TRIETHYLAMINE SOLUBILISED PHOSPHOROUS PENTASULPHIDE AS THIATION REAGENT : A NOVEL ROUTE TO TOTALLY THIATED HETEROCYCLES

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Abstract — Triethylamine solubilised phosphorous pentasulphide (P_4S_{10}) has been evolved as the thiation agent in heterocycles such as substituted benzoxazin-4-ones, 2-pyrazolin-4-ones and pyrimidine-2,5-dione derivatives. The simple and convenient operation involving stirring (24 h) of the reaction mixture at room temperature results in the isolation of the desired products in quantitative yield.

Diverse synthetic methods are available for the facile conversion of ketones to thioketones employing conventional reagents like H_2S/HCl[1] or $P_4S_{10}/NaHCO_3$.[2] Phosphorous and sulphur compounds such as p-methoxyphenylthionophosphine sulphide[3] and phosphorous pentasulphide (P_4S_{10})[4] have received much attention in recent years for the ketone - thioketone conversions in aliphatic and aromatic systems. Conversion in the latter case is generally achieved by the reaction of the substrate with phosphorous pentasulphide in high boiling solvents. The reactions are generally faster in polar solvents like acetonitrile.[5] It is known that the reactivity of P_4S_{10} could be enhanced by rapid cooling of the molten P_4S_{10} and this highly active form might be deactivated to the desired levels by heating it below its melting point.

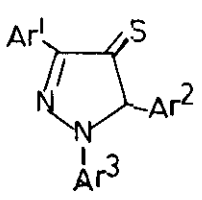
Triethylamine solubilised phosphorous pentasulphide has been effectively used in carbonyl to thiocarbonyl conversions in solvents like acetonitrile and dichloromethane.[5] This reagent has been found to be more effective than the conventional Scheeren's reagent.[2] Such conversion reactions in

heterocyclic systems are scarce in literature. The present study reports the thiation of ketones in heterocycles. The reaction is clean and fast and the products are obtained in quantitative yields. In view of the paramount interest and of the need for improved methods for the preparation of thiated heterocycles,[3,6] we have carefully selected a few nitrogen heterocycles such as 4-pyrazolinones,[7] benzoxazin-4-ones[8] and pyrimidine-2, 5-diones[9] synthesized in our laboratory and studied their thiation behaviour employing this reagent.

The general procedure involves the addition of triethylamine (4 equiv.) to a suspension of P_4S_{10}(1 equiv.) in acetonitrile, which results in an immediate exothermic dissolution of P_4S_{10} giving a clear bright yellow solution turning brown on standing. A vigorous stirring of this solution with the representative heterocyclic ketone followed by washing with cold water, affords the corresponding thione. It is presumed that the interaction of triethylamine with P=S linkage in P_4S_{10} possibly gives rise to a polar structure represented by (1), which could readily account for both the solubility and the greater reactivity of P_4S_{10}. This dipolar intermediate (1) attacks the carbonyl site of the heterocycle, thus resulting in the conversion.

$$P_4S_{10} + Et_3N \longrightarrow \underset{1}{PS_2\text{-}\overset{-}{S}\text{-}PS_2\text{-}\overset{+}{N}(Et)_3}$$

Reactions of 1,3,5-triaryl-2-pyrazolin-4-ones and the 4,6-diaryldihydro-pyrimidine-2,5-diones with Et_3N-P_4S_{10} afforded their thio analogues (2) and (4) respectively. The infrared spectra of the pyrazolin-4-thiones (2) gave peaks at 1680 (C=N), 1310 (C=S) and the PMR spectra (CCl_4) showed a single proton singlet at 5.65 δ (CHPh) and a multiplet corresponding to the



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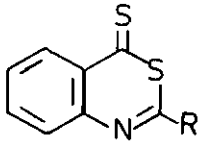

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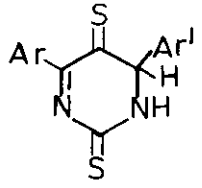

