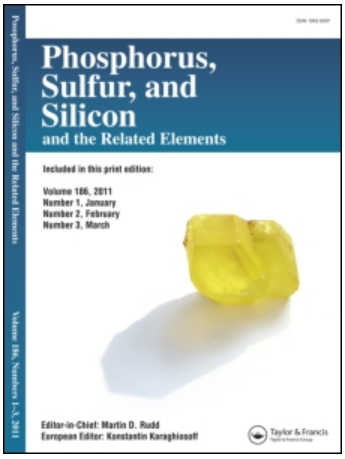


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

A NEW METHOD FOR THE CONVERSION OF ALCOHOLS INTO ALKYL IODIDES

Paul Frøyen[a]; Paul Juvvik[b]
[a] Department of Chemistry, Agricultural University of Norway, Norway [b] Department of Chemistry, University of Bergen, Bergen, Norway

To cite this Article Frøyen, Paul and Juvvik, Paul(1996) 'A NEW METHOD FOR THE CONVERSION OF ALCOHOLS INTO ALKYL IODIDES', Phosphorus, Sulfur, and Silicon and the Related Elements, 116: 1, 217 — 223
To link to this Article: DOI: 10.1080/10426509608040482
URL: http://dx.doi.org/10.1080/10426509608040482

Phosphorus, Sulfur, and Silicon, 1996, Vol. 116, pp. 217–223
Reprints available directly from the publisher
Photocopying permitted by license only

A NEW METHOD FOR THE CONVERSION OF ALCOHOLS INTO ALKYL IODIDES

PAUL FRØYEN[a,*] and PAUL JUVVIK[b]

[a]*Department of Chemistry, Agricultural University of Norway, P. O. Box 5040-1432 Ås-NLH, Norway;* [b]*Department of Chemistry, University of Bergen, N-5007 Bergen, Norway*

(Received 21 May 1996; In final form 18 June 1996)

Treatment of a series of alcohols with triphenylphosphine and cyanogen iodide (a positive halogen source) affords the corresponding alkyl iodides in good yields.

Keywords: Triphenylphosphine; cyanogen iodide; primary and secondary alcohols; replacement of hydroxyl by iodide

Alkyl iodides are considerably more reactive than their halogen analogs and consequently often used in synthesis in preference to chlorides and bromides. A number of methods exist for their preparation, for the most part starting from compounds containing a fairly easily displaceable group such as alcohols, thiols etc.

Alcohols can be converted to alkyl iodides with a number of reagents.[1] The most common is hydrogen iodide, often prepared *in situ* from potassium iodide and phosphoric acid. Although this works well in a number of cases, reduction to the alkane often competes, and rearrangements are common.

Unwanted rearrangements, though not reduction, may be avoided by using PI_3[2], which is usually made from white phosphorus and iodine. Recent work in this area includes the application of diphosphorus tetraiodide[3], aluminium triiodide[4], triphenylphosphite methiodide[5,6], or other quasi—phosphonium compounds (Rydon reagents), trimethylsilyl iodide[7,8], trichloromethylsilane/sodium iodide[9], carbodiimidinium iodide[10], boron trifluoride/sodium iodide[11,12], and fluorobenzothiazolium salts.[13]

*Corresponding author.

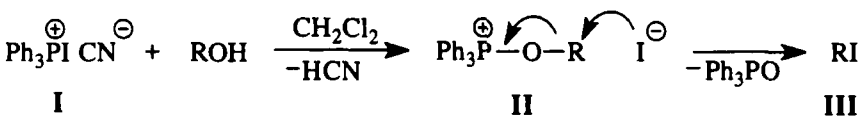
In a previous report[14] we have shown that Ph_3P in combination with NBS or BrCN reacts fairly easily with carboxylic acids, leading to acyl bromides in good yields, whereas similar experiments with Ph_3P/ICN gave poor or negligible yields of acyl iodides. During some initial studies we observed, however, that solutions of Ph_3P/ICN in THF or dichloromethane rapidly converted one equivalent of 1-propanol to 1-iodopropane (Scheme). Thus after 30 min. in boiling CH_2Cl_2 the iodide could be isolated in about 70% yield along with a quantitative amount of triphenylphosphine oxide.

