Convenient Improved Syntheses of Isocyanates or Isothiocyanates from Amines

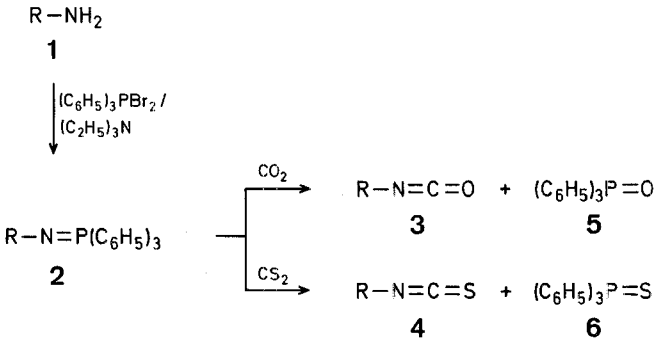
P. MOLINA*, M. ALAJARIN, A. ARQUES

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Murcia, Murcia, Spain

The most widely used methods for the synthesis of isocyanates and isothiocyanates are the reaction of amines or derivatives thereof with carbonyl chloride (phosgene) or thiocarbonyl chloride, respectively. Although these methods are useful and are utilized on an industrial scale the toxicity of the reagents represents a drawback in the laboratory synthesis of isocyanates and isothiocyanates.

Iminophosphoranes (phosphinimines) have been found to be particularly useful in heterocyclic synthesis[1]; however, only few methods for the conversion of primary amino groups into other functionalities via iminophosphorane derivatives have been reported. Iminotriphenylphosphoranes react with isocyanates to give carbodiimides and triphenylphosphine oxide[2-5]. *N*-Aryliminotriphenylphosphoranes react with carbon monoxide in the presence of palladium to give a mixture of aryl isocyanate and a carbonyl complex of palladium[6], with sulfur tetrafluoride to give sulfurdiimides[7], and with acyl halides to give imidoyl halides[8].

It has only been briefly mentioned[9] that the reaction of cyclohexyliminotriphenylphosphorane with carbon dioxide leads to a mixture of cyclohexyl isocyanate (24%) and cyclohexylcarbodiimide (53%). On the other hand, iminophosphoranes can be conveniently used for the synthesis of 1,1,2-substituted hydrazines[10] and *N*-alkylanilines[11]. We describe here an efficient and simple method for the two-step conversion of anilines and alkanamines **(1)** into isocyanates **(3)** or isothiocyanates **(4)**. The key step is the reaction, under mild conditions, of carbon dioxide or carbon disulfide with the iminophosphorane derivatives **2**, readily available from the corresponding amines **(1)** and triphenylphosphine dibromide[12], to give the isocyanate **(3)** and triphenylphosphine oxide **(5)** or the isothiocyanate **(4)** and triphenylphosphine sulfide **(6)**, respectively.



The isocyanates **3** and isothiocyanates **4** thus formed are easily isolated in high yields (73-97%) and are not contaminated by carbodiimide. The reported yields of isothiocyanates from amines and diethylthiocarbamoyl chloride[13] are 21-80% and from amines and carbon disulfide and a Grignard reagent[14] are 24-93%. The reported yields of isocyanates from amines and phosgene[15] are 75-95% and from sulfinylimines and phosgene[16] are 60-75%.

Alkyl- and Aryliminotriphenylphosphoranes (2):
These compounds are prepared according to the procedures of Ref.[12] and Ref.[17].

Table 1. Alkyl and Aryl Isocyanates **(3)** prepared

3	R	Yield[a] [%]	Purity [%]	b.p./torr or m.p. [°C] found	b.p./torr or m.p. [°C] reported
a	C_6H_5	97	93	b.p. 165–167°/760	b.p. 162–163°/751[18]
b	4-Cl—C_6H_4	97		m.p. 32–33°	m.p. 30–31°[18]
c	4-Br—C_6H_4	89	97	b.p. 147–149°/10	b.p. 158°/14[18]
d	4-H_3C—C_6H_4	92	91	b.p. 193–195°/760	b.p. 187°/14[18]
e	4-O_2N—C_6H_4	90		m.p. 55–56°	m.p. 57°[18]
f	CH_3	79	82	b.p. 61–63°/760	b.p. 59.6°/760[18]
g	*c*-C_6H_{11}	73	99	b.p. 60–62°/10	b.p. 62–68°/15[19]
h	C_6H_5—CH_2	92	86	b.p. 95–97°/15	b.p. 88–91°/12[19]

[a] Isolated product.

