A Facile Synthesis of Novel Dihydroindeno[1,2-e][1,2,4]triazolo-[3,4-b][1,3,4]thiadiazines Using HTIB

Om Prakash,[a]* Deepak Kumar Aneja,[b] Deepak Wadhwa,[b] Ravi Kumar,[c] and Sanjiv Arora[b]

[a]Institute of Pharmaceutical Sciences, Kurukshetra University, Kurukshetra 136119Haryana, India
[b]Department of Chemistry, Kurukshetra University, Kurukshetra 136119Haryana, India
[c]Department of Chemistry, Dyal Singh College, Karnal, Haryana, India
*E-mail: dromprakash50@rediffmail.com

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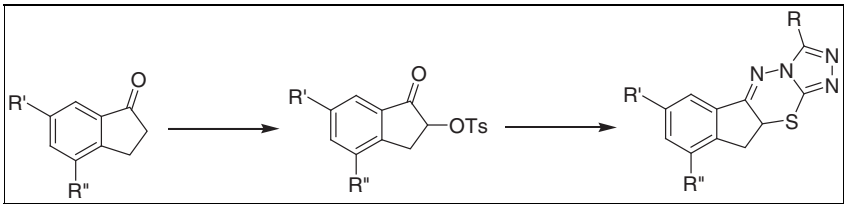

The synthesis of a series of 21 novel 3-alkyl/aryl-7/9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4]thiadiazines (**4**) has been achieved by the cyclocondensation between 4/6-methyl-2-tosyloxy-1-indanones (**2**) and 3-alkyl/aryl-4-amino-5-mercapto-1,2,4-s-triazoles (**3**). 4/6-Methyl-2-tosyloxy-1-indanones (**2**) were readily accessible through hypervalent iodine oxidation of 4/6-methyl-1-indanones using [(hydroxy)tosyloxyiodo]benzene (HTIB, Koser's reagent) in acetonitrile.

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INTRODUCTION

Synthesis of nitrogen containing heterocyclic systems has been attracting increasing interest over the past decade because of their utility in various applications. Compounds bearing the 1,2,4-triazole ring are well known as powerful antihypertensive [1], antimicrobial [2], anticonvulsant [3], antidepressant [4], analgesic [5], and antitumorial [6] agents. Moreover, 1,2,4-triazoles and 1,2,4-triazolo[3,4-*b*][1,3,4]thiadiazines (**A**) derived from 4-amino-3-mercapto-1,2,4-triazoles are associated with diverse pharmacological activities [7–11].

In view of the above facts, it was considered worthwhile to synthesize novel polycyclic fused thiadiazine compounds containing 1,2,4-triazoles of the type **4**, which were modified from 6-phenyl-7*H*-[1,2,4]triazolo[3,4-b][1,3,4] thiadiazines (**A**) as shown in **Figure** 1 [12].

The retrosynthetic strategy outlined in the **Figure** 2 provided us the basis of this work. It was anticipated that the reaction between α-functionalized indan-1-ones (**2**) and 3-alkyl/aryl-4-amino-5-mercapto-1,2,4-s-triazoles (**3**) might lead to cyclocondensation reaction thereby giving target compounds 3-alkyl/aryl-7/9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4-b][1,3,4]thiadiazines (**4**). The α-substitutent in the case of **2** could be halogen, tosyloxy, etc. However, due to the hazardous associated with the halogenation of ketones, instability and toxicity of α-haloketones, alternate approach avoiding these α-haloketones is always preferred. Our previous work [13,14] in the area of I(III) reagents [15] has established that α-tosyloxy ketones, which were readily accessible through the oxidation of α-ketones with HTIB, can offer a superior alternate to α-haloketones.

RESULTS AND DISCUSSION

Synthetic route for 3-alkyl/aryl-7/9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4-b][1,3,4]thiadiazines (**4a–u**) is outlined in **Scheme** 1. Initially, cyclocondensation was carried out starting from 2-tosyloxy-1-indanone (**2a)** and 4-amino-5-mercapto-1,2,4-s-triazoles (**3a)** in ethanol to afford the desired product **4a** in 90% yield (**Scheme** 1). Then we carried out the reaction of different 4/6-methyl-2-tosyloxy-1-indanones (**2b–c**) with 3-alkyl/aryl-4-amino-5-mercapto-1,2,4-s-triazoles (**3a–g**) under similar conditions. It was found that the method in all the cases afforded the desired products **4b–u** in good to excellent yield.

