

STEREOSELECTIVE SYNTHESIS AND THERMAL BEHAVIOR OF (Z)-EPOXYHEXENYNES:
A SIMPLE AND GENERAL ROUTE TO 2-VINYLFURANS

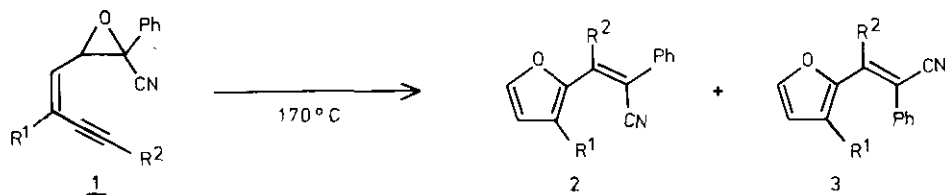
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Abstract - An efficient approach for the synthesis of 2,3-disubstituted furans (2a-j/3a-j) is described by using the thermally induced rearrangement of epoxyhexenyne (1a-j) which are prepared by stereoselective synthesis of the (Z)-pentenynals 10 and subsequent Darzens reaction.

Recently we communicated first results on the unexpected formation of 2-vinylfurans by short-time thermolysis of three 1-phenylepoxyhex-(3Z)-ene-5-ynes 1a. This observation prompted us to further investigations in order to gain more insight into the mechanism of the unprecedented rearrangement and to elaborate the preparative aspects of the reaction as a possible alternative to specifically substituted furans ².

In this contribution we report on the straightforward synthesis of several derivatives of furan bearing bulky substituents not only at the vinyl group but also in 3-position (see structures 2 and 3).



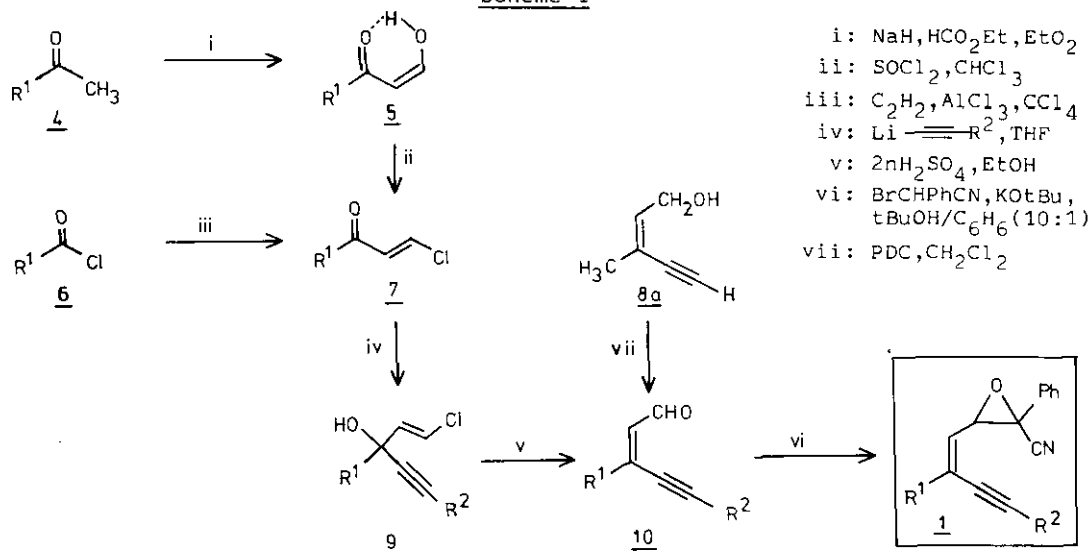
	<u>a</u>	<u>b</u>	<u>c</u>	<u>d</u>	<u>e</u>	<u>f</u>	<u>g</u>	<u>h</u>	<u>i</u>	<u>j</u>
R ¹	CH ₃	iC ₃ H ₇	tC ₄ H ₉	tC ₄ H ₉	tC ₄ H ₉	tC ₄ H ₉	Ph	Ph	Ph	Ph
R ²	H	H	H	Ph	nC ₄ H ₉	tC ₄ H ₉	H	Ph	nC ₄ H ₉	tC ₄ H ₉

The epoxyhexenyne 1a-j, comprising the essential (Z)-geometry of the central double bond, have been selected as appropriate starting materials. In addition to preparative reasons, the substituents R¹/R² were introduced to disclose steric

and/or electronic effects on the course of the rearrangement and (at least in the case of CH_3 , iC_3H_7 , nC_4H_9) for enabling intra- (or inter-³) molecular H-shifts in the potential cycloallene derivatives which have been proposed as high energy intermediates¹ (see below). Furthermore, with the cyano group at the oxirane ring a significant decrease of the reaction temperature is expected providing more suitable conditions for the experimental work.

