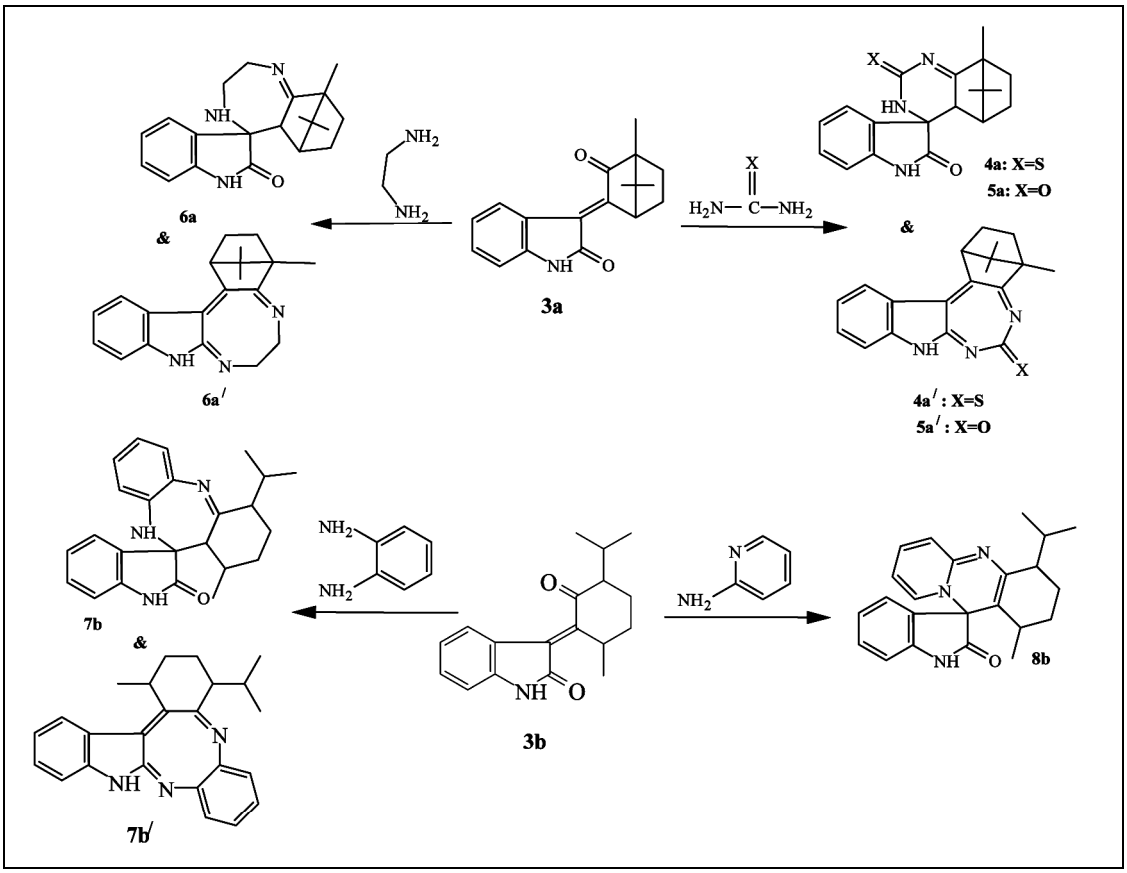
Synthesis of Some Indole Based Spiro and Condensed Heterocycles as Potential Biologically Active Agents

R. L. Sharma*, Daljeet Kour, Jasbir Singh, Surinder Kumar, Poonam Gupta, Shallu Gupta, Bhavneet Kour, Anand Sachar

Department of Chemistry, University of Jammu, Jammu-180006
E-mail: rlsharma_hod@rediffmail.com
Received November 21, 2007



The reactions of isatin with cyclic ketones, *viz* camphor (dl, Mp 174-181°C, specific rotation -1.5° to +1.5°) available from s. d. fine- CHEM LTD and menthone (l, Bp 207°-210° C, density 0.893 g/mL) isolated from peppermint oil, in refluxing ethanol in the presence of t-BuOK afforded the corresponding indolylidene compounds (**3a**) and (**3b**) (a mixture of stereochemical isomers *E* and *Z* in both the cases) respectively, all obtained as racemates. Cyclocondensation of (**3a**) and (**3b**) with thiourea, urea, ethylenediamine and *o*-phenylenediamine afforded new spiro (**4a,b-7a,b**) and condensed systems (**4a',b'-7a',b'**) respectively, whereas with 2-aminopyridine spiro compounds exclusively were obtained (**8a,8b**). All the new spiro and condensed systems generated have been isolated as racemates and evaluated for their antimicrobial activity.

