Expedient Synthesis of 1,1-Diiodoalkenes

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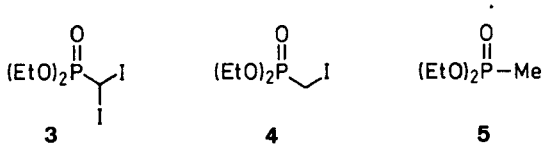
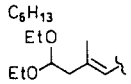
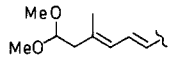
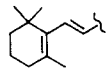
1,1-Diiodoalkenes **1** were readily prepared from carbonyl compounds **2** and diethyl diiodomethylphosphonate (**3**), generated in situ from commercial diethyl iodomethylphosphonate (**4**) or diethyl methylphosphonate (**5**). Starting from aldehydes, iodoacetylenes **6** could be obtained directly in situ by dehydrohalogenation of diiodoalkenes **1**.

1,1-Dichloro- and 1,1-dibromoalkenes are versatile intermediates in organic synthesis whereas there are very few reports devoted to 1,1-diiodoalkenes. Actually, there is no general and convenient synthesis of this class of compounds. Indeed, some 1,1-diiodoalkenes were synthesized using the condensation of aromatic and aliphatic aldehydes with diiodomethylenetriphenylphosphorane prepared in situ from triphenylphosphine and carbon tetraiodide, but this method is reputed to be inefficient starting from ketones.[1,2] Two examples making use of bromine–iodine exchange[3] and two others resorting to the iodination of 1,1-bis(chloromercurio)-1-alkenes have been reported.[4,5] Recently several 1,1-diiodo-2-alkoxyalkenes were also prepared from 1-iodoacetylenes.[6,7]

We wish to report herein an efficient and general synthesis of 1,1-diiodoalkenes **1** using the condensation of carbonyl compounds **2** with diethyl diiodomethylphosphonate (**3**) prepared in situ from commercial diethyl iodomethylphosphonate (**4**) (Methods A and B) or diethyl methylphosphonate (**5**) (Method C) (Scheme 1).

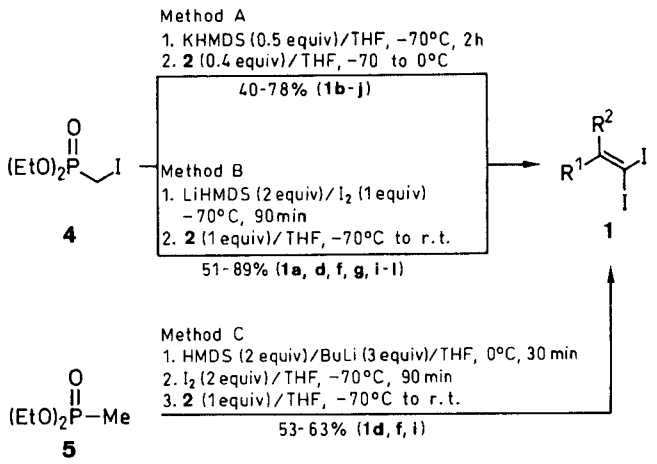


1	R^1	R^2
a	C_5H_{11}	H
b	C_6H_{13}	H
c		H
d	Ph	H
e		H
f	$-(CH_2)_5-$	
g		Me
h		Me
i		Me
j	Ph	Me
k	Ph	Ph
l		Me

Scheme 1

In the first procedure[8] (Method A) (Scheme 2), the iodophosphonate **4** was deprotonated with potassium bis(trimethylsilyl)amide (KHMDS) in tetrahydrofuran at − 70 °C, and condensation of the resulting anion with the starting iodophosphonate **4** leads to diiodophosphonate **3**. Metalation of **3** followed by addition of carbonyl compound **2** gave the diiodoolefins **1** (Table). Diiodoalkenes **1f, g** were also prepared similarly using NaHMDS as the deprotonating reagent. These results are to be considered in relation with the formation of dibromo- (or diiodo-) alkenes previously reported as byproducts, beside the expected monohaloalkenes obtained during the condensation of carbonyl compounds with bromo- or iodomethyltriphenylphosphorane prepared from bromo- or iodomethyl triphenylphosphonium halides.[9,10] Starting from iodophosphonate **4**, the diiodoalkenes **1** were isolated without contamination by any monoiodo derivative.

