# Photocyclizations of Tyrosines, Tyramines, Catecholamines, and Normescaline

**O. Yonemitsu,[1] T. Tokuyama,[2] M. Chaykovsky,[3] and B. Witkop**

*Contribution from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland 20014, and the Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo, Japan.*
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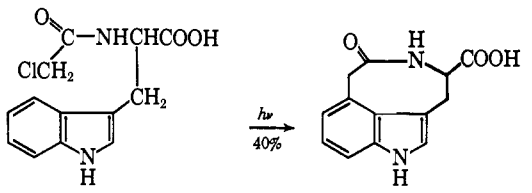
**Abstract:** N-Chloroacetyl-*m*-tyramine (III) and -*m*-tyrosine (IV) on irradiation in aqueous solution are photocyclized to 7-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (V) and its 4-carboxy derivative (VI) which are methylated to the 7-methoxy- (VII) and 7-methoxy-4-carbomethoxy derivative (VIII). The 7-methoxy lactam VII is reduced to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine (IX) by diborane in tetrahydrofuran. N-Chloroacetyl-*p*-O-methyltyramine (XX) and -*p*-O-methyl-L-tyrosine (XIII) on irradiation in aqueous solution undergo a deep-seated photolytic rearrangement to yield 7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-*a*]azepin-3-one (XXI) and L-5-carboxy-7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-*a*]azepin-3-one (XVIII). The structure of XVIII, an asymmetric molecule, was determined by X-ray crystallography of the methyl ester XIX without the benefit of a heavy atom. N-Chloroacetyl-3,4-dihydroxyphenethylamine (XXII) undergoes photocyclization with ring closure into the two positions *para* and *ortho* to the *m*-hydroxy group. After acetylation the crystalline photocyclization products were N-acetyl-7,8-diacetoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXVI) and N-acetyl-8,9-diacetoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXVII). N-Chloroacetyl-3-hydroxy-4,5-dimethoxyphenethylamine (XXIX), a derivative of normescaline, on irradiation gave a single product, the anhalonidine analog 7,8-dimethoxy-9-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXX), resulting from photocyclization into the position *ortho* to the phenolic hydroxyl. N-Chloroacetyl-, N-bromoacetyl-, and N-iodoacetylmescalines in preliminary photocyclization attempts were converted to N-acetylmescaline. N-Chloroacetyl-3,5-dibromotyrosine on irradiation gave no identifiable products.

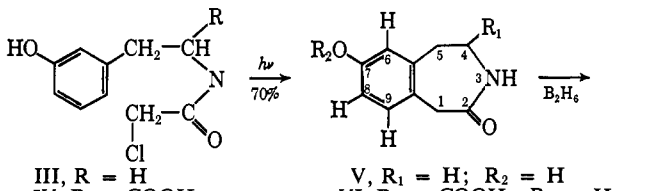
N Chloroacetyl-L-tryptophan (I) on irradiation with a high-pressure mercury lamp in neutral aqueous solution is easily cyclized to the tricyclic lactam II of L-



I II

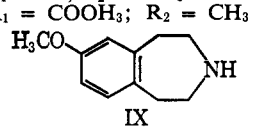
tryptophan-4-acetic acid.[4] This type of photocyclization has now been extended to derivatives of tyrosine and to pharmacodynamic amines, such as tyramine, dopamine, and normescaline.

The photocyclization of N-chloroacetyl-*m*-tyramine (III) leads to one crystalline product in 70% yield.



III, R = H
IV, R = COOH

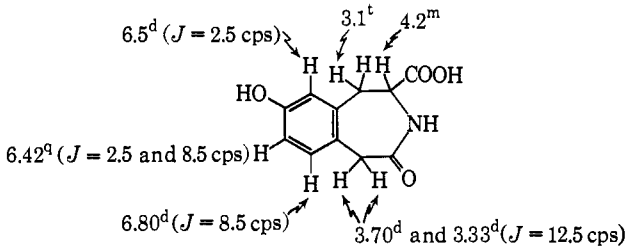
V, $R_1$ = H; $R_2$ = H
VI, $R_1$ = COOH; $R_2$ = H
VII, $R_1$ = H; $R_2$ = $CH_3$
VIII, $R_1$ = $COOH_3$; $R_2$ = $CH_3$



IX

On the basis of its chemical and spectral properties this compound is formulated as 7-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (V).[5]

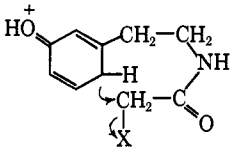
The aromatic protons in the nmr spectrum (dimethyl-$d_6$ sulfoxide) of V and the related acid VI are well separated and easily assignable. The splitting pattern and the coupling constants, *e.g.*, in VIa, are reconcilable only with structures in which the two aromatic protons



VIa

on 9 and 8 are next to each other and the proton on 6 is separate. The alternate structure resulting from ring closure into the position *ortho* to the phenolic hydroxyl group would have the three aromatic protons 7, 8, and 9 in a row and hydroxyl on 6.

The phenol V was methylated to the ether VII which was reduced to the amine IX with diborane in tetrahydrofuran. If the photocyclization were to involve an excited polarized form of the phenol, an intramo-

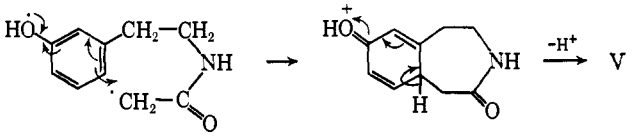


X, X = I

(1) Associate in the Visiting Program of the U. S. Public Health Service, 1964–1966; Hokkaido University, Sapporo, Japan.
(2) Associate in the Visiting Program of the U. S. Public Health Service, 1965–present.
(3) National Institutes of Health Staff Fellow, 1965–1966.
(4) O. Yonemitsu, P. Cerutti, and B. Witkop, *J. Amer. Chem. Soc.*, **88**, 3941 (1966).
(5) *Cf.* M. A. Rehman and G. R. Proctor, *J. Chem. Soc., Sect. C*, 58 (1967).

lecular elimination process should lead to expulsion of halide ion $X^-$ as pictured in X. If this were so, N-iodoacetyl-*m*-tyramine would be expected to undergo photocyclization more readily. This is not the case: the yield of V from X was only 11% with most of the N-iodoacetyl compound having been transformed to N-acetyl-*m*-tyramine. Iodo compounds are known to undergo homolytic fission under the influence of light. With the full output of the mercury lamp it is not possible to excite selectively only the phenolic group without exciting the iodo group. In the photolysis of the iodoacetyl compound cyclization is a minor reaction which probably bears no relation to the mechanism of photolysis of the chloroacetyl compound. It was ascertained in a separate experiment that in the absence of light and in the presence of methoxide ion such an internal SN2 cyclization does not take place.

During the photolysis of N-chloroacetyl-*m*-tyramine hydrogen chloride is liberated and can be continuously titrated in a pH-Stat (Figure 1). The titration curve shows that the half-life time of N-chloroacetyltyramine is only 1.6 min under the specific conditions. By contrast, the liberation of chloride ion from N-chloroacetylmescaline is ten times slower ($t_{1/2}$ = 11.6 min). This means that aqueous solutions of N-haloacylamines undergo photolytic decomposition, presumably homolysis, at a relatively slow rate. This homolysis is considerably accelerated if it is aided by *intramolecular assistance from the photoexcited state of a suitable phenolic group*, as pictured in XI → XII.




XI XII

$Cl + H^{\cdot} \rightarrow HCl$

Photocyclization into the position *ortho* to the phenolic hydroxyl occurs with N-chloroacetylnormescaline (XXIXa → XXXa, see below). The titration curve in this case indicates liberation of halogen at the same slow rate as with mescaline. This may indicate that cyclization in this case proceeds by a different mechanism.

Likewise, N-chloroacetyl-DL-*m*-tyrosine (IV) was cyclized to the benzazepinone VI which was methylated to the ester of the methyl ether VIII. Methylation of the carboxy group with ethereal diazomethane was complete after 5 min. The phenolic group required for complete methylation 2 days at room temperature with excess diazomethane in methanol–ether. Figure 2 shows the fragmentation pattern of the benzazepinone VI and of its methylation products.

There is no significant change in the uv spectrum of N-chloroacetyl-*m*-tyramine and -tyrosine on photocyclization to V and VI. By contrast, the absorption of the phenolic chromophore of N-chloroacetyl-L-tyrosine on irradiation under nitrogen both in aqueous and less so in alkaline solution decreases strongly within 30 min, whereas N-acetyl-L-tyrosine shows no change (Figure 3).

