

which after recrystallization from ethanol-water produced 0.182 g. of hexaethylbenzene, m.p. 128.5–129.0° (lit.³⁶ m.p. 129°).

(35) "Dictionary of Organic Compounds," Vol. II, I. Heilbron and H. M. Bunbury, Ed., Oxford University Press, New York, N. Y., 1953, p. 657.

The infrared spectrum was identical with that published for hexaethylbenzene.³⁶

(36) R. E. Richards and H. W. Thompson, *Proc. Roy. Soc. (London)*, **A195**, 4 (1948).

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The Synthesis, Nuclear Magnetic Resonance Spectrum, Resolution, and Rate of Racemization of 1-Fluoro-12-methylbenzo[*c*]phenanthrene¹

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The synthesis and resolution of 1-fluoro-12-methylbenzo[*c*]phenanthrene is described. The rates of racemization in *o*-dichlorobenzene at 130.5, 109.7, and 91.9° were found to be 7.81×10^{-5} , 9.49×10^{-6} , and 1.27×10^{-6} sec.⁻¹, respectively. From these values, the activation energy was calculated to be 31.1 kcal./mole and the entropy of activation at 109.7°, -2.80 ± 0.6 cal./deg./mole. The molecule showed unexpected n.m.r. properties that are attributed to ring distortion.

A review of the structural features required in compounds which owe their asymmetry to intramolecular overcrowding has been made.³ Later, the synthesis and optical properties of hexahelicene were described.⁴ Of the compounds described in these papers, racemization either occurred too easily or too difficultly to allow for convenient measurement. For example, in the benzo[*c*]phenanthrene series the rate of racemization of a 1-methyl derivative⁵ was too rapid (groups in the 1- and 12-positions, CH₃ and H) whereas in 1,12-dimethyl-5-carboxy-methylbenzo[*c*]phenanthrene³ racemization could not be studied because of thermal decomposition of the compound (groups in the 1- and 12-positions, CH₃ and CH₃) at temperatures suitable for racemization study. Hence it seemed likely that if the groups in the 1- and 12-positions were CH₃ and F perhaps the rate of racemization would be measurable. This hypothesis proved to be correct.

In this paper the synthesis of 1-fluoro-12-methylbenzo[*c*]phenanthrene (VI) and the measurement of its rate of racemization at three temperatures are described. Thus, for the first time, the energy of activation and entropy of activation for the racemization of a compound which owes its asymmetry to intramolecular overcrowding⁶ have been determined.

The synthetic route illustrated was that of Newman and Wolf⁷ modified as described in later similar syntheses.^{3,4,8} The steps from I to III_d proceeded in excellent yields. However, difficulty was experienced in the double ring closure to IV, as in the best cases only about 30–44% yields were obtained. The remainder was a keto acid VII of unproved structure⁹ which was not readily cyclized to the desired diketone IV. Reduction of IV to the diol V proceeded well. Conversion of V to VI was accomplished in 40% yield by heating in refluxing xylene with a small amount of iodine for over 100 hr. Thus, VI was prepared from I in 9.2% over-all yield.

The ultraviolet absorption spectrum of VI is almost the same as that of 1,12-dimethylbenzo[*c*]phenanthrene.⁷ The values are listed in Table I.

(1) This work was taken from the Ph.D. thesis of R. G. M., The Ohio State University, 1962.

(2) We are indebted to the National Science Foundation and The U. S. Public Health Service for support of this work.

(3) M. S. Newman and R. M. Wise, *J. Am. Chem. Soc.*, **78**, 450 (1956).

(4) M. S. Newman and D. Lednicer, *ibid.*, **78**, 4765 (1956).

(5) M. S. Newman and W. Wheatley, *ibid.*, **70**, 1913 (1948).

(6) F. Bell and D. H. Waring, *J. Chem. Soc.*, 2689 (1949).

(7) M. S. Newman and M. Wolf, *J. Am. Chem. Soc.*, **74**, 3225 (1952).

(8) M. S. Newman and D. Phillips, *ibid.*, **81**, 3667 (1959).

(9) We favor the structure 3-carboxymethyl-4-*o*-fluorophenyl-5-methyl- α -tetralone rather than the isomeric structure involving ring closure into the fluorine-containing ring because ring closure *meta* to an aromatic fluorine atom should occur less easily than ring closure *meta* to a methyl group.

