Indian Journal of Chemistry
Vol. 59B, November 2020, pp. 1738-1744

A concise synthesis of pyrazole clubbed imidazolone compounds as antimicrobial agents

N C Desai* & Surbhi B Joshi

Division of Medicinal Chemistry, Department of Chemistry (DST-FIST Sponsored and UGC NON-SAP)
Mahatma Gandhi Campus, Maharaja Krishnakumarsinhji Bhavnagar University, Bhavnagar 364 002, India

E-mail: dnisheeth@rediffmail.com

Received 20 April 2020; accepted (revised) 16 October 2020

We reported an efficient route for the synthesis of pyrazole clubbed imidazolone compounds. The products were characterized by standard techniques like IR, ^{1}H and ^{13}C NMR, and LC-MS. They were investigated for their antimicrobial activity against several strains of bacteria (*E. coli*, *P. aeruginosa*, *S. aureus* and *S. pyogenes*) and fungi (*C. albicans*, *A. niger*,and*A. clavatus*) using broth dilution method. Compounds**3j** (-2-NO_2),**3r** (-4-Br), and **3i** (-2-OCH_3) showed significant antimicrobial activity.

Keywords: Pyrazole,imidazolone, glycine, antimicrobial activity

Increasing the level of antimicrobial resistance makes surveillance difficult for human beings at a global level. Inadequate doses and self-medication make the traditional approaches worthless. This critical issue can only be solved by the research of new and effective antimicrobials. Our research group is focused on the last couple of decades for the synthesis of heterocyclic base antimicrobial agents[1-5]. In continuation, we have synthesized new pyrazole clubbed imidazolone heterocyclic compounds and screened for their antimicrobial activity. It is well known that hybrid molecules show very good activity[6-10] and therefore in this paper we attempted to synthesize pyrazole clubbed imidazole compounds.

Results and Discussion

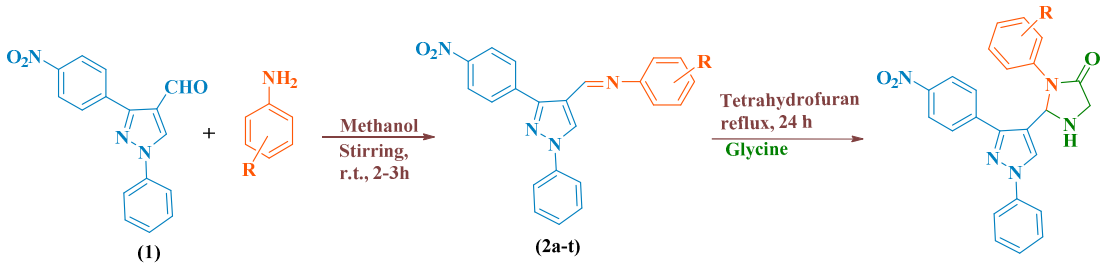
In the present work, we studied the reaction of imines **2a-t** with glycine (Scheme I). 3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **1** was stirred at RT with different derivatives of aniline. This reaction generated imines 1-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-*N*-substituted phenylmethanimines**2a-t**. This was further reacted with glycine in the presence of THF as solvent, synthesized final product 2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-3- substituted phenylimidazolidin-4-ones **3a-t**.

Antimicrobial Assay

Antimicrobial activity was accomplished by Mueller Hinton Broth dilution method (Becton Dickinson, USA)[11,12]. The strains were acquired from CSIR-IMTECH, Chandigarh, India. Antibacterial activity was screened in triple sets at diverse concentrations of 1000, 500, 250 and 200 µg/mL. The compounds which were found to be active in primary analysis were further diluted and evaluated. 10 µg/mL suspensions were further injected on appropriate media and the growth was noted after one or two days. In antifungal evaluation, primary screening was carried out in six sets at different concentrations of 1000, 500, and 250 µg/mL. The compounds found active were similarly diluted to 200, 125, 100, 62.5, 50, 25, and 12.5 µg/mL concentrations for a secondary screening. Minimum Inhibitory Concentration (MIC) is the lowest concentration of compound at which no growth of microbes could be detected after spot subculture for each compound. In this study, Ciprofloxacin and Nystatinwere the standard drugs for evaluating the antibacterial activity and antifungal activity respectively.

