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Electrochemical synthesis and antimicrobial evaluation of some *N*-phenyl α-amino acids†

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In the present report, the authors describe a synthetic route for the generation of *N*-phenyl amino acid derivatives using CO_2 *via* a C–C coupling reaction in an undivided cell containing a combination of Mg–Pt electrodes. The reactions were completed in a short time without the formation of any other side product. The final products were purified *via* a simple recrystallization procedure. The structures of the newly prepared compounds were established using advanced spectroscopic techniques including ^{1}H, ^{13}C NMR, IR, and ESI-MS. All the prepared derivatives show good-to-excellent activity when tested against bacterial and fungal strains. Interestingly, it was observed that the presence of polar groups (capable of forming H-bonds) such as –OH (**4d**) and $-NO_2$ (**4e**) at the *para* position of the phenyl ring show activity equivalent to the standard drugs.

1. Introduction

Amino acids are a type of biomolecule that contains an amino group, a carboxylate group, and a side chain.[1] Although hundreds of different amino acid side chains have been described and synthesized in the literature, only 20 amino acids have been identified as common building blocks of proteins.[2] In addition to their role as protein building blocks, amino acids are used for a variety of other applications in organic chemistry.[1] Because of their inherent chirality, they can act as ligands,[3] organocatalysts[4,5] and as structural linkers in agrochemicals[6] and pharmaceuticals.[7]

Furthermore, these 20 important amino acids have been connected to a number of substrates to achieve potent biological activities, such as antibacterial,[8] antifungal,[9] anticancer[10] inhibition of Type B monoamine oxidase,[11] and anti-fibrotic[12] activities. It has also been observed that *N*-substituted amino acids are more potent for a number of activities, such as PPAR γ-agonist,[13] hyperalphalipoproteinaemic,[14] anti-inflammatory,[9] anti-phlogistic,[10] anti-hypertensive,[15] anti-oxidant,[16] and anti-phlogistic activity.[17]

To date, a number of methods have been proposed for the formulation of amino acids, including simple refluxing,[18] visible light irradiation,[19] microwave irradiation,[20] and ultraviolet irradiation,[21] but these methods all have limitations. In continuation of our work on electro-carboxylation,[22–24] in the present report, we introduced a synthetic route for the production of *N*-substituted amino acids *via* an environmentally friendly electrochemical C–C coupling method using carbon dioxide.

2. Results and discussion

2.1. Optimization of reaction conditions

2.1.1. Investigating the effect of the concentration of the substrate and electrode materials. Under optimized conditions, the effect of sacrificial anodes, such as Al, Ni, and Mg, was critically studied using an electrolyzed mixture of compound **3a** (0.54 mmol), MeCN (100 mL), TPAC (5 mmol), and CO_2 at 20 °C with Pt as the cathode (Table 1). The use of Mg as a sacrificial anode gave the final product **4a** in a high yield of 92% (Table 1, entry 9), while maximum yields of 64% and 72% were obtained using Ni and Al electrodes, respectively (Table 1, entries 1 and 5). In the present research, it was concluded that the use of Pt as an inert cathode with Mg as an anode was the only suitable combination to carry on with exploring other conditions.

2.1.2. Investigation of the relationship of current density with temperature variation and the pressure of carbon dioxide. Other characteristics, such as the CO_2 pressure, temperature, and current density, were studied in order to optimize the reaction conditions. In electrocarboxylation, the current density is a critical factor (Table 2). The experiment was carried out at

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Table 1 Effect of SRP of concentration on the electrocarboxylation and sacrificial electrodes **4a**

Entry	Sacrificial anode	Conc. (mmol L^{-1})	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 2 Standardization of current density and temperature (°C) for the synthesis of **4a**

Entry	Current density (mA cm^{-2})	Temperature (°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

[a] Yield refers to combined yield from all the crops.

three densities *i.e.*, 10, 15 and 20 mA cm^{-2}; among them, the current densities of 10 and 20 mA cm^{-2} gave lower yields of the tested compound **4a**; however, at 15 mA cm^{-2}, a better yield of the same compound was obtained. Determination of the most suitable temperature in combination with an appropriate CO_2 pressure was the next required step. After testing the reaction at temperatures ranging from 0 to 25 °C, it was observed that the yield of the formed product was lower in the low-temperature range and at a current density of 10 mA cm^{-2} (Table 2, entry 1), while a better yield was obtained at a slightly high temperature (25 °C) and a current density of 20 mA cm^{-2} (Table 2, entry 17). Thus, a current density of 15 mA cm^{-2}, temperature of 20–25 °C, and CO_2 pressure of 1 atm were the ideal conditions (Table 2, entries 11 and 12) to obtain a higher yield of the product, *i.e.*, 92% (Table 2, entry 12).

