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FACILE SYNTHESIS OF SPIRO[3*H*-INDOLE-3,2'-OXIRANE]-3'-(2-OXO-2-(THIOPHENE-2-YL))-2(1*H*)ONES AND THEIR ANTIBACTERIAL ACTIVITY

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Abstract
An environmentally benign synthesis of spiro[indole-3,2'-oxirane]-3'(2-oxo-2-(thiophen-2-yl)) 2(1H)ones **(5a-g)** are reported. The spiro[indole-3,2'-oxirane] derivatives were obtained in 90-96% yield exclusively *via* epoxidation of 3-[2-oxo-2-(thiophen-2-yl)ethylidene]-indoline-2-ones **(4a-g)** with 30% aqueous hydrogen peroxide using cetyltrimethyl ammonium bromide as a phase transfer catalyst. The 3-hydroxy-3-(2-oxo-2(thiophen-2yl)ethylene indolin-2ones) **(3a-g)** were synthesized by the reaction of isatin and acetyl thiophene. The **3a-g** on heating with HCl and acetic acid gave **4a-g**. The synthesized compounds have been characterized by analytical and spectral (IR, ^{1}H NMR, ^{13}C NMR, and FAB mass) data. Compounds **5a-g** were screened for antibacterial activity against both gram positive (*E. Coli and P. aeruginuse*) and gram negative (*B. subtilis and S. aureus*) bacteria and showed good to moderate activity.

Keywords: 3-Hydroxy-3-(2-oxo-2(thiophen-2yl)ethylene-indolin-2-ones, cetyltrimethyl ammonium bromide, antibacterial activity.

Introduction:

The indole nucleus, a common and important structural functionality of a variety of both natural and unnatural products is a well known heterocycle.[i] Indole-2,3-dione (isatin) and its derivatives show various biological activities[ii] such as antimicrobial, antitubercular, anticancer, antioxidant, antihistamic, anti HIV, anti-inflammatory, analgesic, antipyretic and antiglycation, etc.

Oxiranes or heterocyclic systems having epoxide ring are found as critical component in many important biologically relevant compounds *e.g.* antitumor,[iii] antibiotics asperline,[iv] and pseudomonic acid [v]A and B.

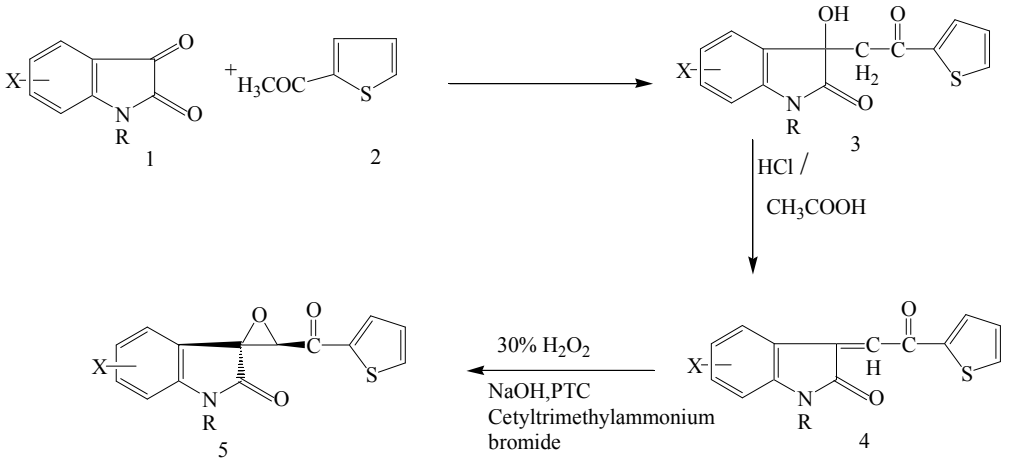
Epoxy carbonyl compounds are widely recognized as versatile intermediate for the synthesis of drug molecules.[vi] The spiro oxindole unit is a privileged heterocyclic motif that forms the core structure of a large family of natural alkaloids and many pharmacological agents with important bioactivity and interesting properties[vii,viii]. The unique structures and the highly pronounced pharmacological activity displayed by the spirooxindoles have made them attractive synthetic target[ix]. Spiro-oxirane-oxindole are a particular class of compounds with both spiro carbon and unstable oxirane feature, can same as important building blocks in organic synthesis of large ring heterocycles.

