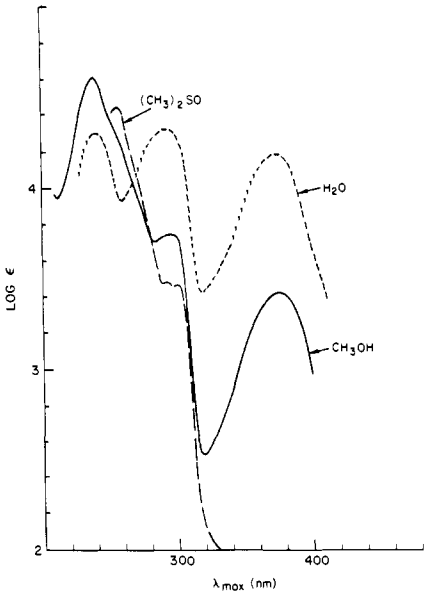

Figure 1. The ultraviolet absorption spectra of **3a** in three solvents.

Table I

Solvent	α^a	β^a	$\alpha - \beta$	E	K
tert-Butyl alcohol	0.44	0.95	−0.51	353	0.021
Isopropyl alcohol	0.68	0.92	−0.24	435	0.026
n-Butyl alcohol	0.71	0.85	−0.14	704	0.043
Ethyl alcohol	0.85	0.77	0.08	948	0.059
Methyl alcohol	0.99	0.62	0.37	2600	0.18
Ethylene glycol	0.79	0.51	0.28	3580	0.27
Water	1.02	0.14	0.88	15300	9.0

[a] Reference 5.

to appear in the ^{1}H NMR spectrum; in 0.2 M CF_3CD_2OH–$CDCl_3$ (10:1) solution only absorption characteristic of the cyclohexa-2,4-dienone **4** could be detected in the ^{1}H NMR spectrum: two broadened singlets at 5.12 and 4.74 ppm, with a methylene singlet superimposed on the broad multiplet of the pyrrolidine rings. In the ^{13}C spectrum, a carbonyl appeared at 183.1 ppm, with four olefinic carbons (164.3, 157.9, 90.7, and 84.7), and a methylene carbon (38.3) among the pyrrolidine signals (48.6, 2C, 48.0 (2C), and 25.1 (4C)). The ultraviolet absorption (λ (max) 370 nm, ε 16 000 L mol^{-1} cm^{-1}) and infrared spectrum (1600 cm^{-1}) in this solvent mixture are well suited to **4**.

Recent studies by Taft and Kamlett[5] have provided parameters characterizing the ability of a solvent to donate hydrogen bonds (the hydrogen bond donor (HBD) acidity, α) and to accept hydrogen bonds (the hydrogen bond acceptor (HBA) basicity, β), of an extensive series of solvents. It seems here that each of these two abilities stabilizes one of the two forms, producing competitive effects. We were therefore interested in seven solvents for which both α and β values have been reported. These values and their differences are listed in Table I with the extinction coefficients observed for **3a**, and the corresponding equilibrium constants.[6] Evidently, for **3a** ⇌ **4**,

$$\ln K = -[(G_p - G_c) - (G_\alpha - G_\beta)]/RT$$

where G_p and G_c represent the free energies of the phenolic and carbonyl forms, respectively, in the absence of hydrogen bonding, and G_α and G_β represent the energies lost in the formation of hydrogen bonds in which the hydrogen is donated and received by the solvent, respectively. Although both the extinction coefficient of **4** and the quantity $G_p - G_c$ must vary somewhat in this series of solvents,[7] the correlation coefficient between ln K and $\alpha - \beta$ is 0.95.[8]

Previous studies have shown the importance of intermolecular hydrogen bonding in stabilizing phenols,[9] but a quantitative estimate of the competitive effect observed here has apparently not been reported.[10-12]

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(6) $K = E(\text{obsd})/E(4)/(1 - E(\text{obsd})/(4)$; $E(4)$ is taken as 17 000, from the extinction coefficient observed in trifluoroethanol and the appearance in the ^{13}C spectrum of peaks which apparently represent approximately 5% of the 2,5 dienone form. The predominance of the 2,5-dienone forms of the ions **1** and **2** apparently reflects the superior charge separation of this form.
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(8) Linear regression provides the relation: $\ln K = -2.5 + 4.3(\alpha - \beta)$; the intercept corresponds to $(G_p - G_c) = 1.5$ kcal.
(9) H. Baba and T. Takemura, *Tetrahedron*, **24**, 4779 (1968).
(10) Crystallographic examination of **3a** indicates that it exists exclusively as the phenol in solid form. R. J. Highet and J. V. Silverton, to be submitted for publication.
(11) Linear regression was performed by MLAB. Cf. G. Knott, "MLAB, an On-line Modeling Laboratory", 4th ed, National Institutes of Health, Bethesda, Maryland, 1974.
(12) We are indebted to a referee for the observation that the correlation confirms that hydrogen bonding in the dienone is primarily by solvent to oxygen. The competitive hydrogen bonding to the amine nitrogen, which would destabilize the dienone by lessening >NC=CC=O resonance, is evidently not significant.

