

On the Relation between Ring Size and Geometry of 2-Bromo-2-cycloalkenyl Acetates Formed from Dibromobicyclo[*n*.1.0]alkanes by Silver Acetate Catalyzed Reactions. Use of $^3J(\text{C-H})$ Couplings To Assign the Geometry of Trisubstituted Olefins

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As part of a study¹ of the chiroptical properties of medium-ring cycloalkenyl *p*-bromobenzoates, several *cis*- and *trans*-2-substituted 2-cycloalkenyl acetates were required. Reese and Shaw² have shown that (*Z*)-2-bromo-2-cyclooctenol and (*Z*)-2-bromo-2-cyclononenol can be conveniently prepared by silver perchlorate promoted solvolyses of the corresponding dibromobicyclo[*n*.1.0]alkanes in aqueous acetone. In order to obtain directly the desired acetates, we modified the Reese and Shaw procedure by reacting the dibromobicyclo[*n*.1.0]alkane with silver acetate in acetonitrile containing a small quantity of acetic acid (see Scheme I). We were surprised to find that compounds **1**, **2**, and **3** obtained under our conditions were not the anticipated *Z* isomers but instead the *E* stereoisomers. The reaction of silver acetate in acetonitrile containing acetic acid with higher homologues of dibromobicyclo[*n*.1.0]alkanes yielded 2-bromo-2-cycloalkenyl acetates in which the size of the ring appeared to influence the geometry about the double bond. The geometry of the double bond in two new compounds has been assigned from data on $^3J(\text{C-H})$ coupling constants obtained from

a new 2D NMR pulse sequence developed by Bax and Freeman.³

Results

A series of *gem*-dibromobicyclo[*n*.1.0]alkanes was prepared by the reaction of dibromocarbene with *cis*- and *trans*-olefins.⁴ Treatment with silver acetate in acetonitrile containing acetic acid afforded 2-bromo-2-cycloalkenyl acetates. Proton NMR spectra (220 MHz) of the crude reaction mixtures established the formation of a single 2-bromo-2-cycloalkenyl acetate; the presence of as little as 5% of the other isomer would have been observable. A comparison of the chemical shifts and splitting patterns of the olefinic proton in the purified acetates (**1a**, **2a**, and **3a**) shows them to be very similar. Enzymic hydrolysis⁵ converted the esters into the corresponding alcohols (**1b**, **2b**, and **3b**); the geometries of the latter were assigned as *E* by a comparison of proton NMR data with data in the literature.^{2,6} The chemical shifts of the methine protons of the allylic acetates **4a**, **5a**, and **6a** and the splitting pattern of the olefinic proton differed from those observed for **1a**, **2a** and **3a** (see Table I). Since compounds **5a** and **6a** were new, it was necessary to assign unambiguously the geometry about the double bond. Compound **4a** was likewise new, but NMR data for **4b** had previously been reported.^{2,6} However, for the reasons given below, the

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(5) (a) Kasai, M.; Kawai, K.; Imuta, M.; Ziffer, H. *J. Org. Chem.* 1984, 49, 675. (b) Ziffer, H.; Kawai, K.; Kasai, M.; Froussios, C. *Ibid.* 1983, 48, 3017.

Scheme I

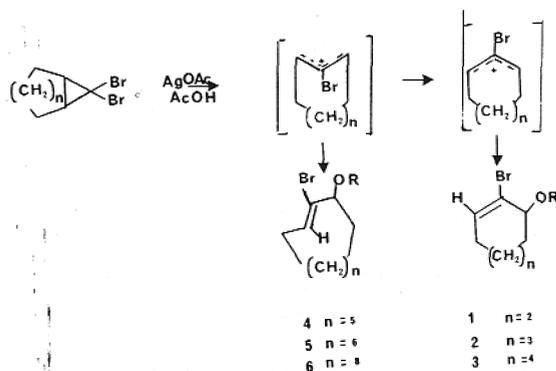


Table I. Chemical Shift and Coupling Constants of Olefinic and Methine Protons of 2-Bromo-2-cycloalkenyl Acetates

compd	ring size	olefinic H (mult, J values)	methine H
1a	7	6.42 (t, 6.5 Hz)	5.56 (br d, 7.5 Hz)
2a	8	6.21 (t, 8.5 Hz)	5.62 (dd, 11.0, 5.0 Hz)
3a	9	6.22 (t, 8.5 Hz)	5.74 (dd, 10.5, 5.0 Hz)
4a	10	6.26 (dd, 8.4, 6.4 Hz)	5.16 (dd, 9.2, 5.2 Hz)
5a	11	6.19 (dd, 9.0, 5.8 Hz)	5.17 (dd, 8.5, 5.0 Hz)
6a	13	6.10 (dd, 9.4, 5.4 Hz)	5.25 (dd, 10.2, 4.0 Hz)

