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5,6,7,8-Tetrahydronaphthalen-1-amine as Precursor for Thiazolidinones and Benzothiazepinones: Synthesis and Atropisomeric Relationship

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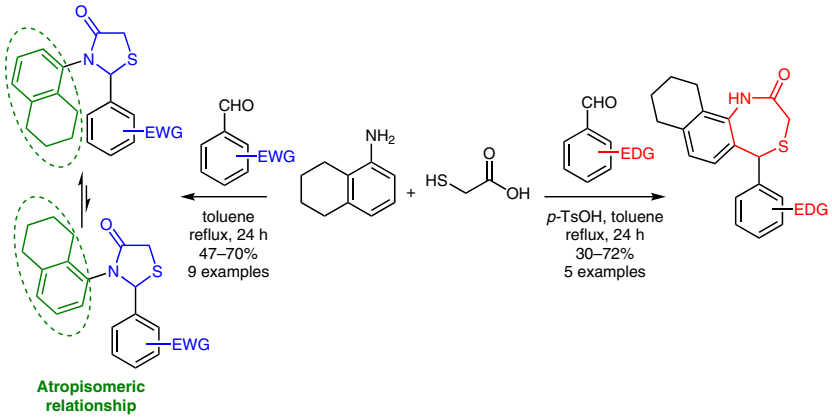

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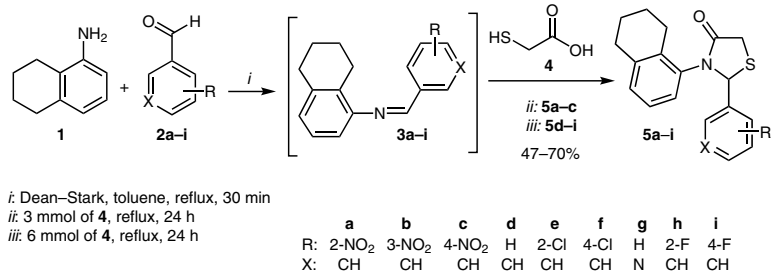
Abstract The one-pot reaction of 5,6,7,8-tetrahydronaphthalen-1-amine, mercaptoacetic acid, and arenealdehydes having strong and weak electron-withdrawing groups gave the corresponding 1,3-thiazolidin-4-ones (47–70%). When arenealdehydes bearing strong and weak electron-donating groups were used as precursors, the 1,4-benzothiazepin-2-ones were obtained (30–72%) by *p*-TsOH catalysis. All compounds are unknown and were characterized by GC-MS and NMR techniques, and available crystals by X-ray diffraction studies. The atropisomerism phenomenon was observed in several 1,3-thiazolidin-4-ones as confirmed by VTNMR method. The Tc was established as 332 K and the energy required for the interconversion of one atropisomer into another is around 16.8 kcal·mol^{-1}. Chemical quantum calculation and NOESY displayed that more stable isomer has the tetrahydronaphthalene portion below the five-ring plane. Only a small difference between isomers (–0.21 to –0.84 kcal·mol^{-1}) was observed by calculated energy.

Key words thiazolidinone, atropisomer, benzothiazepinone, chemical quantum calculation, X-ray

Thiazolidinones and their derivatives are very promising compounds because of their vast action in biological activities, such as antitubercular,[1] anticancer,[2] anti-inflammatory,[3] and as AChE and BChE inhibitors.[4] Generally, 1,3-thiazolidin-4-one synthesis is a reaction of three components: a primary amine, aldehyde or ketone, and mercaptoacetic acid. The synthesis can occur in two-steps or by multicomponent one-pot procedure that can be catalyzed or not.[5] Usually, thermal conventional heating is used most of the times, but alternative sources could also be utilized in the reaction process: ultrasound irradiation[6] or microwave energy.[7] Both methodologies with lower reaction times are faster than conventional thermal heating.

Benzothiazepinone has the same heteroatoms and a carbonyl group that are present in thiazolidinone structure, but in a seven-membered ring fused with benzene. This heterocycle also shows biological importance, among them: neuroprotection,[8] antioxidant,[9] and potential therapeutic for type II diabetes.[10] Nowadays, these heterocycles are in the pharmaceutical market acting as angina-relieving calcium channel blocker (Diltiazem), antihypertensive agent (Clentiazem), and antidepressant GABBA$_A$ blocker (Thiazesim).[11] The benzothiazepinones synthesis is reported in different ways. An approach was developed by the S-alkylation of mercaptoacetic acid with 2-aminobenzhydrol in HCl, but longer reaction times were needed (48–72 h).[12] Also, extreme conditions (–78 °C and *t*-BuLi) are required to promote *o*-lithiation of Boc-protected *p*-chloroaniline.[8,10] But, simpler procedures are currently being published such as the use of high potential microwave irradiation in a multicomponent process[9,13] or by cyclization of 2-aminothiophenol with cinnamic acid by TBAF catalysis.[11]

Our research group has explored the synthesis of 1,3-thiazolidin-4-ones,[14] 1,3-thiazinan-4-ones,[15] and thiazolidin-2,4-diones[16] in the last years. Originally, the purpose of this work was the use of 5,6,7,8-tetrahydronaphthalen-1-amine (**1**) as precursor in the synthesis of 1,3-thiazolidin-4-ones, which were expected to be powerful AChE inhibitors due to the union of heterocyclic thiazolidinone and tetrahydronaphthalene – a tacrine analogue moiety. To our surprise, when arenealdehydes bearing electron-donating

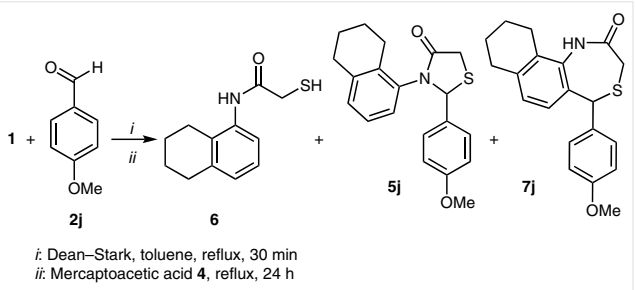


Scheme 1 Synthesis of thiazolidinones **5a–i**

groups were used, unexpected seven-membered rings (benzothiazepinones) were obtained. Interestingly, this heterocycle was not observed in our previously work.[17] Then, considering the possibility to obtain this another important class of heterocycles, the synthesis of 1,4-benzothiazepin-2-ones became another goal in this work.

