

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

Deuterium Isotope Effects in Some Intramolecular Aromatic Substitutions

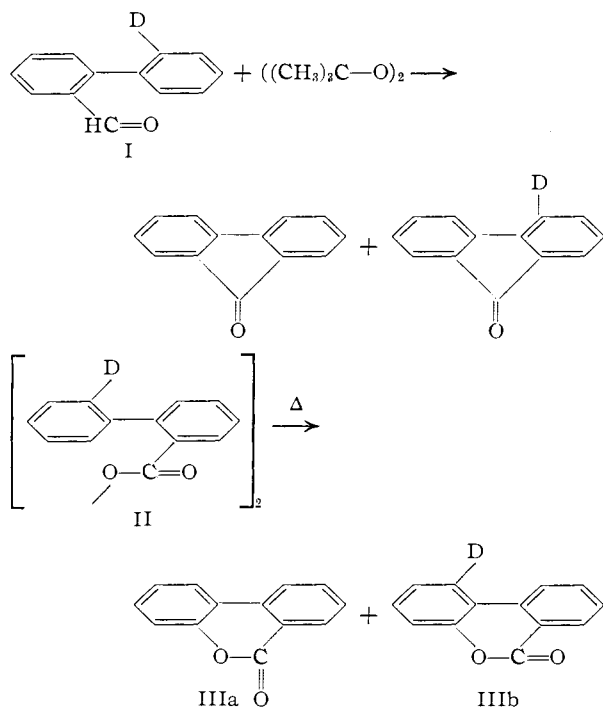
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2-(2-Deuteriophenyl)-benzaldehyde (I) has been allowed to react with di-*t*-butyl peroxide to give fluorenone. An isotope effect, k_H/k_D , of 1.38 was observed for this reaction. 2-(2-Deuteriophenyl)-benzoyl peroxide (II) has been cyclized by heating to give the lactone of 2-carboxy-2'-hydroxybiphenyl (IIIa,b). An isotope effect of 1.32 for k_H/k_D was found for this reaction. Irradiation of 2-(2-deuteriophenyl)-phenyldiazomethane (VI) gave fluorene. The isotope effect for this cyclization was found to be 1.12.

In another paper² we have reported some deuterium isotope effects obtained during the acid-catalyzed cyclization of 2-deuterio-2'-carboxybiphenyl. It seemed of interest to extend our studies to some other types of reactions. In this paper we wish to report results obtained from two free-radical substitutions³ and a carbene substitution.

When 2-(2-deuteriophenyl)-benzaldehyde (I) was heated with di-*t*-butyl peroxide for thirty hours it cyclized to a mixture of fluorenone and deuteriofluorenone.



Deuterium analysis of this mixture indicated an isotope effect, k_H/k_D , of 1.38 for this reaction.

When 2-(2-deuteriophenyl)-benzoyl peroxide (II) was heated in carbon tetrachloride, according to the procedure of Kenner, *et al.*,⁴ it gave a mixture of the lactones, IIIa and IIIb. Analysis of this

(1) Alfred P. Sloan Fellow in Chemistry, 1956-1957.

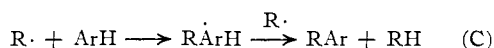
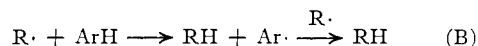
(2) D. B. Denney and P. P. Klemchuk, *THIS JOURNAL*, **80**, 3285 (1958).

(3) Recently it has been reported, C. C. Price and R. J. Convery, *ibid.*, **79**, 2941 (1957), that no isotope effect was observed during the phenylation of a mixture of 2,4-dinitrobenzene and 2,4-dinitrotrithiobenzene. A later communication, C. C. Price, *ibid.*, **79**, 6579 (1957), refutes their earlier findings and they now report that, "Because of the low conversion, no conclusions concerning an isotope effect can be made."

(4) G. W. Kenner, M. A. Murray and C. M. B. Tylor, *Tetrahedron*, **1**, 259 (1957).

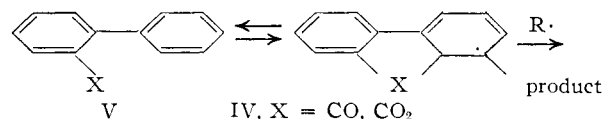
mixture indicated an isotope effect of 1.32 for the lactone formation.

Recently Walling⁵ has discussed free radical substitutions in aromatic systems. He has considered three mechanisms A, B and C. On the basis



of the energies involved for these paths and the products obtained, he has considered mechanisms A and B as being very unlikely and has suggested that path C is the most reasonable. Our results are in agreement with his interpretation since both A and B would most probably lead to rather large isotope effects in the cases reported here. It is not necessarily true that A and B would always show large isotope effects since this will depend on the amount of C-H bond breaking in the transition states. With relatively unreactive radicals such as the carbonyl and carboxyl radicals one predicts that the C-H bonds will be significantly weakened in the transition states and therefore a large isotope effect should be found. With very reactive radicals this might not be the case.

