The preparation of **26f** was carried out on a 1.3-mmol scale from the metal acylate **8b**[23] according to the procedure described above for complex **26a** with the reaction parameters indicated in Table I. A single organometallic product was observed by TLC and purified by chromatography on Florisil in the presence of air. The imino complex **26e** (R_f 0.22) was obtained in 36% yield (212 mg, 0.47 mmol) as an orange/yellow solid: mp 87-88 °C. Spectral data for **26c**: ^{1}H NMR ($CDCl_3$) δ 2.20 (d, 3 H, J = 5.61 Hz), 6.70 (q, 1 H, J = 5.61 Hz), 7.5 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 17.53 (q, J = 131.2 Hz), 112.00 (d, J = 184.51 Hz), 128.23 (d, J = 159.65 Hz), 128.84 (d, J = 165.66 Hz), 131.24 (d, J = 161.69 Hz), 139.33 (s), 186.35 (s), 198.71 (s), 203.31 (s); IR (neat) 2952 m, 2924 s, 2854 m, 2063 w, 1970 w, 1927 s, 1458 w, 1377 w, 699 w cm^{-1}; mass spectrum m/e (% relative intensity) 455 M$^+$ (45, ^{184}W), 427 (15), 399 (15), 371 (36), 343 (36), 343 (84), 317 (100), 286 (65), 272 (41), 258 (25), 156 (25), 84 (35). Anal. Calcd for $C_{14}H_9NO_5W$: C, 36.95; H, 1.99; N, 3.08. Found: C, 36.86; H, 1.95; N, 3.00.

General Procedure for the Reaction of the Methoxy Complexes 1 with *N*-Silyl Imines: Preparation of Pentacarbonyl[methyl[(phenylmethylene)amino]methylene]tungsten (26g). A solution of the silyl imine **24a** (9.35 mmol) in methylene chloride prepared as described above was quickly transferred by syringe to a solution of the methyl methoxy tungsten complex **1d**[25] (2.92 g, 7.62 mmol) in methylene chloride (15 mL) at -20 °C. The solution was warmed to 0 °C slowly over 30 min and then to room temperature for 30 min. The solution was quenched with saturated $NaHCO_3$ and separated. The organic layer was washed with brine (1×), dried over $MgSO_4$, and concentrated. The remaining oil was chromatographed in 1:4 benzene/hexane to give the starting complex (1.07 g, 2.81 mmol, 37%) as a yellow solid and the imino complex **26g** (538 mg, 1.18 mmol, 16%) as an orange-yellow solid: mp 91-92 °C. Spectral data for **26g**: ^{1}H NMR ($CDCl_3$) δ 2.80 (d, 3 H, J = 2.3 Hz), 7.11 (q, 1 H, J = 2.2 Hz), 7.48 (m, 2 H), 7.54 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 35.91 (q, J_{C-H} = 132 Hz), 111.14 (d, J_{C-H} = 185 Hz), 127.51 (s), 128.12 (d, J_{C-H} = 160 Hz), 129.51 (d, J_{C-H} = 164 Hz), 132.15 (d, J_{C-H} = 162 Hz), 189.29 (s), 198.30 (s), 203.34 (s); IR (neat) 3069 w, 3041 w, 2968 m, 2920 m, 2351 w, 2063 s, 1972 sh, 1906 s, 1599 w, 1497 w, 1467 m, 1427 w, 1409 m, 1350 w, 1316 w, 1229 m, 1193 w, 1173 m, 1070 m, 1002 w, 926 m, 866 m, 823 w, 750 s, 688 s cm^{-1}; mass spectrum m/e (% relative intensity) 455 M$^+$ (10, ^{184}W), 427 (9), 399 (9), 371 (17), 343 (33), 330 (11), 315 (75), 302 (11), 286 (37), 272 (36), 260 (16), 247 (11), 233 (21), 222 (10), 210 (11), 191 (9), 178 (50), 156 (21), 143 (15), 130 (51), 115 (74), 103 (97), 90 (100), 77 (84), 69 (9); calcd for $C_{14}H_9NO_5W$ m/e 454.9991, measd m/e 454.9997.

It was subsequently found that it is not necessary to deoxygenate the reaction mixture by the freeze-thaw method but rather this can be done in a flask flushed with argon. This reaction can produce varying amounts of an unidentified polar, red compound whose formation can be suppressed if the reaction is quenched with 1.0 M aqueous HCl. The imino complexes **26a,c,d** were prepared from the methoxy complexes **1a**,[27] **1b**,[25] and **1c**[29] according to the above procedure with the reaction times and equivalents of *N*-silyl imine indicated in Table II. The spectral data for imino complexes **26a,c,d** are presented above.

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Supplementary Material Available: Listings of thermal parameters, least-squares planes, and final fractional coordinates for hydrogen atoms (3 pages); a listing of the observed and calculated structure factors for the X-ray diffraction analysis of compound **13b** (5 pages). Ordering information is given on any current masthead page.

C-Glycoside Synthesis by Palladium-Catalyzed Iodoaglycon–Glycal Coupling

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Efficient coupling of iodo derivatives of anthracycline aglycons with furanoid and pyranoid glycals has been achieved with use of stoichiometric portions of the reactants in the presence of catalytic amounts of palladium(II) acetate and a tertiary amine in dimethylformamide solution at room temperature. This procedure, which occurs regio- and stereospecifically, is an effective route to aryl *C*-glycosides. Demonstration of the efficacy of this palladium-mediated coupling reaction was illustrated by its use in a one-pot four-step sequence that produced the anthracycline *C*-glycoside 4-[2′-deoxy-3′,5′-diacetyl-β-D-*ribo*(=*arabino*)-furanosyl]-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one in 94% isolated yield.

An efficient route to *C*-glycosides[1] developed in our laboratory[2-5] involves, as a key step, palladium-mediated coupling of a 1,2-unsaturated carbohydrate (glycal) with a suitable derivative of an aromatic or heterocyclic aglycon in a regio- and stereospecific[6,7] manner. This reaction utilizes aryl mercurials[3-5] or arylstannanes[2] as aglycon precursors and requires stoichiometric palladium to form the reactive arylpalladium reagent.[6,8] The study of factors that affect the palladium-mediated coupling of enol ethers with aryl halides has led to the development of a glycal-aglycon coupling reaction requiring only catalytic palla-

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(1) For recent reviews of the chemistry and biology of *C*-glycosides, see: Hacksell, U.; Daves, G. D., Jr. *Prog. Med. Chem.* **1985**, *22*, 1-65. Buchanan, J. G. *Prog. Chem. Org. Nat. Prod.* **1983**, *44*, 243-299. Goodchild, J. *Top. Antibiot. Chem.* **1982**, *6*, 99-227.
(2) Outten, R. A.; Daves, G. D., Jr. *J. Org. Chem.* **1989**, *54*, 29-35.
(3) Cheng, J. C.-Y.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3083-3090.
(4) Cheng, J. C.-Y.; Daves, G. D., Jr. *Organometallics* **1986**, *5*, 1753-1755.
(5) Cheng, J. C.-Y.; Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1986**, *51*, 3093-3098.

