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LETTERS

Thermal Rearrangements of 7,7-Dihalo-trans-bicyclo[4.1.0]hept-3-enes.

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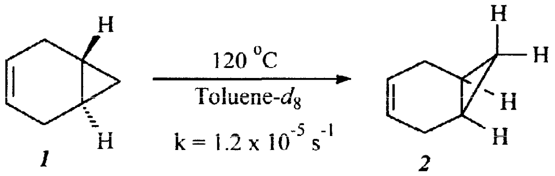
Abstract: Derivatives of *trans*-bicyclo[4.1.0]hept-3-ene with chlorine and bromine substituents the 7 position were synthesized and their thermal rearrangements were examined. Thermolysis of the dichloride leads to the formation of the cis-fused isomer, while heating the dibromide results in ring-expanded products. Thermal rearrangement of the bromochloro derivative provided a mixture of ring-isomerized and ring-expanded products. The halogenated compounds are very labile relative to the unsubstituted molecule with rate accelerations on the order of 1000 or more at 120 °C. When solvents of widely varying polarity were employed, the isomerization rate coefficients for the halogenated derivatives vary by a factor of 1.0-3.2. Therefore, it is unlikely that these compounds rearrange *via* ionic intermediates. © 1998 Elsevier Science Ltd. All rights reserved.

We have been interested in molecules that contain strained carbon-carbon sigma bonds that result from a combination of bond angle distortion and torsional strain. These bonds, which we have termed "twist-bent" bonds,[1,2] occur at the bridgehead carbons of molecules that contain a cyclopropane ring fused to another small ring of 7 carbons or less. Often, enhanced reactivity of the trans-fused molecules is observed when compared to the reactivity of the corresponding cis-fused isomers. For example, at 120 °C *trans*-bicyclo[4.1.0]hept-3-ene (*1*) readily isomerizes to *cis*-bicyclo[4.1.0]hept-3-ene (*2*), which is thermally stable at this temperature.[3,4]



The 7-methyl and 7,7-dimethyl isomers of *1* exhibit similar thermal reactivity, however, ring-opened products also are observed.[4,5] Since methyl substitution caused only a minor alteration in the reactivity of *1*, we were interested in determining whether halogen substitution would lead to different reactivity. Here we report the synthesis and thermal rearrangements of 7,7-dichloro-*trans*-bicyclo[4.1.0]hept-3-ene (*3*), 7,7-dibromo-*trans*-bicyclo[4.1.0]hept-3-ene (*4*), and 7-bromo-7-chloro-*trans*-bicyclo[4.1.0]hept-3-ene (*5*).

Minor adaptations to the technology used for the synthesis of *1* permitted the preparation of *3-5* (Scheme 1).[6] Phase-transfer conditions were used to add the dihalocarbenes to 1,6-dibromo-*trans*-3-hexene (*6*) to provide *bis*-(2-bromoethyl)cyclopropanes *7-9*. These compounds were allowed to react with sodium sulfide to generate the cyclic sulfides *10-12*. Our early studies involved high dilution conditions in ethanol as the solvent for this reaction. However, we found that these reactions could be run using normal concentrations with no appreciable change in yield provided dimethylformamide was substituted as the solvent.[7] Chlorination of the sulfides with N-chlorosuccinamide followed by oxidation with *m*-chloroperbenzoic acid gave the corresponding α-chlorosulfones *13-15*. Reaction of the α-chlorosulfones with potassium *tert*-butoxide in a Ramberg-Bäcklund reaction[8] provided the desired *trans*-bicyclo[4.1.0]hept-3-enes *3-5*.

