Stereo- and Regioselective Palladium-Catalyzed 1,4-Dialkoxylation of Conjugated Dienes

Jan-E. Bäckvall*,[1a] and Jan O. Vågberg[1b]

Department of Organic Chemistry, Royal Institute of Technology, 100 44 Stockholm, Sweden, and Department of Organic Chemistry, University of Uppsala, Box 531, 751 21 Uppsala, Sweden

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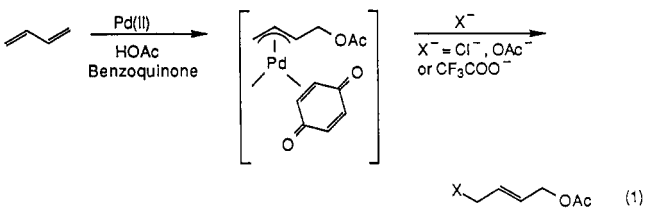
A mild method for stereo- and regioselective 1,4-dialkoxylation of conjugated dienes was developed. The reaction is catalyzed by palladium(II), and *p*-benzoquinone is used as the oxidant. It was found that the reaction rate depended on the presence of catalytic amounts of a strong acid. The role of the acid is probably 2-fold: (i) to create a cationic (π-allyl)palladium intermediate and (ii) to protonate the oxygen in the coordinated benzoquinone in the (π-allyl)palladium(benzoquinone) intermediate.

We have developed several palladium-catalyzed 1,4-oxidations of conjugated dienes.[2-4] In all these reactions acetic acid has served as the solvent and also functioned as at least one of the nucleophiles added to the diene in the oxidation process (eq 1). It would be of great interest



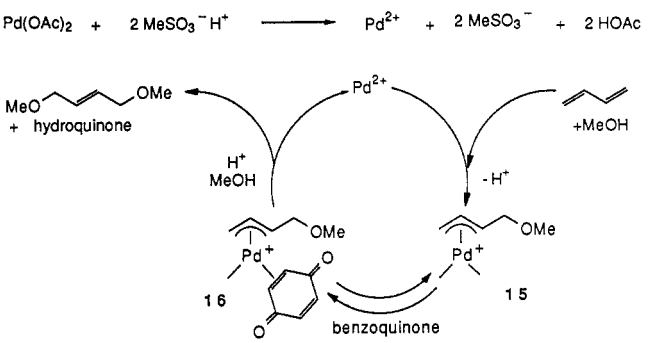
(1)

to extend this methodology to oxygen nucleophiles other than carboxylates. One limitation with the Pd(II)/benzoquinone system is that it seems to require acidic conditions. Thus, initial attempts to transform the palladium-catalyzed 1,4-diacetoxylation of 1,3-dienes into a 1,4-dimethoxylation by replacing acetic acid with methanol failed. However, we found that by adding catalytic amounts of a strong acid to the system the rate drastically increased. We now report a procedure for the stereo- and regioselective palladium-catalyzed 1,4-dialkoxylation of conjugated dienes.

Results and Discussion

The palladium-catalyzed 1,4-dialkoxylation of 1,3-dienes was performed in the corresponding alcohol as solvent with benzoquinone as the oxidant and a catalytic amount of strong acid, e.g. CH_3SO_3H or $HClO_4$. Because of the tendency of the diene to undergo a Diels–Alder reaction with benzoquinone, the former was added slowly during the reaction. Results from 1,4-dialkoxylation of some conjugated dienes are given in Table I. It was found that the presence of acid is essential, and without added acid no reaction occurred. The rate of the diethoxylation of 1,3-cyclohexadiene as a function of added methanesulfonic acid is shown in Figure 1. The rate measured refers to the initial rate. It was found that the rate increases almost linearly with the amount of acid in the range 0–30 mol % and then levels out, and between 75 and 100 mol % the rate increase was small. The role of the acid is possibly 2-fold (Scheme I). First it creates a cationic (π-allyl)-

Scheme I



palladium complex **15**, which facilitates a coordination of *p*-benzoquinone to the metal.[5] The (π-allyl)palladium(benzoquinone) complex **16** formed should be very reactive toward nucleophilic attack. Second, the acid will make the coordinated benzoquinone more electron-withdrawing by protonation of the oxygen. This would also increase the rate of the nucleophilic attack on the π-allyl group. Although the initial reaction rate increased with the concentration of acid, the rate after several hours was usually lower for a high acid concentration than for a lower one. Thus, dimethoxylation of 1,3-cyclohexadiene in two comparable experiments using 10 and 50 mol % of CH_3SO_3H afforded 1 in 59 and 44% yields, respectively, in spite of the higher initial rate of the latter reaction. The reason for this behavior could be explained by the fact that benzoquinone, which is the oxidant, undergoes an acid-catalyzed reaction with methanol and thus will be consumed.[6] In the preparative procedure, therefore, benzoquinone was added in portions in most cases, and CH_3SO_3H (in 10–20 mol %) was preferred over $HClO_4$. The latter, which is the stronger of the two acids, gave a lower yield in the preparative reaction.

It was found that the reaction is highly regio- and stereoselective in cyclic systems resulting in cis-1,4-dialkoxylation products (Table I, entries 1–7). Although 1,3-cyclohexadiene and 1,3-cycloheptadiene and derivatives[7] worked, 1,3-cyclooctadiene did not give a 1,4-dialk-

(1) (a) University of Uppsala. (b) Royal Institute of Technology.
(2) Bäckvall, J. E. In *Organic Synthesis: an Interdiciplinary Challenge*; Streith, J., Prinzbach, H., Schill, G., Eds.; Blackwell Scientific: Oxford, 1985, p 69.
(3) (a) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619. (b) Bäckvall, J. E.; Vågberg, J. O.; Nordberg, R. E. *Tetrahedron Lett.* **1984**, *25*, 2717.
(4) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676.
(5) Bäckvall, J. E.; Gogoll, A. *Tetrahedron Lett.* **1988**, *29*, 2243.
(6) In a control experiment monitored by gas chromatography it was shown that benzoquinone reacts with methanol in the presence of catalytic amounts of CH_3SO_3H. The corresponding reaction between benzoquinone and ethanol was considerably slower. Further control experiments showed that the cyclic 1,4-dialkoxy-2-alkenes were stable toward acid under the reaction conditions. Thus, the presence of 30 mol % of CH_3SO_3H did not lead to any measurable loss of dialkoxide over a period of 45 h.
(7) 6-Methoxy-1,3-cycloheptadiene also gave a diastereoselective 1,4-dialkoxylation and afforded the 1β,4β,6α-product in comparable yields to those in entries 6 and 7.

