ISSN 1070–3632, Russian Journal of General Chemistry, 2018, Vol. 88, No. 12, pp. 2628–2645. © Pleiades Publishing, Ltd., 2018.

Synthesis, Antimicrobial, and Antioxidant Studies of Some New Indolo[3,2-*c*]isoquinoline Derivatives[1]

Vaijinath A. Verma[a]*

[a] *Department of Chemistry, S.S. Margol Degree College of Arts, Science, and Commerce, Shahabad, Kalaburagi, Karnataka, 585228 India*
**e-mail: drvermachem@gmail.com*

Received November 9, 2017
Revised January 6, 2018
Accepted January 6, 2018

Abstract—As a part of systematic study, new series of 6-{[5-(5-substituted 2-phenyl-1*H*-indol-3-yl)-methyleneamino]-1,3,4-oxadiazol-2-yl}-8-substituted-6*H*-indolo[3,2-c]isoquinolin-5(11*H*)-ones and their derivatives are synthesized and evaluated for their biological activities. Compound **8a** displays potent antimicrobial activity against bacteria *E. coli*, *K. penumoniae,* and *S. aureus,* and fungi *A. niger*, *A. flavus,* and *A. fumigates.* Compounds **7a** and **8a** demonstrate promising radical scavenging and chelating with ferrous ions (Fe^{2+}). According to the accumulated data the designed motifs exhibit higher biological activities than the reference compounds.

Keywords: indolo[3,2-*c*]isoquinoline, 1,3,4-oxidiazole, azetidinone, thiazolidinone, antimicrobial, antioxidant activities

DOI: 10.1134/S1070363218120265

INTRODUCTION

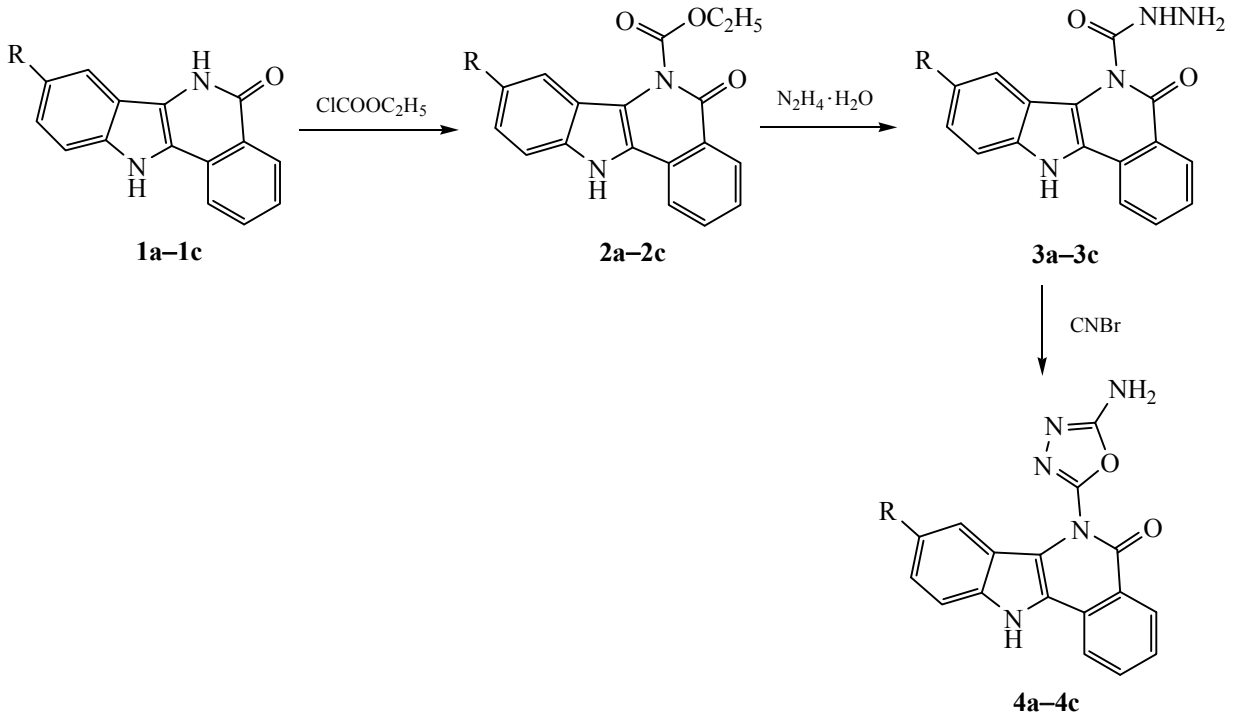
Growing interest in chemistry of carboline (pyrido-indole) and its derivative is initiated by their biological activities, such as anticonvulsant [1], anticoagulant [2], antidepressant [3], anti-HIV [4, 5], anticancer [6], and antioxidant [7]. Indoloisoquinoline and majority of its derivatives demonstrate a broad spectrum of biological activities including bactericidal [8], fungicidal [9], anticancer [9, 10], antimicrobial, anti-inflammatory [11–13], and antimalarial [14]. Analogues of 1,3,4-oxadiazole exhibit anti-inflammatory, anticancer, anti-HIV, antiparkinsonian, and antiproliferative activities [15–20]. In addition, thiazolidinone and azetidinone compounds display wide range of biological properties, acting as antimicrobial and antioxidant agents [21–24]. The synthesis of (8-substituted 6*H*,11*H*-indolo[3,2-*c*]-isoquinolin-5-one-6-yl) carbohydrazides by ligating 1,3,4-oxidiazole, thiazolidinone and azetidinone to indole and evaluation of antimicrobial and antioxidant activities of the target compounds are the objective of the current study.

[1] The text was submitted by the author in English.

RESULTS AND DISCUSSION

The synthetic pathway to the title compounds is illustrated in Schemes 1 and 2. Ethyl(8-substituted 6*H*,11*H*-Indolo[3,2-*c*]isoquinolin-5-one-6-yl)carbohydrazides (**3a–3c**) [25] were synthesized from the prepared precursors 8-substituted 6*H*,11*H*-indolo[3,2-*c*]isoquinolin-5-ones (**1a–1c**) [12], and ethyl (8-substituted-6*H*,11*H*-indolo[3,2-*c*]isoquinolin-5-one-6-yl)-formates (**2a–2c**) [25]. Compounds **3a–3c** were subjected to cyclocondensation with cyanogen bromide in methanol to afford 6-(5-amino-1,3,4-oxadiazol-2-yl)-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (**4a–4c**). Compounds **4a–4c** upon heterocyclization with 5-substituted-2-phenyl-1*H*-indole-3-carbaldehydes (**5a–5c**) [26] in the presence of catalytic amount of glacial acetic acid yielded 6-{[5-(5-substituted 2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (**6a–6i**). The compounds **6a–6i**, when subjected to cyclocondensation with economically viable and commercially available reagents such as thioglycolic acid, chloroacetyl chloride and phenyl acetyl chloride gave 8-substituted-6-{5-[2-(5-substituted 2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-

Scheme 1. Synthetic pathway to compounds **1–4.**



R = Cl (**a**), CH_3 (**b**), H (**c**).

5(11*H*)-ones (**7a–7i**), 6-{5-[3-Chloro-2-(5-substituted 2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (**8a–8i**), and 6-{5-[2-(5-Substituted-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (**9a–9i**), respectively, in high yield. Progress of the reactions was monitored by TLC. All new compounds were characterized by IR, ^{1}H, and ^{13}C NMR, and mass spectra.

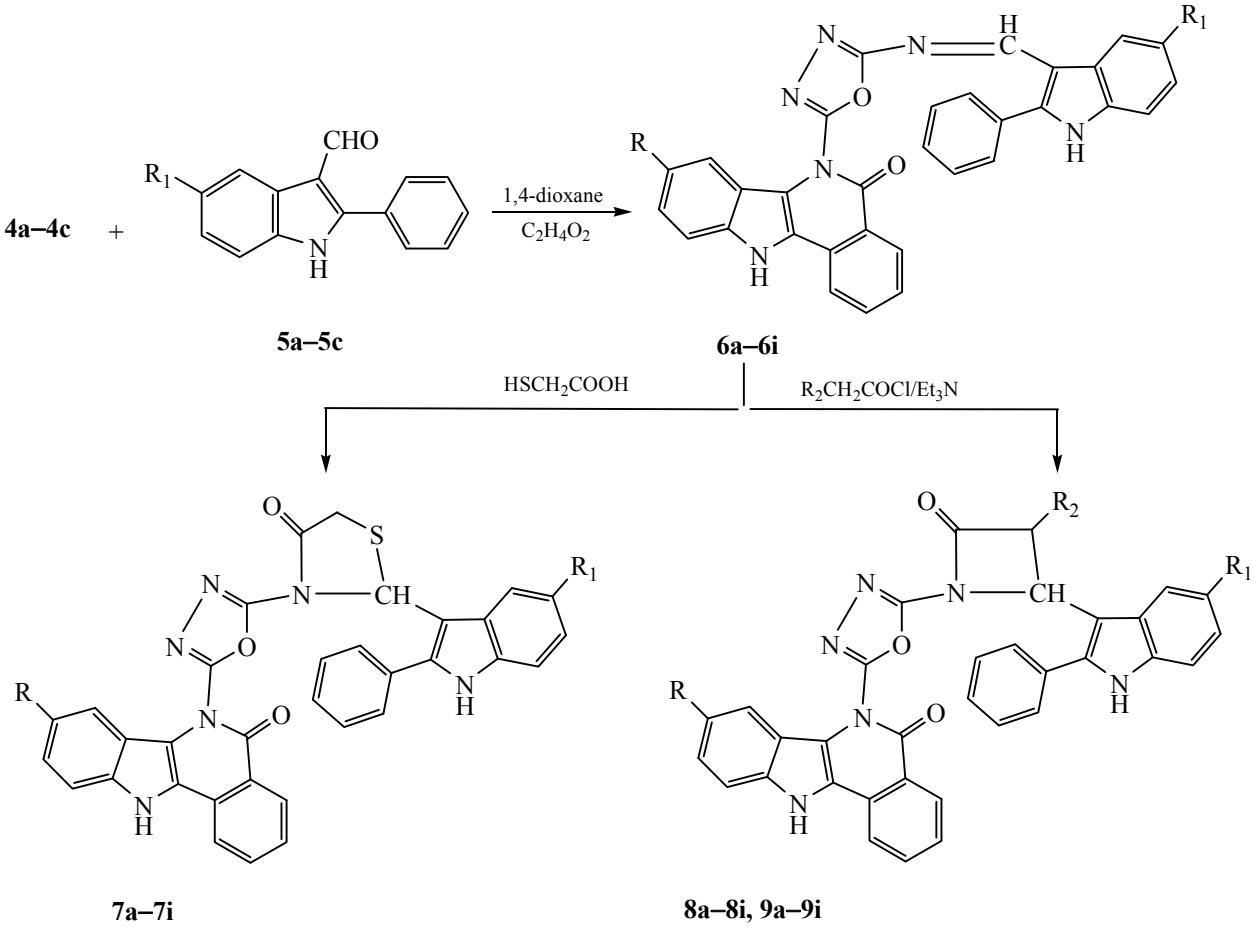
Biological studies. All the synthesized compounds were evaluated for their *in vitro* antibacterial activity against Escherichia coli (ATCC25922), Klebsiella pneumonia (NTCC5221) and Staphylococcus aureus (ATCC25923), and antifungal activity against *Aspergillus niger* (ATCC6275), *Aspergillus flavus* (ATCC9643), and *Aspergillus fumigatus* (ATCC204305) by the cup-plate method (Tables 1 and 2). The zones of inhibition were compared with those of standard drugs streptomycin and fluconazole for antibacterial and antifungal activities, respectively. For the antimicrobial assay, diameter of zones of inhibition above 20 mm at concentration of 100 μg/mL was considered as the best antibiotic display by the compounds.

Antibacterial screening revealed that the compounds **4a**, **6a**, **6e**, **7a**, **8a**, **8b**, **8d**, **8e**, and **9a** exhibited high activities against *E. coli*. Compounds **7a**, **8a**, **8d**, and **8e** were highly active against *K. pneumonia*, and compounds **4a**, **4b**, **6a**, **6e**, **7a**, **7e**, **8a**, **8b**, **8d**, **8e**, and **9a** demonstrated high activity against *S. aureus*. The other compounds were moderately active at various concentrations. Compounds **2c**, **3c**, **6g**, and **8i** started demonstrating inhibitory activity at the concentration of 50 μg/mL.

The antifungal assay showed that compounds **6a**, **7a**, **8a**, **8e**, and **9a** were highly active against *A. niger*, compounds **4a**, **6a**, **7a**, **7b**, **8a**, **8d**, **8e**, **9a**, and the compound **9d** demonstrated high activity against *A. flavus*. Products **7a**, **8a**, **8d**, and **9a** displayed excellent inhibition activity against *A. fumigatus*. Among all the tested compounds **7a** and **8a** demonstrated considerable potential against the targeted microorganisms (Table 3).

Taking in consideration the structure activity relationship (SAR) of the synthesized compounds, it is clear that introduction of the chlorine substituent in molecules of **7a** and **8a** enhanced the antimicrobial potential of the compounds (Scheme 3). The presence of the methyl group in compounds **7e** and **8e**

Scheme 2. Synthetic pathway to compounds **5–9**.