The scope of this reaction was investigated on a number of alcohols (cf. Table). We found that many primary alcohols are converted into iodides simply by adding an equimolar amount of cyanogen iodide to a solution of alcohol and triphenylphosphine in dichloromethane at or below 0°C (in order to modify the exotherm), and thereafter heating the reaction mixture for 1/4 to 3 hours at about 40°C, followed by simple work-up.

Exceptions were sterically hindered alcohols, e.g, neopentyl glycol, which gave low yields of mono or diiodide when the reactions were performed in dichloromethane. However, by changing the solvent to dioxane and operating at 90°C these iodides could be obtained in good yields in a short time (Table, entries **5** and **11**). The best results are generally obtained when ICN is added to an equimolar mixture of alcohol and triphenylphosphine.

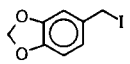
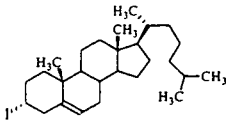
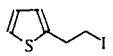
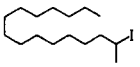
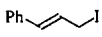
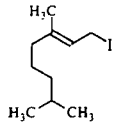
Cyanogen iodide and alcohol should not be mixed before triphenylphosphine has been added to the solution.

In view of the high sensitivity (thermolysis, photolysis) of many of the iodides formed, yields are in most cases quite good, in particular when the raw products are purified by column chromatography. Distillation as a rule tends to lower the yields. For example, purification of crude piperonyl iodide (entry **1**, Table) by distillation (Kugelrohr) gave 52% yield of a slightly discoloured product, whereas silica gel chromatography afforded a nearly quantitative yield of the pure, colourless **1**. The usefulness of the new method for iodination of more complex and sensitive substrates remains to be demonstrated. However, considering its mildness and convenience, and the yields obtained with the present range of alcohols (cf. Table), it seems to be a good alternative to many of the more elaborate methods referred to above. The liberation of hydrogen cyanide (Caution!) constitutes only a slight drawback.



I II III

TABLE I Transformation of alcohols into iodides by means of ph_3P/ICN

Entry	*Iodide*	*Yield (%)*	*Entry*	*Iodide*	*Yield (%)*
1		97			
			6		92
2		73			
			7		79
3		78			
			8		75
4		0	**9**		81
			10		75
5		76	**11**		89

We believe the reaction proceeds via the activated species **II** (Scheme) which is subsequently attacked by the iodide ion in a rate determining second step, forming alkyl iodide and triphenylphosphine oxide.

Together with similar phosphonium salts generated from triphenylphosphine and NBS (or NCS) the present salts **I** (Scheme) constitute versatile intermediates for the preparation of acyl halides,[14] azides,[15] esters,[16] amides,[17] amines,[18] and the present alkyl iodides.

The present transformation of alcohols into the corresponding iodides works well with saturated primary and secondary alcohols, with benzylic alcohols, and in some cases also with allylic alcohols, albeit yields of particularly sensitive iodides e.g., cinnamyl iodide, are generally lower than those of their saturated analogs. The method fails completely in the case of geraniol (entry **4**).

It should be noted, however, that surprisingly good yields are observed in the case of the sterically hindered 2,2-diphenyl-1,3-propandiol, that the sensitive acetal function of piperonyl alcohol is not affected, and that cholesterol when refluxed for about 3 hours in dichloromethane gives 90% yield of cholesteryl iodide **6**, which is better than that reported by Rydon et al.[5] The procedure is likewise more convenient and affords better yields of **6** than the method of Broome et al.[19] based on iodine and amalgamated aluminium. It is furthermore of some interest to notice that the Ph_3P/CCl_4 system fails in the case of cholesterol. The complex mixture of products reported by Aneja et al.[20] indicates that

the intermediate in this particular case undergoes considerable skeletal rearrangements prior to fragmentation into triphenylphosphine oxide and alkyl halide by the regular pathway.

