a methyl decreases the reactivity of disilanes toward perbenzoic acid, and qualitatively this is the same tendency as was observed with the series of phenyl substituted ethylenes.[7]

| Disilanes | $k_2 \times 10^4$, 1. mole$^{-1}$ sec.$^{-1}$ |
|---|---|
| Me₃SiSiMe₃ | 11.7, 11.9 |
| p-MeOC₆H₄SiMe₂SiMe₃ | 11.9, 11.9 |
| p-MeC₆H₄SiMe₂SiMe₃ | 8.79, 8.77 |
| m-MeC₆H₄SiMe₂SiMe₃ | 7.44, 7.32 |
| C₆H₅SiMe₂SiMe₃ | 6.93, 7.00 |
| p-ClC₆H₄SiMe₂SiMe₃ | 6.46, 6.50 |
| C₆H₅SiMe₂SiMe₂C₆H₅ | 3.89, 3.87 |

These results suggest that a possible mechanism for this reaction is direct insertion of an oxygen atom,
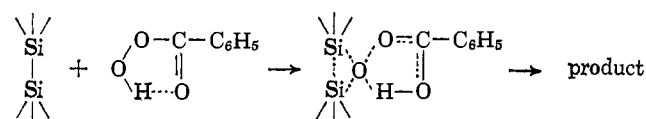


involving electrophilic attack of disilane by a cyclic hydrogen-bonded form of the peracid.[8]

We are investigating the mechanism of the reaction in detail and are extending our studies to the 1,2-diphenyl-tetramethyldisilane system, solvent effect, and stereochemistry.

(7) B. M. Lynch and K. H. Pausacker, J. Chem. Soc., 1525 (1955).

(8) An analogous molecular mechanism was first suggested by Bartlett [P. D. Bartlett, Record Chem. Progr., 11, 47 (1950)] for epoxidation and proposed for the mode of action of perbenzoic acid on 4,4'-dichlorodibenzyl sulfide [C. G. Overberger and R. W. Cummins, J. Am. Chem. Soc., 75, 4250 (1953)], trans-stilbenes,[7] methyl phenyl sulfoxides, and diphenyl sulfoxides [A. Cerniani and G. Modena, Gazz. chim. ital., 89, 843 (1959)], and α,α'-dimethylstilbenes.[4]

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Received June 14, 1965

## Benzocyclobutene Derivatives from the Reactions of Benzyne with Vinyl Ethers and Esters

Sir:

Cycloaddition reactions of benzyne with olefins to give benzocyclobutene derivatives are relatively rare.[1] More generally, reactions with simple olefins yield mixtures of products resulting from hydrogen abstraction.[1a,2]

We wish to report on the synthetically useful reactions of benzyne with the electron-rich systems ethyl vinyl ether and vinyl acetate to form derivatives of benzocyclobutenol. In the case of 1-ethoxyvinyl acetate, benzocyclobutenone is a minor product, the main

(1) (a) H. E. Simmons, J. Am. Chem. Soc., 83, 1657 (1961), observed the first examples of cycloaddition with the strained olefins bicyclo-[2.2.1]heptadiene and bicyclo[2.2.1]heptene; (b) G. Wittig and H. Durr, Ann., 672, 55 (1964), reported the formation of 4-6% of cycloaddition product from the reaction of benzyne with 2,3-dimethylbutadiene; see also (c) M. Kuehne, J. Am. Chem. Soc., 84, 837 (1962), and M. Kuehne and T. Kitagawa, J. Org. Chem., 29, 1270 (1964), for examples of cycloaddition among reaction products of benzyne with enamines.

