Stable Glucopyranosylpalladium Compound with a Cis β Hydrogen

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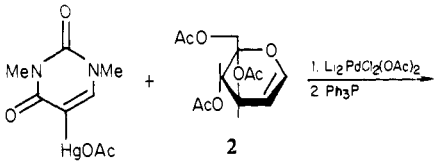
In the course of our studies of palladium-catalyzed reactions of enol ethers[2-6] directed toward the development of new synthetic routes to C-nucleosides,[7] we have succeeded in the stabilization and isolation of a key, palladium-containing reaction intermediate, the adduct **3**[8] formed by regio- and stereospecific addition of a 1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedion-5-ylpalladium(II) reagent (prepared in situ from the corresponding pyrimidinylmercuric acetate[2] (**1**, X = OAc) to 3,4,6-tri-O-acetyl-D-glucal[9] (**2**). The isolation of this adduct (**3**) in which palladium is σ



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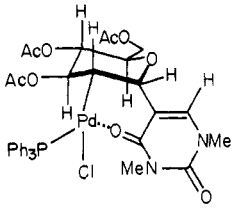

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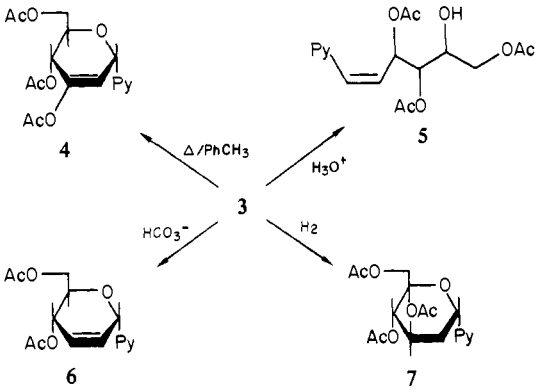
bonded to an aliphatic carbon backbone bearing a cis β hydrogen[10] permits definitive study of the structure and reactions of an organometallic compound type not previously isolated. In this report, we describe four separate decomposition reactions of Pd-adduct **3** (i.e., reactions in which the Pd–C bond is ruptured), each of which yields a single, distinct product. These selective reactions establish **3** and, by analogy, other Pd adducts of glycals as versatile, chiral intermediates for use in stereocontrolled synthetic sequences.

The Pd-adduct **3** was prepared by allowing equimolar quantities of **1**, **2**, palladium (II) acetate, and 2 equiv of lithium chloride in acetonitrile to react at room temperature for 3 days followed by removal of precipitated salts, addition of excess triphenylphosphine, removal of solvent, and purification of the resulting crude adduct by chromatography over silica gel to yield **3** (35–45%) as a nearly colorless powder, mp 138 °C dec, which has been stored at room temperature for periods exceeding 2 months with little decomposition. Adduct **3** was characterized by microanalyses[11] and by ^1H and ^{13}C nuclear magnetic resonance (NMR) spectrometry.[12]

Scheme I. Decomposition Reactions of Pd-Adduct 3 under Selected Conditions[a]



[a] Py = 1,3-dimethyl-2,4-(1*H*,3*H*)-pyrimidinedion-5-yl.

Prior to triphenylphosphine addition, the reaction mixture contained an adduct analogous to **3** in which, presumably, two ligand sites on palladium are occupied by chloride. Attempts to purify this adduct resulted in extensive decomposition. A single triphenylphosphine ligand confers sufficient stability to permit purification.[13] We have studied (by NMR spectrometry and chromatographic techniques) ligand exchange reactions in which **3** adds successively one and two additional triphenylphosphine ligands [forming in the latter instance a positively charged palladium(II) complex ion]. The reverse exchange process is carried out readily by using lithium chloride. The adducts which possess more than one triphenylphosphine ligand lose triphenylphosphine readily and are correspondingly less stable than **3**.

