

SHORT COMMUNICATION

AN $E \rightleftharpoons Z$ ISOMERIZATION OF AN ELECTROPHILIC VINYL AZIDE BY $^{15}\text{N}_3^-$. A PROBE FOR INTERNAL ROTATION PROCESSES IN THE CARBANIONIC INTERMEDIATE OF NUCLEOPHILIC VINYLIC SUBSTITUTION

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The label incorporation and $Z \rightarrow E$ isomerization in the reaction of 3-azidomethylenedihydro-(3H)-furan-2-one with $\text{Na}^{15}\text{NN}_2$ in 1:1 water-acetone were measured as a probe for internal clockwise vs anticlockwise rotation in the intermediate carbanion.

Nucleophilic isomerization of electrophilic alkenes¹ involves an attack of the nucleophile $[\text{Nu}^-]$ on the alkene to form a carbanion which undergoes internal rotation (k_{rot}), followed by nucleophile expulsion (k_{el}). Whether isomerization will be observed when the double bond carries a nucleofuge (LG) depends on the $k_{\text{el}}/k_{\text{rot}}$ ratio. With good nucleofuges, e.g. Br, and moderately electrophilic alkenes, nucleofuge expulsion after 60° rotation gives only substitution with retention and no isomerization.² With longer lived carbanions, $k_{\text{el}}/k_{\text{rot}}$ may be low but most nucleophiles are poorer nucleofuges than Cl and Br, and substitution is favored over isomerization. For $\text{Nu} \neq \text{LG}$, electrophilic vinyl chlorides and bromides isomerize only when $\text{Nu}^- = \text{NCS}^-$.³

For identical nucleophile and nucleofuge, nucleophilic isomerization, e.g., by Br^- , ArS^- or ArO^- , was observed in strongly electrophilic systems.⁴ The concurrent isomerization (isom) and incorporation (ex) of a labelled nucleophile allows the calculation of $k_{\text{ex}}/k_{\text{isom}}$ ratios. In the reaction of (*E*)- and (*Z*)-*p*- $\text{O}_2\text{NC}_6\text{H}_4\text{C}(\text{Cl})=\text{C}(\text{CN})\text{CO}_2\text{Me}$ with $^{36}\text{Cl}^-$, $k_{\text{ex}}/k_{\text{isom}} =$

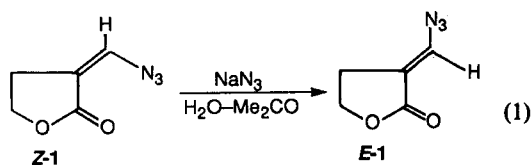
47-136,⁵ but the percentage incorporation in the isomerized material alone could not be determined.

Vinyllyc substitution of highly electrophilic alkenes mostly gives *E/Z* product mixtures. This could be visualized to occur in two ways: (a) competition between 60° (clockwise)⁶ and 120° (anticlockwise)⁶ rotations in the carbanion, each followed by nucleofuge expulsion from a conformation with parallel $\text{sp}^2(\text{C}^-)$ and $\text{C}-\text{X}$ orbitals (the terms clockwise and anticlockwise relate to the specific scheme written; they are mechanistically important only when they are compared with one another); or (b) exclusive 60° rotation and nucleofuge expulsion giving retention, and a further 120° rotation (overall 180°) and nucleophile expulsion giving an isomerized product. These routes are usually indistinguishable but they are distinguishable when a labelled nucleophile, $\text{Nu}^{-*} = \text{LG}$, is used. When $k_{\text{el}} \gg k_{\text{rot}}$ the 120° rotation gives a labelled isomeric product, whereas 180° rotation gives isomerization without incorporation. Up to now the large $k_{\text{ex}}/k_{\text{isom}}$ ratios prevented the use of this probe. We have now found a suitable system for applying it.

(*Z*)-3-azidomethylenedihydro-(3*H*)-furan-2-one, *Z*-1, isomerizes completely in 1:1 water-acetone containing NaN_3 (but not with OH^- or AcO^- or thermally) to the more stable *E*-isomer *E*-1⁶ [equation (1)]. *E*-1 gives no *Z*-1 with NaN_3 .

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Dedicated to Professor G. Modena on the occasion of his 70th birthday.



We measured both the extent of isomerization and label incorporation occurring with equimolar amount of $\text{Na}^{15}\text{NN}_2$ (99%; Cambridge Isotope Laboratories, Switzerland) (NaN_3^*). Starting from *Z*-1 the extent of isomerization to *E*-1 at room temperature between 2 and 36 days was determined by HPLC or ^1H NMR spectrometry. *E*-1 and *Z*-1 were separated by HPLC and the percentage label in each was determined by chemical ionization mass spectrometry from the intensities of the m/z 140 (non-labelled molecular and base peak)/141 (singly labelled) ratio after correction for natural abundance of other isotopes (mass spectra were

determined in the Mass Spectrometry Centre at the Technion, Haifa, with a Finnigan TSQ-70B mass spectrometer). A similar experiment was conducted for 3–45 h at 45°C . There was not enough *E*-1 at the first points to determine the percentage incorporation (Table 1). *E*-1 also reacted with NaN_3^* under the same conditions as in the latter experiment and the extent of N_3^* incorporation is given in the last column in Table 1.

