tion energies was taken from Bergman.[23] Reduction half-wave potentials in dimethylformamide[22] and in 2-methoxyethanol[23] yield similar results. The difference in polarographic oxidation and reduction potentials plus the mean value of k gives the transition energy of the absorption band to within 3% in most cases and to within 5% in all cases.

Monomethylated Benzanthracenes.—The monomethyl derivatives of 1,2-benzanthracene have been studied with respect to many theoretical and experimental parameters. Theoretical calculations of free valence numbers using both molecular orbital[24] and valence bond[25] methods, self-polarizabilities[26] and excitation energies[27] have been reported. Experimental measurements of the ultraviolet spectra and shifts with respect to the spectrum of unsubstituted 1,2-benzanthracene,[26,28] rates of reaction with osmium tetroxide,[29] rates of reaction with silver ion[30] and dissociation constants of charge-transfer complexes with trinitrofluorenone[31] have been reported.

Most of the investigators have been concerned with the varying degree of carcinogenicity within the series. In studies using both injection and skin painting techniques, the 7-, 8- and 12-methyl derivatives were found to be moderately potent, the 5-, 6-, 9-, 10- and 11-methyl derivatives were found to be weakly carcinogenic and the 1-, 2-, 3- and 4-methyl derivatives were found to be inactive. Thus the monomethylated benzanthracenes provide a structurally similar group of compounds with varying degrees of carcinogenicity, against which variation in any other parameter can reasonably be compared.

In several attempts to establish a purely electronic theory of carcinogenicity, data on the methylbenzanthracenes have been presented. The activity of 8-methylbenzanthracene cannot reasonably be attributed to a negligible difference in the calculated free valence numbers or self-polarizabilities. When carcinogenicity is compared with a calculated excitation energy, a significant separation appears between the 8-methyl derivative and the other non-*meso*-methylated compounds, but this is not supported by any experimental measurements.

Polarographic evidence helps clarify the problem. As noted above, the values of $E_{1/2(ox)}$ for the 7- and 12-methyl derivatives are significantly lower than those of the remaining compounds of the series. The variation in the remaining compounds is not more than two times the mean deviation of the values. The difference, however, between the 7-methyl compound and the 8-methyl compound is 0.05 v., which is five times the experimental mean deviation. The experimental results would tend to suggest that the calculations of excitation energies for the series result in a misleading spread of values. It would seem that the potency of the 8-methyl derivative of benzanthracene must be ascribed to non-electronic factors.[32]

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Photochemical Transformations. XIV. Isocolchicine[1,2]

BY WILLIAM G. DAUBEN AND DAVID A. COX

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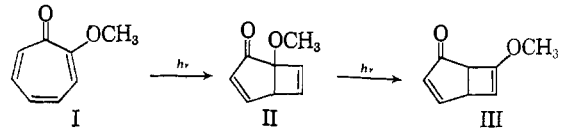
Ultraviolet irradiation of isocolchicine (VII) in methanol gives the valence isomer VIII as the major product, showing the desire of a phenyl-substituted tropolone to retain the styrene chromophore. In addition, a methanol adduct possessing structure XXV, related to γ-lumicolchicine, was formed in lesser amounts.

The photochemical-induced transformation of the tropolone nucleus has been shown to be an excellent synthetic route to the preparation of the $\Delta^{3,6}$-bicyclo[3.2.0]heptadiene-2-one system.[3] For example, α-tropolone methyl ether (I) upon irradiation in methanol by a mercury arc gives rise first to 1-methoxy-$\Delta^{3,6}$-bicyclo[3.2.0]heptadiene-2-one (II) which, in turn, is isomerized to the 7-methoxy derivative III. In a similar manner, γ-tropolone methyl ether is transformed into 5-methoxy-$\Delta^{3,6}$-bicyclo[3.2.0]heptadiene-2-one.[4] In both of these series the first formed valence isomer is the one in which the methoxy group occupies a ring juncture position. In a similar manner to these simple materials, the tropolone ring of the naturally occurring alkaloid colchicine (IV) upon irradiation undergoes a valence isomerization to a bicyclo[3.2.0]-heptadiene. The products, β- and γ-lumicolchicine,[5,6] instead of having the isomeric structures with the methoxy group of a ring juncture such as V, were shown to possess the structure VI, differing only in the stereochemistry. This result raised the question as to whether the different reaction course followed was due to the undue steric strain in V or whether the con-



