Acknowledgment. We thank the University of Toronto and the Natural Sciences and Engineering Research Council, Ottawa, for support of this work.

Registry No. $Mn_2(CO)_{10}$, 10170-69-1; CCl_4, 56-23-5; $Mn(CO)_5Cl$, 14100-30-2; BA, 431-03-8; $Re_2(CO)_8(PPh_3)_2$, 14172-94-2; $Re_2(CO)_{10}$, 14285-68-8; O_2, 7782-44-7.

Definitive Evidence for Cycloheptatetraene from Dehydrobromination of Bromocycloheptatrienes

James W. Harris and W. M. Jones*

Department of Chemistry, University of Florida Gainesville, Florida 32611

Received June 4, 1982

Thermolysis or photolysis of the tosylhydrazone salt of tropone in the presence of styrene gives the cyclopropane product **5**[1] (Scheme I). In the presence of 1,3-diphenylbenzo[*c*]furan, thermolysis[2] gives the adduct **6**. Dehydrobromination of the mixture of bromocycloheptatrienes **4** with base in the presence of the same two acceptors gives the same adducts.[3,4] As photolysis or thermolysis of tosylhydrazone salts typically leads to carbenes[5] and since cyclopropanes are typical carbene–olefin adducts,[5] it has been assumed that **5** arises from addition of the carbene to styrene. Likewise dehydrobromination of bromocycloheptatrienes such as **4** would be expected to occur by β and vinylogous β eliminations[6] to give the allene **3**. Furthermore, adduct **6** is that expected of Diels–Alder addition of an allene to the diene. It has therefore been quite reasonably assumed that **6** arises from the allene **3**. Finally, since both adducts **5** and **6** are formed from both **1** and **4**, it has ben presumed that the intermediates are interconvertible and that both are formed from each precursor.

Unfortunately, as clean as this picture may appear at first sight, on further reflection it loses its crispness. In the first place, as originally pointed out by Waali,[6] both **5** and **6** could originate from a single intermediate, the allene; the latter by a Diels–Alder reaction and the former by an allowed ($\pi^2s + \pi^8s$) cycloaddition by using the termini of the eight-electron conjugated allene π system. He has recently extended this argument with MNDO/3 calculations from which he has concluded that cycloheptatrienylidene does not represent an energy minimum; instead it is the transition state for the interconversion of enantiomeric allenes. As such, of course, it is not available for biomolecular chemistry. On the other hand, in principle the carbene could also be the sole intermediate responsible for biomolecular chemistry since it not only could cycloadd as a typical carbene to give **5** but could also add to one double bond of the furan to give an adduct that could rapidly rearrange to **6**.[1]

In this communication we report experimental data that unequivocally answer some but not all of the above questions. Our results prove the following: (a) dehydrobromination of the bromocycloheptatrienes gives an intermediate that is best represented by the allene structure; (b) this is the intermediate that is responsible for adduct **6**. We also report weak evidence that favors a carbene as the progenitor of the spirononatriene **5**.

Scheme I

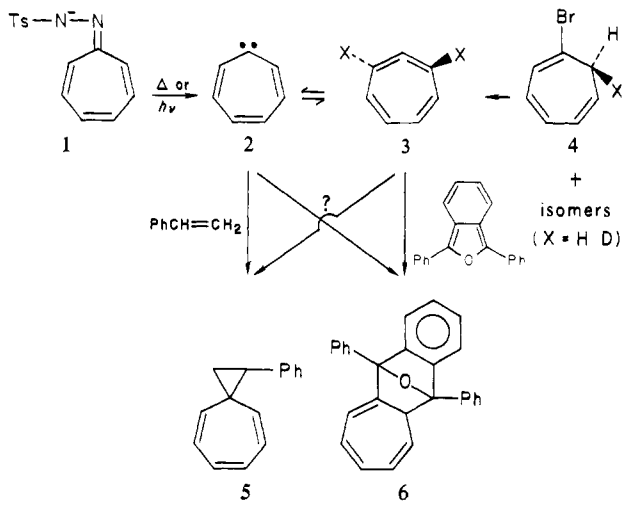


Table I. Specific Rotations of Allene Adducts

bromocycloheptatrienes[a]	base	solvent	T, °C	$[\alpha]^{25}D$,[b] deg
4, X = H	potassium menthoxide	THF	0	3.40
4, X = H	potassium menthoxide	THF	45	2.60
4, X = H	potassium menthoxide	THF	65	0.74
4, X = D	potassium *tert*-butoxide	THF	25	−1.84
4, X = D	potassium *tert*-butoxide	THF	53	−1.38
4, X = D	potassium *tert*-butoxide	diglyme	100[c]	−0.60

