An Improved Method for the Synthesis of 1-Iodoalkynes

José Barluenga,*[a] José M. González,[a] Miguel A. Rodríguez,[a] Pedro J. Campos,[a] Gregorio Asensio,[b]

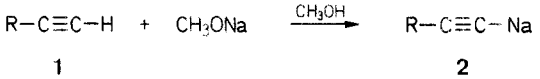
[a] Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, E-33007 Oviedo, Spain
[b] Departamento de Química Orgánica, Facultad de Farmacia, Universidad de Valencia, E-46010 Valencia, Spain

A simple and general one-pot procedure for the synthesis of 1-iodoalkynes is described based on the reaction of terminal acetylenes with bis(pyridine)iodine(I) tetrafluoroborate in the presence of sodium methoxide. The method now reported is superior to the literature procedures in scope, handling, and often yield.

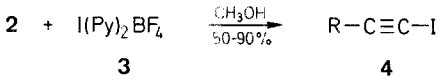
1-Haloalkynes are an interesting group of compounds due to their particular reactivity in substitution, and Cadiot-Chodkiewicz coupling reactions and also to the unexpected effect of the halogens in directing the addition of electrophiles to the triple bond.[1] To date the most general method for the synthesis of 1-iodoalkynes **4** is the reaction of iodine with the corresponding acetylide in liquid ammonia at ca. −30 °C.[1,2]

1-Iodoalkynes **4** also have been produced from the reaction of terminal alkynes and sodium hypoiodite in some instances, but low yields are reported due to side reactions caused by the instability of these compounds in alkaline medium and also due to problems in the purification step.[1,3] On the other hand, the reaction of terminal acetylenes with iodine in methanol assisted by silver ion leads to a mixture of 1-iodoalkynes, 1,2-diiodoalkenes and 1,1-diiodoketones.[4] Recently, we have reported the reaction of alkynes with **(3)**[5] leading to the addition of I^+Nu^- to the triple bond.[6] On this basis it seemed of interest to check the reactivity of **3** towards terminal acetylenes as a potential reagent for the synthesis of compounds **4**.

We have now found that sodium acetylides **2** (prepared *in situ* by reaction of sodium methoxide with the corresponding acetylene) react with **3** at room temperature in methanol to afford 1-iodoalkynes **4** with good to excellent yields in a clean process (Table 1).



1 **2**



3 **4**

All compounds were fully characterized by their IR, ^{1}H-, ^{13}C-NMR and in some cases MS spectra (Table 2). Data for known compounds were found to be in good agreement with those reported in the literature.

The mildness of the reaction conditions allows a variety of functional groups to be present in R in the starting acetylene **1** (Table 1). Since no excess of alkali is used, the 1-iodoalkynes **4** synthesized are stable in the reaction medium and can be easily isolated after an usual work-up procedure.

The general method reported herein for the synthesis of compounds **4** gives similar results as those in the bibliography[1,2] when applied to simple acetylenes but gives much superior yields when these contain a functionalized chain R. On the other hand, our method is superior since the synthesis is carried out in methanol at room temperature avoiding the always cumbersome use of liquid ammonia as solvent. For the above reasons it could become the method of choice for compounds **4**.

Table 1. 1-Iodoalkynes **4** Prepared

Product	R	Yield[a] (%)	m.p. (°C) or b.p. (°C)/mbar	Molecular Formula[b] or Lit. m.p. (°C) or b.p. (°C)/mbar
4a	n-C_4H_9	88	76/27	80/33[4]
4b	n-C_6H_{13}	76	103/13	95/10[7]
4c	CH_2=$CHCH_2$	95	80/93	C_5H_5I (192.0)
4d	CH_2=$C(CH_3)$	75	83/93	C_5H_5I (192.0)
4e	C_6H_5	83	135/13	98/1.6[4]
4f	$HOCH_2$	50	44–45	43–44[8]
4g	CH_3OCH_2	61	77/27	74/27[8]
4h	CH_2=$CHCH(CH_3)OCH_2$	70	oil	C_7H_9IO (236.1)
4i	$ClCH_2$	85	75/27	47/5.3[3]
4j	$BrCH_2$	88	98/27	60/2.7[3]

[a] Based on starting acetylene.
[b] Satisfactory microanalyses obtained: C ± 0.35, H ± 0.24.

