Synthesis of Indane-Based 1,5-Benzothiazepines Derived from 3-Phenyl-2,3-dihydro-1*H*-inden-1-one and Antimicrobial Studies Thereof

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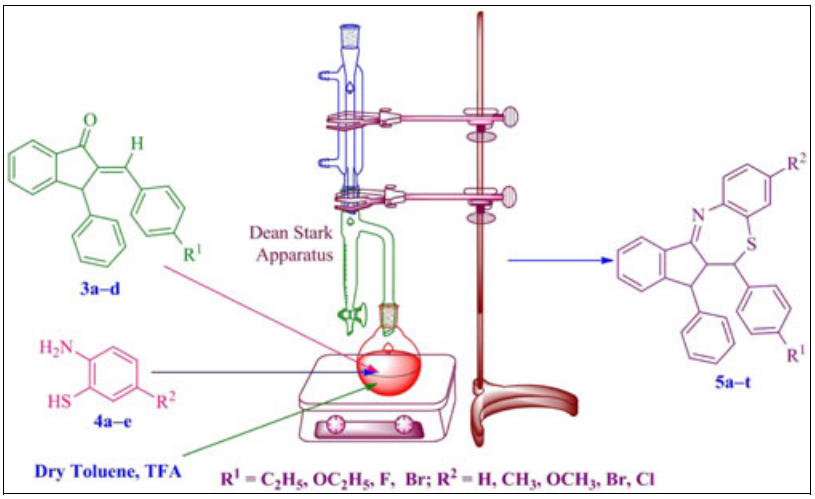

In the present study, a series of 20 indane-based 1,5-benzothiazepines (**5a**–**t**) has been prepared derived from 3-phenyl-2,3-dihydro-1*H*-inden-1-one (**1**). All the synthesized 1,5-benzothiazepines (**5a**–**t**) were screened for their *in vitro* antimicrobial activities against four bacteria [*Bacillus subtilis* (MTCC 441), *Staphylococcus epidermidis* (MTCC 6880), *Escherichia coli* (MTCC 1652), and *Pseudomonas aeruginosa* (MTCC 424)] and two fungi [*Candida albicans* (MTCC 227) and *Aspergillus niger* (MTCC 8189)]. Among all the tested derivatives, **5n** and **5o** against *E. coli* displayed more inhibitory activity than that of the reference drug, ciprofloxacin, while the derivatives **5c**, **5m**–**o**, **5s**, and **5t** against *C. albicans*, and **5d**, **5e**, **5n**, **5o**, **5s**, and **5t** against *A. niger* were found to be more potent than the standard drug, that is, fluconazole.

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INTRODUCTION

The conception of privileged structures has appeared as a rewarding approach in the field of drug discovery and development. The term "privileged structure" refers to a single molecular framework capable to afford ligands for various receptors. Benzothiazepine is one such showcased important class of privileged heterocyclic scaffolds in consequence of their drug-like and versatile binding properties. Exclusively, the 1,5-benzothiazepine skeleton has been the object of immense chemotherapeutic significance and exploration in the field of medicinal chemistry. This seven-membered ring system has extensively been celebrated as prominent cardiac and psychotherapeutic scaffold [1]. At present, 1,5-benzothiazepines are present as a key structural motif in several clinical drugs. For instance, drugs containing 1,5-benzothiazepine moiety are in therapeutic use in the treatment of cardiovascular disorders [2] (diltiazem and clentiazem) and central nervous system disorders [3–5] (thiazesim, quetiapine, and clothiapine); GW-577 for the treatment of lipoprotein disorders; and KT-363 as antihypertensive, antiarrhythmic, and calcium (Ca^{2+}) channel antagonist [6–8]. The 1,5-benzothiazepine functionality has also been identified as a versatile "drug prejudice core" on account of its presence in a variety of bioactive compounds such as Ca^{2+} entry blockers [9], α-glucosidase inhibitors [10], central nervous system depressants [11], calmodulin antagonists [12], bradykinin receptor agonists [13], and angiotensin converting enzyme inhibitors [14]. In addition, dihydro 1,5-benzothiazepines have turned out to be fascinating pharmacophores as many derivatives exhibit a plethora of activities like antimicrobial [15], anti-HIV [16], anticancer [17], antifeedant [18], antiulcer [19], anti-inflammatory [20], anticonvulsant [21], and antiplatelet aggregation [22] activities. The pharmaceutical prominence of 1,5-benzothiazepines has encouraged the researchers all over the world, and many reviews [1,23–26] have been documented in the literature, which compiled

various aspects related to their synthetic advances and biological importance. Consequently, several synthetic protocols have been developed to access this biodynamic skeleton [27–36]. The most convenient method for the synthesis of 1,5-benzothiazepines involves the condensation of α,β-unsaturated carbonyl compounds and 2-aminobenzenethiols [37,38]. The 1,5-benzothiazepines can also be prepared from α,β-unsaturated thioamide [29], from 2-nitrothiophenol [39], from epoxides [30], and so on.

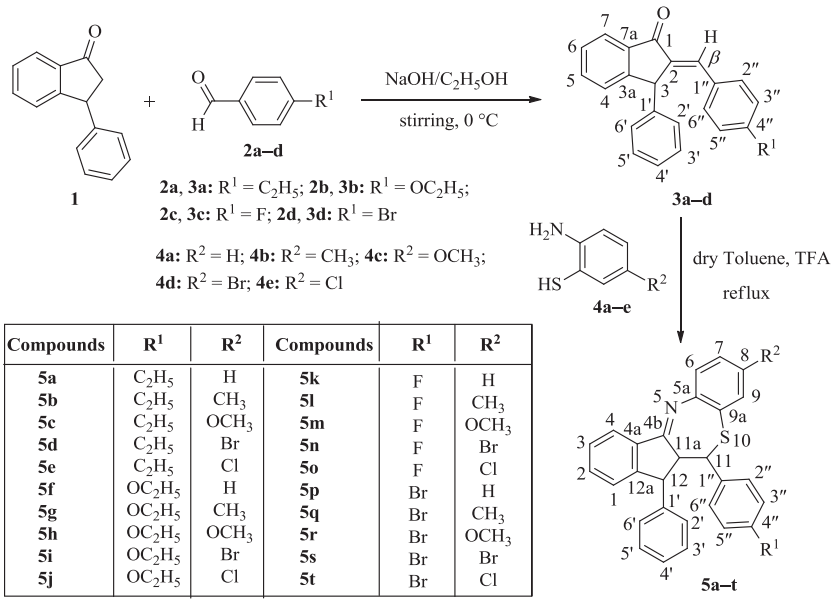
Therefore, in view of remarkable pharmacological activities of 1,5-benzothiazepine derivatives and in continuation of our enduring research on the synthesis of N-containing and S-containing heterocycles [40–46], the current research article has been focused toward the synthesis of indane-based 1,5-benzothiazepines followed by the evaluation of their *in vitro* antimicrobial activities.

RESULTS AND DISCUSSION

Chemistry. The protocol for the synthesis of indane-based 1,5-benzothiazepines (**5a**–**t**) is depicted in Scheme 1. The synthetic route giving rise to the 1,5-benzothiazepines (**5a**–**t**) entailed the reaction of appropriate 2-aminothiophenol (**4a**–**e**) with 2-arylidene-3-phenyl-2,3-dihydro-1*H*-inden-1-ones (**3a**–**d**). At first, 2-arylidene-3-phenyl-2,3-dihydro-1*H*-inden-1-ones (**3a**–**d**) needed for the purpose were prepared by stirring a solution of equimolar quantities of 3-phenyl-2,3-dihydro-1*H*-inden-1-one (**1**) and appropriate benzaldehyde (**2a**–**d**) in $NaOH/C_2H_5OH$ maintaining the temperature of reaction mixture below 5°C as per literature procedure [47]. The 2-aminobenzenethiol (**4a**), being accessible commercially, was purchased from Sigma-Aldrich (St. Louis, MO). The synthesis of other 5-substituted 2-aminobenzenethiols (**4b**–**e**) was achieved via base-catalyzed hydrolytic fission of 6-substituted benzo[*d*]thiazol-2-amines, which in turn were obtained by the reaction of potassium thiocyanate and bromine (generating thiocyanogen, $[(SCN)_2]$, *in situ*) on the respective 4-substituted anilines as described in the literature [48,49]. Thereafter, the equimolar quantities of 2-arylidene-3-phenyl-2,3-dihydro-1*H*-inden-1-ones (**3**) and appropriate 5-substituted 2-aminobenzenethiols (**4**) were refluxed in dry toluene using four to five drops of trifluoroacetic acid as catalyst for 10–12 h to afford the corresponding 1,5-benzothiazepines (**5a**–**t**) in moderate yields (52–68%).

The structures of all the synthesized 1,5-benzothiazepines (**5a**–**t**) have been ascertained by employing different spectral (IR, ^{1}H NMR, ^{13}C NMR, and high-resolution MS) and elemental analysis techniques. The IR spectra of all these compounds (**5a**–**t**) exhibited the characteristic absorption bands in the regions 1599–1611 cm^{-1} owing to C═N stretching [50]. The ^{1}H NMR spectra of compounds (**5a**–**t**), in each case, displayed one doublet of doublet and two doublets, each integrating for one proton in the δ regions 3.41–3.97 (J = 11.65–12.00 and 4.20–5.00 Hz), δ 3.64–4.57 (J = 4.20–5.00 Hz), and δ 3.92–5.08 (J = 11.65–12.00 Hz) ppm, which could easily be assigned to C_{11a}–H, C_{12}–H, and C_{11}–H, respectively, in accordance with the ^{1}H NMR

Scheme 1. Synthesis of indane-based 1,5-benzothiazepines (**5**).