[a] A mixture of 1-, 2-, and 3-bromocycloheptatrienes was used for all runs. [b] Rotations were measured in methylene chloride by using a 1.0-dm polarimeter cell. Sample sizes were typically about 100 mg and gave observed rotations of about 0.100–0.200 ± 0.002°. Repetitive runs showed deviations in specific rotation of 0.15° or less. The rather large deviation is believed to be due to the presence of small amounts of the exo isomer as a contaminant to the primary endo adduct. The former could not be separated by standard chromatography methods. The presence of this contaminant vitiates any conclusions based on changes in rotation. However, conclusions based solely on the presence or absence of rotation should be secure since there was no other detectable contaminant. [c] Optically active adduct did not racemize under these conditions.

Our approach was the same as that used to probe the structure of 1,2-cyclohexadiene, 1,2-cycloheptadiene, and 2,3,6-bicyclo[3.2.1]octatriene:[8] chirality. Since **3** is chiral and **2** is achiral, only the allene could give an optically active adduct **6**. The problem, then, was to generate the intermediate under conditions where by (assuming the allene structure) an excess of one of the enantiomers would be formed. To accomplish this, we used two approaches. In the first, a THF solution of a mixture of bromocycloheptatrienes **4** (X = H) was allowed to react with the potassium salt of menthol. The resulting adducts were isolated and, indeed, found to be active (Table I). This result suggested the allene as the intermediate but was not unequivocal because the presence of menthol (either free or as the salt) could create a chiral environment during the cycloaddition (although probably not[8b]). We therefore used a second less equivocal approach. In this case a primary deuterium isotope effect was used to lead to an enantiomeric excess of the intermediate. Thus, a mixture of optically active monodeuteriobromocycloheptatrienes (**4**, X = D; typical $[\alpha]^{25}D$ −0.164°) was prepared by reducing bromotropylium bromide with $LiAlD_3$-quinine.[9] Since cis elimination of DBr from,

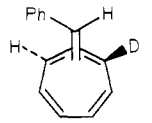
(1) Cf.: Waali, E. E.; Jones, W. M. *J. Am. Chem. Soc.* **1973**, *95*, 8114.
(2) Saito, K.; Omura, Y.; Mukai, T. *Chem. Lett.* **1980**, 349.
(3) Untch, K.; Matthews, G.; Hylton, T. *Int. Symp. Chem. Nonbenzenoid Aromatic Comp., 1st* **1980**.
(4) Duell, B. L.; Jones, W. M. *J. Org. Chem.* **1978**, *43*, 4901; unpublished results of B. L. Duell.
(5) Cf.: Kirmse, W. "Carbene Chemistry", 2nd ed.; Academic Press: New York, 1971.
(6) Waali, E. E.; Lewis, J. M.; Lee, D. E.; Allen, E. W., III; Chappel, A. K. *J. Org. Chem.* **1977**, *42*, 3460. Mayor, C.; Jones, W. M. *Tetrahedron Lett.* **1977**, 3855.
(7) Also see: Waali, E. E. *J. Am. Chem. Soc.* **1981**, *103*, 1980.
(8) (a) Balci, M.; Jones, W. M. *J. Am. Chem. Soc.* **1980**, 102, 7607. (b) Balci, M.; Jones, W. M. *J. Am. Chem. Soc.* **1981**, *103*, 2874.

0002-7863/82/1504-7329$01.25/0

e.g., **4** (X = D) would give one enantiomer while elimination of HBr would give the other, the primary isotope effect should lead to an excess of one enantiomer over the other. Indeed, treatment of the mixture of bromocycloheptatrienes with potassium *tert*-butoxide in THF in the presence of the furan gave optically active adduct **6** (Table I). We take these results as unequivocal evidence for a chiral intermediate as the progenitor of adduct **6**.