J. Heterocyclic Chem., **45**, 1775 (2008).

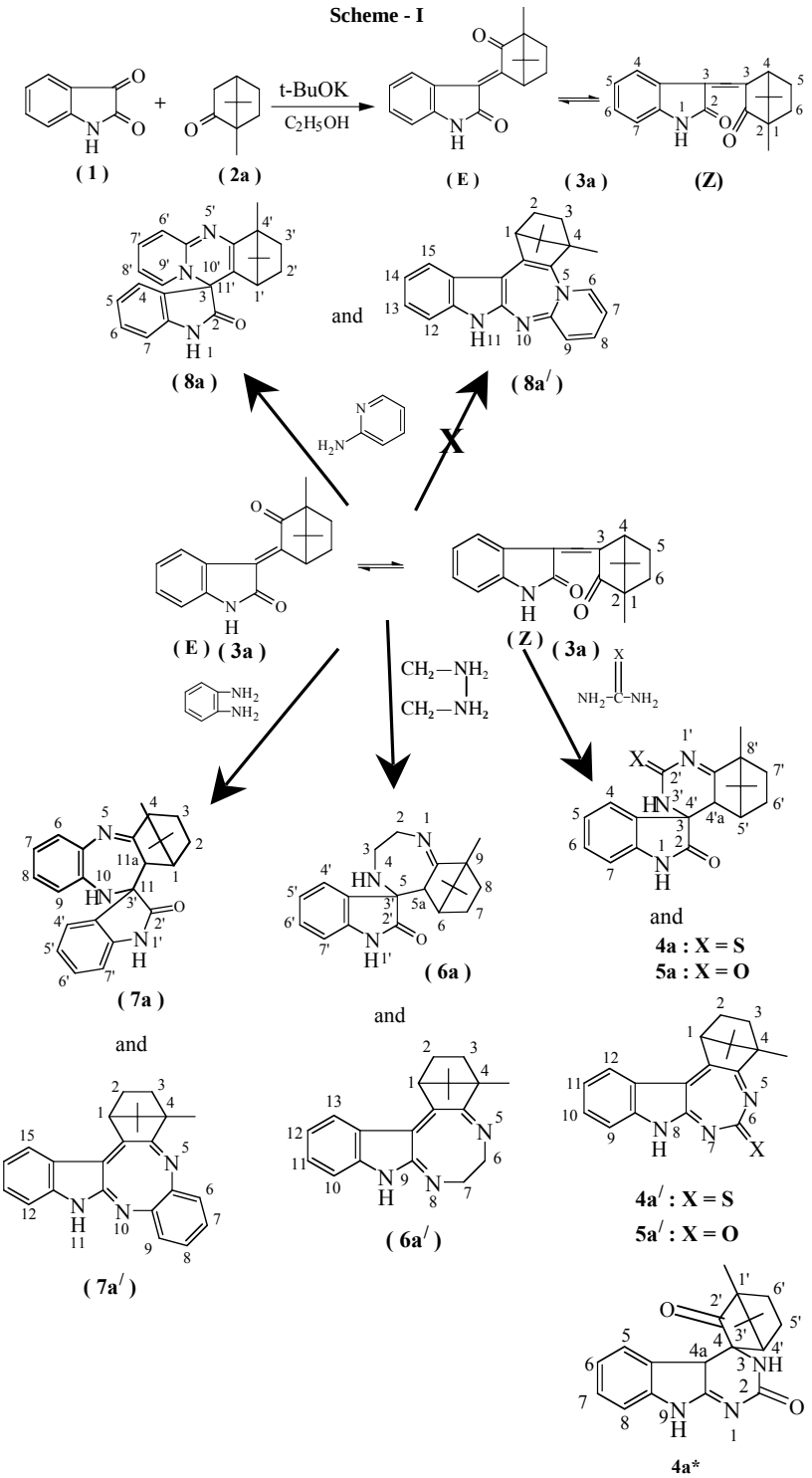
INTRODUCTION

A wide range of biological activities is associated with indole derivatives [1-4]. Systematic investigations of spiro indoles have also drawn much attention due to the fact that if the indole ring is joined to other heterocyclic systems through a spiro carbon atom at C-3, the resulting compounds show an increased spectrum of biological activities *viz.* antibacterial, antituberculosis, anticancer, antifungal, antihypertensive, *etc.* [5-7]. Moreover, varied pharmacological properties are associated with the fused diazepine and diazocine moieties [8-9]. The pharmacological dimensions and importance of pyrimidines and quinazolines are unlimited. In addition, spiro compounds also found application as photochromism [10-11]. These potentially biologically active hitherto unknown systems encouraged us to generate these novel heterocyclic compounds.

