Supplementary

Electrochemical Synthesis and Antimicrobial Evaluation of some N-Phenyl α-Amino Acids

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Materials and Methods

The Sigma Aldrich chemical business provided all of the compounds utilized in the current methods, and they were all used without any further purification. Overnight, 4A molecular sieves were used to preserve the commercially available solvent CH₃CN (Merck). It was collected for further use in the reaction after distillation at a temperature of (80-82°C). The distillate solution was placed in P₂O₅ for roughly a night before being distilled once again to produce dry and pure CH₃CN. Bottles of acetonitrile were kept in a dark, airtight colour. All of the aqueous solutions were created using double-distilled water. We bought all of the solvents of the analytical grade from Loba Chemie. All of the developed heterocyclic compounds had their melting points measured using the open capillary method and a digital melting point instrument. IR spectrum recording is done using a Perkin Elmer Spectrum II with a diamond ATR. Using a Bruker Advanced NMR spectrometer in CDCl₃ and TMS as the internal standard, ¹H and ¹³C NMR data were both collected at 500 MHz. On the LC-MS Spectrometer Model Q-ToF Micromass, Waters, the MS of the compounds was recorded. With the aid of the Thin Layer Chromatography (TLC) method and UV light, the purity of compounds was verified.

Electrochemical Instrumentation:

Power source:

Direct current (DC) was used to power the electrocarboxylation process, and the electrophoresis power supply (Toshniwal) was equipped with a voltmeter that reads from 0-300V and an ammeter that can read 0-100mA.

Undivided cell:

An undivided three-necked electrochemical chamber made of Pyrex glass was utilized for the electrocarboxylation procedure. Cathode and anode electrodes were both submerged through two different openings in the proposed cell, and CO_2 gas was continuously passed through this third hole throughout the reaction.

As an inert cathode and sacrificial anode electrode, platinum gauze and magnesium electrodes with dimensions of (1cm X 1cm X 0.1cm) and (1cm diameter & 5cm length), respectively, were employed. Using a DC power supply, the cathode and anode were eventually connected to the positive and negative ends of the electric circuit, respectively.

Investigating the behaviour of concentrations of substrate and electrode matter

Under optimized conditions, the effect of sacrificial anodes, such as Al, Ni, and Mg was critically studied by electrolysed mixture of compound **3a** (0.54 mmol), MeCN (100 mL), TPAC (5 mmol), CO₂, at 20°C temperature by taking Pt as a cathode **Table S1**. Mg as a sacrificial anode gave the final product **4a** in a high yield of 92% (**Table S1**, **Entries 9**), while the utmost of 64% and 72% yield was obtained with Ni and Al electrode, respectively (**Table S1**, **Entries 1**& **5**). In present research, it was found that Pt as inert cathode with Mg as anode was the only suitable combination to carry on with considering other conditions.

Entry	Sacrificial anode	Conc.(mmol/L)	SRP (Volts)	Yield (%)
1.	Ni	0.64	-0.19	64
2.	Ni	1.12	-0.19	53
3.	Ni	1.53	-0.19	41
4.	Ni	2.15	-0.19	30
5.	Al	0.59	-1.62	72
6.	Al	1.05	-1.62	63
7.	Al	1.61	-1.62	59
8.	Al	2.15	-1.62	47
9.	Mg	0.54	-2.36	92
10.	Mg	1.05	-2.36	89
11.	Mg	1.59	-2.36	77
12.	Mg	2.15	-2.36	65

Table S1. Effect of SRP of concentration on the electrocarboxylation and sacrificial electrodes 4a.

Investigation of the relation of current density with temperature variation and pressure of carbon dioxide:

Other characteristics such as CO₂ pressure, temperature, and current density were studied in order to optimise the reaction conditions. In electrocarboxylation, current density is a critical factor (**Table S2**). The experiment was carried out at three densities *i.e.*, 10, 15 & 20 mA/cm², among them current densities at 10 & 20 mA/cm² gave lesser yield of tested compound **4a** however, at 15 mA/cm² better yield of the same compound was obtained. To determine the suitable temperature in combination with an appropriate CO₂ pressure was the next required step. After testing the reaction at temperature ranges between 0-25°C, it was observed that the yield of the formed product was less at low temperature range and data current density of 10mA/cm^2 (**Table-S2, entry-1**), while, the better yield was obtained at slightly high temperature (25°C) and at a current density of 20mA/cm^2 (**Table-S2, entry-1**). So, the

current density of 15mA/cm², temperature 20-25°C, and CO₂ pressure at 1 atm, were ideal conditions (**Table-S2**, entry-11 & 12) to get a higher yield of product *i.e.* 92%(**Table-S2**, entry-12).