The α-tosyloxyketones **2a–c** were prepared by the oxidation of 1-indanones (**1a–c**) with HTIB in dichloromethane. 3-Alkyl/aryl-4-amino-5-mercapto-1,2,4-s-triazoles (**3a–g)** needed for the present study, were prepared by reported methods [16].

The structures of all the new α-tosyloxyketones **2a–c** and the final products **4a–u** were thoroughly characterized by analyzing their spectral (IR, ^{1}H NMR, ^{13}C NMR) as well as elemental analysis data.

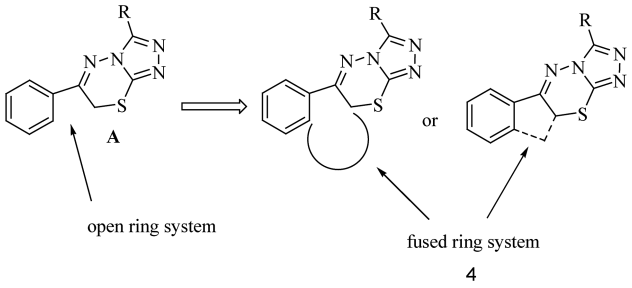


Figure 1. Synthetic plan.

CONCLUSIONS

In this article, we synthesized a series of 21 novel 3-alkyl/aryl-7/9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4]thiadiazines (**4**) from the cyclocondensation between 4/6-methyl-2-tosyloxy-1-indanones (**2**) and 3-alkyl/aryl-4-amino-5-mercapto-1,2,4-s-triazoles (**3**). 4/6-methyl-2-tosyloxy-1-indanones (**2**) were readily accessible through hypervalent iodine oxidation of 4/6-methyl-1-indanones (**1**) using HTIB.

EXPERIMENTAL

Melting points were taken on slides in an electrical apparatus Labindia visual melting range apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1800 FTIR spectrophotometer. ^{1}HNMR and ^{13}CNMR spectra were recorded on Bruker 300 MHz instrument using TMS as an internal standard. All other chemicals used as such as were procured from supplier.

Synthesis of 4/6-methyl-2-tosyloxy-1-indanones (2a-c) ***Typical procedure.*** To a stirred solution of 1-indanone **(1a,** 5g, 38 mmol) in 100-mL acetonitrile, HTIB (16.45g, 41.9 mmol) was added and the reaction mixture was refluxed for 5 h. After that excess of acetonitrile was distilled off under reduced pressure and residual mass was crystallized from ethanol. The product was further washed with cold ethanol and dried to give pure 2-tosyloxy-1-indanone (**2a**, 9.72g, 83%).

2-Tosyloxy-1-indanone (2a). Dark brown; mp 110–111°C; yield 83%; IR (ν_{max}, cm^{-1}): 1728(C O), 1597, 1466, 1404, 1373, 1296, 1188, 1057; ^{1}HNMR (δ, $CDCl_3$, 300 MHz, ppm): 2.484 (s, 3H, CH_3), 3.247–3.320 (dd, 1H, J_1 = 4.5Hz, J_2 = 17.4 Hz), 3.628–3.712 (dd, 1H, J_2 = 17.4 Hz, J_3 = 7.8 Hz), 5.127–5.169 (dd, 1H, J_1 = 4.5 Hz, J_3 = 7.8 Hz), 7.391–7.462 (m, 4H), 7.642–7.690 (m, 1H), 7.735–7.760 (d, 1H, J = 7.5), 7.929–7.955 (d, 2H, J = 7.8 Hz); ^{13}C NMR: 21.70, 30.88, 33.89, 124.68, 126.66, 128.21, 128.42, 129.87, 133.28, 133.64, 136.33, 145.19, 149.95, 197.52. *Anal.* Calcd. for $C_{16}H_{14}O_4S$: C, 63.56; H, 4.67. Found: C, 63.54; H, 4.65. The other derivatives **2b–c** were synthesized by adopting the similar procedure.

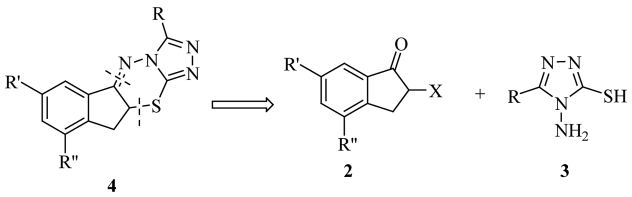
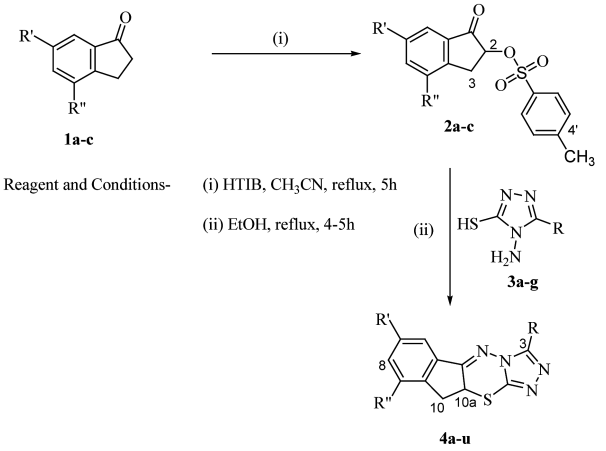