Several features emerge from the data. (a) *E*-1 exchanges with retention (no *Z*-1 was formed) at a reasonable rate at 45°C giving 90% of the expected exchange after 35 h, but the value decreases at 46 h. (b) Starting from *Z*-1, the percentage label in *E*-1 exceeds that in *Z*-1 and at room temperature also exceeds the expected maximum 50% exchange. The statistical value of 50% exchange in *E*-1 + *Z*-1 is achieved after long reaction time. (c) N_3^* incorporation into both isomers is faster than the isomerization.

The results are analysed in Scheme 1, where Y is the

Table 1. N_3^* incorporation and *Z* → *E* isomerization in the reaction of *E*-1 and *Z*-1 with N_3^* in 1 : 1 water–acetone- d_6 ^a

Reaction time (h)	Temperature ($^\circ\text{C}$)	Precursor ^b	<i>E</i> -1 (%) ^c	Label (%) in			
				<i>Z</i> -1	<i>E</i> -1	<i>E</i> -1 + <i>Z</i> -1	<i>E</i> -1 ^d
3	45	<i>Z</i> -1	2.5	8.3			9.7
5			5	10.6 ^e	39.5	12.1	12.5
6.5			7	12.8	24.5	13.6	20.4
23			28				40.0
35			36				45.0
46			52				34.2 ^e
48			r.t. ^f	<i>Z</i> -1	7.7	10.0 ^e	
216	22	23.5 ^e			62.3	30.0	
504	38.8	36.3			56.0	44.0	
864	56	41.8			58.4	51.1	

^a [*E*-1] or [*Z*-1] = $[\text{Na}^{15}\text{N}_3] = 0.4\text{ M}$

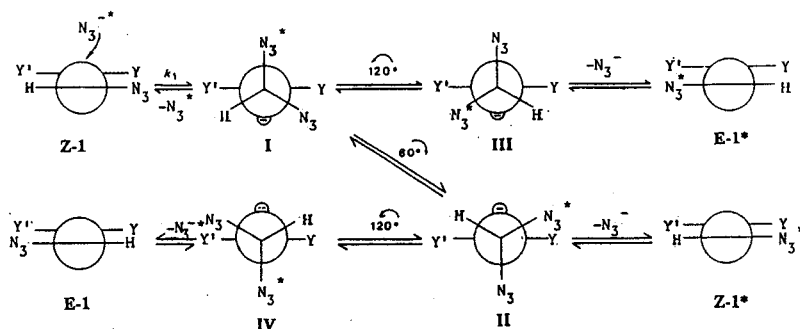
^b Data in the first seven columns.

^c Determined by HPLC at 45°C and by HPLC and ^1H NMR (average given) at room temperature.

^d Precursor is *E*-1 and data are for reaction times, temperature and the percentage label as before.

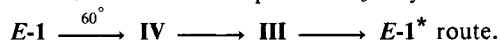
^e Average of two experiments.

^f Room temperature.



Scheme 1

—C(O)— substituent of **1**. Since azide is a poor nucleofuge (in solvolysis of benzyl derivatives, azide is a $ca\ 10^9$ slower nucleofuge than chloride⁷), **1** is moderately electrophilic and concerted vinylic substitution gives retention,² the reaction proceeds via a carbanionic intermediate. The initially formed conformer **I** from **Z-1** can undergo 60° rotation to **II** or 120° rotation to **III**. Loss of N_3^- from **II** and **III** gives labelled retained **Z-1*** and isometric labelled **E-1***, respectively. Further, 120° rotation in **II** gives **IV**, which loses N_3^- to give non-labelled **E-1**. **E-1** incorporates N_3^- by the



The higher percentage labelling starting from **E-1** than from **Z-1** indicates that incorporation and isomerization are connected, i.e. **E-1*** is not entirely formed by exchange of **E-1** formed during the substitution.

If **I-IV** equilibrate rapidly before N_3^-/N_3^* expulsion, since the transition state for elimination from **III/IV** has lower energy than that from **I/II** and $k_{el}(N_3^-)/k_{el}(N_3^*) \approx 1$, the Curtin–Hammett principle predicts that the **E-1** formed should be 50% labelled throughout. If, instead, 60° and 120° rotations are followed by complete N_3^-/N_3^* expulsion without further rotation, only **E-1*** will be formed. If isomerization proceeds by 180° rotation/ N_3^- expulsion, only **E-1** will be obtained. Neither of these predictions is borne out and the non-statistical labelling requires other explanations. Competition between 180° and 120° rotations with $[E-1]/[E-1^*] = k_{rot}^{180}/k_{rot}^{120}$ if $k_{el} \gg k_{rot}$, incomplete equilibration of **I-IV** or isomerization only via $120^\circ/N_3^-$ expulsion followed by an additional 60° rotation/ N_3^- expulsion are other alternatives.

We conclude that in spite of the relatively low nucleofugality of azide, N_3^- expulsion precedes the complete equilibration of conformers **I-IV**. Competition between 60° and 120° rotations is a plausible interpretation if further rotation occurs from conformers **II** and **III**. Our conclusion applies only for an exchange process since the hyperconjugative barriers⁸ for 120° and 180° rotations are similar.

Loss of some **E-1** or **Z-1** by hydrolysis during the reaction and exchange of **E-1** with N_3^* prevent accumulation of more quantitative data. However, for a first use of the exchange in both isomers/isomerization probe, even qualitative results are important. A search for systems capable of giving more quantitative data is continuing.

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