Improved Palladium-Catalyzed 1,4-Haloacyloxylation and 1,4-Diacyloxylation of Cyclic Conjugated Dienes

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Improved procedures for the palladium-catalyzed 1,4-oxidation of cyclic conjugated dienes have been developed. In the new procedures the reactions are performed in acetone or ethyl acetate in the presence of the appropriate carboxylic acid. Thus, palladium-catalyzed oxidations of cyclic conjugated dienes in acetone in the presence of a carboxylic acid and lithium chloride using p-benzoquinone as the oxidant leads to an efficient cis-1,4-chloroacyloxylation. If the reaction is performed in the absence of lithium chloride, but under otherwise identical conditions, a 1,4-diacyloxylation of the conjugated diene takes place. 1,4-Bromoacyloxylation occurs if lithium bromide is used in place of lithium chloride in the palladium-catalyzed oxidation. These new procedures allow the use of a variety of carboxylates in Pd-catalyzed haloacyloxylation and diacyloxylation.

We have recently reported procedures for the palladium-catalyzed 1,4-functionalizations of conjugated dienes. In these reactions two nucleophiles (X\(^{-}\), Y\(^{-}\)) are introduced in the 1- and 4-positions of the diene [eqn. (1)]. In all cases so far, at least one of the nucleophiles added came from the solvent. Thus, in the 1,4-chloroacetoxycarbonylation (X\(^{-}\) = OAc\(^{-}\), Y\(^{-}\) = Cl\(^{-}\)) or 1,4-diacetoxylation (X\(^{-}\) = Y\(^{-}\) = OAc\(^{-}\)) acetic acid served as the solvent. We now report improved procedures for the 1,4-haloacyloxylation and 1,4-diacyloxylation in a non-nucleophilic organic solvent which allows the use of a variety of carboxylates as nucleophiles.

**Results and discussion**

In the palladium-catalyzed 1,4-diacetoxylation the stereochemistry can be controlled to give either cis or trans 1,4-addition. This is explained by the formation of an intermediate trans-4-acetoxy-(α-allyl)palladium complex in which the acetate can be directed towards either cis or trans attack. It would be of great synthetic interest to extend this procedure to other carboxylates which may have better leaving-group properties and/or higher stability towards basic hydrolysis. Carboxylates without α-protons such as pivalate and benzoate are also of interest. One practical limitation to the original procedure is that the carboxylic acid serves as the solvent. However, we have now found that the use of acetone or ethyl acetate as the solvent in the presence of 5–10 equiv. of the appropriate carboxylic acid results in an efficient diacyloxylation reaction. This also leads to simpler work-up procedures.

Reaction of the appropriate conjugated diene with the carboxylic acid in acetone in the presence of Li\(_2\)CO\(_3\), p-benzoquinone and a catalytic amount of a Pd(I) salt afforded the dicarboxylate in good yields [eqn. (2)]. Results from diacyloxylation of 1,3-cyclohexadiene and 1,3-cycloheptadiene are given in Table 1. Acetone was found to be a good solvent for this reaction. The reactions also worked satisfactorily, but slowly, in tetrahydrofuran and ethyl acetate, whereas acetonitrile gave a poor yield. It is interesting to note that the acetone procedure gave a slightly higher trans selectivity in the diacetoxylation compared with the original procedure in acetic acid.

![Diagram](image-url)

\[
\text{cis-}\text{cis} \rightarrow \text{trans-}\text{trans}
\]

A reaction was obtained when the appropriate diene was allowed to react with a carboxylic acid and lithium chloride in acetone in the presence of p-benzoquinone and catalytic amounts of a Pd(I) salt. Several different carboxylic acids afforded a high yield of 1,4-chloroacyloxylation with 1,3-cyclohexadiene. Some results from the 1,4-chloroacyloxylations of 1,3-cyclohexadiene and 1,3-cycloheptadiene are given in Table 2. In all cases the chloroacyloxylations were highly stereoselective (>98% cis). The 1,4-regioselectivity was >98% for the

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Table 1. Palladium-catalyzed 1,4-diacetoxylation of conjugated dienes in acetone.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Diene</th>
<th>Carboxylic Acid</th>
<th>Method\textsuperscript{b}</th>
<th>Product</th>
<th>Yield (%)\textsuperscript{c}</th>
<th>cis/trans</th>
</tr>
</thead>
<tbody>
<tr>
<td>[\text{CH}_2\text{COOH}]</td>
<td>[\text{AcC} ]</td>
<td>A</td>
<td>[\text{cis-1}]</td>
<td>85</td>
<td>83/17</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C</td>
<td>[\text{AcC} ]</td>
<td>87</td>
<td>7/93</td>
</tr>
<tr>
<td>[\text{CF}_3\text{COOH}]</td>
<td>[\text{CF}_3\text{CO} ]</td>
<td>B</td>
<td>[\text{O}_2\text{CCF}_3]</td>
<td>94</td>
<td>23/77</td>
</tr>
<tr>
<td>[\text{PhCOOH}]</td>
<td>[\text{PhCO} ]</td>
<td>A</td>
<td>[\text{cis-3}]</td>
<td>85, 65\textsuperscript{d}</td>
<td>93/7, 99/1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>[\text{PhCO} ]</td>
<td>97, 70\textsuperscript{d}</td>
<td>20/80, 3/97</td>
</tr>
<tr>
<td>[\text{CH}_2\text{COOH}]</td>
<td>[\text{AcC} ]</td>
<td>B</td>
<td>[\text{cis-4}]</td>
<td>100, 80\textsuperscript{d}</td>
<td>92/8, &gt;99% cis</td>
</tr>
<tr>
<td>[\text{PhCOOH}]</td>
<td>[\text{PhCO} ]</td>
<td>A</td>
<td>[\text{O}_2\text{Ph}]</td>
<td>92</td>
<td>70/30</td>
</tr>
<tr>
<td>[\text{CF}_3\text{COOH}]</td>
<td>[\text{CF}_3\text{CO} ]</td>
<td>A</td>
<td>[\text{O}_2\text{CCF}_3]</td>
<td>50</td>
<td>38/62</td>
</tr>
</tbody>
</table>

