Tetrahedron Letters No. 21, pp 1821 - 1824, 1976. Pergamon Press. Printed in Great Britain.

PALLADIUM(II)-CATALYZED CYCLIZATION OF γ,δ-UNSATURATED ALCOHOLS
SYNTHESIS OF 2-VINYLTETRAHYDROFURANS

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(Received in Japan 24 March 1976; received in UK for publication 12 April 1976)

Palladium(II)-catalyzed cyclization of 2-allylphenols is an effective method for the synthesis of 2-substituted benzofurans; in particular, 2-vinyl-2,3-dihydrobenzofuran is readily prepared from 2-(2'-butenyl)phenol.$^{1)}$ As a useful extention of this reaction, we wish here to report a novel palladium(II)-catalyzed synthesis of 2-vinyltetrahydrofurans from γ,δ-unsaturated alcohols.

The reaction of γ,δ-unsaturated alcohols 1a-e with a catalytic amount of $Pd(OAc)_2$ in the presence of $Cu(OAc)_2$-O_2 in MeOH-H_2O proceeded smoothly to give 2-vinyltetrahydrofurans 2a-e in moderate yields as summarized in Table I (see next page).$^{2)}$ The obtained tetrahydrofurans consisted of two diastereoisomers; however, 1a gave a single stereoisomer, *i.e.*, *trans*-2-vinyl-5-phenyltetrahydrofuran (2a).

Table I. Synthesis of 2-vinyltetrahydrofurans 2 from γ,δ-unsaturated alcohols 1.a)

1	R_1	R_2	Yield of 2 b) (%)	Ratio of isomer c) A : B	B.p. (°C)
a	Ph	H	40 d)	100 : 0	70-74 (2 mmHg)
b	Ph	Me	52	41 : 59	106-107 (7 〃)
c	Ph	Et	36	41 : 59	115-117 (5 〃)
d	Ph	Ph	15 e)	——	137-140 (1 〃)
e	Me	H	23	75 : 25	93-94

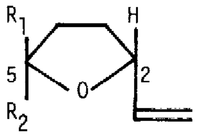
a) A mixture of 1 (5 mmol), $Pd(OAc)_2$ (0.5 mmol), and $Cu(OAc)_2 \cdot H_2O$ (5 mmol) in MeOH (25 ml)-H_2O (2 ml) was reacted at room temperature for 24 hr (1a-d) or 3 hr (1e) under a slow stream of oxygen.

b) Yields are based on charged 1. No attempt was made to optimize the yields.

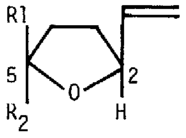
c) A and B refer to the diastereoisomers as shown below. Ratios of the isomers were determined by nmr analysis.

d) 2-Ethyl-5-phenylfuran (10%) was also obtained.

e) Another product was 1,1-diphenyl-1,4-heptadiene (22%).

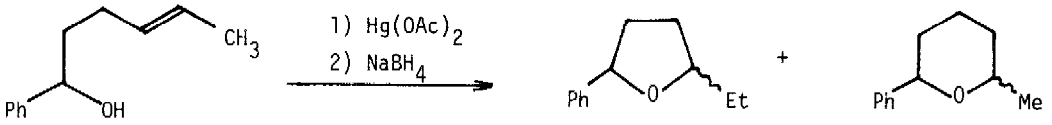


A



B

The stereochemistry of 2a was determined by the comparison of the nmr spectra between the hydrogenated product of 2a and a mixture of cis- and trans-2-ethyl-5-phenyltetrahydrofuran (3) independently synthesized by oxymercuration of 1a with $Hg(OAc)_2$ followed by $NaBH_4$ reduction. The reaction gave a 29 % of 3 (cis : trans = 53 : 47) along with 2-methyl-6-phenyltetrahydropyran (4, 33 %). The nmr spectrum of 3 as a mixture of diastereoisomers shows the resonances



(i)

1a 3 4

of the methyl groups of the C-2 substituent at δ 0.98 and 0.95 ppm. Since the lower field absorption would be due to van der Waals interaction between the ethyl and the phenyl group in one of the contributing conformers of tetrahydrofuran ring,[3) the former absorption is assigned to be due to the *cis*-isomer.

In 2,5-substituted tetrahydrofurans, the absorptions of the C-2 substituents, such as Me and *t*-Bu, being in configurationally different positions are magnetically affected by the C-5 substituents (*vice versa*) and the signals of *cis*-isomer appear at lower fields.4) Therefore, the configurations (A and B) of 2b, 2c, and 2e can be assigned, analogously, by the chemical shift difference of the methyl groups on the C-5 position as summarized in Table II.

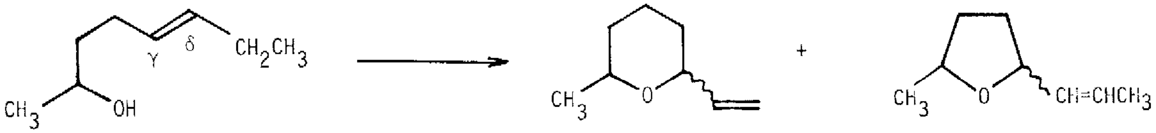
Table II. The methyl signals (δ) of the C-5 substituents.
(Relative configuration to the C-2 vinyl group)

	A	B
2b	1.48 (cis)	1.44 (trans)
2c	0.77 (cis)	0.73 (trans)
2e	1.18 (trans)	1.21 (cis)

The oxidative cyclization can be referred as to a diastereo-selective reaction5) and the selectivity is dependent on the varieties of the substituents on the C-1 position of 1 (Table I). Significantly, the high selectivity is derived from 1a, in contrast to the oxymercuration (reaction i), which would enhance the synthetic utility of this reaction.

Finally, it should be noted that when another methyl group was introduced into the δ-position of 1a, the cyclization also occurred; however, the product was 2,2-dimethyl-6-phenyl-5,6-dihydropyran (45 %).6) Furthermore, when the δ-substituent of 1e was replaced by ethyl

group, 2-vinyl-6-methyltetrahydropyran (10 %) and 2-(1'-propenyl)-5-methyltetrahydrofuran (10 %) were produced.[7] Thus, the substituent on the δ-position of γ,δ-unsaturated alcohols markedly affects the product composition.



Acknowledgement: We wish to acknowledge the support by the Matsunaga Research Grant from Matsunaga Science Foundation.

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2) In the crude reaction mixtures were detected some unidentified products which may be formed by methoxylation of 1a-e with methanol solvent. But, these products decomposed during distillation process. Unreacted starting materials were recovered by distillation.
3) H. Booth in "Progress in Nuclear Magnetic Resonance Spectroscopy", Vol. 5, ed., J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon Press, New York, pp 217-220 (1969).
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6) In addition, a trace amount of 2-isopropenyl-5-phenyltetrahydrofuran was obtained.
7) These products also consist of a mixture of diastereomers; however , the configurations are not yet elucidated.