prising. If the reaction is considered to involve simultaneous homolytic electron displacements ρ would be expected to be small. If simultaneous heterolytic displacements were involved the substituent effects at the *m*- and *p*-positions would be large but opposite in sign. Because of this cancellation the over-all effect would be small.[37]

The present data do not rule out the possibility that an intermediate may be involved in the rearrangement.[38] However, there do not seem to be any reasons for suspecting that this is the case. It appears that the data are consistent with a concerted one-step cyclic mechanism. The geometry of the transition state for such a mechanism has been discussed previously.[5,29]

[37] Ambiguities concerning the nature, *i.e.*, homolytic or heterolytic, and direction of electron displacements in concerted cyclic processes have been discussed by C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 597, 637 and 644.

[38] If an intermediate is involved the apparent first-order rate constant is a composite of three rate constants. The substituent and solvent effects can be predicted for the individual steps but not for the composite.

MADISON 6, WISCONSIN

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS, THE STATE UNIVERSITY]

Deuterium Isotope Effects in Some Acid-catalyzed Cyclizations of 2-Deuterio-2′-carboxybiphenyl

BY DONALD B. DENNEY AND PETER P. KLEMCHUK[1]

RECEIVED DECEMBER 23, 1957

2-Deuterio-2′-carboxybiphenyl has been cyclized to fluorenone with sulfuric acid, polyphosphoric acid and anhydrous hydrogen fluoride. The isotope effects for these reactions have been determined. Hydrogen fluoride cyclization exhibited a k_H/k_D of 3.02, whereas the other acid-catalyzed cyclizations had isotope effects in the range 1.13–1.46. The significance of these results is discussed with respect to possible mechanisms for these substitutions.

Melander's[2] pioneering studies on hydrogen isotope effects in aromatic nitration and bromination are now classics. Since his work was published many papers have appeared in which deuterium and tritium isotope effects have been measured during aromatic substitutions.[3] These studies have led in general to a greater understanding of the mechanisms of these reactions and have specifically provided information concerning intermediates in the reaction sequence as well as to whether or not loss of hydrogen is involved in the rate-determining step.

We wish to report at this time some measurements of deuterium isotope effects obtained during the acid-catalyzed cyclization of 2-deuterio-2′-carboxybiphenyl (I) to 4-deuteriofluorenone (Va) and fluorenone (Vb). As it can be seen, the isotope effects being measured here are those which have been termed intramolecular.[4] This system was chosen because it provides a degree of flexibility not easily obtained when intermolecular isotope effects are measured. For example, it has been possible to measure isotope effects of very fast reactions by this technique, since the isotope effect is obtained simply by analyzing the mixture of Va and Vb for deuterium. We also have been able to measure isotope effects in heterogeneous reactions such as the Friedel–Crafts reaction by the use of this technique.[5] The isotope effects which we have observed can be found in Table I. It is apparent that all of the reactions studied exhibit some isotope effect. The range is considerable from a k_H/k_D of 3.02 in anhydrous hydrogen fluoride to 1.13 in 86.54% sulfuric acid. In order to accept these values as being meaningful, it was necessary to prove that exchange was not taking place during the reaction. This sort of analysis has been accomplished for the sulfuric acid-catalyzed reaction. At various time intervals aliquots of the reaction mixture were removed and the fluorenone was isolated and analyzed for deuterium. All of the samples of fluorenone had the same deuterium content. If exchange was taking place with either the starting acid or the product, fluorenone, then there would be a steady decrease in the deuterium content of the fluorenone. Since this was not observed one knows that the isotope effects ob-

