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(3) **1** was prepared from 2-anthryllithium and 2,3-dichloro-1,4-dioxane in 22% yield: yellow plates, mp 165–167.5 °C ($CHCl_3$–cyclohexane); ^1H NMR (60 MHz, $CDCl_3$) δ 4.37 (m, 4 H, $(CH_2)_2$), 6.99 (s, 1 H, CHO), 7.56 (m, 3 H), 8.08 (m, 4 H), and 8.50 (s, 2 H); satisfactory analysis.
(4) A. P. Schaap, A. L. Thayer, E. C. Blossey, and D. C. Neckers, *J. Am. Chem. Soc.*, **97**, 3741 (1975).
(5) Whether the formation of **3** and **4** is the result of 1,2-cycloaddition of $^1O_2$ to **1** or of rearrangement of **2** to **3** under the reaction conditions is still under investigation.
(6) Yellow solid; mp 137–139 °C; UV (*o*-xylene) λ_{max} (log ϵ) 325 (3.39), 340 (3.61), 358 (3.68), 378 (3.69), and 398 nm (3.67); IR (KBr) 1701 and 1719 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 4.71 (s, 4 H, $(CH_2)_2$), 7.63 (m, 2 H, aromatic), 8.16 (m, 4 H, aromatic), 8.32 (s, 1 H, CHO), 8.54 (s, 1 H, aromatic), 8.67 (s, 1 H, aromatic), and 8.94 (s, 1 H, aromatic); satisfactory analysis.
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(13) J. P. LeRoux and C. Goasdoue, *Tetrahedron*, **31**, 2761 (1975).
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(15) T. Wilson, M. E. Landis, A. L. Baumstark, and P. D. Bartlett, *J. Am. Chem. Soc.*, **95**, 4765 (1973).
(16) The UV spectrum of **3** is identical with that of 2-methylanthracene.
(17) H. H. Wasserman and J. R. Scheffer, *J. Am. Chem. Soc.*, **89**, 3073 (1967).
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(19) Catalysis of the decomposition of **2** at 80 °C by glass wool indicates that surface effects at the vessel walls will have to be investigated.
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(21) D. C.-S. Lee and T. Wilson in "Chemiluminescence and Bioluminescence", M. J. Cormier, D. M. Hercules, and J. Lee, Ed., Plenum Press, New York, N.Y., 1973, p 265.
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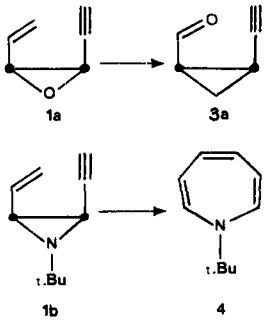
A New Valence Tautomerism: Thermal Rearrangement of *cis*-2-Vinyl-3-ethynyl Three-Membered Heterocycles

Sir:

In recent years, there has been a considerable interest in the Cope rearrangement of 2,3-divinyl[1] and 2,3-diethynyl[2] three-membered rings. Our continuing interest in the thermolytic behavior of 1,5-enynes[3a,b] and the recently published rearrangement of *cis*-1-ethynyl-2-vinylcyclopropane,[3c] prompt us to report on our study of the valence isomerization of *cis*-1-ethynyl-2-vinyloxirane (**1a**) and *cis*-*N*-*tert*-butyl-2-ethynyl-3-vinylaziridine (**1b**).

The desired starting material **1a** was prepared by treatment of 3,4-dihydroxy-1,5-hexenyne[4] (erythro + threo) with 2 equiv of sodium hydride, and 1 equiv of *p*-toluenesulfonyl chloride in ether. A mixture of *cis*- and *trans*-**1a** was obtained (52% yield, cis:trans 1:0.7) and separated by preparative vapor phase chromatography. Deuterated **1c** was prepared by stirring **1a** with BaO in a large excess of D_2O.[5] Aziridine **1b** was prepared conveniently by aminolysis of *cis*-**1a** (46% yield), followed by cyclization of the intermediate threo amino alcohol[6] with Ph_3PCl_2 at room temperature[7] (31% yield). The structures of **1a,b** were established by NMR spectroscopy.[8]

