

b. **4-Hydroxy-O¹⁸-4-methylhexanoate Lactone.**—The labeled lactone (0.86 g.) in 5 ml. of ether was added to a slurry of 0.25 g. of lithium aluminum hydride in 25 ml. of anhydrous ether. The reaction mixture was stirred for 45 min., and was then decomposed with 10 ml. of 30% Rochelle salt solution. The ether layer was decanted, dried over anhydrous potassium carbonate, and concentrated by distillation. The viscous residue was distilled, giving 0.75 g. (85%) of 4-methylhexane-1,4-diol, b.p. 87–89° at 0.5 mm. n_D^{20} 1.4556. About 0.2 g. of the diol and a small piece of iodine were heated to 70° for 1 hr. in a 2.5-ml. gas bulb containing 15 mm. of carbon dioxide. Mass spectrometric analysis of the carbon dioxide permitted the calculation of O¹⁸ content of the tertiary hydroxy position. Absence of reaction at the primary hydroxy position was demonstrated by repeating the equilibration using 4-methyl-1-hexanol-O¹⁸. A negligible amount of exchange (0.9%) occurred under the reaction conditions given above.

Kinetic Studies.—The pH 7 buffer solution was prepared by dissolving 7.465 g. of potassium hydrogen phosphate and 7.776

g. of potassium dihydrogen phosphate in a small amount of boiled distilled water, and diluting this to 1 l. in a volumetric flask (ionic strength 0.243 *M*). The pH 13 solution was prepared by dissolving 3.06 g. of tripotassium phosphate in a small amount of 0.1 *N* potassium hydroxide solution and diluting to 1 l. with the latter.

The solutions of the acids were prepared by weighing out appropriate quantities of the acid, neutralizing with potassium hydroxide, and diluting to volume with the buffer solution. Permanganate solutions were freshly prepared in the same buffers. In one arm of a U-tube attached to a Beckman cell was placed 3 ml. of the acid solution, and in the other was placed 3 ml. of the permanganate solution (about 10⁻⁴ *M*). The solutions were brought to 25° and transferred to the Beckman cell by rapid inversion of the tube. The rate of reaction was determined from the rate of change of optical density at 510 m μ (permanganate). During the run, the cell was maintained in a thermostated water bath placed in the light path of the spectrometer.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY, DURHAM, N. C.]

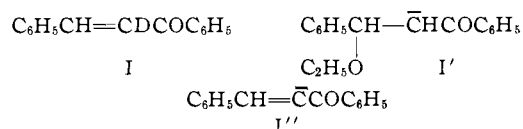
Base-Catalyzed Hydrogen-Deuterium Exchange at the α -Carbon of β -Phenylindenone¹

BY BERNARD W. ROCKETT, THOMAS M. HARRIS, AND CHARLES R. HAUSER

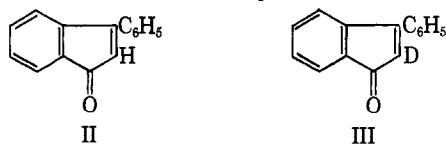
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Deuteration of β -phenylindenone (II) was effected with deuterioethanol by means of sodium ethoxide at 0° to form the α -deuterio derivative III. This result is in agreement with an addition-elimination exchange mechanism, but not with one involving ionization of the α -vinyl hydrogen.

Deuterations of ethyl cinnamate, chalcone, and certain related compounds have recently been effected with deuterioethanol by means of a catalytic amount of sodium ethoxide.² The reaction involved replacement of the α -vinyl hydrogen of the α,β -unsaturated compound by deuterium to form the corresponding α -deuterio derivative; for example, chalcone gave I. Some evidence was presented for an addition-elimination mechanism through carbanion I'. However, an alternative mechanism involving ionization of the α -vinyl hydrogen to form carbanion I'' as the reactive intermediate was not excluded.

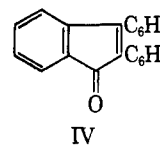


We have now observed a similar deuteration of β -phenylindenone (II), which may be regarded as a cyclic analog of chalcone. The deuteration was effected with deuterioethanol and sodium ethoxide at 0°. To facilitate the hydrogen-deuterium exchange at this temperature a molecular equivalent of sodium ethoxide and a large excess of deuterioethanol were used, although only a catalytic amount of the base should be required. The product III was isolated as its *p*-nitrophenylhydrazone since the free ketone (II or III) was obtained as a liquid which was sensitive to air oxidation. This derivative contained 1.0 deuterium atom per molecule.

