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Stereochemistry of the Vinylic $S_{RN}1$ Reaction of Triarylvinyl Halides. The Structure of the Intermediate α-Arylvinyl Radical

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Evidence for the intermediacy of a vinyl radical in the vinylic $S_{RN}1$ reaction ($S_{RN}1$(V)) of 2-anisyl-1,2-diphenylvinyl bromide **2** is obtained. The photostimulated $S_{RN}1$(V) reaction of pinacolone enolate ion with (*E*)-**2** and (*Z*)-**2**, which are used as stereoindicators, gives complete loss of the original stereochemistry of the two precursors in the substituted and hydrodehalogenated products; i.e., stereoconvergence is found. It is concluded that in the reaction of **2** a *β*-substituted α-phenylvinyl radical is a reactive intermediate and that it has either a linear structure or an average linear structure due to a rapidly interconverting *E*,*Z* mixture of bent radicals. This conclusion is supported by comparing the stereochemical course of the $S_{RN}1$(V) reaction with those of other reactions of the same precursor, which unambiguously give rise to the same α-phenylvinyl radical intermediate by alternative mechanisms. Among the reactions investigated, the hydrodehalogenation of precursor **2** by LAH appears to take place by an ET mechanism.

Nucleophilic substitution reactions of aryl halides via the free radical chain $S_{RN}1$ mechanism proceed by the intermediacy of the aryl radical.[1] Vinyl halides, showing many reactivity features in common with aryl halides, were recently found[2] to react by a comparable substitution mechanism (Scheme 1, where RX is the aryl or vinyl substrate, and Y^- is a suitable nucleophile).

Scheme 1

$$RX \xrightarrow{h\nu/Y^-} RX^{\bullet -} \text{ (initiation)} \qquad (1)$$

$$RX^{\bullet -} \rightarrow R^\bullet + X^- \qquad (2)$$

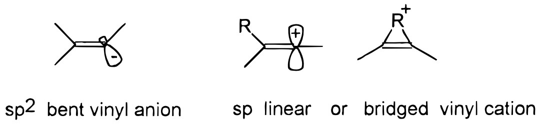
$$R^\bullet + Y^- \rightarrow RY^{\bullet -} \qquad (3)$$

$$RY^{\bullet -} + RX \rightarrow RY + RX^{\bullet -} \qquad (4)$$

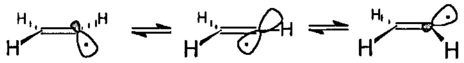
The occurrence of the vinylic $S_{RN}1$ reaction (hereafter, $S_{RN}1$(V)) appears to be strongly dependent on specific structural features of the vinyl halide,[2] which may prevent or minimize competition from alternative ionic processes[3] (e.g., elimination−addition). So far, our investigation in this field has mainly focused on the effect of the structure of the substrate, in particular the role of certain substituents.[4] Questions about the stereochemical course of the $S_{RN}1$(V) reaction, strictly related to the structure of the *vinyl radical* intermediate, were not addressed.

Conceivable alternatives for the structure of vinyl radicals are an sp^2 bent geometry or an sp linear one.[5] If we remember that the structures of the "close neighbors" of the vinyl radical, *viz*. the vinyl anion and the vinyl cation, are bent and configurationally stable for the former,[6] while linear (or bridged) for the latter,[7] an intermediate situation for the vinyl radical is expected.[8,9]

In fact, the parent vinyl radical is suggested to be a



bent species, which rapidly inverts on the ESR time scale owing to a low barrier to inversion (ca. 3 kcal/mol).[10] The linear structure represents the "transition state" for this inversion.



However, α-substituents can modify this situation to a major extent. For example, the $R_2C{=}C(R')^\bullet$ radical, where R′ = Ph, appears linear by ESR investigation,[11] whereas in the case of R′ = Cl or Br there is evidence in

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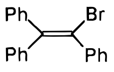
favor of a bent stable structure.[12] Finally, a *halogen-bridged* structure, analogous to an iodine-bridged vinyl cation intermediate that accounted for the stereochemistry of its capture,[13] has been suggested for a β-halogen-substituted vinyl radical.[14] The structure of vinyl radicals thus appears wavering.

The structure of the vinyl radical is expected to affect the stereochemistry of the products: if it is bridged or bent and configurationally stable, the reaction products will retain the original configuration of the precursor.[13] Alternatively, a linear species should give a mixture of retained and inverted products in ratios depending on the relative steric hindrance of the β-substituents. Finally, if it is bent and inverting, the stereochemistry will be determined by the relative rates of inversion and capture (*vide infra*), but again a mixture of isomers is expected.[5,15]

An investigation on the stereochemical outcome of a $S_{RN}1(V)$ reaction was initiated, aimed to characterize the vinyl radical intermediate.[2] To this end, an appropriate pair of *E*/*Z* isomeric precursors was selected, and their behavior was tested under the typical conditions of $S_{RN}1$ nucleophilic processes. The results are reported here and compared with the stereochemical outcome of other exemplary reactions of the same precursor, expected to occur by the same vinyl radical intermediate generated by alternative mechanisms.

Results and Discussion

The $S_{RN}1(V)$ Reaction. For the purpose of our stereochemical investigation, there are two prerequisites for the substituents on the vinyl halide. First, the system should be as close as possible to that of 1-bromo-1,2,2-triphenylethene (**1**), which was shown to react *via* the $S_{RN}1(V)$ route without intervention from competing ionic routes.[2] Second, a pair of configurationally pure *E* and *Z* isomers, which are stable to mutual isomerization under the reaction conditions by routes that are irrelevant to the substitution, should be prepared. After preliminary screening, **2**, differing from **1** by the replacement of one β-Ph by a β-anisyl (An) group, was found as a proper substrate.



