TABLE III

REACTION CONSTANTS FOR ELECTROPHILIC REACTIONS

Reaction	ρ	s^a	c^b	n^c
Solvolysis of phenyldimethylcarbinyl chlorides in 90% aqueous acetone at 25°	− 4.62	0.274	0.980	8[d]
Nitration of monosubstituted benzene in nitromethane or acetic anhydride at 25°	− 6.53	.335	.975	9
Halogenation of monosubstituted benzenes by bromine or chlorine in acetic acid at 25°	−11.35	.690	.987	6
Protonolysis of phenyltrimethylsilanes by perchloric acid in 72% aqueous methanol at 50°	− 4.59	.215	.986	8
Brominolysis of substituted phenylboronic acids in 20% acetic acid and 0.4 *M* sodium bromide at 25°	− 4.30	.224	.991	12

[a] The standard deviation of the experimental measurements from the regression line. [b] The correlation coefficient. [c] The number of compounds involved in the calculation of ρ. [d] The value of ρ determined by a least square treatment of *m*-Me, *m*-Et, H, *m*-F, *m*-Cl, *m*-Br, *m*-I, and *m*-NO$_2$.

ered encouraging for the objective of the present study—the development of a set of substituent constants suitable for the correlation of aromatic substitution data. A rigorous test of the precise utility of these constants must await the availability of additional precise orientation and rate data for aromatic substitution.

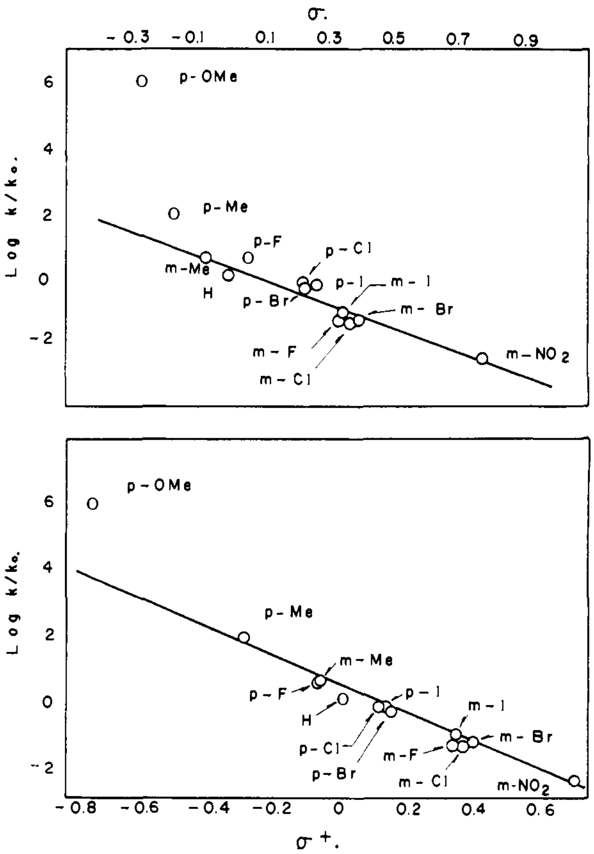

Fig. 5.—Brominolysis of phenylboronic acids in 20% acetic acid at 25°.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE A. AND M. COLLEGE OF TEXAS]

The Kinetics and Mechanism of the Reaction of Benzoic Acid and Substituted Diphenyldiazomethanes in Toluene[1]

BY C. KINNEY HANCOCK, RALPH F. GILBY, JR., AND JOHN S. WESTMORELAND

RECEIVED NOVEMBER 30, 1956

Rate constants at 25° have been determined for the reaction of benzoic acid with twelve *m*- and *p*-substituted diphenyldiazomethanes in toluene. Log k_2 values show a good linear relationship with Hammett's σ-values, the σ-values being additive for disubstituted derivatives. Excluding values for methoxy derivatives, statistical treatment of the data yields the following results: (1) equation of the regression line, $\log k_2 = -0.1440 - 1.570\sigma$, where -1.570 is the reaction constant ρ; (2) standard deviation from the regression line, 0.0422; (3) correlation coefficient, 0.9987. New σ-values may be calculated from the equation, $\sigma = -0.0905 - 0.6353 \log k_2$. The σ-value for the *p*-methoxy group is -0.361. These results support a mechanism for the reaction involving a simultaneous attack of hydroxyl hydrogen and of hydroxyl oxygen (both from benzoic acid) on the diazocarbon.