R. J. Highet,* Feng-te E. Chou
Laboratory of Chemistry
National Heart, Lung and Blood Institute
National Institutes of Health
Bethesda, Maryland 20014

Received January 5, 1977

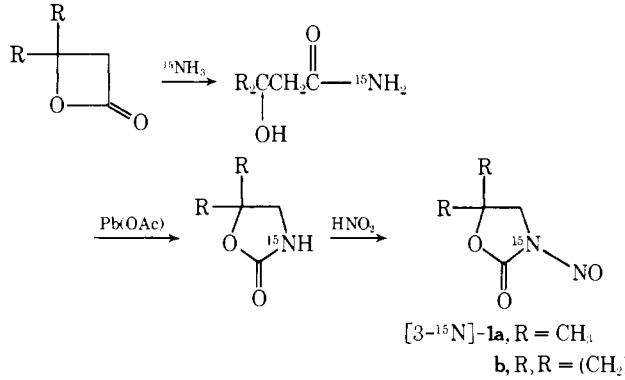
Pathways from Nitrosooxazolidones to Vinyl Azides

Sir:

Reactions of 5,5-dialkyl-*N*-nitrosooxazolidones (**1**) with base and a variety of nucleophiles have been studied.[1-5] The formation of vinyl iodides, azides, isothiocyanates, phosphonates, and ethers was explained by assuming that the vinyl cation (**5**) reacts with nucleophiles.[2] Our interest in azo coupling by aliphatic diazonium ions[6] induced us to reinvestigate the reaction of **1** with azide. We report here on the dissection of various mechanistic pathways from **1** to vinyl azides.

[3-^{15}N]-**1** was prepared as shown in Scheme I.[7] Reaction

Scheme I



[3-^{15}N]-**1a**, R = CH_3
b, R,R = $(CH_2)_5$

Table I. Labeled Products from Nitrosooxazolidones (**1**)

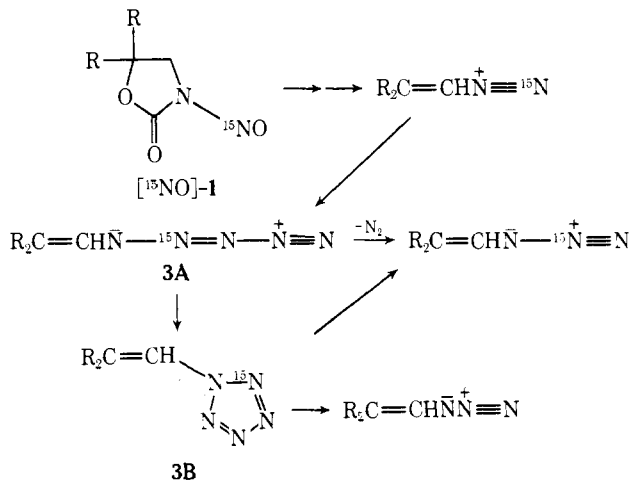
$[LiN_3]$	0.5	1.0	2.0	3.6	6.3	2.0
$[LiOCH_3]$	0	0	0	0	0	0.25
$[3\text{-}^{15}N]$-**1** + CH_3OH						
% ^{15}N in **4a**	88.9	82.2	71.4	45.2	13.8	
% ^{15}N in **4b**	52.4	43.8	31.8	20.2	7.1	0.8
$[^{15}NO]$-**1** + CH_3OH						
% ^{15}N in **4a**	82.0	73.7	63.0	42.1	15.0	1.1
% ^{15}N in **4b**	50.4	41.3	30.8	17.6	5.7	
1 + CH_3OD						
% D in **4a**	48.8	53.3	58.4	55.1	68.4	90.8
% D in **4b**	48.8	57.4	64.7	69.8	81.8	90.2

Table II. Double Labeling Experiments with $[3\text{-}^{15}N]$-**1** in CH_3OD, 1 M LiN_3[a]

	4	$[^{15}N]$-**4**	[D]-**4**	[D, ^{15}N]-**4**	**6**	[D]-**6**
1a	3.2	42.4	17.6	36.8	5.6	94.4
1a + 1 M $LiClO_4$	17.0	31.6	23.4	28.0	Not det.	
1b	2.8	36.6	41.1	19.4	2.5	97.5
1b + 1 M $LiClO_4$	20.1	14.1	50.6	15.2	19.1	80.9

[a] Relative product distribution (%). Absolute yields were 32.0% **4a** and 30.5% **6a** from **1a**, 27% **4b** and 34% **6b** from **1b**.

