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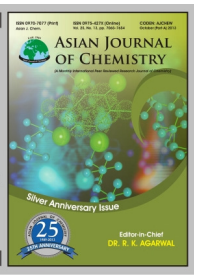

Facile Synthesis of Substituted 3-(1-Ethyl-1*H*-indol-3-yl)-2-(1-methyl-1*H*-indole-3-carbonyl)acrylonitrile and Their Antimicrobial Activities

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Facile syntheses of substituted 3-(1-methyl-1*H*-indol-3-yl)-2-(1-ethyl-1*H*-indole-3-carbonyl)acrylonitriles **5(a-d)** is being reported. L-Tyrosine has been utilized as an efficient and eco-friendly catalyst in water at room temperature for Knoevenagel condensation of N-ethyl indole-3-carboxyaldehyde (**2**) with 3-cyanoacetylindole contain active methylene group **3(a-d),** at room temperature to afford substituted 3-(1-ethyl-1*H*-indol-3-yl)-2-(1*H*-indole-3-carbonyl)acrylonitrile **4(a-d),** respectively. Subsequently these products were treated with dimethyl sulfate in the presence of Na_2CO_3 as a base and triethyl benzylammonium chloride (TEBAC) as phase transfer catalyst in DMF at room temperature for 1 h to afford the corresponding substituted 3-(1-ethyl-1*H*-indol-3-yl)-2-(1-methyl-1*H*-indole-3-carbonyl)acrylonitrile **5(a-d).** The antibacterial and antifungal activities of **4(a-d)** and **5(a-d)** have been studied.

Key Words: Indole-3-carboxyaldehyde, 3-Cyanoacetylindole, L-Tyrosine, Water.

INTRODUCTION

Carbon-carbon bond formation reaction is the most important reaction in organic synthesis[1,2]. The Knoevenagel condensation is one such reaction which facilitates C-C bond formation and has been widely used in synthesis of fine chemicals, carbocyclic and heterocyclic compounds of biological significance as well as in the synthesis of precursors for hetero Diels-Alder reactions[3-5]. These reactions are usually catalyzed by bases[6-8] like primary and secondary amines and their corresponding ammonium salts, potassium fluoride in organic solvents. Lewis acids[9,10], solid supports like alumina[11], Al_2O_3-$AlPO_4$[12], zeolite[13], microwave irradiation[14,15], ultrasound[16,17] grinding techniques[18] and ionic liquids[19-21] have also been added to the existing list of substances that assisted Knoevenagel condensation in organic synthesis. The use of water[22-25] as solvent, the most environmentally benign of all solvents, offers a useful green methodology from both the economical and synthetic points of view. It not only reduces the problem of disposal of organic solvents, but also at times enhances the progress of many organic reactions.

Tyrosine is known to be an efficient, bi-functional, zwitter ionic and eco-friendly catalyst[26-28]. The two functional groups of tyrosine enable it to act both as an acid as well as a base catalyst in chemical condensation reactions.

EXPERIMENTAL

Melting points were measured in open capillary tubes and are uncorrected. TLC was done on plates coated with silica gel-G and spotting was done using iodine or UV lamp. IR spectra were recorded using FT-IR in KBr phase. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz, respectively.

General procedure for the preparation of 4(a-d) from 2 and 3(a-d): A mixture of compounds **2** (10 mmol), **3** (10 mmol), L-tyrosine (2 mmol) and water (25 mL) was stirred at room temperature for a specified period of time (Table-1). After completion of reaction (as shown by TLC checking), the mixture was poured into ice-cold water (50 mL). The separated solid was filtered, washed with water (100 mL) and dried to obtain crude **4**. The latter were then recrystallized from ethyl acetate to afford pure **4(a-d)**.