Since N-chloroacetylmescaline did not change its uv spectrum on irradiation, it was surprising that N-chloroacetyl-O-methyl-L-tyrosine (XIII) on irradiation not only decreased its phenolic absorption, but concomitantly formed a new chromophore with a maximum at 352 mμ (Figure 4).

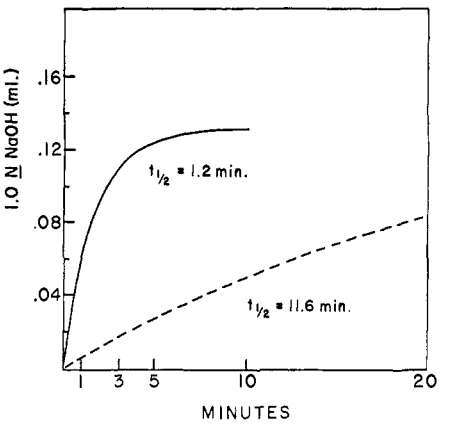



Figure 1. Photolysis of N-chloroacetyl-*m*-tyramine (—), *c* 0.15 × $10^{-3}$ *M* in 100 ml of methanol–water (10:90), and of N-chloroacetylmescaline (----), *c* 0.12 × $10^{-3}$ *M* in 80 ml of methanol–water (10:90), high-pressure Hg lamp with Vycor filter, nitrogen bubbled through solutions.

The crude product, an orange oil (17% yield), was crystallized from acetone to form a yellow microcrystalline powder whose composition was determined by mass spectrometry as $C_{11}H_{11}NO_4$. It differs from the starting material by loss of a methyl group (Figure 5). Methylation with diazomethane in methanol–ether overnight led to mono-, di-, and trimethyl derivatives (Figure 5). Brief treatment with diazomethane (5 min) gave a homogeneous monomethyl derivative, mp 144.5–145.5°. The fragmentation pattern, by its loss of carbomethoxy equivalent, shows this compound to be an ester.

This ester crystallized in the orthorhombic system, space group $P2_12_12_1$, with cell parameters $a$ = 7.17 Å, $b$ = 10.08 Å, and $c$ = 15.99 Å (all ±0.02 Å). An X-ray diffraction analysis of a single crystal of the ester was made using three-dimensional intensity data which were collected with the equiinclination multiple-film Weissenberg technique. Phases for the strong and moderately strong reflections were determined directly from the experimental intensities by the symbolic addition procedure[6] for noncentrosymmetric crystals. The atoms in the molecule were located and identified in a three-dimensional density mass computed with the reflections for which phases had been determined. Hydrogen atoms were located on a difference map. The coordinates and anisotropic thermal parameters for each atom were subjected to a least-squares refinement resulting in a final agreement factor of 7.8%. In this way structure XIX was deduced with the distances and angles as shown in Figure 6[7] and the spatial arrangement indicated in Figure 7.[8] Except for C(6), the carbon and nitrogen atoms in the two rings are nearly coplanar. The ester group is roughly parallel to the aldehyde group.

Nmr and mass spectrometry confirmed this structure (XIX). The strongest peak (176) next to the parent

(6) I. L. Karle and J. Karle, *Acta Cryst.*, **17**, 835 (1965); J. Karle and I. L. Karle, *ibid.*, **21**, 849 (1966).
(7) I. L. Karle, J. Karle, and J. A. Estlin, *Acta Cryst.*, **23**, 494 (1967).
(8) O. Yonemitsu, B. Witkop, and I. L. Karle, *J. Amer. Chem. Soc.*, **89**, 1039 (1967).

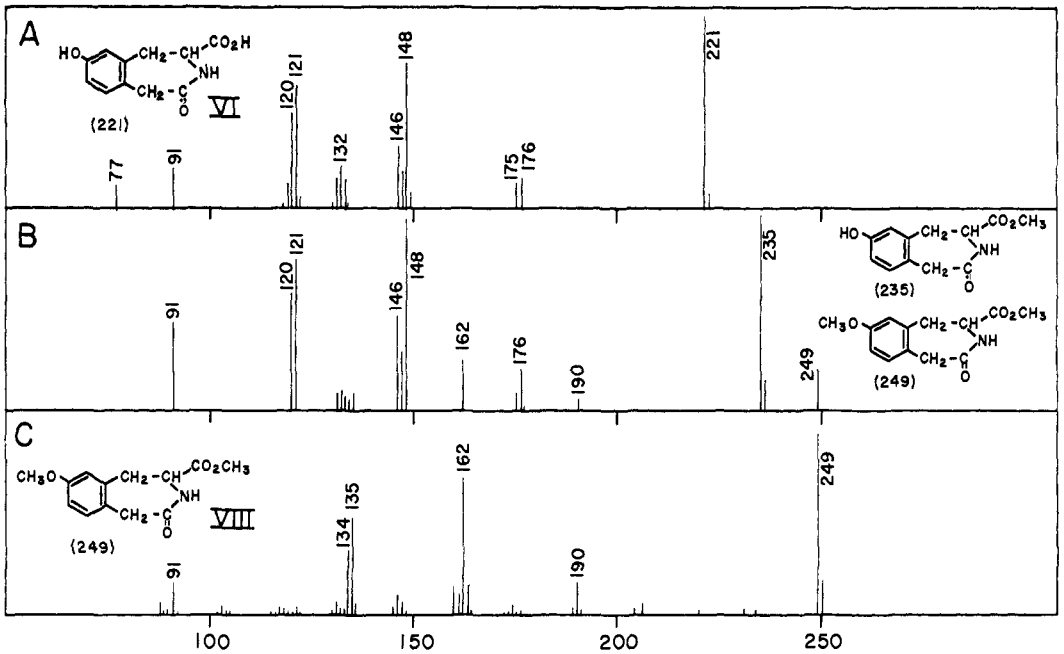



Figure 2. Mass spectra of 4-carboxy-7-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (A) and -4-carbomethoxy-7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one in the pure form (C) and admixed with the phenolic ester (B).

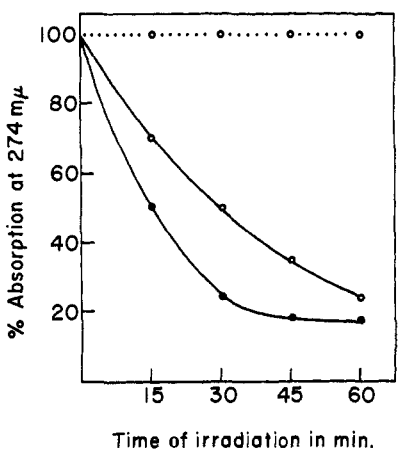



Figure 3. Decrease of absorption of N-chloroacetyl-L-tyrosine in aqueous solution (-●-●-●-) at 274 mμ as a function of the time of irradiation and in alkaline solution (0.06 *N* NaOH, -O-O-O-). By contrast, there is no decrease in the absorption of the phenolic chromophore of N-acetyl-L-tyrosine in water of alkali (·O··O··O·).

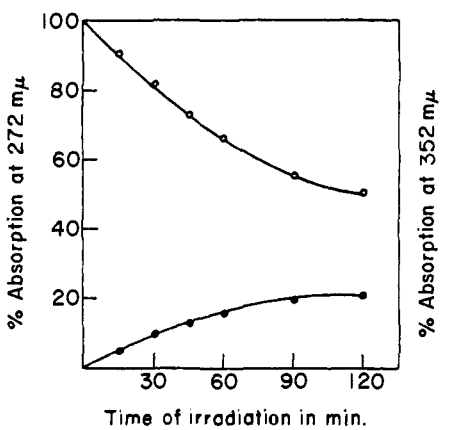
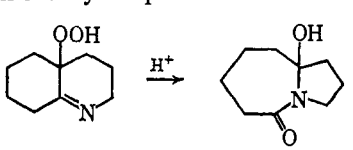



Figure 4. Decrease of the anisol chromophor ($\lambda_{max}$ 272 mμ) of O-methyl-N-chloroacetyl-L-tyrosine in water as a function of irradiation (-O-O-O-) and concomitant increase of the new chromophore at 352 mμ (-●-●-●-).

peak (221 or 235) results from loss of $CO_2$ or $COOCH_3$. Loss of the aldehyde as CHO (29) gives a significant base peak at 148 (Figure 5).

