glycosides can be achieved from similar *C*-arylglycal precursors. These possibilities are currently being explored.

Acknowledgment. We gratefully acknowledge the Natural Sciences and Engineering Research Council of Canada and the University of Toronto for financial support and the University of Toronto for an Open Fellowship (to C.F.S.).

Supplementary Material Available: Physical constants and spectral data for **6–10** and **5b** (2 pages). Ordering information is given on any current masthead page.

Selective Control of the Various Cycloaddition Products from Reactions of Styrenes and 1,4-Benzoquinones: Optimization of the Formal 5 + 2 Cycloadducts

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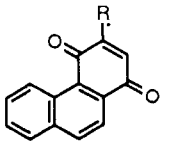
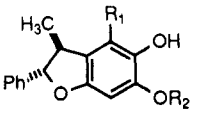
Summary: 7-Aryl-3-hydroxy-6-methylbicyclo[3.2.1]oct-3-ene-2,8-diones **4** and **8** are formed exclusively in Ti(IV)-catalyzed reactions of 2-((4-methoxybenzyl)oxy)-1,4-benzoquinones **5a/d** with *trans*-β-methylstyrene and indene, respectively.

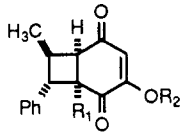
An important issue in the development of synthetically useful reactions is whether or not a single desired product can be obtained selectively in good yield from systems in which several reaction pathways are available. Such is the situation encountered in reactions of styrenes and 1,4-benzoquinones in which, among other processes,[1] as many as four different products of formal cycloaddition[2] can be obtained depending upon reaction conditions. Diels–Alder adducts **1** (4 + 2 cycloadducts) are found under thermal conditions.[3] With Lewis acid catalysis, *trans*-β-methylstyrenes and 2-alkoxy-1,4-benzoquinones produce the dihydrobenzofurans **2** (formal 3 + 2 cycloadducts), the bicyclo[4.2.0]oct-3-ene-2,8-diones **3** (2 + 2 cycloadducts), and/or the bicyclo[3.2.1]oct-3-ene-2,8-diones **4** (5 + 2 cycloadducts).[4] In many cases it is possible to form selectively either the 3 + 2 or 2 + 2 cycloadduct by proper choice of reaction conditions.[4a,c] Herein, we report for the first time a simple variant of the system which results in the direct, exclusive formation of the formal 5 + 2 adducts **4** in good yield. Thus, these reactions provide direct access to biologically important neolignans incorporating the 7-arylbicyclo[3.2.1]octene skeleton as well as the 2-aryl-2,3-dihydrobenzofuran framework and oxidized derivatives.[5]



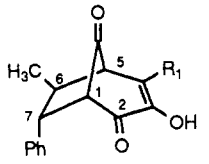
1, R=H, CH_3 or OCH_3



2, R_1=H or CH_3, R_2=CH_3



3, R_1=H or CH_3, R_2=CH_3



4a, R_1=CH_3
4b, R_1=H

The formation of **2**–**4** can be rationalized via intermediates **6** and **7** (Scheme I) which may result from a ($4\pi + 2\pi$) cycloaddition of the Ti(IV)–quinone complex with the styrene to give **6** directly[6] followed by ring opening to **7** (path a). Alternately, **7** may be formed by a stereoselective alkylation of the Ti(IV)–quinone complex by the styrene. Ring closure of **7** via path b gives **6**, and dealkylation of **6** by chloride ion present in the reaction mixture ultimately yields **4** (path c). Bond formation between the carbocation center in **7** and the titanium enolate moiety or the carbonyl group followed by loss of a proton produces **3** and **2**, respectively.[7] In any event,[8] we reasoned that a controlling

(1) Additional reaction manifolds involve hydride or hydrogen atom abstraction processes: (a) Lee-Ruff, E.; Ablenas, F. J. *Can. J. Chem.* **1989**, *67*, 699. (b) Takada, M.; Oshima, R.; Yamauchi, Y.; Kumanotani, J.; Seno, M. *J. Org. Chem.* **1988**, *53*, 3073. For a recent review, see: (c) Becker, H.-D.; Turner, A. B. In *The Chemistry of Quinonoid Compounds, Vol. 2*; Patai, S.; Rappoport, Z., Eds.; John Wiley and Sons: New York, 1988; p 1351.

