In both compounds each carbon atom appears to have five ligands instead of the customary four ligands. To circumvent this anomaly, the concept of carbon participating in the so-called "three-centered bonds" with two boron atoms is accepted. In this connection the two carbon atoms can be visualized as substituting for two boron atoms, but with two additional electrons, thus forming the equivalent stable octahedral $B_6H_6^{-2}$ ion.[8] It already has been suggested[9] that carborane-3 $(B_3C_2H_5)$ may be isoelectronic with $B_5H_5^{-2}$. The structure postulated for $B_3C_2H_5^2$ is indeed that pictured for $B_5H_5^{-2}$.[9]

(8) W. H. Eberhardt, B. Crawford, and W. N. Lipscomb, *J. Chem. Phys.*, **22**, 989 (1954).

(9) E. B. Moore, L. L. Lohr, and W. N. Lipscomb, *ibid.*, **35**, 1329 (1961).

The apparent lack of hydrogen exchange between boron and carbon hydrogens permit the preparation of specifically labeled isotopic compounds. Although the hydrogens originally attached to the carbon and boron atoms in the parent compounds are retained in their same relative environment in the new compounds, the mechanism of formation of the new compounds must be complex since at least the carbon atoms in acetylene must undergo drastic rearrangement in the sym-$B_4C_2H_6$.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE UNIVERSITY OF SCIENCE AND TECHNOLOGY, AMES, IOWA]

Photoisomerization of Isocolchicine[1]

BY O. L. CHAPMAN, H. G. SMITH, AND P. A. BARKS[2]

Irradiation of isocolchicine in aqueous solution gives a photoisomer which is shown to be II. The mode of photochemical valence tautomerization appears to be controlled by electronic factors. The controlling factor in this case appears to be preservation of a trimethoxystyryl unit.

The difference in mode of photochemical valence tautomerization of colchicine[3-5] and simple tropolone methyl ethers[6,7] can be interpreted as a result of steric control in the colchicine photoisomerization and electronic control in the case of simple tropolone ethers.[8] Isocolchicine (I) poses an interesting problem in this light. There is little steric basis for preference for either gross structure II or III for the valence tautomer; consequently the photoisomerization of isocolchicine should be dominated by electronic factors.
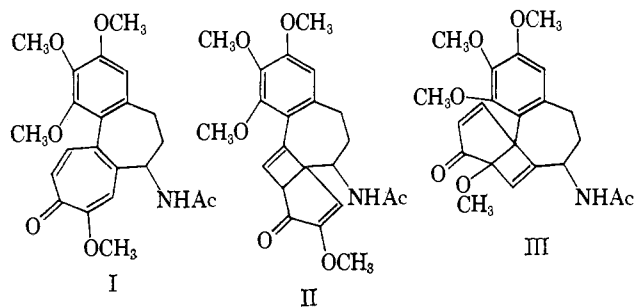
Irradiation of isocolchicine in aqueous solution gives a photoisomer (5.85, 6.01 μ; 218 (4.42) and 260 mμ (log ϵ 4.34)) in 40–50% yield. The ultraviolet absorption of the photoisomer is similar to that of β-lumicolchicine[3,4] and γ-lumicolchicine,[3,4] suggesting that the molecule contains a trimethoxystyryl chromophore. Structure III does not contain a styryl chromophore, and thus structure II is favored by the ultraviolet absorption. The nuclear magnetic resonance spec-

(1) Part IX of the Photochemical Transformation Series.

(2) Petroleum Research Fund Fellow, 1960–1962. Du Pont Teaching Fellow, 1962–1963.

(3) E. J. Forbes, *J. Chem. Soc.*, 3864 (1955).

(4) P. D. Gardner, R. L. Brandon, and G. R. Haynes, *J. Am. Chem. Soc.*, **79**, 6334 (1957).

(5) O. L. Chapman, H. G. Smith, and R. W. King, *ibid.*, **85**, 803, 806 (1963).

(6) O. L. Chapman and D. J. Pasto, *ibid.*, **82**, 3642 (1960).

(7) W. G. Dauben, K. Koch, O. L. Chapman, and S. L. Smith, *ibid.*, **83**, 1768 (1961).

