



Research Article

Microwave-assisted triphenylphosphine catalyzed synthesis of substituted cyanoacrylamides and their antibacterial evaluation

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ARTICLE INFO

Article History

Received: 04 November 2025

Revised: 03 April 2026

Accepted: 07 May 2026

Keywords: Knoevenagel condensation, Microwave, Triphenylphosphine catalyst, Substituted cyanoacetamide.

ABSTRACT

Substituted cyanoacrylamides are important intermediates in the pharmaceutical and agrochemical industries. In this study, we report a triphenylphosphine (TPP)-catalyzed, microwave-assisted Knoevenagel condensation for the efficient synthesis of a series of substituted cyanoacrylamide derivatives from aromatic and heterocyclic aldehydes and cyanoacetamide under solvent-free conditions. The reactions were completed within 1–4 minutes at 300–600 W microwave power, affording the desired products in 75–90% isolated yields. The method eliminates the need for hazardous solvents and tolerates a wide range of functional groups, including fluoro, methyl, methoxy, nitro, cyano, and heterocyclic substituents. Compared with conventional heating, the microwave-assisted protocol offers significant advantages, including shorter reaction times, milder reaction conditions, and higher product yields. The structures of the synthesized compounds were confirmed by FTIR and ¹H NMR spectroscopy. Antibacterial evaluation of selected compounds using the agar well diffusion method revealed activity against both Gram-positive (*Staphylococcus* sp.) and Gram-negative bacteria (*Serratia* sp., *Proteus* sp., and *Klebsiella* sp.).

Introduction

Many solvents are environmentally unfriendly. Eliminating solvents in chemical processes or replacing hazardous solvents is a key area of green chemistry. Because of environmental concerns, organic reactions under solvent-free conditions have increasingly attracted chemists' interest, particularly from a green chemistry perspective (Toda, 1995; Tanaka, 2000).

Unsaturated compounds are among the most important compounds in organic chemistry. For their structural diversity and biological importance, unsaturated compounds have become attractive targets for organic synthesis. Recent development have produced physiologically potent unsaturated

compounds with interesting antiviral (Petrie et al., 1985), antibacterial (Liang Chan, 1998), and antitumor activity.

The use of microwave energy to enhance organic reactions has recently attracted chemists' attention. Microwave irradiation not only considerably reduces reaction times but also minimizes side processes, increases yields, and improves reproducibility. Microwave irradiation reduces environment impact and enable solvent-free protocols. The Knoevenagel condensation of aldehydes with active methylene compounds is an important and widely employed method for carbon-carbon bond formation in organic synthesis with

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numerous applications in the synthesis of fine chemicals (Freeman, 1981), hetero Diels-Alder reactions (Borah et al., 2005), as well as heterocyclic compounds of biological significance (Tietze, 1996).

Bases (Yang et al., 2006), such as sodium hydroxide or sodium ethoxide usually catalyze the reaction in organic solvents. Organic weak bases such as aliphatic amines and piperidine, or corresponding ammonium salts, are also used for the Knoevenagel reaction. (Acker and Hertler, 1962). Lewis acids, such as NbCl_3 and ZnCl_2 , and silica gel have also been employed to catalyze the reaction.

The active methylene cyanoacetamides are highly reactive compounds. The carbonyl and cyano functions of these compounds are suitably situated to react with common reagents and form a variety of heterocyclic compounds. Moreover, cyanoacetamides and their related heterocyclic derivatives have generated great attention due to their interesting biological, therapeutic value and pharmaceutical activities e.g., as herbicidal (Geissler et al., 1980), plant growth regulators (Wayne et al., 1977), anti-inflammatory (Roifman et al., 2000), antitumor (Fahmy et al., 2002) and analgesic properties (Ismail et al., 2007). Microwave-promoted organic synthesis is a fast, efficient heating method used to complete a desired reaction. Microwave irradiation's ability to reduce reaction time led to an idea of carrying out this synthesis under microwave irradiation. The syntheses of some arylidenemalonitriles by the reaction of malonitriles and aldehydes, as well as the synthesis of selective acrylates by condensation reaction, have also been reported (Bhuiyan et al., 2012; Begum et al., 2015; and Jhillu et al., 2004). Yadav also reported the synthesis of α -Cyanoacrylates and α -Cyanoacrylonitriles using a phosphane catalyst (Jhillu et al., 2004). Microwave-assisted, solvent-free reactions (Wang et al., 2001) represent powerful green chemical technologies from both economical and synthetic perspective. In

