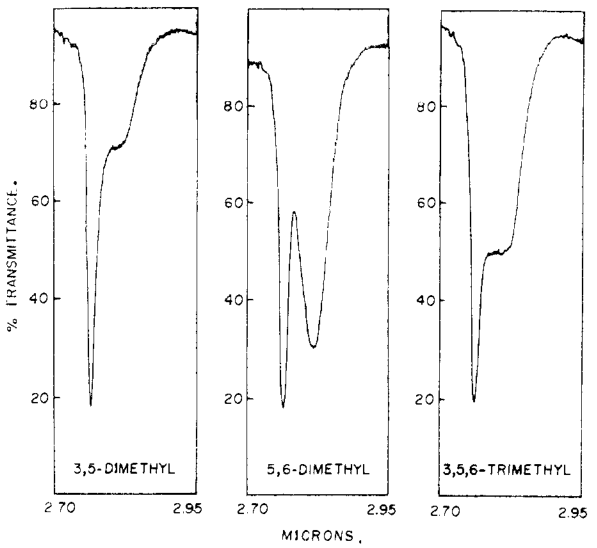

Fig. 4.—The O–H spectra, from left to right, of 2-allyl-3,5-dimethylphenol, 2-allyl-5,6-dimethylphenol and 2-allyl-3,5,6-trimethylphenol.

other than *ortho–ortho*, one finds the expected increase of 2–5 cm.$^{-1}$.

In a forthcoming publication, this *ortho–ortho*-dialkyl effect will be discussed and the suggestion made that it is due to a repulsive steric interaction between the hydrogen of the O–H group and the hydrogens of the alkyl group. Due to the large resonance interaction between the oxygen and the aromatic ring, the steric interaction is not enough to rotate the O–H group out of plane, but instead there is a decrease in the O–H internuclear distance and an increase in the O–H stretching frequency. Consequently, the remarkably high values of ν_{OH} do not reflect the true acidity of such phenols and possibly not their hydrogen bonding powers if these could be determined free from steric complications. (This is to be discussed in detail in a later paper.) This naturally poses the question regarding the way $\Delta\nu_{OH}$ values should be computed for allylphenols. If they are based on the free O–H in each spectrum, then the $\Delta\nu_{OH}$ possibly would be larger for 6-substituted compounds than would be a measure of the energy of the intramolecular hydrogen bond.

The above discussion is amply demonstrated by the data in Table I and the spectra in Fig. 4, which show that ν_{OH} values change from 3612.3 cm.$^{-1}$ in phenol to 3613.6 in 2-allylphenol to 3624.4 cm.$^{-1}$ in 2-allyl-3,5,6-trimethylphenol. In the last compound the buttressing effects of the 3- and 5-methyl groups increase the steric effect of the 2-allyl and 6-methyl groups by 50% or more. This is shown by a comparison with 2-allyl-6-methylphenol which has a ν_{OH} value of 3619.4 cm.$^{-1}$.

The $\Delta\nu_{OH}$ shift of 2-allyl-5,6-dimethylphenol, computed in the usual way, has increased from the value of 64.4 cm.$^{-1}$ in 2-allylphenol to 69.7 cm.$^{-1}$. However, the ν_{OH} value of the associated band is 2 cm.$^{-1}$ higher than that in 2-allylphenol, thus throwing doubt on the validity of $\Delta\nu_{OH}$ values as an index of bonding energy where steric effects are important.

In a previous publication,[1] a 3-methyl group on the ring adjacent to the allyl group was shown to decrease the proportion of the associated O–H because the allyl group is forced slightly out of plane and away from the O–H group. On the other hand, a 6-methyl group, in addition to increasing the $\Delta\nu_{OH}$ shift, as described above, greatly increases the proportion of associated O–H. This may be due mainly to a proton–proton interaction between the methyl and O–H groups, increasing the relative proportion of the in-plane O–H pointing toward the allyl group.

Pittsburg, Calif.

[Contribution from the Department of Chemistry, Oklahoma State University]

Secondary Hydrogen Isotope Effects in the Hydrolysis of Methyl *p*-Methyl-*t*-benzoate

By Ernest M. Hodnett, Ray D. Taylor, Jose-Vicente Tormo and Robert E. Lewis

Received March 13, 1959

Methyl *p*-methyl-*t*-benzoate has been hydrolyzed in basic aqueous alcoholic solution and in 99–100% sulfuric acid. The tritium-labeled compound reacts slower than the ordinary compound in the basic solution but at the same rate as the ordinary compound in 99–100% sulfuric acid. These differences are explained on the basis of (1) greater electron release of the tritium atom through the inductive effect and (2) smaller electron release by the tritium atom through the electromeric effect.