Entry	Current Density(mA/cm ²)	Temperature(⁰ C)	Yield ^a (%)
1.	10	0	61
2.	10	5	65
3.	10	10	69
4.	10	15	75
5.	10	20	79
6.	10	25	75
7.	15	0	63
8.	15	5	74
9.	15	10	79
10.	15	15	80
11.	15	20	90
12.	15	25	92
13.	20	0	65
14.	20	5	69
15.	20	10	73
16.	20	15	75
17.	20	20	81
18.	20	25	79

Table S2. Standardization of current density and temperature (°C) for the synthesis of 4a.

Effect of solvents and supporting electrolyte

The results from distinct supporting electrolytes (TPAB, TPAC, and TBABF₄) with different solvents (*n*-Pentanol, *n*-Butanol, and MeCN) are summarized in **Table S3** on the yield of reference compound. Out of all the three solvents, MeCN along with TPAC as the supporting electrolyte comes out to be the best combination to produce 92% of **4a**. However, the other two solvents were difficult to remove, so it was supposed that the yield of the product was also diminished while evaporating those solvents.

Table S3. Standardization of solvent and supporting electrolyte for the synthesis of 4a.

3.	n-Pentanol	TBABF_4	82	
2.	n-Butanol	$TBABF_4$	83	
1.	MeCN	$TBABF_4$	89	
Entry	Solvent	Supporting Electrolyte	Yield ^a (%)	

5.	n-Butanol	TPAC	84
6.	n-Pentanol	TPAC	79
7.	MeCN	TPAB	81
8.	n-Butanol	TPAB	75
9.	n-Pentanol	TPAB	72

Antimicrobial Activity

Table S4. Minimum inhibitory concentration (MIC in μ g/mL) of synthesized amino acids derivatives **4a-l** against various microbial agents.

	Gram (+ve) bacteria Gram (-ve) bacteria		Fungi					
Compound	В.	S.	<i>E</i> .	К.	<i>S</i> .	А.	А.	А.
	Subtilis	Pyogenes	Coli	Pneumonia	Aureus	Janus	Niger	Sclerotiorum
4a	16	8	8	8	16	8	16	8
4b	16	16	8	16	16	16	8	16
4c	16	32	32	16	32	16	8	32
4d	8	4	8	4	8	16	8	16
4e	4	4	4	8	4	4	4	8
4f	8	8	16	8	16	16	16	8
4g	16	16	8	8	16	8	16	-
4h	64	16	32	16	32	32	32	16
4i	16	32	32	32	16	32	32	32
4j	32	16	8	-	16	32	16	16
4k	8	16	16	32	-	16	16	32
41	8	8	8	16	8	16	32	16
Amoxicillin	4	4	4	4	4	_	_	_
Fluconazole	-	-	_	-	-	2	2	2

General procedure of synthesis

Series **3a-1** has been already reported previously. Here imine derivative **3a** was prepared by the reaction of benzaldehyde (1.01mL, 10mmol) with aniline (0.91mL, 10mmol) at 85°C in ethanol for 2min using in microwave reactor. The completion of the reaction observed by TLC and finally works up in ice-cold water. The crude so obtained was recrystallized with ethanol to obtain colorless crystalline compound.

$$R-CHO + H_2N \xrightarrow{EtOH, 85^0C} R \xrightarrow{N}$$
1a-l 2
$$R \xrightarrow{N}$$

Scheme S1: Synthesis of imine derivatives.