\textsuperscript{a}The reaction was performed in acetone in the presence of 5–10 equiv. of the corresponding acid using 5 mol % of Pd(OAc)\textsubscript{2}. The oxidant was either p-benzoquinone or catalytic p-benzoquinone–MnO\textsubscript{2}. \textsuperscript{b}Method A: no salt of the carboxylic acid was added; Method B: in the presence of the lithium salt of the carboxylic acid; Method C: As method B but with MnO\textsubscript{2}–catalytic p-benzoquinone. \textsuperscript{c}Isolated yields. \textsuperscript{d}Purified by recrystallization or column chromatography.

six-membered ring, but from the seven-membered ring it was in the range 87–93 %. The 1,2-isomer formed in small amounts for the seven-membered ring was shown by \textsuperscript{1}H NMR to be of cis stereochemistry. The procedure works well with 1,3-cyclohexadiene and 1,3-cycloheptadiene, but fails for cyclopentadiene. Acyclic dienes gave poor yields with the acetone procedure. Thus, (E,E)- and (E,Z)-2,4-hexadiene afforded only 18 and 10 %, respectively, of the corresponding chloroacetates using the new procedure. This should be compared with the original chloroacetoxylation which gave 50–60 % yield with the same dienes.\textsuperscript{3} The reason for the slow chloroacetoxylation of these acyclic dienes in acetone is not obvious.

As mentioned above, pivalates are useful in cases where nucleophilic attack at the carbonyl has to be avoided or when strong bases are present. To demonstrate this point, the chloroacetoxyates 7 and 10 were treated with aqueous Na\textsubscript{2}CO\textsubscript{3} in methanol [eqn. (3)]. The chloroacetate 7 was completely hydrolyzed after 1 h at ambient temperature according to GLC analysis.\textsuperscript{7} On the other hand, the chloro-

pivalate 10 was essentially unchanged (>99%) after 1 h under the same reaction conditions.\textsuperscript{8} Chlorobenzoates are also of synthetic interest since after substitution of the chloride, the benzoate may be substituted either classically \(S_n2\), \(S_n2'\) or via metal-catalysis.\textsuperscript{9,10}

We have also extended the halocarboxylation reaction to include bromide as a nucleophile. When the bromoacetoxylation of 1,3-cyclohexadiene was performed in acetone, the stereoselectivity was poor, resulting in an almost 1:1 mixture of the cis- and trans-product. Attempts to replace acetone with acetonitrile, dimethyl sulfoxide or dioxane did
Table 2. Palladium-catalyzed 1,4-chloroacyloxylation of conjugated dienes in acetone.  

<table>
<thead>
<tr>
<th>Diene</th>
<th>Carboxylic acid</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RCO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeCOOH</td>
<td>R = Me</td>
<td>7</td>
<td>88</td>
</tr>
<tr>
<td>MeCH₂COOH</td>
<td>R = Me₂CH</td>
<td>8</td>
<td>82</td>
</tr>
<tr>
<td>Me₂CHCOOH</td>
<td>R = Me₂CH</td>
<td>9</td>
<td>87</td>
</tr>
<tr>
<td>Me₃COOH</td>
<td>R = Me₃C</td>
<td>10</td>
<td>87</td>
</tr>
<tr>
<td>PhCOOH</td>
<td>R = Ph</td>
<td>11</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>RCO₂</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MeCOOH</td>
<td>R = Me</td>
<td>12</td>
<td>69</td>
</tr>
<tr>
<td>Me₂CHCOOH</td>
<td>R = Me₂C</td>
<td>13</td>
<td>56</td>
</tr>
<tr>
<td>PhCOOH</td>
<td>R = Ph</td>
<td>14</td>
<td>60</td>
</tr>
</tbody>
</table>

*The reaction was performed in acetone in the presence of 1.5–2 equiv. of LiCl, 0.5–2 equiv. of Li₂CO₃, and 5–10 equiv. of the corresponding acid using 5 mol % of the Pd²⁺ catalyst. The oxidant was p-benzoquinone. Isolated yields. Contaminated with small amounts of the cis-1,2-isomer: for 12, 1,4:1,2 = 90:10; for 13, 1,4:1,2 = 87:13; for 14, 1,4:1,2 = 93:7.

not improve the stereoselectivity. However, ethyl acetate as the solvent led to a significant improvement in selectivity and yield. The use of 4 equiv. of acetic acid (ethyl acetate-acetic acid = 14:1) gave a cis:trans ratio of 89:11 [eqn. (4)]. In contrast with the chloroacetoxylation, which is highly 1,4-selective, the bromoacetoxylation product was always contaminated with small amounts of the 1,2-isomer (1,4:1,2 = 90:10). An isomerization of cis-1,4-bromoacetate (cis-15) to the 1,2- and trans-1,4-isomer (15' and trans-15) to account for the latter products seems unlikely since the ratio between the three isomers cis-15, trans-15 and 15' was essentially unchanged during the reaction.

