scan width (deg) 3.3 + 1.0 tg θ]. The total number of reflections measured was 3315, of which 2648 had an intensity greater than the standard deviation estimated from counting statistics. The solution and refinement of the crystal structure are based on the latter reflections. The structure was solved by direct methods[14] and refined by full-matrix least squares[15] to a final R factor of 5.5%. All hydrogen atoms were found from Fourier difference syntheses. The number of parameters refined in the last cycles was 316 (scale factor, extinction parameter, positional parameters of all atoms, anisotropic thermal parameters for non-hydrogen atoms, isotropic thermal parameters for hydrogen atoms). The figure was produced by ORTEP.[16]

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Registry No. 1, 67395-20-4; 3, 82281-38-7; 4, 7182-08-3; 5, 82281-39-8; 6a, 31401-28-2; 6b, 31554-37-7; 6c, 7007-34-3; 6d, 31401-27-1; 6e, 25579-44-6; 7a, 82281-40-1; 7b, 82281-41-2; 7e, 82281-42-3; 8c, 82281-43-4; 8d (isomer 1), 82281-44-5; 8d (isomer 2), 82281-45-6; 8e (isomer 1), 82281-46-7; 8e (isomer 2), 82281-47-8.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

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Cope and 1,3-Allylic Rearrangements and Ring Closure of the 1,5-Hexadiene Radical Cation Prior to Decomposition in the Gas Phase

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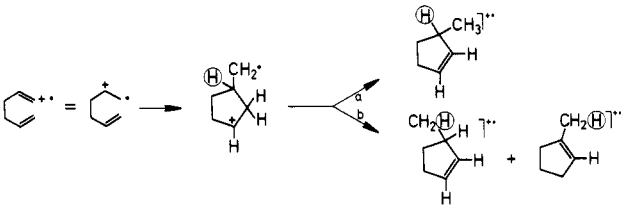
The chemistry of neutral 1,5-hexadiene (1) has been studied extensively. It undergoes the well-known (degenerate) Cope rearrangement under thermal conditions.[1] Facile transformations occur upon irradiation, and depending on the photochemical conditions allylcyclopropane[2] and bicyclo[2.1.1]- and [2.2.0]hexane[3] may be formed. Isotopic separation of deuterated 1 in favor of deuterium situated in the external vinyl sites has been demonstrated with infrared laser;[4] deuterium in the allylic positions, however, is favored under thermal conditions.[5]

In contrast, recent electron impact studies indicate a chemical inertness of the radical cation of 1 ($1^{+\cdot}$). It was shown by photodissociation spectroscopy that $1^{+\cdot}$ remains as an unconjugated diene at low internal energies.[6] Comparison of the heat of formation[7] of $C_5H_7^+$ ions formed by $CH_3\cdot$ loss from isomeric C_6H_{10} radical cations (ions of m/z 67 give rise to base peak in the normal mass spectra of C_6H_{10} isomers[8]) and the kinetic energy release (T)[9] associated therewith showed that $1^{+\cdot}$ among its linear isomers forms the cyclopentenyl cation with the lowest excess energy and smallest T value.[10] This result is in accord with the photodissociation results insofar as $1^{+\cdot}$ cannot isomerize to another linear diene prior to decomposition. The collisional activation mass spectra[11] of C_6H_{10} isomers confirmed that nondecomposing $1^{+\cdot}$ has no or only little resemblance with the radical cations of 1,3-, 1,4-, and 2,4-hexadiene, cyclohexene, and 1-methylcyclopentene.[12]

Scheme I



In light of the apparent retention of structure of $1^{+\cdot}$, this work is concerned with how the cyclopentenyl cation is formed therefrom.

It is necessary to consider which isomeric $C_6H_{10}^{+\cdot}$ ions have heats of formation lying below the energy required for fragmentation of $1^{+\cdot}$ by $CH_3\cdot$ loss and which can display similar kinetic energy release characteristics. From our previous studies,[10,13] these can be reduced to cyclohexene, 2-methyl-1,4-pentadiene, and methylcyclopentene (and methylenecyclopentane); see Table I.

