Tetrahedron Letters Vol. 21, pp 129 - 132
0040-4039/80/0108-0129$02.00/0

THE SYNTHESIS OF 2,5-DIHYDROFURANS FROM α-ALLENIC ALCOHOLS

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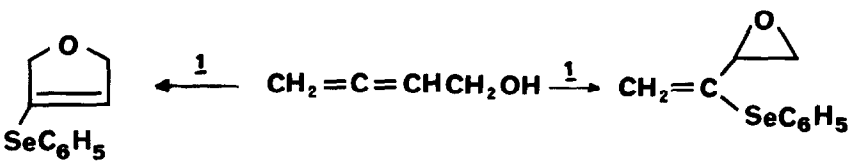
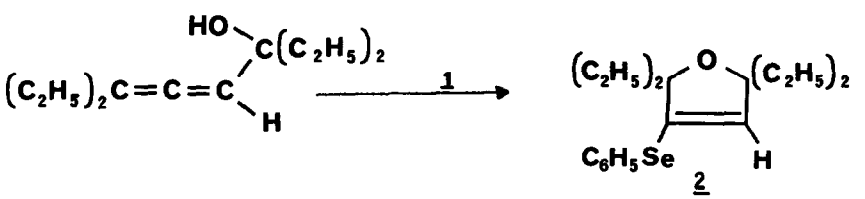
ABSTRACT: α-Allenic alcohols react rapidly with PhSeCl to produce derivatives of 3-phenylseleno-2,5-dihydrofuran in high yields.

The synthesis of heterocycles via the electrophilically-induced cyclization of unsaturated acids,[1] alcohols,[2] and phenols with areneselenenyl halides or derivatives thereof[4] has recently received a great deal of attention by the groups of Clive and Nicolaou. In particular, Clive and coworkers have demonstrated the utility of the reaction of γ,δ unsaturated alcohols with benzeneselenenyl chloride, 1, to produce ring-fused tetrahydrofurans[2a]. While electrophilically-induced ring closures of this type have been known for many years[5], the advantage of such a closure under these conditions arises from the facile nature of the process and the existence of the phenylseleno moiety as a potential synthon for further synthetic transformations[6,7].

The availability of diastereoisomeric α-allenic alcohols[8], plus the known propensity for selenenyl halides to react with carbon-carbon double bonds in an anti stereospecific manner[9], suggested to us the possibility of a facile synthetic route to configurationally well-defined 2,5-dihydrofurans. It must be noted, however, that conceptually there exist two distinct modes of cyclization if the phenylseleno moiety forms a new bond with the central carbon of the allenic system (equation [1]), which seems likely[10].

[1] 

In order to establish the preferred pathway, we treated 3,6-diethyl-4,5-octadien-3-ol with 1 equiv. of 1 in methylene chloride at room temperature and found that it is rapidly transformed into 2,2,5,5-tetraethyl-3-phenylseleno-2,5-dihydrofuran, 2, which was isolable in essentially quantitative yield. The ^{1}H NMR and ^{13}C NMR spectra define the structure of 2, and, as expected,

[2] 

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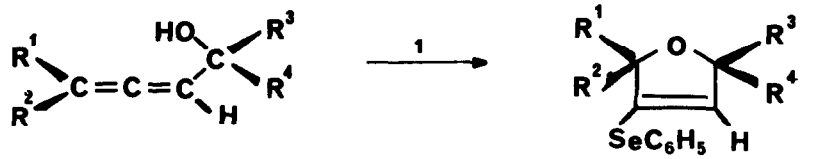
mass spectral analysis shows the production of fragments corresponding to $(M)^{+\cdot}$, $(M-C_2H_5)^{+\cdot}$, $(M-C_2H_5-C_6H_5Se)^{+\cdot}$, and $(C_6H_5Se)^{+\cdot}$ [11].

The generality of the ring closure is demonstrated by the following reactions:

[3] 

	R^1	R^2	R^3	R^4	% Yield
a	CH_3	CH_3	CH_3	C_2H_5	90
b	CH_3	CH_3	CH_3	iC_3H_7	98+
c	CH_3	CH_3	CH_3	tC_4H_9	92
d	CH_3	CH_3	iC_3H_7	iC_3H_7	97
e	CH_3	iC_3H_7	CH_3	iC_3H_7	85
f	CH_3	iC_3H_7	iC_3H_7	CH_3	88
g	H	iC_3H_7	H	iC_3H_7	89
h	H	iC_3H_7	iC_3H_7	H	93
i	CH_3	C_2H_5	H	iC_3H_7	79
j	CH_3	C_2H_5	iC_3H_7	H	86
k	CH_3	iC_3H_7	H	iC_3H_7	90
l	CH_3	iC_3H_7	iC_3H_7	H	91
m	H	H	C_2H_5	C_2H_5	83
n	H	H	iC_3H_7	iC_3H_7	70
o	H	H	CH_3	tC_4H_9	98+
p	H	iC_3H_7	C_2H_5	C_2H_5	95
q	H	iC_3H_7	iC_3H_7	iC_3H_7	98+

Isolated yields are normally > 85%. The reactions involving terminal allenes [3m,n,o], are somewhat sluggish. They proceed faster and in better yields when 1 equiv. of triethylamine is added to react with the HCl which is given off.

