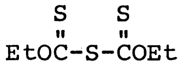
CHEMISTRY LETTERS, pp. 1251-1254, 1986.

Generation and C-Ethoxythiocarbonylation of Enolates Using Ultrasound

Mario A. PALOMINOS, Robinson RODRIGUEZ, and Juan C. VEGA*
Facultad de Química, Pontificia Universidad Católica de Chile,
Casilla 6177, Santiago, Chile

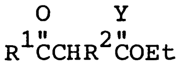
O-Ethyl 3-oxothionoesters were obtained in good yields by reaction of O,O-diethyl trithiodicarbonate with enolate from ketones and NaH in tetrahydrofuran. The enolate formation and thioacylation were performed under ultrasonic irradiation.

The aminolysis[1)] and thiolysis[2,3)] of some unsymmetrical pyrothiocarbonates or thiodicarbonates have been published. The synthesis of symmetrical and unsymmetrical thiodicarbonates has also been reported.[4,5)] In this communication we wish to report the reaction of carbon nucleophiles, e.g., enolates, with O,O-diethyl trithiodicarbonate (**1**), which afforded O-ethyl 3-oxothionoesters (**2**). These compounds have been synthesized by several methods: sulfhydrolysis of hydrochloride 3-oxoimidoesters[6)] (**3**) using H_2S and pyridine in 28-52% yield, desulfuration of S-(acetonyl or phenacyl) O-ethyldithiocarbonate[7)] (**4**) utilizing NaH in tetrahydrofuran (THF), whose yields are 24 and 34% respectively, and ethoxythiocarbonylation of enolates with S-ethyl O-ethyldithiocarbonate (**5**) using ethyl ether as solvent, and $NaNH_2$ as a base to form the enolates.[8)] The latter method is not satisfactory because, in our experience, it gave products of ketone self-condensation which were difficult to separate from 3-oxothionoesters. The oxygen analogues of these compounds, β-ketoesters, have been obtained by C-alkoxycarbonylation of ketone enolates, which is a well known procedure. There are, however, some limitation such as O-acylation, self-condensation of the ketone, and long reaction periods.[9)] A very recent report is available on the preparation of O-ethyl β-ketoesters by reaction of enolates from cyclic ketones with diethyl dicarbonate.[10)] Lately, there has been increasing interest in ultrasound (u.s.) to accelerate multiple types of reactions.[11)] We therefore decided to study the preparation of O-ethyl 3-oxothionoesters (**2**) by C-ethoxythiocarbonylation of ketone enolates under ultrasonic irradiation.



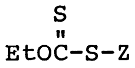
$\mathrm{EtO\overset{S}{\overset{\shortparallel}{C}}{-}S{-}\overset{S}{\overset{\shortparallel}{C}}OEt}$

1



$\mathrm{R^{1}\overset{O}{\overset{\shortparallel}{C}}CHR^{2}\overset{Y}{\overset{\shortparallel}{C}}OEt}$

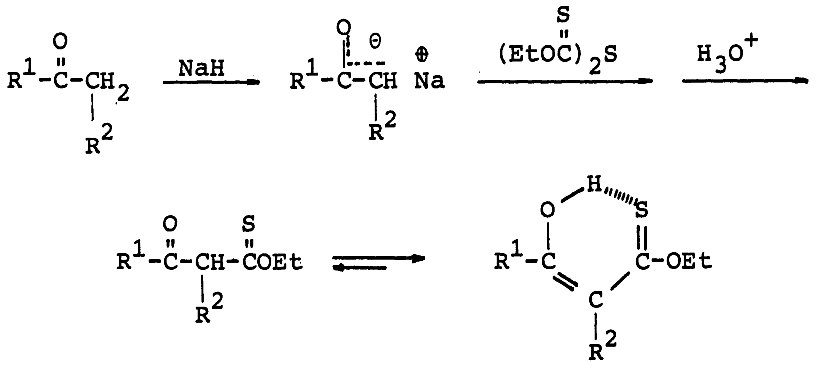
2, Y=S
3, Y=NH·HCl



$\mathrm{EtO\overset{S}{\overset{\shortparallel}{C}}{-}S{-}Z}$

4, $Z=CH_2COCH_3$, CH_2COPh
5, Z=Et

We selected cyclohexanone as a typical substrate, and NaH in THF as a one of the more common bases to generate enolates. Among several thioacylating reagents tested we found that **1** afforded the best result when the enolate was generated from cyclohexanone and NaH suspended in THF under ultrasonic irradiation; subsequently it reacted with **1** under u.s. provided by an ultrasonic lab cleaner. The first step lasted 90 min according to the hydrogen volume formed; the second step lasted 30 min because of the change of the characteristic yellow color of **1**. Both steps were performed at 40 °C. The proportion of enolate to thioacylating reagent was 2.1:1. In these conditions the yield of 2-ethoxythiocarbonylcyclohexanone was 93%. Employing a ratio of 1:1 the yield decreased to 37%. When cyclohexanone, NaH, and **1** in the proportion 1:2:1 were mixed all at once, the yield also dropped because of the inestability of **1** in these conditions. Other thioacylating reagents essayed were $EtOCS_2Et$, EtOCSCl, and $(EtOCS)_2S_2$. Without u.s. and when the 2.1:1 mixture was refluxed in THF, the yield dropped sharply and the self-condensation product appeared. To evaluate the conversion of ketone to enolate with and without u.s. we selected acetophenone because of its reactivity. The formation of its enolate was performed with u.s. under the same conditions as those used for **2f** preparation. After quenching the enolate with chlorotrimethylsilane and working-up, it can be deduced from glc analysis that the silylated product was 75%. Under the same conditions, but without u.s., the yield was 18%.