The related saturated ring system of a 7-hydroxy-2-keto-1-azabicyclo[5.3.0]decane has been obtained previously by acid-catalyzed rearrangement of the hydroperoxide from octahydroquinoline.[9a]




This unusual photolysis of an aromatic ring system is probably initiated by homolysis of the C–Cl bond[9b] with little intramolecular assistance from the photo-excited anisole system as judged by the slow rate of formation compared with that of III → V (Figure 1). The intermediate XIV might undergo hydrolysis of the vinyl ether and retroaldol cleavage of XV to yield the nine-membered keto lactam XVI. Transannular condensation and (vinylogous) β elimination of the carbinolamide XVII would yield the acid XVIII and the methyl ester XIX.

The analogous photolysis of N-chloroacetyl-*p*-O-methyltyramine (XX) gave 7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-*a*]azepin-3-one (XXI).

The photocyclization of N-chloroacetyl-3,4-dihydroxyphenethylamine (XXII), carried out in aqueous solution at pH 6 under nitrogen, led to products whose appearance was followed by thin layer chromatography. By solvent fractionation and extraction two different phenolic products, XXIII and XXIV, were obtained which were stabilized by acetylation to give the diacetate XXV and triacetates XXVI and XXVII in the

(9) (a) L. A. Cohen and B. Witkop, *J. Amer. Chem. Soc.*, 77, 6595 (1955); (b) *cf.* G. A. Russell, *ibid.*, 80, 5002 (1958).

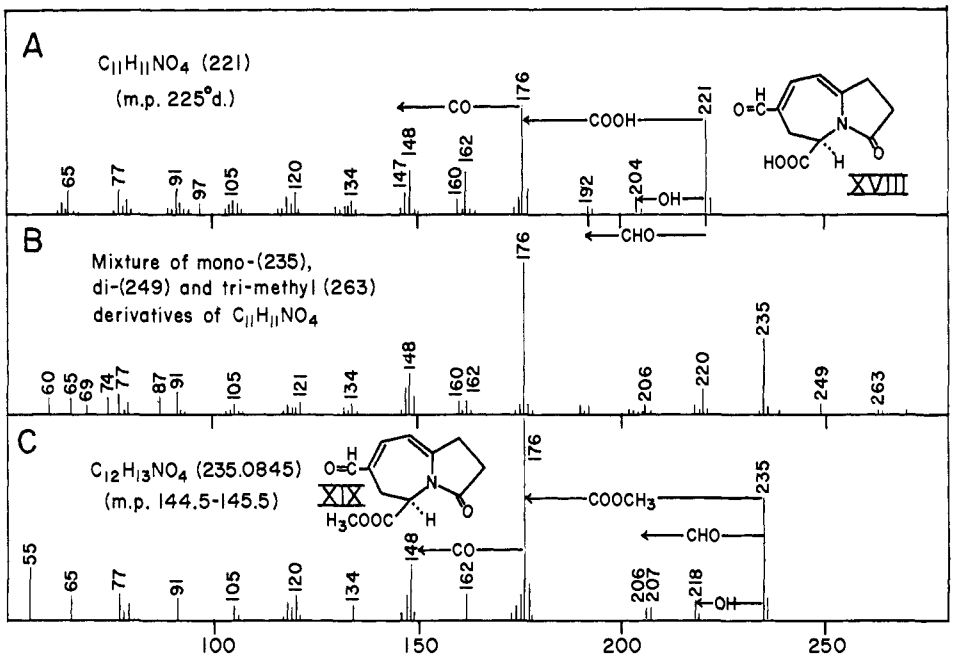
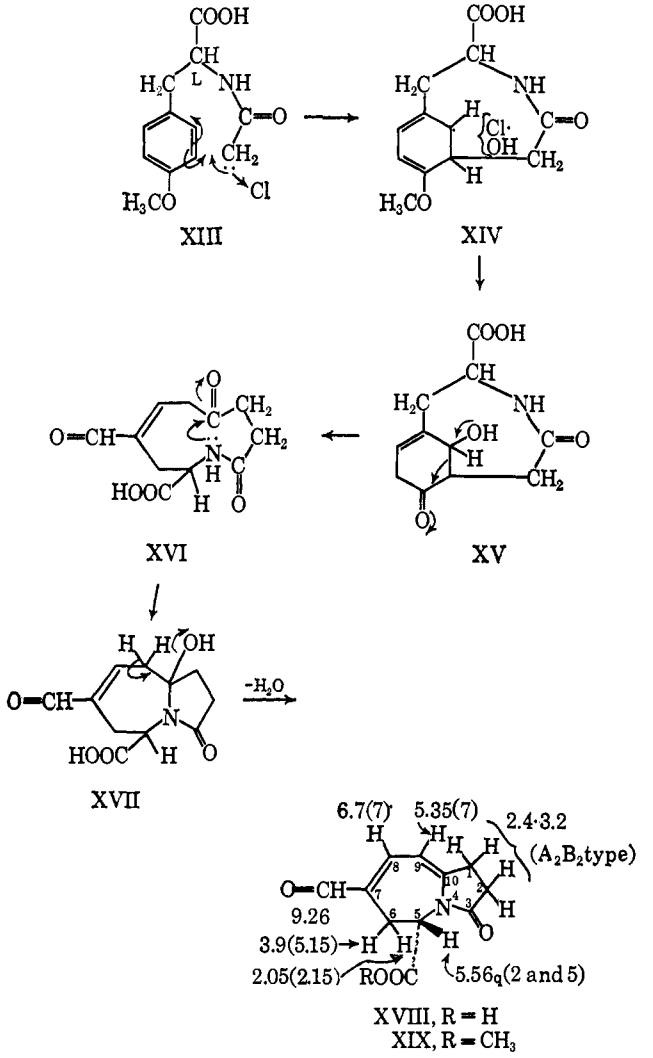



Figure 5. Mass spectra of the $\lambda_{max}$ 352 m$\mu$ ($\epsilon$ 21,600) compound (A) and its monomethyl derivative pure (C) and in admixture with di- and trimethyl homologs (B).

isomeric series. The diacetate XXV still gave positive phenolic reactions and on further acetylation yielded the triacetate XXVI.



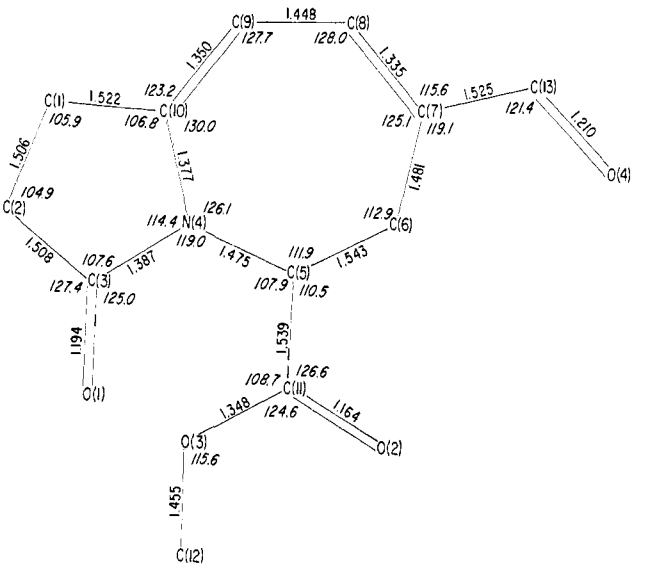
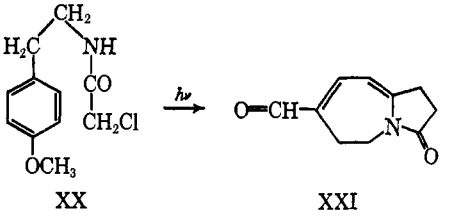



Figure 6. Bond distances and angles of L-5-carbomethoxy-7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-$\alpha$]azepin-3-one (XIX).[7] The standard deviations as computed by the least-squares program are 0.013–0.018 Å for the bond distances and ~1.3° for the bond angles. If all experimental factors were taken into account the values of the standard deviations would increase, perhaps by a factor of 2.

