still afford good yields. It should be noted that *cis*-1,3-pentadiene produces exclusively the trans product (entry 3), consistent with the intermediacy of a syn π-allylpalladium intermediate (see the mechanistic discussion to follow). As noted earlier in entry 8, an allylic alcohol moiety can be accommodated by the process, though a substantial decrease in yield and increase in reaction time was noted.

Mechanistically, heteroannulation no doubt proceeds via intermediate aryl- and π-allylpalladium intermediates as depicted in Scheme I (additional ligands on palladium have been omitted for clarity). While it is impossible with acyclic dienes to tell if intramolecular palladium displacement is proceeding through direct back-side displacement (path A) or via front-side halide displacement and subsequent reductive elimination (path B), it is clear from the 1,3-cyclohexadiene-derived products (entries 1, 6, and 13) that at least where five-membered rings are formed, the latter process predominates.

In conclusion, the palladium-catalyzed heteroannulation of 1,3-dienes is readily effected by a variety of oxygen- and nitrogen-containing aromatic halides. The overall process holds considerable promise for the synthesis of natural products ranging from dihydrobenzofurans to alkaloids.

Acknowledgment. We gratefully acknowledge the National Institutes of Health for their generous financial support and Johnson Matthey, Inc., and Kawaken Fine Chemicals Co., Ltd., for the palladium reagents.

Supplementary Material Available: Physical and spectral data for new compounds (10 pages). Ordering information is given on any current masthead page.

A Mild Method for the Synthesis of Furans. Application to 2,5-Bridged Furano Macrocyclic Compounds

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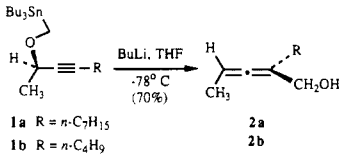
Summary: Upon treatment with $AgNO_3$ or $AgBF_4$ in acetonitrile, allenals **3a** and **3b** and allenones **6** and **8** afford furans **5**, **9**, **10**, and **11** in 72–99% yield. The cyclization is applicable to 2,5-bridged furanocembranoids as well.

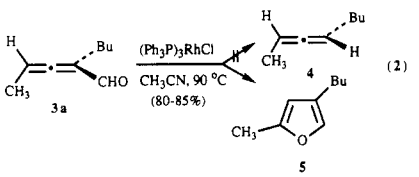
We recently described a stereospecific synthesis of optically active allenes through [2, 3]-Wittig rearrangement of nonracemic propargylic ethers (eq 1).[1] In our efforts



(1)

1a R = *n*-C_7H_{15}
1b R = *n*-C_4H_9 2a 2b

to ascertain the absolute stereochemistry of the allenic products **2** we prepared the formyl derivative **3a**, which we expected to decarbonylate under the influence of $(Ph_3P)_3RhCl$ to the disubstituted allene **4** of known configuration (eq 2).[2] Surprisingly, furan **5** was the sole

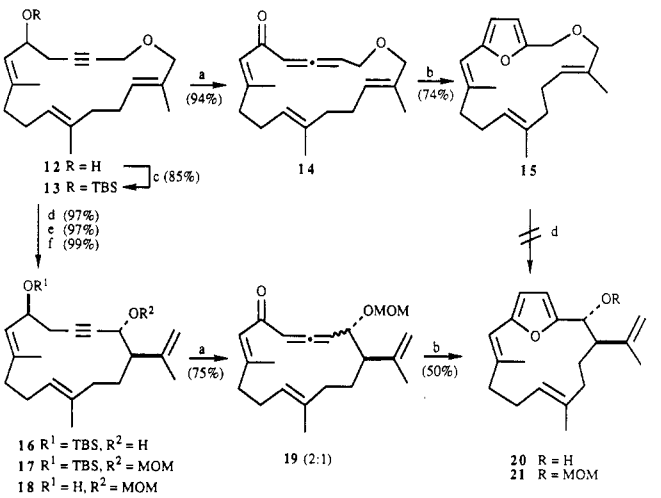


(2)

3a 4 5

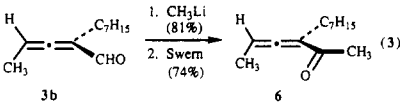
product isolated from the decarbonylation attempt. Furthermore, as little as 10 mol % of catalyst could be employed in this conversion. Assuming that Rh(I) was initiating the cyclization by coordination with the double bond, we briefly examined other π coordinating Lewis acids

