Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron 60 (2004) 10239–10244
Tetrahedron

Sequential alkynylation of ω-bromoalkyl triflates: facile access to unsymmetrical non-conjugated diynes including precursors to diene pheromones

Rosemary J. Armstrong-Chong, Kristopher Matthews and J. Michael Chong*

Department of Chemistry, University of Waterloo, 200 University Ave W, Waterloo, Ont., Canada N2L 3G1

Received 15 July 2004; revised 25 August 2004; accepted 27 August 2004

Available online 22 September 2004

Abstract—Sequential treatment of ω-bromoalkyl triflates with an alkynyllithium at 0 °C followed by addition of a second alkynyllithium and NaI and heating the reaction mixture provides a simple one-pot access to unsymmetrical diynes in good yields. These diynes may be transformed stereoselectively into diene pheromones such as (*Z*,*Z*)- and (*E*,*Z*)-3,13-octadecadienyl acetate.

1. Introduction

There are many insect pheromones which contain non-conjugated dienes as part of their structures.[1] In principle, the corresponding diynes could serve as synthetic intermediates to many of these compounds by taking advantage of well-established stereoselective reduction methods (e.g., semi-hydrogenation over Lindlar-type catalysts or P-2 Ni to prepare *Z* alkenes[2] or Li/NH_3 reductions to produce *E* alkenes[3]). Chemoselective reductions could be achieved using proximity effects such as hydroaluminations of propargyl and homopropargylic alcohols.[4]

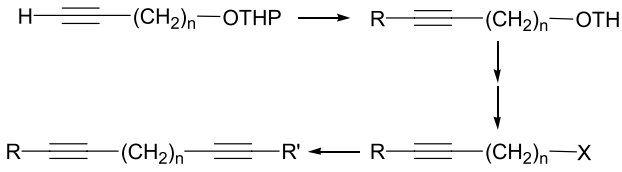
In the past, unsymmetrical diynes have been typically prepared using protecting group chemistry. Thus one might first prepare a THP-protected alkynyl alcohol, alkylate the alkyne, deprotect the alcohol, convert it to a halide, and then alkynylate that alkyl halide (Scheme 1).[5]

A more expeditious route to such diynes would be to sequentially alkynylate difunctional linkers containing leaving groups of widely differing electrofugality (Scheme 2). We now report that this simple approach to unsymmetrical diynes may be implemented in a one-pot procedure using ω-bromotriflates.

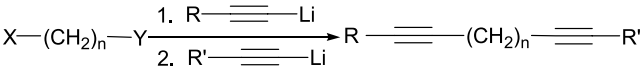
2. Results and discussions

Previous attempts to chemoselectively monoalkynylate chloroiodoalkanes have met with limited success, with variable yields.[6,7] Since iodide is a much better leaving group than chloride, one might expect that selective reaction should be possible. However, the iodide ion formed can participate in Finkelstein reactions generating more reactive alkyl iodides from chlorides. In fact, we have recently shown that bromoalkanes react with alkynyllithiums in THF in the presence of iodide ion but only very slowly in the absence of iodide.[8] This suggests that suppression of Finkelstein reactions is necessary to minimize dialkynylation.

The use of triflates should circumvent any problems with Finkelstein reactions. Alkynylation of alkyl triflates with alkynyllithiums is known to occur under relatively mild



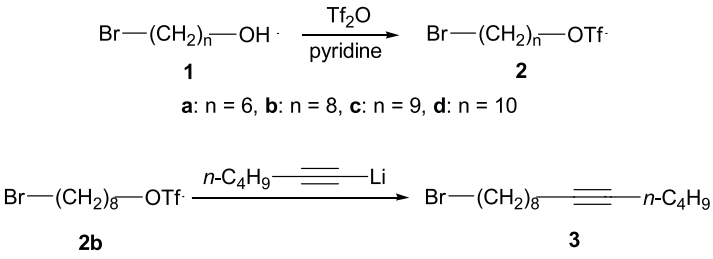
Scheme 1.



Scheme 2.

Keywords: Alkynyllithium; Alkynylation; Diyne; Bromotriflate; Diene pheromone.
* Corresponding author. Tel.: +1-519-888-4567x6643; fax: +1-519-746-0435; e-mail: jmchong@uwaterloo.ca

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2004.08.094



Scheme 3.

conditions.[9] The triflate ion formed, unlike iodide ion, is unlikely to react as a nucleophile. In addition, the selective alkynylation of a primary triflate in the presence of a primary tosylate has previously been demonstrated.[10] As ω-bromoalkanols are readily available,[11] it seemed that the derived ω-bromoalkyl triflates might be good candidates for sequential dialkynylation.