Discussion on antibacterial and antifungal activities

Antimicrobial activity data are as shown in Table I. A few compounds showed a minimum inhibitory concentration (MIC) value less than the standard drug. While some compounds showed the values comparable to the standard drug. Compound **3r** showed excellent activity against *E. coli* at MIC 12.5 µg/mL. Compound **3j** was the most active against *P. aeruginosa*. Results of antifungal activity showed that compound **3i** gave 12.5 µg/mL MIC value against *A. niger*. The standard drug used was Ciprofloxacin and Nystatin for



R= -H, -2-F, -4-F, -2-CH_3, -3-CH_3, -4-CH_3, -2-OCH_3, -3-OCH_3, -4-OCH_3, -2-NO_2, -3-NO_2, -4-NO_2, -2-Cl, -3-Cl, -4-Cl, -2-Br, -3-Br, -4-Br, -4-Br-2-CH_3, -3-Cl-4-F

Scheme I — Synthetic pathway of the newly synthesized compounds

Table I — Results of biological activities of compounds **3a-t**

Compd	-R	Minimum inhibitory concentrations for bacteria(MICB) in µg/mL				Minimum inhibitory concentrations for fungi (MICF) in µg/mL		
		E. c.	*P. a.*	*S. a.*	*S. p.*	*C. a.*	*A. n.*	*A. c.*
3a	-H	200	100	100	125	1000	250	500
3b	-2-F	62.5	125	500	500	>1000	500	500
3c	-4-F	125	200	250	25	>1000	>1000	>1000
3d	-2-CH_3	200	125	200	200	500	100	1000
3e	-3-CH_3	100	200	250	250	1000	200	>1000
3f	-4-CH_3	250	250	500	500	100	1000	50
3g	-2-OCH_3	100	100	500	500	1000	1000	1000
3h	-3-OCH_3	200	250	100	200	>1000	1000	1000
3i	-4-OCH_3	100	125	200	200	500	12.5	1000
3j	-2- NO_2	200	12.5	100	100	1000	250	250
3k	-3-NO_2	250	200	125	125	1000	500	500
3l	-4-NO_2	250	250	200	250	1000	1000	1000
3m	-2-Cl	125	125	250	250	>1000	1000	1000
3n	-3-Cl	125	125	200	200	1000	>1000	>1000
3o	-4-Cl	200	50	200	200	500	1000	1000
3p	-2-Br	250	200	500	500	500	1000	1000
3q	-3-Br	100	200	250	250	250	>1000	>1000
3r	-4-Br	12.5	125	250	100	1000	>1000	>1000
3s	-4-Br-2-CH_3	250	200	200	200	1000	100	1000
3t	-3-Cl-4-F	250	200	250	250	1000	500	500
Ciprofloxacin		25	25	50	50	—	—	—
Nystatin		—	—	—	—	100	100	100

E. c. - Escherichia coli, *P. a. - Pseudomonas aeruginosa*, *S. a. - Staphylococcus aureus*, *S. p. - Streptococcus pyogenes; C.a. - Candida albicans*, *A. n.- Aspergillusniger*, *A. c. - Aspergillusclavatus.*

antibacterial and antifungal activity respectively.

Experimental Section

Synthesis of 3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde, 1

3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **1** was prepared by the literature procedure[13].

Synthesis of 1-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-*N*-substituted phenylmethanimines, 2a-t

A mixture of 3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde **1** (0.01 mol) and substituted aniline (0.01 mol) was continuously stirred in methanol (10 mL) for 2-3 h at RT. Product was filtered off, washed with aqueous methanolic solution and crystallized from ethyl acetate.

Synthesis of 2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-3-substituted phenylimidazolidin-4-ones, 3a-t

Compounds **2a-t** (0.01 mol) were taken in a round bottom flask having tetrahydrofuran (THF) (15 mL) as a solvent. Then solution of glycine (0.02 mol) (in distilled water) was added and refluxed for 24 h. This reaction mixture was poured into crushed ice to obtain the product which was filtered and washed with hot water to

remove excess of reactant, followed by recrystallization from ethanol (95%). All the synthesized compounds were prepared using the same method.