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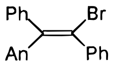
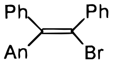
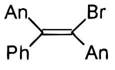


E-**2**

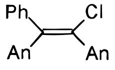


Z-**2**

Compound **2**, which was previously prepared and separated into *E* and *Z* isomers,[16,17] was already investigated as a stereomodel for the vinylic S_N1 reaction[3,18] under stringent conditions.[17] It lacks vinylic or allylic C−H bonds or electron-withdrawing substituents, which can lead to substitution by elimination−addition and addition−elimination routes, respectively,[2,4] and it therefore fulfills the indicated prerequisites for being an $S_{RN}1(V)$ substrate. To our surprise, the structurally similar compounds **3** (86:14 (*Z*)-**3**:(*E*)-**3**) and **4** (91:9 (*E*)-**4**:(*Z*)-**4**) did not lend themselves to the photostimulated $S_{RN}1(V)$ reaction with a ketone enolate ion (see below).



Z-**3**



E-**4**

Determination of the reduction potential of **1**, (*Z*)-**2**, mostly (*Z*)-**3**, and mostly (*E*)-**4** gives the very comparable values of −1.86,[2,4] −1.92, −2.00, and −2.08 V (*vs.* SCE, in THF), respectively. These similar electron affinities would be expected to allow a comparable efficiency in the initiation of the $S_{RN}1(V)$ reaction chain of these precursors. Lack of $S_{RN}1(V)$ reactivity with **3** and **4** is possibly due to the presence of the α-anisyl group that, at variance with the β-anisyl group of **2**, may allow incursion of an ionic vinylic S_N1 route.[3,18−20] Further investigation is in progress along this line, but it has deferred a more extensive use of **3** and **4** in the present study. Once more, we find that the window of occurrence of the $S_{RN}1(V)$ route is narrow,[4] as structurally similar compounds do not behave in the same way.

The photostimulated substitution reaction of (*E*)-**2** and (*Z*)-**2** with the enolate ion of pinacolone ($^{-}CH_2COCMe_3$; **5**) was investigated in Me_2SO solution at room temperature[2] in separate experiments. The substitution product **6** and the hydrodehalogenation product **7** were obtained in ca. 40% and 5% yields, respectively, after 20 min reaction time (Table 1). Both products were *E*,*Z*-pairs, as easily detected by GC and GC−MS analysis. Product **6** was independently prepared as an *E*,*Z*-pair and characterized, while (*E*)-**7** and (*Z*)-**7** were synthesized according to the literature.[16] Under the above reaction conditions,[2] ca. 50% of the precursor was recovered unreacted. The important mechanistic point is that the *E*,*Z* mixtures of products **6** and **7** have the same composition (within 3%) on starting either from (*E*)-**2** or from (*Z*)-**2** (Scheme 2); i.e., the stereochemical outcome is complete stereoconvergence.

When the photostimulated reaction was repeated in the presence of the electron scavenger *p*-dinitrobenzene, no conversion to products was obtained, indicating that electron-transfer steps must play an important role in the process. The stability of the precursors under the adopted photostimulation conditions was investigated with the more largely available (*Z*)-**2**, and the result is taken to hold for (*E*)-**2** as well, due to the close similarity of the two isomeric precursors. After irradiation at a wavelength of 350 nm, at which the substitution took place, but *in the absence* of enolate ion **5**, (*Z*)-**2** was recovered unchanged. Thus, neither *direct* photoinduced[19,21] isomerization nor cleavage−isomerization−recombination[21] of the vinyl halide (VyX in Scheme 3), whereby the original configuration of the reagent would be lost, take place. Configuration of the latter must be lost only *during* the substitution process.

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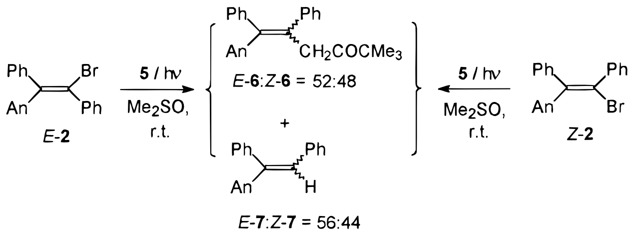
Table 1. Yields and Stereochemical Outcome of the Reactions Investigated