Table S5.	Derivat	ives 3a-l	l with	observed	results
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Entry	Product	R	R _f	Yield	Melting Point	Literature
						Melting Point
1	3a	4-Cl C ₆ H ₄	0.61	98	62	62-64[25]
2	3b	C ₆ H ₅	0.66	98	55	54[25]
3	3c	4-Me C ₆ H ₄	0.63	96	39-41	38-40[25]
4	3d	4-OH C ₆ H ₄	0.69	95	96-97	94-96[25]
5	3e	$4\text{-NO}_2 \text{ C}_6\text{H}_4$	0.71	97	90-93	90-92[25]
6	3f	3-NO ₂ C ₆ H ₄	0.68	98	64-65	65-66[25]
7	3g	4-OMe C ₆ H ₄	0.62	93	64-66	63-65[25]
8	3h	$4\text{-Br }C_6H_4$	0.63	95	75-77	76-77[25]
9	3i	C ₆ H _s CH=CH	0.65	89	103-105	106-108[25]
10	3ј	2-Furyl	0.67	91	56-58	55-57[25]
11	3k	2-Thiopheyl	0.63	92	61-63	-
12	31	2-Pyridyl	0.59	90	65-66	-

^aYield refers to total mass of collection from different crops



3a: Yield 98%, colourless solid, MP 55°C. IR spectrum, v, cm⁻¹: 3060 (sp², C-H), 3028 (Ar-H), 1590 (C=N). ¹H NMR spectrum, δ , ppm (*J*, Hz): 8.13 (s, 1H, CH), 7.10-7.35 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 182 (M+1).



3b: Yield 96%, colourless solid, MP 39-41°C. IR spectrum, υ, cm⁻¹: 3140 (sp² C-H), 3030 (Ar-H), 1586 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.28 (s, 1H, CH), 7.06-7.26 (m, 10H, Ar-H), 2.14 (s, 3H, CH₃). Mass spectrum, *m/z*(*I*_{rel}, %): 196 (M+1).



3c: Yield 95%, colourless solid, MP 96-97°C. IR spectrum, υ, cm⁻¹: 3315(O-H), 3142 (sp² C-H), 3010 (Ar-H), 1584 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 9.1 (s, 1H, OH), 8.28 (s, 1H, CH), 7.09-7.27 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 198 (M+1).



3d: Yield 97%, pale yellow solid, MP 90-93°C. IR spectrum, *v*, cm⁻¹: 3170 (sp² C-H), 3039 (Ar-H), 1610 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.59 (s, 1H, CH), 7.23-7.84 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 227 (M+1).



3e: Yield 98%, pale yellow solid, MP 64-65°C. IR spectrum, v, cm⁻¹: 3152 (sp² C-H), 3033 (Ar-H), 1608 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.52 (s, 1H, CH), 7.22-7.79 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 227 (M+1).



3f: Yield 96%, colourless solid, MP 62°C. IR spectrum, v, cm⁻¹: 3149 (sp² C-H), 3029 (Ar-H), 1597 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.44 (s, 1H, CH), 7.13-7.44 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 216 (M+1), 217(M+2).



3g: Yield 93%, colourless solid, MP 64-66°C. IR spectrum, υ, cm⁻¹: 3122 (sp² C-H), 3019 (Ar-H), 1582 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.24 (s, 1H, CH), 7.09-7.23 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 212 (M+1).



3h: Yield 95%, colourless solid, MP 75-77°C. IR spectrum, υ, cm⁻¹: 3148 (sp² C-H), 3024 (Ar-H), 1599 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.27 (s, 1H, CH), 7.15-7.42 (m, 9H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 261 (M+1), 262 (M+2).



3i: Yield 89%, yellow solid, MP 103-105°C. IR spectrum, υ, cm⁻¹: 3149 (sp² C-H), 3015 (Ar-H), 1581 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.27 (s, 1H, CH), 6.89 (s, 1H, =CH), 7.27 (s, 1H, =CH), 7.11-7.34 (m, 10H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 208 (M+1).



3j: Yield 91%, yellow solid, MP 56-58°C. IR spectrum, v, cm⁻¹: 3144 (sp² C-H), 3033 (Ar-H), 1601 (C=N). ¹H NMR spectrum, δ , ppm (*J*, Hz): 8.43 (s, 1H, CH), 7.17-7.45 (m, 8H, Ar-H). Mass spectrum, $m/z(I_{rel}, \%)$: 172 (M+1).



3k: Yield 92%, yellow-brown solid, MP 61-63°C. IR spectrum, υ, cm⁻¹: 3140 (sp² C-H), 3025 (Ar-H), 1599 (C=N). ¹H NMR spectrum, δ, ppm (*J*, Hz): 8.47 (s, 1H, CH), 7.16-7.48 (m, 8H, Ar-H). Mass spectrum, *m/z*(*I*_{rel}, %): 188 (M+1).



