Stereoselective formation of 1,2-diiodoalkenes and their application in the stereoselective synthesis of highly functionalised alkenes *via* Suzuki and Stille coupling reactions

Nadine Hénaff and Andrew Whiting*

Department of Chemistry, Faraday Building, UMIST, PO Box 88, Manchester, UK M60 1QD

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Treatment of an alkyne with iodine monochloride and sodium iodide at room temperature results in the formation of the thermodynamic (*E*)-diiodoalkene. The corresponding (*Z*)-diiodoalkene can also be produced, by treatment of the alkyne with iodine monochloride at −78 °C in the presence of tetraethylammonium iodide. Such 1,2-diiodoalkenes are useful for the synthesis of more functionalised alkenes by using either Stille or Suzuki cross-coupling protocols.

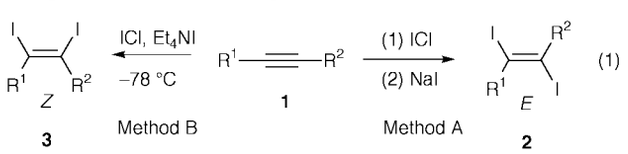
Introduction

1,2-Diiodoalkenes are useful intermediates in direct coupling reactions for forming new carbon–carbon bonds, either involving organo-lithium,[1] organo-copper,[2] or palladium catalysed cross-coupling reactions.[3] They can be prepared by a variety of methods, such as alumina[4] or florisil-assisted[5] iodination of alkynes, direct addition of iodine to alkynes,[6] and using electropositive iodonium species in the presence of iodide ion.[7] In all cases, the predominant diiodoalkene stereochemistry is *E*. As part of a programme aimed at developing flexible methods for the stereoselective synthesis of polyene-containing natural products, we demonstrated the use of a vinylboronate pinacol ester as a vinyl dianion equivalent by employing Heck, followed by Suzuki coupling reactions.[8] In order to extend the utility of these methods, we required a convenient route for the preparation of a range of alkenyl iodides, both *E* and *Z*, to act as coupling partners for palladium-mediated coupling reactions. This has resulted in a preliminary report on the stereoselective formation of either (*E*)- or (*Z*)-alkenyl diiodides from acetylenes using iodine monochloride and an iodide source.[9] Herein we report the full details of this work and demonstrate the use of alkenyl diiodides for the stereoselective formation of tri- and tetra-substituted olefins.

Discussion

Synthesis of diiodoalkenes

In order to effect the stereoselective synthesis of both (*E*)-diiodoalkenes and (*Z*)-diiodoalkenes, we discovered that alkynes react smoothly with iodine monochloride in the presence of certain sources of iodide ion. However, the most important factors for achieving stereocontrol are: (1) controlling the temperature; (2) the order of reagent addition; (3) the source of iodide ion. Thus, treatment of an alkyne **1** with iodine monochloride and sodium iodide at 0 °C produces a highly stereoselective conversion to the thermodynamically favoured *E*-diiodide **2** (eqn. (1) and Table 1) in virtually all cases examined. The only exception is those alkynes with other functional groups which can react in preference, *i.e.* in entry 14 (Table 1), where acetal cleavage is faster than diiodide formation under the reaction conditions. It is worth noting that this acetal cleavage also occurs under the lower temperature conditions, *i.e.* entries 13 and 15 (Table 1).

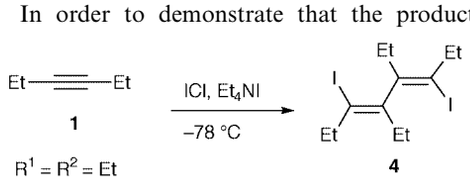


3 **1** **2**

In order to derive the corresponding *Z*-alkenes **3**, various reaction conditions were investigated, which resulted in the discovery that low temperature (−78 °C) conditions were necessary to achieve optimum levels of stereoselectivity. Thus, treatment of the alkyne with iodine monochloride in the presence of iodide ion (tetraethylammonium iodide, which provides sufficient solubility in organic solvents at −78 °C), produces predominantly the (*Z*)-diiodide **3** (eqn. (1), Table 1, Method B). It is noticeable however, that even under these conditions, variable stereocontrol was observed (Table 1); thus, only phenylacetylene and methyl propiolate provide complete *Z*-stereocontrol (entries 3 and 17 respectively, Table 1). For pent-1-yne and hept-1-yne (entries 5 and 7 respectively, Table 1), stereocontrol was a respectable 4:1 (*Z*:*E*), however, this dropped to a poor 3:2 for benzyloxybutyne (entry 10, Table 1). These reactions were generally complete in one to four hours; longer reaction times resulted in slow conversion of the *Z*-diiodide to the *E*-diiodide. It is interesting to note for the case of pent-1-yne (entry 4), that use of dichloromethane produced a mixture (62:38) of (*E*):(*Z*)-diiodoalkenes **3**:**2**, which was changed to 100:0 if THF was used as the solvent.

Other groups[4,7] have claimed to have synthesised (*E*)- and (*Z*)-3,4-diiodohex-3-ene. Unfortunately, in all these reports, analytical data appears to be the same for both *E*- and *Z*-products! However, when (*E*)-3,4-diiodohex-3-ene **2** (R^1 and R^2 = Et) was prepared according to the literature procedure,[4c] all the analytical data were similar to those obtained for Entry 8 (Table 1). However, when Method B was employed, in an attempt to make the *Z*-analogue **3** (R^1 and R^2 = Et), the analytical data were different and could not be attributed to the *Z*-diiodide. Instead, this reaction produced a single compound, to which we have assigned the *Z*,*Z*-diene configuration **4** on mechanistic grounds (*vide infra*) (eqn. (2)), although spectroscopic and analytical data cannot rule out the *E*,*E*-diene configuration.

