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DI-2-PYRIDYL THIONOCARBONATE. A NEW REAGENT FOR THE PREPARATION OF ISOTHIOCYANATES AND CARBODIIMIDES.

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Summary: Reaction of amines with di-2-pyridyl thionocarbonate affords the corresponding isothiocyanates at room temperature, while reaction of N,N'-disubstituted thioureas with di-2-pyridyl thionocarbonate in the presence of 4-dimethylaminopyridine as a catalyst affords the corresponding carbodiimides in high yields.

In the course of studies on the synthetic utility of 2-pyridyl esters and related compounds,[1] we have found that isothiocyanates can be prepared in high yields from amines using di-2-pyridyl thionocarbonate (DPT) as a new thiocarbonyl transfer reagent (eq. 1)[2] and carbodiimides can be conveniently prepared from N,N'-disubstituted thioureas using DPT as a dehydrosulfurization reagent[3] in the presence of a catalytic amount of 4-dimethylaminopyridine (DMAP)[4] (eq. 2).

DPT was easily prepared in 85% yield as a pale yellow crystal by the reaction of thiophosgene with 2 equiv of 2-hydroxypyridine in the presence of 2 equiv of triethylamine in methylene chloride at room temperature and could be stored at room temperature for a long period of time without any decomposition (eq. 3).[5]

$$RNH_2 + DPT \longrightarrow R\text{-}N{=}C{=}S + 2\text{-PyOH} \qquad (1)$$

$$R\text{-}NH\text{-}\overset{\overset{S}{\|}}{C}\text{-}NH\text{-}R' + DPT \xrightarrow{0.1\ eq.\ DMAP} R\text{-}N{=}C{=}N\text{-}R' + CS_2 + 2\text{-PyOH} \qquad (2)$$

$$Cl\text{-}\overset{\overset{S}{\|}}{C}\text{-}Cl + \text{2-PyOH} \xrightarrow{Et_3N} \text{DPT} \qquad (3)$$

The preparation of isothiocyanates was performed on a variety of structurally different alkyl and aryl amines to determine the scope and limitations of the present procedure using 1 equiv of DPT in methylene chloride at room temperature[6] and the results are summarized in Table 1. This procedure was turned out to be general for various alkyl and aryl amines. The reaction was normally complete within 5 min at room temperature, though relatively unreactive aryl amines like p-nitroaniline required 2 h for completion of the reaction.

Several features of this procedure are noteworthy. First, direct conversion of amines into the corresponding isothiocyanates occurred almost instantly at room temperaure using DPT. It is known that the use of 1,1'-thiocarbonyldiimidazole involves 1-(alkylthiocarbamoyl) imidazole, which can be decomposed thermally into isothiocyanates and imidazole under relatively mild conditions,[7] while 1,1'-thiocarbonyldi-1,2,4-triazole results in 1-(alkylthiocarbamoyl)-1,2,4-triazole, which shows no tendency to dissociate isothiocyanates and 1,2,4-triazole.[8] Second, secondary alkyl amines such as diethylamine and dicyclohexylamine yielded the corresponding 2-pyridyl thiocarbamates (R_2N-CS-O-2-Py) in essentially quantitative yields. Finally, this procedure is operationally very simple. Thus, a byproduct, water-soluble 2-hydroxypyridine, can be completely removed by the usual aqueous workup or it can be recovered in high yields (80-90%) by precipitating 2-hydroxypyridine from the reaction mixture with the addition of diethyl ether or petroleum ether.

The synthetic utility of DPT as a dehydrosulfurization reagent was studied with N,N'-disubstituted thioureas. The reaction of N-cyclohexyl-N'-phenylthiourea with equimolar amounts of DPT and pyridine in acetonitrile occurred only to an observable extent, yielding 5% of N-cyclohexyl-N'-phenylcarbodiimide with the recovery of the starting material at room temperature in 24 h and similar results were obtained with the use of triethylamine. We have found that the use of DMAP is exceedingly effective in the conversion of thioureas into carbodiimides in high yields. For example, reaction of N-cyclohexyl-N'-phenylthiourea with 1 euiv of DPT in the presence of 0.01, 0.1, and 1 equiv of DMAP in acetonitrile at room temperature gave N-cyclohexyl-N'-phenylcarbodiimide in essentially quantitative yields in 10 h, 2 h, and 0.1 h, respectively. Thus, remaining reactions were carried out with 1 equiv of DPT in the presence of 0.1 equiv of DMAP in acetonitrile.

As shown in Table 2, N,N'-diaryl or N-aryl-N'-alkyl substituted thioureas were cleanly and rapidly converted into the corresponding carbodiimides in high yields at room temperature. However, the conversion of N,N'-dialkyl substituted thioureas into the corresponding carbodiimides was normally slow and was dependent critically on the nature of alkyl groups. Thus, the reaction of N,N'-di-t-butylthiourea with DPT in the presence of 0.1 equiv of DMAP at room temperature in 6 h gave N,N'-di-t-butylcarbodiimide in 92% yield, whereas the reaction of N,N'-dicyclohexylthiourea required 15 h at 80 °C for completion of the reaction. Furthermore, this procedure reaches a limit with N,N'-primary alkyl disubstituted thioureas. N,N-di-n-butylthiourea and N-methyl-N'-n-butylthiourea were completely inert to DPT in the presence of 1 equiv of DMAP at 80 °C for 12 h and starting materials were recovered unchanged.