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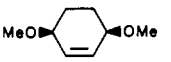
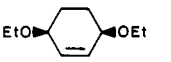
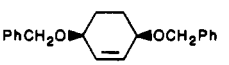
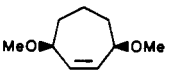
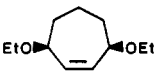
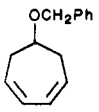
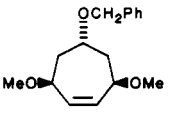
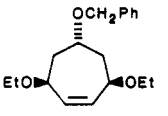
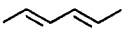
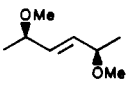
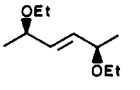
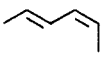
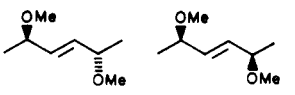
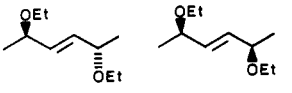
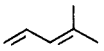
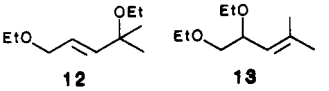
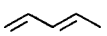
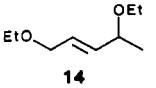
Table I. Palladium(II)-Catalyzed 1,4-Dialkoxylation of 1,3-Dienes[a]

entry	diene	ROH, reaction time (addition time), h	product(s)	yield,[b] %	stereochemistry[c]
1		MeOH, 8 (4)	 **1**	63	>98.8% cis[d]
2		EtOH, 8 (4)	 **2**	72	>98% cis
3		$PhCH_2OH$, 6 (4)	 **3**	53	>98% cis
4		MeOH, 7 (2)	 **4**	69	>98% cis
5		EtOH, 7 (2)	 **5**	82	>98% cis
6		MeOH, 24 (4)	 **6**	52	>96% 1β,4β,6α
7		EtOH, 15 (3)	 **7**	69	>95% 1β,4β,6α
8		MeOH, 24 (18)	 **8**	45	>97% *dl* >98% *E*
9		EtOH, 24 (18)	 **9**	45	>96% *dl* >98% *E*
10		MeOH, 24 (14)	 **10** **8** 87:13	52	>98% *E*
11		EtOH, 24 (14)	 **11** **9** 85:15	58	>98% *E*
12		EtOH, 121 (12)	 **12** **13** 19:81	34	
13		EtOH, 22 (18)	 **14**	25	>98% *E*
14		EtOH, 22 (18)	14	31	>98% *E*

[a] All reactions were run at 20 °C, using 5 mol % of $Pd(OAc)_2$ and 200–300 mol % of *p*-benzoquinone. Unless otherwise noted, 10–20 mol % of methanesulfonic acid was added. [b] Isolated yields after Kugelrohr distillation or flash chromatography. [c] Unless otherwise noted, the stereochemistry was determined by ^1H NMR spectroscopy. [d] The stereochemistry was determined by capillary GC.

oxylation. Also internal acyclic dienes gave a regio- and stereoselective 1,4-dialkoxylation. Thus, dimethoxylation of (*E*,*E*)-2,4-hexadiene afforded the *dl* product **8** (>97% *dl*, entry 8), whereas dimethoxylation of (*E*,*Z*)-2,4-hexadiene gave the meso product **10** (meso:*dl* = 87:13, entry 10). In both cases the double bond was exclusively of *E* configuration. The stereochemical results are consistent with a trans methoxypalladation[8-10] of the diene followed

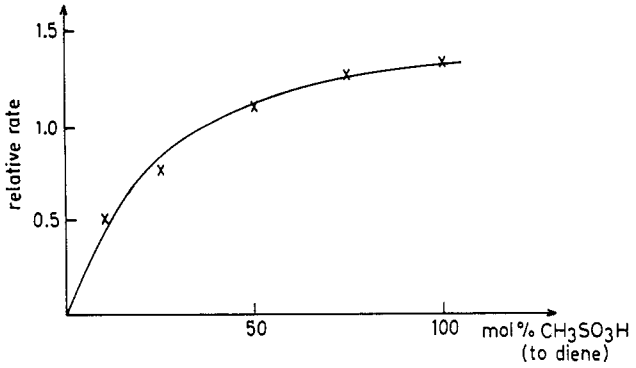
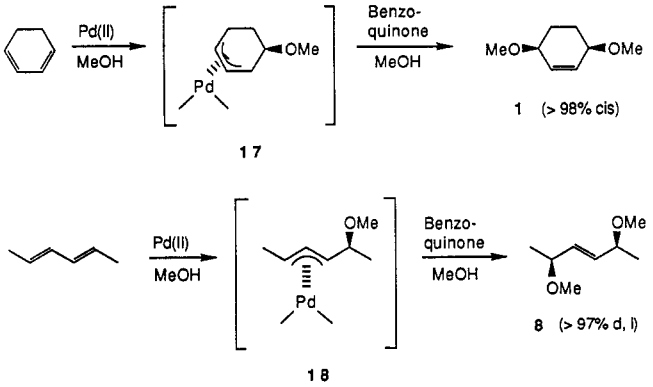


Figure 1. Relative initial rate of palladium-catalyzed 1,4-dimethoxylation of 1,3-cyclohexadiene at different concentrations of methanesulfonic acid.