Our initial investigations centered on bromotriflate **2b** which was easily prepared from 8-bromooctanol (Scheme 3; Tf_2O, py, CH_2Cl_2). Treatment of **2b** with 1-hexynyllithium at 0 °C for 1 h in THF lead to the clean formation of the expected alkynyl bromide **3** (91% isolated yield). There was no evidence (GCMS analysis using an authentic sample) of the possible diyne derived from displacement of both the triflate and bromide groups even when 2 equiv of alkynyllithium were used. It was not surprising that there was a large difference in reactivity between the triflate and bromide in **2b** since it is known that triflates can react 10^7 times faster than bromides.[12]

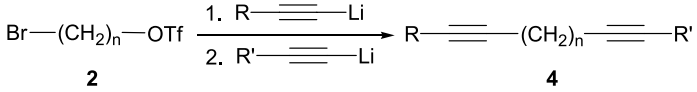
With the monoalkynylation established, we examined the sequential dialkynylation reaction. It has been shown that alkylation of alkynyllithiums with alkyl bromides proceeds well in THF at reflux temperatures if a catalytic amount of NaI or *n*-Bu_4NI is added.[8] Since the alkynylation of triflates is also run in THF but at 0 °C, development of a sequential reaction was relatively simple. Thus the bromotriflate of interest in THF was treated initially with an alkynyllithium at 0 °C and then a second alkynyllithium was added along with 10 mol% NaI and the reaction mixture was heated to reflux. The desired unsymmetrical diynes were isolated in good yields (Table 1).

The bromotriflates could be isolated and purified but were somewhat unstable and showed some decomposition upon column chromatography. Isolated yields of crude triflates were near quantitative but purified material could only be obtained in ~70% yields. Thus triflates were prepared immediately before use and not purified before alkynylation. The yields in Table 1 are only modest in some cases but are quite respectable considering that they are based on bromoalcohol precursors and represent the overall purified yields of products after triflation and two alkynylations. Since many ω-bromoalcohols are commercially available or easily prepared in quantity by treatment of diols with HBr in toluene,[11] this sequence represents a very quick and reasonably efficient route to many unsymmetrical diynes.

Control experiments were run to determine whether higher yields could be obtained by carrying out the sequential dialkynylation with isolation of the alkynylbromide intermediate. In the cases examined, similar or only slightly higher overall yields were obtained when the intermediate alkynylbromide was isolated and purified. For example, yields for the production of **4c** by the 2-step procedure were 78 and 79% for an overall yield of 62%. This is comparable to that obtained in the one-pot reaction (Table 1, entry 3). In practice, it is more convenient to prepare the desired diynes without isolation of intermediates. Of course, the intermediate bromides could serve as useful alkylating agents for other transformations as well.

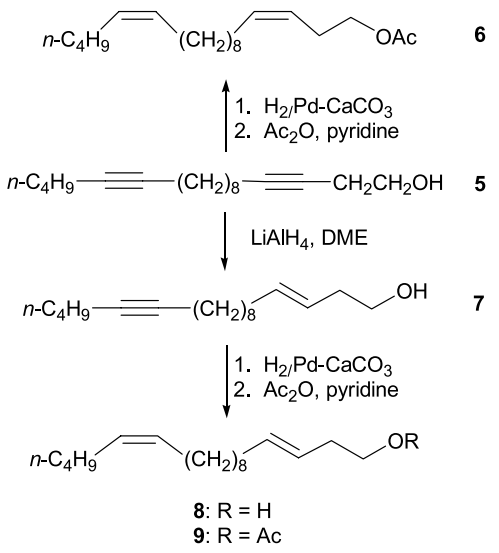
To illustrate a possible use of these diynes, **4d** was converted into (3*E*,13*Z*)-3,13-octadecadienyl acetate and (3*Z*,13*Z*)-3,13-octadecadienyl acetate, both of which are components of the cherrytree borer pheromone[13] (Scheme 4). The *E*,*Z* isomer (or its alcohol) is also a component of many other lepidopteran pheromone blends.[7a] Removal of the THP group in **4d** was readily accomplished (PPTS, EtOH, 99%) to furnish the diynol **5**. Semi-hydrogenation of