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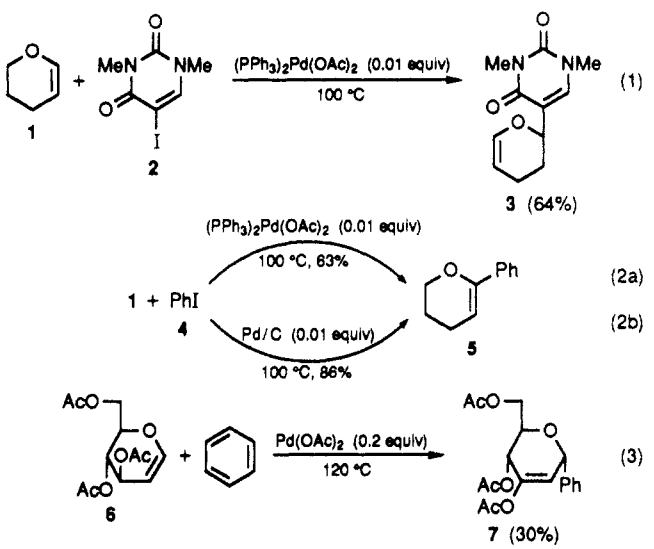
Table I. Formation of *C*-Glycosides by Coupling of 3,4,6-Tri-*O*-Acetyl-D-glucal (6) with 1,3-Dimethyl-5-iodouracil (2) with Use of Catalytic Palladium in Acetonitrile at 40 °C

expt no.	amt of 6/2, equiv	catalyst	X in nBu_4NX[b]	time, days	yields of 8 + 9, %	product ratio (8:9)
1	1.5	$Pd(OAc)_2$		6	5	1:5
2	1.5	$Pd(OAc)_2$	Cl	6	35	2:3
3	3.0	$Pd(OAc)_2$	Cl	6	45	1:5
4	6.0	$Pd(OAc)_2$	Cl	6	60	1:2
5	1.5	$PdCl_2$	Cl	4	20	1:1
6	1.5	$Pd(OAc)_2$	Br	4	0	
7	1.5	$Pd(OAc)_2$	F	4	0	
8	1.5	$Pd(PPh_3)_4$	Cl	3	0	
9	1.5	$(PPh_3)_2Pd(OAc)_2$	Cl	3	0	

[a] The amount of catalyst used was 0.04 equiv, and that of nBu_4NX was 1.0 equiv. [b] The reaction mixture also contained 2.5 equiv of sodium bicarbonate.

dium. This new glycal–aglycon coupling reaction is as effective as the corresponding *C*-glycoside synthesis utilizing metallo derivatives of aryls, which requires stoichiometric palladium.[2-6,8,9] Under defined reaction conditions, glycals and aryl iodides undergo regio- and stereospecific coupling in the presence of 1–10 mol % of palladium acetate at room temperature to form *C*-glycosides in good to excellent yields.

In early studies, we[6d,10,11] and others[12-18] demonstrated coupling reactions between enol ethers and aryl compounds using catalytic quantities of palladium. Thus (eq 1), 3,4-dihydro-2*H*-pyran (**1**, present in excess) and 1,3-dimethyl-5-iodouracil[19] (**2**) underwent coupling in the presence of 1 mol % of a triphenylphosphine-complexed palladium(II) salt at 100 °C producing **3** (64%).[10] Under similar conditions (eq 2a), **1** and iodobenzene (**4**) coupled to form the corresponding product **5** (63%).[11] When the catalyst was palladium on carbon (eq 2b), the yield of **5** increased to 86%.[6d] In each of these cases, double-bond migration[20] occurred. Czernecki has reported[12,13] examples in which glycals (e.g., 3,4,6-tri-*O*-acetyl-D-glucal[21] (**6**)) were regio- and stereospecifically coupled with an aromatic aglycon precursor (e.g. benzene) used as reaction solvent, in the presence of palladium acetate at elevated temperature (eq 3). All of these enol ether–aglycon coupling reactions effected by catalytic portions of palladium require elevated reaction temperatures and several equivalents of either the enol ether or aglycon precursor.



The sensitivity of palladium-mediated reactions to reaction conditions is well recognized; effects of solvent, added salts and ligands, and catalyst nature and form have been noted.[3,6d,20,22-24] We have investigated reaction media effects to define conditions for achievement of a glycal–aglycon coupling reaction which (a) is catalytic in palladium, (b) takes place at or near room temperature, and (c) requires only stoichiometric portions of reactants.

Results and Discussion

Coupling Reactions Catalytic in Palladium. Earlier, we noted that addition of a quaternary ammonium salt to reaction mixtures remarkably accelerates certain palla-

(6) For discussions of the mechanism of these reactions, see: (a) Daves, G. D., Jr. *Acc. Chem. Res.* **1990**, *23*, 201–206. (b) Daves, G. D., Jr. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwhich, CT, in press. (c) Daves, G.D., Jr.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433–1445. (d) Andersson, C.-M.; Hallberg, A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 3529–3536.

(7) One example in which stereospecificity was not observed has been reported.[5]

(8) In reactions requiring Pd(II) for transmetalation, catalytic cycles can sometimes be achieved by including an oxidant to convert Pd(0), formed by decomposition of L_2PdHX following β-hydride elimination from the intermediate σ-organopalladium adduct,[6] back to Pd(II). See: Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. Backvall, J. E.; Nordberg, R. E.; Wilhelm, D. *J. Am. Chem. Soc.* **1985**, *107*, 6892–6898.

(9) RajanBabu, T. V.; Reddy, G. S. *J. Org. Chem.* **1986**, *51*, 5458–5461.

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

(11) Arai, I.; Daves, G. D., Jr. *J. Org. Chem.* **1979**, *44*, 21–23.

(12) Czernecki, S.; Dechavanne, V. *Can. J. Chem.* **1983**, 61, 533–540. Bellosta, V.; Czernecki, S.; Avenil, D.; El Bahij, S.; Gillier-Pandraud, H. *Can. J. Chem.* **1990**, *68*, 1364–1368.

(13) Czernecki, S.; Gruy, F. *Tetrahedron Lett.* **1981**, *22*, 437–440.

(14) Dunkerton, L. V.; Serino, A. J. *J. Org. Chem.* **1982**, *47*, 2812–2814.

(15) Yougai, S.; Miwa, T. *J. Chem. Soc., Chem. Commun.* **1983**, 68–69.

(16) RajanBabu, T. V. *J. Org. Chem.* **1985**, *50*, 3642–3644.

(17) Hallberg, A.; Westfelt, L.; Holm, B. *J. Org. Chem.* **1981**, *46*, 5414–5415.

(18) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 2112–2114.

(19) Evans, C. H.; Jones, A. S.; Walker, R. T. *Tetrahedron* **1973**, *29*, 1611–1614.

(20) Lee, T. D.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 399–402.

(21) Roth, W.; Pigman, W. *Methods in Carbohydrate Chemistry*; Academic Press: New York, 1963; Vol. II, pp 405–408.

(22) Arai, I.; Lee, T. D.; Hanna, R.; Daves, G. D. Jr. *Organometallics* **1982**, *1*, 742–747.

(23) Arai, I.; Hanna, R.; Daves, G. D., Jr. *J. Am. Chem. Soc.* **1981**, *103*, 7684–7685.