We started the preparation of thiazolidinones **5a–c** from nitrobenzaldehydes **2a–c**, 5,6,7,8-tetrahydronaphthalen-1-amine (**1**), and mercaptoacetic acid (**4**), following the procedure described by Masteloto et al. (Scheme 1, conditions *ii*).[17c] For the synthesis of thiazolidinones **5d–i** an optimization was necessary, mainly because no total consumption of imine **3d–i** was observed. The optimization was monitored by TLC or GC-MS analysis. During all the process of evaluation, amine **1** and 4-fluorobenzaldehyde (**2i**) were used as model compounds, changing the following variables: (a) reactions time (24–48 h); (b) one-pot or multicomponent procedure; and (c) mercaptoacetic acid (**4**) proportion. It was found that a reaction time of 24 hours was necessary for the formation of thiazolidinones **5d–i** by the one-pot procedure using Dean–Stark apparatus and an excess of **4** (6 equiv), more than 3 equiv that was generally indicated in the literature[14] (Scheme 1, conditions *iii*). The isolation occurs by neutralization of the organic phase with saturated aqueous $NaHCO_3$. The crude products were purified by column chromatography using hexane–EtOAc (8:2) as eluent or recrystallization from ethanol (**5c** and **5d**) to afford pure compounds **5a–i** in expected yields from an aromatic amine.[17]

However, monitoring the reaction with 4-methoxybenzaldehyde (**2j**) by GC-MS, formation of three compounds was observed: the amide **6**, the expected 1,3-thiazolidin-4-one **5j**, and another compound with the same molecular ion of thiazolidinone (Scheme 2). By column chromatography both compounds were isolated in analytical quantities. The ^1H and ^{13}C NMR spectra revealed characteristic signals corresponding to amide **6** and 1,4-benzothiazepin-2-one **7j**, according to the literature.[13]

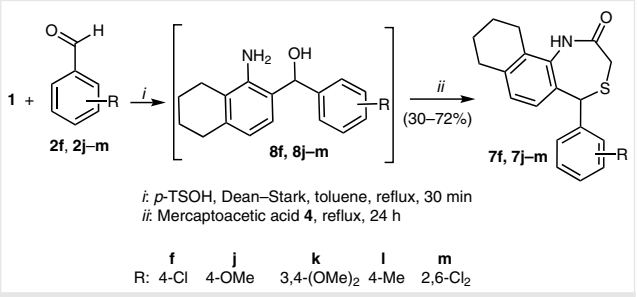


Scheme 2 Products identified by reaction with 4-methoxybenzaldehyde (**2j**)

In trying to avoid the formation of amide **6** and improve the amount of thiazolidinone **5j**, the catalyst BF_3·MeOH (50%) was added to the reaction as previously done by Gouvea et al.[17a] GC-MS showed no amide **6**, but the presence of a mixture of isomers of five- (**5j**) and seven-membered (**7j**) rings with a proportion of 1:3, respectively. The non-significant achievement of thiazolidinone **5j** might be attributed to poor reactivity of carbonyl group in **2j**.

The literature reports that in some cases, reactions between aromatic amines, mercaptoacetic acid, and arenealdehydes substituted with electron-donating groups, induce the benzothiazepinone formation.[9,13] Indeed, in our work this seven-membered heterocycle was observed when 4-methoxybenzaldehyde (**2j**) was the reactant, so we began to focus on specific benzothiazepinone synthesis.

Once catalysis with BF_3·MeOH (50%) favored the seven-membered conversion but mixed with **5j**, another acid catalyst was tested. Then, it was found that 1 mmol of *p*-TsOH worked well in a one-pot procedure. The *p*-TsOH was added together with amine **1** and aldehyde **2j** using a Dean–Stark apparatus. Mercaptoacetic acid (**4**) was added after refluxing in toluene for 30 minutes and the mixture was refluxed continuously for more than 24 hours. This condition resulted in a conversion of 90% (GC-MS) in 1,4-benzothiazepin-2-one **7j** and the yield after recrystallization from ethanol was 72%. This procedure was followed by reaction with arenealdehydes **2f**, **2j–m** (Scheme 3).



Scheme 3 Synthesis of 1,4-benzothiazepin-2-ones **7f**, **7j–m**

Tu et al.[13] described the synthesis of 1,4-benzothiazepin-2-ones from arenealdehydes with strong electron-donating substituents and weak electron-withdrawing groups (F, Cl, or Br). In extreme cases, the seven-membered formation is attributed to the strong electron-donating substituents in amines that can overcome the electron-withdrawing effect on aldehydes. In another work, Shi et al.[9] synthesized benzothiazepinone with the strong electron-withdrawing NO_2, however, the electronic nature effect of the substituent in the course of the reaction was not discussed.

When aldehydes **2a–i** bearing electron-withdrawing groups (strong and weak) were used in the presence of *p*-TsOH, only a small amount of benzothiazepinone **7** was observed. However, it was possible to isolate the benzothiazepinone **7f** in low yield (30%) with 2 equivalents of **2f** (4-Cl).

It is supposed that the thiazolidinone **5m** (R = 2,6-Cl_2) was not obtained because of the *ortho* group hindrance and only imine **3m** was identified. In turn, this *ortho* group does not affect the reaction between the intermediate **8m** and mercaptoacetic acid (**4**) leading to the benzothiazepinone **7m** formation.

A mechanism for 1,3-thiazolidin-4-one is well elucidated in literature,[5,17c] but for benzothiazepinone, a mechanism can be proposed based on the intermediate **8** reported by Tu et al.[13] The mechanism begins with the attack on carbonyl group of arenealdehyde by the *ortho* carbon of aromatic amine, affording an amino alcohol intermediate **8**, which leads to the cyclization to a seven-membered ring, 1,4-benzothiazepin-2-one **7**. In this study, it was observed that *p*-TsOH was necessary in order to improve the yields.

All synthesized compounds are novel. The initial structure analysis was by GC-MS that exhibits the associated fragments and molecular ions of the proposed structures. In the ^{1}H and ^{13}C NMR characterization, the 1,3-thiazolidinones **5a–i** and 1,4-benzothiazepin-2-ones **7f**, **7j–m** structures were differentiated by their diastereotopic hydrogens signals (H3a and H3b for seven-membered, H5a and H5b for five-membered). For 1,4-benzothiazepin-2-ones **7**, the characteristic H3a appears as a doublet (^2J = 12.4–11.8 Hz) that resonates in the range of 2.98–3.57 ppm and H3b shows signals at 2.87–2.96 ppm also as a doublet (except for H3b of **7m**, dd, ^2J = 12.4 and ^4J = 1.4 Hz). In the spectra of 1,3-thiazolidin-4-ones **5a–i**, the signals of the diastereotopic hydrogens are more deshielded. H5a resonates in the range of 3.97–4.09 ppm as a doublet or as a double doublet (**5b**) due to spatial H2 coupling and H5b resonates as doublet from 3.76 to 3.95 ppm. The ^{13}C NMR spectrum exhibits a considerable difference in the asymmetric carbon signal. The C5 in 1,4-benzothiazepin-2-ones **7f**, **7j–m** resonates from 42.8 to 47.1 ppm and C2 in 1,3-thiazolidin-4-ones **5a–i** resonates in the range of 59.9–65.1 ppm.

The ^{1}H and ^{13}C NMR spectral data are in full agreement with the proposed structures; however, an unexpected signal duplication (Figure 1) were observed in the spectra of thiazolidinones **5b**, **5c**, **5d**, **5f**, **5g**, **5h**, and **5i**. This behavior can be attributed to the occurrence of atropisomerism phenomenon, as found in 2-allylidenethiazolidin-4-ones reported by Zapol'skii et al.[18] Atropisomers are spatial isomers generated by the rotation hindrance of an axis bond and has to be considered as temperature dependent asymmetry with a wide rate of energy barrier.[19] Authors who have identified atropisomerism in their compounds cite the NMR duplication signals as the most common proof of occurrence.[20,21] In benzothiazepinones **7f**, **7j–m**, this phenomenon was not observed.