Isomerization of $1^{+\cdot}$ to the cyclohexene radical cation is not likely to occur, because it would involve the formation of bicyclo[2.2.0]hexane$^{+\cdot}$ in the first step, a process having an energy barrier of 16 kcal mol^{-1} (see Table I). Loss of ethylene is an abundant process of the cyclohexene radical cation (RDA elimination),[8] while it is nearly absent in the normal mass spectrum and in the metastable time frame of $1^{+\cdot}$, thus further disfavoring an isomerization.[14]

Ionized 2-methyl-1,4-pentadiene also cannot be involved in the behavior of $1^{+\cdot}$, because the kinetic energy release for the random statistical losses of the deuterium-labeled methyl radicals from 2-methyl-1,4-pentadiene-1,1-$d_2$$^{+\cdot}$ was twice as large as that observed for the unlabeled compound,[13] while this is not the case with labeled 1,5-hexadienes (see also note 23).

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(8) A. Cornu and R. Massot, "Compilation of Mass Spectral Data", 2nd ed., Vol. I, Heyden, London, 1975.
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Table I. Heats of Formation of Some $[C_6H_{10}]^{+\cdot}$ and $[C_5H_7]^+$ Ions and the Kinetic Energy Release ($T_{0.5}$) Associated with the Formation of the Latter

compound	$\Delta H_f[M^{+\cdot}]$, ±1.0 kcal mol^{-1}	$\Delta H_f[(C_5H_7^+]$, ±1.0 kcal mol^{-1}	$T_{0.5}$, meV
1,5-hexadiene[a]	234	202	21.6
3-methylcyclopentene[b]	208	199	17.1
cyclohexene[b]	205	201	17.5
2-methyl-1,4-pentadiene[b]	228	200	18.1
bicyclo[2.2.0]hexane[c]	250 ± 2		
allylcyclopropane[d]	221	211	27.8 ± 1.2

[a] Reference 10. [b] Reference 13 and F. P. Lossing and J. C. Traeger, *Int. J. Mass Spectrom. Ion Phys.*, 19, 9 (1976). [c] IE = 9.6 eV (G. Biene, E. Heilbronner, and T. Kobayshi, *Helv. Chim. Acta*, 59, 2657 (1976); ΔH_f(neutral) = 28.8 kcal mol mol^{-1} estimated by additivity (S. W. Benson, "Thermochemical Kinetics", 2nd ed., Wiley Interscience, New York, 1976). [d] This work, IE = 8.46 ± 0.05 eV, ΔH_f(neutral) = 25.9 kcal mol^{-1} (by additivity), AE = 9.50 ± 0.05 eV, measured for us by Dr. F. P. Lossing. $T_{0.5}$ measured on a Kratos AEI MS 902S mass spectrometer.

Table II. Loss of Methyl from Deuterated 1,5-Hexadienes Following Field Ionization (FI)[a] and Electron Impact (EI).[b] Values in Parentheses Refer to Random Distribution of H and D

	$CH_3\cdot$		$CH_2D\cdot$		$CHD_2\cdot$		$CD_3\cdot$	
loss of	FI	EI	FI	EI	FI	EI	FI	EI
CD_2=CHCH$_2$CH$_2$CH=CD_2 (2)	30 (16.7)	22	33 (50)	52	28 (30)	24	10 (3.3)	2
CH_2=CHCD_2CD$_2$CH=CH_2 (3)	31	21	34	52	23	24	13	2
CH_2=CDCH$_2$CH$_2$CD=CH_2 (4)	51 (46.7)	53.5	44 (46.7)	42	5 (6.7)	4.5[c]		

[a] FI mass spectrum (corrected) on a Varian Mat 711 mass spectrometer at emitter currents of 40 mA, ion source and inlet at ambient temperatures, slits at medium resolution. [b] MIKE spectrum on ZAB-2F mass spectrometer, ion source temperature kept at ca. 100 °C. [c] Metastable peak areas on a Kratos AEI MS 902S mass spectrometer are $CH_3\cdot$ (59), $CH_2D\cdot$ (37), and $CHD_2\cdot$ (4).

It was deemed possible that $1^{+\cdot}$ may communicate with ionized allylcyclopropane, because the consecutive ring closure and reopening of cyclopropane-type ions has been proposed to rationalize the extensive H/D randomizations observed in alkene radical cations.[16] The intermediacy of the allylcyclopropane radical cation could thus explain the behavior of $1^{+\cdot}$, and therefore allylcyclopropane was prepared and its mass spectral behavior was examined. However, the observed results (Table I) for this compound clearly show that $1^{+\cdot}$ cannot communicate therewith.