A close examination of our product (**6**) by TLC, GC/MS and SFC/MS vouched for sample homogeneity and failed to give any evidence of the above-mentioned rearrangements.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were taken at operating frequencies of 200 and 50.3 MHz on a Varian Gemini-200 spectrometer. The mass spectra were obtained on a JMS-DX 303 mass spectrometer. IR spectra were measured as films with a Perkin Elmer 1310 infrared spectrometer. Column chromatography was carried out using Merck No. 9385 silica gel 60. Melting points, determined with a Reichert Thermopan melting point microscope, are uncorrected.

General Procedure for the Preparation of Alkyl Iodides

The reactants, triphenylphosphine and alcohol (5 mmol of each) were dissolved in dichloromethane (6 ml). The mixture was cooled in an ice bath and vigorously stirred while ICN (0.77 g, 5 mmol) was added in small portions. The reaction mixture was thereafter heated for 5–30 min (3 h in the case of cholesterol **6**). The sterically hindered neopentyl glycol was reacted in dioxane, in which heating for about 30 min with one equivalent of Ph_3P/ICN yielded the monoiodide **5**, whereas employment of two equivalents of the same reagent under identical conditions gave the diiodide **10**. After the reaction, most of the solvent was removed by evaporation at reduced pressure and the alkyl iodide either extracted with pentane and distilled *in vacuo*, or freed from contaminants (mostly triphenyphosphine oxide) by column chromatography on Merck No. 9385 silica gel 60 with ether/petrol ether (1 : 8) as eluent. The products were then either crystallized from an appropriate solvent (cyclohexane, pentane, and occasionally, mixtures of pentane/ether) or distilled.

Piperonyl iodide **1**: Chromatography of the raw product followed by evaporation of the eluent (ether) gave virtually pure **1**, a white solid which was recrystallized from pentane. The product melted sharply at 56°C; ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.44 (s, 2H, CH_2), 5.95 (s, 2H, CH_2), 6.68–6.87 (m, 3H, $H_{aromatic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 7.69, 100.94, 107.91, 108.77,

121.54, 132.20, 146.41, 148.88; MS (70 eV): m/z (%) 262 (1.4, M^+), 136 (6.9), 135 (48.3, M^+–I).

2-(2-Thienyl) ethyliodide **2**: Chromatography followed by distillation (Kugelrohr) at about 65°C/0.05 mm Hg gave the pure product, a slightly yellow oil, ^1H NMR (200 MHz, $CDCl_3$): δ 3.38 (s, 4H, CH_2), 6.88–7.18 (m, 2H, $H_{aromatic}$), 7.20–7.22 (m, 1H, $H_{aromatic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 5.93, 34.66, 123.31, 124.55, 126.19, 142.06; MS (70 eV): m/z (%) 238 (65.2, M^+), 111 (17.3), 112 (17.9), 110 (10.8), 97 (53.2), 85 (16.1), 77 (11.5), 67 (18.7).

Cinnamyl iodide **3**: Chromatography of the raw product followed by evaporation of the eluent (ether—petroleum ether 1:8) gave virtually pure **3**, a white solid wich melted at 55°C, lit.[21] 57° and rapidly turned yellow and brown even when kept under nitrogen in a refrigerator; ^1H NMR (200 MHz, $CDCl_3$): δ 4.12 (d, 2H, J = 7.6 Hz, CH_2), 6.36–6.66 (m, 1H, $H_{vinylic}$), 7.22–7.43 (m, 5H, $H_{aromatic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 6.96, 126.50, 126.80, 128.06, 128.54, 133.01, 135.77.

3-Iodo-2,2-dimethyl-1-propanol **5**: Colourless oil; distilled (Kugelrohr) at about 100°C/15 mm Hg, lit.[22] 103°/22 mm, 114°/35 mm; ^1H NMR (200 MHz, $CDCl_3$): δ 1.04 (s, 6H, CH_3), 1.73 (s, 1H, OH), 3.22 (s, 2H, CH_2), 3.44 (s, 2H, CH_2); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 20.84, 24.29, 35.97, 69.83; MS (70 eV): m/z (%) 214 (6.4, M^+), 196 (6.3), 182 (7.6), 127 (7.7).

