate **A**, then a nucleophilic assault by the anion produced from butanamide, generating intermediate **B**. Subsequent cyclization and tautomerization of intermediate **C** afford

The structures of targets **4a** and **4b** were recognized centered on their spectral characteristics. For instance, Compound 4a's IR spectra showed absorption bands at 3452, 3287, and 3107 cm^{-1}, indicating -NH_2 and -NH stretching vibrations, and a band at 2223 cm^{-1} indicating the -CN group. , and a strong absorption at 1646 cm^{-1}consistent with a carbonyl (C=O) functionality. The ^{1}H NMR spectrum of **4a** showed a characteristic singlet

at δ 4.13 ppm corresponding to the H-4 proton of the 4*H*-pyran ring, a singlet at δ 7.50 ppm (exchangeable with D_2O) attributed to the $–NH_2$ group, and two additional singlets at δ 10.37 and 10.56 ppm, consigned to the –NH protons. Furthermore, The mass spectrum of compound 4a exhibited a molecular ion peak at m/z = 704.50, aligning with the molecular formula $C_{36}H_{28}N_6O_8S$.



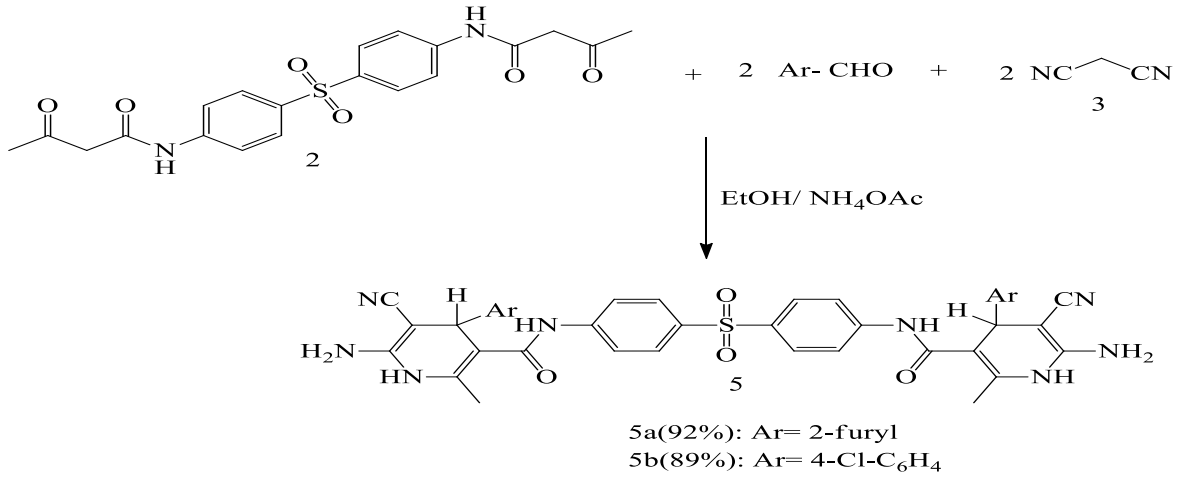
Scheme 2. Synthesis of 4-aryl-4*H*-pyran-3-carboxylic acid arylamide derivatives **4a** and **4b**.



Scheme 2 A. Plausible mechanism for the synthesis of 4-aryl-4*H*-pyran-3-carboxylic acid arylamide derivatives **4a and 4b.**

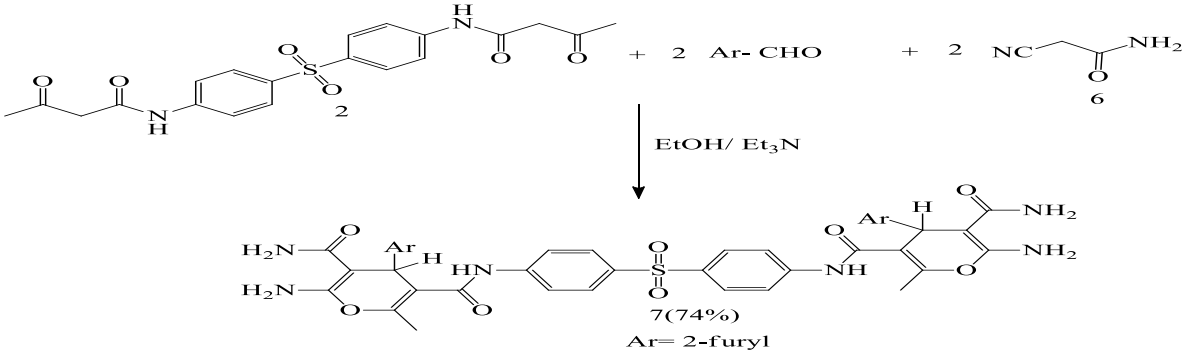
A strategic multicomponent reaction involving butanamide derivative **2**, malononitrile (3),

