

[CONTRIBUTION NO. 1205 FROM THE DEPARTMENT OF CHEMISTRY OF INDIANA UNIVERSITY, BLOOMINGTON, IND.]

## The Effects of Deuterium Substitution on the Rates of Organic Reactions.

### X. The Solvolyses of 4-Chloro-4-methyl-2-pentyne and Its Deuterated Analogs

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RECEIVED FEBRUARY 24, 1964

4-Chloro-4-methyl-2-pentyne (Ia) and its 1,1,1- $d_3$  (Ib) and 4-methyl- $d_4$ -5,5,5- $d_3$  (Ic) analogs have been synthesized and their solvolysis rates measured at 25° in several aqueous solvent mixtures. The rate retardation due to deuterium in compound Ib is a new example of transmission of an isotope effect across an unsaturated linkage. The  $k_H/k_D$  for Ib is about 1.09 and is not appreciably solvent dependent. Compound Ic shows an isotope effect,  $k_H/k_D$ , of 1.66. These results conform to predictions based on hyperconjugation as the governing mode of interaction between isotopic and reaction centers. The contribution to the rate effect of  $\beta$ -deuterium substitution from relief of steric strain is estimated to be at most only a small fraction of the total observed.

#### Introduction

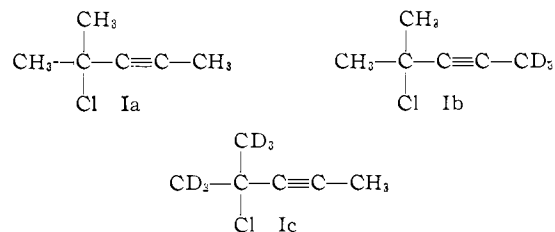
The transmission of isotope effects through unsaturated linkages was first reported by Lewis and Coppinger,<sup>1</sup> who found that  $k_H/k_D$  for *p*-methyl- $d_3$ - $\alpha$ -phenylethyl chloride solvolysis in acetic acid was 1.10. Subsequently, Lewis, Johnson, and Coppinger<sup>2</sup> reported it to be only 1.01 for solvolysis in aqueous acetone. Meanwhile, Shiner and Verbanic<sup>3</sup> had reported  $k_H/k_D$  for *p*-methyl- $d_3$ -benzhydryl chloride solvolysis to vary from 1.06 in "80%" to 1.02 in "66.7%" aqueous acetone.

These authors interpreted their results in terms of hyperconjugation, which had been invoked by Lewis and Boozer<sup>4</sup> and by Shiner<sup>5</sup> as an explanation of solvolysis rate retardations due to  $\beta$ -deuterium substitution. The aromatic system was thought to be able to transmit the electron delocalization from the C-H bonds of the *p*-methyl group to the carbonium ion center, thus accounting for the observed rate retardations due to deuterium substitution rather distant from the reaction center.

In the classic work of Bartlett and Rosen<sup>6</sup> the triple bond was first used to distinguish between steric and electronic effects on reactivity. There have been no reports dealing with the transmission of isotope effects through a triple bond, but Burawoy and Spinner<sup>7</sup> showed that the solvolysis of 3-chloro-3-methyl-1-butyne was accelerated about 2000-fold by a 1-methyl substituent. This large substituent effect should be associated with the ability of the methyl group to release electrons by hyperconjugation and demonstrates that the triple bond is a very efficient conductor of electronic effects. By comparison, a *p*-methyl group accelerates the solvolysis of  $\alpha$ -phenylethyl chloride by only about 60-fold and an  $\alpha$ -methyl group accelerates the solvolysis of isopropyl chloride by an estimated factor of 4000. Burawoy and Spinner further found that a 1-*t*-butyl group accelerated the solvolysis of 3-chloro-3-methyl-1-butyne less than a 1-methyl group. Such "Baker-Nathan" reactivity orders have also been attributed to large hyperconjugation interaction.

