

Molecular Design by Cycloaddition Reactions. Part 32.¹ Transannular Cyclization of Tricyclo[4.2.2.0^{2,5}]deca-3,7-diene Derivatives by Oxypalladation¹

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Reactions of dimethyl tricyclo[4.2.2.0^{2,5}]deca-3,7-diene-9,10-dicarboxylate derivatives with palladium(II) acetate, chloride, and nitrate have been investigated. The products were identified by spectral means and chemical transformations. Mechanisms for their formation are discussed.

WE have investigated extensively the reaction of tricyclo[4.2.2.0^{2,5}]deca-3,7-diene derivatives, which contain two isolated double bonds in spatial proximity, with mercury(II),² lead(IV),³ and thallium(III) salts.³ The reaction can lead to a variety of products depending on the nature of the metal and the solvent. For example the reaction of dimethyl tricyclo[4.2.2.0^{2,5}]deca-3,7-diene-9,10-dicarboxylate (1) † with mercury(II) acetate gave the *exo,cis*-adduct to the cyclobutene unit. Although the organometallic adduct from (1) and lead tetra-acetate was not isolated, it was suggested that

production of an intermediate acetoxy-metal complex preceded formation of the ring-contracted products. It was particularly interesting that oxythallation of (1) gave the products of transannular interaction, indicating the participation of the cyclohexene system in the reaction. In the light of these results it seemed that carbon-carbon bond formation by the reaction of the cyclic diene with palladium salts was a possibility. We now describe the reactions of (1) with palladium(II) chloride, acetate, and nitrate under various conditions.

¹ Part 31, T. Sasaki, K. Kanematsu, and A. Kondo, *Chem. Letters*, 1976, 783.

² T. Sasaki, K. Kanematsu, A. Kondo, and Y. Nishitani, *J. Org. Chem.*, 1974, **39**, 3569.

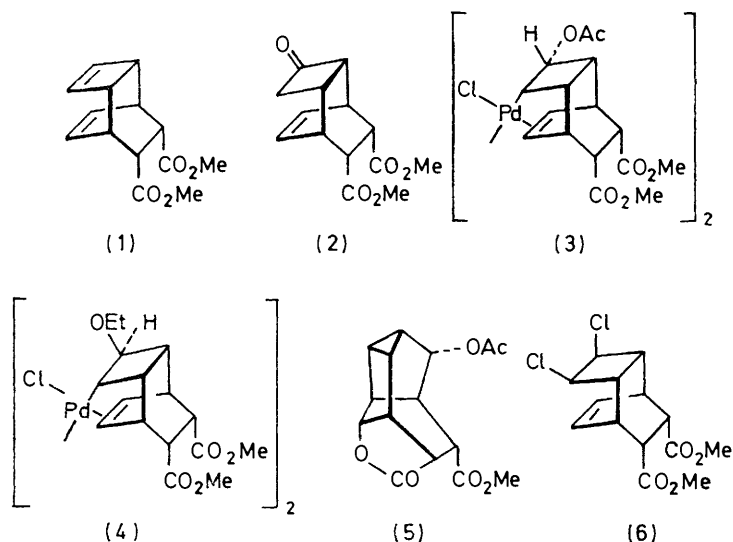
³ T. Sasaki, K. Kanematsu, A. Kondo, and K. Okada, *J. Org. Chem.*, 1976, **41**, 2231.

† Strict application of I.U.P.A.C. rules leads to the name 'dimethyl tricyclo[4.2.2.0^{2,5}]deca-3,9-diene-7,8-dicarboxylate' for structure (1). However, names based on 'tricyclo[4.2.2.0^{2,5}]deca-3,7-diene' will be retained in the present paper, for clarity.

