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PHOTOCHEMICAL ACTIVATION OF THE CARBOXYL GROUP VIA N-ACYL-2-THIONOTHIAZOLIDINES

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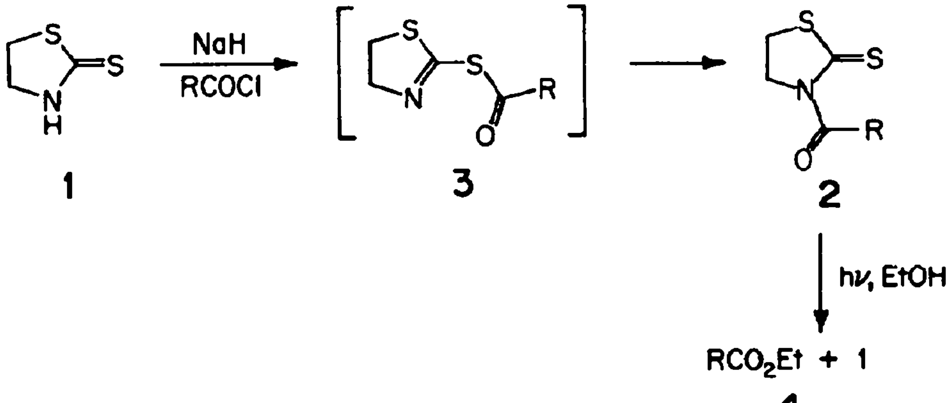
Summary: Photolysis of N-acyl derivatives of 2-thionothiazolidine in the presence of ethanol affords ethyl esters; a mechanism involving γ-hydrogen abstraction by sulfur is postulated.

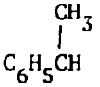
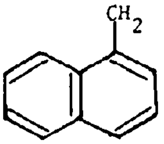
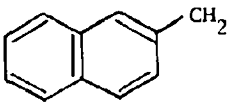
Conventional methodology for activation of the carboxyl group has invariably relied upon conversion of a carboxylic acid to a species (acyl halide, mixed anhydride, active ester, etc.) in which the carboxyl moiety possesses enhanced reactivity towards nucleophilic attack. Although considerable chemical sophistication has been introduced into this technique, particularl in carboxyl activation methods for peptide coupling[2] and recently for macrolide synthesis,[3] ther remains a need for activation of the carboxyl function under mild, neutral conditions using a stable, easily accessible precursor. From this viewpoint, an ideal mode of activation would be photochemical. We describe herein the preparation and photochemical behaviour of N-acyl-2-thionothiazolidines, which suggest that in certain cases, these heterocycles can serve as latent activators of the carboxyl group.[4]

N-Acyl derivatives (2) of 2-thionothiazolidine (1)[5] were conveniently prepared by treatment of the sodium salt of 1 in THF with the corresponding acyl chloride in benzene. The kinetic product from this reaction is probably the S-acyl derivative 3 (the S-isobutyryl intermediate was detected by NMR), but these thioesters apparently undergo a facile, S→N thermal rearrangemen to yield the 3-acylated product 2. The latter are yellow, easily crystallized substances, which exhibit a characteristic carbonyl frequency at 1690-1700 cm^{-1} in their infrared spectra and a pair of two-proton triplets in their NMR spectra at ca δ 3.2 and 4.5.



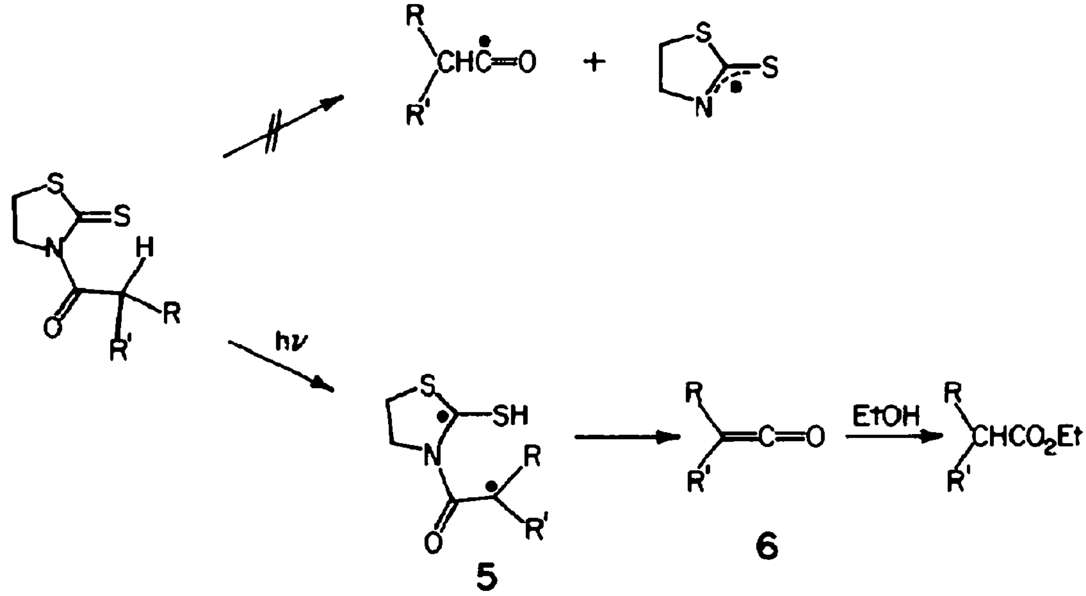
Acylated 2-thionothiazolidines 2 are relatively stable toward both acidic and basic reagents and can be stored indefinitely in the dark. However, upon irradiation with a 450-W mercury lamp through Pyrex, these systems undergo cleavage of the acyl substituent, and 2-thionothiazolidine (1) can be recovered in nearly quantitative yield. If irradiation is carried out in ethanol as solvent, the corresponding ethyl ester 4 is obtained with an efficiency which is markedly dependent on the nature of the R-substituent (see Table I). Thus, arylacetyl derivatives 2a-e afford a generally good yield of ester whereas aliphatic systems such as 2g,h give poor yields. Irradiation of N-benzoyl-2-thionothiazolidone (2f) resulted in a quantitative recovery of starting material. Addition of sensitizers (acetophenone or naphthalene) to the mixture undergoing photolysis produced no significant change in yield, but substitution of Corex or Vycor filters for Pyrex glass gave a considerable quantity of polymeric material. When 2a and 2b were irradiated in benzene solution, only intractable polymeric products were obtained.

