Microwave Assisted Synthesis of Indole Substituted Alkenes Using Knoevenagel Condensation Reaction and their Antibacterial Activity Study

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Abstract: The reaction rate of Knoevenagel condensation can be dramatically enhanced by irradiating the reaction mixture containing an aldehyde, active methylene compound, *L*-proline and chlorobenzene with a commercial microwave oven. Twenty Knoevenagel condensation products were synthesized within 5-17 min in good yields. The new compounds were also screened for their antibacterial activity.

Keywords: Active methylene compounds, Aldehydes, Substituted alkenes, Knoevenagel reaction.

Introduction

The importance of indoles is well recognized by synthetic as well as biological chemists. The most ubiquitous of the known bioactive alkaloids are based on the indole moiety. Medicinal chemists repeatedly turn to indole based compounds as a target pharmacophore for the development of therapeutic agents¹. Nitrogen heterocycles are ubiquitous systems in nature and are consequently considered as privileged structures in drug discovery. Derivatisation of these heterocyclic pharmacophores represents a convenient approach to generate chemical diversity during lead identification and optimization²⁻⁴.

In the recent years the use of microwave irradiation in organic reactions is rapidly increasing, because of the short reaction time and the operational simplicity. It has been reported that a variety of reactions such as Diels-Alder⁵, ene⁶, Claisen reactions⁷, Fischer cyclization⁸, synthesis of heterocycles⁹, hydrolysis of esters¹⁰, phosphoric anhydride¹¹ and adenosine triphosphate¹², hydrogenation¹³, deprotection of benzyl esters¹⁴, deacetylation of diacetates¹⁵, Graebe-Ullmann synthesis¹⁶ and oxazoline formation¹⁷, could be facilitated by microwave irradiation in a good energy transferring medium.

We found that the reaction rate of the Knoevenagel condensation could be enhanced by the microwave irradiation. In the present study, four substituted indole aldehydes *viz.* 5-cyanoindole-3-carbaldehyde (**1a**), 5-bromoindole-3-carbaldehyde (**1b**), 1-methyl indole-3-carbaldehyde (**1c**) and indole-3-carbaldehyde (**1d**) have been condensed with five active methylene compounds namely malononitrile (**2a**), ethyl cyanoacetate (**2b**), meldrum's acid (**2c**), barbituric acid (**2d**) and dimidone (**2e**) using *L*-proline as base are mentioned in Table 1. A large vial with a loose cap or an Erlenmeyer flask with a funnel as a loose top was used as the reaction vessel for the condensation. Mono chlorobenzene was used as an energy-transfer medium since its boiling point (131-133 °C) is about 30 °C higher than water which is to be eliminated in the process. All the reactions were completed within 5-17 min. To the best of our knowledge, there are no reports for the synthesis of indole substituted alkenes by Knoevenagel condensation under microwave irradiation.

Experimental

IR spectra were recorded on a spectrum BX Series. ¹H & ¹³C NMR spectra were recorded on 400 MHZ spectrometer in DMSO-d₆ using TMS as internal standard. Mass spectra were recorded on a DART mass spectrometer. M.ps. were taken on a Haake Bucher melting point apparatus and are uncorrected.

General synthetic procedure

To a solution of malononitrile **2a** (2.2 mmol) in mono chlorobenzene and the catalyst (0.2 mmol) was added indole aldehyde **1a** (2 mmol) rapidly and all at once. The resulting reaction mixture was then irradiated in the microwave oven for 5 min. The progress of the reaction was monitored by TLC. After complete conversion of the starting material as indicated by TLC, the reaction mixture was quenched with water and the solid produced was isolated by simple filtration and dried. The solid product **3a** was identified by spectroscopic measurements and by comparison with an authentic samples and needed no further purification. Similarly, utilizing the aldehydes **1a-d** and active methylene compounds **2a-e**, compounds **3b-t** were synthesized and characterized (Table 1).