Scheme II



by a trans attack by methanol on the intermediate complex (Scheme II). Terminal 1,3-dienes reacted slowly to give moderate yields of the corresponding diethoxides. 1,3-Pentadiene gave only the 1,4-adduct whereas 4-methyl-1,3-pentadiene afforded predominantly the 1,2-adduct **13**. The latter result is probably due to a secondary rearrangement of the 1,4-product **12** to give to 1,2-product **13**. This was supported by the fact that at approximately 10% conversion, **12** and **13** were isolated in a ratio of 6:4. The reason for the low reactivity of terminal 1,3-dienes is probably that the kinetic 4-methoxy-η^3-[1,2,3]alkenylpalladium complex formed[11] would react only slowly with methanol at the terminal position. The π-allyl intermediate in the dialkoxylation is cationic (cf. Scheme I) with considerable carbonium ion character at carbon, which leads to a much lower reactivity at a primary carbon compared to a secondary carbon.[12]

Support for the mechanism given in Scheme II follows from previous work. We have shown that methoxypalladation of 1,3-cyclohexadiene and (*E,E*)-2,4-hexadiene proceeds trans to give complexes **17** and **18**, respectively, which were isolated and characterized as their chloride dimers.[10,13] The intermediacy of **17** and **18** therefore requires an external trans attack by methanol to account for the cis product **1** and *dl* product **8**. It has been suggested without direct evidence, however, that an alkoxy group would be able to add from the same side as the metal[14,15] via a cis migration reaction. Such a mechanism is known to operate for carboxylates,[3,10a,13] where it was proposed that the bidentate property of the carboxylates facilitates a cis migration via a (σ-allyl)palladium intermediate. Ethanol and methanol, which most likely are coordinated to palladium in the cationic (π-allyl)palladium complex show no tendency to migrate from metal to carbon.

A method for dialkoxylation of conjugated dienes based on a mercury-promoted reaction has previously been described.[16] Except for terminal dienes it is 1,4-selective, but the addition is not stereoselective. Thus, cyclic 1,3-dienes afforded mixtures of *cis*- and *trans*-1,4-dialkoxy-2-cycloalkenes. An electrochemical method for the 1,4-dialkoxylation of conjugated dienes has also been reported.[17]

The present palladium-catalyzed procedure should be synthetically useful for cyclic dienes, since it is highly regio- and stereoselective. In one case the reaction was also shown to be diastereoselective toward an existing substituent on the diene. Thus, dialkoxylation of 6-(benzyloxy)-1,3-cycloheptadiene exclusively afforded the 1β,4β,6α product (entries 6 and 7).[7] The reaction is also useful on internal acyclic dienes, whereas terminal 1,3-dienes react too slowly to be synthetically useful.

The 1,4-diethers available from 1,3-dienes by the procedure described here can be used as protected diols that tolerate strong base. In particular, the dibenzyl derivatives (cf. entry 3, Table I) are suitable protected 2-alkene-1,4-diols that tolerate harsh reaction conditions.

Concluding Remarks

It is possible to obtain a regio- and stereoselective 1,4-dialkoxylation of 1,3-dienes catalyzed by Pd(II). The reaction is catalyzed by acids, and the attack by the alcohol on the (π-allyl)palladium intermediate is highly stereospecific and occurs trans. The present results describe an important extension of the palladium-catalyzed 1,4-oxidations[2-4] to solvents other than carboxylic acids.

Experimental Section

Infrared spectra were determined with a Perkin-Elmer 1710 infrared FT spectrophotometer. ^{1}H NMR spectra were recorded with a Bruker WP 200 FT spectrometer (200 MHz) or with a Bruker AM 400 FT spectrometer (400 MHz). ^{13}C NMR spectra were recorded with a Bruker AM 400 FT spectrometer at 100.6 MHz. All NMR spectra were recorded in $CDCl_3$ solutions with tetramethylsilane as internal standard for ^{1}H NMR spectra and $CDCl_3$ (δ 77.00) as internal standard for ^{13}C NMR spectra. DEPT (Distortionless enhancement by polarization transfer) spectra were determined to assign carbon multiplicities (s, C; d, CH; t, CH_2; q, CH_3). Analytical GLC was performed with a Varian Model 3700 gas chromatograph with a FID detector, connected to a computing integrator. A 25-m cross-linked methylsilicone capillary column (0.2-mm i.d.) was used. Kugelrohr distillations were performed with a Büchi Kugelrohr apparatus. For the slow addition of dienes, a Sage Instruments Model 355 syringe pump was used. Thin-layer chromatography (TLC) was performed on 0.2 mm precoated silica gel plates (60 F 254, E. Merck). Flash chromatography was carried out on Merck silica gel 60 (230–400

(8) Stille, J. K.; Morgan, R. A. *J. Am. Chem. Soc.* **1966**, *88*, 5135.
(9) James, D. E.; Hines, L. F.; Stille, J. K. *J. Am. Chem. Soc.* **1976**, *98*, 1806.
(10) (a) Bäckvall, J. E.; Nordberg, R. E.; Björkman, E. E.; Moberg, C. *J. Chem. Soc., Chem. Commun.* **1980**, 943. (b) Bäckvall, J. E.; Nordberg, R. E; Zetterberg, K.; Åkermark, B. *Organometallics* **1983**, *2*, 1625.
(11) Rowe, J. M.; White, D. A. *J. Chem. Soc. A* **1967**, 1451.
(12) The 4-methoxy-η^3-[1,2,3]alkenylpalladium complex initially formed would rearrange slowly to the thermodynamically more stable 1-methoxy-η^3-[2,3,4]alkenylpalladium complex.[11] The latter complex would be more reactive toward nucleophilic attack but because of the slow rearrangement the rate of the whole process will be low also in this case.
(13) Bäckvall, J. E.; Nordberg, R. E.; Wilhelm, D. *J. Am. Chem. Soc.* **1985**, *107*, 6892.
(14) Keinan, E.; Sahai, M.; Roth, Z.; Nudelmann A.; Herzig, J. *J. Org. Chem.* **1985**, *50*, 3558.
(15) Stanton, S. A.; Felman, S. W.; Parkhurst, C. S.; Godleski, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 1964.
(16) Barluenga, J.; Perez-Prieto, J.; Asensio, G. *J. Chem. Soc. Perkin Trans. 1* **1984**, 629.
(17) Baltes, H.; Steckhan, E.; Schäfer, H. *Chem. Ber.* **1978**, *111*, 1294.

mesh), as described by Still.[18] Microanalyses were performed by Analytical Laboratories, Engelskirchen, Germany.