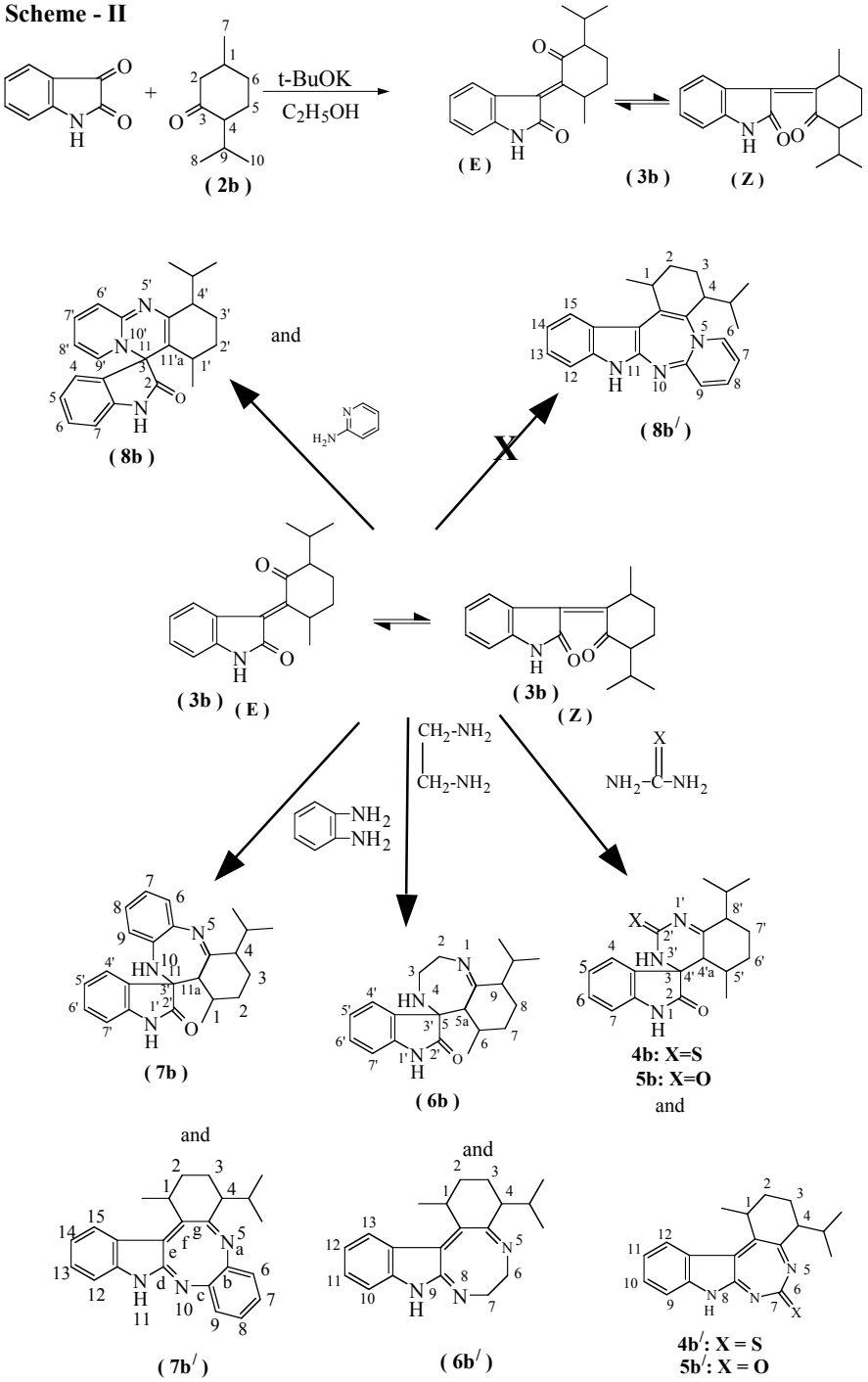
RESULTS AND DISCUSSION

In the present work, isatin (**1**) was reacted with camphor (**2a**) in refluxing ethanol using small amount of potassium *tert*-butoxide to yield 2,3-dihydro-3-{1,7,7-trimethyl-2-oxobicyclo[2.2.1]heptylidene-3-}indole-2-one (**3a**). Compound (**3a**) was found to be a mixture of two sterochemical isomers *E* and *Z*, which could not be separated by repeated crystallization and column chromatography. Compound (**3a**) as such was further refluxed with thiourea, urea, ethylenediamine, *o*-phenylenediamine and 2-aminopyridine to form a variety of novel heterocyclic systems shown in Scheme I. In either

Scheme - I



Scheme - II



condensation, the compound (**3a**) reacted in both the steroisomeric forms to produce a mixture of hitherto unknown spiro and condensed systems respectively. Firstly compound (**3a**) was reacted with thiourea in refluxing ethanol at elevated temperature for about 10-12 hours affording a mixture of two products, the main compound 3',4a',5',6',7',8'-hexahydro-2'*H*-8'-methyl-5',8'-dimethylmethano-2'-thioxospiro[indoline-3,4'-quinazolin]-2-one (**4a**) belonging to spiro system and the minor product 2,3,4,8-tetrahydro-1*H*-4-methyl-1,4-dimethylmethano-indolo[2,3-*d*][1,3]benzodiazepine-6-thione (**4a'**) belonging to condensed system, the characterizations are based on elemental analysis and spectral data.

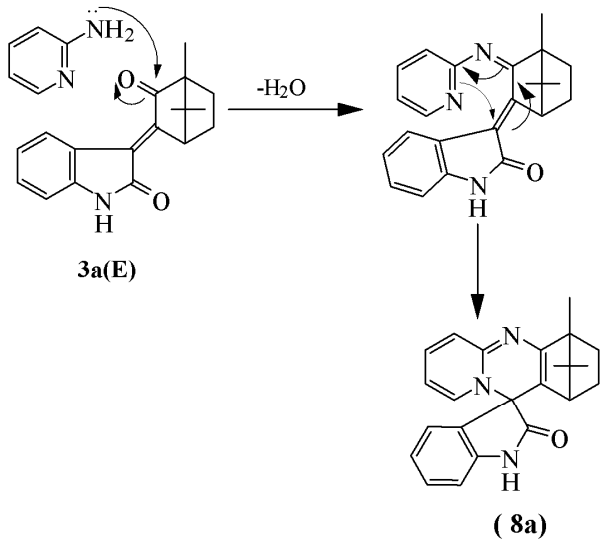
Compound (**4a**), which separated out as brown colored substance, showed characteristic IR absorption at 3280-3325 (NH), 1710 (C=O), 1600 (C=N) and 1230 (C=S). The disappearance of the exocyclic (C=C) absorption at 1620, (C=O) absorption at 1680 and retention of NHCO peak at 1710 cm^{-1} indicated the participation of α,β–unsaturated carbonyl at position-3 of 2-indolinone. The ^{1}H NMR spectrum showed doublet at δ 1.15-1.18 (-CH_3) and singlet at δ1.35-1.40 [$(CH_3)_2$]. The signals for methine proton at position 4'a appeared at δ 4.62; aromatic protons at δ 7.10-7.82 and two NH protons appeared at δ 8.61 (probably NH of pyrimidine moiety) and at δ 9.42 (probably NH of indole moiety). On the basis of this data, the dark brown colored solid was assigned the major spiro structure (**4a**) and was obtained in 48% yield. The alternative site for spirocyclisation leading to the characterization of compound as 4a* was ruled out since in that case, carbonyl group of the amide functionality instead of keto group would be involved which is undesirable comparatively. The filtrate after the separation of (**4a**) was diluted with water and left overnight at low temperature when another brown colored product separated out. Its IR spectrum showed disappearance of both carbonyl absorptions. The ^{1}H NMR spectrum did not display any signal at δ 4.62. This data could substantiate condensed structure (**4a'**) in 22% yield for this latter yellow colored solid compound. Working on similar route of synthesis, compound (**3a**) on condensation with urea afforded a major spiro compound (**5a**) in 53% and a minor condensed compound (**5a'**) in 25%; similarly, compound (**3a**) on condensation with ethylene-diamine by following the same procedure gave a spiro compound (**6a**) in 47% yield and a condensed compound (**6a'**) in 25% yield.