RESULTS

Reaction of the Diene (1) with Palladium(II) Chloride.—Treatment of (1) with an equimolar quantity of palladium(II) chloride in refluxing acetic acid, followed by chromatography on silica gel gave three products [(2) (10%), (3)

characteristic methine proton (H_a) signals at δ 4.90 and 4.48, respectively. The lower-field position of this signal in the latter case is attributable to shielding by the cyclohexene system. Thus, the acetoxy-group in (7) can be assigned the *endo*-configuration. On the other hand,



(2.5%), and (4) (1.3%)]. Increased yields of the products (2) and (3) were obtained by performing the reaction in the presence of sodium acetate. However, the reaction of (1) with a catalytic amount of palladium(II) chloride in the presence of copper(II) chloride and sodium acetate under the same conditions gave compounds (5) (74%) and (6) (17%), and at lower temperature compound (5) was

compound (4) was shown to have an *exo*-ethoxy-group by comparison with an authentic sample⁵ and by further

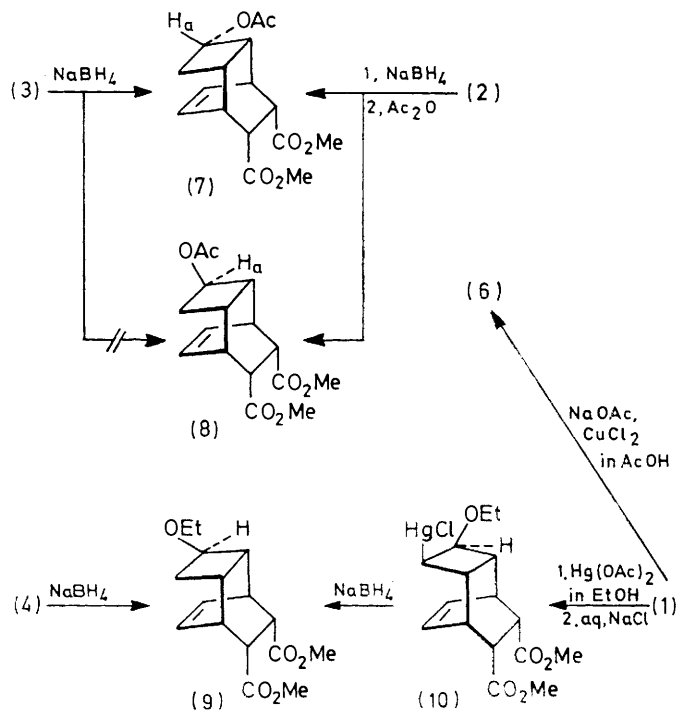
Reactions of the diene (1) with palladium chloride under various conditions

Added reagent(s)	Temp. (°C)	Products (%)				
		(2)	(3)	(4)	(5)	(6)
None	118–120	10	2.5	1.3		
NaOAc	118–120	25	15	1.5		
CuCl ₂ , NaOAc	70–75				54*	
CuCl ₂ , NaOAc	118–120				74	17

* Recovery of (1) 42%.

obtained in 54% yield with unchanged starting material (42%). These results are summarized in the Table.

The product (2) was easily identified by comparison with an authentic sample.⁴ The n.m.r. spectrum of the product (3), C₁₆H₁₉ClO₆Pd, exhibited signals for two olefinic protons at δ 5.93 and 6.38, a methine proton at δ 4.20, two methyl groups at δ 3.65 (2 CO₂Me), one methyl group at δ 2.24 (OAc), and seven methine protons at δ 2.5–3.5, indicating the presence of an acetoxy-palladium complex of the diene. Furthermore, the configuration of acetoxy-group was determined as *endo* by chemical degradation as follows. Reduction of (3) with sodium borohydride in methanol gave compound (7). Similar reduction of (2) with sodium borohydride followed by acetylation with acetic anhydride-pyridine gave compound (7) and the known compound in the ratio 1 : 1. The n.m.r. spectra of (7) and (8)² show