Figure 2. Retrosynthetic analysis.

Scheme 1. Synthesis of 3-alkyl/aryl-7/9-methyl-10,10a-dihydroindeno [1,2-e][1,2,4] triazolo[3,4-b][1,3,4]thiadiazines (**4a–u**).



Compound	R	R′	R″	Compound	R	R′	R″
2a	-	H	H	**4j**	Et	CH_3	H
2b	-	CH_3	H	**4k**	Pr	CH_3	H
2c	-	H	CH_3	**4l**	*i*-Pr	CH_3	H
4a	H	H	H	**4m**	C_6H_5	CH_3	H
4b	CH_3	H	H	**4n**	4-MeC_6H_4	CH_3	H
4c	Et	H	H	**4o**	H	H	CH_3
4d	Pr	H	H	**4p**	Me	H	CH_3
4e	*i*-Pr	H	H	**4q**	Et	H	CH_3
4f	C_6H_5	H	H	**4r**	Pr	H	CH_3
4g	4-MeC_6H_4	H	H	**4s**	*i*-Pr	H	CH_3
4h	H	CH_3	H	**4t**	C_6H_5	H	CH_3
4i	Me	CH_3	H	**4u**	4-MeC_6H_4	H	CH_3

6-Methyl-2-tosyloxy-1-indanone (2b). Light brown; mp 113–114°C; yield 81%; IR (ν_{max}, cm^{-1}): 1728 (C O), 1597, 1489, 1427, 1381, 1281, 1180, 1065; ^{1}HNMR (δ, $CDCl_3$, 300 MHz, ppm): 2.402 (s, 3H, CH_3), 2.485 (s, 3H, CH_3), 3.192–3.262 (dd, 1H, J_1 = 3.9 Hz, J_2 = 16.8 Hz), 3.578–3.661 (d, 1H, J_2 = 16.8 Hz, J_3 = 7.8 Hz), 5.107–5.148 (m, 1H), 7.317–7.344 (d, 1H, J = 8.1 Hz), 7.389–7.416 (d, 2H, J = 8.1 Hz), 7.469–7.541 (m, 2H), 7.927–7.954 (d, 2H, J = 8.1 Hz); ^{13}CNMR: 21.14 (CH_3), 21.74 (CH_3), 33.58, 78.57, 124.55, 126.34, 128.23, 129.88, 133.71, 137.63, 138.57, 145.17, 147.30, 197.62 (CO). *Anal.* Calcd. for $C_{17}H_{16}O_4S$: C, 64.54; H, 4.67. Found: C, 64.52; H, 4.65.

4-Methyl-2-tosyloxy-1-indanone (2c). Light brown; mp 141–142°C; yield 83%; IR (ν_{max}, cm^{-1}): 1728 (C O), 1597, 1489, 1435, 1358, 1281, 1180, 1095; ^{1}HNMR (δ, $CDCl_3$, 300 MHz, ppm): 2.352 (s, 3H, CH_3), 2.486 (s, 3H, CH_3), 3.149–3.221 (dd, 1H, J_1 = 4.2Hz, J_2 = 17.4 Hz), 3.594–3.678 (d, 1H, J_2 = 17.4 Hz, J_3 = 7.8 Hz), 5.116–5.157 (dd, 1H, J_1 = 4.2 Hz, J_3 = 7.8 Hz), 7.307–7.357 (m, 1H), 7.393–7.420 (d, 2H, J = 8.1 Hz),

7.468–7.493 (d, 1H, J = 7.5 Hz), 7.573–7.598 (d, 1H, J = 7.5 Hz); 7.939–7.966 (d, 2H, J = 8.1 Hz) ^{13}CNMR: 17.80, 21.14, 32.75, 78.26, 122.03, 128.25, 128.50, 129.89, 133.12, 133.46, 136.04, 136.83, 145.22, 149.07, 197.94 (CO). *Anal*. Calcd. for $C_{16}H_{14}O_4S$: C, 64.54; H, 4.67. Found: C, 65.53; H, 4.64.