31: Yield 90%, brown solid, MP 65-66°C. IR spectrum, v, cm⁻¹: 3132 (sp² C-H), 3029 (Ar-H), 1597 (C=N). ¹H NMR spectrum, δ , ppm (*J*, Hz): 8.46 (s, 1H, CH), 7.14-7.51 (m, 9H, Ar-H). Mass spectrum, $m/z(I_{rel}, \%)$: 183 (M+1).

To synthesize (4a)



Scheme S2: Synthesis of amino acids derivatives.

Table S6. Derivatives 4a-1 with observed results.

Entry	Product	R1	R _f	Yield ^a	Melting Point
1	4a	4-Cl C ₆ H ₄	0.66	92	196-197
2	4b	C ₆ H ₅	0.69	91	183-185
3	4c	4-Me C ₆ H ₄	0.61	86	174-175
4	4d	4-OH C ₆ H ₄	0.72	84	216-217
5	4e	$4-\mathrm{NO}_2\mathrm{C}_6\mathrm{H}_4$	0.70	91	210-212
6	4f	3-NO ₂ C ₆ H ₄	0.64	89	191-192
7	4g	4-OMe C_6H_4	0.66	86	206-208

1.0						
	8	4h	$4-Br C_6H_4$	0.69	85	178-180
	9	4i	C ₆ H _s CH=CH	0.73	82	225-226
	10	4j	2-Furyl	0.66	87	199-201
	11	4k	2-Thiopehyl	0.67	86	188-190
	12	41	2-Pyridyl	0.63	83	178-181

^aYield refers to total mass of collection from different crops



4a: Yield 92%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3356 (OH), 2970 (Ar-H), 2873 (C-H), 1619 (C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.79 (s, 1H, OH), 9.62 (s, 1H, NH), 8.23 (s, 1H, CH), 7.22-7.53 (m, 9H, ArH). ¹³C NMR spectrum, δ, ppm: 188.3, 145.9, 136.9, 129.7, 129.5, 129.1, 127.5, 120.8, 113.5, 64.3.Mass spectrum, *m/z*(*I*_{rel}, %): 228 (M+1).



4b: Yield 86%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3440 (OH), 3031 (Ar-H), 2978 (C-H), 1628 (C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.83 (s, 1H, OH), 9.51 (s, 1H, NH), 8.37 (s, 1H, CH), 7.14-7.739 (m, 10H, ArH), 2.23 (s, 3H, CH₃). ¹³C NMR spectrum, δ, ppm: 180.5, 155.9, 147.2, 143.9, 139.6, 139.5, 139.4, 130.8, 123.5, 74.3, 31.3. Mass spectrum, *m/z*(*I*_{rel}, %): 242 (M+1).



4c: Yield 84%, colourless solid, MP 183-185°C. IR spectrum, υ, cm⁻¹: 3428 (OH), 3031 (Ar-H), 2978 (C-H), 1610 (C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.87 (s, 1H, OH), 9.55 (s, 1H, NH), 8.42 (s, 1H, CH), 7.21-7.43 (m, 9H,

ArH). ¹³C NMR spectrum, δ , ppm: 180.5, 157.3, 145.9, 129.5, 128.9, 120.8, 116.3, 113.5, 64.3. Mass spectrum, $m/z(I_{rel}, \%)$: 244 (M+1).



4d: Yield 91%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3478 (OH), 3057 (Ar-H), 3020 (C-H), 1625(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 13.15 (s, 1H, OH), 9.87 (s, 1H, NH), 8.69 (s, 1H, CH), 7.38-8.03 (m, 9H, ArH). ¹³C NMR spectrum, δ, ppm: 180.5, 146.7, 145.9, 143.0, 129.5, 128.9, 127.9, 120.8, 113.5, 64.3. Mass spectrum, *m/z*(*I*_{rel}, %): 273 (M+1).



4e: Yield 89%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3470 (OH), 3053 (Ar-H), 3017 (C-H), 1612(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 13.03 (s, 1H, OH), 9.83 (s, 1H, NH), 8.63 (s, 1H, CH), 7.37-7.99 (m, 9H, ArH). ¹³C NMR spectrum, δ, ppm:180.5, 148.3, 145.9, 136.8, 135.8, 130.0, 129.5, 123.5, 122.7, 120.8, 113.5, 63.3. Mass spectrum, *m/z*(*I*_{rel}, %): 273 (M+1).



