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ONE-POT SYNTHESIS OF *trans*-7-ARYL-6*H*-6a,7-DIHYDRO[1]BENZO-PYRANO[3,4-*c*][1,5]BENZOTHIAZEPINES

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Abstract – Green chemical approaches for the condensation reaction of benzenethiols and 3-arylidenenchroman-4-ones as synthons for the synthesis of a series of new*trans*-7-aryl-6*H*-6a,7-dihydro[1]benzo pyrano[3,4-*c*][1,5]benzo-thiazepines which may possess potential biological activity are described.

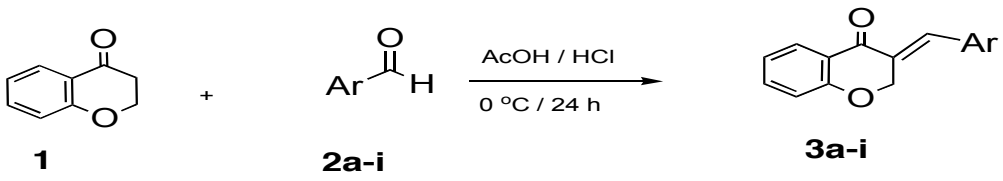
INTRODUCTION

Certain derivatives of 1,5-benzothiazepines, e.g. diltiazem, are used extensively as cardiovascular drugs by acting as calcium channel blockers.[1-5] Extensive synthetic studies have shown that certain substituents on the aromatic ring fused to the 1,5-benzothiazepine nucleus may behave as potential pharmacophores.[6,7] Taking into account the pharmacological activities of the chromane group[8-10] and arylidenechroman-4-ones[11-13] and encouraged by our previous success in the synthesis of potentially biologically active 1,3-thiazoles,[14] we have carried out a one-pot synthesis of tetracyclic [1,5]benzothiazepines with substituents on the fused phenyl ring by the cyclization of 3-arylidenechroman-4-ones with 2-amino-thiophenols with the goal of preparing benzothiazepines with improved cardiovascular activity. The results are reported herein.[15]

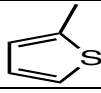
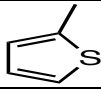
RESULTS AND DISCUSSION

As shown in Table 1, the *trans*-3-arylidenyl derivatives of chroman-4-ones (**3a–i**) were prepared in 87-96% yields by treating 4-chromanone (**1**) with various aromatic aldehydes (**2a–i**) in the presence of AcOH and HCl.[16] The absence of *cis*-3-arylindinyl compounds was ascertained by HPLC. As shown in Scheme 1, the arylidenes (**3a–i**) and 2-aminobenzenethiol (**4**) were then refluxed in a 1:1 (v:v) solution of ethanol/toluene for 2 h in the presence of a strong acid, such as TFA with conc HCl, for 2 h to give *trans*-

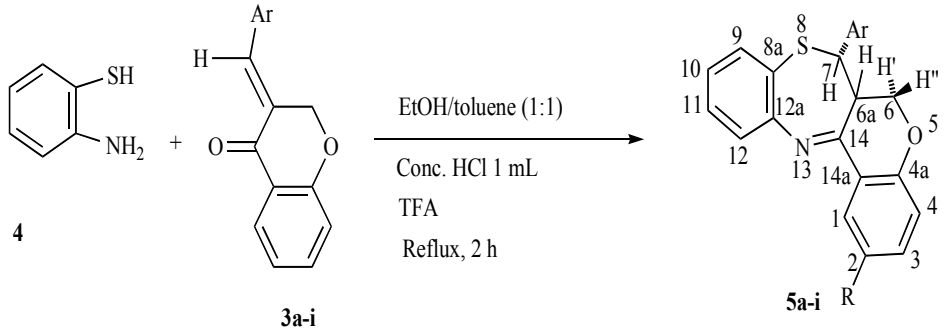
Table 1



1 **2a-i** **3a-i**

a	Ph-		**a**	H	Ph-	96
b	4-MeO-C_6H_4-		**b**	H	4-MeO-C_6H_4-	92
c	4-Me-C_6H_4-		**c**	H	4-Me-C_6H_4-	94
d			**d**	H		84
e	4-Cl-C_6H_4-		**e**	H	4-Cl-C_6H_4-	90
f	4-Br-C_6H_4-		**f**	H	4-Br-C_6H_4-	80
g	2,5-diMeO-C_6H_3-		**g**	H	2,5-diMeO-C_6H_3-	91
h	2,3,4-tri-MeO-C_6H_2-		**h**	H	2,3,4-tri-MeO-C_6H_2-	87
i	3,4,5-tri-MeO-C_6H_2-		**i**	H	3,4,5-tri-MeO-C_6H_2-	95