In the second procedure (Method B) (Scheme 2), we used a cheaper iodination reagent than iodophosphonate **4**, viz iodobis(trimethylsilyl)amide (IHMDS), prepared in situ from lithium bis(trimethylsilyl)amide (LiHMDS) and iodine in tetrahydrofuran at − 70 °C. Addition of phosphonate **4** to a mixture of LiHMDS and IHMDS gave access to diiodophosphonate **3** which was isolated in 95% yield or which could be directly transformed into diiodoolefins **1** (Table). Finally, we also prepared diiodo compounds **1** from diiodophosphonate **3** obtained in situ from diethyl methylphosphonate (**5**) after deprotonation with butyllithium and oxidation with two equivalents of IHMDS (method C) (Scheme 2).



Scheme 2

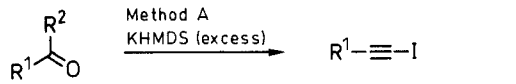
As can be seen from the Table, methods A and B give successful results starting from aldehydes as well as from aliphatic, aromatic and functionalized ketones. It is also worth noting that starting from aldehydes and using these methods in the presence of an excess of base, leads to in

Table. Compounds **1** Prepared

Product[a]	Method	Yield (%)	IR (film) ν (cm^{-1})	^1H NMR (200 MHz/$CDCl_3$) δ, J (Hz)	^{13}C NMR (50 MHz/$CDCl_3$) δ	MS (70 eV)[b] m/z (%)
1a	B	71	1640	0.88 (t, 3H, J = 7.2, CH_3), 1.25–1.50 (m, 6H, H-4, 5, 6), 1.90 (q, 2H, J = 6.9, H-3), 6.92 (t, 1H, J = 6.9, H-2)	11.3 (C-1), 13.9 (C-7), 22.4 (C-6), 27.0 (C-5), 31.1 (C-4), 39.5 (C-3), 153.3 (C-2)	350 (M^+, 44), 293 (12), 280 (24), 95 (100), 67 (36), 81 (8), 55 (68)
1b	A	60	1640	0.87 (t, 3H, J = 5, H-8), 1.23–1.43 (m, 8H, H-4, 5, 6, 7), 1.90 (q, 2H, J = 7.2, H-3), 6.92 (t, 1H, J = 7.0, H-2)	11.3 (C-1), 14.0 (C-8), 22.5 (C-7), 27.3 (C-6), 28.6 (C-5), 31.5 (C-4), 39.6 (C-3), 153.3 (C-2)	–
1c	A	60	1647	Isomer 3*E* (85%):[c] 1.17 (t, 6H, J = 6.8, CH_2CH_3), 1.77 (s, 3H, CCH_3), 2.33 (d, 2H, J = 5.6, H-2), 3.54 (m, 4H, CH_2CH_3), 4.57 (t, 1H, J = 5.6, H-1), 5.61 (d, 1H, J = 10.1, H-4), 7.60 (d, 1H, J = 10.1, H-5)	Isomer 3*E*: 12.9 (C-6), 15.2 (CH_2CH_3), 19.2 (CH_3), 43.9 (C-2), 61.3 (CH_2CH_3), 101.5 (C-1), 129.8 (C-4), 139.8 (C-3), 146.4 (C-5)	447 ($M^+ - C_2H_5OH$, $+C_4H_9$, 1), 429 ($M^+ - C_2H_5OH$, $+C_3H_3$, < 1), 391 ($MH^+ - C_2H_5OH$), 265 (8), 103 ($C_4H_{11}O_2^+$)
				Isomer 3-*Z* (15%):[c] 1.17 (t, 6H, J = 6.8, CH_2CH_3), 1.80 (s, 3H, CCH_3), 2.42 (d, 2H, J = 5.5, H-2), 3.54 (m, 4H, CH_2CH_3), 4.54 (t, 1H, J = 5.5, H-1), 5.61 (d, 1H, J = 10.1, H-4), 7.65 (d, 1H, J = 10.1, H-5)	Isomer 3-*Z*: 12.9 (C-6), 15.2 (CH_2CH_3), 22.4 (CH_3), 38.8 (C-2), 62.0 (CH_2CH_3), 101.5 (C-1), 130.1 (C-4), 139.8 (C-3), 146.4 (C-5)	
1d	A B C	60 70 53	1650, 1600	7.20–7.60 (m, $5H_{arom}$), 8.20 (s, 1H, H-2)	12.1 (C-1), 127.4 (C-4′), 127.7 (C-3′), 128.4 (C-2′), 140.1 (C-1′), 150.9 (C-2)	256 (M^+, 22), 229 (10), 102 (100), 76 (22)
