Stereoselectivity of the Rearrangement of Allyl Siloxyvinyl Ethers. A Highly Stereoselective Synthesis of a Diol Found in the Pheromonal Secretion of the Queen Butterfly

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The [3,3] rearrangement of 3-acetoxy-2-methyl-1-nonene (**1b**), derivatized as the trimethylsiloxyvinyl ether, proceeds in moderate yield (*ca.* 53%) but with very high stereoselectivity (>98%) to give the β,γ-unsaturated acid **2a**. Rearrangement of the *tert*-butyldimethylsiloxyvinyl ether derivative proceeds in higher yield (80%), also with very high stereoselectivity. This rearrangement has been used in a stereoselective synthesis of a terpenoid diol (**8**) found in the phermonal secretion of the queen butterfly, in six steps from geraniol.

Several variants of the [3,3]-Claisen-type rearrangements of allylic ethers have been applied over the past few years to the stereoselective synthesis of trisubstituted olefinic systems.[1] Elegant extensions of this reaction to the repetitive 1,5-diene synthesis have been worked out by Faulkner and his associates.[2] More recent has been the description of rearrangements of enolates[3,4] or enolate equivalents[3] of allylic acetates or thioacetate derivatives.[5] A notable feature of these enolate rearrangements, which would be of advantage in certain systems, is that they proceed at moderate temperatures, under basic conditions, while rearrangement of the ethers requires warming in acid media.

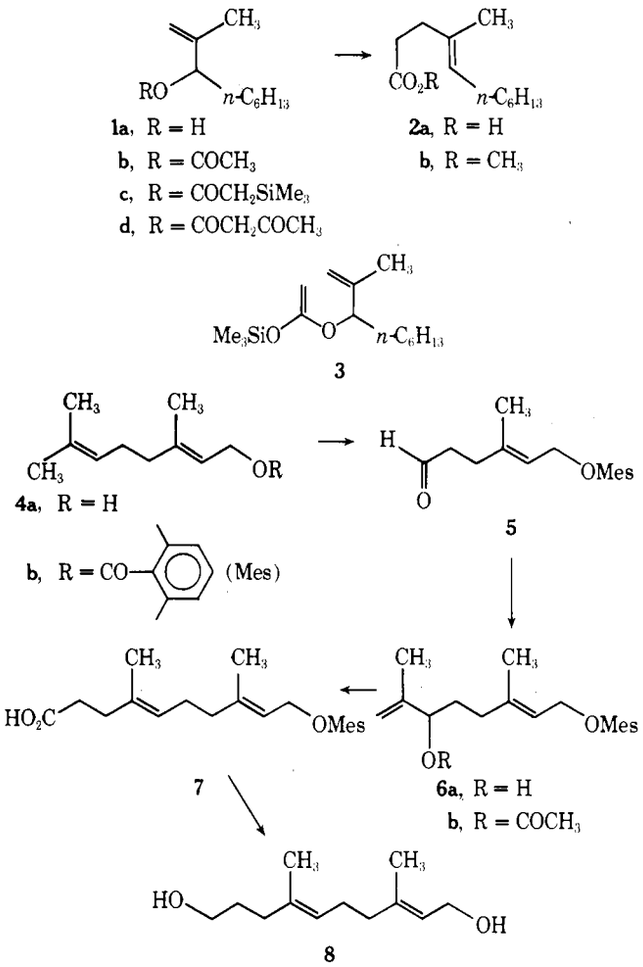
We were intrigued by the report of Ireland[3] that enol silyl ether derivatives of allylic acetates undergo a [3,3]-Claisen-type rearrangement to give β,γ-unsaturated acids under mild conditions. The strategic location of the bulky trimethylsilyl ether function[6] and the mild reaction conditions suggested that this particular rearrangement might proceed with a stereoselectivity[7] greater than the nominal 90–96% generally obtained in such rearrangements. None of the systems detailed by Ireland, however, were of suitable stereochemistry to evaluate this reaction as a method for stereoselective trisubstituted olefin synthesis.

