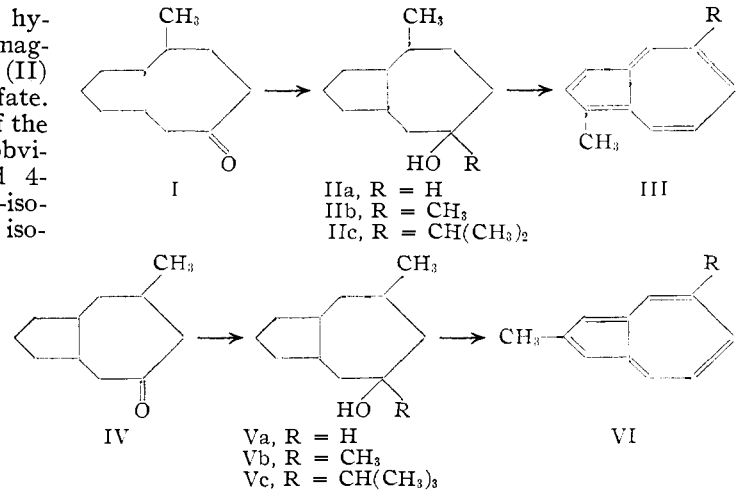
I was treated with lithium aluminum hydride and with methyl- and isopropylmagnesium halide. The resulting alcohols (II) were dehydrated with potassium acid sulfate. Much to our surprise, dehydrogenation of the olefins with sulfur yielded *blue* azulenes obviously not identical with the expected 4-methyl-,[2] 4,7-dimethyl-[3] and 4-methyl-7-isopropylazulenes; no other azulenes were isolated. The visible spectrum and trinitrobenzene complex identified III-a as 1-methylazulene[4] (3%) (λ_{max} 742, 703, 669, 635, 611, 587, m.p.[5] of TNB complex 160°). III-b (isolated in 4% yield) had properties identical with those reported for 1,5-dimethylazulene[3,6] (λ_{max} 765, 715, 681, 650, 622, 602, 565, 545 mμ; m.p. of TNB complex 151–152.5°). III-c, whose spectrum is virtually undistinguishable from IIIb, is therefore assumed to be 1-methyl-5-isopropylazulene,[7] m.p. of TNB complex 137.5–138° (Calcd. for $C_{20}H_{19}N_3O_6$: C, 60.45; H, 4.82; N, 10.58. Found: C, 60.60; H, 5.07; N, 10.7).



The generality of this rearrangement has been demonstrated by subjecting to a similar series of reactions 3-methylbicyclo(5,3,0)-5-decanone (IV), prepared in essentially the same way from cyclopentanone carboxylic ester and ethyl γ-bromodimethylacrylate, b.p. 79–80° (1 mm.) (Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.57; H, 10.92); semicarbazone, m.p. 182–183° (Calcd. for $C_{12}H_{21}N_3O$: C, 64.54; H, 9.48; N, 18.82. Found: C, 64.35; H, 9.67; N, 18.7). V-a yielded 2-methylazulene[4,8] (VI, 6%)[9] (λ_{max} 678, 652, 634, 625, 615, 601, 591, 568, 562, 551, 533, 523, 460 mμ, m.p. of TNB complex 135–136°), V-b gave only the previously unreported 2,5-dimethylazulene (VI-b, 5%), (λ_{max} 693, 668, 655, 628, 603, 578, 558, 545, 480 mμ; m.p. of TNB complex 149–150.5°. Calcd. for $C_{18}H_{15}N_3O_5$: C, 58.53; H, 4.09; N, 11.38. Found: C, 58.67; H, 4.21; N, 11.2), and V-c gave exclusively 2-methyl-5-isopropylazulene[1,11] (λ_{max} 688, 663, 655, 625, 600, 575, 545, 485; m.p. of TNB complex 112.5–114°. Calcd. for $C_{20}H_{19}O_6N_3$: C, 60.45; H, 4.82; N, 10.58. Found: C, 60.58; H, 5.05; N, 10.6).

The demonstration of this apparently transannular rearrangement implies that thermal migration of alkyl groups from position 1 to position 2 of the azulene nucleus is not the only source of error in locating alkyl groups in azulenogens and that reëxamination of certain structures which rest on the dehydration of bicyclodecane derivatives containing hydroxyl groups, particularly hydroxyls in the 5-position, may be in order.

The homogeneity of the azulenic products and their structure suggests that the rearrangement occurs during the dehydration rather than during the dehydrogenation step by a mechanism which involves two 1,3-shifts (or a series of 1,2-shifts). Isomerization during dehydrogenation might have been expected to result in mixtures and to lead to 2- rather than 1-substituted azulenes in the reaction sequence based on I. Studies intended to elucidate this are in progress.