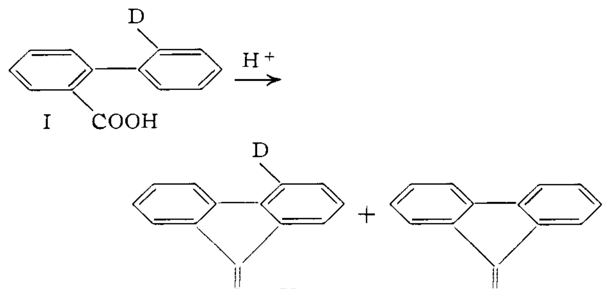


TABLE I

Catalyst	Time, min.	Temp., °C.	k_H/k_D
Concd. sulfuric acid	2–60	1	1.31 ± 0.03
96.63% sulfuric acid	15	1	1.34 ± .03
86.54% sulfuric acid	90	1	1.13 ± .02
Polyphosphoric acid	15	95	1.31 ± .03
Polyphosphoric acid	24 hr.	25	1.46 ± .04
Hydrogen fluoride	30	19	3.02 ± .14

---

[1] Alfred P. Sloan Fellow in Chemistry, 1956–1957.

[2] L. Melander, *Arkiv. Kemi*, **2**, 213 (1950).

[3] (a) W. M. Lauer and W. E. Noland, THIS JOURNAL, **75**, 3689 (1953); (b) T. G. Bonner, F. Bowyer and G. Williams, *J. Chem. Soc.*, 2650 (1953); (c) P. B. D. de la Mare, T. M. Dunn and J. T. Harvey, *ibid.*, 923 (1957); (d) H. Zollinger, *Helv. Chim. Acta*, **38**, 1597 (1955); (e) U. Berglund-Larsson and L. Melander, *Arkiv. Kemi*, **6**, 21 (1953); (f) T. G. Bonner and J. M. Wilkins, *J. Chem. Soc.*, 2358 (1955); (g) E. Grovenstein, Jr., and D. C. Kilby, THIS JOURNAL, **79**, 2972 (1957).

[4] K. B. Wiberg, *Chem. Revs.*, **55**, 713 (1955).

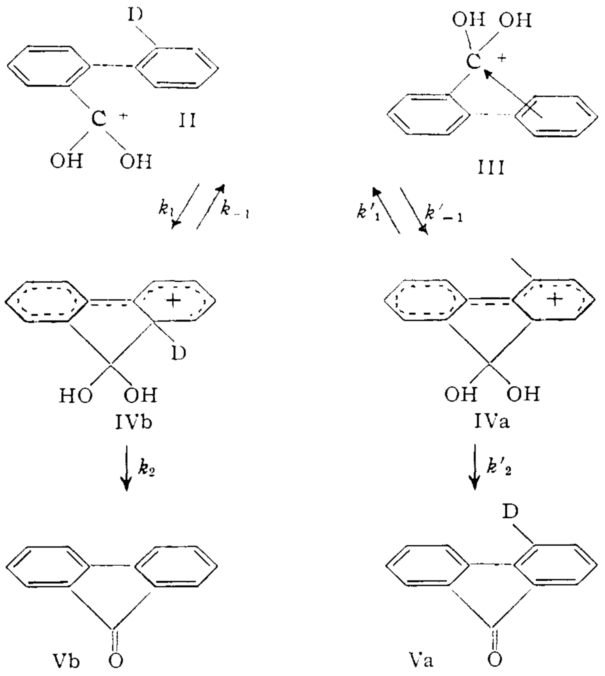
[5] Unpublished work.

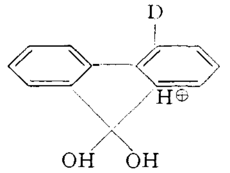
served are the true ones. The other reactions were not scrutinized by this technique; however, it seems reasonable to assume that exchange is not affecting the observed isotope effects.

In his studies of the bromination and nitration of benzene Melander[2] found a $k_H/k_T = 1$. This was interpreted in terms of a slow rate-determining formation of a σ-complex between benzene and the substituting reagent. It was further postulated that the σ-complex loses a proton or triton in a rapid step to give the product. More recently Hammond[6] has pointed out that the same results would obtain if there was a one-step mechanism in which a proton or triton was lost as the electrophilic reagent began bond formation with the carbon. This mechanism requires that there must be very little stretching of the carbon–hydrogen bond in the transition state, since stretching would lead to an observable isotope effect.