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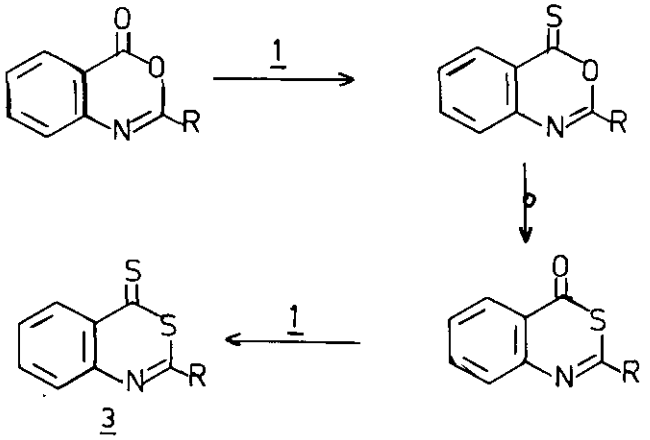
bulk aromatic protons beyond 7.3 δ . The IR spectra of (4) showed sharp peaks at 1310, 1250 (C=S), 1580 (C=N) and 3300 (NH) cm^{-1} and the PMR($CDCl_3$) spectra showed a singlet at 5.8 δ for the benzylic proton and a complex multiplet at 7.6 δ for the bulk aromatic protons and the NH protons. In the case of 2-substituted 3,1-benzoxazin-4-ones, surprisingly, the totally thiated product, 2-substituted 3,1-benzothiazin-4-thiones (3) were obtained in excellent yields as against two products produced with p-methoxyphenyl-thionophosphine sulphide.[6] Compounds (3) gave IR peaks around 1310 cm^{-1} (C=S) and 1580 cm^{-1} (C=N). We propose a tentative mechanism for this conversion, in accordance with that of Lawesson and coworkers,[3] where the benzothiazin-4-one is formed by the rearrangenent of the intermediate which in turn is transformed by (1) to benzothiazin-4-thiones(3) (Scheme).



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EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 137 Infracord Spectrophotometer. PMR spectra were determined on a Varian model A60-D spectrometer. Chemical shifts are reported on solutions as δ values relative to TMS as the internal standard.

Thiated heterocycles with triethylamine solubilised phosphorous pentasulphide (P_4S_{10}): General procedure :

The ketone (1 equiv.) in acetonitrile (generally 10 % solution) was treated

with P_4S_{10} (1 equiv.), and to this stirred suspension was added triethylamine (4 equiv.) in three portions while cooling the mixture in ice-water to moderate the exothermic reaction. The resulting solution was left stirred at room temperature for 24 h and poured into cold-water. The product was filtered and crystallised from ethanol. The physical data of the products are given in the tables I,II and III.

TABLE-I : 1,3,5-Trisubstituted Pyrazolin-4-thiones (2) :

Ar^1	Ar^2	Ar^3	mp (°C)	Yield (%)	Analysis(%) Found (Calcd.) N	S
Ph	Ph	2,4-DNP	117	65	13.25 (13.40)	7.48 (7.66)
p-ClPh	Ph	2,4-DNP	52	17	12.02 (12.14)	6.98 (7.09)
Ph	p-BrPh	2,4-DNP	89	17	11.12 (11.27)	6.32 (6.44)
Ph	Ph	Ph	117	85	8.91 (8.54)	9.62 (9.76)
$p\text{-}NO_2Ph$	Ph	Ph	108	57	11.17 (11.26)	8.45 (8.58)
p-ClPh	Ph	Ph	132	69	7.59 (7.74)	8.77 (8.84)
Ph	p-ClPh	Ph	61	67	7.63 (7.74)	8.81 (8.84)
$p\text{-}CH_3Ph$	Ph	Ph	123	55	9.02 (9.19)	9.16 (9.36)
$p\text{-}CH_3Ph$	$p\text{-}CH_3Ph$	Ph	109	42	7.69 (7.87)	8.82 (8.99)

TABLE-II: 2-Substituted Benzothiazin-4-thiones(3):

R	mp °C	Yield %	Molecular Formula	Analysis(%) N Found	S (Calcd.)
CH_3	79 (lit.[10] 99°)	86	$C_9H_7NS_2$	7.01 (7.25)	32.97 (33.16)
Ph	128 (lit.[10] 128°)	90	$C_{14}H_9NS_2$	5.41 (5.49)	25.00 (25.10)
$PhCH_2$	320	80	$C_{15}H_{11}NS_2$	5.12 (5.20)	23.59 (23.79)
p-NO_2Ph	108	76	$C_{14}H_8N_2O_2S_2$	9.25 (9.33)	21.17 (21.33)

TABLE-III: 4,6-Diarylpyrimidine-2,5-dithiones (4):

Ar	Ar^1	mp (°C)	Yield (%)	Molecular Formula	Analysis(%) N Found	S (Calcd.)
Ph	Ph	95	46	$C_{16}H_{12}N_2S_2$	9.37 (9.46)	21.40 (21.62)
Ph	p-ClPh	134	50	$C_{16}H_{11}N_2S_2Cl$	8.42 (8.48)	19.32 (19.39)
p-ClPh	Ph	108	60	$C_{16}H_{11}N_2S_2Cl_2$	8.35 (8.48)	19.28 (19.39)
p-ClPh	p-ClPh	137	33	$C_{16}H_{10}N_2S_2Cl_2$	7.61 (7.69)	17.44 (17.58)
Ph	p-BrPh	104	46	$C_{16}H_{11}N_2S_2Br$	7.33 (7.47)	17.00 (17.06)
p-CH_3Ph	Ph	120	46	$C_{17}H_{14}N_2S_2$	9.01 (9.03)	20.57 (20.64)

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