(8) O. L. Chapman, Chapter in "Advances in Photochemistry," Vol. 1, edited by W. A. Noyes, Jr., G. S. Hammond, and J. N. Pitts, Jr., John Wiley and Sons, Inc., New York, N. Y., in press.

trum (Table I) of the photoisomer is also in accord with structure II. The two olefinic protons overlap giving a two proton signal at 3.65 τ. It can be demonstrated that this two proton singlet arises from chemically nonequivalent protons by use of pyridine as solvent. The nuclear magnetic resonance spectrum of II in pyridine (Table I) shows three singlet absorptions due to the aromatic proton and the two olefinic protons now rendered magnetically nonequivalent by the specific shielding effect of pyridine. The highly specific shifts of the various proton resonance positions in pyridine offers additional support[5] for Slomp's suggestion[9] that the shielding effect of pyridine is due to attachment of solvent molecules at specific sites on the solute rather than a bulk solvent effect. The remaining proton assignments are straightforward and are given in Table I.

Reduction of II with sodium borohydride gives an enol ether alcohol (6.02 μ, amide; 6.09 μ, C=C—OCH_3) which proved to be very sensitive. The nuclear magnetic resonance spectrum of IV (Table I) shows the aromatic proton and both olefinic protons clearly separated. The shift of one olefinic proton to high field (5.24 τ) identifies it as the enol ether vinyl proton. The bridgehead proton (6.67 τ) is coupled to both the proton on the carbon bearing the hydroxyl group (5.32 τ, $J = 9.4$ c.p.s.) and to the adjacent cyclobutene proton ($J = 0.86$ c.p.s.). The identity of this latter coupling has been confirmed by a double resonance experiment.[10,11] Irradiation of the bridgehead proton 173 c.p.s. upfield from the cyclobutene proton collapsed the cyclobutene proton to a singlet. The small value for this coupling constant is normal for this system in which the coupling constant falls in the range 0–1 c.p.s.[12] Mild acid hydrolysis of IV gives the keto alcohol V. The infrared carbonyl absorption (5.71 μ) of the keto alcohol confirms the presence of a five-membered ring in the photoisomer II. The keto alcohol shows the expected ultraviolet absorption for

(9) G. Slomp and F. MacKellar, *J. Am. Chem. Soc.*, **82**, 999 (1960).

(10) R. Kaiser, *Rev. Sci. Instr.*, **31**, 963 (1960).

(11) R. Freeman, *Mol. Phys.*, **3**, 435 (1960).

(12) L. M. Jackman, "Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N. Y., 1959, p. 86.

TABLE I

NUCLEAR MAGNETIC RESONANCE SPECTRA[a]

							Proton						
Compound	Aromatic	Cyclo-butene	H\=/OMe	N-H[b]	H|C-N	O-CH₃	O‖-C-CH₃	Bridgehead	Methyl-ene	H|>C-O	Hydroxyl	Water of crystn.
II (CDCl₃)	3.48	3.65	3.65	3.74	5.58	6.14 6.18 6.35	8.08	6.54	7.12 7.90	..		7.50[c]
II (pyr.)	3.45	3.34	3.36	..	5.10	6.18 6.22 6.36 6.65	8.02	5.96	7.06 7.68		..	..
IV (CDCl₃)	3.52	3.71	5.24	4.54	5.78	6.17 6.27 6.40	8.07	6.67	7.22 ~8.0	5.32	7.70[c]	..
V (CDCl₃)	3.58	3.73	..	4.02	5.64	6.20 6.36	7.99	~6.3 under OMe	7.23 ~8.0	5.64	6.2 under OMe[c]	..
VI (CDCl₃)	3.45	..	4.52	4.80	5.56	6.18 6.23 6.38 6.42	8.18	~6.15 under OMe	7.13 ~8.0	..	..	7.58[c]

[a] Resonance positions are given in τ-values relative to tetramethylsilane as internal standard. [b] The exact position of this resonance depends strongly on concentration. [c] This resonance disappears when the solution is shaken for a few seconds with 2 drops of D_2O.
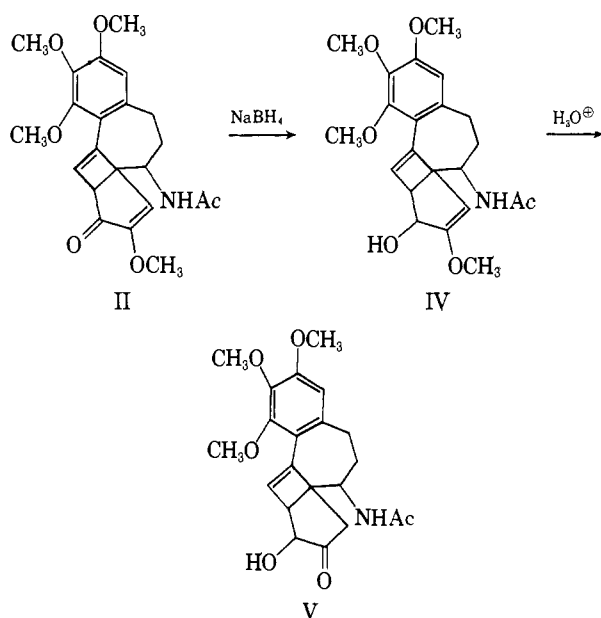

