basis in animals. It also reduces K^+ excretion as compared to Cl^- excretion.

Chlorosulfonation and amination of 5-chloro-*o*-acetotoluide (III) yielded 5-chloro-4-sulfamyl-*o*-acetotoluide (IV) (m.p. >265°; *Anal.* Calcd, for $C_9H_{11}N_2O_3SCl$: C, 41.1; H, 4.20; N, 10.6; S, 12.2; Cl, 13.5. Found: C, 41.0; H, 4.31; N, 10.6; S, 11.9; Cl, 13.8) which was oxidized with $KMnO_4$ to N-acetyl-4-chloro-5-sulfamylanthranilic acid (V) (m.p. 254–256°; *Anal.* Calcd, for $C_9H_9N_2O_5SCl$: C, 36.9; H, 3.08; N, 9.57; S, 11.0; Cl, 12.1. Found: C, 37.3; H, 3.60; N, 9.92; S, 10.7; Cl, 12.3). Treatment of V with urethan at 180–190° gave I (R = CH_3) directly (m.p. >320°; *Anal.* Calcd, for $C_9H_8N_3O_3SCl$: C, 39.6; H, 2.93; N, 15.3; S, 11.7; Cl, 13.0. Found: C, 39.3; H, 3.25; N, 15.2; S, 11.5; Cl, 12.9). Alternately, V was hydrolyzed to 4-chloro-5-sulfamylanthranilic acid VI (m.p. 275°; *Anal.* Calcd. for $C_7H_7N_2O_4SCl$: C, 33.5; H, 2.79; N, 11.2; S, 12.8; Cl, 14.2. Found: C, 33.3; H, 2.85; N, 11.1; S, 12.6; Cl, 14.1) which on fusion with formamide at 170–175° gave I (R = H) (m.p. 310–315°; *Anal.* Calcd. for $C_8H_6N_3O_3SCl$: C, 37.0; H, 2.31; N, 16.2; S, 12.3; Cl, 13.7. Found: C, 37.1; H, 2.60; N, 15.8; S, 12.4; Cl, 13.6).

Reduction of the 4(3H)-quinazolinones (I) with $NaBH_4$ in the presence of $AlCl_3$ gave highly active compounds of the 1,2,3,4-tetrahydro-4-quinazolinone structure (II), for example; 7-chloro-6-sulfamyl-1,2,3,4-tetrahydro-4-quinazolinone (II, R = H) (m.p. 256–258°; *Anal.* Calcd. for $C_8H_8N_3O_3SCl$: C, 36.7; H, 3.06; N, 16.1; S, 12.3. Found: C, 37.2; H, 3.30; N, 16.2; S, 12.2) and 7-chloro-2-methyl-6-sulfamyl-1,2,3,4-tetrahydro-4-quinazolinone (II, R = CH_3) (m.p. 275°; *Anal.* Calcd. for $C_9H_{10}O_3N_3SCl$: C, 39.2; H, 3.63; N, 15.3; S, 11.7; Cl, 12.9. Found: C, 39.1; H, 3.60; N, 15.1; S, 11.8; Cl, 12.7). A number of other compounds in this series have been prepared and will be reported at a later date.

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RECEIVED AUGUST 19, 1959

THE MECHANISM OF ACID-CATALYZED AROMATIC HYDROGEN EXCHANGE[1]

Sir:

Because rates of aromatic hydrogen exchange in strong aqueous acid are proportional to Hammett's acidity function, h_0, this reaction is thought to proceed by the A-1 mechanism,[2] which, in this case, demands a reaction sequence of at least three steps. The evidence for all other electrophilic aromatic substitutions, however, demands nothing more complex than a two-step reaction sequence.[3] An analogous mechanism for aromatic hydrogen exchange would involve a slow proton transfer (A-S_E2 reaction), a reaction whose acidity dependence is not known with certainty.[4] Since there is no reason to consider hydrogen fundamentally different from other electrophilic reagents, it seems desirable to re-examine the mechanism of aromatic hydrogen exchange to see whether it is not, in fact, an A-S_E2 reaction.