The structural assignments rest on the nmr spectra (Table I). A differentiation between the products of *para* ring closure XXVI and the lesser cyclization into the *ortho* position XXVII is possible through the two



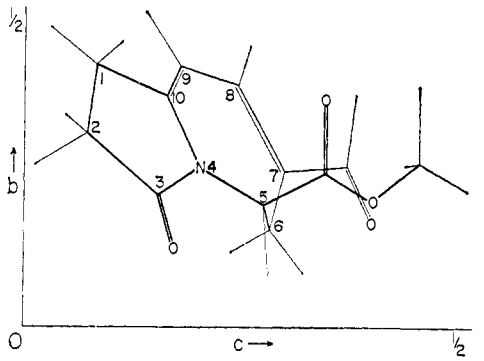
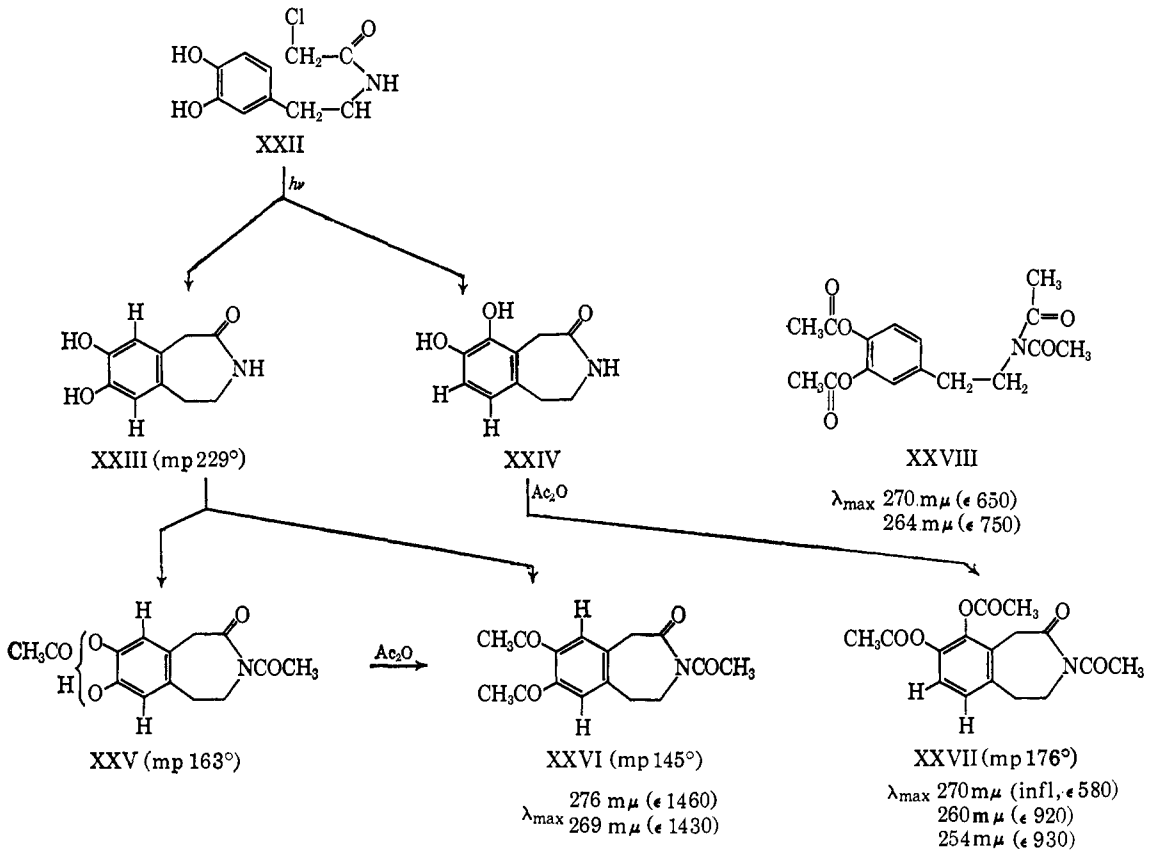


Figure 7. Spatial arrangements of atoms in L-5-carbomethoxy-7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-α]azepin-3-one (XIX).[7,8] The two rings are almost coplanar and the aldehyde group is approximately parallel to the ester group.

aromatic protons which in the diacetate XXV are distinct separate singlets at 6.80 and 6.68 ppm with no sign of *ortho* coupling. In the related triacetate XXVI the two peaks of the protons in positions 6 and 9 coalesce to a singlet at 6.88. The two protons in positions 6 and 7 of the isomeric triacetate XXVII happen to be in the same position. However, the O-acetyl protons in XXVII are well-separated singlets indicating that they are nonequivalent because structure XXVII is much less symmetric than the isomeric triacetate XXVI.

Likewise, the uv spectra were of diagnostic help. When the chromophore of the model compound N,N,-O,O-tetraacetyl-3,4-dihydroxyphenethylamine (XXVIII) was compared with the more symmetric bicyclic triacetate XXVI, the bathochromic effect of cyclization was much more pronounced for XXVI than for the less symmetric XXVII.

N-Chloroacetyl-3-hydroxy-4,5-dimethoxyphenethylamine (XXIX) or normescaline,[10] a metabolite of mescaline,[11] photocyclized in the same manner as described for N-chloroacetyl-3,4-dihydroxyphenethylamine. The crystalline product, mp 205–207°, analyzed correctly (mass spectrum) for 7,8-dimethoxy-9-hydroxy-1,2,4,5-tetrahydro-3H-3- benzazepin - 2 - one (XXXa). Its nmr spectrum showed O-methyl protons at 3.72 (3 H) and 3.75 (3 H), alicyclic protons at 3.82[s] (2 H) and 2.97[t] (2 H), and one aromatic proton at 6.22[s] (Table II). The signal for the aromatic proton at δ 6.22 was shifted downfield by δ 0.42 on acetylation to the diacetyl derivative XXXb. After acetylation to XXIXb the two aromatic protons of the starting material XXIXa showed comparable shifts: the aromatic proton in *ortho* position to the hydroxyl group shifted by δ 0.17; the other proton in the *para* position to the hydroxyl group shifted by δ 0.40.[12] This shift is of diagnostic value. It proves that the aromatic proton in the cyclization product is in the *para* position to the phenolic hydroxyl, *i.e.*, that photocyclization took place *ortho* to the phenolic hydroxyl and that the product is XXXa, the analog of anhalonidine XXXII, and no XXXI.




The successful photolysis of N-chloroacetyl-*p*-methoxyphenethylamine and of N-chloroacetyl-3,4-dimethoxyphenethylamine (unpublished results) prompted preliminary studies in the mescaline series. Attempted

(10) J. Ratcliffe and P. Smith, *Chem. Ind.* (London), 925 (1959).
(11) J. Daly, J. Axelrod, and B. Witkop, *Ann. N. Y. Acad. Sci.*, **96**, 37 (1962).
(12) *Cf.* R. J. Highet and P. F. Highet, *J. Org. Chem.*, 30, 902 (1965).

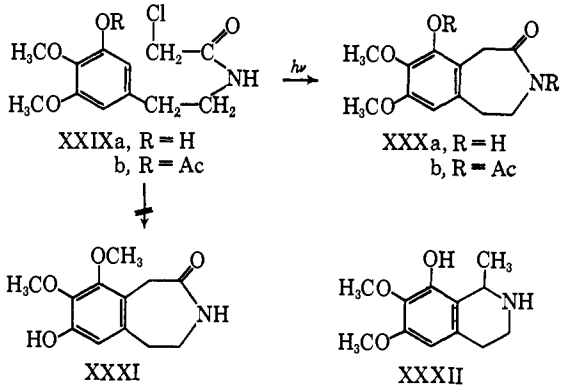
Table I. Nmr Spectra ($\delta$ values) of the Photocyclization Products and Their Acetates from Dopamine ($CDCl_3$)

| Compound | Aromatic protons | Alicyclic protons | | | N-Acetyl protons | O-Acetyl protons |
|---|---|---|---|---|---|---|
| N-Acetyl-7,8-diacetoxy-1,2,4,5-tetrahydro-3H-3-azepin-2-one (XXVI) | 6.88[s] (2 H) | 3.95[s] (2 H) | 3.05[t] (2 H) $J$ = 6.5 cps | 4.21[t] (2 H) $J$ = 6.5 cps | 2.45[s] (2 H) | 2.20[s] (6 H) |
| N-Acetyl-7- (or -8-) acetoxy-8- (or -7-) hydroxy-1,2,4,5-tetrahydro-3H-3-azepin-2-one (XXV) | 6.80[s] (H) 6.68[s] (H) | 3.93[s] (2 H) | 3.05[t] (2 H) $J$ = 6 cps | 4.23[t] (2 H) $J$ = 6 cps | 2.50[s] (3 H) | 2.30[s] (3 H) |
| N-Acetyl-8,9-diacetoxy-1,2,4,5-tetrahydro-3H-3-azepin-2-one (XXVII) | 7.00[s] (2 H) | 3.93[s] (2 H) | 3.15[t] (2 H) $J$ = 6 cps | 4.28[t] (2 H) $J$ = 6 cps | 2.48[s] (3 H) | 2.34[s] (3 H) 2.25[s] (3 H) |
| O,O′-N,N-Tetraacetyldihydrophenethylamine (XXVIII) | ~7.13[m] (3 H) | | ~2.88[m] (2 H) | ~3.85[m] (2 H) | 2.35 (6 H) | 2.28 (6 H) |