Introduction

Roberts and co-workers[2] made a kinetic study of the reaction of diphenyldiazomethane (DDM) in ethanol at 30° with benzoic acid and six *m*- and *p*-substituted benzoic acids. The second-order rate constants, obtained by following the reactions colorimetrically, were correlated with Hammett's[3] σ-values to give a ρ-value of 0.937.

Roberts and others[4a] proposed the two mechanisms shown in Fig. 1 for the reaction of benzoic acid with DDM, but they had no direct evidence in favor of either mechanism over the other. Later

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(1) Presented before the Organic Section at the 11th Southwest Regional A.C.S. Meeting, Houston, Texas, December 1, 1955. Taken in part from the Ph.D. dissertation of R. F. Gilby, Jr., The A. and M. College of Texas, May, 1954.

(2) J. D. Roberts, E. A. McElhill and R. Armstrong, THIS JOURNAL, **71**, 2923 (1949).

(3) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 188.

(4) (a) J. D. Roberts, W. Watanabe and R. E. McMahon, THIS JOURNAL, **73**, 760 (1951); (b) **73**, 2521 (1951).

they[4b] proposed a reasonable alternative mechanism involving an initial slow transfer of a proton from benzoic acid to the diazocarbon with the production of an ion-pair in a solvent "cage."

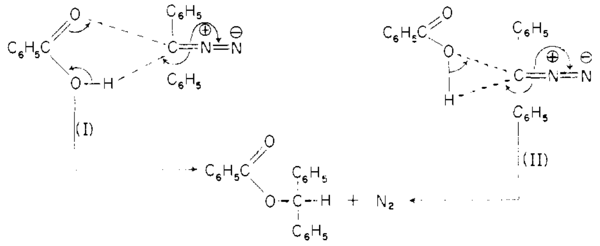

Fig. 1.—Mechanisms proposed by Roberts[4a] for the reaction of diphenyldiazomethane with benzoic acid.

For reactions of *m*- and *p*-disubstituted compounds, an additive effect of the substituents has been proposed.[5a] This means that a substituent in one ring has no effect on the influence of another substituent in the same ring or in another equivalent ring.

With the above information in mind, the objects of the presently reported study were: (1) to make a kinetic study of the reactions of substituted diphenyldiazomethanes (XDDM's) with benzoic acid, (2) to correlate the resulting rate constants with substituent constants[3] by using the additive principle[5a] and (3) to contribute to the theory of the mechanism of the reaction of DDM with benzoic acid.

Experimental

Materials.—3-Nitrobenzophenone was prepared[6a] by the Friedel–Crafts reaction from 3-nitrobenzoyl chloride and benzene. The following were prepared in a similar manner: 3-nitro-4′-methylbenzophenone from 3-nitrobenzoyl chloride and toluene, 4-bromobenzophenone from 4-bromobenzoyl chloride and benzene and 4-methoxybenzophenone from benzoyl chloride and anisole.

3,3′-Dinitrobenzophenone was prepared by nitrating benzophenone by a method similar to that of Barnett and Matthews.[7] 4,4′-Dibromobenzophenone was prepared[6b] by treating bromobenzene with carbon tetrachloride and anhydrous aluminum chloride and then hydrolyzing the bis-(4-bromophenyl)-dichloromethane.

Benzophenone and the other six substituted benzophenones were procured from commercial sources.

Hydrazones of the thirteen ketones were prepared by reaction with 95% hydrazine–5% water (Eastman Kodak Co.) by the method of Szmant and McGinnis.[8] The hydrazones were recrystallized several times from ethanol and dried *in vacuo* for two days. The melting points of the hydrazones of the following substituted benzophenones were not found in the literature: 3,3′-dinitro-, 135° (Calcd. for $C_{13}H_{10}N_4O_4$: C, 54.55; H, 3.52; N, 19.57. Found: C, 54.62; H, 3.68; N, 19.58); 3-nitro-, 84° (Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.54; H, 4.74; N, 17.35); 3-nitro-4′-methyl-, 142° (Calcd. for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 65.85; H, 5.16; N, 16.62.) The melting points of the other ten hydrazones were in good agreement with previously reported values.