The A-1 reaction can be distinguished from the A-S_E2 reaction by the form of its acid catalysis: The A-1 reaction is catalyzed only by hydronium ion, whereas the A-S_E2 reaction shows general acid catalysis.[5] This difference cannot be observed with the usual aromatic substrates because these react at appreciable rates only in strong mineral acids. The accelerating influence of a methoxy group on this reaction is, however, very strong, and a prediction based on known partial rate factors[6] leads to the expectation of measurable rates in dilute aqueous acid for molecules bearing a sufficient number of suitably arranged methoxy groups. This prediction is borne out by experiment: 1,3,5-trimethoxybenzene-2-*t* has an exchange half-life of approximately 30 minutes in 0.05 *N* strong acid. The rate of exchange is proportional to the first power of hydronium ion concentration over the range 1.3×10^{-5} to 5×10^{-2} *N*. In buffers, at constant hydronium ion concentration, the rate is also proportional to buffer concentration; Fig. 1 shows that rate changes by a factor of 3.5 with a change of 10 in acetate

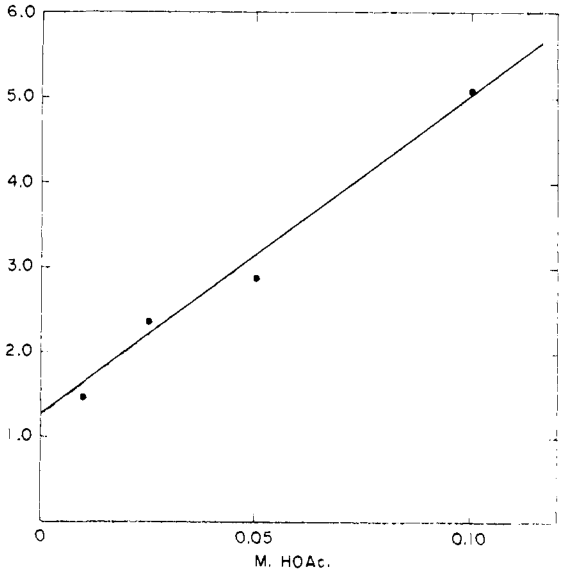

Fig. 1.—Dependence of rate of nuclear hydrogen exchange in 1,3,5-trimethoxybenzene on acetate buffer concentration at constant hydronium ion concentration.

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[1] Work performed under the auspices of the U. S. Atomic Energy Commission.

[2] V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 3609, 3619, 3622 (1955); 1635 (1956).

[3] L. Melander, *Arkiv Kemi*, **2**, 211 (1950); C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 279; P. W. Robertson, *J. Chem. Soc.*, 1267 (1954); P. B. D. de la Mare, T. M. Dunn and J. T. Harvey, *ibid.*, 923 (1957); H. Zollinger, *Experientia*, **12**, 165 (1956); A. J. Kresge, unpublished work on mercuration; A. J. Kresge and D. P. N. Satchell, *Tetrahedron*, in press.

[4] F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 942 (1957); A. J. Kresge and D. P. N. Satchell, *Chem. and Ind.*, 1328 (1958); L. Melander and P. C. Myhre, *Arkiv Kemi*, **13**, 507 (1959).

[5] R. P. Bell, "Acid-Base Catalysis," Oxford University Press, London, 1941, p. 124; A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," John Wiley and Sons, Inc., New York, N. Y., 1953, p. 204; F. A. Long and M. A. Paul, *Chem. Revs.*, **57**, 943 (1957).

[6] D. P. N Satchell, *J. Chem. Soc.*, 3911 (1956).

buffer concentration at constant ionic strength ($\mu = 0.100$, $[HOAc]/[OAc^-] = 1.00$). No exchange was observed in sodium hydroxide solution during the time required for complete exchange in acid at a hydronium ion concentration comparable to the hydroxide ion concentration. Since acetate ion is a much weaker base than hydroxide ion, the dependence of rate on buffer concentration must be the result of catalysis by acetic acid and not by acetate ion. Preliminary results with other acids indicate compliance with the Brönsted relation; α is near 0.5.

This evidence indicates that, in the rate-determining transition state for aromatic hydrogen exchange catalyzed by weak acids, the proton is not yet completely transferred from acid anion to aromatic. This reaction, therefore, must be a slow proton transfer, and the mechanism can be described quite simply as

$$H'Ar + HA \rightleftarrows H'HAr^+ + A^-$$

$$H'HAr^+ + A^- \rightleftarrows HAr + H'A$$

We are grateful to Mr. R. P. Bell, F.R.S., for his interest in this work.

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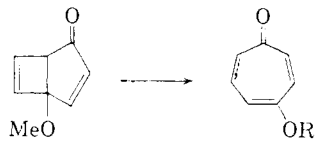
A NOVEL BASE-CATALYZED ISOMERIZATION OF A BICYCLIC SYSTEM TO A TROPONOID SYSTEM

Sir:

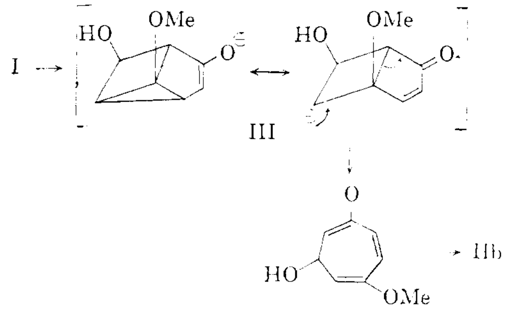
In the course of experiments designed to test the feasibility of anion formation at the bridgehead of photo-γ-tropolone methyl ether (I)[1] (by base-catalyzed exchange of hydrogen for deuterium) it was found that I was rapidly and completely destroyed by 2 *N* aqueous sodium hydroxide with the production of a highly water soluble acidic product. The acidic product was identified quickly as γ-tropolone (IIa) by its characteristic ultraviolet spectra in neutral solution[2] and in 0.1 *N* sodium hydroxide.[2] In dilute base (0.0887 *N* sodium hydroxide) the product initially observed is γ-tropolone methyl ether (IIb, λ_{max} 223 mμ (19,700) and 333 mμ (13,000) in aqueous solution[3] and in 0.1 *N* sodium hydroxide[3]). Brief warming of the basic solution gave γ-tropolone anion[4] which on acidfication gave γ-tropolone. Photo-γ-tropolone methyl ether (I) is quantitatively converted to γ-tropolone methyl ether (IIb) after 110 minutes in 0.0887 *N* sodium hydroxide at 22°. This rapid reaction is in dramatic contrast to the acid-catalyzed opening of I to IIa which does not proceed at a measurable rate in 0.095 *N* sulfuric acid at 22° and which is only 27% complete after 5 hours at 80° in the same acid concentration.[5] The base-catalyzed isomerization of photo-γ-tropolone methyl ether to IIb is without precedent. The facility of this reaction is no less than astonishing. The base-catalyzed reaction fails for dihydro- and tetrahydrophoto-γ-tropolone methyl ether which, however, do undergo acid-catalyzed ring opening.[1] The isomerization of I to IIb can be induced by bases weaker than hydroxide, but the rate is very considerably reduced. Prolonged refluxing of I in 95% ethanol also effects the conversion of I to IIb. Iodide ion does not catalyze the transformation of I to IIb.



I

IIa, R = H
b, R = Me

The transformation of I to IIb is best rationalized on the basis of attack by hydroxide ion on the cyclobutene double bond leading to the anion III which can collapse quite simply to IIb. The Michael-type addition depicted is, to the best of our knowledge, without precedent. Interaction between the non-conjugated double bond and the cyclopentenone system is evident in the ultraviolet spectrum (243 mμ) of I.



Acknowledgment.—The authors wish to acknowledge financial support of this investigation by the Research Corporation through a Frederick Gardner Cottrell grant and by a research grant (CY-4253 PET) from the Cancer Division of the National Institutes of Health, Public Health Service.

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[1] O. L. Chapman and D. J. Pasto, THIS JOURNAL, **80**, 6685 (1958).

[2] In methanol γ-tropolone shows λ_{max} 228 mμ (4.27) and 337 mμ (4.11) and in 0.1 *N* sodium hydroxide 227 mμ (4.30) and 360 mμ (4.33); T. Nozoe, T. Mukai, Y. Ikegami and T. Toda, *Chem. and Ind.*, 66 (1955); R. B. Johns, R. S. Coffey and A. W. Johnson, *ibid.*, 658 (1955); J. Meinwald and O. L. Chapman, THIS JOURNAL, **78**, 4816 (1956).

[3] Authentic γ-tropolone methyl ether shows exactly this spectrum in either water or 0.1 *N* sodium hydroxide.

[4] This was recognized by its characteristic ultraviolet spectrum.[2] The hydrolysis of γ-tropolone methyl ether does not proceed at a significant rate in 0.0887 *N* sodium hydroxide at 22°, but in the same concentration of base at 80° it is quite rapid (unpublished rate measurements of O. L. Chapman and D. J. Pasto).

[5] The hydrolysis of γ-tropolone methyl ether in 0.095 *N* sulfuric acid at 80° is quite rapid and γ-tropolone is thus the observed product (unpublished rate measurements O. L. Chapman and D. J. Pasto).

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COLINEAR BONDS AT THE OXYGEN ATOM

Sir:

Colinear bonds at the oxygen atom were found first in 1935 by G. R. Levi and G. Peyronel[1] in the pyrophosphate anion, and more recently in $H_3Si\text{-}O\text{-}SiH_3$[2] and in the $(Cl_5RuORuCl_5)^{-4}$ an-

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[1] G. R. Levi and G. Peyronel, *Z. Krist.*, **92**, 190 (1935).

[2] R. C. Lord, D. W. Robinson and W. C. Schumb, THIS JOURNAL, **78**, 1327 (1956).