Table1. Synthesis of indole substituted alkenes from the Knoevenagel condensation of aldehydes and active methylene compounds

R1 of 1	R2 of 1	2	Product	Reaction time, min	Yield, %	M.P, °C
CN	H		3a	5	96	289-291
CN	H		3b	8	82	276-278
CN	H		3c	15	82	296-299
CN	H		3d	16	76	263-264

Contd...

CN	H		3e	7	76	240-243
Br	H		3f	4	90	335-336
Br	H		3g	9	87	322-325
Br	H		3h	11	80	291-292
Br	H		3i	17	72	286-288
Br	H		3j	10	61	242-244
H	CH ₃		3k	10	94	277-278
H	CH ₃		3l	10	91	264-267
H	CH ₃		3m	7	79	282-283
H	CH ₃		3n	15	69	249-251
H	CH ₃		3o	9	75	241-243

Contd...

H	H		3p	5	89	187-189 ¹⁸
H	H		3q	5	82	163-166 ¹⁹ (160-162)
H	H		3r	15	74	175-176
H	H		3s	10	65	183-187
H	H		3t	8	71	162-163

Results and Discussion

In our continued interest in the development of a highly expedient methodology for the synthesis of fine chemicals and heterocyclic compounds of biological importance, we report here the first example of the synthesis of indole substituted alkenes from the Knoevenagel condensation of various indole substituted aldehydes (**1**) and active methylene compounds (**2**), for example, malononitrile, ethyl cyanoacetate, barbituric acid, meldrum's acid and dimedone under microwave irradiation (Scheme 1). It was exciting to observe that, cyano group substituted active methylene compounds are more reactive than other active methylene compounds giving excellent yields of Knoevenagel products (**3**).

Scheme 1.

Spectral data of some of the representative compounds

2-((5-Cyano-3-indolyl)methylene)malononitrile (**3a**)

Yellow Solid: M.P. 289-291 °C; (Found: C, 70.55; H, 2.56; N, 25.60. C₁₃H₆N₄ requires C 71.55; H, 2.77; N, 25.68; IR (KBr) 3270, 2915, 2843, 2215, 1566, 1495, 1336, 1225, 1139, 825, 789 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 7.66(d, 1H, 12 Hz), 7.75(d, 1H, 12 Hz),

8.44(s,1H), 8.66(s, 1H, NH-CH=C),9.55(s, 1H, -CH=C(CN)₂),11.20(s, 1H,NH); ¹³C NMR (50 MHz): 94.02, 110.21,102.92, 114.26,114.72, 114.82(2-CN),122.42, 126.72, 128.25, 135.22, 135.62, 146.32.;ES-MS *m/z* 218(M⁺, 100%) .

Ethyl(E)-2-cyano(5-cyano-3- indol)propenoate (3b)

Yellow Needles: M.P.276-278 °C; (Found): C, 67.89; H, 4.16; N, 15.79; O, 12.06. C₁₅H₁₁N₃O₂ requires C 67.92; H, 4.18; N, 15.84; O, 12.08; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590,1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 1.3(t, 3H, 9.6 Hz, CH₃), 4.3(q, 2H, 9.2Hz, CH₂), 7.65(d, 1H,12 Hz), 7.74(d,12H,1H),8.42(s,1H),8.65(s,1H,NH-CH=C), 9.01(s,1H, -CH=C(CN)₂), 11.10(s,1H,NH); ¹³C NMR (50 MHz)14. 13(CH₃), 61.46 (OCH₂), 93.42,102.2, 110.22, 113.83, 114.81(CN), 114.91, 121.33, 126.16, 128.62, 135.02, 135.25, 146.24 , 163.01(CO);ES-MS *m/z* 265(M⁺, 100%).