Decomposition of adduct **3** under four distinct controlled reaction conditions led, in each case, to a single product in essentially quantitative yield (Scheme I). When adduct **3** in toluene was heated under reflux for 10 min, the sole product, resulting from *syn* elimination of a hydridopalladium species,[10,14] was 1,3-dimethyl-5-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*erythro*-hex-2-enopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (**4**). Treatment of adduct **3** with 6 N hydrochloric acid effected rupture of the cyclic ether ring (i.e., anti elimination of Pd and alkoxide) to form selectively the acyclic C-nucleoside (*Z*)-1,2-dideoxy-1-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4(1*H*,3*H*)-dioxo-5-pyrimidinyl)-D-*arabino*-hex-1-enitol 3,4,6-triacetate (**5**).[2,6] Similarly, in the presence of aqueous sodium bicarbonate, **3** underwent anti elimination of acetate and palladium to form 5-(4,16-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)-1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedione (**6**).[2,6] Finally, when **3** in tetrahydrofuran was shaken for 2 h under 2 atm of hydrogen, the Pd–C bond was ruptured with replacement of Pd by hydrogen to form the 2-deoxy C-nucleoside 1,3-dimethyl-5-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-2,4(1*H*,3*H*)-pyrimidinedione (**7**).[6]

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(7) Daves, G. D., Jr.; Cheng, C. C. *Prog. Med. Chem.* **1976**, *13*, 303. Hannessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *3*, 111.
(8) The possibility that **3** exists as a dimer has not been ruled out.
(9) Roth, W.; Pigman, W. In "Methods in Carbohydrate Chemistry"; Academic Press: New York, 1963; Vol. II, p 405.
(10) Adducts of this type undergo facile hydridopalladium elimination and are usually not isolable (see, e.g.: Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146 and references cited therein). Recently, examples of stable Pd adducts containing cis β hydrogens were reported: Newkome, G. R.; Kawato, T.; Kohli, D. K.; Puckett, W. E.; Olivier, B. D.; Chiari, G.; Fronczek, F. R.; Deutsch, W. A. *J. Am. Chem. Soc.* **1981**, *103*, 3423.
(11) Found: C, 53.1; H, 4.76; N, 3.58; Pd 12.8, in accord with empirical formula $C_{36}H_{38}ClN_2O_9PPd$.
(12) ^1H NMR (C_6D_6) δ 1.59, 1.77, 1.79 (OAcs); 2.07 (C-2H, *d* of t, *J* = 5, 13 Hz). 2.67, 3.23 (NMes), 3.55 (C-5H, d of t, *J* = 10, 5 Hz), 4.21 (C-6Hs, d, *J* = 5 Hz), 4.83 (C-4H, t, *J* = 10 Hz), 4.94 (C-1H, br), 5.33 (C-3H, m), 6.82 (PyC-6H, d, *J* = 2 Hz), 7.24, 8.05–8.20 (Ar). Resonances and coupling constant assignments are based on extensive spin–spin decoupling experiments. ^{13}C NMR ($CDCl_3$) δ 20.49 (OAc Mes), 29.75, 38.04 (NMes), 36.74, 63.12, 69.41, 72.44, 72.87, 74.01, 107.28, 146.29, 149.69, 166.76, 169.52, 169.90, 170.33; triphenylphosphine resonances were ignored.
(13) The influences of phosphine ligands on metal complex stabilities has been reviewed: Tolman, C. A. *Chem. Rev.* **1977**, *77*, 313.
(14) For recent studies of the mechanism of elimination and insertion reactions of hydridometallic complexes, see, for example: McCarthy, T. J.; Nuzzo, R. G.; Whitesides, G. M. *J. Am. Chem. Soc.* **1981**, *103*, 3396. Nuzzo, R. G.; McCarthy, T. J.; Whitesides, G. M. *Ibid.* **1981**, *103*, 3404. Huggins, J. M.; Bergman, R. G. *Ibid.* **1981**, *103*, 3002.

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