![Reaction scheme](image)

<table>
<thead>
<tr>
<th></th>
<th>Acetic acid/HOAc</th>
<th>OAc</th>
<th>OAc</th>
<th>Br</th>
<th>Br</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/1²</td>
<td>69 : 23 : 8</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/1³</td>
<td>63 : 28 : 10</td>
<td>83</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14/1⁴</td>
<td>83 : 10 : 8</td>
<td>65</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Acetic acid (100% p.a.), acetone (p.a.), and manganese (IV) oxide (active precipitated) were purchased from Merck, p-Benzoquinone (98%), anhydrous lithium bromide (99%), lithium chloride (99%) and 1,3-cyclohexadiene (distilled before use) were purchased from Aldrich. 1,3-Cycloheptadiene was prepared according to a literature procedure.¹⁵

**General procedure for palladium(II)-catalyzed 1,4-diacyloxylation of conjugated cyclic dienes. Method A.** Unless otherwise noted, all reactions were performed at room temperature in acetone using Pd(OAc)₂ as the catalyst (0.05 equiv.). The amount of acid was 7–10 equiv. and the amount of p-benzoquinone was 2.1 equiv.

**Method B.** As above but with the lithium salt of the acid added.

Experimental

NMR spectra were obtained with a Varian XL 300 FT spectrometer, ¹H NMR at 299.3 MHz, and ¹³C NMR at 75.4 MHz. Assignment of ¹³C NMR spectra was achieved by running 2D NMR shift correlation experiments. The software was supplied by the manufacturer. Some ¹³C–¹H shift correlation experiments were performed with a modified sequence developed recently by Reynolds et al.¹¹ Chemical shifts are reported in δ units, parts per million (ppm) downfield from tetramethylsilane, Me₄Si, for ¹H spectra. For ¹³C spectra the chemical shifts are reported relative to the central peak of internal CDCl₃ (77.00 ppm). Infrared spectra were recorded with a Perkin Elmer 1600 FT-IR spectrometer. Analytical GLC was performed on a Varian 3400 Gas Chromatograph using a 30-m DB5 capillary column. Chemical ionization (CI) spectra were recorded on a Finnigan INCOS 50 mass spectrometer connected to a Varian 3400 Gas Chromatograph, with methane as the ionizing gas. High-pressure liquid chromatography (HPLC) was performed using a Waters 501 HPLC pump with a Waters RCM 8 × 10 equipped with a Resolve silica column (10-μ packing, 0.8×10 cm) connected to a Waters differential refractometer and a Waters differential refractometer electronic unit. Bulb-to-bulb distillations were performed with a Büchi Kugelrohr apparatus. Melting points were obtained on a Büchi apparatus and are uncorrected. Elementary analyses were performed at Engelskirschen Analytische Laboratorien, West Germany.

Acetic acid (100% p.a.), acetone (p.a.), and manganese (IV) oxide (active precipitated) were purchased from Merck, p-Benzoquinone (98%), anhydrous lithium bromide (99%), lithium chloride (99%) and 1,3-cyclohexadiene (distilled before use) were purchased from Aldrich. 1,3-Cycloheptadiene was prepared according to a literature procedure.¹⁵

Conclusions

The introduction of carboxylates other than acetate in the 1,4-haloacyloxylation and 1,4-diacyloxylation of conjugated dienes extends the use of these oxidation products as building blocks. The improved procedures should be useful in the following respects. (a) Compounds that are stable towards hydrolysis and enolization are available. (b) The procedures provide better leaving groups in the classical S₂,2 and S₆,2' reactions as well as milder Pd(0)-catalyzed substitutions. (c) Asymmetric synthesis utilizing readily available acids from the chiral pool could be realized. (d) Annulation reactions with nucelophiles incorporated into the carboxylic acid for the synthesis of lactones and other heterocycles would be possible.
Method C. As method B but with the use of catalytic amount of p-benzoquinone (0.25 equiv.) added together with manganese(IV) oxide (1.25 equiv.).

cis-1,4-Diacetoxy-2-cyclohexene (cis-1). Method A was used. To a stirred solution of Pd(OAc)$_2$ (90 mg, 0.40 mmol), acetic acid (4.80 g, 80.0 mmol) and p-benzoquinone (1.80 g, 16.8 mmol) in acetone (25 ml) was added 1,3-cyclohexadiene (640 mg, 8.00 mmol) via syringe over 2 h 15 min. After a total reaction time of 15 h, the acetone was removed in vacuo and the residue diluted with brine (25 ml) and extracted with ether/pentane (1×40 ml, 3×20 ml, 1:1). The combined organic layers were washed with 2 M NaOH (4×10 ml) whereupon the basic layers were back-extracted with ether/pentane (20 ml, 1:1). After drying (MgSO$_4$) and evaporation of the solvent, the 1.40 g (88%) of a yellow oil was collected which according to $^1$H NMR spectroscopy was 96% of a mixture of cis-1 (83%) and trans-1 (17%) and 4% of the Diels-Alder adduct between 1,3-cyclohexadiene and p-benzoquinone. The NMR data were fully consistent with those previously reported.$^{28}$