3-((2,2-Dimethyl-4,6-dioxo-1,3-dioxan-5-ylidene)methyl)indole-5-carbonitrile (3c)

Yellow solid: M.P.296-299 °C; (Found): C, 64.83; H, 4.02; N, 9.41; O, 21.57. C₁₆H₁₂N₂O₄ requires C 64.86; H, 4.08; N, 9.46; O, 21.60; IR (RBr) 3400-3200, 3100-2910, 2232,1700, 1670, 1600, 1594, 1240, 1108 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 1.33(s, 6H), 7.67(d, 1H, 12 Hz), 7.73(d,1H,12 Hz), 7.98(s,1H), 8.66(s,1H NH-CH=C), 8.7 (s,1H,CH=C), 11.22 (s,1H, NH); ¹³C NMR (50 MHz) :15.2(2CH₃), 102.91, 107.25,1 10.27, 113.92, 114.12, 122.12,125.92,126.21,128.72,135.22, 136.57, 145.92, 164.64 (2CO); ES-MS *m/z* 296(M⁺, 100%).

3-((2,4,6-Trioxo-tetrahydropyrimidin-5 ylidene)methyl)indole-5-carboni trile (3d)

Yellow solid: M.P. 263-264 °C; (Found): C, 59.99; H, 2.83; N, 19.92; O, 17.11. C₁₄H₈N₄O₃ requires C 60.00; H, 2.88; N, 19.99; O, 17.13; IR (RBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590,1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 7.52(d, 1H, 12 Hz), 7.59(d, 1H, 12 Hz), 7.92(s, 1H),8.65(s, 1H, NH-CH=C), 8.72(s, 1H, CH=C), 11.22(s, 1H, NH), 11.31(s, 2H, NH-C=O); ¹³C NMR (50 MHz): 102.32,110.54, 113.12, 113.93, 123.02, 124.06, 125.06, 126.24, 135.21, 136.36, 147.22 , 152.42,160.02 (2CO); ES-MS *m/z* 280(M⁺, 100%).

3-((4,4-Dimethyl-2,6-dioxocyclohexylidene)methyl)indole-5-carbonitrile(3e)

Yellow solid: M.P. 240-243 °C; (Found): C, 73.92; H, 5.50; N, 9.57; O, 10.91.C₁₈H₁₆N₂O₂ requires C 73.95; H, 5.52; N, 9.58; O, 10.95; IR (KBr) 3400-3200, 3070, 3040,2964, 2935, 2870, 2232,1710, 1673, 1600, 1592,1423, 1410, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 1.31(s, 6H), 2.24(s, 4H), 7.65(d,1H,12 Hz),7.72(d,1H,12 Hz), 7.96(s,1H), 8.6 (s,1H, CH=C), 8.64(s,1H,NHCH=C), 11.20(s,1H,NH); ¹³C NMR (50 MHz): 14.72 (2CH₃), 33.43, 50.28, 103.01,110.52,112.96,114.02,122.91,126.24, 128.16, 128.40, 133.65, 135.01, 146.52, 163.02 (2CO); ES-MS *m/z* 292(M⁺, 100%).

2-((5-Bromo-3 indolyl)methylene)malononitrile (3f)

Yellow solid:M.P. 335-336 °C; (Found): C, 52.95; H, 2.21; Br, 29.35, N, 15.41. C₁₂H₆BrN₃ requires C 52.97; H, 2.22; Br, 29.37; N, 15.44; IR (KBr) 3270, 2915, 2843, 2215, 1566, 1495, 1336, 1225, 1139, 825, 789cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 7.42(d, 1H, 8.4 Hz), 7.54(d, 1H, 8.4 Hz), 7.98(s, 1H), 8.58(s, 1H, N-CH=C), 9.50(s, 1H, CH=C (CN) ₂), 11.2(s, 1H, NH); ¹³C NMR (50 MHz): 94.22, 109.55, 115.26, 115.62(2-CN), 118.22, 121.42, 127.20, 128.72, 133.35, 134.98, 147.22.; ES-MS *m/z* 270(M⁺, 100%).