As a consequence, in recent years much attention has been paid to the diastereoselective and enantioselective synthesis of spiro-oxirane-oxindole.[x]

Epoxidation reactions have been done by various methodologies like Darzen Reaction,[x] presence of catalyst/reagent[xi] and under microwave irradiation.[xii] Among various methodology, the use of phase transfer catalyst is unique technique by which reaction between substrate located in mutually immiscible phase are brought about or accelerated literature survey show use of various phase transfer catalyst. We have used cetyltrimethyl ammonium bromide (CTAB) as phase transfer catalyst.

In continuation of our work on biological active compounds[xiii-xvii] we here in report the synthesis of spiro[indole3,2'- oxirane] -3'(2-oxo-2-(thiophen-2-yl))2(1*H*)ones **(5a-g)**.

Indole-2,3-diones reacted with 2-acetylthiophene. We discovered that the aldol condensation proceeded smoothly at 60 ˚C in DMF under catalyzed free conditions within 3-4 hrs stirring instead of stirring at room temperature for 24h.[xviii] The rate of reaction is increased by adding 10.0 mg molecular sieve (MS) 4Å to the reaction system as additive. We supported that molecular sieve might absorb the small amount of water present in the reaction system. The reaction resulted in the formation of 3-hydroxy-3-(2-oxo-2(thiphene-2-yl)ethyl-indolin-2-ones) **(3a-g).** This on heating, on steam bath for 15-30 min. in the presence of HCl and glacial acetic acid affords 3-(2-oxo-2(thiphene-2yl)ethylidine-indol-2-ones) **(4a-g)**. Epoxidation of **4a-g** with 30% hydrogen peroxide using TBAB gives **5a-g (Scheme 1)**.



Compound	X	R	Compound	X	R
3a	F	H	**4e**	H	CH_3
3b	H	H	**4f**	H	$CH_2C_6H_5$
3c	H	C_2H_5	**4g**	Cl	$CH_2C_6H_5$
3d	Cl	H	**5a**	F	H
3e	F	CH_3	**5b**	H	H
3f	H	$CH_2C_6H_5$	**5c**	H	C_2H_5
3g	Cl	$CH_2C_6H_5$	**5d**	Cl	H
4a	F	H	**5e**	F	CH_3
4b	H	H	**5f**	H	$CH_2C_6H_5$
4c	H	C_2H_5	**5g**	Cl	$CH_2C_6H_5$
4d	Cl	H			

Scheme 1: Synthesis of compounds (**5a-g)**

Experimental:

Melting points are uncorrected and taken in open glass capillaries using Gallenkamp melting point apparatus. The IR spectra were recorded on an 8400S SHIMADZU IR spectrometer in KBr pellets and band positions are recorded in wave numbers (cm^{-1}) . ^1H NMR and ^{13}C NMR spectra were recorded on JEOL 300 MHz instrument using $CDCl_3$ at 300 and 75 MHz, respectively and chemical shift (δ) are given in ppm. TMS was used as internal reference. The Mass spectra and elemental analyses were performed at Central Drug Research Institute, Lucknow, India. Chemical were purchased from Acros Organics, the bacterial cultures *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginusa* were procurred from microbial type culture collection, Institute of Microbial Technology, Chandigarh, India. Dimethyl sulfoxide (DMSO) and Chloramphenicol (standard brond spectram antibiotics) were used as controls.

