# ORGANIC AND BIOLOGICAL CHEMISTRY

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## Evidences for the Direct Field Effect. II.[1] The Alkaline Rearrangement of Fluorosubstituted α-Diketones[2]

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Previous papers have reported the migratory ratios in the alkaline rearrangement of substituted benzils and phenanthrenequinones.[1,4] A very marked proximity effect was noted in the rearrangement of 2-chlorobenzil,[1] 1-chlorophenanthrenequinone[1] and 2-methylbenzil.[4d,4e] The migration ratios in the alkaline rearrangement of 2-, 3- and 4-fluorobenzil and 1-fluorophenanthrenequinone have been determined as an extension of this study. The proximity effects observed in the latter two and the proximity effects of fluorine in related reactions are reported as supporting evidence for a direct field effect in the alkaline rearrangement of α-diketones and base-catalyzed hydrolysis of esters.

In the alkaline rearrangement of substituted benzils[1,4] and phenanthrenequinones[1,4b] it has been shown that electron-withdrawing groups in the *m*- and *p*- positions cause preferential migration of the substituted aryl group in the rearrangement. Smith and Ott[1] observed, however, a marked proximity effect in the alkaline rearrangement of 2-chlorobenzil and 1-chlorophenanthrenequinone. The proximity effect, although a well-recognized phenomenon, has received only limited study in near coplanar systems (such as phenanthrenequinone) where a forced steric relationship intensifies the interaction of functional groups.

Because the proximity effect of a strong electronegative group (*e.g.*, chlorine) proved to be very marked,[1] particularly in the case of 1-chlorophenanthrenequinone, the study has been extended to include the corresponding fluoro compound to evaluate the effect of a small, but highly electronegative group, on the rearrangement. For comparison, the rearrangement of 2-, 3- and 4-fluorobenzils have also been included in this study.

The migratory preferences were determined by using radioactive carbon. 1-Fluorophenanthrenequinone-9-$C^{14}$ was particularly difficult to obtain, and the synthesis from 2,4,6-trinitrotoluene required fifteen steps. Only known reactions were used to ensure the position of the radioactive carbon. Carbon-14 labeled fluorobenzils were obtained from fluorotoluenes.

### Results and Discussion

The migration ratios in the alkaline rearrangements of 2-, 3- and 4-fluorobenzils and 1-fluorophenanthrenequinone are summarized in Table I along with other related data. The results obtained parallel those obtained for the corresponding chloro compounds.[1,4b,4c] The 3- and 4-fluorobenzils migrated preferentially on alkaline rearrangement; when included in a Hammett $\sigma\rho$ plot, log aryl/phenyl migration ratios for these compounds showed no deviation from linearity (Fig. 1). However, in spite of the small size of the fluoro group, fluorine causes a proximity effect in the rearrangement of 2-fluorobenzil. This effect is more pronounced in the rearrangement of 1-fluorophenanthrenequinone as is also noted in Fig. 1. In the rearrangement of 1-substituted phenanthrenequinones the unsubstituted rings migrated preferentially at a particularly high ratio illustrating the marked proximity effect by substituents in this coplanar system.

TABLE I

MIGRATIONS IN THE ALKALINE REARRANGEMENT OF α-DIKETONES

| Compound | Migration ratio[a] subst./unsubst. | Migration[a] log subst./unsubst. |
|---|---|---|
| 2-Fluorobenzil | 1.90 | 0.278 |
| 3-Fluorobenzil | 2.67 | .427 |
| 4-Fluorobenzil | 0.964 | − .014 |
| 1-Fluorophenanthrenequinone | .179 | − .749 |
| 2-Chlorobenzil[b] | .409 | − .388 |
| 3-Chlorobenzil[c] | 3.69 | .567 |
| 4-Chlorobenzil[c] | 1.84 | .265 |
| 1-Chlorophenanthrenequinone[b] | $1.44 \times 10^{-2}$ | −1.842 |
| 2-Chlorophenanthrenequinone[d] | 4.45 | 0.648 |
| 3-Chlorophenanthrenequinone[d] | 1.81 | .258 |
| 4-Methoxybenzil[e] | 0.411 | − .381 |
| 4-Methylbenzil[c] | 0.570 | − .244 |
| 2-Methylbenzil[f] | $2.52 \times 10^{-2}$ | −1.599 |

[a] Corrected for $C^{12}/C^{14} = 1.11$ migratory isotope effect (refs. 4b,4c); rearrangements run at room temperature. [b] Ref. 1. [c] Ref. 4c. [d] Ref. 4b. [e] Ref. 4a. [f] Ref. 4d.