2-(3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-3-phenylimidazolidin-4-one,3a: 69%. m.p.187-189°C. IR (KBr): 1641 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1514, 1575 (-N-H bending,imidazolone ring (>NH)), 1456 (-C-H bending,imidazolone ring (>CH_2)), 1387, 1523 (-N=O stretching, -NO_2 group), 1294 (-C-N stretching,imidazolone ring (>NH)), 965 (-C-H bending, aromatic ring), 821 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41 dd (1H,*H*-C-H), 3.52 dd (1H, H-C-*H*), 6.05 s (1H, -C*H* of imidazolone ring), 7.15-8.29 m (14H,Ar-*H*), 7.67 s (1H, -C*H* of pyrazole ring), 7.93 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.2, 73.2, 117.3, 119.8 (2), 123.1, 124.5 (2), 126.3 (2), 126.5, 127.6 (2), 128.1, 128.7 (2), 129.4 (2), 139.3, 139.8, 141.6, 147.7, 149.8, 170.5; LC-MS: *m/z* 425.10 [M^+]. Anal. Calcd for: $C_{24}H_{19}N_5O_3$: C, 67.76; H, 4.50; N, 16.46. Found: C, 67.75; H, 4.52; N, 16.45%.

3-(2-Fluorophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3b: 65%. m.p.137-139°C. IR (KBr): 1652 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1516, 1569 (-N-H bending, imidazolone ring (>NH)), 1463 (-C-H bending, imidazolone ring (>CH_2)), 1352, 1526 (-N=O stretching, -NO_2 group), 1354 (-C-N stretching, imidazolone ring (>NH)), 1078 (-C-F stretching, -F group), 972 (-C-H bending, aromatic ring), 847 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.46 dd (1H, *H*-C-H), 3.53 dd (1H, H-C-*H*), 6.03 s (1H, -C*H* of imidazolone ring), 7.12-8.30 m (13H, Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.87 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 73.3, 115.6, 117.4, 119.7 (2), 123.1, 123.4, 124.6 (2), 124.7, 126.1 (2), 126.4, 127.6, 129.2, 129.5 (2), 139.2, 139.9, 147.8, 149.7, 162.7, 170.3; LC-MS: *m/z* 443.26 [M^+]. Anal. Calcd for: $C_{24}H_{18}FN_5O_3$: C, 65.01; H, 4.09; N, 15.79. Found: C, 65.02; H, 4.11; N, 15.81%.

3-(4-Fluorophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3c: 64%. m.p.160-162°C. IR (KBr): 1643 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1512, 1557 (-N-H bending, imidazolone ring (>NH)), 1453 (-C-H bending, imidazolone ring (>CH_2)), 1346, 1532 (-N=O stretching, -NO_2 group), 1293 (-C-N stretching, imidazolone ring (>NH)), 1053 (-C-F stretching, -F group), 971 (-C-H bending, aromatic ring), 796 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.42 dd (1H, *H*-C-H), 3.56 dd (1H, H-C-*H*), 6.02 s (1H, -C*H* of imidazolone ring), 7.13-8.21 m (13H, Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.92 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 73.5, 115.6 (2), 117.4, 119.7 (2), 123.1, 123.3 (2), 124.4 (2), 126.5 (3), 129.4 (2), 137.4, 139.2, 139.8, 147.7, 150.1, 162.7, 170.5; LC-MS: *m/z* 443.08 [M^+]. Anal. Calcd for: $C_{24}H_{18}FN_5O_3$: C, 65.01; H, 4.09; N, 15.79. Found: C, 65.04; H, 4.07; N, 15.77%.

2-(3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-3-(*o*-tolyl)imidazolidin-4-one,3d: 70%. m.p.191-193°C. IR (KBr): 1647 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1509, 1576 (-N-H bending, imidazolone ring (>NH)), 1476 (-C-H bending, imidazolone ring (>CH_2)), 1392 (-C-H bending, -CH_3 group), 1350, 1522 (-N=O stretching, -NO_2 group), 1285 (-C-N stretching, imidazolone ring (>NH)), 971 (-C-H bending, aromatic ring), 825 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.07 s (1H, -CH_3), 3.43 dd (1H, *H*-C-H), 3.55 dd (1H, H-C-*H*), 6.03 s (1H, -C*H* of imidazolone ring), 6.84-8.27 m (13H, Ar-*H*), 7.61 s (1H, -C*H* of pyrazole ring), 7.94 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.5, 52.3, 73.6, 116.7, 117.3, 120.2 (2), 123.1, 124.5 (2), 125.8, 126.3 (2), 126.4, 129.5 (3), 130.6, 134.2, 138.8, 139.2, 139.9, 147.8, 149.7, 170.3; LC-MS: *m/z* 439.28 [M^+]. Anal. Calcd for: $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.30; H, 4.86; N, 15.91%.