R = Cl (**a**, **d**, **g**), CH_3 (**b**, **e**, **h**), H (**c**, **f**, **i**); R_1 = Cl (**a**–**c**), CH_3 (**d**–**f**), H (**g**–**i**); R_2 = Cl, Ph.

diminished their activity in accord with our previous studies [22, 25].

Scavenging effects of the synthesized compounds on the DPPH radical were compared with the standards BHA, TBHQ and ascorbic acid (AA). The accumulated data (Fig. 1) suggested that the compounds **4a, 4c**, **6a**, **6d**, **6i**, **7a**, **7i, 8a**, **8i**, **9a**, and **9i** exhibited promising activity at concentrations of 75 mg/mL and 100 μg/mL. The compounds **4a**, **6a**, **6i**, **7a**, **8a**, **8i**, **9a**, and **9i** exhibited good activity at 50 μg/mL. The compounds **4a**, **6a**, **6i**, **7a**, **7i**, **8a**, and **9a** showed good activity at 25 μg/mL.

Reductive ability of the synthesized compounds was assessed by the extent of conversion of Fe^{3+}/ferricyanide complex to Fe^{2+}/ferrous form, at different concentrations (25, 50, 75, 100 μg/mL). Reductive ability data (Fig. 2) revealed that compounds **4a**, **6a**, **6e**, **7a**, **7e**, **8a**, and **9e** exhibited promising activity at 25 and 50 μg/mL concentrations. Compounds **4a**, **6a**, **6e**, **7a**, **7b**, **7e**, **8a**, **8e**, **9a**, and **9e** exhibited good activity at 100 μg/mL. Compound **7e** reduced metal ion complex to its lower oxidation state or took part in electron transfer reaction to a high extent at all concentrations. So, the studied compounds demonstrated the ability of scavenging free radicals which was proportional to their concentration.

The ferrous metal-chelating effect of newly synthesized compounds was determined. Ferrozine could quantitatively form a complex with ferrous ion according to this method. In the presence of chelating agents the complex formation was disrupted leading to a decrease in red color of the complex. Measurement of color reduction therefore allowed to estimate the metal chelating activity of the coexisting chelators. Lower absorption indicated higher metal chelating activity. In this assay, synthesized compounds interfered with the formation of ferrous and ferrozine complexes. The results (Fig. 3) suggested that the

Table 1. Antibacterial evaluation of compounds **4** and **6–9**[a,b]

Compounds					Zone of inhibition, mm											
					E. coli				*K. pneumonia*				*S. aureus*			
					concentration of compounds, μg/mL											
	R	R_1	R_2	R_2	25	50	75	100	25	50	75	100	25	50	75	100
4a	Cl	–	–	–	11	16	17	20	10	11	16	20	10	16	19	21
4b	CH_3	–	–	–	11	12	14	19	7	7	10	17	5	8	15	16
4c	H	–	–	–	3	10	14	16	9	8	07	17	8	12	17	14
6a	Cl	Cl	–	–	15	17	18	22	9	10	12	20	18	18	19	22
6b	CH_3	Cl	–	–	12	12	14	15	9	10	12	15	4	10	12	16
6c	H	Cl	–	–	10	13	14	15	10	12	12	17	11	12	14	15
6d	Cl	CH_3	–	–	12	12	16	20	10	14	18	18	8	10	16	18
6e	CH_3	CH_3	–	–	10	16	18	20	9	14	19	20	1	4	18	21
6f	H	CH_3	–	–	10	13	13	15	8	8	12	16	10	10	13	16
6g	Cl	H	–	–	–	2	7	10	11	11	14	17	11	14	14	15
6h	CH_3	H	–	–	6	11	11	13	9	10	15	15	6	10	12	12
6i	H	H	–	–	13	13	16	17	10	11	12	16	4	4	10	14
7a	Cl	Cl	–	–	15	18	20	22	16	18	19	21	17	19	20	23
7b	CH_3	Cl	–	–	10	13	14	15	10	12	18	20	7	11	18	19
7c	H	Cl	–	–	10	12	14	16	11	14	16	17	9	14	17	18
7d	Cl	CH_3	–	–	10	13	13	17	2	8	10	16	6	7	9	13
7e	CH_3	CH_3	–	–	11	9	15	19	6	16	18	20	10	17	19	22
7f	H	CH_3	–	–	8	10	10	17	10	11	11	19	10	13	17	19
7g	Cl	H	–	–	13	13	16	18	11	12	17	17	9	12	18	18
7h	CH_3	H	–	–	10	10	12	13	12	16	16	18	5	13	15	19
7i	H	H	–	–	8	16	19	19	11	14	15	15	9	10	10	14
8a	Cl	Cl	Cl	–	18	19	21	23	17	18	20	22	16	18	21	24
8b	CH_3	Cl	Cl	–	17	18	19	21	09	10	12	18	18	18	20	22
8c	H	Cl	Cl	–	2	04	07	10	11	11	14	16	11	13	15	17
8d	Cl	CH_3	Cl	–	15	17	19	20	15	17	19	21	10	15	17	22
8e	CH_3	CH_3	Cl	–	13	13	16	21	10	11	17	19	4	4	19	21
8f	H	CH_3	Cl	–	11	11	12	15	8	8	12	15	2	6	9	10
8g	Cl	H	Cl	–	10	10	13	13	6	11	13	15	1	4	15	18
8h	CH_3	H	Cl	–	10	15	17	17	5	10	13	16	7	10	14	17
8i	H	H	Cl	–	10	10	10	14	7	8	9	14	–	4	9	16
9a	Cl	Cl	–	Ph	17	18	19	22	9	10	19	20	18	18	21	22
9b	CH_3	Cl	–	Ph	11	12	14	18	11	13	16	16	12	15	15	16
9c	H	Cl	–	Ph	6	13	17	17	11	11	12	13	11	11	15	17

Table 1. (Contd.)

Compounds					Zone of inhibition, mm											
					E. coli				*K. pneumonia*				*S. aureus*			
					concentration of compounds, μg/mL											
	R	R_1	R_2	R_2	25	50	75	100	25	50	75	100	25	50	75	100
9d	Cl	CH_3	–	Ph	13	14	16	16	10	13	16	18	09	13	18	22
9e	CH_3	CH_3	–	Ph	12	17	17	18	12	14	15	19	11	15	17	18
9f	H	CH_3	–	Ph	10	10	15	19	6	10	13	16	7	13	12	15
9g	Cl	H	–	Ph	6	7	11	11	10	10	16	18	4	11	14	15
9h	CH_3	H	–	Ph	10	10	10	14	8	10	16	16	12	13	13	17
9i	H	H	–	Ph	7	10	15	17	13	13	16	18	8	12	15	16
S_1	–	–	–	–	20	20	22	24	18	19	21	23	19	20	23	25
Control DMF					–	–	–	–	–	–	–	–	–	–	–	–

[a] (S_1) Streptomycin. [b] (–) No activity, (1–15) less, (16–19) moderate, and (>20) good activity.

compounds **7a** and **8a** exhibited promising high metal chelating activity (80.35% and 86.42% at 100 μg/mL, respectively).

EXPERIMENTAL

All reagents were obtained commercially and used without further purification. Melting points were determined by an open capillary method and uncorrected. Purity of the compounds was tested by TLC using silica gel-G coated alumininum plates (Merck) and visualized by iodine vapour. IR (KBr) spectra were recorded on a Perkin-Elmer Spectrum spectrophotometer. ^{1}H NMR (DMSO-d_6) spectra were measured on a Marcy Plus (Varian 400 MHz) spectrometer. ^{13}C NMR (DMSO-d_6) spectra were measured on a Bruker NMR (125 MHz) spectrometer. Mass spectra were measured on a ILS-CHU-C^{4}1- VBV4 MS spectrometer. Elemental analysis was carried out using Flash EA 1112 series elemental analyzer.

Scheme 3. Structure–activity relationship (SAR) for antimicrobial and antioxidant activities of thesynthesized 6*H*,11*H*-indolo-[3,2-*c*]isoquinolin-5-one analogues.

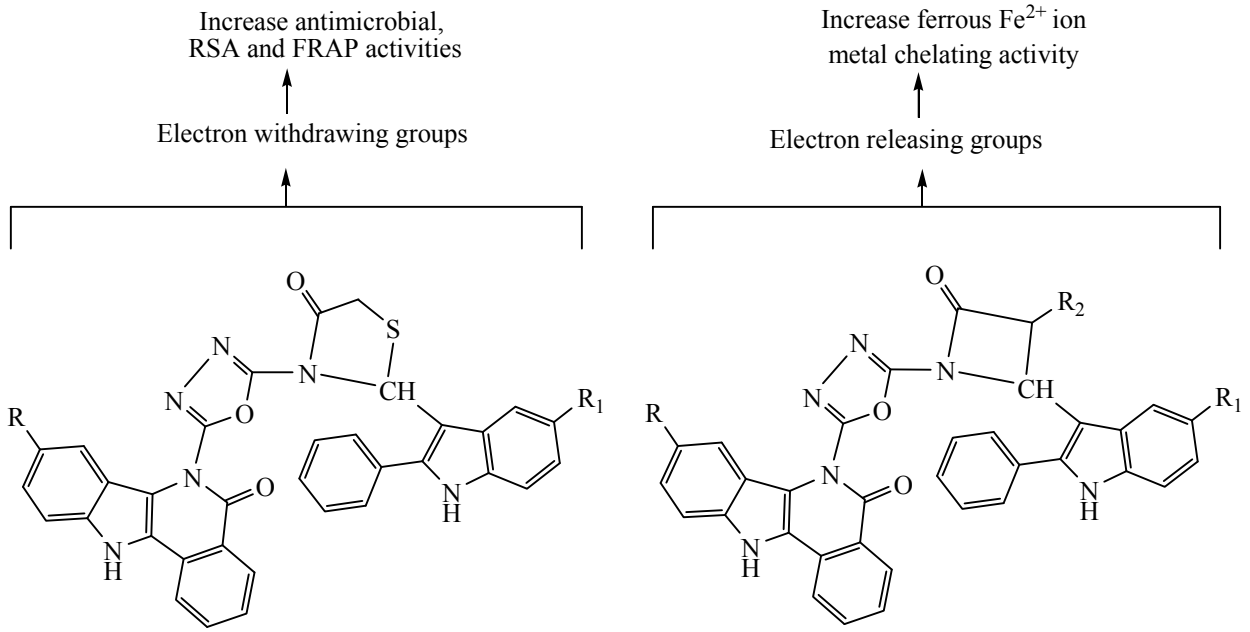


Table 2. Antifungal evaluation of compounds **4** and **6–9**[a,b]

Compounds					Zone of inhibition, mm											
					A. niger				*A. flavus*				*A. fumigatus*			
					concentration of compounds, μg/mL											
	R	R_1	R_2	R_2	25	50	75	100	25	50	75	100	25	50	75	100
4a	Cl	–	–	–	10	15	17	20	7	10	14	23	5	10	13	17
4b	CH_3	–	–	–	10	10	10	19	2	4	9	10	07	8	9	18
4c	H	–	–	–	–	9	12	12	–	3	18	19	6	6	07	13
6a	Cl	Cl	–	–	8	15	19	21	14	14	17	22	10	13	18	19
6b	CH_3	Cl	–	–	12	12	14	15	4	10	19	21	9	10	12	15
6c	H	Cl	–	–	10	13	14	15	11	12	14	15	10	12	12	17
6d	Cl	CH_3	–	–	12	17	18	19	8	10	10	13	10	14	17	18
6e	CH_3	CH_3	–	–	10	11	14	20	1	4	11	12	10	14	17	20
6f	H	CH_3	–	–	10	13	13	15	10	10	13	16	8	8	12	16
6g	Cl	H	–	–	–	2	07	10	11	14	14	15	11	11	14	17
6h	CH_3	H	–	–	6	11	11	13	6	10	12	12	9	10	15	15
6i	H	H	–	–	13	13	16	17	4	4	10	14	10	11	12	16
7a	Cl	Cl	–	–	15	18	19	22	9	13	19	24	10	17	18	21
7b	CH_3	Cl	–	–	10	10	13	13	–	4	19	23	6	11	17	19
7c	H	Cl	–	–	10	15	17	17	07	10	14	17	5	10	13	16
7d	Cl	CH_3	–	–	10	10	18	20	8	10	15	19	07	8	17	18
7e	CH_3	CH_3	–	–	3	9	19	21	–	3	11	16	6	6	16	20
7f	H	CH_3	–	–	8	11	13	17	14	14	16	19	10	11	14	17
7g	Cl	H	–	–	12	12	14	15	4	10	12	16	9	10	12	18
7h	CH_3	H	–	–	10	13	14	15	11	12	14	15	10	12	12	17
7i	H	H	–	–	12	17	17	19	8	10	10	13	10	14	18	15
8a	Cl	Cl	Cl	–	17	19	20	23	9	15	19	25	10	17	19	22
8b	CH_3	Cl	Cl	–	10	13	12	20	10	10	13	16	8	8	19	20
8c	H	Cl	Cl	–	9	12	17	18	11	14	14	15	11	11	14	17
8d	Cl	CH_3	Cl	–	16	18	19	21	12	16	16	23	18	18	19	21
8e	CH_3	CH_3	Cl	–	13	13	17	19	4	4	19	22	10	11	18	20
8f	H	CH_3	Cl	–	11	11	12	15	2	6	16	18	8	8	12	17
8g	Cl	H	Cl	–	10	10	20	21	1	4	11	12	6	11	13	15
8h	CH_3	H	Cl	–	10	15	17	17	7	10	14	17	05	10	13	16
8i	H	H	Cl	–	10	10	10	14	2	04	09	10	7	08	09	14
9a	Cl	Cl	–	Ph	15	17	20	21	15	15	18	23	16	17	18	21
9b	CH_3	Cl	–	Ph	08	11	13	18	14	14	16	18	10	11	17	20
9c	H	Cl	–	Ph	12	12	14	15	04	10	12	16	09	10	12	15

Table 2. (Contd.)