Ethyl 3-(5-Bromo-3-indolyl) 2 cyanoacrylate (3g)

Yellow Needles: M.P. 322-325 °C; (Found): C, 52.68; H, 3.45; Br, 25.03; N, 8.76; O, 10.00. C₁₄H₁₁BrN₂O₂ requires C 52.69; H, 3.47; Br, 25.08; N, 8.78; O, 10.03; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 1.3 (t, 3H, 9.6 Hz, CH₃), 4.3(q, 2H, 9.2 Hz, CH₂), 7.4(d, 1H, 11.2 Hz), 7.50(d, 1H, 11.2 Hz), 8.18(s, 1H), 8.5(s, 1H, N-CH=C, CH=C-CN), 11.17 (broad.s); ¹³C NMR(50 MHz): 14.13(CH₃), 61.46(OCH₂), 93.34, 109.49, 114.81(CN), 114.92, 117.83, 121.33, 126.16, 128.71, 133.35, 134.98, 146.39, 163.01(CO); ES-MS *m/z* 318 (M⁺, 100%).

5((5-Bromo-3-indolyl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (3h)

Yellow solid: M.P. 291-292 °C; (Found): C, 51.40; H, 3.42; Br, 22.80; N, 4.00; O, 18.28. C₁₅H₁₂BrNO₄ requires C 51.45; H, 3.45; Br, 22.82; N, 4.00; O, 18.29; IR (KBr) 3400-3200, 3100-2900, 1700, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 1.2(s, 6H), 7.43(d, 1H, 8.4 Hz), 7.56(d, 1H, 8.4 Hz), 7.96(s, 1H), 8.58(s, 1H, N-CH=C), 9.60(s, 1H, CH=C), 11.3(s, 1H, NH); ¹³C-NMR (50 MHz): 14.2(2CH₃), 106.42, 110.22, 115.37, 118.45, 121.53, 125.06, 127.23, 128.64, 134.22, 136.02, 146.72, 163.64 (2CO); ES-MS *m/z* 348(M⁺, 100%).

5((5-Bromo-3-indolyl)methylene) pyrimidine-2,4,6 trione (3i)

Yellow solid: M.P. 286-288 °C; (Found): C, 46.71; H, 2.40; Br, 23.89; N, 12.54; O, 14.32. C₁₃H₈BrN₃O₃ requires C 46.73; H, 2.41; Br, 23.91; N, 12.58; O, 14.37; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 7.420(d, 1H, 8.4 Hz), 7.536(d, 1H, 8.4 Hz), 7.99(s, 1H), 8.58(s, 1H, N-CH=C), 9.45(s, 1H, CH=CH), 11.16(b.s. 3H, 3NH); ¹³C NMR (50 MHz): 109.27, 114.57, 118.72, 121.33, 124.06, 126.26, 127.02, 134.40, 136.46, 147.92, 152.40, 164.02 (2CO); ES-MS *m/z* 332(M⁺, 100%).

2((5-Bromo-3-indolyl)methylene)-5,5-dimethylcyclohexane-1,3-dione (3j)

Yellow solid: M.P. 286-288 °C; (Found): C, 58.95; H, 4.63; Br, 23.06; N, 4.02; O, 9.21. C₁₇H₁₆BrNO₂ requires C 58.97; H, 4.66; Br, 23.08; N, 4.05; O, 9.24; IR (KBr) 3400-3200, 3070, 3040, 2964, 2935, 2870, 2232, 1710, 1673, 1600, 1592, 1423, 1410, 1100 cm⁻¹; ¹H-NMR(400 MHz, DMSO-d₆) 1.02 (s, 6H), 2.52(s, 4H), 7.44(d, 1H, 8.4 Hz), 7.52(d, 1H, 8.4 Hz), 7.95(s, 1H), 8.57(s, 1H, N-CH=C), 9.51(s, 1H, CH=C), 11.2(s, 1H, NH); ¹³C NMR (50 MHz): 14.62(2CH₃), 32.53, 50.28, 110.02, 116.27, 118.26, 122.42, 126.42, 128.26, 128.40, 134.65, 135.01, 147.52, 165.02 (2CO); ES-MS *m/z* 345(M⁺, 100%).