Synthesis of 3-alkyl/aryl-7/9-methyl-10,10a-dihydroindeno [1,2-e][1,2,4]triazolo [3,4–b][1,3,4] thiadiazines (4a–u). Typical procedure. To a solution of **2a** (1g, 3.31mmol) in 30 ml ethanol was added equimolar amount of 4-amino-5-mercapto-1,2,4-triazole (**3a,** 0.384g) and the reaction mixture was refluxed for 4–5 h. After that the reaction mixture was poured into crushed ice (100 g), followed by basification with ammonia solution. The solid product thus obtained was filtered, washed with water, and recrystalized from aqueous ethanol to give pure 10,10a-dihydroindeno [1,2-e][1,2,4]triazolo[3,4-b][1,3,4]thiadiazine (**4a,** 0.67g, 90%).

10,10a-Dihydroindeno[1,2-e][1,2,4]triazolo[3,4–b][1,3,4] thiadiazine (4a). MP 215–216°C; yield 90%; IR (ν_{max}, cm^{-1}): 1682, 1628, 1605, 1481, 1443, 1366, 1304, 1281, 1287, 1188, 1157, 1095; ^{1}HNMR (δ, $CDCl_3$, 300 MHz, ppm): 3.026–3.193 (m, 1H), 3.731 (m, 1H), 4.398–4.414 (m, 1H), 7.494–7.601 (m, 3H), 7.954 (m, 1H), 8.758 (s, 1H); ^{13}CNMR: 35.06, 37.01, 123.67, 125.85, 128.72, 132.92, 133.90, 147.56, 163.15. *Anal*. Calcd. for $C_{11}H_8N_4S$: C, 57.88; H, 3.53; N, 24.54. Found: C, 57.80; H, 3.50; N, 24.44. All other derivatives **4a–u**, with the exception of **4k** were synthesized by adopting the similar procedure.

In the case of **4k**, after pouring the reaction mixture into crushed ice and basification with ammonia solution, the aqueous mixture was extracted with dichloromethane (3 × 50 mL) and the combined organic layer was dried over anhydrous sodium sulphate. Finally, solvent was removed by distillation and residual mass was obtained, which solidified on standing for 2–3 days. ^{1}H NMR showed that the compound was satisfactorily pure.

3-Methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4–b] [1,3,4] thiadiazine (4b). MP 154–155°C; yield 92%; IR (ν_{max}, cm^{-1}): 1612, 1535, 1466, 1435, 1373, 1304, 1203, 1149, 1095; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.633 (s, 3H, CH_3), 3.127–3.177 (m, 1H), 3.705–3.759 (m, 1H), 4.163 (bs, 1H), 7.489–7.599 (m, 3H), 7.981 (bs, 1H); ^{13}C NMR: 18.40, 34.95, 36.28, 123.57, 125.80, 128.53, 133.33, 133.57, 147.42. *Anal*. Calcd. for $C_{12}H_{10}N_4S$: C, 59.48; H, 4.16; N, 23.12. Found: C, 57.44; H, 4.10; N, 23.10.

3-Ethyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4–b] [1,3,4] thiadiazine (4c). MP 115–116°C; yield 90%; IR (ν_{max}, cm^{-1}): 1713, 1605, 1528, 1458, 1381, 1311, 1273, 1188, 1157, 1095; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.431–1.481 (t, 3H, CH_3), 2.946–3.193 (m, 3H), 3.677–3.763 (dd, 1H, J_1 = 8.4 Hz, J_2 = 17.4 Hz), 4.153–4.243 (m, 1H), 7.496 (m, 2H), 7.580–7.627 (m, 1H), 7.979–8.005(d, 1H, J = 7.8Hz); ^{13}C NMR: 11.30, 18.40, 34.95, 36.28, 123.57, 125.80, 128.53, 133.33, 133.57, 147.42. *Anal*. Calcd. for $C_{13}H_{12}N_4S$: C, 60.91; H, 4.72; N, 21.86. Found: C, 60.88; H, 4.67; N, 21.78.