*5-Fluoro-3-hydroxy-3-(2-oxo-2-(thiophen-2-yl)ethyl)indolin-2-one **(3a):***

To a solution of 5-fluoro isatin **1a** (0.01mol) in freshly distilled DMF (10.0ml) was added 2-acetylthiophene (0.01mol) in the presence of sufficiently activated MS 4Å (10.0 mg). The reaction mixture was stirred at ±60 ˚c for 3-4 h and was monitored by TLC. When the **1a** fully disappeared then solvent was removed under reduced pressure to obtain the crude product. It was further purified by simple re-crystallization by ethanol to give **3a**. Yield: 92%; M.P.156-158 ˚c; IR (KBr, cm^{-1}): 3450(OH), 3310(NH), 1705(CO), 1670(CO); ^1H NMR ($CDCl_3$, δ/ppm) δ: 3.96 (d,2H,CH_2), 6.12 (s, 1H, OH), 6.84-7.95 (m, 6H, Ar-H); 10.27 (s, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, δ/ppm): 45.9, 73.0, 109.5, 121.2, 123.8, 128.8, 129.0, 131.4, 133.9, 135.2, 142.8, 143.5, 178.2, 189.3; Mass(m/z): 288.30 (M^+).;Elemental analysis calculated for $C_{14}H_{10}FNO_3S$: C, 58.32; H, 4.89; N, 4.85; S, 11.12; found: C, 58.35; H, 4.84; N, 4.88; S, 11.16%. Compounds **3b-g** have been prepared similarly their physical and analytical data are recorded in **Table 1**.

*5-Fluoro-3-(2-oxo-2-(thiophen-2-yl)ethylidine)indolin-2-one **(4a)**:*

A mixture of **3a** (0.01mol), conc. HCl (0.5 mol) and glacial acetic acid (10.0 ml) was heated on a steam bath for 15-30 min., ethanol (10.0 ml) was then added to it . On cooling the product obtained was filtered and recrystallized from ethanol to give **4a**: Yield 95%; M.P. 150-152 ˚c ; IR (KBr,cm^{-1}): 3280, 3080, 1710, 1664, 1600, 1490, 1460, 1420, 1330, 1060, 960, 850, 790, 720; ^1H NMR ($CDCl_3$, δ/ ppm) δ: 6.27 (=CH), 6.84-7.89 (m, 6H,Ar-H), 10.20(s, 1H, NH); ^{13}C NMR(75MHz, $CDCl_3$,δ/ppm): 110.3, 120.5, 122.1, 124.1, 128.5, 128.7, 133.0, 133.2, 135.4, 138.0, 145.0, 145.9, 169.4, 182.7: Mass (m/z): 270.28 (M^+). Elemental analysis calculated for $C_{14}H_8FNO_2S$; C, 62.21; H, 2.98; N, 5.18; S, 11.86; found C, 62.18; H, 2.94; N, 5.21; S, 11.90%. Compounds **4b-g** have been prepared similarly their physical and analytical data are recorded in **Table-1**

Table-1: Physical and analytical data of compounds **3a-g** and **4a-g**.

Compd.	X	R	Yield (%)	M.P. (^oC)	Mol. Formula	Analysis % Calcd./(Found)		
						C	H	N
3a	F	H	92	156-158	$C_{14}H_{10}FNO_3S$	58.32/(58.35)	4.89/(4.84)	4.85/(4.88)
3b	H	H	94	180-182	$C_{14}H_{11}NO_3S$	61.52/(61.56)	4.05/(4.08)	5.12/(5.16)
3c	H	C_2H_5	90	170-	$C_{16}H_{15}NO_3S$	63.76/(63.72)	5.01/(4.98)	4.64/(4.61)

