SYNTHESES OF UNCONJUGATED (*Z*, *Z*)-DIOLEFINIC INSECT PHEROMONES ON INSOLUBLE POLYMER SUPPORTS

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Abstract—A 2% cross-linked styrene–divinylbenzene copolymer containing pendant trityl chloride groups was used as the solid support in the synthesis of (*Z*, *Z*)-3,13-octadecadien-1-yl acetate, a component of the sex attractant of the lesser peachtree borer, *Synanthedon pictipes*, the peachtree borer, *Synanthedon exitiosa*, and the cherry tree borer, *Synanthedon hector*. This solid-phase synthesis is compared with a similar synthetic approach in solution. The solid-phase synthesis of (*Z*, *Z*)-7,11-hexadecadien-1-yl acetate, a component of the pheromone of the pink bollworm moth, *Pectinophora gossypiella* is described.

Key Words—(*Z*, *Z*)-3,13-Octadecadien-1-yl acetate, (*Z*, *Z*)-7,11-hexadecadien-1-yl acetate, solid phase synthesis, *Synanthedon pictipes*, lesser peachtree borer, *Synanthedon exitiosa*, peachtree borer, *Synanthedon hector*, cherry tree borer, *Pectinophora gossypiella*, pink bollworm moth, Lepidoptera, Sessiidae, Gelechiidae.

INTRODUCTION

As stated by Henrick (1977): "The structures of many lepidopterous sex pheromones are deceptively simple but their efficient synthesis in high stereochemical purity has offered considerable synthetic challenge." A wide variety of syntheses of insect pheromones has been described (Henrick, 1977; Rossi, 1977). In our own laboratories we have synthesized a large number of stereochemically pure monoolefinic insect pheromones (Svirskaya et al., 1979; Fyles et al., 1977; Leznoff et al., 1977) on insoluble polymer supports (Leznoff, 1978; Fréchet, 1981). One advantage of using the 1 or 2% styrene–divinylbenzene copolymer supports containing trityl chloride groups (Fyles

and Leznoff, 1976; Fréchet et al., 1976) was the selective monoblocking by the polymer of the symmetrical diol starting materials by the "fishhook" principle (Leznoff, 1978). Other advantages include a stereoselective Wittig reaction simulating "salt-free" conditions (Leznoff et al., 1977) and a facile borane addition reaction in which borane impurities are removed by simple filtration of the polymer (Fyles et al., 1977). Finally, the whole procedure of pheromone synthesis on solid phases has the potential to be automated, as shown for polypeptide (Erickson and Merrifield, 1976) and now oligonucleotide synthesis (Alvarado-Urbina et al., 1981).

We now report the preparation of some diolefinic insect pheromones on solid phases using symmetrical difunctional intermediates. Although the synthesis of (*Z*, *Z*)-3,13-octadecadien-1-yl acetate (**1**), a sex pheromone of the lesser peachtree borer, *Synanthedon pictipes* (Grote and Robinson), the peachtree borer, *Synanthedon exitiosa* (Say), and the cherry tree borer, *Synanthedon hector* (Butler), has been accomplished in solution (Doolittle et al., 1980; Uchida et al., 1978; Ebata and Mari, 1979) in several related ways, a retrosynthetic analysis of **1** reveals the presence of a symmetrical difunctional $-(CH_2)_8-$ unit in the middle of **1** and, since solid-phase methodology lends itself to the use of symmetrical difunctional intermediates, the advantageous use of polymer supports in the preparation of **1** is indicated.

METHODS AND MATERIALS

All melting and boiling points are uncorrected. Infrared spectra (IR) were recorded on a Unicam SP1000 IR spectrophotometer as neat films between NaCl disks or KBr plates. Nuclear magnetic resonance spectra (NMR) were recorded on a Varian EM360 spectrometer, with deuteriochloroform as solvent and tetramethylsilane as an internal standard. Mass spectra (MS) were recorded at 70 eV on a VG Micromass 16F mass spectrometer in the EI mode.

High-pressure liquid chromatographs were run with a Waters Associates model 440 instrument, with an R-400 refractive index detector and a 30 × 0.4-cm reverse-phase μBondapak C-18 column using water–acetonitrile (1 : 3) for the C_{16}–C_{18} diyne acetates, and a Zorbax ODS column (25 cm × 0.9 mm) using water–acetonitrile (1 : 9) for the C_{16} diene–acetate and acetonitrile eluant for the C_{18} diene acetate, at a flow rate of 1.0–1.5 ml/min. Experiments involving reactive organometallic reagents or boron hydrides extremely sensitive to air and moisture were carried out under an argon atmosphere, using dry and pure solvents.

Tetrahydrofuran (THF) was refluxed over $LiAlH_4$ for 4 hr and distilled under argon. Freshly distilled THF was always used. Hexamethylphosphoric

triamide (HMPT) (Caution: hazardous) and other solvents were dried and distilled according to standard methods.