Compounds	R^1	R^2	Compounds	R^1	R^2
5a	C_2H_5	H	**5k**	F	H
5b	C_2H_5	CH_3	**5l**	F	CH_3
5c	C_2H_5	OCH_3	**5m**	F	OCH_3
5d	C_2H_5	Br	**5n**	F	Br
5e	C_2H_5	Cl	**5o**	F	Cl
5f	OC_2H_5	H	**5p**	Br	H
5g	OC_2H_5	CH_3	**5q**	Br	CH_3
5h	OC_2H_5	OCH_3	**5r**	Br	OCH_3
5i	OC_2H_5	Br	**5s**	Br	Br
5j	OC_2H_5	Cl	**5t**	Br	Cl

spectra of analogous 1,5-benzothiazepine derivatives [51,52]. Further, the carbons C_{11}, C_{11a}, and C_{12} of 1,5-benzothiazepines (**5a**–**t**) are chiral centers, and their stereochemistry has been established on the basis of their coupling constant (*J*) values. The coupling constant (*J*) values signify that C_{11}–H and C_{11a}–H protons are *trans* oriented, and C_{11a}–H and C_{12}–H are *cis* oriented, which find support from the coupling constant (*J*) values of the similar protons in ^{1}H NMR spectra of analogous derivatives [53–56]. This resemblance also indicates a diastereoselective formation of one diastereoisomer of 1,5-benzothiazepines (**5a**–**t**) as the sole isolable product. The signals due to the remaining protons appeared in their expected regions (see Experimental section). In the ^{13}C NMR spectra of **5a**–**t**, in each case, three characteristic absorption signals were observed in the δ regions 53.15–54.25, 57.53–58.97, and 65.56–67.59 ppm, which could undoubtedly be assigned to the three sp^3 carbons, that is, C_{11a}, C_{12}, and C_{11} [19,57]. Another characteristic feature of ^{13}C NMR spectra is the signal observed in the most downfield δ region 165.46–166.30 ppm easily assignable to C_{4b}. It is worthy to mention that with the variation of R^2, the change in chemical shift value of C_8 signal was observed. The signals due to the remaining carbons were obtained in the expected regions (see Experimental section). Further, the mass spectral data and elemental analysis results of 1,5-benzothiazepines (**5a**–**t**) were found to be in good concord with their molecular formulae (see Experimental section).

Antimicrobial evaluation. The increasing emergence of bacterial resistance to antibiotic therapy and newly emerging pathogens are responsible for generating curiosity in the development of new antimicrobial agents. Regardless of the advancement in antimicrobial therapy, several problems remain to be solved for the majority of accessible antimicrobial drugs. 1,5-Benzothiazepines are recognized to show antimicrobial activities [15,58–66] against various bacterial and fungal strains like *Bacillus substilis*, *Bacillus pumilus*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Klebsiella aerogenes*, *Fusarium oxysporum*, *Candida krusei*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Aspergillus fumigatus*, *Salmonella* Typhi, *Candida violaceum*, *Aspergillus niger*, *Aspergillus flavus*, *Candida albicans*, and *Trichophyton rubrum.* Considering the aforementioned facts, we carried out the *in vitro* antimicrobial screening of all the synthesized indane-based 1,5-benzothiazepines (**5**) against two Gram-positive bacterial strains, namely, *Bacillus subtilis* (MTCC 441) and *S. epidermidis* (MTCC 6880); two Gram-negative bacterial strains, namely, *E. coli* (MTCC 1652) and *P. aeruginosa* (MTCC 424); and two fungal strains, namely, *C. albicans* (MTCC 227) and *A. niger* (MTCC 8189) by using serial dilution method as explained earlier by Mor *et al*. [67]. The results of antimicrobial evaluation were determined in terms of minimum inhibitory concentrations (MICs) in μ*M*/mL. The reference drugs used for antibacterial and antifungal evaluation were ciprofloxacin and fluconazole, respectively. The results of antibacterial evaluation presented in Table 1 and Figure 1 revealed that the derivatives **5d**, **5e**, **5i**–**l**, **5n**, **5o**, and **5s** against *B. subtilis*; **5c**, **5h**, and **5m** against *S. epidermidis*; **5a**, **5b**, **5d**, **5e**, **5i**–**l**, **5s**, and **5t** against *E. coli*; and **5c**, **5h**, **5m**, and **5s** against *P. aeruginosa* showed comparable activity as those of the standard reference drug, ciprofloxacin. However, the derivatives **5n** (MIC, 0.0034 μ*M*/mL) and **5o** (MIC, 0.0031 μ*M*/mL) against *E. coli* displayed more inhibitory activity than those of the reference drug, ciprofloxacin (MIC, 0.0047 μ*M*/mL). Further, the results of antifungal evaluation presented in Table 1 and Figure 2 revealed that derivatives **5c** (MIC, 0.0068 μ*M*/mL), **5m** (MIC, 0.0069 μ*M*/mL), **5n** (MIC, 0.0069 μ*M*/mL), **5o** (MIC, 0.0062 μ*M*/mL), **5s** (MIC, 0.0060 μ*M*/mL), and **5t** (MIC, 0.0056 μ*M*/mL) against *C. albicans*, and **5d** (MIC, 0.0067 μ*M*/mL), **5e** (MIC, 0.0061 μ*M*/mL), **5n** (MIC, 0.0069 μ*M*/mL), **5o** (MIC, 0.0062 μ*M*/mL), **5s** (MIC, 0.0060 μ*M*/mL), and **5t** (MIC, 0.0056 μ*M*/mL) against *A. niger* were found to be more potent than the standard drug, that is, fluconazole (MIC, 0.0102 μ*M*/mL).

Keeping in view of these results, the compounds **5n** and **5o** can be considered as potential antibacterial agents while the derivatives **5c**–**e**, **5m**–**o**, **5s**, and **5t** can be used as potential antifungal agents for further drug development. Moreover, comparison of antibacterial and antifungal evaluation results reveals that both antimicrobial and antifungal activities are prolific.

From the results presented in Table 1 and Figures 1 and 2, the following structure–activity relationships may be inferred:

1. The unsubstitution at C_8 (i.e., C_8–H) of some 1,5-benzothiazepines increased the antimicrobial efficacy against *B. subtilis* and *E. coli*.
2. The electron withdrawing groups like F and Br present at $C_{4''}$ of C_{10a}-phenyl ring, and Cl and Br at C_8 position improved the antimicrobial activity against *B. subtilis*, *E. coli*, *C. albicans*, and *A. niger*.
3. The presence of OCH_3 group at C_8 position enhanced the antimicrobial efficacy against *S. epidermidis*, *P. aeruginosa*, *C. albicans*, and *A. niger*.
4. In contrast to the aforementioned results, electron withdrawing groups such as F and Br present at $C_{4''}$ of C_{10a}-phenyl ring reduced the antibacterial activity against *S. epidermidis* and *P. aeruginosa* in most of the cases.

These results lead to the conclusion that there are different structural requirements for a compound to be

Table 1

In vitro antimicrobial activity of 1,5-benzothiazepines (**5a**–**t**).

	Minimum inhibitory concentration (μ*M*/mL)					
	Gram-positive bacteria		Gram-negative bacteria		Fungi	
Compounds	*B. subtilis*[a]	*S. epidermidis*[b]	*E. coli*[c]	*P. aeruginosa*[d]	*C. albicans*[e]	*A. niger*[f]
5a	0.0145	0.0145	0.0072	0.0145	0.0290	0.0290
5b	0.0140	0.0281	0.0070	0.0140	0.0140	0.0140
5c	0.0135	0.0068	0.0135	0.0068	0.0068	0.0135
5d	0.0067	0.0134	0.0067	0.0134	0.0134	0.0067
5e	0.0061	0.0122	0.0061	0.0122	0.0122	0.0061
5f	0.0279	0.0140	0.0279	0.0279	0.0279	0.0279
5g	0.0271	0.0135	0.0271	0.0271	0.0135	0.0135
5h	0.0131	0.0065	0.0131	0.0065	0.0131	0.0262
5i	0.0065	0.0130	0.0065	0.0130	0.0130	0.0259
5j	0.0059	0.0119	0.0059	0.0119	0.0119	0.0237
5k	0.0074	0.0297	0.0074	0.0297	0.0148	0.0148
5l	0.0072	0.0143	0.0072	0.0574	0.0143	0.0143
5m	0.0138	0.0069	0.0138	0.0069	0.0069	0.0138
5n	0.0069	0.0137	0.0034	0.0137	0.0069	0.0069
5o	0.0062	0.0125	0.0031	0.0125	0.0062	0.0062
5p	0.0259	0.0259	0.0130	0.0130	0.0259	0.0130
5q	0.0252	0.0252	0.0126	0.0126	0.0126	0.0126
5r	0.0244	0.0122	0.0122	0.0122	0.0122	0.0122
5s	0.0060	0.0121	0.0060	0.0060	0.0060	0.0060
5t	0.0223	0.0111	0.0056	0.0223	0.0056	0.0056
Ciprofloxacin	0.0047	0.0047	0.0047	0.0047	—	—
Fluconazole	—	—	—	—	0.0102	0.0102

[a]*Bacillus subtilis* (MTCC 441).
[b]*Staphylococcus epidermidis* (MTCC 6880).
[c]*Escherichia coli* (MTCC 1652).
[d]*Pseudomonas aeruginosa* (MTCC 424).
[e]*Candida albicans* (MTCC 227).
[f]*Aspergillus niger* (MTCC 8189).