TABLE I

ULTRAVIOLET ABSORPTION SPECTRA			
1-Fluoro-12-methylbenzo[<i>c</i>]-phenanthrene		1,12-Dimethylbenzo[<i>c</i>]-phenanthrene	
λ , m μ	log ϵ	λ , m μ	log ϵ
212	4.32 (min.)	215	4.46 (min.)
221	4.55 (max.)	224	4.60 (max.)
240	4.05 (min.)	244	4.07 (min.)
248	4.10 (max.)	250	4.08 (max.)
255	4.09 (min.)	254	4.05 (min.)
289	4.73 (max.)	292	4.78 (max.)
322	3.87 (min.)	324	3.91 (min.)
326	3.88 (max.)	328	3.92 (max.)
361	2.49 (min.)	363	2.46 (min.)
367	2.51 (max.)	370	2.50 (max.)

The resolution of VI was accomplished by the use of (–)- α -(2,4,5,7-tetranitro-9-fluorenylideneaminoxy)-propionic acid¹⁰ as in a similar case.⁴ The maximum resolution afforded VI with $[\alpha]_D^{25} \pm 580 \pm 15^\circ$ in chloroform. The rates of racemization in *o*-dichlorobenzene were 7.81×10^{-5} at 130.5°, 9.49×10^{-6} at 109.7°, and 1.27×10^{-6} sec.⁻¹ at 91.9°. From these values, the activation energy was calculated to be 31.3 kcal./mole and the entropy of activation at 109.7° calculated to be -2.8 ± 0.6 cal./deg./mole. Thus it appears that the transition state for racemization is only slightly more rigid than the reactant.

The variations in the methyl group absorptions of 1-methylbenzo[*c*]phenanthrene, 1-fluoro-12-methylbenzo[*c*]phenanthrene, and 1,12-dimethylbenzo[*c*]phenanthrene in the n.m.r. spectra are of interest.¹¹ The spectrum of 1-methylbenzo[*c*]phenanthrene showed a complex multiplet of relative area eleven centered at about 7.7 δ and 50 c.p.s. in width which was attributed to the aromatic hydrogens. Unlike benzo[*c*]phenanthrene, it lacked unique absorption farther downfield.¹² In the methyl region it showed a singlet of relative area three at 2.36 δ . This methyl absorption was not very greatly shifted (from that for toluene at 2.32 δ) by the presence of the additional rings with their associated ring currents. These results could be attributed to the forcing of the methyl group out of the plane of maximum deshielding anisotropy of the opposing aromatic ring.¹³

(10) M. S. Newman and W. B. Lutz, *J. Am. Chem. Soc.*, **78**, 2469 (1956).

(11) The work on spectra of these compounds and their interpretation was done by Dr. George Slomp of the Upjohn Co., Kalamazoo, Mich. The discussion in our text was written by him. We are much indebted to him for this work. The spectra were taken on deuteriochloroform solutions with a Varian A-60 spectrometer.

(12) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 249.

In the case of 1-methyl-12-fluorobenzo[*c*]phenanthrene, the n.m.r. spectrum showed a complex absorption pattern of relative area ten centered at about 7.4 δ and about 60 c.p.s. in width which was attributed to the aromatic hydrogens. Again they all absorbed in the same region. The methyl peak was a doublet at 2.28 δ , $J = 2.5$ c.p.s. as the methyl group is apparently deshielded by the nearby fluorine atom and twisted out of the plane of the opposing aromatic ring. Possibly this splitting arises from the fluorine *very nearby* in space but seven bonds away. If this is true, the small magnitude of the coupling indicates that the splitting is not transmitted across space,¹⁴ for then it should be much larger, but rather is transmitted through the intervening bonds. The magnitude seems about right for seven bonds, each with partial double bond character. Fluorine-hydrogen splittings of as large as 7 c.p.s. have been observed across five single bonds in 6 β -fluorosteroids (e.g., in 6 β -fluoro-5 α ,11 β ,21-trihydroxy-17(20)-pregnen-3-one, cyclic ethylene acetal, 21-acetate¹⁵ the 19-hydrogens were a doublet at 1.22 δ , $J = 7.0$ c.p.s.)¹⁶ and a hydrogen-hydrogen coupling, $J = 1$ c.p.s., through five bonds having partial double bond character was seen in furocoumarin.¹⁷

The n.m.r. spectrum of 1,12-dimethylbenzo[*c*]phenanthrene showed an aryl-hydrogen multiplet of relative area ten centered at about 7.6 δ and about 45 c.p.s. in width. Owing to the symmetry of the molecule, this multiplet contained about half as many lines as was observed with the two analogs described above. In the methyl region the spectrum showed a singlet at 1.92 δ of relative area six attributed to the hydrogens of the two methyl groups. It is noteworthy that these methyl hydrogens experience additional shielding compared to toluene and the examples cited above. This could indicate that the ring systems were more greatly distorted, thus placing the methyl groups farther out of the deshielding anisotropy plane of the rings because of greater distortion of the aromatic rings.