Silica gel was used for all thin and preparative layer chromatography (TLC) unless otherwise specified. Preparative TLC fractions were extracted with ether in a Soxhlet extractor. Filtration was done under vacuum through sintered glass Buchner funnels. The phrase "polymer was washed below" refers to the following procedure: after a polymer-bound compound was filtered; it was washed at least two times with the same solvent in which the reaction was carried out. The polymer was washed 2–3 times with THF, ethanol, 3–5 times with water, and 2–3 times with ethanol. The polymer was then washed 2–3 times with the solvent in which the reaction was carried out and finally 2–3 times with ethanol and 3–4 times with ether. The polymers, after being washed and air-dried, were transferred to a thimble in a Soxhlet extractor in which molecular sieves (3 Å) had been placed in a second thimble, and the polymer was extracted with dry benzene (or ether) for 3–5 hr under reflux conditions. The polymer was washed with dry ether and dried in vacuo. The reaction schemes are shown in Figures 1 to 4.

Polymer-BoundDiol (3). The slurry of 15 g of **2,** containing 1.3 mmol Cl/g and 15 g of 1,2-ethanediol in 5 ml pyridine was heated at 70–80° (bath) under argon overnight. Polymer **3** was isolated as previously described (Fyles and Leznoff, 1976). Cleavage with acetyl chloride in glacial acetic acid gave 1 mmol/g of 1,2-ethanediyl diacetate.

Polymer-Bound Monomesylate (4). Into a three-necked flask fitted with a magnetic stirrer, a dropping funnel, a thermometer, and a $CaCl_2$ drying tube was placed 15 g of vacuum-dried polymer **3,** 150 ml of dry methylene chloride, and 20 g of dry triethylamine. To this suspension at −10 to 0° was added slowly 10 g of freshly distilled methanesulfonyl chloride. The reaction mixture was stirred at 0° for 12–16 hr, and the resin **4** was filtered, washed, extracted with benzene in a Soxhlet extractor, and vacuum dried. The slightly yellow polymer **(4)** formed showed very strong absorptions at 1170 and 1360 cm^{-1} in its IR spectrum. Standard acid cleavage of 1.0 g of **4** with 0.35 M HCl in dioxane (Fyles, 1976) after preparative TLC gave 0.61 mmol/g of **5.**

Polymer-Bound 3-Butyn-1-ol (6). A slurry of 3 g of the LiC≡CH·EDA complex and 10 g of **4** in 75 ml of a 2:1 mixture of THF and HMPT under argon was heated at 60° (bath) overnight. The reaction mixture was cooled, and the excess of lithium acetylide was quenched with THF–H_2O (1:1). The resin **(6)** was filtered, washed, extracted with ether in a Soxhlet extractor, and dried in vacuo.

Polymer-bound 3-butyn-1-ol **(6)** was also prepared from 5 g of **2** and 5 g of **7** in pyridine according to the procedure described above for **3.**

Polymer-Bound 12-Bromo-3-dodecyn-1-ol **(9).** Into 100 ml of THF in a 250-ml three-necked flask, was placed 8 g of polymer **6.** The flask was

equipped with a magnetic stirrer, thermometer, argon–air inlet, condenser (without water) connected with a large needle directly to the atmosphere, and kept at 60° (oil bath). To the stirred slurry was added, over a 15-min period, 10 ml of *t*-BuLi (2 M in pentane).

The reaction is very exothermic. The pentane was evaporated after the addition of *t*-BuLi was complete, water was passed through the condenser, and the resulting blood-red mixture was stirred for a further 0.75 hr at 60°. The reaction mixture was cooled to room temperature, and 13.5 g of 1,8-dibromooctane **(8)** in 40 ml of HMPT was added (at once). The reaction mixture was stirred overnight, treated with THF–H_2O, and filtered. The excess of **8** was recovered from the filtrate (10 g). The polymer **(9)** was washed, extracted with benzene in a Soxhlet extractor, and dried. Acid cleavage of 1.0 g of **9** and purification by preparative TLC on silica gel (eluant ether–C_6H_6 1:4) gave 87 mg (0.33 mmol/g) of **10.** IR (neat) ν cm^{-1}: 3350 (OH) and 1040 (C-O). NMR: δ 3.8–3.2 (4H, m, overlapping triplets); 2.62–1.10 (17H, broad); 1.4 (s). (Found: C 55.29; H 8.39. Calc. for $C_{12}H_{21}BrO$: C 55.17; H 8.10.) A similar experiment was carried out using **6**, prepared directly from commercial **7.** Acid cleavage gave 0.34 mmol/g of **10.**

Polymer-Bound 3,13-Octadecadiyn-1-ol (12). To a stirred solution of 4.1 g (50 mmol) of 1-hexyne in 20 ml of THF at −10 to 0° was added dropwise 35 ml (51 mmol) of *n*-BuLi in hexane under argon. The reaction mixture was stirred at 0° for 1 hr, and a slurry of 1-lithiohexyne **(11)** was added by syringe to the suspension of 7.5 g of **9**, containing 2.4 mmol of **10** in 50 ml of HMPT. The stirring was continued overnight, the reaction mixture was cooled and hydrolyzed with THF–H_2O. The product **12** was isolated by filtration, washed, and dried. Acid cleavage of 1 g of **12** and purification of the diynol **13** by preparative TLC on silica gel (eluant ether–C_6H_6, 1:4) gave 72 mg (0.27 mmol/g) of pure **13**, mp 27–28°. The IR and NMR spectra were identical with the published spectra (Doolittle et al., 1980; Uchida et al., 1978; Ebata and Mori, 1979). Analysis of the acetate by HPLC (mobile phase H_2O–CH_3CN, 1:3) showed one single peak of chemical purity greater than 99%.