2-(3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-3-(*m*-tolyl)imidazolidin-4-one, 3e: 72%. m.p.111-113°C. IR (KBr): 1648 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1517, 1576 (-N-H bending, imidazolone ring (>NH)), 1456 (-C-H bending, imidazolone ring (>CH_2)), 1395 (-C-H bending, -CH_3 group), 1345, 1536 (-N=O stretching, -NO_2 group), 1297 (-C-N stretching, imidazolone ring (>NH)), 967 (-C-H bending, aromatic ring), 808 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.24 s (3H, -CH_3), 3.41 dd (1H, *H*-C-H), 3.55 dd(1H, H-C-*H*), 6.04 s (1H, -C*H* of imidazolone ring), 7.17-8.28 m (13H, Ar-*H*), 7.66 s (1H, -C*H* of pyrazole ring), 7.88 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.4, 52.1, 73.5, 117.3, 119.7 (2), 121.4, 123.2, 124.5 (2), 124.6, 124.8, 126.1 (2), 126.3, 128.7, 129.4 (2), 138.5, 139.3, 139.8, 141.7, 147.8, 149.9, 170.5;

LC-MS: *m/z* 439.19 [M^+]. Anal. Calcd for: $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.36; H, 4.83; N, 15.99%.

2-(3-(4-Nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)-3-(*p*-tolyl)imidazolidin-4-one, 3f: 59%. m.p.156-158°C IR (KBr): 1657 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1523, 1578 (-N-H bending, imidazolone ring (>NH)), 1469 (-C-H bending, imidazolone ring (>CH_2)), 1391 (-C-H bending, -CH_3 group), 1342, 1516 (-N=O stretching, -NO_2 group), 1293 (-C-N stretching, imidazolone ring (>NH)), 982 (-C-H bending, aromatic ring), 798 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 s (3H, -CH_3), 3.45 dd (1H, *H*-C-H), 3.58 dd (1H, H-C-*H*), 6.00 s (1H, -C*H* of imidazolone ring), 6.93-8.27 m (13H, Ar-*H*), 7.68 s (1H, -C*H* of pyrazole ring), 7.94 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 52.0, 73.5, 117.4, 119.7 (2), 123.1, 124.5 (2), 126.3 (3), 129.3 (2), 129.5 (2), 133.5, 136.7, 138.6, 139.2, 147.8, 150.1, 170.6; LC-MS: *m/z* 439.05 [M^+]. Anal. Calcd for: $C_{25}H_{21}N_5O_3$: C, 68.33; H, 4.82; N, 15.94. Found: C, 68.31; H, 4.80; N, 15.96%.

3-(2-Methoxyphenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one,3g: 60%. m.p.151-153°C. IR (KBr): 1645 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1539, 1564 (-N-H bending,imidazolone ring (>NH)), 1463 (-C-H bending,imidazolone ring (>CH_2)), 1345, 1536 (-N=O stretching, -NO_2 group), 1326 (-C-N stretching,imidazolone ring (>NH)), 1030, 1254 (-C-O-C stretching, -OCH_3 group), 967 (-C-H bending, aromatic ring), 859 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.43 dd (1H, *H*-C-H), 3.55 dd (1H, H-C-*H*), 3.84 s (3H, -OCH_3), 6.03 s (1H, -C*H* of imidazolone ring), 6.98-8.29 m (13H, Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.90 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 55.9, 73.6, 112.7, 117.2, 117.3, 119.9 (2), 121.3, 124.5 (2), 126.3 (3), 128.3, 128.9, 129.4 (2), 139.2, 139.6, 147.8, 149.8, 162.1, 170.5; LC-MS: *m/z* 455.32 [M^+]. Anal. Calcd for: $C_{25}H_{21}N_5O_4$: C, 65.93; H, 4.65; N, 15.38. Found: C, 67.90; H, 4.63; N, 15.35%.