2((1-Methyl-3-indolyl)methylene)malononitrile(3k)

Yellow solid: M.P. 277-278 °C; (Found): C, 75.31; H, 4.33; N, 20.25. C₁₃H₉N₃ requires C 75.35; H, 4.38; N, 20.28; IR (KBr) 3270, 2915, 2843, 2215, 1566, 1495, 1336, 1225, 1139, 825, 789 cm⁻¹; ¹H NMR(400 MHz, DMSO-d₆) 3.98(s, 3H), 7.317-7.375(dt, 2H, *J*=7.2 Hz), 7.7(d, 1H, *J*= 7.6 Hz), 7.97(d, 1H, 7.2 Hz) 8.62(s, 1H), 9.1(s, 1H); ¹³C NMR (50 MHz): 33.82(N-CH₃), 73.45, 110.24, 112.45(2CN), 115.24, 118.70, 122.40, 123.45, 128.63, 135.6, 137.01, 150.48; MS-MS *m/z* 207(M⁺, 100%).

Ethyl-2-cyano-3-(1-methyl-3-indolyl)acrylate(3l)

Yellow crystals: M.P. 264-267 °C; (Found): C, 70.81; H, 5.54; N, 11.00; O, 12.56. C₁₅H₁₄N₂O₂ requires C, 70.85; H, 5.55; N, 11.02; O, 12.58; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆) 1.307(t, 3H, *J*=7.2Hz), 3.977 (s, 3H), 4.286(q, 2H, *J*= 7.2Hz), 7.317-7.375(dt, 2H, *J*= 7.2 Hz), 7.637(d, 1H, *J*= 8Hz), 7.97(d, 1H, 8 Hz), 8.522(s, 1H), 9.01(s, 1H); ¹³C NMR (50 MHz): 14.15(CH₃), 33.82(N-CH₃), 61.42(OCH₂), 73.04, 108.94, 111.41, 117.80, 118.65, 122.55, 123.75, 127.43, 135.8, 136.96, 145.82, 163.30(CO); ES-MS *m/z* 254(M⁺, 100%).

2,2-Dimethyl-5-((1-methyl-3-indolyl)methylene)-1,3-dioxane-4,6-dione (3m)

Yellow solid: M.P. 282-283 °C; (Found): C, 67.35; H, 5.29; N, 4.90; O, 22.40. C₁₆H₁₅NO₄ requires C, 67.36; H, 5.30; N, 4.91; O, 22.43; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 1.75(s, 6H), 3.98(s, 3H), 7.32(t, 1H, 7.6 Hz), 7.37 (1H, t, 7.6 Hz) 7.42(d, 1H, 7.2 Hz), 7.97(d, 1H, 8 Hz), 8.61(s, 1H), 8.7(s, 1H); ¹³C NMR (50 MHz): 14.20(CH₃), 34.12(N-CH₃), 106.42, 110.24, 115.24, 118.70, 122.23, 123.45, 124.02, 126.242, 135.6, 136.02, 146.72, 163.24(2CO); ES-MS *m/z* 285(M⁺, 100%).

5-((1-Methyl-3 indolyl)methylene)pyrimidine-2, 4, 6- trione (3n)

Yellow solid: M.P. 249-251 °C; (Found): C, 62.41; H, 4.10; N, 15.59; O, 17.80. C₁₄H₁₁N₃O₃ requires C, 62.45; H, 4.12; N, 15.61; O, 17.83; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 4.01(s, 3H), 7.35(t, 1H, 7.5 Hz), 7.39(t, 1H, 7.2 Hz), 7.41(d, 1H, 8 Hz), 7.90(d, 1H, 8 Hz), 8.53(s, 1H), 8.62(s, 1H), 11.1(s, 2H); ¹³C NMR (50 MHz): 34.02(N-CH₃), 109.27, 112.20, 118.62, 122.12, 123.45, 124.24, 127.02, 136.40, 136.46, 147.02, 152.40(CO), 163.24(2CO); ES-MS *m/z* 269(M⁺, 100%).