The benzilic acid rearrangement, which occurs in an alkaline medium, is known to be first order in the α-diketone, first order in the base,[5] and in the absence of any complicating factors, *e.g.*, proximity effects, the electropositive properties of the carbonyl groups determine the extent of hydroxide ion attack at a carbonyl group and likewise the migratory ratio of the aryl rings. As a result of the electronegativity of the halogens, substitution of a halogen (or similar electronegative substituent) in one ring increases the electropositive character of the carbon attached directly to the ring

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[1] For the first paper of this series, see G. G. Smith and D. G. Ott, THIS JOURNAL, **77**, 2342 (1955).

[2] (a) Presented in part before the Northwest Regional Meeting of the American Chemical Society, Spokane, Wash., June, 1957. (b) Abstracted from a thesis presented to the Graduate School of the State College of Washington by G. Olof Larson in partial fulfillment of the requirements for the Ph.D. degree, September, 1958.

[3] Dow Research Fellow, Summer, 1957; research assistant at the State College of Washington, 1956–1957, on a National Science Foundation Grant.

[4] (a) J. D. Roberts, D. R. Smith and C. C. Lee, THIS JOURNAL, **73**, 619 (1951); (b) D. G. Ott and G. G. Smith, *ibid.*, **77**, 2325 (1955); (c) M. T. Clark, E. C. Hendley and O. K. Neville, *ibid.*, **77**, 3280 (1955); (d) G. G. Smith, Research Report, National Science Foundation, January, 1958; (e) J. F. Eastham, R. G. Nations and C. J. Collins, *J. Org. Chem.*, **23**, 1764 (1958).

[5] F. H. Westheimer, THIS JOURNAL, **58**, 2209 (1936).

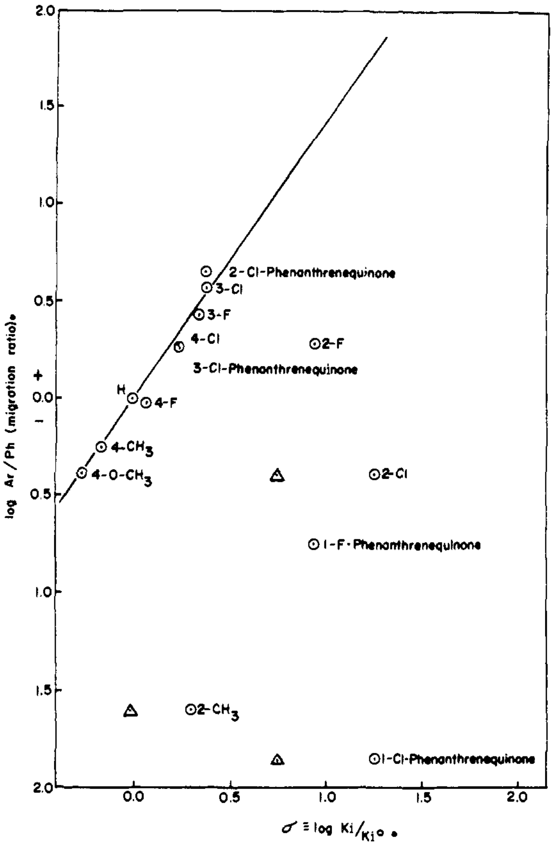

Fig. 1.—Hammett plot of the benzilic acid rearrangement (△ points are from "corrected" *o*-chloro and *o*-methyl σ-values, 0.74 and −0.2, respectively).