Table 1. One-pot preparation of unsymmetrical diynes



Entry	R	R′	*n*	Product (% yield)[a]
1	CH_2OTHP	*n*-C_6H_{13}	6	**4a** (62)
2	$(CH_2)_2OTHP$	*n*-C_4H_9	6	**4b** (70)
3	CH_2OTHP	*n*-C_4H_9	8	**4c** (55)
4	$(CH_2)_2OTHP$	*n*-C_4H_9	8	**4d** (58)
5	$(CH_2)_2OTHP$	*n*-C_6H_{13}	8	**4e** (75)
6	$(CH_2)_2OTHP$	*n*-C_8H_{17}	8	**4f** (78)
7	CH_2OTHP	*n*-C_4H_9	9	**4g** (67)
8	$(CH_2)_2OTHP$	*n*-C_4H_9	10	**4h** (73)

[a] Isolated yield of purified **4**.



Scheme 4.

5 (H_2, $Pd/CaCO_3$) followed by acetylation gave the *Z*,*Z*-isomer **6** (90% yield, 2 steps) with no surprises.

In the hydroalumination of **5**, it was expected that the isolated Δ13 triple bond would not be reduced.[4a] However, prolonged heating of **5** with $LiAlH_4$ (diglyme, 120 °C, 40 h), conditions previously used to affect reductions of homopropargylic alcohols,[14] gave mixtures of the desired enyne **7** and a diene (which, based on GCMS and ^{13}C NMR evidence, likely has *E*,*E*-stereochemistry). Fortunately, formation of this diene could be effectively suppressed by carrying out the reaction at lower temperatures (refluxing DME) for shorter times (18 h). This procedure followed by acetylation and semi-hydrogenation furnished the 3*E*,13*Z*-isomer **9** in 88% overall yield, 3 steps.

3. Conclusions

In summary, we have developed a very convenient route to unsymmetrical diynes which takes advantage of the vastly different reactivities of alkyl triflates and bromides with alkynyllithiums. A wide variety of diynes (and hence the corresponding dienes) should be accessible using this chemistry.

4. Experimental

4.1. General

All reactions were carried out under argon using flame-dried glassware. NMR data were recorded on a 300 MHz instrument in $CDCl_3$ unless otherwise noted. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ. THF was freshly distilled from Na/benzophenone. Dichloromethane and pyridine were distilled from CaH_2. Reagents were purchased from Aldrich Chemical Co. and used without further purification. *n*-BuLi was titrated using *N*-benzylbenzamide before use.[15] Silica gel 60 (40–63 μm) from EM Science was used for flash chromatography. Bromoalcohols were prepared from the corresponding diols.[11]

4.2. General procedure A: preparation of bromotriflates from bromoalcohols

To a cold (−15 °C), stirred solution of bromoalcohol **1** in CH_2Cl_2 (4 mL/mmol) was added pyridine (1.0 equiv) followed by triflic anhydride (1.2 equiv). The reaction was stirred at 0 °C for 1 h then diluted with hexanes (2× volume of CH_2Cl_2) and filtered through a Celite pad. Concentration of the filtrate and removal of volatiles (0.1 mmHg, 30 min) afforded crude triflates which could be used directly for alkynylations. The crude materials could be further purified by filtration through a short column of silica gel using hexanes as eluent.

4.2.1. 1-Trifluoromethanesulfonyloxy-6-bromohexane (2a). This compound was prepared from 6-bromo-1-hexanol using General procedure A (Section 4.2) in 68% yield after purification. ^1H NMR (300 MHz, $CDCl_3$) δ 4.53 (2H, t, $J=6.3$ Hz), 3.40 (2H, t, $J=6.7$ Hz), 1.92–1.77(4H, m), 1.55–1.40 (4H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.58 (q, $J_{C-F}=320$ Hz), 77.36, 33.30, 32.27, 29.00, 27.31, 24.25; IR (neat) 1413, 1248, 1207, 1146, 936 cm^{-1}; MS (EI) *m*/*z* 232 (1), 83 (60), 55 (100).

4.2.2. 1-Trifluoromethanesulfonyloxy-8-bromooctane (2b). This compound was prepared from 8-bromo-1-octanol using General procedure A (Section 4.2) in 70% yield after purification. ^1H NMR (300 MHz, $CDCl_3$) δ 4.52 (2H, t, $J=6.3$ Hz), 3.39 (2H, t, $J=6.7$ Hz), 1.90–1.77 (4H, m), 1.52–1.28 (8H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.61 (q, $J_{C-F}=319$ Hz), 77.61, 33.73, 32.60, 29.12, 28.60, 28.39, 27.89, 24.91; IR (neat) 1413, 1247, 1208, 1146, 934 cm^{-1}; MS (EI) *m*/*z* 260 (1), 69 (100), 55 (55).