Experimental¹⁸

Diethyl *o*-Fluorobenzalmalonate (I), b.p. 142–146° at 1 mm., was obtained in 94% yield from *o*-fluorobenzaldehyde (Columbia Organic Chemical Co.) and diethyl malonate as described for a similar case.¹⁹

Anal. Calcd. for C₁₄H₁₅FO₄: C, 63.2; H, 5.7; F, 7.1. Found*: C, 63.4; H, 5.7; F, 6.9.

2-(2-Fluoro-2-methylbenzhydryl)-1,3-propanediol (IIIa).—To a well-stirred solution of 53.2 g. of I in 125 ml. of ether at 0° was added dropwise during 40 min. the Grignard reagent prepared from 42 g. of *o*-bromotoluene in 200 ml. of ether. The mixture was then refluxed for 1 hr. and worked up as usual to yield 59.6 g. (83%) of crude diethyl (2-fluoro-2-methylbenzhydryl)malonate (II), b.p. 192–200° at 1 mm., as an oil with a faint green color. If compound I were added to the Grignard reagent, the yield of II fell about 10%. If 2 mole % of cuprous chloride were added little change in yields resulted. Lithium aluminum hydride reduction of II in ether afforded the diol IIIa (2.9 μ) as a colorless solid, m.p. 70–76°, in 91% yield after crystallization from petro-

leum ether. If the crude diol were distilled before crystallization the yield of good diol obtained was about 15% less. Several recrystallizations from petroleum ether, b.p. 65–70° (Skellysolve B), afforded colorless crystals of IIIa, m.p. 78.5–80.0°.

Anal. Calcd. for C₁₇H₁₉FO₂: C, 74.7; H, 7.0; F, 6.9. Found*: C, 74.5; H, 6.8; F, 6.8.

3-(2-Fluoro-2-methylbenzhydryl)glutaric Acid (IIIId).—To a solution of 9.5 g. of IIIa, m.p. 70–76°, in 80 ml. of dry pyridine at 0–5° was added dropwise with stirring 13.8 g. of methane-sulfonyl chloride (Eastman White Label) during 30 min. After standing in the cooling bath for 4 hr. the light orange mixture was poured into 250 ml. of cold water. The yellow oil which separated solidified on standing for several hours. The solid was then collected and washed with dilute hydrochloric acid and water. On drying *in vacuo*, 14.2 g. (95%) of bis-methanesulfonate (IIIb) (no band near 2.9 μ present) was obtained. A solution of 13.4 g. of IIIb, 9.8 g. of potassium cyanide, 0.3 g. of potassium iodide, 60 ml. of water, and 125 ml. of dimethylformamide was stirred at 90 \pm 3° for 4.5 hr., then cooled to 60° and poured into 500 ml. of ice water. The light reddish-brown solid was collected, washed, and dried to yield 8.6 g. (95%) of crude dinitrile IIIc (4.5 μ). A solution of 8.0 g. of crude IIIc, 7 g. of sodium hydroxide, and 75 ml. of ethylene glycol was heated to 180° at which point a tan precipitate separated. An additional 20 ml. of ethylene glycol was added and the contents held at reflux for 3 hr. On cooling, the tan solid was collected and dissolved in 100 ml. of water. This solution was filtered and the filtrate added to 50 ml. of cold 4 *N* hydrochloric acid. The colorless precipitate of IIIId melted at 191–194° on drying and weighed 2.9 g. The above ethylene glycol filtrate was diluted with 150 ml. of water and extracted with ether-benzene. The tan-colored aqueous layer was added to excess hydrochloric acid to yield 5.8 g. of less pure IIIId, m.p. 186–192°. The total yield of IIIId was 97%. Recrystallization of the above acid yielded pure IIIId, m.p. 195–196°, with little loss.

Anal. Calcd. for C₁₉H₁₉FO₄: C, 69.1; H, 5.8; F, 5.7. Found*: C, 68.7; H, 6.1; F, 5.7.