SCHEME 1

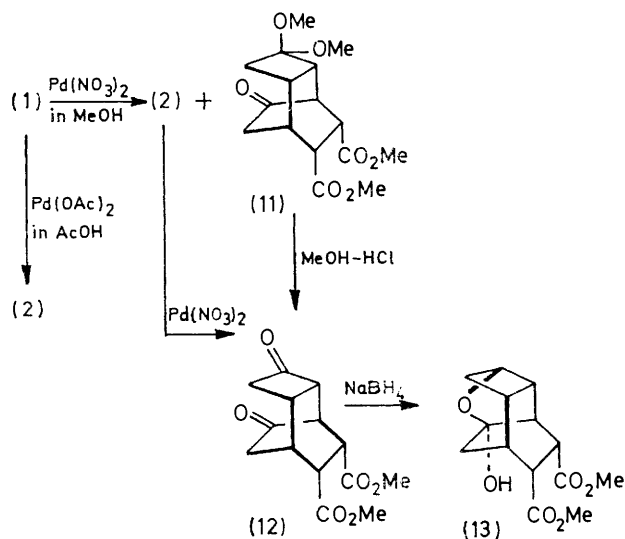
chemical transformation. It is known that diene-palladium chloride complexes react with alkoxide to give the σ - and π -bonded alkoxy-complexes, with the alkoxy-group *exo* to the metal.⁶

⁴ A. C. Cope, S. F. Schaeren, and E. R. Trumbull, *J. Amer. Chem. Soc.*, 1954, **76**, 1096.

⁵ M. Auram, E. Sliam, and C. D. Nenitzescu, *Annalen*, 1960, **636**, 184.

⁶ J. Chatt, L. M. Vallarino, and L. M. Venazi, *J. Chem. Soc.*, 1957, 3413.

Reduction of the product (4) with sodium borohydride in methanol gave (9), which was also obtained by unequivocal independent synthesis. Addition of an equimolar quantity



SCHEME 2

of mercury(II) acetate to the diene (1) in ethanol followed by treatment with aqueous sodium chloride gave the product (10), which was converted into (9) by treatment with sodium borohydride. This ethoxy-complex is probably formed from the palladium–diene 1 : 1 complex during the

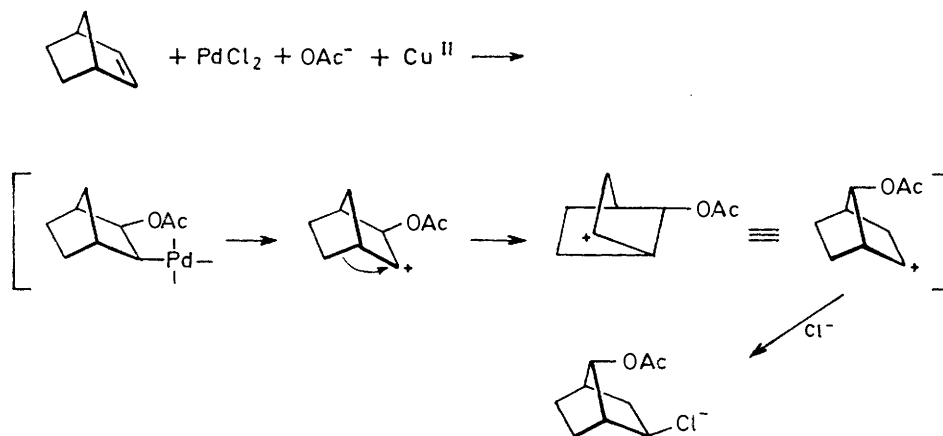
These results are summarized in Scheme 1.

Reactions of the Diene (1) with Palladium Acetate and Nitrate.—The reaction of (1) with an equimolar quantity of palladium acetate in acetic acid at 70–75 °C gave the products (2) (20%) and (4) (6.2%), but at reflux temperature only (2) was obtained, in 50% yield. The reaction of (1) with an equimolar amount of palladium nitrate in methanol at reflux temperature gave the products (2) (51%) and (11) (30%).

The i.r. spectrum of (11) showed carbonyl absorptions at 1 765, 1 740, and 1 730 cm^{-1} . The n.m.r. spectrum exhibited signals at δ 3.63 (2 CO_2Me), 3.12 and 3.05 (2 OMe), 3.2–2.4 (8 H), and 2.2 (2 H). Treatment of (11) with methanol-hydrochloric acid gave a dicarbonyl compound (12), which afforded a transannular cyclization product (13) on reduction with an excess of sodium borohydride in methanol. Compound (12) was also obtained from the reaction of (2) with palladium nitrate in refluxing methanol.