3-(3-Methoxyphenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3h: 62%. m.p.109-111°C. IR (KBr): 1653 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1523, 1570 (-N-H bending, imidazolone ring (>NH)), 1467 (-C-H bending, imidazolone ring (>CH_2)), 1352, 1539 (-N=O stretching, -NO_2 group), 1328 (-C-N stretching, imidazolone ring (>NH)), 1063, 1241 (-C-O-C stretching, -OCH_3 group), 971 (-C-H bending, aromatic ring), 836 cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.42 dd (1H, *H*-C-H), 3.52 dd (1H, H-C-*H*), 3.72 s (3H, -OCH_3), 6.04 s (1H, -C*H* of imidazolone ring), 6.83-8.27 m (13H, Ar-*H*), 7.66 s (1H, -C*H* of pyrazole ring), 7.91 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 55.6, 73.5, 116.3, 117.0, 119.6, 119.7 (2), 123.2, 124.3, 124.5 (2), 125.6, 126.2 (3), 129.4 (2), 139.3, 139.8, 142.6, 147.8, 150.2, 160.7, 170.2; LC-MS: *m/z* 455.20 [M^+]. Anal. Calcd for: $C_{25}H_{21}N_5O_4$: C, 65.93; H, 4.65; N, 15.38. Found: C, 67.97; H, 4.67; N, 15.37%.

3-(4-Methoxyphenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one,3i: 69%. m.p.99-101°C. IR (KBr): 1654 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1511, 1563 (-N-H bending,imidazolone ring (>NH)), 1456 (-C-H bending,imidazolone ring (>CH_2)), 1352, 1530 (-N=O stretching, -NO_2 group), 1290 (-C-N stretching,imidazolone ring (>NH)), 1024, 1264 (-C-O-C stretching, -OCH_3 group), 973 (-C-H bending, aromatic ring), 839cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.40 dd (1H,*H*-C-H), 3.55 dd (1H, H-C-*H*), 3.80 s (3H, -OCH_3),6.03 s (1H, -C*H* of imidazolone ring), 6.94-8.21 m (13H,Ar-*H*), 7.66 s (1H, -C*H* of pyrazole ring), 7.94 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 55.7, 73.5, 114.3 (2), 117.3, 119.7 (2), 122.5 (2), 123.4, 124.5 (2), 126.1 (3), 129.4 (2), 134.1, 139.2, 139.6, 147.8, 149.7, 158.8, 170.3; LC-MS: *m/z* 455.41 [M^+]. Anal. Calcd for: $C_{25}H_{21}N_5O_4$:C, 65.93; H, 4.65; N, 15.38. Found: C, 65.95; H, 4.68; N, 15.40%.

3-(2-Nitrophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one,3j: 72%. m.p.103-105°C. IR (KBr): 1648 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1520, 1578 (-N-H bending,imidazolone ring (>NH)), 1456 (-C-H bending,imidazolone ring (>CH_2)), 1356, 1532 (-N=O stretching, -NO_2 group), 1295 (-C-N stretching,imidazolone ring (>NH)), 968 (-C-H bending, aromatic ring), 802cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.45 dd (1H,*H*-C-H), 3.50 dd (1H, H-C-*H*), 6.03 s (1H, -C*H* of imidazolone ring), 7.45-8.31 m (13H,Ar-*H*), 7.68 s (1H, -C*H* of pyrazole ring), 7.92 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz,

$CDCl_3$): δ 52.1, 72.2, 113.4, 117.4, 120.2 (2), 123.2, 124.5 (2), 125.3, 125.6, 126.3 (3), 129.4 (2), 136.7, 137.8, 139.0, 139.8, 142.5, 147.8, 149.7, 170.6; LC-MS: *m/z* 470.15 [M^+]. Anal. Calcd for: $C_{24}H_{18}N_6O_5$:C, 61.27; H, 3.86; N, 17.86. Found: C, 61.25; H, 3.84; N, 17.83%.

3-(3-Nitrophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one,3k: 75%. m.p.172-174°C. IR (KBr): 1650 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1536, 1562 (-N-H bending,imidazolone ring (>NH)), 1465 (-C-H bending,imidazolone ring (>CH_2)), 1346, 1342 (-N=O stretching, -NO_2 group), 1324 (-C-N stretching, imidazolone ring (>NH)), 974 (-C-H bending, aromatic ring), 821cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.43 dd (1H,*H*-C-H), 3.54 dd (1H, H-C-*H*), 6.02 s (1H, -C*H* of imidazolone ring), 7.45-8.25 m (13H,Ar-*H*), 7.67 s (1H, -C*H* of pyrazole ring), 7.90 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz,$CDCl_3$): δ 52.3, 73.4, 117.3, 119.6, 119.8 (2), 123.2, 124.5 (2), 126.0 (3), 129.4 (2), 129.9, 133.4, 139.3, 139.9, 142.5, 147.8, 148.3, 149.8, 170.2; LC-MS: *m/z* 470.73 [M^+]. Anal. Calcd for: $C_{24}H_{18}N_6O_5$:C, 61.27; H, 3.86; N, 17.86. Found: C, 61.30; H, 3.88; N, 17.89%.