over that of the neighboring carbonyl and in turn causes the halo-substituted ring to migrate preferentially in comparison to phenyl. This has been observed in all cases where the halo-substituted ring was not substituted in the position next to the carbonyl group. Substitution in the *o*-position of benzil (or the 1-position in phenanthrenequinone) effected anomalous results. For example, in 1-halophenanthrenequinones the migration ratios of the substituted ring to phenylene were less than one. Such anomalous results (contrary to the results predicted from the polar effects of halogens) have often been reported for the larger halogens (Cl, Br, I) in a number of different reactions such as in the hydrolyses of *o*-substituted benzoates, but they are not commonly reported for the small fluoro substituent.[6a]

It is recognized that σ-constants for *ortho* substituents obtained in the standard fashion [$\sigma = \log K_i/K_i^0$ (ionization constants for substituted benzoic acids)][6] are subject to error because of the proximity effect (particularly that effect associated with steric inhibition of resonance).[7] Therefore, to evaluate more quantitatively the extent of the proximity effect in the alkaline rearrangement of α-diketones, it was necessary to apply corrected σ-constants.

Recently, McDaniel and Brown[8] proposed the acid dissociation constants, $K_a$, of pyridinium salts as a better reference standard than the ionization constants of benzoic acids for evaluation of purely polar effects of *ortho* substituents. They pointed out that such a system should be relatively free of *ortho* effects, *e.g.*, steric inhibition of resonance, F-strain and steric hindrance to solvation, which contribute to greater acidities in *ortho* substituted benzoic acids than would be expected on polar effects alone. Furthermore, a plot of the $pK_a$ values for substituted benzoic acids *vs.* the $pK_a$ values for substituted pyridines "permits a quantitative estimate to be made of the magnitudes of the *ortho* effects in the benzoic acid system."

From a plot of $\log K_a/K_a^0$ (pyridinium) against σ (Fig. 2 and Table II) it can be seen that all the larger *ortho* groups cause the *ortho* substituted benzoic acids to be proportionately more acidic than would be estimated on the basis of polar effects alone. Using this relationship, Hammett σ-constants for these *ortho* substituents can be corrected to the values they would have if only polar effects were operative in the ionization of an *ortho* substituted benzoic acid.

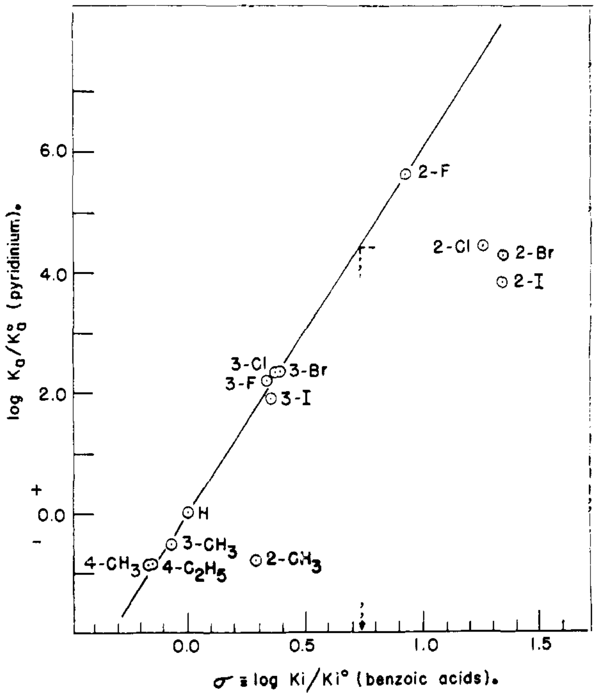

Fig. 2.—Hammett plot of pyridinium salts. Arrow at 0.74 indicates "corrected" σ-constant for *o*-chloro.

For example, $\sigma_{o\text{-chloro}}$ becomes 0.74 when referred to the substituted pyridinium bases as a reference system free of significant *ortho* effects. This value is in excellent agreement with the σ-value reported by Bray and Barnes[9] [$\sigma_{o\text{-chloro}} = 0.78$] from quadrupole resonance measurements. An *o*-fluoro substituent shows no deviation within

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[6] (a) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 204; (b) p. 185.

[7] H. C. Brown, D. H. McDaniel and O. Hafliger, in E. A. Braude and F. C. Nachod, Eds., "Determination of Organic Structures by Physical Methods," Academic Press, Inc., New York, N. Y., 1955, p. 604.