In this report we describe an investigation of this rearrangement in a model system to rigorously establish the minimum reaction temperature and the maximum degree of stereoselectivity. The synthesis of the Queen Butterfly pheromone, using this allyl siloxyvinyl ether rearrangement as the key step, is also described.

Results and Discussion

Rearrangement of 3-Acetoxy-2-methyl-1-nonene (1b). The rearrangement of 3-acetoxy-2-methyl-1-nonene (**1b**), a trisubstituted olefin precursor, was investigated under the conditions described by Ireland.[3] The enol silyl ether was generated using 1.1 equiv of lithium isopropylcyclohexylamide in THF at −78°, followed by 1.05 equiv of trimethylsilyl chloride. Two major products were obtained after the reaction mixture was stirred for 2 hr at 70°. Chromatographic separation on silica gel produced the carboxylic acid (**2a**) and the C-silylated acetate (**1c**). The acid can also be conveniently isolated in 53% yield by extraction into Claisen's alkali[8] causing hydrolysis of **1c** to **1a**. Thus, the yield of rearranged product based on recovered precursors is over 90%. A temperature study showed that the rearrangement was complete within 2 hr at room temperature, but not at 0 or −78°.

We endeavored to improve the yield by increasing the amount of O-silylation relative to C-silylation. Rathke has reported that treatment of lithium enolates derived from acetates with *tert*-butyldimethylsilyl chloride (TBS) in THF–HMPA solutions gave exclusively O-silylated products.[9] Treatment of the lithium enolate of **1b** with TBS and subsequent hydrolysis of the rearranged silyl ester by stirring with acetic acid[10] at room temperature (the trimethylsilyl ester completely hydrolyzes upon washing with 10% HCl) gave **2a** in 80% yield.



Both trimethylsilyl chloride and TBS give rearranged acids with very high stereoselectivity. Nmr analysis of the crude acid shows only one allylic methyl at δ 1.59, consistent with an *E*-type stereochemistry of the trisubstituted olefin (*Z*-type allylic methyl groups generally resonate at 1.67–1.70).[11] Glpc analysis of the methyl ester **2b** (from **2a** with diazomethane) showed it to be identical with the minor component (*E*) of the isomeric esters prepared by the Wittig condensation between levulinic acid and heptylidine triphenylphosphorane. Less than 1% of the *Z* isomer of **2b** was evident upon glpc analysis, indicating a stereoselectivity[7] of greater than 98%.

If the silyl chlorides are omitted from the reaction, a small amount (5–10%) of the rearranged acid is formed; however, the principal products are the allylic alcohol **1a** and the allylic acetoacetate **1d**, resulting from Claisen condensation of the ester enolate. No Claisen condensation product was ever detected under normal conditions (inclusion of the silyl chlorides). In the absence of either silyl chloride the stereoselectivity of the rearrangement of **1b** drops to 85%, which is consistent with predictions of Faulkner and Perrin.[6]

Synthesis of a Queen Butterfly Pheromonal Component. The allyl siloxyvinyl ether rearrangement was utilized in a six-step stereoselective synthesis of a queen butterfly pheromonal component (**8**).[12] The distribution of functionality in this compound makes its synthesis by the Claisen-type rearrangement attractive.

Treatment of geraniol (**4a**) with mesitoyl chloride in pyridine gave geranyl mesitoate **4b** in 80% yield.[13] Ozonolysis of the mesitoate with 1.2 equiv of ozone gave the aldehyde **5** in 30% yield. Since ozonolysis of geranyl acetate under similar conditions produces the related aldehyde in a higher yield (50–60%),[14] it appears that the mesitoate group is less effective in deactivating the allylic double bond toward oxidation. Treatment of the aldehyde **5** with 2 equiv of isopropenylmagnesium bromide at room temperature for 2 hr gave the alcohol **6a**[15] which was generally converted directly to the acetate **6b** (70% overall).

