Thionation of carbonyl compounds using phosphorus pentasulfide and hexamethyldisiloxane under microwave irradiations

Vivek Polshettiwar, Manisha Nivsarkar, Deepak Paradashani and M.P. Kaushik*

Process Technology Development Division, Defence R&D Establishment, Jhansi Road, Gwalior, 474002 (MP) India

A novel and convenient microwave assisted thionation of carbonyl compounds using phosphorus pentasulfide and hexamethyldisiloxane is described. Thionation by this method gave the desired product in higher yield and shorter reaction time as compared to conventional methods.

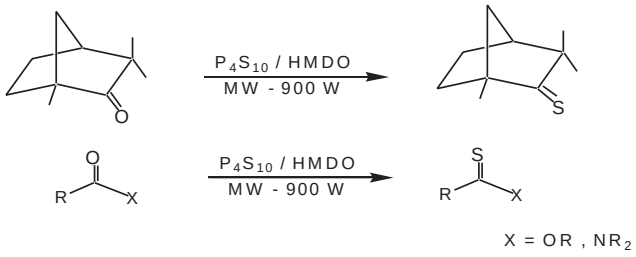
Keywords: thiocarbonyl compounds, thionating agent, microwave, solvent free, HMDO, phosphorus pentasulfide

Thio-analogues of carbonyl compounds *viz*. thioketones, thioesters, thioamides and thiolactams are important intermediates for the synthesis of various biologically active organosulfur compounds of interest.[1,2] Several methods are reported in the literature for the thionation of ketones, esters, amides and lactams[3,4] which make use of various thionating agents (either alone or in combination) such as elemental sulfur,[5] phosphorus pentasulfide[4] and Lawesson's reagent.[6,7] Nevertheless the methods currently available for the synthesis of thio-analogues of carbonyl compounds often involve many steps and transformation is effected at higher temperature (100–150ºC),[8,9] for a long period of time. These methods also involve tedious work-up giving poor to moderate yields of the corresponding thio-derivatives. Recently Curphey[10,11] has shown that combination of phosphorus pentasulfide and hexamethyldisiloxane reagent has efficiently converted esters, lactones, amides and ketones to their corresponding thio-derivatives. Although the method reported is good in terms of selectivity under standard conditions (dry toluene/xylene, thermal heating), but by using P_4S_{10}/HMDO under microwave irradiation has allowed us to increase the selectivity and yields of the product further. In recent chemistry program of Kuhnert,[12] we found that microwave heating can be used to facilitate various transformations effectively. Microwave activation as a non-conventional energy source has become an increasingly popular method that can be used to carry out a variety of reactions within short reaction time, with high yields and high selectivity.[13] This method reduces thermal degradation, formation of byproducts and takes place in the absence of solvents.[14-17]

Acceleration of organic reactions by microwave is well documented. They result from material-wave interactions leading to a thermal effect (connected to dipolar and charge space polarizations) and specific (non thermal) effects resulting from variations in activation parameters and enhancement in molecular impact.[18] We now describe the microwave mediated thionation of ketones, esters, amides and lactam using P_4S_{10}/HMDO as the thionating reagent as shown in Scheme 1. This method has allowed us to improve the selectivity, reduced the reaction time from several hours to few minutes with quantitative yields.

For these studies a newer household MW oven (Samsung) equipped with inverter technology that provides a better control of MW power to a desired level was used. The mixture of corresponding carbonyl compound, HMDO and P_4S_{10} was exposed to microwaves. The reactions were conducted with intermittent heating[19a,b] at power level 900 W and mixing, to obtain better yields and clean products. The intermittent heating is basically to reduce the formation of hot spot. It has been observed that, at elevated power level, a partial decomposition or charring of reaction mixture occurred possibly due to localised overheating of the reaction mixture.

* Correspondence. E-mail: mpkaushik@rediffmail.com



Scheme 1 Thionation by P_4S_{10}/HMDO in microwave oven.

Results obtained with various ketones are shown in Table 1. The yields of thioacetophenone and thiocylcohexanone are low, essentially because both the thioketones are air sensitive and convert back to the corresponding ketones. Similarly, the yield of thiocamphor is also low because of high volatility of the substrate. Relative polarity of the carbonyl compounds also had a profound effect on the yield of the final product, because the more polar the compound is, the better it binds with silica gel during purification and gives lower isolated yields.

In order to explore the utility of our methodology, thionation of the representative set of esters, amides and lactam using P_4S_{10}/ HMDO under microwave were also studied (Table 2).