Scheme II



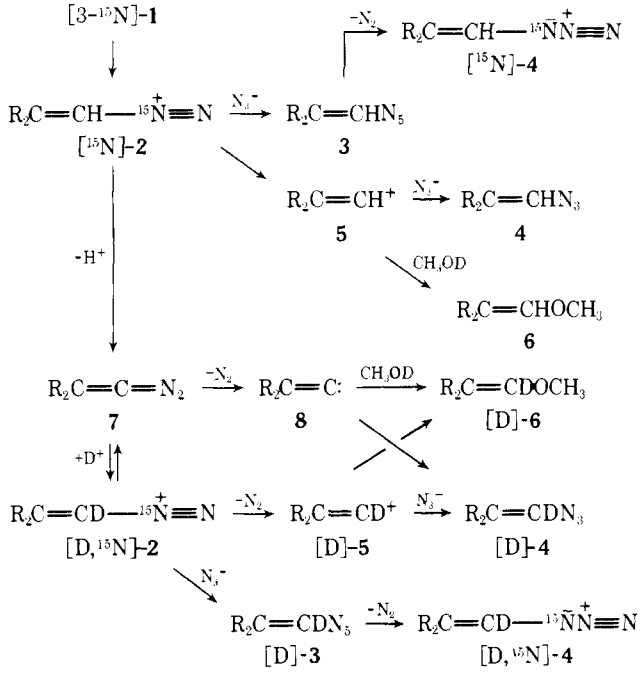
of the nitrosooxazolidones with lithium azide in methanol proceeded smoothly without additional base. Vinyl azides (**4**) and vinyl ethers (**6**) were the major products.[8] The vinyl azides obtained from $[3\text{-}^{15}N]$-**1** retained substantial fractions of the ^{15}N label (Table I), indicating that they arise in part by azo coupling. The coupling reaction of arenediazonium ions with azide is known to proceed by pentazene and pentazole intermediates.[9] Starting with $[3\text{-}^{15}N]$-**1**, the label will be retained regardless of whether a pentazene (**3A**) or a pentazole (**3B**) intervenes. When the nitroso nitrogen is labeled, however, 50% of the label will be lost by intervention of the pentazole **3B** (Scheme II). A comparison of data obtained with $[3\text{-}^{15}N]$-**1** and $[^{15}NO]$-**1** (Table I) indicates a rather modest ($\leq$20%) contribution of **3B**. Pentazoles are more prominent in the coupling of arenediazonium ions (35% at 0 °C)[9] and cyclopropanediazonium ions (40% at 20 °C)[10] with azide.

The fraction of labeled vinyl azide decreases with increasing concentration of lithium azide, and vanishes almost entirely upon addition of 0.25 M lithium methoxide (Table I). What is the source of unlabeled azide? Data obtained from the reaction of $[3\text{-}^{15}N]$-**1** with lithium azide in CH_3OD were helpful in answering this question (Scheme III and Table II).[11] All products which do not contain deuterium originate from $[^{15}N]$-**2**. The high proportion of $[^{15}N]$-**4** among the undeuterated products indicates that azo coupling is the major reaction of **2**; very little vinyl azide is formed via vinyl cation **5**. The contribution of **5** may be increased, however, by addition of lithium perchlorate (salt effect). The substantial amount of [D, ^{15}N]-**4** shows that deuterated diazonium ions [D, ^{15}N]-**2** are produced from $[^{15}N]$-**2** by H–D exchange, presumably via diazoalkene **7**.[12] Neglecting secondary isotope effects, we expect that [D, ^{15}N]-**2** partitions to give [D, ^{15}N]-**4** and [D]-**4** in the same ratio as $[^{15}N]$-**2** gives $[^{15}N]$-**4** and **4**. However, the observed amount of [D]-**4** exceeds by far that expected from [D,^{15}N]-**2**. There must be another source of [D]-**4**, most probably the carbene **8**.[13]