The elucidation of this behavior came from the Variable-Temperature Nuclear Magnetic Resonance (VTNMR) method. The coalescence was observed at 332.15 K (T_C) and the free energy of the transition state ($\Delta G^{\ddagger}$) for conformational interconversion was estimated using the T_C and the frequency difference ($\delta\nu$) of the particular resonances of the two conformers whose coalescence is to be monitored.[22] The rate of conversion (k_T) at a given temperature (generally in the coalescence temperature T_C) was estimated using Eyring Equation.[22c] The data are then analyzed using an Arrhenius type procedure in order to obtain activation parameters. Equations and details are given in the Supporting Information (SI).

As an example, the ^{1}H NMR spectrum of compound **5c** is shown in Figure 1 and exhibits peak multiplicity (in a range of 3.84 to 3.95 ppm for H5B and H5B′; and in a range of 4.10 to 4.20 ppm for H5A and H5A′) as a result of slow to intermediate exchange between conformational isomers (compounds **5c** and **5c′**). Quantification of the interconversion of isomers involves the monitoring of the disappearance of the peak corresponding to the two isomers (i.e., HA and HA′ – HB, and HB') upon heating, these signals broaden, coalesce, and finally sharpen as the rate of exchange increases. Thus, through ^{1}H NMR experiments in DMSO-d_6 as part of the coalescence method, we measured the energy barriers for interconversion of a conformer. Data showed that the energy required for the interconversion of one isomer into another is around 16.8 kcal·mol^{-1} (see Table S1 in the SI). This energy is high and sufficient to impair the rotation of axis bond, but low to permit the isolation of isomers at room temperature.

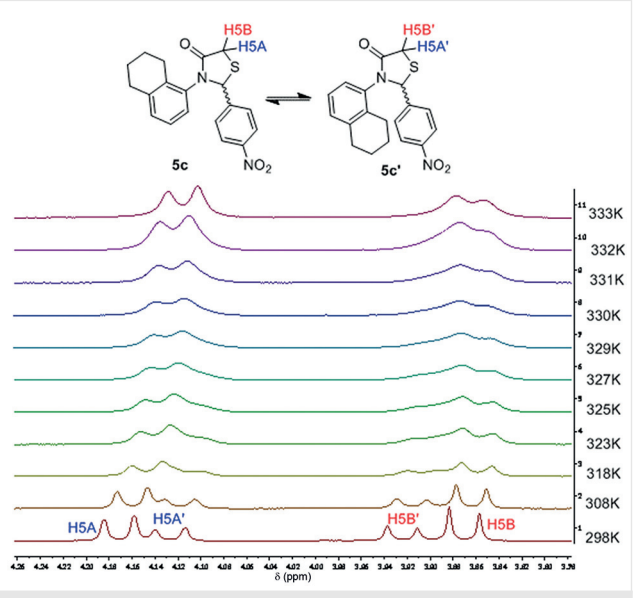


Figure 1 Variable temperature ^{1}H NMR spectra (stacked expansions of the aliphatic region) of compound **5c**

Based on atropisomerism phenomenon in thiazolidinones **5b**, **5c**, **5d**, **5f**, **5g**, **5h**, and **5i**, the stability of these isomers was investigated by chemical quantum calculations. The stability of the isomers was determined from molecular geometry with the lowest global energy for compounds **5b**, **5c**, and **5d**. The molecular geometry found for the two isomers are depicted in the Figure 2. The dihedral angle between tetrahydronaphthalene substituent and five-membered heterocycle are around 90° in both isomers, and in the isomer I, the aliphatic portion of tetrahydronaphthalene is positioned above the plane of the five-membered heterocycle, and in the isomer II, the aliphatic portion of tetrahydronaphthalene is positioned below the plane.

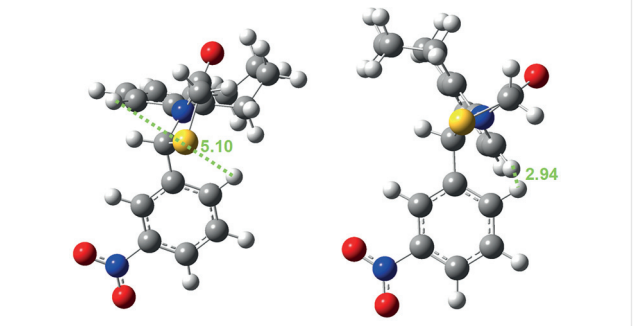
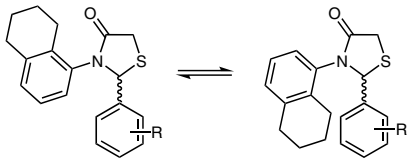


Figure 2 Representation of isomeric relationship for **5b** with aliphatic portion of tetrahydronaphthalene above (isomer I, left) and below (isomer II, right) the plane of thiazolidinone and the distance (Å) of H7 and H21

The different energy values (ΔG°) of the individual products are shown in Table 1. These values indicates a small energy difference between the isomers, ranging from –0.21 to –0.84 kcal·mol^{-1}. These data suggest a slight preference for the formation of the isomer with the aliphatic portion of tetrahydronaphthalene below the plane of five-membered heterocycle (isomer II).

Table 1 Energies Calculated by DFT-B3LYP/cc-pVDZ for Isomers I and II of Compounds **5b**, **5c**, **5d**

	Isomer	ΔG° (kcal·mol^{-1})[a]
5b	I	0
	II	–0.84
5c	I	0
	II	0.44
5d	I	0
	II	–0.21



[a] $\Delta G = [G_{(\text{isomer I})} - G_{(\text{isomer II})}]$.

In addition, molecular geometry revealed by chemical quantum calculations showed that spatial distance of H7 and H21 in isomer II (2.94, 2.97, 2.82 Å for **5b**, **5c**, and **5d**, respectively) is shorter than isomer I (5.10, 3.46, 3.56 Å for **5b**, **5c**, **5d**, respectively). Based on this, a NOESY experiment of **5b** was performed to unambiguously characterize the isomers in solution. Results showed a spatial coupling of the H7 (tetrahydronaphthyl ring) with the H21 (phenyl ring) (see SI) indicating that the favored atropisomer in solution is isomer II, where spatial distance of H7 and H21 is shorter. Absence of spatial coupling of the H7′ with the H21′ confirmed this result.

Considering that isomer II is favored in solution, results of chemical quantum calculation are in agreement with the results observed in the ^{1}H NMR spectrum in $CDCl_3$ at 298 K where the proportion of isomers identified for isomers II/I was 64:36 for the compounds **5c** and **5d** and 62:38 for compound **5b**.

Finally, compounds **5a**, **5d**, and **5e** each formed a crystal available for structure determination by single-crystal X-ray diffraction. ORTEP views of **5e** with thermal ellipsoids at 50% probability are shown in Figure 3 (a). As we can see, torsion angle between tetrahydronaphthalene substituent and five-membered heterocycle is around 90°, which is in accordance with geometry determined by chemical quantum calculation. However, isomer I was isolated as a crystal for **5d** and isomer II was isolated as a crystal for **5a** and **5e**. Structural factors that drove this preferential crystallization are under investigation in our group and will be published later.