[8] D. H. McDaniel and H. C. Brown, THIS JOURNAL, **77**, 3756 (1955).

[9] P. J. Bray and R. G. Barnes, *J. Chem. Phys.*, **27**, 551 (1957).

TABLE II

DATA FOR A HAMMETT PLOT OF SUBSTITUTED PYRIDINIUM SALTS

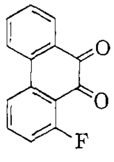
| Substituent | log $K_a/K_a^{\circ a}$ (pyr.) | $\sigma^b$ | Substituent | log $K_a/K_a^{\circ b}$ (pyr.) | $\sigma^b$ |
|---|---|---|---|---|---|
| 4-$C_2H_5$ | −0.85 | −0.151 | 3-Cl | +2.33 | +0.373 |
| 4-$CH_3$ | − .85 | − .170 | 2-Cl | +4.45 | +1.260[c] |
| 3-$CH_3$ | − .51 | − .069 | 3-Br | +2.33 | +0.390 |
| 2-$CH_3$ | − .80 | + .292 | 2-Br | +4.27 | +1.348 |
| 3-F | +2.20 | + .336 | 3-I | +1.92 | +0.352 |
| 2-F | +5.61[c] | + .936 | 2-I | +3.85 | +1.340[c] |

[a] Calculated from data reported by McDaniel and Brown, ref. 8. [b] Calculated from data reported by J. F. J. Dippy, *Chem. Revs.*, **25**, 151 (1939). [c] Corrected $\sigma$ for *c*-Cl, 0.74; see Fig. 2. There is no correction for $\sigma_{o-F}$; see Fig. 2.

experimental error and thus the Hammett $\sigma$-constant for *o*-F needs no correction.

A measure of the proximity effects (deviations from linearity) of chlorine, fluorine and a methyl group in the rearrangements of substituted benzils and phenanthrenequinones is shown in Fig. 1 where the corrected $\sigma$-constants for *o*-chloro and *o*-methyl are also given. (The *o*-fluoro showed no correction; see Fig. 2.)

The proximity effects in phenanthrenequinone are considerably more than the corresponding effects in benzil with the bulkier chlorine causing a larger deviation in both α-diketones than the small halogen (fluorine). However, the electronegative chlorine (although smaller) shows a larger proximity effect than the *o*-methyl group in benzil which gives indication that the proximity effect is not solely steric though it most probably is a major factor. A measure of the proximity effect of a methyl group in the 1-position in phenanthrenequinone will be particularly helpful in evaluation of the relative importance of the steric contribution to the polar factor in the proximity effect. With the larger halogen the proximity effect might logically be considered to include contributions from F-strain, steric hindrance to solvation[10] and possibly the direct field interaction in the near coplanar 1-chlorophenanthrenequinone. With fluorine, however, which shows no steric effect in the dissociation of *o*-fluorobenzoic acid, Fig. 2, the explanation for the proximity effect as noted in the α-diketone rearrangement must, therefore, be attributable to other influences. In 1-fluorophenanthrenequinone the C–F dipole is coplanar (or nearly so) with the neighboring C=O dipole. Therefore, the alignment of these dipoles in the rigid quinone system results in maximizing the direct field effect (dipole–dipole interaction)[11] with the resulting greater diminution of the carbonyl as a favorable site for nucleophilic attack. The direct field effect (coupled with possibly other proximity effects of the fluorine) is, therefore, sufficiently significant to dominate the normal inductive effect of the fluorine. This causes the unsubstituted aryl ring to migrate preferentially by decreasing the hydroxide ion attack on the neighboring carbonyl group and in so doing causing it to attack the more remote carbonyl group. The proximity effect in the benzil system is notably less significant as expected from consideration of the factors which influence a direct field effect. Since it is thought that the hydroxide ion approaches perpendicular to the carbonyl, models do not reveal any more steric hindrance to the approach of the hydroxide ion by a substituent in the 1-position in phenanthrenequinone than an *ortho* substituent in benzil. A greater steric problem may occur, however, in the transition state. The fact that the neutral methyl group shows a smaller proximity effect than chlorine in the rearrangement of *ortho* substituted benzil is further evidence for additional electrical effects of *ortho* halogen substituents.