(2) E. M. Arnett, ibid., 25, 324 (1960).

reaction involving a novel ortho disubstitution of the benzene ring.[3]

Benzenediazonium-2-carboxylate was refluxed with a sixfold excess of ethyl vinyl ether in methylene chloride solution for 45 min. After concentration of the solution, chromatography on neutral alumina, and distillation of the product (35° at 225 μ), ethyl benzocyclobutenyl ether (I) was obtained in ca. 40% yield. Anal. Calcd. for C₁₀H₁₂O: C, 81.04; H, 8.16. Found: C, 80.84; H, 8.06. The structure of the ether follows from its ultraviolet absorption spectrum ($\lambda_{max}^{EtOH}$ 260 mμ (log ε 3.09), 266 (3.27), and 272 (3.25)) and from the n.m.r. spectrum: τ 2.8 (singlet, 4 H), 5.03 (quartet, 1 H), 6.2–7.15 (multiplet, 4 H), and 8.9 (triplet, 3 H).[4] Conversion of the ether to the corresponding acetate (II) using acetic anhydride, boron trifluoride etherate, and lithium bromide[5] confirmed the structure (Chart I).

Chart I
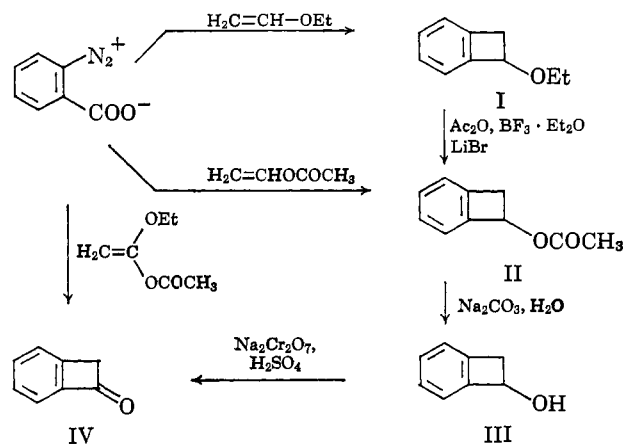


By heating benzenediazonium-2-carboxylate with excess vinyl acetate in methylene chloride and working up the reaction mixture as described above (using silica gel instead of alumina), benzocyclobutenyl acetate (II) could be prepared directly (ca. 45%). Anal. Calcd. for C₁₀H₁₀O₂: C, 74.06; H, 6.21. Found: C, 73.85; H, 6.36. The n.m.r. spectrum shows peaks at τ 2.78 (singlet, 4 H), 4.16 (quartet, 1 H), 6.25–7.05 (octet, 2 H), and 8.02 (singlet, 3 H). Hydrolysis of the acetate with 5% aqueous sodium carbonate[6] in ethanol yielded benzocyclobutenol (III), m.p. 58.5–59.5° (lit. 58°).

The reaction of benzyne with 1-ethoxyvinyl acetate[7] in refluxing methylene chloride followed by distillation and then chromatography on silica gel yielded two products. The minor component (4%) was a liquid showing a split carbonyl absorption in the infrared at $\lambda_{max}^{CCl_4}$ 1782 and 1762 cm.$^{-1}$.[6] The ultraviolet spectrum corresponds exactly to the values reported for benzo-

(3) The benzyne used in this work was generated in methylene chloride solution containing an excess of vinyl ether or ester, according to the procedure of Stiles and co-workers: M. Stiles, R. G. Miller, and U. Burckhardt, J. Am. Chem. Soc., 85, 1792 (1963). We thank Prof. Stiles for a personal communication describing revised details of this procedure.

(4) For related ultraviolet and n.m.r. data on benzocyclobutene derivatives see: (a) M. P. Cava and D. R. Napier, ibid., 80, 2255 (1958); (b) W. Baker, J. F. W. McOmie, and D. R. Preston, J. Chem. Soc., 2971 (1961); (c) H. Nozaki, R. Noyori, and N. Kozaki, Tetrahedron, 20, 641 (1964); (d) G. Fraenkel, Y. Asahi, M. J. Mitchell, and M. P. Cava, ibid., 20, 1179 (1964).

(5) R. D. Youssefyeh and Y. Mazur, Tetrahedron Letters, No. 26, 1287 (1962).

(6) M. P. Cava and K. Muth, J. Am. Chem. Soc., 82, 652 (1960), report a similar hydrolysis of benzocyclobutenyl trifluoroacetate to the alcohol.