Similarly, condensation of (**3a**) with *o*-phenylene-diamine by following the same procedure afforded the main product, a spiro system (**7a**) in 52% yield and a condensed system compound (**7a'**) in 20% yield.

Finally, the ir spectrum of the product formed by the reaction of (**3a**) with 2-aminopyridine in the same way revealed >C=O absorption at 1692 cm^{-1} supporting the formation of the novel spiro system (**8a**) in 63% yield, whereas the corresponding condensed compound if at all possible could not be obtained after the crystallization of (**8a**) even after keeping the filtrate for 4-5 days at low temp.

The present work also includes the condensation of isatin (**1**) with menthone (**2b**) under the same set of conditions which afforded 2,3-dihydro-3-(3-isopropyl-6-methyl-2-oxo-cyclohexylidene-1)-indol-2-one (**3b**). Like (**3a**), (**3b**) was also found to be a mixture of two sterochemical isomers *E* and *Z*. The two isomers could not be separated in this case also even after repeated crystallization. This compound was further refluxed with thiourea, urea, ethylenediamine and *o*-phenylenediamine in the same way to get a series of novel spiro systems (**4b-7b**) and novel tetracyclic condensed ring systems (**4b'-7b'**) respectively as shown in Scheme II. However, on condensation of (**3b**) with 2-aminopyridine, only spiro compound (**8b**) was obtained in good yield. The structure of the spiro compound was confirmed by elemental analysis and spectral data. Hence, for the synthesis of spiro and condensed compounds, the existence of two isomers (*E* and *Z*) of (**3a**) and (**3b**) used as synthons is confirmed.

Mechanism of formation of (8a) (Concerted)



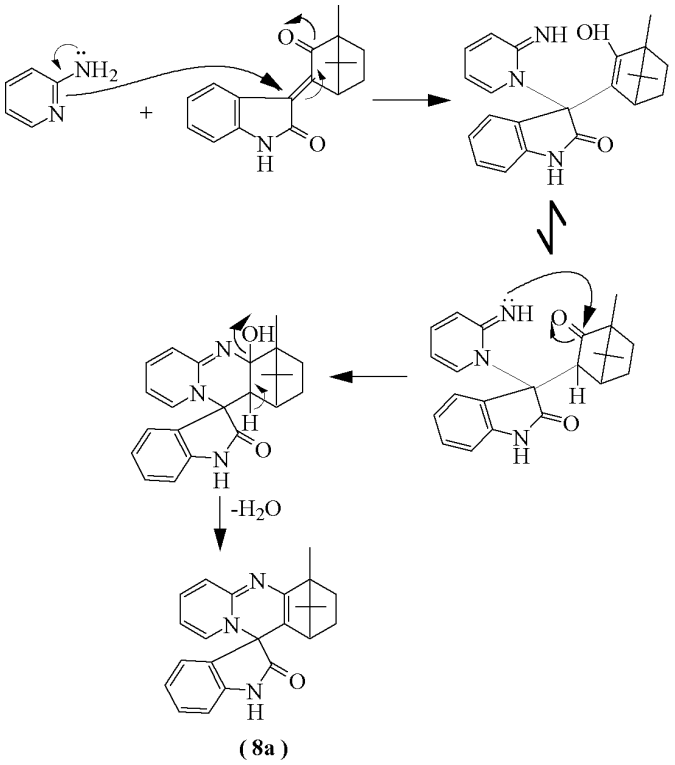
(8a)

Antimicrobial Activity. The compounds were screened for their antibacterial activity against *Escherichia coli*, *Bacillus sublitis* and *Bacillus cereus* at concentration of 1000μg and for antifungal activity against *Aspergillus niger*, *Pencillium* species and *Cladosporium* species at the same concentration by well diffusion technique. Standard antibacterial norfloxacin and antifungal fluconazole were also screened under similar conditions for a comparison. The zones of inhibition formed were measured in mm and are shown in Table-I.

EXPERIMENTAL

All melting points were measured in open capillaries on Perfit melting point apparatus and are uncorrected. TLC checking was done on glass plates coated with Silica gel G and spotting was done using

Alternative Mechanism of formation of (8a) (Micheal type)



(8a)

iodine. IR spectra on KBr were recorded on Alpha Centauri Infrared Spectrometer. ^{1}H NMR and ^{13}C NMR were recorded on a varien unity 200 MHz NMR Spectrophotometer in $CDCl_3$ using TMS as an internal standard. Chemical shift values are in ppm on δ scale. The elemental analyses were performed by the simple CHN analyser.