Mechanism C can be used to explain the rather small isotope effects found in this work. If in the cyclization of I and II an intermediate IV is



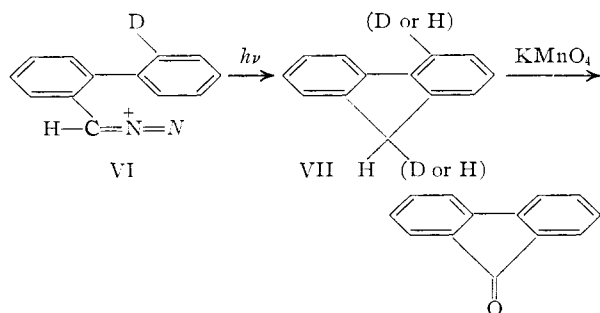
formed and this can return to V or a π -complex derived from V at a rate which can compete with the conversion of IV to products, then one will observe an isotope effect, providing there is an isotope effect in the conversion of IV to the products.⁶ The mechanism by which IV is converted to products is not completely understood; however, one would expect an isotope effect for this process whatever it may be. There seems to be no compelling reason for not accepting an equilibrium between IV and V or the π -complex in these cases since both the carbonyl and carboxyl radicals are relatively stable species. A less stable radical might not return and therefore one would not observe an isotope effect even though the mechanism remained the same.

(5) C. Walling, "Free Radicals in Solution," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 482.

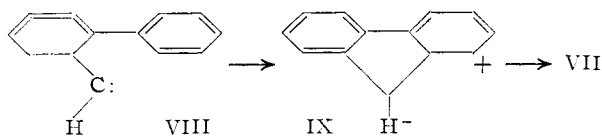
(6) H. Zollinger, *Helv. Chim. Acta*, **38**, 1597 (1955), has derived the kinetic expressions for the entirely analogous case of electrophilic substitution.

There is another way in which these isotope effects could arise; in the formation of IV if there is any radical hyperconjugation of the carbon-hydrogen bond at the carbon being attacked then k_H/k_D will be greater than one. In our first paper we discussed this factor in detail. In these cases it seems somewhat unreasonable to attribute the isotope effects observed to radical hyperconjugation; however, it cannot be eliminated as a possibility.

When 2-(2-deuterophenyl)-phenyldiazomethane (VI) was irradiated it gave a 69% yield of fluorene (VII).



In order to determine the isotope effect for this reaction it was necessary to oxidize the fluorene to fluorenone, which was then analyzed for deuterium; using this procedure k_H/k_D was found to be 1.12. A reasonable mechanism for this reaction involves formation of the carbene VIII, which then reacts to



give the zwitterion IX; IX is converted to the mixture of fluorenes by migration of hydrogen. In this case the isotope effect could arise by processes similar to those outlined for the free radical reactions. In view of the complexity of this reaction and the small amount of information available on its mechanism, it is felt that further discussion at this time would be mere speculation.

Experimental⁷

2-(2-Deuterophenyl)-benzaldehyde (I).—2-(2-Deuterophenyl)-bromobenzene² (6.00 g., 0.00256 mole) dissolved in 80 ml. of dry ether was allowed to react at -30° for 7 min. with 0.00256 mole of *n*-butyllithium in ether. *N*-Methylformanilide (3.80 g., 0.0028 mole) in 5 ml. of ether was added over 5 min. at -30° . The solution was allowed to come to -12° and then was poured onto a mixture of ice and sulfuric acid. The ether solution was washed with three 10-ml. portions of water. The aqueous extracts were washed with 25 ml. of ether, and the combined ether extracts were dried over magnesium sulfate. The ether was evaporated to yield 4.66 g. of crude product. This material was dissolved in hexane and chromatographed on 150 g. of silica gel. The aldehyde was eluted with hexane-benzene (1:2) to give 3.91 g. (83.5%) of product $n_D^{20} 1.6206$. The infrared spectrum of this material was identical to that of a known unlabeled sample except that the 700 cm.^{-1} band of the latter was missing.

Oxidation of I.—Compound I (0.309 g., 0.00169 mole) dissolved in 30 ml. of acetone was oxidized for 22 hr. with a solution of 0.320 g. of potassium permanganate in 13 ml. of water. The reaction mixture was filtered through Celite and

made basic with 10% sodium carbonate solution. The aqueous solution was concentrated to remove acetone treated with Norite A and acidified to yield 0.274 g. (81.4%) of acid, m.p. $110.0\text{--}113.5^\circ$. The acid was purified by crystallization from acetone-hexane (1:9) to give 0.252 g., m.p. $112.5\text{--}114.0^\circ$ (lit.⁸ $113.5\text{--}114.5^\circ$). The acid was analyzed for deuterium; found: 9.88 ± 0.05 , 9.73 ± 0.05 atom % D.

