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NEW METHOD FOR CONVERTING AMINES INTO 1,1-DISUBSTITUTED THIOUREAS BY USING A COMBINED REAGENT OF TRIPHENYLPHOSPHINE AND THIOCYANOGEN

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Although several methods have been reported[1,2] for the preparation of 1,1-disubstituted thioureas (I), the widely used method for these compounds is the reaction of benzoyl or ethoxycarbonyl isothiocyanate with secondary amines followed by acid-hydrolysis of the products.[2,3] In this communication we report a more facile and general synthesis of 1,1-disubstituted thioureas (Ia-g) from secondary amines (IIa-g) and the combined reagent, $Ph_3P(SCN)_2$.[4] This novel method requires only one-pot procedure under mild conditions and gives good yield of the products.

In a typical reaction, a solution of N-methylaniline (IIa, 2 mmole) in dry acetonitrile (5 ml) was added to freshly prepared $Ph_3P(SCN)_2$ (ca. 3 mmole) in dry methylene chloride (10 ml) at -40°. The mixture was stirred for 2 hrs at the same temperature, allowed to warm to room temperature, stirred for 4 hrs, and quenched with aqueous acetonitrile (20 ml) to give N,N-methylphenylthiourea (Ia) in 80% yield. In a similar manner, a number of other secondary amines (IIb-g) were converted to the corresponding thioureas (Ib-g) in good yields. The results are summarized in Table.

The reaction process may be explained by the following scheme, which involves nucleophilic addition of an amine (II) to the reagent to give an intermediate (III), resulting in the formation of the thiourea (I) together with triphenylphosphine oxide and thiocyanic acid by aqueous workup. The presence of the intermediate (III) is strongly supported by the selective formation of the phosphinimine (IV) (m.p. 154-155°) on treatment of two molar equivalent of N-methylbenzylamine (IIc) with the combined reagent under the same conditions, and by smooth conversion of the phosphinimine (IV) into the thiourea (Ic) and triphenylphosphine oxide on treatment with thiocyanic acid in aqueous acetonitrile.

The present results show that the use of the reagent, $Ph_3P(SCN)_2$ is efficient for direct thiocarbamoylation of secondary amines besides for thiocyanation of alcohols,[4] isothiocyanation of carboxylic acids[5] and cyanation of indoles.[4]

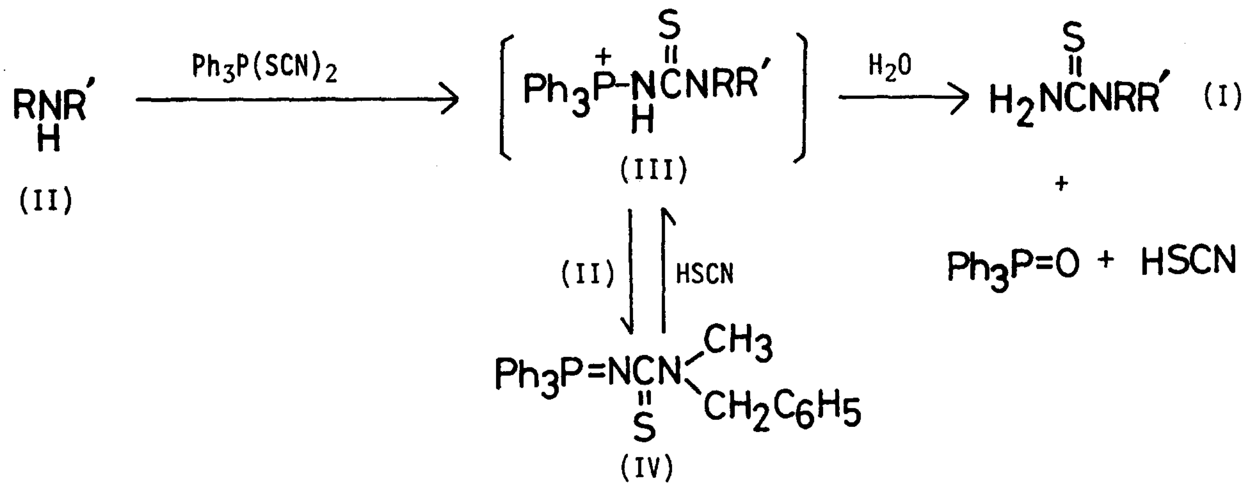

Table The Yield of Thioureas (Ia-g) from Amines (IIa-g)

Product No.*	R	R'	Yield(%)**	m.p.(from)
Ia	CH_3	C_6H_5	80	103-104°(ligroin)
Ib	C_2H_5	C_6H_5	50	111-112°(C_6H_6-n·hexane)
Ic	CH_3	$CH_2C_6H_5$	65	147-149°(EtOH)
Id	$-(CH_2)_5-$		70	125-127°(C_6H_6-n·hexane)
Ie	$-(CH_2)_4-$		77	192-194°(ligroin)
If	C_2H_5	C_2H_5	70	100-101°(i-C_3H_7OH)
Ig	CH_3	cyclo-C_6H_{11}	70	109-110°(i-C_3H_7OH)

* All products have ir, nmr, and mass spectra consistent with the assigned structure.

** Yields(%) are based on the amine used.

REFERENCES

1 H. Salkowski, Ber., 24, 2724 (1891), 26, 2497 (1893); O. Wallach, Ber., 32, 1872 (1899); A.E. Dixon and J. Taylor, J. Chem. Soc., 93, 684 (1908); W.G. Finnegan, R.A. Henry and E. Lieber, J. Org. Chem., 18, 779 (1953); R.H. Sahasrabudhey and R. Singh, J. Ind. Chem. Soc., 29, 636 (1952); R. Singh and T.C. Saikia, ibid., 30, 695 (1953); F. Kurzer and P.M. Sanderson, J. Chem. Soc., 1957, 4461; R.G. Neville and J.J. McGee, Can. J. Chem., 41, 2123 (1963).

2 H. Hartmann and I. Reuther, J. Prakt. Chem., 315, 44 (1973).

3 D.H. Reid, et al., Organic Compounds of Sulfur, Selenium and Tellurium, The Chemical Society, London, vol. 3, p 267 (1975); R. Esmail and F. Kurzer, Synthesis, 1975, 301.

4 Y. Tamura, T. Kawasaki, M. Adachi, M. Tanio and Y. Kita, Tet. Letters, 1977, 4417.

5 Y. Tamura, M. Tanio, T. Kawasaki and Y. Kita, Synthesis, submitted.