Molecules having different isotopes of hydrogen may react at different rates even though a bond to the isotopic atom is not broken or formed in the reaction. These secondary isotope effects are as large as 5% for each deuterium atom in such reactions as the acetolysis of deuterated methyl-*p*-tolylcarbinyl chlorides.[2] In general the effect of the heavier isotope is to slow the reaction,[2,3] but in two reported cases the molecule labeled

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(1) Taken from theses presented by Ray D. Taylor and Jose-Vicente Tormo to the Graduate School of Oklahoma State University in partial fulfillment of the requirements for Master of Science degrees. This investigation was supported in part by the Research Corporation and in part by the U. S. Atomic Energy Commission and the Research Foundation of Oklahoma State University through Contract No. AT(11-1)-71, Project No. 5, and was conducted in the Radioisotopes and Radiations Laboratory.

(2) E. S. Lewis and G. M. Coppinger, This Journal, **76**, 4495 (1954).

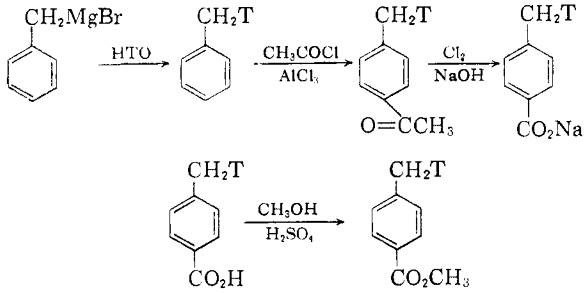
(3) (a) E. S. Lewis, *et al.*, *ibid.*, **74**, 6306 (1952); **76**, 791, 796, 1603 (1954); (b) V. J. Shiner, Jr., *ibid.*, **75**, 2925 (1953); **78**, 2653 (1956); **79**, 3599 (1957); (c) C. E. Boozer, B. W. Ponder, J. C. Trisler and C. E. Wightman, *ibid.*, **78**, 1506 (1956); (d) W. D. Emmons and M. F. Hawthorne, *ibid.*, **78**, 5593 (1956).

with the heavier isotope reacts more rapidly than the normal molecule.[4]

In this study methyl p-methyl-t-benzoate was hydrolyzed in basic aqueous alcoholic solution and in concentrated sulfuric acid. The effect of an atom of tritium in a methyl group which is across the benzene ring from the reacting carboxylate group was determined in each case. In spite of the physical separation of the two groups they are affected by each other electronically. Our hope was to explain the results on the basis of present electronic theory.

Experimental Details

Preparation of Methyl p-Methyl-t-benzoate.—This compound was prepared by the reactions



The radioactive yield of ester was 9.7% based on the tritiated water[5] used. The detailed procedures for these well-known reactions were based on published methods for other compounds.[6] The last dilution of non-radioactive compound was made at the acid stage to avoid an impurity of highly radioactive acid in the ester.[7]

Basic Hydrolysis of the Ester.—Hydrolyses were carried out in sealed vials in a water-bath held at 25° in solutions of 86 volume per cent. methanol and water which were approximately 0.75 M in ester. Sufficient sodium hydroxide was added to react with various amounts of labeled ester. The extent of the reaction was indicated by disappearance of the pink color of phenolphthalein, or by titration with standard acid. The excess ester was extracted with ether, and the sodium salt was converted to the solid p-toluic acid which was separated, recrystallized several times from water, and dried. Another experiment showed that the hydrogen atoms of the p-methyl group of p-toluic acid did not exchange with the tritiated atoms of tritiated water at 100°.

Acidic Hydrolysis of the Ester.—Samples of approximately 1 g. of methyl p-methyl-t-benzoate were dissolved in 20 ml. of cold sulfuric acid which was shown by titration to be 99–100% pure (usually 99.9%). The reaction mixture was held as close to 20° as possible for 4–8 minutes, and then poured into 150 g. of ice and water. The unreacted ester and p-toluic acid were extracted with ether as completely as possible, then the ether solution was extracted several times with sodium bicarbonate solution to remove the p-toluic acid. The latter extract was acidified and extracted with ether. The ether solution was evaporated in a weighed beaker, and the amount of p-toluic acid determined to obtain the extent of hydrolysis. The p-toluic acid was recrystallized and dried before it was assayed. Other experiments showed that the tritium atom in the p-methyl group of p-toluic acid did not exchange with sulfuric acid under these conditions. However, attempts to hydrolyze the ester completely in sulfuric acid resulted in some sulfonation of the ring, so that the 100% hydrolysis was carried out in basic solution.

