

do not form rapidly on the outside of the diver the simplified method described can be applied to weighing tissues much smaller than embryonic hearts. The improvement in the equation given by Zeuthen makes accurate weighings possible under conditions where the diver is or is not suspended at atmospheric pressure.

Reference

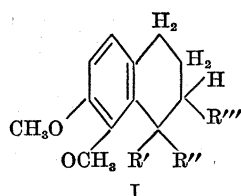
1. ZEUTHEN, E. *Compt. Rend. Trav. Lab. Carlsberg, Serie Chim.*, 1948, **26**, 243.

On the Structure of Morphine and its Derivative Metopon

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Because the unique and valuable analgesic properties of the morphine derivative Metopon (methyl dihydromorphinone) (4) may be due, in large measure, to the influence of the new methyl group, information regarding the latter's position in the molecule is of some moment. With a view toward elucidating this point, a method has been developed for degrading the more accessible dihydrothebaine (Metopon's precursor) to an optically active dimethoxytryalkyltetrahydronaphthalene Ia or Ib.



- (a) $R' = C_2H_5$; $R'' = C_2H_5$;
 $R''' = C_2H_5$
- (b) $R' = CH_3$; $R'' = C_2H_5$;
 $R''' = C_2H_5$

Analysis. Calculated for $C_{18}H_{28}O_2$; C, 78.21; H, 10.21; OCH_3 , 22.46. Found: C, 78.22; H_2 , 10.20; OCH_3 , 22.22. $[\alpha]_D^{20} = -52.7^\circ$ (c, 0.927, ethanol); $n_D^{20} = 1.5295$; $d_4^{20} = 1.027$; bp (evaporative distillation) 97–104° C/0.4 mm.

It is hoped to distinguish between the two possible isomers on the basis of results of synthetic experiments which are now nearly complete.

Degradation of Metopon according to this new scheme should lead to a methyl homologue of either Ia or Ib, distinguishable by synthetic processes.

Of equal and perhaps greater importance is the fact that this method of degradation now affords a complementary means of rigorously proving whether C¹³ is one of the points of closure of the heterocyclic nitrogen ring in morphine. The important synthetic approaches of Grewe (2, 3) and of Gates (1) both favor C¹³ as one point of ring closure; the other point, C⁹, appears well established.

Intimately linked with the above are the stereochemical implications associated with carbon atoms 9, 13, and 14 in the morphine molecule. All the foregoing will be fully reported in papers to be published elsewhere.

References

1. GATES, M., et al. *J. Am. Chem. Soc.*, 1950, **72**, 1141.
2. GREWE, R., and MONDON, A. *Chem. Ber.*, 1948, **81**, 279.
3. GREWE, R., MONDON, A., and NOLTE, E. *Ann. Chemie*, 1949, **564**, 161.
4. SMALL, L., FITCH, H. M., and SMITH, W. R. *J. Am. Chem. Soc.*, 1936, **58**, 1457.

Streaming Birefringence of Denatured Ovalbumin¹

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That the denaturation of globular proteins consists essentially of an unfolding of the polypeptide chain or chains is generally conceded, but evidence for the nature, or even existence, of the unfolded structure in solution is limited and indirect. Intrinsic viscosity data, which have been most used, are difficult to interpret since they yield only a measure of the effective hydrodynamic volume of the solute. Streaming birefringence, which yields essentially a measure of the particle length and is dependent only to a minor extent on molecular asymmetry and hydration, would appear to be a method of great potential value in the study of the denaturation process. Furthermore, results obtained over a wide range of velocity gradients provide an insight into the homogeneity (with regard to length) of the solute (1, 2).

The authors have completed more than 100 flow birefringence runs, in the concentric cylinder apparatus used by one of us previously (3), on ovalbumin denatured in various ways. The orientation angle χ (the angle between the optic axis and the direction of streaming) was measured, as well as the birefringence. The recently computed numerical solutions of Edsall and co-workers (8) for the flow orientation equations developed by Peterlin and Stuart (6, 7) were used for determining α (the ratio of the velocity gradient G to the rotary diffusion constant β) from the χ values obtained. The apparent length of the denatured ovalbumin molecules was calculated by applying the Perrin (5) theory for the case of an elongated ellipsoidal structure.

Denaturation of ovalbumin was carried out under such conditions that no precipitation, gelation, or appreciable turbidity occurred. Heat denaturation was studied in the pH range 1–4 using glycine-buffered and unbuffered solutions, and in the pH range 6–9 in the presence of veronal and phosphate buffers. Urea denaturation was followed in the pH range 6–9. The effect of cationic detergents on the acid side of the isoelectric point and of anionic detergents on the alkaline side was also examined. In a typical heat denaturation experiment 0.100 g of ovalbumin in 15.0 ml of buffer was heated at 100° C for a given period of time; the solution was cooled rapidly and diluted with 42.0 g of 95% glycerol. (The gly-

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