Table 2. Spectral Data of Compounds **4**

Product	IR (Film)[a] $\nu_{C\equiv C}$ (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[b] δ (ppm)	^{13}C-NMR ($CDCl_3$)[b] δ (ppm)[c]
4a	2190	0.9 (t, 3H, J = 6 Hz, CH_3); 1.2–2.5 (m, 4H, CH_2CH_2); 2.3 (t, 2H, J = 6 Hz, $CH_2C\equiv C$)	3.6; 15.7; 22.6; 23.9; 32.6; 96.3
4b	2190	0.8–1.6 [m, 11H, $(CH_2)_4CH_3$]; 2.3 (t, 2H, J = 6 Hz, $CH_2C\equiv C$)	4.9; 15.3; 22.0; 23.8; 29.7; 29.7; 32.5; 95.5
4c	2190	3.0 (d, 2H, J = 5 Hz, $CH_2C\equiv C$); 5.2 (br s, 2H, CH_2=C); 5.5 (m, 1H, C=CH)[d]	0.6; 25.1; 91.2; 116.7; 131.9[e]
4d	2150	1.9 (s, 3H, CH_3); 5.1 (br s, 1H, CH=C); 5.3 (br s, 1H, CH=C)	9.1; 25.1; 97.4; 125.8; 128.8
4e	2170	6.8–7.4 (m, H_{arom})	10.6; 96.3; 124.1; 130.1; 130.6; 134.0
4f	2195[f]	3.5 (br s, 1H, OH); 4.4 (s, 2H, CH_2O)	7.4; 54.3; 94.7
4g	2195	3.4 (s, 3H, CH_3); 4.2 (s, 2H, CH_2O)	7.9; 59.6; 63.1; 92.5
4h	2195[f]	1.2 (d, 3H, J = 10 Hz, CH_3); 4.3 (s, 2H, $OCH_2C\equiv C$); 4.9–5.7 (m, 4H, CH_2=CHCHO)	6.6; 23.3; 58.6; 77.6; 93.0; 119.1; 140.9
4i	2190	4.2 (s, CH_2)	9.2; 34.7; 90.8
4j	2190	4.0 (s, CH_2)	10.6; 19.6; 91.8

[a] Recorded on a Perkin Elmer 298 IR spectrometer.
[b] Recorded on a Varian FT-80A spectrometer.
[c] With reference to the solvent as an internal standard.
[d] Measured in CCl_4 using D_2O capillary lock.
[e] Measured in CCl_4.
[f] Recorded as nujol mull.

1-Iodoalkynes 4; General Procedure:
To a two necked flask containing dry methanol (25 ml) under argon atmosphere, sodium (0.125 g, 5.4 mmol) is added and the mixture stirred until total dissolution. The corresponding acetylene **1** (5 mmol) is then slowly added followed by a stoichiometric amount of bis(pyridine)iodine(I) tetrafluoroborate (**3**; 1.86 g, 5 mmol). After stirring at room temperature for 30 min, the resulting solution is hydrolyzed with water (25 ml), extracted with dichloromethane (3 × 25 ml) and the organic layer succesively washed with **1** normal sulfuric acid (25 ml) and a 5% aqueous solution of sodium thiosulfate (25 ml). The organic layer is dried with sodium sulfate, and evaporated under vacuum to yield the corresponding 1-iodoalkynes **4** as the residue (GC purity of the crude product > 90%). Products **4** are purified by distillation or recrystallization in methanol (Table 1).

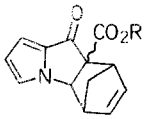
This work was supported in part by the Comisión Asesora de Investigación Científica y Técnica (CAICYT Project No. 2571/83). Two of us (JMG and MAR) acknowledge the Ministerio de Education y Ciencia for a fellowship.

Received: 28 November 1986

(1) Delavarenne, S.Y., Viehe, H.G., in: *The Chemistry of Acetylenes*, Viehe, H.G. (ed.), Marcel Dekker, N.Y., 1969, Chap. 10, p. 651.
(2) Jäger, V., Viehe, H.G., in: Houben-Weyl, *Methoden der Organischen Chemie*, 4th ed., Müller, E. (ed.), Vol. 5/2a. Georg Thieme Verlag, Stuttgart, 1977, pp. 601–610.
(3) Hatch, L.J., Mangold, D.J. *J. Am. Chem. Soc.* **1955**, *77*, 176.
(4) Heasley, V.L., Shellhamer, D.F., Heasley, L.E., Yaeger, D.B., Heasley, G.E. *J. Org. Chem.* **1980**, *45*, 4649.
(5) Barluenga, J., González, J.M., Campos, P.J., Asensio, G. *Angew. Chem.* **1985**, *97*, 341; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 319.
(6) Barluenga, J., Rodríguez, M.A., González, J.M. Campos, P.J., Asensio, G. *Tetrahedron Lett.* **1986**, *27*, 3303.
(7) Vaughn, T.H. *J. Am. Chem. Soc.* **1933**, *55*, 3453.
(8) Beilsteins Handbuch der Organischen Chemie **1**, 455.

Errata and Addenda 1987

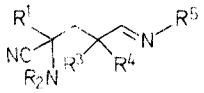
Hall, G., Sugden, J.K., Waghela, M.B.
Page 10. Line 3 of the Abstract should read: dropyrolizines ...
Page 14. The first word of Section 3.11. should be: Benzo[*b*]pyrrolizines.
Page 15. Formula **27** should be:



27

Page 15. The product referred to in Section 4.6., lines 4–5, should be: 10*H*-pyrrolizino[1,2-*b*]quinoline
Page 17. In Section 7., line 4 of the second paragraph should read: **34**.[182] ...

Ahlbrecht, H., von Daacke, A.
Page 24. Formula **8** should be:



8

Costisella, B., Keitel, I.
Page 45. In the heading of the experimental procedure, **6** should read **3** and **8** should read **7**.