In order to demonstrate that the product from entry 8



1 **4**

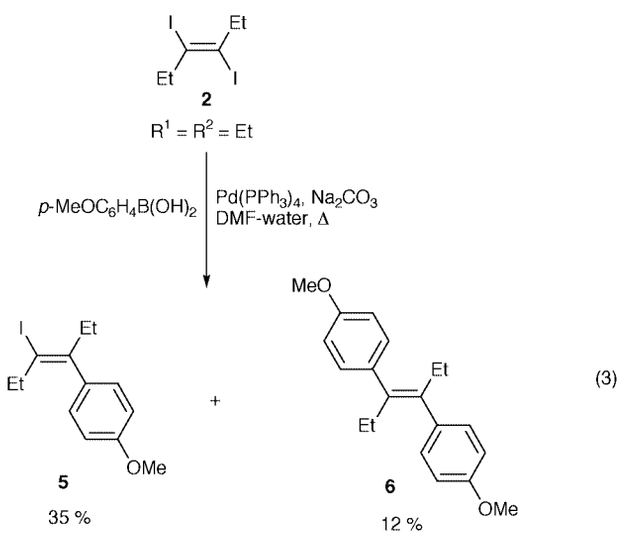
$R^1 = R^2$ = Et

Table 1 Conversion of acetylenes **1** to diiodoalkenes **2** and **3**

Entry	Acetylene	Method[a]	Temp./°C	Solvent	Time/h	*E*:*Z* ratio (**2**:**3**)[b]	Isolated yield[c,d,e] (%)
1	CH≡C–CH_2OAc	A	0–rt	CH_2Cl_2	4	100:0	75
2	CH≡C–Ph	A	0–rt	CH_2Cl_2	6	100:0	86
3	CH≡C–Ph	B	−78	CH_2Cl_2	1	0:100	70
4	CH≡C–^nPr	A	0–rt	THF	12	100:0	65
5	CH≡C–^nPr	B	−78	CH_2Cl_2	3	18:82	42
6	CH≡C–$^nC_5H_{11}$	A	0–rt	CH_2Cl_2	14	100:0	66
7	CH≡C–$^nC_5H_{11}$	B	−78	CH_2Cl_2	0.25	20:80	65
8	Et–C≡C–Et	A	0–rt	CH_2Cl_2	14	100:0	56
9	CH≡C–CH_2CH_2OBn	A	0–rt	CH_2Cl_2	6	100:0	25
10	CH≡C–CH_2CH_2OBn	B	−78	CH_2Cl_2	1	40:60	40
11	CH≡C–CH_2OH	A	0–rt	CH_2Cl_2	16	98:2	65
12	CH≡C–$CH_2CH(OMe)_2$	A	0–rt	CH_2Cl_2	16	76:24	45
13	CH≡C–$CH_2CH(OMe)_2$	B	−78	CH_2Cl_2	16	—	—[f]
14	$^nH_{13}C_6$–C≡C–$CH(OEt)_2$	A	0–rt	CH_2Cl_2	16	—	52
15	$^nH_{13}C_6$–C≡C–$CH(OEt)_2$	B	−78	CH_2Cl_2	16	—	—[g]
16	CH≡C–CO_2Me	A	0–rt	CH_2Cl_2	4	100:0	84
17	CH≡C–CO_2Me	B	−78	CH_2Cl_2	4	0:100	25

[a] See equation 1. [b] Isomeric ratios were determined by both ^1H and ^{13}C NMR. [c] All crude yields were *ca.* quantitative and isolated yields are quoted after silica gel chromatography. [d] All known compounds were identical to those reported in the literature (see refs. 5, 6 and 7). [e] New compounds had satisfactory spectroscopic and analytical properties which agreed with the assigned structures. [f] Decomposition of the starting material. [g] Deprotection occurred to give the aldehyde; IR, ^1H and ^{13}C NMR spectra matched those quoted in literature (see ref. 10).

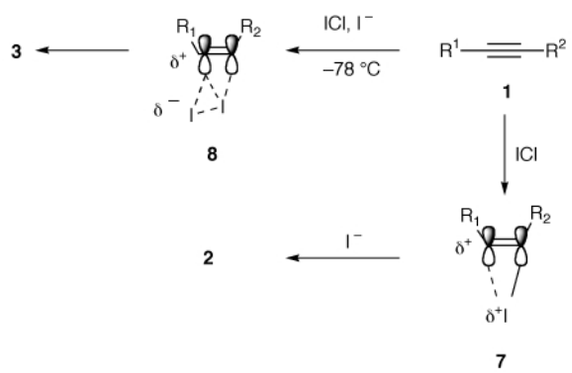
(Table 1) was truly the *E*-diiodide, a Suzuki cross-coupling was attempted. The cross-coupling reaction of 3,4-diiodohex-3-ene **2** (R^1 and R^2 = Et) with *p*-methoxybenzeneboronic acid gave the mono- and bis-cross-coupling products, **5** and **6** respectively, as shown in eqn. (3). The bis-cross-coupling product **6** has been



(3)

reported in the literature[11] and its reported *E*-alkene geometry exactly matches that expected from these results. It can therefore be concluded that the 3,4-diiodohex-3-ene **2** (R^1 and R^2 = Et) from entry 8 (Table 1) does indeed have the *E*-alkene geometry, which matches all other diiodides made by Method A (Table 1).

These results demonstrate the subtle nature of the differences in the mechanisms which produce the *E*- *versus* the *Z*-diiodide. The diiodination reaction can be explained by the formation of two intermediates **7** and **8** (Scheme 1) under the two different reaction conditions. It is reported that such reactions occur through cyclic iodonium ion intermediates such as **7**.[7] Thus, slow nucleophilic *anti*-attack, yields the *E*-diiodide **2**, whereas an ion-paired complex of type **8** would result in formation of the *Z*-diiodide **3**, *via syn*-addition of iodine. As the steric hindrance of the R^1 and R^2 groups increases in **7** and **8**, the bridging by iodine would be weaker and consequently, the iodonium ion becomes less symmetric and one of the iodonium ion carbons will have a higher positive charge density than

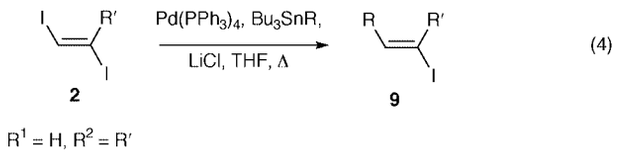


Scheme 1

would be the case with less hindered alkynes. Under these conditions, strong nucleophiles such as iodide will interact to a greater extent with the iodine atom of the iodonium ion, because of the greater positive charge density and hence yielding an overall *syn*-addition of diiodine. Such effects would be reinforced by electronic factors; an electron withdrawing substituent in **8** would enhance the interaction of the incoming iodide with the iodine atom of the iodonium ion, resulting in even more efficient *syn*-addition. This effect is graphically demonstrated by entry 17 (Table 1).

