The new and recalculated values for separate rate constants, and the ratio of k_1/k_2, for the saponification of the five esters are given in Table I.

TABLE I

RATES OF SAPONIFICATION OF DIETHYL ESTERS, 25°. INITIAL CONCENTRATION = 0.025 mole/l.

Diethyl ester	$k_1 \times 10^4$	$k_2 \times 10^4$	k_1/k_2
	l. mole^{-1} sec.$^{-1}$		
2-Methoxyisophthalate, Run 1	45.6	9.31	4.90
Run 2	46.4	9.46	4.90
5-Methoxyisophthalate	89.7	7.40	12.11
Phthalate	13.2	2.65	4.97
Isophthalate, Run 1	82.2	6.07	13.55
Run 2	79.7	5.88	13.55
Terephthalate,[a] Run 1	153	7.10	21.72
Run 2	157	7.20	21.72

[a] Crystals separated from the reaction mixture.

In a previously reported study[5] of the rate of saponification of diethyl phthalate in 91% ethanol a value of $k_1/k_2 = 2.5$ was obtained at 40.° Wegscheider[6] reported a ratio of about 2 for k_1/k_2 at 25°. In the present work the ratio (4.97) was found to be about double those originally reported. As has been noted[7] already the rate of saponification for the isomeric phthalates increases in the order diethyl phthalate, diethyl isophthalate, and diethyl terephthalate, the last being the fastest. The major increase is evidenced in the rate for the saponification of the first ester group, k_1. While attack on the first ester linkage in all five diesters, Table I, is enhanced, to varying extents through the influence of the second ester group, the much lower value of k_1 for the phthalate ester suggests a shielding effect brought about by the proximity of the bulky ethyl group. In the acid-catalyzed hydrolysis of these same esters,[2] the over-all k for diethyl phthalate is again noticeably lower than the others.

In the aliphatic series,[3] *e.g.*, in the saponification of diethyl adipate in dilute aqueous solution at room temperature, the values of k_1/k_2 indicate that the second ester group saponifies at a rate several times slower than the first group. Westheimer[8] attributes such effect to the electrostatic repulsion between the attacking hydroxyl ion and the monoethyl adipate anion. Since, under the conditions of saponification presently used (Table I) the rate constant for the saponification of ethyl benzoate was found[2] to be 6.3×10^{-4} l. mole^{-1} sec.$^{-1}$, which is close to the k_2 values in Table I, the electrostatic repulsion effect of the monoethyl phthalate anions would seem to be of lesser importance than the accelerating influence of the second ester group previously mentioned (indicated by the high k_1 values).

The position effect of the methoxyl groups in the substituted isophthalates on the saponification rate of the first ester linkage appears to be normal. The values for k_1 in Table I agree with the previously observed structural relations in that saponification is slightly faster when the methoxyl is *meta* and slower when *ortho* to the ester groups.

With the exception of the references cited for phthalate, the k_1 and k_2 values, and their ratios, for the isomeric esters had hitherto not been reported.

EXPERIMENTAL

The diethyl esters were purified by distillation in a Podbielniak spinning-band column or by recrystallization: diethyl phthalate, n_D^{20} 1.5021; diethyl isophthalate, n_D^{20} 1.5071; and diethyl terephthalate, m.p. 44°.

Saponification procedure. Reaction mixtures (100 ml.) containing 0.05 equiv. per l. of ethyl ester and of sodium hydroxide in 85% by weight ethanol were prepared. In each case 0.005 equiv. of ester and 40.6 ± 0.2 g. of aqueous ethanol (85% by weight ethanol) were weighed in 250-ml. glass-stoppered flasks and placed in a water bath maintained at 25 ± 0.1°. At the start of a reaction 50 ml. of 0.1*N* alcoholic sodium hydroxide (85% by weight ethanol), also adjusted to 25°, was added by pipet to the ester solution. To effect solution the flask was swirled in the bath for about 2 min. Zero time was taken at half the delivery time of the 50-ml. pipet. During a run at least five 10-ml. aliquots of reaction mixture were taken out at intervals and added to 15 ml. of 0.1*N* aqueous hydrochloric acid which had been cooled in ice to stop the reaction. Sampling time was taken when half the aliquot had been delivered into the acid. The resulting acid solution was promptly titrated with 0.1*N* aqueous sodium hydroxide to a greenish-blue end-point with bromothymol blue. It was established by direct titration of each of the five dibasic acids under consideration that in all cases both carboxyl groups are determined quantitatively under the analytical conditions employed. Duplicate saponification runs gave satisfactory checks.

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(5) G. Semerans, *Gazz. chim. ital.*, **65**, 252 (1935).

(6) R. Wegscheider and W. Von Amann, *Monatsch*, **36**, 549 (1915).

(7) E. Kivinen and E. Tommila, *Suomen Kemistilehti*, **14B**, 7 (1941); *Chem. Abstr.* **36**, 21.

(8) See *Advanced Organic Chemistry* by G. W. Wheland, John Wiley and Sons, Second Ed., p. 440; also F. H. Westheimer, W. A. Jones, and R. A. Lad, *J. Chem. Phys.*, **10**, 478 (1942).

Electronic Effects in the Gomberg Reaction[1]

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Received December 14, 1959

When benzene competes with chlorobenzene or nitrobenzene for phenyl radicals in a Gomberg reaction the substituted benzene reacts more rapidly.[2] If the phenyl radical is substituted by an electron

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(1) Presented at the 135th Meeting of the American Chemical Society at Boston, Mass., April 1959, Abstr., p. 47-O.