4.2.3. 1-Trifluoromethanesulfonyloxy-9-bromononane (2c). This compound was prepared from 9-bromo-1-nonanol using General procedure A (Section 4.2) in 83% yield after purification. ^1H NMR (300 MHz, $CDCl_3$) δ 4.52 (2H, t, $J=6.3$ Hz), 3.39 (2H, t, $J=6.7$ Hz), 1.92–1.77 (4H, m), 1.55–1.30 (10H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.63 (q, $J_{C-F}=319$ Hz), 77.64, 33.85, 32.69, 29.16, 29.09, 28.68, 28.51, 28.01, 24.97; IR (neat) 1413, 1247, 1210, 1147, 934 cm^{-1}; MS (EI) *m*/*z* 274 (1), 135 (15), 83 (35), 69 (100).

4.2.4. 1-Trifluoromethanesulfonyloxy-10-bromodecane (2d). This compound was prepared from 10-bromo-1-decanol using General procedure A (Section 4.2) in 70% yield after purification. ^1H NMR (300 MHz, $CDCl_3$) δ 4.52 (2H, t, $J=6.3$ Hz), 3.39 (2H, t, $J=6.7$ Hz), 1.92–1.78 (4H, m), 1.50–1.28 (12H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.62 (q, $J_{C-F}=319$ Hz), 77.68, 33.88, 32.73, 29.16, 29.15, 29.12, 28.73, 28.60, 28.05, 24.97; IR (neat) 1414, 1247, 1208, 1147, 935 cm^{-1}; MS (EI) *m*/*z* 288 (1), 135 (18), 97 (29), 83 (48), 69 (84), 55 (100).

4.2.5. 1-Bromotetradec-9-yne (3). To a cold (0 °C), stirred solution of 1-hexyne (130 μL, 1.1 mmol) in dry THF (5 mL) was added *n*-BuLi (0.63 mL, 1.60 M in hexanes, 1.0 mmol). The solution was stirred at 0 °C then cooled to −78 °C. Bromotriflate **1a** (338 mg, 0.99 mmol) was slowly added

and the reaction mixture was stirred at −78 °C for 5 min then at 0 °C for 1 h. Standard aqueous work-up using ether and satd aqueous NH_4Cl provided crude material which was purified by flash chromatography on silica gel (15 g) using hexanes as eluent to provide 250 mg (91%) of the known[16] alkyne **3** as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.39 (2H, t, J=7 Hz), 2.12 (4H, m), 1.83 (2H, quintet, J=7 Hz), 1.5–1.2 (14H, m), 0.88 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.07, 79.90, 33.77, 32.71, 31.17, 28.98, 28.85, 28.59, 28.58, 28.02, 21.83, 18.61, 18.33, 13.54; MS (EI) m/z 272 (M^+, ^{79}Br, 0.1), 215 (3), 95 (59), 81 (100), 67 (84).

4.3. General procedure B: sequential dialkynylation of bromotriflates

To a cold (−78 °C), stirred solution of propargyl alcohol THP ether or 3-butyn-1-ol THP ether in THF (3 mL/mmol) was added *n*-BuLi (1.6 M in hexanes, 1.0 equiv). The solution was stirred at 0 °C for 15 min then cooled to −78 °C and a THF solution (2 mL/mmol) of bromotriflate **2** (1.0 equiv, crude material prepared according to General procedure A (Section 4.2)) was slowly added. The mixture was stirred at 0 °C for 1 h to generate the intermediate bromoalkyne. A THF solution (2 mL/mmol) of an alkynyllithium (freshly prepared from a terminal alkyne and *n*-BuLi, −78 °C→0 °C, 15 min, 2.0 equiv) and NaI (10–20 mol%) were then added and the mixture was heated at reflux for 16–30 h (monitor by TLC). After cooling to rt, standard extractive workup (ether/aq NH_4Cl then brine) afforded crude materials which were purified by flash chromatography on silica gel using 3–5% ether in hexanes as eluent to yield the desired diynes as colorless oils.