the trimethoxystyryl chromophore and gives a positive periodate test thereby establishing the juxtaposition of the ketone and hydroxyl functions. The nuclear magnetic resonance spectrum of V (Table I) shows the aromatic proton and the single olefinic proton in agreement with the assigned structure.

TABLE II

ULTRAVIOLET SPECTRA

Compound	$\lambda_{max}^{95\% \text{ EtOH}}$, m$\mu$ (ϵ)
II	218 (26,200), 260 (21,900)
IV	212 (35,530), 270 (14,850)
V	220 (25,000), 265 (15,200)
VI	207 (46,420)

The photoisomer II rapidly absorbs one equivalent of hydrogen over platinum, giving the dihydro derivative VI. Structure VI is based on the change in ultraviolet absorption, the retention of the 5.84 μ carbonyl absorption and the loss of one olefinic proton in the nuclear magnetic resonance spectrum. The nuclear magnetic resonance spectrum of the dihydro derivative VI shows one additional feature of some interest. The remaining olefinic proton appears at 4.52 τ showing

a substantial upfield shift from its position (3.65 τ) in the original photoisomer. The position of this olefinic proton is comparable to that of a similarly situated proton in β-lumicolchicine (3.32 τ).[5] The unexpectedly low-field position of these protons in II and in β-lumicolchicine must arise from paramagnetic shielding by the styryl double bond. The position of the olefinic proton in the dihydro derivative VI may be taken as the normal position. Sodium borohydride
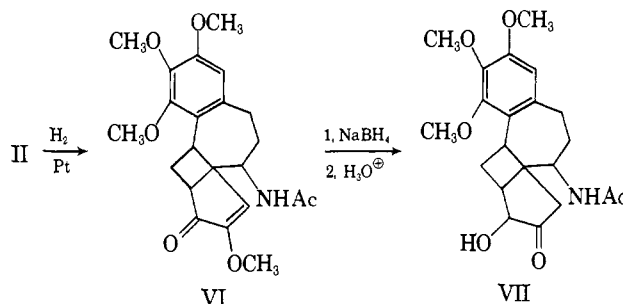
reduction of VI followed by acid hydrolysis gives a ketoalcohol (VII, 5.72 τ) which gives a positive periodate test.

The specific formation of II in the irradiation of isocolchicine suggests strongly that generation of the trimethoxystyryl system in the product is a significant factor in electronic control of product formation both in the colchicine and the isocolchicine irradiation.

Experimental

Colchiceine.—Colchicine (60.0 g., 0.15 mole) was refluxed with stirring in dilute hydrochloric acid (700 ml., 0.1 N)[13] for 1 hr. on a steam bath. After cooling to 15° the amorphous mass which precipitated was broken up, filtered, and washed with cold water. Recrystallization from aqueous ethanol gave colchiceine (31.0 g., 53.6%). A second crop of colchiceine (15.0 g., 26.0%) was obtained by refluxing the acidic filtrate for an additional hour (total yield 46.0 g., 79.6%).

Isocolchicine.[14]—Colchiceine (26.0 g., 0.0675 mole) was dissolved in methylene chloride (25 ml.) and added dropwise to a stirred, ice-cooled methylene chloride solution of diazomethane (from 16.0 g. of N-nitroso-N-methylurea). After the vigorous evolution of nitrogen had ceased (10 min.), the excess diazomethane was removed by gentle boiling. Chloroform (50 ml.) was added, and the solution was concentrated. Ethyl acetate (75 ml.) was added, and the solution was boiled vigorously for several minutes (to remove all halogenated solvents). Pure isocolchicine precipitated from the cooled solution and was fil-

(13) E. Boyland and E. H. Mawson, *Biochem. J.*, **32**, 1204 (1938).