Scheme I



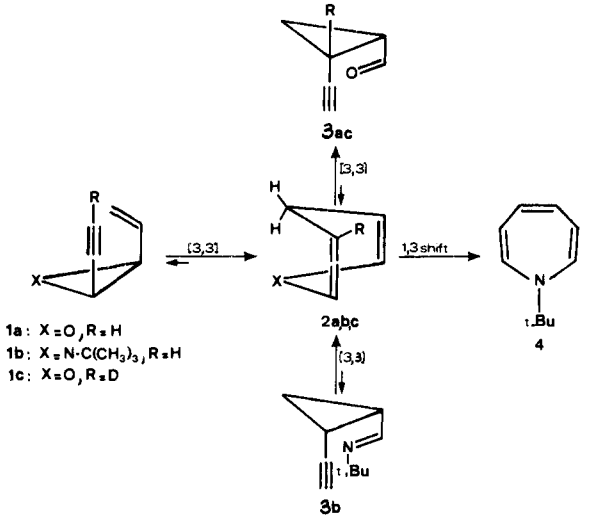
Thermal rearrangements were conducted in sealed tubes in inert solvents (C_6H_6, CCl_4) over the temperature range 80–130 °C. These reactions gave rise to a single product; *cis*-1-carboxaldehyde-2-ethynylcyclopropane (**3a**) and *N*-*tert*-butyl-1*H*-azepine (**4**), respectively, from *cis*-**1a** and *cis*-**1b**. The structure of *cis*-**3a** was established by its straightforward spectral characteristics: ^1H NMR (60 MHz, C_6H_6, δ_{Me_4Si}) O═^{5}—^{4}∇$_6$^{3}—^{2}≡^{1} 9.22 (m, 1 H, H_5), 2.02 (d, 1 H, J = 1.6 Hz, H_1), 1.85–1.50 (m, 2 H, H_4 and H_3) 1.46–0.8 (m, 2 H, H_6); ^{13}C NMR (15.08 MHz, $CDCl_3$, δ_{Me_4Si}) 69.1 (d, C_1), 81.0 (d, C_2), 8.7 (d, C_3), 27.7 (d, C_4), 200.7 (d, C_5), 14.4 (t, C_6); IR ($CHCl_3$, cm^{-1}), 3200, 2100, 1705; MS (70 eV, *m/e*, rel intensity %) 94 (M^+, 5), 65 (100), as well as by its facile conversion to *trans*-**3a**[9] by thermolysis in a flow system[10] at 350 °C.

The structural assignment of **4** was based on its ^1H NMR spectrum (60 MHz, CCl_4, δ_{Me_4Si}) 5.87 (t, 2 H, H-C_4), 5.30 (d, 2 H, J = 7.5 Hz, H-C_2) 4.95 (2t, 2 H, H-C_3), 1.12 (s, 9 H, *t*-Bu); the ethylenic part of the spectrum is very similar to that of *N*-carbalkoxy-1*H*-azepines.[11] The ^{13}C NMR spectrum (15.08 MHz, $CDCl_3$, δ_{Me_4Si}) 26.5 (methyls) 52.4 (quater, C) 114.4, 132.1, and 135.8 (C_2, C_3, and C_4) confirmed this structural assignment.

The rearrangement of **1a** is stereospecific and follows a clean first-order rate law[12] (up to 70% reaction) with respect to starting material. The calculated rate constants ($\times 10^3$ mn) were determined by least-squares analysis of the experimental data: k(102°.8) = 2.70, k(110°.5) = 5.64, k(113°.6) = 7.83, k(116°8) = 10.58, k(120°6) = 14.61, k(130°6) = 29.10. The activation parameters ($\Delta H^{\ddagger}$ = 25.1 ± 1.7 kcal mol^{-1}, $\Delta S^{\ddagger}$ = −3 ± 3 eu) are compatible with a Cope rearrangement. The enthalpy of activation for this rearrangement is only 2.4 kcal mol^{-1} higher than that for the rearrangement of *cis*-divinyloxirane.[1i]

The following mechanism (Scheme II) is proposed to ac-

Scheme II



count for this new thermal isomerization. In the first step, a highly strained seven-membered heterocycle **2a** is formed via a [3,3]sigmatropic rearrangement of **1a.** This species may either give **3a** or return to **1a** by means of [3,3]sigmatropic shifts. Since the estimated heat of formation of **3a** (calculated by the method of Benson et al.[13]) is ~19 kcal mol^{-1} less than that of **1a,** the reaction proceeds in the expected direction, i.e., **1a** → **3a.** In contrast to the isomerization of *cis*-1-ethynyl-2-vinylcyclopropane,[3c] no dimers[14] were formed from the allenic intermediate **2a.** The above mechanism is supported by the analogous conversion of deuterated compound **1c** to **3c.** The structure of **3c** is confirmed by NMR: the spectrum reveals only one cyclopropane hydrogen at δ 1.85–1.50; moreover, the signal of the acetylenic hydrogen appears as a singlet.

