Table II. Solvent and Additive Effects on Methyl Acrylate Dimerization Catalyzed by 1 + $2NaC_{10}H_8$

reactn medium[a]	ca. 1 h			ca. 3 h		
	% convn MA	% yield DHD[b]	TO[c]	% convn MA	% yield DHD[b]	TO[c]
1. MA	8	85	37	28	82	125
2. MA/NMP (1:1)	17	74	66	71	54	208
3. MA/NMP/crown (1:1:0.005)[d]	13	93	64	60	63	205
4. MA/crown (1:0.005)[e]	16	84	75	46	80	198
5. MA/Carbowax (1:0.01)[f]	19	86	88	43	84	195

[a] $(C_6H_6)(MA)_2Ru^0$ (0.005 M) treated with 2 equiv of sodium naphthalenide ($NaC_{10}H_8$/THF), sealed under vacuum in glass, and heated to 140 °C. NMP = N-methylpyrrolidone. [b] 2 × mol of DHD/mol of MA converted. [c] Turnover number = mol of DHD produced/mol of Ru. [d] 18-Crown-6 (see ref 9), approximately 2 equiv/Ru. [e] 18-Crown-6 (see ref 9), approximately 4 equiv/Ru. [f] Carbowax 200 (linear long-chain alkyl polyether).

Treating a solution of the zerovalent complex 1 with very strong reducing agents, e.g., sodium naphthalenide or sodium amalgam, generates a new species of unknown structure[6] which is superior as a catalyst for linear dimerization of acrylate (see Table I). Maximum activity is achieved with 2 equiv of sodium per ruthenium. Excess sodium results in yield loss due to anionic oligomerization of acrylate.[7] Addition of protic acids after reduction inhibits activity, suggesting that ruthenium hydride is not a primary catalytic species. Though solvents are not necessary, highly polar solvents such as *N*-methylpyrrolidone (NMP) increase the activity of the catalyst (see entries 1 and 2 of Table II). These observations can be interpreted to suggest that the active catalytic species is an anionic ruthenium complex.[8]

Hexenedioate (DHD) formation is accompanied by some oligomerization of MA. However, kinetic studies show that the latter arises primarily from decay of the dimerization catalyst to a new catalytic species which promotes oligomerization. The rate of catalyst decay is inversely proportional to the MA concentration: i.e., high MA concentrations inhibit decay. At high MA concentrations and low conversions, little oligomerization occurs but at high conversions large yield losses are observed (see entry 2, Table II). The turnover numbers (TO) indicate that the yield loss is due to an increase in oligomerization rather than a significant decrease in selective dimerization. It is noteworthy that the rate of catalyst decay is also dependent on the nature of the reducing metal and appears to correlate with the size of the corresponding cation so that the rate of catalyst decay increases in the order Li (0.60) < Na (0.99) ≃ Ca (0.99) < K (1.35) ≃ Ba (1.35), where the number in parentheses is the cationic radius. Consistent with the involvement of a cation in the catalyst decay process, the addition of crown ethers, e.g., 18-crown-6,[9] to a sodium-treated system significantly retards catalyst decay and therefore increases selectivity at higher conversions. Indeed we have found that in the presence of catalytic amounts of polyethers such as 18-crown-6 or Carbowax 200, the catalyst performs better, even in the absence of solvent (Table II).

Registry No. MA, 96-33-3; DHD, 6108-58-3; $(\eta\text{-}C_6H_6)(MA)_2Ru(O)$, 103149-99-1; sodium naphthalenide, 3481-12-7.

(6) A cream-colored solid may be isolated by precipitation with excess hexane. This solid is unstable in solution and exhibits a complex ^1H NMR spectrum in THF-d_8 which is dependent upon the temperature at time of isolation (25 °C vs. −30 °C) and changes with time. Coordinated benzene is present but easily lost from the solid isolated at −30 °C but not present in the material isolated at 25 °C. These isolated powders are similar to nonisolated catalyst preparations in catalytic activity.