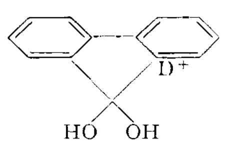
It is of interest to compare the results of this study with these two mechanisms. If the one-step mechanism is operating then a large isotope effect means that there is considerable carbon–hydrogen bond breaking in the rate-controlling step. In this case then the hydrogen fluoride-catalyzed reaction would lead to a transition state in which there is more carbon–hydrogen bond breaking than in the sulfuric and polyphosphoric acid-catalyzed reactions, or putting it another way the transition state in the hydrogen fluoride reaction would be closer to products than those from sulfuric and polyphosphoric acids. A direct consequence of this interpretation is that the hydrogen fluoride-catalyzed reaction should be a slower process than the other reactions. Hammond[6] has discussed this reasoning in great detail. Our observations are that if anything, the hydrogen fluoride-catalyzed reaction is faster than the others. It seems therefore that the one-step mechanism is not particularly acceptable and is inconsistent with the observed data.

It is possible that there is a difference in the mechanism of the hydrogen fluoride reaction and the other acid-catalyzed reactions. If this is the case then the hydrogen fluoride catalyzed reaction must be proceeding by the one-step mechanism and the others by the two-step mechanism. Although a duality of mechanism cannot be ruled out, it seems very improbable and a more reasonable explanation should be sought.





VIa



VIb

If one considers that these reactions proceed by initial formation of II from I, II can then either go directly to IVa and IVb or it could react first to give the π-complex III which would then give rise to IVa and IVb. This work does not distinguish between these possibilities. The conversion of either II or III to IVa or IVb cannot involve a primary isotope effect but it could give rise to a secondary isotope effect. It is difficult to assess the magnitude of this effect; indeed, it is difficult to decide which is larger, k_1 or k_1'. If one considers hyperconjugative structures such as VIa or VIb one would predict that VIa would be more stable than VIb and therefore if this effect can be translated into a stabilization of the transition state then k_1' should be larger than k_1. If this were the only factor affecting the observed isotope effect then k_H/k_D would be greater than one. On the other hand, if the inductive effect of deuterium is greater than that of hydrogen as has been suggested by Halevi[7] then IVb should form more rapidly than IVa. Another factor which could lead to a secondary isotope effect is that the carbon–hydrogen bond on the carbon being attacked is changing from a sp^2-s σ-bond to a sp^3-s σ-bond. Streitwieser[8] has observed in the solvolysis of cyclopentyl-1-D tosylate that the isotope effect k_H/k_D is 1.16. The bond change in their case is opposite to the one reported here, so such an effect if operating in these cases should give a $k_H/k_D < 1.0$. In any event one would not expect the secondary isotope effect to be markedly affected by a change in catalyst. One could therefore assign a tentative maximum to the possible secondary isotope effect of *ca.* 1.13. This figure was derived from the lowest isotope effect observed, *i.e.*, when 86% sulfuric acid was the catalyst. This value is probably larger than the true value, since if secondary isotope effects are of importance in electrophilic substitutions one would expect that they would have appeared in the other experiments.[3] Indeed Swain, *et al.*,[9] have searched for such effects and have

---

(6) G. S. Hammond, THIS JOURNAL, **77**, 334 (1955).

(7) E. A. Halevi, *Tetrahedron*, **1**, 174 (1957).

(8) A. Streitwieser and R. C. Fahey, *Chemistry & Industry*, 1417 (1957).

(9) C. G. Swain, J. E. C. Knee and A. J. Kresge, THIS JOURNAL, **79**, 505 (1957).

found them to be very small; $k_H/k_D = 1.002$ for the nitration of toluene as compared to phenyl-CD_3. Admittedly these experiments were somewhat different from those reported here; however, the effect should operate in the same manner. We will proceed with our discussion on the basis that the observed isotope effects contain a small contribution from secondary isotope effects.