(24) (a) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265–272. (b) Andersson, C.-M.; Karabelas, K.; Hallberg, A.; Andersson, C. *J. Org. Chem.* **1985**, *50*, 3891–3895. (c) Davison, J. B.; Simon, N. M.; Sojka, S. A. *J. Mol. Catal.* **1984**, *22*, 349–352. (d) Chalk, A. J.; Magennis, S. A. *J. Org. Chem.* **1976**, *41*, 273–278. (e) Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287–1289. (f) Benhaddou, R.; Czernecki, S.; Ville, G.; Zegar, A. *Organometallics* **1988**, *7*, 2435–2439. (g) Spencer, A. *J. Organomet. Chem.* **1983**, *258*, 101–108. (h) Ziegler, F. E.; Chakraborty, U. R.; Weisenfeld, R. B. *Tetrahedron* **1981**, *37*, 4035–4040. (i) Kende, A. S.; Roth, B.; Sanfilippo, P. J. *J. Am. Chem. Soc* **1982**, *104*, 1784–1785. (j) Backvall, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 4959–4960. (k) Hosaka, S.; Tsuji, J. *Tetrahedron* **1971**, *27*, 3821–3829. (l) Tsuji, J.; Mori, Y.; Hara, M. *Tetrahedron* **1972**, *28*, 3721–3725. (m) Billips, W. E.; Walker, W. E.; Schield, T. C. *J. Chem. Soc., Chem. Commun.* **1971**, 1067–1068. (n) Trost, B. M.; Strange, P. E.; Weber, L.; Fullerton, T. J.; Dietsche, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 3407–3415. (o) Trost, B. M.; Metzner, P. *J. Am. Chem. Soc.* **1980**, *102*, 3572–3577. (p) Larock, R. C. *Pure Appl. Chem.* **1990**, *62*, 653–660.

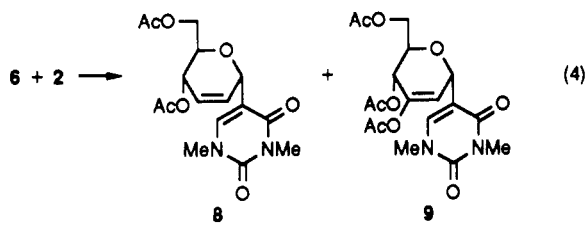
Table II. Coupling Reaction of Cyclic Enol Ethers with 4-Bromo-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one (10)[a]

expt no.	cyclic enol ether	catalyst (equiv)	base (equiv)	added salt or ligand (equiv)	solvent	time, days	temp, °C	product(s) (yield, %)
10	11	$Pd(OAc)_2$ (0.1)	NEt_3 (1.5)		$CHCl_3$	2	55	
11	11	$Pd(OAc)_2$ (0.1)	NEt_3 (1.5)	PPh_3 (0.4)	$CHCl_3$	2	55	**12** (19)
12	11	$Pd(OAc)_2$ (0.1)	NEt_3 (1.5)	P(*o*-tolyl)$_3$ (0.4)	$CHCl_3$	2	55	**12** (20)
13	11	$Pd(OAc)_2$ (1)	NEt_3 (1.5)	P(*o*-tolyl)$_3$ (0.2)	$CHCl_3$	3	55	**12** (34)
14	11	$Pd(OAc)_2$ (0.04)	$NaHCO_3$ (2.5)	nBu_4NCl (1)	CH_3CN	3	40	
15	11	$Pd(CH_3CN)_2Cl_2$ (0.1)	$NaHCO_3$ (1.5)	PPh_3 (0.2)	$CHCl_3$	3	55	
16	1	$Pd(OAc)_2$ (0.1)	NEt_3 (1.5)	P(*o*-tolyl)$_3$ (0.2)	$CHCl_3$	2	65	**13** (15) + **14** (7)
17	6	$Pd(OAc)_2$ (0.1)	NEt_3 (1.5)	P(*o*-tolyl)$_3$ (0.2)	$CHCl_3$	7	65	

[a] The amount of cyclic enol ether used was 1.5 equiv.

dium-mediated coupling reactions.[23] Jeffery has made a similar observation and reported palladium-catalyzed olefin arylation reactions at or near room temperature (rather than the more typical 80–120 °C) when tetrabutylammonium chloride is present in the reaction mixture.[24e] To assess whether quaternary ammonium salts might exert a useful effect on glycal–aglycon coupling reactions, several experiments (Table I) were carried out.

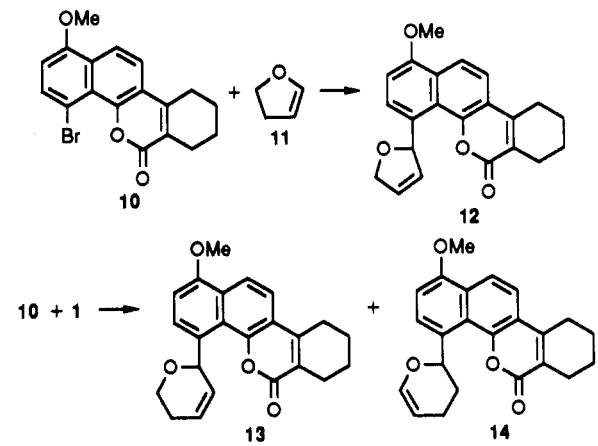
Because the coupling reaction of glycal **6**[21] with (1,3-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)-mercuric acetate,[10] which requires stoichiometric palladium, has been well studied and the resulting *C*-glycosyl products **8** and **9** (and others)[3] have been characterized, glycal **6**[21] and iodopyrimidine **2**[19] were used for preliminary experiments.



Attempted coupling of **6** and **2** in acetonitrile containing sodium bicarbonate as base with palladium acetate as catalyst yielded only 5% of *C*-glycoside product during 6 days (Table I, experiment 1). Addition of 1 equiv of tetra-*n*-butylammonium chloride to this reaction medium improved the yield of coupled products to 35% (experiment 2). Further improvements in yield were attained only by using large stoichiometric excesses of glycal **6**[21] (experiments 3 and 4). A change of palladium catalyst (experiments 5, 8, and 9) was not effective. Surprisingly, use of either tetra-*n*-butylammonium bromide (experiment 6) or fluoride (experiment 7) abolished the beneficial effect of added quaternary ammonium salt.

Work by Heck[24a,25,26] and others[24b,d,g] has shown that aryl bromides can be as effective as aryl iodides in olefin arylation reactions, although somewhat different reaction conditions are required. Chalk and Magennis[24d] have noted that in palladium-catalyzed olefin arylation reactions of aryl bromides inclusion of sodium bicarbonate as base improves yields; Andersson et al.[24b] have demonstrated impressively that whereas in reactions using aryl iodides inclusion of phosphine ligands for palladium retards reaction, such ligands greatly improve the reactivity of aryl bromides in olefin arylations. Perhaps more impressively, Davison and co-workers[24c] have shown that even chlorobenzene[27] is reactive if both phosphine ligands and sodium or potassium acetate are present in a two-phase reaction mixture containing dimethylformamide and water.

