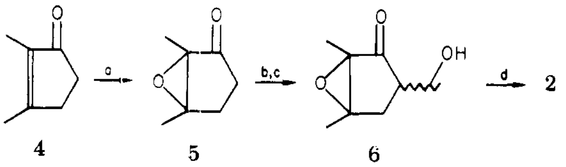
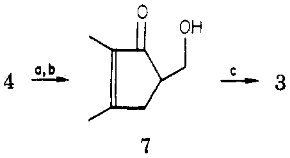
Scheme I



(a) 30% H_2O_2, Na_2CO_3; (b) LDA; (c) CH_2O; (d) DCC, CuCl.

Scheme II

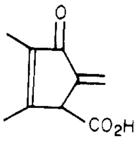


(a) LDA; (b) CH_2O; (c) DCC/CuCl.

and NMR spectra with those previously reported[2] clearly showed that the structure of the material isolated as methylenomycin B should be reassigned as **3**.

The dienone **3** was extremely prone to spontaneous polymerization, and it was therefore surprising to find that with 30% H_2O_2 it formed a stable hemi-hydrogen peroxide complex. This complex (mp 52–54 °C) exhibited spectral characteristics identical with **3** with these exceptions: IR ($CHCl_3$) 3250 cm^{-1} (br); ^1H NMR (Me_2SO-d_6) δ 9.68 (s, H_2O_2); MS m/e 34 (H_2O_2). It dissolved readily in common organic solvents and could be recovered from them unchanged. This stable complex provided us with an excellent means of storing methylenomycin B (**3**). Solvent extraction of an aqueous solution of the H_2O_2 complex readily afforded **3**.

Hornemann[9] recently isolated compound **8** from the bacterial broth that produced methylenomycin A (**1**) and showed that **8** is a precursor to **1**. In view of the known tendency of vinylogues of β-keto acids to undergo decarboxylation at relatively moderate temperatures, it is not unlikely that **3** is actually a chemical decomposition product of **8** formed during the original isolation process.



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Acknowledgment. The authors wish to thank Dr. E. P. Oliveto for his interest and stimulating discussions of this work. We also wish to thank Dr. W. Benz, Dr. V. Toome, and Mr. S. Traiman for mass, UV, and IR spectra, respectively, as well as Dr. J. F. Blount for X-ray structural determination and Dr. F. Scheidl for microanalyses.

Registry No. 2, 52775-77-6; **3**, 52775-77-6; **3** hemihydrogen peroxide, 71719-41-0; **4**, 1121-05-7; **5**, 71719-42-1; **6**, 71719-43-2; **7**, 71719-44-3; 2-hydroxy-3-methylcyclopent-2-en-1-one, 80-71-7; 2-*N*-pyrrolidino-5-methylcyclopent-2-en-1-one, 4933-43-1; pyrrolidine, 123-75-1; methyl iodide, 74-88-4.

Supplementary Material Available: Experimental Section providing preparation details for the compounds in the text (7 pages). Ordering information is given on any current masthead page.

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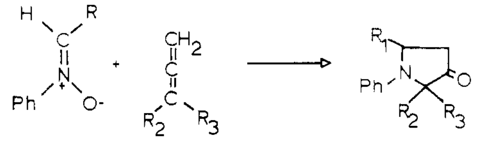
[9] Dr. U. Hornemann, Purdue University, Indiana, personal communication. We wish to thank Dr. Hornemann for communicating his results to us. See U. Hornemann and D. A. Hopwoods, *Tetrahedron Lett.*, 2977 (1978).

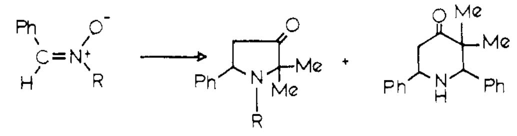
Intermolecular Allene-Nitrone Cycloadditions

Summary: An intermolecular cycloaddition of *C,N*-diphenylnitrone with allene is described which affords three monoadducts, including a pyrrolidinone, an isoxazolidine, and a tetrahydrobenzazapinone.