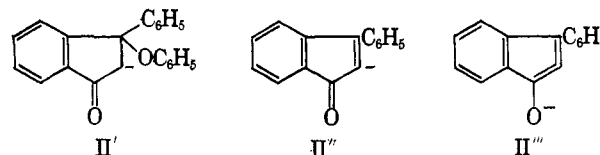


The deuteration of II produced appreciable changes in the infrared spectrum of the *p*-nitrophenylhydrazone. Some bands became weak or disappeared while other bands appeared (see Experimental). Similar spectral changes have been observed previously for other

deuterations.^{2,3} It should be pointed out that both the deuterated and undeuterated compounds showed similar infrared N-H stretching frequencies at 3295 cm.⁻¹. This indicates that deuterium had not replaced substantially the hydrogen on nitrogen in the *p*-nitrophenylhydrazone during the work-up procedure. That deuteration had involved exchange of the α -hydrogen of ketone II, not one or more of the aromatic hydrogens, was supported by the failure of α,β -diphenylindenone (IV) to undergo a significant deuterium-hydrogen exchange (only 0.04 D atom/molecule) under conditions similar to those used for deuteration of II (see Experimental).



The deuteration of II to form III is considered to involve the addition-elimination mechanism through carbanion II', not ionization of the α -vinyl hydrogen to form carbanion II'', since stabilization of II'' would require the unlikely resonance structure II'''.⁴



During the course of this work the related deuteration of Δ^1 -5 α -androsten-3-one to form the compound indicated in V was reported.⁵ The exchange that occurred at the 2-position was considered to involve the addition-elimination mechanism.⁵ This, which resulted in a six-membered ring and ours in a five-membered ring, complement one another.

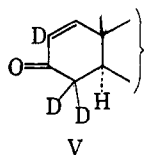
(3) D. S. Noyce, G. L. Woo, and M. J. Jorgenson, *ibid.*, **83**, 1160 (1961); D. S. Noyce, P. A. King, F. B. Kirby, and W. L. Reed, *ibid.*, **84**, 1632 (1962).

(4) See E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, Inc., New York, N. Y., 1959, p. 388.

(5) R. H. Shapiro, J. M. Wilson, and C. Djerassi, *Steroids*, **1**, 1 (1963).

(1) Supported by the National Science Foundation, NSF-G14527.

(2) M. F. Zinn, T. M. Harris, D. G. Hill, and C. R. Hauser, *J. Am. Chem. Soc.*, **85**, 71 (1963).



These results furnish indirect evidence for the operation of the addition-elimination mechanism in the previously reported² hydrogen-deuterium exchanges with acyclic α,β -unsaturated compounds such as chalcone.

Experimental⁶

β -Phenylindenone (II).—This compound was prepared by a new method involving dehydrogenation of β -phenylindanone through its dicarbanion.⁷ The liquid product was characterized as its *p*-nitrophenylhydrazone, m.p. 266–267°, reported⁸ m.p. 266–267°.

Deuteration of II to Form β -Phenylindenone- α - d_1 (III).—To 60 ml. of deuterioethanol (b.p. 79–79.5°)⁹ was added 0.2 g. (0.0087 g.-atom) of sodium. The resulting solution was cooled to 0° and an ethereal solution of 1.8 g. (0.0087 mole) of freshly prepared β -phenylindenone (II) was added. After standing 50–90 hr. at 0°, the reaction mixture was treated with a wet ethanolic solution of *p*-nitrophenylhydrazine hydrochloride (containing a slight excess of hydrochloric acid) to yield 67–88% of the *p*-nitrophenylhydrazone of III, m.p. 266–267° after recrystallization from acetonitrile. Combustion analysis indicated that the material contained 6.69 atom % excess deuterium; calcd.

(6) Melting points were determined with a Mel-Temp capillary melting point apparatus and are uncorrected. Infrared spectra were determined with a Perkin-Elmer Infracord by the potassium bromide pellet method. Deuterium analyses were by Dr. Josef Nemeth, Urbana, Ill.

(7) The details of this and related reactions will be published soon.

(8) K. von Auwers and R. Hugel, *J. prakt. Chem.*, **143**, 157 (1935).

(9) V. J. Shiner, Jr., and M. L. Smith, *J. Am. Chem. Soc.*, **83**, 593 (1961).

for $C_{21}H_{14}N_2O_2D$, 6.67%, corresponding to approximately 1.0 D atom/molecule. The infrared spectrum showed bands at 1185, 1175, 1055, 1030, 922, 780, and 718 cm^{-1} while the undeuterated *p*-nitrophenylhydrazone had bands at 1210, 1130, 1048, 847, and 774 cm^{-1} . The deuterated and the undeuterated compounds showed similar infrared N–H stretching bands at 3295 cm^{-1} .