DISCUSSION

The reaction of the diene (1) with palladium chloride depends on whether or not copper(II) chloride is present. The oxidation of (1) in the presence of copper(II) chloride in acetic acid produces the transannular cyclization product (5). However, in the absence of copper(II) chloride, only oxidation of the cyclobutene system to cyclobutanone occurs. The transannular cyclization product might be formed *via* attack by the cyclohexene system on the initially produced cyclobutene–palladium chloride complex to give the σ -palladium complex (A),



SCHEME 3

separation on silica gel (eluant chloroform–ethanol). Compound (5) was identified by comparison with an authentic sample.³ The n.m.r. spectrum of the product (6), $\text{C}_{14}\text{H}_{16}\text{Cl}_2\text{O}_4$, exhibits signals for two olefinic protons at δ 6.50, and no cyclobutene proton signals. The *exo,cis*-configuration of the chlorine on the cyclobutane ring was supported by the observation of equivalent vinyl protons (a clean triplet) and equivalent protons geminal to chlorine, at δ 4.07.⁷ Since compound (6) was also obtained from (1) under the same conditions in the absence of palladium chloride, this compound must be the product of chlorination by copper(II) chloride.

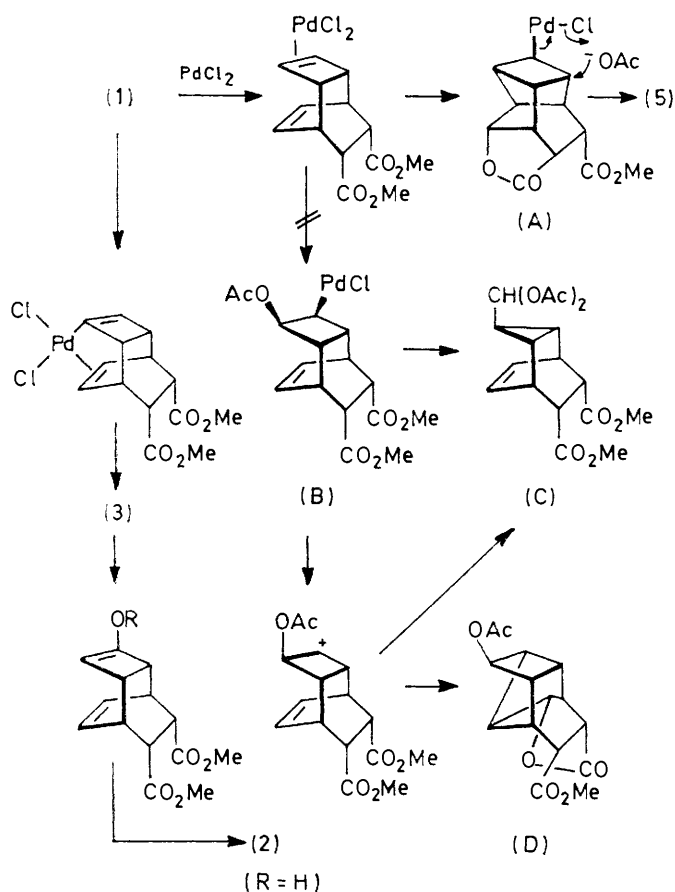
⁷ D. G. Farnum and J. P. Snyder, *Tetrahedron Letters*, 1965, 3861.

the precursor of the rearrangement product (5). Thus, it appears that the cyclobutene–palladium chloride complex might be activated by copper(II) chloride. Oxidation of norbornene with palladium chloride in the presence of copper(II) chloride is reported to give *exo*-2-chloro-*syn*-7-acetoxynorbornene.⁸ This reaction has been rationalized in terms of acetoxy-palladation, followed by heterolysis of the C–Pd bond activated by copper(II) chloride to give an intermediate cation, followed by rearrangement (Scheme 3).