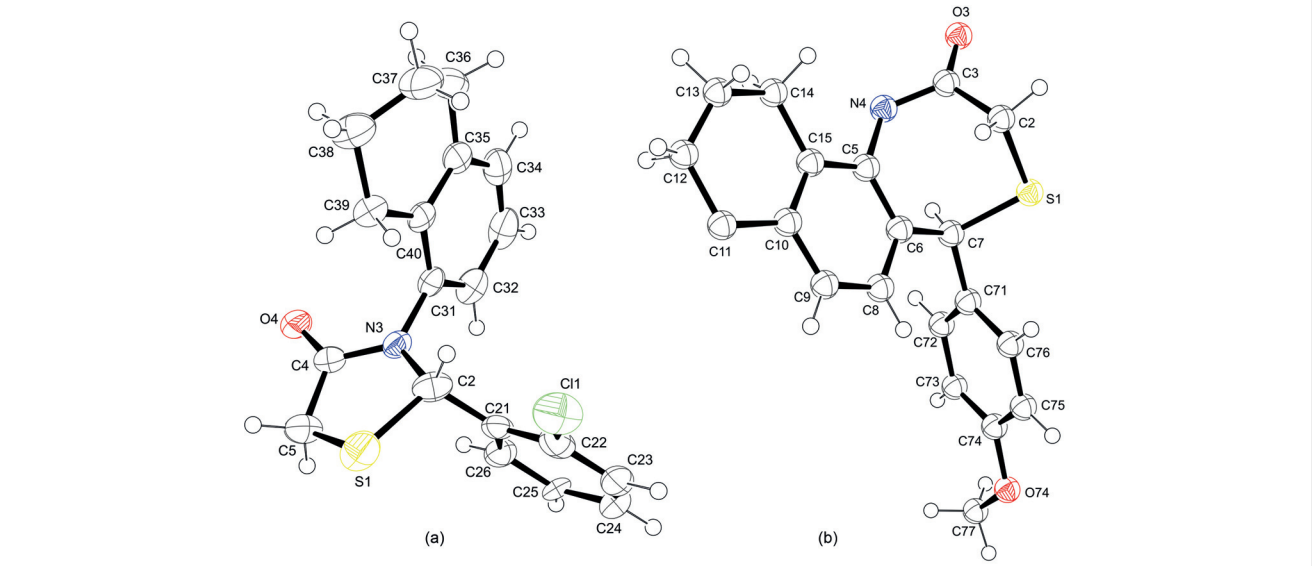


Figure 3 (a) ORTEP views of **5e** with thermal ellipsoids at 50% probability (b) ORTEP views of **7j** with thermal ellipsoids at 50% probability

Additionally, X-ray crystallography data showed that all compounds crystallized in spatial groups that have mirror-symmetry operator (m) indicating that two enantiomers can be found in the crystalline structure. Thus, the assignment of the absolute stereochemistry of the asymmetric center in C2 is arbitrary, and this structure may represent the *R*- or *S*-enantiomer. Benzothiazepinone **7j** also formed a crystal available for structure determination by single-crystal X-ray diffraction. ORTEP views of **7j** with thermal ellipsoids at 50% probability are shown in Figure 3 (b) confirming the benzothiazepinone formation. The crystal data and details concerning data collection and structure refinement are given in the SI.

The present study reported the synthesis of nine unpublished 2-aryl-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-ones **5a–i** by conventional thermal heating through a one-pot procedure. By the same one-pot procedure, but innovating through assistance of *p*-TsOH, a new way to synthesize 1,4-benzothiazepin-2-ones from arenealdehydes substituted with electron-donating groups was found and five 5-aryl-1,5,8,9,10,11-hexahydronaphtho[1,2-*e*][1,4]thiazepin-2(3*H*)-ones **7f**, **7j–m** were obtained. All structural dates are in full agreement with expected for both heterocyclic structures.

The occurrence of atropisomerism phenomenon in some 1,3-thiazolidin-4-ones was elucidated by VTNMR and the energy required for the interconversion of one isomer into another is around 16.8 kcal·mol^{-1}. The stability of isomers was investigated by chemical quantum calculations that were confirmed by NOESY and ^{1}H NMR and the isomer II, with the aliphatic portion of tetrahydronaphthalene below the plane of thiazolidinone ring is more stable. In addition, isomer II was isolated as a crystal for **5a** and **5e**, and isomer I was isolated as a crystal for **5d**.

Finally, in this work we have obtained biologically important compounds: thiazolidinones **5a–i** with a similar fragment of tacrine structure, and benzothiazepinones **7f**, **7j–m** as benzodiazepine analogues. The next step will be to evaluate the potential of AChE inhibition and antidepressant activity of these heterocycles.

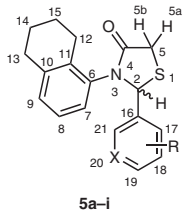
All common reagents and solvents were used as obtained from commercial suppliers without further purification. Reactions progress was monitored by TLC (silica gel 60 F253, hexane–EtOAc (3:1), UV 254 nm). The GC-MS spectra were obtained by a Shimadzu GCMS-QP 2010SE mass spectrometer-coupled gas chromatograph (GC-MS) with an AOC-20i automatic injector and Rtx-5MS 30 m × 0.25 mm × 0.25 µm column. Melting points were determined using open capillaries on a Fisatom model 430 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectrum of **5g** was recorded on a Bruker DRX 400 spectrometer (400.14 MHz for ^{1}H and 100.61 MHz for ^{13}C). All other spectra were recorded on a Bruker Avance III 600 (^{1}H at 600.13 MHz and ^{13}C at 150.62 MHz), in $CDCl_3$ or DMSO-d_6 containing TMS as an internal standard also in this equipment the VT-NMR experiments were recorded in DMSO-d_6/TMS. The sample concentration was 0.17 M and the chemical shifts (δ values) are given in ppm. The experiments were done in a range of 298–333 K. Free energies of activation were calculated using the Eyring equation, $\Delta G^{\neq} = -RT_C \cdot \ln(k_c \cdot h/k_B T_c)$, where $k_c = (\pi\Delta\nu)/\sqrt{2}$ or $k_c = \pi\sqrt{(\Delta\nu 2 + 6J^2)}/\sqrt{2}$, where R, h, and k_B are the gas, Planck and Boltzmann constants, respectively. The ^{1}H-^{1}H NOESY NMR experiment of compound **5b** was recorded on Bruker Avance III (600 MHz) in $CDCl_3$/TMS solutions at 298 K. The number of scans for NOESY were 32, the pulse sequence NOESYGPPHPP relaxation delay 1.5, mixture time 0.5, and acquisition time 0.13. The general reproducibility of chemical shift data was estimated to be not greater than ± 0.01 ppm. All spectra were acquired in a 5 mm tube. Chemical shifts (δ) are given in ppm and *J* values in Hz.