It thus appeared that despite the remoteness of isotopic substitution from the reaction center, a reason-

ably large isotope effect should be observed in the solvolysis of 4-chloro-4-methyl-1-pentyne-1,1,1- $d_3$  (Ib), if hyperconjugation were an important mode of interaction in causing the large effects of  $\beta$ -deuterium substitution on solvolysis reactions. In addition, the solvolysis rate of compound Ic would be useful to give a direct comparison between "remote" and



$\beta$ -deuterium substitution in the same reaction. The syntheses and solvolysis rate measurements of these compounds were accordingly undertaken.

#### Experimental

**2-Methyl-3-butyne-2-ol** was kindly supplied by the Air Reduction Co.

**3-Methoxy-3-methyl-1-butyne.**—The three necks of a 2-l., round-bottom flask were fitted with a Trubore stirrer, a condenser cooled with a Dry Ice-acetone bath, and a gas inlet tube. About 1200 ml. of ammonia was condensed into the flask and about 500 mg. of ferric nitrate nonahydrate was added. Clean sodium cubes (23.5 g., 1.02 g.-atoms) were added during 2 hr. The mixture was then stirred for about 45 min. The gas inlet tube was replaced by a dropping funnel, and 2-methyl-3-butyne-2-ol (83.7 g., 0.995 mole) was added dropwise over a period of 1 hr. Methyl iodide (143.8 g., 1.01 moles) was added dropwise during 75 min. The mixture was allowed to stir for an hour afterward. The dropping funnel was replaced by a bent-necked flask containing 62.3 g. (1.16 moles) of ammonium chloride. The solid was added during 1 hr., and the mixture was stirred for 0.5 hr. after the addition was complete. The stirrer and condenser were replaced by a 13 × 470 mm. vacuum-jacketed Vigreux column fitted with a distilling head cooled with a Dry Ice-acetone bath. The liquid ammonia was evaporated by allowing it to distil through the column. After removal of the ammonia, the reaction mixture was extracted with twelve 50-ml. portions of ether. A few grams of sodium carbonate was added to the ether solution, which was subsequently distilled through a column packed with stainless steel helices. The product was collected over a range of 77–79°; yield 46.9 g. (0.478 mole), 48.0%.

**2-Methoxy-2-methyl-3-pentyne** was prepared by a modification of the method of Hennion and Boisselle.<sup>8</sup> After the final addition of ammonium chloride, the mixture was stirred for 0.5 hr. The ammonia was then allowed to distil through a vacuum-jacketed Vigreux column in the same manner as described above for 3-methoxy-3-methyl-1-butyne. Distillation as before yielded the product, boiling over the range 117–119°; yield 31.0 g. (0.276 mole), 70.3%.

(8) G. F. Hennion and A. P. Boisselle, *J. Org. Chem.*, **26**, 725 (1961).(1) E. S. Lewis and G. M. Coppinger, *J. Am. Chem. Soc.*, **76**, 4495 (1954).(2) E. S. Lewis, R. R. Johnson, and G. M. Coppinger, *ibid.*, **81**, 3140 (1959).(3) V. J. Shiner, Jr., and C. J. Verbanic, *ibid.*, **79**, 373 (1957).(4) E. S. Lewis and C. E. Boozer, *ibid.*, **74**, 6306 (1952).(5) V. J. Shiner, Jr., *ibid.*, **75**, 2925 (1953).(6) P. D. Bartlett and L. J. Rosen, *ibid.*, **64**, 543 (1942).(7) A. Burawoy and E. Spinner, *J. Chem. Soc.*, 3752 (1954).