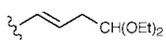
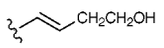
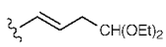
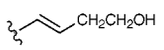
Use of diodooalkenes for the synthesis of tri- or tetra-substituted alkenes

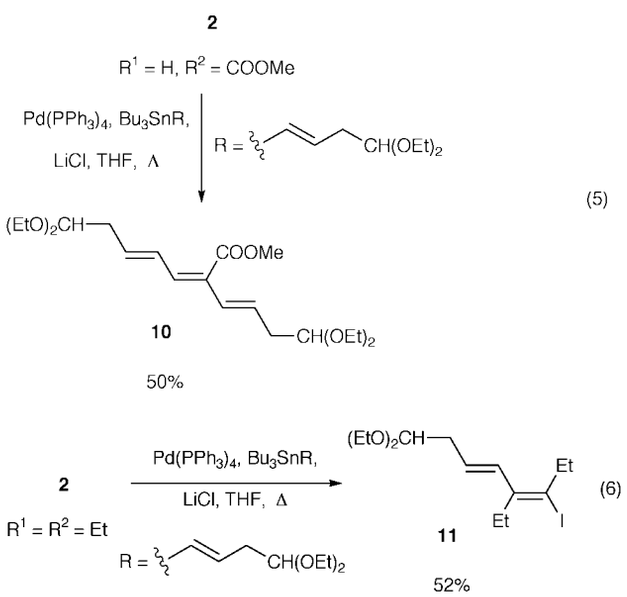
In order to fully utilise the diiodoalkenes **2** and **3** for the synthesis of functionally complex alkenes, we needed to develop coupling reactions which would select just one of the iodine atoms. Subsequent coupling of the remaining iodine function would provide maximum flexibility in the resulting alkene substitution. We therefore investigated the use of common cross-coupling protocols such as Stille (note the application of the Suzuki method in eqn. (3)) for the synthesis of stereo-defined poly-substituted alkenes. *E*-Diiodides **2** were mono-coupled under Stille conditions, as shown in eqn. (4). In all cases (Table 2), it was possible to selectively couple the less hindered iodine atom to provide access to the monoiodides **9**. It was also possible to achieve a clean double Stille coupling reaction, as demonstrated by direct preparation of the tri-substituted triene **10**, *via* the process shown in eqn. (5), and to derive the mono-coupled, highly substituted Stille product **11**, *via* eqn. (6).



(4)

Table 2 Conversion of diiodides **2** to Stille products **9**

Entry	R	R′	Yield/%
1		COOMe	61
2		COOMe	56
3		C_3H_7	46
4		C_5H_{11}	32



(5)

(6)

Conclusions

We demonstrated the highly stereoselective formation of (*E*)-diiodoalkenes using iodine monochloride, followed by sodium iodide. The stereoselective formation of (*Z*)-diiodoalkenes is also possible using iodine monochloride in the presence of tetraethylammonium iodide. Such diiodides can be used under Stille and Suzuki coupling conditons to provide access to stereo-defined polyenes, and functionally complex tri- and tetra-substituted alkenes.

Experimental

All reagents were purchased from Aldrich or Lancaster and used without further purification unless otherwise stated. 4-Benzyloxybut-1-yne was prepared according to the literature.[12] The solvents used were either purchased as anhydrous or distilled before use over either benzophenone–sodium (THF) or calcium hydride (all remaining solvents) under an atmosphere of argon.

All anhydrous reactions were carried out in glassware which was dried prior to use in an oven at 140 °C and cooled under a stream of argon. Concentrations were carried out at 20 mmHg using a Buchi rotary evaporator and evaporation to dryness using the Buchi rotary evaporator followed by drying at pressures <2 mmHg. Column chromatography was achieved under a medium pressure using Acros silica gel, pore size 60A. TLC was carried out on either Merck Kieselgel $60F_{254}$ plastic backed plates or Fluka Kieselgel $60F_{254}$ aluminium backed plates.

Melting points were determined using an Electrothermal melting point apparatus. ^{1}H NMR spectra were recorded at 200, 300 or 400 MHz on Bruker AC200, AC300 or AC400 spectrometers. ^{13}C NMR spectra were recorded at 75.5 MHz on a Bruker AC300 spectrometer. Both ^{1}H and ^{13}C NMR spectra were recorded using a range of deuterated solvents. Electron impact (EI) (70 eV) and chemical ionisation (CI) mass spectra were recorded on a Kratos MS25 spectrometer. Fast atom bombardment (FAB) spectra were recorded on a Kratos MS50 spectrometer using a *m*-nitrobenzyl alcohol matrix. Accurate mass determinations were carried out using a Kratos Concept IS spectrometer. IR spectra were recorded on a Perkin-Elmer 298 spectrometer. UV spectra were recorded on a Perkin-Elmer 115 spectrometer.

Method A

Typical procedure. Anhydrous sodium iodide was added to a freshly prepared solution of iodine monochloride in dry dichloromethane under argon. The resultant suspension was cooled to 0 °C. The alkyne was then added and the mixture was allowed to warm to rt. The reaction mixture was stirred for time, *t*. The suspension was then filtered through Celite and the excess iodine in the product solution was destroyed using the minimum amount of 10% aqueous sodium metabisulfite. The aqueous layer was quickly removed and the organic fraction was washed with water then saturated with aqueous sodium chloride, dried ($MgSO_4$) and evaporated to give the crude product.

Preparation of (*E*)-3-acetoxy-1,2-diiodopropene (Table 1, entry 1). Anhydrous sodium iodide (3.1 g, 20.66 mmol), iodine monochloride (860 mg, 5.15 mmol) in dry dichloromethane (35 ml) and propargyl acetate (prop-2-ynyl acetate) (500 mg, 5.10 mmol), $t = 4$ h. Silica gel chromatography (ethyl acetate–hexane, 2 : 8 as eluant) afforded the pure product (1.3 g, 75%) as a yellow oil. ^{1}H and ^{13}C NMR spectra matched those quoted in the literature;[6] ν_{max} (film)/cm^{-1} 3010 (C=CH), 2950 (aliphatic CH), 2880 (aliphatic CH), 1610 (C=C), 1730 (C=O), 1250 (C–O).