To evaluate the potential utility of readily available aryl bromides for coupling reactions with glycals, reactions of 4-bromo-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho-[1,2-*b*]pyran-6-one[2] (**10**) with 2,3-dihydrofuran (**11**), 3,4-dihydro-2*H*-pyran (**1**), and glycal **6**[21] were studied (Table II). No coupling occurred when **10** and **11** were heated in chloroform containing triethylamine and catalytic palladium acetate (Table II, experiment 10). However,

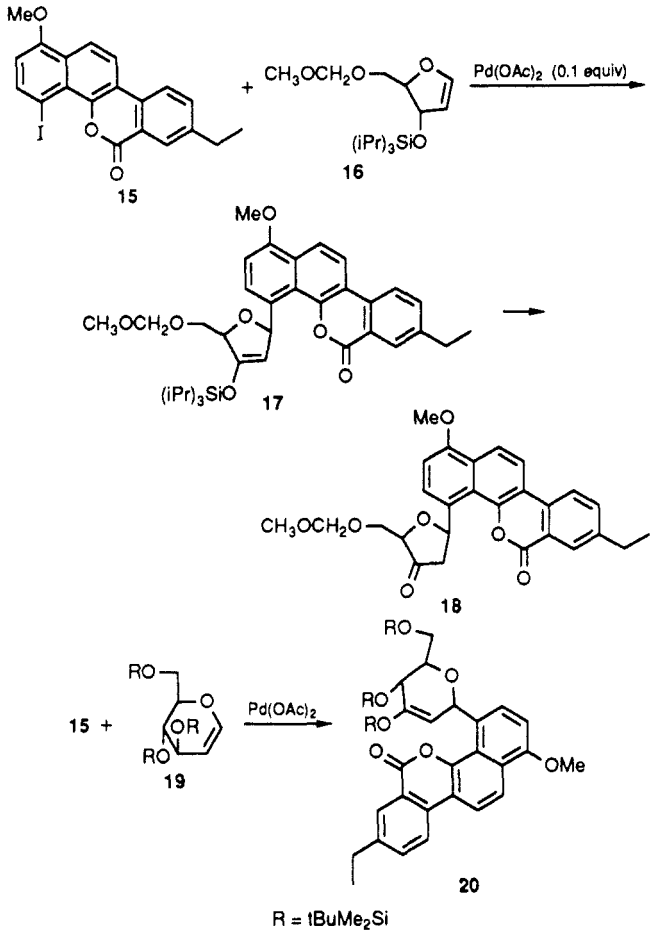


addition of 4 equiv of triphenylphosphine/equiv of palladium acetate to the reaction mixture resulted in coupling to the extent of 20%, yielding **12**[2] (experiment 11). The more sterically hindered tri-*o*-tolylphosphine[28] was equally, but not more, effective (experiment 12); decrease of the P:Pd ratio to 2 improved the yield of coupled product to 34% (experiment 13). When the enol ether was 3,4-dihydro-2*H*-pyran (**1**), low-yield coupling also occurred; unfortunately, however, no coupling was observed when pyranoid glycal **6**[21] was used (experiment 17). No coupling was realized when sodium bicarbonate and tetra-*n*-butylammonium chloride rather than triethylamine and a phosphine were present (experiment 14). Similarly, use of palladium chloride rather than palladium acetate as catalyst was ineffective (experiment 15).

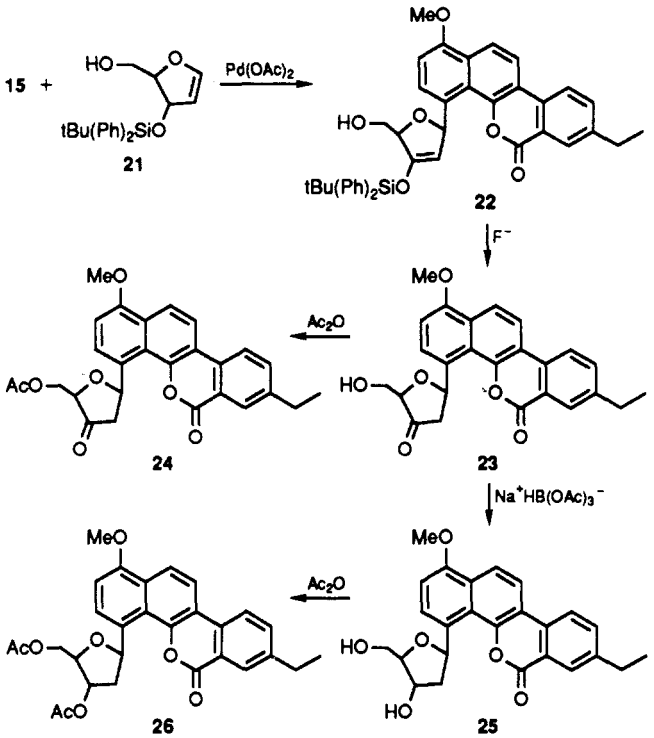
The encouraging results obtained in these preliminary experiments (Tables I and II) and related recent studies[24f,p] led us to undertake an additional series of experiments involving coupling reactions between glycals and iodo derivatives of aglycons with use of catalytic portions of palladium acetate and a tertiary amine base in dimethylformamide solution.[24e,f,p] For these experiments, we prepared 8-ethyl-4-iodo-1-methoxybenzo[*d*]naphtho-[1,2-*b*]pyran-6-one (**15**) by a halogen-exchange reaction[29] employing the corresponding bromo derivative and a mixture of potassium and cuprous iodides at high temperature.[30]

(25) Heck, R. F. *Pure Appl. Chem.* **1978**, *50*, 691–701.
(26) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146–151.
(27) See also: Bozell, J. J.; Vogt, C. E. *J. Am. Chem. Soc.* **1988**, *110*, 2655–2657.
(28) Wilson, N. K.; Zehr, R. D. *J. Org. Chem.* **1978**, *43*, 1768–1773.
(29) Merkushev, E. B. *Synthesis* **1988**, 923–937.

Reactions of the anthracycline iodo derivative **15** with furanoid (**16**[31] and **21**[32]) and pyranoid (**19**[33]) glycals were carried out in a reaction medium containing 10 mol % palladium acetate, 2 equiv of tributylamine/equiv of palladium, and 1 equiv of sodium acetate in dimethylformamide[24e,f,p] at room temperature. Under these conditions, palladium-catalyzed coupling of equivalent portions of iodo derivative **15** with furanoid glycal **16**[31] occurred during 48 h both regio- and stereospecifically[6] to form initially the single *C*-glycoside product **17**, which, under the reaction conditions, underwent desilylation (presumably by iodide ion) to produce the corresponding 3′-keto-β-*C*-glycoside **18** as the only isolated product in 85% yield. A companion experiment, in which tributylamine was replaced by 1 equiv of tetra-*n*-butylammonium chloride[24e] and sodium bicarbonate rather than sodium acetate was used as base, was equally successful. When pyranoid glycal **19**[33] was used, palladium-catalyzed coupling with iodo derivative **15** was slower and the yield (42%) of resulting α[6] *C*-glycoside (**20**) was lower.