**4-Chloro-4-methyl-2-pentyne (Ia).**—2-Methoxy-2-methyl-3-pentyne (11.2 g., 0.097 mole) and about 1 g. of hydroquinone were placed into a three-necked, round-bottom 100-ml. flask. The flask was maintained at 0°, and stirring was provided with a magnetic stirrer. Dry hydrogen chloride was bubbled through the reaction mixture for 15 min. The hydrogen chloride addition was then stopped, a small sample of the reaction mixture to be used for an n.m.r. spectrum was removed, and the flask was immersed in a Dry Ice-acetone bath. The n.m.r. spectrum was immediately taken, and the ratio of the peaks at 8.68  $\tau$  due to the protons on the two equivalent methyl groups of 2-methoxy-2-methyl-3-pentyne, and at 8.22  $\tau$ , due to the corresponding protons of the product, was observed, as a measure of the extent of the reaction. This procedure, involving addition of hydrogen chloride for 15 min., followed by the n.m.r. spectrum, was continued until the total reaction time was 1 hr. At this time, the peak at 8.68  $\tau$  was practically gone, and the peak at 8.31  $\tau$ , due to an allenic impurity, had not yet formed. The reaction mixture was purified by vacuum line fractionation to give the product; yield 8.1 g. (0.068 mole), 69.8%. Although this material slowly decomposed at room temperature, it was found that storage in a Dry Ice-acetone bath over extended periods of a year or more left the n.m.r. spectrum unchanged.

**Trimethylsulfoxonium Iodide- $d_3$ .**—Trimethylsulfoxonium iodide was prepared according to the method of Kulm and Trischmann.<sup>9</sup> It was then subjected to sodium carbonate-catalyzed exchange in deuterium oxide according to the method of Cotton, *et al.*<sup>10</sup>

**Trideuteriomethyl Iodide.**—Trimethylsulfoxonium iodide- $d_3$  was pyrolyzed according to the method of Cotton, *et al.*<sup>10</sup> The product was distilled through a 10  $\times$  390 mm. column packed with 0.25 in. glass helices. The product was collected over the range of 40 to 44°; yield 57.8 g. (0.399 mole), 67.5%. A deuterium analysis by means of n.m.r. showed that the percentage deuterium was 99.7%, corresponding to 2.99 atoms of D per molecule.

**4-Chloro-4-methyl-2-pentyne-1,1,1- $d_3$  (Ib)** was prepared from hydrogen chloride and 2-methoxy-2-methyl-3-pentyne-5,5,5- $d_3$ . The reaction was monitored by n.m.r. by following the same peaks as in the preparation of 4-chloro-4-methyl-2-pentyne. Because of the tendency of this material to give explosions in the combustion train, a deuterium analysis by the combustion method described by Shiner<sup>11</sup> could not be accomplished. As a result, it will be necessary to assume that no undesirable exchange occurred in the synthesis from trideuteriomethyl iodide.

**Acetone- $d_6$**  was prepared by the method of Shiner and Cross.<sup>12</sup> Deuterium analysis by n.m.r. indicated that there was 99.9% deuterium exchange, corresponding to 6.00 atoms of deuterium per molecule.

**2-Methyl- $d_3$ -3-pentyn-2-ol-1,1,1- $d_3$**  was prepared by the action of propynylmagnesium bromide on acetone- $d_6$ , according to the method of Hurd and Cohen.<sup>13</sup>

**4-Chloro-4-methyl- $d_3$ -2-pentyne-5,5,5- $d_3$  (Ic)** was prepared by bubbling dry hydrogen chloride into 2-methyl- $d_3$ -3-pentyn-2-ol-1,1,1- $d_3$  in a manner similar to that used in the preparation of 4-chloro-4-methyl-2-pentyne. The reaction was monitored, as before, by n.m.r. except in this case the disappearance of the peak due to the terminal methyl protons of the alcohol at 8.22  $\tau$  and the appearance of the corresponding peak of the chloride at 8.18  $\tau$  were followed. The total time required for the addition of hydrogen chloride was 35 min. Purification by vacuum line transfer gave 4.2 g. (0.034 mole), yield 79.7%.

**Kinetic Procedure.**—The solvolysis reactions were followed conductometrically. The  $\Delta_\infty$  and  $S_a$  for HCl in "80%" ethanol were determined by Murr,<sup>14</sup> and  $\Delta_\infty$  and  $S_a$  for HCl in "95%" ethanol and "80%" acetone were determined by Shiner and Buddenbaum.<sup>15</sup>

The reactions were followed by the conductance method described by Murr and Shiner.<sup>16</sup> The results of the kinetic runs

were processed by means of a least-squares kinetic program used with IBM 709 digital computer.