Preparation of (*E*)-(1,2-diiodovinyl)benzene (Table 1, entry 2). Anhydrous sodium iodide (700 mg, 4.7 mmol), iodine monochloride (160 mg, 1.0 mmol) in dry dichloromethane (10 ml), phenylacetylene (100 mg, 1.0 mmol), $t = 6$ h, gave a yellow oil which was crystallised in diethyl ether to give the pure product (350 mg, 86%) as a yellow solid. ^{1}H and ^{13}C NMR spectra matched those quoted in the literature;[6] mp 74–76 °C; ν_{max} (Nujol)/cm^{-1} 3020 (C=CH), 1620 (C=C), 1610 (C=C), 750 (monosubstituted aromatic), 700 (monosubstituted aromatic); *m*/*z* (FAB) 356 (M^+, 72%), 229 ($M^+ - I$, 92), 91 ($C_7H_7^+$, 76).

Preparation of (*E*)-1,2-diodopent-1-ene (Table 1, entry 4). Anhydrous sodium iodide (700 mg, 4.7 mmol), iodine monochloride (245 mg, 1.5 mmol) in dry THF (10 ml), pent-1-yne (100 mg, 1.5 mmol), $t = 12$ h. Silica gel chromatography (hexane–ethyl acetate, 4 : 1 as eluant) afforded the pure product (310 mg, 65%) as a yellow oil. IR and ^{1}H NMR spectra matched those quoted in the literature;[5a] δ_C (75.5 MHz; $CDCl_3$) 12.9 (CH_3), 21.6 (Me–CH_2), 46.3 (CH_2CI=CHI), 79.2 (*C*HI=$CICH_2$), 104.1 (CHI=*C*ICH_2); *m*/*z* (EI) 323 (MH^+, 50%), ($MH^+ - C_2H_5$, 45), 195 ($M^+ - I$, 40).

Preparation of (*E*)-1,2-diiodohept-1-ene (Table 1, entry 6). Anhydrous sodium iodide (3.5 g, 23.3 mmol), iodine monochloride (850 mg, 5.2 mmol) in dry dichloromethane (50 ml), hept-1-yne (500 mg, 5.2 mmol), $t = 14$ h. Silica gel chromatography (hexane–ethyl acetate, 4 : 1 as eluant) afforded the pure product (1.2 g, 66%) as a red oil. IR and ^{1}H NMR spectra matched those quoted in the literature;[5a] δ_C (75.5 MHz; $CDCl_3$) 13.9, 22.4, 27.8, 30.2, 44.5, 78.8, 104.4.

Preparation of (*E*)-3,4-diiodohex-3-ene (Table 1, entry 8). Anhydrous sodium iodide (700 mg, 4.7 mmol), iodine monochloride (220 mg, 1.3 mmol) in dry dichloromethane (15 ml), hex-3-yne (100 mg, 1.2 mmol), $t = 14$ h gave the pure product (225 mg, 56%) as a green oil. ^{1}H and ^{13}C NMR spectra matched those quoted in the literature;[7] ν_{max} (film)/cm^{-1} 3010 (C=CH), 2960 (aliphatic CH), 2910 (aliphatic CH), 1600 (C=C), 1470 (aliphatic C–C), 1380 (aliphatic C–C).

Preparation of (*E*)-(3,4-diiodobut-3-enyloxymethyl)benzene (Table 1, entry 9). Anhydrous sodium iodide (700 mg, 4.7 mmol), iodine monochloride (165 mg, 1.0 mmol) in dry dichloromethane (10 ml), 4-benzyloxybut-1-yne (160 mg, 1.0 mmol), $t = 6$ h. Silica gel chromatography (hexane–ethyl acetate, 9:1 as eluant) afforded the pure product (100 mg, 25%) as a yellow oil. ν_{max} (film)/cm^{-1} 1150 (C–O); δ_H (200 MHz; $CDCl_3$) 3.0 (2H, t, *J* 7.1, OCH_2CH_2), 3.7 (2H, t, *J* 7.1, OCH_2CH_2), 4.6 (2H, s, $PhCH_2O$), 7.0 (1H, s, *H*C=C), 7.4–7.6 (5H, m, Ph); δ_C (75.5 MHz; $CDCl_3$) 44.8, 67.6, 72.9, 81.2, 103.1, 127.5, 128.2, 128.6, 140.1.

Preparation of (*E*)-2,3-diiodoprop-2-en-1-ol (Table 1, entry 11). Anhydrous sodium iodide (530 mg, 3.53 mmol), iodine monochloride (145 mg, 0.89 mmol) in dry dichloromethane (10 ml), propargyl alcohol (50 mg, 0.89 mmol), $t = 16$ h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 9:1 as eluant] afforded the pure product (184 mg, 67%). ν_{max}(Nujol)/cm^{-1} 3460 (OH); δ_H (300 MHz; $CDCl_3$) 2.04 (1H, s, O*H*, signal disappears upon addition of D_2O), 4.47 (2H, s, CH_2), 6.77 (1H, s, C=C*H*); δ_C (75.5 MHz; $CDCl_3$) 68.4, 80.2, 126.4; *m*/*z* (CI) 309.8352 (M^+, CH_4I_2O requires *m*/*z* = 309.8352, 25%), 183 ($M^+ - I$, 100).

Preparation of (*E*)-1,2-diiodo-4,4-dimethoxybut-1-ene (Table 1, entry 12). Anhydrous sodium iodide (210 mg, 1.4 mmol), iodine monochloride (70 mg, 0.43 mmol) in dry dichloromethane (10 ml), 4,4-dimethoxybut-1-yne (50 mg, 0.43 mmol), $t = 16$ h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 9:1 as eluant] afforded the pure product (71 mg, 45%); δ_H (300 MHz; $CDCl_3$) 2.87 (2H, d, *J* 6.0, $=CCH_2$), 3.41 (6H, s, OMe), 4.75 [1H, t, *J* 6.0, $CH(OMe)_2$], 7.01 (1H, s, *H*C=); δ_C (75.5 MHz; $CDCl_3$) 47.4, 53.8, 58.5, 82.0, 85.2, 103.3; *m*/*z* (CI) 385.9116 ($M^+ + NH_4$ requires *m*/*z* = 385.9118, 40%), 337 (M − OEt, 70), 322 ($C_4H_4I_2O$, 100).