Palladium acetate ($Pd(OAc)_2$) was purchased from Engelhard. Benzyl alcohol (E. Merck) was purified by fractional distillation at reduced pressure before use. Methanol (p.a., E. Merck), ethanol (99.5%, AB Svensk Sprit), *p*-benzoquinone (EGA Chemie), and methanesulfonic aicd (p.a., E. Merck) were used as received. 1,3-Cyclohexadiene, (*E*,*E*)- and (*E*,*Z*)-2,4-hexadiene, (*E*)- and (*Z*)-1,3-pentadiene, and 4-methyl-1,3-pentadiene were from the Aldrich Chemical Co. and were distilled before use. 1,3-Cycloheptadiene was prepared according to Ter Borg et al.[19] 6-(Benzyloxy)-1,3-cycloheptadiene was prepared from 3,5-cycloheptadienol[20] by reaction with benzyl bromide, in a procedure analogous to the one published for 6-methoxy-1,3-cycloheptadiene.[3a]

General Procedure for Palladium(II)-Catalyzed 1,4-Dialkoxylation of 1,3-Dienes. *cis*-1,4-Diethoxy-2-cyclohexene (2). A solution of 1,3-cyclohexadiene (120 mg, 1.5 mmol) in ethanol (0.86 mL) was added during 3.5 h with a syringe pump to a solution of palladium acetate (16.5 mg, 0.075 mmol), benzoquinone (324 mg, 3.0 mmol), and methanesulfonic acid (14 mg, 0.15 mmol) in ethanol (5 mL) at 20 °C. Stirring was continued for another 3 h at this temperature, and then water (3 mL) and pentane–ether (9:1, 10 mL) were added. The phases were separated, and the aqueous phase was extracted with pentane–ether (9:1, 3 × 10 mL). The combined organic phases were washed with water (5 mL), 2 M NaOH (3 × 5 mL; the last alkaline wash was performed with the addition of small portions of $NaBH_4$ until the organic phase was colorless), and water (5 mL). After drying ($MgSO_4$), the solvents were removed by distillation at ambient pressure through a Vigreux column. Kugelrohr distillation of the crude oil at 75 °C (1 mm) gave 184 mg (72%) of pure **2** as a colorless oil (>98% cis according to ^1H NMR): ^1H NMR (200 MHz), δ 5.89 (d, J = 1.4 Hz, 2 H, H-2 and H-3), 3.78 (m, $W_{1/2}$ = 11 Hz, 2 H, H-1 and H-4), 3.55 (dq, A part of ABX_3 spectrum, J_{AB} = 9.0 Hz, J_{AX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 3.51 (dq, B part of ABX_3 spectrum, J_{AB} = 9.0 Hz, J_{BX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 1.94–1.60 (m, 4 H, CH_2), 1.20 (t, J = 7.0 Hz, 6 H, CH_3CH_2O); ^{13}C NMR δ 130.50 (d, 2 C, C-2 and C-3), 72.02 (d, 2 C, C-1 and C-4), 63.22 (t, 2 C, CH_2O), 24.74 (t, 2 C, C-5 and C-6), 15.40 (q, 2 C, CH_3); IR (neat) 2975, 2946, 2868, 1442, 1390, 1315, 1103, 991 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.38; H, 10.80.

***cis*-1,4-Dimethoxy-2-cyclohexene (1)** was prepared from 1,3-cyclohexadiene (481 mg, 6.0 mmol) by slow addition (4 h) of the diene, dissolved in methanol (0.43 mL), to a solution of $Pd(OAc)_2$ (67 mg, 0.30 mmol), benzoquinone (649 mg, 6.0 mmol + 973 mg, 9.0 mmol after 2 h), and methanesulfonic acid (58 mg, 0.60 mmol) in methanol (20 mL) at 20 °C. After the mixture was stirred for another 4 h, normal extractive workup and Kugelrohr distillation at 120 °C (2 mm) afforded 538 mg (63%) of 1 as a colorless oil (98.8% cis according to analytical GLC): ^1H NMR (200 MHz) δ 5.92 (d, J = 1.4 Hz, 2 H, H-2 and H-3), 3.69 (m, $W_{1/2}$ = 10 Hz, 2 H, H-1 and H-4), 3.359 (s, 6 H, MeO), 1.92–1.62 (m, 4 H, CH_2); ^{13}C NMR δ 130.28 (d, 2 C, C-2 and C-3), 73.63 (d, 2 C, C-1 and C-4), 55.67 (q, 2 C, MeO), 24.04 (t, 2 C, C-5 and C-6); IR (neat) 2942, 2820, 1416, 1685, 1460, 1402, 1194, 1094, 938 cm^{-1}. Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.40; H, 9.84.

To confirm the stereochemical assignment, a sample of *trans*-1,4-dimethoxy-2-cyclohexene was prepared from the known *trans*-2-cyclohexene-1,4-diol[3a] (1.08 mmol) by reaction with sodium hydride (4.0 mmol) and methyl iodide (6.5 mmol) in dry THF (4 mL) at 40 °C. ***trans*-1,4-Dimethoxy-2-cyclohexene**: ^1H NMR (200 MHz) δ 5.89 (s, 2 H, H-2 and H-3), 3.81 (m, $W_{1/2}$ = 14 Hz, 2 H, H-1 and H-4), 3.364 (s, 6 H, MeO), 2.11 (m, 2 H, CH_2), 1.51 (m, 2 H, CH_2); ^{13}C NMR δ 130.47, 74.72, 55.78, 26.16.