Polymer-Bound Dienol (14). To a 10-mmol solution of $(Sia)_2BH$ or slurry of dicyclohexylborane in THF, prepared as described previously (Svirskaya et al., 1980), was added at 0–2° C 2–3 g of **12** containing 0.5–0.7 mmol of **13** under argon. The reaction mixture was stirred at 0–2° (cold plate) for 24 hr. To the cool suspension, 2 ml of AcOH was added dropwise. The cold plate was removed. The mixture was allowed to warm to room temperature and was stirred for an additional 0.5 hr. The polymer was filtered, washed, and dried.

(Z,Z)-*3,13-Octadecadien-1-ol (15).* Acid cleavage of **14** and purification by column chromatography gave product of >99% purity. The IR and NMR spectra of **15** were similar to those of an authentic sample.

(Z,Z)-*3,13-Octadecadien-1-yl Acetate (1).* Acetylation of **15**, as described

in the literature (Uchida eta l., 1978) gave acetate **1**, which was analyzed by HPLC. The μBondapak C_{18} column did not completely separate isomers (>99% purity), but isomers can be separated using a Zorbax ODS (Dupont) column. The analysis indicated ratios of *Z*, *Z* to (*Z*, *E* and *E*, *Z*) as 93:7 (on the polymer) and 95–96:5–4 in solution.

9-Tetradecyn-1-ol (22). Compound **21** was prepared from 8-chlorooctan-1-yl tetrahydropyranyl ether **(20)** (7.44 g, 30 mmol) and 1-lithiohexyne **(11)** (which was formed from 2.87 g, 35 mmol of hexyne and 23 ml, 33 mmol of *n*-BuLi) in a solution of THF–HMPT by the method of Schwartz and Waters (1972). The crude **21** (10 g) was treated with a methanolic solution of *m*-benzenedisulfonic acid to remove the THP-protecting group. The pure alcohol **22** was obtained after column chromatography on silica gel (eluant, ether–benzene, 15:85) and distillation in 84% yield (5.3 g), bp 118–120°/0.35 mm, n_D^{20} 1.4630 [lit. (Uchida eta l., 1978) bp 122–126/0.65 mm, n_D^{22} 1.4621].

1-Bromo-9-tetradecyne (23). The bromination of **22** (5.2 g, 24 mmol) with bromine (4.8 g, 30 mmol), triphenylphosphine (7.5 g, 30 mmol), and pyridine (5 ml) in dioxane (100 ml), as described by Disselnkotter et al. (1976), gave the crude product **23** in quantitative yield. Column purification on silica gel (eluant, hexane–benzene 1:1) and further distillation afforded pure product **23** (5.4 g) in 84% yield, bp 126–128°/0.1 mm. NMR δ: 3.6 (t, 2H, J = 7 Hz), 2.0 (m, 4H), 1.8–1.2 (m, 16H) 0.9 (t, 3H, J = 7 Hz).

3,13-Octadecadiyn-1-ol (13). To a stirred solution of the lithium salt of the tetrahydropyranyl ether of 3-butyn-1-ol **(16)**, prepared from 3.1 g, 20 mmol of the tetrahydropyranyl ether of 3-butyn-1-ol in 20 ml THF, and 20 mmol *n*-BuLi in hexane at −10 to 0° (the mixture was kept 1 hr at 0°), was added dropwise 4.4 g (16 mmol) of 1-bromo-9-tetradecyne **(23)** in 20 ml HMPT. The deep blue solution was stirred for 0.5 hr at 0°, 2 hr at room temperature, and 1 hr at 40°. The mixture was poured into ice-water, the resulting colorless solution was separated, and the aqueous layer was thoroughly extracted with hexane. The combined organic extracts were washed with water and dried over K_2CO_3. Removal of the solvent gave 5 g (90%) of crude tetrahydropyranyl ether of **13**. The hydrolysis of the protecting group was effected by warming the crude product with *m*-benzenedisulfonic acid in aqueous methanol at 50° for 2 hr and at room temperature overnight to give the free alcohol **13**.

Diyne **13** was worked up in the usual manner and purified by column chromatography on alumina (Woelm, neutral, grade II, eluant ether–benzene, 15:85). The pure fraction (3.5 g, 85%) was distilled (Kugelrohr, bath temperature) at 140–145°/0.01 torr, mp 27–28°. Recrystallization from hexane gave **13** mp 29–30°. Analysis of the acetate of **13** on the HPLC showed that the product was >99% pure [lit. (Doolittle et al., 1980; Uchida et al., 1978) mp 26–27, 27–28°].