Compounds					Zone of inhibition, mm											
					A. niger				*A. flavus*				*A. fumigatus*			
					concentration of compounds, μg/mL											
	R	R_1	R_2	R_2	25	50	75	100	25	50	75	100	25	50	75	100
9d	Cl	CH_3	–	Ph	10	13	14	15	11	12	15	22	10	12	12	20
9e	CH_3	CH_3	–	Ph	12	17	19	19	08	10	18	20	10	14	18	19
9f	H	CH_3	–	Ph	10	11	14	17	10	13	15	18	06	11	13	15
9g	Cl	H	–	Ph	10	13	13	19	10	10	13	16	08	08	12	16
9h	CH_3	H	–	Ph	–	2	7	10	11	14	14	15	11	11	14	17
9i	H	H	–	Ph	06	11	11	13	06	10	12	12	09	10	15	15
S_2	–	–	–	–	19	20	22	24	18	20	23	26	19	19	20	23
Control DMF					–	–	–	–	–	–	–	–	–	–	–	–

[a] (S_2) Fluconazole. [b] (–) No activity, (1–15) less, (16–19) moderate, and (>20) good activity.

8-Substituted 6*H*,11*H*-indolo[3,2-*c*]isoquinolin-5-ones **1a–1c** were synthesized according to the reported earlier method [12].

Ethyl(8-substituted 6*H*,11*H*-indolo[2,3-*c*]isoquinolin-5-one-6-yl)carboxylates **2a–2c** were synthesized according to the reported earlier method [25].

Ethyl(8-substituted 6*H*,11*H*-indolo[3,2-*c*]isoquinolin-5-one-6-yl)carbohydrazides **3a–3c** were synthesized according to the developed earlier method [25].

8-Chloro-5-oxo-5*H*-indolo[3,2-*c*]isoquinoline-6(11*H*)-carbohydrazide (3a). Yellow shinning crystals, yield 63%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3325 (indole NH), 3250, 3220 (NH/NH_2), 1720, 1692 (C=O). ^{1}H NMR spectrum, δ, ppm: 12.12 s (1H, indole NH), 8.10 s (1H, CONH), 6.42–7.05 m (7H, Ar-H), 5.00 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 164.0 (NCONH, C^{16}), 160.5 (C=O, C^1), 136.2 (C, C^5), 137.2 (C, C^4), 136.4 (C, C^6), 132.3 (C, C^3), 128.6 (C, C^7), 126.2 (C, C^9), 125.2 (CCl, C^{12}). Found, %: C 58.80; H 3.35; N 17.19. $C_{16}H_{11}N_4O_2Cl$. Calculated, %: C 58.82; H 3.39; N 17.15.

8-Methyl-5-oxo-5*H*-indolo[3,2-*c*]isoquinoline-6(11*H*)-carbohydrazide (3b). Orange crystals, yield 70%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3330 (indole NH), 3200, 3105 (NH/NH_2), 1720, 1700 (C=O). ^{1}H NMR spectrum, δ, ppm: 12.11 s (1H, indole NH), 8.30 s (1H, CONH), 6.35–7.24 m (7H, Ar-H), 5.89 s (2H, NH_2), 2.54 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 163.0

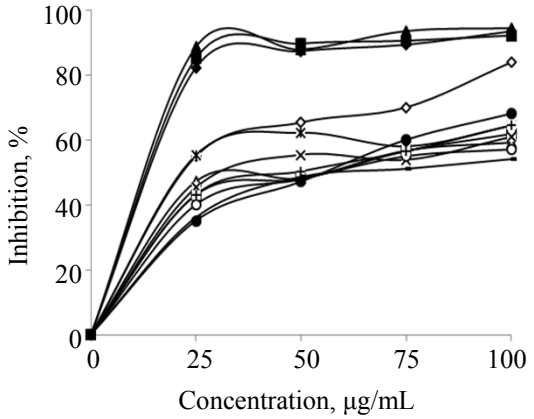


Fig. 1. RSA of compounds **7a–7i**: (◊) **7a**, (□) **7a**, (Δ) **7c**, (×) **7d**, (*) **7e**, (○) **7f**, (|) **7g**, (-) **7h**, (●) **7i**, (♦) BHA, (■) TBHQ, and (▲) AA.

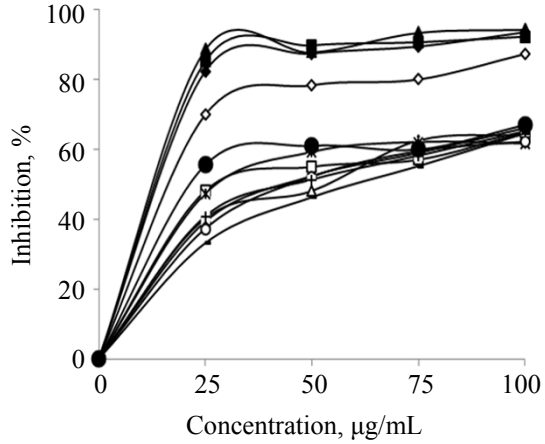


Fig. 2. RSA of compounds **8a–8i**: (◊) **8a**, (□) **8a**, (Δ) **8c**, (×) **8d**, (*) **8e**, (○) **8f**, (|) **8g**, (-) **8h**, (●) **8i**, (♦) BHA, (■) TBHQ, and (▲) AA.

Table 3. Minimum inhibitory concentration (MIC, 100 μg/mL) and IC_{50} of selected compounds[a,b]

Compound	Minimum inhibitory, μg/mL											
	E. coli		*K. pneumoneae*		*S. aureus*		*A. niger*		*A. flavus*		*A. fumigatus*	
	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}	MIC	IC_{50}
4a	–		–	–	15.60	8.3	–	–	8.7	4.4	–	–
6a	9.20	4.1	–	–	14.30	7.3	11.4	5.4	7.4	3.7	–	–
6b	–	–	–	–	–	–	–	–	7.2	3.6	–	–
6e	–	–	–	–	15.30	7.8	–	–	–	–	–	–
7a	6.40	2.8	6.40	3.4	13.26	6.3	6.6	3.4	6.7	3.6	3.3	1.9
7b	–	–	–	–	–	–	–	–	8.4	4.6	–	–
7d	–	–	–	–	–	–	–	–	–	–	–	–
7e	–	–	–	–	14.40	7.2	10.6	5.3	–	–	–	–
8a	5.60	2.4	5.40	2.3	12.20	5.7	6.3	3.2	6.2	3.1	3.1	1.4
8b	6.70	3.4	–	–	14.20	7.3	–	–	–	–	–	–
8d	–	–	7.90	3.5	–	–	9.6	4.8	8.4	4.3	5.5	2.8
8e	9.80	5.1	–	–	15.40	8.1	–	–	9.3	4.2	–	–
9a	6.70	3.4	–	–	13.50	6.7	8.4	4.1	7.1	3.5	4.8	2.5
9d	–	–	–	–	–	–	–	–	8.3	4.2	–	–
S_1	6.25	3.1	6.25	3.3	13.25	6.3	–	–	–	–	–	–
S_2	–	–	–	–	–	–	6.5	3.3	6.5	3.3	3.5	1.9

[a] (S_1) and (S_1) standards. [b] (–) No activity.

(NCONH, C^{16}), 161.3 (C=O, C^1), 138.2 (C, C^5), 138.0 (C, C^4), 136.1 (C, C^6), 132.1 (C, C^3), 129.6 (C, C^7), 127.2 (C, C^9), 19.3 (CCH_3, C^{12}). Found, %: C 66.69; H 4.60; N 18.60. $C_{17}H_{14}N_4O_2$. Calculated, %: C 66.66; H 4.61; N 18.29.

5-Oxo-5*H*-indolo[3,2-*c*]isoquinoline-6(11*H*)-carbohydrazide (3c). Green shiny crystals, yield, 63%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3441 (indole NH), 3212, 3130 (NH/NH_2), 1673, 1663 (C=O). ^{1}H NMR spectrum, δ, ppm: 12.20 s (1H, indole NH), 8.40 s (1H, CONH), 7.05–8.14 m (8H, Ar-H), 6.10 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 164.3 (NCONH, C^{16}), 162.3 (C=O, C^1), 139.2 (C, C^5), 138.4 (C, C^4), 136.2 (C, C^6), 132.5 (C, C^3), 130.6 (C, C^7), 128.3 (C, C^9), 126.3 (C, C^{12}). Found, %: C 65.74; H 4.13; N 19.18. $C_{16}H_{12}N_4O_2$. Calculated, %: C 65.75; H 4.14; N 19.17. MS (EI): *m/z:* 292 $[M]^+$.

Synthesis of 6-(5-Amino-1,3,4-oxadiazol-2-yl)-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (4a–4c). A mixture of an ethyl(8-substituted 6*H*,11*H*-indolo[3,2-*c*]isoquinolin-5-one-6-yl)carbohydrazide (**3a–3c**) (0.01 mol) was stirred with cyanogen bromide (0.015 mol) in methanol for 1–2 h. To the reaction mixture saturated sodium bicarbonate solution (10 mL) was added. The precipitated compound was filtered off, washed with water and recrystallized from dimetheylformamide–methanol mixture to afford the corresponding pure product **4a–4c**.

6-(5-Amino-1,3,4-oxadiazol-2-yl)-8-chloro-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (4a). Yellow

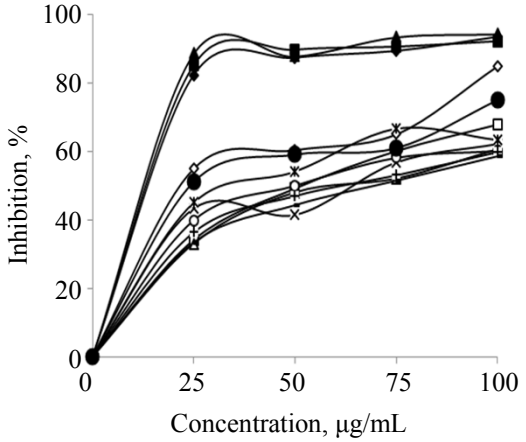


Fig. 3. RSA of compounds **9a–9i**: (◊) **9a**, (□) **9a**, (Δ) **9c**, (×) **9d**, (*) **9e**, (○) **9f**, (|) **9g**, (-) **9h**, (●) **9i**, (♦) BHA, (■) TBHQ, and (▲) AA.

crystals, yield 70%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3419 (indole NH), 3210 (NH_2), 1660 (C=O), 1610 (C=N), 1048 (C–O–C). ^1H NMR spectrum, δ, ppm: 12.40 s (1H, indole NH), 8.80 s (1H, N=CH), 6.70–8.30 m (7H, Ar-H), 6.12 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 164.5 (C=O, C^1), 159.1 (NCN, C^{16}), 157.9 ($NCNH_2$, C^{17}), 139.4 (C, C^5), 137.5 (C, C^4), 135.9 (C, C^6), 130.1 (C, C^2), 129.1(C, C^7) 128.7 (C, C^{10}), 128.4 (C, C^{14}), 127.6 (CCl, C^{12}), 127.4 (C, C^9), 126.2 (C, C^{11}), 122.1 (C, C^{13}), 121.3 (C, C^8), 120.7 (C, C^{15}). Found, %: C 58.02; H 2.88; N 17.16. $C_{17}H_{10}N_5O_2Cl$. Calculated, %: C 58.05; H 2.87; N 19.91.

6-(5-Amino-1,3,4-oxadiazol-2-yl)-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (4b). Yellow crystals, yield 61%, mp 299–300°C. FT-IR spectrum, ν, cm^{-1}: 3413 (indole NH), 3202 (NH_2), 1670 (C=O), 1620 (C=N), 1035 (C–O–C). ^1H NMR spectrum, δ, ppm: 12.38 s (1H, indole NH), 8.45 s (1H, N=CH), 7.00–8.10 m (7H, Ar-H), 5.54 s (2H, NH_2), 2.30 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.1 (C=O, C^1), 158.3 (NCN, C^{16}), 156.4 ($NCNH_2$, C^{17}), 139.3 (C, C^5), 137.4 (C, C^4), 136.1 (C, C^6), 129.4 (C, C^2), 129.2 (C,C^7), 128.6 (C, C^{10}), 128.2 (C, C^{14}), 127.1 (C, C^9), 126.3 (C, C^{11}), 121.5 (C, C^{13}), 121.1 (C, C^8), 120.1(C, C^{15}), 16.5 (CCH_3, C^{12}). Found, %: C 65.24; H 3.92; N 21.12. $C^{18}H_{13}N_5O_2$. Calculated, %: C 65.25; H 3.95; N 21.14.