Synthesis of 2,3-Dihydro-3-{1,7,7-trimethyl-2-oxobicyclo [2.2.1] heptylidene -3 -} indol -2-one (3a). A mixture of isatin (0.01 mole), camphor (0.01 mole) and potassium *tert*-butoxide (0.005 mole) was refluxed for 10 hours in absolute ethanol (100 mL). After completion of reaction as monitored by tlc, the reaction mixture was concentrated in vacuum and about half the solvent (*i.e.* ethanol) was removed. The concentrated reaction mixture was then allowed to crystallize overnight at 0℃ where by a brick red solid (**3a**) crystallized out. The solid was collected by filtration, washed, dried and further crystallized from hot ethanol to give the title compound. Yield : 60%; Mp 268 ℃; IR (KBr, ν, cm^{-1}): NH 3318, C=O 1710, 1680, exo C=C 1620; ^{1}H NMR ($CDCl_3$): δ 1.11 (3H, s, CH_3); 1.34[6H, s, $(CH_3)_2$]; 1.78-1.95(5H, m, 4, 5, 6 -H of camphor moiety); 6.92-7.71(4H, m, Ar-H) and 9.8(1H, s, NH). *Anal.* Calcd.. for $C_{18}H_{19}NO_2$: C, 76.82; H,6.75; N, 4.97. Found: C, 76.86; H, 6.72; N, 4.95.

General procedure for synthesis of spiro heterocycles (4a-7a) and condensed heterocycles (4a'-7a'). A mixture of (**3a**) (0.005 mole) and thiourea/urea/ethylenediamine/*o*-phenyl-enediamine (0.005 mole) in 40-50 mL absolute ethanol was refluxed separately for 10-12 hours. As monitored by tlc, the product gave two spots. The reaction mixture was cooled to room temperature. The dark brown solid was collected by filtration and recrystallized from ethanol to give (**4a-7a**). The filtrate was diluted with water and kept overnight at low temperature when another brown colored product separated out, which on recrystallization from acetic acid afforded (**4a'-7a'**).

3',4a',5',6',7',8'-Hexahydro-2'*H*-8'-methyl-5',8'-dimethylmethano-2'-thioxospiro[indoline-3,4'-quinazolin]-2-one (4a). Yield 48%; Mp 255 ℃; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C=S 1230, C-N 1300-1325, C=N 1600, C=O 1710, NH 3280-3325.^{1}H NMR ($CDCl_3$): δ 1.15(3H, s, CH_3); 1.35[6H, s, $[(CH_3)_2]$; 1.92-2.10(5H, m, 5',6', 7'-H); 4.62(1H, d,4'aH); 7.10-7.82(4H, m, ArH); 8.61and 9.42(2H, s, NH). *Anal.* Calcd. for $C_{19}H_{21}N_3OS$: C, 67.22; H, 6.23; N, 12.37; Found: C, 67.18; H, 6.25; N, 12.39.

Table I

Antimicrobial activity of Compounds **4**, **5**, **6**, **7**, **8**

Antibacterial activity				Antifungal activity		
Compd. No.	E.coli	B.subtilis	B.cereus	A.niger	P.species	C.species
4a	15	14	18	18	16	19
4a'	12	13	16	14	14	17
5a	16	10	20	20	18	18
5a'	13	11	17	15	17	19
6a	17	16	17	19	19	19
6a'	19	13	16	13	17	17
7a	19	14	14	19	16	21
7a'	18	15	13	16	15	20
8a	20	22	20	20	19	16
4b	14	16	18	17	17	14
4b'	10	14	16	16	16	12
5b	11	10	17	14	14	13
5b'	10	12	11	15	13	12
6b	14	18	16	18	17	13
6b'	13	16	14	16	18	17
7b	18	14	15	19	17	18
7b'	16	18	17	18	15	13
8b	22	20	16	15	14	16
NR	28	26	28	---	---	---
Flu	---	---	---	32	25	23

Note:- 11mm, inactive; 12-16mm, weakly active; 17-21mm, moderately active. **NR:- Norfloxacin Flu:- Fluconazole**

2,3,4,8-Tetrahydro-1*H*-4-methyl-1,4-dimethylmethano-indolo[2,3-*d*][1,3]benzodiazepine-6-thione (4a'). Yield 22%; Mp 263 °C; crystallized from AcOH ; IR (KBr, ν, cm^{-1}): C=S 1235, C-N 1320, C=N 1595, NH 3320; ^{1}H NMR ($CDCl_3$): δ 1.12(3H, s, -CH_3); 1.32[6H, s, $(CH_3)_2$]; 1.98-2.11(5H, m, 1, 2, 3-H); 7.12-7.86 (4H, m, ArH) and 9.48(1H, s, NH). *Anal.* Calcd. for $C_{19}H_{19}N_3S$: C, 70.99; H, 5.95; N, 13.07. Found: C, 70.96; H, 5.91; N, 13.03.

3',4a',5',6',7',8'-Hexahydro-2'*H*-8'-methyl-5',8'-dimethyl-methanospiro[indoline-3,4'-quinazoline]-2,2'-dione (5a). Yield 53%; Mp 260 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1300-1325, C=N 1605, 1690 C=O, NH 3330; ^{1}H NMR ($CDCl_3$): δ 1.16-(3H, s, CH_3); 1.33[6H, s, $(CH_3)_2$]; 1.93-2.11(5H, m, 5', 6', 7'-H); 4.68(1H, d, 4'aH); 7.15-7.82(4H, m, ArH); 8.63 and 9.40(2H, s, NH). ^{13}C($CDCl_3$) :δ 12.9, 19.5, 20.1, 26.4, 35.3, 41.6, 43.2, 49.4, 62.6, 120.1, 123.6, 125.7, 128.4, 131.1, 149.1, 164.2, 170.0, 173.0. *Anal.* Calcd. for $C_{19}H_{21}N_3O_2$: C, 70.56; H, 6.54; N, 12.99. Found: C, 70.53; H, 6.52; N, 12.95.