6a,12b-Dihydro-1-fluoro-12-methylbenzo[*c*]phenanthrene-5,8-(6H,7H)-dione (IV).—In one of the best of many runs 25 g. of colorless powdered glutaric acid (IIIId), m.p. 193–195°, was added during 15 sec. to 500 g. of polyphosphoric acid²⁰ (PPA) held at 165° and vigorously stirred. The mixture darkened rapidly. When a deep brown color had been attained after 6 min. the hot mixture was poured on 1 kg. of ice and the whole was then stirred well until no further change in appearance occurred. The solid was collected and on washing with several portions of ether-benzene went into solution with the exception of 2 g. of insoluble material. The dark organic layer was extracted several times with 10% potassium carbonate solution and was then treated in the usual manner. Crystallization of the neutral organic product from benzene yielded 7.3 g. (32%) of yellow diketone IV, m.p. 172–175°, and 2.3 g. (10%) of IV, m.p. 170–174°, as a second crop. The analytical sample, m.p. 176–177° (6.02 μ), was obtained by crystallization from benzene.

Anal. Calcd. for C₁₉H₁₅FO₂: C, 77.5; H, 5.1; F, 6.4. Found*: C, 77.7; H, 5.0; F, 6.2.

The results of many other cyclization attempts are listed in the Ph.D. thesis of R. G. Mentzer.¹

The bis-2,4-dinitrophenylhydrazones melted over 300° dec., on recrystallization from nitrobenzene.

Anal. Calcd. for C₃₁H₂₃FN₂O₈: C, 56.9; H, 3.5. Found*: C, 56.8; H, 3.4.

The potassium carbonate washings were combined and acidified to yield 7.5 g. of an almost black solid. Recrystallization from benzene yielded 5.5 g. (23%) of almost colorless keto acid,⁸ m.p. 143–147°. The analytical sample melted at 147.5–149.0° (3.1, 5.87, 6.02 μ).

Anal. Calcd. for C₁₉H₁₇FO₃: C, 73.1; H, 5.5. Found*: C, 73.0; H, 5.2.

When the cyclization of 10 g. of IIIId in 100 ml. of anhydrous hydrogen fluoride was effected, the yield of the above keto acid was 9.2 g. (97%), m.p. 143–146°. The acid chloride made from this keto acid and thionyl chloride was taken up in 100 ml. of tetrachloroethane and treated at 30° with 5.6 g. of aluminum chloride for 1 hr. A conventional work-up yielded 2 g. (35%) of a yellow diketone, m.p. 193–196° (5.90 μ). Recrystallization from ether-petroleum ether yielded colorless diketone, m.p. 197.0–198.5°, isomeric with IV. No further work was done with this diketone.

Anal. Calcd. for C₁₉H₁₅FO₂: C, 77.5; H, 5.1. Found*: C, 77.3; H, 5.3.

5,6,6a,7,8,12b-Hexahydro-1-fluoro-12-methylbenzo[*c*]phenanthrene-5,8-diol (V).—To a solution of 1.5 g. of lithium alumi-

(13) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 125, and other references cited therein.

(14) A. D. Cross and P. W. Landis, *J. Am. Chem. Soc.*, **84**, 3784 (1962).

(15) U. S. Patent 2,838,497-S.

(16) Private communication, G. Slomp and F. A. MacKellar.

(17) K. D. Kaufman, J. F. W. Klana, R. C. Kelly, D. W. McBride, and G. Slomp, *J. Org. Chem.*, **27**, 2567 (1962).

(18) All melting points are uncorrected. Microanalyses marked * by Galbraith Microanalytical Laboratories, Knoxville, Tenn., * by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. The phrase "treated in the usual manner" means that the solution of the organic products in ether-benzene (about 1:1) was washed with acid and/or alkali as indicated and with saturated sodium chloride solution. The resulting solution was filtered through a layer of anhydrous magnesium sulfate and the solvent distilled or removed under reduced pressure. Infrared absorption bands are noted in parentheses.

(19) C. F. H. Allen and F. W. Spangler, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., p. 377.