Table II. Nmr Spectra ($\delta$ values) of the Photocyclization and Their Acetylation Products from N-Chloroacetylnormescaline ($CD_3OD$)

| Compound | Aromatic protons | Alicyclic protons | | | O-Methyl protons | N- and O-acetyl protons |
|---|---|---|---|---|---|---|
| 7,8-Dimethoxy-9-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXXa) | 6.22[s] (H) | 3.82[s] (2 H) | 2.97[t] (2 H) $J \cong$ 6 cps | 3.48[t] (2 H) $J \cong$ 6 cps | 3.75 (3 H) 3.72 (3 H) | |
| N-Acetyl-7,8-dimethoxy-9-acetoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXXb) | 6.64[s] (H) | 3.90[s] (2 H) | | | 3.79 (3 H) 3.70 (3 H) | 2.34 (3 H) 2.40 (3 H) |
| N-Chloroacetyl-3-hydroxy-4,5-dimethoxyphenethylamine (XXIXa) | 6.23[s] (2 H) | 3.93[s] (2 H) | 2.65[t] (2 H) $J \cong$ 8 cps | 3.38[t] (2 H) $J \cong$ 8 cps | 3.73 (3 H) 3.68 (3 H) | |
| N-Chloroacetyl-3-acetoxy-4,5-dimethoxyphenethylamine (XXIXb) | 6.63[d] (H) 6.40[d] (H) $J \cong$ 2 cps | 3.93[s] (2 H) | 2.75[t] (2 H) $J \cong$ 7 cps | 3.41[t] (2 H) $J \cong$ 7 cps | 3.80 (3 H) 3.70 (3 H) | 2.27 (3 H) |

photocyclization of N-chloroacetyl-, N-bromoacetyl-, and N-iodoacetylmescalines so far have led to N-acetylmescaline in addition to other products now under investigation.




XXXI XXXII

In the tyrosine series it is known that 3,5-dibromotyrosine with N-bromosuccinimide gives a spirocyclohexadienone lactone[13] which is much more stable than the unbrominated spirohexadienone obtainable by electrolysis.[14] It was, therefore, expected that the photocyclization of N-chloroacetyl-3,5-dibromotyrosine might lead to stable products. This was not the case. Irradiation of this compound both in absolute and aqueous ethanol led to dark brown amorphous products which so far have not been further investigated.

(13) G. L. Schmir, L. A. Cohen, and B. Witkop, *J. Amer. Chem. Soc.*, **81**, 2228 (1959).

(14) L. Farber and L. A. Cohen, *Biochemistry*, **5**, 1027 (1966).

## Experimental Section

**N-Chloroacetyl-*m*-tyramine (III).** Chloroacetyl chloride (3.4 g, 30 mmol) was added dropwise over a period of 3 min to a stirred solution of 3.46 g (20 mmol) of *m*-tyramine hydrochloride in 45 ml of 2.0 *N* aqueous sodium hydroxide, cooled in an ice bath. The solution was stirred for 5 min, the ice bath removed, and stirring continued for an additional hr. The solution was adjusted to pH 3 with dilute hydrochloric acid and cooled in an ice bath, and the precipitated solid filtered to yield 3.7 g (86.8%) of the N-chloroacetyl derivative as a colorless solid. Recrystallization from ethanol gave colorless prisms, mp 135–136°.

*Anal.* Calcd for $C_{10}H_{12}ClNO_2$: C, 56.21; H, 5.66; N, 6.56. Found: C, 56.44; H, 5.57; N, 6.36.

The infrared spectrum showed $\lambda_{max}^{CHCl_3}$ 2.7 (w), 2.8 (w), 6.0 (s), 6.25 (m), 6.55 (m), 6.9 (w), and 8.7 (m) $\mu$. The ultraviolet spectrum showed $\lambda_{max}^{EtOH}$ 274 m$\mu$ ($\epsilon$ 2110).

**N-Iodoacetyl-*m*-tyramine.** A solution of 852 mg (4.0 mmol) of N-chloroacetyl-*m*-tyramine in 30 ml of 1.0 *N* solution of sodium iodide in acetone was stirred at room temperature for 24 hr. The acetone was evaporated *in vacuo;* 15 ml of water was added, and the precipitate was filtered to yield 1.15 g (94.2%) of colorless crystals, which after recrystallization from aqueous ethanol showed mp 148–150°.

*Anal.* Calcd for $C_{10}H_{12}INO_2$: C, 39.36; H, 3.96. Found: C, 39.59; H, 4.04.

**7-Hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (V). A. By Photocyclization of N-Chloroacetyl-*m*-tyramine.** The photo equipment consisted of a water-cooled Hanovia quartz immersion well surrounded by a Pyrex jacket which contained the solution to be irradiated. Nitrogen was bubbled through the solution with the aid of a fritted glass disk at the bottom of the Pyrex vessel, and the evolving gas led through a side arm at the top. A 200-W Hanovia mercury discharge tube and a Vycor filter were placed inside the quartz immersion well. A solution of 2.13 g (10 mmol) of N-chloroacetyl-*m*-tyramine in 300 ml of ethanol and 300 ml of water was irradiated for 2 hr. Thin layer chromatography (silica gel; 1-propanol–water, 70:30) indicated the absence of starting material after this time. The solution was stirred with 1 g of silver carbonate for 10 min to remove chloride ions and the silver salts were then removed by filtration through a Büchner funnel con-

taining a matting of Celite filter aid. The filtrate was evaporated *in vacuo* to a volume of 30 ml and cooled in an ice bath and the precipitated solid filtered to yield 1.25 g (70.6%) of the cyclized product as a colorless solid. Recrystallization from ethanol gave colorless crystals, mp 255–259° dec.

*Anal.* Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.59; H, 6.51; N, 7.83.

The infrared spectrum showed $\lambda_{max}^{Nujol}$ 3.10 (m), 3.40 (s), 6.08 (s), 6.25 (m), 7.68 (w), 6.95 (s), 7.22 (m), 7.48 (w), 7.65 (w), 7.80 (w), 8.00 (w), 8.12 (s), 8.68 (m), 8.98 (m), 10.70 (w), 11.10 (w), and 11.50 (m) $\mu$. The nmr spectrum showed a multiplet centered at 2.85 (two protons), a multiplet centered at 3.32 (two protons), a singlet at 3.55 (two protons), a multiplet centered at 6.48 (two protons), a doublet centered at 6.91 (one proton; $J$ = 7.5 cps) and a broad peak at 7.3 ppm (one proton). The mass spectrum showed the mass peak at 177.

**Continuous Titration of Liberated Chlorine During Photocyclization (C. M. Foltz).** The lamp and the cell were contained in a metal cylinder with a polished inner surface of inner diameter 15 cm. All reactions were carried out in a steady stream of nitrogen. In the experiments where the liberation of $Cl^-$ was followed by continuous titration the solvent in all cases was methanol–water (10:90). Titrations were carried out with a Radiometer titrator, type TTTIC, fitted with an Ole Dich recorder and a GK202IC glass electrode. The results are presented in Figure 1.

**B. By Photocyclization of N-Iodoacetyl-*m*-tyramine.** A solution of 610 mg (2 mmol) of N-iodoacetyl-*m*-tyramine in 100 ml of water and 70 ml of ethanol was irradiated for 20 min with a 200-W Hanovia mercury discharge tube under the same conditions as described above. Thin layer chromatography (silica gel; 1-propanol–water, 70:30) indicated the absence of starting material after this time. The solution was treated with silver carbonate, filtered, and concentrated to a volume of 15 ml. The precipitated solid, 40 mg (11.3%) of the benzazepinone V, was identical in all respects with the product obtained from the photocyclization of N-chloroacetyl-*m*-tyramine.

The aqueous filtrate was lyophilized to leave a yellow semisolid residue. The nmr spectrum showed a strong peak at 1.8 ppm ($CH_3C(=O)$—) indicative of N-acetyl-*m*-tyramine.

**Attempted Cyclization of N-Chloroacetyl-*m*-tyramine with Sodium Methoxide in Methanol.** A solution of 426 mg (2.0 mmol) of N-chloroacetyl-*m*-tyramine and 108 mg (2.0 mmol) of sodium methoxide (Fisher Chemicals) in 100 ml of dry methanol was stirred at room temperature for 20 hr, then adjusted to pH 5 with dilute hydrochloric acid. Thin layer chromatography (silica gel; 1-propanol–water, 70:30) indicated the presence of only starting material. The methanol was evaporated at the water pump, 20 ml of water added, and the solid filtered to give an almost quantitative recovery of crude N-chloroacetyl-*m*-tyramine, mp 132–135°.