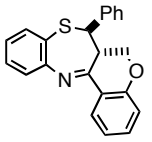
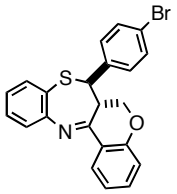
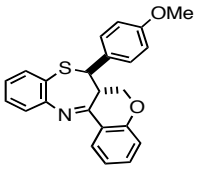
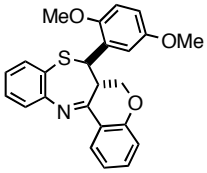
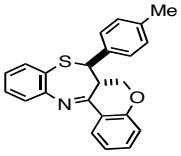
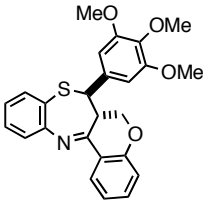
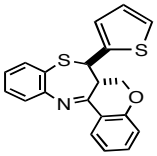
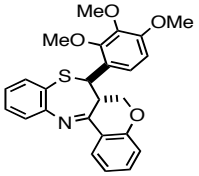
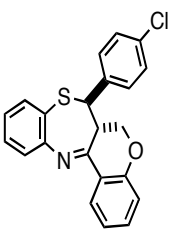
7-aryl-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepines (**5a–i**) in 87-97% yields. The yields are shown in Table 2. Interestingly these reactions did not require the usual work-up since the products (**5a-i**) precipitated from the reaction medium in pure state upon standing.



Scheme 1

During the course of our work, the synthesis of 10-substitutedarylidene-6*H*-6a,7-dihydro-6-phenyl[1]-benzopyrano-[3,4-*c*][1,5]benzothiazepines (**5**) by the reaction of the corresponding chroman-4-one (**3**) and **4** was reported.[16] However, the yields in that study were significantly lower (60-70%) and reaction times were longer (6 h) than those reported here. One of the major differences between the two syntheses is that our method uses dry toluene and ethyl alcohol as co-solvents, whereas the other uses neat toluene. Presumably the ethyl alcohol aids in the formation of and the subsequent precipitation of the benzothi-

Table 2. Preparation of 1,5-Benzothiazepines (**5a–i**)

Entry	1,5-Benzothiazines (**5**)	Yield, %	Entry	1,5-Benzothiazines (**5**)	Yield, %
1	 **5a**	97	6	 **5f**	92
2	 **5b**	92	7	 **5g**	90
3	 **5c**	90	8	 **5h**	94
4	 **5d**	94	9	 **5i**	89
5	 5e	87			

azepines.

The structures of **5a–i** were confirmed by ^{1}H NMR, ^{13}C NMR spectroscopy and in the case of **5a** and **5g**, by X-Ray crystallography. The ORTEP drawings of **5a** and **5g**, which are shown in Figures 1 and 2, respectively, reveal that the H7 and H6a atoms are *trans* to each other with the H7–C7–C6a–H6a angles being 175.09° and 170.62°, respectively. Additionally, the aromatic ring at C_7 occupies the *quasi* equatorial position. Moreover, the ORTEP drawings for **5a** and **5g** reveal that the H7 atom is located at the *quasi* axial position and is *gauche* to the two diastereotopic protons, H6' and H6", and that the diasterotopic protons are *quasi* equatorial. The dihedral angles for H6a—C6a–C6–H6', and H6a—C6a–C6–H6" in compound (**5a**) are -64.1° and 53.4°, respectively, whereas those in compound (**5g**) are –64.9° and 52.1°, respectively. The ORTEP drawings in Figures 1 and 2 also reveal that the seven-membered ring in **5a** and in **5g** exists in a half-chair conformation. These results confirm the structural assignments for **5a** which were made previously on the basis of ^{1}H NMR spectral analysis.[18-20] We further confirmed the *trans, ee* configuration of the other 1,5-benzothiazepines (**5b–5j**) by comparing the multiplicities and coupling constants of the diastereotopic protons H6', H6" and the H6a and H7 protons. These are summarized in Table 3. For example, the 12.0–12.4 Hz splittings of the H7 signals of

