Tetrahedron Letters No. 50, pp 4417 - 4420, 1977. Pergamon Press. Printed in Great Britain.

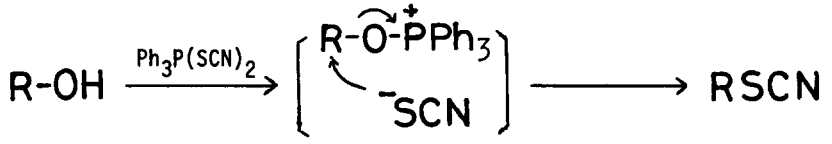
THIOCYANATION AND CYANATION USING A NEW COMBINED REAGENT OF TRIPHENYLPHOSPHINE AND THIOCYANOGEN

Y. Tamura, T. Kawasaki, M. Adachi, M. Tanio, and Y. Kita
Faculty of Pharmaceutical Sciences, Osaka University
133-1, Yamada-Kami, Suita, Osaka, Japan

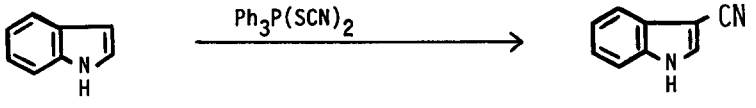
(Received in Japan 26 September 1977; received in UK for publication 20 October 1977)

Tertiary phosphine dihalides are extremely efficient reagents for the preparation of halides from alcohols[1a,2] or phenols,[2] acyl halides from acids[1a,3] or esters,[4] nitriles from amides,[3] amides from oximes,[5] benzils from benzoins,[6] and also for the cleavage of ethers.[4a,7] The ready availability of these reagents and mild reaction conditions have prompted us to investigate a behavior of a combined reagent of triphenylphosphine and disulfide pseudohalogen.

We report herein that a new combined reagent of triphenylphosphine and thiocyanogen reacts smoothly with alcohols to produce directly the corresponding thiocyanates, and with indoles or pyrrole to bring about a different type of reaction, giving nucleus cyanated compounds in high yields. These reactions are outlined by the following equations.



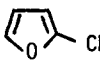
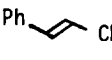
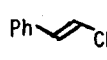
(i)



The reagent, $Ph_3P(SCN)_2$ was prepared by the following method: A suspension of lead thiocyanate in methylene chloride was cooled to 0°, and the calculated amount of bromine was added dropwise with shaking until the color due to the bromine disappeared. The residual solids were allowed to settle, and the thiocyanogen solution was decanted.[8] To the decant, an equimolar amount of triphenylphosphine in dry methylene chloride was added with stirring at -40°, and stirred for additional 30 min under the same condition to give a quantitative yield of the desired reagent as a yellow clear solution.

In a typical experimental procedure for thiocyanation, a solution of benzyl alcohol (4 mmole) in dry methylene chloride (10 ml) was added to a freshly prepared $Ph_3P(SCN)_2$ solution (5 mmole) at -40°, and the reaction mixture was stirred at -30° for 4 hr, allowed to warm to room temperature, kept at room temperature overnight, and concentrated under reduced pressure to give a syrup, from which benzyl thiocyanate was obtained in 80% yield by using a silica gel chromatography. The structure was confirmed by direct comparison with an authentic sample. In a similar manner, a number of other primary alcohols were converted to the corresponding thiocyanates in good yields. The results are summarized in Table I.

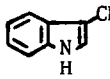
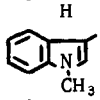
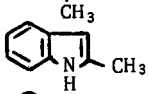
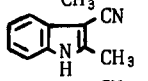
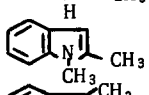
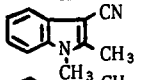
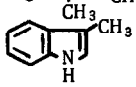
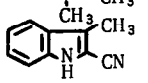
Table I