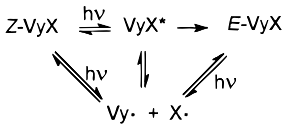
substrate (VyX)	reaction time (min)	% VyX left	% products (stereochem composn)
(a) Photostimulated $S_{RN}1$(V) with **5** in Me_2SO at rt[a]			
(*E*)-**2**	20	47 ((*E*)-**2**)	38 ((*E*)-**6**:(*Z*)-**6** = 52:48) 4 ((*E*)-**7**:(*Z*)-**7** = 55:45)
(*E*)-**2**	20	51 ((*E*)-**2**)	40 ((*E*)-**6**:(*Z*)-**6** = 53:47) 7 ((*E*)-**7**:(*Z*)-**7** = 57:43)
(*Z*)-**2**	20	45 ((*Z*)-**2**)	39 ((*E*)-**6**:(*Z*)-**6** = 55:45) 5 ((*E*)-**7**:(*Z*)-**7** = 56:44)
(*Z*)-**2**	10	61 ((*Z*)-**2**)	21 ((*E*)-**6**:(*Z*)-**6** = 51:49) 2 ((*E*)-**7**:(*Z*)-**7** = 55:45)
(*Z*)-**2** [b]	20	90 ((*Z*)-**2**)	
(*Z*)-**2** [c]	20	98 ((*Z*)-**2**)	
(b) Hydrodehalogenation with Bu_3SnH/AIBN in Refluxing Benzene[d]			
(*E*)-**2**	300	32 ((*E*)-**2**)	62 ((*E*)-**7**:(*Z*)-**7** = 56:44)
(*Z*)-**2**	360		89 ((*E*)-**7**:(*Z*)-**7** = 55:45)
(*Z*)-**2** [e]	360	89 ((*Z*)-**2**)	6 ((*E*)-**7**:(*Z*)-**7** = 58:42)
3 (86% (*Z*)-**3**)	360	23 (82% (*Z*)-**3**)	68 ((*E*)-10:(*Z*)-**10** = 53:47)
4 (91% (*E*)-**4**)	360	27 (89% (*E*)-**4**)	65 ((*E*)-10:(*Z*)-**10** = 57:43)
(c) Hydrodehalogenation with Me_2CHO^-/AIBN in Refluxing Me_2CHOH [f]			
(*E*)-**2**	180	88 ((*E*)-**2**)	8 ((*E*)-**7**:(*Z*)-**7** = 58:42)
(*Z*)-**2**	180	85 ((*Z*)-**2**)	6 ((*E*)-**7**:(*Z*)-**7** = 56:44)
(*Z*)-**2**[e]	180	95 ((*Z*)-**2**)	
(d) Hydrodehalogenation with LAH in THF at rt[g]			
(*E*)-**2**	180	24 ((*E*)-**2**)	71 ((*E*)-**7**:(*Z*)-**7** = 54:46)
(*Z*)-**2**	180	27 ((*Z*)-**2**)	66 ((*E*)-**7**:(*Z*)-**7** = 55:45)
(*Z*)-**2**[b]	180	98 ((*Z*)-**2**)	
(*Z*)-**2**[h]	180	37 ((*Z*)-**2**)	52 ((*E*)-**7**:(*Z*)-**7** = 53:47)

[a] Typical conditions: substrate, 25 μmol; nucleophile, 80 μmol; solvent, 1.5 mL. [b] In the presence of 9 μmol of *p*-dinitrobenzene. [c] Without nucleophile. [d] Typical conditions: substrate, 0.1 mmol; Bu_3SnH, 0.1 mmol; AIBN, 10 μmol; solvent, 0.25 mL. [e] Without AIBN. [f] Typical conditions: substrate, 0.1 mmol; Me_2CHO^-, 0.2 mmol; AIBN, 10 μmol; solvent, 0.25 mL. [g] Typical conditions: substrate, 18 μmol; LAH, 55 μmol; solvent, 0.25 mL. [h] In diethyl ether.

Scheme 2



Scheme 3



Scheme 4

$$2 \xrightarrow{5/h\nu} 2^{\bullet -} \qquad (5)$$

$$2^{\bullet -} \longrightarrow Br^- + AnC(Ph)=\dot{C}(Ph) \qquad (6)$$

$$\underset{}{} \quad 8$$

$$8 \xrightarrow{SH} 7 \qquad (7a)$$

$$8 \xrightarrow{5} 6^{\bullet -} \qquad (7b)$$

$$6^{\bullet -} + 2 \longrightarrow 6 + 2^{\bullet -} \qquad (8)$$

Hence, it is safe to conclude that the products formed according to Scheme 2 are unambiguously produced in a photostimulated $S_{RN}1$(V) route (see Scheme 4). The intermediate α-phenylvinyl radical **8** partitions between hydrogen atom abstraction (e.g., from the solvent) to give **7** and combination with the nucleophile to give the radical anion of **6**. Exchange of an electron from $6^{\bullet -}$ with **2** would yield product **6** and the radical anion of **2** that re-enters the propagation cycle.

The stereoconvergence of the reactions of (*E*)-**2** and (*Z*)-**2** towards equal *E*,*Z* mixtures of **6** and **7** excludes the possibility that radical **8** has a configurationally *stable* bent structure. It is instead either an sp linear or a pair of rapidly interconverting isomeric sp^2 bent radicals: in *both* these cases the original configuration of the reagent would be lost, giving either a static or a dynamically averaged identical intermediate.[5,15] It is appropriate to compare this situation with the stereochemical outcome of the reaction of **2** in a vinylic S_N1 reaction.[17] The linear vinylic carbocation from **2** is captured by 2,2,2-trifluoroethanol giving a 1:1 *E*:*Z* mixture of the 2,2,2-trifluoroethyl ethers. The composition of this *E*:*Z* mixture is very similar to those reported in Scheme 2. It is clear that the ratio of the captured products from a linear intermediate, being either a carbocation or a radical, depends on the relative steric environments of the two faces of the vinylic species. Both faces of **8** are sterically almost the same, and there are only minor electronic differences of An *vs* Ph group. This could be the reason for the ca. 1:1 product ratios in Scheme 2 as well as in the S_N1 reaction.[17]