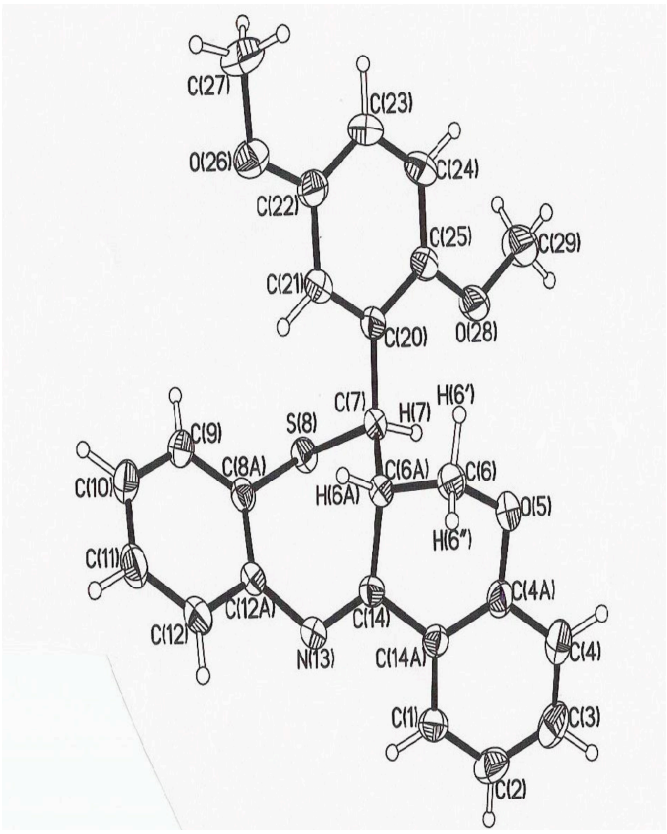


Figure 1 ORTEP of Compound (**5a**)

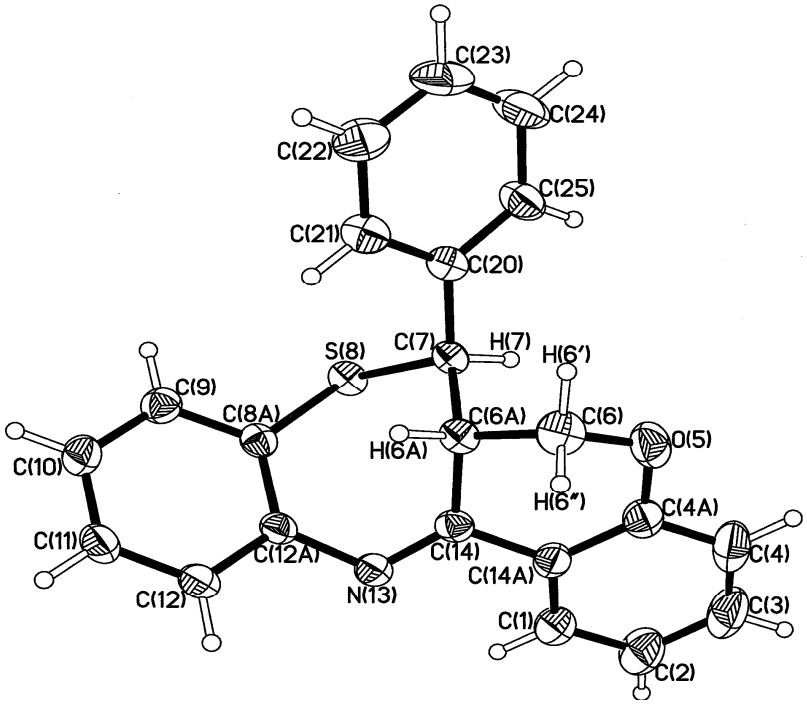


Figure 2 ORTEP of Compound (**5g**)