3-(4-Nitrophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one,3l: 74%. m.p.110-112°C. IR (KBr): 1649 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1526, 1547 (-N-H bending,imidazolone ring (>NH)), 1460 (-C-H bending,imidazolone ring (>CH_2)), 1342, 1536 (-N=O stretching, -NO_2 group), 1347 (-C-N stretching,imidazolone ring (>NH)), 973 (-C-H bending, aromatic ring), 799cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.45 dd (1H,*H*-C-H), 3.56 dd (1H, H-C-*H*), 6.04 s (1H, -C*H* of imidazolone ring), 6.97-8.24 m (13H,Ar-*H*), 7.63 s (1H, -C*H* of pyrazole ring), 7.91 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 73.5, 117.2, 119.7 (2), 123.3, 124.2 (2), 124.5 (2), 126.3 (3), 129.4 (2), 131.3 (2), 139.2, 139.8, 143.6, 147.8, 147.7, 148.1, 149.7, 170.3; LC-MS: *m/z* 470.52 [M^+]. Anal. Calcd for: $C_{24}H_{18}N_6O_5$:C, 61.27; H, 3.86; N, 17.86. Found: C, 61.29; H, 3.85; N, 17.85%.

3-(2-Chlorophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3m: 68%. m.p.149-151°C. IR (KBr): 1653 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1521, 1545 (-N-H bending, imidazolone ring (>NH)), 1458 (-C-H bending, imidazolone ring (>CH_2)), 1347, 1526 (-N=O stretching, -NO_2 group), 1332 (-C-N stretching, imidazolone ring (>NH)), 973 (-C-H bending, aromatic ring), 825 (-C-H bending, pyrazole ring (>C=C(H)N)), 741 cm^{-1} (-C-Cl stretching, -Cl group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.43 dd (1H, *H*-C-H), 3.54 dd (1H, H-C-*H*), 6.02 s (1H, -C*H* of imidazolone ring), 7.19-8.27 m (13H, Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.92 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 72.8, 117.3, 120.2 (2), 123.3 (2), 124.5 (2), 126.5 (3), 127.2, 129.4 (2), 130.3, 131.1, 139.2, 139.9, 140.3, 141.1, 147.8, 150.2, 170.2; LC-MS: *m/z* 459.62 [M^+]. Anal. Calcd for: $C_{24}H_{18}ClN_5O_3$: C, 62.68; H, 3.95; N, 15.23. Found: C, 62.71; H, 3.93; N, 15.20%.

3-(3-Chlorophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3n: 70%. m.p.120-122°C. IR (KBr): 1653 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1513, 1569 (-N-H bending,imidazolone ring (>NH)), 1463 (-C-H bending,imidazolone ring (>CH_2)), 708 (-C-Cl stretching, -Cl group), 1348, 1530 (-N=O stretching, -NO_2 group), 1287 (-C-N stretching,imidazolone ring (>NH)), 965 (-C-H bending, aromatic ring), 831cm^{-1} (-C-H bending, pyrazole ring (>C=C(H)N)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.45 dd (1H,*H*-C-H), 3.56 dd (1H, H-C-*H*), 6.02 s (1H, -C*H* of imidazolone ring), 7.20-8.27 m (13H,Ar-*H*), 7.66 s (1H, -C*H* of pyrazole ring), 7.91 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 73.5, 117.3, 119.7 (2), 123.1, 124.5 (2), 125.7, 126.2 (2), 126.4, 127.8, 129.4 (2), 130.4, 134.6, 135.9, 139.3, 139.6, 143.3, 147.8, 149.7, 170.6; LC-MS: *m/z* 459.27 [M^+]. Anal. Calcd for: $C_{24}H_{18}ClN_5O_3$:C, 62.68; H, 3.95; N, 15.23. Found: C, 62.66; H, 3.97; N, 15.25%.