The diffraction measurements of compounds **5a** and **5e** were carried out by graphite monochromatized MoKα radiation with λ = 0.71073 Å on a Bruker D8 Venture diffractometer. The diffraction measurements

of compound **5d** and **7j** was carried out by graphite monochromatized CuKα radiation with λ = 1.54080 Å on a Bruker D8 QUEST diffractometer. Two diffractometers are equipped with goniometer KAPPA four circles, and with PHOTON II CPAD area detector. The structures were solved with direct methods using the SHELXS program, and refined on F2 by full-matrix least-squares with the SHELXL package.[23] Absorption correction was performed by the Gaussian method.[24] Anisotropic displacement parameters for non-hydrogen atoms were applied. The hydrogen atoms were placed at calculated positions with 0.96 (methyl CH_3), 0.97 (methylene CH_2), 0.98 (methine CH), 0.93 (aromatic CH), and 0.82 Å (OH) using a riding model. Hydrogen isotropic thermal parameters were kept equal to Uiso(H) = xUeq (carrier C atom), with x = 1.5 for methyl groups and x = 1.2 otherwise. The valence angles C–C–H and H–C–H of methyl groups were set to 109.5°, and H atoms were allowed to rotate around the C–C bond. Graphic projections were constructed using Ortep3 for Windows program included in WinGx program package.[25] Parameters in CIF format are available as an electronic supplementary publication.[26] The crystal data and details concerning data collection and structure refinement are given in SI.

All theoretical calculations were performed with the Gaussian09 package of programs.[27] With the aim to obtain the most stable conformer of compounds, a scan of the dihedral angle C–N–C=C changing 360° in steps of 10° at the HF/3-21G was performed A scan of the dihedral angle C(carbonyl)–N–C(aromatic)–C(aromatic) was performed for the compounds **5b**, **5c**, and **5d** changing the angle in 360° in steps of 10° at the HF/3-21G level. The more stable conformers were reoptimized at the B3LYP/cc-pVDZ level. All the other geometries of compounds were fully optimized at the B3LYP/cc-pVDZ level of theory taking into account the effect of the solvent ($CHCl_3$). All geometries were verified as minima on the potential energy by calculating the Hessian matrices by harmonic frequency calculations. The atomic coordinates used in theoretical calculations for compounds **5b**, **5c**, and **5d** are given in the SI.

The general structure of 2-arylthiazolidin-4-ones **5a–i** with numbering of carbon atoms is presented in Figure 4.



5a–i

Figure 4 General structure of 2-arylthiazolidin-4-ones **5a–i**

1,3-Thiazolidin-4-ones 5a–c, General Procedure

The compounds **5a–c** were synthesized according Masteloto et al.[17c] but purified by column chromatography using hexane–EtOAc (8:2) as eluent (for **5a**,**b**) or recrystallization from EtOH (for **5c**).

2-(2-Nitrophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5a)

Yield: 0.184 g (52%); yellow solid; mp 179–181 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.01 (d, *J* = 7.8 Hz, 1 H, ArH), 7.94 (d, *J* = 7.8 Hz, 1 H, ArH), 7.79 (t, *J* = 7.0 Hz, 1 H, ArH), 7.51 (t, *J* = 7.3 Hz, 1 H, ArH), 7.04 (d, *J* = 7.1 Hz, 1 H, H9), 6.93 (t, *J* = 7.3 Hz, 1 H, H8), 6.64 (d, *J* = 7.3 Hz, 1 H, H7), 6.29 (s, 1 H, H2), 3.97 (d, *J* = 15.9 Hz, 1 H, H5a), 3.76 (d, *J* = 15.9 Hz, 1 H, H5b), 2.79–2.75 (m, 2 H, CH_2 cyclohexyl), 2.70–2.62 (m, 2 H, CH_2 cyclohexyl), 1.88–1.76 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.6 (C4), 146.9, 139.8, 136.9, 135.6, 135.1, 134.0, 130.2, 129.3, 127.4, 125.9, 125.5, 125.5, 59.9 (C2), 31.6 (C5), 29.5, 24.9, 22.5, 22.4.

MS (70 eV): *m*/*z* (%) = 354 (M^+, 8), 337 (63), 264 (35), 217 (50), 186 (85), 159 (100), 130 (89).

2-(3-Nitrophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5b and 5b′)

Yield: 0.198 g (56%); off-white solid; mp 147–149 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.6 H′) = 8.23 (br, 1 H′, ArH′), 8.18–8.17 (m, 2 H, ArH), 8.10 (dd, *J* = 8.1, 1.1 Hz, 1 H′, ArH′), 7.70 (d, *J* = 7.7 Hz, 1 H, ArH), 7.65 (d, *J* = 7.7 Hz, 1 H′, ArH′), 7.54 (t, *J* = 8.3 Hz, 1 H, ArH), 7.42 (t, *J* = 7.9 Hz, 1 H′ ArH′), 7.09 (t, *J* = 7.7 Hz, 1 H′, H8′), 7.03–6.99 (m, 2 H, 1 H, H9 and 1 H′, H7′), 6.95 (d, *J* = 7.5 Hz, 1 H′, H9′), 6.86 (t, *J* = 7.7 Hz, 1 H, H8), 6.31 (d, *J* = 7.7 Hz, 1 H, H7), 6.20 (s, 1 H, H2′), 5.76 (1 H, d, *J* = 1.5 Hz, H2), 4.09 (dd, *J* = 15.9, 1.7 Hz, 1 H, H5a), 4.02 (dd, *J* = 15.9, 1.5 Hz, 1 H′,H5a′), 3.95 (d, *J* = 15.9 Hz, 1 H′, H5b′), 3.91 (d, *J* = 15.9 Hz, 1 H, H5b), 2.79–2.53 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′), 2.09–1.56 (m, 8 H, 2 × CH_2 and 2 × CH_2′ cyclohexyl′).

^{13}C NMR (150 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 170.9 (C4), 169.4 (C4′), 148.3, 148.0, 142.6, 139.9, 139.5, 139.3, 135.9, 135.0, 134.8, 134.7, 134.3, 133.6, 130.2, 129.9, 129.5, 129.4, 126.8, 126.0, 124.1, 124.0, 123.4, 122.6, 122.5, 65.7 (C2′), 63.9 (C2), 33.5 (C5′), 32.4 (C5), 29.4, 29.2, 25.2, 24.8, 22.5, 22.5, 22.3, 22.2.

MS (70 eV): *m*/*z* (%) = 354 (M^+, 43), 321 (3), 279 (53), 252 (12), 187 (27), 159 (100), 131 (35).

2-(4-Nitrophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5c and 5c′)

Yield: 0.221 g (60%); yellow solid; mp 191–193 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.5 H′) = 8.19 (d, *J* = 8.6 Hz, 2 H, ArH), 8.09 (d, *J* = 8.6 Hz, 2 H′, ArH), 7.53–7.50 (m, 3 H, 2 H, ArH and 1 H′, ArH), 7.09 (t, *J* = 7.7 Hz, 1 H′, H8′), 7.01 (d, *J* = 7.8 Hz, 1 H, H9 and 1 H′, H7′), 6.96 (d, *J* = 7.5 Hz, 1 H′, H9′), 6.88 (t, *J* = 7.7 Hz, 1 H, H8), 6.33 (d, *J* = 7.8 Hz, 1 H, H7), 6.18 (s, 1 H′, H2′), 5.73 (br, 1 H, H2), 4.07 (d, *J* = 15.8 Hz, 1 H, H5a), 4.01 (d, *J* = 15.9 Hz, 1 H′, H5a′), 3.94 (d, *J* = 15.8 Hz, 1 H′, H5b′), 3.90 (d, *J* = 15.9 Hz, 1 H, H5b), 2.78–2.52 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′), 2.04–1.96 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′).