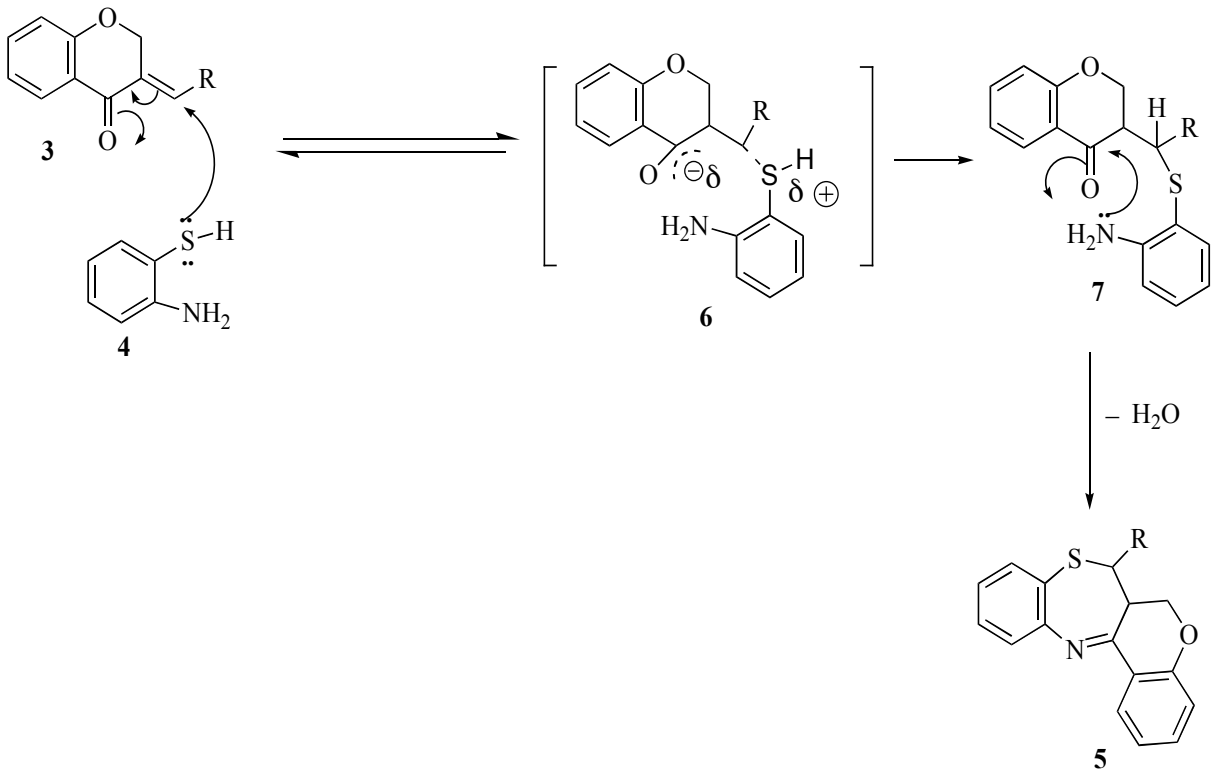
5g are –64.9° and 52.1°, respectively. The ORTEP drawings in Figures 1 and 2 also reveal that the seven-membered ring in **5a** and in **5g** exists in half-chair conformations. These results confirm the structural assignments for **5a** which were made previously on the basis of ^{1}H NMR spectral analysis.[18-20] We further confirmed the *trans, ee* configuration of the other 1,5-benzothiazepines (**5b–f, 5h,i**) by comparing the multiplicities and coupling constants of the diastereotopic protons H6', H6" and the H6a and H7 protons. These are summarized in Table 3. For example, the 12.0–12.4 Hz splittings of the H7 signals at δ 4.79–5.23 ppm are split into a doublet by the H6a protons. This indicates that the H7 and H6a are *trans* to each other and that the aryl groups attached to C7 exist in the *quasi* equatorial position. Additionally, the diastereotopic protons, H6' and H6" appear as ABqx2 patterns in the range of δ 3.90–4.10 and 3.76–3.99 ppm, respectively. Furthermore, the geminal couplings of these protons, which are in the range of 11.8–11.9 Hz, are further split by H6a with coupling constants of 2.7 and 1.6 Hz, respectively. The ^{1}H NMR spectral data for **5a** are in agreement with those previously reported.[18]

The IR spectra of the final products (**5a–i**) were devoid of the characteristic carbonyl absorption peak in the range of 1690–1710 cm^{-1} and the absorption bands in the region of 1710-1690 and 3445-3200 cm^{-1} characteristic of primary amino groups. However, all compounds exhibited strong absorption band in the range of 1602–1618 cm^{-1} indicative of C=N stretching.

A possible mechanism for the formation of titled compounds is given in Scheme 2. Thus, compound (**1**) reacts with **2** by a Michael-type addition to give the adduct (**6**) which then undergoes an intramolecular nucleophilic addition of amino group to the carbonyl moiety to give intermediate (**7**). This intermediate then undergoes dehydration to give **5**.