Table 3 Standardization of solvent and supporting electrolyte for the synthesis of **4a**

Entry	Solvent	Supporting electrolyte	Yield[a] (%)
1	MeCN	$TBABF_4$	89
2	*n*-Butanol	$TBABF_4$	83
3	*n*-Pentanol	$TBABF_4$	82
4	**MeCN**	**TPAC**	**92**
5	*n*-Butanol	TPAC	84
6	*n*-Pentanol	TPAC	79
7	MeCN	TPAB	81
8	*n*-Butanol	TPAB	75
9	*n*-Pentanol	TPAB	72

[a] Yield refers to combined yield from all the crops.

2.1.3. Effect of solvents and supporting electrolyte.

The results for different supporting solutes (TPAC, TPAB, and $TBABF_4$) with different solvents (MeCN, *n*-butanol, and *n*-pentanol) on the production of the reference compound are summarized in Table 3. Out of the three solvents, MeCN with TPAC as the supporting electrolyte was found to be the best combination, producing **4a** in 92% yield. However, the other two solvents were difficult to remove; it was assumed that the yield of the product was also reduced while dissipating those solvents.

Various substitutions on the aldehyde moiety in the imine derivatives were reacted with CO_2 under similar reaction conditions for the generalization of the reaction, and it was discovered that the reactions proceeded smoothly and the desired molecules were collected in high yield as well as high purity. Finally, all the collected synthesized compounds were purified by simple recrystallization in ethanol.

2.2. Chemistry

Primary analysis of the products was conducted by comparing their melting points (MP), and the spectra later assisted in the illustration of the synthesized compounds. The IR spectra of compound **3a** in series **3** shows three considerable absorptions at 3149, 3029, and 1597 cm^{-1} corresponding to the C–H, Ar–H, and C═N groups. In the ^{1}H NMR spectrum (500 MHz, DMSO-d_6), the deshielded signal at δ 8.44 (s) is assigned to the proton of C-1 and the multiplet peak at δ 7.44–7.13 (m) is assigned to the aromatic protons. Furthermore, the presence of [M+1] and [M+2] peaks at 216 and 217 *m*/*z*, respectively, in the mass spectrum validates the formation of the expected compound.

The synthesis of amino acid derivative **4a** was confirmed by the downfield shift in the signal of the aromatic protons from δ 7.25 to δ 7.60, and also the singlet peak for the proton of N–H at δ 9.59 ppm. ^{13}C-NMR exhibits signals at δ 180.5 for the carboxylic group, with other peaks δ 129.5, 129.2, 128.9, 120.8, 113.5, and 64.3 confirming the formation of the targeted compound. In the IR spectrum, an additional broad peak at 3356 cm^{-1} demonstrates the –OH of the carboxylic group and a peak at 2873 cm^{-1} validates the C–H group. Furthermore, ESI-MS fragmentation generated [M+1] and [M+2] peaks at 262 and 263 *m*/*z* respectively, confirming the formation of the desired amino acid derivative.