(2) D. R. Augood, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 2994 (1952).

withdrawing group the relative rate ratio $(C_6H_5X/C_6H_6)K$ is decreased.[3] This decrease in $(C_6H_5X/C_6H_6)K$ is explained by assuming that as the radical nucleus becomes more electron deficient it becomes more difficult for it to react with the already electron deficient substituted benzene. The reverse, of course, is true if one of the substituents either on the benzene or the phenyl radical is electron donating and the other electron withdrawing.[4]

However, an examination of the examples of this phenomena compiled by Augood and Williams[4] suggests that as the substituents on the phenyl radical become more electron withdrawing the $(C_6H_5X/C_6H_6)K$ ratio may approach unity as a limit, rather than decreasing indefinitely: the lowest $(C_6H_5X/C_6H_6)K$ value reported was 0.94 for the competition of nitrobenzene and benzene for *p*-nitrophenyl radicals. This rate ratio we feel is within error of unity. If the $(C_6H_5X/C_6H_6)K$ values are approaching unity (or a related number) as a limit an explanation quite different from the one offered above would be required.

We felt the problem could be resolved by determining the $(C_6H_5Cl/C_6H_6)K$ for 3,4-dichlorophenyl radicals. Since the competitive reaction of benzene and chlorobenzene for phenyl radicals[2] yields a $(C_6H_5Cl/C_6H_6)K$ of 1.4 and for *p*-chlorophenyl radicals[3] a value of 1.0, we expected 3,4-dichlorophenyl radicals to fall below unity, confirming the original explanation, or remain at unity, The results of our experiments are recorded in Fig. 1.

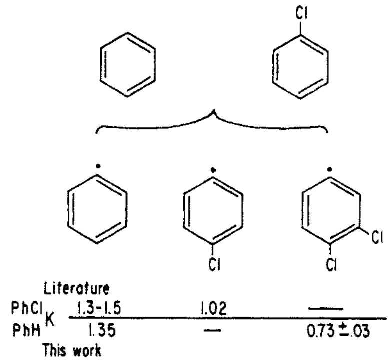

Fig. 1. Competition of benzene and chlorobenzene for various phenyl radicals

The competitive reaction with phenyl radicals was carried out to compare our method of analysis, principally vapor phase chromatography, with those of previous investigators. The $(C_6H_5Cl/C_6H_6)K$ value obtained agrees within error with those previously reported. Competition of benzene and chlorobenzene for 3,4-dichlorophenyl radicals yields a $(C_6H_5Cl/C_6H_6)K$ of 0.73 ± .03 thus confirming the original explanation.

We believe the $(C_6H_5Cl/C_6H_6)K$ of 0.73 represents the first unequivocal example of a substituted benzene reacting more slowly than benzene in a simple Gomberg reaction[5] as a result of electronic influences.[6]

EXPERIMENTAL

Competitive reaction with phenyl radicals. Benzene diazonium chloride (0.1 mole) was prepared in the usual way[7] and the aqueous solution was then stirred vigorously with a mixture of 156 g. (2.0 moles) of benzene and 225 g. (2.0 moles) of chlorobenzene the temperature being maintained between 0° and 10°. To this mixture was rapidly added a solution of sodium acetate trihydrate, 50 g. dissolved in a minimum of water. The reaction mixture was allowed to come to room temperature and the reaction was followed by measuring the nitrogen evolved. Eighty per cent of the theoretical nitrogen was evolved in 12 hr. at room temperature. The temperature was gradually raised to 70° and kept there until nitrogen evolution ceased (total evolved nitrogen, 95%). The organic phase was washed with water, dried over magnesium sulfate and the mixed solvent removed through a 3 ft. Todd distilling apparatus. The biphenyl and chlorinated biphenyl mixture was then distilled from residue through a simple Claisen head, b.p. 115–125°/3 mm., yield 30% (based on analysis of product). The distillate was analyzed directly by vapor phase chromatography.[8] Analysis of the chromatograms indicated a $(C_6H_5Cl/C_6H_6)K$ of 1.35.

Competitive reaction with 3,4-dichlorophenyl radicals. 3,4-Dichlorobenzene diazonium chloride (0.1 mole) was treated exactly as described above. After removal of the mixed solvent the chlorinated biphenyl mixture was distilled from the residue, b.p. 130–170°/3 mm., yield 55% (based on analysis of product).

Analysis: Run No. 1, $(C_6H_5Cl/C_6H_6)K$
(from % C) 0.70, (from % Cl) 0.74,
(from V.P.C.) 0.76; Run No. 2, $(C_6H_5Cl/C_6H_6)K$
(from V.P.C.) 0.75, Average equals 0.73±.03.

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[3] J. I. G. Cadogan, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 1425 (1955).

[4] D. R. Augood and G. H. Williams, *Chem. Revs.*, **57**, 170 (1957).

[5] M. J. S. Dewar and A. N. James have reported a very similar result during the decomposition of 3,5-dibromo-1,4-diazo oxide in aromatic solvents which they believe proceeds through a highly polar diradical. *J. Chem. Soc.*, 4265 (1958).

[6] Similar decreases in activity are recorded for particularly bulky substituents, *i.e.* *t*-butyl. J. I. G. Cadogan, D. H. Hey, and G. H. Williams, *J. Chem. Soc.*, 3352 (1954).

[7] D. F. DeTar and Abdul A. Kazimi, *J. Am. Chem. Soc.*, **77**, 3843 (1955).

[8] Vapor phase chromatograms were obtained with a Perkin Elmer model 154 Vapor Fractometer, using a 1.5 meter 10% silicone impregnated firebrick column at temperatures between 170° and 200°. Areas under the chromatographic peaks were measured with an Ott compensating planimeter.

Fluorinated Diuretic Agents

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Received December 17, 1959

The exceptional diuretic potency of 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide[2] and