2,3,4,8-Tetrahydro-1*H*-4-methyl-1,4-dimethylmethano-indolo[2,3-*d*][1,3]benzodiazepin-6-one (5a'). Yield 25%; Mp 273 °C; crystallized from acetic acid. IR (KBr, ν, cm^{-1}): C-N 1315, C=N 1590, C=O 1690, N-H 3325. ^{1}H NMR ($CDCl_3$): δ 1.14 (3H, s, CH_3); 1.35[6H, s, $(CH_3)_2$]; 1.99-2.10(5H, m, 1,2,3-H); 7.14-7.82(4H, m, ArH) and 9.46(1H, s, NH). *Anal.* Calcd. for $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76. Found: C, 74.70; H, 6.23; N, 13.70.

2,3,4,5a,6,7,8,9-Octahydro-9-methyl-6,9-dimethylmethano-spiro{[1,4]benzodiazepine-5,3'-indolin}-2'-one (6a). Yield 47%; Mp 270 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1305-1320, C=N 1600, C=O 1695, NH 3330-3380; ^{1}H NMR ($CDCl_3$): δ 1.13 (3H, s, CH_3); 1.40[6H, s, $(CH_3)_2$]; 1.98-2.10(5H, m, 6,7,8-H); 2.82-2.87(4H, m, 2 x CH_2), 4.46(1H, d, 5aH); 7.10-7.94(4H, m, ArH); 8.20 (1H, brs, NH at 4 position) and 9.40(1H, s, NH of indole moiety). Anal Calcd. for $C_{20}H_{25}N_3O$; C, 74.26; H, 7.71; N, 13.04. Found: C, 74.30; H, 7.73; N, 13.00.

2,3,4,6,7,9-Hexahydro-1*H*-4-methyl-1,4-dimethylmethano-indolo[2,3-*e*][1,4]benzodiazocine (6a'). Yield 25%; Mp 278 °C; crystallized from dioxane. IR (KBr, ν, cm^{-1}): C = C 1610, C = N 1620, C-N 1325, NH 3335. ^{1}H NMR ($CDCl_3$): δ 1.12 (3H, s, CH_3); 1.40 [6H, s, $(CH_3)_2$]; 1.92-2.30 (5H, m, 1, 2, 3, -H); 2.82-2.87 (4H, m, 2 x CH_2); 7.11-8.13 (4H, m, ArH) and 9.35(1H, s, NH). *Anal.* Calcd. for $C_{20}H_{23}N_3$: C, 78.65; H, 7.59; N, 13.75. Found: C, 78.67; H, 7.56; N, 13.72.

1,2,3,4,10,11a-Hexahydro-4-methyl-1,4-dimethylmethanospiro-{dibenzo[*b*,*f*][1,4]diazepine-11,3'-indolin}-2'-one (7a). Yield 52%; Mp 261 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N1300-1320, C=N1620, C=O1692, NH 3340; ^{1}H NMR ($CDCl_3$): δ 1.00(3H, s, CH_3); 1.36 [6H, s, $(CH_3)_2$]; 1.94-2.28(5H, m, 1, 2, 3-H); 4.42(1H, s, 11aH); 7.15-8.32(8H, m, ArH); 8.85(1H, brs, NH at 10 position) and 9.40(1H, s, NH of indole moiety). *Anal.* Calcd. for $C_{24}H_{25}N_3O$; C, 77.60; H, 6.70; N, 11.33. Found: C, 77.62; H, 6.73; N, 11.32.

2,3,4,11-Tetrahydro-1*H*-4-methyl-1,4-dimethylmethanoindolo-[3,2-d]dibenzo [*b*,*g*] [1,4]diazocine (7a'). Yield 20%; Mp 280 °C; crystallized from acetic acid. IR (KBr, ν ,cm^{-1}): C-N 1315-1325, C=N 1615, NH 3345; ^{1}H NMR ($CDCl_3$): δ 1.14(3H, s, CH_3); 1.43[6H, s, $(CH_3)_2$]; 1.91-2.35[5H, m, 1, 2, 3, H]; 6.92-8.37(8H, m, ArH) and 9.94(1H, s, NH). *Anal.* Calcd. for $C_{24}H_{23}N_3$; C, 81.55; H, 6.55; N, 11.78. Found: C, 81.52; H, 6.56; N, 1181.

1', 2', 3', 4'-Tetrahydro-4'-methyl-1',4'-di-methylmethanospiro-{indoline-3,11'-pyrido[2,1-*b*]quinazolin}-2-one (8a). A mixture of (**3a**) (0.005 mole) and 2-aminopyridine (0.005 mole) was condensed in refluxing ethanol for 11 hours. After the completion of the reaction, as monitored by tlc, the reaction mixture was cooled at low temperature. The yellow colored solid was separated, collected by filtration and recrystallized from ethanol to give (**8a**). Keeping the filtrate for 24 hours at low temperature did not give the expected condensed product (**8a'**).

(8a). Yield 63%; Mp 270 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1320, C=N 1623, C=O 1692, NH 3340; ^{1}H NMR ($CDCl_3$): δ 1.13(3H, s, CH_3); 1.38(6H, s, $(CH_3)_2$]; 2.01-2.42(5H, m, 1', 2', 3'-H); 7.12-8.43(8H, m, ArH); and 9.83(1H, s, NH); ^{13}C NMR ($CDCl_3$): δ 14.5, 14.6, 22.1, 23.2, 43.2, 53.0, 59.3, 73.1, 108.6, 118.0, 120.8, 124.8, 124.6, 125.4, 126, 127.6, 130.2, 135, 137.4, 142.0, 149.1, 168.2. *Anal.* Calcd. for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.48; N, 11.75. Found: C, 77.25; H, 6.44; N, 11.73.