our previous report, we reported microwave-assisted synthesis of arylidene derivatives using NH_4OAc as a catalyst (Ahmed et al., 2018). Triphenylphosphine (TPP) is a well-known organophosphorus compound widely used in organic synthesis due to its nucleophilic properties and ability to stabilize carbanions. However, its potential as a catalyst for synthesizing cyanoacrylamides remains unexplored. This research aims to fill up this gap by developing a TPP-catalyzed method for synthesizing substituted cyanoacrylamides under mild and metal-free conditions.

Continuing our interest to studying organic reactions and transformations using mild, eco-friendly catalysts under microwave irradiation, we report a mild and efficient triphenylphosphine-catalyzed synthesis of known and new substituted cyanoacrylamides, along with preliminary antibacterial evaluation of selected compounds.

In this study, we report a triphenylphosphine (TPP)-catalyzed microwave-assisted Knoevenagel condensation to synthesize a series of substituted cyanoacrylamides under solvent-free conditions. The reactions proceeded efficiently within 1–4 minutes at 300–600 W, affording the target compounds in 75–90% isolated yields. The synthesized compounds were evaluated for antibacterial activity against both Gram-positive and Gram-negative bacterial strains, and several compounds demonstrated notable inhibitory activity.

Experimental

Materials and Methods

General remarks: All Chemicals were obtained from commercial sources (Sigma-Aldrich and Merck, Germany) and were used without further purification. All reactions were performed using standard techniques. GALLER KAMP melting point apparatus was used to record the melting point of the solid compound; heating was done carefully to ensure a steady temperature rise. ^1H NMR spectra were recorded on a JEOL JNM ECS FT NMR at 400 MHz spectrometer using tetramethylsilane as an

internal standard. Coupling constants J are given in Hz. Infrared spectra were observed on a Shimadzu FTIR- spectrometer (IR Prestige 21). Analytical TLC was performed on pre-coated alumina sheet, and the product was visualized by UV light. All reactions were carried out in a domestic microwave oven (Samsung, MW76ND).

General procedure for the synthesis of substituted cyanoacrylamides (3a – k): A mixture of substituted aldehyde (2 mmol), cyanoacetamide (2 mmol), and triphenylphosphine (20% mol) was placed in a Pyrex glass 50 mL beaker and mixed thoroughly with a small amount of ethyl acetate with the help of a glass rod. The reaction mixture was then subjected to microwave irradiation at 100 to 600W for 1- 4 minutes. The reaction progress was monitored by TLC (hexane: ethyl acetate). After cooling, the crude solid product was recrystallized from ethyl acetate and hexane to get the pure substituted cyanoacrylamides 3 (Scheme 1). All the products (3a-3k) were prepared by using the same procedure. We characterized all products by comparing their ^1H NMR and FTIR spectra, TLC data, and physical data with authentic samples. The FTIR and ^1H NMR spectroscopic data of the products were identical to those reported in the literature (Mogilaiah et al., 2003; Moemen et al., 2015; Gerd Kaupp et al., 2003).

2-cyano-3-(4-methylphenyl)acrylamide (3a): White crystal, yield : 82%MF: : $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}$, Mp : 146-148°C.

IR (KBr): ν (cm^{-1}) 3388 and 3319 (N-H str. For NH_2), 3161 (aromatic C-H str.), 3052 (sp^2 C-H str.), 2220 ($\text{C}\equiv\text{N}$ str.), 1697 (CO str.), 1591 (alkene C=C str.), 1563 and 1508 (aromatic C=C str.), 1375 (C-N str), 1215 (C-O str.).

