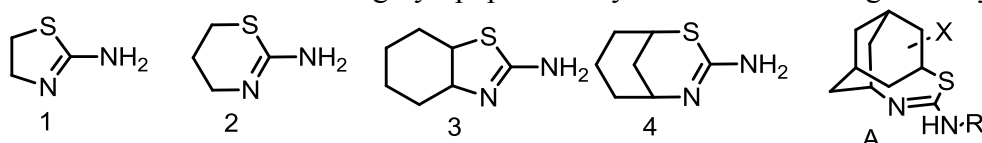


## Novel structural type of bridged urea derivatives

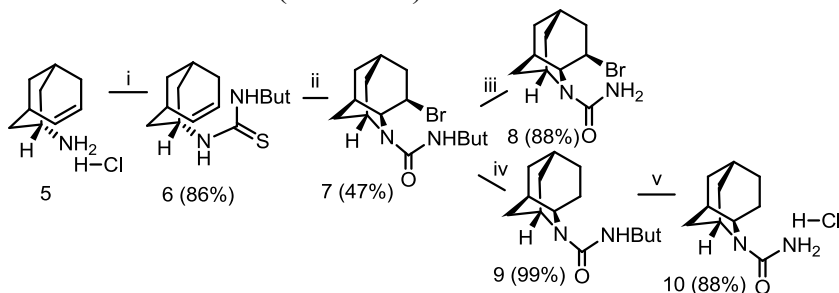
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Cyclic isothioureas, such as 2-amino-2-thiazoline (**1**) and 2-amino-5,6-dihydro-4*H*-1,3-thiazine (**2**), possess pronounced and short-term effect against septic shock and radioactive irradiation due to their ability to inhibit enzyme nitric oxide synthase (NOS). Recently we synthesized more lipophilic bicyclic isothioureas **3** and **4**, which maintained the activity of parent molecules **1** and **2**, but compound **3** displayed prolonged antihypotensive action *in vivo* [1, 2]. These results stimulated us to obtain highly lipophilic tricyclic isothiourea of general type **A**.



In an attempt to synthesize 4-thia-6-azatricyclo[5.3.1.1<sup>3,9</sup>]dodecan-5-imine (**A**, R=H, X=H), a reaction of 1-[(1*RS*,3*SR*,5*SR*)-bicyclo[3.3.1]non-6-en-3-yl]-3-*tert*-butylthiourea **6** in the presence of bromine was undertaken (Scheme 1).



**Scheme 1** i) DIPEA, Bu<sup>t</sup>NCS, CH<sub>2</sub>Cl<sub>2</sub>, rt, 12 h; ii) 1. Br<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>, rt, 24 h; 2. NaHCO<sub>3</sub>, H<sub>2</sub>O; iii) HCl<sub>aq</sub>, reflux, 3 h; iv) *n*-Bu<sub>3</sub>SnH, AIBN, toluene, 100°C, 6 h; v) HCl<sub>aq</sub>, reflux, 3 h; The marked configuration of compounds is relative (they represent racemic mixtures)

The intramolecular cyclization under atmospheric *moisture* conditions however did not lead to a product of intramolecular cyclization by sulphur atom (as was observed earlier for bicyclic compounds **3** and **4**) but was accompanied by precursive oxidation of thiourea to urea fragment and proceeded via nitrogen atom yielding the bridged tricyclic urea derivative **7** (as determined by X-ray analysis and liquid chromatography–mass spectrometry technique for compound **8**). As though the structural template of compounds **7** and **8** is unique and have never been studied earlier, we carried out a reductive debromination of bromine derivative **7** and (via compound **9**, Scheme 1) obtained unsubstituted urea bearing azatricyclo[4.3.1.0<sup>3,8</sup>]decane moiety **10**. It belongs to a novel and unusual structural type of bridged tricyclic ureas.

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### References

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