Attack of palladium chloride on the cyclobutene system from the less hindered side to give the acetoxy-

⁸ W. C. Baird, *J. Org. Chem.*, 1966, **31**, 2411.

palladation product (B) does not occur. If the reaction proceed *via* the intermediate (B), the ring contracted product (C) or transannular cyclization product (D) would be expected, as in oxyplumbation and oxythallation of (1). In the absence of copper(II) chloride, the reaction might proceed *via* a palladium chloride-diene complex. Indeed, the isolation of the *endo*-acetoxy-metal complex (3), which gives (2) on heating in refluxing acetic acid, suggests the following pathway: formation of an acetoxy-metal intermediate followed by intramolecular attack by acetate anion to give (3),



SCHEME 4

which gives (2) by loss of HPdOAc, *via* an enol acetate (Scheme 4).

Generally, the mechanism of the palladium acetate-olefin oxidation which appears to accommodate the facts involves oxypalladation, presumably reversible, of the olefin to give the adduct, which then loses the HPdOAc to yield either an enol acetate or an allylic acetate. However, the reaction of the diene (1) with palladium acetate might proceed in a similar manner to that with palladium chloride, as described above. The fact that an acetoxy-palladium complex was not isolated suggests that the complex with acetoxy-groups as ligands is highly reactive.

By contrast, oxidation of (1) with palladium nitrate

gave compounds (2) and (11). The formation of (11) is the first example of the involvement of the cyclohexene unit in reactions of the diene (1) with oxidizing agents, which indicates the strong oxidation potential of palladium nitrate. This result is compatible with the behaviour of thallium nitrate, which is almost ionic, and is more effective for oxidative ring contraction of cyclic olefins than thallium acetate.

EXPERIMENTAL

M.p.s were measured with a Yanagimoto micro apparatus. Microanalyses were performed on a Perkin-Elmer 240 Elemental Analyser. N.m.r. spectra were determined with a Japan Optics Co. C-60-XL spectrometer with Me₄Si as internal standard. I.r. spectra were taken with a JASCO IR-S spectrophotometer.

Reactions of Dimethyl Tricyclo[4.2.2.0^{2,5}]deca-3,7-diene-9,10-dicarboxylate with Palladium Chloride.—(a) A mixture of the diene (1) (565 mg) and palladium(II) chloride (400 mg) in acetic acid (30 ml) was refluxed for 16 h, then filtered. The filtrate was added to aqueous sodium chloride and the product was extracted with chloroform. Evaporation of the extract at reduced pressure and chromatography on silica gel (chloroform-ethanol) gave the ketone (2) (60 mg), m.p. 94–96° (lit.,⁴ 94–95°), the *dimeric acetoxy-complex* (3) (50 mg), m.p. 220° (decomp.) (Found: C, 42.95; H, 4.3. C₁₆H₁₀ClO₆Pd requires C, 42.8; H, 4.25%), ν_{\max} (KBr) 1745 cm⁻¹, δ (CDCl₃) 6.38 (1 H, t, *J* 6.0 Hz), 5.93 (1 H, t, *J* 6.0 Hz), 4.20 (1 H, t, *J* 6.0 Hz), 3.65 (6 H, s, 2 CO₂Me), 3.5–2.5 (7 H, m), and 2.24 (3 H, s, OAc), and the *dimeric ethoxy-complex* (4) (25 mg), m.p. 180–185° (decomp.) [lit.,⁵ 185–190° (decomp.)].

(b) *In the presence of sodium acetate.* A mixture of the diene (1) (565 mg), palladium chloride (400 mg), and sodium acetate (185 mg) in acetic acid (30 ml) was refluxed for 16 h. Work-up as before gave compounds (2) (150 mg), (3) (300 mg), and (4) (30 mg).