(20) We thank the Victor Chemical Co., Chicago, Ill., for a generous gift of polyphosphoric acid.

num hydride in 150 ml. of ether was added dropwise during 10 min. of stirring a solution of 4.7 g. of IV, m.p. 172–175°, in 90 ml. of dry benzene. An insoluble white precipitate formed immediately. The mixture was refluxed for 30 min., then carefully treated with water. Isolation in the usual way afforded 4.2 g. (89%) of crude diol V, m.p. 159–183°, and 0.3 g. (7%) of diol, m.p. 150–182°, in two crops from benzene. The crude diol (undoubtedly a mixture of isomers) was used directly for dehydration and aromatization as described below. There was no carbonyl peak in the infrared.

A dicarboethoxy derivative was prepared by treating a solution of 2.0 g. of crude diol, m.p. 159–183°, in 40 ml. of dry pyridine at 0° with 6 ml. of ethyl chloroformate (Eastman White Label). After standing at room temperature for 5 hr. and refluxing for 1 hr., the mixture was poured onto ice. The yellow solid which formed was collected after standing at 0° for 12 hr. and recrystallized from ethanol to yield 1.48 g. (48%) of almost colorless solid. Two recrystallizations from ethanol afforded dicarboethoxy derivative of V as colorless needles, m.p. 147–148° (5.8 μ).

Anal. Calcd. for $C_{25}H_{22}FO_6$: C, 67.9; H, 6.2; F, 4.3. Found*: C, 67.5; H, 6.3; F, 4.3.

1-Fluoro-12-methylbenzo[c]phenanthrene (VI).—A solution of 4.25 g. of diol V, m.p. 152–178°, 13 ml. of xylene, and 18 mg. of iodine was heated to reflux. Within a few minutes the iodine color disappeared and a pale yellow color was noted. After 24 hr., 8 mg. of iodine was added. The iodine color again rapidly disappeared. After a total of 100 hr. of reflux the yellow solution was cooled, diluted with ether, washed with sodium bisulfite solution, and worked up as usual to yield a brown gummy residue. Chromatography over alumina yielded 1.55 g. of a colorless oil (ultraviolet max. at 289 $m\mu$, ϵ 47,800) which was rich in VI. Crystallization from absolute ethanol (saturated with nitrogen) yielded 1.4 g. (39%) of colorless VI, m.p. 62–64°. Recrystallization from alcohol yielded pure VI, m.p. 66–67°, with little loss. In other runs similar or lower yields were obtained. Crystallization to yield sharp melting VI was frequently difficult.

Anal. Calcd. for $C_{19}H_{13}F$: C, 87.7; H, 5.0; F, 7.3. Found*: C, 87.5; H, 5.0; F, 7.4.

The dark red 2,4,5,7-tetranitrofluorenone¹⁰ complex, m.p. 200–201°, was prepared in glacial acetic acid.

Anal. Calcd. for $C_{22}H_{17}FN_4O_6$: C, 61.9; H, 2.7; F, 3.1; N, 9.0. Found*: C, 61.8; H, 2.8; F, 3.1; N, 8.9.

Resolution of VI.—Finding the right conditions for crystallization of a complex of VI with optically active α -(2,4,5,7-tetranitro-9-fluorenylideneaminoxy)propionic acid¹⁰ (TAPA) was difficult. Attempted repetitions of successful experiments often failed for unknown reasons. It was found advantageous to saturate all solvents with nitrogen. A solution of 2.0 g. of VI and 1.5 g. of (–)-TAPA in 15 ml. of chloroform was concentrated to 10 ml. and allowed to stand overnight at room temperature. Filtration afforded 1.6 g. of red solid. This was dissolved in ether-benzene and extracted with aqueous sodium bicarbonate. The organic layer was concentrated to yield 0.63 g. of pale red oil. This was chromatographed over alumina using 4:1 Skellysolve B–chloroform. The colorless oil thus obtained (0.58 g.) had $[\alpha]_D^{25} -323^\circ$ in chloroform (c 0.016 g./ml.). A second similar treat-

ment with (–)-TAPA afforded crystals, m.p. 64–67°, $[\alpha]_D^{25} -510^\circ$. Recrystallization from acetic acid then afforded 0.12 g. of VI, m.p. 66–67°, $[\alpha]_D^{25} -580 \pm 15^\circ$ in chloroform, c 0.005 g./ml. In a similar way, when the original complex formation between (–)-TAPA was carried out in acetic acid, the (+)-VI which was obtained had a rotation of $+573 \pm 15^\circ$.