In another experiment, with the same quantities of reagents, the solution was allowed to reflux for 12 hr. Again, only starting material was recovered.

**7-Methoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (VII).** A mixture of 354 mg (2.0 mmol) of 7-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (V), 252 mg (2.0 mmol) of dimethyl sulfate, 552 mg (4.0 mmol) of potassium carbonate, and 100 ml of acetone was reflexed for 21 hr. The mixture was cooled and filtered and the filtrate evaporated to dryness *in vacuo*. The residue was dissolved in 30 ml of chloroform, washed with 20 ml of 0.1 $N$ aqueous sodium hydroxide, then with water, dried over anhydrous sodium sulfate, and evaporated to leave a pale yellow solid. Recrystallization from ethyl acetate gave 250 mg (65.4%) of colorless crystals, mp 150–153°.

*Anal.* Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.94; H, 6.58; N, 7.21.

**7-Methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine Hydrochloride (IX).** To a solution of 245 mg (1.28 mmol) of 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (VII) in 25 ml of dry tetrahydrofuran was added 2.6 ml of a 1.0 $N$ solution of diborane[15] in tetrahydrofuran (Metal Hydrides, Inc.). The solution was refluxed for 2 hr and cooled to room temperature, and 5 ml of 6.0 $N$ hydrochloric acid was added followed by an additional 2 hr of refluxing. The reaction mixture was concentrated *in vacuo* to 5 ml; 10 ml of 5.0 $N$ aqueous sodium hydroxide was added and the mixture extracted with chloroform. The extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated to yield a pale yellow oil. The oil was dissolved in 30 ml of dry ether and filtered, and the filtrate was saturated with dry hydrogen chloride gas at 0°. The precipitated hydrochloride was collected to give 200 mg (73.3%) of a colorless solid. Recrystallization from ethanol gave colorless prisms, mp 235–240° dec.

*Anal.* Calcd for $C_{11}H_{16}ClNO$: C, 61.82; H, 7.55; N, 6.55. Found: C, 61.69; H, 7.30; N, 6.72.

**Photocyclization of N-Chloroacetyl-DL-*m*-tyrosine (IV) to 7-Hydroxy-4-carboxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (VI).** A solution of 257.5 mg (10 mmol) of N-chloroacetyl-DL-*m*-tyrosine (IV) prepared from the reaction of *m*-tyrosine with chloroacetyl chloride, in 100 ml of water, was irradiated for 45 min as described above. During the reaction the uv spectrum remained almost unchanged. The solution was then adjusted to pH 6.5 by the addition of 2.5 $N$ sodium hydroxide and lyophilized. The viscous residue was dissolved in 5 ml of water and the solution adjusted to pH 2 by the addition of 10% hydrochloric acid. The aqueous solution was extracted with ethyl acetate several times. The combined extracts were dried over anhydrous sodium sulfate and evaporated to leave 208 mg of a colorless oil which, dissolved in a small amount of methanol, crystallized on scratching. After filtration and washing with cold ethyl acetate, 56 mg (25%) of the crude cyclization product was obtained. Recrystallization from water furnished 45 mg (21%) of colorless fine needles, mp 245°, which gave an orange Pauli reaction.

*Anal.* Calcd for $C_{11}H_{11}NO_4$: C, 59.72; H, 5.01; N, 6.33. Found: C, 59.54; H, 5.22; N, 6.16.

Spectral analyses were as follows: nmr spectrum (DMSO-$d_6$) 3.70[d], 3.33[d], 4.2[m], 3.1[t], 6.50[d], 6.42[a], 6.80[d]; ir spectrum (Nujol) 3.0, 5.91, 6.18, 6.31, and 13.87 $\mu$; mass spectrum 221 [M], 176, 175, 148, 146, 121, and 120 (Figure 2).

**Incomplete Methylation with Diazomethane. 7-Hydroxy- and 7-Methoxy-4-carbomethoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one.** When the above benzazepinonecarboxylic acid was dissolved in methanol and allowed to react with excess diazomethane in ether for 5 min, the residue left on evaporation of the solvent consisted of a mixture. The main component was the phenolic carbomethoxy derivative and the minor component was the 7-methoxy ester, as was clearly visible from the mass spectrum (Figure 2).

**Complete Methylation with Diazomethane. 7-Methoxy-4-carbomethoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (VIII).** When the benzazepinonecarboxylic acid VI was allowed to react with excess diazomethane in methanol–ether for 2 days at room temperature, there was obtained, after evaporation of the solvent, a pale yellow oil which crystallized when dissolved in a small amount of methanol. Recrystallization from 20% aqueous methanol gave colorless fine leaflets, mp 132–134°; Pauli reaction: negative.

*Anal.* Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.65; H, 6.11; N, 5.41.

Spectral analyses were as follows: ir spectrum 3.08, 3.20, 5.73, 5.99 $\mu$; mass spectrum 249 [M], 190, 162, 135, 134.

**Attempted Photocyclization of N-Chloroacetyl-L-tyrosine.** When a solution of 129 mg (0.5 mmol) of N-chloroacetyl-L-tyrosine (I) in 50 ml of water was irradiated with a Hanovia 654 A36 200-W lamp with Vycor filter, the ultraviolet absorption of the solution decreased rapidly (Figure 3) concomitant with the disappearance of the Pauli reaction as tested by thin layer chromatography.

When the photocyclization was carried out in 0.06 $N$ sodium hydroxide, the rate of disappearance of phenol absorption was not much changed. By comparison a solution of N-acetyl-L-tyrosine on irradiation under analogous conditions showed no changed in uv absorption (Figure 3). So far no crystalline reaction products have been isolated.

**Photolysis of N-Chloroacetyl-O-methyl-L-tyrosine (XIII) to L-5-Carboxy-7-formyl-1,2,5,6-tetrahydro-3H-3-pyrrolo[1,2-*a*]azepin-3-one (XVIII).** A solution of 543 mg (2 mmol) of N-chloroacetyl-O-methyl-L-tyrosine[16] in 200 ml of water was irradiated (200 W, Vycor filter). While the ultraviolet absorption of the anisole chromophore at 272 m$\mu$ slowly decreased, a new characteristic peak at 352 m$\mu$ appeared (Figure 4).

After 2 hr, excess silver carbonate was added to the solution to remove chloride ion. After filtration over Celite and lyophilization a pale brown oil was obtained which was dissolved in cold water and extracted with ethyl acetate several times. The extract was

(15) H. C. Brown and P. Hein, *J. Amer. Chem. Soc.*, **86**, 3566 (1964).

(16) N-Chloroacetyl-O-methyl-L-tyrosine, mp 126°, was prepared according to the method of E. Ronwin, *J. Org. Chem.*, **18**, 1546 (1953). O-Methyl-L-tyrosine was synthesized following the directions of B. R. Baker, J. P. Joseph, and J. H. Williams, *J. Amer. Chem. Soc.*, **77**, 1 (1955).

dried over sodium sulfate and evaporated to give 84 mg of an orange oil. Crystallization and recrystallization from a small volume of acetone furnished 14 mg of a yellow microcrystalline powder, mp 225° dec. The composition of this material according to mass spectrometry was $C_{11}H_{11}NO_4$. The compound gave a positive Tollens reaction when heated on the steam bath.

Spectral results were as follows: mass spectrum 221, 204, 176, 162, 148 (Figure 5); ir spectrum (Nujol) 5.76, 6.12, 6.53 $\mu$; uv spectrum $\lambda_{max}$ 347 m$\mu$ ($\epsilon$ 20,700) in ethanol; $\lambda_{max}$ 347 m$\mu$ ($\epsilon$ 21,600) in 50% ethanol: $\lambda_{max}$ 350 m$\mu$ ($\epsilon$ 21,900) in 1.0 *N* hydrochloric acid in 50% aqueous EtOH; $\lambda_{max}$ 408 m$\mu$ ($\epsilon$ 29,900) in 1.0 *N* sodium hydroxide in 50% aqueous EtOH.

**Methylation of XVIII with Diazomethane. A. Mixture of Methylation Products.** The azepinone XVIII was dissolved in methanol and treated with diazomethane in ether overnight. The resulting pale yellow solution was evaporated to give an unstable oil which turned dark brown on standing for a few hours. The mass spectrum (263 small, 249 small, 235, 220, 176) shows that this oil contains mainly monomethylated (M235) in addition to small amounts of di- (M249) and trimethylated (M263) derivatives.