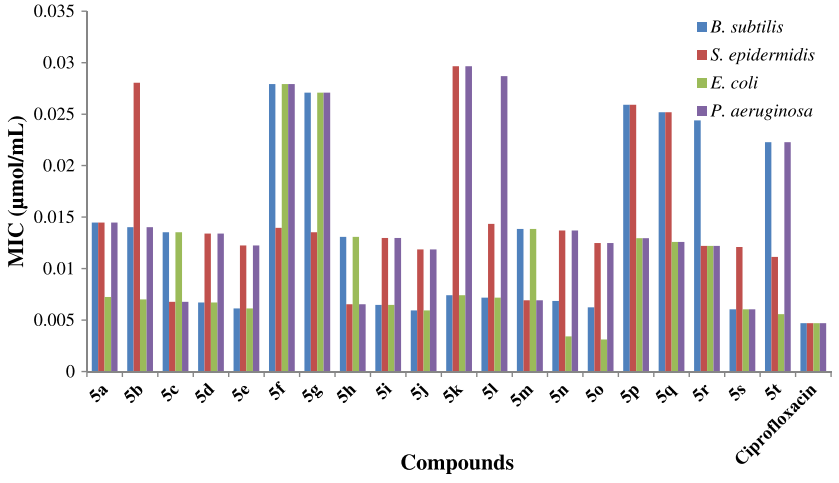


Figure 1. Graphical representation of *in vitro* antibacterial activity of 1,5-benzothiazepines (**5a**–**t**). MIC, minimum inhibitory concentration. [Color figure can be viewed at wileyonlinelibrary.com]

active against different microbial strains. However, no general trend toward structure–activity relationship has been ascertained for antimicrobial activity of the tested 1,5-benzothiazepines (**5**).

EXPERIMENTAL

Chemistry. The commercial reagents were utilized as obtained from suppliers without further purification.

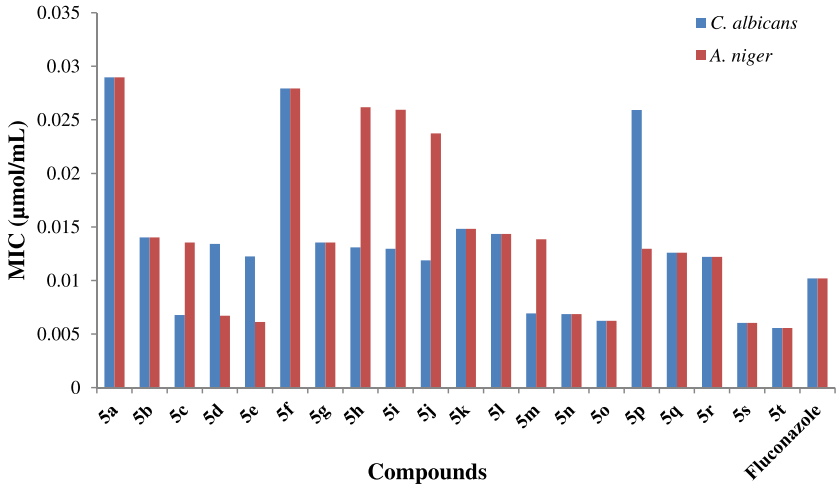


Figure 2. Graphical representation of *in vitro* antifungal activity of 1,5-benzothiazepines (**5a**–**t**). MIC, minimum inhibitory concentration. [Color figure can be viewed at wileyonlinelibrary.com]

2-Aminothiophenol was purchased from Sigma-Aldrich. All the synthesized compounds were characterized by IR, ^{1}H NMR, ^{13}C NMR, electrospray ionization (ESI)–MS/high-resolution MS and elemental analysis. The melting points (°C) were recorded on electrothermal apparatus in open head capillary tubes and were uncorrected. Thin-layer chromatography (TLC) was used for monitoring the progress of the reaction and ascertaining the purity of the synthesized compounds on pre-coated TLC plates (Merck Keiselgel F_{254}, Darmstadt, Germany) using hexane-ethyl acetate solvent system of different polarity, and visualization was achieved by exposure to UV light. Columns were packed as slurry of silica gel (60–120 mesh) in hexane and kept overnight before use. Initially, compounds were adsorbed on silica gel in appropriate solvent and then loaded on column as slurry in hexane. The Fourier transform IR spectra were measured on IR Affinity-1 FTIR (Shimadzu Corporation, Kyoto, Japan) spectrophotometer in the region of 500–4000 cm^{-1}. The apparatus was calibrated by KBr, samples were measured in KBr, and wave numbers (ν) are reported in cm^{-1}. NMR spectra (^{1}H at 400 MHz and ^{13}C at 100 MHz) were scanned on 400 MHz Bruker AVANCE-III spectrometer (Bruker BioSpin AG Industriestrasse, Fallanden, Zurich, Switzerland) using $CDCl_3$ as solvent and tetramethylsilane as internal standard. Chemical shifts (δ) are reported in parts per million (ppm), and coupling constants (J) are expressed in hertz (Hz). Mass spectra were recorded on Waters Q-Tof Micromass spectrometer, Waters Quadrupole Detector (TDQ) (Waters Corporation, Milford, MA), and Agilent 6410B Triple Quad liquid chromatography–MS spectrometer (Agilent Technologies, Santa Clara, CA). Elemental analyses were performed on Thermo Scientific FLASH-2000 CHN analyzer (The Laboratory Glassware Co., Ambala Cantt., India). Analytical results for C, H, and N of all the tested compounds were found to be within ±0.4% of the theoretical values. Nomenclature of the compounds was assigned with the help of CHEMDRAW ULTRA 12.0 (CambridgeSoft, PerkinElmer Inc., Waltham, MA).

General procedure for the synthesis of (*E*)-2-arylidene-3-phenyl-2,3-dihydro-1*H*-inden-1-ones (3). To a solution of 3-phenyl-2,3-dihydro-1*H*-inden-1-one (**1**) (1.32 g, 0.01 mol) and an appropriate 4-substituted benzaldehyde (**2**, 0.1 mol) in ethanol (150 mL) was added NaOH solution (30 mL, 6.7*M*) drop wise under stirring while maintaining the temperature of reaction mixture below 5° C with the aid of an ice bath. The crude product precipitated from the solution within a few minutes. The stirring was continued for further 3 h at room temperature. The solid thus obtained was filtered under reduced pressure; washed with cold ethanol followed by water until the wash out was neutral to pH paper; dried; and crystallized from ethanol to afford the corresponding (*E*)-2-arylidene-3-phenyl-2,3-dihydro-1*H*-inden-1-ones (**3a**–**d**) in excellent yields. The physical, spectral, and elemental analysis data of **3a**–**d** are given as follows.

(E)-2-(4-Ethylbenzylidene)-3-phenyl-2,3-dihydro-1H-inden-1-one (3a). This compound was obtained as white solid, yield 95%; mp 151–153°C (Lit. [68] mp 150–152°C); ir (KBr): 544, 700, 748, 831, 966, 1099, 1258, 1298, 1321, 1458, 1502, 1610 (C═C str.), 1688 (C═O str.), 2878, 2928, 2966 (aliphatic C–H str.), 3024, 3059 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.16 (t, 3H, J = 7.60 Hz, CH_2CH_3), 2.56 (q, 2H, J = 7.60 Hz, CH_2CH_3), 5.31 (s, 1H, C_3–H), 7.07 (d, 2H, J = 8.16 Hz, $C_{3''}$–H, $C_{5''}$–H), 7.11–7.15 (m, 1H, ArH), 7.20–7.26 (m, 4H, ArH), 7.35–7.40 (m, 4H, ArH), 7.47–7.51 (m, 1H,

ArH), 7.84 (d, 1H, J = 1.68 Hz, C_β–H), 7.92 (d, 1H, J = 7.64 Hz, C_7–H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 15.10 (CH_2CH_3), 28.69 (CH_2CH_3), 48.79 (C_3), 124.16, 125.88, 126.89, 127.55 ($C_{2'}$, $C_{6'}$), 127.81, 128.00 ($C_{3''}$, $C_{5''}$), 128.97 ($C_{3'}$, $C_{5'}$), 131.52 ($C_{1''}$), 131.63 ($C_{2''}$, $C_{6''}$), 134.89, 135.72, 136.12, 137.36, 141.61 (C_{7a}), 146.39 ($C_{4''}$), 154.37 (C_{3a}), 194.68 (C_1); ms (ESI) m/z: $[M + H]^+$ calcd. for $C_{24}H_{20}O$, 325.16; found, 325.19. *Anal*. Calcd. for $C_{24}H_{20}O$ (324.41): C, 88.85; H, 6.21. Found: C, 88.92; H, 6.08.