α,β -Diphenylindenone (IV).—A mixture of 12 g. (0.04 mole) of α,β,β -triphenylpropionic acid,¹⁰ 14.3 g. (0.12 mole) of thionyl chloride, and a few drops of pyridine was warmed on the steam bath for 1 hr. The excess thionyl chloride was removed by distillation *in vacuo*, and the residue was dissolved in 40 ml. of benzene. The solution was cooled (ice bath), and 5.4 g. (0.04 mole) of aluminum chloride was added in small portions with stirring during 30 min. After standing at 0° for 1 hr., the reaction mixture was poured onto ice and acidified with dilute hydrochloric acid. The resulting mixture was extracted with ether, and the ethereal extract was dried over anhydrous magnesium sulfate. The solvent was removed, and the viscous oily residue was chromatographed on alumina to give, after recrystallization from cyclohexane, 6.8 g. (60%) of α,β -diphenylindanone, m.p. 99–100°, reported¹¹ m.p. 100–101°.

This compound was dehydrogenated with sulfur by the method of Koelsch¹¹ to give α,β -diphenylindenone (IV), m.p. 152–153°, reported¹² m.p. 150–151°.

Attempted Deuteration of α,β -Diphenylindenone (IV).—To a solution of 0.0013 mole of sodium ethoxide (prepared from 0.03 g., 0.0013 g.-atom, of sodium) in 16 ml. of deuterioethanol at 0° was added an ethereal solution of 0.36 g. (0.0013 mole) of α,β -diphenylindenone (IV). After standing 100 hr. at 0°, the reaction mixture was neutralized with glacial acetic acid and the solvent was removed under reduced pressure. Recrystallization of the residue gave 0.16 g. (89%) of recovered α,β -diphenylindenone, m.p. 151.5–153°. A mixture m.p. with authentic material was undepressed and no alterations were observed in the infrared spectrum. Combustion analysis indicated that the ketone contained 0.31 atom % excess deuterium, corresponding to only 0.04 D atom/molecule.

(10) W. R. Dunnivant and C. R. Hauser, *Org. Syn.*, **40**, 38 (1960).

(11) C. F. Koelsch, *J. Am. Chem. Soc.*, **56**, 1337 (1934).

(12) G. Heyl and V. Meyer, *Ber.*, **28**, 2776 (1895).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY, TECHNOLOGY CENTER, CHICAGO 16, ILL.]

A New Method of Evaluating *ortho* σ -Constants

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A method for evaluating *ortho* σ -constants by using ionization constants and rate of esterification with diphenyldiazomethane of substituted phenylpropionic acids is described. Values for chloro, fluoro, trifluoromethyl, and nitro groups have been determined. The reduced acidities relative to the *p*-isomers of acids substituted in the *o*-position with negative substituents are ascribed to a field effect. A related dipolar field effect is revealed by the infrared and ultraviolet spectra of the acids.

Introduction

In recent years acetylenic compounds have been studied for the purpose of correlating rate and/or equilibrium data with Hammett σ -values for substituents on the aromatic nucleus. Newman and Merrill³ measured the ionization constants and the rates of esterification of *o*-, *m*-, and *p*-chloro-, methoxy-, and nitrophenylpropionic acids, and Roberts and Carboni⁴ made other measurements of reactivities on some of these compounds. More recently, Dessy and his co-workers⁵ examined the effect of various substituents on the rates of deuterium exchange of substituted phenylacetylenes.

A linear free-energy relationship similar to the Hammett equation but applicable to aliphatic and *o*-substituted aromatic compounds has been proposed by Taft.^{6,7} This relationship is valid only for a restricted

number of reaction series, and among the *o*-substituents, fluorine, the amino group, and hydrogen are not included.

We were interested in extending knowledge in this area by obtaining additional data for the *o*-, *m*-, and *p*-fluoro- and trifluoromethyl-substituted phenylpropionic acids. On the basis of these data and the data of Newman and Merrill³ and Roberts and Carboni,⁴ *ortho* σ -constants for the fluoro, trifluoromethyl, chloro, nitro, and methoxy groups have been defined.

Results and Discussion

The ionization constants and the rates of various reactions of several substituted phenylpropionic acids have previously been studied by two groups of workers.^{3,4} The phenylpropionic acid system was chosen because the acetylenic bond is linear and should eliminate steric effects of *o*-substituents more than any other group capable of joining the carboxyl group to the benzene ring. Also, the unsaturated bond should be capable of transmitting polar effects to the reaction site.

The apparent ionization constants of the trifluoromethyl- and fluoro-substituted phenylpropionic acids⁸

(8) See Experimental.

(1) Abstracted from the Ph. D. thesis of I. J. Solomon, January, 1962.

(2) Part of this work was supported by IIT Research Institute (formerly Armour Research Foundation).

(3) M. S. Newman and S. H. Merrill, *J. Am. Chem. Soc.*, **77**, 5552 (1955).

(4) J. D. Roberts and R. A. Carboni, *ibid.*, **77**, 5554 (1955).

(5) R. E. Dessy, Y. Okazumi, and A. Chen, *ibid.*, **84**, 2899 (1962).

(6) R. W. Taft, Jr., *ibid.*, **74**, 2729 (1952).

(7) R. W. Taft, Jr., *ibid.*, **74**, 3120 (1952).