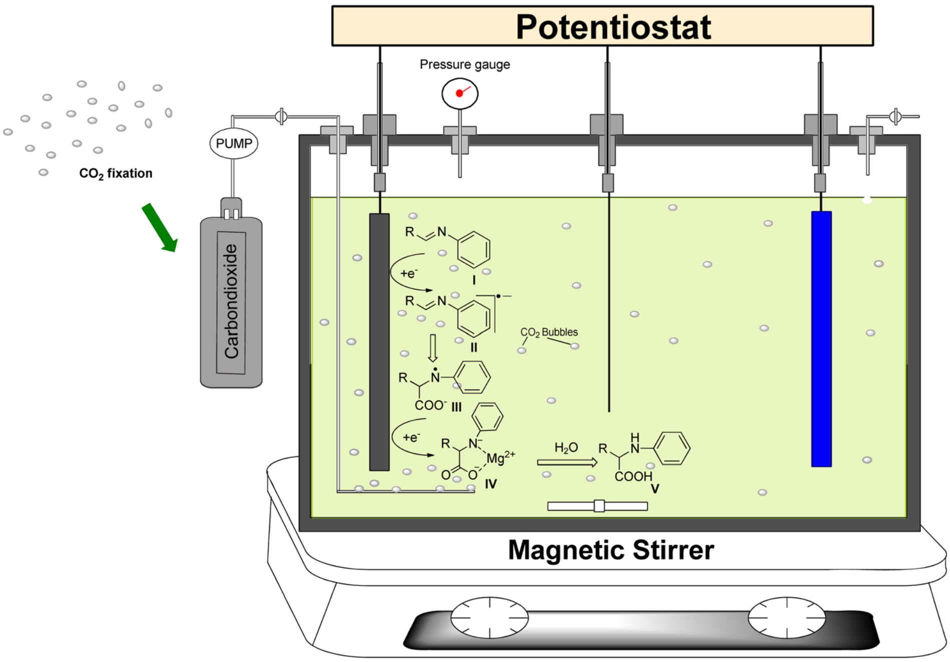


Fig. 1 Plausible reaction mechanism for the synthesis of amino acids.

2.3. Plausible mechanism for the synthesis of amino acid derivatives

Several reports on electrocarboxylation of unsaturated organic imines are available in which an undivided cell with magnesium as a stable sacrificial anode and platinum or silver as a cathode gives a much higher yield and carboxylation selectivity.[25,26] When the carboxylate ions are reduced and dissociated, a reactive radical is formed. These dissociated carboxylate ions react with the anode immediately to form $Mg(OH)_2$. The reactive intermediate **II** is then reduced again to form an intermediate **III** anion. The nucleophile **III** later reacts with CO_2 to produce carboxylate anion **IV** (Fig. 1). Finally, during the work-up, intermediate **IV** absorbs protons from the solution to produce the final compound.

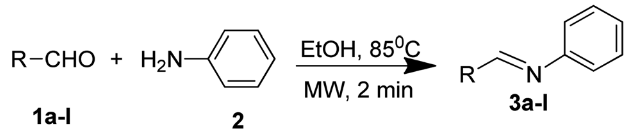
2.4. Antimicrobial activity

The anti-microbial potencies of the synthesized compounds **4a–l** were investigated using the Minimum Inhibitory Concentration (MIC) method. The findings were compared to the reference drugs fluconazole and amoxicillin in their respective areas at 4 g mL^{-1} and 2 g mL^{-1}, respectively. Table 4 shows that series **4a–l** has good-to-great activity against the preferred strain. Only five amino acids (**4a, 4d, 4e, 4f,** and **4g**) were found to be effective against various bacterial

Table 4 Minimum inhibitory concentration (MIC in μg mL^{-1}) of synthesized amino acids derivatives **4a–l** against various microbial agents

	Gram (+ve) bacteria		Gram (−ve) bacteria			Fungi		
Compound	*B. subtilis*	*S. pyogenes*	*E. coli*	*K. pneumonia*	*S. aureus*	*A. janus*	*A. niger*	*A. 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
4l	8	8	8	16	8	16	32	16
Amoxicillin	4	4	4	4	4	—	—	—
Fluconazole	—	—	—	—	—	2	2	2

(*B. subtilis*, *E. coli*, *S. aureus S. pyogenes*, and *K. pneumonia*) and fungal strains (*A. janus* and *A. niger*). Further, it was observed that the presence of polar groups that are capable of forming H-bonds, such as –OH (**4d**) and $–NO_2$ (**4e**) at the *para* position of the phenyl ring show maximum resistance against the microbes, which is equivalent to the standard drugs at MIC 4 μg mL^{-1}.



Scheme 1 Synthesis of imine derivatives **3a–l**.