(E)-2-(4-Ethoxybenzylidene)-3-phenyl-2,3-dihydro-1H-inden-1-one (3b). This compound was obtained as white solid, yield 92%; mp 190–194°C; ir (KBr): 534, 702, 746, 825, 968, 1041, 1095, 1173, 1258, 1294, 1321, 1466, 1508, 1599 (C═C str.), 1688 (C═O str.), 2887, 2930, 2980 (aliphatic C–H str.), 3024, 3080 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.36 (t, 3H, J = 7.00 Hz, OCH_2CH_3), 3.97 (q, 2H, J = 7.00 Hz, OCH_2CH_3), 5.29 (s, 1H, C_3–H), 6.74 (d, 2H, J = 8.84 Hz, $C_{3''}$–H, $C_{5''}$–H), 7.12–7.27 (m, 5H, ArH), 7.36–7.39 (m, 2H, ArH), 7.42 (d, 2H, J = 8.84 Hz, $C_{2''}$–H, $C_{6''}$–H), 7.50–7.27 (m, 1H, 1 ArH), 7.81 (d, 1H, J = 1.76 Hz, C_β–H), 7.91 (d, 1H, J = 7.60 Hz, C_7–H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 14.70 (OCH_2CH_3), 48.83 (C_3), 63.52 (OCH_2CH_3), 114.44 ($C_{3''}$, $C_{5''}$), 124.13, 125.85, 126.61 ($C_{1''}$), 126.96, 127.59 ($C_{2'}$, $C_{6'}$), 127.80, 129.01 ($C_{3'}$, $C_{5'}$), 133.48 ($C_{2''}$, $C_{6''}$), 134.73, 135.59, 135.73, 136.32, 141.53 (C_{7a}), 154.27 (C_{3a}), 160.29 ($C_{4'}$), 194.65 (C_1); ms (ESI) *m/z*: $[M + H]^+$ calcd. for $C_{24}H_{20}O_2$, 341.15; found, 341.11. *Anal*. Calcd. for $C_{24}H_{20}O_2$ (340.41): C, 84.68; H, 5.92. Found: C, 84.83; H, 5.88.

(E)-2-(4-Fluorobenzylidene)-3-phenyl-2,3-dihydro-1H-inden-1-one (3c). This compound was obtained as white solid, yield 94%; mp 188–192°C (Lit. [69] mp 189–191°C); ir (KBr): 509, 702, 744, 831, 968, 1095, 1163, 1230, 1294, 1319, 1462, 1512, 1597, 1603 (C═C str.), 1691 (C═O str.), 3024, 3061 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 5.30 (s, 1H, C_3–H), 689–6.95 (m, 2H, 2 ArH), 7.13–7.23 (m, 5H, ArH), 7.36–7.55 (m, 5H, ArH), 7.81 (d, 1H, J = 1.84 Hz, C_β–H), 7.93 (d, 1H, J = 7.60 Hz, C_7–H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 48.63 (C_3), 115.56 (d, J = 22.00 Hz, $C_{3''}$, $C_{5''}$), 124.28, 125.93, 127.10, 127.58 ($C_{2'}$, $C_{6'}$), 127.98, 129.03 ($C_{3'}$, $C_{5'}$), 130.31 (d, J = 3.00 Hz, $C_{1''}$), 133.30 (d, J = 9.00 Hz, $C_{2''}$, $C_{6''}$), 134.36, 135.12, 135.99, 138.05, 141.09 (C_{7a}), 154.29 (C_{3a}), 163.22 (d, J = 251.00 Hz, $C_{4''}$), 194.47 (C_1); ms (ESI) *m/z*: $[M + H]^+$ calcd. for $C_{22}H_{15}FO$, 315.12; found, 312.15. *Anal*. Calcd. for $C_{22}H_{15}FO$ (314.35): C, 84.06; H, 4.81. Found: C, 84.22; H, 4.91.

(E)-2-(4-Bromobenzylidene)-3-phenyl-2,3-dihydro-1H-inden-1-one (3d). This compound was obtained as white solid, yield 96%; mp 205–208°C (Lit. [69] mp 204–206°C); ir (KBr): 513, 700, 748, 822, 964, 1097, 1255, 1292, 1255, 1292, 1321, 1481, 1587, 1614 (C═C str.), 1691 (C═O str.), 3022, 3078 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 5.29 (s, 1H, C_3–H), 7.14–7.42 (m, 11H, ArH), 7.52–7.56 (m, 1H, ArH), 7.76 (d, 1H, J = 1.92 Hz, C_β–H), 7.93 (d, 1H, J = 7.64 Hz, C_7–H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 48.68 (C_3), 124.13, 124.32, 125.95, 127.16, 127.58 ($C_{2'}$, $C_{6'}$), 128.03, 129.08 ($C_{3'}$, $C_{5'}$), 131.63 ($C_{2''}$, $C_{6''}$), 132.63 ($C_{3''}$, $C_{5''}$), 132.95, 134.19, 135.23 (C_β), 135.94, 139.11, 141.06 (C_{7a}), 154.25 (C_{3a}), 194.36 (C_1); ms (ESI) *m/z*: $[M + H]^+$ calcd. for $C_{22}H_{15}BrO$, 375.04; found, 375.13. *Anal*. Calcd. for $C_{21}H_{12}N_2O_3S$ (375.26): C, 70.41; H, 4.03. Found: C, 70.85; H, 4.25.

General procedure for the synthesis of 2-amino-5-substituted benzenethiols (4). 2-Aminobenzenethiol (**4a**), being commercially available, was procured from Sigma-Aldrich. The other 2-amino-5-substituted benzenethiols (**4b**–**e**) were synthesized in good yields by the base-catalyzed hydrolytic fission of the corresponding 6-substituted benzo[*d*]thiazol-2-amines following exactly the similar procedure as described in literature [48,49].

General procedure for the synthesis of indane-based 1,5-benzothiazepines (5). To a solution of (*E*)-2-arylidene-3-phenyl-2,3-dihydro-1*H*-inden-1-ones (**3**, 0.003 mol) in dry toluene (30 mL) was added an appropriate 2-aminobenzenethiol (**4**, 0.003 mol) and catalytic amount (three to four drops) of trifluoroacetic acid. The reaction mixture was heated at reflux on a heating mantle for 10–12 h equipped with a Dean-Stark apparatus to remove the water formed during the reaction. The progress of reaction was monitored by TLC on aliquots withdrawn from the reaction mixture at different intervals of time. After the completion of reaction, the solvent was removed under reduced pressure. The crude solid thus obtained was purified on silica gel (60–120 mesh) column pre-packed in hexane. Elution of the column with hexane:ethylacetate (24:1, v/v) gave a homogeneous residue, which upon crystallization from chloroform afforded the corresponding 1,5-benzothiazepines (**5**) in moderate yields (52–68%). The physical, spectral, and elemental analysis data of **5a**–**t** are given as follows.

11-(4-Ethylphenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5]benzothiazepine (5a). This compound was obtained as orange crystals, yield 65%; mp 154–158°C; ir (KBr): 1610 (C═N str.), 2968 (aliphatic C–H str.), 3026, 3049 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.10 (t, 3H, J = 7.60 Hz, CH_2CH_3), 2.48 (q, 2H, J = 7.60 Hz, CH_2CH_3), 3.97 (dd, 1H, J = 12.00 and 5.00 Hz, C_{11a}–H), 4.45 (d, 1H, J = 5.00 Hz, C_{12}–H), 5.08 (d, 1H, J = 12.00 Hz, C_{11}–H), 6.83–6.87 (m, 1H, Ar-H), 6.88 (d, 2H, J = 7.96 Hz, $C_{3''}$, $C_{5''}$), 6.99 (d, 2H, J = 7.96 Hz, $C_{2''}$, $C_{6''}$), 7.10 (d, 1H, J = 7.64 Hz, Ar-H),

7.34–7.42 (m, 9H, Ar-H), 7.59 (d, 1H, J = 7.96 Hz, Ar-H), 7.92–7.94 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 15.25 (CH_2CH_3), 28.31 (CH_2CH_3), 53.68 (C_{11a}), 58.33 (C_{12}), 67.47 (C_{11}), 121.08, 121.64, 126.40, 126.79, 127.55 ($C_{2''}$, $C_{6''}$), 127.60, 127.67 ($C_{3''}$, $C_{5''}$), 128.61 ($C_{2'}$, $C_{6'}$), 128.64, 129.08 ($C_{3'}$, $C_{5'}$), 130.27, 131.24, 132.45, 134.28, 136.53, 138.13, 142.71, 146.75, 148.46, 165.75 (C_{4b}); ms [time of flight (TOF) ESI] *m/z*: $[M + H]^+$ calcd. for $C_{30}H_{25}NS$: 432.1786; found, 432.1783. *Anal*. Calcd. for $C_{30}H_{25}NS$ (431.59): C, 83.49; H, 5.84; N, 3.25. Found: C, 83.32; H, 5.58; N, 3.43.

11-(4-Ethylphenyl)-8-methyl-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5b). This compound was obtained as orange crystals, yield 63%; mp 192–195° C; ir (KBr): 1604 (C═N str.), 2868, 2926, 2966 (aliphatic C–H str.), 3044 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.18 (t, 3H, J = 7.60 Hz, CH_2CH_3), 2.49 (s, 3H, CH_3), 2.54 (q, 2H, J = 7.60 Hz, CH_2CH_3), 3.68 (dd, 1H, J = 11.96 and 4.96 Hz, C_{11a}–H), 3.94 (d, 1H, J = 4.96 Hz, C_{12}–H), 4.71 (d, 1H, J = 11.96 Hz, C_{11}–H), 6.75–7.45 (m, 13H, Ar-H), 7.59 (d, 1H, J = 8.35 Hz, Ar-H), 7.65–7.68 (m, 1H, Ar-H), 7.90–7.93 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 15.24 (CH_2CH_3), 21.36 (CH_3), 28.15 (CH_2CH_3), 53.82 (C_{11a}), 58.13 (C_{12}), 67.59 (C_{11}), 121.35, 122.85, 126.83, 127.11, 127.58 ($C_{2''}$, $C_{6''}$), 127.63 ($C_{3''}$, $C_{5''}$), 128.10, 128.53 ($C_{2'}$, $C_{6'}$), 128.61, 129.02 ($C_{3'}$, $C_{5'}$), 130.29, 131.45, 132.51, 134.15, 135.53, 136.51, 138.15, 142.63, 146.65, 148.52, 165.89 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{31}H_{27}NS$: 446.1942; found, 446.1938. *Anal*. Calcd. for $C_{31}H_{27}NS$ (445.62): C, 83.55; H, 6.11; N, 3.14. Found: C, 83.43; H, 6.25; N, 3.28.