1e	A	78	1610	7.00 (dd, 1H, J = 3.6, 5.1, H-3′), 7.27 (dd, 1H, J = 0.7, 5.1, H-4′), 7.32 (dd, 1H, J = 0.6, 3.5, H-2′), 8.42 (s, 1H, H-2)	5.8 (C-1), 126.2 (C-3′), 126.6 (C-2′), 130.6 (C-4′), 141.8 (C-1′), 144.1 (C-2)	362 (M^+, 100), 235 (10), 108 (98)
1f	A B C	74, 71[d] 74 63	1670	1.40–1.60 (m, 6H, H-4, H-5), 2.35–2.45 (m, 1H, H-3)	8.7 (C-1), 25.4 (C-5), 27.0 (C-4), 39.5 (C-3), 155.4 (C-2)	348 (M^+, 84), 221 (4), 94 (6), 79 (84)
1g	A B	70[d] 84	1620	1.95 (s, 3H, CCH_3), 2.55 (d, 2H, J = 6.6, H-3), 3.30 (s, 6H, 2 × CH_3O), 4.45 (t, 1H, J = 6.6, H-4)	14.1 (C-4), 28.9 (CCH_3), 45.0 (C-2), 54.3 (2 × CH_3O), 103.2 (C-1), 148.0 (C-3)	400 (M^+ + 18, 20), 351 (32), 336 (100), 210 (12), 84 (28)[e]
1h	A	40	1632	Isomer 3*E*, 5*E* (85%):[c] 1.80 (s, 3H, CH_3 at C-3), 2.03 (s, 3H, CH_3 at C-7), 2.35 (d, 2H, J = 5.6, H-2), 3.29 (s, 6H, 2 × CH_3O), 4.49 (t, 1H, J = 5.6, H-1, 6.03 (d, 1H, J = 7.3, H-4), 6.51 (dd, 2H, J = 7.3; J = 15.1, H-5, H-6)	Isomer 3*E*, 5*E*: 17.7 (CH_3 at C-3), 19.6 (C-8), 23.9 (CH_3 at C-7), 43.3 (C-2), 52.8 (CH_3O), 103.0 (C-1), 127.6 (C-4), 129.7 (C-5), 132.5 (C-6), 138.0 (C-3), 146.6 (C-7)	447 (M^+, 50), 291 (25), 75 ($C_3H_7O_2^+$, 100)
				Isomer 3*Z*, 5*E* (15%):[c] 1.82 (s, 3H, CH_3 at C-3), 2.03 (s, 3H, CH_3 at C-7), 2.48 (d, 2H, J = 5.6, H-2), 3.29 (s, 6H, 2 × CH_3O), 4.43 (t, 1H, J = 5.6, H-1), 6.08 (d, 1H, J = 7.3, H-4), 6.51 (dd, 2H, J = 7.3, J = 15.1, H-5, H-6)	Isomer 3*Z*, 5*E*: 17.7 (CH_3 at C-3), 19.6 (C-8), 23.9 (CH_3 at C-7), 36.5 (C-2), 52.8 (CH_3O), 103.5 (C-1), 127.6 (C-4), 129.7 (C-5), 132.5 (C-6), 138.0 (C-3), 146.6 (C-7)	447 (M^+, 50), 291 (25), 75 ($C_3H_7O_2^+$, 100)
1i	A B C	70 48 53	1604	1.01 [s, 6H, $(CH_3)_2C$], 1.44 [m, 2H, $(CH_3)_2CCH_2$], 1.61 [m, 2H, $(CH_3)_2CCH_2CH_2$], 1.71 (s, 3H, $=CCH_3$), 1.99 (t, 2H, J = 6.3, $=CCH_2$), 2.06 (s, 3H, CH_3 at C-2), 6.27 (d, 1H, J = 15.8, H-3), 6.44 (d, 1H, J = 15.8, H-4)	18.5 (C-1), 19.0 [$(CH_3)_2CCH_2CH_2$], 22.0 ($=CCH_3$), 23.9 (CH_3 at C-2), 28.9 [$(CH_3)_2C$], 33.1 [$(CH_3)_2CCH_2$], 33.9 [$(CH_3)_2C$], 39.5 ($CH_2C=$), 131.0 ($C=CCH_3$), 132.3 (C-4), 134.6 (C-3), 137.1 ($C=CCH_3$), 146.9 (C-2)	442 (M^+, 88), 316 (6), 188 (24), 158 (18), 145 (28)
1j	A B	42 64	1604	2.25 (s, 3H, CH_3), 7.06–7.20 (m, $2H_{arom}$), 7.25–7.45 (m, $3H_{arom}$)	14.1 (C-1), 30.5 (CH_3), 127.0 (C-4′), 127.6 (C-3′), 128.5 (C-2′), 144.9 (C-1′), 154.4 (C-2)	370 (M^+, 62), 243 (12), 116 (100), 75 (8)
1k	B	51	1658, 1604	7.40–7.62 (m, $6H_{arom}$), 7.75–7.85 (m, $4H_{arom}$)	17.6 (C-1), 128.2 (C-4′), 130.0 (C-3′), 132.4 (C-2′), 137.5 (C-1′), 144.3 (C-2)	432 (M^+, 42), 178 (100), 167 (4), 76 (12)
1l	B	89	1620	0.91 (d, 6H, J = 6.6, 2 × CH_3), 1.89 (qd, 1H, J = 6.6, 7.3, CH), 1.92 (s, 3H, CH_3), 2.22 (d, 2H, J = 7.3, CH_2)	12.0 (C-1), 22.1 [$CH(CH_3)_2$], 27.4 (CCH_3), 27.6 (C-4), 50.5 (C-3), 151.9 (C-2)	350 (M^+, 75), 307 (15), 181 (20), 167 (5), 53 (100)