(7) In the absence of ruthenium, acrylate treated with sodium reducing agents results in nonselective oligomerization.

(8) An apparent reduction of 1 is further suggested by comparing the electrochemical potential of 1 treated with sodium naphthalenide (1.0 V) with that of untreated 1 (0.1 V) and sodium naphthalenide (2.7 V). Measurements were obtained in 0.4 M naphthalene in tetrahydrofuran with platinum electrodes in a small H cell separated by a glass frit. For comparison, other species exhibit the following potentials: Na/Hg, 2.0 V; Ca/Hg, 1.5 V; Mg/Hg, 1.2 V; Mn/Hg, 0.7 V; Zn/Hg, 0.6 V; Cu, 0.1 V.

(9) 18-Crown-6 refers to 1,4,7,10,13,16-hexaoxycyclooctadecane.

Control of Organopalladium Glycal Adduct Decomposition Reactions. Role of Conformational Restriction and β-Carbon Substituents

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Summary: The mode of decomposition of organopalladium adduct intermediates, formed in a palladium-mediated reaction of glycals which leads to *C*-glycosides, is sensitive to adduct conformation and the leaving group ability of substituents β to palladium. Pyranoid glycals conformationally restricted by benzylidene formation through glycal 4- and 6-hydroxyls react with (1,3-dimethyl-2,4(1*H*,3*H*)pyrimidinedion-5-yl)mercuric acetate in the presence of palladium(II) acetate to form an intermediate adduct with palladium and the $C_{3'}$-oxy substituent *trans* diaxially disposed. When the substituent at $C_{3'}$ is a good leaving group (e.g., acetate), anti palladium acetate elimination occurs; when the substituent is a poor leaving group (e.g., alkoxy), the adduct undergoes a conformational change to eclipse palladium and β-hydrogen substituents and syn β-hydride elimination occurs. Similarly, in furanoid glycals the mode of adduct decomposition is determined by the leaving group ability of the $C_{3'}$-oxy substituent; if it is alkoxy, only syn β-hydride elimination is observed; if the substituent is carboxy, only anti palladium carboxylate elimination is observed.

We have developed a palladium-mediated coupling reaction of furanoid[1] and pyranoid[2] glycals, leading to *C*-glycosides,[3] which is direct and efficient. The organometallic chemistry involved is complex, involving four discrete organometallic reactions.[1,2,4-6] In previous reports

(1) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 2870–2876.
(2) Arai, I.; Lee, T. D.; Hanna, R.; Daves, G. D., Jr. *Organometallics* **1982**, *1*, 742–747.
(3) Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1–65. Daves, G. D., Jr.; Cheng, C. C. *Prog. Med. Chem.* **1976**, *13*, 303–349. Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111–188. Buchanan, J. G. *Prog. Chem. Org. Nat. Prod.* **1983**, *44*, 243–299.
(4) Kalinoski, H. T.; Hacksell, U.; Barofsky, D. F.; Barofsky, E.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 6476–6482.
(5) Lee, T. D.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 399–402.

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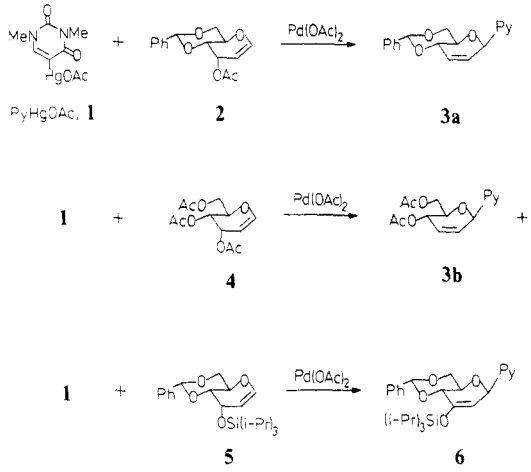
we have considered the first three reactions in the sequence: (1) formation of an organopalladium reagent from an aglycone precursor,[4] (2) π-complex formation whereby the glycal double bond becomes a ligand on palladium,[1,2,4,5] and (3) collapse of the π-complex by insertion of the glycal double bond into a Pd–C bond to form a σ-adduct.[1,2,4-8] These studies have led to effective methods for control of stereochemistry of π-complex formation[1,2,4,5,7-9] and have established that π-complex collapse to σ-adduct is regiospecific.[1,2,4,5,7,8,10]