The Claisen-type rearrangement of **6b** using TBS gave the acid **7** in a 70% yield. Treatment of the acid with excess lithium aluminum hydride both reduces the acid function and cleaves the mesitoate, producing the pheromone **8** in 86% after column chromatography.[16] The spectroscopic properties of this material are fully consistent with its assigned structure, and its bis(α-naphthyl)urethane melts at 128–129.5° (lit.[12c] 127–129°).

Conclusion

The high stereoselectivity observed in the rearrangement of allyl siloxyvinyl ethers to β,γ-unsaturated acids follows the stereochemical predictions based on a chair cyclohexane-like transition state.[6] Good yields are obtained under conditions where the enolate can be selectively O-silylated. The particular utility of this rearrangement reaction is that it proceeds under very mild, nonacidic conditions, using stable, conveniently prepared starting materials.

Experimental Section

Tetrahydrofuran (THF) was dried by distillation from sodium naphthalide. Isopropylcyclohexylamine was distilled from calcium hydride and stored under nitrogen. Hexamethylphosphoramide (HMPA) was distilled from sodium hydride and stored over molecular sieves. Geraniol and 2-bromopropene were obtained from Chemical Samples Co. and used without further purification. Levulinic acid was obtained from Eastman Organics and distilled prior to use. Practical grade heptanal was purchased from Matheson Coleman and Bell and used without further purification. Dimethyl sulfide was from Aldrich. Isopropenylmagnesium bromide solutions in THF were prepared from 2-bromopropene and magnesium and were standardized by the method of Gilman.[17] They were stored under nitrogen in flasks capped with rubber septa. Diazomethane was freshly prepared as alcohol-free ethereal solutions from *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (Diazald, Aldrich) using preparation II as given. Claisen's alkali was prepared as described by Fieser and Fieser.[8] Ozone was generated in a Welsbach Ozonizer (Model T-816); the rate of ozone production was calibrated before use by iodometric titration. A standard procedure for product isolation was used in all reactions: drying of the organic layer over anhydrous magnesium sulfate, filtration, and evaporation of the solvent under reduced pressure on a rotary evaporator. Nmr spectra were recorded on a Varian A-60 spectrometer, and all chemical shifts are given in parts per million downfield from tetramethylsilane (δ scale). Infrared spectra were run on a Perkin-Elmer Model 521 spectrometer. Mass spectra were recorded on a Varian-MAT CH-5 spectrometer. Elemental analyses were performed by the microanalytical service of the University of Illinois.

Analytical glpc analyses were done on a Hewlett-Packard 5750 instrument fitted with flame ionization detectors using a carrier gas (N_2) flow of 30 ml/min. The column used was a 0.125 in. × 20 ft, 5% SE-30 column on an acid-washed dimethyldichlorosilane-treated 80–100 mesh Chromosorb W support. The preparative glpc separation was done on a Varian Aerograph Model 90-P3 chromatograph with a thermal conductivity detector using a carrier gas (He) flow of 120 ml/min. The column used was a 0.375 in. × 10 ft, 15% SE-30 on a 60–80 mesh Chromosorb W support.

3-Hydroxy-2-methyl-1-nonene (1a). Magnesium (8.85 g, 0.37 g-atom) was added to 70 ml of THF along with a few crystals of iodine. A small amount (<1 ml) of 2-bromopropene was added and the mixture stirred at 25° under nitrogen until Grignard formation had begun. The remaining bromide (29.7 g, 0.24 mol) was added dropwise at such a rate as to maintain gentle reflux. After the mixture was stirred for 1 hr at 25°, heptanal (23.4 g, 0.20 mol) in 30 ml of THF was added dropwise. The reaction was stirred overnight at 25°, and then saturated ammonium chloride added to quench the reaction. The precipitate which formed was filtered and washed with ether, and the combined filtrates were washed with saturated sodium chloride. Product isolation gave 29.7 g of an oil. Distillation produced 23 g (72%) of the alcohol **1a:** bp 68–71° (0.3 mm); ir (CCl_4) 3618 (OH) and 1650 cm^{-1} (C=C); nmr (CCl_4) δ 0.93 (m, 3 H), 1.05–1.65 (br s, 10 H), 1.72 (s, 3 H, allylic coupling barely visible), 2.06 (s, 1 H), 4.01 (t, 1 H), and 4.85 (m, 2 H).