6-(5-Amino-1,3,4-oxadiazol-2-yl)-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (4c). Yellow crystals, yield 72%, mp 307–308°C. FT-IR spectrum, ν, cm^{-1}: 3412 (indole NH), 3212 (NH_2), 1720, 1692 (C=O), 1616 (C=N), 1055 (C–O–C). ^1H NMR spectrum, δ, ppm: 12.25 s (1H, indole NH), 8.80 s (1H, N=CH), 7.05–8.20 m (8H, Ar-H), 5.90 s (2H, NH_2). ^{13}C NMR spectrum, δ, ppm: 163.5 (C=O, C^1), 158.1 (NCN, C^{16}), 156.9 ($NCNH_2$, C^{17}), 139.2 (C, C^5), 137.1(C, C^4), 136.2 (C, C^6), 129.8 (C, C^2), 129.1 (C, C^7), 128.9 (C, C^{10}), 128.5 (C, C^{14}), 127.9 (C, C^{12}), 127.3 (C, C^9), 126.4 (C, C^{11}), 121.4 (C, C^{13}) 121.2 (C, C^8), 120.9 (C, C^{15}). Found, %: C 64.32; H 3.47; N 22.04. $C_{17}H_{11}N_5O_2$. Calculated, %: C 64.35; H 3.49; N 22.07. MS (EI) *m/z* 317 $[M]^+$.

Synthesis of 6-{5-[(5-substituted-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-substituted-6H-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (6a–6i). A mixture of a compounds **4a–4c** (0.01 mol) with one of 5-substituted 2-phenyl-1*H*-indol-3-carbaldehydes **5a–5c** (0.01 mol) in 1,4-dioxane (40 mL) containing glacial acetic acid (2 mL) was refluxed for 8 h. Excess of the solvent was removed under reduced pressure and the reaction mixture was poured into ice-cold water. The precipitate was filtered off, washed thoroughly with cold water, dried, and recrystallized from ethanol to give the corresponding products **6a–6i**.

6-{5-[(5-Chloro-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (6a). Yellow crystals, yield, 71%, mp >360°C. FT-IR ν, cm^{-1}: 3405, 3300 (indole NH), 1690 (C=O), 1058 (C–O–C). ^1H NMR spectrum, δ, ppm: 12.00, s (1H, indole NH), 11.75 s (1H, indole NH), 8.52 s (1H, N=CH), 6.20–8.08 m (15H, Ar-H). ^{13}C NMR spectrum, δ, ppm: 163.1 (C=O, C^1), 158.6 (NCN, C^{16}), 155.9 (C, C^{17}), 139.7 (C, C^5), 138.2 (C, C^4), 137.1 (C, C^{26}), 136.2 (C, C^{20}), 135.9 (C, C^{19}), 134.3 (N=CH, C^{18}), 132.4 (C, C^3), 131.8 (C, C^{25}), 130.5 (C, C^2), 128.8, 129.9 (C, C^{29}), 129.5 (C, C^{31}), 128.6 (C, C^4), 128.2 (C, C^{32}), 127.3 (CCl, C^{12}), 126.2 (CCl, C^{28}), 126.1 (C, C^{10}), 125.4 (C, C^{11}), 124.7 (C, C^{27}), 123.4 (C, C^{30}), 122.1 (C, C^{13}), 120.7 (C, C^{23}), 112.5 (C, C^{21}). Found, %: C 65.22; H 3.09; N 14.25. $C_{32}H_{18}N_6O_2Cl_2$. Calculated, %: C 65.21; H 3.08; N 14.26.

6-{5-[(5-Methyl-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (6b). Yellow shiny crystals, yield 62%, mp 305–306°C. FT-IR spectrum, ν, cm^{-1}: 3405, 3315 (indole NH), 1740 (C=O) 1620 (C=N), 1050 (C–O–C); ^1H NMR (DMSO-d_6, δ, ppm); 12.20 s (1H, indole NH), 11.98 s (1H, indole NH), 8.12 s (1H, N=CH), 6.49–7.92 m (15H, Ar-H), 2.25 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.1 (C=O, C^1), 158.4 (NCN, C^{16}), 155.7 (C, C^{17}), 139.3 (C, C^5), 137.9 (C, C^4), 137.2 (C, C^{26}), 136.1 (C, C^{20}), 135.5 (C, C^{19}), 134.1 (N=CH, C^{18}), 132.5 (C, C^3), 131.3 (C, C^{25}), 130.2 (C, C^2), 129.6 (C, C^{29}), 129.2 (C, C^{31}), 128.7 (C, C^4), 128.2 (C, C^{32}), 126.6 (CCl, C^{28}), 126.3 (C, C^{10}), 125.1(C, C^{11}), 124.5 (CCl, C^{12}), 124.1 (C, C^{27}), 123.3 (C, C^{30}), 122.0 (C, C^{13}), 120.5 (C, C^{23}), 112.7 (C, C^{21}), 17.3 (CCH_3, C^{12}). Found, %: C 69.65; H 3.70; N 14.79. $C_{33}H_{21}N_6O_2Cl$. Calculated, %: C 69.66; H 3.72; N 14.77.

6-{5-[(2-Phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]iso-quinolin-5(11*H*)-one (6c). Colorless needles, yield 75%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3441, 3232 (indole NH), 1690 (C=O), 1611(C=N), 1097 (C–O–C). ^1H NMR spectrum, δ, ppm: 12.47 s (1H, indole NH), 12.14 s (1H, indole NH), 9.90 s (1H, N=CH), 7.00–8.20 m (16H, Ar-H). ^{13}C NMR spectrum, δ, ppm: 163.2 (C=O, C^1), 158.5 (NCN, C^{16}),

156.7 (C, C^{17}), 139.7 (C, C^5), 138.2 (C, C^4), 137.1 (C, C^{26}), 136.2 (C, C^{20}), 135.9 (C, C^{19}), 134.3 (N=CH, C^{18}), 132.4 (C, C^3), 131.8 (C, C^{25}), 130.5 (C, C^2), 129.9 (C, C^{29}), 129.5 (C, C^{31}), 128.6 (C, C^4), 128.2 (C, C^{32}), 128.3 (CCl, C^{22}), 127.3 (CCl, C^{12}), 126.1 (C, C^{10}), 125.4 (C, C^{11}), 124.7(C, C^{12}), 124.7 (C, C^{27}), 123.4 (C, C^{30}), 122.1 (C, C^{13}), 120.7 (C, C^{23}), 112.5 (C, C^{21}). Found, %: C 69.26; H 3.43; N 15.12. $C_{32}H_{19}N_6O_2Cl$. Calculated, %: C 69.25; H 3.45; N 15.14. MS (EI): *m/z:* 554 $[M]^+$, 556 $[M+2]^+$.

6-{5-[(5-Chloro-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (6d). Colorless needles, yield 63%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3400, 3290 (indole NH), 1690 (C=O), 1610 (C=N), 1052 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.10 s (1H, indole NH), 11.45 s (1H, indole NH), 8.41 s (1H, N=CH), 6.45–8.02 m (15H, Ar-H), 2.28 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.1 (C=O, C^1), 158.2 (NCN, C^{16}), 156.7 (C, C^{17}), 139.7 (C, C^5), 138.2 (C, C^4), 137.1 (C, C^{26}), 136.2 (C, C^{20}), 135.9 (C, C^{19}), 134.3 (N=CH, C^{18}), 132.4 (C, C^3), 131.8 (C, C^{25}), 130.5 (C, C^2), 129.9 (C, C^{29}), 129.5 (C, C^{31}), 128.6 (C, C^4), 128.2 (C, C^{32}), 127.3 (C, C^{12}), 126.1 (C, C^{10}), 125.4 (C, C^{11}), 125.1 (CCl, C^{12}), 124.7 (C, C^{27}), 123.4 (C, C^{30}), 122.1 (C, C^{13}), 120.7 (C, C^{23}), 112.5 (C, C^{21}), 16.6 (CCH_3, C^{28}). Found, %: C 69.66; H 3.70; N 14.75. $C_{33}H_{21}N_6O_2Cl$. Calculated, %: C 69.66; H 3.72; N 14.77.

6-{5-[(5-Methyl-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-methy-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (6e). Colorless needles, yield 70%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3424, 3300 (indole NH), 1705 (C=O), 1605 (C=N), 1045 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.00 s (1H, indole NH), 11.75 s (1H, indole NH), 8.34 s (1H, N=CH), 6.52–8.00 m (15H, Ar-H), 3.31 s (3H, CH_3), 2.28 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 163.5 (C=O, C^1), 157.1 (NCN, C^{16}), 156.7(C, C^{17}), 139.8 (C, C^5), 138.1 (C, C^4), 137.2 (C, C^{26}), 136.3 (C, C^{20}), 135.3 (C, C^{19}), 134.1 (N=CH, C^{18}), 131.8 (C, C^3), 131.5 (C, C^{25}), 130.4 (C, C^2), 129.7 (C, C^{29}), 129.4 (C, C^{31}), 128.3 (C, C^4), 128.1 (C, C^{32}), 127.3 (C, C^{12}), 126.1 (C, C^{10}), 125.4 (C, C^{11}), 124.5 (C, C^{12}), 124.4 (C, C^{27}), 122.4 (C, C^{30}), 122.3 (C, C^{13}), 120.1 (C, C^{23}), 113.5 (C, C^{21}), 15.7 (CCH_3, C^{28}). Found, %: C 74.45; H 4.40; N 15.34. $C_{34}H_{24}N_6O_2$. Calculated, %: C 74.44; H 4.41; N 15.32.

6-{5-[(2-Phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (6f). Colorless needles, yield 65%, mp 295–296°C. FT-IR spectrum, ν, cm^{-1}: 3315, 3284, (indole NH), 1725 (C=O), 1608 (C=N), 1050 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.11(s, 1H, indole NH), 11.65 s (1H, indole NH), 8.48 s (1H, N=CH). 6.31–7.86 m (16H, Ar-H). 2.45 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 163.6 (C=O, C^1), 158.6 (NCN, C^{16}), 156.8 (C, C^{17}), 139.8 (C, C^5), 138.3 (C, C^4), 137.2 (C, C^{26}), 136.4 (C, C^{20}), 135.4 (C, C^{19}), 134.4 (N=CH, C^{18}), 132.5 (C, C^3), 131.6 (C, C^{25}), 130.4 (C, C^2), 129.7 (C, C^{29}), 129.6 (C, C^{31}), 128.5 (C, C^4), 128.3 (C, C^{32}), 127.4 (C, C^{12}), 126.2 (C, C^{10}), 125.3 (C, C^{11}), 124.8 (C, C^{12}), 124.6 (C, C^{27}), 123.3 (C, C^{30}), 122.2 (C, C^{13}), 120.3 (C, C^{23}), 112.3 (C, C^{21}), 16.1 (CCH_3, C^{28}). Found, %: C 74.11; H 4.13; N 17.72. $C_{33}H_{22}N_6O_2$. Calculated, %: C 74.14; H 4.15; N 15.72.

6-{5-[(5-Chloro-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (6g). Yellow shiny crystals, yield 60%, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3383, 3275 (indole NH), 1750 (C=O), 1616 (C=N), 1052 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 11.99 s (1H, indole NH), 11.85 s (1H, indole NH), 8.38 s (1H, N=CH), 6.32–8.05 m (16H, Ar-H). ^{13}C NMR spectrum, δ, ppm: 163.5 (C=O, C^1), 158.7 (NCN, C^{16}), 156.8 (C, C^{17}), 139.9 (C, C^5), 138.4 (C, C^4), 137.3 (C, C^{26}), 136.5 (C, C^{20}), 135.8 (C, C^{19}), 134.5 (N=CH, C^{18}), 132.6 (C, C^3), 131.9 (C, C^{25}), 130.7 (C, C^2), 129.7 (C, C^{29}), 129.6 (C, C^{31}), 128.7 (C, C^4), 128.4 (C, C^{32}), 127.2 (CCl, C^{12}), 126.3 (C, C^{10}), 125.3 (C, C^{11}), 124.6 (C, C^{28}), 124.4 (C, C^{27}), 123.5 (C, C^{30}), 122.2 (C, C^{13}), 120.9 (C, C^{23}), 112.3(C, C^{21}). Found, %: C 69.23; H 3.42; N 15.13. $C_{32}H_{19}N_6O_2Cl$. Calculated, %: C 69.25; H 3.45; N 15.14.

6-{5-[(5-Methyl-2-phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (6h). Yellow shiny crystals, yield 64%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3405, 3300 (indole NH), 1675 (C=O), 1598 (C=N), 1057 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.10 s (1H, indole NH), 11.45 s (1H, indole NH), 8.75 s (1H, N=CH), 6.55–8.12 m (16H, Ar-H), 3.04 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.2 (C=O, C^1), 159.3 (NCN, C^{16}), 157.7 (C, C^{17}), 138.7 (C, C^5), 138.1 (C, C^4), 137.3 (C, C^{26}), 136.1 (C, C^{20}), 135.5 (C, C^{19}), 134.7 (N=CH, C^{18}), 132.3 (C, C^3), 131.4 (C, C^{25}), 130.3 (C, C^2), 129.4 (C, C^{29}), 129.3 (C, C^{31}), 128.4 (C, C^4), 128.1 (C, C^{32}), 127.4 (C, C^{12}), 126.5 (C, C^{10}), 125.6 (C, C^{11}), 124.3 (C, C^{27}), 123.1 (C, C^{30}), 123.1 (C, C^{13}), 121.7 (C, C^{23}), 113.5 (C, C^{21}), 14.5 (C, C^{12}).