The possibility for any bent vinyl radical to give an *E*,*Z* mixture of product(s) is linked to an *E*,*Z* equilibration being *faster* than the specific reaction channels, e.g., eq 7a,b in Scheme 4. The reactivity of the latter channels can be approximately estimated as follows: the rate of reaction of phenyl radical with a ketone enolate ion is reckoned to be 3×10^8 M^{-1} s^{-1} in liquid NH_3 (−33 °C),[22] while rates of hydrogen atom abstraction by phenyl radical are in the range of 10^5-10^9 M^{-1} s^{-1} (at room

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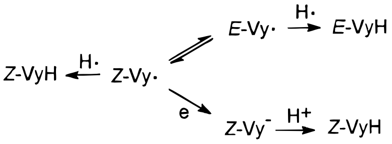
Scheme 5



temperature) depending on the hydrogen donor.[23] Assuming that to a first approximation the reactivity of a vinyl radical resembles that of an aryl radical,[24] we can estimate a *lower* limit to the *E*,*Z* inversion rate of a bent vinyl radical **8** (i.e., $\geq 10^9$ s^{-1}) that is consistent with the observed loss of substrate configuration (Scheme 2). It may be added that circumstantial evidence for homolytic decomposition of some vinylic peroxides or peresters is in favor of the intermediacy of isomeric vinyl radicals that equilibrate much more quickly than they abstract an hydrogen atom.[5,15]

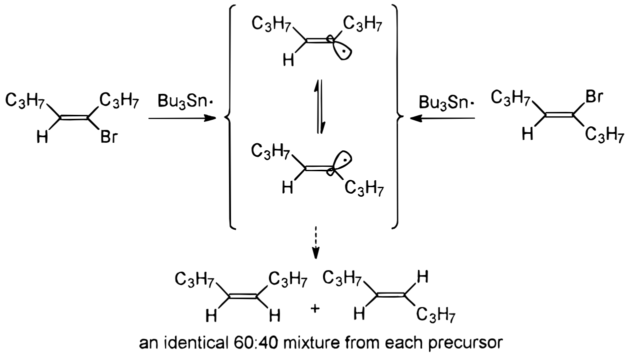
The present results (Scheme 2) are analogous with the stereochemical outcome of an *aliphatic* $S_{RN}1$ substitution.[25] This has been shown to give racemic substitution products owing to the intermediacy of an *alkyl* radical, for which there is a quite general consensus in favor of a *rapidly inverting* shallow pyramidal structure.[26]

Support for the conclusions drawn for the structure of the reactive intermediate of the $S_{RN}1$(V) route was sought. In particular, unambiguous and independent generation of radical **8** was viewed as helpful for selectively studying its stereochemical behavior, in order to compare it with our observations (Scheme 2). Besides that, previous investigation[4,27] has shown that electron transfer to the intermediate vinyl radical (to give a carbanion) can easily occur in a "reducing environment" such as that of an $S_{RN}1$ cycle, where radical anions are involved. Consequently, it is possible, in principle, that reduced product **7** arises from *two* different intermediates: a configurationally stable vinyl anion and the vinyl radical. In contrast to what is found in Scheme 2, however, a larger amount of retention of configuration in product **7** seems likely in this event,[5a,28] if reduction of radical **8** to a configurationally stable carbanion (Vy^-) occurs faster than isomerization of **8** (Scheme 5). Independent generation of **8** from **2** *in the absence* of nucleophile **5** would enable an unequivocal study of its stereochemistry in the absence of ET steps associated with the $S_{RN}1$(V) process.

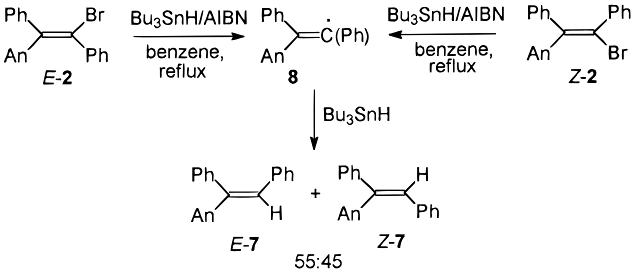
Radical Hydrodehalogenation. Dehalogenation of alkyl or aryl halides by means of trialkyltin radical provides an easy access to the corresponding radical species (eq 9).[24,29]

$$Bu_3SnH \xrightarrow[\Delta]{AIBN} Bu_3Sn^{\bullet} \xrightarrow{RX} Bu_3SnX + R^{\bullet} \qquad (9)$$

Scheme 6



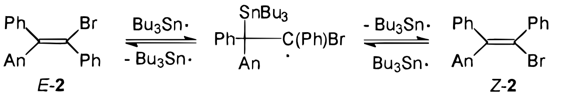
Scheme 7



Vinyl radicals have already been generated by this method from vinyl halides.[5a,24,30] In all the reported cases the double bond was substituted by alkyl groups, and the radicals could be inferred to invert rapidly between *E* and *Z* isomers on the basis of the stereoconvergence obtained[24,30,31] (see, e.g.,[31b] Scheme 6).

This method is exploited here to induce a *bona fide* formation of radical **8** from precursor **2**: the hydrodehalogenated product **7**, resulting from H-atom abstraction from Bu_3SnH,[32] was indeed obtained. In particular, either (*E*)-**2** or (*Z*)-**2** yielded an identical 55:45 (*E*)-**7**:(*Z*)-**7** mixture (Scheme 7). This product distribution is practically identical with that reported for **7** in Scheme 2. The identical product distribution in this radical process and the electron-transfer $S_{RN}1$(V) process strongly supports a common intermediate **8** in both reactions as the origin of the observed stereochemical outcome for the generation of key product **7**.

