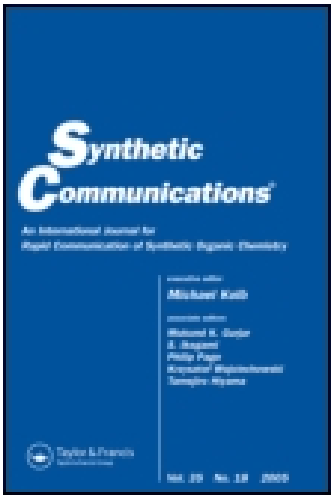

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Synthesis and Characterization of New 2-Oxo-azetidine Derivatives

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SYNTHESIS AND CHARACTERIZATION OF NEW 2-OXO-AZETIDINE DERIVATIVES

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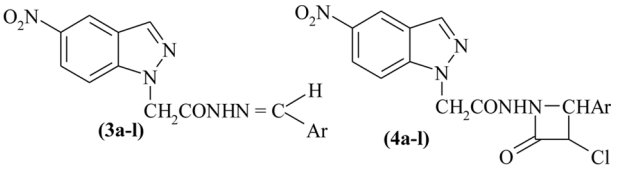
GRAPHICAL ABSTRACT



Where Ar = substituted aryl groups

Abstract *Several new N-[(4-aryl-3-chloro-2-oxo-azetidine)acetamidyl]-5-nitroindazoles* ***4a–l*** *were synthesized from N-(arylidene amino acetamidyl)-5-nitroindazoles* ***3a–l****. The structures of all these compounds were confirmed by infrared,* ^{1}H *NMR,* ^{13}C *NMR, and fast atom bombardment–mass spectra and also by microanalytical data.*

Keywords Arylidene; azetidinones; 5-nitroindazole

INTRODUCTION

Heterocycles constitute one of the biggest classical divisions of organic chemistry and are of immense importance biologically, to the pharmaceutical and agronomic based industries, and indeed to the development of human beings. Heterocycles and medicines have been interconnected recently. Most life-saving modern drugs contain the heterocyclic nucleus. The biological properties of heterocycles in general make them of prime interest to the pharmaceutical, biotechnological, and electronic industries. Organic synthesis is a principal way to produce chemical products of practical applications. The indazole nucleus is a pharmaceutically important and emerging heterocycle with a broad spectrum of activities including anti-inflammatory,[1] antitumor,[2] anti-HIV[3] and antimicrobial activities.[4] Particularly 5-nitroindazole and its derivatives have been found to possess a wide spectrum of activities such as antiprotozoal,[5] antimalarial,[6] and cytotoxic.[7]

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2-Oxo-azetidine derivatives also exhibit antimicrobial,[8–11] antitubercular,[12] anticonvulsant[13,14] and anti-inflammatory properties.[15–17] The incorporation of the 2-oxo-azetidine moiety in 5-nitroindazole through the acetamidyl framework has been found to enhance the activity. Hence, in the present study, position 1 in the 5-nitroindazole moiety having an imino group was used as the target for chemical modification. In view of these, we have synthesized some new N-(arylidene amino acetamidyl)-5-nitroindazoles **3a–l** and N-[(4-aryl-3-chloro-2-oxo-azetidine)acet amidyl]-5-nitroindazoles **4a–l**.

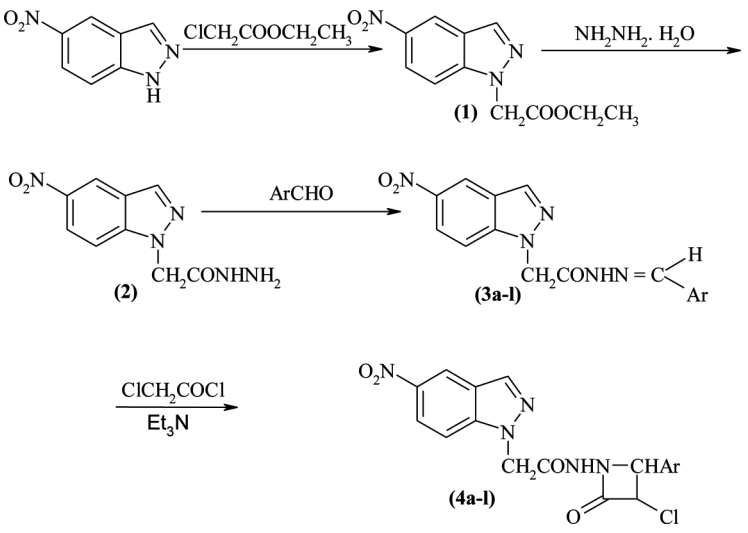
RESULTS AND DISCUSSION

5-Nitroindazole on reaction with ethyl chloroacetate yielded N-(ethyl ethanoate)-5-nitroindazole **1**. In the infrared (IR) spectrum of compound **1**, the absorption band characteristic for the >C=O ester group was identified at 1730 cm^{-1} and in the ^1H NMR spectrum the peaks at δ 1.25 ppm and δ 4.25 ppm were due to CH_3 and CH_2 respectively in $–COOCH_2CH_3$ (J = 7 Hz). Furthermore, in the ^{13}C NMR spectrum, a peak at δ 168.9 ppm appeared due to >C=O of ester, and the peaks at δ 61.1 ppm ($COO\underline{CH_2}CH_3$) and δ 14.5 ppm ($COOCH_2\underline{CH_3}$) confirmed the formation of compound **1**. The compound **1** on amination with hydrazine hydrate yielded N-(acetyl hydrazino)-5-nitroindazole **2**. In the IR spectrum of the compound **2**, the bands at 1678 cm^{-1} for –CONH and 3252, 3378 cm^{-1} for $–NHNH_2$ were observed. In the ^1H NMR spectrum, the peak at δ 8.20 ppm was due to –CONH, and a peak at δ 4.45 ppm was observed due to $–NH_2$. Furthermore in the ^{13}CNMR spectrum a peak at δ 168.0 ppm (-CONH) confirmed the formation of compound **2**. The compound **2** on condensation with various aromatic aldehydes yielded N-(arylidene amino acetamidyl)-5-nitroindazoles **3a–l**. Formation of compounds **3a–l** was evidenced by the appearance of peaks at δ 8.62–8.73 ppm due to N=CH and IR bands at 1635–1647 cm^{-1} for –N=CH of arylidenes. Furthermore, in the ^{13}C NMR spectra, peaks were observed in the range of δ 143.0–144.1 ppm due to a –N=CH group, which confirmed the formation of compounds **3a–l**. The compounds **3a–l** on reaction with chloroacetyl chloride in the presence of triethylamine yielded N-[(4-aryl-3-chloro-2-oxo-azetidine)acetamidyl]-5-nitroindazoles **4a–l** (Scheme 1). Formation of compounds **4a–l** was confirmed by the appearance of peaks at δ 5.01–5.12 ppm due to CH-Cl. In the IR spectra, the bands at 738–749 cm^{-1} for CH-Cl and 1730–1741 cm^{-1} for >C=O, cyclic were observed. Furthermore, in the ^{13}CNMR spectra, peaks at δ 132.1–133.3 ppm appeared due to CH-Cl, and peaks at δ 171.2–172.5 ppm were observed due to >C=O, cyclic which confirmed the formation of compounds **4a–l**.