The hydrazones were converted to XDDM's by oxidation with yellow mercuric oxide[9] in toluene. After recrystallization and on standing, some of the deep-colored solids decomposed rapidly, yielding the ketazines.[10] Because of this decomposition and the danger of explosion[10] with the solid XDDM's, recrystallization was abandoned. The previous careful purification of the hydrazones helped to eliminate impurities in the XDDM's. Also, since the ketazine was the most probable impurity and was formed to only a slight extent in dilute toluene solutions of most of the XDDM's less error was introduced by not purifying than would have been introduced otherwise. This method was successful as indicated by the colorless solutions obtained (except in the case of the methoxy derivatives) after complete reaction with excess benzoic acid.

Attempts to prepare bis-(4-dimethylaminophenyl)-diazomethane from the hydrazone of 4,4′-bis-(dimethylamino)-benzophenone were unsuccessful, a yellow solution being obtained which did not react with benzoic acid. A previous report[11] indicates that the yellow compound was the ketazine and that this XDDM had been impossible to prepare.

Other materials used in this study were obtained from commercial sources and were carefully purified before use.

Rate Measurements.—The procedure was similar to that of Roberts and co-workers.[2] A Beckman model B spectrophotometer was used to follow the reactions. The temperature of the laboratory was maintained at 24.8 ± 0.2°.

After scanning toluene solutions of XDDM's of various concentrations over the spectral range from 500 to 560 mμ, it was decided to use wave lengths of 520 mμ for the nitro derivatives and 550 mμ for the other XDDM's. All of the XDDM's followed Beer's law over the range of concentrations used.

XDDM solutions in toluene were prepared with an approximate optical density (O.D.) of 0.600 which corresponds to an approximate concentration of 0.00600 *M*. The concentrations were determined exactly by treating with an excess of benzoic acid and back-titrating with sodium hydroxide solution. This was done only to ensure that the benzoic acid concentration would be about ten times that of the XDDM, the XDDM concentrations not being used directly in the calculation of the rate constants.

At 25.00 ± 0.01°, 25 ml. of 0.06000 *M* benzoic acid and 25 ml. of approximately 0.00600 *M* XDDM were mixed and reacted at the same temperature. At convenient time intervals, samples of reaction mixture were transferred to the spectrophotometer cell, the O.D. measured and the sample discarded. This required about forty seconds during which no appreciable temperature change was noted. All reactions were followed over a period of at least two half-lives of XDDM decomposition. The completely reacted solutions were colorless, except for yellow solutions in the case of the methoxy derivatives.

In the case of 4,4′-dimethoxydiphenyldiazomethane, because of the short half-life of about two minutes, it was necessary to modify the procedure by retaining in the spectrophotometer cell the first sample of reaction mixture transferred from the 25.00° bath and following the reaction in this sample. No appreciable temperature change of the reaction mixture was observed during the short reaction period.

Six to nine rate determinations were made on each XDDM. The second-order rate constants were obtained by dividing the pseudo first-order rate constants by the acid concentration. The average deviation from the mean of replicate k_2 values exceeded 1% in only the cases of the following four XDDM's: 4,4′-dimethoxy-, 1.9%; 4,4′-dimethyl-, 1.6%; 4-methyl-, 1.5%; 3,3′-dinitro-, 4.4%. The maximum deviation from the mean of replicate k_2 values exceeded 2% in only the cases of the following four XDDM's: 4,4′-dimethoxy-, 2.8%; 4,4′-dimethyl-, 3.2%; 4,4′-dibromo-, 2.6%; 3,3′-dinitro-, 9.1%.

Results and Discussion

Average k_2-values and corresponding Hammett[3] σ-values are given in Table I. For disubstituted

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(5) H. H. Jaffé, *Chem. Revs.*, **[illegible]3** (1953); (a) p. 250, (b) p. 253, (c) p. 230.

(6) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1948: (a) p. 697, Method 2; (b) p. 697, Method 1.

(7) E. D. Barnett and M. A. Matthews, *J. Chem. Soc.*, **125**, 767 (1924).

(8) H. H. Szmant and C. McGinnis, This Journal, **72**, 2890 (1950).

(9) D. A. Shirley, "Preparation of Organic Intermediates," John Wiley and Sons, Inc., New York, N. Y., 1951, p. 134.

(10) H. Staudinger and J. Goldstein, *Ber.*, **49**, 1923 (1916).

