HETEROCYCLES, Vol. 22, No 12, 1984

SYNTHESIS OF 1,3-THIAZOLIDINE-2-THIONE AND (4R)-METHOXYCARBONYL-1,3-THIAZOLIDINE-2-THIONE USING N,N'-THIOCARBONYLDIIMIDAZOLE

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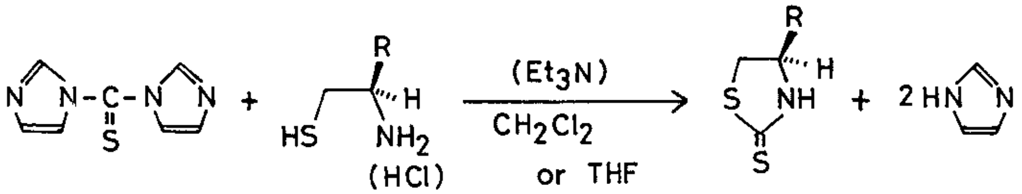
Abstract ——1,3-Thiazolidine-2-thiones are synthesized from β-aminothiols and N,N'-thiocarbonyldiimidazole in good yields.

Derivatives of 1,3-thiazolidine-2-thione(1a) and (4R)-methoxycarbonyl-1,3-thiazolidine-2-thione(1b) have been utilized as important synthetic intermediates for the syntheses of aldehydes, amides, aldols *etc.*[1] Though carbon disulfide is reported to afford (1), its manipulation is not easy because of its foul smelling and its poisonous character.[2] On the other hand, N,N'-thiocarbonyldiimidazole(2) has been known for some time as non-smelling crystals.[3]



(2) (1) (3)

a: $R = H$
b: $R = \underset{\overset{\|}{O}}{C}OCH_3$

Solvent	Yield (%)	
	(1a)	(1b)
CH_2Cl_2	62	81
THF	55	83

Here, we wish to report an improved synthesis of 1,3-thiazolidine-2-thione(**1a**) and (4R)-methoxycarbonyl-1,3-thiazolidine-2-thione(**1b**) using (**2**). When (**2**) was reacted with aminoethanethiol or (R)-cystein methyl ester in dichloromethane or THF, the corresponding thiazolidine-2-thiones(**1a**,**b**) were obtained in good to high yields. The by-product, imidazole(3), was easily removed from the reaction mixture by washing with acid.

The typical experimental procedure is as follows. To a mixture of (R)-cystein methyl ester hydrochloride(0.344g, 2 mmol) in dichloromethane (2.5 ml) or THF (2.5 ml), triethylamine(Et_3N, 0.218g, 2.1 mmol) was added under an argon atmosphere. The mixture was cooled in an ice bath, and N,N'-thiocarbonyldiimidazole(**2**, 0.435g, 2.2 mmol) was added in one portion. The reaction mixture was stirred for additional 20 min, then it was washed with 1M HCl and brine. After organic layer was dried over anhydrous sodium sulfate, the solvent was evaporated under reduced pressure. The residue was purified on preparative silica gel TLC ($CHCl_3$:MeOH = 15:1 as developing solvent). (**1b**) was obtained as a yellow oil(0.289-0.296g, 81-83%). IR (neat): 2975 (C-H), 1750 (C=O) cm^{-1}. ^1H-NMR ($CDCl_3$): 3.5-4.0 (m, 5H, $COOCH_3$, CH_2), 4.8-5.1 (dd, 1H, CH), 8.0-9.0(s, broad, 1H, NH). MS, m/e: Calcd for $C_5H_7O_2NS_2$ (176.9919). Found 176.9922 (94.9). Other peaks (relative intensity, elements) are 117.9792 (100, $C_3H_4NS_2$), 103.0094(3.6, C_3H_5ONS). $[\alpha]_D^{23}$ -64.5° (c = 1.50, $CHCl_3$) [lit. $[\alpha]_D^{21}$ -67.00° (c = 1.10, $CHCl_3$)].[1c] In a similar manner, but without the use of Et_3N, (1a) was obtained in the yields of 55-62%. m.p. 104.0°C (lit. 105-107°C).[4]

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Received, 23rd August, 1984