3-(1-Ethyl-1*H*-indol-3-yl)-2-(1*H*-indole-3-carbonyl)-acrylonitrile (4a): Yellow solid; yield: 3.12 g (96 %); m.p. 176-178 ºC; IR (KBr, ν_{max}, cm^{-1}): 3242 (due to NH), 2212 (due to CN) and1621 (due to CO); ^{1}H NMR spectrum (DMSO/d_6/ TMS): δ 1.43-1.47(t, 3H, CH_3), 4.41-4.46 (q, 2H, -N-CH_2), 7.27-8.24 (m, 8H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s, 1H, D_2O exchangeable, NH proton of the indole ring); its ^{13}C NMR spectrum (DMSO/d_6/TMS): δ 33.38, 41.68,101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z: 326 (M + 1).

3-(1-Ethyl-1*H*-indol-3-yl)-2-(5-methoxy-1*H*-indole-3-carbonyl)acrylonitrile (4b): Yellow solid; yield: 3.33 g (94%); m.p. 258-259 ºC; IR (KBr, ν_{max}, cm^{-1}): 3231 (medium, NH

TABLE-1
SYNTHESIS OF NOVEL KNOEVENAGEL PRODUCTS BY USING L-TYROSINE AS ECO-FRIENDLY CATALYST IN WATER[a,b]

S. No.	Reactants		Product	Time (h)	Yield (%)
1	**1** (R^2= CH_3)	**3a** (R=H, R^1=H)	**4a** (R=H, R^1=H, R^2 = CH_3)	1	96
2	**2** (R^2= CH_3)	**3b** (R=H, R^1=OMe	**4b** (R=H, R^1=OMe, R^2 = CH_3)	1.15	94
3	**2** (R^2= CH_3)	**3c** (R=H,R^1=Br)	**4c** (R=H, R^1= Br, R^2 = CH_3)	1	96
4	**2** (R^2= CH_3)	**3d** (R=H, R^1=NO_2)	**4d** (R=H, R^1= NO_2, R^2 = CH_3)	1.1	95
5	**4a** (R=H,R^1=H, R^2 = CH_3)	DES	**5a** (R= CH_3, R^1=H, R^2 = C_2H_5)	1	91
6	**4b** (R=H,R^1= OMe,R^2=CH_3)	DES	**5b** (R=CH_3,R^1=OMe,R^2=C_2H_5)	1	89
7	**4c** (R=H,R^1= Br, R^2 = CH_3)	DES	**5c** (R= CH_3, R^1= Br, R^2 = C_2H_5)	1	91
8	**4d** (R=H,R^1= NO_2,R^2 = CH_3)	DES	**5d** (R=CH_3,R^1=NO_2, R^2 = C_2H_5)	1	90

[a]Reaction conditions for **4(a-d):** N-ethylindole-3-carboxyaldehyde,3-cyanoacetyl indole, L-tyrosine, water and room temperature. [b]Reaction conditions for **5(a-d):**DMF**,** DES,TEBAC(PTC) and room temperature.

stretching), 2208 (sharp, CN stretching) and 1624 (very strong, carbonyl CO); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47 (t, 3H, CH_3), 4.41-4.46 (q, 2H, N-CH_2), 3.23-3.26 (s, 3H, OCH_3*)*, 7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s, 1H, D_2O exchangeable, NH proton of the indole ring); its ^{13}C NMR spectrum (DMSO/d_6/ TMS): δ 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z = 356 (M + 1).

2-(5-Bromo-1*H*-indole-3-carbonyl)-3-(1-ethyl-1*H*-indol-3-yl) acrylonitrile (4c): Yellow solid; yield: 3.87 g (96 %); m.p. 277-278 ºC; IR (KBr, ν_{max}, cm^{-1}): 3215 (broad, NH stretching), 2211 (sharp, CN stretching) and 1615 (very strong, highly conjugated carbonyl -CO); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47 (t, 3H, CH_3), 4.41-4.46 (q, 2H, -N-CH_2), 7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s, 1H, D_2O exchangeable, NH proton of the indole ring); its ^{13}C NMR spectrum (DMSO/d_6/TMS): δ 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z = 405 (M + 1).