4.3.1. 1-Tetrahydropyranyloxy-2,10-heptadecadiyne (4a). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1a** in 62% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.77 (1H, t, J=3 Hz), 4.20 (2H, AB of ABX_2, $\Delta\nu$=25.6 Hz, J_{AB}=15.2 Hz, J_{AX}=J_{BX}=2 Hz), 3.86–3.74 (1H, m), 3.51–3.41 (1H, m), 2.20–2.07 (6H, m), 1.88–1.25 (22H, m), 0.85 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 96.44, 86.43, 80.19, 79.85, 75.68, 61.79, 54.47, 31.27, 30.18, 29.01, 28.88, 28.42, 28.38, 28.27, 28.19, 25.29, 22.47, 19.01, 18.66, 18.63, 18.58, 13.94; IR (neat) 1480, 1110, 1040, 1020 cm^{-1}; MS (EI) m/z 247 (M^+−THP, 11), 85 (100), 67 (40), 55 (38). Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 79.61; H, 10.97.

4.3.2. 1-Tetrahydropyranyloxy-3,11-octadecadiyne (4b). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1a** in 70% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.62 (1H, t, J=3 Hz), 3.90–3.73 (2H, m), 3.54–3.44 (2H, m), 2.45 (2H, tt, J=7, 3 Hz), 2.12 (6H, br t, J=7 Hz), 1.88–1.36 (18H, m), 0.88 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.52, 81.05, 80.07, 79.87, 76.66, 66.08, 61.95, 31.13, 30.45, 28.90, 28.75, 28.22, 25.35, 21.80, 20.10, 19.28, 18.59, 18.57, 18.30, 13.50; IR (neat) 1137, 1122, 1070, 1034 cm^{-1}; MS (EI) m/z 85 (100), 67 (15), 55 (13). Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.36; H, 10.67.

4.3.3. 1-Tetrahydropyranyloxy-2,12-heptadecadiyne (4c). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1b** in 55% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.78 (1H, t, J=3 Hz), 4.21 (2H, AB of ABX_2, $\Delta\nu$=25.9 Hz, J_{AB}=15.2 Hz, J_{AX}=J_{BX}=2 Hz), 3.87–3.77 (1H, m), 3.53–3.46 (1H, m), 2.23–2.10 (6H, m), 1.85–1.20 (22H, m), 0.87 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 96.50, 86.62, 80.09, 80.04, 75,64, 61.86, 54.54, 31.18, 30.21, 29.05, 28.95 (2C), 28.74, 28.71, 28.51, 25.32, 21.85, 19.03, 18.73, 18.65, 18.36, 13.56; IR (neat) 1132, 1118, 1025 cm^{-1}; MS (EI) m/z 247 (M^+−THP, 1), 85 (100), 67 (59), 55 (72). Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 79.60; H, 10.85.

4.3.4. 1-Tetrahydropyranyloxy-3,13-octadecadiyne (4d). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1b** in 58% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.61 (1H, t, J=3 Hz), 3.91–3.72 (2H, m), 3.51–3.42 (2H, m), 2.12–2.05 (6H, m), 1.81–1.23 (22H, m), 0.87 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.54. 81.17, 80.03, 80.00, 76.61, 66.11, 61.97, 31.16, 30.47, 29.03, 28.96, 28.93, 28.87, 28.70, 28.68, 25.38, 21.81, 20.12, 19.30, 18.62 (2C), 18.32, 13.52; IR (neat) 1130, 1110, 1070, 1040 cm^{-1}; MS (EI) m/z 85 (100), 67 (20), 55 (20). Anal. Calcd for $C_{23}H_{38}O_2$: C, 79.71; H, 11.05. Found: C, 79.90; H, 10.86.

4.3.5. 1-Tetrahydropyranyloxy-3,13-icosadiyne (4e). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1b** in 75% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.61 (1H, t, J=3 Hz), 3.90–3.69 (2H, m), 3.51–3.42 (2H, m), 2.46–2.36 (2H, m), 2.10 (6H, br t, J=7 Hz), 1.82–1.22 (26H, m), 0.85 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.54, 81.18, 80.11, 80.02, 76.61, 66.12, 61.98, 31.29, 30.48, 29.04, 28.98, 28.96, 28.88, 28.72, 28.70, 28.44, 25.37, 22.49, 20.13, 19.31, 18.65, 18.64, 13.96; IR (neat) 1130, 1110, 1060, 1030 cm^{-1}; MS (EI) m/z 289 (M^+−THP, 0.3), 85 (100), 67 (20), 55 (23). Anal. Calcd for $C_{25}H_{42}O_2$: C, 80.16; H, 11.30. Found: C, 80.18; H, 11.05.