The stereochemistry of the ring closure is readily demonstrated by the reaction of 1 with diastereoisomeric α-allenic alcohols. For example, the reaction of 1 with (3-RS, 5-RS)-2,6,7-trimethyl-4,5-octadien-3-ol yields Z-2,5-diisopropyl-2-methyl-3-phenylseleno-2,5-dihydrofuran, 3, stereospecifically, whereas the corresponding (3-RS, 5-SR) allenic alcohol gives the analogous E-2,5-dihydrofuran (equations [4] and [5]).

[4] 

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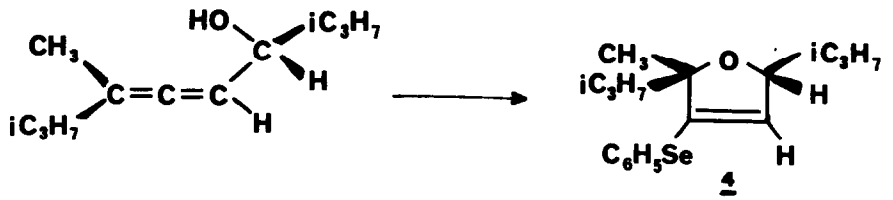
[5] 

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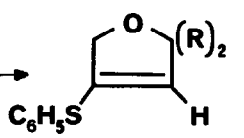
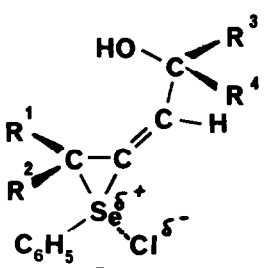
Assignment of 3 and 4 as the Z and E isomers respectively follows directly from their respective ^{1}H NMR spectra. Thus considering only the ring protons of the furan system, we observe for compound 3 a doublet at δ 5.34 1H $^3J_{4,5}$ = 1.50 Hz and a doublet of doublets at δ 4.26 1H $^3J_{4,5}$ = 1.50, $^3J_{5,6}$ = 7.50 Hz, whereas for compound 4 we observe a doublet at δ 5.39 1H $^3J_{4,5}$ = 1.25 Hz and a doublet of doublets at δ 4.26 1H $^3J_{4,5}$ = 1.25, $^3J_{5,6}$ = 4.75 Hz. The significant observation is the magnitude of the coupling constant $^3J_{5,6}$, where H_6 is the methine proton of the isopropyl group directly bonded to C_5. An examination of molecular models reveals a pronounced steric interaction between the two isopropyl groups in compound 3 which gives rise to a conformer distribution favouring the anti conformer with respect to protons H_5 and H_6. As this conformer is expected to be favoured more in compound 3 than in the case of 4 one will observe a larger value of $^3J_{5,6}$ for 3, as assigned. Similar results were observed for the other series of diastereoisomeric allenes studied.

These results have an analog in the reaction of 2,4-dinitrobenzenesulphenyl chloride with a partially resolved β-allenic alcohol[12] to give an optically active 3,4-dihydro-2H-pyran. In this respect we note our analogous results involving the reaction of benzenesulphenyl chloride with α-allenic alcohols to give 3-phenylthio-2,5-dihydrofurans in excellent yield.

[6] $C_6H_5SCl + CH_2=C=CHC(R)_2OH \longrightarrow$ 

In addition to the above, we observe second order kinetics, first-order in electrophile (C_6H_5SeCl or C_6H_5SCl) and first-order in α-allenic alcohol, which establishes the composition of the rate determining transition state as containing one equivalent of each reactant. These data are indicative of a reaction hypersurface containing cyclic intermediate, 5, or a non-resonance stabilized carbonium ion, 6, which collapses to product before bond rotation to the resonance stabilized form 7 can occur.



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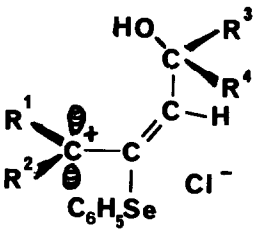

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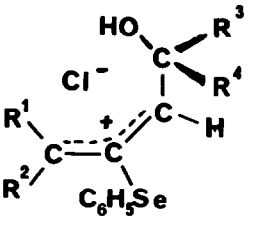

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A continuation of these studies towards the synthesis of 2,5-dihydrothiophenes and 2,5-dihydropyrroles is currently in progress.

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11. Compound 2: ^{1}H NMR (δ, $CDCl_3$) 5.44 s (1H), 1.62 q (4H), 1.57 q (4H), 0.91 t (6H), 0.82 t (6H), 7.3 m (3H), 7.6 m (2H); ^{13}C NMR (δ, $CDCl_3$) 94.0 s, 91.6 s, 31.6 t, 31.0 t, 8.7 q, 8.6 q, 128.1 d, 129.3 d, 134.7 d, 132.7 d, 131.6 s; colorless to pale yellow oil.
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ACKNOWLEDGEMENTS

Continued financial support from the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged, as is a Province of Ontario Scholarship to P.L.B. (1978-1980)

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(Received in USA 24 August 1979)