assignment of the double-bond geometry appeared inconclusive. In a comprehensive study of the silver perchlorate catalyzed reactions of the dibromocarbene adducts of cycloheptene and cyclooctene, Reese and Shaw² provided an extensive discussion of methods available for assigning the stereochemistry of the carbon-carbon double bond in the products formed. In addition to using infrared spectroscopy and chemical reactivities, they employed NMR data on the relative chemical shifts of the methine proton in their alcohols to assign the geometry of the carbon-carbon double bond. The signal of the methine proton in the *E* isomer was reported to occur 0.3–0.75-ppm downfield from that of the corresponding *Z* isomer,² but since the geometric isomers of 5a and 6a were unknown, we were unable to use the relative chemical shift of the methine protons in assigning the geometry of the double bond. Furthermore, since changes in the ring size of these compounds markedly alter their conformations, it was possible that these changes would also affect the relative chemical shifts of the methine proton. Loozen et al.⁶ suggested that the geometry of the double bond in various 2-substituted 2-cycloalkenols could be assigned by NMR from the multiplicity of the signal from the olefinic proton. They found that the proton in the *E* isomers showed a triplet pattern while in *Z* isomers the pattern was a doublet of doublets.

In order to assign the geometry of the double bond in 4a, the compound was hydrolyzed by using *Rhizopus nigricans*⁵ and the NMR data for the resulting alcohol were compared with literature data.^{2,6} The comparison indicated that the alcohol had previously been assigned a *Z* geometry. However, the assignment was questionable since the reported pattern of the olefinic proton was a triplet. If Loozen et al. were correct in assigning the geometry of the double bond from the pattern of the olefinic proton, an *E* assignment was in order, but the relative chemical shifts of the methine proton in the two isomers requires a *Z* geometry. Thus, different geometric assignments can

Table II. Summary of $^3J(\text{C-H})$ Coupling Constants

compd	ring size	stereochemistry of olefin	$^3J(\text{C-H})$, Hz	geometry of C-H couplings
1a	7	<i>E</i>	8.8	trans
2a	8	<i>E</i>	8.5	trans
3a	9	<i>E</i>	8.9	trans
4a	10	<i>Z</i>	5.0	cis
5a	11	<i>Z</i>	4.7	cis
6a	13	<i>Z</i>	4.9	cis

be made depending upon whether the chemical shift differences of the methine proton or the pattern of the olefinic proton were used. Therefore, to resolve this uncertainty a new approach was developed.

In reviewing the literature on long-range proton-carbon coupling constants, Hansen⁷ has indicated that three-bond couplings have been used in studies of the conformation of amino acids. These couplings are sensitive to the substitution pattern, the electronegativity of the substituents, their position along the coupling path, and the geometric relationship of the atoms in question. Vogeli and von Philipsborn⁸ have shown that the numerical value of trans couplings ($^3J(\text{C-H})$) (see top of Figure 1a) are larger than those of cis couplings between the same substituents (Figure 1b). Thus, in our series of compounds an *E* olefin should exhibit a large proton-carbon coupling constant. While the size of the long-range proton-carbon coupling constant (olefinic proton and the carbon bearing an acetoxy group) could in principle establish the geometry about the double bond, the measurement has been difficult to make by conventional techniques. Recently, however, Bax and Freeman⁹ reported a new NMR technique that is specifically designed to facilitate such measurements. This so-called selective proton flip experiment, a low power 180° proton pulse is employed to invert selectively, all resonance lines of a particular multiplet (olefinic proton in these compounds). In the resulting two-dimensional spectrum, resonances from ^{13}C nuclei that are not coupled to the olefinic proton appear as singlets, while the resonances from ^{13}C nuclei which are coupled with J values of 0 to 25 Hz show as doublets in the F1 dimension of the 2D NMR spectrum. The method is sensitive, since nuclear Overhauser enhancement is obtained and the carbon resonances appear as either singlets or doublets. Moreover, with this method it is unnecessary to assign the many long-range proton-carbon coupling constants present in ^1H -coupled ^{13}C spectra thus providing tremendous simplification. The observed patterns for the *E* olefin and the *Z* isomer are shown in Figure 1.⁹ Values of the proton-carbon coupling constants (Table II) demonstrate that for the olefins bearing a bromine atom, cis- $^3J(\text{C-H})$ varies from 4.7 to 5.0 Hz, while the trans value varies from 8.5 to 8.9 Hz. These values are consistent with the work of Vogeli and von Philipsborn and require a *Z* geometry for our 2-bromo-2-cyclodecenols in agreement with the earlier assignment. Since there is no overlap in the numerical values for $^3J(\text{C-H})$ coupling constants in the *E* and *Z* isomers, information on the size of these coupling constants can be used to assign the geometry of trisubstituted olefins. The numerical values of these coupling constants in olefins with different substituents may differ somewhat from those reported here.¹¹