I II III

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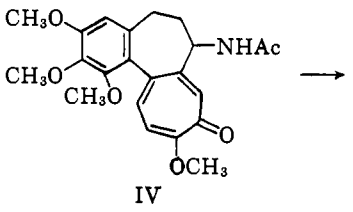
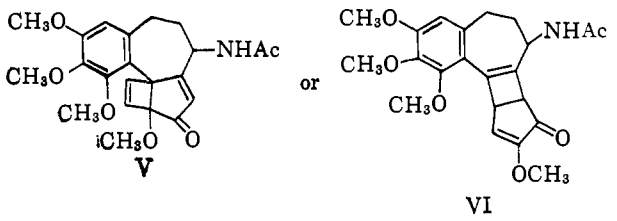


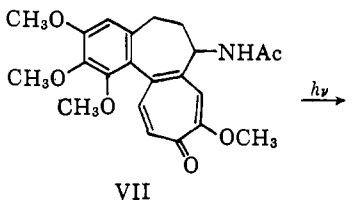
IV



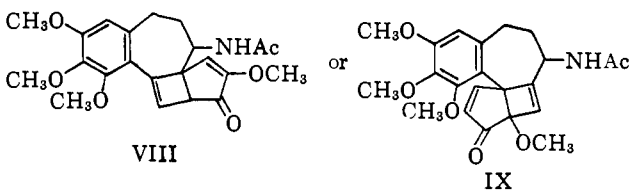
V or VI

trolling factor was the desire to retain the styrene chromophore found in VI.

To investigate these two possibilities, the photochemical transformation of isocolchine (VII)[7] was studied. In this system either valence isomer VIII or IX possesses about equal strain energy and so the role of the residual styrene chromophore can be evaluated. It was found that when VII was irradiated in methanol solution with a mercury arc the rate of



VII



VIII or IX

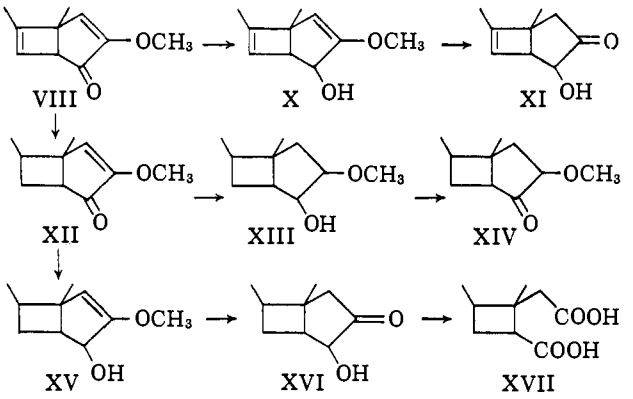
disappearance of the starting material was about one-ninth that found with colchicine. Upon chromatography of the reaction mixture, two materials were obtained, a valence isomer in 56% yield and a methanol adduct in 14% yield.

The major product, lumiisocolchicine, was stable in the liquid phase up to a temperature of 400° and showed infrared absorption bands at 1706 (cyclopentenone), 1650 (amide carbonyl), 1616 (conjugated vinyl hydrogen) and 840 cm.$^{-1}$ (trisubstituted olefin hydrogen). Such absorption could be accounted for by either structure VIII or IX, but the almost identical ultraviolet spectrum of lumiisocolchicine (λ_{max} 218, 260 mμ) with the spectrum of lumicolchicine strongly supported the presence of a styrene chromophore. The low field nuclear magnetic resonance spectrum of lumiisocolchicine clearly indicated the correctness of structure VIII. In the resonance spectrum there were four bands, each equivalent to the absorption of one proton, whereas structure IX would have demanded the presence of five protons. A doublet at τ 3.13 was assigned to the N–H resonance of the acetamide group since when the N–H group was converted to N–D by exchange in deuterium oxide the band disappeared. The three remaining singlets at τ 3.39, 3.48 and 3.60 were assigned to the β-proton of the cyclopentenone, the single aromatic proton and the styrene proton, respectively, on the basis of the following chemical transformations.

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

Reduction of the ketonic carbonyl group in lumiisocolchicine with sodium borohydride yielded an alcohol (X), the infrared spectrum of which lacked the carbonyl absorption at 1706 cm.$^{-1}$ which was present in the starting material. That this carbonyl group was part of a conjugated ketone followed from examination of the n.m.r. spectrum of the reduction product. The low field absorption at τ 3.39 in the starting photo product, characteristic of a β-proton on a conjugated enone system, had shifted to τ 5.23, a position assignable to a vinyl proton of an enol ether system.[3] Chemical evidence for the presence of an enol ether was gained by facile acid hydrolysis of the reduction product to a ketol (XI). The n.m.r. spectrum of XI no longer displayed the τ 5.23 absorption and in the infrared the appearance of a carbonyl absorption at 1748 cm.$^{-1}$ showed that the original enol ether system in VIII was contained in a five-membered ring.