4f: Yield 83%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3448 (OH), 3048 (Ar-H), 2991 (C-H), 1628(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.85 (s, 1H, OH), 9.59 (s, 1H, NH), 8.54 (s, 1H, CH), 7.25-7.60 (m, 9H, ArH). ¹³C NMR spectrum, δ, ppm:180.5, 145.9, 135.0, 133.1, 129.5, 129.2, 128.9, 120.8, 113.5, 64.3. Mass spectrum, *m/z*(*I*_{rel}, %): 262 (M+1), 263(M+2).



4g: Yield 86%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3421 (OH), 3039 (Ar-H), 2983 (C-H), 1605(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.80 (s, 1H, OH), 9.51 (s, 1H, NH), 8.37 (s, 1H, CH), 7.22-7.53 (m, 9H, ArH), 3.98 (s, 3H, OMe). ¹³C NMR spectrum, δ, ppm:180.5, 159.4, 145.9, 129.5, 129.2, 128.5, 120.8, 114.7, 113.5, 64.3, 55.8. Mass spectrum, *m/z*(*I*_{rel}, %): 258 (M+1).



4h: Yield 85%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3446 (OH), 3037 (Ar-H), 2989 (C-H), 1622(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.89 (s, 1H, OH), 9.62 (s, 1H, NH), 8.42 (s, 1H, CH), 7.22-7.57 (m, 9H, ArH), 5.34 (d, 2H). ¹³C NMR spectrum, δ, ppm:180.5, 145.9, 135.9, 132.0, 131.9, 129.5, 121.9, 120.8, 113.5, 64.3. Mass spectrum, *m/z*(*I*_{rel}, %): 307 (M+1), 308(M+2).



4i: Yield 82%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3442 (OH), 3050 (Ar-H), 2987 (C-H), 1616(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.92 (s, 1H, OH), 9.63 (s, 1H, NH), 8.61 (s, 1H, =CH), 7.48 (s, 1H, CH), 7.23-7.58 (m, 10H, ArH), 6.91 (s, 1H, =CH). ¹³C NMR spectrum, δ, ppm:184.1, 147.6, 136.4, 129.5, 128.6, 128.5, 127.9, 123.3, 120.8, 113.5, 72.3. Mass spectrum, *m/z*(*I*_{rel}, %): 254 (M+1).



4j: Yield 87%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3434 (OH), 3049 (Ar-H), 2997 (C-H), 1633(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.95 (s, 1H, OH), 9.57 (s, 1H, NH), 8.62 (s, 1H, CH), 7.28-7.68 (m, 8H, ArH). ¹³C NMR spectrum, δ, ppm:178.5, 145.9, 142.8, 139.3, 129.5, 120.8, 118.6, 113.5, 110.7, 60.0. Mass spectrum, *m/z*(*I*_{rel}, %): 218 (M+1).



4k: Yield 86%, colourless solid, MP 183-185°C. IR spectrum, v, cm⁻¹: 3439 (OH), 3047 (Ar-H), 2998 (C-H), 1628(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.87 (s, 1H, OH), 9.58 (s, 1H, NH), 8.61 (s, 1H, CH), 7.23-7.62 (m, 8H, ArH). ¹³C NMR spectrum, δ, ppm:178.5, 145.9, 137.5, 129.5, 128.1, 126.1, 121.3, 120.8, 113.5, 65.5. Mass spectrum, *m/z*(*I*_{rel}, %): 234 (M+1).



4I: Yield 83%, colourless solid, MP 183-185°C. IR spectrum, υ, cm⁻¹: 3445 (OH), 3055 (Ar-H), 3002 (C-H), 1615(C=O). ¹H NMR spectrum, δ, ppm (*J*, Hz): 12.93 (s, 1H, OH), 9.65 (s, 1H, NH), 8.63 (s, 1H, CH), 7.34-7.79 (m, 9H, ArH). ¹³C NMR spectrum, δ, ppm:178.5, 155.4, 148.6, 145.9, 136.2, 129.5, 121.9, 120.9, 120.8, 113.5, 72.9. Mass spectrum, *m/z*(*I*_{rel}, %): 229 (M+1).



IR spectra of compound 4a



¹H-NMR of compound 4a



¹³C-NMR of compound 4a



Mass spectrum of compound 4a



¹H-NMR of compound **3**k



¹H-NMR of compound **3**l



¹H-NMR of compound **4i**



¹H-NMR of compound 4k



¹H-NMR of compound **4**l