**B. L-5-Carbomethoxy-7-formyl-1,2,5,6-tetrahydro-3H-pyrrolo-[1,2-*a*]-azepin-3-one (XIX).** The acid XVIII was dissolved in methanol and treated with diazomethane in ether for 5 min. Evaporation of the solvent gave a yellow oil which crystallized on trituration in a small amount of methanol. Recrystallization from 20% ethanol furnished fine pale yellow needles, mp 144.5–145.5°. The composition of the compound was $C_{12}H_{13}NO_4$ (235) according to the mass spectrum. Other prominent peaks were: 235 [M], 218, 207, 176, 148; ir spectrum: 5.72, 5.79, 6.02, 6.32, 12.79 $\mu$; uv spectrum $\lambda_{max}$ 249 m$\mu$ ($\epsilon$ 22,100) in 50%e thanol; $\lambda_{max}$ 349 m$\mu$ ($\epsilon$ 33,100) in 1.0 *N* hydrochloric acid in 50% ethanol; $\lambda_{max}$ 409 m$\mu$ ($\epsilon$ 27,500) in 1 *N* sodium hydroxide in 50% ethanol.

**N-Chloroacetyl-*p*-methoxyphenylethylamine (XX).** Chloroacetyl chloride (16.8 g; 150 mmol) was added dropwise over a period of 10 min to a stirred mixture of 15.1 g (100 mmol) of *p*-methoxyphenylethylamine and 100 ml of 2.0 *N* aqueous sodium hydroxide, cooled in an ice bath. Stirring was continued for 30 min at room temperature. The mixture was again cooled in ice and the precipitated solid filtered to yield 15.9 g (70%) of the chloroacetyl derivative as a pale yellow solid. Recrystallization from aqueous ethanol gave colorless needles, mp 99–100°. The ultraviolet spectrum showed $\lambda_{max}^{EtOH}$ 276 m$\mu$ ($\epsilon$ 1790) and 283 m$\mu$ ($\epsilon$ 1540).

*Anal.* Calcd for $C_{11}H_{14}ClNO_2$: C, 58.03; H, 6.20; N, 6.15. Found: C, 57.92; H, 6.11; N, 6.20.

**7-Formyl-1,2,5,6-tetrahydro-3H-pyrrolo[1,2-*a*]azepin-3-one (XXI).** A solution of 227.5 mg (1 mmol) of N-chloroacetyl-*p*-O-methyltyramine (XX) in 200 ml of water was irradiated with a 100-W high-pressure lamp. After 90 min the pale yellow solution was saturated with sodium chloride and extracted with ethyl acetate three times. The combined extracts were washed with water and saturated with sodium chloride. The pale yellow oil which remained after evaporation of the ethyl acetate was chromatographed on a silica gel column (2 × 20 cm) and eluted with methylene chloride to give 45 mg of a yellow oil which was unstable and turned red after a few hours at room temperature. The oil was treated with active charcoal in aqueous solution at room temperature and recrystallized from water to give 10 mg of yellow prisms, mp 85–87°.

*Anal.* Calcd for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.91. Found: C, 67.92; H, 6.53; N, 7.62.

**N-Chloroacetyl-3,4-dihydroxyphenethylamine (XXII).** To an aqueous solution of 1.89 g of 3,4-dihydroxyphenethylamine (dopamine) hydrochloride was added, under nitrogen, 25 ml of 2.0 *N* sodium hydroxide (5 equiv) and then an ethereal solution of 1.71 g of chloroacetic anhydride. Vigorous stirring was continued for 0.5 hr. More sodium hydroxide (10 ml, 2 equiv) and 1.71 g of chloroacetic anhydride were added under stirring. The reaction mixture was kept stirring for 1 hr more. The reaction mixture was neutralized to pH 6 by the addition of hydrochloric acid and extracted with ethyl acetate four times. The combined extracts left an oily residue, 2.4 g, which was chromatographed on a column of 45 g of silica gel. The column was eluted with chloroform containing 4% methanol, and fractions of 7 ml were collected. Fractions 30–50 contained pure N-chloroacetyl-3,4-dihydroxyphenethylamine which was recrystallized from chloroform to yield colorless crystalline granules (1.52 g), mp 108–109°.

*Anal.* Calcd for $C_{10}H_{12}ClNO_3$: C, 52.29; H, 5.27; N, 6.10. Found: C, 52.64; H, 5.14; N, 5.81.

The ir spectrum showed 2.85, 2.95, 3.07, 6.05, 6.48, and 6.61 $\mu$.

**Photocyclization of N-Chloroacetyl-3,4-dihydroxyphenethylamine (XXII).** The light source used for photocyclization was a quartz mercury arc lamp, Hanovia 679A-36, 450 W. The solution was irradiated with the light source inside a quartz cooling jacket surrounded by two semicircular quartz irradiation chambers whose mean distance from the light source was about 4 cm. A solution of 1.52 g of N-chloroacetyl-3,4-dihydroxyphenethylamine (XXII) in 40 ml of methanol was diluted with 620 ml of 0.06 *N* phosphate buffer solution, pH 6. The solution was irradiated for 1 hr, while a steady stream of nitrogen was bubbled through it. The irradiated solution was concentrated *in vacuo* to 150 ml. The precipitate, 0.25 g, was collected by filtration. The filtrate was extracted four times with ethyl acetate. The extract on evaporation left 0.14 g of a microcrystalline powder which was combined with the precipitate (fraction A, XXIII). The aqueous layer was then subjected to continuous extraction for 5 days to afford 0.29 g of a crystalline powder (fraction B, XXIV). These crystalline products were completely insoluble in almost all organic solvents. Fraction A was recrystallized twice from alcohol–water to yield a colorless powder, 0.17 g, mp 229° dec, which showed a single spot on tlc (silica gel, developed with toluene–ethyl formate–formic acid, 5:3:1). The ir spectrum showed an amide carbonyl at 5.99 $\mu$ (amide I). The mother liquor was evaporated to dryness and combined with the fraction from the continuous extraction (fraction B).

**N-Acetyl-7,8-diacetoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXVI).** The product which had been recrystallized from alcohol–water (0.16 g) was warmed in 3 ml of acetic anhydride on a steam bath for 3 hr and evaporated to dryness *in vacuo*. The residue was treated with ethyl acetate and sodium bicarbonate solution to remove a trace of acetic anhydride. The ethyl acetate layer was evaporated to leave an oil, 0.27 g, which was purified by chromatography on a column containing 4.0 g of silica gel. Elution with chloroform containing 12 and 15% ethyl acetate gave three products. The first minor fraction was an oil. The second elution gave 0.18 g of colorless crystals, mp 145°, after recrystallization from benzene.

*Anal.* Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.07; H, 5.29; N, 4.53.

The ir spectrum showed absence of NH and OH stretching bands, 5.67 and 5.90 $\mu$ ($\nu_{C=O}$).

**N-Acetyl-7- (or -8-) -hydroxy-8- (or -7-) -acetoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXV).** The elution following the above triacetyl compound XXVI afforded colorless crystals (55 mg), mp 162–163°, after recrystallization from benzene. This product showed positive color tests for a phenol group. Further acetylation of this diacetate gave the triacetate XXVI.

*Anal.* Calcd for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.97; H, 5.61; N, 5.05.

The ir spectrum showed major bands at 3.00, 5.66, 5.83, 5.89, and 5.94 $\mu$.

**N-Acetyl-8,9-diacetoxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXVII).** Acetylation of the more water-soluble fraction B (XXIV) was carried out in the same manner as described above. The reaction mixture, 0.60 g, was purified by chromatography on a column of silica gel (12 g). Elution with chloroform containing 1% methanol afforded colorless crystals (0.45 g), mp 175–176° after recrystallization from ethyl acetate.

*Anal.* Calcd for $C_{16}H_{17}NO_6$: C, 60.18; H, 5.37; N, 4.39. Found: C, 60.44; H, 5.54; N, 4.65.

The ir spectrum showed no NH or OH stretching bands and peaks at 5.66, 5.86, and 5.90 $\mu$.

**N-Chloroacetyl-3-hydroxy-4,5-dimethoxyphenethylamine (XXIX).** An aqueous solution of 0.34 g of 3-hydroxy-4,5-dimethoxyphenethylamine hydrochloride was treated three times with 0.25 g of chloroacetic anhydride and 3.0 ml of 1.0 *N* sodium hydroxide under ice cooling in the course of three hr. The reaction mixture was adjusted to pH 6 by the addition of hydrochloric acid and then extracted with ethyl acetate. The oily residue of the extract was purified on a silica gel column (10 g) from which elution with chloroform containing 1.5% methanol gave a crystalline product (0.20 g), mp 100–101°, after recrystallization from benzene.