EXPERIMENTAL

General Methods and Materials

All the melting points were taken in open capillary tubes. Formation of the compounds was routinely checked by thin-layer chromatography (TLC) using silica gel G, and the spots were exposed to iodine vapors for visualization. IR spectra were recorded in Shimadzu 8201 PC spectrophotometer. The ^1H NMR spectra were



Scheme 1. Synthesis of new 2-oxo-azetidine derivatives **4a–l**.

recorded at 400 MHz, and ^{13}C NMR spectra were recorded at 100 MHz on Bruker DRX-300 in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard on δ scale. The fast atom bombardment (FAB)–mass spectra were recorded on a Jeol SX102 mass spectrometer. All the compounds gave satisfactory C, H, and N percentages within the experimental limits.

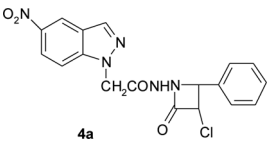
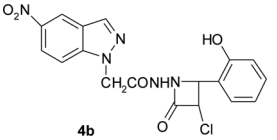
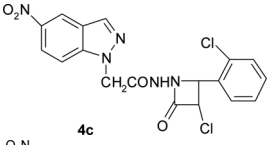
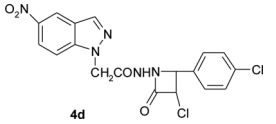
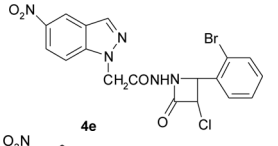
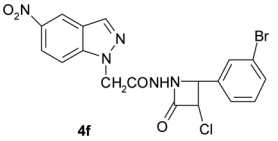
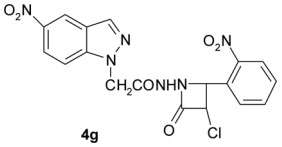
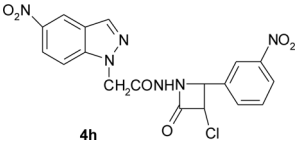
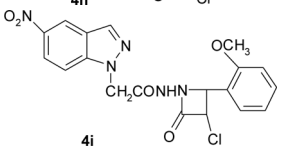
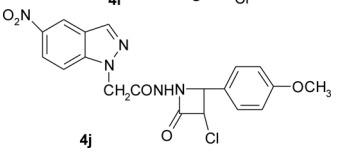
Synthesis of N-(Ethyl ethanoate)-5-nitroindazole (1)

Equimolar solution of 5-nitroindazole (30 g, 0.18 mol) and ethyl chloroacetate (22.55 g, 0.18 mol) in acetone (100 ml) was stirred for about 2 h. The solvent was removed in vacuo, and the residue thus obtained was purified over the column of silica-gel and recrystallized from acetone to furnish compound **1**. Yield 78%; mp 264–266 °C; IR (ν, cm^{-1}, KBr): 3046 (C-H, Ar-H), 1730 (>C=O, ester), 1601 (N=CH−, cyclic), 1530, 1338 ($ArNO_2$), 1430 (N−CH_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H, N=CH−, cyclic), 7.26–7.60 (m, 3H, Ar-H), 4.25 (q, 2H, $J = 7$ Hz, $COOCH_2CH_3$), 2.51 (s, 2H, N−CH_2), 1.25 (t, 3H, $J = 7$ Hz, $COOCH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9 (>C=O of ester), 142.0 (C-NO_2, aromatic), 135.0 (N=CH−, cyclic), 110.9–122.2 (C of aromatic ring), 61.1 ($COO\underline{CH_2}CH_3$), 33.3 (N−CH_2), 14.5 ($COOCH_2\underline{CH_3}$). Mass (m/z): 249 [M^+], 204, 203, 176, 162, 134, 88. Anal. (%) for $C_{11}H_{11}N_3O_4$, calcd. C, 53.01; H, 4.42; N, 16.87. Found: C, 52.98; H, 4.39; N, 16.83.

Synthesis of N-(Acetyl hydrazino)-5-nitroindazole (2)

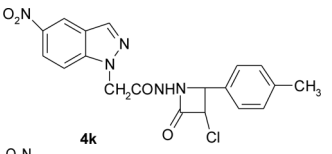
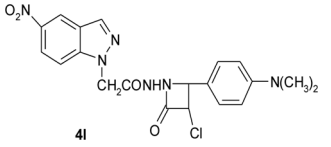
Equimolar solution of the compound **1** (27 g, 0.11 mol) and hydrazine hydrate (5.43 g, 0.11 mol) in dioxane (90 ml) was stirred for about 8 h. The solvent was removed in vacuo, and the residue thus obtained was purified over the column of

Table 1. Synthesized new 2-oxo-azetidine derivatives (**4a–l**)

Entry	Ar	Product	Yield (%)	Melting point (°C)
1	C_6H_5	 **4a**	72	197–198
2	2-OHC_6H_4	 **4b**	70	215–216
3	2-ClC_6H_4	 **4c**	68	175–176
4	4-ClC_6H_4	 **4d**	73	177–178
5	2-BrC_6H_4	 **4e**	69	185–186
6	3-BrC_6H_4	 **4f**	71	180–181
7	2-$NO_2C_6H_4$	 **4g**	74	205–206
8	3-$NO_2C_6H_4$	 **4h**	76	201–202
9	2-$CH_3OC_6H_4$	 **4i**	72	210–211
10	4-$CH_3OC_6H_4$	 **4j**	75	207–208

(*Continued*)