The conclusion that can be drawn from the above data is that $1^{+\cdot}$ only decompose via isomerization to ionized methylcyclopentene.[17] This may proceed as follows (see Scheme I): Nucleophilic attack of C-6 on C-2 acting as an electrophile produces a methylcyclopentene-like ion, which either by a 1,3-H shift (route a) or two successive 1,2-H shifts (route b) forms 1- or 3-methylcyclopentene radical cations.[18]

1 was labeled with deuterium in positions 1,2 (2), 3,4 (3), and 2,5 (4) to distinguish between the two routes (see Table II). According to Scheme I, $2^{+\cdot}$ should lose both $CD_3\cdot$ (route a) and $CHD_2\cdot$ (route b), $3^{+\cdot}$ should lose only $CH_3\cdot$, while $4^{+\cdot}$ would lose both $CH_3\cdot$ (route b) and $CH_2D\cdot$ (route a).

The distributions of labeled cyclopentenyl cations formed from $2^{+\cdot}$ and $3^{+\cdot}$ were found to be time dependent,[22,23] as shown by the difference between the results for ions of short lifetime (FI source generated $C_5H_7^+$, 10^{-9}–10^{-11} s) and those of longer lifetime (EI generated metastable ions, ca. 2×10^{-5} s). Losses of $CH_3\cdot$ and $CD_3\cdot$ following field ionization of 2 and 3 were slightly greater than their random values (assuming complete mixing of H and D atoms), and this together with the observation that the daughter ion distributions were nearly the same whether starting from 2 or 3, permits us to propose that $2^{+\cdot}$ and $3^{+\cdot}$ interconvert in a Cope-like manner (by a 3,3-allylic shift, i.e., C-1 and C-6 become C-3 and C-4, respectively).[24] At longer times (electron impact) $CH_3\cdot$ loss is still greater than random, and $CD_3\cdot$ loss has diminished; this is compatible with the suggestion that at longer times $3^{+\cdot}$ is favored over $2^{+\cdot}$ (cf. ref 5).

It becomes evident from the significant loss of $CH_2D\cdot$ from both $2^{+\cdot}$ and $3^{+\cdot}$ that a 1,3-allylic shift (C-1 becomes C-3 and vice versa) prior to ring closure also is an important additional rearrangement of $1^{+\cdot}$. The suppression of this loss at short times (FI) is compatible with its more complex route to a reactive configuration. (This 1,3-allylic shift is absent under thermal conditions of 1; cf. ref 5.)

Experimental Section

Materials. Allylcyclopropane was prepared as follows: 5-pentenol →[25] 3-cyclopropylpropanol →[26] 3-bromo-1-cyclo-

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(18) The ionizing energy of 1 corresponds to that of an isolated C–C double bond,[19] which means that one double bond remains un-ionized and can act as a nucleophile. MINDO/3 calculations on 1 using the geometry by McIver[20] give ΔH_f (neutral) = 22.5 kcal mol^{-1} (obsd[21] 20.1 kcal mol^{-1}) and $\Delta H_f(1^{+\cdot}$ doublet) = 230 kcal mol^{-1} (obsd[10] 234 kcal mol^{-1}); the calculations show that C-2 carries 26% of the positive charge, followed by 16% at C-1, while C-5 and C-6 carry only 2% total.

(19) H. M. Rosenstock, K. Draxl, B. W. Steiner, and J. T. Herron, *J. Phys. Chem. Ref. Data, Suppl. 1* 6, (1977).

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(22) The distributions are not likely to be due to nonspecific mixing, because allyl cation formation from 2 and 3 following FI showed very little mixing across the C-3–C-4 bond; $C_3H_3D_2^+$ was 80% (random 48%).

(23) The metastable peaks are of the same shape (within experimental error) as that of 1, thus any H/D mixing after ring closure must be within the ring, otherwise mixing from a ring-opened species would give rise to $T_{0.5}$ values of about double those observed.[13]

(24) To our knowledge the only reported case of a formal Cope-like rearrangement of radical cations is that of T. C. Jain, J. E. McCloskey, and C. M. Banks, *Org. Mass Spectrom.*, 5, 751 (1971). We thank Dr. S. Hammerum for pointing this out.

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(26) S. W. Baldwin and J. C. Tomesh, *J. Org. Chem.*, 45, 1455 (1980).

propylpropane →[27] allylcyclopropane; the NMR was identical with that reported.[28] The deuterated 1,5-hexadienes were made according to Sunko et al.;[5] the reduction step of the bis(dimethylamide) was done in THF, thus reducing the reaction time to only 2 h.