4.3.6. 1-Tetrahydropyranyloxy-3,13-docosadiyne (4f). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1b** in 78% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.61 (1H, t, J=3 Hz), 3.90–3.70 (2H, m), 3.52–3.42 (2H, m), 2.40 (2H, br t, J=7 Hz), 2.09 (6H, br t, J=7 Hz), 1.82–1.23 (30H, m), 0.84 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.57, 81.20, 80.14, 80.05, 76.63, 66.14, 62.01, 31.78, 30.50, 29.16, 29.09, 29.07, 29.00, 28.98, 28.90, 28.80, 28.75, 28.73, 25.39, 22.60, 20.15, 19.33, 18.67, 18.65, 14.03; IR (neat) 1130, 1110, 1070, 1030 cm^{-1}; MS (EI) m/z 85 (100), 67 (24), 55 (20). Anal. Calcd for $C_{27}H_{46}O_2$: C, 80.54; H, 11.51. Found: C, 80.22; H, 11.13.

4.3.7. 1-Tetrahydropyranyloxy-2,13-octadecadiyne (4g). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1c** in 67% yield after purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.76 (1H, t, J=3 Hz), 4.18 (2H, AB of ABX_2, $\Delta\nu$=24.2 Hz, J_{AB}=15.2 Hz, J_{AX}=J_{BX}=2 Hz), 3.82–3.73 (1H, m), 3.49–3.41 (1H, m), 2.18–2.07 (6H, m), 1.82–1.22 (24H, m), 0.84 (3H, t, J=7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 96.39, 86.51, 79.97 (2C), 75.60, 61.76, 54.45, 31.14, 30.16, 29.27, 29.01, 28.97,

28.94, 28.72, 28.68, 28.47, 25.28, 21.79, 18.99, 18.67, 18.60, 18.29, 13.49; IR (neat) 1130, 1110, 1060, 1040 cm^{-1}; MS (EI) *m/z* 261 ($M^+ - THP$, 1), 85 (100), 67 (50), 55 (50). Anal. Calcd for $C_{23}H_{38}O_2$: C, 79.71; H, 11.05. Found: C, 79.60; H, 10.92.

4.3.8. 1-Tetrahydropyranyloxy-3,15-icosadiyne (4h). This compound was prepared following General procedure B (Section 4.3) from bromoalcohol **1d** in 73% yield after purification. ^1H NMR (300 MHz, $CDCl_3$) δ 4.61 (1H, t, $J=3$ Hz), 3.89–3.71 (2H, m), 3.53–3.42 (2H, m), 2.46–2.38 (2H, m), 2.14–2.08 (6H, m), 1.82–1.25 (26H, m), 0.87 (3H, t, $J=7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 98.56, 81.22, 80.06, 80.03, 76.60, 66.13, 62.00, 31.19, 30.49, 29.43, 29.40, 29.08, 29.06, 28.91, 28.76, 25.38, 21.83, 20.14, 19.32, 18.65, 18.35, 13.55; IR (neat) 1130, 1110, 1060, 1030 cm^{-1}; MS (EI) *m/z* 85 (100), 67 (20), 55 (19). Anal. Calcd for $C_{25}H_{42}O_2$: C, 80.16; H, 11.30. Found: C, 79.86; H, 11.17.

4.3.9. 3,13-Octadecadiyn-1-ol (5). A solution of THP ether **4d** (1.53 g, 4.4 mmol) and PPTS (200 mg) in ethanol (25 mL) was heated at 60 °C for 4 h. It was cooled to rt and solid $NaHCO_3$ was added before removal of volatiles by rotoevaporation. Standard extractive workup (ether, satd $NaHCO_3$ then brine) gave crude material which was purified by flash chromatography on silica gel using hexanes/ether, 2:1 to yield the known[17] alcohol **5** (1.15 g, 99%) as a low-melting colorless solid. ^1H NMR (300 MHz, $CDCl_3$) δ 3.63 (2H, t, $J=7$ Hz), 2.42–2.35 (2H, m), 2.14–2.07 (6H, m), 1.48–1.23 (16H, m), 0.86 (3H, t, $J=7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 82.54, 80.10, 80.06, 76.23, 61.28, 31.17, 29.03, 28.94, 28.88 (2C), 28.75, 28.70, 23.06, 21.84, 18.64 (2C), 18.34, 13.54.

