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AN IMPROVED CONVERSION OF 1,4,6-TRISUBSTITUTED 2(1H)-PYRIMIDINONES INTO THE CORRESPONDING THIONES

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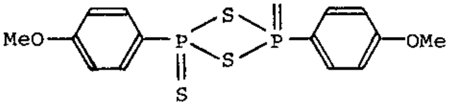
Abstract —— 1,4,6-Trisubstituted 2(1H)-pyrimidinones (**2a-j**) are easily converted into the corresponding thiones (**3a-j**) in high yields by reacting with 2,4-bis(p-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (**1**). Further, other diazines, e.g., 2-methyl-6-phenyl-3(2H)-pyridazinone (**4**) and 1-methyl-5,6-diphenyl-2(1H)-pyrazinone (**6**) are also converted into the corresponding thiones **5** and **7** in 99 and 91% yield, respectively.

Recently we have shown that 1,4,6-trisubstituted 2(1H)-pyrimidinethiones exhibit the antiinflammatory activity[1] and are useful synthons for the preparation of various heterocyclic compounds.[2,3] (Scheme 1) The conversion of 2(1H)-pyrimidinones into the corresponding thiones has hitherto been carried out in the presence of phosphorus pentasulfide in xylene, tetralin, or pyridine.[4] However, these classical O/S exchange reactions require high temperature and rather long reaction time. On the other hand, althogh 2,4-bis(p-methoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulfide (Lawesson's reagent, **1**) has been found to be a potent reagent for the thiation of diverse carbonyl compounds,[5] few papers concerning the thiation of carbonyl groups in heterocyclic compounds have been reported.



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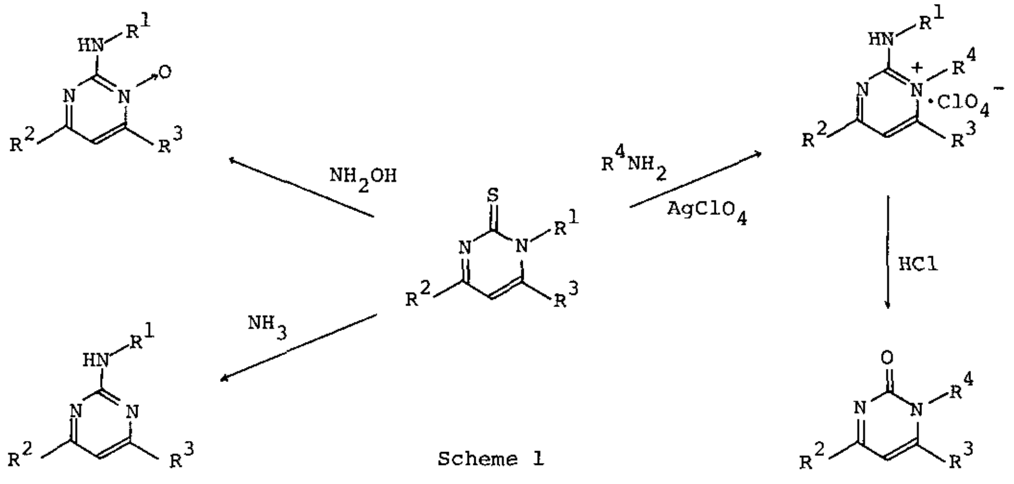
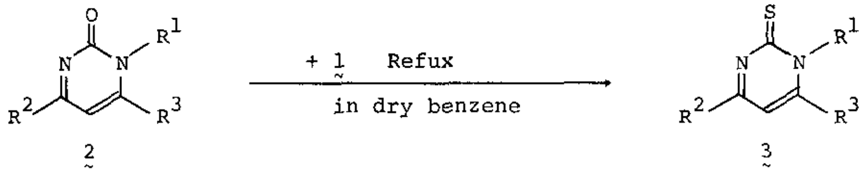
In this paper, we wish to describe the application of Lawesson's reagent to O/S exchange reaction of diazines, especially 1,4,6-trisubstituted 2(1H)-pyrimidinones.