(11) F. K. Beilstein, "Handbuch der Organischen Chemie," Vol. XIV, 4th Ed., J. Springer, Berlin, 1929, p. 393.

XDDM's, the σ-values listed are the sums[5a] of the σ-values for the two substituents. A plot of log k_2 *versus* σ is shown in Fig. 2.

Excluding values for the methoxy derivatives, statistical treatment[5b] of the data of Table I yields the following results: equation of the regression line

$$\log k_2 = -0.1440 - 1.570\sigma \qquad (1)$$

where -0.1440 is the value of $(\log k_2^0)_{\text{calcd.}}$ and -1.570 is the slope ρ of the regression line; standard deviation from the regression line, 0.0442; correlation coefficient, 0.9987. The regression line is shown in Fig. 2.

TABLE I

RATE AND SUBSTITUENT CONSTANTS FOR THE REACTION OF BENZOIC ACID WITH SUBSTITUTED DIPHENYLDIAZOMETHANES IN TOLUENE AT 25°

No.	Substituents	k_2, l. mole^{-1} min.$^{-1}$	$\sigma^{3,5a}$
1	4,4'-Dimethoxy-	10.06	−0.536
2	4-Methoxy-	2.65	− .268
3	4,4'-Dimethyl-	2.48	− .340
4	4-Methyl-	1.27	− .170
5	None	0.649	.000
6	4-Chloro-	.314	+ .227
7	4-Bromo-	.289	+ .232
8	4,4'-Dichloro-	.155	+ .454
9	4,4'-Dibromo-	.132	+ .464
10	3-Nitro-4'-methyl-	.119	+ .540
11	3-Nitro-	.0601	+ .710
12	3,3'-Dinitro-	.00375	+1.420

In Fig. 2, it can be seen that the rate constants decrease as the values of σ increase, the only exception being that of 4-methoxydiphenyldiazomethane which has a larger rate constant than 4,4'-dimethyldiphenyldiazomethane even though the latter has the smaller σ-value. Also, the value for 4,4'-dimethoxydiphenyldiazomethane deviates considerably from the regression line. At first it was thought that these two deviations might be due to side reactions since yellow solutions remained after complete reaction of the methoxy compounds, and it was suspected that the color was caused by ketazines formed by acid catalysis.[8] Moreover, it was observed repeatedly that the methoxy derivatives are relatively unstable on standing.

On the other hand, Jaffé[5c] has noted the unreliability of the σ value for the p-methoxy group and the following is significant in this respect. Equation 1 corresponds to minimizing the squares of the deviations along the log k_2-axis. By minimizing the squares of the deviations along the σ-axis, equation 2 may be obtained.[5b] Because of the

$$\sigma = -0.0905 - 0.6353 \log k_2 \qquad (2)$$

nearness to unity of the correlation coefficient, an equation almost identical to eq. 2 may be obtained by simply solving eq. 1 for σ. Equation 2 may be used to calculate new σ-values from experimental k_2-values. In this manner, the first two rate constants from Table I yield σ-values of -0.727 for p,p'-dimethoxy- and -0.359 for p-methoxy- which are almost in exact agreement with the additive principle[5a] of substituent effects. In view of this fact and the evidence presented below, it is believed that a σ-value of -0.361 for the p-methoxy group applies to the reaction studied. The fact that toluene solutions of the methoxy derivatives of DDM followed Beer's law shows that the rates of decomposition of these compounds were too slow to affect the kinetic study. Further, the reactions of the methoxy compounds with benzoic acid exactly followed pseudo first-order kinetics, and it is believed that the over-all rate was that of the very fast XDDM–benzoic acid reaction; that is, the rate of the slower side reactions, if any, had no appreciable effect on the over-all rate. Consequently, the large apparent deviations with the methoxy compounds are not real but are due to the inapplicability of Hammett's σ-value for the p-methoxy group. Also, the exclusion from the statistical treatment of rate constants *versus* Hammett's σ-values for the methoxy derivatives is justified.