Anal. Calcd for $C_{10}H_{20}O$: C, 76.86; H, 12.90. Found: C, 76.63; H, 12.76.

3-Acetoxy-2-methyl-1-nonene (1b). A solution of alcohol **1a** (7 g, 0.045 mol), acetic anhydride (13.8 g, 0.135 mol), and pyridine (35.5 g, 0.450 mol) was stirred for 40 hr at 25°. The reaction mixture was then poured into ice water, and the aqueous layer was extracted three times with ether. The combined organic extracts were washed with 10% HCl, 10% $NaHCO_3$, water, and saturated sodium chloride. Chromatography on silica gel (16% ether in hexane) gave 8.11 g (92%) of the acetate **1b:** ir (CCl_4) 1745 (C=O), 1650 (C=C), 1460, 1370, 1245 (C—O), and 1020 cm^{-1}; nmr (CCl_4) δ 0.93 (m, 3 H), 1.09–1.61 (m, 10 H), 1.69 (s, 3 H, allylic coupling barely visible), 1.96 (s, 3 H), 4.80 (m, 2 H), and 5.07 (t, J = 6.5 Hz, 1 H).

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.62; H, 11.29.

(*E*)-4-Methyl-4-undecenoic Acid (2a)–Trimethylsilyl Chloride Method. A solution of 10 ml of THF and isopropylcyclohexylamine (1.5 g, 10.6 mmol) was cooled to −78° under nitrogen and was treated with a 1.25 *M* (8.25 ml, 10.6 mmol) solution of *n*-BuLi followed by the addition of **1b** (2 g, 10.1 mmol). The reaction mixture was stirred for 10 min, and trimethylsilyl chloride (1.1 g, 10.3 mmol) was added. After the mixture was warmed to 70° over a 30-min period and stirred for 2 hr (precipitate evident), it was cooled and diluted with ether. The ether was extracted twice with 10% HCl, and the product was isolated to give a yellow oil. Chromatography on silica gel (18% ether in hexane, then 50% ether in hexane) gave 1.05 g (53%) of the acid **2a.**

Treatment of **2a** with diazomethane produced the methyl ester **2b.** The ester was analyzed by glpc (182°), and it was found to contain *ca.* 0.7% of the *Z* isomer. An analytical sample was obtained by preparative tlc on silica gel (16% ether in hexane): ir (CCl_4) 1740 (C=O), 1458, 1438, and 1150 cm^{-1}; nmr (CCl_4) δ 0.93 (m, 3 H), 1.26 (br s, 8 H), 1.59 (s, 3 H), 1.95 (m, 2 H), 2.28 (s, 4 H), 3.59 (s, 3 H), and 5.13 (t, J = 7 Hz, 1 H).

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.51; H, 11.39.

***tert*-Butyldimethylsilyl Chloride Method.** A solution of 3 ml of THF and isopropylcyclohexylamine (456 mg, 3.3 mmol) was cooled to −78° under nitrogen and was treated with a 1.9 *M* (1.74 ml, 3.3 mmol) solution of *n*-BuLi followed by the addition of **1b** (594 mg, 3 mmol). After the reaction was stirred for 10 min, HMPA (0.45 ml) and *tert*-butyldimethylsilyl chloride in 0.5 ml of THF (475 mg, 3.15 mmol) were added to it. The reaction was warmed to 70° over a 30-min period and was stirred for 2 hr. Then 15 ml of acetic acid, 5 ml of water, and 2 ml of THF were added and the solution was stirred for 12 hr at 25°. After the reaction mixture was diluted with ether, it was extracted with water and the product was isolated to give 956 mg of a yellow oil. Chromatography on silica gel (20% ether in hexane, then 25% ether in hexane) gave 475 mg (80%) of the acid **2a.** The acid was characterized as its

methyl ester **2b** (CH_2N_2), and it had spectral properties identical with the ester **2b** produced by the trimethylsilyl chloride method above.