Assay of p-Toluic Acid.—The pure samples of p-toluic acid were prepared for tritium assay by the method of Wilzbach, Kaplan and Brown,[8] and assayed on a model 30, Applied Physics Corporation vibrating reed electrometer. To minimize small differences in operation of the electrometer, the samples of a given experiment were assayed on the same day in random order.

Results of the experiments are shown in Tables I and II, with the isotope effects, k^*/k, calculated by the method of Stevens and Attree.[9] It is evident that the tritium-labeled ester reacts slower than the ordinary ester in basic solution but at practically the same rate in 99.9% sulfuric acid.

TABLE I

ALKALINE HYDROLYSIS OF METHYL p-METHYL-t-BENZOATE

Extent of hydrolysis, %	Radioactivity of p-toluic acid, μc./mmole		Isotope effect, k^*/k
5	6.26 6.18 6.14 6.16	6.18 ± 0.04	0.955
40	6.24 6.14 6.25 6.22	6.21 ± .04	.950
100	6.46 6.47 6.42 6.49	6.46 ± .02	
4.4	5.78 5.79 5.81 5.76	5.78 ± .02	.951
35	5.89 5.83 5.87 5.85	5.86 ± .02	.957
100	6.05 6.08 6.05 6.10	6.07 ± .02	
		Average	0.953

TABLE II

HYDROLYSIS OF METHYL p-METHYL-t-BENZOATE IN 99–100% SULFURIC ACID

Extent of hydrolysis, %	Radioactivity of p-toluic acid, μc./mmole		Isotope effect, k^*/k
6.9	8.43 8.56 8.50 8.56	8.51 ± 0.05	1.005
16.4	8.54 8.50 8.44 8.50	8.49 ± .03	1.003
29.0	8.51 8.56 8.33	8.46 ± .09	0.999
100[a]	8.49 8.51 8.44 8.47	8.47 ± .02	
20	7.02 7.17 7.02 7.15 7.20	7.11 ± .07	0.989
100[a]	7.18 7.20 7.18 7.16	7.18 ± .02	
		Average	0.999

[a] Basic hydrolysis.

These results may be explained on the basis of two considerations: (1) greater electron release for the heavier hydrogen isotope by the inductive effect and (2) smaller electron release for the heavier hydrogen isotope by the electromeric process, particularly by the hyperconjugative mechanism. Halevi[10] has demonstrated that these considera-

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(4) (a) E. S. Lewis, J. L. Kinsey and R. R. Johnson, THIS JOURNAL, **78**, 4294 (1956); (b) E. M. Hodnett and L. Kaplan, Abstracts of the 125th Meeting of the American Chemical Society, Kansas City, Mo., April, 1954.

(5) E. M. Hodnett, C. F. Feldman and J. J. Flynn, Jr., *Experientia*, **13**, 96 (1957).

(6) (a) L. Melander, *Arkiv Kemi*, **2**, 211 (1950); (b) H. Pines, D. R. Stehlan and V. N. Ipatieff, THIS JOURNAL, **71**, 3534 (1949); (c) A. M. Van Arendonk and M. E. Cupery, *ibid.*, **53**, 3186 (1931).

(7) G. A. Ropp, *J. Chem. Ed.*, **34**, 60 (1957).

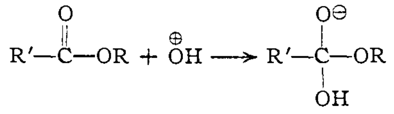
(8) K. E. Wilzbach, L. Kaplan and W. G. Brown, *Science*, **118**, 522 (1953).

(9) W. H. Stevens and R. N. Attree, *Can. J. Research*, **B27**, 807 (1949).

(10) (a) E. A. Halevi and M. Nussim, *Bull. Research Council of Israel*, **5A**, 263 (1956); (b) E. A. Halevi, *Tetrahedron*, **1**, 174 (1957); (c) E. A. Halevi, *Trans. Faraday Soc.*, **54**, 1441 (1958).

tions allow secondary hydrogen isotope effects to be used as criteria for elucidation of mechanisms of organic reactions. Halevi[10a] has shown that the acid-dissociation constant of phenylacetic acid is greater than that of phenylacetic-α,α-d_2 acid; this difference is due to more effective electron release from the C–D bond than from the C–H bond. This difference in acid-dissociation constants must arise from a difference in the ground states of the two molecules. On the other hand, some experiments[3] show that the heavier hydrogen isotope has a smaller electron release through conjugative mechanisms.