3-Propyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4–b] [1,3,4] thiadiazine (4d). MP 129–130°C; yield 85%; IR (ν_{max}, cm^{-1}): 1713, 1605,1528, 1458, 1389, 1311, 1265, 1196, 1149, 1095, 1057, 1026; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.069 (m, 3H, CH_3), 1.886 (m, 2H, CH_2), 2.975 (m, 2H, CH_2), 3.127–3.160 (m, 1H), 3.696 (m, 1H), 4.166(m, 1H), 7.475–7.578 (m, 3H), 7.980 (m, 1H); ^{13}C NMR: 13.84, 20.48, 26.57, 34.94, 36.29, 123.56, 125.80, 128.52, 133.52, 133.58, 139.32, 147.43, 154.26, 162.61. *Anal*. Calcd. for $C_{14}H_{14}N_4S$: C, 62.20; H, 5.22; N, 20.72. Found: C, 62.17; H, 5.18; N, 20.69.

3-Isopropyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4–b][1,3,4] thiadiazine (4e). MP 114–115°C; yield 70%; IR (ν_{max}, cm^{-1}): 1713, 1605, 1520, 1458, 1389, 1304, 1196, 1157, 1095; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.402–1.426 (d, 3H, CH_3), 1.491–1.502 (d, 3H, CH_3), 3.086–3.161 (dd, 1H, J_1 = 5.4 Hz, J_2 = 17.1 Hz), 3.378–3.448 (m, 1H), 3.662–3.746 (m, 1H), 4.149–4.195 (dd, 1H, J_1 = 5.4 Hz, J_3 = 8.4 Hz), 7.415–7.489 (m, 2H), 7.560–7.585 (d, 1H, J = 7.5 Hz), 7.951–7.976 (d, 1H, J = 7.5 Hz); ^{13}C NMR: 19.79, 20.81, 25.50, 34.95, 36.21, 123.52, 125.83, 128.52, 133.31, 133.60, 139.63, 147.47, 158.40, 162.11. *Anal*. Calcd. for $C_{14}H_{14}N_4S$: C, 62.20; H, 5.22; N, 20.72. Found: C, 62.18; H, 5.18; N, 20.66.

3-Phenyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4–b] [1,3,4] thiadiazine (4f). MP 214–215°C; yield 88%; IR (ν_{max}, cm^{-1}): 1597, 1466, 1366, 1296, 1196, 1165, 1103, 1072, 1026; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 3.163–3.220 (m, 1H), 3.731–3.815 (dd, 1H, J_1 = 8.1Hz, J_2 = 17.1Hz), 4.232 (bs, 1H), 7.489–7.612 (m, 6H); 7.992–8.015(m, 1H), 8.209(m, 2H); ^{13}C NMR: 34.98, 35.86, 123.78, 125.87, 126.21, 128.25, 128.57, 128.61, 130.23, 133.21, 133.81, 140.97, 147.63, 152.18, 163.05. *Anal*. Calcd. for $C_{17}H_{12}N_4S$: C, 67.08; H, 3.97; N, 18.41. Found: C, 67.02; H, 3.93; N, 18.38.

3-(p-Tolyl)-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4–b] [1,3,4] thiadiazine (4g). MP 115–116°C; yield %; IR (ν_{max}, cm^{-1}): 1705, 1605, 1458, 1350, 1296, 1157, 1065, 1018; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.438 (s, 3H, CH_3), 3.161–3.206 (m, 1H), 3.755 (bs, 1H), 4.233 (bs, 1H), 6.785–8.097 (m, 8H); ^{13}C NMR: 21.53, 34.98, 35.84, 123.10, 123.78, 125.86, 126.42, 128.28, 128.60, 129.35, 129.80, 133.20, 133.81, 140.06, 140.91, 142.93, 147.63, 152.32. *Anal*. Calcd. for $C_{18}H_{14}N_4S$: C, 67.90; H, 4.43; N, 17.60. Found: C, 67.86; H, 4.41; N, 17.55.

7-Methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4-b] [1,3,4]thiadiazine (4h). MP 208–209°C; yield 78%; IR (ν_{max}, cm^{-1}): 1612, 1481, 1443, 1358, 1288, 1234, 1188, 1149, 1034; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.480 (s, 3H, CH_3), 3.117–3.188 (dd, 1H, J_1 = 4.5 Hz, J_2 = 16.8 Hz), 3.728–3.811 (dd, 1H, J_2 = 16.8 Hz, J_3 = 8.1 Hz), 4.560 (bs, 1H), 7.361–7.388 (d, 1H, J = 8.1 Hz), 7.467–7.492 (d, 1H, J = 8.1 Hz), 7.786 (s, 1H), 8.918 (s, 1H); ^{13}C NMR: 21.28, 34.77, 37.20, 123.78, 125.57, 135.53, 139.96, 142.35, 146.62, 163.62. *Anal*. Calcd. for $C_{12}H_{10}N_4S$: C, 59.48; H, 4.16; N, 23.12. Found: C, 59.44; H, 4.10; N, 23.09.