Sir: The reaction of a nitrone with a cumulatively unsaturated system was first investigated by E. Beckmann[1] in 1890 and involved the addition of *N*-benzylidenebenzylamine *N*-oxide to phenyl isocyanate. In the intervening 89 years, nitrone cycloadditions involving isothiocyanates, carbon disulfide, allenes, ketenes, ketene imines, and carbodiimides have undergone some study.[2] LeBel[3] investigated the intramolecular cycloaddition reactions of allenic nitrones and, indeed, two reports[4,5] have focused on the intermolecular reactions of nitrones with simple allenes. Thus *C*-benzoyl-*N*-phenylnitrone (**1a**) was reported[4] to provide the 3-pyrrolidinone **3a** in 85% yield as the sole product isolated upon reaction with allene, while *C,N*-diphenylnitrone (**1b**) gave **3b** upon reaction with 1,1-dimethylallene (**2b**). In addition to the 3-pyrrolidinones obtained from the reaction of *N*-arylnitrones with allenes, *N*-alkylnitrones also are reported[5] to afford 4-piperidinones (e.g., **6**) upon reaction with dimethylallene.



1a, R_1=COPh 2a, R_2= R_3= H 3a, R_1= COPh, R_2= R_3= H
b, R_1=Ph b, R_2= R_3=Me b, R_1= Ph, R_2=R_3= Me



4 5 6

In contrast with the results noted above, we find that the reaction of *C,N*-diphenylnitrone (**1b**) with excess allene in a sealed tube at 72 °C for 60 h leads to the formation of three products. After opening the reaction vessel at −78

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[1] E. Beckmann, *Ber. Dtsch. Chem. Ges.*, **23**, 1680, 331 (1890); **27**, 1957 (1894).

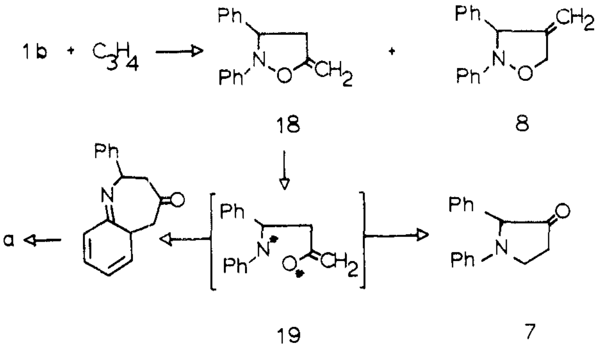
[2] For an excellent review of such transformations, see D. St. C. Black, R. F. Crozier, and V. C. Davis, *Synthesis*, **7**, 205 (1975).

[3] N. A. LeBel and E. Banucci, *J. Am. Chem. Soc.*, **92**, 5278 (1970).

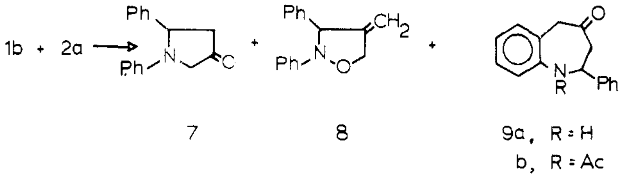
[4] M. C. Aversa, G. Cum, and N. Uccella, *J. Chem. Soc., Chem. Commun.*, 156 (1971).

[5] G. Cum, G. Sindona, and N. Uccella, *J. Chem. Soc., Perkin Trans. 1*, 719 (1976).

