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A NEW SYNTHESIS OF THIAZOLES FROM TOSYLMETHYLISOCYANIDE AND CARBOXYMETHYL DITHIOATES[1]

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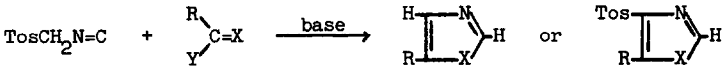
In a previous series of papers[2,3] the synthetic utility of tosylmethylisocyanide (TosMIC, I) has been advocated. TosMIC reacts, under basic conditions, with carbonyl compounds to provide in good yields oxazoles (III, X = O), or 4-tosyl-substituted oxazoles (IV, X = O), depending on the nature of Y in II (Y = H resp. Cl or RCOO).[2] Similarly, reaction with imidoyl chlorides (II, X = NR', Y = Cl) leads to 4-tosylimidazoles (IV, X = NR').[3]



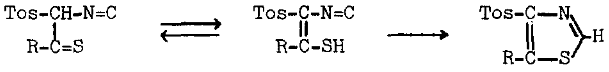
(I) (II) (III) (IV)

X = O,NR',S; Y = see text

We now wish to describe the reaction of TosMIC with thiocarbonyl compounds. Since monomeric thioaldehydes are not available, our attention thus far has been focused on thioacylating substrates. Positive results were indeed obtained with the easily prepared carboxymethyl dithioates[4] (II, X = S, Y = SCH_2COOH), which are known to be highly efficient thioacylating agents for various amino compounds.[5,7]

According to the general scheme, 4-tosylthiazoles (IV, X = S) are obtained in fair yields when 3 equiv. of crushed KOH are added to a solution of 2 equiv. of TosMIC and 1 equiv.

of carboxymethyl dithioate (II, X = S, Y = SCH$_2$COOH) in t-BuOH.[6] The reaction is assumed to take place through initial thioacylation of TosMIC at C$_\alpha$, as indicated below. This equation also stresses an essential feature of the use of TosMIC in heterocyclic syntheses: the 2-position in the products remains unsubstituted.



(V, equals IV for X = S)

R (in V)	m.p. °C	% yield
p-CH$_3$O-C$_6$H$_4$	183-185	79
p-CH$_3$-C$_6$H$_4$	142-143	62
C$_6$H$_5$	148-149	53
p-Cl-C$_6$H$_4$	180-181	48
2-furyl	137-138	58

Apparently, the above reaction requires an efficient thioacylating agent, since under the same conditions no reaction was observed with mono- or dithiocarboxylates (II, X = S, Y = OR, or SR). On the other hand, the esters of carboxymethyl dithioates (II, X = S, Y = SCH$_2$COOCH$_3$) react equally well as the corresponding carboxylic acids (Y = SCH$_2$COOH).

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NOTES AND REFERENCES

1. This communication is considered Part 4 of Chemistry of Sulfonylmethylisocyanides. For previous Parts, see ref. 2 and 3.
2. A.M. van Leusen, B.E. Hoogeboom, and H. Siderius, Tetrahedron Letters 1972, in press. Likewise, under milder conditions Δ^2-oxazolines are obtained from aldehydes and certain ketones.
3. A.M. van Leusen and O.H. Oldenziel, Tetrahedron Letters 1972, in press. Remarkably, in some cases aldoimines lead to Δ^2-oxazolines rather than Δ^2-imidazolines; to be published.
4. K.A. Jensen and C. Pedersen, Act. Chem. Scand. 15, 1087 (1961).
5. Review: F. Kurzer, Chem. and Ind. 1961, 1333.
6. After stirring for 6-12 hrs., t-BuOH is stripped off, water is added, and the solid residue is crystallized from benzene-pentane. The thiazole structure is supported by elemental analyses and spectral data.
7. A. Kjaer, Act. Chem. Scand. 6, 327 (1951); G.C. Barrett, J. Chem. Soc. 1965, 2825.