Lumiisocolchicine on hydrogenation in ethanol over platinum absorbed three moles of hydrogen, the first mole being taken up more rapidly. The hexahydro derivative XIII lacked carbonyl absorption in the



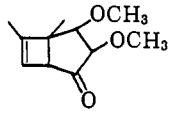
infrared showing that the carbonyl group had been reduced and from the low intensity of the ultraviolet spectrum it was apparent that the styrene double bond also had been attacked to leave a substituted benzene derivative. The n.m.r. spectrum possessed a low field doublet (τ 3.68) assignable to the N–H resonance and a singlet at τ 3.53 which must arise from the single aromatic proton. The hydroxyl group of the hexahydro derivative was oxidized and the resulting tetrahydro ketone XIV showed a carbonyl absorption in the infrared indicating the presence of a saturated five-ring ketone. Since the carbonyl group must be the same one present in the original photo product VIII, it follows that the unsaturated methoxylated enone system must be of the homoannular type.

When the hydrogenation was stopped after absorption of one mole of hydrogen, a dihydro derivative XII was readily obtained. The ultraviolet spectrum of the product was similar to that of the hexahydro derivative, showing the disappearance of the styrene double bond. The n.m.r. spectrum in addition to the N–H and benzenoid bands at τ 4.61 and 3.46, respectively, possessed a singlet at τ 4.49 which must be assigned to the β-proton of the five-ring enone system. The upfield shift of this latter band in the dihydro derivative as compared to lumiisocolchicine showed the interaction of the enone system and the styrene double bond. Direct evidence for the presence of the enol ether system in XII was obtained by reduction of the carbonyl group with sodium borohydride to yield a dihydroalcohol XV. The remaining enol ether was readily hydrolyzed with hydrochloric acid to give rise to the dihydroketol XVI. Reduction of XVI with hydride followed by oxidation with potassium permanganate-

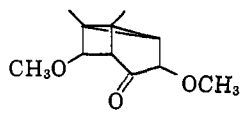
sodium periodate reagent[8] yielded a diacid (XVII). This cleavage showed the retention in a juxtaposition of the two oxygen functions of the tropolone ring system during the irradiation.

These chemical transformations coupled with spectroscopic evidence establish the presence of a styrene system containing a trisubstituted double bond and a homocyclic α-methoxycyclopentenone unit, both features demanded by structure VIII. In further agreement with this latter structure are all the coupling constants in the n.m.r. spectra. The lack of coupling between the styrene vinyl proton and the adjacent hydrogen on the ring juncture is not unexpected since in the analogous simple compounds as II and III[3] little if any coupling is seen, a result due to an unfavorable dihedral angle relationship. These data, when considered along with known photo-induced valence isomerizations of the tropolone system,[3-5] indicate the correctness of structure VIII for lumiisocolchicine. The formation of such a product clearly shows the dominant role played by the desire to retain the strongly conjugated styrene in this valence isomerization reaction of a tropolone molecule.

The minor photo product, the methanol adduct, was next examined. The material showed a band in the infrared spectrum at 1736 cm.$^{-1}$, characteristic of a cyclopentanone ring. The presence of a conjugated cyclopentenone system in the major photo product suggested that methanol may have added to the conjugated system to yield XVIII since such photochemically-induced additions are known.[9] Also, since it is known that there is an electronic interaction between

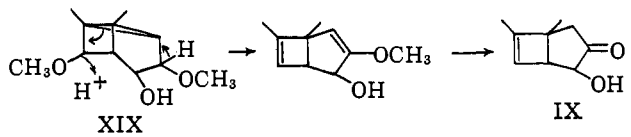


XVIII



XIX

the cyclobutene double bond and the cyclopentenone system in a bicyclo[3.2.0]heptadiene,[4] structure XIX warranted consideration. Both of these structures could readily be discarded, however, when the following observations were considered. The ultraviolet spectrum of the adduct had intense maxima at 229 and 280 mμ, characteristic of the styrene system, but the bathochromic shift of the bands when compared with similar bands in lumiisocolchicine indicated a different spatial arrangement of the chromophore. The n.m.r. spectrum had only two low field absorptions, a doublet at τ 4.01 for the N–H resonance and a singlet at τ 3.53 for the single aromatic proton. Thus, a double bond conjugated with the benzenoid ring must be tetrasubstituted, ruling out structure XVIII. In contrast to lumiisocolchicine, hydrogenation of the adduct reduced only the carbonyl group and the ultraviolet spectrum of the dihydro derivative was practically identical with that of the starting material. The dihydro material was extremely sensitive toward acid and was converted to a ketol with the concomitant loss of two moles of methanol. Considering the possible course for this hydrolytic reaction and using structure XIX as an example, it follows that the product

