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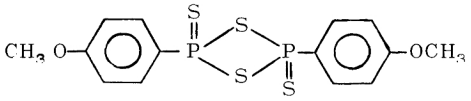
NOVEL AND CONVENIENT METHODS FOR THE PREPARATION OF SUBSTITUTED THIOPHENES, THIAZOLES, AND 1,3,4-THIADIAZOLE-2(3H)-THIONES FROM BIFUNCTIONAL SUBSTRATES[1)]

I. THOMSEN, U. PEDERSEN, P. B. RASMUSSEN, B. YDE, T. P. ANDERSEN, and S.-O. LAWESSON*

Department of Organic Chemistry, Institute of Chemistry, University of Aarhus, DK-8000 Aarhus C, Denmark

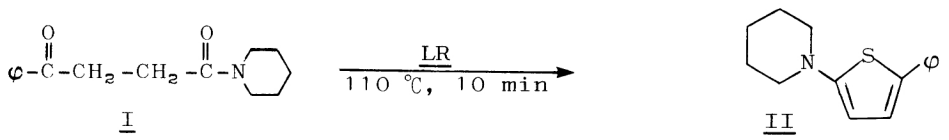
The reactions of LR (Lawesson's Reagent) with 4-oxocarboxylic acid derivatives I, N-acyl aminoacid derivatives III, and N-acyl-N'-ethoxycarbonylhydrazines V, smoothly produce substituted thiophenes II, thiazoles IV, and 1,3,4-thiadiazole-2(3H)-thiones VI.

Recently it was shown by this group[2)] that the reaction of Lawesson's Reagent (LR) with N,N'-dibenzoylhydrazine produced 2,5-diphenyl-1,3,4-thiadiazole in high yields.



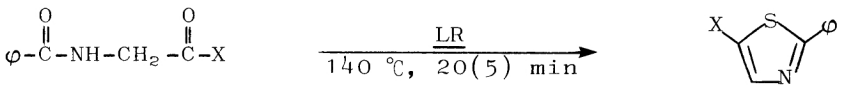
LR

As an extension of this work the reaction of LR with different bifunctional substrates has been investigated. Thus, 1-(4-oxo-4-phenyl-butanoyl)-piperidine I, on reaction with LR at 110 °C for 10 min gives 82% yield of 2-phenyl-5-piperidinothiophene, II.



I II

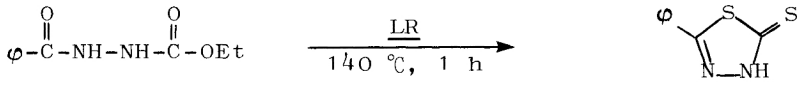
Also 1-(N-benzoyl-glycyl)-ethyl ester, IIIa, and 1-(N-benzoyl-glycyl)-piperidine, IIIb produce 2-phenyl-5-ethoxythiazole, IVa, and 2-phenyl-5-piperidinothiazole, IVb, in high yields, respectively.



IIIa (X = OEt)
IIIb (X = N⟨⟩)

IVa (85%)
IVb (78%)

N-Benzoyl-N′-ethoxycarbonyl hydrazine, V, when refluxed in xylene with LR for 1 h gave 78% yield of 5-phenyl-1,3,4-thiadiazole-2(3H)-thione, VI.



V VI

Literature search shows that the yields by this method are better than earlier reported [3-5]. Full papers on thiophenes[6], thiazoles[7], and 1,3,4-thiadiazoles[8] will appear elsewhere.

2-Phenyl-5-piperidinothiophene, II: 0.01 mol of 1-(4-oxo-4-phenyl-butanoyl)-piperidine, I (mp 53 ℃) and 0.01 mol of LR were refluxed in toluene for 10 min. After cooling to room temp, the product II was separated by silica gel column chromatography with 10% Et_2O/P.E. as eluent, in 82% yield (mp 70 ℃).

2-Phenyl-5-ethoxythiazole, IVa: 0.01 mol of 1-(N-benzoyl-glycyl)-ethyl ester, IIIa, and 0.01 mol of LR were refluxed in xylene for 20 min. The product IVa was isolated in 85% yield by silica gel column chromatography with 20% Et_2O/P.E. as eluent (bp 125-128 ℃/1 mmHg).

2-Phenyl-5-piperidinothiazole, IVb: The product was prepared as above from 1-(N-benzoyl-glycyl)-piperidine, IIIb (mp 91 ℃) and LR. Reflux in xylene for 5 min. Yield: 78% (mp 83 ℃).

5-Phenyl-1,3,4-thiadiazole-2(3H)-thione, VI: 0.01 mol of N-benzoyl-N′-ethoxycarbonyl hydrazine, V, and 0.02 mol of LR were refluxed in xylene for 1 h. After cooling to room temp, the product VI was isolated in 78% yield by silica gel column chromatography with 5% Et_2O/CH_2Cl_2 as eluent (mp 149 ℃).

All compounds were characterized by microanalyses, MS, ^1H and ^{13}C NMR spectroscopy.

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5) J. Sandström, Adv.Het.Chem. 9 (1968) 165.
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8) P. B. Rasmussen, U. Pedersen, I. Thomsen, B. Yde, and S.-O. Lawesson, to be published.

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