## Results

The table gives the results of the kinetic runs, along with an indication of their reliability.

TABLE I  
SOLVOLYSIS RATES AND ISOTOPE EFFECTS AT 25°

Compound	Solvent	Rate constant, sec. <sup>-1</sup>	$k_H/k_D$
Ia	"80%" EtOH-H <sub>2</sub> O	5.420 $\pm$ 0.005 $\times 10^{-4}$	...
	"95%" EtOH-H <sub>2</sub> O	3.1649 $\pm$ .0002 $\times 10^{-5}$	...
	"80%" acetone-H <sub>2</sub> O	5.87 $\pm$ .015 $\times 10^{-5}$	...
Ib	"80%" EtOH-H <sub>2</sub> O	4.9653 $\pm$ .0007 $\times 10^{-4}$	1.092 $\pm$ 0.001
	"95%" EtOH-H <sub>2</sub> O	2.8907 $\pm$ .0008 $\times 10^{-5}$	1.0949 $\pm$ .0004
	"80%" acetone-H <sub>2</sub> O	5.403 $\pm$ .005 $\times 10^{-5}$	1.087 $\pm$ .004
Ic	"80%" EtOH-H <sub>2</sub> O	3.275 $\pm$ .005 $\times 10^{-4}$	1.655 $\pm$ .004

The inconsistency in the observed errors appears to be due to a deviation from precise first-order kinetics. This appears to be due to an isomerization of the type described by Shiner and Wilson<sup>17</sup> causing the formation of an allenic chloride which also solvolyzes, but at a much slower rate.

## Discussion

The table above shows that  $\beta$ -deuteration retards the solvolysis rate by an amount similar to that observed for other *t*-alkyl halides.<sup>18</sup> The effect is, however, significantly smaller than 1.84, the  $k_H/k_D$  value previously observed in the solvolysis of 3-bromo-3-methyl- $d_3$ -1-butyne-4,4,4- $d_3$ .<sup>19</sup> The  $\beta$ -deuterium isotope effect in the solvolysis of  $\alpha$ -phenylethyl bromide has been found to be very similar to that for the chloride.<sup>15</sup> Thus it may be inferred that the methyl group in compound Ic causes, relative to hydrogen, a decrease in the  $\beta$ -effect from 1.84 to 1.655. Similar reductions in the  $\beta$ -effect are associated with electron-releasing ring substituents in the solvolysis of  $\alpha$ -phenylethyl chloride<sup>15</sup> and are apparently due to the ability of these groups to disperse the positive charge developed in the transition state and reduce the demand for hyperconjugation. The methyl group reduces the isotope free energy effect in the same proportion to its reduction of the free energy of activation in both cases.

$\delta$ -Deuteration also causes a significant effect, about one-third as large per D atom as  $\beta$ -deuteration. Further, in a set of solvents in which *p*-methyl- $d_3$ -benzhydryl chloride showed a strong solvent dependency of the isotope rate effect,<sup>3</sup> the effect of  $\delta$ -deuteration is relatively constant and somewhat larger. It is also larger than the solvolysis isotope effect shown by *p*-methyl- $d_3$ - $\alpha$ -phenylethyl chloride in similar solvents.<sup>2</sup> Thus the present results confirm and strengthen the conclusion originally drawn from the experiments designed after the classic method of organic chemistry to show that the  $\beta$ -deuterium isotope effect was caused by an *electronic* interaction with the reaction center. Although these earlier results have subsequently been ignored or discounted for being small and solvent dependent,<sup>20,21</sup> by the proponents

(9) P. Kuhn and H. Trischmann, *Ann.*, **611**, 117 (1958).

(10) F. A. Cotton, J. H. Fassnacht, W. D. Horrocks, Jr., and N. A. Nelson, *J. Chem. Soc.*, 4138 (1959).

(11) V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **74**, 5285 (1952).