Table 1. Continued

Entry	Ar	Product	Yield (%)	Melting point (°C)
11	4-$CH_3C_6H_4$	 4k	70	192–193
12	4-$N(CH_3)_2C_6H_4$	 4l	65	195–196

silica gel and recrystallized from acetone to furnish compound **2**. Yield 80%; mp 210–211 °C; IR (ν, cm^{-1}, KBr]: 3252, 3378 ($-NHNH_2$), 3045 (C-H, Ar-H), 1678 (>C=O, amide), 1600 (N=CH−, cyclic), 1527, 1333 ($ArNO_2$), 1427 ($N-CH_2$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H, CONH), 7.89 (s, 1H, N=CH−, cyclic), 7.25–7.61 (m, 3H, Ar-H), 4.45 (s, 2H, NH_2), 2.49 (s, 2H, $N-CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.0 (CONH), 142.2 (C-NO_2, aromatic), 135.2 (N=CH−, cyclic), 111.9–122.0 (C of aromatic ring), 33.5 ($N-CH_2$). Mass (m/z): 235 [M^+], 204, 189, 176, 162, 134, 88. Anal. (%) for $C_9H_9N_5O_3$: calcd. C, 45.96; H, 3.83; N, 29.79. Found: C, 45.90; H, 3.79; N, 29.76.

Synthesis of N-(Benzylidene amino acetamidyl)-5-nitroindazole (3a)

Equimolar solution of the compound **2** (1.8 g, 0.008 mol) and benzaldehyde (0.81 g, 0.008 mol) in dioxane (30 ml) was stirred for about 1 h. The solvent was removed in vacuo, and the residue thus obtained was purified over the column of silica gel and recrystallized from chloroform to furnish compound **3a**. Yield 80%; mp 200–202 °C; IR (ν, cm^{-1}, KBr): 3043 (C-H, Ar-H), 1674 (>C=O, amide), 1635 (N=CH−, acyclic), 1604 (N=CH−, cyclic), 1524, 1329 ($ArNO_2$), 1428 ($N-CH_2$); ^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (s, 1H, CONH), 8.70 (s, 1H, N=CH−, acyclic), 7.86 (s, 1H, N=CH−, cyclic), 7.27–7.63 (m, 8H, Ar-H), 2.52 (s, 2H, $N-CH_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.1 (CONH), 143.2 (N=CH, acyclic), 142.3 (C-NO_2, aromatic), 135.6 (N=CH−, cyclic), 112.1–122.2 (C of aromatic ring), 33.4 ($N-CH_2$). Mass (m/z): 323 [M^+], 277, 219, 204, 176, 162, 161, 147, 134, 119, 104, 88. Anal. (%) for $C_{16}H_{13}N_5O_3$: calcd. C, 59.44; H, 4.02; N, 21.67. Found: C, 59.40; H, 3.98; N, 21.63.

Other compounds **3b–l** were prepared similarly by treating **2** with various aromatic aldehydes.

N-(2-Hydroxybenzylidene amino acetamidyl)-5-nitroindazole (3b)

Yield 81%; mp 260–261 °C; IR [ν, cm^{-1}, KBr): 3246 (Ar-OH), 3047 (C-H, Ar-H), 1672 (>C=O, amide), 1637 (N=CH−, acyclic), 1602 (N=CH−, cyclic),

1520, 1324 ($ArNO_2$), 1431 (N−CH_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.95 (s, 1H, Ar-OH), 8.71 (s, 1H, −N=CH−, acyclic), 8.22 (s, 1H, CONH), 7.84 (s, 1H, N=CH−, cyclic), 7.23–7.59 (m, 7H, Ar-H), 2.50 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9 (CONH), 165.1 (C-OH, aromatic), 143.1 (N=CH−, acyclic), 142.4 (C-NO_2, aromatic), 135.4 (N=CH−, cyclic), 112.3–122.6 (C of aromatic ring), 33.6 (N−CH_2). Mass (*m/z*): 339 [M^+], 293, 219, 204, 177, 176, 163, 162, 135, 134, 120, 88. Anal. (%) for $C_{16}H_{13}N_5O_4$: calcd. C, 56.64; H, 3.83; N, 20.65. Found: C, 56.59; H, 3.79; N, 20.61.

N-(2-Chlorobenzylidene amino acetamidyl)-5-nitroindazole (3c)

Yield 72%; mp 152–155 °C; IR (ν, cm^{-1}, KBr): 3042 (C-H, Ar-H), 1669 (>C=O, amide), 1639 (N=CH−, acyclic), 1605 (N=CH−, cyclic), 1523, 1327 ($ArNO_2$), 1432 (N−CH_2), 754 (Ar-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 1H, N=CH−, acyclic), 8.18 (s, 1H, CONH), 7.87 (s, 1H, N=CH−, cyclic), 7.20–7.55 (m, 7H, Ar-H), 2.54 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7 (CONH), 143.0 (N=CH−, acyclic), 142.7 (C-NO_2, aromatic), 135.8 (N=CH−, cyclic), 134.3 (C-Cl, aromatic), 112.8–122.3 (C of aromatic ring), 33.8 (N−CH_2). Mass (*m/z*): 357.5 [M^+], 311, 219, 204, 195, 181, 176, 162, 153, 138, 134, 88. Anal. (%) for $C_{16}H_{12}N_5O_3Cl$: calcd. C, 53.71; H, 3.36; N, 19.58. Found: C, 53.67; H, 3.31; N, 19.52.

N-(4-Chlorobenzylidene amino acetamidyl)-5-nitroindazole (3d)

Yield 78%; mp 156–158 °C; IR [ν, cm^{-1}, KBr]: 3041 (C-H, Ar-H), 1671 (>C=O, amide), 1636 (N=CH−, acyclic), 1603 (N=CH−, cyclic), 1528, 1325 ($ArNO_2$), 1434 (N−CH_2), 757 (Ar-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (s, 1H, -N=CH−, acyclic), 8.16 (s, 1H, CONH), 7.85 (s, 1H, N=CH−, cyclic), 7.21–7.57 (m, 7H, Ar-H), 2.55 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5 (CONH), 143.3 (N=CH−, acyclic), 142.5 (C-NO_2, aromatic), 135.3 (N=CH−, cyclic), 134.0 (C-Cl, aromatic), 112.0–122.1 (C of aromatic ring), 33.7 (N−CH_2). Mass (*m/z*): 357.5 [M^+], 311, 219, 204, 195, 181, 176, 162, 153, 138, 134, 88. Anal. (%) for $C_{16}H_{12}N_5O_3Cl$: calcd. C, 53.71; H, 3.36; N, 19.58. Found: C, 53.68; H, 3.34; N, 19.54.