***cis*-1,4-Bis(benzyloxy)-2-cyclohexene (3)** was prepared by slow addition (4 h) of 1,3-cyclohexadiene (120 mg, 1.5 mmol), dissolved in *n*-pentane (0.86 mL), to a benzyl alcohol solution (5 mL) containing $Pd(OAc)_2$ (16.5 mg, 0.075 mmol), benzoquinone (324 mg, 3.0 mmol), and methanesulfonic acid (14 mg, 0.15 mmol) at 20 °C. Stirring was continued for another 2 h, and then the mixture was filtered. After normal workup, excess benzyl alcohol was removed by Kugelrohr distillation at 80 °C (0.5 mm). Further distillation at 230 °C (0.3 mm) gave 236 mg (53%) of **3** as a colorless oil (>98% cis according to ^1H NMR): ^1H NMR (200 MHz) δ 7.38–7.20 (m, 10 H, Ph), 5.95 (d, J = 1.4 Hz, 2 H, H-2 and H-3), 4.60 (d, A part of AB spectrum, J_{AB} = 12.0 Hz, 2 H, one of two diasterotopic CH_2Ph), 4.56 (d, B part of AB spectrum, J_{AB} = 12.0 Hz, 2 H, one of two diasterotopic CH_2Ph), 3.90 (m, $W_{1/2}$ = 12 Hz, 2 H, H-1 and H-4), 2.05–1.66 (m, 4 H, CH_2); ^{13}C NMR δ 138.85 (s), 130.81 (d), 128.31 (d, 2 C), 127.54 (d, 2 C), 127.42 (d), 71.86 (d, 2 C, C-1 and C-4), 70.14 (t, 2 C, CH_2Ph), 24.87 (t, 2 C, C-5 and C-6); IR (neat) 3030, 2943, 2862, 1497, 1454, 1089, 1064, 1028, 734, 697 cm^{-1}. Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.54; H, 7.55.

***cis*-1,4-Dimethoxy-2-cycloheptene (4)** was prepared from 1,3-cycloheptadiene (565 mg, 6.0 mmol) by the general procedure above, using 20 mol % of methanesulfonic acid (115 mg, 1.2 mmol) and $Pd(OAc)_2$ (67 mg, 0.3 mmol) in methanol (20 mL). Benzoquinone was added in two portions (1.30 g, 12.0 mmol + 649 mg, 6.0 mmol after 2 h). The addition time of the diene was 2 h, and the total reaction time was 7 h. Normal workup and Kugelrohr distillation at 130 °C (2 mm) afforded 647 mg (69%) of **4** as colorless oil (>98% cis according to ^1H NMR): ^1H NMR (200 MHz) δ 5.77 (s, 2 H, H-2 and H-3), 3.79 (br d, J = 10.5 Hz, 2 H, H-1 and H-4), 3.34 (s, 6 H, MeO), 2.12–1.23 (m, 6 H, CH_2); ^{13}C NMR δ 134.46 (d, 2 C, C-2 and C-3), 80.76 (d, 2 C, C-1 and C-4), 56.16 (q, 2 C, MeO), 32.13 (t, 2 C, C-5 and C-7), 24.83 (t, C-6); IR (neat) 2978, 2932, 2859, 2818, 1454, 1393, 1189, 1157, 1097, 978 cm^{-1}. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.95; H, 10.24.

***cis*-1,4-Diethoxy-2-cycloheptene (5)** was prepared from 1,3-cycloheptadiene (565 mg, 6.0 mmol) as described for the preparation of **4**, but methanol was exchanged for ethanol. After normal workup and Kugelrohr distillation at 140 °C (2 mm), 907 mg (82%) of **5** could be isolated as a colorless oil (>98% cis according to ^1H NMR): ^1H NMR (200 MHz) δ 5.76 (s, 2 H, H-2 and H-3), 3.88 (br d, J = 11.0 Hz, 2 H, H-1 and H-4), 3.52 (dq, A part of ABX_3 spectrum, J_{AB} = 8.8 Hz, J_{AX} = 7.0 Hz, 2 H, one of two diasterotopic CH_3CH_2O), 3.44 (dq, B part of ABX_3 spectrum, J_{AB} = 8.8 Hz, J_{BX} = 7.0 Hz, 2 H, one of two diasterotopic CH_3CH_2O), 2.1–1.3 (m, 6 H, CH_2), 1.20 (t, J = 7.0 Hz, 6 H, CH_3CH_2O); ^{13}C NMR δ 134.98 (d, 2 C, C-2 and C-3), 79.16 (d, 2 C, C-1 and C-4), 63.86 (t, 2 C, CH_2O), 32.75 (t, 2 C, C-5 and C-7), 25.18 (t, C-6), 15.49 (q, 2 C, CH_3); IR (neat) 2975, 2932, 2864, 1445, 1385, 1300, 1159, 1109, 1022 cm^{-1}. Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.81; H, 10.91.

1β,4β-Dimethoxy-6α-(benzyloxy)-2-cycloheptene (6) was prepared from 6-(benzyloxy)-1,3-cycloheptene (300 mg, 1.5 mmol), $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), CH_3SO_3H (14 mg, 0.15 mmol), and benzoquinone (324 mg, 3.0 mmol + 81 mg, 0.75 mmol after 9 h) in methanol (5 mL) according to the general procedure described above. The addition time was 4 h, and the total reaction time was 24 h. Purification by flash chromatography (hexane–EtOAc, 85:15) gave 203 mg (52%) of **6** as a colorless oil (>96% 1β,4β,6α according to ^1H NMR): ^1H NMR (200 MHz) δ 7.40–7.25 (m, 5 H, Ph), 5.82 (d, J = 1.2 Hz, 2 H, H-2 and H-3), 4.62 (s, 2 H, $PhCH_2O$), 4.24 (br d, $J_{1,7a} = J_{4,5a}$ = 11.0 Hz, 2 H, H-1 and H-4), 3.91 (tt, $J_{6,5e} = J_{6,7e}$ = 5.2 Hz, $J_{6,5a} = J_{6,7a}$ = 2.7 Hz, 1 H, H-6), 3.34 (s, 6 H, MeO), 2.19 (ddd, $J_{5e,5a} = J_{7e,7a}$ = 13.5 Hz, $J_{5e,6} = J_{7e,6}$ = 5.2 Hz, $J_{5e,4} = J_{7e,1}$ = 2.2 Hz, 2 H, H-5e and H-7e), 1.67 (ddd, $J_{5a,5e} = J_{7a,7e}$ = 13.5 Hz, $J_{5a,4} = J_{7a,1}$ = 11.0 Hz, $J_{5a,6} = J_{7a,6}$ = 2.7 Hz, 2 H, H-5a and H-7a); ^{13}C NMR δ 138.7 (s), 134.57 (d, 2 C), 128.34 (d, 2 C), 127.49 (d, 2 C), 127.36 (d, 2 C), 74.54 (d, 2 C, C-1 and C-4), 73.14 (d, C-6), 70.21 (t, $PhCH_2O$), 56.34 (q, 2 C, MeO), 36.65 (t, 2 C, C-5 and C-7); IR (neat) 2927, 2819, 1455, 1394, 1114, 1093, 1070, 983 cm^{-1}. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.09, H, 8.47.