11-(4-Ethylphenyl)-8-methoxy-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5c). This compound was obtained as orange crystals, yield 57%; mp 187–191°C; ir (KBr): 1607 (C═N str.), 2855, 2926, 2963 (aliphatic C–H str.), 3019, 3059 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$): δ 1.17 (t, 3H, J = 7.60 Hz, CH_2CH_3), 2.50 (q, 2H, J = 7.60 Hz, CH_2CH_3), 3.41 (dd, 1H, J = 11.95 and 4.95 Hz, C_{11a}–H), 3.85 (s, 3H, OCH_3), 4.35 (d, 1H, J = 4.95 Hz, C_{12}–H), 4.71 (d, 1H, J = 11.95 Hz, C_{11}–H), 6.64 (d, 2H, J = 2.64 Hz, Ar-H), 6.90 (d, 2H, J = 7.96 Hz, Ar-H), 6.99 (d, 2H, J = 7.96 Hz, Ar-H), 7.10–7.43 (m, 10H, Ar-H), 7.58 (d, 1H, J = 7.92 Hz, Ar-H), 7.90–7.92 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 15.12 (CH_2CH_3), 28.22 (CH_2CH_3), 53.73 (C_{11a}), 55.46 (OCH_3), 58.04 (C_{12}), 67.50 (C_{11}), 115.13, 118.13, 121.05, 123.052, 126.81, 127.11, 127.26 ($C_{2''}$, $C_{6''}$), 127.56 ($C_{3''}$, $C_{5''}$), 128.31, 128.49 ($C_{2'}$, $C_{6'}$), 129.98 ($C_{3'}$, $C_{5'}$), 130.40, 132.36, 134.27, 136.41, 138.32, 142.68, 146.78, 157.62 (C_8), 165.79 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{31}H_{27}NOS$: 462.1892; found, 462.1890. *Anal*. Calcd. for $C_{31}H_{27}NOS$ (461.62): C, 80.66; H, 5.90; N, 3.03. Found: C, 80.43; H, 6.15; N, 3.28.

8-Bromo-11-(4-ethylphenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5d). This compound was obtained as yellow crystals, yield 54%; mp 192–196° C; ir (KBr): 1611 (C═N str.), 2849, 2918, 2963 (aliphatic C–H str.), 3019, 3044 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$): δ 1.14 (t, 3H, J = 7.60 Hz, CH_2CH_3), 2.52 (q, 2H, J = 7.60 Hz, CH_2CH_3), 3.68 (dd, 1H, J = 12.00 and 5.00 Hz, C_{11a}–H), 3.95 (d, 1H, J = 5.00 Hz, C_{12}–H), 4.59 (d, 1H, J = 12.00 Hz, C_{11}–H), 6.93 (d, 2H, J = 8.10 Hz), 6.99 (d, 2H, J = 8.10 Hz, Ar-H), 7.24–7.44 (m, 10H, Ar-H), 7.58 (d, 1H, J = 8.8 Hz, Ar-H), 7.98–8.02 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 15.18 (CH_2CH_3), 28.13 (CH_2CH_3), 53.55 (C_{11a}), 58.10 (C_{12}), 67.48 (C_{11}), 120.38, 121.68, 124.51, 126.58, 126.75, 127.32, 127.36 ($C_{2''}$, $C_{6''}$), 127.65 ($C_{3''}$, $C_{5''}$), 128.44, 128.51 ($C_{2'}$, $C_{6'}$), 129.11 ($C_{3'}$, $C_{5'}$), 130.26, 130.34, 132.34, 134.12, 136.45, 138.28, 142.69, 146.68, 148.13, 165.72 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{30}H_{24}BrNS$: 510.0891 (^{79}Br), 512.0871 (^{81}Br); found, 510.0895 (^{79}Br), 512.0875 (^{81}Br). *Anal*. Calcd. for $C_{30}H_{24}BrNS$ (510.49): C, 70.58; H, 4.74; N, 2.74. Found: C, 70.67; H, 4.52; N, 2.81.

8-Chloro-11-(4-ethylphenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5e). This compound was obtained as orange solid, yield 59%; mp 194–198°C; ir (KBr): 1611 (C═N str.), 2849, 2918, 2963 (aliphatic C–H str.), 3022, 3049, 3073 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$): δ 1.15 (t, 3H, J = 7.55 Hz, CH_2CH_3), 2.70 (q, 2H, J = 7.55 Hz, CH_2CH_3), 3.69 (dd, 1H, J = 12.00 and 5.00 Hz, C_{11a}–H), 3.96 (d, 1H, J = 5.00 Hz, C_{12}–H), 4.58 (d, 1H, J = 12.00 Hz, C_{11}–H), 6.92 (d, 2H, J = 8.00 Hz, Ar-H), 6.90 (d, 2H, J = 7.96 Hz, Ar-H), 6.99 (d, 2H, J = 7.96 Hz, Ar-H), 7.10–7.43 (m, 10H, Ar-H), 7.58 (d, 1H, J = 7.92 Hz, Ar-H), 7.90–7.92 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 15.18 (CH_2CH_3), 28.15 (CH_2CH_3), 53.51 (C_{11a}), 58.12 (C_{12}), 67.52 (C_{11}), 119.42, 121.22, 121.69, 124.11, 126.85, 127.23, 127.39 ($C_{2''}$, $C_{6''}$), 127.73 ($C_{3''}$, $C_{5''}$), 128.50, 128.65 ($C_{2'}$, $C_{6'}$), 128.99 ($C_{3'}$, $C_{5'}$), 129.21, 130.46, 132.49, 134.40, 136.23, 137.89, 142.59, 146.63, 148.11, 166.30 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{30}H_{24}ClNS$: 466.1396 (^{35}Cl), 468.1367 (^{37}Cl); found, 466.1390 (^{35}Cl), 468.1365 (^{37}Cl). *Anal*. Calcd. for $C_{30}H_{24}ClNS$ (466.04): C, 77.32; H, 5.19; N, 3.01. Found: C, 77.53; H, 5.37; N, 3.25.

11-(4-Ethoxyphenyl)-12-phenyl-11a,12-dihydro-11H-indeno [2,1-c][1,5]benzothiazepine (5f). This compound was obtained as orange crystals, yield 55%; mp 190–194°C; ir (KBr): 1610 (C═N str.), 2853, 2922, 2978 (aliphatic C–H str.), 3055 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$): δ 1.32 (t, 3H, J = 7.00 Hz, OCH_2CH_3), 3.80 (dd, 1H, J = 11.65 and 4.45 Hz, C_{11a}–H), 3.87 (q, 2H,

J = 7.00 Hz, OCH_2CH$_3$), 4.01 (d, 1H, J = 4.45 Hz, C_{12}–H), 4.35 (d, 1H, J = 11.65 Hz, C_{11}–H), 6.59 (d, 2H, J = 8.70 Hz, $C_{3''}$–H, $C_{5''}$–H), 6.86–6.89 (m, 1H, Ar-H), 6.99 (d, 2H, J = 8.70 Hz, $C_{2''}$–H, $C_{6''}$–H), 7.11 (dd, 1H, J = 8.25 and 1.20 Hz, Ar-H), 7.24–7.41 (m, 9H, Ar-H), 7.60 (dd, 1H, J = 7.95 and 1.15 Hz, Ar-H), 7.92–7.93 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 14.74 (OCH$_2$CH$_3$), 53.15 (C_{11a}), 57.53 (C_{12}), 63.20 (OCH$_2$CH$_3$), 65.56 (C_{11}), 113.96 ($C_{3''}$, $C_{5''}$), 121.05, 121.58, 126.38, 126.90, 127.56, 128.56 ($C_{2'}$, $C_{6'}$), 128.66, 128.83 ($C_{2''}$, $C_{6''}$), 129.01 ($C_{3'}$, $C_{5'}$), 129.06, 130.24, 131.24, 132.37, 134.23, 138.03, 142.61, 146.58, 148.36, 157.47, 165.68 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{30}H_{25}NOS$: 448.1735; found, 448.1730. *Anal*. Calcd. for $C_{30}H_{25}NOS$ (447.17): C, 80.50; H, 5.63; N, 3.13. Found: C, 80.43; H, 5.75; N, 3.38.