Table 3 ^{1}H Chemical Shifts (δ, Multiplicities and Coupling Constants (Hz) for H7', H6a, H6' and H6" of Compounds (**5a**)

5	H7 (d)		H6a (ddd)		H6' (dd)		H6" (dd)	
	δ	*J* (Hz)	δ	*J* (Hz)	δ	*J* (Hz)	δ	*J* (Hz)
a	4.92	12.3	3.09	12.3, 2.7, 1.6	4.04	11.8, 2.7	3.79	11.8, 1.6
b	4.89	12.3	3.03	12.3, 2.7, 1.5	4.04	11.8, 2.7	3.79	11.9, 1.6
c	4.89	12.3	3.01	12.3, 2.7, 1.6	4.04	11.8, 2.7	3.81	11.8, 1.6
d	5.23	12.0	2.99	12.0, 2.7, 1.5	4.10	11.8, 2.7	3.99	11.9, 1.6
e	4.88	12.2	3.04	12.1, 2.7, 1.6	4.05	11.9, 2.5	3.77	11.8, 1.6
f	4.87	12.1	3.05	12.1, 2.7. 1.6	4.05	11.8, 2.5	3.76	11.7, 1.6
g	4.09	12.4	3.01	12.4, 2.7, 1.6	3.90	11.8, 2.7	3.81	11.9, 1.6
h	4.09	12.3	3.01	12.4, 2.7, 1.6	3.90	11.8, 2.7	3.81	11.9, 1.6
i	4.79	12.4	3.05	12.4, 2,7, 1.6	4.06	11.9, 2.6	3.05	11.9, 1.6



Scheme 2

CONCLUSIONS

In conclusion, we have shown that a variety of 1,5-benzothiazepines can be prepared in excellent yields. by the acid catalyzed cyclization of 3-benzylidinechroman-4-ones with 2-aminothiophenol. To our knowledge this is the best method in terms of yields and ease of work-up for the synthesis of seven-membered ring compounds.

EXPERIMENTAL

Melting points were determined using a Mel-Temp capillary apparatus and were uncorrected. NMR spectra were recorded on a Bruker Avance DRX400 instrument at 400 MHz (^{1}H) or 100 MHz (^{13}C NMR) in $CDCl_3$. Chemical shifts (δ values) were reported in parts per million and coupling constants (*J* values) in Hz. IR spectra were recorded in a KBr pellet on a Perkin-Elmer spectrophotometer FT Paragon 1000 PC. Elemental analyses were obtained from SMU Analytical Laboratories. Flash chromatography was performed on silica gel (Ultrapure 230-400 mesh). TLC was performed on pre-coated silica gel plates (silica gel 60, F_{254}, 20 x 20 cm). Solvents were HPLC grade or were purified by standard procedures. All reagents were of commercial quality and were purified before use. The glassware was heated overnight in an oven at 125 ºC prior to use. The reactions were carried out under an atmosphere of dry O_2-free Ar *via* balloon.

Preparation of Arylidenechroman-4-ones (3a-j).

These compounds were synthesized by a literature method.[16] The following have been reported and were identified on the basis of their mp.

3-Benzylidenechroman-4-one (3a): mp 109 °C (MeOH); lit.,[21]110 °C.

3-(4'-Methoxybenzylidene)chroman-4-one (3b): mp 131–132 °C (MeOH); lit.,[21] 132 °C.

3-(4'-Methylbenzylidene)chroman-4-one (3c): mp 117–118 °C (MeOH); lit.,[21] 118 °C.

3-(Thiophen-2-ylmethyl)chroman-4-one (3d): mp 79 °C (MeOH); lit.,[22] 80–81 °C.

3-(4'-Chlorobenzylidene)chroman-4-one (3e): mp 160–162 °C (MeOH): lit.,[21] 168 °C.

3-(4'-Bromobenzylidene)chroman-4-one (3f): mp 174–175 °C (MeOH); lit.,[21] 174 °C.

3-(3', 4', 5'-Trimethoxybenzylidene)chroman-4-one (3i): mp 108-109 °C (MeOH); lit.,[21]107 °C.

The physical and spectral properties of new arylidenechroman-4-ones (**3g, 3h**, and **3j**) follow.

3-(2', 5'-Dimethoxybenzylidene)chroman-4-one (3g): Yellow solid, mp 77–79 °C (EtOH). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.67 (s, 3 H), 3.77 (s, 3 H), 5.23 (s, 2 H), 6.66 (s, 1H), 6.90–6.98 (m, 4H), 7.07 (d, *J* = 7.45 Hz, 1 H), 7.49 (d, *J* = 7.45 Hz, 1 H), 7.97 (s, 1H), 8.04–8.06 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.3, 55.5, 68.5, 112.4, 116.1, 116.6, 118.1, 118.3, 122.2, 122.6, 124.6, 128.4, 131.6. 134.0, 136.1, 152.9, 153.5, 161.8. Anal. Calcd for $C_{18}H_{16}O_4$: C, 72.96; H, 5.44. Found: C, 73.05; H, 5.50.