Scheme 1

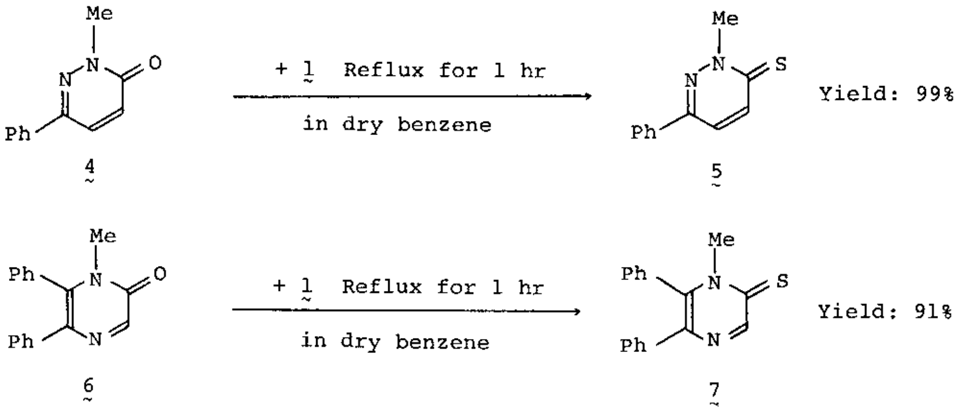
Table I Conversion of 2(1H)-Pyrimidinones into the Corresponding Thiones



Compd.	R^1	R^2	R^3	Condition (hr)	Product	Yield (%)	Mp (°C)
2a	H	Ph	Me	2	3a(a)	69	198-200*
2b	Me	Me	Me	4	3b(a)	15	155.5-157**
2c	Ph	Me	Me	4	3c(a)	71	209(decomp.)
2d	p-MeC$_6$H$_4$	Me	Me	1.5	3d(a)	80	219(decomp.)
2e	m-MeC$_6$H$_4$	Me	Me	1.5	3e(b)	82	178.5(decomp.)
2f	Ph	Ph	Me	5	3f(a)	90	213-215
2g	Ph	p-ClC$_6$H$_4$	Me	2	3g(a)	100	252(decomp.)
2h	Me	Ph	Ph	2	3h(b)	90	205-207
2i	PhCH$_2$	Ph	Ph	3	3i(c)	86	231-232
2j	Ph	Ph	Ph	1	3j(d)	98	202-203.5

(a) Recrystallized from EtOH. (b) Recrystallized from AcOEt. (c) Recrystallized from acetone. (d) Recrystallized from benzene. *Lit.[6] mp 199-200 °C. **Lit.[7] mp 156.5 °C.

A typical experimental procedure for the conversion of 1,4,6-trisubstituted 2(1H)-pyrimidinones into the corresponding thiones is as follows. A mixture of 4-(p-chlorophenyl)-6-methyl-1-phenyl-2(1H)-pyrimidinone (2g, 1 mmol) and Lawesson's reagent (1, 0.5 mmol) in dry benzene (5 ml) was refluxed for 2 hr. After cooling the solvent was evaporated off under reduced pressure. The crude product was purified by flash chromatography[8] on silica gel 60 (230-400 mesh) with chloroform/benzene/ethyl acetate (2:2:1), followed by recrystallization from ethanol to give 4-(p-chlorophenyl)-6-methyl-1-phenyl-2(1H)-pyrimidinethione (3g)[9] in 100% yield; mp 252 °C(decomp.); ir $\nu_{max.}$(KBr) 1590, 1485, 860, 820, 810, 765, and 700 cm^{-1}; ^{1}H-nmr(δ, $CDCl_3$) 2.11 (d, 3H, J=0.7 Hz), 7.12 (q, 1H, J=0.7 Hz), 7.2-7.6 (m, 7H), and 8.1-8.3 ppm (m, 2H). Similarly, the O/S exchange reactions of other 2(1H)-pyrimidinones were examined, and the results are listed in Table I.[9]



Scheme 2

Since compounds 3f and 3g cannot be obtained at all by the reaction of N-phenylthiourea with benzoylacetones,[10] this route is of highly preparative value for these and analogous compounds.

Further, this reagent was applied to the O/S exchange reactions of other diazines. 2-Methyl-6-phenyl-3(2H)-pyridazinone (4) was treated with Lawesson's reagent to afford 2-methyl-6-phenyl-3(2H)-pyridazinethione (5), mp 151-153 °C(Lit.[11] mp 151 °C), in 99% yield. 1-Methyl-5,6-diphenyl-2(1H)-pyrazinone (6) was also treated with Lawesson's reagent to give 1-methyl-5,6-diphenyl-2(1H)-pyrazinethione (7), mp 163-164.6 °C,[9] in 91% yield. (Scheme 2)

It is concluded that Lawesson's reagent is consistently superior to phosphorus pentasulfide with respect to ease of manipulation, reaction time, and excellent yields of diazines such as 2(1H)-pyrimidinethione, 3(2H)-pyridazinethione, and 2(1H)-pyrazinethione.

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9. The microanalyses were in good agreement with the calculated values: C, ± 0.28; H, ± 0.07; N, ± 0.16.
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