Preparation of (*E*)-2,3-diiodonon-2-en-1-al diethyl acetal (Table 1, entry 14). Anhydrous sodium iodide (150 mg, 1.0 mmol), iodine monochloride (80 mg, 0.49 mmol) in dry dichloromethane (10 ml), non-2-yn-1-al diethyl acetal (50 mg, 0.24 mmol), $t = 16$ h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 9:1 as eluant] afforded the pure product (62 mg, 52%); δ_H (300 MHz; $CDCl_3$) 1.26–1.68 (19H, m, $C_6H_{13} + 2 \times OCH_2CH_3$), 3.49–3.72 (4H, m, $2 \times OCH_2CH_3$), 4.72 [1H, s, $CH(OCH_2CH_3)_2$]; δ_C (75.5 MHz; $CDCl_3$) 14.0 (CH_3), 15.1 (OCH_2CH_3), 28.2 (CH_2), 28.6 (CH_2), 28.8 (CH_2), 30.8 (CH_2), 31.6 (CH_2), 53.2 (OCH_2), 62.5 (OCH_2), 102.6 [$CH_2(I)C$=], 107.4 [*C*H(OEt)], 124.7 [=*C*(I)CH(OEt)]; *m*/*z* (CI) 420.9530 (M − OEt requires *m*/*z* = 420.9529, 100%), 391 ($C_9H_{13}I_2O$, 50).

Preparation of (*E*)-2,3-diiodoacrylic acid methyl ester (Table 1, entry 16). Anhydrous sodium iodide (8.4 g, 5.6 mmol), iodine monochloride (1.8 g, 11.2 mmol) in dry dichloromethane (100 ml), methyl propiolate (1 ml, 11.2 mmol), $t = 4$, gave the pure product as a yellow oil (3.1 g, 84%). IR and ^{1}H NMR spectra matched those quoted in the literature;[13] δ_C (75.5 MHz; $CDCl_3$) 53.6 (CH_3), 85.8 (HI*C*=C), 88.0 (C=*C*HCO$_2$Me), 164.2 (*C*=O); *m*/*z* (EI) 337.8313 (M^+, $C_4H_4I_2O_2$ requires *m*/*z* = 337.8301, 100%), 307 ($M^+ - OCH_3$, 28), 211 ($M^+ - I$, 64), 127 (I^+, 76).

Method B

Typical procedure. Tetraethylammonium iodide was added to a freshly prepared solution of iodine monochloride in dry dichloromethane under argon at −78 °C. The alkyne was added and the mixture was stirred at −78 °C for time *t*. The suspension was then filtered through Celite and the excess iodine in the product solution was destroyed using a minimum amount of 10% aqueous sodium metabisulfite. The aqueous layer was quickly removed and the organic fraction was washed with water then saturated with aqueous sodium chloride, dried ($MgSO_4$) and evaporated to give the crude product which was recrystallised from diethyl ether to give the product.

Preparation of (*Z*)-(1,2-diiodovinyl)benzene (Table 1, entry 3). Tetraethylammonium iodide (1.0 g, 3.9 mmol), iodine monochloride (160 mg, 1.0 mmol) in dry dichloromethane (15 ml), phenylacetylene (100 mg, 1.0 mmol), $t = 1$ h. The crude product was recrystallised from diethyl ether to give the pure product (249 mg, 70%) as a yellow solid. IR and ^{1}H NMR spectra matched those quoted in the literature;[6] mp 72–74 °C; δ_C (75.5 MHz; $CDCl_3$) 73.0, 103.0, 128.3, 129.0, 130.2, 134.1; *m*/*z* (FAB) 356 (M^+, 70%), 229 ($M^+ - I$, 87), 91 ($C_7H_7^+$, 70).

Preparation of (*Z*)-1,2-diiodopent-1-ene (Table 1, entry 5). Tetraethylammonium iodide (1.0 g, 3.9 mmol), iodine monochloride (245 mg, 1.5 mmol) in dry dichloromethane (15 ml), pent-1-yne (100 mg, 1.5 mmol), $t = 3$ h. The pure product (200 mg, 42%) was obtained as a yellow oil without any further purification. ν_{max} (film)/cm^{-1} 3010 (C=CH), 2950 (aliphatic CH), 2880 (aliphatic CH), 1600 (C=C), 1440 (aliphatic C–C), 1370 (aliphatic C–C); δ_H (200 MHz; $CDCl_3$) 0.91 (3H, t, *J* 7.0, CH_3), 1.64 (2H, quintet, *J* 7.0, $MeCH_2CH_2$), 2.52 (2H, t, *J* 7.0, CH_2C=C), 6.20 (1H, s, *H*C=C); δ_C (75.5 MHz; $CDCl_3$) 13.1, 29.7, 44.1, 79.2, 101.8; *m*/*z* (EI) 322.8791 (MH^+, $C_5H_9I_2$ requires *m*/*z* = 322.8794, 45%), ($MH^+ - C_2H_5$, 35), 195 ($M^+ - I$, 40).

Preparation of (*Z*)-1,2-diiodohept-1-ene (Table 1, entry 7). Tetraethylammonium iodide (1.1 g, 4.3 mmol), iodine monochloride (180 mg, 1.1 mmol) in dry dichloromethane (10 ml), hept-1-yne (100 mg, 1.1 mmol), $t = 15$ min. Silica gel chromatography (hexane–ethyl acetate, 4:1 as eluant) afforded the pure compound (250 mg, 65%) as a yellow oil. ν_{max} (film)/cm^{-1} 3010 (C=CH), 2920 (aliphatic CH), 2880 (aliphatic CH), 1700, 1450 (aliphatic C–C), 1360 (aliphatic C–C); δ_H (200 MHz; $CDCl_3$) 0.90 (3H, t, *J* 7.0, CH_3), 1.31 (2H, m, $MeCH_2$), 1.65 (2H, m, CH_2), 2.10 (2H, m, CH_2), 2.40 (2H, t, *J* 8.0, CH_2C=C); δ_C (75.5 MHz; $CDCl_3$) 10.3, 13.3, 20.3, 29.7, 53.4, 76.3, 102.0.