3-(2', 3', 4'-Trimethoxybenzylidene)chroman-4-one (3h): viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.76 (s, 3 H), 3.86 (s, 3 H), 4.01 (s, 3 H), 5.23 (s, 2 H), 7.00-7.04 (m, 2H), 6.64 (d, *J* = 7.5 Hz, 1 H), 6.21–6.24 (m, 2 H), 6.17 (d, *J* = 7.5 Hz, 1 H), 7.97 (s, 1H). Anal. Calcd for $C_{19}H_{18}O_5$: C, 69.93, H, 5.56. Found: C, 70.13; H, 5.63.

General Procedure for the Synthesis of *trans*-7-Phenyl-6*H*-6a,7-dihydro [1]benzopyrano-[3,4-*c*]-[1,5]-benzothiazepine (5a).

A mixture of 3-arylidenechroman-4-one (**2a**) (200 mg, 0.84 mmol) and 2-aminothiophenol (**4a**) (106 mg, 0.84 mmol) was solubilized in ethanol/toluene (1:1) (20 mL) with 1 mL of conc. HCl with a catalytic amount of TFA (0.2 mL). The resulting solution was refluxed until TLC revealed the absence of reactants. The solvent was removed under reduced pressure, and the residue left was recrystallized to give **5a** (280 mg, 97%) as light yellow crystals, mp 170–172 ^{0}C (EtOH). IR (KBr, ν_{max}) 1602 cm^{-1} (C=N); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.09 (ddd, *J* = 12.3, 2.7, 1.6 Hz, H-6a), 3.79 (dd, *J* = 11.7,1.2 Hz, H-6"), 4.04 (dd, *J* = 11.8, 2.7 Hz, H-6'), 4.92 (d, *J* = 12.3 Hz, H-7), 7.00–8.40 (m, 13H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.1(C-6a), 59.7(C-7), 67.1(C-6), 118.0(C-4), 120.4(C-4a), 122.4(C-2), 124.4(C-8a), 125.7(C-12), 125.8(C-10), 127.2(C-1), 127.4(C-2', C-6'), 128.5(C-4'), 129.3(C-3', C- 5'), 130.4(C-9), 133.7(C-3), 135.5(C-11), 143.2(C-1'), 152.1(C-12a), 158.4(C-4a), 163.3(C-14). Anal. Calcd for $C_{22}H_{17}NOS$: C, 76.94; H, 4.99; N, 4.08. Found: C, 76.85; H, 4.82; N, 4.15.

General Procedure for the HPLC Analysis of 5a-i.

The purity of compounds (**5a-1**) was ascertained by HPLC analysis. The HPLC analysis wee performed on a Waters 484UV detector using a (S,S)Whelk-O 1 column obtained from Regis Technologies. The flow rate was 1 ml/min and the solvent composition was hexane-isopropyl in a ratio of 75:25. The compounds were detected at 254 nm.

The physical and spectral of compounds **5b-i** follow.

***trans*-7-(4'-Methoxyphenyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5b):** Colorless crystals, mp 193–195 ºC (EtOH). IR (KBr, ν_{max}): 1615.2 cm^{-1} (C=N). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.03 (ddd, *J* = 12.4, 2.7, 1.5 Hz, H-6a), 3.79 (dd, *J* = 11.9, 1.6 Hz, H-6"), 3.82 (3H, MeO-4'), 4.04 (dd, *J* = 11.9, 2.7 Hz, H-6'), 4.89 (d, *J* = 12.4 Hz, H-7), 6.86–8.38 (m, 12H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.3(6a), 55.7(MeO-4'), 59.3(C-7), 67.1(C-6), 114.6(C-4), 118.0(C-14a), 120.4(C-2), 122.4(C-8a), 124.4(C-12), 125.6(C-10), 125.8(C-1), 127.4(C-2', 6'), 128.3(C-1'), 130.3(C-3', 5'), 133.7(C-9), 135.5(C-3), 136.7(C-11), 152.1(C-12a), 158.4(C-4'), 159.7(C-4a), 163.3(C-14). Anal. Calcd for $C_{23}H_{19}NO_2S$: C, 73.97; H, 5.13; N, 3.75. Found: C, 74.11; H, 5.10; N, 3.69.