3. Materials and methods

The commercial supplier Sigma Aldrich provided all of the compounds utilized in the current methods, which were all used without any further purification. 4A molecular sieves were used to preserve the commercially available solvent CH_3CN (Merck) overnight. It was collected for further use in the reaction after distillation at a temperature of 80–82 °C. The distillate was placed in P_2O_5 for about 24 h before being diluted once to produce dry and pure CH_3CN. Acetonitrile was stored in a dark-coloured and airtight bottles. All of the aqueous solutions were created using double-distilled water. We bought all of the solvents of analytical grade from Loba-Chemie. The melting points of all the developed heterocyclic compounds were measured using the open capillary method and a digital melting point instrument. Recording of IR spectra was conducted using a PerkinElmer Spectrum II with a diamond ATR. Using a Bruker Advanced NMR spectrometer, $CDCl_3$ as the solvent and TMS as the reference, ^1H and ^{13}C NMR data were both collected at 500 MHz. The mass spectra of the compounds was recorded on the LC-MS Spectrometer Model Q-ToF-Micromass, Waters. The purity of compounds was determined using the Thin Layer Chromatography (TLC) method and UV light.

3.1. Electrochemical instrumentation involved in setup

3.1.1. 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 0–300 V and an ammeter that can read 0–100 mA.

3.1.2. Undivided cell. An undivided three-necked electrochemical chamber made of Pyrex glass was utilized for the electrocarboxylation procedure. The 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 1 cm × 1 cm × 0.1 cm and 1 cm diameter and 5 cm 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.

4. Experimental

4.1. Synthesis of (*E*)-*N*,1-diphenylmethanimine (3a)

Imine derivative **3a** was prepared by the reaction of 4-chlorobenzaldehyde (1.40 g, 10 mmol) with aniline (0.91 mL, 10 mmol) at 85 °C in ethanol for 2 min using a microwave reactor. The progress of the reaction was observed *via* thin layer chromatography (TLC) and finally worked up in chilled water. The recrystallization was conducted with ethanol to yield colorless crystalline product **3a** (Scheme 1). Similarly, other imine derivatives have been synthesized using aldehydes **1b–l** with aniline **2** using the same procedure to obtain **3b–l** in excellent yield (Table 5).

3a: yield 98%, colourless solid, mp 62 °C. IR spectrum, ν, cm^{-1}: 3149 (sp^2 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).

3b: yield 98%, colourless solid, mp 55 °C. IR spectrum, ν, cm^{-1}: 3060 (sp^2, 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, 10H, Ar–H). Mass spectrum, *m*/*z* (I_{rel}, %): 182 (M+1).

3c: yield 96%, colourless solid, mp 39–41 °C. IR spectrum, ν, cm^{-1}: 3140 (sp^2 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, 9H, Ar–H), 2.14 (s, 3H, CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 196 (M+1).

3d: yield 95%, colourless solid, mp 96–97 °C. IR spectrum, ν, cm^{-1}: 3315 (O–H), 3142 (sp^2 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).

3e: yield 97%, pale yellow solid, mp 90–93 °C. IR spectrum, ν, cm^{-1}: 3170 (sp^2 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).

3f: yield 98%, pale yellow solid, mp 64–65 °C. IR spectrum, ν, cm^{-1}: 3152 (sp^2 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).

3g: yield 93%, colourless solid, mp 64–66 °C. IR spectrum, ν, cm^{-1}: 3122 (sp^2 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), 3.92 (s, 3H, OCH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 212 (M+1).

3h: yield 95%, colourless solid, mp 75–77 °C. IR spectrum, ν, cm^{-1}: 3148 (sp^2 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, ν, cm^{-1}: 3149 (sp^2 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, ν, cm^{-1}: 3144 (sp^2 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).