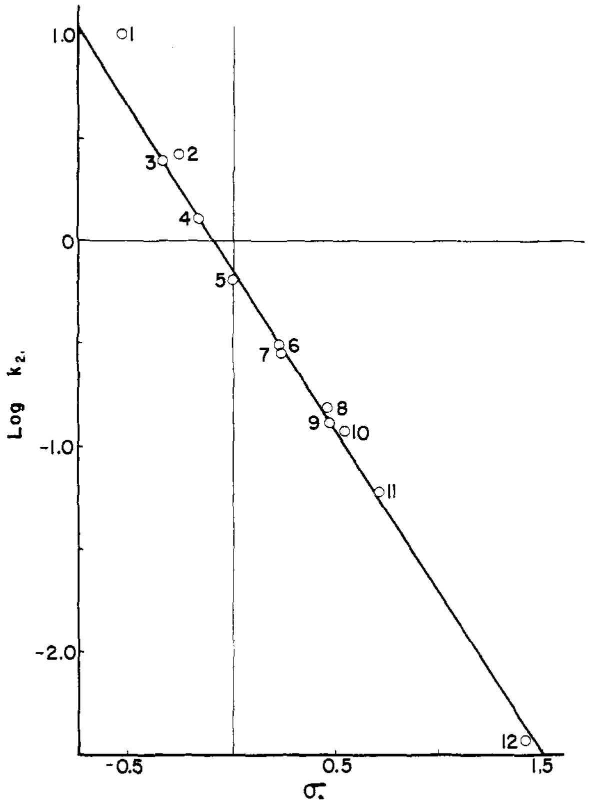

Fig. 2.—Correlation between the second-order rate constants for the reaction of benzoic acid with substituted diphenyldiazomethanes in toluene at 25° and Hammett's substituent constants.

Previously reported values have been found for only two of the rate constants given in Table I. Hoefelmeyer,[12] using the same method and equipment but materials from different sources, found a rate constant of 0.642 l. mole^{-1} min.$^{-1}$ for DDM which is in good agreement with no. 5 of Table I. Norris and Strain,[13] by following the reaction with an azotometer, found a rate constant of 2.44 l. mole^{-1} min.$^{-1}$ for 4,4'-dimethyldiphenyldiazomethane which agrees satisfactorily with no. 3 of Table I.

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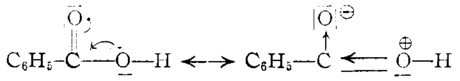
[12] A. B. Hoefelmeyer and C. K. Hancock, THIS JOURNAL, **77**, 4746 (1955).

[13] J. F. Norris and W. H. Strain, *ibid.*, **57**, 187 (1935).

The negative ρ-value means that the reaction rate is increased by the substitution of groups which increase the electron density on the diazocarbon. It is interesting to note[2] that the rate is also increased by the substitution of electron-withdrawing groups on the benzoic acid.

In the five cases where the effect of a substituent on one ring was compared to the effect of two of the same substituents on different rings, it was found that the σ-values are satisfactorily additive.[5a] The good correlation for 3-nitro-4′-methyldiphenyldiazomethane, where the nitro group with a strong deactivating effect and the methyl group with a moderate activating effect are both influencing the same reaction center, offers striking proof of the additive principle of substituent effects.

The results show that an increase in the electron density on the diazocarbon increases the rate of the reaction. This fact is consistent with either of the mechanisms shown in Fig. 1. However, consideration of resonance in the carboxyl group of benzoic acid, and the resulting partial positive charge on



$$C_6H_5-\overset{\overset{\large\cdot\cdot}{O}\,\|}{C}-\overset{..}{\underset{..}{O}}-H \longleftrightarrow C_6H_5-\overset{|\overline{O}|^{\ominus}\,\uparrow}{C}\Longleftarrow\overset{\oplus}{\underset{..}{O}}-H$$

the hydroxyl oxygen and partial negative charge on the carbonyl oxygen indicates that mechanism II, involving a simultaneous attack of hydroxyl oxygen and of hydroxyl hydrogen, is more probable since the more positive of the two oxygens is more likely to attack the nucleophilic diazocarbon.

Acknowledgment.—This study was supported in part by a research grant from the Robert A. Welch Foundation.