***E* and *Z* Isomers of 4-Methyl-4-undecenoic Acid (2a).** To a mixture of heptyl triphenylphosphonium bromide (20 g, 45.4 mmol) and 100 ml of THF at 0° under nitrogen was added a 2.31 *M* (19.7 ml, 45.4 mmol) solution of *n*-BuLi, producing a red solution of ylide which was stirred for 2 hr at 25°. A precipitate appeared upon the addition of levulinic acid (2.63 g, 22.7 mmol), and the mixture was refluxed for 67 hr. The reaction was cooled to 25°, acidified with 10% HCl, and extracted three times with ether. Product isolation from the combined extracts gave 3.8 g of a yellow oil. Chromatography on silica gel (18% ether in hexane, then 50% ether in hexane) produced 922 mg (20%) of a mixture of the *E* and *Z* isomers of 4-methyl-4-undecenoic acid. Analysis of the esterified (CH_2N_2) mixture by glpc (182°) showed the *Z*/*E* ratio as 2/1. The isomers were separated by preparative glpc (150°): nmr (*E* isomer) (CCl_4) δ 0.93 (m, 3 H), 1.26 (br s, 8 H), 1.59 (s, 3 H), 1.95 (m, 2 H), 2.28 (s, 4 H), 3.59 (s, 3 H), and 5.13 (t, *J* = 7 Hz, 1 H); nmr (*Z* isomer) (CCl_4) δ 0.93 (m, 3 H), 1.27 (br s, 8 H), 1.66 (s, 3 H, cisoid allylic coupling barely visible), 1.94 (m, 2 H), 2.25 (s, 4 H), 3.57 (s, 3 H), and 5.08 (t, *J* = 7 Hz, 1 H).

(*E*)-8-Mesitoyloxy-2,6-dimethyl-2,6-octadiene (geranyl mesitoate) (4b) was prepared in 80% yield from geraniol and mesitoyl chloride[18] as previously described.[13]

(*E*)-6-Mesitoyloxy-4-methyl-4-hexenal (5). A solution of geranyl mesitoate (**4b**) (10 g, 33 mmol) and 600 ml of methanol was cooled to −78° and ozone (36.9 mmol) was passed through. After adding excess dimethyl sulfide to the reaction mixture at −78°, it was stirred for 12 hr at 25°. Evaporation of the dimethyl sulfide and methanol left a residue which was diluted with ether, and the ether was washed with water and saturated sodium chloride. Product isolation and chromatography on silica gel (16.6% ether in hexane) gave 2.65 g (30%) of the desired aldehyde **5** and 2.3 g of starting material. An analytical sample was obtained by preparative tlc on silica gel (30% ether in hexane, two developments): ir (CCl_4) 2720 (aldehyde C—H), 1725 (aldehyde and ester C=O), 1615, 1445, 1263, 1169, and 1080 cm^{-1}; nmr (CCl_4) δ 1.77 (s, 3 H), 2.22 (s, 9 H), 2.38 (m, 4 H), 4.73 (d, *J* = 7 Hz, 2 H), 5.45 (t, *J* = 7.5 Hz, 1 H), 6.75 (s, 2 H), and 9.66 (t, *J* = 1 Hz, 1 H); mass spectrum (70 eV) *m/e* (rel intensity) 274 (M^+, 2), 164 (12), 148 (13), 147 (M − OR, 100), 146 (31), 119 (M − CO_2R, 19), 110 (M − mesitoic acid, 7), 93 (30), 55 (30), 43 (41), and 31 (69).

Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.31; H, 8.17.

(*E*)-3-Hydroxy-8-mesitoyloxy-2,6-dimethyl-1,6-octadiene (6a). A 1.28 *M* solution (6.25 ml, 8 mmol) of isopropenylmagnesium bromide was treated dropwise at 25° with a solution of **5** (1 g, 3.6 mmol) and 7 ml of THF, and the reaction was stirred under nitrogen for 2 hr. The reaction was quenched with saturated ammonium chloride and extracted twice with ether. Product isolation from the combined organic extracts gave 1.04 g of the crude alcohol **6a.** An analytical sample was obtained by preparative tlc on silica gel (30% ether in hexane, two developments): ir (CCl_4) 3622 (OH), 1722 (C=O), 1612, 1442, 1257, 1162, and 1072 cm^{-1}; nmr ($CDCl_3$) δ 1.53–2.22 (m, 11 H), 2.27 (s, 9 H), 4.05 (t, *J* = 6 Hz, 1 H), 4.75–5.00 (m, 4 H, CH_2=CCH_3 and CH_2OCO), 5.53 (t, *J* = 7.5 Hz, 1 H), and 6.81 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 316 (M^+, 0.18), 298 (M − H_2O, 0.73), 165 (21), 164 (86), 152 (M − mesitoic acid, 37), 151 (16), 148 (28), 147 (100), 146 (67), 119 (42), 93 (28), 81 (27), 55 (26), and 43 (39).

Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.64; H, 8.91.

(*E*)-3-Acetoxy-8-mesitoyloxy-2,6-dimethyl-1,6-octadiene (6b). A dark red solution of crude alcohol **6a** (1.04 g, *ca.* 3.5 mmol) and 10 ml of pyridine was treated with acetic anhydride (1.30 g, 12.7 mmol), and the reaction mixture was stirred for 12 hr at 25°. The reaction mixture was poured into ice water, and the water extracted three times with ether. The combined organic extracts were washed with 10% HCl, 10% $NaHCO_3$, water, and saturated sodium chloride. Product isolation gave 1.2 g of a dark red oil. Chromatography on silica gel (16.6% ether in hexane) gave 900 mg (69% from **5**) of a colorless oil: ir (CCl_4) 1740 and 1727 (C=O), 1612, 1445, 1260 and 1240 (C—O), 1168, and 1078 cm^{-1}; nmr (CCl_4) δ 1.53–1.88 (m, 8 H), 1.89–2.18 (m, 2 H, allylic methylene), 2.06 (s, 3 H, $COCH_3$), 2.27 (s, 9 H), 4.7–5.03 (m, 4 H), 5.18 (t, *J* = 6.5 Hz, 1 H), 5.53 (t, *J* = 7.5 Hz, 1 H), and 6.81 (s, 2 H); mass spectrum (70 eV) *m/e* (rel intensity) 358 (M^+, 0.76), 299 (M − OAc, 8), 195 (6), 148 (11), 147 (100), 146 (18), 135 (11), 134 (11), 119 (21), 93 (14), 55 (18), and 43 (37).

Anal. Calcd for $C_{22}H_{30}O_4$: C, 73.71; H, 8.41. Found: C, 73.77; H, 8.51.