Table 2. Alkyl and Aryl Isothiocyanates **(4)** prepared

4	R	Yield[a] [%]	Purity [%]	b.p./torr or m.p. [°C] found	b.p./torr or m.p. [°C] reported
a	C_6H_5	92	93	b.p. 90–92°/10	b.p. 95°/12[18]
b	4-Cl—C_6H_4	96		m.p. 43–44°	m.p. 45°[18]
c	4-Br—C_6H_4	96		m.p. 59–60°	m.p. 60–61°[18]
d	4-H_3C—C_6H_4	94	91	b.p. 113–115°/15	b.p. 115°/15[20]
e	4-O_2N—C_6H_4	88		m.p. 111–112°	m.p. 112°[21]
f	CH_3	80		m.p. 34–36°	m.p. 36°[18]
g	*c*-C_6H_{11}	75	92	b.p. 221–223°/760	b.p. 219°/746[18]
h	C_6H_5—CH_2	93	96	b.p. 118–120°/10	b.p. 124–125°/12[18]

[a] Isolated product.

0039-7881/82/0732-0596 $ 03.00

Isocyanates (3); General Procedure:
A stream of dry carbon dioxide is passed through a solution of the iminophosphorane **2** (10 mmol) in dry benzene (100 ml). The solution is heated at reflux temperature for 2 h. After cooling, the solvent is removed under reduced pressure. The residue is extracted with petroleum ether (3 × 40 ml), the combined organic extracts are concentrated, and the residual product is distilled or recrystallized to give the isocyanate **3**; purity of liquid products **3**: > 80%, as checked by G.L.C. analysis (10% SE-30 on 60/80 mesh Chromosorb W, 6 ft × 1/8 in column, column temperature after injection: 210 °C).

Isothiocyanates (4); General Procedure:
Carbon disulfide (1.52 g, 20 mmol) is added to a solution of the iminophosphorane **2** (10 mmol) in dry benzene (100 ml), the mixture is heated at reflux temperature for 2 h, and then allowed to cool. The solvent is removed under reduced pressure and the residue extracted with petroleum ether (3 × 40 ml). The extract is concentrated and the residual product distilled or recrystallized to give the isothiocyanate **4**; purity of liquid products **4**: > 90%, as checked by G.L.C. analysis (10% SE-30 on 60/80 mesh Chromosorb W, 6 ft × 1/8 in column, column temperature after injection: 210 °C).

Received: November 3, 1981
(Revised form: December 16, 1981)

* Address for correspondence.

[1] See, for example: *Organophosphorus Reagents in Organic Synthesis*, J. I. G. Cadogan, ed., Academic Press, New York, 1979.
[2] H. Staudinger, J. Meyer, *Helv. Chim. Acta* **2**, 635 (1919).
[3] V. I. Gorbatenko, N. V. Melnichenko, L. I. Samarai, *Zh. Obshch. Khim.* **48**, 1425 (1978); *J. Gen. Chem. USSR* **48**, 1309 (1978).
[4] V. I. Gorbatenko, V. N. Fetyukhim, L. I. Samarai, *Zh. Org. Khim.* **12**, 2472 (1976); **13**, 2449 (1977).
[5] G. Aksnes, P. Froyam, *Acta Chem. Scand.* **23**, 2697 (1969).
[6] J. Kiji et al., *J. Chem. Soc. Chem. Commun.* **1975**, 751; *Bull. Chem. Soc. Jpn.* **50**, 2731 (1977).
[7] R. Appel, J. R. Lundehn, E. Lassmann, *Chem. Ber.* **109**, 2442 (1976).
[8] E. Zbiral, E. Bauer, *Phosphorus* **35**, 2 (1972).
[9] W. S. Wadsworth, W. D. Emmons, *J. Am. Chem. Soc.* **84**, 1316 (1962).
[10] H. Zimmer, G. Singh, *J. Org. Chem.* **29**, 1579 (1964).
[11] E. M. Briggs, G. W. Brown, J. Jiricny, M. F. Meidine, *Synthesis* **1980**, 295.
[12] L. Horner, H. Oediger, *Justus Liebigs Ann. Chem.* **627**, 142 (1959).
[13] A. A. R. Sayigh, H. Ulrich, J. S. Potts, *J. Org. Chem.* **30**, 2465 (1965).
[14] S. Sakai, T. Fujinami, T. Aizawa, *Bull. Chem. Soc. Jpn.* **48**, 2981 (1975).
[15] A. A. Artemev, Z. A. Strepikheev, Y. A. Shmidt, B. M. Babkin, *French Patent* 1578808 (1969); *C. A.* **72**, 131650 (1970).
[16] H. Ulrich, B. Tucker, A. A. R. Saylor, *J. Org. Chem.* **34**, 3200 (1969).
[17] H. Zimmer, M. Jayawant, P. Gutsch, *J. Org. Chem.* **35**, 2826 (1970).
[18] *Handbook of Chemistry and Physics*, 51st Edition, Chemical Rubber Co., Inc., Cleveland, Ohio, 1970–1971.
[19] D. Martin, A. Weise, *Angew. Chem.* **79**, 145 (1967); *Angew. Chem. Int. Ed. Engl.* **6**, 168 (1967).
[20] G. Barnikow, H. Kunzek, *J. Prakt. Chem.* [4] **29**, 323 (1965).
[21] D. W. Browne, G. M. Dyson, *J. Chem. Soc.* **1931**, 3299.

0039-7881/82/0732-0597 $ 03.00