3-Methyl-7-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4] thiadiazine (4i). MP 233–234°C; yield 80%; IR (ν_{max}, cm^{-1}): 1582, 1535, 1466, 1373, 1311, 1257, 1219, 1188, 1149, 1041; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.467(s, 3H, CH_3), 2.627 (s, 3H, CH_3), 3.047–3.122 (dd, 1H, J_1 = 5.7 Hz, J_2 = 16.8 Hz), 3.620–3.704 (dd, 1H, J_2 = 16.8 Hz, J_3 = 8.4 Hz), 4.117–4.163 (dd, 1H, J_1 = 5.7 Hz, J_3 = 8.4 Hz), 7.341–7.7.368 (d, 1H, J = 7.4 Hz), 7.397–7.423 (d, 1H, J = 7.4 Hz), 7.784 (s, 1H) ; ^{13}C NMR: 10.36,

21.28, 34.59, 36.56, 123.55, 125.49, 133.28, 134.94, 138.71, 139.49, 144.81, 151.00, 162.56. *Anal*. Calcd. for $C_{13}H_{12}N_4S$: C, 60.91; H, 4.72; N, 21.86. Found: C, 60.88; H, 4.68; N, 21.81.

3-Ethyl-7-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4-b][1,3,4] thiadiazine (4j). MP 180–181°C; yield 88%; IR (ν_{max}, cm^{-1}): 1666, 1612, 1528, 1466, 1389, 1311, 1257, 1188, 1149, 1119, 1057, 1003; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.474 (s, 3H, CH_3), 2.868 (bs, 3H), 3.011–3.125 (m, 3H), 3.659–3.738 (dd, 1H, J =7.2 Hz, J = 16.5 Hz), 4.287 (bs, 1H), 7.356–7.444 (m, 2H), 7.785 (s, 1H); ^{13}C NMR: 11.21, 21.30, 34.69, 36.50, 123.78, 125.57, 135.53. *Anal*. Calcd. for $C_{14}H_{14}N_4S$: C, 62.20; H, 5.22; N, 20.72. Found: C, 62.15; H, 5.16; N, 20.68.

3-Propyl-7-methyl-10,10a-dihydroindeno[1,2-e][1,2,4] triazolo[3,4-b][1,3,4] thiadiazine (4k). Semisolid; yield 67%; IR (ν_{max}, cm^{-1}): 1612, 1582, 1528, 1458, 1389, 1281, 1219, 1180, 1119, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.050–1.098 (t, 3H, CH_3, J = 7.2 Hz), 1.838–1.938 (sextet, 2H, CH_2), 2.475 (s, 3H, CH_3), 2.931–3.122 (m, 3H), 3.624–3.707 (dd, 1H, J = 8.1 Hz, J = 16.8 Hz), 4.140–4.187 (dd, 1H, J = 5.7 Hz, J = 8.4 Hz), 7.343–7.425 (d, 1H, J = 8.1 Hz), 7.665–7.692 (d, 1H, J = 8.1 Hz), 7.781 (s, 1H); ^{13}C NMR: 13.88, 20.48, 21.28, 26.52, 34.61, 36.51, 123.55, 125.50, 125.92, 128.54, 133.29, 134.98, 138.71, 144.85, 154.22, 162.59. *Anal*. Calcd. for $C_{15}H_{16}N_4S$: C, 63.35; H, 5.67; N, 19.70. Found: C, 63.31; H, 5.61; N, 19.66.

3-Isopropyll-7-methyl-10,10a-dihydroindeno[1,2-e][1,2,4] triazolo[3,4-b][1,3,4]thiadiazine (4l). MP 150–151°C; yield 69%; IR (ν_{max}, cm^{-1}): 1612, 1520, 1458, 1389, 1311, 1281, 1196, 1157, 1095, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.411–1.434 (d, 3H, CH_3), 1.497–1.520 (d, 3H, CH_3), 2.455 (s, 3H, CH_3), 3.026–3.100 (dd, 1H, J_1 = 5.4 Hz, J_2 = 16.8 Hz), 3.373–3.488 (m, 1H), 3.620–3.704 (dd, 1H, J_2 = 16.8 Hz, J_3 = 8.4 Hz), 4.159–4.205 (m, 1H), 7.331–7.412 (m, 2H), 7.752 (s, 1H); ^{13}C NMR: 20.29, 21.05, 21.26, 25.49, 34.63, 36.45, 123.49, 125.33, 133.25, 135.04, 138.70, 139.92, 144.93, 158.27, 162.60. *Anal.* Calcd. for $C_{15}H_{16}N_4S$: C, 63.35; H, 5.67; N, 19.70. Found: C, 63.30; H, 5.64; N, 19.68.