(*E,E*)-10-Mesitoyloxy-4,8-dimethyl-4,8-decadienoic Acid (7). A solution of 1 ml of THF and isopropylcyclohexylamine (131 mg, 0.92 mmol) was cooled to −78° under nitrogen and was treated with a 2.06 *M* (0.45 ml, 0.92 mmol) solution of *n*-BuLi. The solution was stirred for 20 min, and **6b** (300 mg, 0.84 mmol) was added producing a red solution. HMPA (0.15 ml) was then added followed by the addition of *tert*-butyldimethylsilyl chloride (132 mg, 0.88 mmol) in 0.5 ml of THF, and the reaction was warmed to 25° over a 30-min period. After stirring the reaction mixture for 3 hr, it was diluted with ether and extracted with 10% HCl and Claisen's alkali. Dropwise acidification at 0° of the alkaline extract with 10% HCl and extraction with ether gave 260 mg of the acid **7** after product isolation. Chromatography on silica gel (40% hexane in ether) gave 210 mg (70%) of pure **7**: nmr ($CDCl_3$) δ 1.63 (s, 3 H), 1.77 (s, 3 H), 2.08 (m, 4 H), 2.28 (s, 9 H), 2.38 (s, 4 H, $HO_2CCH_2CH_2$), 4.81 (d, *J* = 7 Hz, 2 H), 5.20 (m, 1 H), 5.50 (t, *J* = 8 Hz, 1 H), and 6.81 (s, 2 H).

Treatment of **7** with diazomethane gave the corresponding methyl ester. An analytical sample was obtained by preparative tlc on silica gel (30% ether in petroleum ether, two developments): ir (CCl_4) 1744 and 1728 (C=O), 1616, 1438, 1262, 1168, and 1076 cm^{-1}; nmr ($CDCl_3$), identical with **7** except for the addition of δ 3.64 (s, 3 H); mass spectrum (70 eV) *m/e* (rel intensity) 372 (M^+, 0.58), 208 (M − mesitoic acid, 11) 164 (12), 148 (13), 147 (100), 146 (23), 121 (17), 119 (23), 81 (35), 80 (35), and 43 (14).

Anal. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 74.24; H, 8.76.

(*E,E*)-3,7-Dimethyl-2,6-decadiene-1,10-diol (8). A 0.67 *M* (5.57 ml, 3.74 mmol) filtered solution of lithium aluminum hydride was treated with a solution of **7** (134 mg, 0.37 mmol) in a small amount of THF, and the reaction mixture was stirred under nitrogen for 40 min at 70°. The reaction was quenched at 0° with ethyl acetate, and it was diluted with saturated ammonium chloride. After the mixture was extracted twice with ether, the product was isolated from the combined ether extracts and was chromatographed on silica gel (50% chloroform in ehter) to give 64 mg (87%) of the diol **8**: nmr ($CDCl_3$) δ 1.5–1.92 (m, 8 H), 1.93–2.36 (m, 8 H, allylic methylenes and OH's), 3.63 (t, *J* = 6.5 Hz, 2 H), 4.15 (d, *J* = 7 Hz, 2 H), 5.18 (m, 1 H), and 5.43 (t, *J* = 7 Hz, 1 H); mass spectrum (10 eV) *m/e* (rel intensity) 198 (M^+, 0.64), 180 (M − H_2O, 5), 167 (M − CH_2OH, 5), 152 (M − H_2O + CH_2=CH_2, 8), 121 (32), 97 (34), 95 (92), 84 (100), 69 (44), and 68 (48).

Treatment of 8 with α-naphthyl isocyanate gave a bis(α-naphthyl)urethane which melts at 128–129.5° (lit.[12c] 127–129°) after recrystallization from hexane–ether.

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Registry No.—**1a,** 52500-37-5; **1b,** 52500-38-6; (*E*)-**2a,** 52500-39-7; (*Z*)-**2a,** 52500-40-0; (*E*)-**2b,** 52500-41-1; (*Z*)-**2b,** 52500-42-2; **4b,** 1674-04-0; **5,** 52500-43-3; **6a,** 52500-44-4; **6b,** 52500-45-5; **7,** 52500-46-6; **7** methyl ester, 52500-47-7; **8,** 24048-35-9; 2-bromopropene, 557-93-7; heptanal, 111-71-7.

References and Notes

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Palladium-Catalyzed Carboalkoxylation of Aryl, Benzyl, and Vinylic Halides

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Aryl and vinylic bromides and iodides and benzyl chloride react with carbon monoxide and an alcohol at 100° or below and atmospheric pressure in the presence of a tertiary amine and a catalytic amount of a palladium–triphenylphosphine complex to form esters. The reaction is tolerant of a variety of functional groups and shows appreciable stereospecificity at 60–80° with cis and trans vinylic halides producing esters with retained configuration.