(12) V. J. Shiner, Jr., and S. Cross, *ibid.*, **79**, 3593 (1957).

(13) C. D. Hurd and F. L. Cohen, *ibid.*, **53**, 1068 (1931).

(14) B. L. Murr, Jr., Ph.D. Thesis, Indiana University, 1961, p. 77.

(15) V. J. Shiner, Jr., and W. E. Buddenbaum, unpublished results.

(16) B. L. Murr, Jr., and V. J. Shiner, Jr., *J. Am. Chem. Soc.*, **84**, 4672 (1962).

(17) V. J. Shiner, Jr., and J. W. Wilson, *ibid.*, **84**, 2402 (1962).

(18) V. J. Shiner, Jr., B. L. Murr, and G. Heinemann, *ibid.*, **85**, 2413 (1963).

(19) V. J. Shiner, Jr., J. W. Wilson, G. Heinemann, and N. Solliday, *ibid.*, **84**, 2408 (1962).

(20) L. S. Bartell, *ibid.*, **83**, 3567 (1961); *Iowa State J. Sci.*, **36**, 137 (1961). The simple steric model ignoring charge delocalization predicts a null effect for isotopic substitution at these remote sites. In the second

of the steric origin of all secondary isotope rate effects, it appears unlikely that the present results can be explained by change in either steric or solvent interactions on activation without the incursion of electronic interactions with the reaction center.

If the  $\delta$ -effect is entirely electronic in origin, it remains to predict from this what fraction of the approximately 3-fold larger effect in the  $\beta$ -position is similarly electrical in origin and to estimate by difference what residual amount could be attributed to changes in nonbonded interactions. It has been found that the triple bond generally attenuates the inductive effect by a factor around three or four.<sup>22</sup> However, the present effect is certainly mainly conjugative in nature. Kochi

paper this problem is met by a model involving charge delocalization. This is tantamount to invoking hyperconjugation but includes the novel idea that relief of nonbonded interactions assists hyperconjugative electron release.

(21) M. J. S. Dewar, "Hyperconjugation," The Ronald Press, New York, N. Y., 1962, p. 141.

(22) R. E. Dessy and J.-Y. Kim, *J. Am. Chem. Soc.*, **83**, 1167 (1961), and references there cited.

and Hammond<sup>23</sup> have estimated that the carbon-carbon triple bond is a four- or fivefold poorer conjugative electron releaser than the double bond. Thus we can infer that the part of the  $\beta$ -effect caused by electronic interactions would be much larger than 1.10 and *might* be large enough to account for the total observed. Nevertheless, it is not possible at the present time to conclude that there is *no* small "steric" component in the  $\beta$ -effect. The strong solvent dependencies of isotope effects transmitted by conjugation through the benzene ring remain to be elucidated by further experiments.

**Acknowledgment.**—This research was supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund. The facilities of the Indiana University Computing Center were used for the machine computations.

(23) J. K. Kochi and G. S. Hammond, *ibid.*, **75**, 3452 (1953).

[CONTRIBUTION NO. 3051 FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA, CALIF., AND THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASS.]

## Small-Ring Compounds. XLII. Synthesis and Reactions of 3-Phenyl-2-cyclobutenone and Some Related Compounds<sup>1,2</sup>

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RECEIVED JANUARY 20, 1964

Hydrogenation of either 1,1-difluoro-2,2-dichloro-3-phenylcyclobutane (VII) or 1,1-difluoro-2,2-dichloro-2-phenylcyclobutene (VI) over a palladium-on-charcoal catalyst gave 1,1-difluoro-3-phenylcyclobutane (V). Bromination of V by *N*-bromosuccinimide produced 1,1-difluoro-3-bromo-3-phenylcyclobutane (IX) which on dehydrobromination by potassium hydroxide in ethanol afforded 1,1-difluoro-3-phenyl-2-cyclobutene (IV). Hydrolysis of IV by concentrated sulfuric acid gave 3-phenyl-2-cyclobutenone (I). Treatment of I with hot dilute aqueous base produced mixtures of benzoic acid, acetophenone, and benzoylacetone. The ring opening of I in boiling acetic acid gave  $\beta$ -methyl-*trans*-cinnamic acid. Catalytic hydrogenation of I produced 3-phenylcyclobutanone (XI). Sodium borohydride reduction of I afforded 3-phenyl-2-cyclobutenol (XII) which on catalytic hydrogenation gave *cis*-3-phenylcyclobutanol (XIII); XIII was also obtained by catalytic hydrogenation of 2-chloro-3-phenyl-2-cyclobutenol (XVI) from the sodium borohydride reduction of 2-chloro-3-phenyl-2-cyclobutenone (XV).