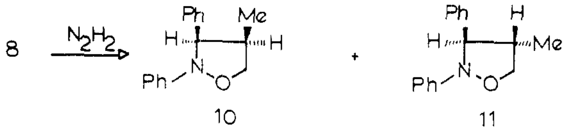
Scheme I

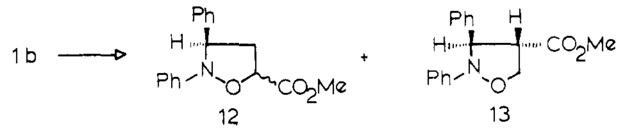


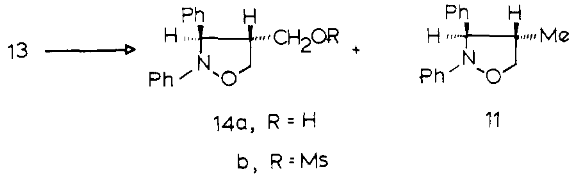
°C, excess allene was removed by passing nitrogen through the cold solution. The resulting light yellow reaction product was chromatographed on silica gel to afford three adducts, **7**, **8**, and **9a**. Two of these (i.e., **7** and **9a**) derive from one regiochemical mode of cycloaddition of **1b** to allene, while the other (i.e., **8**) derives from the alternate mode of addition (vide infra; Scheme I). The 3-pyrrolidinone **7**, formed in 23% yield, is readily characterized by its spectral properties. It displays the expected carbonyl absorption at 5.71 μm, characteristic of a carbonyl group in a five-membered ring. The ^{1}H NMR spectrum [($CDCl_3$, 60 MHz) δ 6.5–7.4 (m, 10), 5.2 (dd, 1), 4.0 (br s, 2), 3.2 and 2.6 (AB portion of ABX, J_{45} = 9, $J_{45'}$ = 5, $J_{44'}$ = 19 Hz)] closely resembles that reported[4] for **3a**. Mass spectral analysis indicates the presence of the molecular ion at *m/e* 237 (30%). These findings support the structural assignment attributed to pyrrolidinone **7** and are in accord with earlier reports.[4,5]



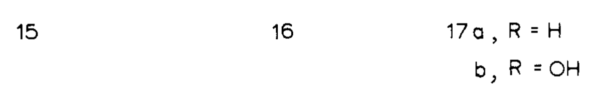
Adduct **8** (mp 42 °C), formed in 22% yield, displays no carbonyl absorption in the IR, but does exhibit significant absorptions at 6.26 (C=C stretch) and 11.1 μm (C=CH_2). In the NMR spectrum ($CDCl_3$, 60 MHz) there appear signals at δ 4.6 (m, 2), 4.9 (m, 3), and 6.8–7.7 (m, 10). Moreover, **8** was reduced with diimide (hydrazine hydrate, copper sulfate, air)[6] to approximately equivalent amounts of a pair of separable diastereomers (TLC, silica gel, benzene). The NMR spectrum of the crude isomeric mixture displays two doublets (*J* = 7 Hz) of equal intensity at δ 0.72 and 1.12. The former is attributed to the more highly shielded methyl group of isoxazolidine **10**. This structural interpretation gains further support from the following considerations. When *C*,*N*-diphenylnitrone (**1b**) was added to methyl acrylate at 110 °C (toluene, sealed tube) there resulted a mixture of regioisomeric adducts, **12** and **13**, in a 2:1 ratio, respectively. The adduct **13** was separated (TLC, silica gel; CH_2Cl_2) and reduced with lithium aluminum hydride to afford alcohol **14a** (97%). The corresponding methanesulfonate **14b** was converted into **11** by Super-Hydride[7] reduction. The isoxazolidine produced in this manner proved to be identical with one of the diimide reduction products (i.e., **11**) derived from **8**. This suggests that the stereochemistry of **13** may be depicted as indicated.







The structure assigned to the major product **9**, formed in 31% yield, rests solidly on both spectral and chemical evidence. Thus, **9a** exhibits absorptions at 5.88 (carbonyl stretch) and 2.98 μm (NH stretch). The ^{1}H NMR spectrum ($CDCl_3$, 60 MHZ) exhibits signals at δ 2.4–3.2 (m, 2), 3.75 (AB, 2, *J* = 14 Hz), 4.65 (dd, 1, *J* = 4.5, 10 Hz), 6.5–7.4 (m, 9 H). The mass spectrum displays a molecular ion at *m/e* 237. That **9a** is indeed an amine was confirmed by conversion to the corresponding acetamide upon refluxing with acetic anhydride. The amide **9b** no longer exhibits an NH stretching absorption in the IR (i.e., at 3.0 μm) but rather displays two carbonyl absorptions at 5.87 and 6.08 μm. The ^{1}H NMR spectrum of **9b** ($CDCl_3$, 100 MHz) exhibits signals at δ 1.79 (s, 3, Me), 2.60 and 2.97 (AB portion of ABX, 2, *J* = 5.3, 13, 13 Hz), 3.68 (AB, 2, *J* = 18 Hz), 6.10 (dd, 1, *J* = 5.3, 13 Hz), and 6.8–7.4 (m, 9). Finally, the structural assignment for the tetrahydrobenzazepinone **9a** was supported by its reduction (Wolff–Kishner) to **17a**, whose structure was confirmed by an independent synthesis from the tetrahydrobenzazepine **15**. Oxidation of **15** to the corresponding nitrone **16** with *m*-chloroperbenzoic acid (CH_2Cl_2)[8] was followed by a Grignard procedure[9] (e.g., using phenylmagnesium bromide) to give a mixture of **17a** and **17b** in modest yield. Hydroxylamine **17b** was converted into the amine **17a** by hydrogenolysis with zinc and acetic acid. This amine (**17a**) is identical in every respect with that obtained from **9a** by Wolff–Kishner reduction.