N-(2-Bromobenzylidene amino acetamidyl)-5-nitroindazole (3e)

Yield 74%; mp 190–192 °C; IR (ν, cm^{-1}, KBr): 3040 C−H, Ar-H), 1666 (>C=O, amide), 1638 (N=CH−, acyclic), 1607 (N=CH−, cyclic), 1526, 1323 ($ArNO_2$), 1436 (N−CH_2), 618 (Ar-Br); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (s, 1H, -N=CH−, acyclic), 8.14 (s, 1H, CONH), 7.88 (s, 1H, N=CH−, cyclic), 7.22–7.58 (m, 7H, Ar-H), 2.53 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8 (CONH), 143.6 (N=CH−, acyclic), 141.9 (C-NO_2, aromatic), 135.1 (N=CH−, cyclic), 118.2 (C-Br, aromatic), 111.7–122.4 (C of aromatic ring), 33.9 (N−CH_2). Mass (*m/z*): 401.9 [M^+], 356, 240, 226, 219, 208, 198, 183, 176, 162, 134, 88. Anal. (%) for $C_{16}H_{12}N_5O_3Br$; calcd. C, 47.76; H, 2.98; N, 17.41. Found: C, 47.71; H, 2.93; N, 17.37.

N-(3-Bromobenzylidene amino acetamidyl)-5-nitroindazole (3f)

Yield 72%; mp 188–190 °C; IR (ν, cm^{-1}, KBr): 3044 (C−H, Ar-H), 1661 (>C=O, amide), 1640 (N=CH−, acyclic), 1606 (N=CH−, cyclic), 1522, 1326 ($ArNO_2$), 1433 (N−CH_2), 620 (Ar-Br). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1H, −N=CH−, acyclic), 8.11 (s, 1H, CONH), 7.91 (s, 1H, N=CH−, cyclic), 7.24–7.56 (m, 7H, Ar-H), 2.56 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2 (CONH), 143.4 (N=CH−, acyclic), 141.7 (C-NO_2, aromatic), 135.5 (N=CH−, cyclic), 118.4 (C-Br, aromatic), 111.5–122.8 (C of aromatic ring), 34.0 (N−CH_2). Mass (m/z): 401.9 [M^+], 356, 240, 226, 219, 208, 198, 183, 176, 162, 134, 88. Anal. (%) for $C_{16}H_{12}N_5O_3Br$: calcd. C, 47.76; H, 2.98; N, 17.41. Found: C, 47.73; H, 2.94; N, 17.38.

N-(2-Nitrobenzylidene amino acetamidyl)-5-nitroindazole (3g)

Yield 83%; mp 210–212 °C; IR (ν, cm^{-1}, KBr): 3048 (C−H, Ar-H), 1662 (>C=O, amide), 1642 (N=CH−, acyclic), 1609 (N=CH−, cyclic), 1525, 1328 ($ArNO_2$), 1429 (N−CH_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (s, 1H, −N=CH−, acyclic), 8.13 (s, 1H, CONH), 7.93 (s, 1H, N=CH−, cyclic), 7.28–7.62 (m, 7H, Ar-H), 2.60 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.5 (CONH), 143.5 (N=CH−, acyclic), 141.6 (C-NO_2, aromatic), 135.7 (N=CH−, cyclic), 111.2–122.5 (C of aromatic ring), 34.1 (N−CH_2). Mass (m/z): 368 [M^+], 322, 219, 206, 204, 192, 176, 164, 149, 134, 88. Anal. (%) for $C_{16}H_{12}N_6O_5$: calcd. C, 52.17; H, 3.26; N, 22.82. Found: C, 52.13; H, 3.21; N, 22.80.

N-(3-Nitrobenzylidene amino acetamidyl)-5-nitroindazole (3h)

Yield 85%; mp 214–215 °C; IR (ν, cm^{-1}, KBr): 3050 (C−H, Ar-H), 1664 (>C=O, amide), 1641 (N=CH−, acyclic), 1608 (N=CH−, cyclic), 1529, 1332 ($ArNO_2$), 1435 (N−CH_2), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.66 (s, 1H, −N=CH−, acyclic), 8.12 (s, 1H, CONH), 7.92 (s, 1H, N=CH−, cyclic), 7.31–7.65 (m, 7H, Ar-H), 2.59 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3 (CONH), 143.7 (N=CH−, acyclic), 141.8 (C-NO_2, aromatic), 135.9 (N=CH−, cyclic), 111.3–122.7 (C of aromatic ring), 34.3 (N−CH_2). Mass (m/z): 368 [M^+], 322, 219, 206, 204, 192, 176, 164, 149, 134, 88. Anal. (%) for $C_{16}H-_{12}N_6O_5$: calcd. C, 52.17; H, 3.26; N, 22.82. Found: C, 52.14; H, 3.23; N, 22.83.

N-(2-Methoxybenzylidene amino acetamidyl)-5-nitroindazole (3i)

Yield 72%; mp 220–222 °C; IR [ν, cm^{-1}, KBr]: 3049 (C−H, Ar-H), 2825 (Ar-OCH_3), 1663 (>C=O, amide), 1644 (N=CH−, acyclic), 1610 (N=CH−, cyclic), 1533, 1331 ($ArNO_2$), 1437 (N−CH_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (s, 1H, −N=CH−, acyclic), 8.15 (s, 1H, CONH), 7.94 (s, 1H, N=CH−, cyclic), 7.30–7.67 (m, 7H, Ar-H), 3.96 (s, 3H, OCH_3), 2.58 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4 (CONH), 144.0 (N=CH−, acyclic), 142.6 (C-NO_2, aromatic), 136.1 (N=CH−, cyclic), 110.5–122.9 (C of aromatic ring), 55.8 (OCH_3), 34.5 (N−CH_2). Mass (m/z): 353 [M^+], 219, 204, 191, 177, 176, 162, 149, 134, 88. Anal. (%) for $C_{17}H_{15}N_5O_4$: calcd. C, 57.79; H, 4.25; N, 19.83. Found: C, 57.73; H, 4.21; N, 19.79.

