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Palladium-Assisted (*Z*)–(*E*) Isomerization of Styrenes

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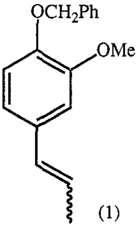
Abstract

It is shown that treatment of stereoisomeric mixtures of styrenes with a catalytic amount of bis(acetonitrile)dichloropalladium(II) achieves smooth stereoisomerization of the (*Z*)-isomers to the (*E*)-isomers.

Methods that are completely stereoselective for the production of both (*E*)- and (*Z*)-alkenes are of enormous importance in synthetic organic chemistry. These objectives can often be partly fulfilled by reduction of alkynes or by the stereochemical control of the Wittig reaction.[1,2] Nevertheless, the inversion of the stereochemistry of an alkene is still an important method.[3]

In connection with the total synthesis of the aphid pigments it became necessary to synthesize a number of (*E*)-styrenes in order to control the stereochemistry of the pyran rings in these systems.[4,5] As a consequence we have synthesized a number of styrenes, as mixtures of stereoisomers, by the Wittig reaction, and have studied their isomerization to afford predominantly the (*E*)-isomers. Thus, the styrenes (1)–(4) were each obtained by separate



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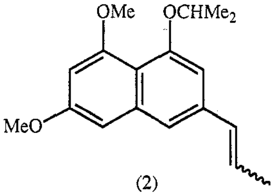

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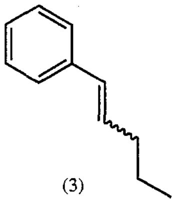

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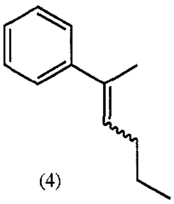

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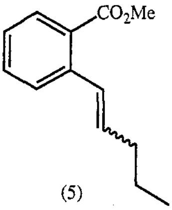
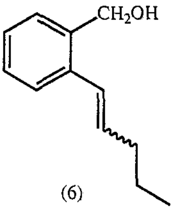
Wittig reactions between the appropriate aromatic aldehyde or ketone and either ethylidene- or butylidene-triphenylphosphorane. In general the (*Z*)-stereoisomers (as determined by ^{1}H n.m.r. spectroscopy) predominated in the mixtures of alkenes resulting from these reactions. The styrene (5) was obtained as a mixture of stereoisomers by Wittig reaction between butanal and the phosphorane generated from 2-methoxycarbonylbenzyltriphenylphosphonium bromide, and on reduction with lithium aluminium hydride it afforded the alcohol (6). These compounds (5) and (6) have previously been obtained as the pure (*E*)-isomers by an alternative route.[4]



(5)



(6)

These styrenes were each separately treated with bis(acetonitrile)dichloropalladium(II) in dichloromethane or (D)chloroform solution, normally at 35°. In the case of the last-mentioned solvent the course of the reactions was conveniently followed by ^{1}H n.m.r. spectroscopy. In the cases of compounds (1)–(3) and (6) these conditions led to efficient isomerization, and the resultant products, which were obtained in good yield, contained the (*E*)-isomer in a proportion of better than 95% as estimated by 300-MHz ^{1}H n.m.r. spectroscopy. In the case of the ester (5), however, the proportion of the (*E*)-isomer was only 81%.

We then sought to apply this method to a styrene with a trisubstituted double bond. Thus it was found that compound (4) required prolonged exposure to the reaction conditions to effect isomerization, and the proportion of the (*E*)-isomer obtained was only 81%.

Previous studies have shown that transition-metal complexes are capable of isomerizing 3-arylprop-1-enes into 1-arylprop-1-enes and that the predominant isomer produced has the (*E*)-stereochemistry,[6–10] but this method has not been studied in any depth.