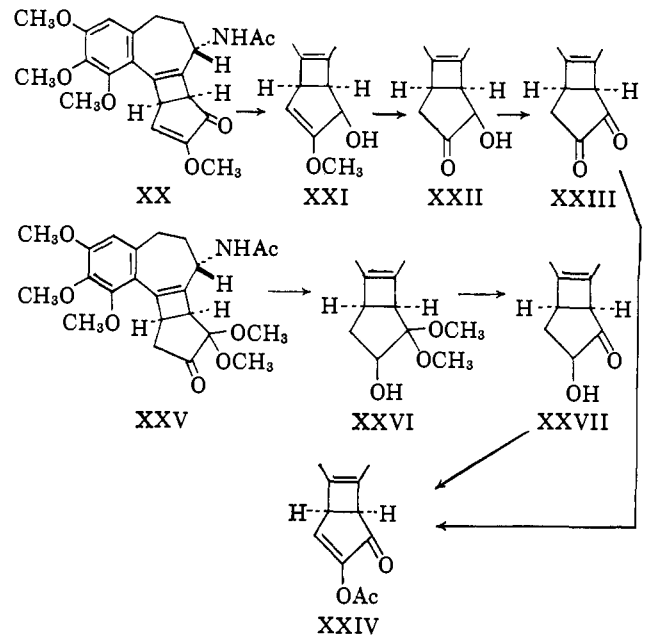


XIX IX

should be related to IX prepared in the lumiisocolchicine series. The ketol formed, however, possessed no vinyl proton absorption in the n.m.r. spectrum, thus ruling out structure XIX for the adduct.

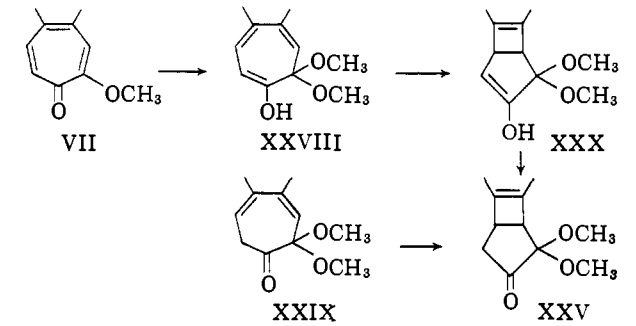
The ketol possessed a band at 1739 cm.$^{-1}$ in the infrared spectrum, indicating the presence of a cyclopentanone grouping; the carbonyl group was part of an α-ketol system since the hydroxyl group could be oxidized with cupric acetate to yield an α-diketone. This reaction sequence showed that the adduct was an α-diketone monoketal which, in turn, was converted to an α-hydroxy ketal, an α-hydroxyketone and an α-diketone.

A similar α-diketone was prepared from β- and γ-lumicolchicines (XX) by hydride reduction to XXI, followed by acid hydrolysis to ketol XXII, and oxidation to diketone XXIII. The diketone and its related



enol acetate XXIV derived from γ-lumicolchicine were i entical with the compound prepared from the methanol adduct. This interconversion of the series establishes the structure XXV for the methanol adduct derived from isocolchicine and XXVI and XXVII for the corresponding α-hydroxy ketal and ketol, respectively.

In analogy to the well known 1,8-additions to troponoid systems,[10] the formation of the methanol adduct must first involve the addition of a mole of solvent to isocolchicine to yield XXVIII. In the simple troponoid



VII XXVIII XXX XXIX XXV

series[9] the adduct ketonizes to form a structure related to XXIX, but in the simple series such cycloheptadienones upon ultraviolet irradiation do not undergo valence isomerization but expel carbon monoxide and

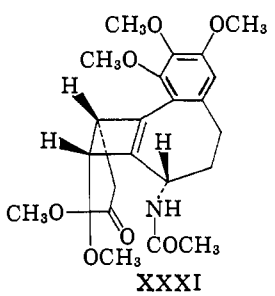
(8) R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701, 1710, 1714 (1955).

(9) R. Stoermer and H. Stockman, *Ber.*, **47**, 1786 (1914); A. M. Moore and C. H. Thompson, *Can. J. Chem.*, **35**, 163 (1957); S. Y. Yang, *J. Am. Chem. Soc.*, **80**, 6196 (1958).