### Introduction

The cycloaddition reactions of styrene and phenylacetylene with either 1,1-difluoro-2,2-dichloroethylene, 1,1,2-trifluoro-2-chloroethylene, or tetrafluoroethylene give adducts whose conversion to substituted (either halogen- or alkoxy-substituted) 3-phenyl-2-cyclobutenones has been described in earlier papers.<sup>4</sup> The ring-opening reactions of a number of substituted 3-phenyl-2-cyclobutenones have also been discussed previously.<sup>4a,4c,5</sup>

(1) Presented in part at the Fourteenth National Organic Chemistry Symposium of the American Chemical Society, Lafayette, Ind., June, 1955, and at the 138th National Meeting of the American Chemical Society, New York, N. Y., Sept. 15, 1960, Abstracts of Papers, p. 72P.

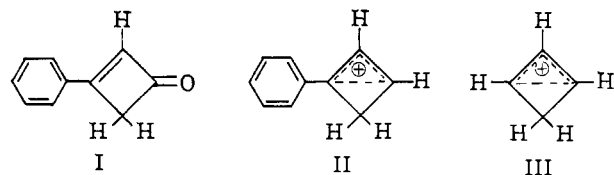
(2) Supported in part by the National Science Foundation.

(3) Monsanto Chemical Co. Predoctoral Fellow, 1957-1958.

(4) (a) J. D. Roberts, G. B. Kline, and H. E. Simmons, Jr., *J. Am. Chem. Soc.*, **75**, 4765 (1953); (b) E. F. Silversmith and J. D. Roberts, *ibid.*, **80**, 4083 (1958); (c) E. F. Silversmith, Y. Kitahara, M. C. Caserio, and J. D. Roberts, *ibid.*, **80**, 5840 (1958); (d) E. J. Smutny, M. C. Caserio, and J. D. Roberts, *ibid.*, **82**, 1793 (1960); (e) M. C. Caserio, H. E. Simmons, Jr., A. E. Johnson, and J. D. Roberts, *ibid.*, **82**, 3102 (1960); (f) Y. Kitahara, M. C. Caserio, F. Scardiglia, and J. D. Roberts, *ibid.*, **82**, 3106 (1960).

(5) (a) E. F. Jenny and J. D. Roberts, *ibid.*, **78**, 2005 (1956); (b) E. F. Silversmith and J. D. Roberts, *ibid.*, **78**, 4023 (1956); (c) L. Skattebøl and J. D. Roberts, *ibid.*, **80**, 4085 (1958); (d) E. F. Silversmith, Y. Kitahara, and J. D. Roberts, *ibid.*, **80**, 4088 (1958).

The present research was concerned with the synthesis and ring-opening reactions of 3-phenyl-2-cyclobutenone itself (I) as well as the chemistry of some of its derivatives. A synthesis of I was desired as a precursor to derivatives from which a 3-phenyl-2-cyclobutenyl cation (II) might be generated by suitable solvolyses or deamination reactions. Simple LCAO-molecular orbital calculations suggest that delocaliza-



tion of electrons as the result of  $\pi$ -overlap between the p-orbitals on the 1- and 3-positions in the cations II and III could well result in significant enhancement of the  $S_N1$  solvolysis rates of substances which could yield II and III over those for suitable model compounds.

The cations in question are of the homocyclopropenyl type and are expected to possess at least some of the stabilization predicted by the simple LCAO-MO