In previous papers we and others have noted the ready formation of organopalladium complexes by reaction of finely divided palladium metal[1,2] or palladium(0)–organophosphine complexes[3,4] with aryl, benzyl, and vinyl halides.

Since these organopalladium complexes reacted easily with olefins,[1-3] it seemed reasonable to expect that they would also react with carbon monoxide to form acylpalladium derivatives. The last compounds could then possibly reductively eliminate acyl halide or at least react with alcohols to form esters and an unstable metal hydride which could re-form the palladium(0) starting material. Therefore a catalytic synthesis of acyl halides or esters from aryl, benzyl, and vinyl halides and carbon monoxide appeared possible analogous to the known reactions of allylic chlorides.[5,6] A similar reaction is known to occur with bromo-

$$H_2C{=}CHCH_2Cl + CO \xrightarrow{Pd} H_2C{=}CHCH_2COCl$$
$$\xrightarrow[ROH]{Pd} H_2C{=}CHCH_2COOR + HCl$$

π-allylnickel(II) dimer, from allyl bromide and tetracarbonylnickel(0), and carbon monoxide.[7] A related carboalkoxylation of organomercury compounds with palladium salts, carbon monoxide, and an alcohol is known, but generally mixtures of esters, biaryls, and ketones were obtained with only low yields of esters being formed in most instances.[8,9] Tetracarbonylnickel(0) is an excellent reagent for the carboalkoxylation of aryl, benzyl, and vinyl halides particularly in the presence of bases.[10,11] The nickel reaction has two problems which we hoped to overcome by the use of palladium catalysts: (1) tetracarbonylnickel vapor is extremely toxic while the palladium reagents are not volatile and (2) tetracarbonylnickel is either required in stoichiometric quantities or at least in relatively large catalytic amounts while the palladium complexes may react highly catalytically.

Preliminary experiments showed that acyl halides were not formed catalytically from aryl halides at 100° and with 1 atm of carbon monoxide even in the presence of tertiary amines, but in the presence of an alcohol and a tertiary amine a highly catalytic reaction ensued forming esters in good yields.

$$ArX + CO + ROH + R_3'N \xrightarrow{\text{"Pd"}} ArCOOR + R_3'NH^+X^-$$

Results

Initial experiments were carried out with aryl iodides adding palladium acetate as catalyst. The palladium(II) acetate was reduced by the carbon monoxide in the reaction mixture. Little carbon monoxide was absorbed at 100° and at 1 atm unless a tertiary amine and an alcohol were added. We used *n*-butyl alcohol as the alcohol and tri-*n*-butylamine as the tertiary amine, since they boiled well above the reaction temperature. Generally, the reactions with 1–2 mol % of catalyst at 100° required 14 hr or more to reach completion and were usually allowed to go longer to be sure the aryl halide had completely reacted. Reactions were carried out in a gasometric apparatus as described previously so that the reaction rate and the amount of gas absorbed could be measured.[12] Products were isolated by ether extraction, acid washing, and distillation. The esters were obtained very pure by this simple procedure. The yields and product properties of representative examples are show in Table I. Nmr data on the products are given in Table III which will appear in the microfilm edition of the journal. See paragraph at the end of paper regarding supplementary material. Substituent effects in the aromatic halide appeared to be less significant than in the reactions of the same halides with olefins.[1,3] Both strongly electron supplying and withdrawing substituents could be present.

The reaction with palladium acetate as catalyst at 100° was limited to aryl iodides; bromides did not react unless they were strongly activated with electron withdrawing substituents. We found, however, that adding 2 equiv of triphenylphosphine would cause unactivated aryl bromides to react at practical rates and produce esters in good yields. Aryl iodides reacted at about the same rates with the phosphine catalysts as they did with the palladium acetate cata-