point with an authentic 2-chloropyridine picrate gave no depression.

Anal. Calcd. for $C_{11}H_7N_4O_7Cl$: N, 16.36. Found: N, 16.53.

ELECTROCHEMICALS DEPT.
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The Biosynthesis of Valine in *Aerobacter Aerogenes*[1]

BY MAX E. RAFELSON, JR.

RECEIVED APRIL 9, 1955

Strassman, *et al.*,[2] have shown by isotopic studies in *Torulopsis utilis* that pyruvic acid was apparently the sole source of the carbon chain of valine. The distribution of the carbon atoms of glycine and acetate as well as carbon 1 of glucose was in accord with their prior conversion to pyruvate *via* known biochemical processes.

As a result of experiments designed to study the biosynthesis of tryptophan,[3,4] various radioactive valine samples were isolated from *Aerobacter aerogenes* grown on acetate-1-C^{14}, glucose-1-C^{14} and glucose-3,4-C^{14}. These valine samples were subjected to degradation in order to determine the intramolecular distribution of the isotope. The results are presented in Table I and are identical with those obtained by Strassman, *et al.*,[2] in *T. utilis*. This may be interpreted as indicating that the biosynthetic pathways for valine in these two organisms are very similar, if not identical. The present data are in accord with the proposed mechanism for valine biosynthesis.[2] This visualized the prior conversion of glucose and acetate to pyruvate and the subsequent condensation of pyruvate and acetaldehyde (derived from pyruvate by decarboxylation) to yield α-acetolactate which undergoes a pinacol-like rearrangement to form the keto analog of valine.

TABLE I

INTRAMOLECULAR DISTRIBUTION OF GLUCOSE AND ACETATE CARBON IN VALINE

Valine carbon atom	Total activity in valine, % Glucose C-1	Glucose C-3,4	Acetate C-1
1	2	100	99
2	4	0	0
3	4	0	0
4,4[1]	90	0	0

Experimental

The cultivations of the organism on acetate-1-C^{14} and on glucose-3,4-C^{14} have been described in previous publications.[3,4] The details of the glucose-1-C^{14} cultivation[5] were very similar to those of the cultivation on glucose-3,4-C^{14}. The procedures for the assay of radioactivity have also been presented in detail.[3,4,6]

Following the removal of tryptophan, tyrosine and phenylalanine from the hydrolysates,[3,6] glutamic and aspartic acids were separated from the hydrolysate according to Cannan.[7] The remaining amino acids were separated on a column of Dowex-50.[8] The fractions containing valine were treated as described by Ehrensvärd, *et al.*[9] The identity and purity of the valine samples were determined by filter paper chromatography and radioautography.

The methods for the degradation of valine were essentially those of Strassman, *et al.*,[2] the differences being minor.

(1) Supported in part by a grant (G-4175) from the National Institutes of Health, United States Public Health Service.

(2) M. Strassman, A. J. Thomas and S. Weinhouse, THIS JOURNAL, **77**, 1261 (1955).

(3) M. E. Rafelson, G. Ehrensvärd, M. Bashford, E. Saluste and C. G. Hedin, *J. Biol. Chem.*, **211**, 725 (1954).

(4) M. E. Rafelson, *ibid.*, **213**, 479 (1955).

(5) M. E. Rafelson, to be published.

(6) M. E. Rafelson, G. Ehrensvärd and L. Reio, *Exptl. Cell Research*, in press (1955).

(7) R. K. Cannan, *J. Biol. Chem.*, **152**, 401 (1944).

(8) W. H. Stein and S. Moore, *Cold Spring Harbor Symposia Quant. Biol.*, **14**, 179 (1950).

(9) G. Ehrensvärd, L. Reio, E. Saluste and R. Stjernholm, *J. Biol. Chem.*, **189**, 93 (1951).

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Steric Effects on Migration Aptitudes. Reaction of Some *o*-Substituted Benzophenones with Peroxyacetic Acid

BY WILLIAM H. SAUNDERS, JR.

RECEIVED FEBRUARY 16, 1955

It has been known for some time that the migration aptitude of a *p*-substituted phenyl group in the pinacol and allied rearrangements depends upon the electron-releasing ability of the substituent. The abnormally low migration aptitudes of *o*-substituted phenyl groups have been explained on the basis of a steric effect,[1] and recently the nature of this steric effect has been discussed in some detail.[2] According to this viewpoint the migrating aryl group must adopt a rotational conformation such that the π-electrons of the ring may effectively overlap the vacant (or partially vacant) *p*-orbital left by the departing group on the migration terminus. An *o*-substituent interferes with this process and thus lowers the mobility of the group.

