

**MICROWAVE THERMOLYSIS VII : OXIDATIVE  
COUPLING OF THIOL ACETATES AND ESTERS USING  
"CLAYAN" IN DRY MEDIA**

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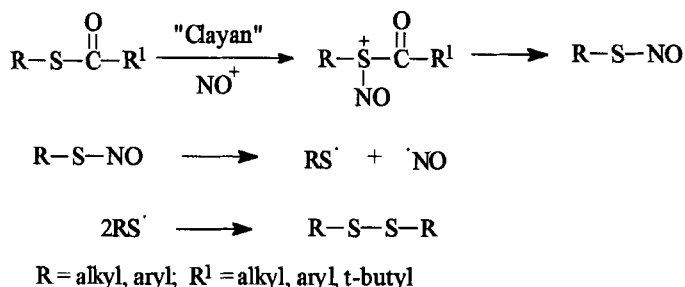
**Abstract :** Disulfide bond formation by the oxidative cleavage of thiol acetates and thiol esters using "Clayan" under microwave irradiation is described. The non-metallic and inexpensive nature of the reagent are the important features of the procedure.

Disulfide bond formation is important in peptide synthesis,<sup>1</sup> protein stabilization<sup>2</sup> and in bioactive molecules.<sup>3</sup> Thiols are the main precursor for disulfides but they are highly susceptible to air oxidation and can not survive in multistep synthesis. Therefore, the protection of thiols as acetates or esters and their subsequent transformation into -S-S- linkage is important.

There are few methods<sup>4</sup> for the cleavage of thiol acetates under abnormal conditions like, longer reaction time<sup>4a</sup> (12 days), argon atmosphere<sup>4b</sup> and photolysis<sup>4c</sup>. However, the scope and limitations are not studied systematically. Recently, among the improved methods, one

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### Scheme

of the procedure needs activation by stannates<sup>5</sup> while the another uses a metallic reagent<sup>6</sup> with a longer reaction time. The last decade has witnessed much research activity in the area of solid supported catalysts<sup>7,8</sup> or in combination with microwave<sup>9</sup> because of its simple workup and ease of manipulation. In continuation of our work in the development of non-metallic catalysts, we have devised an efficient and inexpensive method for dethioacetalization,<sup>10a</sup> deoximation<sup>10b</sup> and MPM deprotection.<sup>10c</sup> Herein, we wish to report a rapid and convenient method for the oxidative cleavage of thiol derivatives using clay supported ammonium nitrate "Clayan" under microwave irradiation.

The present method is very rapid and avoids the use of activating reagents or excess of solvent for reaction. We have noticed that when both the acid and thiol parts are aromatic, the C-S bond cleavage is very slow (entry 12, 13). But the reaction is efficient if the acid counterpart is aliphatic. The utility of the procedure is exemplified by the smooth cleavage of long chain thiol ester (entry-6). Nitrates are well known source of NO<sup>+</sup>.<sup>12</sup> So we presume that nitrosonium ion is the attacking species which further gives disulfide as shown in the scheme.

**Table : Thiol acetate or ester into disulphide using "Clayan"**

Entry	Thiol acetate or ester	Acetate or ester : Clayan ratio	Reaction time (min.)	Disulphide <sup>a</sup> Yield (%)	M.P.(°C)	
					Found	Reported <sup>11</sup>
1.		1 : 5	4	98	62	62
2.		1 : 7	5	95	70	71
3.		1 : 5	6	73	34	34.5
4.		1 : 5	4	95	62	62
5.		1 : 7	6	95	34	34.5
6.		1 : 5	5	95	34	34.5
7.		1 : 5	4	95	62	62
8.		1 : 5	5	90	61	62
9.		1 : 7	4	95	34	34.5
10.		1 : 7	6	90	61	62
11.		1 : 7	6	80	61	62
12.		1 : 5	4	61 <sup>b</sup>	62	62
13.		1 : 5	4	57 <sup>b</sup>	61	62

a : All the products are characterized by Mass, NMR, m.p. and by comparison with a TLC of an authentic sample.

b : Reaction remained incomplete even with more clayan (1:8) and longer reaction time (7 min). Starting material recovered.

In conclusion, we have developed a very rapid and convenient method for the formation of S-S bond from thiol derivatives. The inexpensive and non-metallic nature of reagent demonstrates the economic and environmental advantages of the procedure.

## EXPERIMENTAL

Boiling points and melting points are uncorrected. Melting points were recorded on Buchi R535 apparatus. Unless mentioned the chemicals were obtained commercially and used without further purification.  $^1\text{H}$  NMR spectra were recorded on FT 200 (Gemini) spectrometer. Mass spectra were recorded on either micromass 7070H or Finnigan Mat 1020B mass spectrometer operating at 70 eV. Thin layer chromatography was done on precoated silicagel 60f 254 (0.5 mm) glass plates. The reagent "Clayan" was prepared according to known procedure<sup>10b</sup>.

*CAUTION : These procedures are worked out safely in our hands but as the nitrates are dangerous compounds, appropriate precaution is recommended for the reaction at elevated temperature. We suggest that the microwave oven be operated for a shorter time because of the possible higher localised temperature.*

**General Procedure :** In a typical procedure, thiol acetate or ester (1 mmole) is mixed with "clayan"<sup>10a</sup> (see table for ratio) in solid state and transferred to a test tube. It is then irradiated in a microwave oven (BPL make, BMO, 700T, 650w operating at a frequency 2450 MHz) for stipulated period (table). The mixture is extracted with dichloromethane (3 x 20 ml) and solvent is evaporated under reduced pressure. The residue is purified by column chromatography (hexane : ethyl acetate, 95:5) to obtain the pure disulfide.

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