Anthracycline *C*-Glycoside Synthesis. The effective use of this palladium-catalyzed coupling reaction was illustrated further by reaction of iodoanthracycline **15** with furanoid glycal **21**.[32] In this case, the reaction was complete after 10 h; tetrabutylammonium fluoride was then added to complete desilylation[5,31] of the intermediate silyl enol ether (**22**) and the free 5′-hydroxyl of the resulting 5′-hydroxy-3′-keto-*C*-glycoside **23** was acetylated in situ to facilitate product isolation. This one-pot three-step reaction sequence yielded *C*-glycoside **24** as the single isolated product in 89% yield. More dramatically, a one-pot four-step synthetic sequence to yield the acetylated *C*-glycoside **26** was accomplished in an isolated yield of 94%. This latter sequence incorporated the stereospecific reduction of the 3′-keto group of the furanosyl moiety of *C*-glycoside **23**. We have demonstrated previously[32] the stereospecific reduction of a 3′-keto group of a furanosyl *C*-glycoside from the most hindered face of the carbonyl. This carbonyl reduction utilizes sodium triacetoxyborohydride,[32,34] which requires activation by acetoxy displacement by the β-hydroxy group prior to internal hydride delivery to the carbonyl.



Assignment of *C*-Glycoside Structures. These palladium-mediated coupling reactions are known to be regio- and stereospecific, yielding *C*-glycosyl products derived from a single σ-organopalladium species, the structure and stereochemistry of which is now readily predicted.[6] In the case of pyranoid glycal **6**.[21] decomposition of the intermediate σ-organopalladium adduct that formed occurred in two competing ways to yield a mixture of the previously characterized[3] *C*-glycosides **8** and **9**. The other glycal coupling reactions reported here yielded, in each case, a single C-glycosidic product. The structures of these products were assigned unambiguously on the basis of detailed nuclear magnetic resonance (NMR) spectrometric studies described previously. For example, the magnitude of the coupling constant $J_{1,4}$ observed in ^{1}H NMR spectra of 2,3-unsaturated furanosyl compounds **17** and **22** permits assignment of these compounds as 1,4-cis i.e. β-*C*-glycosides.[2,5] Structures **18** and **23–26** were assigned with use of NMR techniques described previously

(30) Suzuki, H.; Kondo, A.; Inouye, M.; Ogawa, T. *Synthesis* **1986**, 121-122.
(31) Hacksell, U.; Daves, G. D., Jr. *J. Org. Chem.* **1983**, *48*, 2870–2876.
(32) Farr, R. N.; Daves, G. D., Jr. *J. Carbohydr. Chem.* **1990**, *9*, 653–660.
(33) Nicolaou, K. C.; Hwang, C. K.; Duggan, M. E. *J. Chem. Soc., Chem. Commun.* **1986**, 925–926. Hanessian, S.; Martin, M.; Desai, R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926-927.
(34) (a) Gribble, G. W.; Ferguson, D. C. *J. Chem. Soc., Chem. Commun.* **1975**, 535–536. (b) Nutaitis, C. F.; Gribble, G. W. *Tetrahedron Lett.* **1983**, *24*, 4287–4290. (c) Saksena, A. K.; Mangiaracina, P. *Tetrahedron Lett.* **1983**, *24*, 273–276. (d) Turnbull, M. D.; Hatter, G.; Ledgerwood, D. E. Tetrahedron *Lett.* **1984**, *25*, 5449–5452. (e) Nieminen, T. E. A.; Hase, T. A. *Tetrahedron Lett.* **1987**, *28*, 4725–4728. (f) Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578. (g) Wender, P. A.; Kogen, H.; Lee, H. Y.; Munger, J. D., Jr.; Wilhelm, R. S.; Williams, P. D. *J. Am. Chem. Soc.* **1989**, *111*, 8957–8958.

for assignment of 2′-deoxy C-nucleosides.[35] All assignments of stereochemistry at the anomeric carbon were confirmed by observation of appropriate nuclear Overhauser effects (NOE).[36,37] For β-ribofuranosyl *C*-glycosides, irradiation of the resonance for the anomeric hydrogen, H-1, gave rise to an NOE signal at H-4. For the α-pyranosyl *C*-nucleoside **20**, irradiation of the H-1 resonance gave rise to NOE signals at H-4 and H-6.

Conclusions

The iodoaglycon–glycal coupling procedure, which requires only stoichiometric portions of reactants and catalytic palladium acetate, complements previously described palladium-mediated coupling reactions[2-6,9,12,22,23,31,32] leading to *C*-glycosides[1,6a] and extends the utility of these synthetically important reactions. The concise synthesis of anthracycline *C*-glycoside **26** constitutes a key development in our synthetic program directed toward synthesis of *C*-glycosides of the benzo[*d*]naphtho[1,2-*b*]pyran-6-one series[38-40] related to the ravidomycin, gilvocarcin, chrysomycin class of antibiotics.[1,41]

Experimental Section

General Comments. Thin-layer chromatography (TLC) was carried out on prescored silica gel GF plates (Analtech). Preparative TLC was carried out on 1 mm thick, 20 × 20 cm, silica gel GF plates (Analtech). For flash chromatography, silica gel 60 (230–400 mesh ASTM, E. Merck) was used. Columns were eluted with a positive nitrogen pressure. Nuclear magnetic resonance (NMR) spectra were obtained on either a JEOL FX-90Q or a Bruker AM 500 spectrometer and are referenced to tetramethylsilane. Melting points were measured with a Thomas-Hoover capillary apparatus and are uncorrected. Elemental analyses were carried out by Quantitative Technologies, Bound Brook, NJ.

Coupling of 3,4,6-Tri-*O*-acetyl-D-glucal[21] (6) with 1,3-Dimethyl-5-iodouracil[19] (2). Coupling reactions of 3,4,6-tri-*O*-acetyl-D-glucal[21] (**6**) and 1,3-dimethyl-5-iodouracil[19] (**2**) were carried out as indicated in Table I. Reaction workup, product isolation, and structure assignments were accomplished as previously described.[3]

4-(3′,4′-Dihydrofuran-2′-yl)-1-methoxy-7,8,9,10-tetrahydrobenzo[*b*]naphtho[1,2-*b*]pyran-6-one[2] (12). A solution of 4-bromo-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one[2] (**10**; 359 mg, 1 mmol), 2,3-dihydrofuran (**11**; 105 mg, 1.5 mmol), palladium acetate (24 mg, 0.11 mmol), triphenylphosphine (105 mg, 0.4 mmol), and triethylamine (0.2 mL, 1.5 mmol) in 10 mL of chloroform was heated at 50–55 °C with stirring for 2 days. The reaction mixture was then cooled and filtered through Celite. The volume of the resulting filtrate was reduced until crystallization of unreacted **10** occurred. The recovered **10** was removed by filtration, and the residue from the filtrate was separated by preparative TLC with 19:1 chloroform–acetonitrile as eluent to yield **12** (67 mg, 19%) as pale yellow crystals, mp 177–178 °C (lit.[2] mp 177–179 °C).

This procedure is experiment 11 of Table II; experiments 10 and 12–15 were carried out similarly with the changes noted in Table II.