3-(4-Chlorophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3o: 72%. m.p.157-159°C. IR (KBr): 1647 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1518, 1564 (-N-H bending, imidazolone ring (>NH)), 1459 (-C-H bending, imidazolone ring (>CH_2)), 1348, 1526 (-N=O stretching, -NO_2 group), 1297 (-C-N stretching, imidazolone ring (>NH)), 973 (-C-H bending, aromatic ring), 829 (-C-H bending, pyrazole ring (>C=C(H)N)), 796 cm^{-1} (-C-Cl stretching, -Cl group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.43 dd (1H, *H*-C-H), 3.54 dd (1H, H-C-*H*), 6.00 s (1H, -C*H* of imidazolone ring), 7.34-8.24 m (13H, Ar-*H*), 7.62 s (1H, -C*H* of pyrazole ring), 7.89 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 51.9, 73.6, 117.3, 119.7 (2), 123.1, 124.5 (2),

125.7 (2), 126.3 (3), 129.1 (2), 129.4 (2), 133.4, 139.2, 139.9, 140.1, 148.2, 149.9, 170.5. LC-MS: *m/z* 459.13 [M^+]. Anal. Calcd for: $C_{24}H_{18}ClN_5O_3$: C, 62.68; H, 3.95; N, 15.23. Found: C, 62.70; H, 3.94; N, 15.21%.

3-(2-Bromophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3p: 69%. m.p.145-147°C. IR (KBr): 1648 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1526, 1569 (-N-H bending,imidazolone ring (>NH)), 1462 (-C-H bending,imidazolone ring (>CH_2)), 1356, 1514 (-N=O stretching, -NO_2 group), 1298 (-C-N stretching,imidazolone ring (>NH)), 968 (-C-H bending, aromatic ring), 829 (-C-H bending, pyrazole ring (>C=C(H)N)), 526cm^{-1} (-C-Br stretching, -Br group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.42 dd (1H,*H*-C-H), 3.55 dd (1H, H-C-*H*), 5.99 s (1H, -C*H* of imidazolone ring), 7.11-8.26 m (13H,Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.91 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.3, 72.9, 117.4, 119.8 (2), 122.5, 123.2, 124.5 (2), 126.3 (3), 127.8, 128.4, 129.2 (2), 131.7 (2), 139.2, 139.8, 143.6, 147.7, 149.8, 170.6; LC-MS: *m/z* 502.89 [M^+]. Anal. Calcd for: $C_{24}H_{18}BrN_5O_3$:C, 57.16; H, 3.60; N, 13.89. Found: C, 57.19; H, 3.62; N, 13.92%.

3-(3-Bromophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3q: 68%. m.p.126-128°C. IR (KBr): 1648 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1521, 1567 (-N-H bending,imidazolone ring (>NH)), 1456 (-C-H bending,imidazolone ring (>CH_2)), 1342, 1526 (-N=O stretching, -NO_2 group), 1287 (-C-N stretching,imidazolone ring (>NH)), 967 (-C-H bending, aromatic ring), 821 (-C-H bending, pyrazole ring (>C=C(H)N)), 552cm^{-1} (-C-Br stretching, -Br group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.41 dd (1H,*H*-C-H), 3.54 dd (1H, H-C-*H*), 6.03 s (1H, -C*H* of imidazolone ring), 7.10-8.27 m (13H,Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.91 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.1, 73.5, 117.4, 119.7 (2), 120.7, 123.2, 123.5, 124.2 (2), 126.5 (3), 127.3, 129.5 (2), 130.1, 139.0, 139.8, 143.7, 147.8, 149.9, 170.5; LC-MS: *m/z* 503.14 [M^+]. Anal. Calcd for: $C_{24}H_{18}BrN_5O_3$:C, 57.16; H, 3.60; N, 13.89. Found: C, 57.18; H, 3.63; N, 13.88%.

3-(4-Bromophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3r:70%. m.p.173-175°C. IR (KBr): 1648 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1512, 1547 (-N-H bending,imidazolone ring (>NH)), 1468 (-C-H bending,imidazolone ring (>CH_2)), 1345, 1536 (-N=O stretching, -NO_2 group), 1285 (-C-N stretching,imidazolone ring (>NH)), 969 (-C-H bending, aromatic ring), 830 (-C-H bending, pyrazole ring (>C=C(H)N)), 514cm^{-1} (-C-Br stretching, -Br group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.44 dd (1H,*H*-C-H), 3.55 dd (1H, H-C-*H*), 6.03 s (1H, -C*H* of imidazolone ring), 7.43-8.25 m (13H,Ar-*H*), 7.63 s (1H, -C*H* of pyrazole ring), 7.91 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 52.0, 73.3, 117.3, 120.2 (2), 122.4, 123.2, 124.5 (2), 126.3, 129.5 (2), 131.7 (2), 136.8 (2), 139.2, 139.9, 140.5, 147.8, 149.7, 170.4; LC-MS: *m/z* 503.25 [M^+]. Anal. Calcd for: $C_{24}H_{18}BrN_5O_3$:C, 57.16; H, 3.60; N, 13.89. Found: C, 57.15; H, 3.58; N, 13.86%.