Because a proximity effect of unexpected magnitude was observed for the small fluorine atom in the alkaline rearrangement of α-diketones, other reactions were considered. A Hammett plot was drawn (which includes some "corrected" $\sigma$-constants) of the log of the rate constants in the alkaline hydrolysis of ortho substituted ethyl benzoates (Fig. 3, Table III) and *ortho* substituted *trans*-ethyl cinnamates (Fig. 4, Table IV). A proximity effect, as shown in Fig. 3, was observed not only for the bulky *o*-groups (Cl, Br, $CH_3$) but also with ethyl *o*-fluorobenzoate.

TABLE III

DATA FOR HAMMETT PLOT OF THE BENZOIC ESTER HYDROLYSIS

| Substituent | log $k/k^\circ$ | $\sigma^a$ | Substituent | log $k/k^\circ$ | $\sigma^a$ |
|---|---|---|---|---|---|
| *p*-$OCH_3$ | −0.670[b] | −0.268 | *m*-$CH_3$ | −0.153[b] | −0.069 |
| | − .680[c] | | | − .157[d] | |
| *p*-$CH_3$ | − .331[b] | − .170 | *m*-F | + .801[e] | + .337 |
| | − .341[c] | | *m*-Cl | + .870[b] | + .373 |
| *p*-F | + .283[b] | + .062 | | + .885[d] | |
| | + .307[d] | | *m*-Br | + .906[b] | +0.391 |
| *p*-Cl | + .636[b] | + .226 | *o*-$CH_3$ | − .904[d] | + .292 |
| | + .634[c] | | *o*-F | + .744[b] | + .937 |
| *p*-Br | + .693[b] | + .232 | | + .572[d] | |
| | + .722[b] | | *o*-Cl | + .281[b] | +1.260 |
| *p*-$NO_2$ | +2.016[b] | + .778 | | + .350[d] | |
| | +2.063[d] | | *o*-Br | + .276[b] | +1.348 |
| *m*-$NO_2$ | +1.802[b] | + .710 | | | |
| | +1.840[d] | | | | |

[a] Calculated from data reported by J. F. J. Dippy, *Chem. Revs.*, **25**, 151 (1939). [b] K. Kindler, *Ann.*, **464**, 278 (1928); **450**, 1 (1926). [c] C. K. Ingold and W. S. Nathan, *J. Chem. Soc.*, 222 (1936). [d] D. P. Evans, J. J. Gordon and H. P. Watson, *ibid.*, 1431 (1937). [e] K. Kindler, *Ber.*, **69B**, 2792 (1936).

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[10] In a recent paper (J. Hine and H. W. Haworth, THIS JOURNAL, **80**, 2274 (1958)) it was shown that the rate of reaction was not affected appreciably by a change in the solvent from dioxane–water (2:1) to 60% dioxane–40% water. Because the change in solvent was only slight the steric effects in solvation are included until more results are known concerning the extent of the solvent effects in this reaction.

[11] The direct field effect (dipole–dipole or ion–dipole interaction) has been considered as the best explanation for the marked difference in the first and second dissociation constants of dibasic acids and the higher second dissociation constant of fumaric over maleic acid (G. N. Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalogue Co. (Reinhold Publ. Corp.), New York, N. Y., 1923, p. 144).