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3d	Cl	H	93	179-181	$C_{14}H_{10}ClNO_3S$	54.64/(54.60)	3.27/(3.30)	4.55/(4.59)
3e	H	CH_3	90	166-168	$C_{15}H_{13}NO_3S$	62.70/(62.73)	4.56/(4.54)	4.87/(4.83)
3f	H	CH_2Ph	88	132-134	$C_{21}H_{17}NO_3S$	69.40/(69.45)	4.71/(4.75)	3.85/(3.89)
3g	Cl	CH_2 Ph	89	128-130	$C_{21}H_{16}ClNO_3S$	63.39/(63.42)	4.05/(4.09)	3.52/(3.56)
4a	F	H	95	150-152	$C_{14}H8FNO_2S$	62.21/(62.18)	2.98/(2.94)	5.18/(5.21)
4b	H	H	96	176-178	$C_{14}H_9NO_2S$	65.87/(65.91)	3.55/(3.58)	5.48/(5.52)
4c	H	C_2H_5	92	165-167	$C_{16}H_{13}NO_2S$	67.82/(67.86)	4.62/(4.66)	4.94/(4.97)
4d	Cl	H	93	173-175	$C_{14}H_8ClNO_2S$	58.03/(58.08)	2.78/(2.81)	4.83/(4.88)
4e	H	CH_3	94	160-162	$C_{15}H_{11}NO_2S$	66.89/(66.92)	4.11/(4.15)	5.20/(5.24)
4f	H	CH_2 Ph	90	125-127	$C_{21}H_{15}NO_2S$	73.02/(73.07)	4.37/(4.39)	4.05/(4.09)
4g	Cl	CH_2 Ph	90	120-122	$C21H_{14}ClNO_2S$	66.40/(66.44)	3.71/(3.74)	3.68/(3.64)

General method for the synthesis of spiro(3H-indole-3,2-oxirane)- 3'-(2-oxo-2-thiophene-2yl) 2(1H)-ones ***(5a-g)***:

The 3-(2-oxo-2-(2-thienyl)ethylidine)indol-2-ones **4a-g** (1.0 mmol) aquous 30% hydrogen peroxides (1.5 mmol) CTAB (0.05 mmol), water (5.0 ml) and sodium hydroxide (1.0 mmol) were taken in round bottom flask and stirred at room temperature for 30-60 min. completion of reaction was monitored by TLC. The solid that was formed was filtered off and then washed thoroughly with water to obtain the pure compounds **(5a-g)**.

*5-Fluoro-spiro[3*H- *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5a)***:

Yield: 93%; M.P.193-195˚c; IR (KBr, cm^{-1}): 3250(NH), 1700(CO), 1680(CO), ^{1}H NMR ($CDCl_3$, δ/ ppm) δ: 4.00 (s,1H,CH-oxirane), 6.93-7.53 (m, 6H,Ar-H), 9.14(s, 1H, NH); ^{13}CNMR (75MHz, CDCl3, δ/ppm): 67.8 (C-oxirane), 68.3 (CH-oxirane), 120.3, 124.0, 125.6, 127.6, 128.2, 129.6, 132.7, 134.4, 137.7, 145.5, 172.7 (CONH), 191.3(CO), Mass (m/z): 286.28 (M^+). Elemental analysis calculated for $C_{14}H_8FNO_3S$; C, 58.73; H, 2.81; N, 4.89; S, 11.19; found C, 58.76; H, 2.84; N, 4.91; S, 11.22%.

*Spiro[3*H *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5b)***:

Yield: 90% ; M.P.210-212˚c; IR (KBr, cm^{-1}): 3250(NH), 1700(CO), 1680(CO), ^{1}H NMR $CDCl_3$, ppm) δ: 4.01(s,1H,CH-oxirane), 6.93-7.48(m, 7H,Ar-H), 9.15(s, 1H, NH); ^{13}C NMR (75 MHz, CDCl3, δ/ppm): 67.8(C-oxirane), 68.3 (CH-oxirane), 120.3, 124.0, 125.6, 128.1, 128.2, 129.6, 132.7, 134.4, 137.7, 145.5, 172.7(CONH), 191.3(CO), Mass (m/z): 271.29 (M^+). Elemental analysis calculated for $C_{14}H_9FNO_3S$; C, 61.98; H, 3.34; N, 5.16; S, 11.81; found C, 61.94; H, 3.30; N, 5.14; S, 11.84%.