Borane Reduction of Diynol 13 to 15 in Solution. The diynol **13** was

reduced with dicyclohexylborane in THF at −5 to 0° for 4 hr and for an additional 2 hr at room temperature, or with disiamylborane for 24 hr at 0°. (Reduction of the diynol **13** with $(Sia)_2BH$ for 6 hr gave a mixture of mono and bis reduction product.)

Products were hydrolyzed with glacial acetic acid at 40–50° for 5 hr and oxidized with 30% H_2O_2 in 6 N NaOH. The dienol was worked up and purified by column chromatography on alumina (grade 2) to give the *Z, Z* isomer in 80–85% yield of >99% purity. HPLC analysis of the acetate (Zorbax ODS column) gave 95–93% of the *Z, Z* isomer.

Polymer-Bound Diol (27). A slurry of 20 g of **2** and 18 g of **26** in 125 ml of pyridine was stirred at room temperature for 48 hr to give polymer **27.** Cleavage of **27** with 0.3 N HCl in dioxane, as previously described (Fyles and Leznoff, 1976), gave 1.1 mmol of **26**/g of **27.**

Polymer-Bound Monomesylate (28). Compound **28** was prepared according to the procedure described for **4** above. Cleavage of **28** as before yielded 0.62 mmol of 1,6-hexanediol monomesylate **(29)**/g of **28.**

Polymer-Bound 7-Octyn-1-ol (30). Compound **30** was prepared according to the procedure described for **6** above. Acid cleavage of **30** gave 0.31 mmol of 7-octyn-1-ol **(31)**/g of **30.**

Reaction of Polymer-Bound 7-Octyn-1-ol (30) with t-BuLi and 3-Octyn-1-yl Mesylate (32). Cleavage of polymer, which formed in the usual coupling reaction described for **9,** from polymer **30,** *t*-BuLi and 3-octyn-1-ol mesylate **(32)** gave only 0.30 mmol/g of the starting alcohol 7-octyn-1-ol **(31).**

Reaction of Lithium Salt of Tetrahydropyranyl Ether of 7-Octyn-1-ol with 1-Bromo-3-octyne (32a). Conditions of the coupling reaction were analogous to those for compound **13.** After the organic layer was separated, washed, dried; the solvent was distilled (short path); and the residue was chromatographed on silica gel. The first component isolated from the column (eluant pentane) as a colorless oil was 1-octen-3-yne **(33).** The physical and spectroscopic data were identical with those described by Anzilotti (1939). The compound eluted with benzene was the starting tetrahydropyranyl ether of 7-octyn-1-ol.

Polymer-Bound 7,11-Dodecadiyn-1-ol (35). The coupling reaction was carried out as for **12,** but the reaction mixture was stirred for 1 hr at room temperature and 1 hr at 40°. The product after cleavage was isolated by preparative TLC (solvent ether–benzene, 3 : 7) to give 30 mg (0.17 mmol/g) of 7,11-dodecadiyn-1-ol **(36).**

Polymer-Bound 7,11-Hexadecadiyn-1-ol (37). Polymer **37** was prepared in a typical procedure described above from the lithium salt of polymer-bound 7,11-dodecadiyn-1-ol and butyl bromide and in a separate experiment from polymer-bound 1,6-hexanediol monomesylate **(28)** and 1-lithio-1,5-decadiyne **(38).** After cleavage and purification using flash chromatography (Still,

1978), 30 mg (0.12 mmol/g) of 7,11-hexadecadiyn-1-ol (**39**) was isolated in the first experiment, and 50 mg (0.21 mmol/g) of **39** in the second.

Polymer-Bound (Z,Z)-*7,11-Hexadecadien-1-ol (40).* Reduction of the polymer **37** as for **12** gave **40.**

(Z,Z)-*7,11-Hexadecadien-1-ol (41).* Acid cleavage of 1 g of **40** gave 39 mg or 0.16 mmol/g of (*Z,Z*)-7,11-hexadecadien-1-ol (**41**). HPLC analysis of the acetate, prepared as before, using the μBondapak C_{18} column showed only a single peak (>99% purity), but isomers were separated on a Zorbax ODS column. Analysis by HPLC showed that reduction of diynols **37** and **39** with dicyclohexylborane gave dienols of higher stereochemical purity (93–96%) than reduction with disiamylborane (90%).