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(8) Vogeli, U.; von Philipsborn, W. *Org. Magn. Reson.* 1975, 7, 617.

(9) During a study of the chiroptical properties of *p*-bromobenzoates of these allylic alcohols, it became necessary to assign the absolute stereochemistry of (+)-5b. An X-ray crystallographic analysis of the camphanate ester confirmed the trans geometry of the double bond in 5a.¹

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(6) (a) Loozen, H. J. J.; Robben, W. M. M.; Richter, T. L.; Buck, H. M. *J. Org. Chem.* 1976, 41, 384. (b) Loozen, H. J. J.; de Haan, J. W.; Buck, H. M. *J. Org. Chem.* 1977, 42, 418.

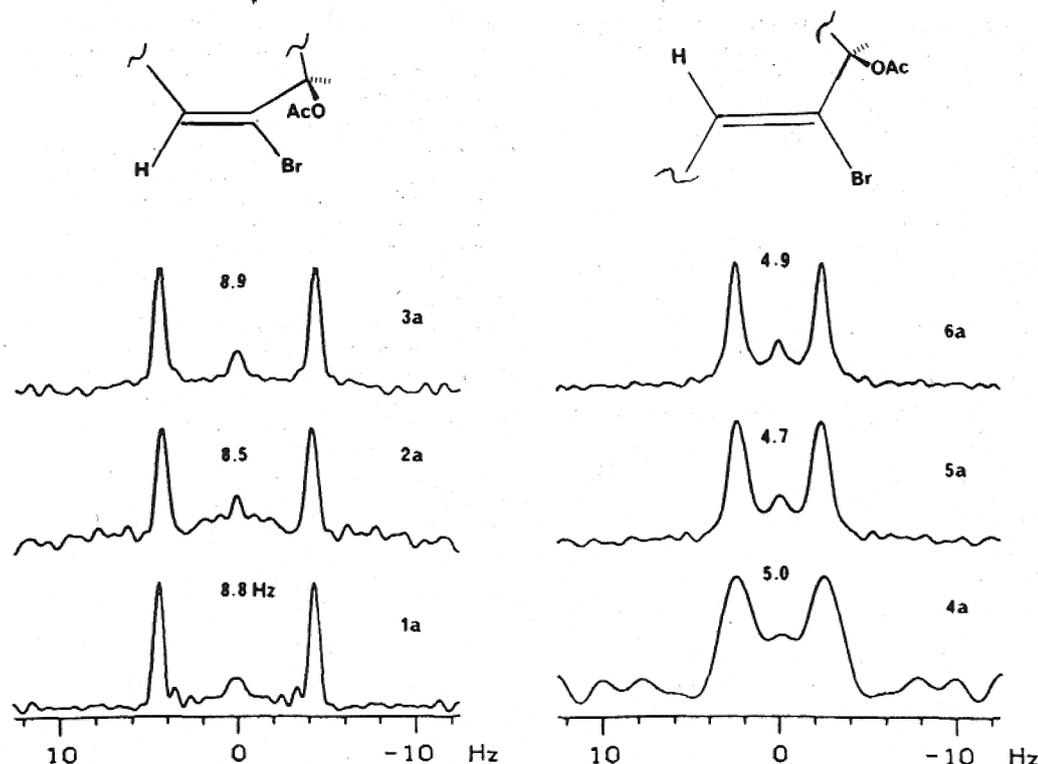


Figure 1. The relation between the geometry about the double bond and the size of $^3J(\text{C}-\text{H})$. Each of the doublets represents a cross-section through the 2D selective proton-flip NMR spectrum, taken parallel to the F_1 axis at the F_2 frequency of the brominated olefinic carbon. The measuring times for the 2D spectra was approximately 1 h each.