Table I. Irradiation of N-Acyl-2-thionothiazolidines (2)

R		Irradiation Time (hr)	Isolated Yield of Ester 4 (%)
$C_6H_5CH_2$	(2a)	14	71
$(C_6H_5)_2CH$	(2b)	12	84
 $C_6H_5CH(CH_3)$	(2c)	12	86
	(2d)	12	73
	(2e)	12	59
C_6H_5	(2f)	20	0
$(CH_3)_2CH$	(2g)	12	17
$CH_3(CH_2)_7$	(2h)	23	24

The failure of 2f to undergo photolysis, when taken with the general absence of products characteristic of acyl radical intermediates in these irradiations, argues against a primary photodissociative process[6] of the type shown in Scheme I. A plausible alternative appeared to be γ-hydrogen abstraction by sulfur, analogous to the pathway observed by Barton and coworkers in their study of the photolysis of O-phenylethylthiobenzoates.[7] Thus, removal of a hydrogen from the carbon α to the acyl function by the sulfur atom of the thione leads to diradical 5; the latter can subsequently collapse to a ketene 6 with the regeneration of 1.[8]

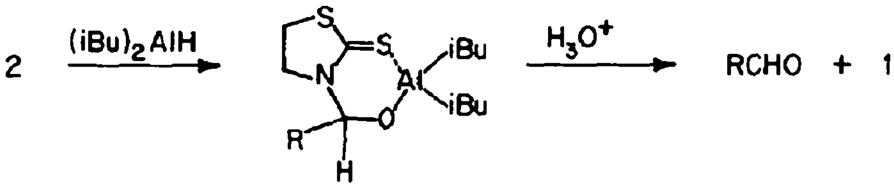
SCHEME I



A distinction between the mechanisms implicit in Scheme I is afforded when a N-acyl-thionothiazolidine carrying an optically active carbon α to the carbonyl group is subjected to photolysis. For this purpose, hydrotropic acid ($[\alpha]_D^{21}$ +46.6°, resolved via its strychnine salt[9]) was converted to the corresponding thionothiazolidine 2c ($[\alpha]_D^{21}$ -11.7°). Irradiation of this substance in ethanol gave ethyl hydrotropate with $[\alpha]_D^{21}$ -0.18°.[10] This finding is consistent with a mechanism proceeding through ketene 6.

Although this photochemical activation process appears, for practical purposes, restricted to cases where hydrogen abstraction and subsequent ketene formation is favored by aryl substitution, the N-acyl-2-thionothiazolidine nucleus affords an attractive device for masking latent reactivity of the acyl group. For example, it has recently been shown that these substances are reduced in excellent yield to aldehydes with diisobutylaluminum hydride via an aluminum chelate

7.[11] Other properties of this interesting heterocyclic system will be reported subsequently.[12]



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REFERENCES AND NOTES

(1) National Institutes of Health Research Career Development Awardee, 1976-81.
(2) Yu. V. Mitlin and N.P. Zapevalova, Russian Chem. Rev., **46**, 499 (1977).
(3) K.C. Nicolaou, Tetrahedron, **33**, 683 (1977), T.G. Back, Tetrahedron, **33**, 3041 (1977); S. Masamune, G.S. Bates, and J.W. Corcoran, Angew. Chem. Internat. Edn., **16**, 585 (1977).
(4) For a recent review of the photochemistry of carboxylic acid derivatives, see J.D. Coyle, Chem. Rev., **78**, 97 (1978).
(5) C.S. Dewey and R.A. Bafford, J. Org. Chem., **30**, 491 (1965).
(6) J.G. Calvert and J.N. Pitts, "Photochemistry", Wiley, New York, 1966, p 427.
(7) D.H.R. Barton, M. Bolton, P.D. Magnus, and P.J. West, J. Chem. Soc. Perkin Trans. I, 1580 (1973).
(8) Unlike the photolysis of O-phenethylthiobenzoates, where an intermediate oxetane was isolated,[7] no evidence for a β-lactam from **5** could be found.
(9) H.S. Roper, J. Chem. Soc., **123**, 2557 (1923).
(10) Ethyl hydroatopate, prepared from hydrotropic acid ($[\alpha]_D^{21}$ -27.0°) by treatment with phosphorus trichloride and then ethanol, had $[\alpha]_D^{21}$ -43.0°.
(11) T. Izawa and T. Mukaiyama, Bull. Chem. Soc. Japan, **52**, 555 (1979).
(12) It has very recently been shown that **2** reacts with primary and secondary amines to yield amides in high yield (Y. Nagao, K. Seno, K. Kawabata, T. Miyasaka, S. Takao, and E. Fujita, Tetrahedron Lett., 841 (1980)).

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