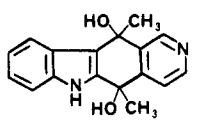
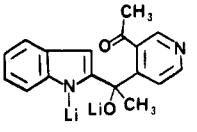
indole and aryl ketone chromophores, respectively.[15]

In accord with expectations, **8** reacted with methyllithium (2 equiv, -100 °C, THF) to afford diol **9**[10,16] as a mixture of diastereomers. This reaction presumably involves the successive generation of ketone **10** followed by cyclization to the indole β-position to afford **9**.



9



10

Without purification the crude diol mixture (**9**) was treated with sodium borohydride (EtOH, reflux)[5b] to afford ellipticine (**1a**), mp 311-315 °C dec, in 82% yield from **8** after flash chromatography[17] on silica gel (THF-EtOAc, 7:3) and in 54% overall yield from indole (**2a**). The material so obtained was identical in all respects (IR, TLC, UV, MS, mmp 311-315 °C dec) with an authentic sample of ellipticine.

Further studies to explore the generality of this pyrido[4,3-*b*]carbazole synthesis are in progress.

Acknowledgment. This investigation was supported in part by Merck Sharp and Dohme Research Laboratories, by Grant CH-200 from the American Cancer Society, and by Biomedical Research Support Grants RR-05392 and RR-07056 from the Biomedical Research Support Branch, Division of Research Facilities and Resources, National Institutes of Health. We also thank Dr. Catherine E. Costello (Massachusetts Institute of Technology) for the high-resolution mass spectra (National Institutes of Health Resource Grant FR00317 from the Division of Research Facilities and Resources), the Colorado State University Regional NMR Center, funded by National Science Foundation Grant No. CHE 78-18581, for high-resolution NMR spectra, Professors John A. Joule, Victor A. Snieckus, Jan Bergman, and Dr. Norbert Neuss for authentic samples and/or spectra of **1a** and **7**, and Mr. Al Barefoot for low-resolution mass spectra. We also thank Professor Joule for communicating his results to us prior to publication.

Registry No. **1a**, 519-23-3; **2a**, 120-72-9; **2b**, 40899-71-6; **3**, 4664-08-8; **4**, 40900-03-6; **5a**, 81940-21-8; **5b**, 81940-22-9; **6**, 81940-23-0; **7**, 73326-98-4; **8**, 81940-24-1; **9**, 81940-25-2; **10**, 81940-26-3.

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(16) **9**: mass spectrum, *m/e* 280.1202 (M^+, calcd 280.1212).
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Mark G. Saulnier, Gordon W. Gribble*
Department of Chemistry
Dartmouth College
Hanover, New Hampshire 03755
Received February 17, 1982

Palladium-Assisted C-Glycosylation. Addition of Carbanions to Cyclic Enol Ethers

Summary: Pd(II) effects the regiospecific addition of carbanions to dihydrofuran at the ring oxygen-bearing carbon. A similar regiospecific alkylation of acetoxydihydropyrans catalyzed by Pd(0) is also reported. Initial examples of the stereoselectivity of these reactions are also given.

Sir: The alkylation of furanosides and pyranosides constitutes a very important step in the synthesis of a variety of biologically active natural products. Methodology for this purpose continues to be developed and applied to the stereoselective asymmetric syntheses of *C*-glycoside-containing natural products. *C*-Glycofuranosides can be viewed as precursors to C-nucleosides and other natural products containing alkylated tetrahydrofuran moieties. Some recent examples include syntheses of showdomycin[1] and the elaboration of chiral furenone components of germacranolide sesquiterpenes.[2-4] *C*-Glycosides have also been prepared by a variety of methods, including enolate Claisen rearrangements,[5,6] Lewis acid catalyzed nucleophilic additions to glycals,[7,8] hetero-Diels-Alder reactions,[9-12] and allyl stannane coupling with glycosyl halides.[13]

As a part of a general study directed toward the development of transition metal controlled asymmetric functionalization of carbohydrates, the palladium-assisted alkylation of cyclic enol ethers has been investigated.[14] Herein we report examples of two regiospecific methods for the alkylation of cyclic enol ethers, both of which alkylate exclusively at the ring oxygen-bearing carbon atom.