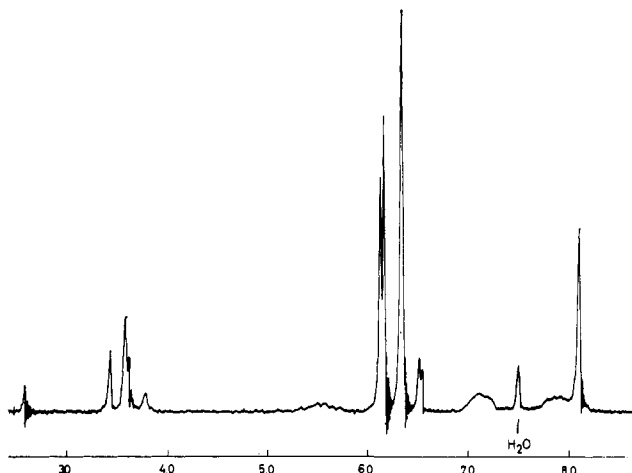(14) M. Sorkin, *Helv. Chim. Acta*, **29**, 246 (1946).

Fig. 1.—Nuclear magnetic resonance spectrum of photoisomer II (100 mg. in 400 μl. of CDCl₃). The scale is calibrated in τ-values relative to internal tetramethylsilane.

tered and washed with cold ethyl acetate. The isocolchicine was purified by boiling in ethyl acetate or recrystallization from ethyl acetate with a few drops of chloroform (m.p. 220–222°, 6.5 g., 25%).

Irradiation of Isocolchicine.—Isocolchicine (3.0 g., 0.0075 mole) was dissolved in water (2 l.) and flushed with nitrogen for 1 hr. The mercury arc lamp (Hanovia Type A, 550 watts) was inserted in a Pyrex immersion well, cooled with water (12°). The reaction solution was stirred (Teflon stirring bar), and a slow stream of nitrogen was bubbled through the solution for the duration of the irradiation. The progress of the irradiation was followed by the disappearance of the 343 mμ band in the ultraviolet. The maximum yield of photoproduct was obtained after 60–65 hr. irradiation (40% complete).

The aqueous solution was saturated with sodium chloride and extracted with chloroform (4 × 250 ml.) and the extract dried over magnesium sulfate. Filtration and evaporation gave a red viscous mass (3 g.) which was dissolved in hot ethyl acetate and placed in a beaker. After boiling the solution (to remove all the chloroform) and then cooling, unreacted isocolchicine was precipitated, filtered, and washed with cold ethyl acetate (recovery 1.2–1.5 g., 40–50%). The combined filtrates were concentrated to dryness, dissolved in benzene–chloroform (15 ml., 3:1), and chromatographed on a neutral alumina column (50 g.). Elution with benzene–chloroform (1:1) gave crude II as a yellow glass (1.0 g.). Elution with chloroform gave crude isocolchicine (0.6 g.), which crystallized from boiling ethyl acetate, giving pure isocolchicine (0.5 g.). The crude photoisomer II crystallized from aqueous methanol, ethanol, or dioxane giving pure II (0.5 g., 38–50% based on unrecovered isocolchicine) as small, colorless needles of the monohydrate, m.p. 119.5–121.5°, λ$_{max}^{95\%EtOH}$ 218 (26,200) and 260 mμ (ε 21,900); λ$_{max}^{CHCl}$ 5.85, 6.02 μ. The nuclear magnetic resonance spectrum of II showed the water of crystallization as a singlet at 7.50 τ which was removed by shaking with deuterium oxide for a few seconds.

Anal. Calcd. for C₂₂H₂₅O₆N·H₂O: C, 63.30; H, 6.52; N, 3.36. Found: C, 63.56; H, 6.63; N, 3.09.

High vacuum drying of II monohydrate (78°, 24 hr., 0.05 mm.) gives II which showed no water in the nuclear magnetic resonance spectrum (m.p. 115.5–116.5°, resolidified from 130–145°, second m.p. 196–199°).

Reduction of II to IV.—Sodium borohydride (0.2 g., 98% purity) and water (2 ml.) were added to a stirred solution of II (0.150 g., 0.38 mmole) in tetrahydrofuran (20 ml.). The stirred mixture was refluxed for 2 hr., then cooled to room temperature. Water (12 ml.) was added, and the reaction mixture was concentrated (*in vacuo*) to 10 ml. The solution (pH 11) was extracted with chloroform (4 × 3 ml.), dried over magnesium sulfate and potassium carbonate, filtered, and concentrated (*in vacuo*), giving a colorless, viscous oil. Trituration with benzene (3 ml.) gave IV as a colorless powder which was recrystallized from acetone–methanol giving colorless diamond-shaped crystals (0.070 g., 47%, m.p. 206–209° dec.); λ$_{max}^{95\%EtOH}$ 212 mμ (ε 35,530), λ$_{max}^{95\%EtOH}$ 270 mμ (ε 14,850), λ$_{max}^{CHCl₃}$ 6.02 and 6.09 μ.