(7) H. H. Wasserman and P. S. Wharton, ibid., 82, 661 (1960).

cyclobutenone (IV).[8] Comparison with an authentic sample prepared by the oxidation of benzocyclobutenol[8] confirmed the identity. The ketone undoubtedly arises from breakdown of the intermediate ethoxyacetoxybenzocyclobutene (VI). The main component of the reaction, m.p. 65.5–66° (25%), was identified as the ethyl ester of o-acetylphenylacetic acid (VII) by comparison with an authentic sample prepared by esterification of the known acid.[9] *Anal.* Calcd. for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 70.05; H, 6.82.
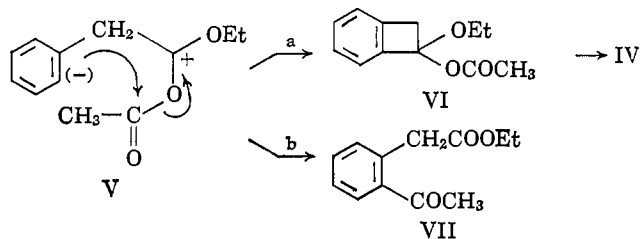


In the above reactions with electron-rich olefinic systems, benzyne appears to behave as an electrophilic agent, forming an intermediate such as V. Collapse of V to the four-membered ring (path a) or intramolecular acylation (path b, arrows) represent alternate reaction paths. Further studies on this aspect of benzyne chemistry are in progress.

(8) M. P. Cava, D. Mangold, and K. Muth, *J. Org. Chem.*, **29**, 2947 (1964).

(9) J. O. Halford and B. Weissmann, *ibid.*, **18**, 30 (1953).

(10) National Science Foundation Cooperative Fellow, 1962–1965.

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## The Anomeric Linkage of Streptose in Streptomycin and Bluensomycin

*Sir:*

With the assignment of absolute stereochemistry to the substituted streptidine fragment of streptomycin[1a,2] and confirmation of the previously assigned[3] stereochemistry of the streptose fragment by its synthesis,[4] the structure of this medicinally important antibiotic appeared to be complete[1a,b] except for the anomeric configuration of streptose in its attachment to streptidine. The usually quoted[1a,b] assignment is β-L-,[5] made in 1954[6] from rotational arguments on polybenzoyl derivatives, though the 1947 assignment of α-L- configuration,[7] based on rotations of polyacetyl de-

rivatives, appears now to have greater validity. We present nuclear magnetic resonance evidence here which assigns as α-L- the anomeric configuration of streptose in its attachment to streptidine in streptomycin (reversing the 1954 assignment[6] but agreeing with the 1947 assignment)[7] and related evidence which confirms as α-L- the earlier[6,7] stereochemical assignment of the anomeric configuration of N-methyl-L-glucosamine in its attachment to streptose.

The nuclear magnetic resonance spectra[8] of dihydrostreptomycin (I), of dihydrostreptomycin sulfate, of streptomycin (II) sulfate, and of tri-N-acetyldideguanyldihydrostreptomycin (III) contain two signals in the anomeric proton region (Table I). The signal for the anomeric proton of the N-methyl-L-glucosamine fragment is, predictably, shifted downfield in the sulfate and, less predictably, shifted upfield in the N-acetylated compounds. Its coupling constant ($J \sim 3.0$ c.p.s.) corresponds clearly to an axial–equatorial (but not axial–axial) H-1–H-2 relationship and thus to the α-L- configuration for N-methyl-L-glucosamine, in agreement with that previously assigned from rotational arguments.[6,7] Of greater interest, the anomeric proton of streptose, found near $\tau$ 4.70 in all compounds, occurs as a broad singlet ($J \leq 1$ c.p.s.). In accordance with the previously enunciated rule,[9] this can only be the case when the C-1 and C-2 protons of a furanoside are *trans* to one another. Since streptose has been established[3,4] to have the L-*lyxo* configuration, a C-1 proton *trans* to the C-2 proton corresponds to the α-L- configuration for streptose, and the complete stereochemical formula for dihydrostreptomycin (I) (and for streptomycin, II, which can be reduced to dihydrostreptomycin) is that shown.[10]
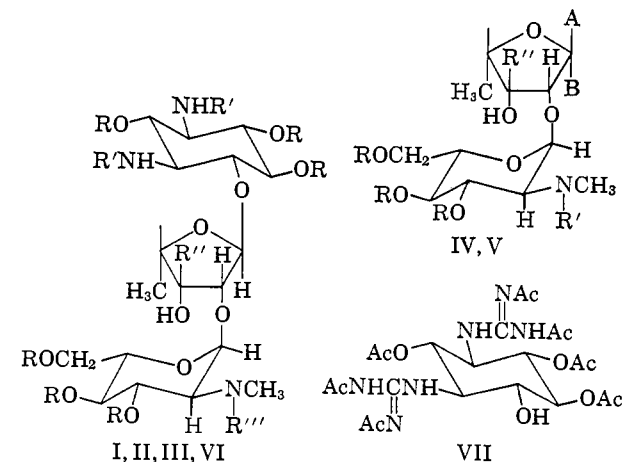