Primary alcohols	Thiocyanates[9]	Yield (%)	m.p.(b.p.)[10] (°C)
$PhCH_2OH$	$PhCH_2SCN$	80	41-2.5
p-Cl-$C_6H_4CH_2OH$	p-Cl-$C_6H_4CH_2SCN$	99	(176-9/10 mmHg)
p-CH_3O-$C_6H_4CH_2OH$	p-CH_3O-$C_6H_4CH_2SCN$	95	(135-9/0.7 mmHg)
		78	(105-8/14 mmHg)
		63	71.5-2.5
$PhCH_2CH_2OH$	$PhCH_2CH_2SCN$	48	(161-5/15 mmHg)
n-$CH_3(CH_2)_4OH$	n-$CH_3(CH_2)_4SCN$	80	(85-9/15 mmHg)
n-$CH_3(CH_2)_{11}OH$	n-$CH_3(CH_2)_{11}SCN$	60	(170-5/10 mmHg)

In contrast to the primary alcohols the reagent reacted with tertiary alcohols to give the corresponding isothiocyanates instead of the thiocyanates, and with secondary alcohols to give a mixture of the thiocyanates and the isothiocyanates [e.g., α,α-dimethylbenzyl alcohol: α,α-dimethylbenzyl isothiocyanate (80%), t-butyl alcohol: t-butyl isothiocyanate (8%), cyclopentyl alcohol: cyclopentyl thiocyanate (62%) and cyclopentyl isothiocyanate (4%), cyclooctyl alcohol: cyclooctyl thiocyanate (53%) and cyclooctyl isothiocyanate (2%)]. The reaction seems to proceed through a phosphonium salt (i) which reacts with SCN anion to form the thiocyanates, which may isomerize to the isothiocyanates when the thiocyanates are unstable.[11]

We also found this reagent can act as a cyanation agent for indoles and pyrrole. The procedure for cyanation is analogous to that described for thiocyanation: To an excess of $Ph_3P(SCN)_2$ (5 mmole) in dry methylene chloride, a solution of indoles or pyrrole (2 mmole) in dry methylene chloride was added at -40° and the reaction mixture was stirred for 4 hr under the same condition to give the cyanated compounds in fairly good yields. The results obtained for some representative indoles and pyrrole, are summarized in Table II. The structures were proved by spectral and analytical data.

Table II

Indoles and pyrrole	Products[9]	Yield (%)	m.p.(b.p.)[10] (°C)
		93	183-4
		64	65
		99	204-6
		70	104-5
		85	103-4
		50	(113-5/11 mmHg)

As can be seen in Table II, the cyanation of indoles by $Ph_3P(SCN)_2$ occurred selectively at C-3 position unless 3-position was already substituted. Common nucleophilic attack of 3-position of indoles to CN-carbon accompanied with formation of $Ph_3P=S$ can account for the product, but other mechanisms can be envisaged.

It is worth noting a ready availability of this reagent and smooth reactions at low temperature under mild condition. The investigation of scope, limitation and reaction mechanisms are now in progress.

REFERENCES

1a, L. Horner, H. Oediger and H. Hoffmann, Ann., 626, 26 (1959).

b, A.V. Bayless and H. Ziminer, Tet. Letters, 1968, 3811, Y. Kobayashi and C. Akashi, Chem. Pharm. Bull., 16, 1009 (1968), J.I.G. Cadogan and R.K. Mackie, Chem. Soc. Rev., 3 121 (1974).

2, G.A. Wiley, R.L. Hershkowitz, B.M. Rein and B.C. Chung, J. Amer. Chem. Soc., 86, 964 (1964).

3, H.J. Bestmann, J. Lienert and L. Mott, Ann., 718, 24 (1968).

4a, A.G. Anderson, Jr. and D.H. Kono, Tet. Letters, 1973, 5121.

b, D.J. Burton and W.M. Koppes, Chem. Commun., 1973, 425.

5, M. Ohno and I. Sakai, Tet. Letters, 1965, 4541.

6, T.L. Ho, Synthesis, 1972, 697.

7, H.P. Marchand and W.R. Weimar, Jr., Chem. and Ind., 1969, 200, A.G. Anderson, Jr. and F.J. Freenor, J. Org. Chem., 37, 626 (1972).

8, J.L. Wood, Org. Reactions, Vol. 3, 240 (1946).

9, Products were identified by comparison of spectral and physical data with that for authentic samples.

10, bath temperature

11, R.G.R. Bacon, Organic Sulfur Compounds, Vol 1, 306 (1961).