We envisage that the isomerization reactions presently studied involve a ligand exchange between the catalyst and the styrene (see Scheme 1) with the formation of an olefinic palladium complex which then undergoes reversible formation of a mobile π-allyl(hydrido)palladium intermediate. This intermediate prefers the *anti*-stereochemistry (8) since the *syn*-form (7) suffers from greater steric repulsion.[11]

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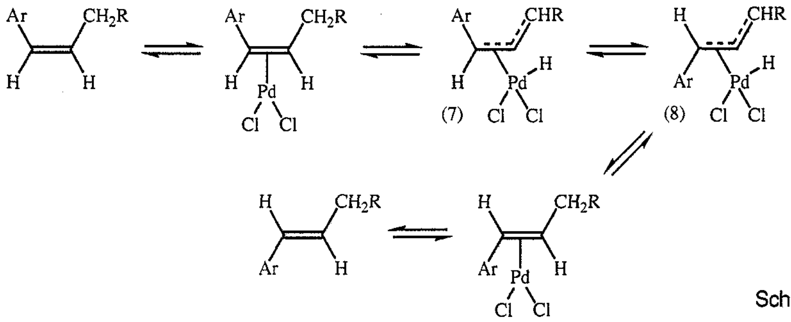

Scheme 1

We have also treated pure (*Z*)-oct-4-ene with a catalytic amount of bis(acetonitrile)dichloropalladium(II) in (D)chloroform, and, in agreement with previous workers, who had studied oct-1-ene[12] and (*E*)-oct-4-ene,[13] have found that this reaction gave a stereoisomeric mixture of positional isomers. In this case there is less steric repulsion in the *syn*-complex analogous to (7).

Experimental

General directions have been given previously.[14] Bis(acetonitrile)dichloropalladium(II) was prepared by the method of Hegedus *et al.*[15]

1-(4-Benzyloxy-3-methoxyphenyl)prop-1-ene (1)

A solution of butyllithium (1·66 M) in hexane (6·1 ml) was added dropwise at room temperature to a stirred suspension of ethyltriphenylphosphonium bromide (3·77 g) in anhydrous tetrahydrofuran (50 ml) under an atmosphere of dry nitrogen. The solution was stirred at room temperature for 15 min and next a solution of *O*-benzylvanillin[16] (2·42 g) in tetrahydrofuran (10 ml) was added dropwise, and the solution was stirred for 30 min. The solution was poured into water, and the crude product was isolated by extraction with ethyl acetate, and next purified by chromatography over silica gel with 5% ethyl acetate/light petroleum as eluent to afford the alkene (1) (2·10 g, 83%) as an oily mixture of stereoisomers which had b.p. 220°/0·2 mm Hg (Kugelrohr). A solution of the isomeric mixture (1) (317 mg) and bis(acetonitrile)dichloropalladium(II) (4 mg, 1·2 mole %) in (D)chloroform (1 ml) was placed in an n.m.r. tube and maintained at 35°. After 6·5 h no further change could be detected in the ^{1}H n.m.r. spectrum. The solvent was evaporated, and the residue was rapidly chromatographed through a short column of silica gel with 10% ethyl acetate/light petroleum as eluent. The oily product (290 mg, 90%) was crystallized from light petroleum and afforded the (*E*)-*isomer* as prisms, m.p. 53–54° (Found: C, 80·6; H, 7·3. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·2%). δ_H (300 MHz) 1·85, dd, 3, *J* 6·5, 1·5 Hz, Me; 3·89, s, 3, OMe; 5·14, s, 2, **CH**$_2$Ph; 6·09, dq, 1, *J* 15·7, 6·5 Hz, CH; 6·32, dd, 1, *J* 15·7, 1·5 Hz, CH; 6·79, narrow dd, 2, ArH; 6·91, d, 1, ArH; 7·20–7·48, m, 5, Ph. Examination of the 300 MHz ^{1}H n.m.r. spectrum of the material obtained from the mother liquors showed no sign of signals due to the (*Z*)-isomer.

1-(4-Isopropoxy-5,7-dimethoxynaphthalene-2-yl)prop-1-ene (2)

A solution of butyllithium (1·15 M) in hexane (0·88 ml) was added dropwise at 0° to a stirred suspension of ethyltriphenylphosphonium bromide (377 mg) in anhydrous ether

