of the possible modes of decomposition of PH_5 has been presented.[15]

Acknowledgment. It is a pleasure to acknowledge the assistance and instruction in gas-handling techniques given us by Professor A. C. Bond.

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Kinetics of the Cycloaddition of cis-Bicyclo[6.1.0]nona-2,4,6-triene with Halosulfonyl Isocyanates

Sir:

The adducts from *cis*-bicyclo[6.1.0]nona-2,4,6-triene or methyl-substituted derivatives and chlorosulfonyl isocyanate (CSI) are formed with a remarkably high degree of stereoselectivity: methyl labels in the starting material **1** appear in the *trans*-10-azabicyclo-[7.2.0]undeca-2,5,7-triene product, **2**, according to the positional transformation 124 → 328; the 9-anti methyl-labeled triene **3** gives **4**, but its 9-syn isomer fails to react.[1–3] Bicyclo[6.1.0]nonatrienes and tetracyanoethylene behave analogously.[4–6]

1, R = H
3, R = CH₃

2, R = H
4, R = CH₃
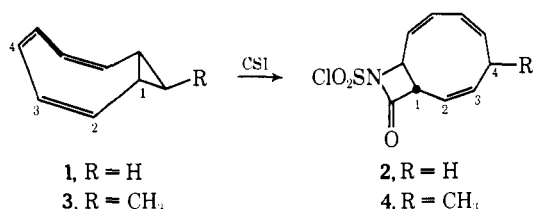
The reactions are thought to involve formation of a transient dipolar intermediate through rate-limiting combination of the less stable folded conformer of bicyclo[6.1.0]nonatriene (**5**) with CSI.[1–3,6,7]
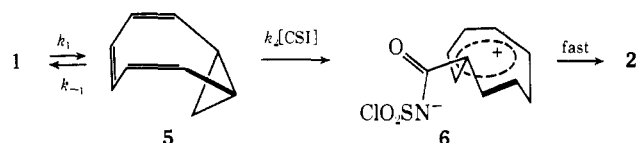
An alternate mechanism, based on the known pro-

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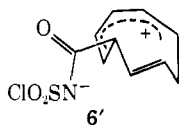
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(7) Another representation for the postulated zwitterionic inter-

mediate would be **6′**.[3]

pensity of bicyclo[6.1.0]nonatriene to undergo cycloaddition reactions by way of one or another valence isomer,[8–13] would postulate reversible formation of *cis,trans,cis,cis*-cyclononatetraene (**8**) by way of the [5.2.0] isomer, **7**, followed by cycloaddition with CSI in a normal (2 + 2) process.
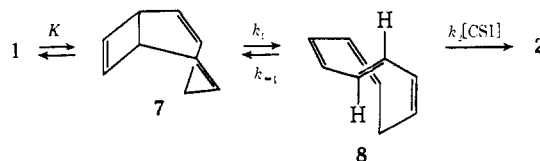
Both mechanisms have identical rate expressions, $d[2]/dt = Ak_2[CSI][1]/(k_{-1} + k_2[CSI])$. In the Paquette mechanism, $A = k_1$, the unimolecular rate constant for the conformational change **1** → **5**; in the second mechanism, $A = Kk_1$, the product of the equilibrium constant for **1** ⇌ **7** and the rate constant for **7** → **8**.

Experimental data from three types of kinetic runs have been used to measure the kinetic parameters A and k_{-1}/k_2. First in deuteriochloroform using cyclopropylmethylene nmr absorptions near δ 0 integrated against adamantane at δ 1.8 as internal standard, pseudo-first-order rate constants for the disappearance of **1** were measured as a function of [CSI]. Second, the triene reaction with excess fluorosulfonyl isocyanate was followed by the same method; the proton nmr spectrum of the fluorosulfonyl adduct was essentially identical with that of the chlorosulfonyl compound **2**.[1] Third, the FSI reaction with excess triene was followed by ^{19}F nmr. The appropriate linear plots of k_{obsd}^{-1} vs. $[XSI]^{-1}$, or of $[1]k_{obsd}^{-1}$ vs. $[FSI]$,[14] gave the results summarized in Table I.

Table I. Kinetic Parameters for the Reaction of *cis*-Bicyclo[6.1.0]nona-2,4,6-triene with Halosulfonyl Isocyanates at 33.7°

Reactant in excess	[XSI] range (M)	k_{obsd} values in linear least-squares plot	A, sec⁻¹	k_{-1}/k_2, M
CSI	0.5–2.0	6	$(2.5 \pm 0.3) \times 10^{-4}$	1.2 ± 0.2
FSI	0.3–3.7	8	$(2.5 \pm 0.6) \times 10^{-4}$	3.4 ± 0.9
1	0.13–1.0	6	$(2.5 \pm 1.3) \times 10^{-4}$	1.9 ± 1.0

All three determinations gave $A = 2.5 \times 10^{-4}$ sec⁻¹; the slightly higher k_{-1}/k_2 value for the reactions with FSI might have been expected.[15] This observed A value is smaller than the rate constants for ring inversions of cycloocta-1,3,5-triene and cyclooctatetraene by