^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.33(s, 1H), 7.88(d, $J=8$, 2H), 7.33(d, $J=8$, 2H), 6.33(s, 1H, N-H), 5.80(s, 1H, N-H), 2.46(s, 3H).

2-cyano-3-(4-methoxyphenyl)acrylamide(3b): Light yellow crystal,yield: 87% MF: $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_2$, Mp: 195-197 °C.

IR (KBr): ν (cm^{-1}) 3448and 3367 (N-H str. For NH_2), 3307 (aromatic C-H str.), 3180 (sp^2 C-H str.), 2208 ($\text{C}\equiv\text{N}$ str.), 1697 (CO str.), 1585 (alkene C=C str.), 1510 and 1427 (aromatic C=C str.), 1386 (C-N str), 1263 (C-O str.).

^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.23(s, 1H), 7.98(d, $J=8.8$, 2H), 7.02(d, $J=8.8$, 2H), 6.29(s, 1H, N-H), 5.70(s, 1H, N-H), 3.92(s, 3H).

2-cyano-3-(2,3,4-trimethoxyphenyl)acrylamide (3c) : Yellow crystal,yield: 85%, MF : $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}$, Mp: 135-136 °C.

IR (KBr): ν (cm^{-1}) 3444and 3419 (N-H str. For NH_2), 3172 (aromatic C-H str.), 2945 (sp^2 C-H str.), 2210 ($\text{C}\equiv\text{N}$ str.), 1697 (CO str.), 1577 (alkene C=C str.), 1486 and 1460 (aromatic C=C str.), 1290 (C-N str), 1106 (C-O str.). NMR (CDCl_3 , 400 MHz): ^1H NMR (CDCl_3 , 400 MHz): δ (ppm) 8.68(s, 1H), 8.10(d, $J=9.2$, 2H), 6.80(d, $J=8.8$, 2H), 6.29(s, 1H, N-H), 5.82(s, 1H, N-H), 4.00(s, 3H), 3.97(s, 3H), 3.89(s, 3H).

2-cyano-3-(4-hydroxyphenyl)acrylamide(3d): Yellow crystal, yield: 90%MF: $\text{C}_{10}\text{H}_8\text{N}_2\text{O}_2$,Mp: 243-244 °C. IR (KBr): ν (cm^{-1}) 3454and 3366 (N-H str. For NH_2), 3200 (O-H str.), 3079 (aromatic C-H str.), 3030 (sp^2 C-H str.), 2229 ($\text{C}\equiv\text{N}$ str.), 1658 (CO str.), 1624 (alkene C=C str.), 1600 and 1514 (aromatic C=C str.), 1290 (C-N str), 1251 (C-O str.). ^1H NMR ($\text{DMSO}-d_6$, 400 MHz) δ (ppm) 10.53(br s, 1H), 8.05(s, 1H), 7.87(d, $J=8.8$, 2H), 7.74(s, 1H, NH), 7.61(s, 1H, NH), 6.93(d, $J=8.8$, 2H).

2-cyano-3-(4-nitrophenyl)acrylamide(3e): Red crystal, yield: 85%MF: $\text{C}_{10}\text{H}_7\text{N}_3\text{O}_3$: Mp 230-232 °C. IR (KBr): ν (cm^{-1}) 3442and 3346 (N-H str., NH_2), 3196 (aromatic C-H str.), 3024 (sp^2 C-H str.), 2224 ($\text{C}\equiv\text{N}$ str.), 1695 (CO str.), 1622 (alkene C=C str.), 1600 and 1494 (aromatic C=C str.), 1510 and 1346 (nitro N=O str.), 1327 (C-N str), 1203 (C-O str.).

^1H NMR ($\text{DMSO}-d_6$, 400 MHz): δ (ppm) 8.39(d, $J=8.8$ Hz, 2H), 8.30(s, 1H), 8.13(d, $J=8.8$, 2H), 8.05(s, 1H, N-H), 7.91(s, 1H, N-H).