Acknowledgment. This work was supported by the Danish Natural Science Research Council. We thank Professor N. M. M. Nibbering and his staff (University of Amsterdam) for assistance with the FI measurements and Dr. J. K. Terlouw (University of Utrecht) for access to and help with the ZAB measurements.

Registry No. 1, 592-42-7; $1^{+\cdot}$, 74056-39-6.

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Efficient Preparation of 6,6-Dihalopenicillanic Acids. Synthesis of Penicillanic Acid *S,S*-Dioxide (Sulbactam)

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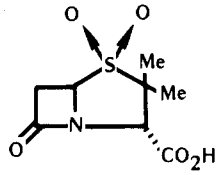
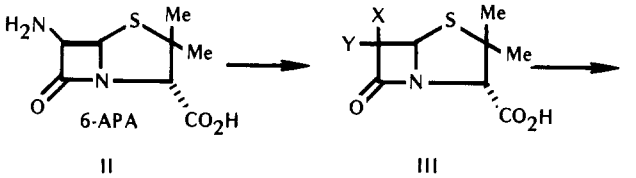
The discovery of novel β-lactam antibiotics[1] in recent years is largely responsible for the continued synthetic interest in the chemical manipulations of readily available β-lactam structures. The penicillin nucleus has, in fact, been utilized in the construction of nonclassical β-lactams such as the Woodward penems,[2] oxacephems,[3] and carbapenems.[4] In this paper we report a similar strategy in the synthesis of the novel β-lactamase inhibitor sulbactam I (CP-45,899).[5]



I

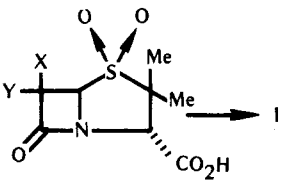
Key to an efficient synthesis of sulbactam is the development of technology for eliminating the 6-β-amido (amino) side chain of the penicillin framework. A solution to this problem was suggested by the work of Clayton,[6] who studied the diazotization/halogenation of 6-aminopenicillanic acid (II) in aqueous media. Accordingly, Clayton was able to generate 6,6-dibromopenicillanic acid (IIIa), a most useful β-lactam intermediate,[7] in approximately 34% yield and was able to convert this product via a reduction to penicillanic acid (IIIb). While this diazotization/halogenation procedure conceptually provided a solution to our problem, the low yield for this transformation was unacceptable for our purposes and similarly has plagued those who have used IIIa in β-lactam syntheses.

This diazotization reaction, in our hands, generated varying amounts of α-bromopenicillanic acid (IIIc) in addition to the desired 6,6-dibromopenicillanic acid (IIIa).[8] The inefficiency of this transformation, we thought, could be attributed to the presence of hydrogen bromide in the reaction media, which was intercepting the diazo intermediate to form IIIc, and also to the prolonged exposure of the desired dihalogenated product IIIa to strongly acidic conditions. We therefore reasoned that a high-yield conversion of 6-APA (II) to 6,6-dibromopenicillanic acid (IIIa)



6-APA II III

a) X, Y = Br
b) X, Y = H
c) X = H, Y = Br
d) X = Cl, Y = I
e) X = Br, Y = I



IV

might best be achieved if the diazo intermediate, once formed, were more effectively exposed to bromine. To this end, a two-phase diazotization/bromination reaction was designed to exploit the solubility of bromine and the 6-diazopenicillanic acid intermediate in organic solvents and the solubility of hydrogen bromide in water. Following this rationale, we added 6-APA (II) as a solid charge to a cooled methylene chloride/sulfuric acid mixture containing sodium nitrite and bromine, and it was converted exclusively to the desired 6,6-dibromopenicillanic acid (IIIa, ~80% yield). Other halogen atoms[9] were similarly introduced on the penicillin framework. For example, ICl and IBr addition generated IIId (53% yield) and IIIe (72% yield), respectively.

6,6-Dibromopenicillanic acid (IIIa), once formed, need not be isolated and could be converted in high yield (~90%) to the corresponding sulfone IVa by a potassium permanganate oxidation.[10] Finally, 6,6-dibromo-

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(9) This technology did not appear useful for the preparation of 6,6-diiodopenicillanic acid, which was obtained in low yield (~15%), and of 6,6-dichloropenicillanic acid.
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