The conversion of esters to thioesters is a difficult of thionation to effect because of the generally low reactivity of the ester carbonyl group towards the usual thionation reagent, but using P_4S_{10}/HMDO under microwave irradiation, the conversion has taken place with high yield in a short period of time. The amide carbonyl group, is generally the most easily thionated of the common carbonyl group derivatives. Thionation of amide occurred in a very short period of time with excellent yield. In case of lactams, the conversion is 100%, but due to the polar nature of thiolactam, it strongly binds with silica gel on column during workup and hence lowers the isolated yield. When this paper was under communication, solvent free thionation of γ-lactones under microwave irradiation appeared,[20] which is also supportive of data presented in this paper.

The reaction time and yields of the product under microwave conditions were compared with the conventional heating also. In a conventional heating procedure, a three neck reaction flask fitted with a reflux condenser was charged with carbonyl compound, P_4S_{10} and HMDO in xylene as a solvent. The mixture was refluxed under a nitrogen atmosphere and the reaction was monitored by TLC and GC. In comparison with conventional heating protocol, microwave heating has advantages in terms of reaction time and product yield (Table 3).

In summary, we have developed a highly efficient microwave-assisted protocol for the thionation of variety of carbonyl compounds *viz.* ketones, esters, amides and lactam that occurs remarkably fast, under mild reaction condition using P_4S_{10}/HMDO and an unmodified household microwave oven as an irradiations source. The advantages of this method

Table 1 Microwave assisted thionation of ketones by P_4S_{10}/HMDO

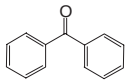
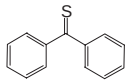
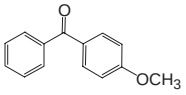
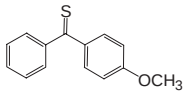
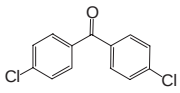
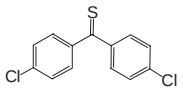
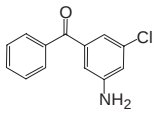
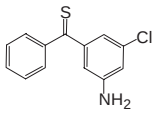
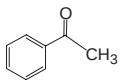
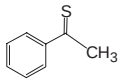
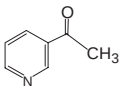
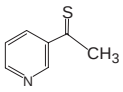
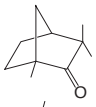
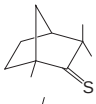
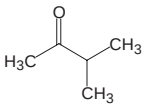
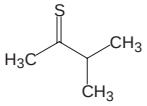
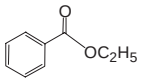
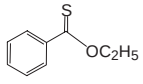
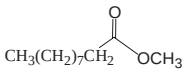
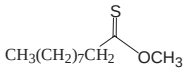
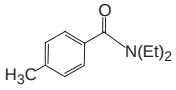
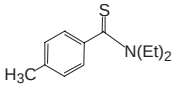
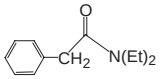
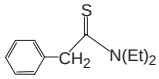
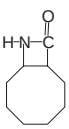
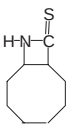
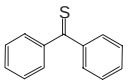
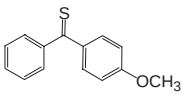
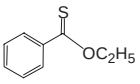
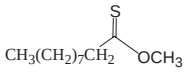
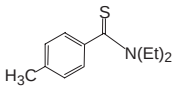
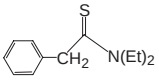
S.No.	Ketone	Reaction time (s) at 900 W	Thioketone	Isolated yield %
1		30+30+30+30+30+30+30+30		91
2		15+15+15+15+15+15+15+15+15		85
3		30+30+30+30+15+15 +15+15+15+30+30+30		90
4		30+30+30+60+30+30+30 +30+60+60+60+30+30		81
5		30+30+30+30		72
6		30+15+15+15+30		84
7		30+30+30+30+30+30 +30+30+30+30+30+30 +60+60+60+30+30		80
8		30+30+30+30+30+30+30		69
9		30+30+30+30+30+30+30+30		74
10		30+30+30+30+30		92

Table 2 Microwave assisted thionation of ester, amide and lactam by P_4S_{10}/HMDO

S.No.	Reactant	Reaction time (s) at 900 W	Product	Isolated yield %
1		30+30+30+30+15+30 +30+30		90
2		15+15+15+15+30+30 +30+60+60+60+120 +120+60+120		89
3		15+15+15		92
4		15+15+15		89
5		30+30+30+30+30+30+30 +30+30+30+30+30+60		29

All compounds had satisfactory IR, NMR and MS data and were compared with authentic samples.

Table 3 Comparative study of microwave heating and conventional heating under optimised conditions

Entry	Thio carbonyl compound	MW heating time/min	Yields/%	Conventional heating time/hr	Yield/%
1		4	91	1.5	93
2		2.25	85	1	80
3		3.75	90	8	73
4		12.5	89	24	75
5		0.75	92	3	82
6		0.75	89	3	80

are, simple reaction set up, safe technique, high product yield and very short reaction time as well as elimination of solvents.