Thermal rearrangement of **1b** to **3b** should also occur since the heat of formation of **3b** is estimated[13] to be less than ~9 kcal mol^{-1} that of **1b.** Nevertheless, only the formation of **4** is observed when **1b** is heated at 90 °C for 20 min. A pathway consistent with this fact would be a 1,3-hydrogen shift from the proposed intermediate **2b.** Since a thermal concerted 1,3-shift is forbidden by the Woodward–Hoffman rules,[15] we suggest that the hydrogen transfer occurs intramolecularly and is catalyzed by the nitrogen atom in **2b:** one of the two allylic hydrogens is near the nitrogen atom, because the six centered transition state leading to **2b** must generate a cis double bond. This hypothesis for the formation of the intermediate **2b** is further supported by the fact that **4** is the only product formed when *cis*-**3b**[16] is subjected to flow pyrolysis[10] at 350 °C.[17]

It may be asked why different pathways are observed when **1a** and **1b** are submitted to pyrolysis. This can be attributed to the higher basicity of the nitrogen atom over the oxygen atom.

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(4) S. Galaj and Y. L. Pascal, *Bull. Soc. Chim. Fr.*, 3979 (1972).

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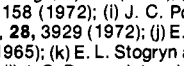
(6) CH_2=CHCH(NH-*t*-Bu)CH(OH)C≡CH, ^{1}H NMR (60 MHz, CCl_4, δ_{Me_4Si}) 1.15 (s, 9 H, *t*-Bu), 2.32 (d, 1 H, J = 2.32 Hz, HC≡), 2.9 (2 H, NH and OH) 3.26 (br t, 1 H, J = 7.5 Hz, HCN), 3.90 (2d, 1 H, J = 2.15 Hz, HCO) 5.03–5.38 (m, 2 H, CH_2=), 5.60–6.20 (m, 1 H, –CH=).

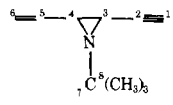
(7) (a) R. Appel and R. Kleinstuck, *Chem. Ber.*, **107,** 5 (1974); (b) J. C. Pommelet and J. Chuche, *Can. J. Chem.*, **54,** 1571 (1976).

(8) cis-**1a:** ^{1}H NMR (60 MHz, CCl_4, δ_{Me_4Si}) 2.32 (d, 1 H, J = 1.6 Hz, H_1),



cis-**1a**

3.26–3.50 (m, 2 H, H_3 and H_4), 5.16–6.00 (m, 3 H, H_5 and H_6). ^{13}C NMR (15.08 MHz, $CDCl_3$, δ_{Me_4Si}) 74.1 (d, C_1), 78.6 (d, C_2), 46.0 (d, C_3), 57.9 (d, C_4), 132.6 (d, C_5), 122.3 (t, C_6). MS (70 eV, *m/e*, rel intensity %) 94 (M^+, 5), 65 (100). cis-**1b:** ^{1}H NMR (60 MHz, CCl_4, δ_{Me_4Si}) 0.98 (s, 9 H, H_8), 1.88



cis-**1b**

(m, 1 H, H_5), 2.25 (m, 2 H, H_1 and H_3), 5.01–5.70 (m, 3 H, H_5 and H_6). ^{13}C NMR (15.08 MHz, $CDCl_3$, δ_{Me_4Si}) 69.0 (d, C_1) 82.0 (d, C_2), 26.9 (d, C_3), 39.9 (d, C_4), 136.2 (d, C_5), 118.0 (t, C_6), 54.1 (s, C_7), 26.3 (q, C_8). MS (70 eV, *m/e*, rel intensity %) 149 (M^+, 32), 93 (100).