Following the same procedure but using 1.25 equiv. MnO$_2$ and only 0.25 equiv. of p-benzoquinone (method C) gave 59% yield of a mixture of cis-1 (58%) and trans-1 (42%).

trans-1,4-Diacetoxy-2-cyclohexene (trans-1). Method C was used. To a stirred mixture of Pd(OAc)$_2$ (16.8 mg, 0.075 mmol), LiOAc $\cdot$ 2H$_2$O (171 mg, 1.65 mmol), p-benzoquinone (46 mg, 0.043 mmol), MnO$_2$ (158 mg, 1.82 mmol), and acetic acid (0.50 ml, 8.3 mmol) in 2.5 ml acetone was added 1,3-cyclohexadiene (120 mg, 1.50 mmol) and pentadecane (50 μl, internal standard). Work-up was performed as for cis-1 after 11 h at room temperature. GLC analysis indicated 92% yield, HPLC and $^1$H NMR analyses indicated a trans:cis ratio of 93:7. Chromatography on silica (hexane, hexane-ether = 85:15) afforded 260 mg (87%) of trans-1. The $^1$H NMR spectrum was consistent with that previously reported.$^{28}$

1,4-Bis(trifluoroacetoxy)-2-cyclohexene (2). Following method B, 1,3-cyclohexadiene (640 mg, 8.00 mmol) was added over 2.5 h to a solution of Pd(OAc)$_2$ (90 mg, 0.40 mmol), trifluoroacetic acid (9.50 g, 83.3 mmol), lithium trifluoroacetate (202 mg, 0.170 mmol) and p-benzoquinone (1.82 g, 16.8 mmol) in acetone (24 ml). After the reaction had been stirred for 23 h, the acetone was removed in vacuo and the residue was extracted thoroughly with pentane-ether (total 125 ml, 1:1). The organic phase was washed with satd. Na$_2$CO$_3$ (4×30 ml) and dried (MgSO$_4$). Concentration in vacuo afforded an oil, 2.31 g (94%), which solidified slowly. According to $^1$H NMR and GLC it consisted of trans-2 and cis-2 in a ratio of 77:23 contaminated with a small amount of monoalcohol.$^{15}$ Further characterization was obtained through the mild hydrolysis of the stereoisomeric mixture to the known diols.$^{28}$

cis-1,4-Dibenzoxoxy-2-cyclohexene (cis-3). Method A was used. To a stirred mixture of Pd(OAc)$_2$ (46 mg, 0.20 mmol), benzoic acid (3.71 g, 30.4 mmol), and p-benzoquinone (950 mg, 8.80 mmol) in acetone (25 ml) was added 1,3-cyclohexadiene (320 mg, 4.00 mmol) via syringe over 4 h. After 17 h at room temperature, the acetone was removed in vacuo, followed by addition of ether (75 ml) to the residue. The ether phase was washed with 2 M NaOH (2×20 ml)$^{14}$ and finally once with 2 M NaOH (10 ml) with some NaBH$_4$ added. The combined basic layers were back-extracted with ether (2×10 ml) whereupon the combined organic layers were dried (MgSO$_4$). Evaporation of the solvent afforded 1.10 g (85%) of an oil which slowly solidified. The $^1$H NMR and GLC showed 93% cis-3 and 7% trans-3. Recrystallization from hexane afforded pure (>99%) cis-3 in 65% yield, m.p. 79.5–82.5°C. Further characterization was obtained by hydrolysis to the known diol.$^{28}$ $^1$H NMR (CDCl$_3$): $\delta$ 8.09 (m, 2 H, ortho), 7.56 (m, 1 H, para), 7.44 (m, 2 H, meta), 6.10 (br d, 1 J 1.5 Hz, 2 H, olefinic), 5.54 (m, 2 H, CHO$_2$CPh), 2.10 (m, 4 H, CH$_2$$_2$). $^{13}$C NMR (CDCl$_3$): $\delta$ 165.98 (O=CPh), 132.96 (para), 130.46 (olefinic), 130.20 (ipso), 129.60 (ortho), 128.29 (meta), 67.82 (CHO$_2$CPh), 25.05 [(CH$_2$)$_2$], IR (KBr): 1709 (br), 1342, 1316, 1265, 1121, 1108, 1012, 710 cm$^{-1}$. MS (Cl–CH$_2$)$_2$: m/z (rel. intensity) 229 (2), 202 (15), 201 (100), 200 (3), 151 (4), 123 (22), 106 (2), 105 (33), 81 (2), 79 (7); Found: C, 74.44; H, 5.54. Calc. for C$_{12}$H$_{14}$O$_2$: C, 74.50; H, 5.63.