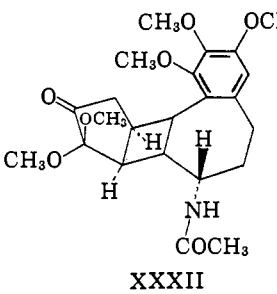
(10) O. L. Chapman, D. J. Pasto and A. A. Griswold, *ibid.*, **84**, 1213 (1962).

give rise to an acyclic triene.[11] In the more complex materials, however, it could be possible that the isomerization reaction could prevail and lead to the photo product XXV. Alternately, the presence of the phenyl ring may cause the adduct to exist largely as the conjugated trienol XXVIII and valence isomerization of cycloheptatrienes to a structure related to XXX is well known.[12] At the present time no decision can be rendered as to the course of the photo reaction. Also, it is not known whether the solvent addition occurs in the photoexcited state or in a ground vibrationally excited state. It is interesting to note in this first example of a photo-induced addition of a protic solvent to a tropolone system that the valence isomerization reaction is one-ninth that found in the similar isomerization reaction of colchicine. This retardation of the valence isomerization reaction must permit an alternate pathway to compete, a competition which is not favorable in the other tropolones studied.

Finally, it should be noted that the photo methanol adduct XXV belongs to the γ-series, the isomer produced in the lesser amount in the colchicine series. Using the accepted stereochemistry of β- and γ-lumicolchicine,[6] the former has the cyclopentenone ring *cis* to the acetylamino group while in the latter isomer these groupings are *trans*. Examination of structures XXXI and XXXII possessing the β- and γ-stereochemistry, respectively, shows that in the *cis* structure XXXI there is interference between the methoxyl group of the ketal and the acetylamino group. Such a steric interaction is lacking in the *trans* structure XXX and this latter



XXXI



XXXII

orientation would be preferred. In the β- and γ-lumicolchines the tetrahedral ketalated carbon is replaced by a trigonal atom and in this arrangement the lone methoxy of the enol system does not interfere with the acetylamino group.

Experimental[13]

Isocolchicine (VII).—Isocolchicine was prepared from purified colchicine[14] following the procedure of Sorkin[7] and the material recrystallized from acetone–hexane; m.p. 225–226°, reported m.p. 225–226°; λ_{max} 245 mμ (ϵ 35,900), 345 mμ (ϵ 21,400).

Irradiation of Isocolchicine.—In a typical experiment, a solution of 2.00 g. (5.0 mmoles) of isocolchicine in 750 ml. of methanol was placed into a cylindrical vessel which was fitted with an internal, water-cooled quartz probe. Into the probe was placed a Pyrex filter and a 450-watt Hanovia mercury lamp (type L). A small Teflon-coated magnetic stirring bar was placed in the bottom of the cylindrical flask and the solution was stirred magnetically while being purged with helium. These same conditions were used for the irradiation. The progress of the irradiation reaction was followed by examination of the ultraviolet spectra of aliquots withdrawn through a rubber serum cap with a hypodermic syringe. As the irradiation proceeded, the maximum at 345 mμ gradually diminished and new maxima at 217 and 260 mμ appeared. After 23 hours of irradiation, at which time the reaction was terminated, the 345 mμ band had virtually disappeared and maximum extinction coefficients had been obtained for the 217 and 260 mμ bands.

The methanolic solution was concentrated under reduced pressure and the residual brown foam was chromatographed on Woelm neutral alumina (Act. III). Elution with chloroform–benzene (4:1) and chloroform gave 0.25 g. (13%) of a colorless oil which upon crystallization from acetone–hexane yielded the methanol adduct XXV as white feathery crystals, m.p. 220–221°, $[\alpha]^{22.5}D$ +44.5° (*c* 0.625); λ_{sh} 219 mμ (22,450), λ_{max} 229 mμ (ϵ 25,750), 280 mμ (ϵ 20,780); ν_{max} 1640, 1736 and 3365 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.53(s), 4.01(d).

Anal. Calcd. for $C_{23}H_{29}O_7N$ (431.47): C, 64.02; H, 6.77; N, 3.25. Found: C, 63.93; H, 6.74; N, 3.38.

Continued elution with chloroform followed by 2% methanol in chloroform gave 1.11 g. (56%) of crude lumiisocolchicine (VIII) as a pale yellow foam which was recrystallized from acetone–hexane to yield the photo product as a hydrate in the form of colorless, massive needles, m.p. 115–115.5°, $[\alpha]^{24}D$ −210° (*c* 0.68). The material after melting resolidifies at about 130° and melts again sharply at 203–204°. An infrared spectrum of the last melt was practically identical with that of the hydrate. The spectral properties of the hydrate were: λ_{max} 218 mμ (ϵ 28,000), 260 mμ (23,000), 339 mμ (ϵ 1030); ν_{max} 3585, 3450, 3300, 1706, 1650, 1616 and 840 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.46(s), 3.63(s, two H) and 3.97(d). It was found that two of the bands in the n.m.r. spectrum were shifted downfield when a sample of the hydrate was heated above 100° under reduced pressure in the presence of phosphorus pentoxide, the sample having been molten during the drying; the values were 3.13(d), 3.39, 3.48, and 3.60. Crystallization of the melt regenerated unchanged hydrate, identical in all respects with starting hydrate.