3-(1-Ethyl-1*H*-indol-3-yl)-2-(5-nitro-1*H*-indole-3-carbonyl)-acrylonitrile (4d): Yellow solid, yield: 3.51 g (95 %), m.p. 164-167 ºC, IR (KBr, ν_{max}, cm^{-1}), 3199 (very broad, NH stretching), 2211 (sharp, CN stretching) and 1621 (very strong, highly conjugated carbonyl CO); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47 (t, 3H, CH_3), 4.41-4.46 (q, 2H, -N-CH_2), 7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring),12.18 (br s,1H, D_2O exchangeable, NH proton of the indole ring); its ^{13}C NMR spectrum (DMSO/d_6/TMS): δ 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z = 371 (M + 1).

General procedure for the preparation of 5(a-d) from 4(a-d): A mixture of **4** (10 mmol), diethyl sulphate (DES) (10mmol) and TEBAC as phase transfer catalyst in DMF at room temperature for1h. At the end of this period, the mixture was poured into ice-cold water (50 mL). The separated solid was filtered, washed with water (100 mL) and dried to obtain crude **5**. The latter were then recrystallized from ethyl acetate to afford pure compounds **5(a-d)**.

3-(1-Ethyl-1*H*-indol-3-yl)-2-(1-methyl-1*H*-indole-3-carbonyl)-acrylonitrile (5a): Yellow solid; yield: 3.21 g (91 %); m.p. 245-246 ºC; IR (KBr, ν_{max}, cm^{-1}): 2201 (medium, due to CN stretching), 1621 (strong, due to CO stretching); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47(t, 3H, N-CH_3), 3.93 (s, 3H, N-CH_3), 4.41-4.46 (q, 2H, N-CH_2), 7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s, 1H, D_2O exchangeable, NH proton of the indole ring); ^{13}C NMR spectrum(DMSO/d_6/TMS): 1511, 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z = 354 (M + 1).

3-(1-Ethyl-1*H*-indol-3-yl)-2-(5-methoxy-1-methyl-1*H*-indole-3-carbonyl)-acrylonitrile (5b): Yellow solid; yield: 3.40 g (89 %); m.p. 228-229 ºC; IR (KBr, ν_{max}, cm^{-1}): 2167 (sharp, CN stretching) and1616 (very strong, highly conjugated carbonyl C=O); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47 (t, 3H, N-CH_3), 3.93 (s, 3H, N-CH_3), 4.41-4.46 (q, 2H, N-CH_2), 3.23-3.26 (s, 3H, OCH_3*)*, 7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s, 1H, D_2O exchangeable, NH proton of the indole ring); ^{13}C NMR spectrum (DMSO/d_6/TMS): δ 15.11, 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z = 384 (M + 1).

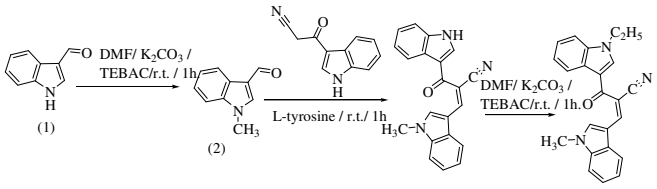
2-(5-Bromo-1-methyl-1*H*-indole-3-carbonyl)-3-(1-ethyl-1*H*-indol-3-yl)acrylonitrile (5c): Yellow solid; yield: 3.93 g (91 %); m.p. 281-282 ºC; IR (KBr, ν_{max}, cm^{-1}): 2212 (sharp, CN stretching) and 1616 (very strong, highly conjugated carbonyl C=O); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47 (t, 3H, N-CH_3), 3.93 (s, 3H, N-CH_3), 4.41-4.46 (q, 2H, N-CH_2), 7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s,1H, D_2O exchangeable, NH proton of the indole ring); Its ^{13}C NMR spectrum (DMSO/d_6/TMS): δ 15.11, 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.68; MS m/z = 433 (M + 1).