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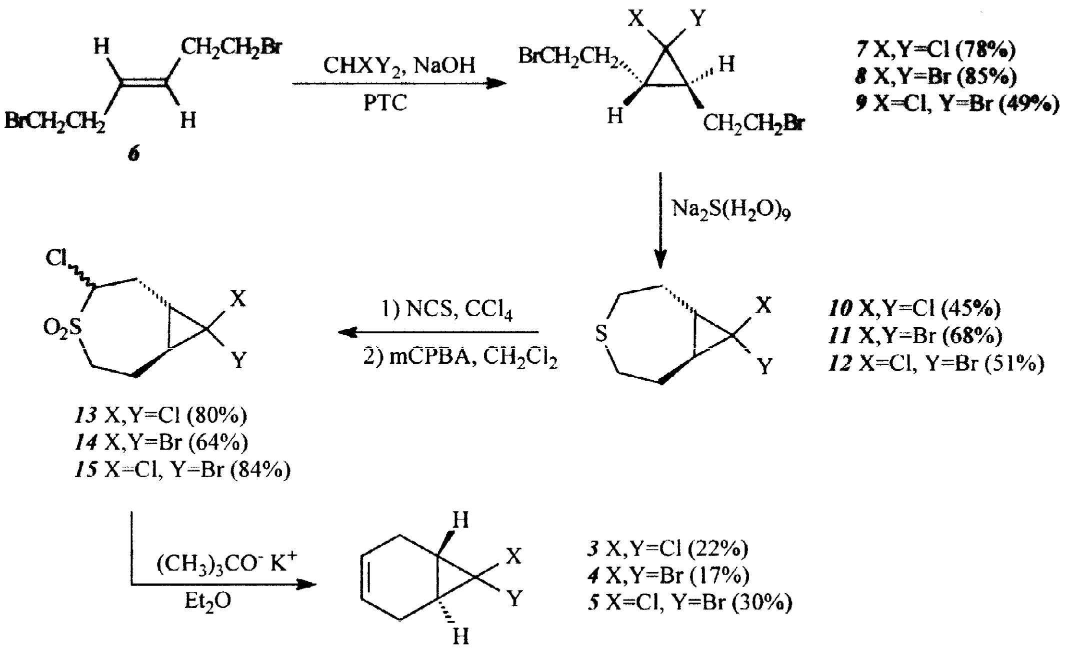
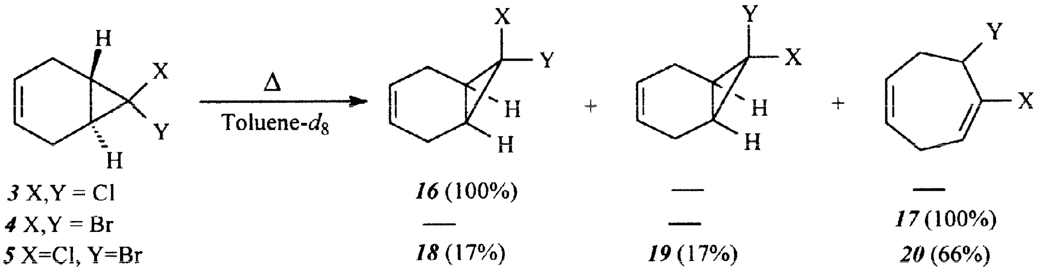
SCHEME 1



When ***3*** was heated at 75-105 °C in toluene-d_8 a clean isomerization to 7,7-dichloro-*cis*-bicyclo-[4.1.0]hept-3-ene (***16***) was observed. In contrast, dibromide ***4*** isomerizes at lower temperatures (50-70 °C), and the initially observed product is 1,7-dibromo-1,4-cycloheptadiene (***17***). Independent experiments showed that 7,7-dibromo-*cis*-bicyclo[4.1.0]hept-3-ene was stable under the conditions used to isomerize ***4***. Interestingly, compound ***5*** displayed intermediate reactivity. When this compound was heated in toluene-d_8 at temperatures ranging from 60-79 °C a 1:2 mixture of ring-isomerized to ring-opened products was observed. The migration of the bromine substituent and not chlorine in the ring-opening of ***5*** was determined by the similarity of the ^{1}H and ^{13}C NMR spectra for ***17*** and ***20***.[9] The cis fused isomers and compound ***20*** were stable under the thermolysis conditions, while compound ***17*** underwent further thermal reactions to give a mixture of products that were not characterized further.



The first-order rate coefficients for the rearrangement of compounds ***3-5*** were measured using variable temperature NMR kinetics. Measurement of the rates of isomerization at three different temperatures permitted us to obtain the Arrhenius parameters for these processes (Table 1). These values were used to obtain extrapolated rate constants for the isomerizations of ***3-5*** so that a comparison could be made to the reactivity of ***1***. As can be seen from the data in Table 1, halogen substitution at the 7 position causes a substantial increase in the thermal lability of ***1***. Rate accelerations approximately three orders of magnitude were observed, with bromine substitution leading to the most pronounced effect.

Table 1. Rate Coefficients and Arrhenius Parameters for the Thermal Rearrangement of *1* and *3-5*.