We now present initial results directed toward control of the fourth reaction in the sequence: decomposition of the σ-adduct with elimination of palladium and *C*-glycoside product formation. Control of the mode of organopalladium adduct decomposition was achieved (a) by restriction of adduct conformational mobility and (b) by selection of glycal substituents on carbon 3 which is β to palladium in the resulting intermediate adduct.

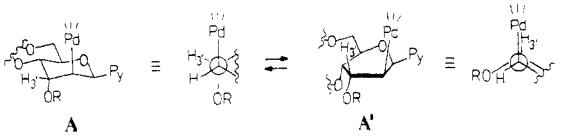
The complex, chiral glycalpalladium adducts encountered in the synthetic sequence leading to *C*-glycosides are ideal for study of stereochemical features of organopalladium reactions. Four decomposition modes[1,2,7,8] for organopalladium glycal adducts have been observed;[11] each involves an elimination reaction with apparent strict steric requirements in which palladium and a substituent on carbon β to palladium are lost. Thus, palladium acetate elimination[2,7] and palladium alkoxide elimination (with opening of the carbohydrate ring)[2,7,12] involve an anti-periplanar arrangement of palladium and oxygen substituent whereas palladium hydride[2,5-7] and palladium oxide[8,9] eliminations involve a syn-periplanar arrangement of palladium and β-hydrogen or -oxygen substituent respectively. Isolatable σ-palladium adducts with β-substituents suitable for elimination possess structures with significant barriers to the stereochemical alignments associated with these elimination reactions.[13,14]

In the present work, conformational mobility in σ-palladium adducts derived from pyranoid glycals was restricted by incorporation of hydroxyls at C-4 and C-6 into a six-membered ring by reaction with benzaldehyde. When equimolar portions of (1,3-dimethyl-2,4(1*H*,3*H*)-pyrimidinedion-5-yl)mercuric acetate[15] (**1**), 3-*O*-acetyl-1,5-anhydro-2-deoxy-4,6-*O*-phenylmethylene-D-*ribo*-hex-1-enitol[16] (**2**), and palladium(II) acetate in acetonitrile were allowed to react for 24 h at room temperature, a single C-nucleoside product (**3a**)[17] was formed by anti elimination of palladium acetate from the intermediate σ-palladium adduct. In contrast, similar reaction of the corresponding conformationally mobile 3,4,6-tri-*O*-acetyl derivative of the glycal[18] **4** produced a 1:1 mixture of **3b** and an enol acetate as a result of competing anti elimination of palladium acetate and syn elimination of palladium hydride.



If the 3-acetoxy substituent of the conformationally restricted glycal **2** was changed to (triisopropylsilyl)oxy **5**,[16,17,19] which is a much poorer leaving group, the barrier for anti elimination was raised sufficiently that only syn β-hydride elimination was observed with formation of **6**.[17]

These results suggest that the conformation of the intermediate organopalladium adducts derived from **2** and **5** has palladium in an axial position anti-periplanar to the oxygen substituent at $C_{3'}$ (A). When this substituent is an effective leaving group (acetate), anti elimination of palladium and $C_{3'}$-oxy substituent occurs. When the leaving group is poor (alkoxy), the adduct must assume the higher energy half-chair conformation (A') in which carbohydrate ring carbons C_1–$C_{4'}$ are coplanar and palladium and the $C_{3'}$–H are syn-periplanar permitting syn β-hydride elimination. The energy difference between the conformers of the adduct derived from **4** is minimal and gives rise to mixtures.