**7,8-Dimethoxy-9-hydroxy-1,2,4,5-tetrahydro-3H-3-benzazepin-2-one (XXXa).** A solution of 110 mg of N-chloroacetyl-3-hydroxy-4,5-dimethoxyphenethylamine in 3.3 ml of 0.1 *N* sodium hydroxide and 60 ml of 0.66 *N* phosphate buffer (pH 7.0) was irradiated for 4 hr in the manner described. The irradiated solution was extracted with ethyl acetate. Recrystallization of the extract from chloroform gave colorless crystals, mp 205–207°. Composition ($C_{12}H_{15}NO_4$) and molecular weight (237) were determined by mass spectrometry. The structure was elucidated on the basis of nmr data (Table II).

**N-Chloroacetylmescaline.** Chloroacetyl chloride (1.68 g, 15 mmol) was added dropwise over a period of 3 min to a stirred solution of 2.78 g (5 mmol) of mescaline sulfate dihydrate in 30 ml of 1.0 *N* aqueous sodium hydroxide, cooled in an ice bath. After stirring for 10 min the ice bath was removed and stirring continued for 30 min. The mixture was cooled in an ice bath and the precipitated solid collected to yield 1.8 g (62.7%) of a colorless solid. Recrystallization from water gave long fine colorless needles, mp 78–79°.

*Anal.* Calcd for $C_{13}H_{18}ClNO_4$: C, 54.26; H, 6.30; N, 4.87. Found: C, 54.46; H, 6.46; N, 4.67.

The ir spectrum showed $\lambda_{max}^{CHCl_3}$ 2.85 (w), 3.38 (m), 6.00 (s), 6.30 (s), 6.60 (m), 6.88 (s), 7.10 (w), 7.40 (w), 7.52 (w), 7.65 (w), 8.90 (s), and 10.0 (m) $\mu$. The ultraviolet spectrum showed $\lambda_{max}^{EtOH}$ 269 m$\mu$ ($\epsilon$ 700).

**N-Bromoacetylmescaline.** The same procedure as described for N-chloroacetylmescaline, *i.e.*, the reaction of 2.78 g (5.0 mmol) of mescaline sulfate dihydrate with 3.02 g (15 mmol) of bromoacetyl bromide, yielded 1.77 g (53.3%) of N-bromoacetylmescaline as a colorless solid. Recrystallization from water gave long fine colorless needles, mp 83–84°.

*Anal.* Calcd for $C_{13}H_{18}BrNO_4$: C, 47.00; H, 5.46; N, 4.22. Found: C, 47.05; H, 5.34; N, 4.16.

The uv spectrum showed $\lambda_{max}^{EtOH}$ 268 m$\mu$ ($\epsilon$ 760).

**Attempted Photocyclization of N-Bromoacetylmescaline.** A solution of 540 mg (1.62 mmol) of N-bromoacetylmescaline in 100 ml of water and 70 ml of alcohol was irradiated with a 200-W Hanovia mercury discharge tube (Vycor filter) under nitrogen for 1 hr. The pale yellow solution was stirred with 500 mg of silver carbonate for 10 min and the silver salts were then removed by filtration through a Büchner funnel containing a matting of Celite filter aid. The filtrate was concentrated to a volume of 50 ml and then lyophilized to leave an orange oil which failed to crystallize. The oil was taken up in 5 ml of ethyl acetate and placed on a chromatography column containing 40 g of alumina (Merck). Ethyl acetate (100 ml) was passed through the column to elute the product. Evaporation of the ethyl acetate left a colorless crystalline solid, mp 87–89°. Recrystallization from isopropyl ether gave 125 mg (30.8%) of colorless needles, mp 90–91°. The compound was identified as N-acetylmescaline (lit.[17] mp 93–94°).

(17) E. Spath and J. Bruck, *Chem. Ber.*, 71B, 1275 (1938).

*Anal.* Calcd for $C_{13}H_{19}NO_4$: C, 61.65; H, 7.56; N, 5.53. Found: C, 61.54; H, 7.51; N, 5.51.

The nmr spectrum showed a singlet at 1.98 (three protons), multiplets centered at 2.80 and 3.50 (two protons each), a singlet at 3.90 (nine protons), a broad peak at 5.95 (one proton), and a singlet at 6.50 (two protons) ppm.

**Attempted Photocyclization of N-Chloroacetylmescaline.** A solution of 2.09 g (7.28 mmol) of N-chloroacetylmescaline in 600 ml of alcohol was irradiated with a 200-W Hanovia mercury discharge tube (Vycor filter), under nitrogen for 24 hr. Treatment of the solution with silver carbonate as described above, filtration, and evaporation left a yellow oil. The oil was taken up in 10 ml of ethyl acetate and filtered through 50 g of Merck alumina using 250 ml of ethyl acetate as eluent. Evaporation left a pale yellow crystalline solid which was taken up in 50 ml of hot isopropyl ether, treated with Norit, filtered, and cooled to yield 400 mg of colorless needles, mp 70–86°. Thin layer chromatography (silica gel; 1-propanol–water, 70:30) showed that the solid was mostly N-acetylmescaline, slightly contaminated with some unchanged N-chloroacetylmescaline.

**N-Chloroacetyl-3,5-dibromotyrosine.** Chloroacetyl chloride (2.69 g; 24 mmol) was added dropwise over a period of 5 min to a stirred solution of 5.7 g (16.8 mmol) of 3,5-dibromotyrosine in 35 ml of 2.0 *N* aqueous sodium hydroxide, cooled in an ice bath. After removing from the ice bath and stirring for 1 hr longer the solution was adjusted with dilute hydrochloric acid to pH 2 and the precipitated solid collected to yield 4.5 g (64.6%) of the N-chloroacetyl derivative as a pale yellow solid. Recrystallization from water gave fine colorless needles, mp 159–161°.

*Anal.* Calcd for $C_{11}H_{10}Br_2ClNO_4$: C, 31.80; H, 2.43; N, 3.37. Found: C, 32.00; H, 2.57; N, 3.37.

The infrared spectrum showed $\lambda_{max}^{KBr}$ 2.91 (s), 5.70 (s), 6.00 (s), 6.45 (s), 6.65 (s), 7.00 (m), 7.50 (w), 7.95 (m), and 8.45 (m) $\mu$. The uv spectrum showed $\lambda_{max}^{EtOH}$ 285 m$\mu$ ($\epsilon$ 2680) and 292 m$\mu$ ($\epsilon$ 2810).

**Attempted Photocyclization of N-Chloroacetyl-3,5-dibromotyrosine.** Photolysis was conducted with a 200-W Hanovia mercury discharge tube (Vycor filter) under nitrogen in both absolute ethanol and in ethanol–water solution. In all cases only dark brown resinous material was isolated and was not further investigated.

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# Chlorophyll–Ligand Interactions from Nuclear Magnetic Resonance Studies[1]

**Joseph J. Katz, Harold H. Strain, Daniel L. Leussing,[2] and Ralph C. Dougherty[2]**

*Contribution from the Chemistry Division, Argonne National Laboratory, Argonne, Illinois 60439, and the Department of Chemistry, The Ohio State University, Columbus, Ohio 43210.* *Received September 28, 1967*

**Abstract:** Chlorophyll–ligand coordination interactions, revealed by nmr spectra, have been studied by observing ring-current effects on proton chemical shifts of the ligands bound to chlorophyll. The use of deuteriochlorophyll simplifies interpretation of the nmr spectra. The equilibrium constant for the disaggregation of chlorophyll *a* dimers by methanol in $CCl_4$ to form chlorophyll monosolvate is found to be $K_1 = 56$ l. mol$^{-1}$. Equilibria involving the disolvate are less important, $K_2 = 1.3$ l. mol$^{-1}$. Pentacoordinate magnesium(II) appears to dominate the equilibria. Data are given for the interaction of other aliphatic alcohols and deuteriochlorophylls *a* and *b* and deuteriobacteriochlorophyll. Solvent and temperature dependence were examined. The Mg–O bond distance deduced from ring-current considerations for alcohol–chlorophyll interactions in halocarbon solvents is 3.1 Å.

It has long been known that chlorophyll interacts with nucleophilic ligands. Chlorophyll coordinates water[3,4] strongly. Livingston[5] found that chlorophylls *a* and *b* form stable monosolvates with nucleophiles such as water, alcohols, amines, ketones, and ethers and

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(2) The Ohio State University, Columbus, Ohio 43210.

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