3-(1-Ethyl-1*H*-indol-3-yl)-2-(1-methyl-5-nitro-1*H*-indole-3-carbonyl)acrylonitrile (5d): Yellow solid; yield: 3.58 g (90 %); m.p. 284-286 ºC; IR (KBr, ν_{max}, cm^{-1}): 2222

(sharp, CN stretching) and 1618 (very strong, highly conjugated carbonyl C=O); ^{1}H NMR spectrum (DMSO/d_6/TMS): δ 1.43-1.47(t, 3H, N-CH_3), 3.93 (s, 3H, N-CH_3), 4.41-4.46 (q, 2H, N-CH_2),7.27-8.24 (m, 7H, aryl protons of the two indole rings), 8.46-8.57 (m, 2H, α-protons of the two indole rings), 8.63 (vinylic proton of the indole ring), 12.18 (br s, 1H, D_2O exchangeable, NH proton of the indole ring); Its ^{13}C NMR spectrum (DMSO/d_6/ TMS): δ 15.11, 33.38, 41.68, 101.97, 109.63, 110.78, 111.24, 113.11, 119.02, 120.29, 121.68, 122.10, 122.36, 123.30, 123.51, 126.86, 127.98, 132.85, 135.84, 137.13, 137.45, 144.34, 180.6 ; MS m/z = 399 (M + 1).

RESULTS AND DISCUSSION

Treatment of N-ethyl indole-3-carboxyaldehyde (**2**) with 3-cyanoacetylindoles [**3(a-d)**] in the presence of L-tyrosine in water at room temperature for 1 h resulted in the formation of substituted 3-(1-ethyl-1*H*-indol-3-yl)-2-(1*H*-indole-3-carbonyl)acrylonitriles [**4(a-d)**] in 94-96 % yields (Table-1) (**Scheme-I**). This method is very facile and convenient for the preparation of large amount of Knoevenagel adducts with high yields in less time. L-Tyrosine acts as a base to induce the reaction.



Scheme-I: Knoevenagel condensation of N-ethyl indole-3-carboxy-aldehyde with 3-cyanoacetylindole in presense of L-tyrosine in water

In the absence of L-tyrosine, the reaction does not proceed the reactants in water at room temperature for 24 h. The use of L-tyrosine as a catalyst helps to avoid the use of environmentally unfavourable organic solvents (DMF, C_6H_6, toluene, DMSO, *etc*.,) as reaction medium. It is inexpensive, readily available and found to retain its activity even in the presence of water and other active functional groups such as CHO, CO, NO_2 and CN present in the substrates. In all cases, the reaction proceeded smoothly with catalytic amount of L-tyrosine to give products of good purity. In the above reaction, the product has been assigned E-configuration (first and second priority groups *i.e*., indolyl and 3-cyanoacetylindol, respectively are *trans* to each other) on the basis of the assumption that the groups with maximum stereochemical bulk would be more stable in a trans configuration.

The above reactions of N-ethyl indole-3-carboxyaldehyde **(1)** with 3-cyanoacetylindoles **3(a-d)** were attempted in the presence of various bases like NaOH, KOH were too strong bases to result in more by products. K_2CO_3, ammonium acetate can not catalyze effectively this reaction under same conditions. Low yield was obtained and long reaction time is needed using piperidine and triethylamine as catalyst for condensation of N-ethyl indole-3-carboxyaldehyde with 3-cyanoacetylindole containing active methylene group in water at room temperature.

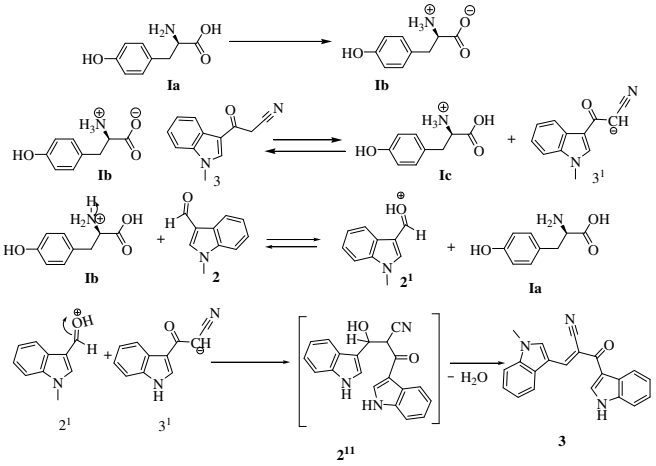
Table-1 showed that the condensation of 3-cyanoacetyl-indole with electron withdrawing group such as Br and NO_2 at 5-th position of indole ring with N-ethyl indole-3-carboxyaldehyde can be carried out in relatively shorter time and higher yield than with electron donating group such as OCH_3 in the water at room temperature.