Table III. Comparison of ^1H Chemical Shift Values (ppm) for 2b, 3b, and 4b with Literature Values (Coupling constants are given in hertz)

proton	<i>E</i> isomer		<i>Z</i> isomer
		2b	
methine	4.71 (dd, $J = 10, 5$) ⁶	4.65 (bd, $J = 10$)	4.18 (dd, $J = 5, 10$) ⁶
olefinic	6.21 (t, $J = 8.5$)	6.17 (t, $J = 9.5$)	6.11 (dd, $J = 4.5, 10.5$)
		3b	
methine	4.71 (dd, $J = 5, 10$)	4.72 (dd, $J = 7.5, 8.5$)	4.18 (dd, $J = 5, 10$)
olefinic	6.18 (t, $J = 11$)	6.17 (t, $J = 9.0$)	6.11 (dd, $J = 5, 10$)
		4b	
methine	4.82 (t, $J = 8$) ⁶	4.12 (br m)	4.18 (dd, $J = 9, 5$) ⁶
olefinic	5.98 (dd, $J = 12, 6$)	6.21 (dd, $J = 6.4, 7.6$)	6.24 (t, $J = 9$)
methine	4.67 (dd, $J = 6, 9$) ²		4.07 (dd, $J = 5, 8$) ²
olefinic	5.86 (dd, $J = 5, 12$)		6.18 (t, $J = 8$)

Discussion

The early studies^{2,6} of silver ion promoted reactions of dibromocyclopropane derivatives were done at a time when there was considerable interest in concerted reactions. The reaction conditions employed by Reese and Shaw and others generated the less stable *Z* double-bond isomers and were therefore consistent with expectations for concerted reactions. Several compounds prepared by Loozen et al.⁶ were assigned as *Z* primarily upon these expectations. However, an examination of NMR data published by these authors reveals inconsistencies between the splitting pattern of the olefinic proton and the assigned geometries about the double bond. Data on $^3J(\text{C}-\text{H})$ coupling constants could be used to verify the earlier assignments.

Studies of Loozen et al.⁶ and Shaw and Reese² demonstrated clearly that both *E* and *Z* isomers are formed from dibromobicyclo[7.1.0]decane; the results were best explained by assuming formation of intermediate free cations that could isomerize (*Z* → *E*) or react with nucleophiles

(see Scheme I). Furthermore, Sandler¹⁰ reported that the same product, a *trans*-pentadiene, is formed from the reaction of two isomeric 1,1-dibromo-2,3-dimethylcyclopropanes with silver acetate in acetic acid, but oddly enough the logical inferences of this observation were not pursued. While the importance of this observation was not apparent at the start of our studies, it is entirely consistent with the postulate that these silver acetate and acetic acid catalyzed reactions probably proceed via free cations rather than via concerted reactions. Although our reaction conditions differ from those employed by Sandler, Shaw and Reese, and Loozen et al., these authors also have employed polar solvents. Therefore, the differences in the geometry of the cyclooctene and cyclononene derivatives formed in their studies and ours probably do not reflect different reaction mechanisms but rather may arise only from differences in the rates of the isomerization of the *Z* cation and the reaction rates of each cation with acetate. The *Z* geometries of the 11- and 13-membered 2-cycloalkenyl acetates also differ from that anticipated for a concerted reaction where the predominant isomer should have been the (*E*)-2-bromo-2-cycloalkenyl acetate. All our

(11) Hight¹² has recently described a procedure for obtaining these coupling constants with a simpler spectrometer.

observations are consistent with the postulate that the reaction rate of acetate with the carbocation is relatively slow in comparison with that by which the initially formed ion isomerizes to the more stable one. Calculations and experimental data on the heats of hydrogenation¹³ indicate that cyclic cis olefins with nine or fewer carbons are more stable than the corresponding trans isomer. For cyclodecene and larger cyclic olefins the trans compound is the more stable. Our results on the geometry of the allylic acetate formed in these reactions as a function of ring size parallel the calculated and experimentally observed stabilities of the most stable cyclic olefins.

Conclusion

This study has shown that it is possible to control the stereochemistry of the eight- and nine-membered olefins formed from silver ion promoted solvolyses of the same intermediates by modifying the reaction conditions. Our results suggest that these solvolyses yield the most stable cycloalkenes. Three-bond proton-carbon coupling constants, obtained using the selective proton-flip experiment, have been shown to permit a facile assignment of the geometry of trisubstituted olefins. Since three-bond proton-carbon coupling constants have been shown to be useful for stereochemical assignments increased use of this NMR technique may be anticipated.

Experimental Section

EI-mass spectra were obtained by the NIH microanalytical laboratory. ¹H NMR spectra were collected on a Varian H-220 spectrometer, and ¹³C NMR spectra were measured with a Nicolet 270 spectrometer (67.8 MHz). CDCl₃ was used for measuring ¹H NMR spectra and acetone-*d*₆ for ¹³C NMR spectra.