RESULTS AND DISCUSSION

The solution-phase synthesis of **1** by Doolittle et al. (1980) used 1-chloro-8-iodooctane prepared in 41% yield from the symmetrical 1,8-dichlorooctane, while an alternate synthesis by Uchida et al. (1979) used the tetrahydropyranyl ether of 8-chlorooctan-1-ol, itself prepared from the symmetrical 1,8-octanediol. Polymer-bound trityl chloride (**2**) reacted with excess 1,2-ethanediol to give the monoreacted polymer-bound monotrityl ether of 1,2-ethanediol (**3**) by methods previously described (Fyles and Leznoff, 1976). Subsequent reaction of **3** with methanesulfonyl chloride (MsCl) in methylene chloride and triethylamine (Svirskaya et al., 1979) yielded the polymer-bound monotrityl ether of 1,2-ethanediol monomesylate (**4**). This modified mesylation procedure affords the monomesylate **4** in high yield as acid cleavage (Svirskaya et al., 1979; Leznoff et al., 1977) of **4** liberates 0.61 mmol of 1,2-ethanediol monomesylate (**5**) per g of polymer **4.** Coupling of **4** with the lithium acetylide-ethylenediamine (LiC≡CH·EDA) complex in 2:1 tetrahydrofuran (THF)–hexamethylphosphoric triamide (HMPT) yielded the polymer-bound trityl ether of 3-butyn-1-ol (**6**). Alternatively, **2** reacted directly with commercially available 3-butyn-1-ol (**7**) to give **6** in one step, but from the more expensive precursor **7.** Treatment of **6** with *n*-BuLi and a large excess of the symmetrical 1,8-dibromooctane (**8**) led to the polymer-bound bromoalkyne (**9**). Acid cleavage of **9** gave 12-bromo-3-dodecyn-1-ol (**10**) in 54% yield based on **4** and showed that **9** contained at least 0.33 mmol of **10** per gram of polymer **9.** Coupling of **9** with 1-lithiohexyne (**11**) in THF-HMPT gave the polymer-bound diyne (**12**). Acid cleavage of **12** gave 3,13-octadecadiyn-1-ol (**13**) in 82% yield based on polymer **9.** Reduction of **12** with dicyclohexylborane (Zweifel and Polston, 1970) or disiamylborane (Brown and Zweifel, 1961) yielded the polymer-bound *cis,cis*-diene **14.** Acid cleavage of **14** gave (*Z,Z*)-3,13-octadecadien-1-ol (**15**) in 67% yield based on polymer **12.** Acetylation of **15** gave **1** (Figure 1) in nearly quantitative yield.

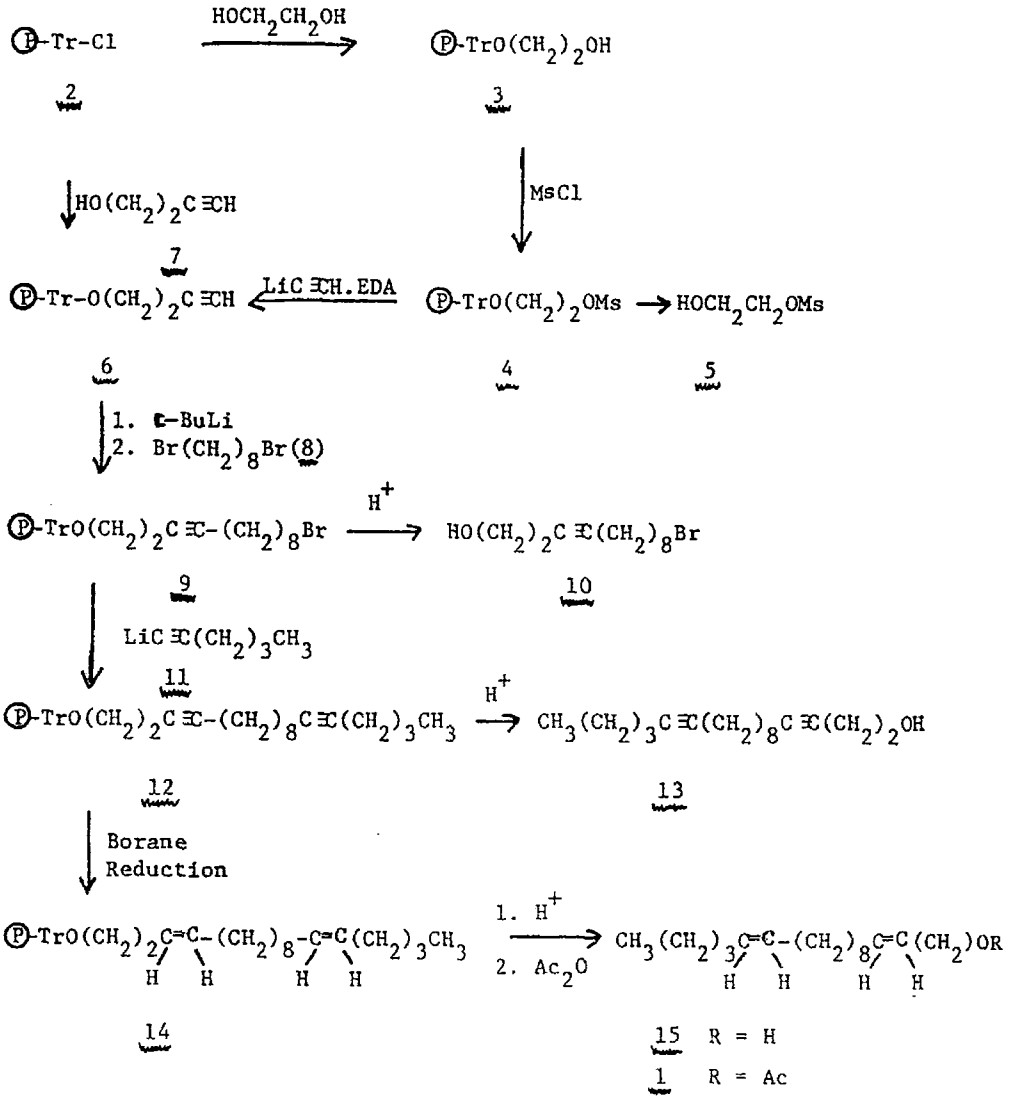

FIG. 1.