5,5-Dimethyl-2-((1-methyl-3indolyl)methylene)cyclohexane-1,3-dione (3o)

Yellow solid: M.P. 241-243 °C; (Found): C, 76.81; H, 6.79; N, 4.97; O, 11.34. C₁₈H₁₉NO₂ requires 76.84; H, 6.81; N, 4.98; O, 11.37; IR (KBr) 3400-3200, 3070, 3040, 2964, 2935, 2870, 2232, 1710, 1673, 1600, 1592, 1423, 1410, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 1.26(s, 6H), 2.24(s, 4H), 3.96(s, 3H), 7.29(t, 1H, 7.61Hz), 7.35(t, 1H, 7.23 Hz), 7.42(d, 1H, 8 Hz), 7.96(d, 1H, 8 Hz), 8.52(s, 1H), 8.95(s, 1H); ¹³C NMR (50 MHz): 14.74 (2CH₃), 32.44(2CH₂), 34.22(N-CH₃), 50.28, 110.26, 112.62, 118.62, 122.22, 123.42, 125.01, 128.11, 135.76, 136.66, 148.69, 165.40(2CO); ES-MS *m/z* 281(M⁺, 100%).

2-((1H-indol-3-yl)methylene)malononitrile (3p)

Yellow solid: M.P. 187-189 °C; (Found): C, 74.60; H, 3.65; N, 21.75. C₁₂H₇N₃ requires C, 74.62; H, 3.67; N, 21.77; IR (KBr) 3270, 2915, 2843, 2215, 1566, 1495, 1336, 1225, 1139, 825, 789 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 7.31(t, 1H, 7.65 Hz), 7.36(t, 1H, 7.23), 7.54(d, 1H, 8 Hz), 7.92(d, 1H, 8 Hz), 8.52(d, 1H), 9.2(s, 1H), 11.2(d, 1H); ¹³C NMR (50 MHz): 73.45, 110.24, 112.45 (2CN), 115.24, 118.70, 122.40, 123.45, 128.63, 135.6, 137.01, 150.48; ES-MS *m/z* 193(M⁺, 100%).

Ethyl 2-cyano-3-(1H-indol-3-yl)acrylate (3q)

Yellow Needles: M.P. 160-162 °C; (Found): C, 69.94; H, 5.00; N, 11.64; O, 13.31. C₁₄H₁₂N₂O₂ requires C, 69.99; H, 5.03; N, 11.66; O, 13.32; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 1.30(t, 3H, 7.2 Hz), 4.27(q, 2H, 7.2 Hz), 7.31(t, 1H, 7.6 Hz), 7.37(t, 1H, 7.2 Hz), 7.63(d, 1H, 8 Hz), 7.97(d, 1H, 8 Hz), 8.52(s, 1H), 8.91(s, 1H), 11.1(s, 1H); ¹³C NMR (50 MHz): 14.15(CH₃), 61.42(OCH₂), 73.04, 108.94, 111.41, 117.80, 118.65, 122.55, 123.75, 127.43, 135.8, 136.96, 145.82, 163.30(CO); ES-MS *m/z* 240(M⁺, 100%).

3-((2,2-Dimethyl-4,6-dimethylene-1,3-dioxan-5-ylidene)methyl)indole (3r)

Yellow solid: M.P. 175-176 °C; (Found): C, 66.40; H, 4.80; N, 5.12; O, 23.51. C₁₅H₁₃NO₄ requires C, 66.41; H, 4.83; N, 5.16; O, 23.59; IR (KBr) 3400-3200, 3100-2910, 2232, 1700, 1670, 1600, 1594, 1240, 1108 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 1.37(s, 6H), 7.31(t, 1H, 7.6 Hz), 7.37(t, 1H, 7.2 Hz), 7.62(d, 1H, 8 Hz), 7.95(d, 1H, 8 Hz), 8.52(s, 1H), 8.61(s, 1H), 11.0(s, 1H); ¹³C NMR (50 MHz): 14.20(CH₃), 106.42, 110.24, 115.24, 118.70, 122.23, 123.45, 124.02, 126.242, 135.6, 136.02, 146.72, 163.24(2CO); ES-MS *m/z* 271(M⁺, 100%).