Anal. Calcd. for $C_{22}H_{25}O_6N \cdot H_2O$ (417.44): C, 63.30; H, 6.52; N, 3.36. Found: C, 63.29; H, 6.63; N, 3.39; mol. wt., 438 (osmometer).

Lumiisocolchicine Alcohol (X).—To a solution of 1.30 g. (3.12 mmoles) of lumiisocolchicine hydrate in 40 ml. of methanol there was added 0.13 g. (3.4 mmoles) of sodium borohydride. The resulting solution was allowed to stand at room temperature for 24 hours, neutralized with dilute hydrochloric acid, and the solution evaporated under reduced pressure to a volume of about 3 ml. The residue was diluted with water, the mixture extracted four times with chloroform, the chloroform extracts combined and washed with water, and dried. The solvent was removed under reduced pressure and the residue crystallized from acetone–hexane; yield 1.19 g. (95%), m.p. 219–220°; λ_{max} 213 mμ (ϵ 31,150), 271 mμ (ϵ 13,600); ν_{max} 3330, 1634 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.53(s), 3.73(s), 4.38(d) and 5.23(s).

Anal. Calcd. for $C_{22}H_{27}O_6N$ (401.44): C, 65.82; H, 6.78; N, 3.49. Found: C, 65.62; H, 6.80; N, 3.88.

A solution of 120 mg. (0.3 mmole) of lumiisocolchicine alcohol (X) and 0.36 ml. of deuterium oxide in purified tetrahydrofuran (prepared by distilling from sodium a previously dried sample which had been "wetted" with deuterium oxide) was allowed to stand for 2 hours at room temperature. The solution was concentrated to dryness under reduced pressure, taking special precautions to exclude air, and dried in a vacuum desiccator. The n.m.r. spectrum of the material was (τ, p.p.m.): 3.53(s), 3.73(s) and 5.25(s).

Lumiisocolchicine Ketol (XI).—To a hot solution of 0.99 g. (2.48 mmoles) of lumiisocolchicine alcohol (X) in 4 ml. of ethanol was added 50 ml. of 0.5 *N* hydrochloric acid which had been preheated to 95°. After the reaction cooled to room temperature, the mixture was extracted with chloroform, the extracts washed with water, dried over sodium sulfate, and the solvent removed. The residual material was crystallized from acetone–hexane; yield 0.77 g. (81%), m.p. 235–236°, λ_{max} 221 mμ (ϵ 26,800), 266 mμ (ϵ 16,600); ν_{max} 3367, 3225, 1748, 1656 and 1639(sh) cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.55(s), 3.70(s) and 4.13(d).

Anal. Calcd. for $C_{21}H_{25}O_6N$ (387.42): C, 65.10; H, 6.50; N, 3.62. Found: C, 65.04; H, 6.55; N, 3.61.

Dihydrolumiisocolchicine (XII).—A solution of 520 mg. (1.25 mmoles) of lumiisocolchicine hydrate in 50 ml. of ethanol was hydrogenated at atmospheric pressure over prereduced platinum prepared from 52 mg. of the oxide. After the rate of hydrogen uptake had decreased and approximately one mole of gas had been absorbed, the reaction was stopped, the catalyst filtered, and the solvent removed under reduced pressure. The remaining white solid which gave only one spot when eluted on a silicic acid thin layer chromatogram with acetone–hexane (4:1) was crystallized from acetone–hexane; yield 388 mg. (77%), m.p. 239–240°; λ_{max} 208 mμ (ϵ 53,200), λ_{sh} 232 mμ (ϵ 12,100), λ_{sh} 253 mμ (ϵ 7600), 277 mμ (ϵ 2700) and 307 mμ (ϵ 220); ν_{max} 3365, 1701 and 1669 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.46(s), 4.61(d) and 4.49(s).

Anal. Calcd. for $C_{22}H_{27}O_6N$ (401.44): C, 65.82; H, 6.78; N, 3.49. Found: C, 65.75; H, 6.40; N, 3.49.

(11) O. L. Chapman, D. J. Pasto, G. W. Borden and A. A. Griswold, *J. Am. Chem. Soc.*, **84**, 1220 (1962).

(12) W. G. Dauben and R. L. Cargill, *Tetrahedron*, **12**, 186 (1961).

(13) All analyses were performed by the Microanalytical Laboratory, University of California. All melting points were taken in evacuated capillaries. The ultraviolet spectra were determined in methanol and unless otherwise stated Nujol mulls were utilized for infrared spectra. The n.m.r. spectra were measured in deuteriochloroform with tetramethylsilane as an internal standard. Optical rotations were determined in chloroform.