4.3.10. (3*Z*,13*Z*)-3,13-Octadecadien-1-yl acetate (6). A mixture of diyne **5** (135 mg) and 5% Pd/$CaCO_3$ poisoned with lead (28 mg) in hexanes (2 mL) was stirred under an atmosphere of H_2 for 18 h. The mixture was filtered through Celite and volatiles were removed by rotoevaporation. The residue was stirred with pyridine (1.5 mL), Ac_2O (0.5 mL) and DMAP ($\sim$3 mg). Removal of volatiles in vacuo followed by flash chromatography on silica gel using hexanes/ether, 50:1 as eluent provided *Z,Z*-diene **6**[12] (141 mg, 90%) as a colorless liquid. Diene **6** co-eluted with its 3*E*,13*Z* and 3*E*,13*E* isomers on GC (DB-5 column) but high stereochemical purity was ascertained by the absence of ^{13}C signals at δ 124.9 and 133.5 (3E olefinic carbons) and 130.2 (13E olefinic carbons). ^1H NMR (300 MHz, $CDCl_3$) δ 5.50–5.25 (4H, m), 4.02 (2H, t, $J=7$ Hz), 2.33 (2H, app q, $J=7$ Hz), 2.05–1.95 (6H, m), 1.99 (s, 3H), 1.36–1.22 (16H, m), 0.86 (3H, t, $J=7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 132.9, 129.8 (2C), 124.2, 63.9, 31.9, 29.7, 29.5, 29.4, 29.2, 27.2, 27.1, 26.8, 26.7, 22.3, 20.9, 13.9.

4.3.11. (*E*)-Octadec-3-en-13-yn-1-ol (7). To a solution of diene **5** (156 mg, 0.6 mmol) in DME (4 mL) was carefully added $LiAlH_4$ (92 mg, 2.4 mmol) and the mixture was heated at reflux for 18 h. The reaction mixture was cooled to 0 °C, diluted with ether and carefully quenched with satd NH_4Cl. Standard aqueous workup with 1 M HCl then brine afforded crude alcohol **7** which was directly acetylated. An analytical sample was purified by flash chromatography on silica gel using hexanes/ether, 2:1 to afford **7** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 5.56–5.25 (2H, m), 3.57 (2H, t, $J=7$ Hz), 2.23 (2H, app q, $J=7$ Hz), 2.15–2.04 (4H, m), 1.94 (2H, app q, $J=7$ Hz), 1.75–1.20 (16H, m), 0.86 (3H, t, $J=7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.26, 125.63, 80.14 (2C), 61.98, 35.91, 32.62, 31.21, 29.39, 29.32, 29.09, 29.05, 28.98, 28.78, 21.87, 18.69, 18.38, 13.58; IR (neat) 3351, 1466, 1048 cm^{-1}; MS (EI) *m/z* 233 ($M^+ - CH_2OH$, 0.2), 95 (43), 81 (90), 67 (100), 55 (93). Anal. Calcd for $C_{18}H_{32}O$: C, 81.75; H, 12.20. Found: C, 81.81; H, 12.01.

4.3.12. (*E*)-Octadec-3-en-13-yn-1-yl acetate (8). Crude alcohol **7** from the previous reaction was stirred with pyridine (1.5 mL), Ac_2O (0.5 mL) and DMAP ($\sim$3 mg). Removal of volatiles in vacuo followed by flash chromatography on silica gel using hexanes/ether, 50:1 as eluent provided acetate **8** (166 mg, 91%) as a colorless liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 5.55–5.25 (2H, m), 4.02 (2H, t, $J=7$ Hz), 2.27 (2H, app q, $J=7$ Hz), 2.15–2.05 (4H, m), 2.00 (3H, s), 1.95 (2H, app q, $J=7$ Hz), 1.50–1.20 (16H, m), 0.87 (3H, t, $J=7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.10, 133.53, 124.91, 80.12, 80.11, 64.10, 32.54, 31.89, 31.21, 29.31, 29.09, 29.05, 29.01, 28.78, 21.87, 20.92, 18.68, 18.38, 13.58; IR (neat) 1743, 1238 cm^{-1}; MS (EI) *m/z* 264 ($M^+ - C_2H_2O$, 0.2), 93 (48), 81 (69), 79 (62), 67 (100), 55 (55). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.42; H, 11.10.