and either furfural or 4-chlorobenzaldehyde, conducted in absolute ethanol with ammonium acetate as a catalyst, led to the formation of 1,4-dihydropyridine derivatives 5a and 5b **(Scheme 3)**. The infrared spectrum of compound **5a** showcased distinct absorption bands at 3480, 3345, and 3103 cm^{-1}which are related to the stretching vibrations of the NH_2 and NH groups. Additionally, the characteristic nitrile stretch appeared at 2195 cm^{-1}, and the carbonyl stretch was observed at 1664 cm^{-1}. The ^1H NMR spectrum of 5a exposed the incidence of the 4*H*-pyridine H-4 proton at δ 4.09 ppm, along with a singlet at δ 7.52 ppm (exchangeable with D_2O), indicative of the NH_2 group. The mass spectrum of 5a displayed a molecular ion peak at m/z = 702.11, which aligned with the molecular formula $C_{36}H_{30}N_8O_6S$, confirming the structure.



Scheme 3. Synthesis of 4-aryl-1, 4-dihydropyridine-3-carboxylic acid arylamide derivatives **5a and 5b**.

To assess the broader applicability of this multicomponent reaction, the reaction was explored using a different cyanomethylene reagent, after optimizing the aforementioned conditions. When acetoacetanilide **2** was reacted with furfural and 2-cyanoacetamide **(6)** in absolute ethanol with drops of triethylamine, the 4*H*-pyran derivative **7** was successfully obtained **(Scheme 4)**. The infrared (IR) spectrum of compound **7** displayed characteristic absorption bands at 3454, 3364, and 3102 cm^{-1}, corresponding to the NH_2 and NH stretching vibrations, as well as peaks at 1719 and 1633 cm^{-1} recognized to the carbonyl (C=O) groups. In the ^1H NMR spectrum of compound **7**, the 4*H*-pyran H-4 proton appeared at δ 4.08 ppm, while a singlet at δ 9.56 ppm was assigned to the NH group. The NH_2 groups were spotted as a singlet at δ 7.98 ppm, which is consistent with the anticipated structure for 7. Additionally, the mass spectrum revealed a molecular ion peak at m/z = 740.46, which matched the molecular formula $C_{36}H_{32}N_6O_{10}S$.



Scheme 4. Synthesis of N^3, $N^{3'}$-(sulfonylbis(4,1-phenylene))bis(6-amino-4-(furan-2-yl)-2-methyl-4*H*-pyran-3,5-dicarboxamide **(7)**.

3.2. Antimicrobial Activity:

The percentage activity index of the chemical was considered according to the following formula:

$$\%\text{Activity Index} = \left(\frac{\text{Zone of Inhibition by Test Compound (mm)}}{\text{Zone of Inhibition by Standard (mm)}}\right) \times 100$$

As presented in Table **1**, all synthesized dapsone-based derivatives exhibited notable antimicrobial activity, with compound **7**, pyran-3,5-dicarboxamido derivative, demonstrating the highest efficacy among the tested chemicals, and achieved activity indices of **75.33%**, **73.12%**, **78.12%**, **76.66%**, and **78.33%** against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*,

Candida albicans, and *Aspergillus niger*, respectively.

The chlorine atom is present at the para-position (C-4) of the aryl ring in targets **4b** and **5b** appeared to enhance their antimicrobial profiles. Notably, the 1,4-dihydropyridine derivative **4b** exhibited considerable inhibitory effects, with activity indices of **60%**, **77.5%**, **74.37%**, **72.77%**, and **72.22%** against the aforementioned strains. Similarly, the furyl-substituted analogues **4a** and **5a** showed appreciable antibacterial potential. For instance, compound **4a** demonstrated inhibition indices of 53.12%, 61.25%, 53.75%, 57.77%, and 74.44%, respectively.

Overall, these findings highlight the broad-spectrum antimicrobial capabilities of the synthesized dapsone derivatives (4a, 4b, 5a, 5b, and 7), indicating their potential as promising therapeutic candidates. Nevertheless, the observed lack of activity of compound **5b**, a 4*H*-pyran-3,5-dicarboxamido derivative, (against *S. aureus* warrants further mechanistic studies to elucidate the structural or biochemical factors contributing to its selective antimicrobial behavior.