11-(4-Ethoxyphenyl)-8-methyl-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5g). This compound was obtained as light orange crystals, yield 58%; mp 145–148°C; ir (KBr): 1601 (C═N str.), 2887, 2930, 2980 (aliphatic C–H str.), 3080 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.34 (t, 3H, J = 7.00 Hz, OCH$_2$CH_3), 2.41 (s, 3H, CH$_3$), 3.58 (dd, 1H, J = 11.76 and 4.64 Hz, C_{11a}–H), 3.86 (q, 2H, J = 7.00 Hz, OCH_2CH$_3$), 4.34 (d, 1H, J = 4.64 Hz, C_{12}–H), 4.97 (d, 1H, J = 11.76 Hz, C_{11}–H), 6.58 (d, 2H, J = 8.68 Hz, $C_{3''}$–H, $C_{5''}$–H), 6.43–6.85 (m, 9H, Ar-H), 6.98 (d, 2H, J = 8.68 Hz, $C_{2''}$–H, $C_{6''}$–H), 7.58 (d, 1H, J = 8.32 Hz, Ar-H), 7.64–7.67 (m, 1H, Ar-H), 7.90–7.94 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 14.73 (OCH$_2$CH$_3$), 21.43 (CH$_3$), 53.80 (C_{11a}), 57.95 (C_{12}), 63.21 (OCH$_2$CH$_3$), 66.92 (C_{11}), 113.94 ($C_{3''}$, $C_{5''}$), 121.48, 122.87, 126.84, 127.14, 128.15, 128.62 ($C_{2'}$, $C_{6'}$), 128.81 ($C_{2''}$, $C_{6''}$), 129.01 ($C_{3'}$, $C_{5'}$), 130.42, 132.45, 132.45, 134.38, 135.50, 138.24, 142.58, 146.60, 148.55, 157.51, 165.75 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{31}H_{27}NOS$: 462.1892; found, 462.1887. *Anal*. Calcd. for $C_{31}H_{27}NOS$ (461.62): C, 80.66; H, 5.90; N, 3.03. Found: C, 80.83; H, 5.75; N, 3.27.

11-(4-Ethoxyphenyl)-8-methoxy-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5h). This compound was obtained as yellow crystals, yield 52%; mp 156–160°C; ir (KBr): 1603 (C═N str.), 2887, 2966 (aliphatic C–H str.), 3019, 3073 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.33 (t, 3H, J = 7.00 Hz, OCH$_2$CH_3), 3.64 (dd, 1H, J = 11.68 and 4.40 Hz, C_{11a}–H), 3.68 (s, 3H, OCH$_3$), 3.85 (q, 2H, J = 7.00 Hz, OCH_2CH$_3$), 4.39 (d, 1H, J = 4.40 Hz, C_{12}–H), 5.02 (d, 1H, J = 11.68 Hz, C_{11}–H), 6.60 (d, 2H, J = 8.60 Hz, $C_{3''}$–H, $C_{5''}$–H), 6.65 (d, 1H, J = 2.60 Hz, Ar-H), 6.98 (d, 2H, J = 8.60 Hz, $C_{2''}$–H, $C_{6''}$–H), 7.13–7.43 (m, 9H, Ar-H), 7.58 (d, 1H, J = 7.95 Hz, Ar-H), 7.92–7.93 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 14.75 (OCH$_2$CH$_3$), 53.68 (C_{11a}), 55.42 (OCH$_3$), 58.10 (C_{12}), 63.18 (OCH$_2$CH$_3$), 67.42 (C_{11}), 113.95 ($C_{3''}$, $C_{5''}$), 115.01, 118.10, 121.15, 123.50, 126.92, 127.75, 128.60 ($C_{2'}$, $C_{6'}$), 128.65, 128.81 ($C_{2''}$, $C_{6''}$), 129.03 ($C_{3'}$, $C_{5'}$), 130.31, 132.40, 134.21, 138.10, 142.65, 146.62, 148.71, 157.48, 157.84, 165.70 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{31}H_{27}NO_2S$: 478.1841; found, 478.1845. *Anal*. Calcd. for $C_{31}H_{27}NO_2S$ (477.62): C, 77.96; H, 5.70; N, 2.93. Found: C, 77.68; H, 5.95; N, 2.75.

8-Bromo-11-(4-ethoxyphenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5i). This compound was obtained as yellow solid, yield 55%; mp 196–198°C; ir (KBr): 1604 (C═N str.), 2930, 2963 (aliphatic C–H str.), 3022, 3059 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.31 (t, 3H, J = 7.00 Hz, OCH$_2$CH_3), 3.70 (dd, 1H, J = 11.70 and 4.20 Hz, C_{11a}–H), 3.83 (q, 2H, J = 7.00 Hz, OCH_2CH$_3$), 4.41 (d, 1H, J = 4.20 Hz, C_{12}–H), 4.80 (d, 1H, J = 11.70 Hz, C_{11}–H), 6.57 (d, 2H, J = 8.60 Hz, $C_{3''}$–H, $C_{5''}$–H), 6.97 (d, 2H, J = 8.60 Hz, $C_{2''}$–H, $C_{6''}$–H), 7.14–7.44 (m, 10H, Ar-H), 7.59 (d, 1H, J = 8.32 Hz, Ar-H), 7.97–8.02 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 14.72 (OCH$_2$CH$_3$), 53.83 (C_{11a}), 58.17 (C_{12}), 63.19 (OCH$_2$CH$_3$), 66.80 (C_{11}), 113.97 ($C_{3''}$, $C_{5''}$), 119.48, 121.25, 121.61, 124.13, 126.86, 127.28, 128.59 ($C_{2'}$, $C_{6'}$), 128.62, 128.82 ($C_{2''}$, $C_{6''}$), 128.99 ($C_{3'}$, $C_{5'}$), 129.23, 130.32, 132.48, 134.39, 137.98, 142.61, 146.55, 148.52, 157.49, 165.91 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{30}H_{24}BrNOS$: 526.0840 (^{79}Br), 528.0820 (^{81}Br); found, 526.0835 (^{79}Br), 528.0816 (^{81}Br). *Anal*. Calcd. for $C_{30}H_{24}BrNOS$ (526.49): C, 68.44; H, 4.59; N, 2.66. Found: C, 68.57; H, 4.33; N, 2.51.

8-Chloro-11-(4-ethoxyphenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5j). This compound was obtained as yellow solid, yield 53%; mp 124–128°C; ir (KBr): 1605 (C═N str.), 2876, 2918, 2963 (aliphatic C–H str.), 3024, 3063 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 1.32 (t, 3H, J = 7.00 Hz, OCH$_2$CH_3), 3.69 (dd, 1H, J = 11.70 and 4.40 Hz, C_{11a}–H), 3.84 (q, 2H, J = 7.00 Hz, OCH_2CH$_3$), 4.42 (d, 1H, J = 4.40 Hz, C_{12}–H), 4.79 (d, 1H, J = 11.68 Hz, C_{11}–H), 6.59 (d, 2H, J = 8.56 Hz, $C_{3''}$–H, $C_{5''}$–H), 6.96 (d, 2H, J = 8.56 Hz, $C_{2''}$–H, $C_{6''}$–H), 7.21–7.43 (m, 10H, Ar-H), 7.60 (d, 1H, J = 8.20 Hz, Ar-H), 7.96–8.01 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 14.73 (OCH$_2$CH$_3$), 53.87 (C_{11a}), 58.15 (C_{12}), 63.21 (OCH$_2$CH$_3$), 66.83 (C_{11}), 113.92 ($C_{3''}$, $C_{5''}$), 120.35, 121.63, 124.53, 126.51, 126.88, 127.31, 128.58 ($C_{2'}$, $C_{6'}$), 128.63, 128.85 ($C_{2''}$, $C_{6''}$), 128.99 ($C_{3'}$, $C_{5'}$), 130.21, 130.37, 132.47, 134.35, 138.29, 142.63, 146.54, 148.54, 157.50, 165.89 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{30}H_{24}ClNOS$: 482.1345 (^{35}Cl), 484.1316 (^{37}Cl); found, 482.1342 (^{35}Cl), 484.1313

(^{37}Cl). *Anal*. Calcd. for $C_{30}H_{24}ClNOS$ (482.04): C, 74.75; H, 5.02; N, 2.91. Found: C, 74.58; H, 5.26; N, 2.72.

11-(4-Fluorophenyl)-12-phenyl-11a,12-dihydro-11H-indeno [2,1-c][1,5]benzothiazepine (5k). This compound was obtained as orange crystals, yield 57%; mp 145–150°C; ir (KBr): 1601 (C═N str.), 3059 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$): δ 3.48 (dd, 1H, *J* = 12.00 and 5.00 Hz, C_{11a}–H), 4.31 (d, 1H, *J* = 5.00 Hz, C_{12}–H), 4.77 (d, 1H, *J* = 12.00 Hz, C_{11}–H), 6.77 (t, 2H, *J* = 8.65 Hz, Ar-H), 6.87–6.91 (m, 1H, Ar-H), 6.87–6.91 (m, 1H, Ar-H), 7.06–7.50 (m, 11H, Ar-H), 7.60 (dd, 1H, *J* = 7.95 and 1.35 Hz, Ar-H), 7.89–7.94 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 53.86 (C_{11a}), 58.15 (C_{12}), 65.87 (C_{11}), 116.17 (d, *J* = 22.50 Hz, $C_{3''}$, $C_{5''}$), 121.19, 121.68, 126.42, 126.98, 127.76, 128.66 ($C_{2'}$, $C_{6'}$), 128.96 ($C_{3'}$, $C_{5'}$), 129.21, 129.51 (d, *J* = 8.75 Hz, $C_{2''}$, $C_{6''}$), 129.93 (d, *J* = 3.75 Hz, $C_{1''}$), 130.37, 131.23, 132.23, 134.22, 137.96, 142.48, 148.35, 164.44 (d, *J* = 250.00 Hz, $C_{4''}$), 165.62 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{28}H_{20}FNS$: 422.1379; found, 422.1375. *Anal*. Calcd. for $C_{28}H_{20}FNS$ (421.53): C, 79.78; H, 4.78; N, 3.32. Found: C, 79.92; H, 4.53; N, 3.48.