A comparative study of the progress of condensation reactions **2** and **3(a-d)** were carried out in different solvents contaning along with L-tyrosine as catalyst and is summarized in Table-2.

TABLE-2
PROGRESS OF REACTION IN DIFFERENT SOLVENT MEDIA

Entry	Solvent	Time(h)	Temp. (ºC)	Yield (%)
1	L-Tyrosine/water	1	r.t.	94-96
2	L-Tyrosine/EtOH	2-5	r.t.	76-78
3	L-Tyrosine/benzene	8	r.t.	43-46
4	L-Tyrosine/DMSO	10	r.t.	37-45
5	Withoutcatalyst inwater	24	r.t./reflux at 100	Nil
6	L-Tyrosine/DMF	7	r.t.	24-28
7	L-Tyrosine/CH_3CN	12	r.t.	19-20
8	L-Tyrosine/$CHCl_3$	18	r.t.	Nil

A plausible mechanism for the formation of compunds **4** from **2** and **3** in the presence of L-tyrosine as catalyst is shown in the **Scheme-II**.



Scheme-II: Plausible mechanism for the formation of **4** from **2** and **3** in the presence of L-tyrosine in water at room temperature

In the mechanism shown in **Scheme-II**, L-tyrosine, in its zwitter ionic form **(Ib),** abstracts a proton from 3-cyanoacetyl-indole **(3)** forming the carbanion of 3-cyanoacetyl indole *i.e*. **(3^1)** which then attacks the protonated N-ethyl indole-3-carboxyaldehyde **(2^1)** forming the corresponding intermediate **(3^{II})** that loses water to form the end product **4** which on alkylation results the title compound **5**.

Treatment of compounds **4(a-d)** each with dimethyl sulfate independently, Na_2CO_3 as base and TEBAC as phase transfer catalyst in DMF at room temperature for 1hr. resulted substituted 3-(1-ethyl-1*H*-indol-3-yl)-2-(1-methyl-1*H*-indole-3-carbonyl)acrylonitriles **4(a-d)**, respectively in 89-91 % yields (**Scheme-I**). Treatment of indole-3-carboxyldehyde with diethyl sulfate, Na_2CO_3 as base and TEBAC as phase transfer catalyst in DMF at room temperature for 1 h resulted N-ethyl

indole-3-carboxyaldehyde (**2**). All the above reactions are summarized in **Scheme-I**.

Antimicrobial activity

Antibacterial activity: All the compounds **4(a-d)** and **5(a-d)** were screened for their antibacterial activities[29] against gram-positive bacteria such as *Bacillus subtilis*, *Staphylococcus aureus* (ATCC6538) and also against gram-negative bacteria such as *Klebsiella pneumonia, Escherichia coli* (ATCC8739) bacterial strains[30] at concentrations of 50, 100, 200, 300 and 500 µg/mL. Streptomycin was used as a reference standard. Petri plates and necessary glassware were sterilized in hot air oven at 190 ºC for 45 min. The Muller Hinton Agar and saline (0.82 % NaCl) media were sterilized in autoclave (121 ºC, 15 psi, 20 min). Inoculum was prepared in sterile saline (0.82 % NaCl) and the optical density of all pathogens was adjusted to 0.10 at 625 nm on a chemito spectra scan UV 2600 spectrophotometer that is equivalent to 0.5 Mc Farland standards[31]. The Mueller Hinton Agar plates were prepared by the pour plate method. The activity of the compounds was tested by agar disc diffusion method. All the bacterial cells were cultured in Mueller Hinton Agar plates and the compounds to be tested were dissolved in N,N-dimethyl formamide and were soaked in agar disc and the petri plates incubated at 37 ºC for 24 h. The diameter (mm) of the zone of inhibition around each agar disc was measured and results were recorded in Table-3. The compounds **4(a-d)** and **5(a-d)** tested were found to have excellent antibacterial activity against *Klebsiella pneumoniae* and *Escherichia coli*. However, they were found to have moderate activity against *Staphylococcus aureus* and *Bacillus subtilis.*