4-(5′,6′-Dihydro-2′*H*-pyran-2′-yl)-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one (13) and 4-(3′,4′-dihydro-2′*H*-pyran-2′-yl)-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one (14). A solution of 4-bromo-1-methoxy-7,8,9,10-tetrahydrobenzo[*d*]naphtho[1,2-*b*]pyran-6-one[2] (**10**; 359 mg, 1 mmol), 3,4-dihydro-2*H*-pyran (**1**; 126 mg, 1.5 mmol), palladium acetate (24 mg, 0.11 mmol), tri-*o*-tolylphosphine[28] (65 mg, 0.21 mmol), and triethylamine (0.21 mL, 1.5 mmol) in 10 mL of chloroform was heated at 60–65 °C with stirring for 2 days. The reaction mixture was then cooled and filtered through Celite. The filtrate was concentrated until crystallization began. Unreacted **10** was removed by filtration, and the residue obtained by evaporation of the filtrate was separated by preparation TLC with 19:1 chloroform–acetonitrile as eluent to afford two products, **14** (R_f 0.4; 24 mg, 7%) and **13** (R_f 0.7; 50 mg, 15%). Spectral data for **13**: IR (neat) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65–2.95 (12 H, H-5′, H-6′, H-7, H-8, H-9, H-10), 3.95 (3 H, s, OMe), 4.71–4.95 (1 H, m, H-4′), 6.49–6.57 (1 H, m, H-3′), 6.91 (1 H, d, H-2), 7.51 (1 H, d, H-11), 7.77 (1 H, dd, H-3), 8.13 (1 H, d, H-12). Spectral data for **14**: MS *m/z* 362 ($M^{+\cdot}$), 306 ($M - C_3H_4O$), 280 ($M - C_5H_7O$); IR (neat) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65–2.45 (8 H, H-3′, H-4′, H-8, H-9), 2.45–2.95 (4 H, m, H-7, H-10), 3.97 (3 H, s, OMe), 5.85–6.05 (2 H, m, H-2′, H-5′), 6.55–6.73 (1 H, m, H-6′), 6.86 (1 H, d, H-2), 7.53 (1 H, dd, H-11), 7.81 (1 H, d, H-3), 8.13 (1 H, d, H-12). Anal. Calcd for $C_{22}H_{19}O_3$: C, 64.2; H, 4.66. Found: C, 64.2; H, 4.52.

4-Bromo-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one. To a suspension of 8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one[36] (2.0 g, 6.6 mmol) in 50 mL of dry dimethylformamide was added *N*-bromosuccinimide (1.29 g, 7.2 mmol). After the solution became clear, an off-white precipitate formed. The reaction was complete in 2 h on the basis of TLC. The resulting mixture was poured into 500 mL of ice water, and the precipitate that formed was collected and recrystallized from chloroform-ethanol to give 2.21 g (88%) of 4-bromo-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one as off-white crystals, mp 185 °C. ^1H NMR ($CDCl_3$): δ 1.32 (3 H, t, CH_3), 2.79 (2 H, q, benzylic), 3.92 (3 H, s, OCH_3), 6.60 (1 H, d, $J_{2,3}$ = 8.3 Hz, H-2), 7.61 (1 H, q, $J_{7,9}$ = 1.7 Hz, $J_{9,10}$ = 8.2 Hz, H-9), 7.68 (1 H, d, $J_{2,3}$ = 8.3 Hz, H-3), 7.88 (1 H, d, $J_{11,12}$ = 9.1 Hz), 7.98 (1 H, d, $J_{9,10}$ = 8.3 Hz, H-10), 8.04 (1 H, d, $J_{11,12}$ = 9.1 Hz), 8.15 (1 H, d, $J_{7,9}$ = 1.6 Hz, H-7). ^{13}C NMR ($CDCl_3$): δ 15.15, 28.56, 55.77, 106.13, 106.82, 115.02, 118.70, 119.13, 120.74, 122.13, 122.30, 127.77, 128.64, 132.47, 134.18, 134.89, 145.50, 145.85, 154.43, 160.23. Anal. Calcd for $C_{20}H_{15}BrO_3$: C, 62.7; H, 3.95. Found: C, 62.5; H, 3.92.

8-Ethyl-4-iodo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (15). To a mixture of 4-bromo-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (1.05 g, 2.7 mmol) and potassium iodide (9.1 g, 54.8 mmol) in 25 mL of dimethylformamide was added cuprous iodide (2.6 g, 13.7 mmol). The mixture was heated under reflux for 2 h, at which time TLC indicated that reaction was complete. After the reaction mixture was cooled to room temperature, the solvent was removed in vacuo. Chloroform (100 mL) was added, and the suspension was filtered through a small amount of silica gel. The filtrate was washed with a saturated solution of sodium thiosulfate and distilled water and then dried over sodium sulfate. The solvent was removed, and the residue was recrystallized from chloroform–ethanol to give 1.06 g (90%) of 8-ethyl-4-iodo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (**15**) as white crystals, mp 205 °C. ^1H NMR ($CDCl_3$): δ 1.30 (3 H, t, CH_3), 2.75 (2 H, q, benzylic), 3.91 (3 H, s, OCH_3), 6.44 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.60 (1 H, dd, $J_{7,9}$ = 1.9 Hz, $J_{9,10}$ = 8.1 Hz, H-9), 7.87 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.01 (1 H, d, $J_{9,10}$ = 8.1 Hz, H-10), 8.05 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.10 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-3), 8.13 (1 H, d, $J_{7,9}$ = 1.9 Hz, H-7). ^{13}C NMR ($CDCl_3$): δ 15.19, 28.58, 55.75, 73.80, 107.05, 114.69, 118.67, 118.94, 120.88, 122.35, 123.62, 127.53, 128.70, 132.55, 134.93, 142.29, 144.91, 145.51, 155.42, 160.04. Anal. Calcd for $C_{20}H_{15}IO_3$: C, 55.8; H, 3.51. Found: C, 55.8; H, 3.41.

4-[2′-Deoxy-5′-(methoxymethyl)-β-D-*glycero*-pentofuran-3′-ulos-1′-yl]-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (18). To a mixture of 8-ethyl-4-iodo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (**15**; 50 mg, 0.12 mmol), sodium acetate (10 mg, 0.12 mmol), and tributylamine (6 μL, 0.024 mmol) in 5 mL of dry dimethylformamide was added 1,4-anhydro-2-deoxy-5-*O*-(methoxymethyl)-3-*O*-[tris-1-methylethyl)silyl]-D-*erythro*-pent-1-enitol[3] (**16**; 44 mg, 0.14 mmol) and palladium acetate (3 mg, 0.012 mmol). After the mixture was stirred at room temperature for 48 h, the volatiles were removed

(35) Hacksell, U.; Cheng, J. C.-Y.; Daves, G. D., Jr. *J. Carbohydr. Chem.* **1986**, *5*, 287–297.
(36) Farr, R. N.; Anderson, W. R., Jr.; Daves, G. D., Jr. Unpublished results.
(37) Cornia, M.; Casiraghi, G.; Zetta, L. *Tetrahedron* **1990**, *46*, 3071–3076.
(38) Kwok, D. I.; Daves, G. D., Jr. *J. Org. Chem.* **1989**, *54*, 4496–4497.
(39) Kwok, D. I.; Outten, R. A.; Huhn, R.; Daves, G. D., Jr. *J. Org. Chem.* **1988**, *53*, 5359–5361.
(40) Outten, R. A.; Daves, G. D., Jr. *J. Org. Chem.* **1987**, *52*, 5064–5066.
(41) McGee, L. R.; Misra, R. *J. Am. Chem. Soc.* **1990**, *112*, 2386–2389 and references cited therein.