N-(4-Methoxybenzylidene amino acetamidyl)-5-nitroindazole (3j)

Yield 80%; mp 224–225 °C; IR (ν, cm^{-1}, KBr): 3053 (C−H, Ar-H), 2828 (Ar-OCH_3), 1665 (>C=O, amide), 1643 (N=CH−, acyclic), 1613 (N=CH−, cyclic), 1532, 1335 ($ArNO_2$), 1439 (N−CH_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (s, 1H, −N=CH−, acyclic), 8.17 (s, 1H, CONH), 7.95 (s, 1H, N=CH−, cyclic), 7.29–7.66 (m, 7H, Ar-H), 3.95 (s, 3H, OCH_3), 2.57 (s, H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6 (CONH), 143.8 (N=CH−, acyclic), 143.1 (C-NO_2, aromatic), 136.3 (N=CH, cyclic), 110.4–123.0 (C of aromatic ring), 55.5 (OCH_3), 34.2 (N−CH_2). Mass (m/z): 353 [M^+], 219, 204, 191, 177, 176, 162, 149, 134, 88. Anal. (%) for $C_{17}H_{15}N_5O_4$: calcd. C, 57.79; H, 4.25; N, 19.83. Found: C, 57.76; H, 4.22; N, 19.78.

N-(4-Methylbenzylidene amino acetamidyl)-5-nitroindazole (3k)

Yield 70%; mp 200–201 °C; IR (ν, cm^{-1}, KBr): 3051 (C−H, Ar-H), 2920 (Ar-CH_3), 1667 (>C=O, amide), 1645 (N=CH−, acyclic), 1611 (N=CH−, cyclic), 1534, 1337 ($ArNO_2$), 1440 (N−CH_2), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.62 (s, 1H, −N=CH−, acyclic), 8.19 (s, 1H, CONH), 7.96 (s, 1H, N=CH−, cyclic), 7.32–7.68 (m, 7H, Ar-H), 2.61 (s, 2H, N−CH_2), 2.37 (s, 3H, Ar-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8 (CONH), 143.9 (N=CH−, acyclic), 142.8 (C-NO_2, aromatic), 136.0 (N=CH−, cyclic), 110.0–123.2 (C of aromatic ring), 34.4 (N−CH_2), 22.5 (CH_3). Mass (m/z): 337 [M^+], 291, 219, 204, 190, 176, 162, 147, 134, 88. Anal. (%) for $C_{17}H_{15}N_5O_3$: calcd. C, 60.53; H, 4.45; N, 20.77. Found: C, 60.51; H, 4.41; N, 20.72.

N-(4-Dimethylaminobenzylidene amino acetamidyl)-5-nitroindazole (3l)

Yield 73%; mp 205–206 °C; IR (ν, cm^{-1}, KBr): 3054 (C−H, Ar-H), 2910, 2852 (N−CH_3), 1668 (>C=O, amide), 1647 (N=CH−, acyclic), 1612 (N=CH−, cyclic), 1536, 1336 ($ArNO_2$), 1438 (N−CH_2); ^{1}H NMR [400 MHz, $CDCl_3$]: 8.63 (s, 1H, −N=CH−, acyclic), 8.23 (s, 1H, CONH), 7.98 (s, 1H, N=CH−, cyclic), 7.34–7.64 (m, 7H, Ar-H), 3.12 (s, 6H, $2 \times CH_3$), 2.63 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7 (CONH), 144.1 (N=CH−, acyclic), 143.0 (C-NO_2, aromatic), 136.4 (N=CH−, cyclic), 110.3–123.1 (C of aromatic ring), 34.7 (N−CH_2), 23.7 (NCH_3). Mass (m/z): 366 [M^+], 320, 219, 204, 190, 176, 162, 147, 134, 88. Anal. (%) for $C_{18}H_{18}N_6O_3$: calcd. C, 59.02; H, 4.92; N, 22.95. Found: C, 58.97; H, 4.88; N, 22.90.

Synthesis of N-[(4-Phenyl-3-chloro-2-oxo-azetidine) acetamidyl]-5-nitroindazole (4a)

An equimolar solution of the compound **3a** (1 g, 0.003 mol) and chloroacetyl chloride (0.35 g, 0.003 mol) with triethylamine (0.31 g, 0.003 mol) in acetone (25 ml) was stirred for about 5 h. The solvent was removed in vacuo, and the residue thus obtained was purified over a column of silica gel and recrystallized from chloroform

to furnish compound **4a**. Yield 72%; mp 197–198 °C; IR (ν, cm^{-1}, KBr): 3055 (C−H, Ar-H), 1730 (>C=O, cyclic), 1672 (>C=O, amide), 1613 (N=CH−, cyclic), 1535, 1339 ($ArNO_2$), 1442 (N−CH_2), 738 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H, CONH), 8.01 (s, 1H, N=CH−, cyclic), 7.38–7.71 (m, 8H, Ar-H), 5.01 (d, 1H, $J = 5$ Hz, CHCl), 4.19 (d, 1H, $J = 5$ Hz, −N−CH−), 2.66 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2 (>C=O, cyclic), 167.5 (CONH), 143.7 (C-NO_2, aromatic), 137.1 (N=CH−, cyclic), 132.1 (CH-Cl), 112.2–124.3 (C of aromatic ring), 39.1 (N−CH-), 35.1 (N−CH_2). Mass (m/z): 399 [M^+], 371, 353, 325, 237, 223, 219, 209, 204, 195, 180, 176, 167, 162, 152, 134, 88. Anal. (%) for $C_{18}H_{14}N_5O_4Cl$: calcd. C, 54.07; H, 3.50; N, 17.52. Found: C, 54.04; H, 3.46; N, 17.48.

Other compounds **4b–l** were prepared similarly by using **3b–l** respectively.

N-[{4-(2-Hydroxyphenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4b)

IR [ν, cm^{-1}, KBr]: 3244 (Ar-OH), 3057 (C−H, Ar-H), 1733 (>C=O, cyclic), 1674 (>C=O, amide), 1615 (N=CH−, cyclic), 1537,1340 ($ArNO_2$), 1444 (N−CH_2), 739 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.96 (s, 1H, Ar-OH), 8.28 (s, 1H, CONH), 8.03 (s, 1H, N=CH−, cyclic), 7.40–7.70 (m, 7H, Ar-H), 5.03 (d, 1H, $J = 5$ Hz, CHCl), 4.22 (d, 1H, $J = 5$ Hz, −N−CH−), 2.67 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.3 (>C=O, cyclic), 167.8 (CONH), 165.3 (C-OH, aromatic), 143.5 (C-NO_2, aromatic), 137.3 (N=CH−, cyclic), 132.2 (CH-Cl), 112.5–124.1 (C of aromatic ring), 39.3 (N−CH-), 35.3 (N−CH_2). Mass (m/z): 415 [M^+], 387, 369, 341, 253, 239, 225, 219, 211, 204, 196, 183, 176, 168, 162, 134, 88. Anal. (%) for $C_{18}H_{14}N_5O_5Cl$; calcd. C, 51.98; H, 3.37; N, 16.85. Found: C, 51.95; H, 3.33; N, 16.81.