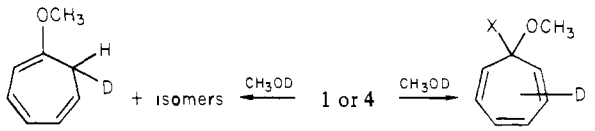
The effect of change in temperature[8] on the specific rotation of the adduct is also recorded in Table I. However, as described in footnote b of Table I, the endo adduct could not be separated from small (and varying) amounts of exo isomer. As a result, the only valid conclusion from these results is that up to 100 °C at least some of the activity persists. This requires that if the allene is competitively racemizing, at least some is bled off before complete racemization occurs.

In principle, chirality might also be used to assign the structure of the precursor to the spirononatriene. Thus, if styrene traps cycloheptatetraene in an allowed ($\pi^2s + \pi^8s$) reaction, the mode of attack on the double bond should be as pictured in **7**. Furthermore, solely on the basis of steric arguments, the phenyl ring would have a favored orientation; most likely the one shown. If this is the case, then optically active allene should give an excess of one enatiomeric transition state and the resulting spirononatriene (**5**) should be optically active. Of course, the achiral carbene would give racemic adduct.



7

The optically active bromide (**4**, X = D) was therefore treated with potassium *tert*-butoxide in the presence of styrene at −30 °C (to maximize asymmetric induction) for 5.5 h. The resulting spirononatriene (**5**) showed NO rotation (α_{obsd} 0.002 ± 0.002°; $[\alpha]^{25}_D$ 0.018°; limit of experimental method). This result must be taken as preliminary (a more sterically demanding system needs to be studied) and, admittedly, is negative evidence. Nonetheless, it is the result that would be expected if the carbene is the intermediate being trapped. At this point it should also be mentioned that Kirmse[10] has very recently reported that the intermediate from either **1** or **4** is trapped by alcohols to give **8**. This is the product expected of a carbene but not a strained cyclic allene, which should give **9**.[11]



+ isomers 9

8, X = H or D

Acknowledgment. We gratefully acknowledge financial support from the National Science Foundation. We are also indebted to Professor Ronald Breslow of Columbia University for a conversation that led to using chirality as a probe to distinguish between the structures discussed in this manuscript.

Registry No. **1**, 83527-70-2; **2**, 17476-70-9; (+)-**3**, 83527-68-8; (−)-**3**, 83527-69-9; **4** (X = H), 32743-67-2; **4** (X = D), 83527-67-7; **5**, 50517-62-9; **6**, 83572-17-2; $PhCH{=}CH_2$, 100-42-5; 1,3-diphenylbenzo[*c*]furan, 5471-63-6; 2-bromocycloheptatriene, 3046-02-4; 3-bromocycloheptatriene, 3046-03-5; 7-deuterio-2-bromocycloheptatriene, 83527-71-3; 7-deuterio-3-bromocycloheptatriene, 83527-72-4; potassium methoxide, 865-33-8; potassium *tert*-butoxide, 865-47-4.

(9) Cervinka, O. *Collect. Czech. Chem. Commun.* **1965**, *30*, 1684, 2403.
(10) Kirmse, W.; Loosen, K.; Sluma, H. D. *J. Am. Chem. Soc.* **1981**, *103*, 5935.
(11) Mohanakrishnan, P.; Toyal, S. R.; Vaidyanathaswamy, R.; Devaprabhakara, D. *Tetrahedron Lett.* **1972**, 2871. Bottini, A. T.; Anderson, B. *Ibid.* **1973**, 3321.

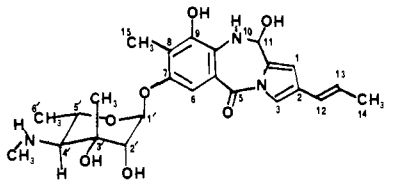
Revision of Assignment of Structure to the Pyrrolodiazepinone Antitumor Antibiotic Sibiromycin

Kathlyn A. Parker* and Robert E. Babine†

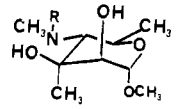
Department of Chemistry, Brown University
Providence, Rhode Island 02912

Received August 9, 1982

Studies directed toward the synthesis of sibiromycin recently led us to revise the structure of the carbohydrate portion of this antitumor antibiotic.[1] Further comparison of the synthetic material derived from the natural product and examination of the spectroscopic properties of anhydrosibiromycin now allow us to reassign the structure of sibiromycin as the α-L-glycoside **1**.