I, R = R''' = H; R' = C(=NH)NH₂; R'' = CH₂OH
II, R = R''' = H; R' = C(=NH)NH₂; R'' = CHO
III, R = H; R' = R''' = Ac; R'' = CH₂OH
IV, R = H; R' = Ac; R'' = CH₂OH
 a, A = OCH₃; B = H; b, A = H; B = OCH₃
V, R = R' = Ac; R'' = CH₂OAc
 a, A = OCH₃; B = H; b, A = H; B = OCH₃
VI, R = R''' = Ac; R = C(=NAc)NHAc; R'' = CH₂OAc

Application of Hudson's rules[5,11] to compound III allows the same conclusion (that streptose has the

(1) (a) J. R. Dyer and A. W. Todd, *J. Am. Chem. Soc.*, **85**, 3896 (1963). This reference provides a concise review of earlier streptomycin chemistry. (b) Other recent reviews of streptomycin chemistry: H. Umezawai, "Recent Advances in Chemistry and Biochemistry of Antibiotics," Microbial Chemistry Research Foundation, Tokyo, 1964, p. 67; J. D. Dutcher, *Advan. Carbohydrate Chem.*, **18**, 360 (1963).

(2) S. Tatsuoka, S. Horii, K. L. Rinehart, Jr., and T. Nakabayashi, *J. Antibiotics* (Tokyo), **A17**, 88 (1964).

(3) F. A. Kuehl, Jr., M. N. Bishop, E. H. Flynn, and K. Folkers, *J. Am. Chem. Soc.*, **70**, 2613 (1948).

(4) J. R. Dyer, W. E. McGonigal, and K. C. Rice, *ibid.*, **87**, 654 (1965).

(5) The terms "α-L-" and "β-L-" are employed in accordance with the Hudson nomenclature convention [C. S. Hudson, *ibid.*, **31**, 66 (1909)].

(6) M. L. Wolfrom, M. J. Cron, C. W. DeWalt, and R. M. Husband, *ibid.*, **76**, 3675 (1954).

(7) (a) R. U. Lemieux, C. W. DeWalt, and M. L. Wolfrom, *ibid.*, **69**, 1838 (1947); (b) R. U. Lemieux and M. L. Wolfrom, *Advan. Carbohydrate Chem.*, **3**, 337 (1948).

(8) N.m.r. spectra were determined on deuterium oxide solutions at 20°, employing the methyl signal of 3-trimethylsilyl-1-propanesulfonic acid as standard.

(9) K. L. Rinehart, Jr., W. S. Chilton, M. Hichens, and W. von Phillipsborn, *J. Am. Chem. Soc.*, **84**, 3216 (1962).

(10) The proton of the streptose C-3 formyl group of II (see Table I), in the hemiacetal or hydrate form, appears as a sharp singlet at $\tau$ 4.93.

(11) C. S. Hudson, *J. Am. Chem. Soc.*, **38**, 1566 (1916); **46**, 483 (1924).