***trans*-7-(4'-Tolyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5c):** Yellow crystals, mp 153–155 ºC (EtOH-EtOAc). IR (KBr, ν_{max}): 1618 cm^{-1} (C=N). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (3H, Me-4'), 3.07 (ddd, *J* = 12.3, 2.7, 1.6 Hz, H-6a), 3.81 (dd, *J* = 11.8 Hz, 1.6 H-6"), 4.04 (dd, *J* = 11.8, 2.7 Hz, H-6'), 4.89 (d, *J* = 12.3 Hz, H-7), 7.00–8.39 (m, 12H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.6(Me-4'), 44.1(C-6a), 59.5(C-7), 67.1(C-6), 118.0(C-4), 120.4(C-14a), 122.4(C-2), 124.5(C-8a), 125.6(C-12), 125.8(C-10), 127.0(C-1), 127.4(C-2', 6'), 130.0(C-1'), 130.3(C-3', 5'), 133.7(C-9),

135.5(C-3), 138.3(C-11), 140.3(C-12a), 152.1(C-4'), 158.4(C-4a), 163.3(C-14). Anal. Calcd for $C_{23}H_{19}NOS$: C, 77.28; H, 5.36; N, 3.92. Found: C, 77.18; H, 5.29; N, 3.89.

***trans*-7-(Thiophen-2-yl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5d):** Yellow solid, mp 136–138 ºC (EtOH). IR (KBr, ν_{max}): 1613 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 2.97 (ddd, *J* = 12.0, 2.7, 1.5 Hz, H-6a), 3.99 (dd, *J* = 11.9, 1.6 Hz, H-6"), 4.10 (dd, *J* = 11.8, 2.7 Hz, H-6'), 5.23 (d, *J* = 12.0 Hz, H-7), 6.96–8.38 (m, 11H, thiophene and ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 45.2(C-6a), 55.2(C-7), 67.2(C-6), 118.1(C-4), 120.4(C-14a), 122.5(C-2), 123.3(C-8a), 125.4(C-10, C-12), 125.5(C-1), 125.6(C-4'), 126.9(C-2'), 127.4(C-3'), 130.7(C-9), 133.8(C-3), 136.1(C-11), 146.8(C-1'), 152.2(C-12a), 158.4(C-4a), 162.9(C-14). Anal. Calcd for $C_{20}H_{15}NOS_2$: C, 68.74; H, 4.33; N, 4.01. Found: C, 68.68; H, 4.26; N, 3.97.

***trans*-7-(4'-Chlorophenyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5e):** Colorless crystals mp 178–180 ºC (EtOH). IR (KBr, ν_{max}): 1617 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 3.04 (ddd, *J* = 12.2, 2.7, 1.6 Hz, H-6a), 3.77 (dd, *J* = 11.8, 1.6 Hz, H-6"), 4.05 (dd, *J* = 11.9, 2.5 Hz, H-6'), 4.88 (d, *J* = 12.2 Hz, H-7), 7.00–8.39 (m, 12H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.0(C-6a), 58.9(C-7), 67.0(C-6), 118.1(C-4), 120.4(C-14a), 122.6(C-2), 124.0(C-8a), 125.8(C-12), 126.0(C-10), 127.5(C-1), 128.6(C-2', 6'), 129.5(C-3', 5'), 130.6(C-9), 133.9(C-3), 134.2(C-4'), 135.5(C-11), 141.7(1'), 152.2(C-12a), 158.4(C-4a), 163.0(C-14). Anal. Calcd for $C_{22}H_{16}NClS$: C, 69.92; H, 4.27; N, 3.71. Found: C, 69.97; H, 4.35; N, 4.78.

***trans*-7-(4'-Bromophenyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5f):** Light yellow solid, mp 153-155 ºC (EtOH). IR (KBr, ν_{max}): 1618 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 3.05 (ddd, *J* = 12.1, 2.7, 1.6 Hz, H-6a), 3.76 (dd, *J* = 11.7, 1.6 Hz, H-6"), 4.05 (dd, *J* = 11.8, 2.5 Hz, H-6'), 4.87 (d, *J* = 12.1 Hz, H-7), 7.05–8.41 (m, 12H, Ar H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.0(C-6a), 58.7(C-7), 67.2(C-6), 118.4(C-4), 120.1(C-14a), 122.5(C-2), 124.3(C-8a), 125.6(C-12), 126.2(C-10), 127.8(C-1), 128.4(C-2', 6'), 129.8(C-3', 5'), 130.2(C-9), 133.6(C-3), 134.5(C-4'), 135.8(C-11), 141.6(C-1'), 152.7(C-12a), 158.5(C-4a), 163.2(C-14). Anal. Calcd for $C_{22}H_{16}NOBrS$: C, 62.56; H, 3.82; N, 3.32. Found: C, 62.54; H, 3.79; N, 3.30.