Antifungal activity: All the compounds **4(a-d)** and **5(a-d)** were screened for antifungal activity against *Rhizoctonia solani, Fusarium oxysporum, Aspergillus Niger* and *Aspergillus flavus at* concentrations of 50, 100, 200, 300 and 500 µg/mL. Mycostatin was used as a reference standard. Potato dextrose agar (PDA) was used as basal medium for test fungi. Glass petridishes used were sterilized. Sterilized melted PDA medium (*ca.* 45 ºC) was poured at the rate of 15 mL into each petridish (90 mm). After solidification of the medium, small portions of the mycelium of each fungus were spread carefully over the centre of each PDA plate with the help of sterilized needles. Thus, each fungus was transferred to a number of PDA plates, which were then incubated at (25 ± 2) ºC and

TABLE-3
ANTIBACTERIAL ACTIVITY OF **4(a-d)** AND **5(a-d)** AGAINST *Klebsiella pneumonia, Escherichia coli, Staphylococcus aureus* AND *Bacillus subtilis*

S. No.	Compound No.	Types of bacteria	Zone of inhibition in mm for concentration of				
			50 (µg/mL)	100 (µg/mL)	200 (µg/mL)	300 (µg/mL)	500 (µg/mL)
1	**4a**	*Klebsiella pneumonia*	9	14	18	23	31
		Escherichia coli	8	13	16	20	30
		Staphylococcus aureus	6	10	14	18	25
		Bacillus subtilis	4	9	12	15	23
2	**4b**	*Klebsiella pneumonia*	9	14	18	23	32
		Escherichia coli	8	13	15	20	31
		Staphylococcus aureus	6	10	13	16	26
		Bacillus subtilis	4	9	11	14	22
3	**4c**	*Klebsiella pneumonia*	9	14	18	23	32
		Escherichia coli	8.4	13.5	14	21	30
		Staphylococcus aureus	6	10	13	17	25
		Bacillus subtilis	5	9.5	11	15	23
4	**4d**	*Klebsiella pneumonia*	9	14	18	23	32
		Escherichia coli	8	13	15	20	31
		Staphylococcus aureus	6	10	13	16	26
		Bacillus subtilis	4	9	11	14	22
5	**5a**	*Klebsiella pneumonia*	9	14	18	23	31
		Escherichia coli	8	13	16	20	30
		Staphylococcus aureus	6	10	14	18	25
		Bacillus subtilis	4	9	12	15	23
6	**5b**	*Klebsiella pneumonia*	9	14	18	23	32
		Escherichia coli	8	13	15	20	31
		Staphylococcus aureus	6	10	13	16	26
		Bacillus subtilis	4	9	11	14	22
7	**5c**	*Klebsiella pneumonia*	9	14	18	23	32
		Escherichia coli	8.4	13.5	14	21	30
		Staphylococcus aureus	6	10	13	17	25
		Bacillus subtilis	5	9.5	11	15	23
8	**5d**	*Klebsiella pneumonia*	9	14	18	23	31
		Escherichia coli	8	13	16	20	30
		Staphylococcus aureus	6	10	14	18	25
		Bacillus subtilis	4	9	12	15	23
13	Streptomycin	*Klebsiella pneumonia*	11	16	22	26	35
		Escherichia coli	10	15	21	24	34
		Staphylococcus aureus	8	13	17	20	29
		Bacillus subtilis	7	12	15	18	26

ready for use after 5 days of incubation. Prepared discs of samples were placed gently on solidified agar plates, freshly seeded with the test organisms with sterile forceps. A control disc was also placed on the test plates to compare the effect of the test samples and to nullify the effect of solvent, respectively. The plates were then kept in a refrigerator at 4 ºC for 24 h so that the materials had sufficient time to diffuse over a considerable area of the plates.After this, the plates were incubated at 37 ºC for 72 h. N,N-dimethyl formamide was used as solvent to prepare desired solutions of the compounds and also to maintain proper control. The diameter (mm) of the zone of inhibition around each agar disc was measured and results were recorded in Table-4. **4(a-d)** and **5(a-d)** compounds tested were found to have very good antifungal activity against *Rhizoctonia solani* and *Fusarium oxysporum.* However, they were found to good activity against *Aspergillus niger* and *Aspergillus flavus.*