3-Phenyl-7-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4] thiadiazine (4m). MP 218–219°C; yield 79%; IR (ν_{max}, cm^{-1}): 1612, 1574, 1458, 1373, 1304, 1219, 1180, 1149, 1119, 1080, 1041, 1011; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.475 (s, 3H, CH_3), 3.091–3.164 (dd, 1H, J_1 = 4.8 Hz, J_2 = 16.8 Hz), 3.679–3.763 (dd, 1H, J_2 = 16.8 Hz, J_3 = 8.4 Hz), 4.191–4.236 (m, 1H), 7.363–7.441 (m, 2H), 7.543–7.564 (m, 3H), 7.784 (s, 1H), 8.194–8.213 (m, 2H); ^{13}C NMR: 21.28, 34.64, 36.10, 123.69, 125.55, 126.18, 128.27, 128.61, 130.24, 135.16, 138.80, 141.14, 145.00, 163.22. *Anal*. Calcd. for $C_{18}H_{14}N_4S$: C, 67.90; H, 4.43; N, 17.60. Found: C, 67.85; H, 4.39; N, 17.56.

3-(p-Tolyl)-7-methyl-10,10a-dihydroindeno[1,2-e][1,2,4] triazolo[3,4-b][1,3,4] thiadiazine (4n). MP 150–151°C; yield 83%; IR (ν_{max}, cm^{-1}): 1612, 1489, 1458, 1350, 1288, 1173, 1119, 1065, 1011; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.419 (s, 6H, $CH_3 \times 2$), 3.129–3.393 (m, 1H), 3.571–3.852 (m, 1H), 4.583 (bs, 1H), 7.100 (m, 1H), 7.266–8.071 (m, 8H); ^{13}C NMR: 21.14, 21.71, 34.66, 36.01, 125.58, 126.43, 128.23, 128.49, 129.48, 129.83, 142.98, 145.16. *Anal.* Calcd. for $C_{19}H_{16}N_4S$: C, 68.65; H, 4.85; N, 16.85. Found: C, 68.54; H, 4.78; N, 16.78.

9-Methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo[3,4-b] [1,3,4]thiadiazine (4o). MP 207–208°C; yield 89%; IR (ν_{max}, cm^{-1}): 1597, 1481, 1443, 1373, 1288, 1149, 1065, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.377 (s, 3H, CH_3), 3.005–3.137 (m, 1H), 3.612–3.696 (dd, 1H, J = 8.1 Hz, J = 16.5 Hz), 4.207–4.250 (m, 1H), 7.312–7.415 (m, 2H), 7.620–7.777 (bs, 1H), 8.637 (s, 1H); ^{13}C NMR: 18.35, 33.92, 36.91, 121.01, 128.97, 132.60, 134.48, 135.44, 139.96, 142.25, 146.72, 163.80. *Anal*. Calcd. for $C_{12}H_{10}N_4S$: C, 59.48; H, 4.16; N, 23.12. Found: C, 59.44; H, 4.10; N, 23.08.

3-Methyl-9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4] thiadiazine (4p). MP 219–220°C; yield 91%; IR (ν_{max}, cm^{-1}): 1597, 1535, 1458, 1373, 1311, 1203, 1057; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.380 (s, 3H, CH_3), 2.636 (s, 3H, CH_3), 2.979–3.053 (dd, 1H, J_1 = 5.4 Hz, J_2 = 16.8 Hz), 3.605–3.690 (dd, 1H, J_2 = 16.8 Hz, J_3 = 8.4 Hz), 4.138–4.184 (dd, 1H, J_1 = 5.4 Hz, J_3 = 8.4 Hz), 7.398–7.412 (m, 2H), 7.80–7.85 (m, 1H) ; ^{13}C NMR: 9.80, 17.85, 33.18, 35.64, 120.25, 128.24, 132.34, 133.68, 134.96, 138.81, 146.56, 150.10, 162.97. *Anal*. Calcd. for $C_{13}H_{12}N_4S$: C, 60.91; H, 4.72; N, 21.86. Found: C, 60.85; H, 4.67; N, 21.77.