N-[{4-(2-Chlorophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4c)

IR (ν, cm^{-1}, KBr): 3059 (C−H, Ar-H), 1731 (>C=O, cyclic), 1673 (>C=O, amide), 1614 (N=CH−, cyclic), 1536, 1338 ($ArNO_2$), 1443 (N−CH_2), 755 (Ar-Cl), 740 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H, CONH), 8.02 (s, 1H, N=CH−, cyclic), 7.41–7.72 (m, 7H, Ar-H), 5.02 (d, 1H, $J = 5$ Hz, CHCl), 4.21 (d, 1H, $J = 5$ Hz, -N−CH-), 2.69 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4 (>C=O, cyclic), 167.6 (CONH), 143.6 (C-NO_2, aromatic), 137.6 (N=CH−, cyclic), 134.1 (C-Cl, aromatic), 132.4 (CH-Cl), 112.3–124.2 (C of aromatic ring), 39.2 (N−CH-), 35.2 (N−CH_2). Mass (m/z): 434 [M^+], 406, 388, 360, 272, 258, 244, 230, 219, 215, 204, 202, 187, 176, 162, 134, 88. Anal. (%) for $C_{18}H_{13}N_5O_4Cl_2$: calcd. C, 49.77; H, 2.99; N, 16.13. Found: C, 49.74; H, 2.95; N, 16.10.

N-[{4-(4-Chlorophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4d)

IR (ν, cm^{-1}, KBr): 3061 (C−H, Ar-H), 1734 (>C=O, cyclic), 1671 (>C=O, amide), 1616 (N=CH−, cyclic), 1538, 1341 ($ArNO_2$), 1445 (N−CH_2), 756 (Ar-Cl), 741 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H, CONH), 8.04 (s, 1H,

N=CH−, cyclic), 7.43–7.73 (m, 7H, Ar-H), 5.04 (d, 1H, $J = 5$ Hz, CHCl), 4.23 (d, 1H, $J = 5$ Hz, -N−CH-), 2.68 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.6 (>C=O, cyclic), 167.7 (CONH), 143.3 (C-NO_2, aromatic), 137.4 (N=CH−, cyclic), 134.1 (C-Cl, aromatic), 132.3 (CH-Cl), 112.4–124.4 (C of aromatic ring), 39.4 (N−CH-), 35.4 (N−CH_2). Mass (m/z): 434 [M^+], 406, 388, 360, 272, 258, 244, 230, 219, 215, 204, 202, 187, 176, 162, 134, 88. Anal. (%) for $C_{18}H_{13}N_5O_4Cl_2$: calcd. C, 49.77; H, 2.99; N, 16.13. Found: C, 49.75; H, 2.96; N, 16.11.

N-[{4-(2-Bromophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4e)

IR (ν, cm^{-1}, KBr): 3060 (C−H, Ar-H), 1732 (>C=O, cyclic), 1675 (>C=O, amide), 1618 (N=CH−, cyclic), 1539, 1342 ($ArNO_2$), 1446 (N−CH_2), 743 (CH-Cl), 623 (Ar-Br); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H, CONH), 8.06 (s, 1H, N=CH−, cyclic), 7.45–7.69 (m, 7H, Ar-H), 5.06 (d, 1H, $J = 5$ Hz, CHCl), 4.25 (d, 1H, $J = 5$ Hz, -N−CH-), 2.70 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7 (>C=O, cyclic), 168.1 (CONH), 143.1 (C-NO_2, aromatic), 137.5 (N=CH−, cyclic), 132.5 (CH-Cl), 118.1 (C-Br, aromatic), 112.6–124.6 (C of aromatic ring), 39.6 (N−CH-), 35.5 (N−CH_2). Mass (m/z): 478 [M^+], 450, 432, 404, 316, 302, 288, 274, 259, 246, 231, 219, 204, 176, 162, 134, 88. Anal. (%) for $C_{18}H_{13}N_5O_4ClBr$: calcd. C, 45.14; H, 2.72; N, 14.63. Found: C, 45.11; H, 2.69; N, 14.58.

N-[{4-(3-Bromophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4f)

IR (ν, cm^{-1}, KBr): 3062 (C−H, Ar-H), 1735 (>C=O, cyclic), 1676 (>C=O, amide), 1617 (N=CH−, cyclic), 1541, 1343 ($ArNO_2$), 1448 (N−CH_2), 742 (CH-Cl), 619 (Ar-Br); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (s, 1H, CONH), 8.08 (s, 1H, N=CH−, cyclic), 7.42–7.74 (m, 7H, Ar-H), 5.05 (d, 1H, $J = 5$ Hz, CHCl), 4.24 (d, 1H, $J = 5$ Hz, -N−CH-), 2.72 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.9 (>C=O, cyclic), 168.3 (CONH), 143.2 (C-NO_2, aromatic), 137.7 (N=CH−, cyclic), 132.6 (CH-Cl), 118.3 (C-Br, aromatic), 112.7–124.7 (C of aromatic ring), 39.7 (N−CH-), 35.7 (N−CH_2). Mass (m/z): 478 [M^+], 450, 432, 404, 316, 302, 288, 274, 259, 246, 231, 219, 204, 176, 162, 134, 88. Anal. (%) for $C_{18}H_{13}N_5O_4ClBr$: calcd. C, 45.14; H, 2.72; N, 14.63. Found: C, 45.10; H, 2.68; N, 14.60.

N-[{4-(2-Nitrophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4g)

IR (ν, cm^{-1}, KBr): 3065 (C−H, Ar-H), 1736 (>C=O, cyclic), 1678 (>C=O, amide), 1619 (N=CH−, cyclic), 1540, 1344 ($ArNO_2$), 1447 (N−CH_2), 744 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (s, 1H, CONH), 8.10 (s, 1H, N=CH−, cyclic), 7.46–7.76 (m, 7H, Ar-H), 5.07 (d, 1H, $J = 5$ Hz, CHCl), 4.26 (d, 1H, $J = 5$ Hz, −N−CH−), 2.71 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.2 (>C=O, cyclic), 168.2 (CONH), 143.4 (C-NO_2, aromatic), 137.8 (N=CH−, cyclic), 132.7 (CH-Cl), 112.9–124.8 (C of aromatic ring), 39.5 (N−CH-), 35.6 (N−CH_2). Mass (m/z): 444 [M^+], 416, 398, 376, 282, 268, 254, 240, 225, 219, 212, 204, 197, 176,

162, 134, 88. Anal. (%) for $C_{18}H_{13}N_6O_6Cl$: calcd. C, 48.59; H, 2.92; N, 18.90. Found: C, 48.55; H, 2.88; N, 18.86.