Conclusion

In summary, L-tyrosine has been employed as an efficient catalyst for the preparation of indolo olefinic compounds by a Knoevenagel reaction in water at room temperature. This method is applicable to a wide range of N-alkyl indole-3-carboxyldehydes (**2**) and 3-cyanoacetyl indole contain active methylene group. The attractive features of this procedure are the mild reaction conditions, high conversions, operational simplicity and inexpensive and ready availability of the catalyst, all of which make it a useful and attractive strategy for the preparation of olefins.

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REFERENCES

1. G. Jones, The Knovenagel Condensation Reaction in Organic Reactions Wiley New York, Vol. 15, p. 204 (1967).
2. L.F. Tietze and U. Beifuss, In eds.: B.M. Trost, I. Fleming and C.H. Heathcock, Comprehensive Organic Synthesis, Pergamon: Oxford., Vol. 2, p. 341 (1991).
3. F. Freeman, *Chem. Rev.,* **80**, 329 (1980).

TABLE-4
ANTIFUNGAL ACTIVITY OF **4(a-d)** AND **5(a-d)** AGAINST *Rhizoctonia solani, Fusarium oxysporum, Aspergillus niger* AND *Aspergillus flavus*

S. No.	Compound No.	Types of bacteria	Zone of inhibition in mm for concentration of				
			50 (µg/mL)	100 (µg/mL)	200 (µg/mL)	300 (µg/mL)	500 (µg/mL)
1	**4a**	*Rhizoctonia solani*	9	14	18	23	31
		Fusarium oxysporum	9	13.8	17	22.6	30
		Aspergillus niger	6	10	14	18	25
		Aspergillus flavus	6.5	11	13.6	18.3	25.2
2	**4b**	*Rhizoctonia solani*	8	13	15	20	31
		Fusarium oxysporum	8	13	14	19	30
		Aspergillus niger	4	9	11	14	22
		Aspergillus flavus	4.3	8.9	11.1	13.9	22.1
3	**4c**	*Rhizoctonia solani*	8.4	13.5	14	21	30
		Fusarium oxysporum	8	13	13	20	29
		Aspergillus niger	5	9.5	11	15	23
		Aspergillus flavus	5	9	10.8	14.8	23
4	**4d**	*Rhizoctonia solani*	9	14	18	23	32
		Fusarium oxysporum	8	13	15	20	31
		Aspergillus niger	6	10	12	15	23
		Aspergillus flavus	4	9	11	14	22
5	**5a**	*Rhizoctonia solani*	9	14	18	23	31
		Fusarium oxysporum	8	13	16	20	30
		Aspergillus niger	6	10	14	18	25
		Aspergillus flavus	4	9	12	15	23
6	**5b**	*Rhizoctonia solani*	9	14	18	23	32
		Fusarium oxysporum	8	13	15	20	31
		Aspergillus niger	6	10	13	16	26
		Aspergillus flavus	4	9	11	14	22
7	**5c**	*Rhizoctonia solani*	9	14	18	23	32
		Fusarium oxysporum	8.4	13.5	14	21	30
		Aspergillus niger	6	10	13	17	25
		Aspergillus flavus	5	9.5	11	15	23
8	**5d**	*Rhizoctonia solani*	9	14	18	23	32
		Fusarium oxysporum	8	13	15	20	31
		Aspergillus niger	6	10	13	16	26
		Aspergillus flavus	4	9	11	14	22
13	Mycostanin	*Rhizoctonia solani*	13	16	20	28	35
		Fusarium oxysporum	13	16	19	27	35
		Aspergillus niger	9.2	11	14.6	21	30
		Aspergillus flavus	9	11	14	20	29