in vacuo. The residue was dissolved in chloroform and purified by column chromatography to give 46 mg (85%) of **18** as white crystals, mp 194 °C. ^{1}H NMR ($CDCl_3$): δ 1.34 (3 H, t, CH_3), 2.39 (1 H, dd, $J_{1',2'a}$ = 10.0 Hz, $J_{2'a2'b}$ = 18.5 Hz, H-2'a), 2.83 (2 H, q, benzylic), 3.43 (3 H, s, OCH_3), 3.65 (1 H, dd, $J_{1',2'b}$ = 6.1 Hz, H-1'), 4.00 (2 H, ddd, $J_{4',5'}$ = 2.6 Hz, $J_{4',5''}$ = 4.4 Hz, $J_{5',5''}$ = 11.1 Hz, H-5', H-5''), 4.04 (3 H, s, $ArOCH_3$), 4.38 (1 H, dd, H-4), 4.75 (2 H, dd, J = 11.1 Hz, OCH_2O), 6.58 (1 H, dd, H-1'), 6.97 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.71 (1 H, dd, $J_{7,9}$ = 1.8 Hz, $J_{9,10}$ = 8.4 Hz, H-9), 8.02 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.13 (1 H, d, H-3), 8.18 (1 H, d, H-10), 8.23 (1 H, d, H-7), 8.25 (1 H, d, $J_{11,12}$ = 9.0 Hz). ^{13}C NMR ($CDCl_3$): δ 15.22, 28.58, 46.37, 55.31, 55.68, 66.39, 75.87, 81.15, 96.61, 105.51, 114.79, 118.40, 119.19, 120.30, 121.93, 122.43, 125.01, 126.76, 128.69, 129.60, 132.94, 135.19, 145.51, 147.05, 154.49, 160.62, 213.96. Anal. Calcd for $C_{27}H_{26}O_7$: C, 70.1; H, 5.67. Found: C, 70.0; H, 5.68.

3,4,6-Tri-*O*-[(1,1-dimethylethyl)dimethylsilyl]-D-glucal[33] **(19).** To a solution of 3,4,6-tri-*O*-acetoxy-D-glucal[21] (1.0 g, 3.68 mmol) in 50 mL of methanol was added potassium carbonate (5.07 g, 36.8 mmol). The reaction was complete after 1 h on the basis of TLC. The volatiles were removed in vacuo, and the residue was dried under vacuum for 1 h. The residue was then dissolved in 15 mL of dimethylformamide, and imidazole (2.50 g, 36.8 mmol) was added. After 1 min, *tert*-butyldimethylsilyl chloride (2.77 g, 18.4 mmol) was added and the reaction mixture was stirred at room temperature for 10 h, at which time the reaction was complete on the basis of TLC. Ether (200 mL) was added, and the resulting solution was washed with brine and distilled water. The organics were dried over sodium sulfate, and the volatiles were removed in vacuo. The crude product was purified by column chromatography to give 1.76 g (98%) of 3,4,6-tri-*O*-[(1,1-dimethylethyl)dimethylsilyl]-D-glucal[33] (**19**) as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 0.08 (18 H, br, Si–CH_3), 0.85 (27 H, br, *tert*-butyl), 3.74 (1 H, dd, $J_{5,6}$ = 3.5 Hz, $J_{6,6'}$ = 11.2 Hz, H-6), 3.77 (1 H, m), 3.88 (1 H, m), 3.92 (1 H, dd, $J_{5,6'}$ = 7.4 Hz, H-6'), 3.97 (1 H, m), 4.67 (1 H, m, H-2), 6.30 (1 H, d, $J_{1,2}$ = 6.26 Hz, H-1). ^{13}C NMR ($CDCl_3$): δ −5.23, −5.19, −4.71, −4.38, −4.31, −4.21, 18.00, 18.08, 18.44, 25.71, 25.87, 25.99, 61.76, 66.77, 70.19, 80.07, 101.38, 142.97. Anal. Calcd for $C_{24}H_{52}O_4Si_3$: C, 59.0; H, 10.7. Found: C, 59.3; H, 10.9.

4-(2'-Deoxy-3,4,6-tri-*O*-[(1,1-dimethylethyl)dimethylsilyl]-α-D-*erythro*-hex-2-enopyranosyl)-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (20). To a solution of 8-ethyl-4-iodo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (**15**; 200 mg, 0.47 mmol), sodium acetate (38 mg, 0.47 mmol), and tributylamine (22 μL, 0.09 mmol) in 10 mL of dry dimethylformamide was added 3,4,6-tri-*O*-[(1,1-dimethylethyl)dimethylsilyl]-D-glucal (**19**; 340 mg, 7.0 mmol) and palladium acetate (21 mg, 0.09 mmol). The reaction mixture was stirred for 4 days at room temperature, and the volatiles were removed in vacuo. The residue was purified by column chromatography (5:1 ether–petroleum ether) to give 154 mg (42%) of **20** as a pale yellow solid. An analytical sample was recrystallized from chloroform–ethanol; mp 172 °C. ^{1}H NMR ($CDCl_3$): δ 0.05–0.21 (18 H, br, Si–CH_3), 0.85–0.97 (27 H, br, *tert*-butyl), 1.33 (3 H, t, CH_3), 2.80 (2 H, q, benzylic), 3.84 (1 H, d, $J_{5',6'}$ = 4.6 Hz, H-6'), 4.00 (1 H, d, $J_{5',6''}$ = 4.7 Hz, H-6''), 4.01 (3 H, s, $ArOCH_3$), 4.12 (1 H, dd, $J_{4',5'}$ = 6.3 Hz, H-5'), 4.70 (1 H, d, H-4), 5.29 (1 H, d, $J_{1',2'}$ = 2.3 Hz), 6.77 (1 H, s, H-1'), 6.93 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.68 (1 H, dd, $J_{7,9}$ = 1.9 Hz, $J_{9,10}$ = 8.3 Hz, H-9), 8.01 (1 H, d, $J_{11,12}$ = 9.1 Hz), 8.08 (1 H, d, H-3), 8.13 (1 H, d, H-10), 8.23 (1 H, d, $J_{11,12}$ = 9.1 Hz), 8.25 (1 H, d, H-7). ^{13}C NMR ($CDCl_3$): δ −5.23, −5.17, −4.52, −4.21, −2.76, 15.27, 18.17, 18.22, 25.79, 25.87, 25.93, 25.98, 28.62, 55.73, 62.18, 67.28, 70.07, 80.16, 105.88, 108.37, 114.69, 118.04, 119.13, 120.62, 122.46, 126.86, 128.50, 128.69, 130.61, 133.22, 134.97, 145.21, 147.32, 154.40, 160.51. Anal. Calcd for $C_{44}H_{66}O_7Si_3$: C, 66.8; H, 8.41. Found: C, 66.7; H, 8.31.