A control experiment makes it clear that no thermal isomerization of the precursors occurs, since (*Z*)-**2** is recovered configurationally unchanged from refluxing benzene containing Bu_3SnH *but no* AIBN. Moreover, recovery of unreacted (*E*)-**2** after reaction with Bu_3SnH (Scheme 7) reveals no isomerization; this ensures that a conceivable loss of configuration of the precursor or products due to $Bu_3Sn^{\bullet}$ addition−isomerization−elimination (eq 10)[21,29] cannot be the major cause for the formation of the *E*,*Z*-mixtures of **7** in Scheme 7.



(10)

The results of Scheme 7 were confirmed with the two other stereoindicators, namely, **3** (86% *Z*) and **4** (91% *E*).

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[23] (a) *Methods in Free Radical Chemistry*; Huyser, E. S., Ed.; Marcel Dekker: New York, 1969−1974; Vols. 1−5. (b) For a more recent compilation, see: Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry;* Masson-Wiley: Paris, 1995.

[24] Curran, D. P. *Synthesis* **1988,** 417.

[25] Norris, R. K.; Smyth-King, R. J. *Tetrahedron* **1982**, *38*, 1051.

[26] (a) Lisle, J. B.; Williams, L. F.; Wood, D. E. *J. Am. Chem. Soc.* **1976**, *98*, 227. (b) Bonazzola, L.; Leray, N.; Roncin, J. *Ibid.* **1977**, *99*, 8348. (c) Paddon-Row, M. N.; Houk, K. N. *Ibid.* **1981**, *103*, 5046.

[27] Gatti, N.; Jugelt, W.; Lund, H. *Acta Chem. Scand.* **1987**, *B41*, 646.

[28] Sargent, G. D.; Browne, M. W. *J. Am. Chem. Soc.* **1967**, *89*, 5363.

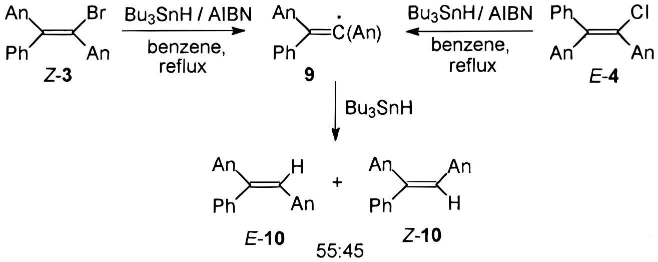
[29] Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Baldwin, J. E. Ed.; Organic Chemistry Series 5; Pergamon: Oxford, 1986.

[30] Stork, G.; Baine, N. H. *J. Am. Chem. Soc.* **1982**, *104*, 2321.

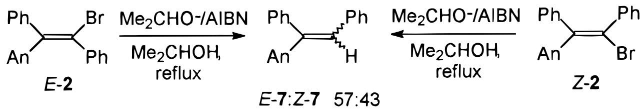
[31] (a) Jasperse, C. P.; Curran, D. P.; Ferig, F. L. *Chem. Rev.* **1991**, *91*, 1237. (b) Curran, D. P.; Jasperse, C. P.; Totleben, M. J. *J. Org. Chem.* **1991**, *56*, 7169.

[32] Reference 24 quotes k_H 3 × 10^8 s^{-1} at 30 °C as the rate of H-atom abstraction by vinyl radical from Bu_3SnH.

Scheme 8



Scheme 9



These vinylic precursors had been prepared according to the literature[16] and were available from a previous investigation.[33] Tin radical-induced hydrodehalogenations of mostly (*Z*)-**3** or mostly (*E*)-**4** gave *equal E,Z*-mixtures of product **10** (Scheme 8).

This stereoconvergence resulting from the same vinylic radical generated from two different precursors is again rationalized either by an sp linear or by a configurationally unstable sp^2 structure for the radical intermediate **9**.

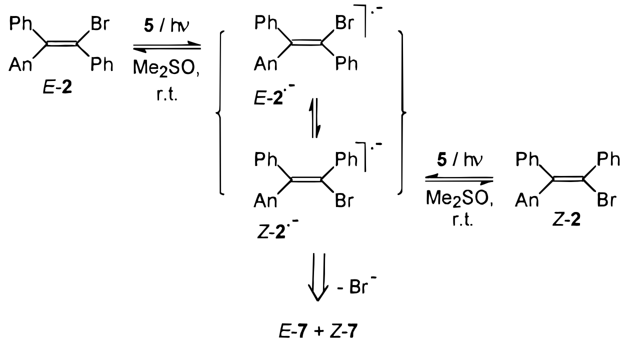
Electron-Transfer-Induced Hydrodehalogenation. As an additional corroboration of the structural conclusions derived from the tin-induced radical dehalogenation, it appeared desirable to study a *bona fide* electron-transfer induced hydrodehalogenation of **2** that would proceed through the intermediacy of radical **8** and compare its stereochemical outcome with those reported in Schemes 2 and 7. Inspiration for this experimental method derives from previous studies of the groups of Bunnett[34] and Savéant.[35] It is a dehalogenation of the vinyl halide induced by 2-propoxide ions; radicals from an initiator (AIBN) remove a hydrogen atom from the alkoxide ion, transforming it into a powerful electron donor,[36] i.e., acetone radical anion. The radical anion of the vinyl halide is generated from it by electron transfer (eq 11). The subsequent steps are similar to those