Organopalladium adducts of furanoid glycals behaved similarly. Thus, furanoid glycals which possess poor leaving groups at C-3, i.e., 1,4-anhydro-2-deoxy-5,3-bis-*O*-(methoxymethyl)-D-*erythro*-pent-1-enitol[1,20] (**7**) or the corresponding 3-*O*-triisopropylsilyl glycal[1] **8**, give rise to intermediate σ-palladium glycal adducts which yield single C-nucleoside products **9**[1] by syn β-hydride elimination.

(6) Henry, P. M. *Palladium Catalyzed Oxidation of Hydrocarbons*; Kiewer Boston: Boston, MS, 1980. Collman, J. P.; Hegedus, L. S. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1980. Heck, R. F. *Organotransitional Metal Chemistry*; Academic Press: New York, 1974.

(7) Arai, I.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 7683.

(8) Hacksell, U.; Daves, G. D., Jr. *Organometallics* **1983**, *2*, 772–775.

(9) We have recently found a reaction yielding products which arise from attack of palladium on both α and β faces of the glycal double bond (Cheng, J. C. Y.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.*, in press). Mixtures involving stereoisomeric complex formation have also been observed in a related palladium-mediated coupling reaction of glycals (Czernecki, S.; Dechavanne, V. *Can. J. Chem.* **1983**, *61*, 533–540).

(10) Regiospecificity is lost in acyclic enol ethers or when strongly electron-deficient organopalladium reagents are used. See: Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1979**, *44*, 21–23. Hallberg, A.; Westfelt, L. *J. Chem. Soc., Perkin Trans. 1* **1984**, 933–935. Hallberg, A.; Westfelt, L.; Holm, B. *J. Org. Chem.* **1981**, *46*, 5414–5415.

(11) A fifth mode of adduct decomposition is accessible when adducts are isolatable or stable in the reaction mixture. Subjecting them to 1–2 atm of hydrogen results in replacement of palladium with hydrogen. See ref 7 and 8.

(12) Observed only when reaction mixtures containing stabilized adducts were decomposed by using protic (H_2S) reagents.

(13) Hacksell, U.; Kalinoski, H. T.; Barofsky, D. F.; Daves, G. D., Jr. *Acta Chem. Scand., Ser. B* **1985**, *B39*, 469–476.

(14) Kurosawa, H.; Emoto, M.; Urabe, A.; Miki, K.; Kasai, N. *J. Am. Chem. Soc.* **1985**, *107*, 8253–8254.

(15) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1978**, *43*, 4110–4112.

(16) Feast, A. A.; Overend, W. G.; Williams, N. R. *J. Chem. Soc.* **1965**, 7378–7388.

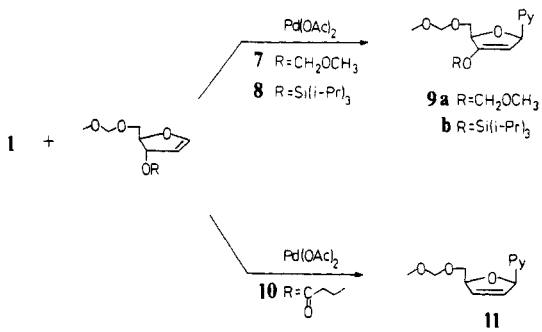
(17) New compounds **3a**, **3b**, **5**, **6** and **11** were characterized by ^1H and ^{13}C nuclear magnetic resonance spectrometry, elemental analysis, and/or high-resolution mass spectrometry. Unoptimized yields of the coupling reactions reported were in the range of 20–30%. These yields are lower than those experienced in related reactions;[1,2] possibly conformational restriction in glycals adversely affects π-complex and/or σ-adduct formation.

(18) Richtmyer, N. *Methods Carbohydr. Chem.* **1962**, *1*, 107–113. Lemieux, R. U.; Fraga, E.; Watanabe, K. A. *Can. J. Chem.* **1968**, *46*, 61–69. Guthrie, R. D.; Irvine, R. W. *Carbohydr. Res.* **1979**, *72*, 285–288.

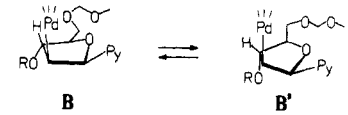
(19) Cunico, R. F.; Bedell, L. *J. Org. Chem.* **1980**, *45*, 4797–4798.