The alkylation of dihydrofurans was first investigated. Palladium(II) reagents were used in these reactions following the recently developed methodology to alkylate alkenes.[15,16] The alkylation of 2,3-dihydrofuran was carried out by activation with bis(acetonitrile)palladium(II) chloride. Formation of the Pd(II) π complex was accomplished by addition of 2,3-dihydrofuran to a solution of $Pd(CH_3CN)_2Cl_2$ in 1:1 THF/DMF at room temperature under argon. The complex was cooled to -78 °C followed by addition of Et_3N (2.0 equiv/Pd). A carbanion (1 equiv) (**1-7**, Table I) was introduced at -78 °C and the reaction

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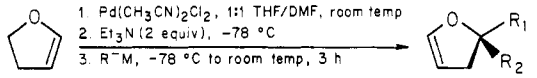
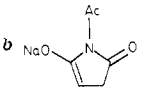
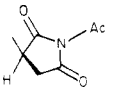
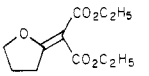
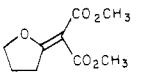
Table I. Pd(II)-Assisted Alkylation of Dihydrofuran

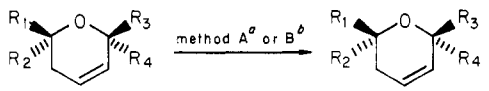


8-12

carbanion	% yield [a]	product compd	R_1	R_2
1, $NaC(NHCHO)(CO_2C_2H_5)_2$	76	8	H	$C(NHCHO)(CO_2C_2H_5)_2$
2, $NaC(NHAc)(CO_2C_2H_5)_2$	73	9	H	$C(NHAc)(CO_2C_2H_5)_2$
3, $NaC(NHAc)(CO_2CH_3)_2$	64	10	H	$C(NHAc)(CO_2CH_3)_2$
4, [b] $NaC(CH_3)(CO_2C_2H_5)_2$	50	11	H	$C(CH_3)(CO_2C_2H_5)_2$
5, [b]  in DMF	55	12	H	
6, [b] $NaCH(CO_2C_2H_5)_2$	76	13		
7, [b] $NaCH(CO_2CH_3)_2$	78	14		

[a] Based on Pd after chromatography. [b] In THF.

Table II. Pd(0)-Catalyzed Alkylation of Dihydropyranyl Acetates



reactants no.	R_1	R_2	R_3	R_4	carbanion, % yield [c]	products no.	R_5	R_6
15	H	H	OAc	H	1, 83 [a]	17	$C(NHCHO)(CO_2C_2H_5)_2$	H
15	H	H	OAc	H	2, 88 [a]	18	$C(NHAc)(CO_2C_2H_5)_2$	H
15	H	H	OAc	H	3, 80 [a]	19	$C(NHAc)(CO_2CH_3)_2$	H
16 [d]	CH_3OCH_2	H	OAc	H	3, 90 [a]	20	$C(NHAc)(CO_2CH_3)_2$	H
16 [d]	CH_3OCH_2	H	OAc	H	C_6H_5ZnCl, 94 [b,e]	21	H	C_6H_5
16 [d]	CH_3OCH_2	H	OAc	H	$CH_2=CHZnCl$, 97 [b,e]	22	H	$CH=CH_2$

[a] Method A: (1) 0.1 equiv of $Pd(PPh_3)_4$, 1 equiv of PPH_3, DMF, room temperature, 30 min; (2) carbanion, 70 °C, 18 h. [b] Method B: (1) 0.05 equiv of $Pd(PPh_3)_4$, THF, room temperature, 15 min; (2) RZnCl (from 1:1 RMgBr + $ZnCl_2$), THF, room temperature, 3 h.[29] [c] Yield based on acetate, after chromatography, NMR data in Tables III and IV. [d] Reference 28. [e] Phenylzinc chloride was at least 90% stereoselective; tentative data for the minor epimer 23 is included in Table III; vinylzinc chloride was 100% stereoselective.

Table III. ^{13}C NMR Data (50.3 MHz, $CDCl_3$, δ)

compd	C-2	C-3	C-4	C-5	C-6	CH_2OCH_3		other
16	89.01	128.54	122.73	26.86	67.98	74.43	59.32	$OCOCH_3$, 21.87, 168.27
20	69.40	124.38	123.86	26.91	69.55	74.53	59.37	$NHCOCH_3$, 26.77, 167.45 CO_2CH_3, 23.67, 165.95, 164.94
21 (major)	73.99	128.24	125.26	27.04	66.54	75.16	59.16	C_6H_5, 127.45, 127.86, 127.53, 140.87
22	73.19	127.29	124.66	26.97	66.80	75.38	59.18	$CH=CH_2$, 136.85, 116.85
23	76.07				68.24			