Experimental

General procedure for synthesis of thioketones by P_4S_{10}/HMDO in microwave oven: Ketone (0.015 mole), P_4S_{10} (0.00275 mole) and HMDO (0.025 mole) were placed in a 100ml conical flask and mixed thoroughly on a cyclomixer. After initial exposure for 30 seconds to microwaves (Samsung CE2977N operating at 2450 MHz with oven cavity 336 × 241 × 349 mm and 28 litre volume) at power level 900 W the reaction mixture was taken out, mixed for 10 seconds and then heated at the same power for additional time as mentioned in Tables 1 and 2. The temperature recorded of the reaction mixture was in the range of 80–90ºC. This sequence was repeated until the formation of the thio compounds ensued. The formation of the product was monitored with the help of TLC (silica plates, 10% acetone in benzene) and GC. A Nucon GC model 5765 instrument was used with flame ionisation detector (FID). A capillary column (30m × 0.25mm I.D-BP5) packed with 5% phenyl and 95% dimethyl polysiloxane (SGE) coated on fused silica was employed. The injection port and detector block were maintained at 280°C and 260°C respectively and the column oven was at programmed temperature profile started at 50°C, ramped up to 280°C at 25°C/min. Dinitrogen was used as a carrier gas (at a flow rate of 30ml/min). Air for FID was supplied at 300ml/min and dihydrogen at 30ml/min. In all analysis, 1 µl samples were injected and peaks recorded on a computerised data acquisition station. After completion of reaction, the reaction mixture was dissolved in dichloromethane, filtered, and purified by column chromatography taking toluene/benzene as an eluent. The phosphorus-containing by product formed during reaction was retained on the column.

Synthesis of thioestes, thioamides and thiolactam by P_4S_{10}/HMDO in microwave oven: The reaction was carried out according to general thionation procedure as given above but with different mole ratios. The mole ratio for esters: ester (0.03 mole), P_4S_{10} (0.01 mole) and HMDO (0.05 mole) and for amides and lactam: amide/lactam (0.012 mole), P_4S_{10} (0.00228 mole) and HMDO (0.02 mole).

We thank Shri K. Sekhar, Director, DRDE, Gwalior for his keen interest and encouragement. Thanks are also to DRDO, New Delhi for financial support to VP.

Received 23 March 2004; accepted 29 June 2004
Paper 042400

References

1 E. Block, *Reactions of organosulfur compounds*, Academic Press: New York, 1978.
2 R.J. Cremlyn, *An introduction to organosulfur chemistry*, John Wiley & sons: New York, 1996.
3 D. Brillon, *Sulfur Rep.*, 1992, **12**, 297.
4 U. Schmidt, A. Luttringhaus and H. Trefzger, *Justus Liebigs Ann. Chem.*, 1960, **631**,129.
5 B.S. Pedersen, S. Scheibye, N.H. Nilsson and S.O. Lawesson, *Bull. Soc. Chem. Belg.*, 1978, **87**, 223.
6 B.S. Pedersen and S.O. Lawesson, *Tetrahedron*, 1979, **35**, 2433.
7 M.P. Cava and M.I. Levinson, *Tetrahedron*, 1985, **41**, 5061.
8 T.J. Curphey, *Tetrahedron Lett.* 2000, **41**, 9963.
9 N. Lozac'h and L. Legrand, *C.R. Seances Acad. Sci.*, 1952. **234**, 1291.
10 T.J. Curphey, *J. Org. Chem.*, 2002, **67**, 6461.
11 T.J. Curphey *Tetrahedron Lett.*, 2002, **43**, 371.
12 N. Kuhnert, *Angew. Chem. Int. Ed.* , 2002, **41**, 1863.
13 H.E. Blackwell, *Org. Biomol. Chem*, 2003, **1**, 1251.
14 A. Loupy, A. Petit, J. Hamelin, F. Texier-Boullet, P. Jacqualt and D. Mathe, *Synthesis*, 1998, 1213.
15 R.S. Varma, *Green Chem.*, 1999, **1**, 43.
16 S. Deshayes, M. Liagre, A. Loupy, J.L. Luche and A. Petit, *Tetrahedron*, 1999, **55**, 10851.
17 H. Rodriguez, R. Perez, M. Suarez, A. Law, N. Cabrales and A. Loupy, *Hetrocycles*, 2001, **55**,291.
18 P. Lidstrom, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, 2001, **57**, 9225.
19 (a) A. Vass, J. Dadas, J. Toth and R.S. Varma, *Tetrahedron Lett.*, 2001, **42**, 5347; (b) V.V. Namboodiri and R.S. Varma, *Tetrahedron Lett.*, 2002, **43**, 5381.
20 J.J. Filippi, X. Fernandez, L. Lizzani-Cuvelier and A.M. Loiseau, *Tetrahedron Lett.*, 2003, **44**, 6647.