(9) Spectral data for *trans*-**3a:** ^{1}H NMR (60 MHz, C_6H_6, δ_{Me_4Si}) 8.96 (d, 1 H, J = 3.8 Hz, H_5), 2.10–1.36 (m, 2 H, H_3 and H_4) 1.88 (d, 1 H, J = 1.6 Hz, H_1), 1.30–0.50 (m, 2 H, H_6). MS (70 eV, *m/e*, rel intensity %) 94 (M^+, 4), 65 (100).

(10) The products were dropped through a hot vertical Pyrex tube 80-cm in length; all pyrolyses carried out at ~15 Torr.

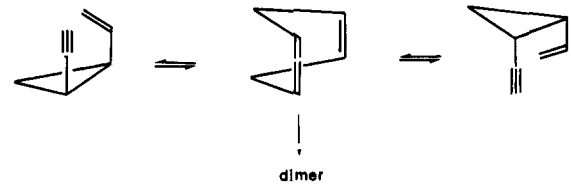
(11) L. A. Paquette, D. E. Kuhla, J. H. Barrett, and R. J. Haluska, *J. Org. Chem.*, **10,** 2866 (1969).

(12) The rates of disappearance of **1a** were determined in sealed tubes; 300 μL of a solution of **1a** in CCl_4 was placed in the tubes. The tubes were then frozen in dry ice–acetone, evacuated (0.1 Torr) and sealed off under nitrogen, while frozen. The contents of the tube were analyzed by NMR.

(13) S. W. Benson, "Thermochemical Kinetics", Wiley, New York, N.Y., 1968.

(14) It is likely that *cis*-1-ethynyl-2-vinylcyclopropane[3c] might undergo the degenerate rearrangement shown below.

Scheme III

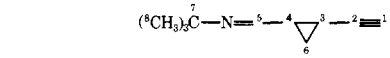


dimer

The authors would like to thank a referee for this suggestion.

(15) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8,** 829 (1969).

(16) **3b** was prepared in 45% yield by treatment of *cis*-**3a** with *tert*-butylamine and $CaCl_2$ in ether. ^{1}H NMR (60 MHz, $CDCl_3$, δ_{Me_4Si}) 7.30 (d, 1 H, J = 6.2



Hz, H_5), 2.25–1.60 (m, 2 H, H_3 and H_4) 1.95 (d, 1 H, H 1.8 Hz, H_1), 1.53–0.82 (m, 2 H, H_6), 1.20 (s, 9 H, H_8). ^{13}C NMR (15.08 MHz, $CDCl_3$, δ_{Me_4Si}) 67.4 (d, C_1), 82.9 (d, C_2), 6.9 (d, C_3), 22.7 (d, C_4), 158.6 (d, C_5), 14.3 (t, C_6), 57.1 (s, C_7), 29.8 (q, $_8$). MS (70 eV, *m/e*, rel intensity %) 149 (M^+, 28), 93 (100).

(17) Compound **3b** is stable under the milder conditions (90 °C) used for rearrangement of **1b.**

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The Crystal Structure of the Mushroom Toxin β-Amanitin[1]

Sir:

The deadly poisonous mushroom *Amanita phalloides* contains a number of cyclic peptides which can be classified as phallotoxins (heptapeptides), amatoxins (octapeptides), and antamanide, a decapeptide antagonist of the phallotoxins. The amatoxins cause death by destroying liver cells and damaging the secretory cells of the convoluted tubules in the kidney via inhibition of RNA polymerase II.[2,3] Although the chemical sequences of these cyclopeptides have been determined, only antamanide has been subjected to a three-dimensional structure analysis.[4]

We wish to report the x-ray crystallographic structure determination of the amatoxin β-amanitin, isolated and purified from American *Amanita phalloides.*[5] β-Amanitin (**1**), $C_{39}H_{53}SO_{15}N_9$, has the chemical sequence cyclo (L-α-aspartyl-4-hydroxy-L-prolyl-4,5-dihydroxy-L-isoleucyl-6-hydroxy-2-mercapto-L-tryptophyl-glycyl-L-isoleucyl-glycyl-L-cysteinyl) cyclo(4 → 8)-*S*-oxide. The octapeptide ring is bridged through the sulfur atom of the sulfoxide form of cysteine to the 2 position of the indole ring. The resulting bicyclic structure contains two 18-membered rings.

Crystals were grown by slow evaporation from a 95% eth-