Found, %: C 74.16; H 4.14; N 15.71. $C_{33}H_{22}N_6O_2$. Calculated, %: C 74.14; H 4.15; N 15.72.

6-{5-[(2-Phenyl-1*H*-indol-3-yl)methyleneamino]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (6i). Yellow shiny crystals, yield 69%, mp >300°C. FT-IR spectrum, ν, cm^{-1}: 3340, 3290 (indole NH), 1715 (C=O), 1608 (C=N), 1053 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.30 s (1H, indole NH), 11.75 s (1H, indole NH), 8.33 s (1H, N=CH), 6.39–8.01 m (17H, Ar-H). ^{13}C NMR spectrum, δ, ppm: 163.5 (C=O, C^1), 157.7 (NCN, C^{16}), 156.4 (C, C^{17}), 137.9 (C, C^5), 137.5 (C, C^4), 136.1 (C, C^{26}), 136.0 (C, C^{20}), 135.6 (C, C^{19}), 134.2 (N=CH, C^{18}), 132.3 (C, C^3), 131.3 (C, C^{25}), 130.4 (C, C^2), 129.2 (C, C^{29}), 129.1 (C, C^{31}), 128.3 (C, C^4), 128.2 (C, C^{32}), 127.5 (C, C^{12}), 126.4 (C, C^{10}), 125.3 (C, C^{11}), 124.2 (C, C^{12}), 124.2 (C, C^{27}), 123.4 (C, C^{30}), 123.3 (C, C^{13}), 121.6 (C, C^{23}), 114.6 (C, C^{21}). Found, %: C 73.86; H 3.81; N 16.15. $C_{32}H_{20}N_6O_2$. Calculated, %: C 73.84; H 3.87; N 16.14.

Synthesis of 8-substutited 6-{5-[2-(5-substituted-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (7a–7i). To the solution of compounds **6a–6i** (0.02 mol) in DMF (45 mL), thioglycolic acid (0.02 mol) and anhydrous zinc chloride (0.02 mol) were added, and the mixture was refluxed for 6 h. Upon completion of the reaction, excess of the solvent was removed under reduced pressure, and the mixture was poured onto crushed ice. The precipitated product was filtered off, washed with cold water and recrystallized from ethanol to afford the corresponding compounds **7a–7i**.

8-Chloro-6-{5-[2-(5-chloro-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7a). Yellow solid, yield 63%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3342, 3285 (indole NH); 1700, 1695 (C=O), 1600 (C=N), 1052 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.12 s (1H, indole NH), 11.79 s (1H, indole NH), 6.51–8.05 m (15H, Ar-H), 4.81 d (1H, NCH), 3.80 d (2H, CH_2CO). ^{13}C NMR spectrum, δ, ppm: 163.8 (C=O, C^{18}), 161.1 (C=O, C^1), 157.2 (C, C^{17}), 156.2 (NCN, C^{16}), 139.3 (CCl, C^{12}), 139.2 (CCl, C^{24}), 138.4 (C, C^4), 136.4 (C, C^5), 135.7 (C, C^5), 134.3 (C, C^{21}), 133.4 (C, C^{28}), 131.3 (C, C^{32}), 129.5 (C, C^4), 129.3 (C, C^{22}), 128.7 (C, C^9), 128.6 (C, C^{14}), 127.5 (C, C^{31}), 126.2 (C, C^{10}), 125.4 (C, C^{26}),123.4 (C, C^{25}), 122.5 (C, C^{13}), 121.6 (C, C^{15}), 120.7 (C, C^8), 40.1 (SCH_2, C^{19}). Found, %: C 61.55; H 3. 04; N 12.63. $C_{34}H_{20}N_6O_3SCl_2$. Calculated, %: C 61.54; H 3.04; N 12.67.

8-Chloro-6-{5-[2-(5-methyl-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7b). Yellow solid, yield 62 %, mp >360°C. FT-IR spectrum, ν, cm^{-1}: 3420, 3342 (indole NH), 1750, 1675 (C=O), 1615 (C=N), 1047 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.04 s (1H, indole NH), 11.99 s (1H, indole NH), 6.41–8.00 m (15H, Ar-H), 4.79 d (1H, NCH), 3.79 d (2H, CH_2CO), 2.86 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 162.8 (C=O, C^{18}), 160.1 (C=O, C^1), 156.2 (C, C^{17}), 154.2 (NCN, C^{16}), 139.1 (CCl, C^{24}), 138.1 (C, C^4), 136.8 (C, C^5), 135.8 (C, C^5), 134.1 (C, C^{21}), 133.2 (C, C^{28}), 131.1 (C, C^{32}), 129.4 (C, C^4), 129.2 (C, C^{22}), 128.8 (C, C^9), 128.5 (C, C^{14}), 127.4 (C, C^{31}), 126.3 (C, C^{10}), 125.6 (C, C^{26}),123.3 (C, C^{25}), 122.5 (C, C^{13}), 121.9 (C, C^{15}), 120.9 (C, C^8), 39.5 (SCH_2, C^{19}), 15.1 (CH_3, C^{12}). Found, %: C 65.39; H 3.59; N 13.04. $C_{35}H_{23}N_6O_3SCl$. Calculated, %: C 65.37; H 3.60; N 13.07.

8-Chloro-6-{5-[2-(2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (7c). Yellow solid, yield 64%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3441, 3229 (indole NH), 1722, 1683 (C=O), 1605 (C=N), 1074 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.20 s (1H, indole NH), 11.79 s (1H, indole NH), 6.41–8.00 m (16H, Ar-H), 4.81 d (1H, NCH), 4.00 d (2H, CH_2CO). ^{13}C NMR spectrum, δ, ppm: 162.8 (C=O, C^{18}), 160.1 (C=O, C^1), 156.2 (C, C^{17}), 154.2 (NCN, C^{16}), 139.1 (CCl, C^{24}), 138.1 (C, C^4), 136.8 (C, C^5), 135.8 (C, C^5), 134.1 (C, C^{21}), 133.2 (C, C^{28}), 131.1 (C, C^{32}), 129.4 (C, C^4), 129.2 (C, C^{22}), 128.8 (C, C^9), 128.5 (C, C^{14}), 127.4 (C, C^{31}), 126.3 (C, C^{10}), 125.6 (C, C^{26}), 123.3 (C, C^{25}), 122.5 (C, C^{13}), 121.9 (C, C^{15}), 120.9 (C, C^8), 39.5 (SCH_2, C^{19}). Found, %: C 64.91; H 3.33; N 13.39. $C_{34}H_{21}N_6O_3SCl$. Calculated, %: C 64.91; H 3.36; N 13.36. MS (EI): *m/z*: 629 $[M]^+$; 631 $[M+2]^+$.

8-Methyl-6-{5-[2-(5-chloro-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7d). Yellow solid, yield 61%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3388, 3300 (indole NH); 1700, 1658 (C=O), 1608 (C=N), 1030 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.32 s (1H, indole NH), 11.85 s (1H, indole NH), 6.65–7.95 m (15H, Ar-H), 4.84 d (1H, NCH), 3.80 d (2H, CH_2CO), 2.58 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 162.8 (C=O, C^{18}), 161.2 (C=O, C^1), 155.2 (C, C^{17}), 154.4 (NCN, C^{16}), 138.4 (CCl, C^{12}), 137.4 (C, C^4), 136.6 (C, C^5), 135.4 (C, C^5), 134.3 (C, C^{21}), 133.5 (C, C^{28}), 131.3 (C, C^{32}), 129.5 (C, C^4), 129.3 (C, C^{22}), 128.9 (C, C^9), 128.7 (C, C^{14}), 127.5 (C, C^{31}), 126.7 (C,

C^{10}), 125.3 (C, C^{26}), 123.4 (C, C^{25}), 122.4 (C, C^{13}), 121.8 (C, C^{15}), 120.8 (C, C^{8}), 39.4 (SCH_2, C^{19}), 15.4 (CH_3, C^{24}). Found, %: C 65.35; H 3.62; N 13.05. $C_{35}H_{23}N_6O_3SCl$. Calculated, %: C 65.37; H 3.60; N 13.07.

8-Methyl-6-{5-[2-(5-methyl-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7e). Yellow solid, yield 73%, mp 330–331°C. FT-IR spectrum, ν, cm^{-1}: 3408, 3295 (indole NH), 1720, 1678 (C=O), 1603 (C=N), 1062 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.07(s, 1H, indole NH), 11.85 s (1H, indole NH), 6.42–8.02 m (15H, Ar-H), 4.85 d (1H, NCH), 3.56 d (2H, CH_2CO), 2.43 s (3H, CH_3), 2.23 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.5 (C=O, C^{18}), 162.3 (C=O, C^{1}), 155.4 (C, C^{17}), 154.7 (NCN, C^{16}), 138.3 (C, C^{4}), 136.7(C, C^{5}), 135.5 (C, C^{5}), 134.4 (C, C^{21}), 133.4 (C, C^{28}), 131.2 (C, C^{32}), 129.5 (C, C^{4}), 129.2 (C, C^{22}), 128.6 (C, C^{9}), 128.4 (C, C^{14}), 127.5 (C, C^{31}), 126.6 (C, C^{10}), 125.2 (C, C^{26}), 124.1 (C, C^{25}), 123.5 (C, C^{13}), 122.9 (C, C^{15}), 121.9 (C, C^{8}), 39.1 (SCH_2, C^{19}), 15.8 (CH_3, C^{12}), 14.6 (CH_3, C^{24}). Found, %: C 69.46; H 4.20; N 13.49. $C_{36}H_{26}N_6O_3S$. Calculated, %: C 69.44; H 4.21; N 13.50.

8-Methyl-6-{5-[2-(2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7f). Yellow solid, yield 70%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3295, 3245 (indole NH), 1684, 1650 (C=O), 1615 (C=N), 1058 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 11.97 s (1H, indole NH), 11.49 s (1H, indole NH), 6.46–8.00 m (16H, Ar-H), 4.86 d (1H, NCH), 3.64 d (2H, CH_2CO), 2.43 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 162.8 (C=O, C^{18}), 160.1 (C=O, C^{1}), 156.2 (C, C^{17}), 154.2 (NCN, C^{16}), 138.1 (C, C^{4}), 136.8 (C, C^{5}), 135.8 (C, C^{5}), 134.1 (C, C^{21}), 133.2 (C, C^{28}), 131.1 (C, C^{32}), 129.4 (C, C^{4}), 129.2 (C, C^{22}), 128.8 (C, C^{9}), 128.5 (C, C^{14}), 127.4 (C, C^{31}), 126.3 (C, C^{10}), 125.6 (C, C^{26}), 123.3 (C, C^{25}), 122.5 (C, C^{13}), 121.9 (C, C^{15}), 120.9 (C, C^{8}), 39.5 (SCH_2, C^{19}), 14.7 (CCH_3, C^{24}). Found, %: C 69.03; H 3.98; N 13.80. $C_{35}H_{24}N_6O_3S$. Calculated, %: C 69.06; H 3.97; N 13.81.

6-{5-[2-(5-Chloro-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7g). Yellow solid, yield 65%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3395, 3255 (indole NH); 1690, 1660 (C=O), 1620 (C=N), 1038 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.20 s (1H, indole NH), 11.78 s (1H, indole NH), 6.61–8.00 m (16H, Ar-H), 4.78 d (1H, NCH), 3.80 d (2H, CH_2CO). ^{13}C NMR spectrum, δ, ppm: 164.4 (C=O, C^{18}), 163.1 (C=O, C^{1}), 156.5 (C, C^{17}), 155.2 (NCN, C^{16}), 139.4 (CCl, C^{12}), 138.6 (C, C^{4}), 136.4 (C, C^{5}), 135.6 (C, C^{5}), 134.1 (C, C^{21}), 133.5 (C, C^{28}), 131.3 (C, C^{32}), 129.2 (C, C^{4}), 129.1 (C, C^{22}), 128.7 (C, C^{9}), 128.4 (C, C^{14}), 127.3 (C, C^{31}), 126.5 (C, C^{10}), 125.3 (C, C^{26}), 123.4 (C, C^{25}), 122.4 (C,C^{13}), 121.8 (C, C^{15}), 120.2 (C, C^{8}), 39.5 (SCH_2, C^{19}). Found, %: C 64.92; H 3.35; N 13.36. $C_{34}H_{21}N_6O_3SCl$. Calculated, %: C 64.91; H 3.36; N 13.36.

6-{5-[2-(5-Methyl-2-phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (7h). Yellow solid, yield 72%, mp > 360°C. FT-IR spectrum, ν cm^{-1}: 3405, 3345 (indole NH), 1720, 1650 (C=O), 1610 (C=N), 1058 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.00 s (1H, indole NH), 11.88 s (1H, indole NH), 6.60–8.00 m (16H, Ar-H), 4.87 d (1H, NCH), 3.81 d (2H, CH_2CO), 2.75 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 163.8 (C=O, C^{18}), 161.1 (C=O, C^{1}), 157.2 (C, C^{17}), 155.2 (NCN, C^{16}), 139.1 (C, C^{4}), 137.3 (C, C^{5}), 135.8 (C, C^{5}), 135.1 (C, C^{21}), 133.2 (C, C^{28}), 131.1 (C, C^{32}), 129.4 (C, C^{4}), 129.2 (C, C^{22}), 128.8 (C, C^{9}), 128.5 (C, C^{14}), 127.4 (C, C^{31}), 126.3 (C, C^{10}), 125.6 (C, C^{26}), 123.3 (C, C^{25}), 122.5 (C, C^{13}), 121.9 (C, C^{15}), 120.9 (C, C^{8}), 38.5 (SCH_2, C^{19}), 15.1 (CH_3, C^{12}). Found, %: C 69.08; H 3.99; N 13.83. $C_{35}H_{24}N_6O_3S$. Calculated, %: C 69.06; H 3.97; N 13.81.

