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Tetrahedron Letters 45 (2004) 6255–6257

Tetrahedron Letters

A new, efficient and simple method for the thionation of ketones to thioketones using P_4S_{10}/Al_2O_3

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Received 27 May 2004; revised 17 June 2004; accepted 22 June 2004

Abstract—A simple, efficient and new method has been developed for the synthesis of thioketones by thionation of ketones using P_4S_{10}/Al_2O_3 in acetonitrile. It has been found that the P_4S_{10}/Al_2O_3 combination provides a simple and convenient method for the synthesis of thioketones.

Organosulfur compounds are valued not only for their rich and varied chemistry, but also for many important biological properties.[1] Since organosulfur compounds have become increasingly useful and important in organic synthesis, the development of convenient and practical methods for the preparation of thioketones is desirable. Thioketones have been used in the pharmaceutical, polymer, pesticide and herbicide industries.[2] Thionation, the conversion of a carbonyl group to a thiocarbonyl group, is a commonly used procedure for the synthesis of thioketones. Several methods are reported in the literature for this transformation, which makes use of elemental sulfur,[3] P_4S_{10},[4] Lawesson's reagent[5,6] and P_4S_{10}/HMDO (hexamethyldisiloxane).[7–10] Thionation of ketones to thioketones can be effected by P_4S_{10}, but typically in rather low yield.[4,11] In recent years Lawesson's reagent (LR) and a combination of P_4S_{10}/HMDO has replaced P_4S_{10} as the reagent of choice for many thionations. However, besides its high cost, LR results in the formation of by-products derived from the reagent itself, which cannot be easily removed by an extractive procedure and require chromatography, making the method more expensive. The combination of P_4S_{10}/HMDO is good in terms of reactivity but the use of HMDO makes the method expensive and the by-products formed need to be removed by column chromatography. Despite this wide range of synthetic methods for the conversion of ketones to thioketones, no attempt has been made to use the readily accessible P_4S_{10} on a solid support for the thionation of ketones. In recent years, the use of reagents and catalysts supported on solid supports has received much attention. Such reagents not only simplify purification processes but also help prevent release of reaction residues into the environment. This has led to growth in the field of solid supported reagents on alumina.[12]

Herein we report a new procedure for the conversion of ketones into thioketones using phosphorus pentasulfide supported on alumina in acetonitrile (Scheme 1).

The reaction was carried out by refluxing a mixture of the ketone and P_4S_{10}/Al_2O_3 in acetonitrile as solvent. A series of experiments established that 0.34 mol of P_4S_{10}/Al_2O_3 per mole of ketone were required to obtain maximum yield of the thioketone. Using standard conditions, the thionation of a series of ketones was examined. The carbonyl substrates were chosen to reflect a variety of structural types. Alkyl and aryl ketones reacted smoothly with P_4S_{10}/Al_2O_3 under these reaction conditions to produce the corresponding thioketones in good to excellent yields. The results are summarized in Table 1.

The catalytic role of Al_2O_3 was also studied by carrying out the reaction in the absence of Al_2O_3 using P_4S_{10} alone. It was found that the yield of the thioketones using the combination of P_4S_{10}/Al_2O_3 were greater than those with P_4S_{10} alone. The beneficial effect of

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Keywords: P_4S_{10}/Al_2O_3; Thionation; Thioketones.

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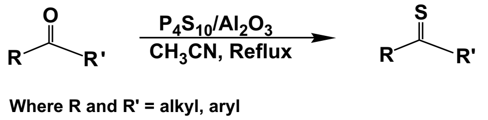
doi:10.1016/j.tetlet.2004.06.091



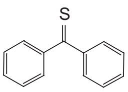
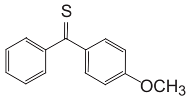
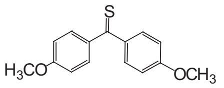
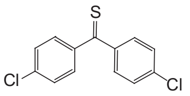
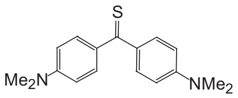
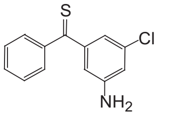
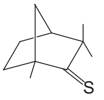
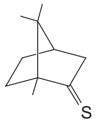
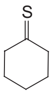
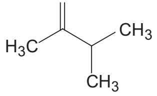
Scheme 1. Thionation of ketones by P_4S_{10}/Al_2O_3.

Al_2O_3 may be due to the scavenging of yield-lowering intermediates formed during the course of the reaction.

Although the yield and reaction times are comparable with LR, the P_4S_{10}/Al_2O_3 combination still offers advantages over LR. LR needs 2 mol of the reagent per mole of ketone and the high equivalent weight of Lawesson's reagent means that the substrate comprises only a small percentage by weight of the crude reaction mixture, whereas P_4S_{10}/Al_2O_3 requires only 0.34 mol/mol of ketone making the method less expensive. The combination P_4S_{10}/Al_2O_3 provides clean products in comparison to LR, which gives by-products, which can be difficult to remove. Also this method is economic and practical as compared to the expensive P_4S_{10}/HMDO method. The use of a solid support for P_4S_{10}/Al_2O_3 is advantageous over LR and P_4S_{10}/HMDO because the supported reagent can be removed easily by filtration, avoiding an aqueous workup and decreasing waste solvent. In addition, since the thioketones never covalently bind to the solid support, reaction monitoring and analysis can be accomplished using standard methods (i.e., GC, TLC).

The application of this new thionation procedure to other types of substrates and attempts to understand its mechanism are in progress and will be reported in due course.

Table 1. Thionation of ketones by P_4S_{10}/Al_2O_3 in acetonitrile under reflux[13,14]

Entry	Thioketone	P_4S_{10}/Al_2O_3		P_4S_{10}	
		Time (h)	% Yield	Time (h)	% Yield
1		1.5	89	12	46
2		2	82	10	52
3		0.75	93	1.5	88
4		2	86	12	58
5		0.5	95	1	92
6		2	86	8	50
7		2	88	8	58
8		2	68	8	52
9		2	73	12	46
10		2	65	12	49

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

Acknowledgements

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

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14. Experimental: The reagent was prepared by the combination of phosphorus pentasulfide (6 g) and alumina (Al_2O_3, basic, 10 g) in a mortar and pestle by grinding together until a fine, homogeneous powder was obtained (10–15 min). 0.00085 mol of P_4S_{10} (i.e., 1 g of P_4S_{10}/Al_2O_3) were added to 0.0025 mol of ketone in 50 mL acetonitrile and then the mixture refluxed under a nitrogen atmosphere. The reaction was monitored by TLC and GC. After completion of reaction, the reagent was removed by filtration and the solvent was evaporated. The resultant viscous liquid was then extracted with hexane or diethyl ether. On evaporation of the solvent, pure thioketones were obtained.