

Heterocycles from Ylides. Part V (1).
Reactivity of 4-Arylmethylene- Δ^2 -isoxazolin-5-ones with Stabilized Sulfur Ylides

Piero Dalla Croce

Istituto di Chimica Industriale dell'Università di Milano, C.N.R.,
Centro di studio sulla sintesi e stereochimica di speciali sistemi organici, Via Golgi, 19 20133 Milano, Italy

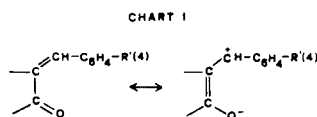
Received April 7, 1976

4-Arylmethylene- Δ^2 -isoxazolin-5-ones react with carbonyl-stabilized sulfur ylides yielding spiro[cyclopropane-1,4'- Δ^2 -isoxazolin]-5'-ones identified from spectroscopic data and chemical behaviour.

J. Heterocyclic Chem., 13, 1109 (1976).

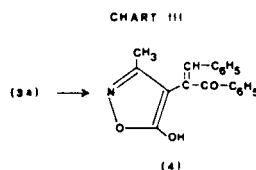
The use of carbonyl-stabilized sulfur ylides in organic synthesis has become very important in recent years (2). The acyl, diacyl and ethoxycarbonyl-stabilized sulfur ylides have been shown to give cyclopropane derivatives with Michael acceptors (3).

Herein is reported the reaction between carbonyl-stabilized sulfonium ylides and 4-arylmethylene- Δ^2 -isoxazolin-5-ones. These compounds, analogous to 4-arylmethylene- Δ^2 -pyrazolin-5-ones (4), can show the mesomerism illustrated in Chart I. The different contribution of the diene and dipolar forms is influenced by the nature of substituent R' in the arylmethylene group. Accordingly products derived from [1,2] versus [1,4] addition reactions might be expected.



Reaction of dimethyl sulfoniumphenacylide (1) with several (*Z*) 4-arylmethylene- Δ^2 -isoxazolin-5-ones (2a-e) gave only the spiro[cyclopropane-1,4'- Δ^2 -isoxazolin]-5'-ones

(3a-e) deriving from a [1,4-conjugate] addition reaction (5) (Chart II). This behaviour is closely related to that of stabilized sulfur ylides with α,β -unsaturated carbonyl compounds (6). The principal characteristics of compounds (3a-e) are summarized in Table I.



The structure of compounds (3a-e) was confirmed on the basis of spectroscopic data (Table II). The infrared spectrum (two carbonyl absorptions) was consistent with the spiro[cyclopropane-isoxazolinonic] structure. The ^1H nmr spectrum showed an AB splitting pattern for the cyclopropane hydrogen atoms allowing the assignment to the $\text{H}_2\text{-H}_3$ system of the *cis* configuration on the basis of the coupling constants (7,8).

The products (3a-e) might have two alternative configurations: *cis-exo* (see Chart II) and *cis-endo*. The exami-

Table I

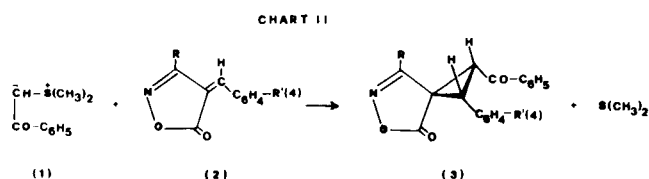
Compound	Substituents		M.p. °C	Crystallization Solvent	Yield %	Molecular Formula	Analysis					
	R	R'					Calcd.		Found			
						C	H	N	C	H	N	
3a	CH ₃	H	120-121	Ethanol	90	C ₁₉ H ₁₅ NO ₃	74.74	4.95	4.59	74.83	4.96	4.47
b	CH ₃	OCH ₃	118-119	Ethanol	86	C ₂₀ H ₁₇ NO ₄	71.63	5.11	4.18	71.68	5.13	4.01
c	CH ₃	NO ₂	119-120	Buthanol	70	C ₁₉ H ₁₄ N ₂ O ₅	65.14	4.03	8.00	65.19	3.88	8.00
d	C ₆ H ₅	H	182-183	Ethanol	86	C ₂₄ H ₁₇ NO ₃	78.46	4.66	3.81	78.18	4.64	3.67
e	C ₆ H ₅	NO ₂	180-181	Ethanol	95	C ₂₄ H ₁₆ N ₂ O ₅	69.90	3.91	6.79	70.10	4.23	6.69

Table II

Compound	Ir ν CO cm^{-1}	Nmr (Perdeuteriobenzene)		
		τ H ₂	τ H ₃	J _{2,3} (cps)
3a	1770, 1680	5.96	6.15	9.0
b	1770, 1670	5.93	6.10	9.1
c	1760, 1670	5.20	5.46	9.0
d	1770, 1670	5.61	6.05	9.1
e	1760, 1675	5.20	5.40	9.0

nation of molecular models revealed that the first appears the most probable owing to the (*Z*) configuration of starting 4-arylmethylene- Δ^2 -isoxazolin-5-ones (9) and to less steric interaction between the isoxazoline 3'-substituent and the cyclopropane 2- and 3-substituents.