1



2a R=H
2b R=Tos

Sibiromycin was obtained from a culture of *Streptosporangium sibiricum* (American Type Culture Collection, original specimen contributed by Gause)[2] grown as outlined by Hurley.[3] Degradation[4] followed by tosylation[1] and isolation by flash chromatography gave material that proved to be levorotatory,[5] whereas compound **2b** (synthetic, from D-glucose) was dextrorotatory. We conclude therefore that natural sibirosamine is L-4,6-dideoxy-3-*C*-methyl-4-(methylamino)mannose. The large negative rotational shift observed by Mesentsev when tetraminecopper(II) sulfate was added to methyl sibirosaminide[4,6] is consistent with this assignment.

We were able to address the question of anomeric configuration (previously assigned β[7]) by comparison of the nuclear Overhauser effects of the axial C-3′ methyl group on the axial C-5′ proton and the anomeric C-1′ proton in anhydrosibiromycin (N-10, C-11 anhydro).[8,9] NOE difference spectroscopy[10,11] (irradiation of C-3′ methyl resonance at δ 1.35) indicated enhancement of the signals for H-2′ (δ 3.87) and H-5′ (δ 3.74) but not for H-1′ (δ 5.74). Therefore we conclude that sibiromycin is an α-glycoside.

Finally, we sought to verify the original designation of the natural product as a C-7 (rather than C-9) glycoside by spectroscopic means.[12] The selectively decoupled ^{13}C NMR spectrum

† Present address: American Cyanamid Co., Medical Research Division, Lederle Laboratories, Pearl River, NY 10965.

(1) Parker, K. A.; Babine, R. E. *Tetrahedron Lett.* **1982**, *23*, 1763 and references therein.
(2) The American Type Culture Collection, *Catalog of Strains I*, 13th ed.; Rockville, MD, 1978; p 175, catalog no. ATCC 29053.
(3) Hurley, L. H.; Lasswell, W. L.; Malhotra, R. K.; Parry, R. *Biochemistry* **1979**, *18*, 4225.
(4) Mesentsev, A. S.; Kuljaeva, V. V. *Tetrahedron Lett.* **1973**, 2225.
(5) Optical rotation data: methyl *N*-tosyl α-sibirosaminopyranoside. Synthetic **2b** from D-glucose[1] (*c* 1.56, $CHCl_3$): +62° (589 nm), +73° (578 nm), +81° (546 nm), +138° (436 nm), +211° (365 nm). Degradation product, from sibiromycin (*c* 0.08, $CHCl_3$): −54° (589 nm), −65° (578 nm), −78° (546 nm), −162° (436 nm), −202° (365 nm).
(6) Umezawa, S.; Tsuchija, T.; Tatsuta, K. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1235.
(7) Mesentsev, A. S.; Kuljaeva, V. V.; Rubasheva, L. M. *J. Antibiot.* **1974**, *27*, 866.
(8) The studies described below were carried out on anhydrosibiromycin, which may be obtained as very clean (but noncrystalline solid) material; sibiromycin itself is difficult to purify. H-4′ and H-5′ must be axial because of the large coupling (J = 9.6 Hz) between them. Also the C-3′ methyl must be trans to the C-4′ proton because methyl *N*-tosyl-α-D-sibirosaminide is prepared by 3,4-epoxide opening with the sodium salt of *N*-methyltosylamide.[1] Therefore the C-3′ methyl group is necessarily axial in anhydrosibiromycin.
(9) Refer to Table I for complete ^1H NMR data.
(10) Hall, L. D.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1980**, *102*, 5703.
(11) All spectra discussed in this paper were measured in a Bruker WM 250 NMR spectrometer.
(12) We felt it was necessary to check the previous assignment, which was based on the failure to observe reaction of the phenolic hydroxyl of anhydrosibiromycin with diazomethane.

0002-7863/82/1504-7330$01.25/0