Dibromocyclopropane derivatives were prepared by the procedure of Skottebol and Solomon.⁴ General procedure for silver ion catalyzed solvolysis: An acetonitrile solution (5 ml) of the dibromo compound (5 mmol) was heated in the presence of 1.1 equiv of AgOAc and 1 mL of AcOH on a steam bath for 2 h. The solution was filtered and the precipitate washed with ether. The combined filtrates were washed with aqueous NaHCO₃, dried, and concentrated. The crude acetates were purified by column chromatography on silica gel.

(Z)-2-Bromo-2-cyclodecen-1-yl Acetate (4a). Cyclononene was prepared from cyclononene (5 g) by reduction with sodium borohydride in methanol to yield cyclononanol, which was dehydrated at 170 °C, by heating with 85% H₃PO₄ for 1 h. The

reaction mixture was cooled, diluted with water, and extracted into hexane. The hexane solution was passed through silica gel to remove polar impurities. The crude olefin (3.17 g) was used to prepare dibromobicyclo[7.1.0]decane (2.48 g, bp 129–134 °C/2.6 torr) by treatment with potassium *tert*-butoxide and bromoform as described by Skottebol and Solomon.⁴ Solvolysis of the dibromobicycloalkane with AgOAc, MeCN, and AcOH as described above yielded, after chromatography on silica gel, 731 mg of 4a: colorless oil; EI-MS, found 195.1384 (C₁₂H₁₉O₂, M⁺ - Br); ¹H NMR 1.06–1.84 (m, 12 H), 2.08 (s, 3 H), 2.06–2.23 (m, 1 H), 2.25–2.45 (m, 1 H), 5.16 (dd, *J* = 5.2, 9.2 Hz, 1 H), 6.26 (dd, *J* = 6.4, 8.4 Hz, 1 H).

(Z)-2-Bromo-2-cycloundecen-1-yl Acetate (5a). Cyclodecene was prepared by heating cyclodecanol (obtained from sodium borohydride reduction of the ketone) with 85% H₃PO₄ at 170 °C for 1 h. The crude olefin was isolated and reacted with potassium *tert*-butoxide and bromoform as described above. Solvolysis of the crude dibromobicyclo[8.1.0]undecane as described above yielded after chromatography a sample of pure 5a: colorless oil; EI-MS found 209.1525 (C₁₃H₂₁O₂, M⁺ - Br); ¹H NMR 1.06–1.88 (m, 14 H), 2.09 (s, 3 H), 2.23 (m, 1 H), 2.48 (m, 1 H), 5.17 (dd, *J* = 8.5, 5.0 Hz, 1 H), 6.19 (dd, *J* = 9.0, 5.8).

(Z)-2-Bromo-2-cyclotridecen-1-yl Acetate (6a). Commercial *trans*-cyclododecene was used in the reaction sequence described above to prepare (*E*)-2-bromo-2-cyclotridecen-1-yl acetate (6a): colorless oil; EI-MS found 237.1857 (C₁₅H₂₅O₂, M⁺ - Br); ¹H NMR 1.12–1.53 (m, 15 H), 1.57–1.78 (m, 2 H), 1.81–1.99 (m, 1 H), 2.06 (s, 3 H), 2.09–2.25 (m, 1 H), 2.28–2.47 (m, 1 H), 5.25 (dd, *J* = 4.0, 10.2 Hz, 1 H), 6.10 (dd, *J* = 9.4, 5.4 Hz, 1 H).

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Registry No. 1, 14310-05-5; 2, 100206-51-7; 3, 100296-00-2; 4, 100206-52-8; 5, 100206-53-9; 6, 100206-54-0; AgOAc, 563-63-3; 7,7-dibromobicyclo[4.1.0]heptane, 2415-79-4; 8,8-dibromobicyclo[5.1.0]octane, 7124-41-6; 9,9-dibromobicyclo[6.1.0]nonane, 1196-95-8; 10,10-dibromobicyclo[7.1.0]decane, 36262-23-4; 11,11-dibromobicyclo[8.1.0]undecane, 64480-09-7; 13,13-dibromobicyclo[10.1.0]tridecane, 17301-57-4; cyclononene, 100206-56-2; cyclononanol, 24469-56-5; cyclononene, 3618-11-9; cyclodecene, 100206-55-1; cyclodecanol, 1724-39-6; cyclodecene, 3618-12-0; *trans*-cyclododecene, 1486-75-5.

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