The seven step synthesis of **1** on insoluble polymer supports in an overall yield of 30% represents a synthesis long enough to set up for the automated procedures possible in solid-phase methodology. In addition, the use of the solid phase to monoprotect 1,2-ethanediol to form **3**, to monoreact with 1,8-dibromooctane **(8)**, and to facilitate the work-up of the borane reduction step leading to **14** (hydrogen peroxide does not have to be used to make borane impurities water soluble) illustrates some of the advantages of solid-phase synthesis of diolefinic pheromones.

As a control to the solid phase synthesis of **1**, we prepared **1** by solution methods related to, but not identical with, those previously described (Doolittle et al., 1980; Uchida et al., 1978) and to our solid-phase method

described above. Treatment of the lithium salt of the tetrahydropyranyl ether of 3-butyn-1-ol **(16)** with a large excess of the symmetrical 1,8-dibromooctane **(8)** in THF-HMPT gave the tetrahydropyranyl ether of 12-bromo-3-dodecyn-1-ol **(17)** in only 23% yield accompanied by many by-products, despite the fact that a similar sequence of reactions gave a monobromoalkyne in high yield from a symmetrical dibromo compound using the dihalide in excess (Burgstahler et al., 1977). This similar reaction was accomplished on solid phases in 54% yield with the additional advantage that the product was purified by simple filtration, the by-products and excess dihalide remaining in the filtrate. In a second synthetic approach to **1** in solution, 1,8-octanediol **(18)** was converted to 8-chloro-1-octanol **(19)** and hence to 8-chloro-1-octanol tetrahydropyranyl ether **(20)**. Coupling of **20** with 1-lithio-1-hexyne **(11)**, as before, yielded the tetrahydropyranyl ether of 9-tetradecyn-1-ol **(21)**. Acid hydrolysis of **21** gave 9-tetradecyn-1-ol **(22)** in 84% yield from **20** as shown in Figure 2. Conversion of **22** into 1-bromo-9-tetradecyne **(23)** with bromine and triphenylphosphine in pyridine (Disselnkötter et al., 1976) was achieved in 84% yield. This procedure represents an improvement over previous methods (Doolittle, 1980; Uchida, 1978). Coupling of **23** with **16**, as before, followed by acid hydrolysis, gave 3,13-octadecadiyn-1-ol **(13)** in 85% yield. Reduction of **13** with dicyclohexylborane or disiamylborane, as above, yielded (*Z*, *Z*)-3,13-octadecadien-1-ol **(15)** in 85% yield. Acetylation of **15** yielded **1** in nearly quantitative yield.

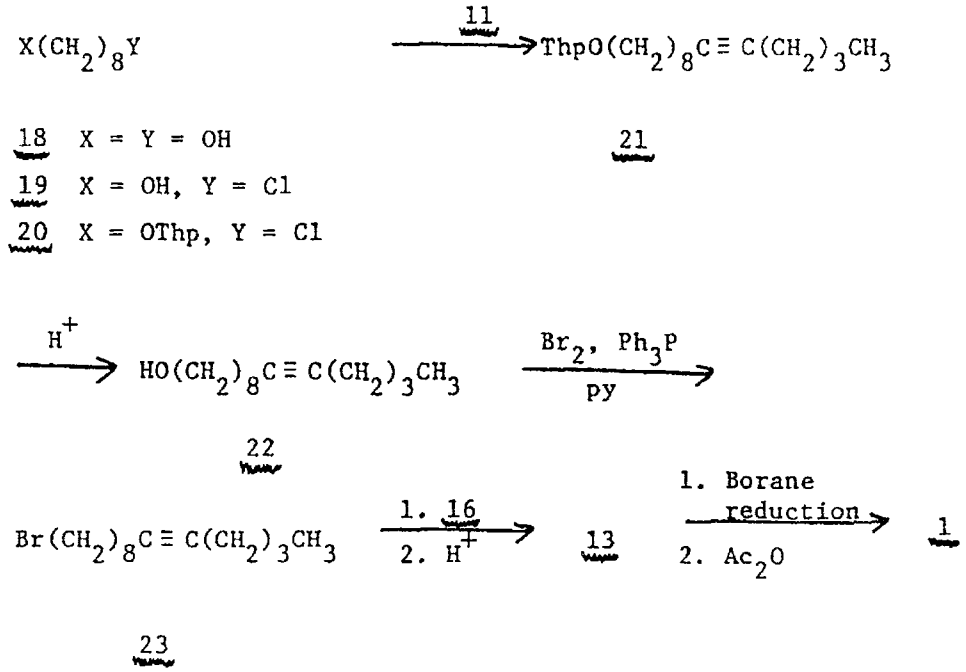

FIG. 2.

