

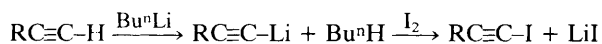
Copper(I)- and Phase-Transfer-Catalysed Iodination of Terminal Alkynes

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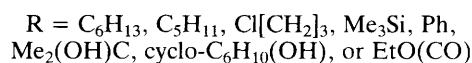
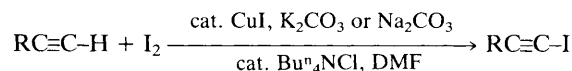
A convenient synthesis of 1-iodoalk-1-yne is reported, involving copper(I)-catalysed iodination of terminal alkynes with molecular iodine under solid–liquid phase-transfer conditions.

1-Iodoalk-1-yne are useful synthetic intermediates,¹ they may also have fungicidal² and antimicrobial³ activity. Although several routes to this type of compound are known,^{4–7} the more usual preparative methods involve iodination of metal acetylides $\text{RC}\equiv\text{CM}$ ($\text{M} = \text{Li}, \text{Na}, \text{Mg}, \text{Hg}, \text{Cu},$ or Ag) preformed from alk-1-yne. Among the various procedures available, the most convenient is that based on the stoichiometric formation of lithium acetylides from readily available *n*-butyl-lithium and alk-1-yne followed by iodination with molecular iodine⁵ (Scheme 1). This communication describes a catalytic procedure for the direct iodination of terminal alkynes.



Scheme 1

As shown in Table 1, good yields of 1-iodoalk-1-yne can be obtained by treating terminal alkynes with a solution of iodine in *N,N*-dimethylformamide (DMF), in the presence of a catalytic amount of copper(I) iodide, under solid–liquid phase-transfer conditions, with potassium or sodium carbonate as base and tetra-*n*-butylammonium chloride as phase-transfer agent (Scheme 2).



Scheme 2

Table 1. Copper(I)- and phase-transfer-catalysed synthesis of 1-iodoalk-1-yne from terminal alkynes.^a

Run no.	Alk-1-yne	CuI (equiv.)	Bu ⁿ ₄ NCl (equiv.)	Inorganic base	Product ^b	% Yield ^c
1	C ₆ H ₁₃ C≡CH	0	0	K ₂ CO ₃	C ₆ H ₁₃ C≡CI	0
2	C ₆ H ₁₃ C≡CH	0	1	K ₂ CO ₃	C ₆ H ₁₃ C≡CI	0
3	C ₆ H ₁₃ C≡CH	0.1	0	K ₂ CO ₃	C ₆ H ₁₃ C≡CI	(18)
4	C ₆ H ₁₃ C≡CH	0.1	1	K ₂ CO ₃	C ₆ H ₁₃ C≡CI	(98)
5	C ₆ H ₁₃ C≡CH	0.05	0.20	K ₂ CO ₃	C ₆ H ₁₃ C≡CI	90 ^d
6	C ₅ H ₁₁ C≡CH	0.1	0.30	K ₂ CO ₃	C ₅ H ₁₁ C≡CI	70 ^d
7	Cl[CH ₂] ₃ C≡CH	0.1	0.20	Na ₂ CO ₃	Cl[CH ₂] ₃ C≡CI	88
8	Me ₃ SiC≡CH	0.05	0.20	Na ₂ CO ₃	Me ₃ SiC≡CI	82 ^{d,e}
9	PhC≡CH	0.1	0.25	K ₂ CO ₃	PhC≡CI	80 ^d
10	Me ₂ C(OH)C≡CH	0.1	0.30	Na ₂ CO ₃	Me ₂ C(OH)C≡CI	77
11	[CH ₂] ₅ C(OH)C≡CH	0.1	0.30	K ₂ CO ₃	[CH ₂] ₅ C(OH)C≡CI	85
12	EtO ₂ CC≡CH	0.05	0.30	Na ₂ CO ₃	EtO ₂ CC≡CI	80 ^f

^a Reactions were carried out in DMF with terminal alkyne (1 equiv.), Na₂CO₃ or K₂CO₃ (2 equiv.), Buⁿ₄NCl (as indicated), copper(I) iodide (as indicated), and molecular iodine (1 equiv.) at room temperature overnight unless otherwise noted. ^b All compounds were characterised by mass spectra, i.r., ¹H and ¹³C n.m.r. data. ^c Yield of spectroscopically pure product isolated by flash chromatography for small-scale reactions (5–15 mmol of alkyne) or by distillation for larger scale reactions (30–50 mmol of alkyne). Yields in parenthesis were determined by g.l.c. analysis. ^d Reaction performed with 30–50 mmol of alkyne. ^e After 6 h at room temperature. ^f After 4 h at –30 °C and overnight at room temperature.

The reaction does not take place without copper(I) iodide (run 1 and 2). The rate is greatly enhanced by tetra-n-butylammonium chloride (run 4), which is also effective in catalytic amounts (run 5). No attempts were made to minimize the amounts of the two catalysts. It has been observed however, that the reaction yields are directly influenced by the addition rate of the iodine solution and, to maintain good yields, lower percentages of copper(I) iodide and tetra-n-butylammonium chloride must be accompanied by a lower rate of addition.