Anal. Calcd. for C₂₂H₂₇O₆N: C, 65.82; H, 6.78; N, 3.49. Found: C, 65.88; H, 7.00; N, 3.70.

Keto Alcohol V.—A solution of IV (0.075 g., 0.19 mmole), ethanol (95%, 1 ml.), water (4.0 ml.), and sulfuric acid (1.0 N, 1.0 ml.) was heated in a test tube on a steam bath for 5 min. The cooled reaction mixture was extracted with chloroform (3 × 1.5 ml.) and the combined extracts were dried over magnesium sul-
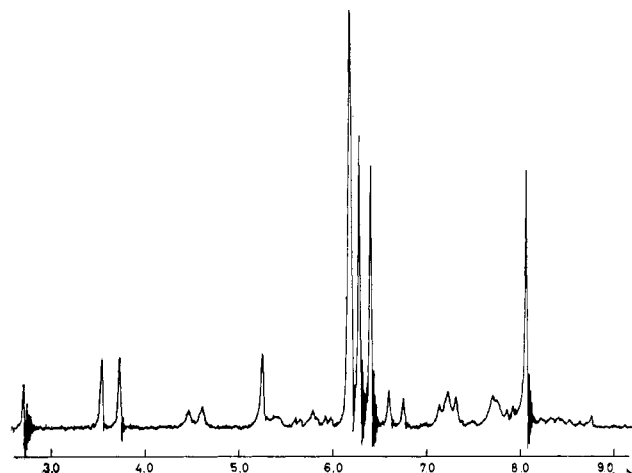
Fig. 2.—Nuclear magnetic resonance spectrum of the enol ether alcohol IV (40 mg. in 400 μl. of CDCl₃). The scale is calibrated in τ-values relative to tetramethylsilane.

Fig. 3.—Double resonance experiment on IV. Before irradiation of the bridgehead proton the cyclobutene proton appears as a doublet (J = 0.86 c.p.s.). After irradiation of the bridgehead proton the doublet collapses to a singlet.

fate. Filtration and concentration (*in vacuo*) gave a colorless viscous oil which was treated with ethanol (1.0 ml.) and evaporated again (to remove chloroform). The crude product gave a positive periodic acid test. Colorless platelets were obtained by crystallization from aqueous ethanol or aqueous acetone; m.p. 229–231°, λ$_{max}^{95\%EtOH}$ 220 mμ (ε 25,000), λ$_{max}^{95\%EtOH}$ 265 mμ (ε 15,200), λ$_{max}^{CHCl₃}$ 5.71 and 6.00 μ.

Anal. Calcd. for C₂₁H₂₃O₆N: C, 65.10; H, 6.50; N, 3.62. Found: C, 65.40; H, 6.73; N, 3.47.

Reduction of II to VI.—A solution of II (1.10 g.) in 95% ethanol (70 ml.) was reduced with hydrogen over Adams catalyst (52 mg.). After 1.05 moles of hydrogen was taken up the catalyst was filtered and the filtrate concentrated (*in vacuo*). The yellow oil was crystallized from ethanol–water (1:3, 20 ml. total) giving colorless needles (m.p. 113.5–115.5°, resolidified between 140–170° and remelted 219–225°), λ$_{max}^{95\%EtOH}$ 207 mμ (ε 46,420), λ$_{max}^{CHCl₃}$ 5.84 and 6.01 μ.

Anal. Calcd. for C₂₂H₂₇O₆N·H₂O: C, 62.99; H, 6.97; N, 3.34. Found: C, 62.89; H, 6.95; N, 3.64.

Conversion of VI to VII.—Reduction of VI (0.125 g.) with sodium borohydride (0.125 g.) as above gave a colorless oil (λ$_{max}^{CHCl₃}$ 6.03, 6.11 μ) which was hydrolyzed with sulfuric acid (1.0 ml., 1.0 N) in water (4 ml.) and ethanol (4 ml.). The reaction mixture was extracted with chloroform (3 × 4 ml.) and dried over anhydrous magnesium sulfate, filtered, and concentrated to dryness giving VII as a colorless powder (m.p. 140–148°) which could be crystallized from ethyl acetate–ethanol (m.p. 146–149°); λ$_{max}^{CHCl₃}$ 5.72 and 6.00 μ. The product gave a positive periodic acid test.