The almost identical approach to the synthesis of **15** on polymer supports and in solution via the symmetrical **8** favors the solid-phase approach. The much better solution-phase synthesis of **1** (Figure 2) went in 32% yield based on the symmetrical **18** and **16** in eight steps. The polymer-based synthesis gave **15** in 30% overall yield from **8** and **16** in only five steps, or from **8** and the more simple 1,2-ethanediol in seven steps with the advantages outlined before. The main disadvantage of polymer-based synthesis arises from the fact that the solid-phase syntheses work more efficiently using polymers containing only 10–25% of the phenyl groups of **2** functionalized and hence reaction volumes tend to be five to ten times larger than comparable reactions in solution. One long standing problem in organic synthesis on polymer supports has been recently alleviated using [^{13}C]NMR spectroscopy (Jones et al., 1982). In fact, we have recently characterized polymer-bound trityl alcohol (**2**, Cl=OH), **3**, **4**, **6**, and **9** by this method. Cleavage of a polymer-bound substrate from the polymer still remains the major quantitative method of evaluating the yield of each reaction step.

The solid-phase synthesis of (*Z*, *Z*)-7,11-hexadecadien-1-yl acetate **(24)**, a sex pheromone component of the pink bollworm moth, *Pectinophora gossypiella*, has been reported by many synthetic routes (Henrick, 1977; Rossi, 1977; Disselnkötter, 1976; Su, 1974; Sonnet, 1979; Mori, 1975; Anderson, 1975) in solution. In the same retrosynthetic analysis of **24** as that described above for **1**, the symmetrical synthon in the middle of the molecule is simply 1,2-dibromoethane **(25)**. We felt, however, that the coupling of an acetylene to **25** would give a β-bromoacetylenic intermediate, which on subsequent reaction would lead to elimination instead of coupling. This prediction was in fact borne out, as shown in Figure 3.

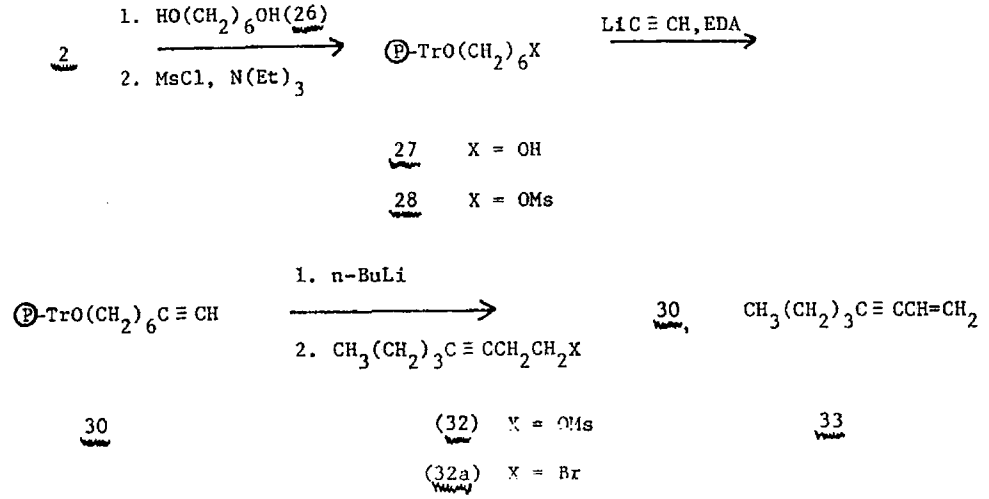

FIG. 3.