5-((1H-3-indolyl)methylene)pyrimidine-2,4,6-trione (3s)

Yellow solid; M.P. 183-187 °C; (Found): C, 61.15; H, 3.52; N, 16.41; O, 18.79. C₁₃H₉N₃O₃ requires C, 61.18; H, 3.55; N, 16.46; O, 18.81; IR (KBr) 3400-3200, 3100-2900, 2210, 1670, 1600, 1590, 1240, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 7.31-7.37(dt, 2H, 7.2 Hz, 7.8 Hz), 7.62(d, 1H, 8 Hz), 7.93(d, 1H, 8 Hz), 8.52(s, 1H), 8.62(s, 1H), 11.0(s, 1H), 11.21(s, 2H); ¹³C NMR (50 MHz): 109.27, 112.20, 118.62, 122.12, 123.45, 124.24, 127.02, 136.40, 136.46, 147.02, 152.40(CO), 163.24(2CO); ES-MS *m/z* 255(M⁺, 100%).

2-((1H-3-indolyl)methylene)-5,5-dimethylcyclohexane-1,3-dione (3t)

Yellow solid; M.P. 162-163 °C; (Found): C, 76.31; H, 6.37; N, 5.21; O, 11.94. C₁₇H₁₇NO₂ requires C, 76.38; H, 6.41; N, 5.24; O, 11.97; IR (KBr) 3400-3200, 3070, 3040, 2964, 2935, 2870, 2232, 1710, 1673, 1600, 1592, 1423, 1410, 1100 cm⁻¹; ¹H NMR (400 MHz, DMSO-d₆), 1.26(s, 6H), 2.5(s, 4H), 7.32-7.37(dt, 2H, 7.2 Hz, 7.8 Hz), 7.61(d, 1H, 8.1 Hz), 7.92(d, 1H, 8.2 Hz), 8.52(s, 1H), 8.62(s, 1H), 11.1(s, 1H); ¹³C NMR (50 MHz): 14.74(2CH₃), 32.44(2CH₂), 50.28, 110.26, 112.62, 118.62, 122.22, 123.42, 125.01, 128.11, 135.76, 136.66, 148.69, 165.40(2CO); ES-MS *m/z* 267(M⁺, 100%).

Antibacterial activity

Biological activity of compounds 3a-3t was studied by disc diffusion technique. Some of the compounds showing the interesting results are tabulated in the Table 2. Most bromo substituted and cyano substituted compounds showed the potent activity against the tested bacteria.

Table 2. Antimicrobial screening results of synthesized indole compounds

Compd.	Fungi		Gram(+Ve) bacteria			Gram(-Ve) bacteria		
	<i>A.niger</i>	<i>P.notatum</i>	<i>S.aureus</i>	<i>S.faecalis</i>	<i>B.Subtillis</i>	<i>E.coli</i>	<i>K.pneumoniae</i>	<i>S.typhi</i>
3a	+++	++	+++	-	+++	+	+	+++
3g	+	-	++	-	-	+	+	-
3d	-	-	+	+	++	-	-	+
3i	-	-	+++	-	+++	+++	++++	+
3l	++	-	+	+++	-	-	+	+

Inhibition values beyond control are + = 6–10 mm, ++ = 11–15 mm, +++ = 16–20 mm, ++++ = 21–25 mm and – = not active

(The values are including disc diameter); R = Terbinafin (antifungal agent) and Tetracycline (antibacterial agent). The standards are in the form of sterile Hi-Disc cartridges, each disc containing 10 µg of the drug

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