(2) For a recent review, see: Finley, K. T. in ref 1c, p 537.

(3) (a) Kita, Y.; Okunaka, R.; Honda, T.; Shindo, M.; Tamura, O. *Tetrahedron Lett.* **1989**, *30*, 3995. (b) Manning, W. B. *Ibid.* **1981**, *22*, 1571. (c) Kelly, T. R.; Magee, J. A.; Weibel, F. R. *J. Am. Chem. Soc.* **1980**, *102*, 798. (d) Rosen, B. I.; Weber, W. P. *J. Org. Chem.* **1977**, *42*, 3463. (e) Inouye, Y.; Kakisawa, H. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 563. (f) Lora-Tamayo, M. *Tetrahedron* **1958**, *4*, 17. (g) For a review, see: Wagner-Jauregg, T. *Synthesis* **1980**, 769 and references cited in the above.

(4) (a) Engler, T. A.; Combrink, K. D.; Ray, J. E. *J. Am. Chem. Soc.* **1988**, *110*, 7931. (b) Engler, T. A.; Combrink, K. D.; Takusagawa, F. *J. Chem. Soc., Chem. Commun.* **1989**, 1573. (c) Engler, T. A.; Reddy, J. P.; Combrink, K. D.; Vander Velde, D. *J. Org. Chem.* **1990**, *55*, 1248 and references cited therein.

(5) For recent reviews and leading references on the pharmacological activity of neolignans, see: (a) Gottlieb, O. R. In *New Natural Products and Plant Drugs with Pharmacological, Biological or Therapeutic Activity*, Proceedings of the First International Congress, 1976; Wagner, H., Wolff, P. M., Eds.; Springer Verlag: Berlin, 1977; p 277. (b) Gottlieb, O. R. *Quim. Nova* **1984**, *7*, 250. For current reviews on the isolation, chemistry, and synthesis of lignans and neolignans, see: (c) Gottlieb, O. R. *Fortsch. Chem. Org. Naturst.* **1978**, *35*, 1. (d) Gottlieb, O. R. *Rev. Latinoamer. Quim.* **1974**, *5*, 1. (e) Gottlieb, O. R. *Phytochemistry* **1972**, *11*, 1537. (f) Ward, R. S. *Chem. Soc. Rev.* **1982**, *11*, 75. (g) Whiting, D. A. *Nat. Prod. Rep.* **1985**, *2*, 191. (h) Whiting, D. A. *Nat. Prod. Rep.* **1987**, *4*, 499.

(6) For related reactions of 3,4-dialkoxy- or 3-alkoxy-4-alkyl-1-oxocyclohexa-2,5-dien-4-yl cations, see: (a) Büchi, G.; Mak, C.-P. *J. Am. Chem. Soc.* **1977**, *99*, 8073. (b) Büchi, G.; Chu, P.-S. *J. Org. Chem.* **1978**, *43*, 3717. (c) Büchi, G.; Mak, C.-P. *J. Org. Chem.* **1981**, *46*, 1. (d) Büchi, G.; Chu, P.-S. *J. Am. Chem. Soc.* **1981**, *103*, 2718. (e) Shizuri, Y.; Yamamura, S. *Tetrahedron Lett.* **1983**, *24*, 5011. (f) Thomas, E. J.; Mortlock, S. V.; Seckington, J. K. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2305.

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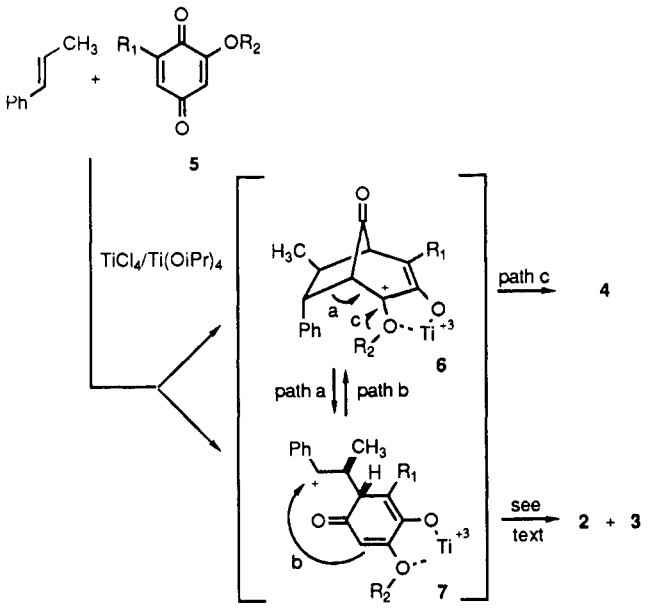
Table I. Titanium(IV)-Catalyzed Reactions of 2-Alkoxy-1,4-benzoquinones and *trans*-β-Methylstyrene[a]