The foregoing results are most easily rationalized (cf. Scheme I) by a modification of the mechanism previously suggested[4,5] for the generation of 3-pyrrolidinone **3b** from **1b**. The nitrogen–oxygen bond in **18** is expected to be cleaved readily, since such heteroatom–heteroatom bonds are known[10,11] to be relatively weak. Moreover, the scission of this bond to afford **19** is facilitated by conjugative stabilization at both incipient radical (or ionic) centers.

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(6) (a) E. E. van Tamelen and R. J. Timmons, *J. Am. Chem. Soc.*, **84**, 1087 (1962); (b) M. Ohno and M. Ocomoto, *Tetrahedron Lett.*, 2423 (1964).

(7) S. Krishnamurthy and H. C. Brown, *J. Org. Chem.*, 41, 3064 (1976).

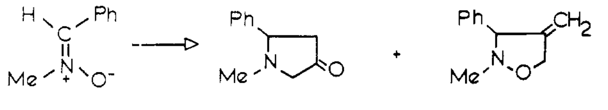
(8) A. H. Beckett, R. T. Coutts, and F. A. Ogunbona, *Tetrahedron*, **29**, 4189 (1973).

(9) J. Hamer and A. Macaluso, *Chem. Rev.*, **64**, 473 (1964).

(10) J. E. Baldwin, R. G. Pudussery, A. K. Qureshi, and B. B. Sklarz, *J. Am. Chem. Soc.*, **90**, 5326 (1968).

(11) (a) J. A. Kerr, *Chem. Rev.*, **66**, 496 (1966); (b) T. I. Cottrell, "The Strengths of Chemical Bonds", 2nd ed., Butterworths, London, 1958.

We have demonstrated that the product distribution reflects kinetic rather than thermodynamic factors by refluxing each of the products (i.e., **7**, **8**, and **9a**) separately in acetone and recovering each unchanged. Finally, Scheme I argues that nitrones not bearing an *N*-aryl substituent should afford only two products upon exposure to allene. Indeed, *C*-phenyl-*N*-methylnitrone undergoes cycloaddition with allene to afford pyrrolidinone **20** and isoxazolidine **21** in a 2:3 ratio, respectively. As expected from the absence of an *N*-aryl substituent in the starting nitrone, no benzazepinone (i.e., corresponding to **9a**) was formed. The structure of **20** follows from the presence of carbonyl absorption at 5.71 μm in the infrared and its ^{1}H NMR spectrum [(CDCl$_3$, 100 MHz) δ 2.20 (s, 3), 1.8–3.0 (m, 3 besides Me), 3.50 (m, 2), and 7.24 (br s, 5)]. Isoxazolidine **21** shows no significant absorption in the 5–6-μm region of the infrared. Its ^{1}H NMR spectrum [(CDCl$_3$, 100 MHz) δ 2.60 (s, 3), 3.85 (br s, 1), 4.50 (br s, 3), 4.93 (br s, 1), and 7.25 (s, 5)] is consistent with the structural assignment.



20 21

We have shown herein that the intermolecular reactions of nitrones with allene can result in the production of regioisomeric adducts, one of which (e.g., **18**) undergoes spontaneous further rearrangement. When an *N*-aryl substituent is present in the nitrone, the production of a benzazepinone (e.g., **9a**) can be anticipated as a major product.

Acknowledgment. We gratefully acknowledge the generous financial assistance provided by the National Institutes of Health (Institute of General Medical Sciences, GM 25303).

Registry No. 1b, 26505-49-7; **2a**, 463-49-0; 4 (R = Me), 34285-49-9; **7**, 5469-56-7; **8**, 71718-69-9; **9a**, 71718-70-2; **9b**, 71718-71-3; **10**, 71718-72-4; **11**, 71718-73-5; **12**, 19344-95-7; **13**, 69284-39-5; **14a**, 71718-74-6; **14b**, 71718-75-7; **15**, 1701-57-1; **16**, 71718-76-8; **17a**, 71718-77-9; **17b**, 71718-78-0; **20**, 23770-12-9; **21**, 71718-79-1; methyl acrylate, 96-33-3.