trans-1,4-Dibenzoxoxy-2-cyclohexene (trans-3). Method B was used. 1,3-Cyclohexadiene (640 mg, 8.00 mmol) was added to a mixture of Pd(OAc)$_2$ (90 mg, 0.40 mmol), benzoic acid (9.20 g, 75.4 mmol), lithium benzoate (0.90 g, 7.0 mmol), and p-benzoquinone (1.82, 16.8 mmol) in acetone (25 ml) at 32°C over 4 h. After 14 h, a work-up as for cis-3 yielded 2.50 g (97%) of a pale yellow solid which according to $^1$H NMR spectroscopy was trans-3 (80%) and cis-3 (20%). Flash chromatography on silica (hexane:ethanol-acetate 95:5) afforded 1.80 g (70%) of trans-3 as a colorless solid (contaminated with 3% of cis-3), m.p. 95.5–98.0°C. Further characterization was obtained by hydrolysis to the known diol.$^{28}$ HPLC: $k'$ = 2.0 (hexane:ethanol acetate 90:10);
cis-1,4-Diacetoxy-2-cycloheptene (cis-4). Method B was used. Pd(OAc)₂ (22.4 mg, 0.10 mmol), acetic acid (1.20 g, 20.0 mmol), LiOAc · 2H₂O (816 mg, 8.00 mmol), p-benzoquinone (454 mg, 4.20 mmol) and 1,3-cycloheptadiene (188 mg, 2.00 mmol) in acetone (6.0 ml) was heated to 40°C for 2 h. Work-up as for cis-1 afforded 430 mg (100%) of a solid, which according to ¹H NMR spectroscopy was 92% cis-4 and 8% trans-4. Recrystallization from hexane yielded 340 mg (80%) of isomerically pure cis-4 (>99% cis). The ¹H NMR data were fully consistent with those previously reported.¹⁹

1,4-Dibenzoxyl-2-cycloheptene (5). Method A was used. Pd(OAc)₂ (45 mg, 0.20 mmol), benzoic acid (4.88 g, 40.0 mmol), p-benzoquinone (908 mg, 8.40 mmol) and 1,3-cycloheptadiene (380 mg, 4.00 mmol) in acetone (12 ml) were stirred for 183 h at room temperature. Work-up as for cis-3 afforded 1.24 g (92%) of an almost pure (>96%) oil which according to ¹H NMR was a mixture of cis-5 and trans-5 (ratio 7:3). The isomers were separated by flash chromatography (hexane-ethyl acetate 95:5) on silica. Further characterization was obtained by hydrolysis to the diols. Samples of cis- and trans-2-cycloheptene-1,4-diols were obtained by hydrolysis of the known corresponding diacetates.²⁰

cis-5: m.p. 89.5–91.0°C; ¹H NMR (CDCl₃): δ 8.07 (m, 2 H, ortho), 7.57 (m, 1 H, para), 7.45 (m, 2 H, meta), 5.90 (br s, 2 H, olefinic). ¹³C NMR (CDCl₃): δ 165.64 (OCH₃), 132.98 (para), 132.69 (olefinic), 130.30 (ipso), 129.61 (ortho), 128.33 (meta), 74.09 (CHO,CH₂), 32.50 (CH₂,CH₃), 22.75 (CH₃,CH₃). IR (KBr): 2925, 1718, 1704, 1330, 1274, 1108, 712 cm⁻¹. MS (CI-CH₃): m/z (rel. intensity) 243 (2), 216 (16), 215 (100), 214 (2), 151 (2), 123 (9), 106 (4), 105 (5), 95 (3), 93 (8).

trans-5: m.p. 78.5–81.5°C; ¹H NMR (CDCl₃): δ 8.07 (m, 2 H, ortho), 7.57 (m, 1 H, para), 7.45 (m, 2 H, meta), 6.00 (br d, J 2.0 Hz, 2 H, olefinic), 5.74 (m, 2 H, CHO,CH₂), 2.04 (br s, 6 H, CH₃). ¹³C NMR (CDCl₃): δ 165.69 (OCH₃), 133.21 (olefinic), 132.96 (para), 130.31 (ipso), 129.59 (ortho), 128.36 (meta), 72.16 (CHO,CH₂), 31.96 (CH₂,CH₃), 20.14 (CH₃,CH₃). IR (neat): 1705, 1335, 1266, 1108, 1068, 1024, 937, 709 cm⁻¹. MS (CI-CH₃): m/z (rel. intensity) 216 (16), 215 (100), 151 (5), 123 (13), 106 (7), 105 (92), 95 (5), 93 (13).

By using 8 equiv. of benzoic acid and 4 equiv. of lithium benzoate in refluxing acetone (method A), a mixture enriched in trans-5 product (55% trans) was obtained in a quantitative yield.

1,4-Bis(trifluoroacetoxy)-2-cycloheptene (6). Method A was used. Pd(OAc)₂ (46 mg, 0.20 mmol), trifluoroacetic acid (4.56 g, 40.0 mmol), p-benzoquinone (908 mg, 8.40 mmol) and 1,3-cycloheptadiene (380 mg, 4.00 mmol) in acetonitrile (12 ml). After 70 h at room temperature, a work-up as for 2 gave 638 mg (50%) of an oil which according to NMR spectroscopy was trans-6 (62%) and cis-6 (38%) contaminated with small amounts of the mono-alkanol.³³ Further characterization was obtained by means of mild hydrolysis to the diols. Samples of cis- and trans-2-cycloheptene-1,4-diols were obtained by hydrolysis of the known corresponding diacetates.²⁰

cis-6: ¹H NMR (CDCl₃): δ 5.96 (br d, 2 H, olefinic), 5.60 (m, 2 H, CHO,CCF₃), 1.99 (br s, 6 H, (CH₃)₂). MS (CI-CH₃): m/z (rel. intensity) 208 (6), 207 (55), 151 (2), 95 (2), 94 (9), 93 (100).
trans-6: ¹H NMR (CDCl₃): δ 5.84 (br s, 2 H, olefinic), 5.55 (m, CH₂,CCF₃), 2.17–1.83 (m, 6 H, (CH₃)₂). MS (CI-CH₃): m/z (rel. intensity) 208 (7), 207 (58), 206 (3), 95 (2), 94 (7), 93 (100).