COLLEGE STATION, TEXAS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of the Ivanov and Reformatsky Reactions. I

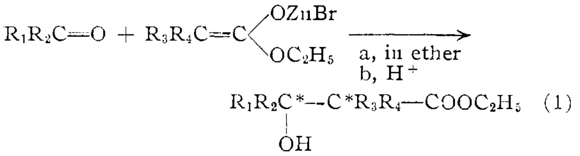
BY HOWARD E. ZIMMERMAN AND MARJORIE D. TRAXLER

RECEIVED NOVEMBER 1, 1956

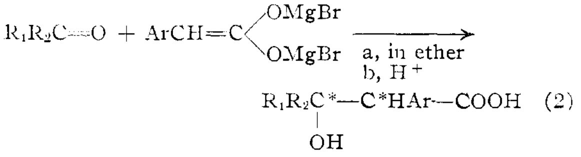
The stereochemistry of the reaction of benzaldehyde with the magnesium enolate of phenylacetic acid has been studied. In addition to the known 178° isomer of 2,3-diphenyl-3-hydroxypropionic acid, its diastereomer, m.p. 144°, was isolated as a minor product. By means of a stereospecific degradation the former was shown to be the *threo* isomer while the latter was found to have the *erythro* configuration. The ratio of the diastereomeric reaction products was determined and a hypothesis advanced to account for the preferential formation of the *threo* isomer.

The Reformatsky reaction has been known for over sixty years; its synthetic utility is undisputed. Nevertheless, little is known about its stereochemistry. Similarly, the stereochemical course of the mechanistically analogous but more recent Ivanov reaction has not been investigated.

Thus, in the reaction of an aldehyde or unsymmetrically substituted ketone with an unsymmetrically substituted Reformatsky reagent (equation 1) or Ivanov reagent (equation 2), no theory



$$R_1R_2C{=}O + R_3R_4C{=}C\begin{matrix}\nearrow OZnBr\\ \searrow OC_2H_5\end{matrix}\xrightarrow[\text{a, in ether}\atop \text{b, }H^+]{} \underset{OH}{R_1R_2C^*}-C^*R_3R_4-COOC_2H_5 \quad (1)$$



$$R_1R_2C{=}O + ArCH{=}C\begin{matrix}\nearrow OMgBr\\ \searrow OMgBr\end{matrix}\xrightarrow[\text{a, in ether}\atop \text{b, }H^+]{} \underset{OH}{R_1R_2C^*}-C^*HAr-COOH \quad (2)$$

exists for predicting whether both possible diastereomers will be formed and, if so, which will predominate. Such information would be not only of synthetic but also of intrinsic mechanistic interest. The present paper relates efforts directed toward an elucidation of the stereochemistry of these reactions, efforts which began with study of an example of the Ivanov reaction.

Perusal of the literature[1] on the Ivanov reaction showed that almost without exception[2] only one diastereomer[3] had been obtained in situations where two might have been expected. Thus it appeared that a stereospecific reaction was involved.

The present work began with the Ivanov condensation of benzaldehyde with phenylacetic acid. Previously this reaction had been reported by Ivanov[1a] to yield 2,3-diphenyl-3-hydroxypropionic acid, m.p. 175°, in 60% yield; the same product, reported as melting at 173–174°, was isolated by Blicke[1c] in an 80% yield.

In the present investigation it was found that by crystallization 53% of 2,3-diphenyl-3-hydroxypropionic acid, m.p. 177.0–178.0°, could be isolated without difficulty. Further quantities could be isolated, however, with more difficulty. By means of systematic recrystallization small quantities of a stereoisomer melting at 142.0–143.5° were isolable. With much less difficulty these acids could be separated by silica gel chromatography; in fact, it was found that this procedure could be utilized

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(1) (a) D. Ivanov and N. Nicoloff, *Bull. soc. chim.*, **51**, 1325 (1932), and earlier references cited therein; (b) A. Weston and R. DeNet, THIS JOURNAL, **73**, 4221 (1951); (c) F. Blicke and H. Raffelson, *ibid.*, **74**, 1730 (1952); (d) F. Blicke and R. Cox, *ibid.*, **77**, 5401 (1955); (e) F. Blicke and H. Zinnes, *ibid.*, **77**, 6247 (1955); (f) C. Rondestvedt and E. Rowley, *ibid.*, **78**, 3804 (1956).

(2) Ivanov (ref. 1a) reported a major and a minor product from the reaction of phenylacetic acid and isobutyraldehyde. The yield was not reported and more recent workers (ref. 1c) have been unable to isolate the minor product and to reproduce the melting point of the major product. Recently (ref. 1f) two sets of diastereomers have been reported; however, in each case the total yield was below 25% with no indication of the proportion of the isomers.

(3) The reported yields vary from much below 50% to considerably above this. In the latter situation there is a suggestion of stereospecificity; in the former case no conclusion can be drawn from isolation of only one isomer.