Cholesteryl iodide **6**: Chromatography of the raw product followed by evaporation of the eluent (ether/petroleum ether 1:8) gave virtually pure **6**, a colourless solid which after recrystallization from pentane melted at 105–107°C, lit.[19] 107–108°; ^1H NMR (200 MHz, $CDCl_3$): δ 0.67 (s, 3H, CH_3), 0.86 (d, 6H, J = 6.6 Hz, CH_3), 0.91 (d, 3H, J = 6.5 Hz, CH_3), 1.04 (s, 3H, CH_3), 0.94–1.01 and 1.05–1.65 (m, 22H, CH_2), 1.65–3.02 (m, 6H, CH), 4.05 (m, 1H, CH), 5.33 (m, 1H, $H_{vinylic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 12.62, 19.41, 19.92, 21.45, 23.23, 23.48, 24.47, 24.88, 28.59, 28.79, 31.10, 32.15, 32.27, 36.26, 36.65, 36.93, 37.06, 39.95, 40.10, 42.32, 42.69, 46.75, 50.65, 56.36, 56.91, 121.13, 141.96; MS (70 eV): m/z (%) 497 (0.1, M^+), 370 (34.5, M^+–I), 388.5 (100, M^+–HI), 246.5 (12.6), 242.5 (12.4), 174.6 (30.8), 164.7 (14.1), 160.6 (64.5), 150.6 (12.8), 148.6 (39.3), 146.6 (59.1), 134.7 (39.2), 132.7 (10.5), 122.7 (19.6), 120.7 (26.8). $[\alpha]^{21}_D = -12.7°$ (C = 4 in $CHCl_3$), lit.[19] $[\alpha]^{21}_D = -12°$ ($CHCl_3$).

2-Iodohexadecane **7**: Column chromatography followed by evaporation of the eluent (ether/petroleum ether 1: 8) gave virtually pure **7**, a colourless oil; ^1H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, 3H, J = 5.8 Hz, CH_3), 1.26 (m, 26H, CH_2), 1.92 (d, 3H, J = 6.8 Hz, CH_3), 4.18 (m, 1H, CH); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 14.88, 23.34, 29.33, 29.49, 29.93, 30.05, 30.14, 30.26, 31.19, 32.46, 43.32; MS (70 eV): m/z (%) 352 (27.3, M^+), 263 (24.3), 262 (13.8), 226 (15.2),

225 (80.5, $M^+ - I$), 183 (11.1), 169 (15.2), 155 (21.1), 141 (25.4), 127 (28.8), 113 (34.3), 99 (46.1), 85 (99.9), 71 (100).

Benzyl iodide **8:** Oil; distilled (Kugelrohr) at about 60°C/0.05 mm Hg, m.p. 24°; lit.[23] m.p. 25°; ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.47 (s, 2H, CH_2), 7.20–7.44 (m, 5H, $H_{aromatic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 6.70, 127.16, 126.02, 128.09, 138.41; MS (70 eV): m/z (%) 218 (3.5, M^+), 127 (2.7, I^+), 91 (100, $M^+ - I$), 65 (17.0).

(2-Iodoethyl)benzene **9:** distilled (Kugelrohr) at about 70°C/0.05 mm Hg, lit.[23] 125–128°C/18–20 mm; ^{1}H NMR (200 MHz, $CDCl_3$): δ 3.12–3.17 (m, 2H, CH_2), 3.17–3.44 (m, 2H, CH_2), 7.15–7.40 (m, 5H, $H_{aromatic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 6.48, 40.65, 126.16, 127.61, 127.92, 138.76; MS (70 eV): m/z (%) 232 (6.0, M^+), 105 (100, $M^+ - I$), 103 (10), 91 (7.5), 79 (16.3), 77 (17).