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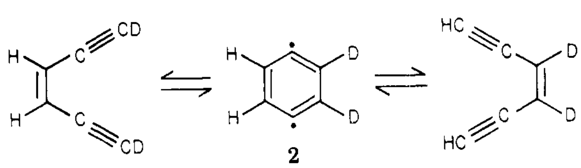
Evidence for the Formation of 1,3-Dehydrobenzene Diradicals by Silicon Shift in 1,4-Dehydrobenzenes at High Temperature

Summary: Evidence is presented that high temperature pyrolysis of three isomeric disubstituted 1,5-hexadiyn-3-enes proceeds by initial cyclization to 1,4-dehydrobenzene intermediates, and that these initially formed species are capable of rearranging to 1,3-dehydrobenzenes. Both types of intermediates appear to behave as diradicals at these temperatures.

Sir: Thermal rearrangement of 1,5-hexadiyn-3-ene (**1** and **3**, eq 1) proceeds through a 1,4-dehydrobenzene intermediate which we believe has diradical structure **2** at the temperatures required for rearrangement.[1,2] We now find that substituted systems also undergo cyclization to derivatives of **2**, and at higher temperatures than those required for rearrangement, chemistry involving interaction of the aryl radical centers with the substituents occurs. In one case formation of the observed product is most easily understood by postulating the intervention of 1,3-dehydrobenzene, or *m*-benzyne, intermediates. Furthermore, as in the 1,4 case, the 1,3 intermediates appear to behave as diradicals at these temperatures.



1 **2** **3** (1)

Our studies involve the synthesis (Chart I) and gas-phase flow pyrolysis of diynes **4**, **5**, and **6**. Both stereoisomers[3] of **4** and **5** were stable at temperatures substantially above those (ca. 150 °C) normally required for the $1 \rightleftharpoons 3$ rearrangement. At temperatures near 300 °C, thermal interconversion of **4a** and **5a** (Chart II) was observed, the equilibrium lying predominantly (99:1) on the side of **5a**. At 450 °C cis/trans isomerization set in, and irreversible conversion to new products was also observed. Four major products, along with several unidentified materials in minor amount, were formed (Chart II). The structures of **7** and **9** were assigned by independent synthesis, and **8** and **10** were assigned on the basis of mass spectroscopic and NMR data. Most importantly, only *m*-(trimethylsilyl)isobutenylbenzene (**7**) was formed; the ortho and para isomers were not observed. The quantitative product distributions are shown in Table I.

In the case of diyne **6**, the presence of two bulky substituents at the terminal positions made cyclization an even slower process. Cis/trans isomerization once again was observed near 450 °C but irreversible conversion to new products required temperatures near 530 °C. Three major products were formed in >95% total yield (Chart II). Two are isomeric isopropenyl(trimethylsilyl)toluenes: only one of the two possible 1,2,3 isomers (**11**) and one of the two possible 1,2,4 isomers (**12**).[4] The third product was once

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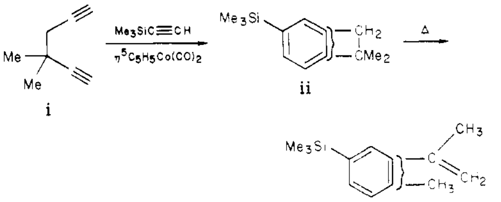
(1) Jones, R. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660.

(2) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25.

(3) Application of the *E*/*Z* nomenclature to the hexenediynes discussed here requires that some of the compounds having the two alkynyl groups in cis relationship be termed the *E* isomer, and in other cases the *Z*. Because this makes discussion of our results somewhat clumsy, we have taken the liberty of reverting to the older (somewhat arbitrary) system, and will refer in all cases to those compounds with the two alkynyl groups in cis relationship as the cis isomer.

(4) The two pyrolysis products were determined to be isopropenyl(trimethylsilyl)toluenes on the basis of analytical and NMR spectral data.



i ii 12

A mixture of 2,2-dimethyl-3- and 4-(trimethylsilyl)benzocyclobutenes (ii) were prepared from diyne i as shown above.[4a] Pyrolysis of this mixture gave 1-methyl-2-isopropenyl-4-(trimethylsilyl)benzene and 1-isopropenyl-2-methyl-4-(trimethylsilyl)benzene (**12**). This result allowed us to distinguish the set of compounds **11** from the set **12**. It also demonstrated that the two isomeric compounds present in **12** could be resolved gas chromatographically, and that compounds ii were unstable to the conditions used for pyrolysis of the diynes, rearranging only to **12**: Hillard, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1977**, *99*, 4058.