$$\mathrm{Me_2CHO^-} \xrightarrow[\mathrm{Me_2CHOH,\ reflux}]{\mathrm{AIBN}} \mathrm{Me_2CO^{\cdot -}} \xrightarrow[\mathrm{-\,Me_2CO}]{\mathrm{VyX}} \mathrm{VyX^{\cdot -}} \xrightarrow[\mathrm{-\,X^-}]{\mathrm{Me_2CHO^-}} \mathrm{VyH} \qquad (11)$$

described in Scheme 4, with the only exception that nucleophile **5** is absent and only hydrodehalogenation may occur (Scheme 9).

When the reaction was conducted with (*E*)-**2** and (*Z*)-**2**, hydrodehalogenation took place, giving identical (*E*)-**7**:(*Z*)-**7** mixtures either from (*E*)-**2** or (*Z*)-**2**. This is again the same 57:43 (*E*)-**7**:(*Z*)-**7** composition reported in Schemes 2 and 7. A control experiment had shown that the (*Z*)-**2** precursor was recovered unchanged from reflux in 2-propoxide/2-propanol solution *without* AIBN. The generation of **2**$^{\bullet-}$ by ET step, and the presence of **8** in the product-determining route of Scheme 9, are thus warranted.

Scheme 10



As a *bona fide* counterpart of the ET steps invoked in Schemes 2 and 9, we add that electrochemical reduction of vinyl halides has already been investigated.[27,37] Results consistent with ours are reported, indicating that, after the uptake of one electron, a vinyl radical is produced. It can undergo isomerization *prior to* accepting a second electron and a proton, ultimately affording a *cis,trans* mixture of the alkene product.[27,38]

It is finally fitting to comment on a subtle source of complexity in the results of Scheme 2. In fact, another reactive intermediate of the S$_{\mathrm{RN}}$1(V) route does exist, in addition to **8**, i.e., **2**$^{\bullet-}$. The same intermediate is shared by the 2-propoxide/AIBN route of Scheme 9. In principle, a vinylic radical anion can be configurationally unstable because it hosts the extra electron in a π^* MO. The antibonding character of the double bond has been held at the origin of the *cis,trans* isomerization observed with vinylic radical anions lacking suitable leaving groups such as the halogens.[39] Isomerization of the *cis*-stilbene radical anion into the *trans*-radical anion[40] and a few other examples of isomerizations of vinylic radical anions are known.[41] Consequently, the stereochemical result of our S$_{\mathrm{RN}}$1(V) reaction could be masked by occurrence of a (*E*)-**2**$^{\bullet-}$ $\Leftrightarrow$ (*Z*)-**2**$^{\bullet-}$ isomerization *before that* dehalogenation to form radical **8** has taken place (Scheme 10).

An argument against this route is that the unambiguous generation of **8** by means of tin radical (Scheme 7) has already delineated the stereochemical behavior of that particular vinyl radical as a species capable of loss of memory of the configuration of its vinyl halide precursor(s), as testified by the stereoconvergence obtained in the formation of key product **7**. This has been confirmed in Scheme 8 for radical **9**. Moreover, isomerization of **2**$^{\bullet-}$ could become appreciable only if it is *faster* than the rate of C–Br bond cleavage. Typical rates of cleavage of radical anions of aryl bromides are in the range[42] of 10^7–10^9 s^{-1}. However, for the isomerization of *cis*-stilbene radical anion, a rate of 1.4×10^5 s^{-1} is reported,[40] and the isomerization of diethyl maleate → diethyl fumarate radical anions is even slower,[41a] the rate constant being 10 s^{-1}. It seems reasonable to conclude that any (*E*)-**2**$^{\bullet-}$ $\Leftrightarrow$ (*Z*)-**2**$^{\bullet-}$ isomerization will be slower than the following

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[33] Rappoport, Z.; Apeloig, Y. *J. Am Chem. Soc.* **1969**, *91*, 6734; **1975**, *97*, 821, 836.

[34] (a) Bunnett, J. F.; Wamser, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 6712. (b) Bunnett, J. F. *Acc. Chem. Res.* **1992**, *25*, 2.

[35] Amatore, C.; Badoz-Lambling, J.; Bonnel-Huyghes, C.; Pinson, J.; Savéant, J.-M.; Thiébault, A. *J. Am. Chem. Soc.* **1982**, *104*, 1979.

[36] Wardman, P. *J. Phys. Chem. Ref. Data* **1989**, *18*, 1637.

[37] *Encyclopedia of Electrochemistry of the Elements, Org. Sect.*; Bard, A. J., Lund, H., Eds.; Marcel Dekker: New York, 1980; Vol. 14.

[38] Elving, P. J.; Rosenthal, I.; Hayes, J. R.; Martin, A. J. *Anal. Chem.* **1961**, *33*, 330.

[39] Todres, Z. V. *Tetrahedron* **1987**, *43*, 3839; *Acta Chem. Scand.* **1990**, *44*, 535.

[40] Jensen, B. S.; Lines, R.; Pagsberg, P.; Parker, V. D. *Acta Chem. Scand.* **1977**, *B31*, 707.