(14) J. N. Ashley and J. O. Harris, *J. Chem. Soc.*, 677 (1944).

Hexahydrolumiisocolchicine (XIII).—A solution of 440 mg. (1.06 mmoles) of lumiisocolchicine hydrate in 40 ml. of ethanol was hydrogenated over 44 mg. of platinum oxide as described above except the reaction was allowed to proceed until about 3 moles of hydrogen had been absorbed (13 hours). The catalyst was filtered, the solvent removed under reduced pressure, and the residue chromatographed on Woelm neutral alumina (Act. III). Elution with chloroform–benzene (4:1) gave eleven oily fractions. The latter six (94 mg.) yielding 73 mg. of hexahydro derivative were combined and recrystallized from acetone–hexane; m.p. 193–194°; λ_{max} 209 mμ (ε 54,800), λ_{sh} 227 mμ (ε 10,600) and λ_{max} 278 mμ (ε 1330); ν_{max} 3535, 3310, 1665 and 1639 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.53(s) and 3.68(d).

Anal. Calcd. for $C_{22}H_{32}O_6N$ (405.48): C, 65.16; H, 7.71; N, 3.45. Found: C, 65.24; H, 7.71; N, 3.71.

The first five fractions (330 mg.) could not be crystallized and were combined and rechromatographed. Elution with chloroform–benzene (7:3) gave 29 mg. (7%) of dihydrolumiisocolchicine; elution with chloroform–benzene (8:1) and pure chloroform yielded a trace of a gum; and finally elution with chloroform–methanol (50:1) gave 255 mg. of hexahydro derivative which upon crystallization from acetone–hexane yielded 170 mg. of pure material. The combined yield of hexahydrolumiisocolchicine was 57%.

Tetrahydrolumiisocolchicine (XIV).—To an ice-cold solution of 145 mg. of hexahydrolumiisocolchicine (0.36 mmole) in 12 ml. of purified acetone there was added with stirring 0.1 ml. of a 2.67 *M* solution of chromium trioxide in sulfuric acid.[15] The reaction was quenched with a few drops of methanol after 15 minutes, diluted with water, and the mixture extracted six times with chloroform. The organic extract was washed with aqueous sodium bicarbonate, then water, and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the remaining pale yellow oil showed two spots when analyzed by a thin layer silicic acid chromatogram. Chromatography on Woelm neutral alumina (Act. III) and elution with chloroform–benzene (4:1) and chloroform gave tetrahydrolumiisocolchicine as a colorless oil (76 mg., 53%) which crystallized from acetone–hexane; m.p. 227–228°. Elution with acetone returned 36 mg. (25%) of unchanged hexahydro starting material. The spectral properties of the tetrahydro derivative were: λ_{max} 206 mμ (ε 59,300), λ_{sh} 225 mμ (ε 11,500), λ_{sh} 275 mμ (ε 1160) and λ_{max} 280 mμ (ε 1190); ν_{max} 3380, 1730 and 1670 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.43(d) and 3.50(s).

Anal. Calcd. for $C_{22}H_{29}O_6N$ (403.46): C, 65.49; H, 7.25; N, 3.47. Found: C, 65.51; H, 6.99; N, 3.61.

seco-**Diacid XVII.**—A solution of dihydrolumiisocolchicine was reduced with sodium borohydride in methanol, the non-crystalline product (ν_{max} 3300, 1639 cm.$^{-1}$) allowed to react with a hot 0.5 *N* solution of hydrochloric acid, and the ketol (ν_{max} 3235, 1740, 1645 cm.$^{-1}$) formed could not be crystallized. The ketol was reduced with sodium borohydride to yield a sirupy diol (ν_{max} 3290, 1645 cm.$^{-1}$).

To a solution of 180 mg. (0.45 mmole) of the dihydrodiol and 30 mg. of potassium carbonate in 100 ml. of 5% *tert*-butyl alcohol in water under a nitrogen atmosphere there was added 40 ml. of the standard sodium periodate–potassium permanganate solution[8] and the reaction diluted with water to a volume of 200 ml. The solution was stirred for 24 hours, acidified with dilute sulfuric acid, saturated with sodium chloride, and extracted with chloroform. The extract was dried, the solution concentrated to about a 5-ml. volume, and an ethereal solution of diazomethane (three times excess) added. After standing 12 hours, the solvent was evaporated and the residue (125 mg., ν_{max} 1725 cm.) chromatographed on Woelm neutral alumina (Act. III). Elution with chloroform gave 37 mg. of a colorless oil which was crystallized from acetone–hexane; yield 13 mg. (6.5% from dihydrodiol), m.p. 153–154°; λ_{max} 208 mμ (ε 58,000), λ_{sh} 227 mμ (ε 12,000) and λ_{max} 275 mμ (ε 1320); ν_{max} 1730 and 1635 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{31}O_8N$ (449.49): C, 61.45; H, 6.95. Found: C, 61.97; H, 7.06.