6-{5-[2-(2-Phenyl-1*H*-indol-3-yl)-4-oxothiazolidin-3-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (7i). Yellow solid, yield 67%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3400, 3345 (indole NH), 1720, 1690 (C=O), 1605(C=N), 1050 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.12 s (1H, indole NH), 11.79 s (1H, indole NH), 6.91–8.05 m (17H, Ar-H), 4.87 d (1H, NCH), 3.70 d (2H, CH_2CO). ^{13}C NMR spectrum, δ, ppm: 164.3 (C=O, C^{18}), 163.1 (C=O, C^{1}), 156.4 (C, C^{17}), 154.5 (NCN, C^{16}), 138.3 (C, C^{4}), 136.7 (C, C^{5}), 135.6 (C, C^{5}), 134.1 (C, C^{21}), 133.2 (C, C^{28}), 131.1 (C, C^{32}), 129.4 (C, C^{4}), 129.2 (C, C^{22}), 128.8 (C, C^{9}), 128.5 (C, C^{14}), 128.4 (C, C^{31}), 127.3 (C, C^{10}), 126.6 (C, C^{26}), 123.5 (C, C^{25}), 123.3 (C, C^{13}), 121.6 (C, C^{15}), 120.7 (C,C^{8}), 37.9 (SCH_2, C^{19}). Found, %: C 68.67; H 3.73; N 14.13. $C_{34}H_{22}N_6O_3S$. Calculated, %: C 68.67; H 3.73; N 14.13.

Synthesis of 6-{5-[3-chloro-2-(5-substituted-2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (8a–8i). To the solution of

compounds **6a–6i** (0.02 mol) in dioxane, chloroacetyl chloride (0.04 mol) and TEA (0.04 mol) were added upon constant stirring at 0–5°C within the period of 10 min. After the addition was over, the reaction mixture was refluxed for 8–10 h, and excess of the solvent was removed under reduced pressure. The precipitate was filtered off, washed with 1,4-dioxane, dried and recrystallized from ethanol to give the corresponding pure products **8a–8i**.

6-{5-[3-Chloro-2-(5-chloro-2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8a). Brown crystals, yield 69%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3385, 3305 (indole NH), 1725, 1700 (C=O), 1621 (C=N), 1050 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.02 s (1H, indole NH), 11.89 s (1H, indole NH), 7.07–8.06 m (15H, Ar-H), 6.31 d (1H, NCH), 5.75 d (1H, CHCO). ^{13}C NMR spectrum, δ, ppm: 166.9 (C=O, C^{18}), 163.5 (C=O,C^1), 158.1 (NCN,C^{16}), 157.7 (C, C^{17}), 154.7 (CCl, C^{12}), 140.4 (C, C^5), 135.8 (C, C^4), 135.3 (C, C^6), 135.1 (C, C^3), 134.5 (C, C^{29}), 133.2 (C, C^{28}), 133.0 (C, C^{22}), 130.9 (C, C^{33}), 130.4 (C, C^{34}), 130.2 (C, C^{32}), 129.8 (C, C^7), 129.3 (C, C^{30}), 129.2 (C, C^2), 128.3 (C, C^{31}), 128.2 (C, C^{14}), 127.4 (C, C^9), 127.2 (C, C^{10}), 126.6 (CCl, C^{24}), 126.0 (C, C^{11}), 125.8 (C, C^{26}), 125.6 (C, C^{27}), 121.8 (C, C^8), 121.5 (C, C^{23}), 121.4 (C, C^{15}), 121.3 (C, C^{13}), 112.7 (C, C^{21}), 65.1 (CCl, C^{19}), 50.1 (NCH, C^{20}). Found, %: C 61.30; H 2.89; N 12.65. $C_{34}H_{19}N_6O_3Cl_3$. Calculated, %: C 61.32; H 2.88; N 12.62.

6-{5-[3-Chloro-2-(5-methyl-2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8b). Yellow crystal, yield 59%, mp 305–306°C. FT-IR spectrum, ν, cm^{-1}: 3400, 3306 (indole NH), 1760, 1705 (C=O), 1620 (C=N), 1062 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.01 s (1H, indole NH), 11.78 s (1H, indole NH), 6.17–8.00 m (15H, Ar-H), 5.74 d (1H, NCH), 5.32 d (1H, CHCO), 2.23 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 166.5 (C=O, C^{18}), 163.2 (C=O, C^1), 158.3 (NCN, C^{16}), 157.5 (C, C^{17}), 140.2 (C, C^5), 135.3 (C, C^4),135.2 (C, C^6), 135.1 (C, C^3), 134.3 (C, C^{29}), 133.1 (C, C^{28}), 133.0 (C, C^{22}), 130.5 (C, C^{33}), 130.2 (C, C^{34}), 130.1 (C, C^{32}), 129.5 (C, C^7), 129.2 (C, C^{30}), 129.1 (C, C^2), 128.4 (C, C^{31}), 128.3 (C, C^{14}), 127.3 (C, C^9), 127.1 (C, C^{10}), 126.5 (CCl, C^{24}), 126.1 (C, C^{11}), 125.2 (C, C^{26}), 125.1 (C, C^{27}), 121.7 (C, C^8), 121.4 (C, C^{23}), 121.3 (C, C^{15}), 121.2 (C, C^{13}), 112.2 (C, C^{21}), 65.2 (CCl, C^{19}), 50.3 (NCH, C^{20}), 15.7 (CCH_3, C^{12}). Found, %: C 65.15; H 3.46; N 13.05. $C_{35}H_{22}N_6O_3Cl_2$. Calculated, %: C 65.12; H 3.44; N 13.02.

6-{5-[3-Chloro-2-(2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8c). Brown solid, yield 63%, mp 301–302°C. FT-IR spectrum, ν, cm^{-1}: 3321, 3214 (indole NH), 1732, 1720 (C=O), 1601 (C=N), 1048 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.00 s (1H, indole NH), 11.92 s (1H, indole NH), 7.00–8.02 m (16H, Ar-H), 6.35 d (1H, NCH), 6.00 d (1H, CHCO), 2.73 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 166.6 (C=O, C^{18}), 163.1 (C=O, C^1), 157.8 (NCN, C^{16}), 156.5 (C, C^{17}), 141.2 (C, C^5), 135.5 (C, C^4), 135.3 (C, C^6), 135.2 (C, C^3), 134.2 (C, C^{29}), 133.3 (C, C^{28}), 133.1 (C, C^{22}), 130.4 (C, C^{33}), 130.1 (C, C^{34}), 129.7 (C, C^{32}), 129.2 (C, C^7), 129.1 (C, C^{30}), 129.0 (C, C^2), 128.3 (C, C^{31}), 128.2 (C, C^{14}), 127.5 (C, C^9), 127.6 (C, C^{10}), 126.3 (C, C^{12}), 126.1 (CCl, C^{24}), 125.9 (C, C^{11}), 125.1 (C, C^{26}), 124.8 (C, C^{27}), 121.5 (C,C^8), 121.3 (C, C^{23}), 121.1 (C, C^{15}), 121.0 (C, C^{13}), 112.3 (C, C^{21}), 66.1 (CCl, C^{19}), 50.5 (NCH, C^{20}). Found, %: C 64.69; H 3.20; N 13.33. $C_{34}H_{20}N_6O_3Cl_2$. Calculated, %: C 64.67; H 3.19; N 13.31.

6-{5-[3-Chloro-2-(5-chloro-2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8d). Brown crystals, yield 55%, mp 309–310°C. FT-IR spectrum, ν, cm^{-1}: 3450, 3350 (indole NH), 1713, 1695 (C=O), 1620 (C=N), 1055 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.11 s (1H, indole NH), 11.93 s (1H, indole NH), 6.67–8.00 m (15H, Ar-H), 6.30 d (1H, NCH), 6.10 d (1H, CHCO), 2.82 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 165.8 (C=O, C^{18}), 163.5 (C=O, C^1), 158.2 (NCN, C^{16}), 157.2 (C, C^{17}), 152.3 (CCl, C^{12}), 140.4 (C, C^5), 135.7 (C, C^4), 135.5 (C, C^6), 135.3 (C, C^3), 134.2 (C, C^{29}), 133.1 (C, C^{28}), 132.9 (C, C^{22}), 130.1 (C, C^{33}), 129.8 (C, C^{34}), 129.6 (C, C^{32}), 129.3 (C, C^7), 129.2 (C, C^{30}), 128.9 (C, C^2), 128.1 (C, C^{31}), 127.9 (C, C^{14}), 127.5 (C, C^9), 127.2 (C, C^{10}), 125.7 (C, C^{11}), 125.3 (C, C^{26}), 124.6 (C, C^{27}), 121.4 (C, C^8), 121.2 (C, C^{23}), 121.1 (C, C^{15}), 121.0 (C, C^{13}), 112.4 (C, C^{21}), 65.5 (CCl, C^{19}), 49.8 (NCH, C^{20}), 16.1 (CCH_3, C^{24}). Found, %: C 65.14; H 3.42; N 13.00. $C_{35}H_{22}N_6O_3Cl_2$. Calculated, %: C 65.12; H 3.44; N 13.02.

6-{5-[3-Chloro-2-(5-methyl-2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8e). Yellow crystal, yield 60%, mp 294-295°C. FT-IR spectrum, ν,

cm^{-1}: 3406, 3324 (indole NH), 1720, 1675 (C=O), 1613 (C=N), 1046 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 11.92 s (1H, indole NH), 11.85 s (1H, indole NH), 6.95–8.01 m (15H, Ar-H), 6.35 d (1H, NCH), 5.78 d (1H, CHCO), 3.23 s (3H, CH_3), 2.42 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 166.8 (C=O, C^{18}), 163.1 (C=O, C^1), 157.2 (NCN, C^{16}), 156.2 (C, C^{17}), 140.2 (C, C^5), 135.8 (C, C^4), 135.6 (C, C^6), 135.2 (C, C^3), 134.1 (C, C^{29}), 133.2 (C, C^{28}), 133.1 (C, C^{22}), 131.2 (C, C^{33}), 130.8 (C, C^{34}), 130. 6 (C, C^{32}), 129.1 (C, C^7), 129.0 (C, C^{30}), 128.7 (C, C^2), 128.4 (C, C^{31}), 127.3 (C, C^{14}), 127.1 (C, C^9), 127.0 (C, C^{10}), 125.8 (C, C^{11}), 125.5 (C, C^{26}), 124.8 (C, C^{27}), 121.3 (C, C^8), 121.1 (C, C^{23}), 121.0 (C, C^{15}), 120.9 (C, C^{13}), 112.5 (C, C^{21}), 66.3 (CCl, C^{19}), 51.8 (NCH, C^{20}), 17.3 (CCH_3, C^{12}), 16.1 (CCH_3, C^{24}). Found, %: C 69.19; H 4.05; N 13.47. $C_{36}H_{25}N_6O_3Cl$. Calculated, %: C 69.17; H 4.03; N 13.44.

6-{5-[3-Chloro-2-(5-methy-2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8f). Yellow crystal, yield 70%, mp 295–296°C. FT-IR spectrum, ν, cm^{-1}: 3342, 3281 (indole NH), 1735, 1709 (C=O), 1610 (C=N), 1058 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.00 s (1H, indole NH), 11.70 s (1H, indole NH), 6.77–8.04 m (15H, Ar-H), 6.38 d (1H, NCH), 5.69 d (1H, CHCO), 2.73 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 166.5 (C=O, C^{18}), 163.4 (C=O, C^1), 158.1 (NCN, C^{16}), 157.2 (C, C^{17}), 140.1 (C, C^5), 135.7 (C, C^4), 135.6 (C, C^6), 135.2 (C, C^3), 134.1 (C, C^{29}), 133.2 (C, C^{28}), 133.1 (C, C^{22}), 131.2 (C, C^{33}), 130.8 (C, C^{34}), 130. 6 (C, C^{32}), 129.1 (C, C^7), 129.0 (C, C^{30}), 128.7 (C, C^2), 128.4 (C, C^{31}), 127.3 (C, C^{14}), 127.1 (C, C^9), 127.0 (C, C^{10}), 126.6 (C, C^{12}), 125.8 (C, C^{11}), 125.5 (C, C^{26}),124.8(C,C^{27}), 121.3 (C,C^8), 121.1 (C,C^{23}), 121.0 (C,C^{15}), 120.9 (C,C^{13}), 112.5 (C,C^{21}), 66.3 (CCl, C^{19}), 51.8 (NCH, C^{20}), 15.5 (CCH_3, C^{24}). Found, %: C 68.83; H 3.81; N 13.77. $C_{35}H_{23}N_6O_3Cl$. Calculated, %: C 68.80; H 3.79; N 13.75.