Preparation of (*Z*)-(3,4-diiodobut-3-enyloxymethyl)benzene (Table 1, entry 10). Tetraethylammonium iodide (1.0 g, 3.9 mmol), iodine monochloride (206 mg, 1.3 mmol) in dry dichloromethane (15 ml), benzyloxybutyne (200 mg, 1.2 mmol), $t = 1$ h. Silica gel chromatography (hexane–ethyl acetate, 9:1 as eluant) afforded the pure compound (200 mg, 40%) as a yellow oil. ν_{max} (film)/cm^{-1} 3100 (C=CH), 3060 (C=CH), 2900 (aliphatic CH), 2850 (aliphatic CH), 1620 (C=C), 1600 (C=C), 1140 (C–O), 750 (monosubstituted aromatic), 700 (monosubstituted aromatic); δ_H (200 MHz; $CDCl_3$) 3.09 (2H, t, *J* 6.5, OCH_2CH_2), 3.70 (2H, t, *J* 6.5, OCH_2CH_2), 4.62 (2H, s, $PhCH_2O$), 7.05 (1H, s, *H*C=C), 7.40–7.62 (5H, m, Ph); δ_C (75.5 MHz; $CDCl_3$) 39.1, 66.5, 72.9, 80.3, 99.1, 128.3, 128.4, 128.6, 138.2.

Preparation of (*Z*)-2,3-diiodoacrylic acid methyl ester (Table 1, entry 17). Tetraethylammonium iodide (300 mg, 1.2 mmol), iodine monochloride (50 mg, 0.3 mmol) in dry dichloromethane (5 ml), methyl propiolate (25 mg, 0.3 mmol). Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 95:5 as eluant] afforded the pure compound (25 mg, 25%) as a

yellow oil. IR and ^{1}H NMR spectra matched those quoted in the literature;[13] *m/z* 338 (M^+, 100%), 211 ($M - I^+$, 50).

Preparation of (*Z*,*Z*)-4,5-diethyl-3,6-diiodoocta-3,5-diene 4

Tetraethylammonium iodide (2.60 g, 10.12 mmol), iodine monochloride (450 mg, 2.77 mmol) in dry dichloromethane (30 ml), hex-3-yne (200 mg, 2.44 mmol). Silica gel chromatography (hexane–ethyl acetate, 98:2 as eluant) afforded the pure compound (700 mg, 69%) as a yellow oil. δ_H (300 MHz; $CDCl_3$) 0.96 (6H, t, *J* 7.5, 2 × C*H*$_3$), 1.02 (6H, t, *J* 7.5, 2 × C*H*$_3$), 2.56 (8H, q, *J* 7.5, 4 × C*H*$_2$); *m/z* (CI) 291.0607 ($M^+ - I$, $C_{12}H_{20}I$ requires *m/z* = 291.0610, 100%).

Preparation of (*E*)-1-(1-ethyl-2-iodobut-1-enyl)-4-methoxybenzene 5 and (*Z*)-3,4-bis(4-methoxyphenyl)hex-3-ene 6

3,4-Diiodohex-3-ene (150 mg, 0.45 mmol), *p*-methoxyphenylboronic acid (70 mg, 0.46 mmol) and sodium bicarbonate (60 mg, 0.57 mmol) were degassed in DMF and water (7 and 1 ml respectively) for one hour. $Pd(PPh_3)_4$ (21 mg, 18.2 μmol) was then added to the reaction mixture and degassed for a further 30 minutes before heating overnight at 100 °C. The reaction mixture was then allowed to cool down to room temperature, washed with HCl 10% (20 ml), extracted with diethyl ether (3 × 15 ml), washed with water (10 ml), dried ($MgSO_4$), filtered and evaporated. Purification by silica gel chromatography [petroleum ether (40–60) as eluant] gave the pure products **5** (50 mg, 35%) and **6** (15 mg, 12%), both as yellow oils. **5**, δ_H (300 MHz; $CDCl_3$) 0.96 (3H, t, *J* 7.5, C*H*$_3$), 1.11 (3H, t, *J* 7.5, C*H*$_3$), 2.04 (2H, q, *J* 7.5, C*H*$_2$), 2.33 (2H, q, *J* 7.5, C*H*$_2$), 3.86 (3H, s, OC*H*$_3$), 6.98 (2H, AB quartet, 9.1 and 146.5, aromatic protons), 7.49 (2H, AB quartet, 9.1 and 146.5, aromatic protons); *m/z* (CI) 189.1277 ($M^+ - I$, $C_{13}H_{17}O$ requires *m/z* = 189.1279, 35%), 107 ($C_7H_7O^+$, 45); **6**, ^{1}H NMR spectrum matched that quoted in the literature;[10] *m/z* (FAB) 205 (C_6H_{13}, 40%), 107 (C_7H_7, 90).

Preparation of tri-*n*-butyl(4-hydroxybut-1-enyl)stannane

But-3-yn-1-ol (0.5 g, 6.9 mmol), tri-*n*-butyltin hydride (2.4 ml, 9.0 mmol) and AIBN (100 mg, 0.6 mmol) were heated at 80 °C for 7 h under argon. The reaction mixture was allowed to cool to rt. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the pure product[14] (2.1 g, 84%) as a colourless oil (^{1}H NMR data was identical to that reported in the literature[14]). ν_{max}(film)/cm^{-1} 3320 (OH), 3010 (=CH), 2960 (CH aliphatic), 2880 (CH aliphatic), 1590 (C=C), 1080 (C–O); δ_C (75.5 MHz; $CDCl_3$) 9.7, 13.8, 27.6, 29.1, 40.9, 61.6, 132.3, 145.0; *m/z* (EI) 363.1713 (MH^+, $C_{16}H_{35}SnO$ requires *m/z* = 363.1709, 10%), 332 ($MH^+ - CH_2OH$, 5), 306 ($Bu_3SnCH_2^+$, 70).

Preparation of tri-*n*-butyl(4,4-diethoxybut-1-enyl)stannane

4,4-Diethoxybut-1-yne (380 mg, 2.7 mmol), tri-*n*-butyltin hydride (0.9 ml, 3.5 mmol) and AIBN (50 mg, 0.3 mmol) were heated at 80 °C for 7 h under argon. The reaction mixture was allowed to cool to rt. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the pure product (1.1 g, 94%) as a colourless oil. ν_{max} (film)/cm^{-1} 3010 (=CH), 2940 (CH aliphatic), 2900 (CH aliphatic), 1590 (C=C), 1050 (C–O); δ_H (300 MHz; $CDCl_3$) 0.83 (6H, t, *J* 7.7, 3 × SnC*H*$_2$), 0.87 (9H, t, *J* 7.0, 3 × C*H*$_3$CH$_2$CH$_2$), 1.19 (6H, t, *J* 7.0, 2 × C*H*$_3$CH$_2$O), 1.30 (6H, quintet, *J* 7.0, 3 × C*H*$_2$-CH$_2$Sn), 1.46 [6H, sextet, *J* 7.0, (CH$_3$C*H*$_2$CH$_2$CH$_2$)$_3$Sn], 2.47 (2H, t, *J* 5.6, =CHC*H*$_2$), 3.45–3.70 (4H, m, 2 × OCH$_2$), 4.52 [1H, t, *J* 5.6, C*H*(OCH$_2$CH$_3$)$_2$], 5.91 (1H, dt, *J* 5.6 and 19.0, HC=C*H*CH$_2$), 6.02 (1H, d, *J* 19.0, *H*C=CHCH$_2$); δ_C (75.5 MHz; $CDCl_3$) 9.2, 13.5, 15.5 , 27.2 (CH_2), 29.1, 42.3, 60.9, 102.4, 131.0, 143.6; *m/z* (CI) 435.2289 (MH^+, $C_{20}H_{43}SnO_2$ requires *m/z* = 435.2285, 10%), 389 ($C_{18}H_{37}O^+$, 35), 331 ($C_{16}H_{32}^+$, 55).