2 **2'**

After work-up glc showed that esters **2** were obtained in good yields, with the only exception of **2b**. The formation of the O-thioacylated product is less than 5%. Table 1 shows the conditions and yields of this method, which is simpler and more efficient than those reported. As expected the more reactive ketones were cyclopentanone and acetone. Acetophenone was also very reactive.

Products **2** were formed as follows: A mixture of ketone (15 mmol) and NaH (15 mmol) in THF (20 mL; sodium-benzophenone) under nitrogen in a round bottom flask was partially submerged in an ultrasonic lab cleaner12) filled with water at the temperature indicated in Table 1. After the time shown in this table, **1** (7 mmol) dissolved in THF (15 mL) was added through a septum by means of a hypodermic syringe, and cavitational agitation was kept up for some time (see

Table 1. Preparation of O-ethyl 3-oxothionoesters, R^1COCHR^2CSOEt (**2**)

2	R^1	R^2	Time of enolate formation/min	Time of thio-acylation/min	Temp °C	Yield[a)] %
a	$-(CH_2)_4-$		90	30	40	93
b	$-(CH_2)_3-$		30	15	25	52[b)]
c	C_2H_5	CH_3	90	30	40	74
d	CH_3	H	45	15	25	88
e	t-C_4H_9	H	75	30	40	82
f	C_6H_5	H	30	15	40	95

a) Isolated yield based on **1**. b) Purified by preparative tlc using silica gel, Merck Art. 7747, and cyclohexane.

Table 1) at the same temperature. The crude product was poured into cold 5% hydrochloric acid, extracted with dichloromethane and dried with magnessium sulphate. The filtered solution was evaporated, and the residue was submitted to fractional distillation at reduced pressure. The physical properties of **2** and their enol form (**2'**) percentages are shown in Table 2.

Table 2. Physical properties and enol contents of **2**

2	Bp/°C (Torr) Found	Bp/°C (Torr) Reported[8)]	n_D^{20}	IR(ν/cm^{-1})[b)] C=O	IR(ν/cm^{-1})[b)] C=C	^{1}H-NMR (δ, ppm)[c)] O-H	^{1}H-NMR (δ, ppm)[c)] C-H	% enol[d)] Found	% enol[d)] Reported[13)]
a	85(0.5)	105-8(1.5)	1.5532	1708	1570	14.18		96	<100
b	48(mp)[a)]	108-110(3)			1580	12.98		100	100
c	78(2)	-[a)]	1.5000	1723	1565	14.60		85	
d	50(2)	43(0.8)	1.5143	1712	1605	13.79	5.72	82	82
e	63(0.5)	-[a)]	1.5078	1710	1590	14.02	5.82	90	
f	116(0.3)	122-5(0.5)	1.6250	1685	1590	14.19	6.38	86	89

a) Satisfactory microanalysis obtained. b) KBr plates. c) $CDCl_3$. d) According to ^{1}H-NMR spectra at 32 °C in $CDCl_3$ at equilibrium.

It can be seen from Table 2 that 3-oxothionoesters **2** are highly enolised. In connection with enol contents it must be mentioned that **2c** and **2f** keto forms are slowly displaced in favour of enol forms until equilibrium is reached, as described.[7] This final value is shown in Table 2.

M.A.P. thanks PNUD-UNESCO through project CHI-84-006 and FONDECYT-CHILE for financial support.

References

1) M.A. Palominos, J.G. Santos, J.A. Valderrama, and J.C. Vega, Phosphorus Sulfur, 15, 245 (1983).

2) M.A. Palominos, J.G. Santos, J.A. Valderrama, and J.C. Vega, J. Chem. Soc., Perkin Trans.1, 1983, 2641.

3) E.A. Castro, S.A. Peña, J.G. Santos, and J.C. Vega, J. Org. Chem., 49, 863 (1984).

4) S. Juliá, G. Tagle, and J.C. Vega, Synth. Commun., 12, 897 (1982).

5) M.A. Palominos, J.G. Santos, J.C. Vega, and M.A. Martínez, Phosphorus Sulfur, 25, 91 (1985).

6) G. Barnikow and G. Strickmann, Chem. Ber., 100, 1428 (1967).

7) A.J. Bridges and G.H. Whitham, J. Chem. Soc., Perkin Trans.1, 1975, 1603.

8) S. Scheithauer and H. Pech, Ger. (East) Pat., 94 361 (1972); Chem. Abstr., 79, 5176 (1973); S. Scheithauer, personal communication.

9) "Carbon-Carbon Bond Formation," ed by R.L. Augustine, Marcel Dekker, Inc., New York (1978), Vol. 1.

10) J. Hellou, J.F. Kingston, and A.G. Fallis, Synthesis, 1984, 1014.

11) For leading references see: B.H. Hang and P. Boudjouk, Tetrahedron Lett., 23, 1643 (1982); R. Newmann and Y. Sasson, J. Chem. Soc., Chem. Commun., 1985, 616.

12) Cole-Palmer, model Nª 8845-46 operating at 230 W.

13) S. Scheithauer and R. Mayer, "Thio- and Dithiocarboxylic Acids and Their Derivatives," "Topics in Sulfur Chemistry," ed by A. Senning, Georg Thieme Verlag, Stuttgart (1979), Vol. 4, pp. 220-222.

(Received April 22, 1986)