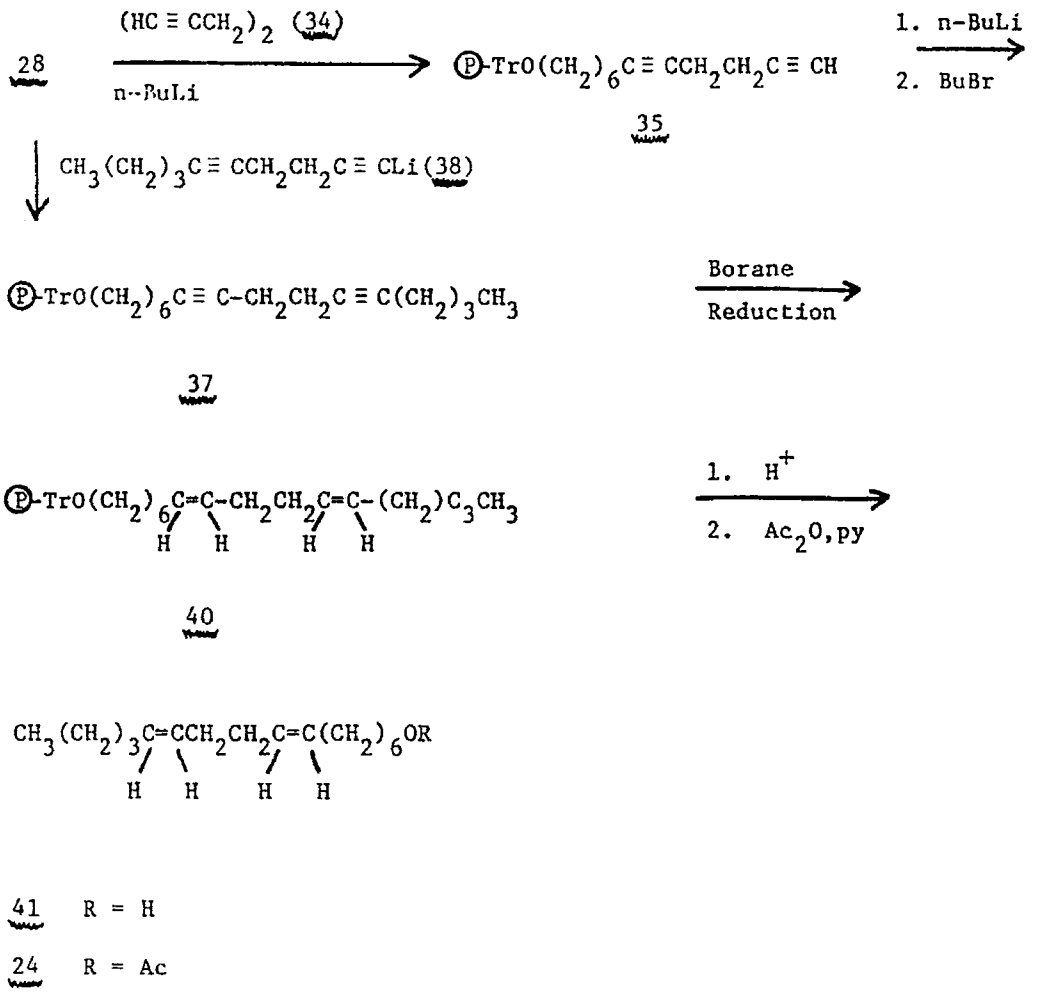

FIG. 4.

Thus polymer **2** reacted with 1,6-hexanediol **(26)** at one end only to give the polymer-bound monotrityl ether of 1,6-hexanediol **(27)** (Svirskaya et al., 1979; Fréchet, 1981) which was mesylated, as for **4**, to give the polymer-bound monotrityl ether of 1,6-hexanediol monomesylate **(28)** (Leznoff et al., 1977). Acid cleavage of **28** liberated 0.62 mmol of 1,6-hexanediol monomesylate **(29)**. Treatment of **28** with the lithium acetylide complex, as before, gave the polymer-bound monotrityl ether of 7-octyn-1-ol **(30)**. Acid cleavage of **30** gave 7-octyn-1-ol **(31)** (Ames and Goodburn, 1967) in 50% yield based on **28**. When **30** reacted with *t*-BuLi and 3-octyn-1-yl mesylate **(32)**, only **30** was recovered. In a model reaction, 1-bromo-3-octyne **(32a)** (Disselnkötter et al., 1976) reacted with *n*-BuLi to give the known elimination product 1-octen-3-yne **(33)** (Anzilotti and Vogt, 1939). Thus, 1,2-dibromoethane would not be a suitable symmetrical intermediate for the synthesis of 1,4-diynes. Another symmetrical synthon derived from **24** can be envisioned, namely, 1,5-

hexadiyne **(34)**. Thus, treatment of **28** with the lithium salt of **34** led to the polymer-bound trityl ether of 7,11-dodecadiyn-1-ol **(35)**. Acid cleavage of **35** gave 7,11-dodecadiyn-1-ol **(36)** in 27% yield based on **28**. Subsequent coupling of **35** with *n*-BuLi and butyl bromide gave polymer-bound trityl ether of 7,11-hexadecadiyn-1-ol **(37)**. Alternatively **37** was prepared by direct coupling of **28** with *n*-BuLi and 1,5-decadiyne **(38)**. Acid cleavage of **37** liberated 0.21 mmol of 7,11-hexadecadiyn-1-ol **(39)** per g showing that **37** was formed in 37% yield using **38** but in only 20% yield using **34**. Borane reduction of **37** via **38**, as before, gave the polymer-bound trityl ether of (*Z*, *Z*)-7,11-hexadecadien-1-ol **(40)**. Acid cleavage of **40** afforded (*Z*, *Z*)-7,11-hexadecadien-1-ol **(41)** in 67% yield based on polymer **37**. Acetylation of **41** gave the desired pheromone **24** in high yield (Figure 4).

The overall yields of **24** synthesized via **38** on solid phases, as shown in Figure 4, are similar to the yields obtained by similar solution methods. The advantages and disadvantages of solid-phase synthesis were similar to those described above for the synthesis of **1**, except that for 1,4-diynes, one cannot use the inexpensive symmetrical dihalide. Unfortunately the symmetrical synthon **34** gives low yields, probably due to allenic impurities (Mori et al., 1975). Analysis of **1** and **24** by high-pressure liquid chromatography (HPLC) showed that all the products exhibited not less than 90% and more commonly 93–98% of the *cis, cis* isomer. The stereochemical purity of **1** was identical when **1** was synthesized by solid phase or solution methods.

The syntheses of **1** and **24** demonstrate a practical synthesis of unconjugated diolefinic pheromones using solid-phase methodology. Furthermore, one can see that unconjugated tri-, tetra-, and oligoacetylenic compounds can be prepared by the repetitive additions of symmetrical difunctionalized synthons to a growing polymer-bound hydrocarbon chain.

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