[a] All the products obtained are oils. Satisfactory HRMS values obtained: ± 0.0029 amu.
[b] Chemical ionisation (isobutane).
[c] Determined from the configuration of the starting material.
[d] Using NaHMDS instead of KHMDS.
[e] Chemical ionisation (ammonia).

situ dehydrohalogenation of diiodoalkenes **1**, thus yielding iodoacetylenes **6** which are versatile intermediates classically prepared from acetylenic compounds[11,12] (Scheme 3).



Scheme 3

On the other hand, method C presents some limitations. It gave satisfactory results for cyclohexanone **(2f)** and β-ionone **(2i)** but very poor yields for acetophenone **(2j)** and ketone **2g** and mixtures of **1d** and **6d** when benzaldehyde **(2d)** was used. In fact, the formation of the diiodophosphonate **3** is not complete owing to the voluminous precipitate of lithium iodide which prevents proper stirring of the mixture. Consequently, the residual base (LiHMDS) leads in these cases to a partial formation of acetylenic product **6**, starting from aldehydes. Diethyl diiodophosphonate **(3)** and diiodoalkenes **1**, except **1d**[1,2] and **1f**[3,4] are new compounds.

IR spectra were recorded on a Perkin-Elmer 377 spectrometer as thin films. Mass spectra were recorded on a Jeol AX 500 (EI) at 30 to 70 eV, if not otherwise stated. NMR spectra were obtained on a Bruker AC 200 spectrometer operating at 200 MHz for protons and at 50 MHz for carbon. No TMS was added; rather, shifts were referenced to the solvent line ($CDCl_3$) (chemical shifts in ppm). For the carbon spectra a relaxation delay of 20 sec was required to observe the quaternary carbon atom substituted by the two iodine atoms. All reagents were of commercial quality or purified before use. Organic solvents were purified by standard procedures. THF was distilled under Ar atmosphere from purple solutions of sodium/benzophenone ketyl. All reactions were carried out under dry Ar. TLC was performed on silica gel 60 F-254 plates and column chromatography over silica gel (230–400 mesh). ***Warning***: although thermal decompositions were never observed, the explosive character of alkynes and *N*-iodoamines has to be kept in mind.

1,1-Diiodoalkenes 1:

Method A: A solution of diethyl iodomethylphosphonate (**4**; 1.40 g, 5.0 mmol) in THF (2 mL) was slowly added to a stirred solution of KHMDS (0.5 g, 2.51 mmol) in THF (10 mL) cooled at −70 °C. The mixture was stirred at −70 °C for 2 h, then a solution of carbonyl compound **2** (2 mmol) in THF (1 mL) was added. The mixture was stirred 5 min at −70 °C then warmed up to 0 °C. When compound **2** had completely reacted (TLC) (0.5 to 2 h), water (5 mL) was added. The aqueous solution was extracted with Et_2O (5 × 35 mL). The combined organic layers were dried ($MgSO_4$) and evaporated. The diiodoalkenes **1** were chromatographed over silica gel [light petroleum (bp 50–55 °C)/Et_2O, 3:1]. Compounds **1i,j** obtained from ketones were prepared using an excess of KHMDS (**4**/KHMDS = 1:1).