The observed isotope effects can arise quite easily if k_2 and k_2' are not equal; *i.e.*, $k_2' > k_2$ and k_{-1} and k_{-1}' are large enough so that return from IVb and IVa to a symmetrical intermediate like II or III can occur.

It is possible to derive an expression for the isotope effect in terms of the rate constants for the formation of the intermediates from the reactant and for the conversion of the intermediates to reactant or to products.[10] Unfortunately since we do not know the magnitude of any of these constants, our discussion must remain qualitative.

If the two-step mechanism is operating, then the hydrogen fluoride-catalyzed reaction must have considerably different rate constants from the other reactions. We feel that this is the case with a larger difference between k_2 and k_2' than in the other acid-catalyzed reactions. The reason for suggesting this is that it is well known that hydrogen fluoride forms σ-complexes with aromatic hydrocarbons quite easily.[11] This suggests that in hydrogen fluoride IVa and IVb may be more stable with respect to hydrogen loss than in the other acids. If this is the case it will mean that in going from these two intermediates the structure of the transition state will shift toward the products Va and Vb; this will necessarily lead to a larger difference in k_2 and k_2' since there is more carbon–hydrogen bond stretching in such a transition state. There may be of course other factors which will modify the isotope effect in this medium; however, this would appear to be the main one. This suggestion is amplified by the effect observed on adding water to sulfuric acid; the over-all rate becomes considerably smaller as would be expected. At the same time the isotope effect drops from 1.34 to 1.13. This change may arise because it is easier to lose a hydrogen in 86% sulfuric acid than in 96% sulfuric acid. This would tend to bring k_2 and k_2' closer together since there would be less bond stretching in the transition state leading to products.

The effect of increased temperature found with the polyphosphoric acid cyclizations is normal and in agreement with these postulates.

It is not to be construed from the data reported here that all intramolecular acid-catalyzed cyclizations will have similar isotope effects, since different structural factors will undoubtedly affect the pertinent rate constants. For example, the cyclization of I is somewhat unique in that one is forming a biphenyl which gains some resonance energy which should make k_2 and k_2' large. On the other hand, in order to gain this resonance energy one must create a planar system and in order to do this energy must be put into the system to overcome the steric repulsions of the two ortho hydrogens. The net effect is not known; but if the structure of biphenyl[12] is taken as a model then it would seem that to overcome the non-bonded interactions requires more energy than is gained by the creation of the planar system. If this is true one would observe larger isotope effects for this system than most others.

Experimental

2-Bromo-2'-deuterobiphenyl.—2,2'-Dibromobiphenyl[13] (124.8 g., 0.400 mole) dissolved in 1600 ml. of dry ether (distilled from ethylmagnesium bromide) was allowed to react under a dry nitrogen atmosphere at −30° for five minutes with 0.400 mole of *n*-butyllithium in ether. Deuterium oxide (99.5%, 25 g., 1.40 mole) was added in about 10 sec. with vigorous stirring to the reaction mixture which was held at −30°. The stirred reaction mixture was allowed to warm to 0° and then treated with 300 ml. of water. The phases were separated and the ether phase was extracted with three 100-ml. portions of water. The ether solution was dried over magnesium sulfate and then concentrated to give 95.9 g. of residue. This material was distilled through a short column to separate unreacted 2,2'-dibromobiphenyl from 2,2'-dideuterobiphenyl and 2-bromo-2'-deuterobiphenyl. The mixture of these two compounds was fractionated through a 36-inch spinning-band column to yield one main fraction, 40.33 g. (43.1%), b.p. 147.5–148.5° (10 mm.), $n^{20}D$ 1.6283.