Iododiphenylmethane **10:** Column chromatography followed by evaporation of the eluent (ether/petroleum ether 1: 8) gave pure **10**, a colourless oil which immediately was transferred to a refrigerator and stored under nitrogen at −78°; ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.59 (s, 1H, CH), 7.26–7.32 (m, 6H, $H_{aromatic}$), 7.49–7.54 (m, 4H, $H_{aromatic}$); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 127.11, 127.91, 128.15, 141.62; MS (70 eV): m/z (%) 254 (11.4, I_2), 168 (53.6), 167 (98.4, $M^+ - I$), 166 (56.9, $M^+ - HI$), 165 (100), 153 (11.2), 152 (43.9), 139 (13), 128 (13.1), 127 (38.1, I), 115 (13), 106 (18), 105 (55.6), 89 (11.5), 83 (25.1).

2,2-Dimethyl-1,3-diiodopropane **11:** Oil; distilled (Kugelrohr) at about 100°C/15 mm Hg; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.25 (s, 6H, CH_3), 3.28 (s, 4H, CH_2); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ 22.25, 26.69, 34.10; MS (70 eV): m/z (%) 324 (20.5, M^+), 197 (64.1, $M^+ - I$), 128 (13.4), 127 (13.6), 70 (11.2), 69 (10.6), 55 (30.4).

Acknowledgements

One of us, P. F., would like to thank professor J. Skramstad for making laboratory space available at the Department of Chemistry, University of Oslo during this work. A thank also to Mr. D. Ekeberg, Department of Chemistry, Agricultural University of Norway, for recording the mass spectra.

References

[1] J. March "Advanced Organic Chemistry," 4. ed. Wiley; p. 431 (1992).
[2] W.W. Hartmann, J.R. Byers and J.B. Dickey, *Org. Synth., Coll. Vol. II*, 322 (1943).
[3] M. Lauwers, B. Regnier, M. Van Eenoo, J.N. Denis and A. Krief, *Tetrahedron Lett.*, **33**, 1801 (1963).
[4] P. Sarmah and N.C. Barua, *Tetrahedron Lett.*, **45**, 2659 (1989) and references therein.
[5] S.R. Landauer and H.N. Rydon, *J. Chem. Soc.*, 2224 (1953).

[6] H.N. Rydon, Org., *Synth., Coll. Vol. VI*, 830 (1988).
[7] M.E. Jung and P.L Ornstein, *Tetrahedron Lett.*, **31**, 2659 (1977).
[8] G.A. Olah, S.C. Narang, B.G.B. Gupta and R. Malhotra, *Angew. Chemie*, **91**, 648 (1979).
[9] G.A. Olah, A. Husain, B.P. Singh and A.K. Mehrotra, *J. Org. Chem.*, **48**, 3667 (1983).
[10] R. Scheffold and E. Saladin, *Angew. Chemie*, **84**, 158 (1972).
[11] Y.D. Vankar and C.T. Rao, *Tetrahedron Lett.*, **26**, 2717 (1985).
[12] Y.D. Vankar and C.T. Rao, *J. Chem. Res. (S)*, 232 (1985).
[13] K. Hojo and T. Mukaiyama, *Chem. Lett.*, 619 (1975).
[14] P. Frøyen, *Phosphorus, Sulfur and Silicon*, **102**, 253 (1995).
[15] P. Frøyen, *Phosphorus, Sulfur and Silicon*, **89**, 57 (1994).
[16] P. Frøyen, *Phosphorus, Sulfur and Silicon*, **91**, 145 (1994).
[17] P. Frøyen, *Synth. Commun.*, **25**, 959 (1995).
[18] P. Frøyen and P. Juvvik, *Tetrahedron Lett.*, **52**, 9555 (1995).
[19] J. Broome, B.R. Brown and G.H.R. Summers, *J. Chem. Soc.*, 2071 (1957).
[20] R. Aneja, A.P. Davies and J.A. Knaggs, *Tetrahedron Lett.*, **31**, 67 (1974).
[21] J. Meisenheimer and J. Link, *Lieb. Ann.*, **479**, 211 (1930).
[22] P. Meyersberg, *Monatsh. Chem.*, **26**, 41 cited after *Beilstein's Handbuch d. Org. Chem.*, **1**, 407 (1905).
[23] G.H. Coleman and C.R. Hauser, *J. Am. Chem. Soc.*, **50**, 1193 (1928).