General procedure for palladium(II)-catalyzed 1,4-chloroacyloxylation of conjugated cyclic dienes. The reactions were performed at ambient temperature in acetonitrile (3 ml mmol⁻¹ diene) with 1.5–2 equiv. of LiCl and 0.5–2 equiv. of Li₂CO₃ (or the lithium carboxylate of the acid) using PdCl₂, Li₂PdCl₄, or Pd(OAc)₂ as the catalyst (0.05 equiv.). The amount of acid used was 5–10 equiv. p-Benzoquinone (2.1 equiv.) was used as the oxidant unless otherwise noted. Addition of 1,3-cyclohexadiene was performed via syringe over 2–4 h, while 1,3-cycloheptadiene was added in one portion.

cis-1-Acetoxy-4-chloro-2-cyclohexene (7). 1,3-Cyclohexadiene (641 mg, 8.00 mmol) was added over 2 h via syringe to a solution of Pd(OAc)₂ (90 mg, 0.40 mmol), LiCl (509 mg, 12.00 mmol), acetic acid (4.80 g, 80.0 mmol), and p-benzoquinone (1.82 g, 16.8 mmol) in acetonitrile (24 ml) with added Li₂CO₃ (296 mg, 4.00 mmol). After 18 h at room temperature, a work-up as for cis-1 afforded a pale yellow oil (1.25 g, 89%) which according to ¹H NMR spectroscopy was a >97% pure product contaminated with small amounts of Diels–Alder adduct. The ¹H NMR spectrum was consistent with that previously reported.³
cis-1-Chloro-4-isobutyroyloxy-2-cyclohexene (9). Performed as above with 10 equiv. of isobutyric acid. The reaction mixture was stirred for 12 h at room temperature. Work-up for cis-1 yielded a colorless oil which according to NMR was a pure product, 1.36 g (87%): 1H NMR (CDCl3): δ 5.87 (dddt, J 10.0, 3.8, 1.7, 0.5 Hz, 1 H, CH=CHCHI), 5.69 [dddt, J 10.0, 2.9, 1.0, 0.5 Hz, 1 H, CH=CHCHO2CC(CHOH)], 5.17 [m, 1 H, CHOOCCH(CH3)], 4.46 [m, 1 H, CHCl], 2.45 [m, J 7.0 Hz, 1 H, CH(CH3)], 2.60–1.99 [m, 2 H, CH2CH(CH3)], 1.89–1.81 [m, 2 H, CH2CHO2CC(CHOH)], 1.073 [d, J 7.0 Hz, 1 CH2CH2], one of two diastereotopic, 1.073 [d, J 7.0 Hz, 1 CH2CH2], one of two diastereotopic. 13C NMR (CDCl3): δ 176.42 O2CC(CHOH), 131.40 (CH=CHCHI), 129.40 [CH=CHCHO2CC(CHOH), 67.17 [CHOOCCH(CH3)], 53.44 (CHCl), 33.87 [CH2CH2], 29.45 [CH2CH2CO2CC(CHOH)], 18.82 [CH2CH2], one of two diastereotopic, 18.75 [CH2CH2], one of two diastereotopic]. IR (neat): 2973, 1732, 1256, 1228, 1189, 1157, 1071, 1018 cm−1; MS (CI–CH3), m/z (rel. intensity) 203 [M+1, 5], 168 (12), 167 (100), 117 (20), 115 (35), 89 (73), 79 (53), 75 (13), 71 (34).

cis-1-Chloro-4-pivaloyloxy-2-cyclohexene (10). To a mixture of PdCl2 (71 mg, 0.40 mmol), Li2CO3 (1.18 g, 16.0 mmol), pivalic acid (8.18 g, 80.0 mmol), LiCl (640 mg, 15.2 mmol), and p-benzoquinone (1.82 g, 16.8 mmol) in acetone (24 ml) was added 1.3-cyclohexadiene (641 mg, 8.00 mmol) over 2 h via syringe. After 25 h, work-up as for cis-3 afforded 1.51 g (87%) of a colorless oil of >98% purity: 1H NMR (CDCl3): δ 5.96 (dddd, J 10.0, 3.8, 1.8, 0.8 Hz, 1 H, CH=CHCHI), 5.78 [dddt, J 10.0, 2.9, 1.0, 0.7 Hz, 1 H, CH=CHCHO2CC(CHOH)], 5.25 [m, 1 H, CHOOCCH(CH3)], 4.57 [m, 1 H, CHCl], 2.17–2.09 (m, 2 H, CH2CHCl), 1.98–1.90 [m, 2 H, CH2CHO2CC(CHOH)], 1.21 [s, 9 H, (CH3)], 13C NMR (CDCl3): δ 178.0 [O2CC (CH3)], 131.42 (CH=CHCHI), 129.60 [CH=CHCHO2CC(CHOH)], 67.32 [CHOOCCH(CH3)], 53.66 (CHCl), 38.67 [CH2CH2], 29.58 (CH2CH2), 27.06 [(CH3)], 24.37 [CH2CHO2CC(CHOH)]: IR (neat): 2969, 1728, 1480, 1280, 1228, 1156, 1035, 1016 cm−1; MS (Cl–CH3): m/z (rel. intensity) 217 [M+1]−, 2, 182 (13), 181 (100), 143 (4), 131 (10), 123 (4), 117 (8), 115 (26), 104 (5), 103 (90), 96 (3), 95 (27), 86 (9), 85 (21), 84 (12), 80 (3), 79 (40). Found: C, 60.83; H, 7.81. Calcd. for C31H32Cl2O2: C, 60.97; H, 7.91.