3-(4-Bromo-2-methylphenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3s:72%. m.p.194-196°C. IR (KBr): 1687 (C=O stretching, imidazolone ring (-C(=O)-N<)), 1502, 1598 (-N-H bending, imidazolone ring (>NH)), 1454 (-C-H bending, imidazolone ring (>CH_2)), 1392 (-C-H bending, -CH_3 group), 1334, 1535 (-N=O stretching, -NO_2 group), 1294 (-C-N stretching, imidazolone ring (>NH)), 958 (-C-H bending, aromatic ring), 833 (-C-H bending, pyrazole ring (>C=C(H)N)), 547 cm^{-1} (-C-Br stretching, -Br group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.13 s (3H, -CH_3), 3.43 dd (1H, *H*-C-H), 3.54 dd (1H, H-C-*H*), 6.02 s (1H, -C*H* of imidazolone ring), 7.05-8.26 m (12H, Ar-*H*), 7.64 s (1H, -C*H* of pyrazole ring), 7.92 s (1H, -N*H* of imidazolone ring); ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.8, 52.5, 73.6, 116.8, 117.4, 118.6, 119.7 (2), 123.4, 124.6 (2), 126.3 (3), 129.3 (2), 133.1, 134.2, 136.7, 137.7, 139.1, 139.8, 147.8, 149.9, 170.6. LC-MS: *m/z* 517.46 [M^+]. Anal. Calcd for: $C_{25}H_{20}BrN_5O_3$: C, 57.93; H, 3.89; N, 13.51. Found: C, 57.95; H, 3.87; N, 13.52%.

3-(3-Chloro-4-fluorophenyl)-2-(3-(4-nitrophenyl)-1-phenyl-1*H*-pyrazol-4-yl)imidazolidin-4-one, 3t: 67%. m.p.184-186°C. IR (KBr):1647 (C=O stretching,imidazolone ring (-C(=O)-N<)), 1517, 1563 (-N-H bending,imidazolone ring (>NH)), 1458 (-C-H bending,imidazolone ring (>CH_2)), 1347, 1527 (-N=O stretching, -NO_2 group), 1287 (-C-N stretching, imidazolone ring (>NH)), 1078 (-C-F stretching, -F group), 965 (-C-H bending, aromatic ring), 823 (-C-H bending, pyrazole ring (>C=C(H)N)), 741 cm^{-1} (-C-Cl stretching, -Cl group); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.46 dd (1H, *H*-C-H), 3.53 dd (1H, H-C-*H*), 6.02 s (1H, -C*H* of imidazolone ring), 7.11-8.28 m (12H, Ar-*H*), 7.63 s (1H, -C*H* of pyrazole ring), 7.94 s (1H, -N*H* of imidazolone ring); ^{13}C NMR

(100 MHz, $CDCl_3$): δ 52.3, 73.2, 113.5, 117.3, 119.7 (2), 120.8, 121.4, 123.2, 123.7, 129.5 (2), 138.8, 139.3, 147.8, 149.8, 154.3, 170.3; LC-MS: *m/z* 477.26 [M^+]. Anal. Calcd for: $C_{24}H_{17}ClFN_5O_3$: C, 60.32; H, 3.59; N, 14.66. Found: C, 60.30; H, 3.56; N, 14.63%.

Conclusion

We have revealed a concise and easy synthetic procedure for pyrazole and imidazolone derivatives. From the antimicrobial activity of the mentioned compounds, it may be concluded that compounds **3j** (-2-NO_2), **3r** (-4-Br) and **3i** (-2-OCH_3) showed excellent antimicrobial activity. Additional research on biological profiles of these compounds is worth.

Supplementary Information

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

Acknowledgements

One of the authors, Prof. N. C. Desai is thankful to UGC for awarding BSR faculty fellowship-2019 [No. F 18-1/2011 (BSR)] and financial assistance. The authors are thankful to the University Grants Commission (UGC) New Delhi, and Department of Science and Technology (DST), New Delhi (DST-FIST-SR/FST/CSI-212/2010), for financial support under the NON-SAP and DST-FIST programs [No.F.4-7/2008(BSR)/ 11-8/2008(BSR)] respectively.

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