The infrared absorption band at *ca.* 700 cm.$^{-1}$ which is characteristic of monosubstituted benzenes was absent completely in the infrared spectrum of the 2-bromo-2'-deuterobiphenyl. The spectrum is compatible with an *o*-disubstituted benzene derivative. The position of the deuterium atom in the molecule is confirmed.

Anal. Calcd. for $C_{12}H_8DBr$: Br, 34.14. Found: Br, 32.48.

The analytical results indicated that this product was 95.3% pure; this was arrived at by assuming that 2,2'-dideuterobiphenyl was the major impurity. The product was not further purified, since the contaminant was removed easily in the next step.

2-Carboxy-2'-deuterobiphenyl (I).—2-Bromo-2'-deuterobiphenyl (35.1 g., 0.150 mole) in 425 ml. of ether (distilled from ethylmagnesium bromide) was allowed to react under a dry nitrogen atmosphere with 101 ml. of a *n*-butyllithium solution, which contained 0.150 mole of *n*-butyllithium, at −30 to −35° for seven minutes. The resulting thin slurry was poured rapidly onto about 450 g. of powdered Dry Ice suspended in sufficient dry ether to permit stirring. The reaction mixture was allowed to warm to 25° and then was hydrolyzed with dilute hydrochloric acid. The ether was extracted with 470 ml. of dilute sodium carbonate solution. The basic extract was acidified with 6 *N* hydrochloric acid. The product was isolated by filtration, washed with water and dried *in vacuo* over sulfuric acid. The yield of I was 27.1 g. (90.6%), m.p. 112–113°. The acid was recrystallized from 40% aqueous ethanol and then sublimed, bath 115–120° (0.05 mm.). The yield of I after this treatment was 25.1 g. (84.0%), m.p. 112–113.0° (lit.[14,15] 111°; 113.5°–114.5°). A small sample of this material was recrystallized from acetone–hexane (1:9), m.p. 112.5–114.0°. This material was analyzed for deuterium; found: 9.90 ± 0.06, 9.79 ± 0.06, 9.89 ± 0.06 atom % D in the acid. The average atom % D was 9.86 ± 0.06 and the mole fraction of labeled acid was 0.986 ± 0.006.

Cyclization of I with Concentrated Sulfuric Acid.—To 100 ml. of concentrated sulfuric acid, reagent grade, at 1° was added with stirring 2.00 g. of I. Samples of about 25 ml. were removed at intervals, poured onto ice and extracted with ether. The ether solution, after extraction with sodium carbonate solution and drying over magnesium sulfate, was evaporated to dryness to afford fluorenone.

---

[10] H. Zollinger, *Helv. Chim. Acta*, **38**, 1597 (1955).

[11] M. Kilpatrick and F. E. Luborsky, THIS JOURNAL, **75**, 577 (1953).

[12] G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N.Y., 1955, p. 157, discusses the structure of biphenyl in considerable detail and comes to the conclusion that it is not planar, but has a moderate departure from coplanarity.

[13] H. W. Schwechten, *Ber.*, **65**, 1605 (1932).

[14] K. Mieleitner, *Z. Kryst. Min.*, **55**, 61 (1915).

[15] M. Weger and K. Doring, *Ber.*, **36**, 881 (1903).

The sodium carbonate solution was acidified to yield recovered acid. The samples of fluorenone were recrystallized from hexane (0.5 ml./0.01 g.) and sublimed. They all melted at 84.0–85.0° (lit.[16] 83.0–83.5°).

Sample	Time, sec.	Fluorenone, g.	Atom % D in fluorenone
A	135	0.020	7.04 ± 0.04
B	435	.036	6.97 ± .05
C	900	.043	7.00 ± .04; 7.01 ± 0.05
D	3610	.048	7.04 ± .04; 6.99 ± 0.05

The average deuterium content of the fluorenone was found to be 6.99 ± 0.05 atom % D, after a correction for the average molecular weight was made.