*1-Ethyl spiro[3*H- *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5c)***:

Yield: 90%, M.P. 207-209˚c; IR (KBr, cm^{-1}): 1700(CO), 1680(CO), ^{1}H NMR ($CDCl_3$, δ /ppm) δ: 1.13 (t,3H,-CH_3), 3.42 (q,2H,CH_2CH_3), 4.08 (s, 1H-oxirane), 6.96-7.58 (m,7H,Ar-H); ^{13}C NMR (75 MHz, CDCl3, δ/ppm): 12.8(CH_3), 43.0(-NCH_2CH_3), 65.6(C-oxirane), 68.6 (CH-oxirane), 120.3, 124.0, 125.6, 128.2, 128.4, 129.6, 132.7, 134.4, 137.7, 145.5, 170.9 (CO), 191.3 (CO), Mass (m/z):299.35 (M^+). Elemental analysis calculated for $C_{16}H_{13}NO_3S$; C, 64.19; H, 4.37; N, 4.68; S, 10.71; found C, 64.15; H, 4.41; N, 4.64; S, 10.73%.

*5-Chloro spiro[3*H- *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5d)***:

Yield: 94%; M.P. 199-201˚c; IR (KBr,cm^{-1}) : 3250(NH), 1700(CO), 1680(CO), ^{1}H NMR ($CDCl_3$, ppm)δ: 4.02(s,1H,CH-oxirane), 6.93-7.57(m,6H,Ar-H), 1.17(s, 1H,NH); ^{13}C NMR (75 MHz, CDCl3,δ/ppm): 67.8(C-oxirane), 68.3(CH-oxirane), 120.3, 124.0, 125.6, 128.2, 129.6, 130.4, 132.7,134.4, 137.7, 145.5, 172.7(CONH), 191.3(CO), Mass (m/z): 305.74(M^+); Elemental analysis calculated for $C_{14}H_8ClNO_3S$; C, 54.99; H, 2.64; N, 4.58; S, 10.48; found C, 54.96; H, 2.60; N, 4.62; S, 10.50%.

*1-Methyl spiro[3*H *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5e)***:

Yield: 92%; M.P. 200-202˚c; IR (KBr,cm^{-1}): 1700(CO), 1680(CO); ^{1}H NMR ($CDCl_3$, ppm)δ: 3.78(s,3H,CH_3), 4.03(s,1H,CH-oxirane), 6.96-7.48(m,7H,Ar-H); ^{13}C NMR (75 MHz, CDCl3, δ/ppm): 35.3(NCH_3), 65.3(C-oxirane), 68.6(CH-oxirane) ,120.4, 124.0, 125.6, 128, 128.2, 129.6, 132.7, 134.4, 137.7, 145.6, 171.0(CO), 191.3(CO), Mass (m/z): 285.32(M^+); Elemental analysis calculated for $C_{15}H_{11}NO_3S$; C, 63.14; H, 3.88; N, 4.91; S, 11.24; found C, 63.12; H, 3.84; N, 4.95; S, 11.22%.

*1-Benzyl spiro[3*H *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5f)***:

Yield: 94%; M.P. 197-199˚c; IR (KBr,cm^{-1}): 1710(CO), 1690(CO); ^{1}H NMR ($CDCl_3$, ppm)δ: 4.64(s,2H,$NCH_2C_6H_5$), 4.02(s,1H,CH-oxirane), 6.82-7.53(m,12H,Ar-H); ^{13}C NMR (75 MHz, CDCl3,δ/ppm): 55.7($NCH_2C_6H_5$), 65.6(C-oxirane), 68.6(CH-oxirane), 120.3, 124.0, 125.6, 126.5, 127.1(2C), 128.2(2C), 128.3(2C), 129.6, 132.7, 134.4, 137.7, 142.4, 145.5, 170.2(CONH), 191.3(CO),Mass(m/z): 361.42(M^+); Elemental analysis calculated for $C_{21}H_{15}NO_3S$; C, 69.79; H, 4.18; N, 3.87; S, 8.87; found C, 69.82; H, 4.14; N, 3.90; S, 8.83%.