***trans*-7-(2',5'-Dimethoxyphenyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5g):** Yellow crystals, mp 180–183 ºC (EtOH). IR (KBr, ν_{max}): 1615 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 3.01 (ddd, *J* = 12.4, 2.7, 1.6 Hz, H-6a), 3.73 (3H, OMe), 3.74 (3H, OMe), 3.81 (dd, *J* = 11.9, 1.6 Hz, H-6"), 3.90 (dd, *J* = 11.8, 2.7 Hz, H-6'), 4.09 (d, *J* = 12.4 Hz, H-7), 6.75 (s, 1H, Ar H), 6.79–8.37 (m, 8H, Ar H), 8.38 (d, *J* = 6.8 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.1(C-6a), 56.0(C-7), 61.2(C-6), 67.3(C-4), 112.9(C-4a), 113.7(C-2), 118.0(C-8a), 120.5(C-12), 122.2(C-10), 123.7(C-5'), 125.3(C-1)), 125.6(C-2'), 127.4(C-9), 130.2(C-3), 133.6(C-11), 135.7(C-1'), 152.2(C-12a), 154.0(C-3',

6'), 158.5(C-4a), 163.5(C-14). Anal. Calcd for $C_{24}H_{21}NO_3S$: C, 71.44; H, 5.25; N, 3.47. Found: C, 71.49; H, 5.31; N, 4.51.

***trans*-7-(3', 4', 5'-Trimethoxyphenyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5h):** Light yellow solid, mp 151–153 ºC (EtOH). IR (KBr, ν_{max}): 1612 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 3.01 (ddd, *J* = 12.4, 2.7, 1.6 Hz, 1H, H-6a), 3.73 (3H, OMe), 3.74 (3H, OMe), 3.74 (3H, OMe), 3.81 (dd, *J* = 11.9, 1.6 Hz, 1H, H-6"), 3.90 (dd, *J* = 11.9, 2.7 Hz, 1H, H-6'), 4.09 (d, *J* = 12.3 Hz, 1H, H-7), 6.75 (s, 1H, ArH), 6.79–8.37 (m, 8H, Ar H), 8.38 (d, *J* = 6.8 Hz, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.1(C-6a), 56.5(MeO x 3), 60.0(C-7), 67.1(C-6), 104.0(C-4), 118.0(C-14a), 120.4(C-2), 122.4(C-8a), 124.4(C-12), 125.5(C-10), 125.8(C-1), 127.3(C-2', 6'), 130.6(C-4'), 133.8(C-9), 135.4(C-3), 138.0(C-11), 139.0(C-1'), 152.3(C-3', 5'), 153.7(C-12a), 158.5(C-4a), 163.3(C-14). Anal. Calcd for $C_{25}H_{23}NO_4S$: C, 69.26; H, 5.35; N, 3.23. Found: C, 69.29; H, 5.38; N, 3.26.

***trans*-7-(2',3',4'-Trimethoxyphenyl)-6*H*-6a,7-dihydro[1]benzopyrano[3,4-*c*][1,5]benzothiazepine (5i):** Light yellow crystals, mp 158–160 ºC (EtOH). IR (KBr, ν_{max}): 1617 cm^{-1} (C=N). ^1H NMR (400 MHz, $CDCl_3$): δ 3.05 (ddd, *J* = 12.4, 2.7, 1.6 Hz, H-6a), 3.82 (3H, OMe), 3.84 (3H, OMe), 3.85 (3H, OMe), 3.87 (dd, *J* = 11.9, 1.6 Hz, H-6"), 4.06 (dd, *J* = 11.9, 2.6 Hz, H-6'), 4.79 (d, *J* = 12.4 Hz, H-7), 6.64 (d, *J*= 8.6 Hz, 1H, ArH), 6.86 (d, *J* = 8.5 Hz, 1H, ArH), 7.00–8.39 (m, 8H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.2(C-6a), 56.3(MeO x 3), 61.1(C-7), 67.2(C-6), 108.4(C-4), 118.0(C-14a), 120.4(C-2), 120.7(C-8a), 122.3(C-12), 123.9(C-10), 125.4(C-3'), 125.6(C-1'), 127.4(C-2'), 129.2(C-1), 130.2(C-9), 133.7(C-3), 135.8(C-11), 142.5(C-5'), 150.9(C-4'), 152.2(C-6'), 153.5(C-12a), 158.4(C-4a), 163.3(C-14). Anal. Calcd for $C_{25}H_{23}NO_4S$: C, 69.26; H, 5.35; N, 3.23. Found: C, 69.30; H, 5.38; N, 3.26.

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