4.3.13. (3*E*,13*Z*)-3,13-Octadecadien-1-yl acetate (9). A mixture of enyne **8** (150 mg) and 5% Pd/$CaCO_3$ poisoned with lead (15 mg) in hexanes (2 mL) was stirred under an atmosphere of H_2 for 40 h. The mixture was filtered through Celite and volatiles were removed by rotoevaporation. Purification of the residue by flash chromatography on silica gel using hexanes/ether, 50:1 as eluent provided the known[7a] *E,Z*-diene **9** (147 mg, 97%) as a colorless liquid. ^1H NMR (300 MHz, $CDCl_3$) δ 5.50–5.24 (4H, m), 4.01 (2H, t, $J=7$ Hz), 2.25 (2H, app q, $J=7$ Hz), 2.02–1.90 (6H, m), 1.99 (s, 3H), 1.34–1.20 (16H, m), 0.85 (3H, t, $J=7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 133.5, 129.7 (2C), 124.9, 64.0, 32.5, 31.9, 31.8, 29.7, 29.6, 29.4, 29.3, 29.2, 29.0, 27.1, 26.8, 22.3, 22.1, 20.8, 13.9.

Acknowledgements

We thank the Natural Sciences and Engineering Research Council of Canada (NSERC) for financial support.

References and notes

1. Mori, K. The Synthesis of Insect Pheromones, 1979–1989. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1992; Vol. 9, pp 1–534.
2. Rylander, P. N. *Hydrogenation Methods*; Academic: San Diego, 1985; pp 53–65.
3. Brandsma, L.; Nieuwenhuizen, W. F.; Zwikker, J. W.; Mäeorg, U. *Eur. J. Org. Chem.* **1999**, 775–779.

4. (a) Bailey, W. J.; Pfeifer, C. R. *J. Org. Chem.* **1955**, *20*, 1337–1341. (b) Kang, M. J.; Jang, J. S.; Lee, S. G. *Tetrahedron Lett.* **1995**, *36*, 8829–8832.
5. Schwarz, M.; Klun, J. A.; Leonhardt, B. A.; Johnson, D. T. *Tetrahedron Lett.* **1983**, *24*, 1007–1010.
6. Alkynylation of $I(CH_2)_7Cl$ was reported to give a mixture of chloroalkyne and iodoalkyne: Grimmer, G.; Krqacht, J. *Chemische Berichte* **1963**, *96*, 3370–3373 as quoted in CA 60:22944.
7. For apparently similar reactions, reported yields vary from 33–93%: (a) Capdevila, A.; Prasad, A. R.; Quero, C.; Petschen, I.; Bosch, M. P.; Guerrero, A. *Org. Lett.* **1999**, *1*, 845–848. (b) Crundwell, E.; Cripps, A. L. *J. Med. Chem.* **1972**, *15*, 754–756. (c) Romeril, S. P.; Lee, V.; Claridge, D. W.; Baldwin, J. E. *Tetrahedron Lett.* **2002**, *43*, 327–329. (d) Barrot, M.; Fabriás, G.; Camps, F. *Tetrahedron* **1994**, *50*, 9789–9796. (e) van der Louw, J.; Komen, C. M. D.; Knol, A.; de Kanter, F. J. J.; van der Baan, J. L.; Bickelhaupt, F.; Klumpp, G. W. *Tetrahedron Lett.* **1989**, *30*, 4453–4456.
8. Buck, M.; Chong, J. M. *Tetrahedron Lett.* **2001**, *42*, 5825–5827.
9. (a) Evans, D. A.; Fitch, D. M.; Smith, T. E.; Cee, V. J. *J. Am. Chem. Soc.* **2000**, *122*, 10033–10046. (b) Mori, Y.; Hayashi, H. *Tetrahedron* **2002**, *58*, 1789–1797. (c) Suzuki, K.; Nakata, T. *Org. Lett.* **2002**, *4*, 3943–3946.
10. Kotsuki, H.; Kadota, I.; Ochi, M. *Tetrahedron Lett.* **1990**, *31*, 4609–4612.
11. Chong, J. M.; Heuft, M. A.; Rabbat, P. *J. Org. Chem.* **2000**, *65*, 5837–5838.
12. Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis* **1982**, 85–126.
13. Uchida, M.; Mori, K.; Matsui, M. *Agric. Biol. Chem.* **1978**, *42*, 1067–1070.
14. Pop, L.; Oprean, I.; Barabas, A.; Hodosan, F. *J. Prakt. Chem.* **1986**, *328*, 867–878.
15. Burchat, A. F.; Chong, J. M.; Nielsen, N. *J. Organomet. Chem.* **1997**, *542*, 281–283.
16. Svirskaya, P. I.; Leznoff, C. C. *J. Chem. Ecol.* **1984**, *10*, 321–333.
17. Abrams, S. R.; Nucciarone, D. D.; Steck, W. F. *Can. J. Chem.* **1983**, *61*, 1073–1076.