cis-1-Benzoyloxy-chloro-2-cyclohexene (11). To a stirred solution of Li2PdCl4 (105 mg, 0.40 mmol), LiCl (509 mg, 12.0 mmol), lithium benzoate (549 mg, 4.30 mmol), benzoic acid (7.80 g, 63.9 mmol) and p-benzoquinone (1.82 g, 16.8 mmol) in acetone (30 ml), was added 1,3-cyclohexadiene (651 mg, 8.00 mmol) via syringe over 4 h. After an additional 14 h the reaction was worked up as cis-3 to afford a yellow oil (1.50 g) of 94% purity. The Diels–Alder adduct between 1,3-cyclohexadiene and p-benzoquinone, 6% in the crude product, was easily removed by flash chromatography (hexane–ethyle acetate 90:10) on silica to yield 1.33 g (70%) of pure product, HPLC: k’ = 1.6 (hexane–ethyle acetate 90:10). 1H NMR (CDCl3): δ 8.05 (m, 2 H, ortho), 7.55 (m, 1 H, para), 7.43 (m, 2 H, meta), 6.01 (ddd, J 10.0, 3.7, 1.6 Hz, 1 H, CH=CHCHI), 5.92 (ddt, J 10.0, 2.8, 0.8 Hz, 1 H, CH=CHCHO2CPh), 5.53 (m, 1 H, CHOOCPh), 4.58 (m, 1 H, CHCl), 2.21–2.04 [m, 4 H, (CH2)]. 13C NMR (CDCl3): δ 165.83 (O2CPh), 132.90 (para), 131.74 (CH=CHCHI), 129.98 (ipso), 129.49 (ortho), 129.22 (CH=CHCHO2CPh), 128.20 (meta), 68.04 (CHOOCPh), 53.47 (CHCl), 29.50 (CH2CHO2CPh), 24.94 (CHCl): IR (neat): 1716, 1452, 1315, 1270, 1109, 1070, 1026, 1014, 712 cm−1; MS (Cl–CH3): m/z (rel. intensity) 237 [M+1]−, 222 (20), 215 (20), 151 (100), 151 (39), 117 (23), 115 (61), 105 (84), 81 (11), 79 (96). Found: C, 65.78; H, 5.52. Calcd. for C31H32Cl2O2: C, 65.96; H, 5.55.

cis-1-Acetoxy-4-chloro-2-cycloheptene (12) was prepared as for cis-13 and worked up as for cis-1. Bulb-to-bulb distillation (75–85 °C/0.05 mmHg) afforded 648 mg (69%) of a colorless oil which according to 1H NMR spectroscopy was cis-12 (90%) and cis-4-acetoxy-3-chloro-2-cycloheptene (cis-12*) (10%). The 1H NMR spectrum of cis-12 was completely consistent with data previously reported.3 Compound cis-12* was isolated by preparative HPLC: k’ = 2.1 (hexane–ethyle acetate 98:2). 1H NMR (CDCl3): δ 6.05 (ddd, J 11.1, 6.5, 5.5 Hz, 1 H, CH=CHCHI), 5.82 (ddd, J 11.1, 7.4, 1.7, 1.0 Hz, 1 H, CH=CHCHI), 5.10 (ddd, J 10.4, 4.0, 2.0 Hz, 1 H, CHOCa), 4.68 (dddt, J 7.4, 3.2, 2.0, 0.5 Hz, 1 H, CHCl), 2.37–2.12 (m, 1 H, CH2CH2), and 2 H, CH2CH2), 2.09 (s, 3 H, CH3CO2), 2.01–1.77 (m, 2 H, CH2CHCl), 1.67–1.55 [m, 1 H, CH2CH2]. MS (Cl–CH3): m/z (rel. intensity) 189 [M+1]+, 354 (5), 153 (49), 131 (33), 130 (9), 129 (100), 111 (18), 93 (57), 88 (10), 86 (62), 84 (99).

cis-1-Chloro-4-pivaloyloxy-2-cyclohexene (13). 1.3-Cyclohexadiene (470 mg, 5.0 mmol) was added to a solution of Li2PdCl4 (65 mg, 0.25 mmol), Li2CO3 (165 mg, 2.50 mmol), and p-benzoquinone (1.19 g, 11.0 mmol) in ace-
tone (15 ml). After 72 h of stirring at room temperature only 5–10% of the diene remained. Work-up as for cis-3 gave an oil which was bulb-to-bulb distilled (100°C/0.05 mmHg) to yield 645 mg (56%) of a solid which melts at RT, 87% of cis-13 and 13% of cis-13-chloro-4-pivaloyl-2-cyclohexene (cis-13').