mixture stirred at −78 °C for 30 min followed by slow warming to room temperature over 2.5 h. Isolation and purification afforded 2-substituted 2,3-dihydrofurans 8–14 shown in Table I.[17] No products derived from carbanion attack at C-3 were observed. The migration of the double bond was expected on the basis of previous Pd(II)-assisted nucleophilic additions performed in our laboratories.[14,18] After β elimination of "PdH", it is presumed a series of readdition–elimination reactions occur, terminating when the double bond is endocyclic and in conjugation with the ring oxygen. It is noteworthy that the succinimide adduct 12 was formed stereoselectively[19] and that double-bond migration terminated in the endocyclic manner. Migration exocyclic to the ring was observed during the reactions of diethyl and dimethyl sodiomalonate, affording products 13 and 14. The regioselectivity can be rationalized on the basis of electronic effects similar to that reported by Rosemblum for enol ether iron complexes.[19-23] Experiments

(17) All compounds gave satisfactory ^1H NMR (100, 200, or 500 MHz), ^{13}C NMR (25.2, 50.3, or 125 MHz), infrared, and mass spectra.
(18) Dunkerton, L. V.; Mohamed, F. unpublished results.

(19) The >90% diastereoselectivity is assigned primarily on the basis of ^{13}C NMR with some supporting evidence from the ^1H NMR. The major product 12 was assigned the threo configuration while the minor product was assigned as the tetrahydro threo analogue. The suggested diastereoselectivity is that predicted based on the preferred orientation of the reactants in which the cyclic enol ether is exo to the enolate. This diastereoselectivity has also been observed by Rosenblum in the alkylation of enol ether iron complexes.[20-22] NOE difference experiments failed to unequivocally assign the threo configuration to 12.
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Table IV. ^{1}H NMR Data Relevant to Stereochemical Assignment (500 MHz, $CDCl_3$, δ)

compd	H-2	$J_{2,3}$, Hz	$H_{3,4}$	H-6	CH_2
16	6.31-6.33	1.0	6.10-6.19	4.05-4.17	3.44-3.57
20	5.09-5.11	1.56	H_3, 6.04-6.07; H_4, 5.89-5.93	3.94-3.98	3.47-3.54
21	5.30 (whh = 6 Hz)	1.83	5.99-6.61	3.75-3.80	3.34-3.46
22	4.71 (whh = 9 Hz)	2.16	H_3, 5.85-5.89; H_4, 5.69-5.73	3.82-3.87	3.36-3.50

to extend the scope of this reaction to substituted enol ethers and to other carbanions are in progress, including intramolecular examples. The extent of double-bond migration and the overall stereoselectivity will be determined.

The other method which was investigated was the Pd(0)-catalyzed alkylation of acetoxydihydropyrans. Dihydropyranyl acetates **15** and **16** were prepared by a modification of the method of Hurd and Edwards, using $Pb(OAc)_4$.[24] In a typical experiment **15** was treated with diethyl sodioformamidomalonate (**1**; 1 equiv) in the presence of $Pd(PPh_3)_4$ (0.1 equiv) and PPh_3 (1 equiv) in dry DMF under argon at 70 °C for 18 h to give 2-[formamidobis(ethoxycarbonyl)methyl]-5,6-dihydro-2*H*-pyran (**17**) in 83% yield after column chromatography.[25-27] Similarly, adducts **18–22** were prepared and the results are shown in Table II.[17] No products derived from carbanion attack at C-4 were observed. The stereoselectivity in the alkylation of *cis*-(methoxymethyl)dihydropyranyl acetate **16**[28] to give **20** occurred with net retention via the same double inversion observed by Trost and co-workers in both cyclic and acylic examples.[25,26] In contrast, the alkylation of **16** with phenylzinc chloride or vinylzinc chloride in the presence of 0.05 equiv of $Pd(PPh_3)_4$ in THF to give **21** or **22** occurred with inversion similar to that observed by Negishi and co-workers for cyclic allylic acetates.[29,30] The stereochemical assignments of products **20–22** were made on the basis of their ^{13}C and ^{1}H NMR spectra as shown in Tables III and IV. A very important criterion is the ^{13}C NMR γ effect rule which assigns the less shielded C-6 to the cis isomer.[7]

These initial palladium-assisted alkylations of dihydropyranylacetates are completely regioselective and highly stereoselective, and the stereoselectivity thus far observed is identical with that observed for alkylations of carbocyclic allylic acetates. Experiments to extend the scope of this reaction to other substituted acetoxydihydropyrans and to other carbanions are in progress, including applications to the synthesis of *C*-glycoside-containing natural products.