Method B: BuLi (0.90 mL of a 2.5 M solution in hexane, 2.23 mmol), freshly titrated,[13] was added at 0 °C to a solution of 1,1,1,3,3,3-hexamethyldisilazane (HMDS) (0.36 g, 2.23 mmol) in THF (6 mL). The solution was stirred 30 min at 0 °C, then cooled to −70 °C. A solution of I_2 (0.26 g, 1.02 mmol) in THF (2 mL) was added, then after 5 min, a solution of diethyl iodomethylphosphonate (**4**; 0.28 g, 1.02 mmol) in THF (2 mL) was added. After 90 min at −70 °C, the carbonyl compound **2** (1.02 mmol) in THF (1 mL) was added. The mixture was stirred 5 min at −70 °C, then warmed 1 h at 0 °C and 2 h at r.t. After addition of water (2 mL), the separation and purification was carried out as described in method A to afford the diiodoalkenes **1**.

Method C: BuLi (2.4 mL of a 1.65 M solution in hexane, 3.96 mmol) was added at 0 °C to a solution of HMDS (0.43 g, 2.64 mmol) in THF (10 mL). The solution was stirred 30 min at 0 °C, then cooled to −70 °C. A solution of methylphosphonate **5** (0.2 g, 1.32 mmol) in THF (2 mL) was added and the mixture was stirred at −70 °C for 90 min. Then a solution of I_2 (0.67 g, 2.64 mmol) in THF (2 mL) was added. After 90 min at −70 °C a solution of the carbonyl compound **2** (1.32 mmol) in THF (1 mL) was added. The mixture was stirred 5 min at −70 °C, then warmed 1 h à 0 °C and 2 h at r.t. and worked up as above to give the diiodoalkenes **1**.

Diethyl Diiodomethylphosphonate (3):

Following Method B, a sat. aq NaCl solution (3 mL) was added instead of the carbonyl compound **2**. After the usual workup, the crude diiodophosphonate **3** was isolated as a yellow oil; yield: 98 %.

IR (film): ν = 2950, 1455, 1400, 1244 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 1.35 (t, 6 H, J = 7.1, CH_3), 4.22–4.33 (m, 4 H, CH_2), 4.92 (d, 1 H, J = 4.6, CHI_2)

^{13}C NMR ($CDCl_3$): δ = 16.21 (d, $J_{C,P}$ = 5.7, CH_3), 29.48 (d, $J_{C,P}$ = 155.8, CI_2), 65.26 (d, $J_{C,P}$ = 6.6, CH_2).

^{31}P NMR ($CDCl_3$, reference: triphenylphosphine): δ = 17.89.

MS: *m/z* (%) = 404 (M^+, 100), 277 (M^+ − I, 60), 249 (55).

HRMS: *m/z* Calc. for $C_5H_{11}I_2O_3P$ 403.8535, found 403.8544.

1-Iodo-1-heptyne (6a):

Prepared according to method A and starting from iodophosphonate **4** (0.66 g, 2.38 mmol) KHMDS (0.48 g, 2.38 mmol), and hexanal (**2a**; 0.094 g, 0.95 mmol); yield: 0.120 g (58 %).[11,14]

IR (film): ν = 2195 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 0.87 (t, 3 H, J = 6.8, H-7), 1.17–1.53 (m, 6 H, H-4, 5, 6), 2.33 (t, 2 H, J = 6.9, H-3).

^{13}C NMR ($CDCl_3$): δ = 4.85 (C-1), 13.91 (C-7), 20.73 (C-6), 22.10 (C-5), 28.13 (C-4), 29.65 (C-3), 94.74 (C-2).

MS: *m/z* (%) = 207 (M^+–CH_3, 10), 96 (M^+–I,50).

1-Iodophenylacetylene (6d):

Prepared according to method A starting from iodophosphonate **4** (0.53 g, 1.3 mmol), KHMDS (0.38 g, 1.3 mmol) and benzaldehyde (**1d**; 0.081 g, 0.76 mmol); yield: 0.160 g (85 %).[6,11,12,15]

IR (film): ν = 2910, 2175 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 7.29–7.34 (m, 3 H, H-3′, 4′), 7.40–7.46 (m, 2 H, H-2′).

^{13}C NMR ($CDCl_3$): δ = 11.54 (C-1), 94.07 (C-2), 123.30 (C-1′), 128.19 (C-3′), 128.76 (C-4′), 132.27 (C-2′).

MS: *m/z* (%): 228 (M^+, 55), 202 (100), 101 (40).

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