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Synthesis of Novel Chiral Phenyl Ethyl Amine Derivatives of Thiadiazines with their Antiulcer and Antioxidant Activities

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Introduction:

In several clinical pharmaceuticals, 3,5-Disubstituted tetrahydro-2*H*-1,3,5-thiadiazine thione have been reported as a well-known bioactive pharmacophore, that possess a major role in numerous biological activities like antibacterial (**1**)[1], antifungal (**2**)[2] and antileishmaniasis (**3**)[3] (Figure 1).

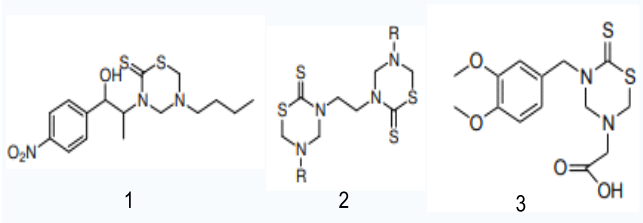

Figure 1. Biological Active THTT Analogues

Our recent studies[3] found this pharmacophore as potent antileishmanial backbone. Inspired by literature and our own recent findings, here, we extended our studies by synthesizing the enantiopure THTT derivatives which were further screened for their antiulcer and antioxidant activities.

Experimental:

S or R isomers of THTT derivatives were synthesized at 10mmol scale by following the literature[3] (Scheme 1). The reaction involves the treatment of appropriate amine with carbon disulphide in presence of potassium hydroxide to deliver the corresponding dithiocarbamate salts. Subsequent treatment with formaldehyde gives the intermediates, which were further allowed to react with amine. Column chromatography provided the enantiopure THTT analogues in good yields (40-60%). Noteworthy antiulcer and antioxidant activities are also presented (Table 1).

Scheme-1

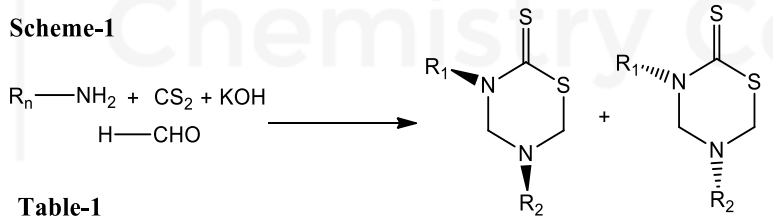

Table-1

Activity	THTT (S- Isomer)	THTT (R-Isomer)	Racemic Form	Standard
Anti-oxidant	30.52 µM	30.73 µM	30.49 µM	BHA (44.20 µM)
Anti-ulcer	69.90 µM	65.90 µM	57.80 µM	Thiourea (25.63 µM)

(i) 3,5-bis (S)-1-phenylethyl-THTT (S Isomer):

^{1}H NMR (δ) 0.8 (d, 3H), 1.45 (d, 3H), 3.91 (q, 1H), 3.99 (d, 1H), 4.08 (d, 1H), 4.17 (d, 1H), 4.41 (d, 1H), 7.240-7.582 (m, 10H), 7.59 (q, 1H)

(ii) 3,5-bis (R)-1-phenylethyl-THTT (R Isomer):

^{1}H NMR (δ) 0.82 (d, 3H), 1.45 (d, 3H), 3.90 (q, 1H), 4.0 (d, 1H), 4.1 (d, 1H), 4.19 (d, 1H), 4.4 (d, 1H), 7.254-7.291 (m, 10H), 7.32 (t, 3H), 7.38 (d, 2H), 7.57 (q, 1H)

Conclusion:

In conclusion, an efficient preparation for enantiopure R and S isomers along with racemic THTT analogues have been developed. Both enantipure isomers and their racemic mixture were also identified as significant antioxidant and antiulcer agents.

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