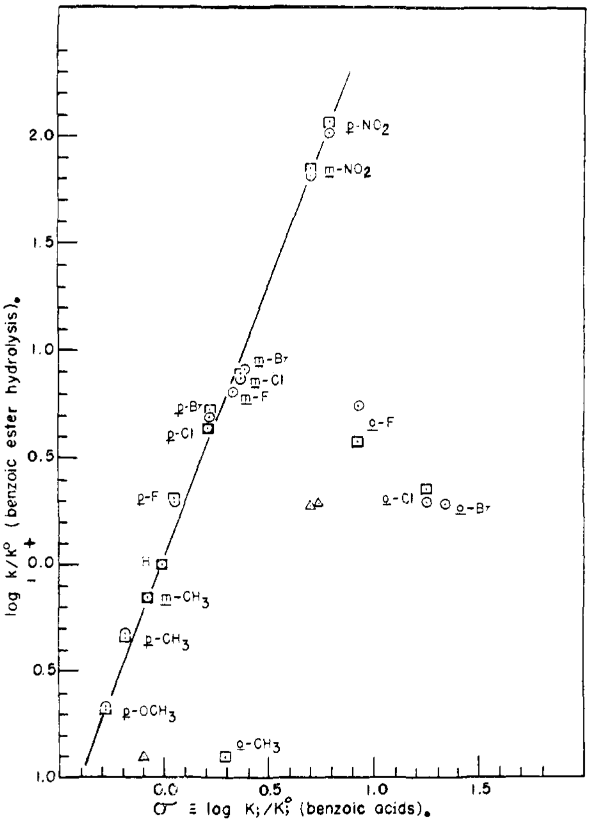

Fig. 3.—Hammett plot of benzoic ester hydrolysis; ⊙ and ⊡ are from two sources of data; see Table III (△ points are from "corrected" *o*-chloro and *o*-bromo σ-values, 0.74 and 0.70, respectively).

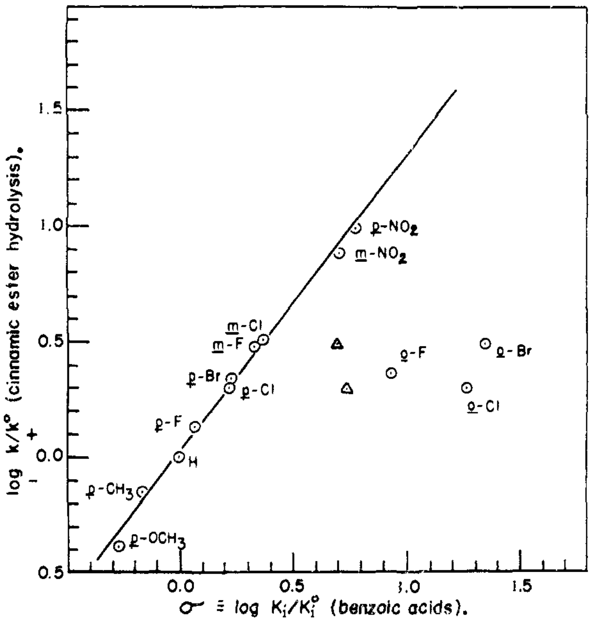

Fig. 4.—Hammett plot of cinnamic ester hydrolysis (△ points are from "corrected" *o*-chloro and *o*-bromo σ-values, 0.74 and 0.70, respectively).

Even more interesting was the discovery of a proximity effect, as measured by the deviation from linearity in a Hammett plot using corrected σ-constants, for an *o*-fluoro group in the alkaline hydrolysis of substituted *trans*-ethyl cinnamates (Fig. 4). With the reaction site sufficiently removed from the *ortho* substituents, significant steric effects from an *o*-fluoro group in this reaction (to cause the observed effect) seems improbable. These results provide further evidence for the direct field effect as part of the proximity effect with *ortho* halogen substituents in base-promoted reactions.

## Experimental[12]

**Synthesis and Rearrangement of 1-Fluorophenanthrenequinone-9-C$^{14}$. 2-Amino-6-fluorotoluene** (VII).—Compound VII was synthesized in a six-step synthesis from 2,4,6-trinitrotoluene (I) using modifications of standard procedures already reported in the literature. Brief mention of the procedures will be listed. For the details of the modifications reference is made to G. O. Larson's thesis, ref. 2b.