2-cyano-3-(3-nitrophenyl)acrylamide(3f) : Light brown crystal, yield: 80%MF: $C_{10}H_7N_3O_3$, Mp: 146-148 °C, R_f : 0.53 (hexane: ethyl acetate = 1:1)

IR (KBr): ν (cm^{-1}) 3415 and 3321 (N-H str. For NH_2), 3116 (aromatic C-H str.), 3105 (sp^2 C-H str.), 2223 ($C\equiv N$ str.), 1708 (CO str.), 1604 (alkene C=C str.), 1527 (aromatic C=C str.), 1352 (C-N str), 1209 (C-O str.).

1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.76(s, 1H), 8.44(s, 1H), 8.42(d, $J=1.2$, 1H), 8.32(d, $J=7.6$, 1H), 7.76(t, $J=8$, 1H), 6.34(s, 1H, N-H), 5.85(s, 1H, N-H).

2-cyano-3-(4-fluorophenyl)acrylamide(3g)

: White crystal, yield : 88%MF: $C_{10}H_7N_2OF$, Mp: 153-154 °C.

IR (KBr): ν (cm^{-1}) 3488 and 3381 (N-H str. For NH_2), 3169 (aromatic C-H str.), 3024 (sp^2 C-H str.), 2216 ($C\equiv N$ str.), 1701 (CO str.), 1687 (alkene C=C str.), 1600 and 1504 (aromatic C=C str.), 1386 (C-N str), 1233 (C-O str.). 1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.32(s, 1H), 8.01(d, $J=8.4$, 2H), 7.22(d, $J=8.4$, 2H), 6.38(s, 1H, N-H), 6.11(s, 1H, N-H).

2-cyano-3-(4-cyanophenyl)acrylamide (3h): White crystal, yield: 75%MF: $C_{11}H_7N_3O$

Mp: 140-142 °C.

IR (KBr): ν (cm^{-1}) 3427 and 3313 (N-H str. for NH_2), 3176 (aromatic C-H str.), 2231 ($C\equiv N$ str.), 1697 (CO str.), 1600 (alkene C=C str.), 1558 and 1506 (aromatic C=C str.), 1377 (C-N str.), 1209 (C-O str.). 1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.37(s, 1H), 8.04(d, $J=8.4$, 2H), 7.82(d, $J=8.4$, 2H), 6.37(s, 1H, N-H), 5.79(s, 1H, N-H).

2-cyano-3-(furan-2-yl)acrylamide(3i): Brown crystal, yield: 83%MF: $C_8H_6N_2O_2$ Mp: 93-94 °C.

IR (KBr): ν (cm^{-1}) 3488 and 3381 (N-H str. For NH_2), 3169 (aromatic C-H str.), 3024 (sp^2 C-H str.), 2216 ($C\equiv N$ str.), 1701 (CO str.), 1687 (alkene C=C str.), 1600 and 1504 (aromatic C=C str.), 1386 (C-N str), 1233 (C-O str.). 1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.10(s, 1H), 7.76(d, $J=1.6$, 1H), 7.25(d, $J=3.6$, 1H), 6.66(dd, $J=3.6$, $J=1.6$, 1H), 6.29(s, 1H, N-H), 5.76(s, 1H, N-H).

2-cyano-3-(thiophen-2-yl)acrylamide(3j): Light yellow crystal, yield: 85%MF: $C_8H_6N_2OS$ Mp: 120-121 °C.

IR (KBr): ν (cm^{-1}) 3140 (aromatic C-H str.), 2980 (sp^2 C-H str.), 2800 (sp^3 C-H str.), 2207 ($C\equiv N$ str.), 1702 (C=O str.), 1617 (alkene C=C str.), 1580 and 1487 (aromatic C=C str.)

1H NMR ($CDCl_3$, 400 MHz): δ (ppm) 7.81(s, 1H), 7.25 (t, $J=8.0$, 1H), 7.79(d, $J=8.0$ Hz, 1H), 8.45(s, 1H), 6.25(s, 1H, N-H), 6.92(s, 1H, N-H).