The data on the pinacol rearrangement give no indication as to whether the major source of interference with the *o*-substituent lies in other groups on the migration origin or in groups on the migration terminus. An answer to this question would be of considerable assistance in formulating a more precise picture of the transition state for the rearrangement. One possible approach is the selection of a system in which there are no interfering substituents on the migration terminus. Kharasch[3] found that in the treatment of tertiary aromatic alcohols with hydrogen peroxide under acidic conditions, which leads to phenols and ketones, both *o*-anisyl and *o*-tolyl migrated better than phenyl, in contrast to behavior of these groups in the pinacol rearrangement. Here there is no possibility of interference by groups on the migration terminus, since the only such group in the protonated hydroperoxide intermediate is the departing $-OH_2^+$, which must be *trans* to the migrating group. Unfortunately there was not a sufficient variety of substituents employed to permit a decision concerning the degree of similarity between this reaction and the pinacol rearrangement. Another recent study of the *ortho* effect, in which Smith[4] deter-

(1) C. H. Beale and H. H. Hatt, THIS JOURNAL, **54**, 2405 (1932).

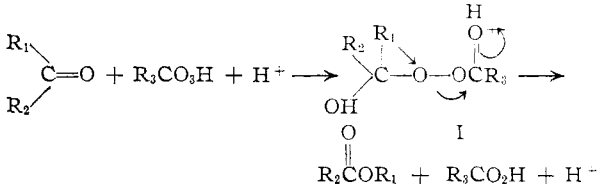
(2) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 478.

(3) M. S. Kharasch, A. Fono, W. Nudenberg and A. C. Poshkus, *J. Org. Chem.*, **15**, 775 (1950).

(4) P. A. S. Smith, THIS JOURNAL, **76**, 431 (1954).

mined product ratios in the Schmidt reaction on *o*-substituted benzophenones, does not seem to have direct bearing on the present problem. The controlling factor apparently was the relative stabilities of the isomeric intermediates, and the intrinsic migration aptitudes of the groups had little effect on the results.

The aim of the present work was to study further the migration of *o*-substituted aryl groups to cationic oxygen. For this purpose the peroxyacetic acid oxidation of appropriate benzophenones was chosen, since this reaction has been investigated thoroughly with respect to *p*-substituents[5] and was found to show qualitatively the same order of migration aptitudes as the pinacol rearrangement. A recent investigation[6] has established the mechanism of this reaction as involving addition of the peroxyacid to the ketone followed by migration of an R group to oxygen along with (probably simultaneous) departure of an acid molecule.



The results of the current study are given in Table I. It is obvious that the *ortho* effect assumes complete control when other factors are substantially equal (*o*-chlorophenyl *vs. p*-chlorophenyl) and can even overcome to some extent an electronic effect in the opposite direction (*o*-tolyl *vs.* phenyl). The electronic effect becomes dominant with *o*-anisyl, in contrast with results in the pinacol rearrangement.[1] This may be ascribed in part to the strong electron-releasing properties of the methoxyl group and in part to its ability to rotate so as to offer relatively little interference. Winstein[7] has observed that substitution of either an *o*- or *p*-methoxyl group on 2-phenylethyl *p*-bromobenzenesulfonate has about the same accelerating effect on its rate of solvolysis, which indicates similar degrees of participation in both cases.

TABLE I

REACTION OF *o*-SUBSTITUTED BENZOPHENONES WITH PEROXYACETIC ACID

Ketone RCOR'		Yields,[a] %		M.p. of
R	R'	RCOOR'	R'COOR	acid, °C.
C_6H_5	*o*-ClC_6H_5	..	71	141–142
p-ClC_6H_5	*o*-ClC_6H_5	..	80	139–142
C_6H_5	*o*-$CH_3C_6H_5$	12	38	89–95[b]
C_6H_5	*o*-$CH_3OC_6H_5$	82	..	121–122

[a] Figures are the yields of acids (based on ketone) obtained by hydrolysis of the ester products. A blank indicates the apparent absence of any isomeric product (see Experimental). [b] M.p. of mixture of acids. Total yield of crude acid was 50%.

The data available suggest that there is no essential difference between migration to carbon and migration to oxygen. Large groups on the migration origin are shown to offer a significant degree of hindrance to rotation of an *o*-substituted migrating aryl group. The more striking *ortho* effect with the pinacols suggests that interference on the migration terminus also may be involved. Another possible explanation is that these differences are simply due to varying degrees of stretching of the C-aryl bond of different systems in the transition states, which result in varying degrees of interference by the same groups on the migration origin.

An interesting consequence of these ideas is the prediction that a group which is normally a poor migrator might hinder the migration of another group to the extent that the former rather than the latter would migrate preferentially. Friess[8] has observed that reaction of cyclohexyl phenyl ketone with peroxybenzoic acid leads to a mixture of esters, cyclohexyl migrating better than phenyl by a ratio of 5:1. Models of the intermediate (I, $R_1 = C_6H_5$, $R_2 = C_6H_{11}$) show that the bulky cyclohexane ring offers considerable resistance to the attainment of the preferred rotational conformation by the benzene ring. The cyclohexyl group presumably has no such requirements and thus can migrate freely when the energy barrier to phenyl migration has been raised sufficiently. Work aimed at providing further information on this hypothesis is in progress.