Cyclization of I.—Compound I (1.83 g., 0.010 mole) was heated under nitrogen with 1.00 ml. of di-*t*-butyl peroxide in an oil-bath at $143 \pm 3^\circ$. After 17 hr. an additional 1.00 ml. of peroxide was added and the reaction was continued for 13 hr. The solution was concentrated *in vacuo* and then evaporatively distilled to yield 1.33 g. of a clear yellow liquid. The distillate was chromatographed to give 0.89 g. of recovered aldehyde and 0.37 g. of fluorenone. The fluorenone was purified by crystallization from hexane, m.p. $83.5\text{--}85.0^\circ$.

Anal. Found: D, 7.08 ± 0.04 , 7.21 ± 0.04 , 7.13 ± 0.04 .

A portion of the recovered aldehyde was oxidized to the corresponding acid, m.p. $112.0\text{--}114.0^\circ$. This material was analyzed for deuterium. This result shows quite clearly that no exchange took place during this reaction.

Anal. Found: D, 9.78 ± 0.06 , 9.86 ± 0.06 .

Cyclization of 2-(2-Deuterophenyl)-benzoyl Peroxide.—The procedure of Kenner, *et al.*,³ was followed. From 1.00 g. of 2-(2'-deuterophenyl)-benzoic acid there was obtained 0.788 g. of peroxide, m.p. $107\text{--}109^\circ$ (lit.³ $107\text{--}108^\circ$). This material (0.548 g.) was converted to 0.067 g. of lactone, m.p. $88\text{--}91^\circ$, by Kenner's method. After further purification by crystallization from hexane there was obtained 0.025 g. of lactone, m.p. $92.0\text{--}94.0^\circ$ (lit.^{3,9} $86\text{--}88^\circ$, 92.5°). This material was analyzed for deuterium; found: 7.01 ± 0.04 atom % D.

Preparation and Cyclization of 2-(2-Deuterophenyl)-phenyldiazomethane.—2-(2-Deuterophenyl)-benzaldehyde (0.910 g., 0.00496 mole) was refluxed for one hour with 0.590 g. (0.010 mole) of 85% aqueous hydrazine hydrate in 10 ml. of absolute ethanol. The solution was evaporated *in vacuo* to yield an oil which was dissolved in 25 ml. of ether. The ether was washed with water and dried over magnesium sulfate. The stirred ether solution of the hydrazone was treated with 0.5 g. of magnesium sulfate and 1.40 g. of silver oxide. After 25 min. the mixture was filtered through Celite and the bright orange-red ether solution of 2-(2-deuterophenyl)-phenyldiazomethane was irradiated with a General Electric sunlamp for 24 hours. The light yellow solution was evaporated to dryness to yield 0.82 g. of yellowish crystalline solid. This material was chromatographed to yield 0.57 g. (68.6% based on aldehyde) of fluorene, m.p. $115.0\text{--}115.5^\circ$. This material was crystallized from ethanol to yield 0.54 g., m.p. and mixed m.p. with an authentic sample of fluorene $115.0\text{--}116.0^\circ$. This material was analyzed for deuterium; found: 9.84 ± 0.07 , 9.73 ± 0.05 atom % D. The average atom % D in the fluorene, 9.79 ± 0.07 , corresponds to a mole fraction of 0.979 ± 0.07 of labeled material. This compares favorably with that of the starting aldehyde, 0.984 ± 0.05 .

Conversion of Labeled Fluorene to Labeled Fluorenone.—To a solution of 0.20 g. (0.00120 mole) of labeled fluorene in 20 ml. of pyridine was added a solution of 0.320 g. (0.00202 mole) of potassium permanganate in 12 ml. of water. The solution was allowed to remain at room temperature for 23 hours. The solution was then filtered and concentrated *in vacuo*. Water, 20 ml., was added and the solution was concentrated to about 5 ml. The concentrate was diluted with 20 ml. of water and acidified with dilute sulfuric acid. A dilute solution of ferrous sulfate was added until the permanganate color was discharged.

The resulting aqueous slurry of fluorenone was extracted with ether. The ether solution was dried over magnesium sulfate and then evaporated to yield 0.202 g. (93.4%) of fluorenone, m.p. $80.0\text{--}83.5^\circ$. The fluorenone was recrystallized from hexane and sublimed, m.p. $83.5\text{--}84.5^\circ$.

Anal. Found: D, 6.50 ± 0.05 , 6.53 ± 0.06 , 6.52 ± 0.04 .

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(7) The method of analysis and the calculation of errors has been discussed already (see ref. 2).

(8) M. Weger and K. Doring, *Ber.*, **36**, 881 (1903).

(9) C. Graebe and P. Schestakow, *Ann.*, **384**, 316 (1895).