Typical procedure for the Stille couplings

A solution of diiodine, tri-*n*-butyl(4,4-diethoxybut-1-enyl)-stannane and lithium chloride in THF was degassed at rt. $Pd(PPh_3)_4$ was then added and the mixture was again degassed before heating at 70 °C for 2 days under argon. The reaction mixture was allowed to cool to rt and was partitioned between water (5 ml) and dichloromethane (5 ml). The organic layer was dried ($MgSO_4$), filtered and evaporated.

Preparation of 7,7-diethoxy-2-iodohepta-2,4-dienoic acid methyl ester (Table 2, entry 1). (*E*)-2,3-Diiodoacrylic acid methyl ester (135 mg, 0.4 mmol), tri-*n*-butyl(4,4-diethoxybut-1-enyl)stannane (172 mg, 0.4 mmol) and lithium chloride (17 mg, 0.4 mmol) in THF (2 ml), $Pd(PPh_3)_4$ (18 mg, 15.6 μmol), *T* = 70 °C, *t* = 48 h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the pure product (86 mg, 61%) as a yellow oil. ν_{max} (film)/cm^{-1} 3025 (=CH), 2950 (CH aliphatic), 2860 (CH aliphatic), 1725 (C=O), 1600 (C=C), 1120 (C–O); δ_H (300 MHz; $CDCl_3$) 1.20 (6H, t, *J* 7.0, 2 × C*H*$_3$CH$_2$O), 2.50 [2H, d, *J* 5.9, (EtO)$_2$CHC*H*$_2$], 3.45–3.70 (4H, m, 2 × CH$_3$-C*H*$_2$O), 3.82 (3H, s, C*H*$_3$O), 4.53 [1H, t, *J* 5.9, (EtO)$_2$C*H*], 6.02 (1H, d, *J* 15.3, IC=CHCH=C*H*), 7.08 (1H, dd, *J* 11.2 and 15.3, IC=CHC*H*=CH), 7.37 (1H, d, *J* 11.2, IC=C*H*); *m/z* (CI) 308.9983 (M^+ − OEt, $C_{10}H_{14}O_3I$ requires *m/z* = 308.9987, 80%), 182 (M^+ − OEtI, 30).

Preparation of 7-hydroxy-2-iodohepta-2,4-dienoic acid methyl ester (Table 2, entry 2). (*E*)-2,3-Diiodoacrylic acid methyl ester (135 mg, 0.40 mmol), tri-*n*-butyl(4-hydroxybut-1-enyl)stannane (145 mg, 0.40 mmol) and lithium chloride (17 mg, 0.41 mmol) in THF (2 ml), $Pd(PPh_3)_4$ (18 mg, 15.6 μmol), *T* = 70 °C, *t* = 40 h. Purification by silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the product (63 mg, 56%) as a yellow oil. δ_H (300 MHz; $CDCl_3$) 1.77 (1H, br s, OH, disappears upon addition of D_2O), 2.43 (2H, t, *J* 6.2, HOCH$_2$-C*H*$_2$), 3.74 (2H, t, *J* 6.2, HOC*H*$_2$), 3.81 (3H, s, OC*H*$_3$), 6.05 (1H, dt, *J* 6.2 and 15.1, IC=CHCH=C*H*), 6.10 (1H, dd, *J* 11.3 and 15.1, IC=CHC*H*=CH), 7.37 (1H, d, *J* 11.3, IC=C*H*CH=CH); δ_C (75.5 MHz; $CDCl_3$) 29.3, 53.1, 61.4, 83.1, 130.5, 141.3, 153.6, 205.7; ν_{max} (film)/cm^{-1} 3400 (OH), 3030 (=CH), 2960 (CH aliphatic), 2865 (CH aliphatic), 1730 (C=O), 1600 (C–C); *m/z* (CI) 300.0096 ($M + NH_4^+$, $C_8H_{11}IO_3 + NH_4$ requires *m/z* = 300.0097, 52%); *m/z* (EI) 282 (M^+, 100%), 59 ($C_2H_3O_2^+$, 70).

Preparation of 1,1-diethoxynona-6-iodo-3,5-diene (Table 2, entry 3). (*E*)-1,2-Diiodopent-1-ene (100 mg, 0.3 mmol), tri-*n*-butyl(4,4-diethoxybut-1-enyl)stannane (129 mg, 0.3 mmol) and lithium chloride (13 mg, 0.3 mmol) in THF (2 ml), $Pd(PPh_3)_4$ (14 mg, 12.1 μmol), *T* = 68 °C, *t* = 48 h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the pure product (47 mg, 46%) as a yellow oil. ν_{max} (film)/cm^{-1} 3010 (=CH), 2980 (CH aliphatic), 2870 (CH aliphatic), 1600 (C=C), 1060 (C–O); δ_H (300 MHz; $CDCl_3$) 0.90 (3H, t, *J* 7.0, C*H*$_3$CH$_2$CH$_2$), 1.20 (6H, t, *J* 7.1, 2 × OCH$_2$C*H*$_3$), 1.25–1.51 (4H, m, CH$_3$C*H*$_2$C*H*$_2$), 2.51 [2H, d, *J* 5.9, (EtO)$_2$CHC*H*$_2$], 3.46–3.75 (4H, m, 2 × OCH$_2$), 4.52 [1H, t, *J* 5.9, (EtO)$_2$C*H*], 5.95 (1H, d, *J* 18.8, IC=CHCH=C*H*), 5.98 (1H, d, *J* 6.9, IC=C*H*CH=CH), 6.50 (1H, dd, *J* 6.9 and 18.8, IC=CHC*H*=CH); *m/z* (CI) 293.0400 (M^+ − OEt, $C_{11}H_{18}OI$ requires *m/z* = 293.0402, 70%), 166 (M^+ − OEtI, 10).