4. N. Zidar, T. Tomasic and R. Sink, *J. Med. Chem.,* **53**, 6584 (2010).
5. M. Oguchi, K. Wada and H. Honma, *J. Med. Chem*., **43**, 3052 (2000).
6. M.S. Malamas, J. Sredy and J.I. Gunawan, *J. Med. Chem.,* **43**, 995 (2000).
7. R. Murugan, S. Anbazhagan and S.S. Narayanan, *Eur. J. Med. Chem.,* **44**, 3272 (2009).
8. U.V. Desai, D.M. Pore, R.B. Mane, S.B. Solabanavar and P.P. Wadgaonkar, *Synth. Commun.*, **34**, 25 (2004).
9. D. Fildes, V. Caignaert, D. Villemin and P. Jaffres, *Green Chem.,* **3**, 52 (2001).
10. F. Texier-Boullet and A. Foucod, *Tetrahedron Lett.*, **23**, 4927 (1982).
11. J.A. Cabello, J.M. Campelo, A. Garcia, D. Luna and J.M. Marians, *J. Org. Chem.*, **49**, 5195 (1984).
12. J.S. Yadav, B.V.S. Reddy, A.K. Basak, B. Visali, A.V. Narsaiah and K. Nagaiah, *Eur. J. Med. Chem.,* **67**, 546 (2004).
13. D.H. Yang, B.H. Yang, B.C. Chen and S.Y. Chen, *Org. Prep. Proced. Int.*, **38**, 81 (2006).
14. A.V. Narsaiah, A.K. Basak, B. Visali and K. Nagaiah, *Synth. Commun.,* **34**, 2893 (2004).
15. I. Rodriguez, S. Iborra, A. Corma, F. Rey and J.L. Jorda, *Chem. Commun*., **35**, 593 (1999).
16. P.S. Rao and R.V. Ratnam, *Tetrahedron Lett.,* **32**, 5821 (1991).
17. A.V. Narsaiah and K. Nagaiah, *Synth. Commun.,* **33**, 3819 (2003).
18. L. Martins, K.M. Vieira, L.M. Rios and D. Cardoso, *Catal. Today*, **133**, 706 (2008).
19. T.I. Reddy and R.S. Verma, *Tetrahedron Lett*., **38**, 1721 (1997).
20. P. Formentin, H. Garcia and A. Leyva, *J. Mol. Catal.* **214**, 137 (2004).
21. N. Tavakoli-Hoseini, M.M. Heravi and F.F. Bamoharram, *Asian J. Chem.*, **22**, 7208 (2010).
22. H. McNab, *Chem. Soc. Rev.,* **7**, 345 (1978).
23. G.A. Kraus and M.E. Krolski, *J. Org. Chem.*, **51**, 3347 (1986).
24. X. Huang and L. Xie, *Synth. Commun.*, **16**, 1701 (1986).
25. S. Nakamura, H. Rao and T. Ohwada, *J. Org. Chem.,* **69**, 4309 (2004).
26. P.S. Rao and R.V. Venkataratnam, *Indian J. Chem.*, **32B**, 484 (1993).
27. S. Miroslav, P. Daniel, A. Marta, F.Andres, C. Carmen, A. Fernando and A. Mercedes, *J. Med. Chem.,* **52**, 6217 (2009).
28. L.S.K. Tara and W.G. Gordon, *Tetrahedron Lett.,* **42**, 4783 (2001).
29. V. Ravichandran, R. Harish, K.S. Kumar and A.R. Kishore, *Lett. Drug Design Discov.*, **8**, 82 (2011).
30. Md. Kaspady, V.K. Narayanaswamy, M. Raju and G.K. Rao, *Lett. Drug Design Discov.*, **6**, 21 (2010).
31. S. Frankel, S. Reitman and A.C. Sonnenwirth, Gradwohl's Clinical Laboratory Methods and Diagnosis, Textbook on a Laboratory Procedure and their Interpretation, edn. 7, Vol. 2, p. 1406 (1970).