The synthesis of 1a-j was accomplished as outlined in Scheme 1, using the pentenynals 10 as direct precursors. While 10a was readily prepared by PDC-oxidation of commercially available 'cis-1-pentol' (8a), the other aldehydes were synthesized by sulfuric acid promoted transformation of the vinyl ethynyl carbinols 9, the alkynylation products of the vinyl ketones 7 which themselves are accessible from 4 and 6, respectively. Due to the directing effect of the substituents R^1 the conversion of 9 to 10 took place with remarkably high stereoselectivity leading almost exclusively (> 95%) to the desired (Z)-isomers. The concluding Darzens reaction to 1 resulted in the formation of the oxirane derivatives (ca. 60% yield) with the expected trans-configuration⁴ of the bulky phenyl- and enyne-groups. The overall-yields of 1a-j are between 20 and 53% (starting with 4c, g, 6b and 8a, respectively)⁵.

Scheme 1



Compared to the previously studied 1-phenylepoxyhexenyne 1a the thermal reactivity of the doubly activated derivatives 1a-j is indeed much higher: thermolysis experiments, carried out in isooctane and followed by tlc, revealed a slow decrease of the educts already at 160°C ; after heating up to 190°C quantitative

conversion is reached within 5 - 10 min.

For preparative purposes a temperature of 170 °C is specially convenient resulting in reaction periods of 40 to 150 min. Only two products were formed in each case (73 - 92% according to $^1\text{H-NMR}$ analysis) which have been identified as 2-vinylfurans (2/3)⁵. After work up by preparative tlc pure mixtures of the diastereomers were obtained (see Table 1) which could be separated in most cases either by repeated chromatography or by crystallization⁵ (for some $^1\text{H-NMR}$ -data see Table 2).

Table 1. Thermolysis of the Epoxyhexenyne 1a-j^{a)}

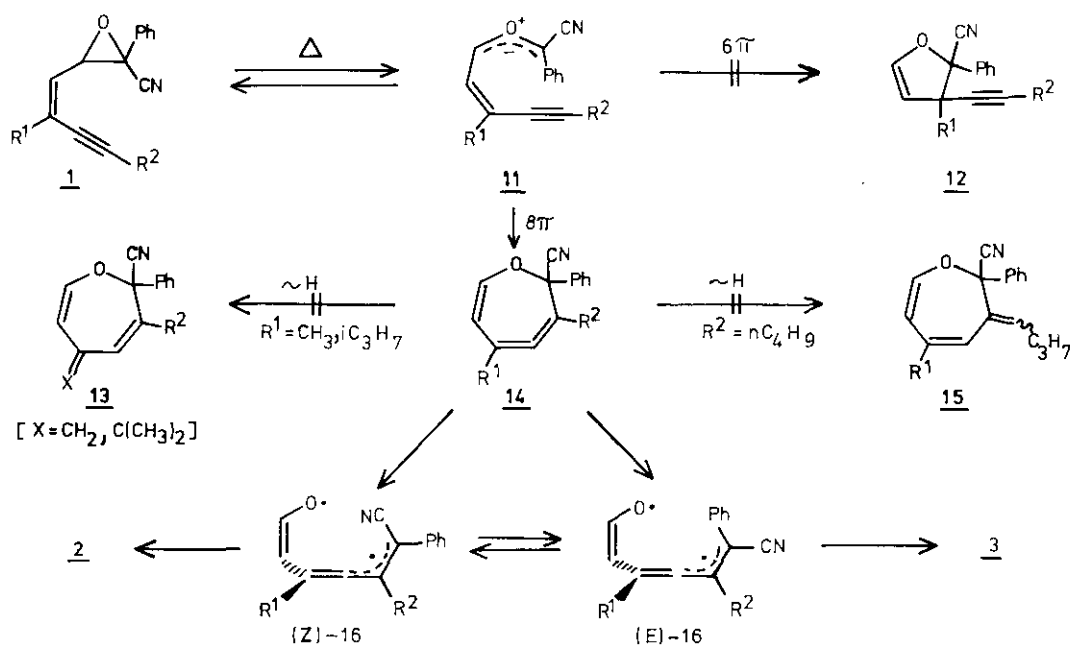
	<u>1a</u>	<u>1b</u>	<u>1c</u>	<u>1d</u>	<u>1e</u>	<u>1f</u>	<u>1g</u>	<u>1h</u>	<u>1i</u>	<u>1j</u>
t [min] ^{b)}	40	50	60	60	80	150	60	60	90	90
(<u>2+3</u>) [%] ^{c)}	88	73	75	87	83	85	91	92	73	78
^{d)}	77	63	61	68	75	72	79	89	68	77
ratio <u>2</u> : <u>3</u>	90/10	89/11	92/8	56/44	38/62	6/94	89/11	53/47	44/56	7/93

a) $2 \cdot 10^{-2}\text{M}$ in isooctane, 170 °C. b) Time for complete conversion. c) Crude products ($^1\text{H-NMR}$). d) After tlc.