6-{5-[3-Chloro-2-(2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-chloro-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8g). Yellow crystals, yield 59%, mp > 360°C. FT-IR spectrum, ν, cm^{-1}: 3454, 3381 (indole NH), 1704, 1675 (C=O), 1615 (C=N), 1040 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.14 s (1H, indole NH), 12.09 s (1H, indole NH), 6.94–8.03 m (16H, Ar-H), 6.40 d (1H, NCH), 5.80 d (1H, CHCO). ^{13}C NMR spectrum, δ, ppm: 166.2 (C=O, C^{18}), 160.1 (C=O, C^1), 157.1 (NCN, C^{16}), 156.2 (C, C^{17}), 151.6 (CCl, C^{12}), 140.2 (C, C^5), 136.7 (C, C^4), 135.6 (C, C^6), 135.3 (C, C^3), 134.1(C, C^{29}), 133.2 (C, C^{28}), 133.1 (C, C^{22}), 131.2 (C, C^{33}), 130.8 (C, C^{34}), 130. 6 (C, C^{32}), 129.1 (C, C^7), 129.0 (C, C^{30}), 128.7 (C, C^2), 128.4 (C, C^{31}), 127.3 (C, C^{14}), 127.1 (C, C^9), 127.0 (C, C^{10}), 125.8 (C, C^{11}), 125.5 (C, C^{26}), 124.8 (C, C^{27}), 121.3 (C, C^8), 121.1 (C, C^{23}), 121.0 (C, C^{15}), 120.9 (C, C^{13}),112.5 (C, C^{21}), 66.3 (CCl, C^{19}), 51.8 (NCH, C^{20}), 15.5 (CCH_3, C^{24}). Found, %: C 64.69; H 3.20; N 13.32. $C_{34}H_{20}N_6O_3Cl_2$. Calculated, %: C 64.67; H 3.19; N 13.31.

6-{5-[3-Chloro-2-(2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (8h). Yellow crystal, yield 77%, mp 298–299°C. FT-IR spectrum, ν, cm^{-1}: 3440, 3230 (indole NH), 1700, 1682 (C=O), 1600 (C=N), 1060 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.25 s (1H, indole NH), 11.76 s (1H, indole NH), 6.77–7.98 m (16H, Ar-H), 6.30 d (1H, NCH), 5.79 d (1H, CHCO), 2.82 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 166.4 (C=O, C^{18}), 163.1 (C=O, C^1), 158.1 (NCN, C^{16}), 156.2 (C, C^{17}), 140.2 (C, C^5), 136.7 (C, C^4), 135.6 (C, C^6), 135.3 (C, C^3), 134.1 (C, C^{29}), 133.2 (C, C^{28}), 133.1 (C, C^{22}), 131.2 (C, C^{33}), 130.8 (C, C^{34}), 130. 6 (C, C^{32}), 129.1 (C, C^7), 129.0 (C, C^{30}), 128.7 (C, C^2), 128.4 (C, C^{31}), 127.3 (C, C^{14}), 127.1 (C, C^9), 127.0 (C, C^{10}), 126.5 (CCl, C^{24}), 125.8 (C, C^{11}), 125.5 (C, C^{26}), 124.8 (C, C^{27}), 121.3 (C, C^8), 121.1 (C, C^{23}), 121.0 (C, C^{15}), 120.9 (C, C^{13}), 112.5 (C, C^{21}), 66.3 (CCl, C^{19}), 51.8 (NCH, C^{20}), 19.5 (CCH_3, C^{12}). Found, %: C 68.79; H 3.80; N 13.76. $C_{35}H_{23}N_6O_3Cl$. Calculated, %: C 68.80; H 3.79; N 13.75.

6-{5-[3-Chloro-2-(2-phenyl-1*H*-indol-3-yl)-4-oxoazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (8i). Yellow crystal, yield 73%, mp 304–305°C. FT-IR spectrum, ν, cm^{-1}: 3405, 3248 (indole NH), 1690, 1640 (C=O), 1625 (C=N), 1063 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.19 s (1H, indole NH), 12.01 s (1H, indole NH), 6.27–7.97 m (17H, Ar-H), 5.42 d (1H, NCH), 4.68 d (1H, CHCO), 2.85 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 166.9 (C=O, C^{18}), 163.5 (C=O, C^1), 158.1 (NCN, C^{16}), 157.7 (C, C^{17}), 140.4 (C, C^5), 135.8 (C, C^4), 135.3 (C, C^6), 135.1 (C, C^3), 134.5 (C, C^{29}), 133.2 (C, C^{28}), 133.0 (C, C^{22}), 130.9 (C, C^{33}), 130.4 (C, C^{34}), 130.2 (C, C^{32}), 129.8 (C, C^7), 129.3 (C, C^{30}), 129.2 (C, C^2), 128.3 (C, C^{31}), 128.2 (C, C^{14}), 127.4 (C, C^9), 127.2 (C, C^{10}), 126.7 (C, C^{12}), 126.6 (CCl, C^{24}), 126.0 (C, C^{11}), 125.8 (C, C^{26}), 125.6 (C, C^{27}), 121.8 (C, C^8), 121.5 (C, C^{23}), 121.4 (C, C^{15}), 121.3 (C, C^{13}), 112.7 (C, C^{21}),

65.1 (CCl, C^{19}), 50.1 (NCH, C^{20}). Found, %: C 68.42; H 3.56; N 14.06. $C_{34}H_{21}N_6O_3Cl$. Calculated, %: C 68.40; H 3.55; N 14.08.

Synthesis of 6-{5-[2-(5-Substituted-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-substituted-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-ones (9a–9i). To a Schiff base **6a–6i** (0.02 mol) in dry benzene (30 mL) containing few drops of TEA, phenyl acetyl chloride (0.02 mol) was added upon stirring within the period of 10 min at room temperature. After the addition was over, the reaction mixture was refluxed for 1 h. Triethyl amine hydrochloride formed was filtered off and washed several times with dry benzene. The filtrate and washings were combined and concentrated under reduced pressure. After cooling down to room temperature the product obtained was filtered off, washed with petroleum ether (40:60) and recrystallized in aq. ethanol.

8-Chloro-6-{5-[2-(5-chloro-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9a). Brown crystals, yield, 67%, mp > 360°C, FT-IR spectrum, ν, cm^{-1}: 3245, 3200 (indole NH), 1743, 1675 (C=O), 1607 (C=N), 1084 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.13(s, 1H, indole NH), 11.77 s (1H, indole NH), 6.34–8.20 m (20H, Ar-H), 6.25 s (1H, NCH), 6.04 s (1H, CHCO). ^{13}C NMR spectrum, δ, ppm: 163.5(NC=O, C^{18}) 161.2 (C=O, C^1), 156.4 (NCN, C^{17}), 155.4 (NCN, C^{16}), 152.2 (CCl, C^{12}), 139.5 (C, C^5), 137.3 (C, C^4), 136.4 (C, C^3), 136.2 (C, C^6), 134.6 (C, C^{20}), 133.5 (C, C^{25}), 131.2 (C, C^{34}), 130.4 (C, C^{26}), 129.7 (C, C^{23}), 129.5 (C, C^2), 129.2 (C, C^{23}), 128.6 (C, C^{10}), 128.4 (C, C^{14}), 127.5 (C, C^9), 127.2 (C, C^{11}), 126.3 (C, C^{28}). Found, %: C 67.92; H 3.40; N 11.90. $C_{40}H_{24}N_6O_3Cl_2$. Calculated, %: C 67.90; H 3.42; N 11.88.

8-Chloro-6-{5-[2-(5-methyl-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9b). Brown crystals, yield 64%, mp > 302°C. FT-IR spectrum, ν, cm^{-1}: 3330, 3298 (indole NH), 1715, 1690 (C=O), 1627 (C=N), 1097 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.00 s (1H, indole NH), 11.69 s (1H, indole NH), 6.34–8.20 m (20H, Ar-H), 4.31 s (1H, NCH), 6.08 s (1H, CHCO), 2.62 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 163.3 (NC=O, C^{18}), 162.2 (C=O, C^1), 156.4 (NCN, C^{17}), 154.2 (NCN, C^{16}), 139.4 (C, C^5), 137.5 (C, C^4), 136.4 (C, C^3), 136.3 (C, C^6), 134.4 (C, C^{20}), 133.5 (C, C^{25}), 131.1 (C, C^{34}), 130.2 (C, C^{26}), 129.3 (C, C^{23}), 129.1 (C, C^2), 129.0 (C, C^{23}), 128.7 (C, C^{10}), 128.2 (C, C^{14}), 127.2 (C, C^9), 127.0 (C, C^{11}), 126.3 (CCl, C^{28}), 15.2 (CCH_3, C^{12}). Found, %: C 71.64; H 3.95; N 12.22. $C_{41}H_{27}N_6O_3Cl$. Calculated, %: C 71.66; H 3.96; N 12.23.

8-Chloro-6-{5-[2-oxo-3-phenyl-4-(2-phenyl-1*H*-indol-3-yl)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9c). Brown crystals, yield 72%, mp 298–299°C. FT-IR spectrum, ν, cm^{-1}: 3344, 3130 (indole NH), 1692, 1655 (C=O), 1615 (C=N), 1096 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.10 s (1H, indole NH), 11.82 s (1H, indole NH), 7.30–8.30 m (21H, Ar-H), 6.50 d (1H, NCH), 6.07 d (1H, CHCO). ^{13}C NMR spectrum, δ, ppm: 164.8 (NC=O, C^{18}) 163.1 (C=O, C^1), 157.4 (NCN, C^{17}), 154.3 (NCN, C^{16}), 150.2 (CCl, C^{28}), 139.5 (C, C^5), 137.1 (C, C^4), 136.9 (C, C^3), 136.1 (C, C^6), 134.5 (C, C^{20}), 133.4 (C, C^{25}), 131.5 (C, C^{34}), 130.4 (C, C^{26}), 129.9 (C, C^{23}), 129.8 (C, C^2), 129.1 (C, C^{23}), 128.9 (C, C^{10}), 128.5 (C, C^{14}), 127.3 (C, C^9), 127.1 (C, C^{11}). Found, %: C 71.39; H 3.72; N 12.51. $C_{40}H_{25}N_6O_3Cl$. Calculated, %: C 71.37; H 3.74; N 12.49. MS (EI): *m/z:* 673 $[M]^+$; 675 $[M+2]^+$.

6-{5-[2-(5-Chloro-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-8-methyl-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9d). Brown crystals, yield, 65%, mp 331–332°C. FT-IR spectrum, ν, cm^{-1}: 3330, 3298 (indole NH), 1724, 1700 (C=O), 1623 (C=N), 1086 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.23 s (1H, indole NH), 11.86 s (1H, indole NH), 6.54–8.24 m (20H, Ar-H), 6.32 d (1H, NCH), 5.73 d (1H, CHCO), 2.85 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 163.5 (NC=O, C^{18}) 160.1 (C=O, C^1), 156.5 (NCN, C^{17}), 153.7 (NCN, C^{16}), 138.5 (C, C^5), 137.5(C, C^4), 136.3 (C, C^3), 136.2 (C, C^6) 134.3 (C,C^{20}), 133.3 (C,C^{25}), 131.2 (C,C^{34}), 130.2 (C, C^{26}), 129.2 (C, C^{23}), 129.1 (C, C^2), 129.0 (C, C^{23}), 128.7 (C, C^{10}), 128.4 (C, C^{14}), 127.2 (C, C^9), 127.1 (C, C^{11}), 126.3 (C, C^{28}). Found, %: C 71.69; H 3.94; N 12.21. $C_{41}H_{27}N_6O_3Cl$. Calculated, %: C 71.66; H 3.96; N 12.23.

8-Methyl-6-{5-[2-(5-methyl-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9e). Brown crystals, yield 61%, mp > 305°C. FT-IR spectrum, ν, cm^{-1}: 3404, 3238 (indole NH), 1732, 1695 (C=O), 1619 (C=N), 1068 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.13 s (1H, indole NH), 1.88 s (1H,

indole NH), 6.35–8.15 m (20H, Ar-H), 6.21 d (1H, NCH), 6.00 d (1H, CHCO), 3.02 s (3H, CH_3), 2.62 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.3 (NC=O, C^{18}), 163.4 (C=O, C^1), 156.6 (NCN, C^{17}), 154.4 (NCN, C^{16}), 139.5 (C, C^5), 137.1 (C, C^4), 136.9 (C, C^3), 136.1 (C, C^6), 134.5 (C, C^{20}), 133.4 (C, C^{25}), 131.5 (C, C^{34}), 130.4 (C, C^{26}), 129.7 (C, C^{23}), 129.4 (C, C^2), 129.2 (C, C^{23}), 128.3 (C, C^{10}), 128.2 (C, C^{14}), 127.5 (C, C^9), 127.2 (C, C^{11}), 16.3 (CCH_3, C^{12}), 15.3 (CCH_3, C^{28}). Found, %: C 75.64; H 4.56; N 12.61. $C_{42}H_{30}N_6O_3$. Calculated, %: C 75.66; H 4.54; N 12.60.

