HETEROCYCLES, Vol. 23, No. 11, 1985

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

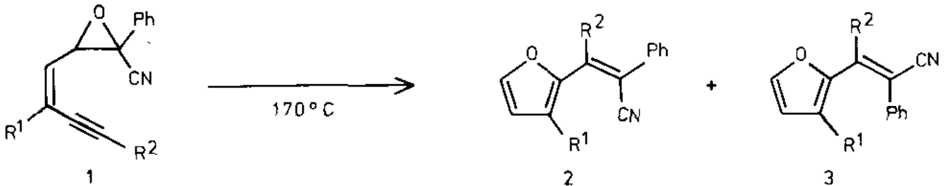
Wolfgang Eberbach* and Joachim Roser

Institut für Organische Chemie und Biochemie der Universität
Albertstrasse 21, D-7800 Freiburg, West Germany

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 epoxyhexenynes (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).



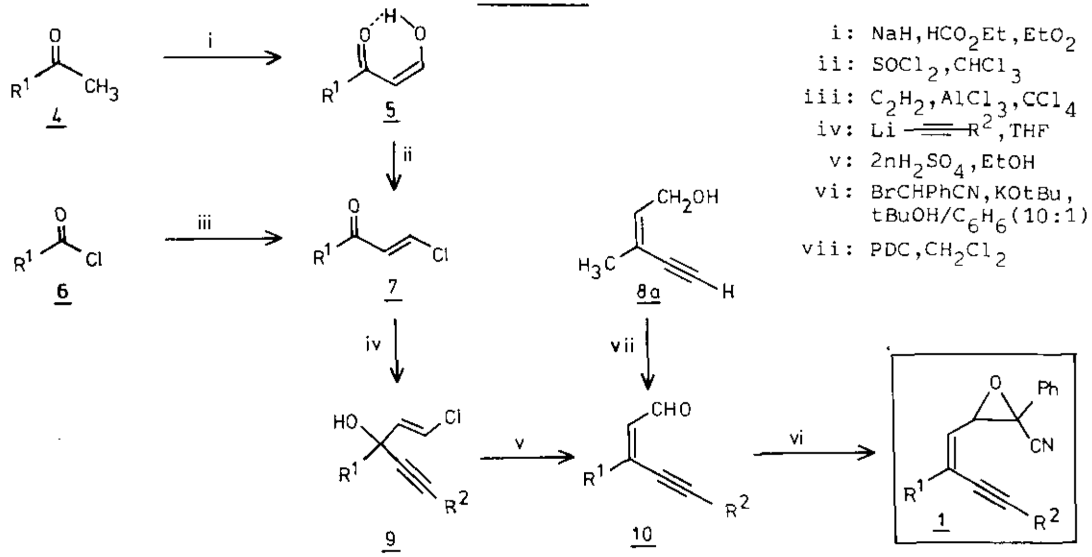
1 2 3

	a	b	c	d	e	f	g	h	i	j
R^1	CH_3	iC_3H_7	tC_4H_9	tC_4H_9	tC_4H_9	tC_4H_9	Ph	Ph	Ph	Ph
R^2	H	H	H	Ph	nC_4H_9	tC_4H_9	H	Ph	nC_4H_9	tC_4H_9

The epoxyhexenynes 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 R^1/R^2 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 intermediates [1] (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-configuration [4] 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



i: NaH, HCO_2Et, EtO_2
ii: $SOCl_2$, $CHCl_3$
iii: C_2H_2, $AlCl_3$, CCl_4
iv: $Li-\!\!\equiv\!\!-R^2$, THF
v: $2nH_2SO_4$, EtOH
vi: BrCHPhCN, KOtBu, $tBuOH/C_6H_6$ (10:1)
vii: PDC, CH_2Cl_2

Compared to the previously studied 1-phenylepoxyhexenynes [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}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 crystallization [5] (for some ^{1}H-NMR-data see Table 2).

Table 1. Thermolysis of the Epoxyhexenynes 1a - j [a)]

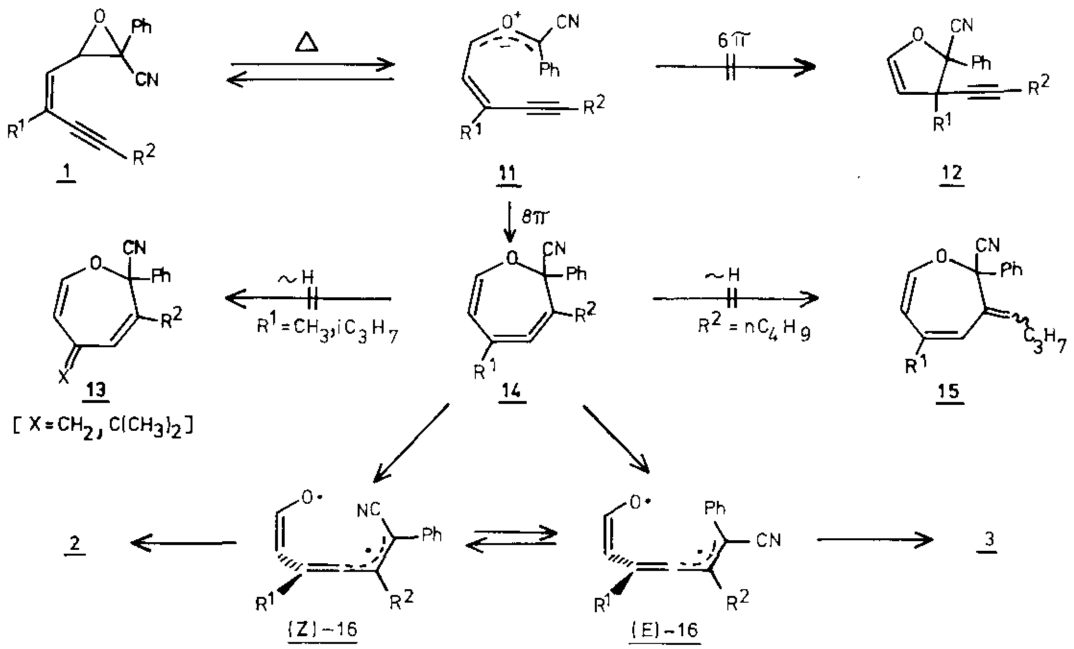
		1a	1b	1c	1d	1e	1f	1g	1h	1i	1j
t [min] [b)]		40	50	60	60	80	150	60	60	90	90
(2 + 3) [%]	c)	88	73	75	87	83	85	91	92	73	78
	d)	77	63	61	68	75	72	79	89	68	77
ratio 2 : 3		90/10	89/11	92/8	56/44	38/62	6/94	89/11	53/47	44/56	7/93