(c) *In the presence of sodium acetate and copper(II) chloride.* (i) A mixture of the diene (1) (600 mg), palladium chloride (100 mg), sodium acetate (200 mg), and copper(II) chloride (595 mg) in acetic acid (40 ml) was refluxed for 16 h. Work-up as before gave the lactone (5) (520 mg), m.p. 181–183° (lit.,³ 181–183°), and the *dichloride* (6) (130 mg), m.p. 193–195° (Found: C, 52.7; H, 5.05. C₁₄H₁₆Cl₂O₄ requires C, 52.7; H, 5.05%), ν_{\max} (KBr) 1740 cm⁻¹, δ (CDCl₃) 6.50 (2 H, t, *J* 4.5 Hz), 4.07 (2 H, d, *J* 3.0 Hz), 3.60 (6 H, s, 2 CO₂Me), 3.20 (2 H, m), and 2.85br (4 H, s).

(ii) A mixture of the diene (1) (600 mg), palladium chloride (100 mg), sodium acetate (200 mg), and copper chloride (595 mg) in acetic acid (40 ml) was stirred for 16 h at 75 °C. Work-up as before gave compound (5) (375 mg) and unchanged (1) (250 mg).

Reduction of the Acetoxy-complex (3) with Sodium Borohydride.—To a solution of the complex (3) (200 mg) in methanol (20 ml) sodium borohydride (30 mg) was added, and the mixture was stirred for 1 h and filtered. The filtrate was added to water (50 ml) and the product was extracted with chloroform. Evaporation of the extract at reduced pressure and chromatography on silica gel (benzene) gave the *acetate* (7) (50 mg) (Found: C, 62.45; H, 6.6. C₁₆H₂₀O₆ requires C, 62.3; H, 6.55%), ν_{\max} (neat) 1740 cm⁻¹, δ (CDCl₃) 6.37 (2 H, m), 4.90 (1 H, m), 3.60 (6 H, s, 2 CO₂Me), 3.2–2.7 (6 H, m), 2.40 (2 H, m), and 2.03 (3 H, s, OAc), n_D^{20} 1.507 0.

Dimethyl exo- and endo-3-Acetoxytricyclo[4.2.2.0^{2,5}]dec-7-ene-9,10-dicarboxylates (7) and (8).—To a solution of the ketone (2) (300 mg) in methanol (20 ml), sodium borohydride (50 mg) was added. After stirring at room temperature for 2 h, the mixture was decomposed by addition to water. The product was added to pyridine (5 ml) and acetic anhydride (3 ml). After stirring at room temperature for 1 day, the mixture was added to water (20 ml) and extracted with chloroform. Evaporation of the extract gave a 1 : 1 mixture of products (7) and (8) (280 mg) (by n.m.r. analysis). The mixture could not be separated by chromatography on silica gel.

Reaction of the Diene (1) with Mercury(II) Acetate.—A solution of the diene (1) (750 mg) and mercury(II) acetate (960 mg) in ethanol (20 ml) was stirred for 12 h at room temperature, then evaporated under reduced pressure. The residue was treated with an excess of aqueous sodium chloride and the product was extracted with chloroform. Evaporation of the extract, followed by recrystallization from benzene-n-hexane, gave the *ethoxy-complex* (10) (1.49 g), m.p. 70–72° (Found: C, 36.4; H, 4.1. C₁₀H₂₀ClHgO₅ requires C, 36.3; H, 4.0%), ν_{\max} (KBr) 1745 cm⁻¹, δ (CDCl₃) 6.62 (2 H, t, *J* 4.5 Hz), 3.60 (6 H, s, 2 CO₂Me), 3.6–2.6 (10 H, m), and 1.20 (3 H, t, *J* 7.5 Hz).

Reduction of the Ethoxy-complex (10).—To a solution of the complex (10) (800 mg) in methanol (20 ml), sodium borohydride (100 mg) was added. The mixture was stirred for 1 h. Work-up as before gave the *ethoxy-olefin* (9) (250 mg) (Found: C, 65.5; H, 7.45. C₁₆H₂₂O₅ requires C, 65.3; H, 7.55%), ν_{\max} (neat) 1745 cm⁻¹, δ (CDCl₃) 6.43 (2 H, t, *J* 4.5 Hz), 3.60 (7 H, s, 2 CO₂Me and 1 H), 3.30 (2 H, q, *J* 6.9 Hz), 3.1–2.8 (2 H, m), 2.48 (2 H, m), 1.80 (2 H, m), and 1.17 (3 H, t, *J* 6.95 Hz), n_D^{20} 1.508 6.