Scheme I[a,b]



[a] (a) Dess–Martin periodinane reagent;[6] (b) $AgNO_3$, CH_3CN; (c) TBSCl, Et_3N, DMAP; (d) *n*-BuLi, THF–pentane; (e) MOMCl, CH_2Cl_2, *i*-Pr_2NEt; (f) TBAF, THF. [b] All compounds are racemic.

and found that $AgNO_3$ and $AgBF_4$ were also highly effective. Allenyl aldehyde **3b** and ketones **6** (eq 3) and **8**



(3)

3b 6

afforded furans **9**, **10** and **11** in high yield upon heating with these catalysts in acetonitrile (Table I).[3-5]

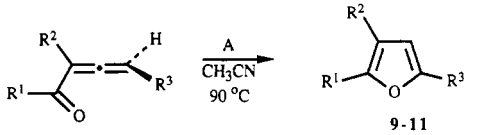
(1) Marshall, J. A.; Robinson, E. D.; Zapata, A. *J. Org. Chem.* **1989**, *54*, 5854.

(2) Cf.: Tsuji, J.; Okno, K. *Synthesis* **1969**, 157. Pirkle, W. H.; Boeder, C. W. *J. Org. Chem.* **1978**, *43*, 1950.

(3) A previous report describes the conversion of allenones to furans upon pyrolysis at 800 °C. Jullien, J.; Pechine, J. M.; Perey, F.; Piade, J. J. *Tetrahedron* **1982**, *38*, 1413. For leading references to furan synthesis and furanoid natural products, see: Danheiser, R. L.; Stoner, E. J.; Koyama, H.; Yamashita, D. S.; Klade, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 4407.

0022-3263/90/1955-3450$02.50/0

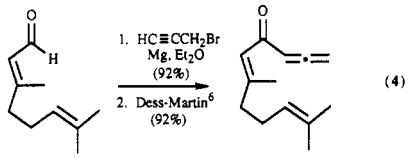
Table I. Cyclization of Allenyl Aldehydes and Ketones



9-11

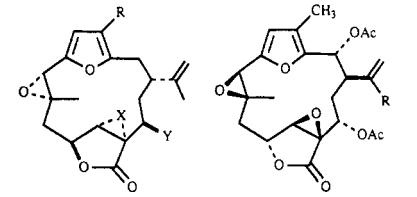
allene	R^1	R^2	R^3	A	furan	yield, %
3b	H	n-C_7H_{15}	CH_3	$(Ph_3P)_3RhCl$, 15 min	**9**	80
6	CH_3	n-C_7H_{15}	CH_3	$(Ph_3P)_3RhCl$, 30 min	**10**	85
3b	H	n-C_7H_{15}	CH_3	$AgBF_4$, 30 min	**9**	72
6	CH_3	n-C_7H_{15}	CH_3	$AgNO_3$, 30 min	**10**	74
6	CH_3	n-C_7H_{15}	CH_3	$AgBF_4$, 30 min	**10**	99
8	C_9H_{15}	H	H	$AgBF_4$, 1 h	**11**	90

Ketone **8** was conveniently prepared by addition of propargylmagnesium bromide to geranial (**7**) followed by Dess–Martin oxidation (eq 4).[6] None of the propargylic ketone isomer was isolated from this oxidation.[7]



7 8 (4)

The successful preparation of furan **11** suggested an application of this novel allenone cyclization to furan bridged cembranoids such as lophotoxin,[8] pukalide,[9] and their congeners.[10] As a model system we selected the