Whereas the reaction rate of the transformations varies only slightly in this series, there is a significant influence of the substituents on the stereochemical outcome (Table 1). Especially R^2 exerts a marked effect on the ratio of the isomers 2/3: with $\text{R}^2 = \text{H}$ (a, b, c, g) formation of the vinylfurans 2 predominates by a factor of about 9, with $\text{R}^2 = \text{Ph}$ (d, h) or nC_4H_9 (e, i) the yields of both isomers are nearly the same, and with $\text{R}^2 = \text{tC}_4\text{H}_9$ (f, j) the furans 3 are by far the major products (ca. 14 : 1).

This observation is in agreement with a reaction mechanism involving heterocycloallenes (14) as central intermediates¹ (see Scheme 2). One possible route to 2/3 implies the formation of the diradicals 16 which could proceed to either diastereomer, depending on the geometry of the allylic unit. It is reasonable to assume that with increasing size of the substituents R^2 the geometry of (E)-16 is favored over (Z)-16; consequently, the activation energy for the recyclisation affording isomer 3 should be lowered. Although this explanation is supported by a fairly good correlation between the ratio of 2/3 and the space-filling parameters for R^2 ⁶ the cyclopropene-carbene pathway¹ cannot be unambiguously excluded as a mechanistic alternative.

Scheme 2



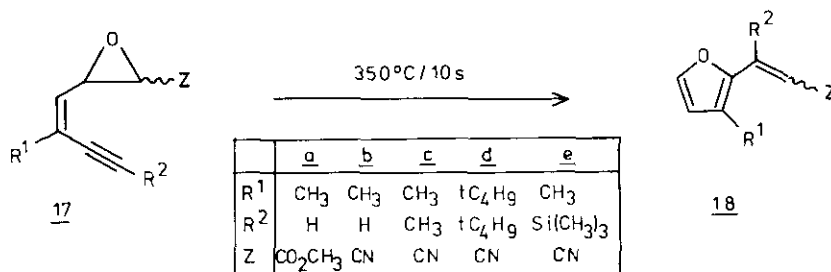
Two comments have to be made concerning the formation and the reactivity of the cycloallenes **14**: (1) The electrocyclicalisation of the conjugated dipoles proceeds with complete periselectivity (8π -reaction); there is no indication for the 6π -process leading to 2,3-dihydrofurans **12** ^{7,8}. (2) The possible H-shifts in **14a**, **b**, **e**, **i** producing the more stable seven-membered derivatives **13**/**15** do not compete with the "normal" reaction sequence (to **2** and **3**, see Scheme 2) ⁹.

Table 2. Selected ¹H-NMR-Data of **2a-j** and **3a-j** ^{a)}

	2a	2b	2c	2d	2e	2f	2g	2h	2i	2j
	3a	3b	3c	3d	3e	3f	3g	3h	3i	3j
δ_{4-H}	6.36 6.28	6.46 6.37	6.47 6.37	6.47 6.31	6.42 6.25	6.39 6.15	6.67 6.59	6.69 6.49	6.65 6.40	6.66 6.31
δ_{5-H}	7.52 7.17	7.53 7.17	7.51 7.10	7.43 7.29	b) 7.40	b) 7.39	7.65 7.27	7.61 7.44	7.59 7.43	7.46 7.43
$\delta_{H(R^1)}$	2.18 2.13	c) d)	1.39 1.36	1.23 0.91	1.35 0.84	1.01 0.75	d) d)	d) d)	d) d)	d) d)
$\delta_{H(R^2)}$	7.19 6.97	7.26 7.03	7.53 7.30	d) d)	f) g)	1.40 1.43	7.31 7.08	d) d)	f) g)	0.98 1.50

^{a)} 250 MHz, CDCl₃. ^{b)} Signals covered. ^{c)} 3.04(1H), 1.22(6H). ^{d)} Arom.H. ^{e)} 2.98(1H), 1.20(6H). ^{f)} 0.8(3H), 1.14-1.45(4H), 2.50(2H). ^{g)} 0.96(3H), 1.36-1.64(4H), 2.86(2H).

With regard to the preparative scope of the described reaction it is important to note that, according to recent results, this method proved also practicable for the synthesis of non-phenylated 2-vinylfurans ¹⁰. For instance, the main products after short-time thermolysis of the epoxyhexenynes 17a-e are the vinylfurans 18a-e ¹⁰.



In summary, the thermal transformation of epoxyhexenynes (type 1 or 17) offers a new and simple approach to 2,3-disubstituted furans ¹¹ which compares favorably with existing methods ².

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9. Meanwhile we obtained further evidence for intermediates like 14 by using systems designed for [1,5]- (instead of [1,3]-) H-shifts.
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11. Results on the synthesis of higher substituted furans, including 3,4-annelated derivatives, will be published elsewhere.

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