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factors of $10^{6.6}$ and 10^{12}, respectively.[16-21] Thus it seems awkward to interpret it as the $1 \rightarrow 5$ ring inversion rate constant k_1 as required by the originally proposed mechanism. The $A = 2.5 \times 10^{-4}$ sec^{-1} value is, however, entirely reasonable in terms of the alternative in which $A = Kk_1$. The constant K might well be 10^{-2} or 10^{-3}, and E_a for the conversion $7 \rightarrow 8$ could be on the order of 20 kcal/mol.[22]

In terms of this alternative and kinetically plausible mechanism, the stereochemistry of adducts from methyl-substituted analogs of **1** would depend on the relative rates of isomerization $7 \rightarrow 8$ in two distinct conrotatory modes.[3] Further work on the conformational, valence isomerization, and cycloaddition chemistry of triene **1** will be required to test this deduction.

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D-Glucosamine and L-Citrulline, Precursors in Mitomycin Biosynthesis by *Streptomyces verticillatus*

Sir:

The mitomycins (I, mitomycin B; II, mitomycin C) are a group of anticancer antibiotics which contain a unique carbon–nitrogen ring skeleton[1] and which are produced by *Streptomyces verticillatus* and other strains of *Streptomyces*.[2] Previous studies on their biosynthesis have shown that L-[methyl-^{14}C]methionine provides *O*- and *N*-methyl groups but not the *C*-methyl group,[3-5] that L-[guanidino-^{14}C]arginine labels the carbamoyl group,[4] that label from D-glucose[5] and from D-ribose[4] appears in the methylbenzoquinone moiety, and that D-[1-^{14}C,6-^{3}H,^{15}N]glucosamine is incorporated in a manner suggesting its utilization as an intact unit.[4,6]

To further examine the intact incorporation of this amino sugar, D-[1-^{13}C,^{15}N]glucosamine was prepared from D-arabinose, [^{15}N]benzylamine (99 atom % ^{15}N), and H^{13}CN (90 atom % ^{13}C).[7] Fifty milligrams of

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Ion	Designation	Rel abundance $\times$ 100
C$_4$H$_8$N	a	55.6
C$_4$H$_8$^{15}N	b	8.4
C$_3$^{13}CH$_8$N	c	4.9
C$_3$^{13}CH$_8$^{15}N	d	31.1
C$_2$^{13}C$_2$H$_8$N	e	<2

this material was mixed with 5 μCi of D-[1-^{14}C]glucosamine administered to doubly replaced mycelia of *S. verticillatus* and approximately 4 mg of a mixture of mitomycins A, B, and C and porfiromycin were isolated 24 hr later. Carbon-14 incorporation[8] into this mixture was 1.8%. Mitomycin B was purified and analyzed by mass spectrometry as described previously.[6] The relevant ions of the cluster C$_4$H$_8$N (m/e 70), which according to Van Lear[9] comprise C-1, C-2, and C-3, N-1a, and its attached methyl group, were identified in high-resolution mass spectra (CEC 21 110B, direct inlet probe, 200°, 70 eV, mass marker: perfluorokerosene at m/e 69.99856; accuracy, 3 mmass units). Their relative intensities (Table I) were determined using an average of ten scans per ion. It can be calculated from the intensity data that the specific incorporation of ^{13}C into the C$_4$H$_8$N fragment, most likely into its C-3, was 36.9%, while the specific incorporation of ^{14}C^{10} into mitomycin B was 41.2%. This close agreement, the small value observed for ion c, and the virtual absence of ion e in the spectrum show that only a negligible fraction of the carbon label is randomized and indicate that the incorporation is specific. The amino group of D-glucosamine apparently provides directly the nitrogen atom of the aziridine ring, yet the configuration at C-2 of the mitomycins[11] is opposite to that at C-2 of this aminohexose. Since the intensities of ions b and c were very weak the ^{13}C and the ^{15}N labels are never separated, and it can be concluded that the nitrogen atom is not removed from the carbon skeleton and reincorporated during the inversion of the configuration.

In another feeding experiment D-[6-^{14}C]glucosamine (5 μCi, 5 mg) which was synthesized from D-[6-^{14}C]-gluconic acid *via* D-[5-^{14}C]arabinose[7] gave 5.1% incorporation into mitomycins A, B, and C and porfiromycin. Mitomycin C after purification to constant specific radioactivity (first recrystallization, 9.37 $\times$ 10^4 dpm/mmol; second recrystallization, 9.34 $\times$ 10^4 dpm/mmol) was converted into 2-amino-1,7-dihydroxydecarbamoyl-mitosene (III).[12,13] This compound was subjected to periodate oxidation to give formaldehyde, which arises predominantly from C-10.[14] The latter was purified

(8) Incorporation: total radioactivity in mitomycins/total radioactivity administered.
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(10) Specific incorporation: specific radioactivity of mitomycin B/specific radioactivity of D-[1-^{14}C]glucosamine.
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(14) This reaction was utilized by Webb, *et al.*, in the structure determination of the mitomycins.[15] Mitosene III gave formaldehyde in 50–70% yield while a derivative of III containing a carbamoyl group at C-10 gave formaldehyde in 16–22% yield.
(15) J. S. Webb, *et al.*, manuscript in preparation, and personal communication.