2-cyano-3-(pyridine-4-yl)acrylamide(3k): Brown crystal: 88%, MF: $C_9H_7N_3O$, Mp: 210-212 °C (decompose).

: ν (cm^{-1}) 3429 and 3329 (N-H str. For NH_2), 3026 (aromatic C-H str.), 2789 (sp^2 C-H str.), 2216 ($C\equiv N$ str.), 1708 (CO str.), 1639 (alkene C=C str.), 1598 and 1546 (aromatic C=C str.), 1361 (C-N str), 1240 (C-O str.).

1H NMR ($DMSO-d_6$, 400 MHz): δ (ppm) 8.79(d, $J=6$, 2H), 8.18(s, 1H), 8.06(s, 1H, N-H), 7.92(s, 1H, N-H), 7.78(d, $J=6$, 2H).

Results and Discussion

Initially, the condensation reaction of *para*-methylbenzaldehyde (**1a**) with cyanoacetamide was carried out at 300W for 1-3 min without triphenylphosphine catalyst. The reaction did not proceed. The starting material was recovered. However, when the reaction was conducted using triphenylphosphine (TPP), the desired product, cyanoacrylamide, was formed in good yield. In this study, triphenylphosphine (TPP) has been employed as a mild and efficient catalyst for this condensation. Accordingly, treatment of *para*-methylbenzaldehyde with cyanoacetamide **2** in the presence 20 mol % of TPP catalyst at 300W/1-3 min resulted in the formation of **3a** in 82% yield under solvent-free conditions. We subjected a series of other aldehydes with electron-donating and electron-withdrawing substituents to obtain the corresponding acrylamide **3**. Therefore, in a similar manner, a wide range of substrates such as 4-methoxy, 2,3,4-trimethoxy, 4-hydroxy, 4-nitro, 3-nitro aldehydes, etc with active methylene cyanoacetamide **2** react efficiently under

the same conditions to give the corresponding olefins **3b**, **3c**, **3d**, **3e**, **3f**, **3g**, and **3h**, respectively. We also examined heterocyclic aldehydes to obtain the corresponding products. Heterocyclic aldehydes, such as 2-furaldehyde, thiophene-2-carboxaldehyde, and pyridine-3-carboxaldehyde, reacted with cyanoacetamide to give the corresponding olefin derivatives **3i**, **3j**, and **3k** in 83%, 85 %, and 88% yield, respectively, under the same conditions (Table 1). Both electron-rich and electron-deficient aldehydes gave high product yields. Table 1 shows that yields vary for both electron-rich and electron-deficient aldehydes. The reactions were completed within a short time (1-4 min), and the products were obtained by simple recrystallization from hexane without chromatographic purification. Functional groups such as nitro, hydroxyl, cyano, and heterocyclic moieties were well tolerated. The reaction does not proceed under similar conditions

without the triphenylphosphine catalyst, only the starting materials were obtained in the reaction mixture.

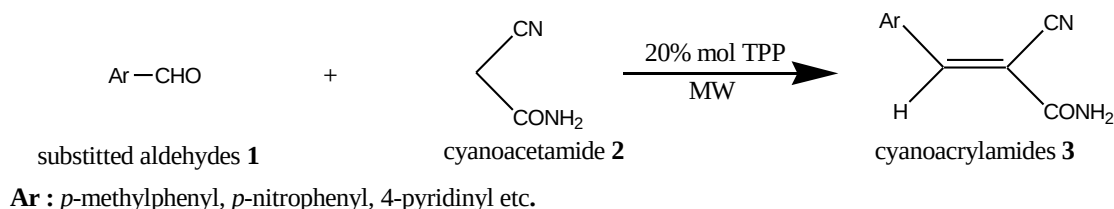
All the synthesized compounds were characterized by NMR spectral data analysis. The proton NMR spectra of the products **3a–3k** showed the olefinic proton around δ 7 – 9 ppm in CDCl_3 as a singlet. In the FTIR spectrum, the absorption peak observed at 1705 - 1730 cm^{-1} due to carbonyl, and the band at 2214 - 2225 cm^{-1} is due to the $-\text{CN}$ groups. The spectroscopic data of all the products are given sequentially. The spectroscopic data of all the products were identical to those reported in the literature (Mogilaiah et al., 2003; Moemen et al., 2015; Kaupp et al., 2003).

