## A CONVENIENT ONE-POT PROCEDURE FOR SYNTHESIS OF THIOL ESTERS USING MAGNESIUM ION AS A CATALYST

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Summary: Various thiol esters  $(R^1 \text{COSR}^2)$  were prepared in high yields by treatment of 1-acylimidazole with thiols in the presence of a catalytic amount of  $\text{Mg(OEt)}_2$ . Malonic half-thiol esters  $[R^1 \text{OCOCH}(R^3) \text{COSR}^2]$  were also prepared in good yields by treating magnesium monoalkyl malonate  $[R^1 \text{OCOCH}(R^3) \text{COOMg}_{1/2}]$  with carbonyl-1,1'-diimidazole followed by addition of thiols.

Thio-esterification of carboxylic acid by the known methods  $^1$ ) has been associated generally with some disadvantages such as use of toxic materials and heavy metals, less applicability to hindered alkanethiols and tedious procedure. Although Masamune reported that 1-acylimidazole ( $\underline{2}$ , Im : 1-imidazolyl group) reacted with benzenethiol to give the corresponding thiol ester  $\underline{4}$  but not with alkane thiols  $^{1b}$ , the authors have found that the reaction of  $\underline{2}$  with thiols including alkane thiols was accelerated in the presence of a catalytic amount of Mg(0Et)<sub>2</sub> to give the thiol esters ( $\underline{4}$ ) in excellent yields (eq. 1 and Table 1).

$$R^{1}COOH \xrightarrow{Im_{2}CO} [R^{1}COIm] \xrightarrow{\tilde{R}^{2}SH (\underline{3}) / r.t.} R^{1}COSR^{2}$$

$$\underline{1} \xrightarrow{In DMF / r.t. (\underline{2}, in situ)} \frac{\tilde{R}^{2}SH (\underline{3}) / r.t.}{cat. amt. of Mg(OEt)_{\underline{2}}} R^{1}COSR^{2} \qquad (eq. 1)$$

For example, in the absence of  ${\rm Mg(OEt)}_2$ , a reaction of  $\frac{1}{2}$  ( ${\rm R}^1$  = o-chlorophenyl, 3 mmole) with t-BuSH (3 mmole) in DMF (3 ml) at r.t. (20°) did not proceed satisfactorily even after being stirred for 24 hr (6.2 % formation of the corresponding thiol ester  $\frac{4}{2}$  was observed on HPLC analysis), but in the presence of 0.03 molar equivalent of  ${\rm Mg(OEt)}_2$  (11.5 mg), the reaction proceeded smoothly and almost completed after being stirred overnight at r.t. to give  $\frac{4}{2}$  as oil (o-Cl-C<sub>6</sub>H<sub>4</sub>-COS-t-Bu) in quantitative yield after usual work-up.

Monomethyl malonate (MeOCOCH<sub>2</sub>COOH) was readily converted to dimethyl  $\beta$ -ketoglutarate in quantitative yield when treated with  ${\rm Im}_2{\rm CO}$ , on the other hand, magnesium monomethyl malonate (5, R<sup>1</sup> = H, R<sup>2</sup> = Me) reacted with  ${\rm Im}_2{\rm CO}$  accompanied by evolution of  ${\rm CO}_2$  gas, and subsequent addition of thiols to the mixture gave the malonic half-thiol esters (9)<sup>2</sup>) in good yields (eq. 2 and Table 1). The manipulation is similar as that for o-Cl-C<sub>6</sub>H<sub>4</sub>-COS-t-Bu. The product of entry 10 could be easily converted to the corresponding half malonic ester (10, R<sup>1</sup> = H, R<sup>3</sup> = C<sub>6</sub>H<sub>5</sub>, viscous material) by treating with trifluoroacetic acid (eq. 2).

Table 1 Thiol Ester obtained by the New Method<sup>3)</sup>

entry	thiol ester (bp <sup>*1</sup> )	yıeld <sup>*2</sup>	entry	thiol ester (bp <sup>*1</sup> or mp)	yıeld <sup>*2</sup>
1	C <sub>6</sub> H <sub>5</sub> COS-t-Bu (bp <sub>1.0</sub> 125 - 127°)	87.1	7	c-C <sub>6</sub> H <sub>11</sub> COS-2-pyridyl (mp 88 - 90°) <sup>*3</sup>	83.0
2	o-OH-C <sub>6</sub> H <sub>4</sub> -COS-Et (bp <sub>1.0</sub> 118 - 120°)	87.0	8	Bz1-OCONHCH <sub>2</sub> CH(OH)CH <sub>2</sub> COSEt (viscous material)	85.4
3	o-Cl-C <sub>6</sub> H <sub>4</sub> -COS-t-Bu (bp <sub>1.0</sub> 145 - 148°)	quant.	9	Me0C0CH <sub>2</sub> COS-C <sub>6</sub> H <sub>5</sub> (bp <sub>1.0</sub> 160 - 163°)	quant.
4	3-pyridyl-COS-t-Bu (bp <sub>1.0</sub> 137 - 140°)	quant.	10	t-Bu-0C0CH <sub>2</sub> COS-C <sub>6</sub> H <sub>5</sub> (bp <sub>1.0</sub> 169 — 173°)	85.5
5	t-Bu-COS-t-Bu (bp <sub>21</sub> 101 - 103°)	87.2	1 1	Et0C0CH(Bzl)COS-t-Bu (bp <sub>1.0</sub> 175 — 178°)	quant.
6	c-C <sub>6</sub> H <sub>11</sub> -COS-t-Bu (bp <sub>2.0</sub> 90 - 92°)	90.0	12	EtOCOCH(CH <sub>2</sub> CH=CH <sub>2</sub> )COSEt (bp <sub>2.0</sub> 134 - 135°)	76.2

## References and Footnotes

- 1) a) H.-U.Reigig and B.Scherer, Tetrahedron Lett., 21, 4259 (1980); literatures therein.
  - b) G.S.Bates, J.Diakur, and S.Masamune, 1bid., 17, 4423 (1976); literatures therein.
  - c) H-J.Liu, S.P.Lee, and W.H.Chan, Synth. Commun., 9, 91 (1979); literatures therein.
  - d) H-J.Liu, S.K.Attah-Poku, and H.K.Lai, ibid., 9, 883 (1979); literatures therein.
- 2) Malonic half-thiol esters are of interest because of close relations to malonyl S-CoA and have been noticed recently as useful materials for organic synthesis. [D.W.Brooks, L-D.Lu, and S.Masamune, Angew. Chem. Int. Ed. Engl., 18, 72 (1979)]
- Spectral and analytical data of all compounds shown in Table 1 were consistent with their structures.

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