The structure of spiro[cyclopropane-isoxazolin]ones was also supported by the following chemical transformation. Treatment of compound (**3a**) with potassium *t*-butoxide in dimethyl sulfoxide prompted abstraction of the 3-proton followed by cleavage of the cyclopropane 1,2-bond. This led to 4-(α -benzylidenephenacyl)-5-hydroxy-3-methyl-isoxazole (**4**) (Chart III).



The easy entry to spiro[cyclopropane-isoxazolin]ones by this regiospecific and stereospecific route contribute to the general utility of carbonyl-stabilized sulfur ylides in heterocyclic synthesis.

EXPERIMENTAL

Melting points are uncorrected. Nmr spectra were recorded with a Varian A-60 spectrometer (TMS as internal standard). Ir spectra were recorded on a Perkin-Elmer model 137 Infracord spectrophotometer as a ca. 2% chloroform solution.

4-Arylmethylene- Δ^2 -isoxazolin-5-ones (**2a-e**).

These were prepared by reported methods (12,13,14) from 3-methyl or 3-phenyl- Δ^2 -isoxazolin-5-ones and the appropriate aldehyde.

General Procedure for the Preparation of Spiro Cyclopropane-isoxazolinones (**3a-e**).

A solution of dimethyl sulfoniumphenacylide (**1**) (15) (0.01 mole) in 1,2-dimethoxyethane (25 ml.) was added to a stirred suspension, cooled to -20° , of the 4-arylmethylene- Δ^2 -isoxazolin-5-one (0.01 mole) in the same solvent (50 ml.). The mixture was stirred for 2 hours and then the solvent was evaporated and the residue was crystallized (see Table I).

4-(α -Benzylidenephenacyl)-5-hydroxy-3-methylisoxazole (**4**).

A mixture of compound **3a** (1 g.) and of potassium *t*-butoxide (0.3 g.) in dimethyl sulfoxide (25 ml.) was allowed to stand overnight at room temperature. The solvent was evaporated under vacuum and the residue was taken up with water (25 ml.) and ether (25 ml.). The aqueous layer was acidified with 10% aqueous acetic acid and the precipitate filtered off. The product was purified from ethanol, m.p. $137-138^\circ$, yield 57%; ir: ν OH 3140 cm^{-1} ; ν CO 1670 cm^{-1} .

Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{NO}_3$: C, 74.74; H, 4.95; N, 4.59. Found: C, 75.01; H, 4.88; N, 4.32.

REFERENCES AND NOTES

- (1) Part IV. P. Dalla Croce and D. Pocar, *J. Chem. Soc., Perkin Trans. 1*, 620 (1976).
- (2) B. M. Trost and L. S. Melvin Jr., "Sulfur Ylides," Academic Press, 1975, pp. 1-107.
- (3) H. Nzaki, M. Takaku and K. Kondo, *Tetrahedron*, **24**, 2141 (1966).
- (4) G. Cellerino, G. Desimoni, P. Righetti and G. Tacconi, *Gazz. Chim. Ital.*, **103**, 1247 (1973).
- (5) The use of solvents of increased polarity (acetonitrile, dimethyl sulfoxide) at several temperatures (0, 25, 65°) did not influence the reaction path. Products derived from [1,2] or [1,4-dipolar] addition reactions with formation respectively of oxirane or dihydrofuran derivatives were not detected.
- (6) G. B. Payne, *J. Org. Chem.*, **32**, 3351 (1967).
- (7) H. Booth, *Progr. Nmr Spectros.*, **5**, 167 (1969); L. M. Jackmann and S. Sternhell, "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, Oxford, 1969.
- (8) Y. Tamuru, T. Migamoto, H. Kiyokawa and Y. Kita, *J. Chem. Soc.*, 1125 (1974).
- (9) For 3-substituted compounds the configuration is (*Z*) owing to steric interaction (10,11).
- (10) J. Meunier-Piret, P. Piret, G. German, J. P. Putzeys and M. Van Meerse, *Acta Cryst.*, **B 28**, 1308 (1972).
- (11) A. Maquestiau, Y. Van Haverbeke and R. N. Muller, *Tetrahedron Letters*, 1147 (1972).
- (12) J. J. Douleavy and E. E. Gilbert, *J. Am. Chem. Soc.*, **59**, 1074 (1937).
- (13) G. Lo Vecchio, G. Lamonica and G. Cum, *Biochim. Appl.*, **10**, 131 (1963).
- (14) G. Lo Vecchio, G. Grassi, F. Risitano and F. Foti, *Tetrahedron Letters*, 3777 (1973).
- (15) A. W. Johnson and R. T. Amel, *J. Org. Chem.*, **34**, 1240 (1969).