^{13}C NMR (150 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 170.9 (C4), 169.4 (C4′), 148.2, 148.1, 147.4, 144.6, 139.5, 139.3, 135.8, 135.0, 134.9, 134.7, 130.2, 129.6, 129.4, 128.4 (2 C), 126.5, 126.1, 126.0, 124.1 (2 C), 123.5, 122.5, 65.7 (C2′), 63.8 (C2), 33.5 (C5′), 32.3 (C5), 29.4, 29.2, 25.1, 24.8, 22.5, 22.5, 22.3, 22.2.

MS (70 eV): *m*/*z* (%) = 354 (M^+, 62), 279 (58), 251 (11), 205 (11), 187 (21), 159 (100), 131 (34).

1,3-Thiazolidin-4-ones 5d–i, General Procedure

A mixture of 5,6,7,8-tetrahydronaphthalen-1-amine (**1**; 0.147 g, 1 mmol) and the corresponding arenealdehyde **2d–i** (1 mmol) in toluene (30 mL) was heated to reflux using a Dean–Stark apparatus for 30 min. Then, mercaptoacetic acid (**4**; 0.42 mL, 6 mmol) was added and the mixture was heated until the reaction was complete (24 h). The organic layer was washed with sat. aq $NaHCO_3$ (3 × 20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude

compounds **5e–i** were purified by column chromatography on silica gel using hexane–EtOAc (8:2) as eluent. The crude **5d** was recrystallized from EtOH.

2-Phenyl-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5d and 5d′)

Yield: 0.157 g (51%); off-white solid; mp 184–186 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.6 H′) = 7.32 (br, 5 H, ArH and 2 H′, ArH′), 7.22–7.21 (m, 3 H′, ArH′), 7.08 (t, *J* = 7.4 Hz, 1 H′, H8′), 7.01 (d, *J* = 7.6 Hz, 1 H, H7′), 6.99 (d, *J* = 7.4 Hz, 1 H, H9), 6.93 (d, *J* = 7.1 Hz, 1 H′, H9′), 6.84 (t, *J* = 7.6 Hz, 1 H, H8), 6.33 (d, *J* = 7.7 Hz, 1 H, H7), 6.07 (s, 1 H′, H2′), 5.64 (s, 1 H, H2), 4.06 (d, *J* = 15.8 Hz, 1 H, H5a), 4.00 (d, *J* = 15.7 Hz, 1 H′, H5a′), 3.90 (d, *J* = 15.8 Hz, 1 H′, H5b′), 3.86 (d, *J* = 15.7 Hz, 1 H, H5b), 2.77–2.45 (m, 8 H, 2 × CH_2 cyclohexyl and 4 H′ 2 × CH_2′ cyclohexyl′), 2.03–1.22 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′).

^{13}C NMR (150 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 171.1 (C4), 169.7 (C4′), 140.2, 139.0, 138.9, 137.3, 136.3, 135.6, 135.4, 134.7, 129.8, 129.2, 129.2, 129.1, 128.7 (2 C), 128.5, 128.2, 127.5 (2 C), 126.8, 125.8, 125.8, 123.0, 67.1 (C2′), 65.1 (C2), 33.7 (C5′), 32.6 (C5), 29.5, 29.3, 24.9, 24.8, 22.7, 22.6, 22.4, 22.2.

MS (70 eV): *m*/*z* (%) = 309 (M^+, 70), 276 (56), 234 (100), 206 (47), 177 (21), 159 (83), 135 (73).

2-(2-Chlorophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5e)

Yield: 0.195 g (57%); off-white solid; mp 154–156 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.75 (br, 1 H, ArH), 7.39–7.17 (m, 4 H, ArH and $CHCl_3$), 7.02–7.01 (m, 1 H, ArH), 6.91–6.91 (m, 1 H, ArH), 6.55 (d, *J* = 7.4 Hz, 1 H, H7), 6.25 (br, 1 H, H2), 3.98 (d, *J* = 15.4 Hz, 1 H, H5a), 3.80 (d, *J* = 13.7 Hz, 1 H, H5b), 2.78–2.72 (m, 4 H, 2 × CH_2 cyclohexyl), 1.84–1.77 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 171.7 (C4), 139.2, 135.5, 135.1, 135.0, 129.9, 129.7, 127.7, 127.3, 127.2, 126.1, 125.8, 60.6 (C2), 33.7 (C5′), 32.0 (C5), 29.5, 24.9, 22.6, 22.6.

MS (70 eV): *m*/*z* (%) = 343 (M^+, 70), 308 (36), 268 (59), 234 (31), 186 (22), 159 (100), 135 (63).

2-(4-Chlorophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5f and 5f′)

Yield: 0.185 g (54%); orange oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.7 H′) = 7.29 (d, *J* = 8.5 Hz, 2 H, ArH), 7.27–7.25 (m, 4 H, 2 × ArH, 2 × ArH′ and $CHCl_3$), 7.19 (d, *J* = 8.4 Hz, 2 H′, ArH′), 7.07 (t, *J* = 7.7 Hz, 1 H′, H8′), 7.00–6.97 (m, 2 H, H9 and H7′), 6.95 (d, *J* = 7.5 Hz, 1 H′, H9′), 6.88 (t, *J* = 7.7 Hz, 1 H, H8), 6.32 (d, *J* = 7.7 Hz, 1 H, H7), 6.05 (s, 1 H, H2′), 5.62 (br, 1 H, H2), 4.03 (dd, *J* = 15.8, 1.5 Hz, 1 H, H5a), 3.96 (d, *J* = 15.9 Hz, 1 H, H5a), 3.89 (d, *J* = 16.0 Hz, 1 H, H5b′), 3.86 (d, *J* = 15.8 Hz, 1 H, H5b), 2.78–2.50 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′), 2.05–1.61 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′).

^{13}C NMR (150 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 170.9 (C4), 169.5 (C4′), 139.2, 139.1, 138.7, 136.1, 135.8, 135.3, 135.1, 135.0, 134.8, 134.6, 130.0, 129.9, 129.3, 128.9, 128.4, 126.8, 125.9, 125.8, 122.7, 119.6, 66.2 (C2′), 64.3 (C2), 33.6 (C5′), 32.5 (C5), 29.4, 29.3, 24.9, 24.8, 22.6, 22.5, 22.3, 22.2.

MS (70 eV): *m*/*z* (%) = 343 (M^+, 46), 310 (8), 268 (60), 240 (23), 187 (21), 159 (100), 135 (62).