[a)] $2 \cdot 10^{-2}$m in isooctane, 170 °C. [b)] Time for complete conversion. [c)] Crude products (^{1}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 R^2 = H (a, b, c, g) formation of the vinylfurans 2 predominates by a factor of about 9, with R^2 = Ph (d, h) or nC_4H_9 (e, i) the yields of both isomers are nearly the same, and with R^2 = tC_4H_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 intermediates [1] (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 pathway [1] cannot be unambigously excluded as a mechanistic alternative.

Scheme 2



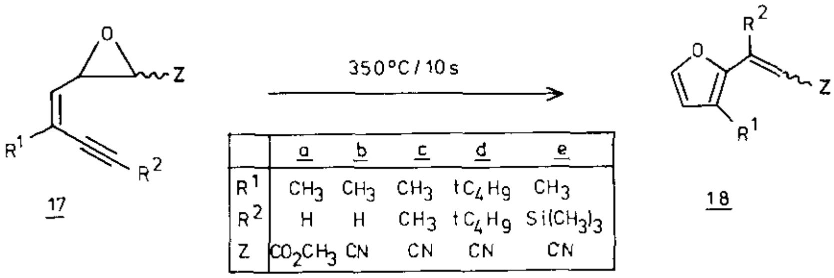
Two comments have to be made concerning the formation and the reactivity of the cycloallenes 14: (1) The electrocyclisation of the conjugated dipoles proceeds with complete periselectivity (8π-reaction); there is no indication for the 6π-process leading to 2,3-dihydrofurans 12 [7,8]. (2) The possible 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 ^{1}H-NMR-Data of 2a - j and 3a - j [a]

	2a 3a	2b 3b	2c 3c	2d 3d	2e 3e	2f 3f	2g 3g	2h 3h	2i 3i	2j 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, CDCl$_3$. [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].



	a	b	c	d	e
R^1	CH_3	CH_3	CH_3	tC_4H_9	CH_3
R^2	H	H	CH_3	tC_4H_9	$Si(CH_3)_3$
Z	CO_2CH_3	CN	CN	CN	CN

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].

ACKNOWLEGDEMENTS

Financial support of this work by the DEUTSCHE FORSCHUNGSGEMEINSCHFT and the FONDS DER CHEMISCHEN INDUSTRIE is gratefully acknowledged.

REFERENCES

1. (a) J.Roser and W.Eberbach, Tetrahedron Lett. 1984, 2455. (b) J.Roser and W. Eberbach, 5th International Conference On Organic Synthesis, Freiburg, August 27 - 30, 1984, Poster M 20.
2. For extensive review articles on furans, see: Comprehensive Heterocyclic Chemistry, Vol. 4, p. 89, 531, 599, 657, Pergamon Press, 1984.
3. F.Bourelle-Wargnier, M.Vincent and J.Chuche, Tetrahedron Lett. 1978, 283.
4. G.Kryriakakou and J.Seyden-Penne, Tetrahedron Lett. 1974, 1737; J.Brokatzky-Geiger and W.Eberbach, Chem.Ber. 117, 2157 (1984).
5. The experimental details of the syntheses and the spectral data of 1a - j as well as the full characterization of the 2-vinylfurans 2a - j/3a - j will be given in our forthcoming full paper.
6. M.Charton, J.Am.Chem.Soc. 97, 1552 (1975).

7. W.Eberbach and B.Burchardt, *Chem.Ber.* **111**, 3665 (1978); W.Eberbach, W.Seiler and H.Fritz, *Chem.Ber.* **113**, 875 (1980).

8. For other examples on the preference of 8π- over 6π-cyclisation reactions, see: W.Eberbach and U.Trostmann, *Chem.Ber.* **114**, 2979 (1981); *Chem.Ber.* in press; D.P.Munroe and J.T.Sharp, *J.Chem.Soc., Perkin* I 1984, 849; I.R.Robertson and J.T.Sharp, *J.Chem.Soc.,Chem.Commun.* **1983**, 1003; see also ref. [1].

9. Meanwhile we obtained further evidence for intermediates like *14* by using systems designed for [1,5]- (instead of [1,3]-) H-shifts.

10. W.Eberbach and J.Roser, in preparation.

11. Results on the synthesis of higher substituted furans, including 3,4-annelated derivatives,will be published elsewhere.

Received, 8th August, 1985