[41] (a) Bard, A. J.; Puglisi, V. J.; Kenkel, J. V.; Lomax, A. *Faraday Disc. Chem. Soc.* **1973**, *56*, 353. (b) Yeh, L.-S. R.; Bard, A. J. *J. Electrochem. Soc.* **1977**, *124*, 189.

[42] Andrieux, C. P.; Savéant, J.-M.; Zann, D. *Nouv. J. Chim.* **1984**, *8*, 107.

cleavage of the radical anion, so that the stereoconvergence observed in the ET pathways of Schemes 2 and 9 is due only to the intermediacy of vinyl radical **8**. Our own experience with radical anions of vinyl halides generated by cyclic voltammetry confirms fast cleavage rates of the C-halogen bond.[4] In addition, no isomerization of the *recovered precursor* is detected from the ET-induced experiments (Schemes 2 and 9). This is consistent with the fact that the (*E*)-$\mathbf{2}^{\bullet-}$ or (*Z*)-$\mathbf{2}^{\bullet-}$ generated by ET steps are lost by a consecutive and very fast cleavage step. In conclusion, *E,Z* isomerization of $\mathbf{2}^{\bullet-}$, followed by return to the isomeric vinylic halides, does not appear to appreciably interfere with the stereochemical fate of intermediate **8**. The possibility to study the isomerization of the radical anion of a vinyl halide, in competition with its cleavage, represents *per se* an interesting experimental challenge, which could be addressed in the future on proper precursors.[43,44]

Hydrodehalogenation with LAH. Hydrodehalogenation of alkyl and aryl halides by lithium aluminum hydride (LAH) takes place easily, but its mechanism has been strongly debated, as summarized in a recent paper.[34b] One possibility is a radical-chain mechanism with a propagating cycle similar to that of Scheme 4,[45] even though its initiation step is uncertain (see Scheme 11, where substrate **2** is used for demonstration).

Scheme 11

$$\mathbf{2} \Rightarrow \mathbf{8}\ \text{(initiation)}$$

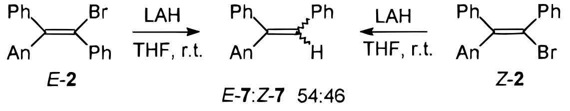
$$\mathbf{8} + \mathrm{AlH_4}^{-} \rightarrow \mathbf{7} + \mathrm{AlH_3}^{\bullet-}$$

$$\mathrm{AlH_3}^{\bullet-} + \mathbf{2} \rightarrow \mathrm{AlH_3} + \mathbf{2}^{\bullet-}$$

$$\mathbf{2}^{\bullet-} \rightarrow \mathbf{8} + \mathrm{Br}^{-}$$

Without generalization to other kinds of substrates, we report our results with (*E*)-**2** and (*Z*)-**2**, which were exploited as stereoindicators of the hydrodehalogenation reaction with LAH in THF at room temperature. An (*E*)-**7**/(*Z*)-**7** mixture was again obtained from the two isomeric precursors (Scheme 12), with the "usual" composition of 54:46 (*E*)-**7**:(*Z*)-**7** identical with that previously reported in Schemes 2, 7, and 9. The unreacted (*Z*)-**2** was recovered configurationally unchanged. This reduction reaction cannot be an ionic bimolecular vinylic substitution, in which the predicted stereochemical outcome is retention of configuration.[3]

Scheme 12



Reaction in the presence of the electron scavenger *p*-dinitrobenzene gave no conversion to **7** within the same time span. From these facts, the intermediacy of **8** and the relevance of ET steps in this reaction, as delineated in Scheme 11, seem likely.

Conclusions. Our investigation excludes the possibility of a bridged or a bent and configurationally stable structure for radical **8**. It cannot distinguish between an sp linear structure or a pair of rapidly interconverting isomeric sp^2 bent radicals. Ongoing calculations,[46] however, preliminarly show that a conjugated α-vinylvinyl radical is linear. If the latter is taken as a model for the α-phenylvinyl radical in solution, it seems reasonable that the stereochemistry described in this paper can be ascribed to the intermediacy of *linear* **8**. The very presence of this vinylic radical in the $S_{RN}1$(V) propagation cycle has been confirmed by comparison of the stereochemical outcome of this reaction with that of different reactions that unambiguously give rise to **8** through the agency of alternative mechanisms. Evidence for an ET step of hydrodehalogenation of vinyl halide **2** by LAH is also provided.

Experimental Section

The instrumentation has already been described.[2,4] Determination of the reduction potential of compounds **2**−**4** by cyclic voltammetry was conducted in THF (at a 500 mV s^{-1} sweep rate) as reported in a previous paper.[4] Precursors **2**−**4** and products (*E*)-**10**:(*Z*)-**10** (72:28) were prepared as previously described.[17,33] Products (*E*)-**7** (mp 58−59 °C) and (*Z*)-**7** (mp 90−91 °C) were prepared according to Curtin *et al.*[16] Pinacolone was distilled from anhydrous K_2CO_3; freshly sublimed *t*-BuOK was used to generate the enolate ion from pinacolone. Commercial Me_2SO (C. Erba RPE, 99.5%) was dried on activated molecular sieves and thoroughly purged with argon for 30 min prior to use in order to remove volatile acidic impurities.[4] Benzene was dried over sodium, and THF was distilled from benzophenone radical anion. Commercial $LiAlH_4$, Me_2CHOH, AIBN, and Bu_3SnH were used.