Table 5 Derivatives **3a–l** with observed results

Entry	Product	R	R_f	Yield[a] (%)	Melting point (°C)	Literature melting point (°C)
1	**3a**	4-Cl C_6H_4	0.61	98	62	62–64 (ref. 25)
2	**3b**	C_6H_5	0.66	98	55	54 (ref. 25)
3	**3c**	4-Me C_6H_4	0.63	96	39–41	38–40 (ref. 25)
4	**3d**	4-OH C_6H_4	0.69	95	96–97	94–96 (ref. 25)
5	**3e**	4-NO_2 C_6H_4	0.71	97	90–93	90–92 (ref. 25)
6	**3f**	3-NO_2 C_6H_4	0.68	98	64–65	65–66 (ref. 25)
7	**3g**	4-OMe C_6H_4	0.62	93	64–66	63–65 (ref. 25)
8	**3h**	4-Br C_6H_4	0.63	95	75–77	76–77 (ref. 25)
9	**3i**	C_6H_s CH=CH	0.65	89	103–105	106–108 (ref. 25)
10	**3j**	2-Furyl	0.67	91	56–58	55–57 (ref. 25)
11	**3k**	2-Thiophenyl	0.63	92	61–63	—
12	**3l**	2-Pyridyl	0.59	90	65–66	—

[a] Yield refers to total mass of collection from different crops.

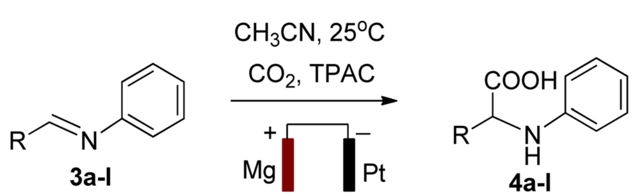
3k: yield 92%, yellow-brown solid, mp 61–63 °C. IR spectrum, ν, cm^{-1}: 3140 (sp^2 C–H), 3025 (Ar–H), 1599 (C=N). ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.47 (s, 1H, CH), 7.16–7.48 (m, 8H, Ar–H). Mass spectrum, *m/z* (I_{rel}, %): 188 (M+1).

3l: yield 90%, brown solid, mp 65–66 °C. IR spectrum, ν, cm^{-1}: 3132 (sp^2 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).

4.2. Synthesis of anilino(phenyl)acetic acid (4a)

To obtain amino acid derivative **4a**, an undivided electrochemical cell consisting of Mg as a sacrificial anode and Pt as an inert cathode was used, which was cleaned with diluted HNO_3, rinsed with distilled water and dried in an oven. Then, 0.54 mmol of imine derivative **3a** was added to a 100 mL quantity of CH_3CN containing 5 mmol of TPAC as a supporting electrolyte. In the next step, the designed electrolytic solution mixture was electrolyzed at 25 °C by maintaining a constant current density of 15 mA cm^{-2}. A continuous flow of CO_2 gas was also passed into the solution to maintain the required pressure (1 atm) over a 10 hours period to obtain compound **4a**.

Following this, the excess solvent was reduced under low pressure, while the solid residue was retained. Furthermore, to eliminate ionic residues from the solid, the extraction was carried out in a separating funnel with diethyl ether, and the product was left to dry using anhydrous $MgSO_4$. Finally, compound **4a** was obtained by recrystallizing the isolated crude product with ethanol (Scheme 2). Similarly, the other imine derivatives **3b–l** were converted into amino acid derivatives **4b–l** using the same procedure (Table 6).



Scheme 2 Synthesis of *N*-substituted amino acids **4a–l**.

4a: yield 92%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3356 (OH), 2970 (Ar–H), 2873 (C–H), 1619 (C=O). ^1H NMR spectrum, δ, ppm (*J*, Hz): 12.85 (s, 1H, OH), 9.59 (s, 1H, NH), 8.54 (s, 1H, CH), 7.14–7.80 (m, 9H, ArH). ^{13}C 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).

4b: yield 91%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3455 (OH), 3052 (Ar–H), 2825 (C–H), 1628 (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, 10H, ArH). ^{13}C 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).

4c: yield 86%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3440 (OH), 3031 (Ar–H), 2978 (C–H), 1610 (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, 9H, ArH), 2.23 (s, 3H, CH_3). ^{13}C 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).