*1-Benzyl-5-chlorospiro[3*H *indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1*H*) one* ***(5g)***:

Yield: 93% M.P. 194-196˚c; IR (KBr,cm^{-1}): 1700(CO), 1680(CO); ^{1}H NMR ($CDCl_3$, ppm)δ: 4.64(s,2H,$NCH_2C_6H_5$), 4.03(s,1H,CH-oxirane), 6.82-7.75(m,12H,Ar-H); ^{13}C NMR (75 MHz, CDCl3,δ/ppm): 55.7($NCH_2C_6H_5$), 65.6(C-oxirane), 68.6(CH-oxirane), 120.3, 124.0, 125.6, 126.5, 127.1(2C), 128.2(2C), 128.3(2C), 129.6, 132.7, 134.4, 137.7, 142.4, 145.5, 170.2(CO), 191.3(CO), Mass(m/z): 395.86(M^+); Elemental analysis calculated for $C_{21}H_{14}ClNO_3S$; C, 63.71; H, 3.56; N, 3.54; S, 8.09; found C, 63.75; H, 3.52; N, 3.58; S, 8.11%.

Antibacterial activities:

For antibacterial assay the zone of inhibition was performed at 128μgml^{-1} concentration for all the compounds (**5a-g**) using discs diffusion method,[xix,xx] for this purpose DMSO was used as diluents, Mueller-Hilton (Himedia, India) agar medium was prepared and sterilized by autoclaving at 121˚c at 15 psi for 15 min. The medium was poured into sterile petri dishes under aseptic condition using laminar airflow chamber. After the solidification of medium the suspension of the test organism (10^6 cfu ml^{-1}) was swabbed onto the individual media plates using a sterile glass spreader. A sterile discs (9.0mm diameter) impregnated with compounds was placed over media surface and the plates were incubated at 37˚c for 18-24 h under dark condition. The determination as to whether the organism is susceptible, intermediate, or resistant was made by measuring the zone of inhibition in comparison with standard antibiotic.

MIC assay was performed to determine the lowest concentration of compound necessary to inhibit a test organism. MIC values were evaluated for all the compounds **(5a-g)** using broth

micro-dilution method as per the standard guideline.[xxi] Assay was carried out for the compounds at 0.5, 1.0, 2.0, 4.0, 8.0, 16.0, 32.0, 64.0 and 128.0 μg ml^{-1} concentrations. A set of tubes containing Muller Hilton broth medium with different concentrations of compounds were prepared. The tubes were inoculated with bacterial culture (10^6 cfu ml^{-1}) and incubated on a rotator shaker (180 rpm) at 37˚c for 18-24h under dark condition. MIC values were defined as lowest concentration of compound that prevented the visible growth of bacteria after the incubation period. All the experiments were performed in three replicates,

Table-3: Antibacterial activity **5a-g.**

Compound	*E. coli*	*P.aeruginusa*	*B.subtilis*	*S.aureus*
	Zone of Inhibition (mm)			
5a	22	23	23	24
5b	17	21	22	17
5c	16	17	20	15
5d	20	22	22	20
5e	18	19	22	19
5f	17	18	21	16
5g	18	20	23	21
Chloramphenicol	21	23	24	22

Table-4: MIC (μg ml^{-1}) values **5a-g.**

Compound	*E. coli*	*P.aeruginusa*	*B.subtilis*	*S.aureus*
	MIC (μgml^{-1})			
5a	64	64	64	64
5b	128	128	128	128
5c	128	128	128	128
5d	32	32	64	64
5e	128	128	128	128
5f	128	128	128	128
5g	64	64	64	64
Chloramphenicol	16	16	16	16

Result and Discussion:

We have developed an efficient aldol reaction of acetylthiophene with isatin using DMF as solvent in the presence of molecular sieve. The process is more efficient and convenient from the viewpoint of green chemistry.