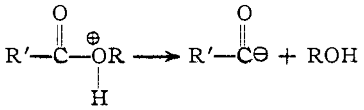
The rate-determining step in the basic hydrolysis of most esters generally is thought to be an attack of a hydroxyl ion on the carboxylate carbon[11]



$$R'-\overset{\overset{\large O}{\|}}{C}-OR + \overset{\oplus}{O}H \longrightarrow R'-\underset{\underset{\large OH}{|}}{\overset{\overset{\large O\ominus}{|}}{C}}-OR$$

Electron-releasing groups attached to the benzene ring of benzoates cause a reduction in the rate of hydrolysis. In this case, the tritium atom in the p-methyl group slows the reaction by its greater ability to release electrons by the inductive process. Since the release of electrons is not demanded by the attacking reagent, the electromeric mechanism is not called into play.

The rate-determining step in the hydrolysis of esters in 99–100% sulfuric acid is thought to be the production of an acylium ion[12]



$$R'-\overset{\overset{\large O}{\|}}{C}-\underset{\underset{\large H}{|}}{\overset{\oplus}{O}}R \longrightarrow R'-\overset{\overset{\large O}{\|}}{C}\ominus + ROH$$

Esters of p-toluic acid react approximately four times as rapidly as corresponding benzoate esters.[13] In this case the electromeric effect probably operates since electron release from the p-methyl group speeds the reaction. If the tritium atom releases electrons less readily than the protium atom, the reaction rate for the labeled molecule would be less than for the ordinary molecule. On the other hand, the greater release of electrons by inductive effect of tritium would cause the reaction to be faster for the tritium-labeled compound. These effects oppose one another, and in this particular case they cancel one another within experimental error. The labeled molecule reacts at the same rate as the ordinary molecule.

Acknowledgment.—The authors are grateful to Professor E. A. Halevi for his interest in this work and for copies of manuscripts of his papers.

[11] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 754.

[12] *Ibid.*, p. 769.

[13] E. D. Hughes and J. Graham, private communication.

STILLWATER, OKLA.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF THE ILLINOIS INSTITUTE OF TECHNOLOGY AND BRANDEIS UNIVERSITY]

The Structure and Chemistry of Ferrocene. IV. Intraannular Resonance Effects[1]

BY MYRON ROSENBLUM[2]

RECEIVED FEBRUARY 10, 1959

Both phenylferrocene and 1,1′-diphenylferrocene have been subjected to Friedel–Crafts acetylation, and the structures of the resulting isomeric acetylphenylferrocenes and acetyl-1,1′-diphenylferrocenes have been established. The structures of all the isomers also have been correlated with their infrared and ultravolet absorption spectra. Relative site reactivities for non-equivalent ring positions in phenyl- and in 1,1′-diphenylferrocene have been determined from the proportions in which the various isomers are formed. For phenylferrocene these are 1′:2:3 = 1.1:1.0:1.0, while for 1,1′-diphenylferrocene they are 2:3 = 1.0:1.0. It is suggested that a phenyl substituent inductively deactivates the substituted ferrocene ring toward acylation, but that superimposed resonance effects render positions adjacent to the phenyl substituent relatively more accessible to electrophilic attack than the more remote ring sites.

In a previous communication[3] evidence pertaining to the ring rotational barrier in ferrocene was presented, and it was demonstrated that rotation of the rings with respect to one another was essentially unhindered at normal temperatures in all but the solid state.[4]

In the present paper we consider the general problem of electronic interactions in ferrocene derivatives, and in particular the effect of such interactions in determining the ease and position of entry of an acetyl group into the substituted ferrocene ring during the course of electrophilic substitution.

The acetylation of ethylferrocene (Ia) has been shown to lead to the formation of three isomeric acetyl-ethylferrocenes (IIa, IIIa, IVa).[3] From the proportion in which these isomers are formed, the relative reactivities of each of the non-equivalent ring cites in ethylferrocene were estimated to be 1′:2:3 = 1:1.4:4.2.

The somewhat greater reactivity of both positions within the alkylated ring compared with sites in the unsubstituted ring is most readily understandable in terms of a more effective inductive or hyperconjugative activation of the substituted ring by the alkyl group. Such activation bears a close qualitative analogy with the effect of alkyl substitution on the reactivity of

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[1] Presented in part at the 133rd Meeting of the American Chemical Society, San Francisco, Calif., April, 1958.

[2] Department of Chemistry, Brandeis University, Waltham 54, Mass.

[3] M. Rosenblum and R. B. Woodward, THIS JOURNAL, **80**, 5443 (1958).

[4] Yu. T. Struchkov, *Zhur. Obshch. Khim.*, **27**, 2039 (1957), has estimated that the potential barrier to rotation of the rings in ferrocene is appreciably higher than in ethane, but somewhat lower than in biphenyl.