Preparation of 6-iodo-1-hydroxyundeca-3,5-diene (Table 2, entry 4). (*E*)-1,2-Diiodohept-1-ene (140 mg, 0.4 mmol), tri-*n*-butyl(4-hydroxybut-1-enyl)stannane (144 mg, 0.4 mmol) and lithium chloride (17 mg, 0.4 mmol) in THF (3 ml), $Pd(PPh_3)_4$ (37 mg, 32.1 μmol), *T* = 68 °C, *t* = 48 h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the pure product (37 mg, 32%) as a yellow oil. ν_{max} (film)/cm^{-1} 3340 (OH), 3010 (=CH), 2980 (CH aliphatic), 2870 (CH

aliphatic), 1600 (C=C), 1060 (C–O); δ_H (300 MHz; $CDCl_3$) 0.83–1.64 (11H, m, $CH_3CH_2CH_2CH_2CH_2$), 1.96 (1H, br s, OH, disappears upon addition of D_2O), 2.35 (2H, m, $HOCH_2CH_2$), 3.67 (2H, t, *J* 6.4, $HOCH_2$), 5.61 (1H, dt, *J* 6.4 and 14.0, IC=CHCH=CH), 6.14 (1H, dt, *J* 2.5 and 10.3, IC=CHCH=CH), 6.67 (1H, dd, *J* 10.3 and 14.0, IC=CHCH=CH); δ_C (75.5 MHz; $CDCl_3$) 12.0, 15.1, 17.2, 20.0, 27.1, 35.2, 50.6, 65.0, 67.9, 73.4, 109.2; *m*/*z* (CI) 313.0901 ($MH^+ + NH_4$, $C_{11}H_{20}OI + NH_4$ requires *m*/*z* = 313.0903, 70%), 275 ($M^+ - H_2O$, 20).

Preparation of 2-(4,4-diethoxybut-1-enyl)-7,7-diethoxyhepta-2,4-dienoic acid methyl ester 10. (*E*)-2,3-Diiodoacrylic acid methyl ester (100 mg, 0.3 mmol), 1-tri-*n*-butyl(4,4-diethoxybut-1-enyl)stannane (260 mg, 0.6 mmol) and lithium chloride (13 mg, 0.3 mmol) in THF (2 ml), $Pd(PPh_3)_4$ (28 mg, 24.3 μmol), *T* = 68 °C, *t* = 16 h. Silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 4:1 as eluant] gave the pure product **10** (55 mg, 53%) as a yellow oil. ν_{max} (film)/cm^{-1} 3020 (=CH), 2960 (CH aliphatic), 2860 (CH aliphatic), 1725 (C=O), 1600 (C=C), 1060 (C–O); δ_H (300 MHz; $CDCl_3$) 1.20 (12H, t, *J* 7.1, 4 × CH_3CH_2O), 2.49 (2H, m, CH_2C=C), 2.57 (2H, m, CH_2C=C), 3.43–3.73 (8H, q, m, 4 × CH_2O), 3.83 (3H, s, OCH_3), 4.53 and 4.57 [each 1H, t, *J* 5.6, $CH(OCH_2)$], 5.77 (1H, d, *J* 19.2, OCCC*H*=CHCH$_2$), 5.90–6.01 (2H, m, C*H*=CHCH=C and OCCCH=C*H*CH$_2$), 7.08 (1H, dd, *J* 11.2 and 23.2, CH=CHC*H*=C), 7.38 (1H, d, *J* 11.2, MeO_2CC=C*H*); δ_C (75.5 MHz; $CDCl_3$) 14.1, 15.3, 29.3, 29.7, 53.5, 61.5, 61.6, 102.4, 102.5, 134.2, 142.4, 147.9, 150.5, 153.9, 164.1, 205.0; λ_{max} (EtOH)/nm 254 (ε/dm^3 mol^{-1} cm^{-1} 33800); *m*/*z* (CI) 279.1602 ($M^+ - 2 \times$ OEt, $C_{16}H_{23}O_4$ requires *m*/*z* = 279.1596, 100%), 222 ($C_{12}H_{14}O_4$, 20).

Preparation of 5-ethyl-1,1-diethoxy-6-iodoocta-3,5-diene 11. A solution of (*E*)-3,4-diiodohex-3-ene (100 mg, 0.31 mmol), tri-*n*-butyl(4,4-diethoxybut-1-enyl)stannane (129 mg, 0.30 mmol) and lithium chloride (13 mg, 0.31 mmol) in THF (5 ml) was degassed at rt. $Pd(PPh_3)_4$ (14 mg, 12.11 μmol) was then added and the mixture was again degassed before heating at 68 °C for 16 h under argon. The reaction mixture was allowed to cool to rt, partitioned between water (5 ml) and dichloromethane (5 ml). The organic layer was dried ($MgSO_4$), filtered and evaporated. Purification by silica gel chromatography [petroleum ether (40–60)–ethyl acetate, 95:5 as eluant] gave the pure product **11** (55 mg, 52%) as a yellow oil. ν_{max} (film)/cm^{-1} 3010 (=CH), 2950 (CH aliphatic), 2860 (CH aliphatic), 1600 (C=C), 1050 (C–O); δ_H(300 MHz; $CDCl_3$) 0.80–0.90 (12H, m, 2 × CH_3CH_2C + 2 × OCH_2CH_3), 2.46–2.57 (4H, m, 2 × CH_3CH_2C), 2.35–2.39 [2H, m, $(EtO)_2CHCH_2$], 3.45–3.71 (4H, m, 2 × OCH_2), 4.49 [1H, t, *J* 5.7, $CH(OEt)_2$], 5.95 (1H, d, *J* 18.7, CH_2CH=C*H*), 6.51 (1H, dt, *J* 7.0 and 18.7, CH_2CH=CH); *m*/*z* (CI) 308 ($MH^+ - OEt$, 100%), 307.0556 ($M^+ - OEt$ requires *m*/*z* = 307.0559, 80), 263 ($MH^+ - 2 \times OEt$, 15).

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