Synthesis of 2,3-Dihydro-3-(3-isopropyl-6-methyl-2-oxo-cyclohexylidene-1)-indol-2-one (3b). A mixture of isatin (0.01 mole), menthone (0.01 mole) and ammonium acetate (0.005 mole) was refluxed for about 10 h in absolute ethanol by the same procedure as mentioned for (**3a**). Yield 65%; Mp 275 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): NH 3320, conj C=O 1710, 1675, exo C=C 1615; ^{1}H NMR ($CDCl_3$): δ 1.05-1.10(3H, d, CH_3, J=2.71 Hz); 1.11-1.27[6H, d, $(CH_3)_2$]; 1.30-2.10 (6H, m, 3, 4, 5, 6-H of cyclohexanone moiety); 2.27-2.35(1H, m, -CH of isopropyl gp); 6.62-7.52(4H, m, ArH) and 9.3(1H, s, NH). *Anal.* Calcd. for $C_{18}H_{21}NO_2$. C, 76.29; H, 7.47; N, 4.94. Found: C, 76.25; H, 7.43; N, 4.92.

Synthesis of spiro heterocycles (4b-7b) and condensed heterocycles (4b'- 7b'). These compounds were obtained by condensing (**3b**) (0.005 mole) with thiourea (0.005 mole) in refluxing ethanol by the same procedure as mentioned for (**4a**) and (**4a'**).

3',4'a,5',6',7',8'-Hexahydro-2'*H*-8'-isopropyl-5'-methyl-2'-thioxospiro{indoline-3,4'-quinazolin} -2-one (4b). Yield 50%; Mp 271 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C=S 1220, C-N 1300-1335, C=N 1590, C=O 1710; ^{1}H NMR ($CDCl_3$): δ 1.07-1.11(3H, d, CH_3, J=2.75 Hz);1.15-1.29[6H, d, -$(CH_3)_2$]; 1.35-2.18(6H, m, 5',6',7',8'-H); 2.30-2.37(1H, m, -CH of isopropyl gp); 4.21(1H, d, 4'aH); 6.90-7.72(4H, m, ArH); 8.10 & 9.62 (2H, s, NH). ^{13}C NMR (DMSO-d_6): δ (PPm) 17.3, 20.2, 21.8, 25.3, 26.8, 34.8, 42.6, 43.9, 70.8, 120.9, 123.6, 125.9, 128.6, 131.4, 140.8, 167, 171, 188. *Anal.* Calcd. for $C_{19}H_{23}N_3OS$: C, 66.83; H, 6.78; N, 12.30. Found: C, 66.81; H, 6.75; N, 12.32

2,3,4,8-Tetrahydro-1*H*-4-isopropyl-1-methylindolo[2,3-*d*]-[1,3]benzodiazepine-6-thione (4b'). Yield 30%; Mp 279 °C; crystallized from dioxane. IR (KBr, ν, cm^{-1}): C=S 1230,C-N 1320-1330, C=N 1590, NH 3340; ^{1}H NMR ($CDCl_3$): δ 1.09-1.10(3H, d, CH_3, J = 2.72 Hz); 1.16-1.27[6H, d (CH_3)$_2$]; 1.45-2.20(6H, m, 1, 2, 3, 4-H) 2.18-2.30(1H, m, -CH of isopropyl gp); 6.45-7.05(4H, m, ArH) and 9.52(1H, s, NH). *Anal.* Calcd. for $C_{19}H_{21}N_3S$: C, 70.55; H, 6.54; N, 12.99. Found : C, 70.52; H, 6.50; N, 12.95.

3',4'a,5',6',7',8'-Hexahydro-2'*H*-8'-isopropyl-5'-methylspiro-{indoline-3,4'-quinazoline]-2,2'-dione (5b) and 2,3,4,8-Tetrahydro-1*H*-4-isopropyl-1-methylindolo[2,3-*d*][1,3]benzodiazepin-6-one (5b'). Compounds (**5b**) and (**5b'**) were obtained by condensing (**3b**) and urea in the mole ratio of 1:1 by following the same procedure as that of (**4b**) and (**4b'**).

(5b). Yield 58%; Mp 270 °C; crystallized from ethanol. IR(KBr, ν, cm^{-1}): C-N 1300-1330, C=N 1610, C=O 1695-1705, NH 3335; ^{1}H NMR ($CDCl_3$): δ 1.10-1.25(3H, d, CH_3, J = 2.70 Hz); 1.15-1.25[6H, d, $(CH_3)_2$]; 1.55-2.19(6H, m, 5',6',7',8'-H); 2.20-2.33(1H, m, CH of

isopropyl gp); 4.50(1H, d, 4'aH); 6.48-7.08(4H, m, ArH); 8.68 & 9.82(2H, s, NH). *Anal.* Calcd. for $C_{19}H_{23}N_3O_2$; C, 70.13; H, 7.12; N, 12.91. Found: C, 70.09; H, 7.10; N, 12.94.

(5b'). Yield 28%; Mp 289 °C; crystallized from dioxane. IR(KBr, ν, cm^{-1}) : C-N 1310,C=N 1600, C=O 1700, NH 3320;^{1}H NMR ($CDCl_3$) δ : 1.12-1.20(3H, d, CH_3, J=2.69 Hz); 1.16-1.26[6H, d, $(CH_3)_2$]; 1.59-2.20(6H, m, 1,2,3,4-H); 2.16-2.25(1H, m, CH of isopropyl gp); 6.50-7.07(4H, m, ArH) and 9.63(1H, s, NH). *Anal.* Calcd. for $C_{19}H_{21}N_3O$; C, 74.24; H, 6.88; N, 13.67. Found: C, 74.21; H, 6.85; N, 13.63.