cis-13': HPLC: *k* = 1.6 (hexane–ethyl acetate 98:2). 1H NMR (CDCl3): δ 5.88 (ddd, J 12.0, 4.4, 2.3, 0.6 Hz, 1 H, CH=CHCH2Cl), 5.67 (ddd, J 12.0, 3.0, 1.7, 1.0 Hz, CH=CH2OCC(C3H7)2), 5.35 [m, 1 H, CHOCC(C3H7)2], 4.65 (m, 1 H, CHCl), 2.21–1.71 [m, 6 H, (CH3)2], 1.21 [s, 9 H, (CH3)3]; 13C NMR (CDCl3): δ 177.65 [O2CC(CH3)2], 133.85 [CH=CHCHOCC(C3H7)2], 133.29 [CH=CHC(CH2)3], 72.10 [CHOCC(C3H7)2], 58.57 (CHCl), 36.03 (CH2CHCl), 31.92 [CH2OCC(C3H7)2], 27.02 [CH3], 22.60 [CH2(CH3)2]. IR (neat): 2971, 2936, 1728, 1480, 1281, 1158, 1033, 992 cm⁻¹. MS (CI−CH3): m/z (rel. intensity) 231 [(M+1)⁺, 3], 196 (13), 195 (83), 143 (4), 131 (21), 129 (33), 111 (7), 104 (3), 103 (42), 95 (4), 94 (10), 93 (100), 86 (3), 85 (54).

cis-13' (in mixture with cis-13): 1H NMR (CDCl3): δ 6.04 (ddd, J 11.3, 6.5, 5.6 Hz, 1 H, CH=CHCH2Cl), 5.81 (ddd, J 11.3, 7.0, 1.7, 0.5 Hz, 1 H, CH=CHCH2Cl), 5.07 (ddd, J 9.9, 4.0, 2.0 Hz, 1 H, CHOCC(C3H7)2), 4.66 (m, 1 H, CHCl), 13C NMR (CDCl3): δ 137.44 (CH=CH2Cl), 127.26 (CH=CH2Cl), 73.29 [CHOCC(C3H7)2], 60.79 (CHCl), 38.56 (CH2CH=CH2), 30.73 [CH2OCC(C3H7)2], 27.43 [(CH3)2], 23.16 [CHF2(C3H7)2]. MS (CI−CH3): m/z (rel. intensity) 231 [(M+1)⁺, 13], 196 (12), 195 (77), 131 (38), 130 (10), 129 (100), 111 (11), 103 (28), 93 (22), 85 (44), 75 (10).

cis-1-Benzoyloxy-4-chloro-2-cyclohexene (14). This was prepared as for cis-13 but using a slightly larger volume of acetone (20 ml) and with lithium benzoate (961 mg, 1.50 mmol) in place of Li2CO3. Work-up as for cis-3 and subsequent bulb-to-bulb distillation (190–200°C/0.05 mmHg) afforded 749 mg (60%) of a solid, which consisted of cis-14 (93%) and cis-4-benzoyloxy-3-chloro-2-cyclohexene (cis-14) (7%).

cis-14: 1H NMR (CDCl3): δ 8.06 (m, 2 H, ortho), 7.56 (m, 1 H, para), 7.44 (m, 2 H, meta), 5.94 (ddd, J 12.2, 6.4, 2.1 Hz, 1 H, CH=CHCH2Cl), 5.83 (ddd, J 12.2, 3.1, 1.4, 1.0 Hz, 1 H, CH=CHCHOCH2P), 5.63 (m, 1 H, CHOCH2P), 4.69 (m, 1 H, CHCl), 2.24–1.77 [m, 6 H, (CH3)3]; 13C NMR (CDCl3): δ 165.66 (O2P), 133.65 (CH=CHCHOCH2P), 133.55 (CH=CHCH2Cl), 133.02 (para), 129.72 (ipsO), 129.60 (ortho), 128.34 (meta), 73.00 (CHOCH2P), 58.53 (CHCl), 36.06 (CH3CH2Cl), 32.12 (CH2OCCP), 22.64 [(CH3)2]. IR (neat): 1717, 1450, 1316, 1272, 1113, 1070, 1026, 712 cm⁻¹; MS (CI−CH3): m/z (rel. intensity) 251 [(M+1)⁺, 9], 216 (12), 215 (56), 153 (8), 151 (15), 131 (39), 130 (9), 129 (100), 123 (36), 105 (92), 95 (13), 95 (56). Found: C, 66.95; H, 6.03. Calcd. for C18H12O2: C, 67.06; H, 6.04.

References
6. The amount of p-benzoquinone can be lowered significantly if MnO2 is added as an oxidant for hydroquinone (method C).
7. The chloro-alcohol initially formed reacts further to give a mixture of products (via the epoxide) which were not characterized.

13. Characterized by $^1$H NMR and chemical ionization mass spectrometry.
14. The formation of emulsions at this stage can usually be overcome by the addition of NaBH₄.

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