Rate of Racemization Experiments.—Since it proved so difficult to obtain large amounts of completely resolved VI, the rate of racemization experiments were carried out on partly resolved material ($[\alpha]_D^{25}$ 300–400°). In a typical run, a weighed amount, 0.1570 g. of VI, $[\alpha]_D^{25} -323^\circ$, was dissolved in *o*-dichlorobenzene (single peak by v.p.c. analysis) and made up to 12.00 ml. Ten vials were filled with 1.20 ml. of this solution and were sealed up. The sealed vials were weighed before and after heating to ensure that no loss had occurred. These vials were placed in a glycerine bath in an apparatus arranged so that the bath was heated with a constant boiling liquid. The temperatures recorded by the same thermometer (corrected, standardized) were constant to $\pm 0.1^\circ$ during each run. At the indicated time intervals, a vial was removed and cooled. The rotation was then determined at 25° with the sodium D line in a Rudolph polarimeter. The rate constants were shown to be first order with respect to VI by the fact that straight lines were obtained on plotting $\log \alpha$ vs. time (in min.) until material initially about 50–60% resolved was almost completely racemized. The values of the rate constants were obtained by using the intercepts on the axes of the above plots and substituting in eq. 1.²¹ The rate constants are listed in Table II.

$$\ln(\alpha_1/\alpha_2) = 2k(t_1 - t_2) \quad (1)$$

where α = observed rotation and t = time.

TABLE II
RATES OF RACEMIZATION OF
(l)-1-FLUORO-12-METHYLBENZO[c]PHENANTHRENE

Temp., °C.	k , sec. ⁻¹
130.6 \pm 0.1	7.90 \times 10 ⁻⁶
130.4 \pm .1	7.73 \times 10 ⁻⁶
109.7 \pm .1	9.52 \times 10 ⁻⁶
109.7 \pm .1	9.45 \times 10 ⁻⁶
91.7 \pm .1 ^a	1.24 \times 10 ⁻⁶
92.0 \pm .1	1.30 \times 10 ⁻⁶

^a See text near ref. 22 for explanation of temperature variation.

The temperature variation for the two runs at about 92 and at 130° was caused by the fact that the atmospheric pressure was different on different days. The temperature near 92° was obtained with the water–butanol azeotrope.²²

The values of $\log k$ vs. $1/T$ were plotted to yield a straight line. From the slope obtained by drawing the best line through the points, the activation energy was calculated to be 31.3 kcal./mole. The statistical error was calculated to be 0.2 kcal./mole.²³

(21) For derivation see D. Smith, *J. Am. Chem. Soc.*, **49**, 43 (1927).

(22) Lange's "Handbook of Chemistry," 9th Ed., Sandusky, Ohio, p. 1484.

(23) R. W. Taft, Jr., and C. DeFazio, *J. Am. Chem. Soc.*, **77**, 837 (1955).

[CONTRIBUTION FROM THE GERONTOLOGY BRANCH, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MD., AND BALTIMORE CITY HOSPITALS, BALTIMORE, MD.]

The Reaction of Mercury(II) with Nucleosides

BY GUNTHER L. EICHHORN AND PATRICIA CLARK

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The attachment of mercury to the nucleosides has been elucidated by a variety of techniques. Titration studies reveal that binding occurs at the N_3O^6 grouping of uridine and guanosine. Experiments in which the amino group is masked by reaction with formaldehyde show that mercury is bound to the amino group in adenosine and cytidine. These results are confirmed by spectrophotometric observations. Support for the mercury–DNA structure proposed by Katz is obtained from titration data with mercury–DNA solutions.

The importance of an understanding of the interaction of metal ions with the nucleic acids becomes evident when it is realized that metals of various kinds, under various conditions, can stabilize the secondary and tertiary macromolecular structures,¹ or labilize these structures,² or even bring about the decomposition of the primary structure.^{3,4} Of fundamental impor-

tance to such an understanding is the knowledge of whether the metal ions bind to the phosphate groups on the polynucleotide chain, or whether they bind to electron donors on the purine or pyrimidine bases.

The discovery of the reaction of mercury(II) ion with DNA by Katz⁵ was followed by the demonstration of

(1) J. Shack, R. J. Jenkins, and J. M. Thompsett, *J. Biol. Chem.*, **203**, 373 (1953).

(2) G. L. Eichhorn, *Nature*, **194**, 474 (1962).

(3) E. Bamann, H. Trapmann, and F. Fischler, *Biochem. Z.*, **328**, 89 (1954).

(4) G. L. Eichhorn and J. J. Butzow, in preparation.

(5) S. Katz, *J. Am. Chem. Soc.*, **74**, 2238 (1952).