2,3,4,5a,6,7,8,9-Octahydro-9-isopropyl-6-methylspiro{[1,4]-benzodiazepine-5,3'-indolin}-2'-one (6b) and 2,3,4,6,7,9-Hexa-hydro-1*H*-4-isopropyl-1-methylindolo[2,3-*e*][1,4]benzodiazocine (6b'). Compounds (**6b**) and (**6b'**) were obtained by condensing (**3b**) (0.005 mole) and ethylenediamine (0.005 mole) by following the same procedure as above.

(6b). Yield 47%; Mp 278 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1310-1320, C=N 1595, C=O 1705, NH 3315-3400; ^{1}H NMR ($CDCl_3$): δ 1.18-1.22(3H, d, CH_3, J=2.70 Hz); 1.20-1.24[6H, d, $(CH_3)_2$]; 1.60-2.25[6H, m, 6,7,8,9-H); 2.20-2.25(1H, m, CH of isopropyl gp.); 2.80-2.85(4H, m, 2x CH_2); 4.22(1H, d, 5aH); 6.95-8.00(4H, m, ArH); 8.5(1H, brs, NH at 4 position) and 9.51(1H, s, NH of indole moiety). ^{13}C NMR (DMSO) :δ (PPm) 17.2, 20.1, 22.9, 24.9, 26.1, 34.8, 41.2, 42.6, 44.3, 49.4, 69.7, 120.1, 123.8, 125.8, 128.4, 131.1, 140.4, 164.4, 171.8. *Anal.* Calcd. for $C_{20}H_{27}N_3O$; C, 73.81; H, 8.36; N, 12.91. Found: C, 73.78; H, 8.33; N, 12.94.

(6b'). Yield 25%; Mp 289 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1305, C=N 1595, NH 3345; ^{1}H NMR ($CDCl_3$) δ : 1.15-1.27(3H, d, CH_3, J=2.74 Hz); 1.25-1.30[6H, d, $(CH_3)_2$]; 1.58-2.20[6H, m, 1,2,3,4-H); 2.22-2.30(1H, m, CH of isopropyl gp.); 2.82-2.90(4H, m, 2 x CH_2); 6.42-7.50(4H, m, ArH) and 9.23(1H, s, NH). *Anal.* Calcd. for $C_{20}H_{25}N_3$; C, 78.13; H, 8.19; N, 13.68. Found : C, 78.09; H, 8.15; N, 13.65.

1,2,3,4,10,11a-Hexahydro-4-isopropyl-1-methylspiro{dibenzo-[*b,f*][1,4]diazepine-11,3'-indolin}-2'-one (7b) and 2,3,4,11-Tetra-hydro-1*H*-4-isopropyl-1-methylindolo[3,2-*d*]dibenzo[*b,g*][1,4]-diazocine (7b'). Compounds (**7b**) and (**7b'**) were obtained by condensing (**3b**) (0.005 mole) and *o*-phenylenediamine (0.005 mole) by following the same procedure as that for (**4b**) and (**4b'**).

(7b). Yield 42%; Mp 263 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1300-1320, C=N 1600, C=O 1690, NH. 3320-3350; ^{1}H NMR ($CDCl_3$): δ 1.18-1.30(3H, d, CH_3, J=2.79 Hz); 1.35-1.40[6H, d, $(CH_3)_2$]; 1.55-2.25[6H, m, 1,2,3,4-H); 2.20-2.35(1H, m, CH of isopropyl gp); 4.35(1H, d, 11aH); 6.40-7.80(8H, m, ArH); 8.80 and 9.20(2H, s, NH). *Anal.* Calcd. for $C_{24}H_{27}N_3O$; C, 77.18; H, 7.28; N, 11.25. Found: C, 77.15; H, 7.32; N, 11.21.

(7b'). Yield 29%; Mp 288 °C; crystallized from acetic acid. IR (KBr, ν, cm^{-1}): C-N 1310-1325, C=N 1610-1615, NH 3350; ^{1}H NMR ($CDCl_3$): δ 1.20-1.28(3H, d, CH_3, J=2.80 Hz);1.30-1.38[6H, d, $(CH_3)_2$]; 1.40-2.30[6H, m, 1,2,3,4-H); 2.18-2.40(1H, m, CH of isopropyl); 6.45-7.35(8H, m, ArH) and 9.81(1H, s, NH). *Anal.* Calcd. for $C_{24}H_{25}N_3$; C, 81.09; H, 7.08; N, 11.82. Found : C, 81.06; H, 7.04; N, 11.80.

1',2',3',4'-Tetrahydro-4'-isopropyl-1'-methylspiro{indoline-3,11'-[2,1-*b*]quinazolin}-2-one (8b). A mixture of (**3b**) (0.005 mole) and 2-aminopyridine (0.005 mole) in 40-50 mL absolute ethanol was refluxed for 10 to 12 hours. As monitored by tlc the product gave a single spot. The reaction mixture was cooled to room temperature. The brown colored solid product was separated, collected by filtration and recrystallized from ethanol to give (**8b**). No condensed product was obtained by keeping the filtrate at room temperature for even 2 to 3 days.

(8b). Yield 60%; Mp 291 °C; crystallized from ethanol. IR (KBr, ν, cm^{-1}): C-N 1300-1330, C=N 1610, NH 3345; ^{1}H NMR ($CDCl_3$): δ 1.20-1.30(3H, d, CH_3, J = 2.79 Hz); 1.25-1.32[6H, d, $(CH_3)_2$]; 1.28-2.25[6H, m, 1',2',3',4'-H); 2.10-2.35(1H, m, CH of isopropyl gp); 6.89-7.80(8H, m, ArH) and 9.65(1H, s, NH). *Anal.* Calcd. for $C_{23}H_{25}N_3O$; C, 76.85; H, 7.01; N, 11.68. Found: C, 76.81; H, 6.95; N, 11.69.

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