Table III. Labeled Products from 4,5,5-Trimethyl-*N*-nitrosooxazolidone (**11**)

$[LiN_3]$	$[LiClO_4]$	$[LiOCH_3]$	% ^{15}N in **13**
0.3	0	0	20.1
1.0	0	0	17.2
2.0	0	0	11.8
1.0	0.007	0	18.2
1.0	0.027	0	16.8
1.0	0.066	0	14.7
1.0	0.20	0	10.0
1.0	0.33	0	ca. 6
1.0	0	0.2	17.5
1.0	0	1.0	20.2
1.0	0	2.0	23.6

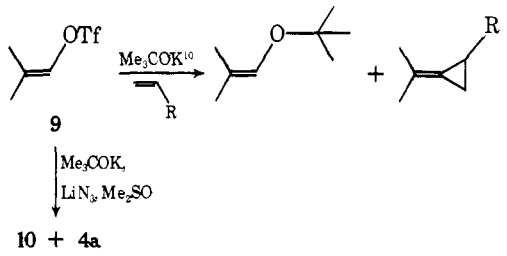
Scheme III



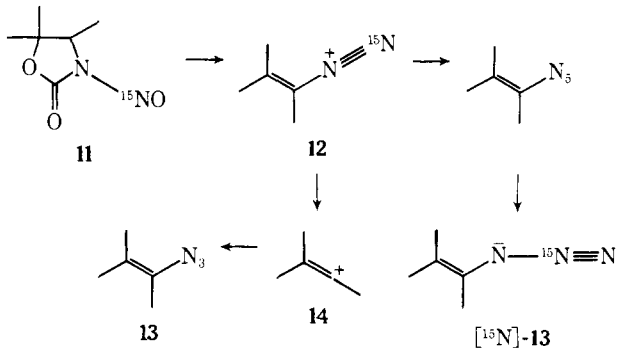
Alkylidenecarbenes (**8**) are known to intervene in the base-catalyzed decomposition of nitrosooxazolidones (**1**), and have been trapped by addition to alkenes.[1,14] Although addition of carbenes to anions has not received much attention, the reversible reaction of dihalocarbenes with halide ions[15] may be cited as an example. The high deuterium content of vinyl ether **6** (Table II, cf. ref 1 and 2) suggests that **6** derives largely from the carbene **8**. In the formation of vinyl azide **4**, the carbene reaction increases with increasing concentration of base at the expense of azo coupling.

The intermediacy of **8** is supported by the reaction of 2-methyl-1-propenyl triflate (**9**) with potassium *tert*-butoxide and lithium azide in dimethyl sulfoxide which produced vinyl azide **4a** and vinyl ether **10** in a 1:1 ratio, albeit in low yield (Scheme IV). Stang has shown that treatment of **9** with po-

Scheme IV



Scheme V



tassium *tert*-butoxide generates carbene **8** which may be trapped by addition to alkenes.[16]

Additional support comes from a comparison of **1** with 4,5,5-trimethyl-*N*-nitrosooxazolidone (**11**) (Scheme V). Although the yields of vinyl derivatives from trisubstituted nitrosooxazolidones are notoriously low,[5] recovery of a ^{15}N label from [^{15}NO]-**11** in vinyl azide **13** is informative (Table III). The greater stability of vinyl cation **14** (as compared to **5**) promotes loss of nitrogen from diazonium ions **12** and decreases the amount of azo coupling. The fraction of [^{15}N]-**13** is further diminished by addition of lithium perchlorate and, less strongly, by increasing the concentration of lithium azide (salt effect). Addition of lithium methoxide, however, does not affect the retention of ^{15}N (even a slight increase is found) as **12** cannot form a carbene.

We conclude that vinyl azides can arise from vinyldiazonium ions via pentazenes (azo coupling), vinyl cations, and alkylidene carbenes. The relative contributions of these mechanistic pathways may be influenced in a predictable manner by the choice of reaction conditions and by structural variations.

Acknowledgment. We are grateful to Dr. Dietrich Müller for mass spectrometric analyses of the vinyl azides.