Reduction of the Ethoxy-complex (4).—To a solution of the complex (4) (540 mg) in methanol (20 ml) sodium borohydride (50 mg) was added. The mixture was stirred for 1 h. Work-up as before gave compound (9) (250 mg).

Reaction of the Diene (1) with Copper(II) Chloride and Sodium Acetate.—A mixture of the diene (1) (300 mg), copper chloride (300 mg), and sodium acetate (100 mg) in acetic acid (20 ml) was refluxed for 16 h. Work-up as before gave the dichloride (6) (380 mg).

Thermolysis of the Acetoxy-complex (3).—A solution of the complex (3) (560 mg) in acetic acid (20 ml) was refluxed

for 10 h. Evaporation followed by chromatography on silica gel gave starting material (3) (330 mg) and the ketone (2) (35 mg).

Reaction of the Diene (1) with Palladium Acetate.—(a) A mixture of (1) (800 mg) and palladium acetate (700 mg) in acetic acid (20 ml) was stirred for 20 h at 75 °C. Work-up gave the ketone (2) (180 mg) and the ethoxy-complex (4) (240 mg).

(b) A mixture of (1) (700 mg) and palladium acetate (615 mg) in acetic acid (20 ml) was refluxed for 16 h. Work-up as before gave the ketone (2) (370 mg).

Reaction of the Diene (1) with Palladium Nitrate.—A mixture of (1) (760 mg) and palladium nitrate (700 mg) in methanol (20 ml) was refluxed for 7 h. Work-up as before gave the ketone (2) (587 mg) and the *oxo-acetal* (11) (300 mg), m.p. 104–105° (Found: C, 59.05; H, 6.65. C₁₆H₂₂O₇ requires C, 58.55; H, 6.8%), ν_{\max} (KBr) 2840, 1765, 1740, and 1725 cm⁻¹, δ (CDCl₃) 3.63 (6 H, s, 2 CO₂Me), 3.12 (3 H, s, OMe), 3.05 (3 H, s, OMe), 3.2–2.5 (8 H, m), and 2.25 (2 H, m).

Reaction of the Oxo-acetal (11) with Methanol-Hydrochloric Acid.—A solution of compound (11) (120 mg) in methanol (12 ml) and hydrochloric acid (2 ml) was refluxed for 4 h. Evaporation, followed by chromatography on silica gel, gave the *dione* (12) (70 mg), m.p. 140–141° (Found: C, 60.15; H, 5.7. C₁₄H₁₆O₆ requires C, 60.0; H, 5.75%), ν_{\max} (KBr) 1790 and 1740 cm⁻¹, δ (CDCl₃) 3.67 (3 H, s, CO₂Me), 3.65 (3 H, s, CO₂Me), 3.5–3.0 (5 H, m), and 3.0–2.5 (5 H, m).

Reaction of the Ketone of (2) with Palladium Nitrate.—A mixture of the ketone (2) (300 mg) and palladium nitrate (260 mg) in methanol (20 ml) was refluxed for 10 h. Work-up as before gave the *dione* (12) (80 mg).

Reduction of the Dione (12) with Sodium Borohydride.—To a solution of the dione (12) (120 mg) in methanol (20 ml), sodium borohydride (50 mg) was added. The solution was stirred for 2 h at room temperature. Work-up as before gave the *hemiacetal* (13) (50 mg), m.p. 143–145° (Found: C, 59.55; H, 6.45. C₁₄H₁₈O₆ requires C, 59.55; H, 6.45%), ν_{\max} (KBr) 3300, 1725, and 1730 cm⁻¹, δ (CDCl₃) 4.52 (1 H, m), 3.69 (7 H, s, 1 H D₂O-exchangeable, 2 CO₂Me and OH), 3.5–3.0 (2 H, m), and 2.6–1.8 (8 H, m).

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