1β,4β-Diethoxy-6α-(benzyloxy)-2-cycloheptene (7) was prepared from 6-(benzyloxy)-1,3-cycloheptadiene (300 mg, 1.5 mmol) by the procedure shown for **6** except that methanol was exchanged for ethanol. The addition time was 3 h, and the total reaction time was 15 h. Normal workup and flash chromatography (hexane–EtOAc, 85:15) afforded 303 mg (69%) of **7** as a colorless oil (>95% 1β,4β,6α according to ^1H NMR): ^1H NMR (200 MHz),

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(19) Ter Borg, A. P.; Bickel, A. F. *Recl. Trav. Chim.* **1961**, *80*, 1229.
(20) Schuster, D. I.; Palmer, J. M.; Dickerman, S. C. *J. Org. Chem.* **1966**, *31*, 4281.

δ 7.40–7.25 (m, 5 H, Ph), 5.80 (d, J = 1.3 Hz, 2 H, H-2 and H-3), 4.62 (s, 2 H, PhCH_2O), 4.34 (br d, $J_{1,7a} = J_{4,5a}$ = 11.0 Hz, 2 H, H-1 and H-4), 3.91 (tt, $J_{6,5e} = J_{6,7e}$ = 5.0 Hz, $J_{6,5a} = J_{6,7a}$ = 2.8 Hz, 1 H, H-6), 3.54 (dq, A part of ABX_3 spectrum, J_{AB} = 9.2 Hz, J_{AX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 3.45 (dq, B part of ABX_3 spectrum, J_{AB} = 9.2 Hz, J_{BX} = 7.0 Hz, 2 H, one of two diasterotopic CH_3CH_2O), 2.18 (ddd, $J_{5e,5a} = J_{7e,7a}$ = 13.5 Hz, $J_{5e,6} = J_{7e,6}$ = 5.0 Hz, $J_{5e,4} = J_{7e,4}$ = 2.1 Hz, 2 H, H-5e and H-7e), 1.68 (ddd, $J_{5a,5e} = J_{7a,7e}$ = 13.5 Hz, $J_{5a,4} = J_{7a,1}$ = 11.0 Hz, $J_{5a,6} = J_{7a,6}$ = 2.8 Hz, 2 H, H-5a and H-7a); ^{13}C NMR δ 138.80 (s), 134.96 (d, 2 C), 128.27 (d, 2 C), 127.38 (d, 2 C), 127.27 (d, 2 C), 73.35 (d, C-6), 72.71 (d, 2 C, C-1 and C-4), 70.11 (t, PhCH_2O), 63.92 (t, 2 C, CH_3CH_2O), 37.04 (t, 2 C, C-5 and C-7), 15.41 (q, 2 C, CH_3CH_2O); IR (neat) 2978, 2931, 2901, 2819, 1448, 1372, 1200, 1116, 1094, 1043, 974 cm^{-1}. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.39; H, 8.99.

(*E*)-*dl*-2,5-Dimethoxy-3-hexene (8) was prepared by slow addition (18 h) of (*E*,*E*)-2,4-hexadiene (493 mg, 6.0 mmol) to $Pd(OAc)_2$ (67 mg, 0.3 mmol), methanesulfonic acid (58 mg, 0.6 mmol), and benzoquinone (649 mg, 6.0 mmol + 1.30 g, 12.0 mmol after 6 h) in ethanol (20 mL). The total reaction time was 24 h. Normal extractive workup and Kugelrohr distillation at 110 °C (2–3 mm) gave 387 mg (45%) of **8** as a slightly yellow oil (>97% *dl*, >98% *E* according to ^{1}H NMR): ^{1}H NMR (200 MHz) δ 5.514 (apparent dd, AA′ part of AA′XX′$M_3M'_3$ spectrum,[21] $|J_{AX} + J_{AX'}| = |J_{3,2} + J_{3,5}|$ = 6.7 Hz, $J_{AA'} = J_{3,4}$ = 15.5 Hz, $J_{XX'} = J_{2,5}$ = 0, 2 H, H-3 and H-4), 3.74 (apparent 13-line m, XX′ part of AA′XX′$M_3M'_3$ spectrum, 2 H, H-2 and H-4), 3.290 (s, 6 H, MeO), 1.243 (d, J = 6.4 Hz, 6 H, H-1 and H-6); ^{13}C NMR δ 133.82 (d, 2 C, C-3 and C-4), 77.44 (d, 2 C, C-2 and C-5), 55.90 (q, 2 C, MeO), 21.25 (q, 2 C, C-1 and C-6); IR (neat) 2978, 2931, 2901, 2819, 1448, 1372, 1200, 1116, 1094, 974 cm^{-1}. The ^{1}H NMR data are in full accordance with those reported previously.[13]