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(4) Base catalyzed decompositions of *N*-nitrosooxazolidones have been shown to be complex. In order to obtain reactions through a vinyl diazonium ion, C-5 must generally be disubstituted.[5]
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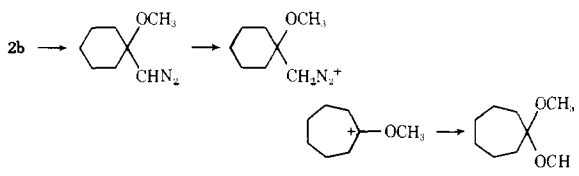
(7) The ammonia used in the preparation of [3-^{15}N]-**1** contained 96.2% ^{15}N. The results reported in Tables I and II have been corrected to 100% isotopic purity.
(8) Minor products arise by addition of nucleophiles to the activated double bond of **2**,[5] e.g., cycloheptanone dimethyl acetal was found among the products from **1b**:



(9) R. Huisgen and I. Ugi, *Angew. Chem.*, **68**, 705 (1956); I. Ugi, R. Huisgen, K. Clusius, and M. Vecchi, *ibid.*, **68**, 753 (1956).
(10) W. Kirmse and O. Schnurr, unpublished results.
(11) Mass spectrometric analysis (15 eV) of the vinyl azides rests on relative peak intensities of M^+, $(M + 1)^+$, and $(M + 2)^+$. High resolution mass spectrometry resolved the $(M + 1)^+$ peak into [D]-**4** and [^{15}N]-**4** (*m/e* 98.0703 and 98.0610 for **4a**; *m/e* 138.1016 and 138.0923 for **4b**).
(12) Nitrosooxazolidones (**1**) do not undergo H–D exchange prior to decomposition. No deuterium was found, within the limits of NMR detection (<5%), in **1a,b** recovered after ca. 50% conversion.
(13) The lower retention of ^{15}N in **4b** (as compared to **4a**, Table I) may be traced to an increased contribution of the carbene mechanism with **1b** (about twice as much [D]-**4** is produced from **1b**, Table II). In terms of Scheme III this result indicates a higher rate of decomposition vs. protonation of **7b** (ca. 2) as compared to **7a** (ca. 0.5).
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Wolfgang Kirmse,* Otto Schnurr
Abteilung für Chemie der Ruhr-Universität
4630 Bochum, West Germany
Received January 31, 1977

Biosynthetic Origin of the C_2 Units of Geldanamycin and Distribution of Label from D-[6-^{13}C]Glucose[1,2]

Sir:

Considerable interest has been evidenced recently in the biosynthesis of the ansamycin antibiotics, which are both active antibacterial agents and potent inhibitors of reverse trascriptase.[3] The aliphatic ansa ring carbons of rifamycin S,[4] streptovaricin D,[5] and geldanamycin[2] have been shown to be derived mainly from propionate (Figure 1),[6] while the biogenetic C_2 units in the ansa chains of streptovaricin D[5a,b] and rifamycin S[4a,b] have been shown to be derived from acetate or malonate. Recently, White and co-workers[4a] showed that part of the naphthoquinone ring of rifamycin S is derived from acetate (or malonate) and propionate (as is part of the naphthoquinone methide ring of streptovaricin D[5a,b,7]), while the remaining C_7N unit (see Figure 1) is derived from glucose or glycerate by a shikimate-type pathway (Figure 2).[4c,d] In the present communication we present evidence from D-[6-^{13}C]glucose administration which provides remarkable insight into the intermediary metabolism of *Streptomyces hygroscopicus*, demonstrating that 21 of the 29 carbons of geldanamycin arise from C-6 of glucose and, in particular, that the aromatic (benzoquinone) C_7N unit of geldanamycin, like that of rifamycin S (and presumably that of streptovaricin D), arises

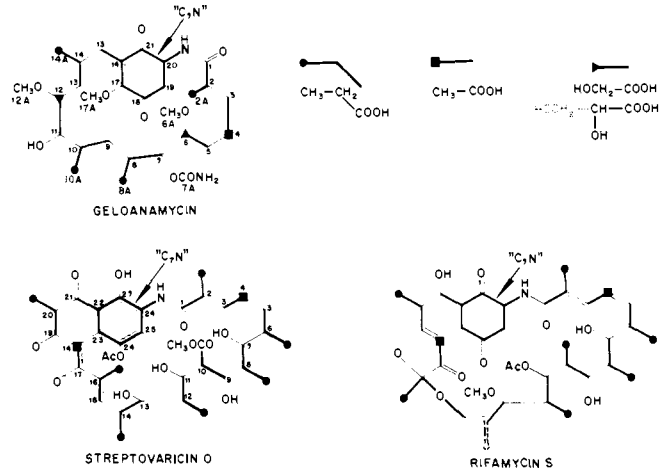

Figure 1. Ansamycin antibiotics and the origin of their carbon skeletons.