entry	quinone	catalyst $TiCl_4$–$Ti(OiPr)_4$[c]	temp, °C	yield,[b] % 4	2	3
1	**5a**	1:1[d]	−78 to rt[e]	76	−[f]	−
2	**5b**	2:1[d]	−78 to 10	54	−	−
3	**5d**	1:1[d]	−78 to rt	59	−	−
4	**5c**	3:1[g]	−78	41–51	4–10	7–17[h]
5	**5c**	3:1	−78 to rt	18	8	13
6	**5c**	2:1[g]	−78 to rt[i]	19–28	6–7	≤7
7	**5e**	2:1[d]	−78	27	19	8
8	**5f**	1:0	−78	−	30	19
9	**5f**	3:1	−78	−	20	27
10	**5f**	2:1	−78 to 0	−	32	29
11	**5f**	1:1	−78 to 0	−	6	−[j]

[a] All reactions were carried out in dry CH_2Cl_2 under an atmosphere of N_2 or Ar. [b] Yield of material(s) isolated after addition of *i*-PrOH/solid $NaHCO_3$ and water, extractive isolation (CH_2Cl_2), and silica gel chromatography and/or recrystallization. [c] Equivalents of Ti^{4+} with respect to quinone was 1.0–1.1, except where noted, and the ratio of styrene to quinone was 1.2–1.5 for each case. [d] A range of catalyst mixtures (4:1 to 1:1), equiv of Ti^{4+} (1–2) and reaction temperatures were examined. The results shown represent the optimum conditions for formation of **4**: other experiments produced mixtures of **2**–**4** and/or low material balance. [e] Indicates that the reaction mixture was allowed to warm from −78 °C to the temperature indicated; rt = room temperature. [f] Indicates that none of this product was found. [g] The ratio of Ti(IV):quinone was varied from 1.0:1 to 2.0:1 in several different experiments. [h] In these experiments, 32–43% of the starting quinone was recovered. [i] Several reaction temperatures were examined. [j] In this experiment, 52% of the starting quinone was recovered.

Scheme I



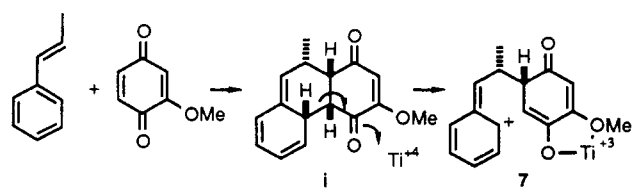
For **2**-**7**: **a**, R_1=CH_3, R_2=CH_2Ph-4-OCH_3; **b**, R_1=CH_3, R_2=CH_2Ph; **c**, R_1=CH_3, R_2=CH_3; **d**, R_1=H, R_2=CH_2Ph-4-OCH_3; **e**, R_1=H, R_2=CH_2Ph **f**, R_1=H, R_2=CH_3

factor in the formation of **4** versus **2**/**3** may be the relative ease of path a versus c. A modification of the system resulting in the preference for path c over path a would lead to more of the cycloadduct **4**. Following this premise, we explored the reactions of styrenes with 2-(benzyloxy)-1,4-benzoquinones[9] **5a**/**b** and **5d**/**e** in which the corresponding bicyclic cations **6**, if formed, should lead to higher proportions of **4** relative to **2**/**3** by more facile displacement (S_N1 or S_N2) of the benzyl moieties relative to CH_3.