Acknowledgment. Support for this research from the National Cancer Institute (CA 21162) and from the American Cancer Society Institutional Research Grant IN-21-1 to the LAC–USC Comprehensive Cancer Center are gratefully acknowledged. A.J.S. is particularly thankful to Dr. William Croasmun for assistance at the Southern California Regional Nuclear Magnetic Resonance Spectrometer Facility located at the California Institute of Technology. Low-resolution mass spectra were obtained on an HP 5985 GC/MS funded by an instrumental grant from NSF. Some high-resolution mass spectra were obtained from the mass spectrometry laboratory, School of Chemical Sciences, University of Illinois, supported in part by a grant from NIH (GM 27029). The HREI assistance from Professor K. L. Rinehart, Jr., and J. Carter Cook, Jr., is gratefully acknowledged. Additional high-resolution mass spectra were obtained from the Midwest Center for Mass Spectrometry, Department of Chemistry, University of Nebraska, supported in part by the National Science Foundation. This assistance by Professor M. L. Gross and Dr. Ken Tomar is gratefully acknowledged. A generous loan of palladium chloride from Engelhard Industries is also very gratefully acknowledged.

Registry No. **1**, 59227-56-4; **2**, 30412-43-2; **3**, 72071-39-7; **4**, 18424-77-6; **5**, 81790-57-0; **6**, 996-82-7; **7**, 18424-76-5; **8**, 81790-58-1; **9**, 81790-59-2; **10**, 81790-60-5; **11**, 81790-61-6; **12**, 81790-62-7; **13**, 54362-89-9; **14**, 81790-63-8; **15**, 52416-79-2; **16**, 81790-64-9; **17**, 81802-28-0; **18**, 81790-65-0; **19**, 81790-66-1; **20**, 81790-67-2; **21**, 81790-68-3; **22**, 81790-69-4; **23**, 81790-70-7; $Pd(CH_3CN)_2Cl_2$, 14592-56-4; $Pd(PPh_3)_4$, 14221-01-3; C_6H_5ZnCl, 28557-00-8; CH_2=$CHZnCl$, 78389-90-9; dihydrofuran, 1191-99-7.

Lois V. Dunkerton,*[33] Anthony J. Serino[34]
Department of Chemistry
University of Southern California
University Park
Los Angeles, California 90089
Received May 27, 1981

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(27) Approximately 15% of 4-acetoxy-3,4-dihydro-2*H*-pyran formed in the allylic oxidation of dihydropyran could be conveniently removed by chromatography after the alkylation step. This suggests that allylic isomerization of **16** does not occur under the reaction conditions.
(28) Compound **16** was prepared as follows from 2-formyl-3,4-dihydro-2*H*-pyran:[31] (1) $NaBH_4$, CH_3CH_2OH, -5 °C[32]; (2) NaH, THF, CH_3I; (3) $Pb(OAc)_4$, PhH;[24] 40% overall yield. The $Pb(OAc)_4$ oxidation to give **16** was greater than 80% regioselective. In addition, this cis stereoselective allylic acetoxylation greatly enhanced the synthetic utility of this reaction. Additional examples which further define the stereoselectivity and mechanism of $Pb(OAc)_4$ oxidation of dihydropyrans will be the subject of a forthcoming paper (Dunkerton, L. V.; Serino, A. J., manuscript to be submitted for publication).
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(33) Address effective Aug 15, 1982: Department of Chemistry and Biochemistry, Southern Illinois University, Carbondale, IL 62901.
(34) Stauffer Fellow (1982).

Reduction of α,β-Acetylenic Ketones to (*S*)-Propargyl Alcohols of High Enantiomeric Purity

Summary: (*S*)-Propargyl alcohols may be obtained in 86–96% enantiomeric purity by asymmetric reduction of α,β-acetylenic ketones with the 9-borabicyclo[3.3.1]nonane (9-BBN) adduct of nopol benzyl ether.

Sir: Optically-active propargyl alcohols are very useful precursors and intermediates in synthetic organic chemistry. The acetylene unit provides a convenient handle which may be transformed into a variety of functionalities. Thus propargyl alcohols have been used successfully in the synthesis of alkaloids,[1] pheromones,[2] prostaglandins,[3]

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