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Spotlight 226

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Lawesson's Reagent: Endowed With Wide Utility in Organic Synthesis

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Introduction

Lawesson's Reagent (LR, Figure 1), 2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphethane-2,4-disulfide is a versatile and effective thionation reagent;[1] it is best known for the conversion of a wide variety of carbonyl into thiocarbonyl compounds, including the synthesis of phosphorus- and sulfur-containing heterocycles, such as thiazolidinediones,[2] thiothalidomides,[3] 2*H*-benzo[1,4]thiazine,[4] among others. However, this reagent can efficiently be applied to many other reactions, in particular for the deoxygenation of heterocyclic halobenzyl alcohols,[5] to heterocyclization of acetohydrazidepyridines, which yields [1,2,4]triazolo[4,3-*a*]pyridines,[6] to afford pyrazoles,[7] to [4+2] cycloaddition of α,β-unsaturated ketones,[8] and as a racemization-free coupling reagent in peptide synthesis.[9] LR is stable in solvents like toluene, THF, dichloromethane, and pyridine,[10] it can be used under microwave irradiation and for automated parallel synthesis; it is commercially available and easily prepared by reaction of P_4S_{10} with anisole under heating.[1]

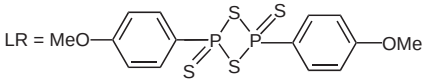
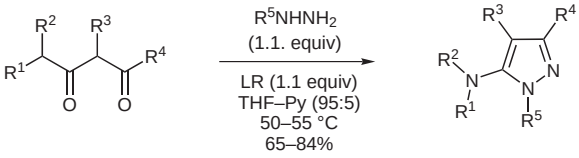


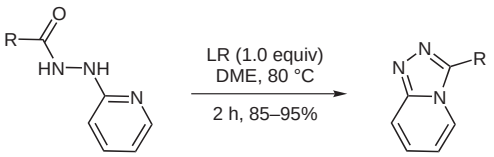
Figure 1

Abstracts

(A) Dodd and Martinez[7] have described a mild one-pot synthesis of 5-substituted aminopyrazoles using LR to promote an efficient cyclization to afford the desired pyrazoles in high yields and to suppress the undesired pyrazolone byproducts. The method is also suitable for solid-phase synthesis.



(B) Moulin and co-workers[6] showed that LR is an excellent promoter for heterocyclization of a variety of acetohydrazidepyridines to the corresponding [1,2,4]triazolo[4,3-*a*]pyridines in high yields.



R = amino acid

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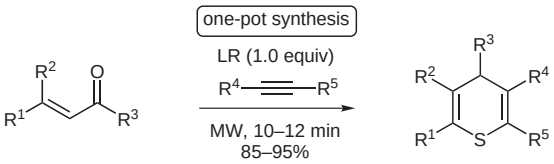
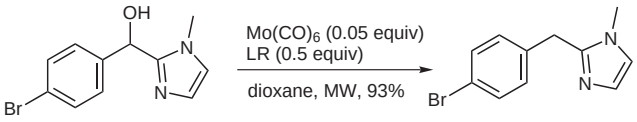
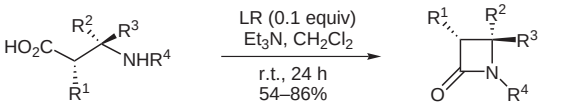
(C) Recently, Barthakur and co-workers[8] used a three-component reaction of α,β-unsatured ketones, LR, and alkynes under MW irradiation for a rapid synthesis of substituted 4*H*-thiopyrans in high yields. The method offers several advantages over previously known methods in terms of simplicity, applicability, and purity.



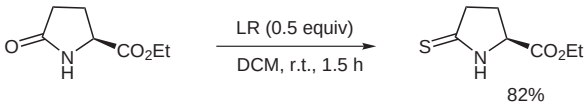
(D) Wu et al.[5] developed a fast and chemoselective deoxygenation of heterocyclic halobenzyl alcohols with LR catalyzed by $Mo(CO)_6$ under MW irradiation, which provided the deoxygenated products in high yields after only 30 min and also without producing dehalogenated byproducts.



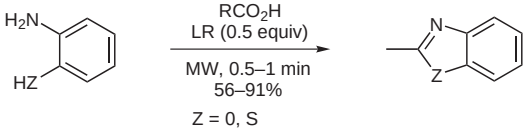
(E) Kanwar and Sharma[9] provide a convenient route for the synthesis of monocyclic 2-azetidinones in high stereoselectivity and yields, by using LR in basic medium to mediate the intramolecular cyclodehydration of β-amino acids. These authors related the advantageous properties of the LR to other cyclodehydrating agents in terms of cost, reaction conditions, and also quantities of reactants.



(F) Hussaini and Moloney[10] reported a short approach to *cis*-2,5-disubstituted pyrrolidines, from the conversion of pyrroglutamic acid ethyl ester into the thiolactam, employing LR in dichoromethane at r.t., giving an excellent yield of thiolactam in high purity. The high efficiency of this method is attributed to the greater solubility of LR in dichoromethane compared to other solvents (such as toluene, THF and pyridine) and also the r.t. conditions, which avoid the formation of a phosphorus impurity reported previously.[11]



(G) More recently, Seijas et al.[12] used LR under microwave irradiation as an efficient promoter system for the synthesis of 2-substituted benzoxazoles or benzothiazoles from carboxylic acids and 2-aminophenol. This method is known as fast, general, and suitable for parallel synthesis.



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