2-(Pyridin-3-yl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5g and 5g′)

Yield: 0.217 g (70%); orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.15 H′) = 8.56 (dd, *J* = 4.8, 1.5 Hz, 1 H, ArH), 8.49 (dd, *J* = 4.8, 1.4 Hz, 1 H′, ArH′), 8.46 (d, *J* = 1.8 Hz, 1 H′, ArH′), 8.44 (d, *J* = 1.9 Hz, 1 H, ArH), 7.81–7.78 (m, 2 H, ArH), 7.34 (dd, *J* = 7.9, 4.9 Hz, 1 H, ArH), 7.22 (dd, *J* = 7.9, 4.9 Hz, 1 H′, ArH′), 7.10 (t, *J* = 7.6 Hz, 1 H′, H8′), 7.03–6.99 (m, 2 H, H9 and H7′), 6.96 (d, *J* = 7.4 Hz, 1 H′, H9′), 6.87 (t, *J* = 7.7 Hz, 1 H, H8), 6.29 (d, *J* = 7.7 Hz, 1 H, H7), 6.10 (s, 1 H′, H2′), 5.71 (d, *J* = 1.4 Hz, 1 H, H2), 4.08–3.99 (m, 1 H, H5a and 1 H′, H5a′), 3.95–3.89 (m, 1 H′, H5b′ and 1 H, H5b), 2.77–1.26 (m, 16 H, 4 × CH_2 cyclohexyl and 4 × CH_2′ cyclohexyl′).

^{13}C NMR (100 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 170.9 (C4), 169.4 (C4′), 150.3, 150.2, 149.6, 149.6, 148.7, 139.4, 139.2, 136.2, 135.8, 135.7, 135.5, 134.7, 134.6, 133.1, 130.1, 129.6, 126.9, 126.0, 125.0, 123.7, 123.2, 122.8, 104.9, 64.3 (C2′), 62.3 (C2), 33.5 (C5′), 32.5 (C5), 29.4, 29.2, 24.9, 24.8, 22.5, 22.5, 22.2, 22.1.

MS (70 eV): *m*/*z* (%) = 310 (M^+, 75), 277 (29), 235 (80), 207 (37), 187 (49), 159 (100), 136 (67).

2-(2-Fluorophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5h and 5h′)

Yield: 0.153 g (47%); off-white solid, mp 142–145 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.4 H′) = 7.54 (t, *J* = 7.2 Hz, 1 H′, ArH′), 7.41 (t, *J* = 7.1 Hz, 1 H, ArH), 7.30–7.27 (m, 1 H, ArH), 7.23–7.17 (m, 1 H′, ArH′), 7.13 (t, *J* = 7.5 Hz, 1 H, ArH), 7.07 (d, *J* = 6.5 Hz, 1 H, ArH), 7.01–6.98 (m, 2 H, H9 and H7′), 6.94 (d, *J* = 5.4 Hz, 1 H′, H9′), 6.88 (t, *J* = 7.7 Hz, 1 H, H7), 6.44 (br, 1 H and H2′), 5.94 (s, 1 H, H2), 4.07–4.01 (m, 2 H, H5a and H5a′), 3.88 (d, *J* = 15.6 Hz, 1 H, H5b′), 3.82 (d, *J* = 15.6 Hz, 1 H, H5b), 2.78–2.53 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′), 1.85–1.73 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′).

^{13}C NMR (150 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 171.2 (C4), 169.5 (C4′), 160.6 (d, ^1J = 248.5 Hz, 1 C′), 160.4 (d, ^1J = 249.1 Hz, 1 C), 139.1, 138.7, 135.9, 135.2, 134.9, 130.8 (d, ^3J = 8.4 Hz, 1 C′), 130.6 (d, ^3J = 8.4 Hz, 1 C), 129.9, 129.2, 128.8 (d, ^4J = 2.4 Hz, 1 C), 127.5, 127.4, 126.1, 125.8, 124.4, (d, ^4J = 3.4 Hz, 1 C), 124.1, 123.0, 116.0 (d, ^2J = 21.4 Hz, 1 C), 115.5 (d, ^2J = 22.0 Hz, 1 C′), 59.5 (C2′), 58.8 (C2), 33.6 (C5′), 32.5 (C5), 29.4, 29.3, 24.8, 24.7, 22.6, 22.5, 22.3, 22.2.

MS (70 eV): *m*/*z* (%) = 327 (M^+, 70), 294 (30), 252 (86), 224 (48), 186 (21), 159 (100), 130 (44).

2-(4-Fluorophenyl)-3-(5,6,7,8-tetrahydronaphthalen-1-yl)thiazolidin-4-one (5i and 5i′)

Yield: 0.173 g (53%); light orange solid; mp 145–148 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ_H and $\delta_{H'}$ (1 H:0.7 H′) = 7.33–7.28 (m, 4 H, 2 × ArH and 2 ArH′), 7.08 (t, *J* = 7.7 Hz, 1 H′, ArH′), 7.01–6.99 (m, 2 H, ArH′ and H7′), 6.95 (d, *J* = 7.6 Hz, 1 H′, ArH′), 6.90 (t, *J* = 8.5 Hz, 1 H, ArH′), 6.86 (t, *J* = 7.7 Hz, 1 H, H8), 6.29 (d, *J* = 7.7 Hz, 1 H, H7), 6.06 (s, 1 H′, H2′), 5.65 (s, 1 H, H2), 4.03 (d, *J* = 15.8 Hz, 1 H, H5a), 3.97 (d, *J* = 15.8 Hz, 1 H′, H5a′), 3.91–3.86 (m, 1 H, H5b and 1 H′, H5b′), 2.78–2.46 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′), 2.02–1.25 (m, 8 H, 2 × CH_2 cyclohexyl and 2 × CH_2′ cyclohexyl′).

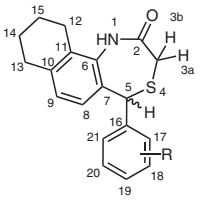
^{13}C NMR (150 MHz, $CDCl_3$): δ_C and $\delta_{C'}$ = 171.1 (C4), 169.6 (C4′), 162.9 (d, ^1J = 248.8 Hz), 162.8 (d, ^1J = 248.6 Hz), 139.1, 139.0, 136.1, 135.8 (d, ^4J = 3.1 Hz, 1 C), 135.3, 135.1, 134.6, 133.0 (d, ^4J = 2.7 Hz, 1 C′), 130.3 (d, ^3J = 8.5 Hz, 2 C′), 129.9, 129.5 (d, ^3J = 8.2 Hz, 2 C), 129.3, 126.9,

125.8, 125.8, 122.9, 115.7 (d, ^2J = 21.9 Hz, 2 C), 115.2 (d, ^2J = 21.8 Hz 2 C′), 66.2 (C2′), 64.3 (C2), 33.6 (C5′), 32.6 (C5), 29.4, 29.3, 24.9, 24.8, 22.6, 22.5, 22.3, 22.2.

MS (70 eV): *m*/*z* (%) = 327 (M^+, 67), 294 (54), 252 (83), 224 (47), 187 (18), 159 (100), 130 (45).

1,4-Benzothiazepin-2-ones 7f and 7j-m; General Procedure

General structure of 5-aryl-1,4-benzothiazepin-2-ones **7f**, **7j–m** with numbering of carbon atoms is presented in Figure 5.