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(20 ml). The solution was cooled to −78° and a solution of 4-isopropoxy-5,7-dimethoxynaphthalene-2-carbaldehyde[17] (109 mg) in anhydrous ether (10 ml) was added dropwise. The reaction mixture was allowed to warm to room temperature, and the usual workup gave a crude product which was purified by chromatography over silica gel with 5% ethyl acetate/light petroleum as eluent to afford the alkene (2) (85 mg, 75%) as an oily mixture of stereoisomers. A solution of the isomeric mixture (2) (149 mg) and bis(acetonitrile)dichloropalladium(II) (14 mg, 10·4 mole %) in dichloromethane (2 ml) was heated under reflux for 3 h. The usual workup followed by chromatography over silica gel with 5% ethyl acetate/light petroleum as eluent afforded the (*E*)-isomer as an oil (120 mg, 80%). δ_H (90 MHz) 1·36, d, 6, Me_2C; 1·90, d, 3, *J* 6 Hz, Me; 3·85 and 3·87, each s, 3, OMe; 4·52, septet, 1, CH; 6·04–6·47, m, 3, 2×=CH and H6; 6·66, d, 1, *J* 2 Hz, H8; 6·86, d, 1, *J* 1·5 Hz, H3; 7·16, d, 1, *J* 1·5 Hz, H1. *m/z* 286 (M, 31%), 260 (39), 244 (53), 216 (100), 201 (10), 175 (35). Signals due to the (*Z*)-isomer could not be detected in the ^1H n.m.r. spectrum.

This alkene (48·5 mg) and palladized charcoal (10%, 30 mg) were stirred under hydrogen in ethyl acetate (3 ml) until absorption ceased. The usual workup gave *1-isopropoxy-6,8-dimethoxy-3-propylnaphthalene* (47·6 mg, 98%) as an oil (Found: C, 75·1; H, 8·4. $C_{18}H_{24}O_3$ requires C, 75·0; H, 8·3%). *m/z* 288 (M, 42%), 246 (100) 218 (83), 203 (15), 175 (19), 115 (11).

1-Phenylpent-1-ene (3)

A Wittig reaction between benzaldehyde (3·18 g) and the phosphorane generated from butyltriphenylphosphonium bromide (11·97 g) was carried out during 12 h in a manner similar to that used in the preparation of compound (1). The alkene (3) was obtained as an oily mixture of stereoisomers (3·38 g, 77%), b.p. 140°/23 mm Hg (Kugelrohr) [lit.,[18] for (*E*)-isomer, 100–101°/22 mm Hg]. Treatment of the isomeric mixture of alkenes (3) (92 mg) with the complex (5 mg, 2·9 mole %) in (D)chloroform (1 ml) at 35° during 24 h gave the (*E*)-isomer (85 mg, 92%) as an oil (b.p. 140°/23 mm Hg). δ_H (300 MHz) 0·95, t, 3, *J* 7·3 Hz, Me; 1·49, m, 2, CH_2; 2·18, dq, 2, *J* 6·8, 1·0 Hz, CH_2; 6·22, dt, 2, *J* 15·8, 6·8 Hz, CH; 6·38, d, 1, *J* 15·8 Hz, CH; 7·00–7·41, m, 5, Ph. Signals due to the (*Z*)-isomer in this ^1H n.m.r. spectrum were negligible.

2-Phenylhex-2-ene (4)

A Wittig reaction between acetophenone and the phosphorane generated from butyltriphenylphosphonium bromide was performed in a manner similar to that described for the preparation of compound (3). The alkene (4) was obtained as an oily mixture of stereoisomers (20%), b.p. 120°/27 mm Hg (Kugelrohr) [lit.,[19] for (*E*)-isomer, 105°/15 mm Hg]. The isomeric mixture of alkenes (4) (117 mg) in (D)chloroform (3 ml) was treated with the complex (14 mg, 7·4 mole %) at 60° during 98 h. The usual workup gave the alkene (4) (50 mg, 43%) which contained 81% (*E*)-isomer. δ_H (300 MHz) (*E*)-isomer 0·95, t, 3, *J* 7·4 Hz, Me; 1·47, m, 2, CH_2; 2·02, d, 3, *J* 1·4 Hz, Me; 2·17, dq, 2, *J* 7·4, 0·7 Hz, CH_2; 5·78, dt, 1, *J* 7·4, 1·4 Hz, CH; 7·16–7·41, m, 5, Ph; (*Z*)-isomer 0·84, t, 3, *J* 7·4 Hz, Me; 1·35, m, 2, CH_2; 1·94, dq, 2, *J* 7·4, 0·7 Hz, CH_2; 2·02, d, 3, *J* 1·4 Hz, Me; 5·46, dt, 1, *J* 7·4, 1·4 Hz, CH; 7·08–7·47, m, 5, Ph.