In the experiments, bicyclo[3.2.1]oct-3-ene-2,8-dione **4a**[10] is isolated in 76% yield upon addition of *trans*-β-methylstyrene to a mixture of 2-((4-methoxybenzyl)-oxy)-6-methyl-1,4-benzoquinone (**5a**) and a 1:1 mixture of $TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$ in dichloromethane at −78 °C followed by warming to room temperature (Table I). In a similar manner, **4a** is produced from **5b** and **4b**[10] is formed from **5d** in 54 and 59% yields, respectively. For comparison, results of reactions involving 2-(benzyloxy)-1,4-benzoquinones **5b**/**e** and 2-methoxy-1,4-benzoquinones **5c**/**f** are also presented in the table. The experiments suggest that the efficiency of the reaction and the ratio of products formed is dependent on several factors including the ratio of $TiCl_4$:$Ti(OiPr)_4$ utilized as catalyst and the reaction temperature. A systematic study to define the effects of these variables on the product ratios observed in reactions involving ≥10 different quinones and ≥16 styrenes is underway, and the results will be reported in due course. However, at this time, the experiments demonstrate that the yield of the 5 + 2 adduct **4** is considerably improved by the use of the benzyloxyquinones in the reactions and, in fact, cycloadduct **4** is the only product isolated in reactions of **5a**/**d**; products **2**/**3** are present in only trace amounts (TLC). As an additional example, indene reacts with **5a** to give **8** in 63% yield[11a] whereas reactions of indene with **5c** give a mixture of **8** and products analogous to **2** and **3**[4b] in 32–36, 3–9, and 19–22% yields,[11b] respectively. In keeping with our initial premise, 4-methoxybenzyl chloride is found in reactions of **5a**/**d**.

The structure of **4a** is firmly established by single-crystal X-ray analysis. The stereochemistry in **4a** and **4b** is also

(7) A third possible mechanism involves a Diels–Alder reaction of the styrene and the quinone via an endo transition state to give i which may open to **7** and then proceed to **6**. This process also explains the diastereospecificity observed in the formation of **3** from reactions of (*E*)- and (*Z*)-β-methylstyrenes.[4a] However, a reason for the absence of dihydroxyphenanthrene or phenanthrenedione products via such a mechanism is not obvious (for example, see ref 3).

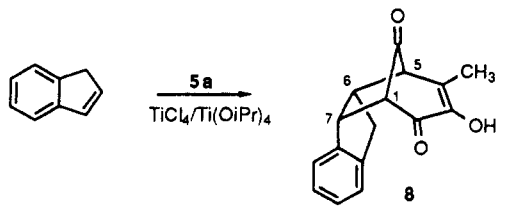


(8) The divergent reaction pathways available to intermediates similar to **6**/**7** have also been suggested as part of the biosynthesis of a number of classes of neolignans; see, Angle, S. R.; Turnbull, K. D. *J. Am. Chem. Soc.* **1990**, *112*, 3698 and references cited therein.

(9) Prepared via Fremy's salt oxidation of the corresponding phenols; see, for example: Ishii, H.; Ohtake, R.; Ohida, H.; Mitsui, H.; Ikeda, N. *J. Pharm. Soc. Jpn.* **1970**, *90*, 1283 (Cf: Zimmer, H.; Lankin, D. C.; Horgan, S. W. *Chem. Rev.* **1971**, *71*, 229).

(10) All compounds have been characterized by 300- or 500-MHz ^1H NMR, ^{13}C NMR, IR, UV, HRMS, and/or elemental analysis; see the supplementary information.

(11) (a) The conditions are the same as for the reactions of *trans*-β-methylstyrene with **5a**. (b) The range is for several experiments.



evident from a J_{H1-H7} of 6–7 Hz and the lack of a measurable coupling constant between H5 and H6.[6f] In the indene adduct 8, an endo orientation is indicated by J_{H1-H7} and J_{H5-H6} of 8–9 Hz. The structures of 2 and 3 have been reported previously.[4]

The mechanism(s) of the reactions remains to be firmly established;[4b,7] however, the rationale presented here is a useful guide for the design of experiments and reaction conditions to control the various reaction manifolds available to styrenes and quinones. In addition, since the quinones and styrenes are readily available and the reactions are stereoselective, this new methodology should be valuable for the efficient and stereoselective preparation of a number of different naturally occurring carbocyclic and heterocyclic systems.

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Supplementary Material Available: Representative experimental procedures for the preparation of **4a/b** and **8**, including complete physical and spectral data; ^1H and ^{13}C NMR spectra of **4a/b** and **8**; full crystallographic data and an ORTEP representation of **4a** (24 pages). Ordering information is given on any current masthead page.