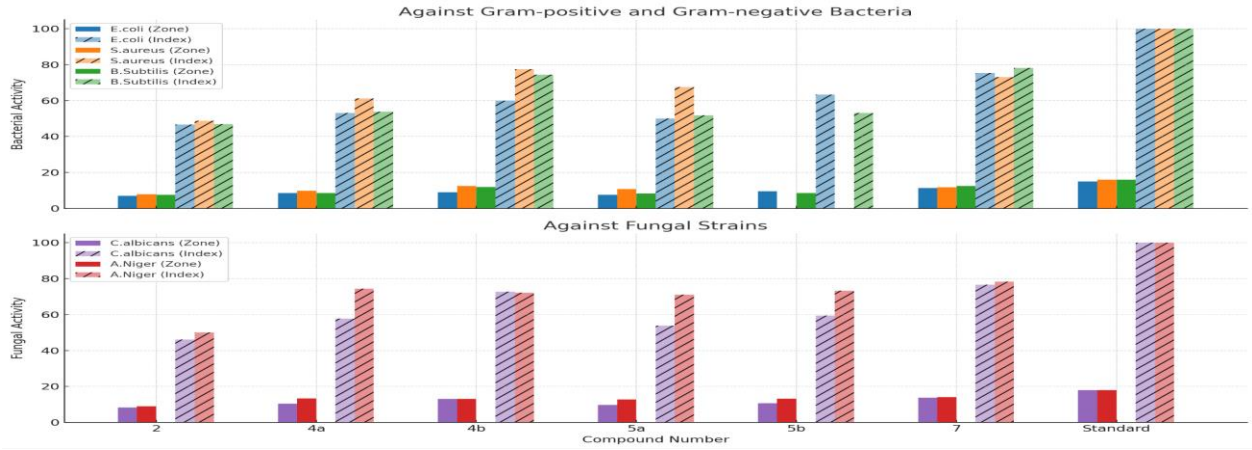


Figure 3. Antimicrobial activity (zone of inhibition and activity index) of dapsone derivatives against a spectrum of microbial strains.

Table 1: The antimicrobial activities of dapone derivatives:

Bacte-ria	***E.coli***		***S.aureus***		***B.Subtilis***		**Fungi**	***C.albicans***		***A.Niger***	
Compd. No.	**Diameter of inhibition zone (mm)**	**Activity index %**	**Diameter of inhibition zone (mm)**	**Acti-vity index %**	**Diameter of inhibition zone (mm)**	**Acti-vity index %**	**Compd. No.**	**Diameter of inhibition zone (mm)**	**Activity index %**	**Diameter of inhibition zone (mm)**	**Activity index %**
2	7	46.6	7.8	48.75	7.5	46.87	2	8.3	46.11	9	50.00
4a	8.5	53.12	9.8	61.25	8.6	53.75	4a	10.4	57.77	13.4	74.44
4b	9	60.00	12.4	77.5	11.9	74.37	4b	13.1	72.77	13	72.22
5a	7.5	50.00	10.8	67.5	8.3	51.87	5a	9.7	53.88	12.8	71.11
5b	9.5	63.33	NA	---	8.5	53.12	5b	10.7	59.44	13.2	73.33
7	11.3	75.33	11.7	73.12	12.5	78.12	7	13.8	76.66	14.1	78.33
Gentam-ycin	15	100	16	100	16	100	*Keto-conazo le*	18	100	18	100

A well diffusion test was used to measure antimicrobial activity; the well diameter was

6.0 mm, and 100 µL of each sample was added. Gentamycin at 4 mg/mL obliged as an indicator

of effective bacterial suppression, and keto-

conazole at 4 mg/mL assisted as an indicator of effective bacterial suppression. The concentration of the test compounds was standardized at 10 mg/mL. For bacterial and yeast strains, the plates were kept

warm at 37°C for 24-48 hours. For filamentous

fungus, the temperature was set at 28°C for 48 hours. Antimicrobial effectiveness was verified by measuring the width of the

inhibition zones (millimeters). Dimethyl sulfoxide (DMSO) served as the solvent for the test substances and was also employed as the negative control; no inhibitory action was detected with DMSO, demonstrating its lack of effect on microbial evolution. A measurement was taken of the inhibitory zone to determine activity, and "NA" denoted no activity.

Conclusion:

In summary, a straightforward synthetic approach was employed to design innovative 1,4-dihydropyridine and 4*H*-pyran derivatives. The regioselective reactivity of various reagents with the active site moiety of dapsone derivative **2** facilitated the generation of a diverse range of compounds. Several of the newly synthesized derivatives demonstrated promising antimicrobial activity. Notably, compounds **4b** and **7** exhibited potent antimicrobial efficacy, comparable to the reference standards, gentamycin and ketoconazole.

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