Experimental

Melting points are uncorrected. Analysis by Miss A. Smith.

Materials.—A sample of *o*-methoxybenzophenone was kindly furnished by Dr. P. A. S. Smith. The 2,4'-dichlorobenzophenone was a commercial product (Eastman Kodak Co.). *o*-Chlorobenzophenone was obtained by chromic acid oxidation of *o*-chlorobenzhydrol.[9] *o*-Methylbenzophenone was prepared by the action of *o*-tolylmagnesium bromide on benzonitrile.

General Procedure.—The ketone (0.010 mole) was mixed at room temperature with 15–20 ml. of glacial acetic acid and 4–6 ml. of 40% peroxyacetic acid. The quantity of concd. sulfuric acid added was 3–4 ml., except in the case of *o*-methoxybenzophenone, where 0.2 ml. sufficed. A reaction time of 4–6 days was allowed. The reaction mixture then was diluted with 2–3 times its volume of water and extracted with an ether–pentane mixture. The extract was washed with sodium carbonate solution and dried over magnesium sulfate. The crude ester (85% yield or better in all cases) obtained on removal of the solvent was hydrolyzed by refluxing for 1–2 days with 20% sodium hydroxide. Separation of the acidic and phenolic fractions of the product was effected by conventional means. Quoted yields (Table I) are based upon crude acid which, except for the product from *o*-methylbenzophenone (see below), melted within a few degrees of the pure acid and appeared on subsequent recrystallization to be homogeneous. The phenols were not isolated in the pure state but were identified by standard derivatives. Although no consistent attempt was made to obtain these derivatives quantitatively, the yields of crude phenols approximated the acid yields.[10] Unsaponifiable material (presumably ke-

(5) W. von E. Doering and L. Speers, THIS JOURNAL, **72**, 5515 (1950).

(6) W. von E. Doering and E. Dorfman, *ibid.*, **75**, 5595 (1953).

(7) S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *ibid.*, **75**, 147 (1953).

(8) S. L. Friess and N. Farnham, *ibid.*, **72**, 5518 (1950).

(9) G. Lock and E. Rödiger, *Ber.*, **72**, 861 (1939).

(10) A referee has suggested that the ester may be unstable with respect to the conditions of reaction or of work-up. To test this possibility phenyl benzoate (m.p. 70–71°) was subjected to the reaction conditions and recovered in 83% yield (m.p. 65–68°). A similar mixture was worked up immediately after preparation to give 95% recovery of ester (m.p. 66–69°). For various reasons it seems likely that these results represent an upper limit of instability as far as the compounds used in the present work are concerned. Consequently it is doubtful that this source of error would change the qualitative trend appreciably. Unfortunately the greatest uncertainty is in *o*-tolyl *vs.* phenyl. The relatively low over-all acid yield could not be improved in three tries.

tone) was always less than 10% of the total weight of ester.

The literature value[11] (118°) for the m.p. of guiacol α-naphthylurethan was found to be erroneous. This derivative, both from our product and from an authentic sample, had m.p. and mixed m.p. 134–135° (from chloroform–hexane).

Anal. Calcd. for $C_{18}H_{15}O_3N$: C, 73.70; H, 5.16. Found: C, 73.73; H, 5.20.

Products from *o*-Methylbenzophenone.—The acid from the hydrolysate was obviously a mixture, since on crystallization from hot water two successive fractions melted at 99–101° and 105–115°. In order to determine the composition, 0.60 g. of the total acid was oxidized with alkaline potassium permanganate and the resulting 0.49 g. of colorless solid treated with hot carbon tetrachloride.[12] The insoluble phthalic acid amounted to 0.35 g. and evaporation of the extract left 0.08 g. of benzoic acid. The molar ratio of *o*-toluic to benzoic acid was thus about 3:1. From the phenolic fraction was obtained a small amount of *o*-cresoxyacetic acid by treatment with chloroacetic acid and base. The remainder of this derivative was impure phenoxyacetic acid.

(11) H. E. French and A. F. Wirtel, THIS JOURNAL, **48**, 1736 (1926).

(12) W. E. Bachmann and M. X. Barton, *J. Org. Chem.*, **3**, 300 (1938).