The use of triphenylphosphine as a catalyst helps to avoid the use of environmentally unfavorable organic solvents as reaction medium since the reaction proceeds smoothly under solvent free conditions.

Table 1. Products of triphenylphosphine (TPP) catalyzed microwave-assisted Knoevenagel condensation of aldehydes with active methylene compound.

Entry	Aldehyde substrate	Product ^a	Reaction Time & Watt	Melting point ^c (°C)	Yield ^b (%)
1	4-MeC ₆ H ₄ CHO	3a	2 min/600 W	146 - 148	82
2	4-MeOC ₆ H ₄ CHO	3b	2.5 min/ 600W	195 -197	87
3	2,3,4-(MeO) ₃ C ₆ H ₂ CHO	3c	1.5 min/450W	135 - 136	85
4	4-OHC ₆ H ₄ CHO	3d	1 min/300W	243 – 244 (245 °C)	90
5	4-NO ₂ -C ₆ H ₄ CHO	3e	1.5 min/300W	230 - 232	85
6	3-NO ₂ C ₆ H ₄ CHO	3f	1 min/300W	146 - 148	80
7	4-FC ₆ H ₄ CHO	3g	3 min/450W	153 - 154	88
8	4-CNC ₆ H ₄ CHO	3h	4 min/300W	140 - 142	75
9	2-furylaldehyde	3i	1 min/300W	93 - 94	83
10	thiophene-2-carboxaldehyde	3j	1 min/300W	120 – 121 (117-118 °C)	86
11	pyridine-4-carboxaldehyde	3k	2 min/600W	210- 212 (209-211°C)	88

^aAll products were characterized by melting point and spectral analysis (FTIR and ¹H NMR); melting point was compared with reported literature values. ^b Isolated yield; ^c Values in parenthesis are lit Mp.



Scheme 1 : Triphenylphosphine catalyzed synthesis of substituted cyanoacrylamides

Study of antibacterial activity

The antibacterial activity of four selected synthesized compounds, namely 2-cyano-3-(4-fluorophenyl)acrylamide (3g), 2-cyano-3-(2,3,4-trimethoxyphenyl)acrylamide (3c), 2-cyano-3-(furan-2-yl)acrylamide (3i), and 2-cyano-3-(pyridine-4-yl)acrylamide (3k), was evaluated against four bacterial isolates: *Serratia* sp., *Proteus* sp., *Klebsiella* sp. (Gram-negative), and *Staphylococcus* sp. (Gram-positive), using the agar well diffusion method.

Table 2 presents the antibacterial screening results. The zone of inhibition values ranged from 0 mm (no activity) to 7 mm across the four bacterial isolates tested. None of the compounds demonstrated inhibitory activity against *Serratia* sp. under the experimental conditions used. Variable activity was observed against the remaining three organisms, depending on the compound's structural features.

2-Cyano-3-(4-fluorophenyl)acrylamide (3g) showed the broadest spectrum of activity among the compounds tested, inhibiting *Proteus* sp. (5 mm), *Klebsiella* sp. (3 mm), and *Staphylococcus* sp. (4 mm), while showing no activity against *Serratia* sp. The electron-withdrawing fluorine substituent at the *para* position of the phenyl ring likely enhances the electrophilicity of the α,β -unsaturated system, potentially facilitating interaction with bacterial membrane proteins or intracellular targets.

The notable activity against the Gram-positive organism *Staphylococcus* sp. may be attributed to the capacity of fluorinated aromatic systems to penetrate the lipid-rich bacterial cell wall (Li and Chan, 1998).