4-(5'-Acetyl-2'-deoxy-β-D-*glycero*-pentofuran-3'-ulos-1'-yl)-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (24). To a mixture of 8-ethyl-4-iodo-1-methoxybenzo[*d*]-naphtho[1,2-*b*]pyran-6-one (**15**; 700 mg, 1.63 mmol), sodium acetate (133 mg, 1.63 mmol), and tributylamine (77 μL, 0.33 mmol) in 25 mL of dry dimethylformamide was added 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[32] (**21**; 692 mg, 1.95 mmol) and palladium acetate (37 mg, 0.17 mmol). After the mixture was stirred for 6 h at room temperature, acetic acid (195 mg, 3.26 mmol) and a 1 M solution of tetrabutylammonium fluoride in tetrahydrofuran (2.0 mL, 2.0 mmol) was added. After the mixture was stirred for an additional 10 min, volatiles were removed in vacuo. Pyridine (10 mL) and acetic anhydride (2 mL) were then added. The reaction mixture was then stirred for an additional 8 h, at which time TLC indicated the reaction was complete. The volatiles were removed in vacuo, and the residue was purified by column chromatography to give **24** (666 mg, 89%) as off-white crystals, mp 190 °C. ^{1}H NMR ($CDCl_3$): δ 1.34 (3 H, t, CH_3), 2.12 (3 H, s, $COCH_3$), 2.35 (1 H, dd, $J_{1',2'}$ = 9.9 Hz, $J_{2'a,2'b}$ = 18.7 Hz, H-2'a), 2.81 (2 H, q, benzylic), 3.67 (1 H, dd, $J_{1',2'b}$ = 6.2 Hz, H-2b), 4.02 (3 H, s, $ArOCH_3$), 4.42 (2 H, dd, $J_{4',5'}$ = 4.6 Hz, $J_{5',5''}$ = 15.1 Hz, H-5',5''), 4.69 (1 H, dd, $J_{4',5''}$ = 5.5 Hz, H-4'), 6.52 (1 H, dd, H-1'), 6.94 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.69 (1 H, dd, $J_{7,9}$ = 1.8 Hz, $J_{9,10}$ = 8.2 Hz, H-9), 7.98 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.04 (1 H, dd, $J_{1',3}$ = 0.8 Hz, H-3), 8.08 (1 H, d, H-10), 8.19 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.20 (1 H, d, H-7). ^{13}C NMR ($CDCl_3$): δ 15.19, 20.86, 28.56, 46.11, 55.67, 62.92, 75.98, 79.56, 105.40, 114.78, 118.44, 119.17, 120.22, 121.79, 122.41, 124.57, 126.76, 128.64, 129.23, 132.85, 135.19, 145.54, 146.90, 154.53, 160.55, 170.68, 212.95. Anal. Calcd for $C_{27}H_{24}O_7$: C, 70.4; H, 5.17. Found: C, 70.0; H, 5.19.

4-[2'-Deoxy-3',5'-diacetyl-β-D-*ribo*-(=*arabino*)-furanosyl]-8-ethyl-1-methoxybenzo[*d*]naphtho[1,2-*b*]-pyran-6-one (26). To a solution of 8-ethyl-4-iodo-1-methoxybenzo[*d*]naphtho[1,2-*b*]pyran-6-one (**15**; 1.80 g, 4.19 mmol), sodium acetate (0.34 g, 4.19 mmol), and tributylamine (200 μL, 0.84 mmol) in 50 mL of dry dimethylformamide was added 1,4-anhydro-2-deoxy-3-*O*-[(1,1-dimethylethyl)diphenylsilyl]-D-*erythro*-pent-1-enitol[32] (**21**; 1.78 g, 5.02 mmol) and palladium acetate (94 mg, 0.42 mmol). The reaction mixture was stirred at room temperature for 10 h, at which time acetic acid (0.50 g, 8.37 mmol) and a 1 M solution of tetrabutylammonium fluoride in tetrahydrdofuran (6.28 mL) were added. After 10 min, the volatiles were removed in vacuo and the residue was dried under high vacuum for 2 h. Dimethylformamide (100 mL) and acetic acid (100 mL) were then added. Sodium triacetoxyborohydride (2.65 g, 12.56 mmol) was added, and the reaction was complete in 10 min on the basis of TLC. Volatiles were removed in vacuo, and pyridine (40 mL) and acetic anhydride (2 mL, 20.9 mmol) were added. The reaction mixture was then stirred for an additional 10 h. Volatiles were removed, and the residue was dissolved in chloroform. Purification was accomplished by column chromatography to give 1.98 g (94%) of **26** as an off-white solid. An analytical sample was recrystallized from chloroform–ethanol; mp 169 °C. ^{1}H NMR ($CDCl_3$): δ 1.30 (3 H, t, CH_3), 1.94 (1 H, ddd, $J_{1',2'a}$ = 9.7 Hz, $J_{2'a,2'b}$ = 13.7 Hz, $J_{2'a,3'}$ = 6.0 Hz, H-2'a), 2.10, 2.27 (6 H, 2 s, $COCH_3$), 2.78 (2 H, q, benzylic), 3.05 (1 H, ddd, $J_{1',2'b}$ = 5.2 Hz, $J_{2'b,3'}$ = 5.3 Hz, H-2'b), 3.98 (3 H, s, $ArOCH_3$), 4.32 (1 H, dd, $J_{4',5'}$ = 4.6 Hz, $J_{5',5''}$ = 11.3 Hz, H-5'), 4.42 (1 H, m, H-4), 4.48 (1 H, dd, $J_{4',5'}$ = 4.2 Hz, H-5''), 5.23 (1 H, m, H-3'), 6.45 (1 H, dd, H-1'), 6.90 (1 H, d, $J_{2,3}$ = 8.4 Hz, H-2), 7.66 (1 H, dd, $J_{7,9}$ = 1.7 Hz, $J_{9,10}$ = 8.4 Hz, H-9), 7.96 (1 H, d, H-3), 7.97 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.08 (1 H, d, H-10), 8.18 (1 H, d, $J_{11,12}$ = 9.0 Hz), 8.19 (1 H, d, H-7). ^{13}C NMR ($CDCl_3$): δ 15.24, 20.95, 21.27, 28.58, 41.89, 55.66, 64.48, 76.54, 79.16, 81.01, 105.47, 114.68, 118.33, 119.09, 120.39, 121.92, 122.40, 124.26, 126.84, 128.63, 129.97, 132.99, 135.05, 145.34, 147.29, 154.26, 160.49, 170.88, 171.25. Anal. Calcd for $C_{29}H_{28}O_8$: C, 69.0; H, 5.59. Found: C, 69.2; H, 5.46.

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Registry No. **1**, 110-87-2; **2**, 40738-83-8; **6**, 2873-29-2; **8**, 80242-47-3; **9**, 80242-46-2; **10**, 117408-10-3; **11**, 1191-99-7; **12**, 130277-26-8; **13**, 130277-27-9; **14**, 130277-28-0; **15**, 130277-29-1; **15** (bromo derivative), 130277-35-9; **15** (deiodo derivative), 114862-65-6; **16**, 86436-81-9; **18**, 130277-30-4; **19**, 79999-47-6; **20**, 130277-31-5; **21**, 130277-32-6; **24**, 130277-33-7; **26**, 130277-34-8; $Pd(OAc)_2$, 3375-31-3; $PdCl_2$, 7647-10-1; $Pd(PPh_3)_4$, 14221-01-3; $(PPh_3)_2Pd(OAc)_2$, 14588-08-0; Bu_4NCl, 1112-67-0; Bu_4NBr, 1643-19-2; Bu_4NF, 429-41-4; $Pd(CH_3CN)_2Cl_2$, 14592-56-4; Et_3N, 121-44-8; tri-*o*-tolylphosphine, 6163-58-2.