(*E*)-*dl*-2,5-Diethoxy-3-hexene (9) was prepared from (*E*,*E*)-2,4-hexadiene (493 mg, 6.0 mmol) according to the procedure for the preparation of **8** except that 20 mol % of methanesulfonic acid (115 mg, 1.2 mmol) was used and methanol was exchanged for ethanol. Kugelrohr distillation at 125 °C (2–3 mm) gave 467 mg (45%) of **9** as a slightly yellow oil (>96% *dl*, >98% *E* according to ^{1}H NMR): ^{1}H NMR (200 MHz) δ 5.515 (apparent dd, AA′ part of AA′XX′$M_3M'_3$ spectrum, $|J_{AX} + J_{AX'}| = |J_{3,2} + J_{3,5}|$ = 6.5 Hz, $J_{AA'} = J_{3,4}$ = 15.5 Hz, $J_{XX'} = J_{2,5}$ = 0 Hz, 2 H, (apparent 13-line m, XX′ part of AA′XX′$M_3M'_3$ spectrum, 2 H, H-2 and H-5), 3.51 (dq, A part of ABX_3 spectrum, J_{AB} = 9.3 Hz, J_{AX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 3.36 (dq, B part of ABX_3 spectrum, J_{AB} = 9.3 Hz, J_{BX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 1.238 (d, J = 6.4 Hz, 6 H, H-1 and H-6), 1.193 (t, J = 7.0 Hz, 6 H, CH_3CH_2O); ^{13}C NMR δ 133.77 (d, 2 C, C-3 and C-4), 75.63 (d, 2 C, C-2 and C-5), 63.42 (t, 2 C, CH_2O), 21.54 (q, 2 C, C-1 and C-6), 15.21 (q, 2 C, CH_3CH_2O); IR (enat) 2976, 2931, 2868, 1445, 1371, 1319, 1158, 1105, 975, 958 cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.76; H, 11.58.

(*E*)-*meso*-2,5-Dimethoxy-3-hexene (10) was prepared by slow addition (14 h) of (*E*,*Z*)-2,4-hexadiene (493 mg, 6.0 mmol) according to the procedure for **8**. The total reaction time was 24 h. After the normal workup and Kugelrohr distillation at 105 °C (2–3 mm), 452 mg (52%) of **10** could be isolated as a colorless oil (meso:*dl* = 87:13, δ 98% *E* according to ^{1}H NMR): ^{1}H NMR (200 MHz) δ 5.524 (apparent dd, AA′ part of AA′XX′$M_3M'_3$ spectrum, $|J_{AX} + J_{AX'}| = |J_{3,2} + J_{3,5}|$ = 6.5 Hz, $J_{AA'} = J_{3,4}$ = 15.5 Hz, $J_{XX'} = J_{2,5}$ = 0, 2 H, H-3 and H-4), 3.74 (apparent 13-line m, XX′ part of AA′XX′M_3M_3 spectrum, 2 H, H-2 and H-5), 3.270 (s, 6 H, MeO), 1.257 (d, J = 6.4 Hz, 6 H, H-1 and H-6); ^{13}C NMR δ 133.69 (d, 2 C, C-3 and C-4), 77.32 (d, 2 C, C-2 and C-5), 55.85 (q, 2 C, MeO), 21.33 (q, 2 C, C-1 and C-6); IR (neat) 2978, 2931, 2901, 2819, 1448, 1372, 1200, 1116, 1094, 974 cm^{-1}. The ^{1}H NMR data are in full accordance with those reported previously.[13]

(*E*)-*meso*-2,5-Diethoxy-3-hexene (11) was prepared from (*E*,*Z*)-2,4-hexadiene (493 mg, 6.0 mmol) by using the procedure described for **8** except that 20 mol % of methanesulfonic acid (115 mg, 1.2 mmol) was used and methanol was exchanged for ethanol. The addition time of the diene was 14 h, and the total reaction time was 24 h. Kugelrohr distillation at 110 °C (2–3 mm) yielded 604 mg (58%) of **11** as a colorless oil (meso:*dl* = 85:15, >98% *E* according to ^{1}H NMR): ^{1}H NMR (200 MHz) δ 5.523 (apparent dd, AA′ part of AA′XX′$M_3M'_3$ spectrum, $|J_{AX} + J_{AX'}| = |J_{3,2} + J_{3,5}|$ = 6.4 Hz, $J_{AA'} = J_{3,4}$ = 15.5 Hz, $J_{XX'} = J_{2,5}$ = 0 Hz, 2 H, H-3 and H-4), 3.84 (apparent 13-line m, XX′ part of AA′XX′$M_3M'_3$ spectrum, 2 H, H-2 and H-5), 3.48 (dq, A part of ABX_3 spectrum, J_{AB} = 9.3 Hz, J_{AX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 3.35 (dq, B part of ABX_3 spectrum, J_{AB} = 9.3 Hz, J_{BX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2O), 1.252 (d, J = 6.5 Hz, 6 H, H-1 and H-6), 1.187 (t, J = 7.0 Hz, 6 H, CH_3CH_2O); ^{13}C NMR δ 133.68 (d, 2 C, C-3 and C-4), 75.56 (d, 2 C, C-2 and C-5), 63.37 (t, 2 C, CH_2O), 21.64 (q, 2 C, C-1 and C-6), 15.34 (q, 2 C, CH_3CH_2O); IR (neat) 2978, 2931, 2819, 1448, 1372, 1200, 1116, 1094, 974 cm^{-1}. Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.92; H, 11.58.

A mixture of (*E*)-1,4-diethoxy-4-methyl-2-pentene (12) and 1,2-diethoxy-4-methyl-3-pentene (13) was prepared from 4-methyl-1,3-pentadiene (123 mg, 1.5 mmol) by the general procedure by using 50 mol % of methanesulfonic acid (72 mg, 0.75 mmol). The addition time was 12 h, and the total reaction time was 121 h. After Kugelrohr distillation at 90 °C (1 mm), 87 mg (34%) of a colorless oil could be isolated. According to ^{1}H NMR analysis, the oil consisted of **12** and **13** in a ratio of 19:81.