11-(4-Fluorophenyl)-8-methyl-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5l). This compound was obtained as yellow crystals, yield 76%; mp 114–118°C; ir (KBr): 1599 (C═N str.), 2853, 2922, 2955 (aliphatic C–H str.), 3049 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (500 MHz, $CDCl_3$): δ 2.43 (s, 3H, CH_3), 3.58 (dd, 1H, *J* = 11.90 and 4.95 Hz, C_{11a}–H), 4.57 (d, 1H, *J* = 4.95 Hz, C_{12}–H), 4.92 (d, 1H, *J* = 11.90 Hz, C_{11}–H), 6.78–7.49 (m, 13H, Ar-H), 7.60 (d, 1H, *J* = 8.60 Hz, Ar-H), 7.66–7.69 (m, 1H, Ar-H), 7.92–7.95 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 21.42 (CH_3), 53.92 (C_{11a}), 58.12 (C_{12}), 65.90 (C_{11}), 115.72 (d, *J* = 22.50 Hz, $C_{3''}$, $C_{5''}$), 121.53, 122.78, 127.14, 127.18, 128.13, 128.65 ($C_{2'}$, $C_{6'}$), 128.95 ($C_{3'}$, $C_{5'}$), 129.42 (d, *J* = 8.75 Hz, $C_{2''}$, $C_{6''}$), 129.95 (d, *J* = 3.75 Hz, $C_{1''}$), 130.21, 132.41, 134.61, 135.58, 138.03, 142.54, 148.58, 164.30 (d, *J* = 250.00 Hz, $C_{4''}$), 165.80 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{29}H_{22}FNS$: 436.1535; found, 436.1530. *Anal*. Calcd. for $C_{29}H_{22}FNS$ (435.56): C, 79.97; H, 5.09; N, 3.22. Found: C, 79.76; H, 5.36; N, 3.47.

11-(4-Fluorophenyl)-8-methoxy-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5m). This compound was obtained as yellow crystals, yield 59%; mp 148–152°C; ir (KBr): ν_{max} 1605 (C═N str.), 2829, 2928 2849, 2918, 2963 (aliphatic C–H str.), 3003, 3073, 3115 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 3.45 (dd, 1H, *J* = 11.68 and 4.48 Hz, C_{11a}–H), 3.65 (d, 1H, *J* = 4.48 Hz, C_{12}–H), 3.69 (s, 3H, OCH_3), 3.92 (d, 1H, *J* = 11.68 Hz, C_{11}–H), 6.64 (d, 1H, *J* = 2.64 Hz, Ar-H), 6.79–7.41 (m, 13H, Ar-H), 7.58 (d, 1H, *J* = 8.80 Hz, Ar-H), 7.90–7.92 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 53.72 (C_{11a}), 55.49 (OCH_3), 58.20 (C_{12}), 65.82 (C_{11}), 114.99, 115.14 (d, *J* = 22.00 Hz, $C_{3''}$, $C_{5''}$), 118.15, 121.02, 121.39, 127.53, 127.84,128.63 ($C_{2'}$, $C_{6'}$), 128.98 ($C_{3'}$, $C_{5'}$), 129.02, 129.33 (d, *J* = 8.00 Hz, $C_{2''}$, $C_{6''}$), 129.92, 130.08 (d, *J* = 4.00 Hz, $C_{1''}$), 132.48, 133.66, 138.01, 142.52, 148.52, 148.72, 158.02, 163.85 (d, *J* = 242.00 Hz, $C_{4''}$), 165.46 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{29}H_{22}FNOS$: 452.1484; found, 452.1478. *Anal*. Calcd. for $C_{29}H_{22}FNOS$ (451.55): C, 77.14; H, 4.91; N, 3.10. Found: C, 77.40; H, 4.73; N, 3.32.

8-Bromo-11-(4-fluorophenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5n). This compound was obtained as yellow solid, yield 62%; mp 153–158°C; ir (KBr): 1603 (C═N str.), 3073, 3113 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 3.49 (dd, 1H, *J* = 11.96 and 4.96 Hz, C_{11a}–H), 3.68 (d, 1H, *J* = 4.96 Hz, C_{12}–H), 4.33 (d, 1H, *J* = 11.96 Hz, C_{11}–H), 6.80 (t, 1H, *J* = 8.48 Hz, Ar-H), 7.08–7.11 (m, 1H, Ar-H), 7.15–7.48 (m, 12H, Ar-H), 7.60 (d, 1H, *J* = 8.64 Hz, Ar-H), 7.85–7.91 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 53.61 (C_{11a}), 58.97 (C_{12}), 66.48 (C_{11}), 115.18 (d, *J* = 22.00 Hz, $C_{3''}$, $C_{5''}$), 119.45, 121.28, 121.48, 124.16, 127.23, 127.45, 128.63 ($C_{2'}$, $C_{6'}$), 128.96 ($C_{3'}$, $C_{5'}$), 129.08, 129.21, 129.32 (d, *J* = 8.00 Hz, $C_{2''}$, $C_{6''}$), 130.01 (d, *J* = 4.00 Hz, $C_{1''}$), 130.10, 132.41, 133.62, 138.96, 142.50, 148.51, 163.81 (d, *J* = 240.00 Hz, $C_{4''}$), 165.89 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{28}H_{19}BrFNS$: 500.0484 (^{79}Br), 502.0463 (^{81}Br); found, 500.0480 (^{79}Br), 502.0458 (^{81}Br). *Anal*. Calcd. for $C_{28}H_{19}BrFNS$ (500.42): C, 67.20; H, 3.83; N, 2.80. Found: C, 67.55; H, 3.52; N, 2.65.

8-Chloro-11-(4-fluorophenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5o). This compound was obtained as yellow solid, yield 54%; mp 156–159°C; ir (KBr): 1607 (C═N str.), 3059, 3115 (aromatic C–H str.) cm^{-1}; ^{1}H nmr (400 MHz, $CDCl_3$): δ 3.50 (dd, 1H, *J* = 11.96 and 4.96 Hz, C_{11a}–H), 3.67 (d, 1H, *J* = 4.96 Hz, C_{12}–H), 4.34 (d, 1H, *J* = 11.96 Hz, C_{11}–H), 6.81 (t, 1H, *J* = 8.44 Hz, Ar-H), 7.05–7.09 (m, 1H, Ar-H), 7.15–7.49 (m, 12H, Ar-H), 7.58 (d, 1H, *J* = 8.60 Hz, Ar-H), 7.84–7.90 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 53.65 (C_{11a}), 58.94 (C_{12}), 66.53 (C_{11}), 115.14 (d, *J* = 22.00 Hz, $C_{3''}$, $C_{5''}$), 120.36, 121.50, 124.58, 126.48, 127.32, 127.32, 127.43, 128.61 ($C_{2'}$, $C_{6'}$), 128.92 ($C_{3'}$, $C_{5'}$), 129.11, 129.30 (d, *J* = 8.00 Hz, $C_{2''}$, $C_{6''}$), 130.05 (d, *J* = 4.00 Hz, $C_{1''}$), 130.08, 130.33, 132.42, 133.65, 138.99, 142.53, 148.58, 163.85 (d, *J* = 240.00 Hz, $C_{4''}$), 165.92 (C_{4b}); ms (TOF ESI) *m/z*: $[M + H]^+$ calcd. for $C_{28}H_{19}ClFNS$: 456.0989 (^{35}Cl), 458.0960 (^{37}Cl); found, 456.0990 (^{35}Cl), 458.0957 (^{37}Cl). *Anal*. Calcd. for $C_{28}H_{19}ClFNS$ (455.97): C, 73.75; H, 4.20; N, 3.07. Found: C, 73.54; H, 4.35; N, 3.31.

11-(4-Bromophenyl)-12-phenyl-11a,12-dihydro-11H-indeno [2,1-c][1,5]benzothiazepine (5p). This compound was obtained as yellow solid, yield 63%; mp 148–150°C; ir (KBr): 1604 (C═N str.), 3022, 3059 (aromatic C–H str.) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 3.47 (dd, 1H, J = 11.96 and 4.96 Hz, C_{11a}–H), 4.34 (d, 1H, J = 4.96 Hz, C_{12}–H), 4.78 (d, 1H, J = 11.96 Hz, C_{11}–H), 6.78 (t, 2H, J = 8.60 Hz, Ar-H), 6.86–6.90 (m, 1H, Ar-H), 7.05–7.48 (m, 11H, Ar-H), 7.59 (dd, 1H, J = 7.96 and 1.36 Hz, Ar-H), 7.88–7.93 (m, 1H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 54.25 (C_{11a}), 58.10 (C_{12}), 65.93 (C_{11}), 121.26, 121.62, 124.89, 126.46, 127.36, 127.78, 128.11, 128.65 ($C_{2'}$, $C_{6'}$), 129.03 ($C_{3'}$, $C_{5'}$), 129.23, 130.69, 131.23 ($C_{2''}$, $C_{6''}$), 131.25, 132.13 ($C_{3''}$, $C_{5''}$), 132.66, 134.19, 136.51, 138.52, 142.58, 148.39, 165.73 (C_{4b}); ms (TOF ESI) m/z: $[M + H]^+$ calcd. for $C_{28}H_{20}BrNS$: 482.0578 (^{79}Br), 484.0558 (^{81}Br); found, 482.0575 (^{79}Br), 484.0560 (^{81}Br). *Anal*. Calcd. for $C_{28}H_{20}BrNS$ (482.43): C, 69.71; H, 4.18; N, 2.90. Found: C, 69.47; H, 4.35; N, 2.72.