Methyl 2-(Pent-1-enyl)benzoate (5)

1,5-Diazabicyclo[5.4.0]undec-5-ene (547 mg) was added to a stirred mixture of 2-methoxycarbonylbenzyltriphenylphosphonium bromide[20] (1·47 g) and butanal (0·54 ml) in anhydrous acetonitrile (10 ml) under dry nitrogen at room temperature. The solution was next heated under reflux for 6 h. The usual workup gave a crude product which was chromatographed over silica gel with 10% ethyl acetate/light petroleum as eluent, and was next distilled

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[20] Dunn, J. P., Green, D. M., Nelson, P. H., Rooks, W. H., II, Tomolonis, A. J., and Untch, K. G., *J. Med. Chem.*, 1977, **20**, 1557.

under diminished pressure, a procedure which afforded the ester (5) as an oily mixture of stereoisomers (230 mg, 38%), b.p. 125°/0·1 mm Hg (Kugelrohr).[4] The isomeric mixture of alkenes (5) (104 mg) in dichloromethane (5·0 ml) was heated under reflux for 18·75 h with the complex (5 mg, 3·8 mole %). The usual workup gave the alkene (5) (84 mg, 81%) as an oil which contained the (*E*)-isomer (81%). δ_H (300 MHz) (*E*)-isomer 0·97, t, 3, Me; 1·52, m, 2, CH_2; 2·23, dq, 2, *J* 7·1, 0·8 Hz, CH_2; 3·89, s, 3, OMe; 6·14, dt, 1, *J* 15·5, 7·1 Hz, CH; 7·13, d, 1, *J* 15·5 Hz, CH; 7·21–7·85, m, 4, ArH; (*Z*)-isomer 0·87, t, 3, Me; 1·43, m, 2, CH_2, 2·09, dq, 2, *J* 7·1, 1·5 Hz, CH_2; 3·97, s, 3, OMe; 5·71, dt, 1, *J* 12·0, 7·1 Hz, CH; 6·86, d, 1, *J* 12·0 Hz, CH; 7·20–8·00, m, 4, ArH.

2-(Pent-1-enyl)benzyl Alcohol (6)

A solution of the foregoing isomeric mixture of esters (5) (408 mg) in anhydrous ether (10 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (500 mg) in ether (25 ml). After 15 min at room temperature the reaction mixture was cooled to 0°, and an excess of saturated aqueous sodium sulfate was added. The usual workup gave the alcohol (6) (340 mg, 97%) as an oily mixture of stereoisomers.[4] This mixture (54 mg) in (D)chloroform (0·5 ml) was treated during 0·5 h at 35° with the complex (1·5 mg, 1·9 mole %). The usual workup gave the (*E*)-alkene[4] (6) (46 mg, 85%), b.p. 110°/0·01 mm Hg (Kugelrohr). δ_H (300 MHz) 0·96, t, 3, Me; 1·50, m, 2, CH_2; 1·93, br, 1, OH; 2·21, dt, 2, *J* 7·3, 1·5 Hz, CH_2; 4·70, s, 2, $\mathbf{CH_2}$OH; 6·14, dt, 1, *J* 15·7, 7·3 Hz, CH; 6·70, d, 1, *J* 15·7 Hz, CH; 7·17–7·47, m, 4, ArH.

(Z)-*Oct-4-ene*

A solution of butyllithium (1·29 M) in hexane (15·1 ml) was added by syringe to a stirred suspension of butyltriphenylphosphonium bromide (11·97 g) in anhydrous tetrahydrofuran (60 ml) under an atmosphere of dry argon at −78°. The stirred suspension was allowed to warm to room temperature, and anhydrous hexamethylphosphoric triamide (20·8 ml) was added; the solution was stirred at room temperature for 15 min and next cooled to −78°, and butanal (1·91 g) was added. The solution was stirred at −78° for 15 min, and then allowed to warm to room temperature and next poured into water. The crude product was isolated by extraction with pentane, and the pentane was removed by distillation (Vigreux column). The octene (1·90 g, 64%) was obtained as an oil, b.p. 120° (lit.[21] 121·7°/739 mm Hg). δ_H (300 MHz) 0·94, t, 3, Me; 1·40, m, 2, 2-CH_2; 2·04, br q, 2, 3-CH_2; 5·40, m, 2, =CH. δ_C (75·5 MHz) 13·79 (C 1), 22·94 (C 2), 29·41 (C 3), 129·60 (C 4).

Acknowledgments

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