2-Cyano-3-(pyridine-4-yl)acrylamide (3k) displayed selective activity against *Klebsiella* sp. (6 mm) and *Staphylococcus* sp. (5 mm), with no detectable inhibition of *Serratia* sp. or *Proteus* sp. The pyridyl nitrogen may contribute to antibacterial activity by accepting hydrogen bonds with bacterial protein targets or by facilitating membrane permeability, as reported for related nitrogen-heterocyclic cyanoacrylate derivatives (Bhuiyan et al., 2012).

2-Cyano-3-(furan-2-yl)acrylamide (3i) exhibited moderate activity exclusively against *Proteus* sp. (7 mm), which represented the largest single zone of inhibition recorded in this study. The furanyl system, known for its inherent biological activity, may contribute synergistically with the cyanoacrylamide scaffold to inhibit *Proteus* sp. growth.

2-Cyano-3-(2,3,4-trimethoxyphenyl)acrylamide (3c) showed activity limited to *Proteus* sp. (5 mm), with no inhibition observed for the remaining isolates. The three methoxy substituents on the phenyl ring increase electron density across the aromatic system, which may restrict broad-spectrum activity but does not preclude selective interaction with certain bacterial strains.

Table 2. Zone of inhibition (mm) of selected synthesized cyanoacrylamide derivatives against four bacterial isolates.

Compound	<i>Serratia</i> sp. (mm)	<i>Proteus</i> sp. (mm)	<i>Klebsiella</i> sp. (mm)	<i>Staphylococcus</i> sp. (mm)	Control (mm)
2-Cyano-3-(4-fluorophenyl)acrylamide (3g)	0	5	3	4	0
2-Cyano-3-(pyridine-4-yl)acrylamide (3k)	0	0	6	5	0
2-Cyano-3-(2,3,4-trimethoxyphenyl)acrylamide (3c)	0	5	0	0	0
2-Cyano-3-(furan-2-yl)acrylamide (3i)	0	7	0	0	0

Values represent mean of triplicate measurements. 0 = no inhibition.

Conclusion

In conclusion, we developed a simple, efficient microwave-assisted method to synthesize substituted cyanoacrylamides using triphenylphosphine as a catalyst. We synthesized a series of eleven substituted cyanoacrylamide derivatives bearing electron-donating, electron-withdrawing, and heterocyclic substituents via a triphenylphosphine (TPP)-catalyzed Knoevenagel condensation under microwave-assisted, solvent-free conditions. The reactions were completed within 1–4 minutes, affording products in 75–90% isolated yield—significantly superior to conventional thermal methods that typically require 2–6 hours and give lower yields. The methodology requires no chromatographic purification; products are obtained by simple recrystallization from ethyl acetate and hexane. Antibacterial evaluation by the agar well diffusion method demonstrated that 2-cyano-3-(4-fluorophenyl) acrylamide (3g) exhibited the broadest spectrum of activity, inhibiting *Proteus* sp. (5 mm), *Klebsiella* sp. (3 mm), and *Staphylococcus* sp. (4 mm). 2-Cyano-3-(pyridine-4-yl)acrylamide (3k) showed activity against *Klebsiella* sp. (6 mm) and *Staphylococcus* sp. (5 mm). These results demonstrate that the present method provides a practical, green, and efficient route to biologically relevant cyanoacrylamide scaffolds. This methodology provides a convenient and environmentally friendly approach to synthesizing cyanoacrylamide derivatives of potential synthetic and biological importance.

Acknowledgment

The authors are grateful to the Department of Chemistry, Shahjalal University of Science and Technology, Sylhet, for providing laboratory facilities, contributory support, and chemicals and reagents. The authors are also grateful to the Wazed Miah Science Research Centre, Jahangirnagar University, Savar, for measuring the ^1H NMR spectra.

Authors contribution

Professor Md. Mizanur Rahman and Shameem Ara Begum: contributed to the idea, supervision, data

analysis, and manuscript writing; Sadia Jannat, Md. Mahibur Rahman and Rashed Mahmud: performed laboratory experiments, data analysis, and literature review and prepared the table scheme and figure; Sadia Jannat: also contributed to the Microbial assay of the synthesized compounds.

Conflict of interest

The authors declare no conflict of interest.

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