11-(4-Bromophenyl)-8-methyl-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5q). This compound was obtained as yellow solid, yield 55%; mp 192–194°C; ir (KBr): 1602 (C═N str.), 2926, 2963 (aliphatic C–H str.), 3019, 3063 (aromatic C–H str.) cm^{-1}; ^1H nmr (500 MHz, $CDCl_3$): δ 2.42 (s, 3H, CH_3), 3.57 (dd, 1H, J = 11.65 and 4.45 Hz, C_{11a}–H), 4.57 (d, 1H, J = 4.45 Hz, C_{12}–H), 4.91 (d, 1H, J = 11.65 Hz, C_{11}–H), 6.75–7.51 (m, 13H, Ar-H), 7.61 (d, 1H, J = 8.35 Hz, Ar-H), 7.65–7.68 (m, 1H, Ar-H), 7.91–7.94 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 21.42 (CH_3), 53.61 (C_{11a}), 58.17 (C_{12}), 65.89 (C_{11}), 121.49, 122.83, 124.93, 127.16, 127.35, 128.17, 128.20, 128.63 ($C_{2'}$, $C_{6'}$), 128.99 ($C_{3'}$, $C_{5'}$), 130.61, 131.42, 131.48 ($C_{2''}$, $C_{6''}$), 132.12 ($C_{3''}$, $C_{5''}$), 132.73, 134.22, 135.52, 136.55, 138.43, 142.53, 148.54, 165.78 (C_{4b}); ms (TOF ESI) m/z: $[M + H]^+$ calcd. for $C_{29}H_{22}BrNS$: 496.0735 (^{79}Br), 498.0714 (^{81}Br); found, 496.0732 (^{79}Br), 498.0710 (^{81}Br). *Anal*. Calcd. for $C_{29}H_{22}BrNS$ (496.46): C, 70.16; H, 4.47; N, 2.82. Found: C, 70.37; H, 4.25; N, 2.63.

11-(4-Bromophenyl)-8-methoxy-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5r). This compound was obtained as yellow solid, yield 58%; mp 196–198°C; ir (KBr): 1601 (C═N str.), 2849, 2918, 2957 (aliphatic C–H str.), 3001, 3065 (aromatic C–H str.); 3028, 3055, 3088, 3123 (aromatic C–H str.) cm^{-1}; ^1H nmr (500 MHz, $CDCl_3$): δ 3.43 (dd, 1H, J = 11.70 and 4.60 Hz, C_{11a}–H), 3.64 (d, 1H, J = 4.60 Hz, C_{12}–H), 3.70 (s, 3H, OCH_3), 3.93 (d, 1H, J = 11.70 Hz, C_{11}–H), 6.65 (d, 1H, J = 2.90 Hz, Ar-H), 6.82–6.85 (m, 1H, Ar-H), 7.08–7.42 (m, 10H, Ar-H), 7.60 (d, 1H, J = 8.55 Hz, Ar-H), 7.90–7.96 (m, 2H, Ar-H), 8.03–8.05 (m, 1H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 53.72 (C_{11a}), 55.90 (OCH_3), 58.18 (C_{12}), 65.84 (C_{11}), 115.73, 118.20, 121.06, 121.28, 124.96, 127.32, 127.65, 128.13, 128.67 ($C_{2'}$, $C_{6'}$), 129.07 ($C_{3'}$, $C_{5'}$), 130.63, 131.46 ($C_{2''}$, $C_{6''}$), 132.25 ($C_{3''}$, $C_{5''}$), 132.78, 134.26, 136.26, 136.53, 138.36, 142.62, 148.71, 157.85, 165.65 (C_{4b}); ms (TOF ESI) m/z: $[M + H]^+$ calcd. for $C_{29}H_{22}BrNOS$: 512.0684 (^{79}Br), 514.0663 (^{81}Br); found, 512.0679 (^{79}Br), 514.0668 (^{81}Br). *Anal*. Calcd. for $C_{29}H_{22}BrNOS$ (512.46): C, 67.97; H, 4.33; N, 2.73. Found: C, 67.83; H, 4.52; N, 2.62.

8-Bromo-11-(4-bromophenyl)-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5s). This compound was obtained as yellow solid, yield 59%; mp 236–240°C; ir (KBr): 1601 (C═N str.), 3055, 3115 (aromatic C–H str.) cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 3.52 (dd, 1H, J = 11.96 and 4.96 Hz, C_{11a}–H), 3.66 (d, 1H, J = 4.96 Hz, C_{12}–H), 4.31 (d, 1H, J = 11.96 Hz, C_{11}–H), 6.81 (t, 1H, J = 8.48 Hz, Ar-H), 7.06–7.50 (m, 11H, Ar-H), 7.58 (dd, 1H, J = 8.72, 1.84 Hz, Ar-H), 7.86–7.90 (m, 1H, Ar-H), 8.01–8.05 (m, 2H, Ar-H); ^{13}C nmr (100 MHz, $CDCl_3$): δ 54.16 (C_{11a}), 58.23 (C_{12}), 66.28 (C_{11}), 119.46, 121.24, 121.53, 124.11, 124.95, 127.18, 127.38, 128.19, 128.65 ($C_{2'}$, $C_{6'}$), 129.05 ($C_{3'}$, $C_{5'}$), 129.23, 130.74, 131.40 ($C_{2''}$, $C_{6''}$), 132.20 ($C_{3''}$, $C_{5''}$), 132.61, 134.15, 136.50, 138.83, 142.59, 148.54, 166.01 (C_{4b}); ms (TOF ESI) m/z: $[M + H]^+$ calcd. for $C_{28}H_{19}Br_2NS$: 559.9683 (^{79}Br and ^{79}Br), 561.9663 (^{79}Br and ^{81}Br), 563.9642 (^{81}Br and ^{81}Br); found, 559.9680 (^{79}Br and ^{79}Br), 561.9661 (^{79}Br and ^{81}Br), 563.9639 (^{81}Br and ^{81}Br). *Anal*. Calcd. for $C_{28}H_{19}Br_2NS$ (561.33): C, 59.91; H, 3.41; N, 2.50. Found: C, 60.12; H, 3.58; N, 2.37.

11-(4-Bromophenyl)-8-chloro-12-phenyl-11a,12-dihydro-11H-indeno[2,1-c][1,5] benzothiazepine (5t). This compound was obtained as orange crystals, yield 57%; mp 214–216°C; ir (KBr): 1605 (C═N str.), 3019, 3073 (aromatic C–H str.) cm^{-1}; ^1H nmr (500 MHz, $CDCl_3$): δ 3.51 (dd, 1H, J = 12.00 and 5.00 Hz, C_{11a}–H), 3.68 (d, 1H, J = 5.00 Hz, C_{12}–H), 4.32 (d, 1H, J = 12.00 Hz, C_{11}–H), 6.82 (t, 1H, J = 8.50 Hz, Ar-H), 7.01–7.10 (m, 1H, Ar-H), 7.18–7.51 (m, 10H, Ar-H), 7.59 (dd, 1H, J = 8.75 and 1.85 Hz, Ar-H), 7.88–7.93 (m, 1H, Ar-H), 8.03–8.08 (m, 2H, Ar-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 54.12 (C_{11a}), 58.21 (C_{12}), 66.23 (C_{11}), 120.33, 121.55, 124.57, 124.91, 126.54, 127.29, 127.41, 128.21, 128.69 ($C_{2'}$, $C_{6'}$), 129.06 ($C_{3'}$, $C_{5'}$), 130.36, 130.71, 131.38 ($C_{2''}$, $C_{6''}$), 132.22 ($C_{3''}$, $C_{5''}$), 132.63, 134.18, 136.48, 138.82, 142.57, 148.52, 166.15 (C_{4b}); ms (TOF ESI) m/z: $[M + H]^+$ calcd. for $C_{28}H_{19}BrClNS$: 516.0188 (^{79}Br and ^{35}Cl), 518.0168 (^{81}Br and ^{35}Cl), 518.0159 (^{79}Br and ^{37}Cl), 520.0138 (^{81}Br and ^{37}Cl); found, 516.0185 (^{79}Br and ^{35}Cl), 518.0164 (^{81}Br and ^{35}Cl), 518.0156 (^{79}Br and ^{37}Cl), 520.0140 (^{81}Br and ^{37}Cl). *Anal*. Calcd. for $C_{28}H_{19}BrClNS$ (516.88): C, 65.06; H, 3.71; N, 2.71. Found: C, 65.34; H, 3.56; N, 2.59.

Antimicrobial evaluation. *In vitro* antimicrobial evaluation of all the newly synthesized indane-based 1,5-benzothiazepines (**5a**–**t**) was carried out against two Gram-positive bacteria, namely, *B. subtilis* (MTCC 441) and *S. epidermidis* (MTCC 6880); two Gram-negative bacteria, namely, *E. coli* (MTCC 1652) and *P. aeruginosa* (MTCC 424); and two fungi, namely, *A. niger* (MTCC 8189) and *C. albicans* (MTCC 227) using serial dilution method [67]. The results of the antimicrobial activity in terms of MIC (μ*M*/mL) are presented in Table 1 and Figures 1 and 2.

CONCLUSION

The present investigation reports the synthesis of a series of 20 new 1,5-benzothiazepines (**5**) using easily obtainable starting materials under environmentally benign conditions in good yields. The synthesized compounds exhibited *in vitro* antimicrobial activities with a degree of variation. Some of the tested derivatives possessed more inhibitory antimicrobial activities than did the standard reference drugs and can be used as potential antimicrobial agents for further drug development. Working on these foundations, the more potent antibacterial and antifungal agents of therapeutic significance may be designed.

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