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(2) Pl. A. Plattner, E. Heilbronner and A. Fürst, *Helv. Chim. Acta*, **30**, 1100 (1947).

(3) H. Pommer, *Ann.*, **579**, 47 (1953).

(4) Pl. A. Plattner and J. Wyss, *Helv. Chim. Acta*, **24**, 483 (1941); Plattner and G. Büchi, *ibid.*, **29**, 1608 (1946).

(5) Melting points determined on Kofler block.

(6) H. Arnold and H. Schachtner, *Ber.*, **86**, 1445 (1953).

(7) Yield not reported because the reaction of I and IV with isopropylmagnesium bromide or isopropyllithium resulted in a mixture of I and II and IV and Vc consisting largely of starting material. This was used directly for further work.

(8) Pl. A. Plattner and E. Heilbronner, *Helv. Chim. Acta*, **30**, 910 (1947).

(9) This experiment also yielded a small amount of a blue azulene which could not be characterized but whose spectrum was identical with that of 5-methylazulene,[10] the "expected" product.

(10) F. Sorm, *Coll. Czech. Chem. Commun.*, **12**, 251 (1947).

(11) Pl. A. Plattner, A. Fürst, A. Müller and W. Keller, *ibid.*, **37**, 271 (1954).

OXYGEN EXCHANGE DURING THE ACIDIC AND BASIC HYDROLYSES OF AMIDES AND THE ENZYMATIC HYDROLYSIS OF ESTERS[1]

Sir:

Oxygen exchange has been found to occur between benzamide-O^{18} and water during the basic hydrolysis of benzamide, but no exchange was observed during its acidic hydrolysis. Oxygen exchange was not observed during the α-chymotrypsin catalyzed hydrolysis of methyl β-phenylpropionate-*carbonyl*-O^{18}. These results are in contrast to those obtained during the basic and acidic hydrolyses of ethyl benzoate.[2] In both ethyl benzoate hydrolyses, exchange between the carbonyl oxygen of the ester and the water occurred. This phenomenon was attributed to the reversible formation of a symmetrical addition intermediate, $RC(OH)_2OR$.[3]

Benzamide-O^{18} was prepared from benzoic acid-

(1) This investigation has been supported by grants from the Research Corporation and the U. S. Public Health Service. III in the series, Intermediates in the Reactions of Carboxylic Acid Derivatives.

(2) M. L. Bender, THIS JOURNAL, **73**, 1626 (1951).

(3) Infrared evidence for stable addition compounds related to this structure is given in M. L. Bender, *ibid.*, **75**, 5986 (1953).

O^{18} *via* the acid chloride.[2] The kinetics of the hydrolysis of benzamide in aqueous solutions of hydrochloric acid or sodium hydroxide at 109.0 ± 0.2° were measured by the spectrophotometric determination of the liberated ammonia, using Nessler's reagent.[4] Labeled benzamide was hydrolyzed under conditions identical to those used in the kinetic determinations. After periods of time corresponding to 0–85% hydrolysis, the reaction was quenched and the unreacted benzamide was isolated (m.p. 127–127.5°). The benzamide samples were pyrolyzed to carbon dioxide[5] which was analyzed mass spectrometrically.[6]

Oxygen exchange experiments between benzamide-O^{18} (0.58 atom %) and water during basic hydrolysis revealed significant exchange. Benzamide from runs including 21, 25, 28, 37, 55, 75% hydrolysis gave values of 0.33, 0.29, 0.28, 0.24, 0.21, 0.20 atom % O^{18}, respectively. By plotting these data[2] the ratio of the rate constant of hydrolysis to the rate constant of exchange was evaluated as 0.21. This value should be compared with the value of 4.8 for the k_h/k_{ex} found for the oxygen exchange during ester hydrolysis. The fact that $k_{ex} > k_h$ in the amide hydrolysis, but $k_h > k_{ex}$ in the ester hydrolysis may be related to the competitive breakdown of the addition intermediate $RC(OH)_2X$. The ease of removal of groups is presumably in the order: $OH^- > NH_2^-$ from the amide intermediate and $OR^- > OH^-$ from the ester intermediate. In the amide case the order is in accord with the relative anionic stabilities of the groups, but not in the ester case, in which the large steric requirement of the OR^- group may be important.

However, oxygen exchange experiments between benzamide-O^{18} (0.58 atom %) and water during acid hydrolysis indicated no exchange. Benzamide recovered from runs including 60, 70 and 85% hydrolysis gave values of 0.57, 0.58, 0.58 atom % O^{18}, respectively.[7] The lack of oxygen exchange in the acid hydrolysis of benzamide may be attributed to the greater basicity of nitrogen relative to oxygen, which results in a displacement reaction without the formation of an addition intermediate.[8] That the basicity of the nitrogen atom is a factor in determining the course of the hydrolysis is demonstrated by the acid-catalyzed hydrolysis of *p*-benzotoluide-O^{18} (0.98 atom %) in which exchange has been observed (0.93 atom % O^{18} after 25% hydrolysis, $k_h/k_{ex} \sim 5$).