DPT can be successfully applied for the preparation of carbodiimides from amines by a three-step, one-pot procedure. N-Cyclohexyl-N'-phenylcarbodiimide was prepared in 92% yield without isolation of intermediates as shown below.[9]

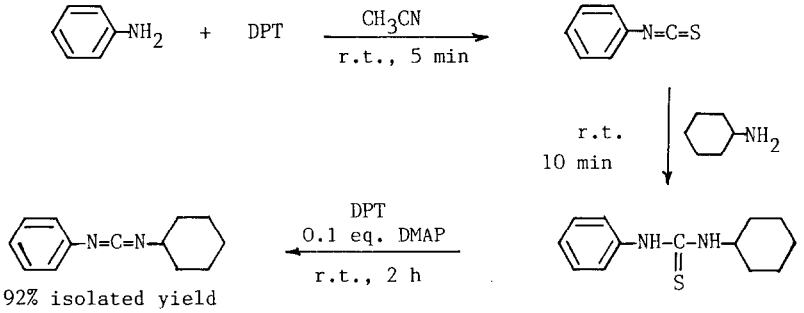

Table 1. Preparation of Isothiocyanates[a]

$$RNH_2 + DPT \xrightarrow[r.t.]{CH_2Cl_2} R\text{-}N{=}C{=}S + 2\text{-PyOH}$$

RNH_2	Isolated Yield, % R-N=C=S	RNH_2	Isolated Yield, % R-N=C=S
$C_6H_5CH_2NH_2$	90	$(CH_3)_3CNH_2$	87
$CH_3(CH_2)_2CH_2NH_2$	94	$C_6H_5NH_2$	90
$CH_2{=}CHCH_2NH_2$	85	$p\text{-}CH_3C_6H_4NH_2$	95
$CH_3CH_2CH(CH_3)NH_2$	85	$p\text{-}NO_2C_6H_4NH_2$[b]	90
Cyclohexylamine	85	α-Naphthylamine[c]	95

[a] The reaction was carried out with equimolar amounts of an amine and DPT for 5 min, unless specified. [b] Reaction time: 2 h. [c] Reaction time: 10 min.

Table 2. Preparation of Carbodiimides

$$R\text{-}NH\text{-}\overset{\overset{S}{\|}}{C}\text{-}NH\text{-}R' + DPT \xrightarrow[CH_3CN,\ r.t.]{0.1\ eq.\ DMAP} R\text{-}N{=}C{=}N\text{-}R' + CS_2 + 2\text{-PyOH}$$

R[a]	R'[a]	Time, h	Isolated Yield, % R-N=C=N-R'	Bp, °C (mmHg)[c]
C_6H_5	C_6H_5	0.5	84	130–133 (1.0)
C_6H_5	$o\text{-}CH_3C_6H_4$	0.5	89	137–139 (0.6)
C_6H_5	$CH_3(CH_2)_3$	1	91	90–92 (0.5)
C_6H_5	C_6H_{11}	2	87	95–97 (0.7)
C_6H_5	$(CH_3)_3C$	1	90	85–88 (0.5)
C_6H_{11}	$(CH_3)_3C$	12	90	65–67 (1.8)
		2[b]	85	
C_6H_{11}	C_6H_{11}	15[b]	84	101–103 (0.6)
$(CH_3)_3C$	$(CH_3)_3C$	6	92	71–73 (50)
		1[b]	86	
$CH_3(CH_2)_3$	$CH_3(CH_2)_3$	12[b]	0	
CH_3	$CH_3(CH_2)_3$	12[b]	0	

[a] C_6H_{11} indicates cyclohexyl group. [b] The reaction was carried out at 80 °C.
[c] Reported boiling points are those observed during distillation with Kugelrohr apparatus and are uncorrected. All values are in accord with reported values.

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References and Notes

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3. For reviews, see: (a) F. Kurzer and K. Douraghi-Zadeh, Chem. Rev., 67, 107 (1967). (b) A. Williams and I. T. Ibrahim, Chem. Rev., 81, 589 (1981).
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5. Di-2-pyridyl Thionocarbonate (DPT): mp 98-100 °C; NMR($CDCl_3$)δ7.10-7.47 (m, 2H), 7.72-8.07 (m, 1H), 8.37-8.57 (m, 1H); IR(KBr) 3030, 1600, 1575, 1470, 1440, 1310,1280, 1225, 1150 cm^{-1}. Calcd for $C_{11}H_8O_2N_2S$: C, 56.89; H, 3.47; N, 12.06. Found: C, 56.71; H, 3.42; N, 12.20.
6. The reaction was normally complete within 10 min in acetonitrile at room temperature.
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9. Spectral and physical data of all products obtained here were in accord with reported data.

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