3-Ethyl-9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (4q). MP 223–225°C; yield 93%; IR (ν_{max}, cm^{-1}): 1636, 1597, 1528, 1458, 1381, 1350, 1311 1281, 1203, 1165, 1065, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.421–1.470 (t, 3H, CH_3), 2.376 (s, 3H, CH_3), 2.910–3.131 (m, 3H), 3.598–3.683 (dd, 1H, J_1 = 8.4 Hz, J_2 = 17.1 Hz), 4.145–4.190 (m, 1H), 7.390–7.403 (m, 2H), 7.799–7.825 (m, 1H); ^{13}C NMR: 11.30, 18.35, 18.41, 33.81, 36.20, 120.92, 128.82, 133.06, 134.13, 135.35, 139.50, 146.51, 155.30, 162.70. *Anal.* Calcd. for $C_{14}H_{14}N_4S$: C, 62.20; H, 5.22; N, 20.72. Found: C, 62.16; H, 5.18; N, 20.68.

3-Propyl-9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (4r). MP 80–81°C; yield 89%; IR (ν_{max}, cm^{-1}): 1597, 1520, 1458, 1389, 1342, 1304, 1273, 1203, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 0.912–1.102 (m, 3H, CH_3), 1.801–1.928 (m, 2H, CH_2), 2.245 (s, 3H, CH_3), 2.910–3.101 (m, 3H), 3.510–3.720 (m, 1H), 4.201–4.230 (m, 1H), 7.293–7.800 (m, 3H); ^{13}C NMR: 13.86, 18.36, 20.43, 26.45, 33.85, 36.19, 121.01, 128.85, 132.88, 134.35, 135.42, 139.77, 146.70, 163.42. *Anal*. Calcd. for $C_{15}H_{16}N_4S$: C, 63.35; H, 5.67; N, 19.70. Found: C, 63.30; H, 5.64; N, 19.65.

3-Isopropyl-9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4] triazolo[3,4-b][1,3,4]thiadiazine (4s). MP 187–188°C; yield 86%; IR (ν_{max}, cm^{-1}):1597, 1520, 1458, 1389, 1350, 1311, 1281, 1203, 1157, 1095, 1065, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 1.501–1.60 (m, 6H), 2.865 (s, 3H), 2.969–3.025 (m, 1H), 3.450–3.682 (m, 2H), 4.217 (bs, 1H), 7.293–7.800 (m, 3H); ^{13}C NMR: 18.35, 19.77, 20.80, 25.49, 33.83, 36.13, 120.89, 128.81, 133.01, 134.19, 135.38, 139.76, 146.60, 158.32, 162.76. *Anal*. Calcd. for $C_{15}H_{16}N_4S$: C, 63.35; H, 6.67; N, 19.70. Found: C, 63.28; H, 6.62; N, 19.65.

3-Phenyl-9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (4t). MP 255°C (dec); yield 79%; IR (ν_{max}, cm^{-1}): 1597, 1528, 1458, 1373, 1304, 1203, 1119, 1034; ^1H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.384 (s, 3H, CH_3), 3.019–3.070 (m, 1H), 3.687 (bs, 1H), 4.274 (bs, 1H), 7.441–8.612

(m, 8H); ^{13}C NMR: 18.39, 33.91, 35.79, 121.15, 128.23, 128.57, 128.90, 130.22, 132.96, 134.35. *Anal*. Calcd. for $C_{18}H_{14}N_4S$: C, 67.90; H, 4.43; N, 17.60. Found: C, 67.84; H, 4.40; N, 17.56.

3-(P-tolyl)-9-methyl-10,10a-dihydroindeno[1,2-e][1,2,4]triazolo [3,4-b][1,3,4]thiadiazine (4u). MP 290–291°C; yield 76%; IR (ν_{max}, cm^{-1}):1597, 1450, 1366, 1304, 1180, 1111, 1034; ^{1}H NMR (δ, $CDCl_3$, 300 MHz, ppm): 2.392 (s, 3H, CH_3), 2.461 (s, 3H, CH_3), 3.018–3.074 (m, 1H), 3.665–3.746 (dd, 1H, J_1 = 16.8 Hz, J_2 = 6.9 Hz), 4.263 (bs, 1H), 7.342–7.368 (d, 2H, J = 7.8 Hz), 7.417 (bs, 2H), 7.825 (bs, 1H), 8.099–8.124 (d, 2H, J = 7.8 Hz); ^{13}C NMR: 18.38, 21.56, 33.90, 35.78, 121.12, 128.21, 128.88, 129.32, 132.99, 134.33, 135.43, 140.56, 146.71, 163.51. *Anal*. Calcd. for $C_{19}H_{16}N_4S$: C, 68.65; H, 4.85; N, 16.85. Found: C, 68.60; H, 4.79; N, 16.80.

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