6-*p*-Anisyl-2,2-dimethyl-5,6-diphenyl-5-hexen-3-one (6). Reaction of 0.9 g of pinacolone (9 mmol), 1.0 g of sublimed *t*-BuOK (9 mmol), and 1.1 g of (*Z*)-**2** (3 mmol) in 25 mL of Me_2SO was conducted in a Rayonet photochemical reactor (16 "350 nm" lamps) for 90 min.[2] After usual workup,[2] the crude mixture (1.5 g) was chromatographed on silica gel with 5:1 petroleum ether (40−70 °C)/diethyl ether and then with 2:1 petroleum ether (40−70 °C)/benzene eluents to yield 400 mg (35%) of **6**, mp 75−80 °C, as an *E:Z* mixture: ^{1}H NMR δ ($CDCl_3$) 7.3−6.3 (m,14H), 3.75 (s, 2H), 3.6 (s, 3H), 0.96 and 0.92 (s, 9H, *E,Z* CMe_3); ^{13}C NMR δ ($CDCl_3$) 213.6 and 213.5 (*E,Z* *C*=O), 158.6, 143.3, 142,2, 135−125, 113, 55.1, 44.7, 44.2, 26.3; HRMS 384.2084, $C_{27}H_{28}O_2$ requires 384.2082.

Procedures. Details on $S_{RN}1$ experiments under photostimulation and on the radical dehalogenation experiments by AIBN/Bu_3SnH have been given described previously.[2,4] Description of a typical *i*-PrO$^-$/AIBN procedure of hydrodehalogenation follows. One mL of a freshly prepared 0.4 M *i*-PrONa/*i*-PrOH solution was added to a 2 mL *i*-PrOH solution of 44 mg of (*Z*)-**2** (0.12 mmol), 6 mg AIBN (0.04 mmol), and 10 mg of biphenyl (internal standard; 0.065 mmol). The solution was refluxed for 5 h and directly analyzed (GC and GC−MS; no workup). Similarly, a LAH-induced dehalogenation was conducted in 2 mL of anhydrous THF with 22 mg of (*E*)-**2** (0.06 mmol) and 2 mg of $LiAlH_4$ (0.053 mmol); after being stirred at room temperature for 4 h, the internal standard was added and the solution analyzed by GC and GC−MS. In cases where

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(43) A reviewer had pointed out that the radical anion of the substitution product ($\mathbf{6}^{\bullet-}$), having no leaving group, could live long enough to isomerize. This cannot be excluded. However, if the vinyl radical **8** is already linear or behaves like it (i.e., a rapidly interconverting mixture), then whatever its successor species $\mathbf{6}^{\bullet-}$ is doing it is irrelevant to the stereochemical outcome. At any rate, our stereochemical conclusions are drawn on the loss of the original stereochemistry that is verified in the formation of hydrodehalogenation product **7**, whose generation (in Schemes 2, 7, and 9) directly stems from radical **8**. However, we do plan to investigate the rate of isomerization of radical anions from **6**, or similar compounds, by means of cyclic voltammetry.[44]

(44) Work in progress, in collaboration with the group of Prof. H. Lund, Århus University, Denmark.

(45) Ashby, E. C. *Acc. Chem. Res.* **1988**, *21*, 414. Ashby, E. C.; Deshpande, A. K.; Patil, G. S. *J. Org. Chem.* **1995**, *60*, 663.

(46) Galli, C.; Mencarelli, P.; Rappoport, Z. Work in progress. The calculations are carried out by an *ab initio* DFT (BLYP/6-31G**) method.

p-dinitrobenzene was added as an inhibitor, it was employed in a 20−40% molar amount with respect to the substrate.

Analysis of Diastereoisomeric Composition of Reagents and Products. Quantitative GC analyses of the reaction mixtures were performed by the internal standard method, suitable response factors being determined on pure samples of compounds **6** and **7**. The peaks of (*E*)-**6** and (*Z*)-**6**, as well as those of (*E*)-**7** and (*Z*)-**7**, were sufficiently well separated by the capillary columns employed in GC and GC-MS analyses (30 m × 0.25 mm SE-54 and 25 m × 0.20 mm methyl silicone gum, respectively) in order for reliable integration of the corresponding areas to be performed. Products **10** were less efficiently separated to the *E* and *Z* isomers by gas chromatographic analysis. However, ^{1}H NMR analysis was a suitable analytical tool in this case. The signals of the MeO groups,[33] at δ 3.84 and 3.74 for (*Z*)-**10** and δ 3.80 and 3.73 for (*E*)-**10** could be followed and integrated. The diastereoisomeric composition of recovered **2** was checked by GC and GC-MS, while ^{1}H NMR analysis was again employed in the case of **3** and **4**.[33]

Photostimulated reactions of mostly (*Z*)-**3**, as also of mostly (*E*)-**4**, with the enolate ion of pinacolone did not produce the expected substitution product or the hydrodehalogenated product, while consumption of the starting reagents was indeed verified. Only *p*-methoxybenzophenone (ca. 30−40%) was detected as a product after 20 min reaction. Formation of this product is in agreement[33,47] with the intermediacy of a vinylic carbocation.[18,20]

Acknowledgment. Support from the Italian MURST and from the U.S.−Israel Binational Science Foundation (BSF), Jerusalem, Israel (to Z.R.), are gratefully acknowledged.

JO961007V

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[47] Ruberu, S. R.; Fox, M. A. *J. Am. Chem. Soc.* **1992**, *114*, 6310.