Methyl β-phenylpropionate-*carbonyl*-O^{18} was prepared from β-phenylpropionic acid.[2] The kinetics of the α-chymotrypsin catalyzed hydrolysis were followed by titration to constant *p*H.[9] After 50% hydrolysis, the enzyme was precipitated with trichloroacetic acid and the unreacted ester was isolated, distilled, and pyrolyzed to carbon dioxide[5] which was analyzed mass spectrometrically. The O^{18} content of the unreacted ester and of a blank (excluding enzyme) were identical, indicating no exchange.[10] The lack of oxygen exchange in enzymatic hydrolysis may be attributed to a concerted reaction, to an intermediate involving unsymmetrical oxygens, or to a double displacement involving enzyme.[11]

Oxygen exchange investigations involving the hydrolysis of acid chlorides, esters, amides, and peptides during acidic, basic and enzymatic hydrolysis are in progress in this laboratory.

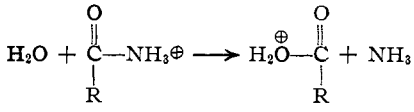
(4) I. Meloche and K. J. Laidler, THIS JOURNAL, **73**, 1712 (1951).

(5) W. E. Doering and E. Dorfman, *ibid.*, **75**, 5595 (1953).

(6) A Consolidated–Nier Model 21-201 Isotope-Ratio Mass Spectrometer was used through the courtesy of Dr. H. Taube, University of Chicago under A.E.C. Contract At(11-1)-92.

(7) Private communication from C. A. Bunton, University College, London, confirms the above results qualitatively.

(8) Compare the mechanism in reference 4.



(9) G. W. Schwert, H. Neurath, S. Kaufman and J. E. Snoke, *J. Biol. Chem.*, **172**, 221 (1948).

(10) S. S. Stein and D. E. Koshland, *Arch. Biochem. Biophys.*, **45**, 467 (1953), reported no oxygen exchange during the hydrolysis of acetylcholine by acetylcholinesterase. D. B. Sprinson and D. Rittenberg, *Nature*, **167**, 484 (1951), and D. G. Doherty and F. J. Vaslow, THIS JOURNAL, **74**, 931 (1952), report oxygen exchange between three amino acids (involving the β-phenylpropionyl structure) and water using α-chymotrypsin as catalyst.

(11) M. L. Barnard and K. J. Laidler, THIS JOURNAL, **74**, 6099 (1952); D. E. Koshland in W. D. McElroy and B. Glass, "Mechanisms of Enzyme Action," Johns Hopkins University Press, Baltimore, Md., 1954.

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RECEIVED MAY 10, 1954

THE YIELDS OF HYDROGEN AND HYDROGEN PEROXIDE IN THE IRRADIATION OF OXYGEN SATURATED WATER WITH COBALT GAMMA-RAYS

Sir:

In the radiation chemistry of water and aqueous solutions, many observations have been interpreted on the basis of the intermediate formation of H, OH, H_2 and H_2O_2 by decomposition of the water. The initial yield of H_2 from oxygen saturated water irradiated with X-rays has been reported[1] to be the same as that from solutions in which the solute prevented secondary reaction of H_2 with OH. This observation was an important consideration in a mechanism proposed[2] to interpret H_2O_2 formation in oxygen saturated water. Studies of H_2O_2 formation in potassium bromide solutions[3] have indicated that this mechanism is not adequate. Previous studies[4] have indicated that the secondary reaction of H_2 with OH occurs readily, and should lead to a low H_2 yield in oxygen saturated water. The H_2 consumed in this secondary reaction should result in the formation of an equivalent amount of H_2O_2. We have therefore measured H_2 and H_2O_2 yields from oxygen saturated water in ampoules having no gas space, and also H_2O_2 yields from water through which oxygen was continuously swept during irradiation in order to remove the H_2 produced.

A cobalt-60 γ-ray source giving a dose rate of about 1.7×10^{20} ev./liter-min. was used for these irradiations. All yields are based upon the ferrous sulfate dosimeter with a yield of 15.6 ferrous ions oxidized per 100 ev.

(1) E. R. Johnson and A. O. Allen, THIS JOURNAL, **74**, 4147 (1952).

(2) A. O. Allen, *Radiation Research*, **1**, 86 (1953).

(3) T. J. Sworski, THIS JOURNAL, in press.

(4) C. J. Hochanadel, *J. Phys. Chem.*, **56**, 587 (1952).