Stoss, P., Merrath, P., Schlüter, G.
Page 174. Numbers 1 and 3 should be exhanged in formula **2a–f**.

Singh, G., Deb, B., Ila, H., Junjappa, H.
Page 286. Compounds **1** are 2-aroyl-2-arylthioketene dithioacetals.

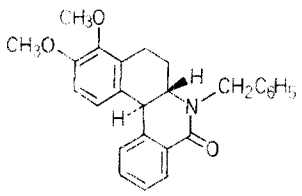
Asaad, F.M., Becher, J., Møller, J., Varma, K.S.
Page 301. Under the reaction scheme, the X group in compounds **3b,d** and **4b,d** should be $CO_2C_2H_5$.

Legrel, P., Baudy-Floc'h, M., Robert, A.
Page 306. The title should read: A One-Pot Synthesis of α-Halohydrazides from 2,2-Dicyanooxiranes.
Page 306. In the table under the reaction scheme, the second heading R^1 should be R^2.

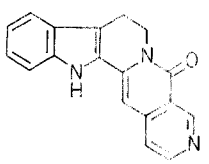
van der Goorbergh, J.A.M., van der Steeg, M., van der Gen, A.
Pages 314–317. The systematic names for the heterocycles involved are: 4,5-dioxo-3,4-dihydro-2*H*,5*H*-thiopyrano[3,2-*c*][1]benzopyrans **4** (RF 24756), 4,5-dioxo-2*H*,5*H*-thiopyrano[3,2-*c*][1]benzopyrans **7** (RF 24756), and 4,5-dioxo-1,3,4,4a,5,10b-hexahydro-2*H*-[1]benzopyrano[4,3-*b*]pyridines **8** (RF 24539).

Attanasi, O.A., Filippone, P., Santensanio, S., Serra-Zanetti, F.
Page 382. In the table under the reaction scheme, R^3 for **1b** should be $CO_2C_2H_5$ and R^3 for **1c** should be CO_2CH_3.

Campbell, A.L., Lenz, G.R.
Pages 428 and 446. Formulae **95** and **298** should be:



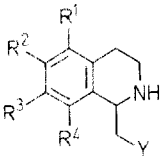
95



298

Page 437. The heading for Table 3 should be: Intermolecular ...

Pelletier, J.C., Cava, M.P.
Page 476. Formula **1a–m** should be:



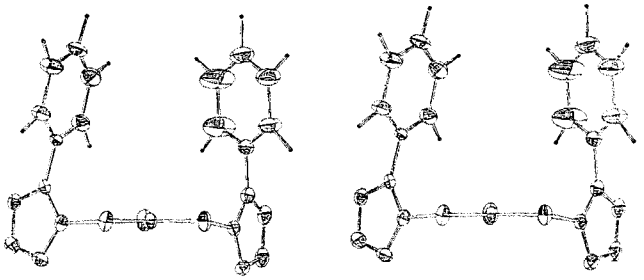
1a-m

L'abbé, G.
Page 528. Compound **45** should be named: 3-(2-pyridyl)-2,4-dithioxo-3,4-dihydro-2*H*-pyrido[1,2-*a*][1,3,5]triazine (RF 9177).

Evans, R.D., Schauble, J.H.
Page 551. Compounds **10** and **11** are tricyclo[2.2.1.$0^{2,6}$]heptane derivatives.

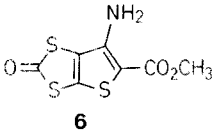
Takeda, K., Tsuboyama, K., Hoshino, M., Kishino, M., Ogura, H.
Page 559. The Y-group for **2g** and **2j** should be furfuryloxy.

Takeda, K., Tsuboyama, K., Takayanagi, H., Ogura, H.
Page 560. The following figure should appear after the 4th paragraph:



Eicher, T., Stapperfenne, U.
Page 625. Compounds **13a,b** are 6,7-dihydrofuro[2,3-*b*]pyridines (RF 7431), and compounds **15a,b** are 1,4-dihydrocyclopentimidazoles (RF 5892).

Dölling, W., Augustin, M., Ihrke, R.
Page 655. Formula **6** should be:



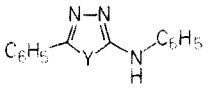
6

Mikołajczyk, M., Bałczewski, P.
Page 661. The second paragraph of ref. 21 should be ref. 22; refs. 22 and 23 should be 23 and 24, respectively.

Rösch, W., Regitz, M.
Page 692. Compounds **21a,b** are 2*H*-1,2,3-diazaphospholes.

Tietze, L.-F., Brumby, T., Pretor, M.
Page 702. Compounds **8** and **9** are 4a,10b-dihydro-4*H*,5*H*-pyrano[3,4-*c*][1]benzopyran-2-carboxylic esters.

Wamhoff, H., Zahran, M.
Page 877. Formula **18a,b** should be:



18a,b

Castaldi, G., Giordano, C.
Page 1039. The target compounds **3** are 1-bromoalkyl aryl ketones.