4d: yield 84%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3428 (OH), 3031 (Ar–H), 2978 (C–H), 1625 (C=O). ^1H

Table 6 Derivatives **4a–l** with observed results

Entry	Product	R1	R_f	Yield[a] (%)	Melting point (°C)
1	**4a**	4-Cl C_6H_4	0.66	92	196–197
2	**4b**	C_6H_5	0.69	91	183–185
3	**4c**	4-Me C_6H_4	0.61	86	174–175
4	**4d**	4-OH C_6H_4	0.72	84	216–217
5	**4e**	4-NO_2 C_6H_4	0.70	91	210–212
6	**4f**	3-NO_2 C_6H_4	0.64	89	191–192
7	**4g**	4-OMe C_6H_4	0.66	86	206–208
8	**4h**	4-Br C_6H_4	0.69	85	178–180
9	**4i**	C_6H_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	**4l**	2-Pyridyl	0.63	83	178–181

[a] Yield refers to total mass of collection from different crops.

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). ^{13}C 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).

4e: yield 91%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3478 (OH), 3057 (Ar–H), 3020 (C–H), 1612 (C=O). ^{1}H 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). ^{13}C 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).

4f: yield 89%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3470 (OH), 3053 (Ar–H), 3017 (C–H), 1628 (C=O). ^{1}H 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). ^{13}C 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).

4g: yield 86%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3421 (OH), 3039 (Ar–H), 2983 (C–H), 1605 (C=O). ^{1}H 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). ^{13}C 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, ν, cm^{-1}: 3446 (OH), 3037 (Ar–H), 2989 (C–H), 1622 (C=O). ^{1}H 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). ^{13}C 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, ν, cm^{-1}: 3442 (OH), 3050 (Ar–H), 2987 (C–H), 1616 (C=O). ^{1}H 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). ^{13}C 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, ν, cm^{-1}: 3434 (OH), 3049 (Ar–H), 2997 (C–H), 1633 (C=O). ^{1}H 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). ^{13}C 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, ν, cm^{-1}: 3439 (OH), 3047 (Ar–H), 2998 (C–H), 1628 (C=O). ^{1}H 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). ^{13}C 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).

4l: yield 83%, colourless solid, mp 183–185 °C. IR spectrum, ν, cm^{-1}: 3445 (OH), 3055 (Ar–H), 3002 (C–H), 1615 (C=O). ^{1}H 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). ^{13}C 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).

4.3. Anti-microbial evaluation

The newly synthesized compounds **4a–l** were tested against three Gram −ve (*Escherichia coli* MTCC 443, *Klebsiella pneumonia* MTCC 3384, and *Staphylococcus aureus* MTCC 96), two Gram +ve (*Bacillus subtilis* MTCC 441, and *Streptococcus pyogenes* MTCC 442) and Fungus (*Aspergillus janus* MTCC 2751, *Aspergillus niger* MTCC 281, and *Aspergillus sclerotiorum* MTCC 1008) samples. Nutrient broth was used to store the bacteria samples after they had been cultured at 37 °C for 24 hours. The fungal strains, on the other hand, were grown in malt extract for 72 hours at 28 °C before inoculation. A serial dilution procedure was used to test each produced chemical in triplicate after it was dissolved in DMSO at doses of 128, 64, 32, 16, 8, 4, and 2 g mL^{-1}.

5. Conclusion

In this work, the authors synthesized 12 potent *N*-phenyl amino acid derivatives from imines and CO_2 *via* direct C–C coupling reaction in an undivided cell containing a combination of Mg–Pt electrodes. The products are obtained in a single step with adaptability and diversity in excellent yield and superior purity. This procedure is efficient in terms of labor, cost, and waste production, as well as the absence of harsh reaction conditions. All the synthesized amino acid derivatives show good-to-excellent resistance against the microbes. However, those with polar groups like –OH and $–NO_2$ at the *para* position on the phenyl ring show equivalent resistance compared to the standard drugs amoxicillin and fluconazole.

Abbreviations

TPAC	Tetrapropylammonium chloride
TPAB	Tetrapropylammonium bromide
$TBABF_4$	Tetrapropylammonium tetrafluoroborate
MIC	Minimum inhibitory concentration
SRP	Standard reduction potential
ATR	Attenuated total reflectance
TLC	Thin layer chromatography

Conflicts of interest

The authors declare that they have no conflict of interest.

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