12: ^{1}H NMR (400 MHz, assigned peaks in mixture of **13**) δ 5.70 (d, A part of AB spectrum, $J_{AB} = J_{2,3}$ = 16.0 Hz, 1 H, H-3), 5.67 (dt, B part of AB spectrum, $J_{AB} = J_{3,2}$ = 16.0 Hz, $J_{2,1}$ = 4.5 Hz, 1 H, H-2), 3.98 (d, J_{12} = 4.5 Hz, 2 H, H-1), 3.60–3.32 (m, 4 H), 1.28 (s, 6 H, CH_3), 1.22 (t, J = 7.0 Hz, 3 H, CH_3CH_2O), 1.15 (t, J = 7.0 Hz, 3 H, CH_3CH_2O); ^{13}C NMR δ 138.75 (d), 125.79 (d), 74.34 (s, C-4), 70.90 (t, C-1), 65.51 (t, CH_3CH_2O), 57.75 (t, CH_3CH_2O), 26.19 (q, 2 C, C-5 and C-4-CH_3), 15.99 (q, CH_3CH_2O), 15.08 (q, CH_3CH_2O).

13: ^{1}H NMR (400 MHz, assigned peaks in mixture with **12**) δ 5.07 (d of heptet, J = 9.0, 1.4 Hz, 1 H, H-3), 4.21 (ddd, J = 9.0, 7.2, 4.0 Hz, 1 H, H-2), 3.60–3.32 (m, 6 H), 1.75 (d, J = 1.4 Hz, 3 H, CH_3), 1.70 (d, J = 1.5 Hz, 3 H, CH_3), 1.20 (t, J = 7.0 Hz, 3 H, CH_3CH_2O), 1.19 (t, J = 7.0 hZ, 3 H, CH_3CH_2O); ^{13}C NMR δ 136.78 (s, C-4), 123.26 (d, C-3), 75.17 (d, C-2), 73.56 (t, C-1), 66.67 (t, CH_3CH_2O), 63.52 (t, CH_3CH_2O), 25.81 (q, C-5), 18.30 (q, C-4-CH_3), 15.36 (q, CH_3CH_2O), 15.04 (q, CH_3CH_2O).

(*E*)-1,4-Diethoxy-2-pentene (14) was prepared from (*Z*)-1,3-pentadiene (409 mg, 6.0 mmol) by the general procedure above by using 20 mol % of methanesulfonic acid (115 mg, 1.2 mmol). The addition time of the diene was 18 h, and the total reaction time was 22 h. Normal workup and Kugelrohr distillation at 120 °C (2–3 mm) afforded 297 mg (31%) of **14** as a slightly yellow oil (>95% *E* according to ^{1}H NMR): ^{1}H NMR (400 MHz) δ 5.71 (dt, A part of ABX_2Y spectrum, $J_{AB} = J_{2,3}$ = 15.6 Hz, $J_{AX} = J_{2,1}$ = 5.5 Hz, 1 H, H-2), 5.62 (ddt, B part of ABX_2Y spectrum, $J_{AB} = J_{3,2}$ = 15.6 Hz, $J_{BY} = J_{3,4}$ = 7.0 Hz, $J_{BX} = J_{3,1}$ = 1.2 Hz, 1 H, H-3), 3.97 (dd, J_{12} = 5.5 Hz, $J_{1,3}$ = 1.2 Hz, 2 H, CH_2OEt), 3.86 (dq, apparent quintent, J = 6.6 Hz, 1 H, H-4), 3.49 (q, J = 7.0 Hz, 2 H, CH_3CH_2OC-1) that is superimposed on 3.51 (dq, A part of ABX_3 spectrum, J_{AB} = 9.0 Hz, J_{AX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2OC-4), 3.37 (dq, B part of ABX_3 spectrum, J_{AB} = 9.0 Hz, J_{BX} = 7.0 Hz, 2 H, one of two diastereotopic CH_3CH_2OC-4), 1.24 (d, $J_{5,4}$ = 6.4 Hz, 3 H, H-5), 1.22 (t, J = 7.0 Hz, 3 H, CH_3CH_2O), 1.18 (t, J = 7.0 Hz, 3 H, CH_3CH_2O); ^{13}C NMR δ 135.06 (d), 128.02 (d), 75.56 (d, C-4), 70.59 (t, C-1), 65.59 (t, CH_3CH_2O), 63.46 (t, CH_3CH_2O), 21.42 (q, C-5), 15.35 (q, CH_3CH_2O), 15.14 (q, CH_3CH_2O); IR (neat) 2976, 2931, 2867, 1445, 1374, 1105, 972 cm^{-1}.

Registry No. **1**, 59415-77-9; **2**, 90786-01-9; **3**, 116910-21-5; **4**, 116910-22-6; **5**, 90786-03-1; **6**, 116910-23-7; **7**, 116910-24-8; **8**, 98721-08-5; **9**, 116910-25-9; **10**, 98721-09-6; **11**, 116910-26-0; **12**, 116910-27-1; **13**, 116910-28-2; **14**, 116910-29-3; $Pd(OAc)_2$, 2004-70-8; 1,3-cyclohexadiene, 592-57-4; *trans*-1,4-dimethoxy-2-cyclohexene, 59415-76-8; *trans*-2-cyclohexene-1,4-diol, 41513-32-0; 1,3-cycloheptadiene, 4054-38-0; 6-(benzyloxy)-1,3-cycloheptene, 115522-58-2; (*E*,*E*)-2,4-hexadiene, 5194-51-4; (*E*,*Z*)-2,4-hexadiene, 5194-50-3; 4-methyl-1,3-pentadiene, 926-56-7; (*Z*)-1,3-pentadiene, 1574-41-0.

(21) Homonuclear decoupling of the methyl groups at δ 1.24 collapsed the AA′XX′$M_3M'_3$ spectrum to an AA′XX′ spectrum consisting of two identical half spectra at δ 5.51 and at δ 3.73. Each half spectrum consisted of a doublet (J = 6.7 Hz) and an AB quartet (J_{AB} = 15.5 Hz).