Hydrogenation of Photo Methanol Adduct XXV.—A solution of 138 mg. (0.32 mmole) of XXV in 15 ml. of ethanol was hydrogenated at atmospheric pressure over prereduced platinum prepared from 14 mg. of the oxide. After 8 hours one mole of hydrogen had been absorbed, the reaction was stopped, the catalyst filtered, and the solvent removed. The remaining white solid was crystallized from acetone–hexane; yield 123 mg. (89%), m.p. 210–211°, 243–245°; λ_{sh} 217 mμ (ε 20,250), λ_{max} 229 mμ (ε 23,600), λ_{max} 280 mμ (ε 20,500); ν_{max} 3440, 3205 and 1630 cm.$^{-1}$; n.m.r. spectrum (τ, p.p.m.): 3.56(s) and 3.86(d).

Anal. Calcd. for $C_{23}H_{31}O_7N$ (433.49): C, 63.72; H, 7.21; N, 3.23. Found: C, 63.44; H, 7.24; N, 3.19.

Hydrolysis of Dihydro Photo Methanol Adduct XXVI.—To a solution of 27 mg. (0.062 mmole) of dihydro adduct XXV in 1 ml. of ethanol was added 2 ml. of 0.5 *N* hydrochloric acid. The mixture was heated on a steam-bath for 30 minutes, poured into a saturated aqueous sodium chloride solution, the organic material removed by chloroform extraction, and the chloroform extract washed and dried. The solvent was evaporated under reduced pressure and the ketol XXVII was recrystallized from acetone–hexane; yield 20 mg. (83%), m.p 257–258°; λ_{max} 228 mμ (ε 26,800), 278 mμ (ε 21,300); ν_{max} 3290, 3195, 1739 and 1637 cm.$^{-1}$.

Anal. Calcd. for $C_{21}H_{25}O_6N$ (387.42): C, 65.10; H, 6.50; N, 3.62. Found: C, 64.82; H, 6.64; N, 3.73.

Preparation of Keto–Enol Acetate XXIV. (a) From Ketol XXVII.—To a solution of 40 mg. (0.1 mmole) of ketol XXVII in 3.2 ml. of methanol there was added a solution of 30 mg. of cupric acetate monohydrate in 1.6 ml. of methanol and 0.4 ml. of water. The mixture was heated under reflux for 30 minutes during which time a brown precipitate slowly formed. The cooled mixture was shaken with chloroform and 0.5 *N* hydrochloric acid, the colorless aqueous layer extracted three times with chloroform, and the organic extracts combined, washed and dried. The solvent was removed under reduced pressure and the residue was 42 mg. of an orange solid (XXIII) which could not be crystallized; $\nu_{max}^{CHCl_3}$ 1751, 1701 and 1656 cm.$^{-1}$.

The crude orange solid diketone XXIII was dissolved in 5 ml. of a 4:1 mixture of pyridine and acetic anhydride and the solution allowed to stand at room temperature for 12 hours. The solution was diluted with ice-cold 2 *N* hydrochloric acid, the mixture extracted with chloroform, and the organic extract washed with water and dried. The solvent was evaporated under reduced pressure and the residual pale yellow solid was crystallized from acetone–hexane; yield 9 mg., m.p. 286–287° dec. The mother liquor was chromatographed on alumina (Act. III) and an additional 8 mg. of product was obtained; combined yield 17 mg. (38.5%), $[\alpha]^{21}D$ −71.7° (*c* 0.48); λ_{max} 229 mμ (ε 27,400), 280 mμ (ε 21,700); ν_{max} 3344, 1733 and 1712 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{25}O_7N$ (427.44): C, 64.62; H, 5.90; N, 3.28. Found: C, 64.71; H, 5.99; N, 3.53.

(b) **From Ketol XXII.**—The ketol XXII was prepared as described by Forbes[5] from γ-lumicolchine and was oxidized and processed as described in part a. The crude orange diketone possessed an infrared spectrum identical with that found for the diketone prepared in part a. The diketone was acetylated and worked up as described above to yield crystalline enol acetate XXIV, m.p. 286–287°, identical (by mixture m.p., rotation, and comparison of infrared spectra) with the enol acetate prepared in part a.

In a similar manner, an enol acetate was prepared from β-lumicolchicine and was found to melt from 193–194°, $[\alpha]^{23}D$ +430° (*c* 0.57).

Anal. Found: C, 64.61; H, 5.79; N, 3.28.

(15) K. Bowden, I. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); C. Djerassi, R. R. Engle and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).