SYNTHESIS OF HETEROCYCLIC COMPOUNDS USING 1,3-OXATHIOLIUM CATIONS: SYNTHESIS OF THIENO[3,2-e][1,4]DIAZEPINE, THIAZOLO[4,5-e][1,4]DIAZEPINE, AND S-TRIAZOLO[3,4-c]THIAZOLO[4,5-e][1,4]DIAZEPINE DERIVATIVES

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1,3-Oxathiolium cation (1) reacts easily with nucleophiles and is a versatile intermediate for a variety of heterocyclic compounds. As an extension of our studies on 1,3-oxathiolium cation, we investigated the fusion of heterocyclic rings to the seven membered diazepine ring system resulting in novel hetero 1,4-diazepines.

The starting 3-amino-2-benzoyl-4-cyano-5-dialkylaminothiophene (2) and 4-amino-5-benzoyl-2-dialkylamino(or 2-aryl)-thiazole (3) were readily obtained from 2-dialkylamino(or 2-aryl)-1,3-oxathiolium salts by the reaction with malononitrile or cyanamide, respectively, in high yields. N-Monomethylated 2 was coupled with chloroacetyl chloride or Z-Gly-Cl and then converted into 8-cyano-1-methyl-5-phenyl-7-piperidino(or morpholino)-1,3-dihydro-2H-thieno[3,2-e][1,4]-diazepin-2-one (4). Smiles rearrangement was observed when phthalylglycyl-N-methylaminothiophene was heated with hydrazine hydrate giving N^2-substituted thiopheneglycinamide. 4-Amino-5-benzoyl-2-piperidinothiazole (3) was coupled with chloroacetyl chloride or Pht-Gly-Cl. Aminolysis or hydrazinolysis of the resulting chloroacetamide or phthalylglycylamide failed to cyclize into thiazolodiazepines and starting aminothiazole was recovered. Cyclization was finally achieved by reaction of chloroacetamide with hexamethylenetetramine in $CHCl_3$ and then treatment with EtOH-HCl. Another method to obtain thiazolodiazepine is conversion of 3 into Z-glycylamide and then deprotection with HBr-HOAc followed by treatment with DABCO or Et_3N. Through this method , we obtained a series of thiazolodiazepines (5) having various substituents at 2, 4, and 6 positions. Triazolothiazolodiazepine was obtained from 5 by several steps.