Only traces of dimers and/or 1,2-di-iodoalk-1-enes were observed under the conditions described, as evidenced by coupled g.l.c.-mass spectrometric analysis of the crude products, whereas mixtures of 1-iodoalk-1-yne, 1,2-di-iodoalk-1-enes, and di-iodo ketones have been obtained when terminal alkynes were treated with iodine in methanol, even in the presence of a stoichiometric amount of silver nitrate.⁸ No halogen exchange was observed with ω -halogenoalk-1-yne; a 1-iodoalk-1-yne having a hydroxy or a carbonyl moiety in its structure can also be prepared in good yield by the described procedure without protection of the functional group.

The reactions were carried out under an inert atmosphere; a typical procedure is as follows. A solution of iodine (30 mmol) in DMF (20 ml) was added very slowly (3–4 h) to a well stirred suspension in DMF (15 ml) of potassium or sodium carbonate (60 mmol), tetra-n-butylammonium chloride (6–9 mmol), terminal alkyne (30 mmol), and copper(I) iodide (1.5–3 mmol). Decolorisation of the iodine was generally observed until almost the end of the addition. Stirring was continued for 2 h or overnight, after which ether was added and the mixture was rapidly filtered through a bed of Celite. Water was added and the mixture extracted with ether, and the organic layer was successively washed with aqueous 0.05 M-sodium thiosulphate and brine and dried (MgSO_4). Removal of solvent under reduced pressure and purification by distillation or chromatography on silica gel gave the pure product.

The described procedure compares well with other methods in terms of yield. Moreover it has the advantages of being catalytic and tolerant towards functionalities. The simplicity

of the operation and the availability of the starting materials should also make it synthetically useful.

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References

- 1 For recent examples, see W. R. Roush, S. M. Peseckis, and A. E. Walts, *J. Org. Chem.*, 1984, **49**, 3429; F. Björkling, T. Norin, and R. Unelius, *Synth. Commun.*, 1985, **15**, 463; R. H. Boutin and H. Rapoport, *J. Org. Chem.*, 1986, **51**, 5320.
- 2 For recent examples, see: G. Jaeger, W. Paulus, and H. Genth (A. G. Bayer), Ger. Offen. DE 3 122 263/1982 (*Chem. Abstr.*, 1983, **98**, 197757); G. Jaeger, W. Brandes, and P. E. Frohberger (A. G. Bayer), Eur. Pat. Appl. EP 66 771/1982 (*Chem. Abstr.*, 1983, **98**, 197764); B. W. Krueger, U. Priesnitz, G. Jaeger, W. Paulus, and H. Genth (A. G. Bayer), Ger. Offen. DE 3 305 834/1984 (*Chem. Abstr.*, 1984, **101**, 186137); W. Singer and C. C. Versfelt (Troy Chemical Corp.), Brit. Pat. Appl. GB 2 138 292/1984 (*Chem. Abstr.*, 1985, **102**, 057826); A. G. Makhsumov and M. A. Atakhodzhaeva, *Khim. Farm. Zh.*, 1985, **19**, 1455 (*Chem. Abstr.*, 1986, **105**, 225980); B. F. Rose (Chevron Research Co.), U.S. Pat. US 4 639 460/1987 (*Chem. Abstr.*, 1987, **106**, 156456).
- 3 For recent examples, see: W. Gerhardt and R. Lehmann (K. Henkel), Ger. Offen. DE 3 216 895/1983 (*Chem. Abstr.*, 1984, **100**, 51107); W. Gerhardt and R. Lehmann (K. Henkel), Ger. Offen. DE 3 224 504/1984 (*Chem. Abstr.*, 1984, **100**, 209179); G. Schade, W. Paulus, and H. G. Schmitt (A. G. Bayer), Ger. Offen. DE 3 526 789/1987 (*Chem. Abstr.*, 1987, **106**, 98104).
- 4 S. Y. Delavarenne and H. G. Viehe in 'Chemistry of Acetylenes,' ed. H. G. Viehe, Dekker, New York, 1969, p. 651, and references cited therein.
- 5 L. Brandsma, 'Preparative Acetylenic Chemistry,' Elsevier, Amsterdam, London, and New York, 1971, p. 99.
- 6 V. Jäger and H. G. Viehe in Houben-Weyl, 'Methoden der Organischen Chemie,' ed. E. Müller, Vol. V/2a, Thieme Verlag, Stuttgart, 1977, p. 601 and references cited therein.
- 7 For recently reported procedures, see: H. Hofmeister, K. Annen, H. Laurent, and R. Weichert, *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 727; J. Barluenga, J. M. Gonzalez, M. A. Rodriguez, P. J. Campos, and G. Asensio, *Synthesis*, 1987, **7**, 661.
- 8 V. L. Heasley, D. F. Shellhamer, L. E. Heasley, D. B. Yaeger, and G. E. Heasley, *J. Org. Chem.*, 1980, **45**, 4649.