Lophotoxin X = O, R = CHO, Y = OAc
Pukalide X = double bond, R = CO_2Me, Y = H

Bipinnatin a, R = CO_2Me
Bipinnatin b, R = CHO

known macrocyclic ether **12**, readily prepared from farnesyl acetate.[11] Dess–Martin oxidation[6] afforded the allenone **14** in high yield.[7] Cyclization to furan **15** was readily effected upon treatment with $AgNO_3$ in acetonitrile (see Scheme I). However, attempted [2, 3]-Wittig ring contraction[12] of the furan gave none of the desired 14-membered product **20**. Only 16-membered [1, 2]-rearrangement products were produced. Accordingly, we carried out the [2, 3]-isomerization prior to furan ring closure. Thus, treatment of the TBS derivative **13** of racemic ether **12**, as previously described, with n-BuLi in THF–hexane followed by protection of the resulting alcohol and TBS cleavage yielded a mixture of diastereomeric 14-membered homopropargylic alcohols, principally **18** (~80%).[11] Oxidation of this mixture gave rise to a 15:85 mixture of propargylic ketone and diastereomeric allenones **19**. Treatment of the major allenone with $AgNO_3$ afforded only the bridged furan **21** in 50% isolated yield and recovered starting material (50%). The minor diastereomer was likewise converted to bridged furan **21** (50% yield) and a 1:1 mixture of recovered allenone and its diastereomer.

These preliminary results illustrate the potential applicability of this new furan synthesis to furanocembranes and related natural products.[13] Previous approaches to these compounds have suffered from complications in attempted ring closures owing to the chemical reactivity and stereochemical constraints engendered by a preformed furan moiety.[14] The present approach defers introduction of the furan until macrocyclization has been effected. The mild conditions of furan construction should be compatible with functionalized intermediates appropriate to the targets of interest.

Acknowledgment. This work was supported by a research grant from the National Institutes of Health, National Institute of General Medical Sciences (2GM29475), to whom we are grateful. The able assistance of Shiping Xie in the preparation of multigram quantities of macrocyclic ether **12** is warmly acknowledged.

Supplementary Material Available: ^1H NMR, IR, MS data and experimental procedures for compounds **8**, **11**, **14**, **15**, **17–19**, and **21** and ^1H NMR spectra for compounds **8–11**, **17–19**, and **21** (16 pages). Ordering information is given on any current masthead page.

(4) Typical procedure for **2-[(1E)-2,6-Dimethyl-1,5-heptadienyl]-furan (11).** To a solution of 310 mg (1.63 mmol) of the allenic ketone **8** in 3 mL of CH_3CN was added 63 mg (0.33 mmol) of $AgBF_4$. The mixture was stirred at 100 °C for 1 h, cooled to room temperature, and filtered through silica gel. The eluant was concentrated, and the residue was purified by column chromatography on silica gel to afford 278 mg (90%) of the furan **11**: ^1H NMR ($CDCl_3$) 7.32 (d, 1 H, J = 1.8 Hz, furan H), 6.36 (dd, 1 H, J = 1.8, 3.3 Hz, furan H), 6.16 (d, 1 H, J = 3.3 Hz, furan H), 6.07 (s, 1 H, vinyl H), 5.11 (t, 1 H, J = 1.4 Hz, vinyl H), 2.15 (m, 4 H, CH_2's), 1.95 (s, 3 H, vinyl CH_3), 1.67 (s, 3 H, vinyl CH_3), 1.54 ppm (s, 3 H, vinyl CH_3); IR ν 3020–2870, 1660, 1500, 1460, 1390, 1270, 1170, 1120, 1030 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.08; H, 9.54. MS $C_{13}H_{18}O$: 190 (M), 121 (M – C_4H_5O).

(5) All new compounds have been satisfactorily characterized by their ^1H NMR and IR spectra and by C/H and/or MS analysis.

(6) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156.

(7) We have found that oxidations of homopropargylic alcohols by a wide variety of oxidizing agents leads to allenones as the major products.

(8) Fenical, W.; Okuda, R. K.; Bandurraga, M. M.; Culver, P.; Jacobs, R. S. *Science* **1981**, *212*, 1512.

(9) Missakian, M. G.; Burreson, B. J.; Scheuer, P. J. *Tetrahedron* **1975**, *31*, 2513.

(10) Cf.: Wright, A. E.; Burres, N. S.; Schulte, G. K. *Tetrahedron Lett.* **1989**, *30*, 3491.

(11) Marshall, J. A.; Robinson, E. D.; Lebreton, J. *J. Org. Chem.* **1990**, *55*, 227.

(12) Marshall, J. A.; Jenson, T. M.; DeHoff, B. S. *J. Org. Chem.* **1987**, *52*, 3860.

(13) Cf.: Bandurraga, M. M.; Fenical, W.; Donovan, S. F.; Clardy, J. *J. Am. Chem. Soc.* **1982**, *104*, 6463.

(14) Cf.: Marshall, J. A.; Nelson, D. J. *Tetrahedron Lett.* **1988**, *29*, 741.