Formation of 3-hydroxy-3-(2-oxo-2-(2-thienyl)ethyl)indole-2-ones were confirmed by the IR spectrum in which band at 3450-3310 cm^{-1} due to OH stretching combined with NH stretching and two peaks at 1705 and 1670 cm^{-1} due to carbonyl groups were observed. In the ^{1}HNMR spectra, signals at δ 6.0 and 3.4 ppm clearly indicates the presence of –OH and CH_2- groups, respectively. The ^{13}CNMR spectra also corresponded well with respective carbon atoms. In the mass spectrum,it shows M^+ at m/z 288.30 (**3a**) the dehydration of hydroxyl compound **3a-g** to afford 3-(2-oxo-2-(2-thienyl)ethylidene)indol-2-one **4a-g** was indicated by the IR spectrum of the later where the peak due to –OH group disappeared. However, the absorptions at 3280 cm^{-1} due to NH,1710 and 1640 cm^{-1} due to carbonyl

groups and at 1600cm^{-1} due to =CH- were observed. In the ^{1}HNMR spectrum appearance of singlet corresponding to =CH- at δ 6.27 ppm alongwith disappearance of peak due to –OH group confirmed the formation of **4a-g**.In the mass spectrum it shows M^{+} at m/z 270.28 (**4a**).
The formation of spiro(indole-oxirane) **5a-g** were confirmed by ^{1}HNMR spectra in which CH- oxirane appeared at δ 4.00 ppm. In ^{13}CNMR spectrum, C-oxirane appeared at δ 67.8 ppm while CH- oxirane appeared at δ 68.3 ppm which confirm the formation of epoxide ring. Further,in the mass spectrum it shows M^{+} at m/z 286.28 (**5a**).
The synthesized spiro[indole-3,2-oxirane]-3'-(2-oxo-2-(thiophen-2-yl)2(1H) one **(5a-g)** can exist in the form of two isomer differing in the stereochemical arrangement of the hydrogen atom of oxirane ring. In the present investigation using PTC high diastereoselectivity was observed with excellent yield. with very easily work up methodology. The stereochemistry of the products formed is found to be trans because the ^{1}H NMR spectral data are similar to a report in which trans geometry is confirmed on the basis of X-ray crystal structure [x,xxii] Also, appearance of one singlet at about 4.00 ppm for one proton of the epoxy unit, clearly indicates that only one isomer exists for all the compounds. It is also observed in some derivatives of spiro[indoline-3,2-oxiran]-2-ones in which singlet appeared for CH- oxirane.
The compounds **5a-g** were screened for antibacterial activities against *B. subtilis*, *S. aureus*, *E. coli* and *P. aeruginuse*. It was observed that compounds **5a, 5d** and **5g** show better zone of inhibition and lower MIC μg ml^{-1} values. Among all, **5a** shows excellent activity. It was due to fluoro substitution in the ring. Compound **5d** is more active against gram negative bacteria. Other compounds show good to moderate activity. The results suggest that analog **5a,5d** and **5g** can be used a potential broad spectrum antibacterial agents as they are potent against both gram positive and gram negative bacteria.

Conclusions:
We described here that cetyltrimethylammonium bromide catalyst is highly efficient per the green protocol for diastereoselective synthesis of spiro(indole3,2-oxirane)3'-(2-oxo-2-thiophene-2yl)2(1H)-ones by the reaction of 3-(2-oxo-2-thiophene-2yl) ethylene-indole-2-ones with 30% aqueous hydrogen peroxide in excellent yield. The present methodology offers several advantages such as simple procedure, low cost, easy work-up, short reaction time and milder condition. These compounds can be used as potent antibacterial agents.

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