Cmpd	Temp (°C)	Rate (s^{-1})	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (eu)	k_{rel} @ 120 °C
1[a]	120	$1.19 \pm 0.01 \times 10^{-5}$	33.4 ± 1.7	3.5 ± 4.4	1
3	105	$1.8 \pm 0.1 \times 10^{-3}$	29.7 ± 0.5	7.1 ± 1.5	740
	90	$3.6 \pm 0.1 \times 10^{-4}$			
	75	$5.6 \pm 0.1 \times 10^{-5}$			
4	70	$6.8 \pm 0.1 \times 10^{-4}$	23.7 ± 0.5	-4.1 ± 1.5	5500
	60	$2.1 \pm 0.1 \times 10^{-4}$			
	50	$7.9 \pm 0.4 \times 10^{-5}$			
5	79	$2.9 \pm 0.2 \times 10^{-4}$	26.7 ± 0.5	0.8 ± 1.5	1500
	70	$1.0 \pm 0.1 \times 10^{-4}$			
	60	$2.9 \pm 0.1 \times 10^{-5}$			

[a]Data obtained from reference 4.

The formation of the ring-opened products in the thermal rearrangements of brominated compounds *4* and *5* is indicative of a cyclopropyl-allyl rearrangement that is symmetry-allowed by the Woodward-Hoffman rules.[10] The mechanism of this general type of reaction involves ionization and ring opening of the halogenated cyclopropane to an allyl cation followed by collapse of the ion pair to provide an allylic halide.[11] The ionic nature of these reactions is evident by a large solvent effect when the rearrangement is carried out in solvents of different polarity.[12,13] The rate coefficients for rearrangement of compounds *3-5* were examined in a variety solvents with a range of polarities in order to determine whether these particular reactions proceed *via* ionic intermediates (Table 2).

Table 2. Relative Rates of Isomerization for Compounds *3-5* in Various Solvents.

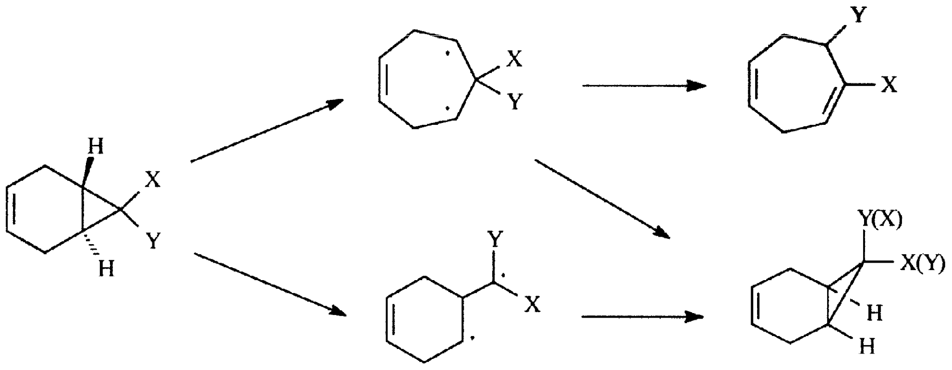
Cmpd	Solvent	Dielectric Constant (D)	Temp (°C)	Rate (s^{-1})	k/k(toluene-d_8)[a]
3	Nitrobenzene-d_5	34.6	75	$5.7 \pm 0.5 \times 10^{-5}$	1.0
	65:35 Dioxane-d_8:D_2O	45.7	75	$1.2 \pm 0.1 \times 10^{-4}$	2.2
4	Acetonitrile-d_3	37.5	70	$1.4 \pm 0.1 \times 10^{-3}$	2.0
	Methanol-d_4	32.6	70	1.8×10^{-4}[b]	2.7
5	Nitrobenzene-d_5	34.6	70	$1.9 \pm 0.1 \times 10^{-4}$	1.9
	Ethanol-d_6	24.3	70	$3.2 \pm 0.3 \times 10^{-4}$	3.2

[a]The dielectric constant of toluene is 2.4 D.

[b]This value was obtained from rate coefficients measured at lower temperatures.

The rather modest rate accelerations observed provide strong evidence against ionic intermediates for these reactions. In addition, the isomerizations of *4* and *5* performed in nucleophilic solvents still generated products *17* and *20*. Had an allylic cation intermediate been formed, then products corresponding to trapping of this species by the solvent would have been expected. The observation that compounds *4* and *5* do not undergo a symmetry-allowed ring opening is probably due to the fact that a disrotatory ring opening in these trans-fused cyclopropanes would form a highly strained cis-trans allyl cation within a seven-membered ring.

The proposed mechanism of isomerization for compounds *3-5* involves initial cleavage of either the bridgehead or peripheral bond of the three-membered ring. Ring-closure of the corresponding biradicals would lead to the cis-fused isomers, while a 1,2-shift of a bromine atom in the intermediate generated by cleavage of the bridgehead bond would produce the observed cycloheptadiene products.



The relatively weak carbon-bromine bond could account for only the brominated species leading to ring-opened products.

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