Direct Preparation of 2-Deoxy-D-glucopyranosides from Glucals without Ferrier Rearrangement

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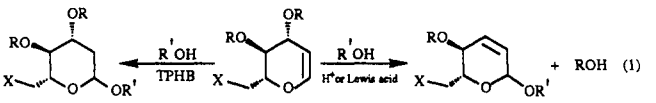
Summary: An efficient catalytic procedure for the preparation of 2-deoxyglucosides from glucals without allylic or Ferrier rearrangement using triphenylphosphine hydrobromide and a wide variety of hydroxylic nucleophiles is described.

2-Deoxyglycosides are versatile synthetic intermediates[1] as well as common structural units in many biologically significant substances.[2] Their preparation by electrophilic glycosylation[3] of hydroxylic donors with readily available glycals[4] is complicated in many instances by the proclivity of the cyclic enol toward allylic rearrangement resulting in 2,3-unsaturated glycosides (eq 1). This is commonly



known as the Ferrier reaction[5] and is most prevalent when the C(3)-hydroxyl is derivatized or under the influence of Lewis acid catalysts.[6]

Although several procedures have been introduced recently to circumvent rearrangement, they generally involve introduction of an auxiliary derived from a toxic, expensive, or difficult to handle reagent.[7] By necessity, one or more further steps are required to remove or transpose the auxiliary. Herein, we describe an efficient catalytic procedure using triphenylphosphine hydrobromide (TPHB) for the preparation of 2-deoxyglucosides directly from substituted glucals and a wide selection of hydroxylic nucleophiles. We have reported previously that stoichiometric amounts of TPHB add to enol ethers to give α-

(1) For example: Falck, J. R.; Lumin, S.; Yadagiri, P.; Shin, D.-S. *Adv. Prost. Throm. Leuk. Res.* **1989**, *19*, 635–638. Lumin, S.; Falck, J. R. *Tetrahedron Lett.* **1990**, *31*, 2971–2974.

(2) Williams, N. R.; Wander, J. D. In *The Carbohydrates*; Pigman, W., Horton, D., Eds.; Academic Press: New York, 1980; Vol. 1B, p 761. Gould, R. F. *Deoxy Sugars*; American Chemical Society: Washington, D.C., 1968.

(3) For alternative approaches to 2-deoxyglycosides, see: (a) Kahne, D.; Yang, D.; Lim, J. J.; Miller, R.; Paguaga, E. *J. Am. Chem. Soc.* **1988**, *110*, 8716–8717. (b) Michalska, M.; Borowiecka, M. *J. Carbohydr. Chem.* **1983**, *2*, 99. (c) Tavecchia, P.; Trumtel, M.; Veyrieres, A.; Sinay, P. *Tetrahedron Lett.* **1989**, *30*, 2533. (d) Crich, D.; Ritchie, T. J. *J. Chem. Soc., Perkin Trans. 1* **1990**, 945–954. (e) Giese, B.; Gilges, S.; Groninger, K. S.; Lamberth, C.; Witzel, T. *Liebigs Ann. Chem.* **1988**, 615–617. (f) Catelani, G.; Colonna, F.; Rollin, P. *Gazz. Chim. Ital.* **1989**, *119*, 389–393.

(4) Ireland, R. E.; Thaisrivongs, S.; Vanier, N.; Wilcox, C. S. *J. Org. Chem.* **1980**, *45*, 48–61. Wittman, M. D.; Halcomb, R. L.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 1979–1981.

(5) Ferrier, R. J. *Adv. Carbohydr. Chem. Biochem.* **1969**, *24*, 199–266. Ferrier, R. J.; Prasad, N. *J. Chem. Soc. C* **1969**, 570.

(6) Descotes, G.; Martin, J.-C. *Carbohydr. Res.* **1977**, *56*, 168–172. Grynkiewicz, G.: Priebe, W.; Zamojski, A. *Ibid.* **1979**, *68*, 33–41. Hadfield, A. F.; Sartorelli, A. C. *Ibid.* **1982**, *101*, 197–208. Lundt, I.; Pedersen, C. *Acta Chem. Scand.* **1970**, *24*, 240–246.

(7) For recent examples, see: Ramesh, S.; Kaila, N.; Grewal, G.; Franck, R. W. *J. Org. Chem.* **1990**, *55*, 5–7 and references cited therein. Also: Bock, K.; Lundt, I.; Pedersen, C. *Carbohydr. Res.* **1984**, *130*, 125–134.

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