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Spectral Detection of a Transient Ion Pair Intermediate in the Reaction of a Triarylmethyl Chloride with Pyrrole in Benzene Solution[1,2]

BY C. GARDNER SWAIN, LAURA E. KAISER AND TERENCE E. C. KNEE

RECEIVED DECEMBER 13, 1954

Spectral detection of a transient carbonium ion intermediate has been reported previously only by Roberts and Hammett, who observed a transient yellow color in the reaction of 1.3 *M* mercuric nitrate with 1.0 *M* benzyl chloride in 60% dioxane–40% water mixture at 25°.[3] Experiments of this sort if done quantitatively should be able to furnish the concentration of reaction intermediates and the separate kinetic orders and absolute rate constants for their formation and decay. We have investigated the reaction of trianisylmethyl chloride with pyrrole at 25° in benzene solution, which gives α-trianisylmethylpyrrole, and found a transient absorption in the green region of the spectrum. The absorption maximum is at 498 mμ, close to the maximum at 483 mμ observed with trianisylcarbinol or trianisylmethyl chloride in 100% sulfuric acid. It was assumed that both colors are due to the same carbonium ion and that its extinction coefficient is the same in the two media; this was supported by showing that the extinction coefficient of trianisylmethyl perchlorate in benzene differs from that in sulfuric acid by less than a factor of four. Figure 1 is the resulting plot of carbonium concentration *vs.* time for a typical run. Table I gives data for 21 runs in which similar behavior was observed.

The maximum concentration of intermediate in all runs is proportional to the product of concentrations of chloride and pyrrole. This is demonstrated by the fact that the last column of Table I ($I_{max}/[RCl][PH]$) has an average deviation of only 7% whereas $I_{max}[PH]/[RCl]$, $I_{max}/[RCl]$, $I_{max}/[RCl][PH]^2$ and $I_{max}/[RCl][PH]^3$ have average deviations of 54, 26, 30 and 61%, respectively. This relationship suggests that all steps consuming the intermediate are of lower order by one with respect to pyrrole than the step forming it.

(1) For complete experimental data see L. E. Kaiser, Ph.D. thesis, M.I.T., February, 1954.

(2) This work was supported by the Office of Naval Research, Contract No. N5ori-07838, Project No. NR 055-198.

(3) I. Roberts and L. P. Hammett, THIS JOURNAL, **59**, 1063 (1937).

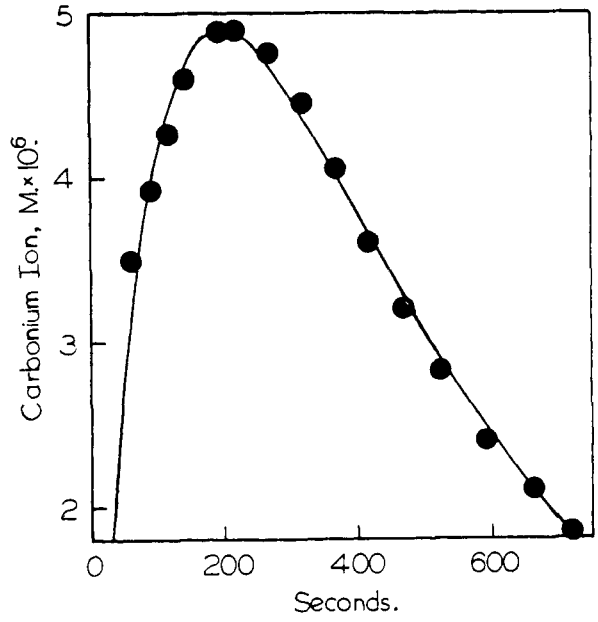

Fig. 1.—Observed points and calculated curve for trianisylmethyl ion concentration *vs.* time in the reaction of trianisylmethyl chloride with pyrrole in benzene solution at 25°, run no. 46.

TABLE I

MAXIMUM INTERMEDIATE CONCENTRATIONS[a]

Run	[RCl], $M \times 10^3$	[PH], M	I_{max},[a] $M \times 10^6$	$I_{max}/[RCl][PH]$ $M^{-1} \times 10^3$
2	2.72	0.099	1.34	4.99
5	2.45	.189	2.40	5.19
11	1.58	.198	1.62	5.18
13	3.28	.198	3.31	5.11
14	3.26	.148	2.63	5.45
16	3.26	.247	4.53	5.64
19	2.53	.142	2.24	6.24
20	2.17	.276	3.38	5.65
23	2.17	.294	3.70	5.80
27	2.00	.184	2.12	5.76
28	2.00	.163	1.70	5.22
31	3.41	.113	2.59	6.73
33	1.74	.318	3.73	6.74
35	1.74	.212	1.98	5.37
36	1.74	.269	2.82	6.02
38	2.87	.212	3.25	5.35
39	2.87	.226	3.48	5.37
42	4.10	.283	6.08	5.25
44	2.96	.339	5.84	5.82
46	4.09	.226	4.90	5.31
47	4.09	.113	2.44	5.28
			Av.	5.60 ± 0.39

[a] Maximum intermediate concentrations assuming the same extinction coefficient as in 100% sulfuric acid.