N-[{4-(3-Nitrophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4h)

IR (ν, cm^{-1}, KBr): 3064 (C−H, Ar-H), 1738 (>C=O, cyclic), 1677 (>C=O, amide), 1620 (N=CH−, cyclic), 1542, 1346 ($ArNO_2$), 1449 (N−CH_2), 745 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 1H, CONH), 8.09 (s, 1H, N=CH−, cyclic), 7.47–7.78 (m, 7H, Ar-H), 5.09 (d, 1H, $J = 5$ Hz, CHCl), 4.27 (d, 1H, $J = 5$ Hz, −N−CH−), 2.73 (s, 2H, N−CH_2); ^{13}CNMR (100 MHz, $CDCl_3$): δ 172.1 (>C=O, cyclic), 168.4 (CONH), 143.8 (C-NO_2, aromatic), 137.9 (N=CH−, cyclic), 132.9 (CH-Cl), 112.8–125.1 (C of aromatic ring), 39.8 (N−CH-), 35.8 (N−CH_2). Mass (m/z): 444 [M^+], 416, 398, 376, 282, 268, 254, 240, 225, 219, 212, 204, 197, 176, 162, 134, 88. Anal. (%) for $C_{18}H_{13}N_6O_6Cl$: calcd. C, 48.59; H, 2.92; N, 18.90. Found: C, 48.56; H, 2.89; N, 18.87.

N-[{4-(2-Methoxyphenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4i)

IR (ν, cm^{-1}, KBr): 3063 (C−H, Ar-H), 2823 (Ar-OCH_3), 1737 (>C=O, cyclic), 1680 (>C=O, amide), 1622 (N=CH−, cyclic), 1544, 1348 ($ArNO_2$), 1450 (N−CH_2), 747 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (s, 1H, CONH), 8.07 (s, 1H, N=CH−, cyclic), 7.48–7.77 (m, 7H, Ar-H), 5.08 (d, 1H, $J = 5$ Hz, CHCl), 4.29 (d, 1H, $J = 5$ Hz, −N−CH−), 3.94 (s, 3H, OCH_3), 2.75 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3 (>C=O, cyclic), 168.5 (CONH), 144.1 (C-NO_2, aromatic), 138.1 (N=CH−, cyclic), 132.8 (CH-Cl), 113.1–125.2 (C of aromatic ring), 55.7 (OCH_3), 39.9 (N−CH-), 35.9 (N−CH_2). Mass (m/z): 429 [M^+], 401, 383, 355, 267, 253, 239, 225, 219, 210, 204, 197, 182, 176, 162, 134, 88. Anal. (%) for $C_{19}H_{16}N_5O_5Cl$: calcd. C, 53.08; H, 3.72; N, 16.30. Found: C, 53.05; H, 3.69; N, 16.26.

N-[{4-(4-Methoxyphenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4j)

IR (ν, cm^{-1}, KBr]: 3066 (C−H, Ar-H), 2824 (Ar-OCH_3), 1739 (>C=O, cyclic), 1682 (>C=O, amide), 1621 (N=CH−, cyclic), 1543, 1347 ($ArNO_2$), 1452 (N−CH_2), 746 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.36 (s, 1H, CONH), 8.11 (s, 1H, N=CH−, cyclic), 7.50–7.80 (m, 7H, Ar-H), 5.10 (d, 1H, $J = 5$ Hz, CHCl), 4.28 (d, 1H, $J = 5$ Hz, -N−CH-), 3.97 (s, 3H, OCH_3), 2.74 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.4 (>C=O, cyclic), 168.7 (CONH), 143.9 (C-NO_2, aromatic), 138.3 (N=CH−, cyclic), 133.1 (CH-Cl), 113.2–125.4 (C of aromatic ring), 55.9 (OCH_3), 40.0 (N−CH-), 36.1 (N−CH_2). Mass (m/z): 429 [M^+], 401, 383, 355, 267, 253, 239, 225, 219, 210, 204, 197, 182, 176, 162, 134, 88. Anal. (%) for $C_{19}H_{16}N_5O_5Cl$: calcd. C, 53.08; H, 3.72; N, 16.30. Found: C, 53.04; H, 3.68; N, 16.27.

N-[{4-(4-Methylphenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4k)

IR [ν, cm^{-1}, KBr]: 3067 (C−H, Ar-H), 2921 (Ar-CH_3), 1740 (>C=O, cyclic), 1681 (>C=O, amide), 1623 (N=CH−, cyclic), 1545, 1349 ($ArNO_2$), 1451 (N−CH_2), 748 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H, CONH), 8.12 (s, 1H, N=CH−, cyclic), 7.49–7.79 (m, 7H, Ar-H), 5.11 (d, 1H, $J = 5$ Hz, CHCl), 4.30 (d, 1H, $J = 5$ Hz, −N−CH−), 2.76 (s, 2H, N−CH_2), 2.36 (s, 3H, Ar-CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.5 (>C=O, cyclic), 168.6 (CONH), 144.2 (C-NO_2, aromatic), 138.2 (N=CH−, cyclic), 133.2 (CH-Cl), 113.3–125.3 (C of aromatic ring), 40.1 (N−CH-), 36.2 (N−CH_2), 22.7 (CH_3). Mass (m/z): 413 [M^+], 385, 367, 339, 251, 237, 223, 219, 209, 204, 194, 181, 176, 166, 162, 134, 88. Anal. (%) for $C_{19}H_{16}N_5O_4Cl$: calcd. C, 55.14; H, 3.87; N, 16.93. Found: C, 55.11; H, 3.83; N, 16.89.