7f, 7j–m

Figure 5 General structure of 5-aryl-1,4-benzothiazepin-2-ones **7f**, **7j–m**

A mixture of 5,6,7,8-tetrahydronaphthalen-1-amine (**1**; 0.147g, 1 mmol), the corresponding arenealdehyde **2f** (0.143 g, 2 mmol) or **2j–m** (1 mmol), and *p*-TsOH (0.190 g, 1 mmol) in toluene (30 mL) was heated to reflux using a Dean–Stark apparatus for 30 min. Then, mercaptoacetic acid (**4**; 0.21 mL, 3 mmol) was added and the mixture was heated until the reaction was complete (24 h). The organic layer was washed with sat. aq $NaHCO_3$ (3 × 20 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude compounds were purified by recrystallization from EtOH, except **7l**, which was purified by column chromatography on silica gel using hexane–EtOAc (8:2) as eluent.

5-(4-Chlorophenyl)-1,5,8,9,10,11-hexahydronaphtho-[1,2-*e*][1,4]thiazepin-2(3*H*)-one (7f)

Yield: 0.102 g (30%); yellowish solid; mp 201–203 °C.

^{1}H NMR (600 MHz, DMSO-d_6): δ = 8.96 (s, 1 H, NH), 7.47–7.43 (m, 4 H, ArH), 6.95 (d, *J* = 7.9 Hz, 1 H), 6.71 (d, *J* = 7.7 Hz, 1 H), 5.54 (s, 1 H, H5), 2.98 (d, *J* = 12.0 Hz, 1 H, H3a), 2.90 (d, *J* = 11.9 Hz, 1 H, H3b), 2.70–2.49 (m, 4 H, 2 × CH_2 cyclohexyl), 1.72–1.64 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, DMSO-d_6): δ = 167.6 (C2), 136.9, 134.8, 131.5, 131.4, 130.8, 130.0 (2 C), 127.7 (2 C), 126.9, 124.1, 46.0 (C5), 30.3 (C3), 28.3, 23.9, 21.6, 21.4.

MS (70 eV): *m*/*z* (%) = 343 (M^+, 100), 301 (78), 268 (65), 232 (35), 218 (21), 165 (8), 118 (27).

5-(4-Methoxyphenyl)-1,5,8,9,10,11-hexahydronaphtho-[1,2-*e*][1,4]thiazepin-2(3*H*)-one (7j)

Yield 0.244 g (72%); golden colored solid; mp 206–209 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.15 (s, 1 H, NH), 7.40 (d, *J* = 8.5 Hz, 2 H, ArH), 6.91–6.89 (m, 3 H, ArH), 6.70 (d, *J* = 8.0 Hz, 1 H), 5.65 (s, 1 H, H5), 3.81 (s, 3 H, OCH_3), 3.27 (d, *J* = 11.8 Hz, 1 H, H3a), 2.94 (d, *J* = 11.8 Hz, 1 H, H3b), 2.78–2.63 (m, 4 H, 2 × CH_2 cyclohexyl), 1.90–1.66 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.6 (C2), 159.2, 137.9, 134.4, 132.0, 131.3, 130.5 (2 C), 129.2, 128.2, 125.1, 113.9 (2 C), 55.2 (OCH_3), 47.1 (C5), 31.7 (C3), 29.4, 25.2, 22.7, 22.3.

MS (70 eV): *m*/*z* (%) = 339 (M^+, 86), 306 (50), 297 (73), 264 (100), 250 (14), 184 (31), 121 (38).

5-(3,4-Dimethoxyphenyl)-1,5,8,9,10,11-hexahydronaphtho-[1,2-*e*][1,4]thiazepin-2(3*H*)-one (7k)

Yield 0.258 g (70%); off-white solid; mp 182–185 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.72 (s, 1 H, NH), 7.04–7.01 (m, 2 H, ArH), 6.92 (d, *J* = 8.0 Hz, 1 H, ArH), 6.86 (d, *J* = 8.2 Hz, 1 H, ArH), 6.74 (d, *J* = 8.0 Hz, 1 H, ArH), 5.64 (s, 1 H, H5), 3.88 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.26 (d, *J* = 11.8 Hz, 1 H, H3a), 2.95 (d, *J* = 10.8 Hz, 1 H, H3b), 2.75–2.60 (m, 4 H, 2 × CH_2 cyclohexyl), 1.88–1.71 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.3 (C2), 148.9, 148.8, 138.0, 134.4, 132.2, 131.3, 129.8, 128.3, 125.2, 121.6, 112.8, 111.2, 55.9 (2 × OCH_3), 47.6 (C5), 31.7 (C3), 29.5, 25.3, 22.7, 22.4.

MS (70 eV): *m*/*z* (%) = 369 (M^+, 100), 336 (38), 312 (40), 294 (61), 278 (10), 231 (17), 184 (20).

5-(*p*-Tolyl)-1,5,8,9,10,11-hexahydronaphtho[1,2-*e*][1,4]thiazepin-2(3*H*)-one (7l)

Yield: 0.180 g (56%); beige solid; mp 229–231 °C.

^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.87 (s, 1 H, NH), 7.28 (d, *J* = 7.9 Hz, 2 H, ArH), 7.10 (d, *J* = 7.7 Hz, 2 H, ArH), 6.82 (d, *J* = 8.0 Hz, 1 H, ArH), 6.63 (d, *J* = 8.0 Hz, 1 H, ArH), 5.58 (s, 1 H, H5), 3.18 (d, *J* = 11.8 Hz, 1 H, H3a), 2.87 (d, *J* = 11.5 Hz, 1 H, H3b), 2.66–2.59 (m, 4 H, 2 × CH_2 cyclohexyl), 2.28 (s, 3 H, CH_3), 1.79–1.63 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.4 (C2), 137.9, 137.7, 134.5, 134.4, 132.1, 131.3, 129.3 (2 C), 129.2 (2 C), 128.2, 125.2, 47.5 (C5), 31.7 (C3), 29.5, 25.2, 22.7, 22.4, 21.1 (CH_3).

MS (70 eV): *m*/*z* (%) = 323 (M^+, 100), 336 (38), 312 (40), 294 (61), 278 (10), 231 (17), 184 (20).

5-(2,6-Dichlorophenyl)-1,5,8,9,10,11-hexahydronaphtho-[1,2-*e*][1,4]thiazepin-2(3*H*)-one (7m)

Yield: 0.215 g (57%); off-white solid; mp 232–235 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.40 (d, *J* = 8.0 Hz, 2 H, ArH), 7.29 (br, 1 H, NH), 7.24 (t, *J* = 8.1 Hz, 1 H, ArH), 6.93 (d, *J* = 8.1 Hz, 1 H, ArH), 6.85 (d, *J* = 8.1 Hz, 1 H, ArH), 6.73 (s, 1 H, H5), 3.57 (d, *J* = 12.4 Hz, 1 H, H3a), 2.96 (dd, *J* = 12.4, 1.4 Hz, 1 H, H3b), 2.77–2.56 (m, 4 H, 2 × CH_2 cyclohexyl), 1.94–1.67 (m, 4 H, 2 × CH_2 cyclohexyl).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.2 (C2), 138.7, 134.9, 132.9, 131.4, 129.7, 127.9, 126.5, 126.1, 42.9 (C5), 31.6 (C3), 29.5, 25.6, 22.7, 22.3.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0036-1590866.

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