(20) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48–61.

However, if the 3-hydroxyl substituent of this glycal was converted to an ester[21] (**10**), the directing effect on adduct formation[1] was retained while the improved leaving group changed the relative energetics for adduct decomposition modes. The observed product, formed by anti loss of palladium carboxylate, was (2′*R*)-*cis*-5-[2′,5′-dihydro-5′-[(methoxymethoxy)methyl]-2′-furanyl]-1,3-dimethyl-2,4-(1*H*,3*H*)pyrimidinedione[17] (**11**) which is a direct precursor to various important ribofuranosyl C-nucleosides.[22,23]



In the five-membered ring series, unlike the six, it is typical that multiple, essentially isoenergetic conformations coexist in solution.[24] The nature, number, and position of substituents on the furanosyl ring affect conformational preferences significantly,[25] making difficult the prediction of favored conformation(s) for specific molecules. In conformation B, which has the large groups at $C_{1'}$ and $C_{4'}$ in favorable pseudoequatorial positions, palladium and β-hydrogen are essentially syn-periplanar[26] as required for syn β-hydride elimination (which is facile in furanoid systems).[1,5] However, the favorable leaving ability of carboxylate diverts the reaction to anti palladium carboxylate elimination, presumably following a suitable conformational change to B′.



The combination of regio- and stereocontrol of adduct formation previously achieved and stereoelectronic control of adduct decomposition provides an effective and versatile synthetic approach to C-nucleosides. Continued experimental and theoretical[27] study of mechanistic details of organometallic reactions foreshadows the development of synthetic procedures of increasingly impressive specificity.

Acknowledgment. We thank the American Cancer Society for financial support. We thank H. Henrik Johnsson for preparation of starting materials for pyranoid glycals.

(21) Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 1988–2006.
(22) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 4144–4147.
(23) Hirota, K.; Watanabe, K. A.; Fox, J. J. *J. Org. Chem.* **1978**, *43*, 1193–1197.
(24) Lesyng, B.; Saenger, W. *Carbohydr. Res.* **1984**, *133*, 187–197.
(25) Wiorkiewicz-Kuczera, J.; Rabczenko, A. *J. Chem. Soc., Perkin Trans. 2* **1985**, 789–797.
(26) The agostic interaction between these substituents[27a] helps stabilize the conformation.
(27) (a) Koga, N.; Obara, S.; Kitaura, K.; Morokuma, K. *J. Am. Chem. Soc.* **1985**, *107*, 7109–7116. (b) Backvall, J. E.; Bjorkman, E. E.; Pettersson, L.; Siegbahn, P. *J. Am. Chem. Soc.* **1985**, *107*, 7265–7267. (c) Brainard, R. L.; Whitesides, G. M. *Organometallics* **1985**, *4*, 1550–1557. (d) Bryndza, H. E. *J. Chem. Soc., Chem. Commun.* **1985**, 1696–1698.

Additions and Corrections

Robert W. Armbruster, Michael M. Morgan, James L. Schmidt, Chun Man Lau, Rose M. Riley, Daniel L. Zabrowski, and Harold A. Dieck*: Palladium-Catalyzed Additions of Amines to Conjugated Dienes: Alteration of Behavior of (Triphenylphosphine)palladium Catalysts with Amine Hydroiodide Salts. **1986**, *5*, 234–237.

On page 236, left column, line 51, the word "not" should be deleted. Thus the sentence beginning on line 49 should read: "After 9 h, greater than 85% conversion (GLC) to the 1,4-addition product *N*-(1-buten-1-yl)-*p*-toluidine had occurred."

T. K. Dutta, J. C. Vites, and T. P. Fehlner*: On the Mechanism of the Hydrogenation/Dehydrogenation of a C_2 Fragment on a Triiron Site. **1986**, *5*, 385–386.

In the caption to Figure 1 the calculated mass for $HD_2Fe_3(CO)_9CCH_3$ should read 451.8186.