8-Methyl-6-{5-[2-oxo-3-phenyl-4-(2-phenyl-1*H*-indol-3-yl)azetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9f). Brown crystals, yield 58%, mp 300–301°C. FT-IR spectrum, ν, cm^{-1}: 3400, 3239 (indole NH), 1721, 1675 (C=O), 1610 (C=N), 1064 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.21 s (1H, indole NH), 12.09 s (1H, indole NH), 6.32–8.10 m (21H, Ar-H), 6.20 d (1H, NCH), 5.79 d (1H, CHCO), 2.74 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.5 (NC=O, C^{18}), 161.2 (C=O, C^1), 155.6 (NCN, C^{17}), 153.5 (NCN, C^{16}), 139.5 (C, C^5), 139.1 (C, C^4), 136.5 (C, C^3), 136.3 (C, C^6) 134.2 (C, C^{20}), 133.5 (C, C^{25}), 131.3 (C, C^{34}), 130.8 (C, C^{26}), 129.5 (C, C^{23}), 129.3 (C, C^2), 129.0 (C, C^{23}), 128.5 (C, C^{10}), 128.3 (C, C^{14}), 127.2 (C, C^9), 127.1 (C, C^{11}), 126.5 (C, C^{12}), 15.2 (CCH_3, C^{28}). Found, %: C 75.47; H 4.30; N 12.90. $C_{41}H_{28}N_6O_3$. Calculated, %: C 75.45; H 4.32; N 12.88.

6-{5-[2-(5-Chloro-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9g). Brown crystals, yield 60%, mp 307–308°C. FT-IR spectrum, ν, cm^{-1}: 3334, 3264 (indole NH), 1700, 1659 (C=O), 1620 (C=N), 1064 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.25 s (1H, indole NH), 12.09 s (1H, indole NH), 6.54–8.23 m (21H, Ar-H), 6.31 d (1H, NCH), 5.73 d (1H, CHCO). ^{13}C NMR spectrum, δ, ppm: 163.8 (NC=O, C^{18}), 161.1 (C=O, C^1), 156.4 (NCN, C^{17}), 154.3 (NCN, C^{16}), 138.5 (C, C^5), 137.3 (C, C^4), 136.2 (C, C^3), 136.0 (C, C^6), 134.2 (C, C^{20}), 133.2 (C, C^{25}), 131.3 (C, C^{34}), 130.2 (C, C^{26}), 129.5 (C, C^{23}), 129.3 (C, C^2), 129.2 (C, C^{23}), 128.3 (C, C^{10}), 128.2 (C, C^{14}), 127.1 (C, C^9), 127.0 (C, C^{11}), 126.2 (CCl, C^{12}). Found, %: C 71.35; H 3.72; N 12.50. $C_{40}H_{25}N_6O_3Cl$. Calculated, %: C 71.37; H 3.74; N 12.49.

6-{5-[2-(5-Methyl-2-phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]isoquinolin-5(11*H*)-one (9h). Brown crystals, yield 61%, mp 299–300°C. FT-IR spectrum, ν, cm^{-1}: 3430, 3308 (indole NH), 1740, 1680 (C=O), 1616 (C=N), 1084(C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.06 s (1H, indole NH), 11.64 s (1H, indole NH), 6.41–8.21 m (21H, Ar-H), 6.10 d (2H, NCH), 5.71 d (1H, CHCO), 2.76 s (3H, CH_3). ^{13}C NMR spectrum, δ, ppm: 164.2 (NC=O, C^{18}), 163.2 (C=O, C^1), 156.3 (NCN, C^{17}), 155.2 (NCN, C^{16}), 137.5 (C, C^5), 137.1 (C, C^4), 136.4 (C, C^3), 136.3 (C, C^6) 134.3 (C, C^{20}), 133.2 (C, C^{25}), 131.4 (C, C^{34}), 130.3 (C, C^{26}), 129.8 (C, C^{23}), 129.6 (C, C^2), 129.1 (C, C^{23}), 128.7 (C, C^{10}), 128.6 (C, C^{14}), 127.4 (C, C^9), 127.2 (C, C^{11}), 16.3 (CCH_3, C^{12}). Found, %: C 75.47; H 4.34; N 12.90. $C_{41}H_{28}N_6O_3$. Calculate, %: C 75.45; H 4.32; N 12.88.

6-{5-[2-(2-Phenyl-1*H*-indol-3-yl)-4-oxo-3-phenylazetidin-1-yl]-1,3,4-oxadiazol-2-yl}-6*H*-indolo[3,2-*c*]-isoquinolin-5(11*H*)-one (9i). Brown crystals, yield 59%, mp 308–309°C. FT-IR spectrum, ν, cm^{-1}: 3400, 3323 (indole NH), 1723, 1690 (C=O), 1619 (C=N), 1063 (C–O–C). ^{1}H NMR spectrum, δ, ppm: 12.08 s (1H, indole NH), 11.99 s (1H, indole NH), 6.65–8.23 m (22H, Ar-H), 6.49 d (1H, NCH), 5.78 s (1H, CHCO). ^{13}C NMR spectrum, δ, ppm: 163.8 (NC=O, C^{18}), 163.1 (C=O, C^1), 157.1 (NCN, C^{17}), 154.2 (NCN, C^{16}), 139.4 (C, C^5), 137.3 (C, C^4), 136.3 (C, C^3), 135.1 (C, C^6), 134.4 (C,C^{20}), 133.3 (C, C^{25}), 131.3 (C, C^{34}), 130.2 (C, C^{26}), 129.7 (C, C^{23}), 129.5 (C, C^2), 129.4 (C, C^{23}), 128.7 (C, C^{10}), 128.4 (C, C^{14}), 127.2 (C, C^9), 127.1 (C, C^{11}), 126.4 (C, C^{12}). Found, %: C 75.20; H 4.09; N 13.17. $C_{40}H_{26}N_6O_3$. Calculated, %: C 75.22; H 4.10; N 13.16.

Biological studies. Antimicrobial activity of the synthesized compounds was tested against three bacteria and three fungal species using nutrient agar and PDA medium by the cup plate method [27] (concentrations 25, 50, 75, and 100 mg/mL). The precise values of MIC and IC_{50} values were appraised by the broth dilution method [28, 29].

Antioxidant activity. 2,2-Diphenyl-2-picryl-hydrazil (DPPH) radical scavenging activity (RSA) was tested in methanolic solution at concentrations 25, 50, 75, and 100 μg/mL containing freshly prepared DPPH solution (0.004 % w/v) according to the reported method [30].

Ferric ion (Fe^{3+}) reducing antioxidant power (FRAP). The reducing power of the synthesized compounds was determined according to the literature method [31] using BHA, TBHQ and AA as standards.

Different concentrations of samples (25, 50, 75, and 100 μg/mL) in DMSO (1 mL) were mixed with phosphate buffer (2.5 mL, 0.2 M, pH = 6.6) and potassium ferricyanide (2.5 mL, 1%).

Ferrous (Fe^{2+}) ion metal chelating activity. Chelating activity of the ferrous ions by the synthesized compounds and BHA, TBHQ, and AA as standards was estimated by the reported earlier method [32] with test samples concentrations of 25, 50, 75, and 100 μg/mL.

CONCLUSIONS

New indolo[3,2-*c*]isoquinoline derivatives are synthesized. Probably high antimicrobial and antioxidant activities of the compounds is initiated by the chlorine substituent. The MIC/IC_{50} values of the synthesized compounds are higher than those of standard drugs. All tested compounds demonstrate significant antioxidant activity. Compounds **7a** and **8a** are the most effective as RSA and metal chelaters. The compound **7e** has a benevolent ferric ions (Fe^{3+}) reducing antioxidant power. The same activities are reduced probably due to the methyl group attached.

So, the combination of the parent indolo[3,2-*c*]-isoquinoline moiety with 1,3,4-oxidiazole, thiazolidinone and azetidinone in one molecule creates a number of new bioactive compounds.

ACKNOWLEDGEMENTS

The author is grateful to the Chairman, Department of Chemistry, Gulbarga University, Kalaburagi for providing laboratory facilities, Principal, S. Margol Degree College of Arts, Science, and Commerce, Shahabad, Kalaburagi, and the Director, IIT Madras, Chennai for providing spectral data.

CONFLICT OF INTEREST

No conflict of interest was declared by the author.

REFERENCES

1. Saxena, V.-C., Bapat, S.-K., Dhawan, B.-N., *Jpn. J. Pharmacol*., 1969 vol. 19, p. 477, *Chem. Abstr*., 1970, vol. 72, 65152.
2. Cohen, A., US Patent 1967, no. 3 316 271. *Chem Abstr*., vol. 67, 21900s
3. Garmaise, D.-L. and Parks, G.V., US Patent 1973, no. 3 705 901; *Chem Abstr*., vol. 78, 72103.
4. Wang, Y.-H., Tang, J.-G., Wang, R.-R., Yang, L.-M., Dong, Z.-J., Shen, L. D.-X., Liu, J.-K., and Zheng, T., *BioChem. Bioph. Res. Comm*., 2007, vol. 355(4), p. 1091. doi 10.1016/j.bbrc.2007.02.081
5. Ishida, J., Wang, H.-K., Oyama, M., Cosentino, M.-L., Hu, C.-Q., and Lee, K.-H., *J. Nat. Prod*., 2001, vol. 6(7), p. 958. doi 10.1021/np0101189
6. Anelise, S., Formagio, N., Tonin, L.T.-D., Foglio, M.A., Madjarof, C., de Carvalho, J.E., da Costa, W.F., Cardoso, F-P., and Sarragiotto, M.-H., *Bioorg. Med. Chem*., 2008, vol. 16, p. 9660. doi 10.1016/j.bmc.2008.10.008
7. Hadjaz, F., Besret, S., and Martin-Nizard, F., *Eur. J. Med. Chem*., 2011, vol. 46(6), p. 2575. doi 10.1016/j.ejmech.2011.03.048
8. Winter, G., Dimola, N., Berti, M., and Ariali, V., *Farmaco. Ed. Sci*., 1979, vol. 34(6), p. 507.
9. Ishizumi, K. and Katsube, J., Brit. Patent, 1980, 2 025 932, *Chem. Abstr.,* vol. 93, 186322e
10. Sumitomo Chemical Co. Ltd and Jpn. Kokai Tokkyo Hoho, Jap. Pantent, 1983, 5869 882 (8369 882); *Chem. Abstr.,* 1983, vol. 99, 88182p
11. Kosuge, T., Zenda, H., Tamamoto, H., and Torigoe, Y., Jap. Pantent, 1973, 7391 210, *Chem Abstr.*, 19780, 112616p.
12. Hiremath, S.-P., Saundane, A.-R., and Mruthyunjayaswamy, B.H.-M., *J. Heterocycl. Chem.,* 1993, vol. 30, p.6 03.
13. Saundane, A.-R., Ranganath, S.-H., Prayagrai, G., Rudresh, K., and Satyanayana, N.D., *Orient. J. Chem*., 1998, vol. 14(2), p. 251.
14. Hoorocks, P., Fallon, S., Denman, L., Devine, O., Duffy, L.J., Harper, A., Meredith, E. L., Hasenkam, P.-S., Sidaway, A., Monnery, D., and Phillips, T.-R., *Bioorg. Med. Chem. Lett*., 2011, vol. 22(4), p. 1770. doi 10.1016/j.bmcl.2011.12.071
15. Zheng, X., Li, Z.-Y., and Wang, *J. Flu. Chem*., 2003, vol. 123(2), p. 163.
16. Amir, M.-S. and Shahani., *Ind. J. Het. Chem*., 1998, vol. 8, p. 107.
17. Shah, H.-P., Shah, B.-R., Bhatt, J.-J., Desai, N.-C., Trivedi, P.-B., and Undavia, N.-K., *Ind. J Chem*., 1998, vol. 37B, p.180.
18. Hazarika, J. and Kataky, J.C.-S., *Indian. J. Heterocycl. Chem*., 1998, vol. 7, p. 83.
19. Liszkiewicz, H., Kowalska, M.-W., Wietrzyk, J., and Opolski, A., *Ind. J. Chem.,* 2003, vol. 42B, p. 2846.
20. Mallick, S.-K., Martin, A.-R., and Lingard, R.-G.,

J. Med. Chem., 1971, vol. 14(6), p. 528.

21. Freddy, H., Havaldar, Sushil, K., and Mishra, J., *Ind. J. Heterocycl. Chem*., 2004, vol. 13, p. 197
22. Saundane, A.-R., Vaijinath, A.-V., and Vijaykumar, K., *Heterocyclic. Lett*., 2012, vol. 2(3), p. 333.
23. Sies, H., *Am. J. Med.* 1991, vol. 91(3C), p. 31S. doi 10.1016/0002-9343(91)90281-2
24. Stocker, R., *Curr. Opi. Lip*., 1999, vol. 10(6), p. 589.
25. Saundane, A.-R., Vaijinath, A.-V., and Vijaykumar, K., *Med. Chem. Res*., 2013,vol. 22, p. 3787.
26. Hiremath, S.-P., Biradar, J.-S., and Purohit, M.-G., *Ind. J. Chem B*., 1982, vol. 21, p. 249.
27. *Indian Pharmacopoeia, Government of India*, New Delhi Appendix IV, 3rd ed., 1985, vol. 90
28. Janovska, D., Kubikova, K., and Kokoska, L., *Czech. J. Food. Sci*., 2003, vol. 21, p. 107.
29. Bishnu, J., Sunil, L., and Anuja, S., *J. Sci. Eng and Tech*., 2009, vol. 5, p. 143.
30. Hatano, H., Kanawa, T., and Yasuhara, O., *Chem. Pharm. Bull*., 1988, vol. 36, p. 2090.
31. Oyaizu, M., *Jap. J. Nutr*., 1986, vol. 44(6), p. 307.
32. Dinis, T. C.-P., Madeira, V. M.-C., and Almeida, L.-M., *Arch. Biochem and Biophys*., 1994, vol. 315 (1), p. 161.