In a similar manner Compound I was cyclized in concentrated sulfuric acid, which was shown to be 96.63% sulfuric acid by analysis. The atom % D in the sample of fluorenone obtained was 7.09 ± 0.04 and 7.00 ± 0.04.

Cyclization of I with 86.54% Sulfuric Acid.—Compound I was allowed to react for 90 minutes at 1° in 86.54% sulfuric acid. The fluorenone was isolated and purified as described above, m.p. 82.0–83.0°; found: 6.58 ± 0.04, 6.52 ± 0.04 atom % D.

Cyclization of I with Polyphosphoric Acid.—Polyphosphoric acid was prepared by the reaction of 9.5 ml. of 85% phosphoric acid with 14.8 g. of phosphorus pentoxide. To the polyphosphoric acid at 33° was added 0.50 g. of I. The reaction mixture was stirred for 24 hours at 33°, and then quenched by the addition of ice. The aqueous solution was extracted with ether. The ether was washed with water, 10% sodium carbonate solution and water. The ether was dried and evaporated to afford fluorenone which was recrystallized from hexane, yield 0.330 g., m.p. 83.5–84.5°. The fluorenone was sublimed and analyzed for deuterium; found: 7.32 ± 0.05, 7.30 ± 0.05 atom % D.

The same reaction was conducted at 95°. The fluorenone, m.p. 83.5–84.5°, was purified as before and analyzed for deuterium. Found: 7.03 ± 0.04, 6.95 ± 0.04 atom % D.

Cyclization of I with Anhydrous Hydrogen Fluoride.—To 15 g. of anhydrous hydrogen fluoride 0.50 g. of I was added. The solution was allowed to stand for 30 minutes, and then the hydrogen fluoride was removed in a stream of nitrogen. The dark red residue was treated with water and 10% sodium carbonate was added until a *p*H of 8 was attained. Ether was added and the phases were separated. The fluorenone was isolated from the ether and purified as described above. It had m.p. 83.5–84.5°.

Anal. Found: D, 9.24 ± 0.06, 9.26 ± 0.07.

Method of Analysis and Calculations.—The analyses for deuterium were performed according to the procedure of Trenner and his co-workers.[17] A Perkin–Elmer model 21, double beam, recording infrared spectrophotometer with sodium chloride optics was used for the analyses.

An initial calculation of the atom % D was made from the combustion data. This was then corrected by using an average molecular weight, since the samples which were analyzed consisted of a mixture of deuterated and undeuterated compounds. This correction lowered the atom % D of the fluorenones by 0.01–0.02 atom % D. The isotope effects were calculated from these corrected values.

The largest error in these analyses appears to be in the measurement of the optical densities of the water samples. The error in the optical density was calculated by the equation

$$\text{error} = s_1 = \sqrt{\frac{\Sigma d^2}{n-1}}$$

where s_1 = standard error, d = deviation of a value from the mean and n = number of values averaged to obtain the mean.

The error in the atom % D of the water was calculated from the equation

$$\text{error} = 5\sqrt{(s_1)^2 + (s_2)^2} = \Delta W$$

where s_1 = standard error calculated above and s_2 = standard error of a known sample of approximately the same deuterium content.

The error in the atom % D of the sample was calculated as

$$\text{error} = \Delta S = \Delta W/A$$

where

$$A = \frac{\dfrac{\text{wt. of sample}}{\text{mol. wt. of sample}}\,N}{\dfrac{\text{wt. of sample}}{\text{mol. wt. of sample}}\,N + \dfrac{\text{wt. of diluent}}{\text{mol. wt. of diluent}}\,N^1}$$

N and N^1 are the total number of hydrogens in the sample and diluent, respectively.

NEW BRUNSWICK, N. J.

---

[16] E. H. Huntress, E. B. Hershberg and I. S. Cliff, THIS JOURNAL, **53**, 2720 (1931).

[17] N. R. Trenner, B. Arison and R. W. Walker, *Appl. Spectros.*, **7**, No. 4 (1953).