N-[{4-(4-Dimethylaminophenyl)-3-chloro-2-oxo-azetidine}acetamidyl]-5-nitroindazole (4l)

IR (ν, cm^{-1}, KBr): 3068 (C−H, Ar-H), 2911, 2851 (N−CH_3), 1741 (>C=O, cyclic), 1683 (>C=O, amide), 1624 (N=CH−, cyclic), 1546, 1350 ($ArNO_2$), 1453 (N−CH_2), 749 (CH-Cl); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H, CONH), 8.13 (s, 1H, N=CH−, cyclic), 7.51–7.81 (m, 8H, Ar-H), 5.12 (d, 1H, $J = 5$ Hz, CHCl), 4.31 (d, 1H, $J = 5$ Hz, −N−CH−), 3.15 (s, 6H, $2 \times CH_3$), 2.77 (s, 2H, N−CH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6 (>C=O, cyclic), 168.8 (CONH), 144.3 (C-NO_2, aromatic), 138.4 (N=CH−, cyclic), 133.3 (CH-Cl), 113.4–125.5 (C of aromatic ring), 40.2 (N−CH-), 36.3 (N−CH_2), 23.8 (NCH_3). Mass (m/z): 442 [M^+], 414, 396, 374, 280, 266, 252, 238, 223, 219, 210, 204, 195, 176, 162, 134, 88. Anal. (%) for $C_{20}H_{19}N_6O_4Cl$; calcd. C, 54.24; H, 4.29; N, 18.98. Found: C, 54.20; H, 4.26; N, 18.94.

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REFERENCES

1. Caron, S.; Vazquez, E. The synthesis of a selective PDE_4/TNF α inhibitor. *Org. Process Res. Dev.* **2001**, *5*, 587–592.
2. Jakupec, A. M.; Reisner, E.; Eichinger, A.; Pongratz, M.; Arion, V. B.; Galanski, M.; Hartinger, C. G.; Keppler, B. K. Redox-active antineoplastic ruthenium complexes with indazole: Correlation of in vitro potency and reduction potential. *J. Med. Chem.* **2005**, *48*, 2831–2837.

3. Sun, J. H.; Teleha, C. A.; Yan, J. S.; Rodgers, J. D.; Nugiel, D. A. Efficient synthesis of 5-(bromomethyl)-and 5-(aminomethyl)-1-THP-indazole. *J. Org. Chem.* **1997**, *62*, 5627–5629.
4. Li, X.; Chu, S.; Feher, V. A.; Kahalili, M.; Nie, Z.; Margosiak, S.; Nikulin, V.; Levin, J.; Sprankle, K. G.; Tedder, M. E.; Almassy, R.; Appelt, K.; Yager, K. M. Structure-based design, synthesis, and antimicrobial activity of indazole-derived SAH/MTA nucleosidase inhibitors. *J. Med. Chem.* **2003**, *46*, 5663–5673.
5. Olea-Azar, C.; Cerecetto, H.; Gerpe, A.; Gonzalez, M.; Aran, V. J. Rigol, C.; Opazo, L. ESR and electrochemical study of 5-nitroindazole derivatives with antiprotozoal activity. *Spectrochim. Acta Part A* **2006**, *63*, 36–42.
6. Alho, M. M.; Garcia-Sanchez, R. N.; Nogel-Ruiz, J. J.; Escario, J. A.; Gomez-Barrio, A.; Martinez-Fernandez, A. R.; Aran, V. J. Synthesis and evaluation of 1, 1′-hydrocarbylenebis (indazole-3-ols) as potential antimalarial drugs. *Chem. Med. Chem.* **2009**, *4*, 78–87.
7. Aran, V. J.; Ochoa, C.; Boiani, L.; Buccino, P.; Cerecetto, H.; Gerpe, A.; Gonzalez, M.; Montero, D.; Nogal, J. J.; Gomez-Barrio, A.; Azqueta, A.; Lopez de Cerain, A.; Piro, O. E.; Castellano, E. E. Synthesis and biological properties of new 5-nitroindazole derivatives. *Bioorg. Med. Chem.* **2005**, *13*, 3197–3207.
8. Sonwane, S. K.; Srivastava, S. D.; Srivastava, S. K. Synthesis and antimicrobial activity of 2-(2′-arylidene-hydrazino-acetyl-amino)-4-phenyl-1,3-thiazoles and 2-[2′-{4″-substituted-aryl-3″-chloro-2″-oxo-azetidine}-acetyl-amino]-4-phenyl-1,3-thiazoles. *Indian J. Chem.*, **2008**, *47B*, 633–636.
9. Singh, G. S.; Pheko, T. Formation and antimicrobial activity of 2-azetidinones from selective ester cleavage in 1,3,3-trisubstituted-4-[2′-(O-diarylacyl) hydroxyphenyl]-2-azetidinones. *Indian J. Chem.*, **2008**, *47B*, 159–162.
10. Singh, G. S.; Mbukwa, E.; Pheko, T. Synthesis and antimicrobial activity of 2-azetidinones from N-(salicylidene)amines and 2-diazo-1,2-diarylethanones. *Arkivoc* **2007**, *9*, 80–90.
11. Ansari, K. F.; Lal, C. Synthesis and biological activity of some heterocyclic compounds containing benzimidazole and β-lactam moiety. *J. Chem. Sci.* **2009**, *121*, 1017–1025.
12. Yadav, R.; Srivastava, S.; Srivastava, S. K.; Srivastava, S. D. Synthesis and biological activity of benzothiazolylthiomethyl-1,3,4-thiadiazol-2-oxo-azetidines and 5-arylidene-1, 3-thiazolidine-4-ones. *Chem. Indi. J.*, **2003**, *1*, 95–103.
13. Mistry, K.; Desai, K. R. Microwave-assisted rapid and efficient synthesis of nitrogen- and sulphur-containing heterocyclic compounds and their pharmacological evaluation. *Indian J. Chem.*, **2006**, *45B*, 1762–1766.
14. Kohli, P.; Srivastava, S. D.; Srivastava, S. K. Synthesis and pharmacological evaluation of (N-phenothiazinomethyl)-4-[N-(3-chloro-2-oxo-4-substituted-azetidine)]-5-mercapto-1,2,4-triazoles. *J. Ind. Chem. Soc.*, **2008**, *85*, 326–327.
15. Kumar, A.; Rajput, C. S. Synthesis and anti-inflammatory activity of newer quinazolin-4-one derivatives. *Eur. J. Med. Chem.*, **2009**, *44*, 83–90.
16. Srivastava, S. K.; Srivastava, S.; Srivastava, S. D. Synthesis of new carbazolyl-thiadiazol-2-oxo-azetidines: Antimicrobial, anticonvulsant, and anti-inflammatory agents. *Indian J. Chem.*, **1999**, *38B*, 183–187.
17. Biradar, J. S.; Manjunath, S. Y. Synthesis of novel 2-(5′-substituted-2′-phenylindole-3′-yl)-5-(coumarin-3″-yl)-1,3,4-oxadiazoles and 4-(5′-substituted-2′-phenylindole-3′-yl)-1-(coumarin-3″-amido)azetidin-2-one and their antimicrobial activity. *Indian J. Chem.*, **2004**, *43B*, 141–143.