2,4,6-Trinitrotoluene (I) was reduced to 2,6-dinitro-*p*-toluidine (II) in a 43.6–55.6% yield, m.p. 170–171°,[13] by a procedure adapted from those of Holleman[13] and Finger and Reed.[14] Compound II was diazotized and reduced to 2,6-dinitrotoluene (III), m.p. 63–64°,[15] in a 50.4% yield. The deamination was a modification of Morton and McGookin's[16] procedure. Compound III was reduced with ammonium sulfide by the procedure described for the reduction of I. The yield of 2-amino-6-nitrotoluene (IV) was 60.4% after recrystallization from 40% acetic acid, m.p. 89–91°.[17] This amine (IV) was diazotized in the presence of fluoborate ion according to a procedure described by Roe.[18] The crude fluoborate salt V, which was formed in 82.6% yield, was pyrolyzed according to a known procedure.[19] The product, 2-fluoro-6-nitrotoluene (VI), was distilled at 90–92° (10 mm.)[20] and obtained in 49.1% yield as a light yellow-green liquid. The 2-fluoro-6-nitrotoluene was reduced with stannous chloride in hydrochloric acid following the procedure of Lock[20] and the product was obtained in 90.4% yield. The acetyl derivative melted at 131–131.5°.[21]

TABLE IV

DATA FOR HAMMETT PLOT OF THE CINNAMIC ESTER HYDROLYSIS

| Substituent | log $k/k°$ | $\sigma^a$ | Substituent | log $k/k°$ | $\sigma^a$ |
|---|---|---|---|---|---|
| *p*-OCH$_3$ | $-0.382^b$ | $-0.268$ | *m*-NO$_2$ | $+0.877^c$ | $+0.710$ |
| *p*-CH$_3$ | $-\ .148^{b,c}$ | $-\ .170$ | *m*-Cl | $+\ .504^b$ | $+\ .373$ |
| *p*-F | $+\ .136^{b,c}$ | $+\ .062$ | *m*-F | $+\ .480^b$ | $+\ .337$ |
| *p*-Cl | $+\ .307^{b,c}$ | $+\ .226$ | *o*-F | $+\ .369^c$ | $+\ .937$ |
| *p*-Br | $+\ .348^b$ | $+\ .232$ | *o*-Cl | $+\ .298^c$ | $+1.260$ |
| *p*-NO$_2$ | $+\ .990^c$ | $+\ .778$ | *o*-Br | $+\ .486^c$ | $+1.348$ |

[a] Calculated from data reported by Dippy (footnote *a*, Table III). [b] Footnote *e*, Table III. [c] Footnote *b*, Table III.

**3-Fluoro-2-methylbiphenyl** (VIII) was obtained by the Gomberg–Bachmann coupling reaction[22] according to the

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[12] All melting points are corrected. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn., and by Weiler and Strauss Microanalytical Laboratory, Oxford, England. Radiochemical analyses were performed by New England Nuclear Corp., Boston, Mass.

[13] A. F. Holleman and J. Boeseken, *Rec. trav. chim.*, **16**, 425 (1897), reported m.p. 171°.

[14] G. C. Finger and F. H. Reed, THIS JOURNAL, **66**, 1972 (1944).

[15] W. H. Gibson, R. Buckham and R. Fairbairn, *J. Chem. Soc.*, **121**, 270 (1922), reported m.p. 64.6°.

[16] R. A. Morton and A. McGooken, *ibid.*, 901 (1934).

[17] H. L. Wheeler, *Am. Chem. J.*, **44**, 126 (1910), reported m.p. 91.5°.

[18] A. Roe, in R. Adams, Ed., "Organic Reactions," Vol. V, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 205.

[19] A. Roe, *ibid.*, p. 211.

[20] G. Lock, *Ber.*, **69**, 2253 (1936), reported b.p. 97° (11 mm.).

[21] G. Lock, *ibid.*, reported m.p. 132°.

[22] W. E. Bachmann and R. H. Hoffmann, in R. Adams, Ed., "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 224.

procedure of Ott[23] for the preparation of 3-chloro-2-methylbiphenyl. Ether was used instead of benzene for extracting the reaction mixture. The yield from 32.9 g. of VI was 3.09 g. (6.31%); b.p. 88–90° (1.2 mm.) and 74–77° (0.5 mm.). An analytical sample of the yellow distillate was collected at 88° (1.2 mm.).

*Anal.* Calcd. for $C_{13}H_{11}F$: C, 83.84; H, 5.95. Found: C, 83.88; H, 5.89.

**2-Chloromethyl-3-fluorobiphenyl (IX).**—Chlorination of 3.05 g. (16.4 mmoles) of 3-fluoro-2-methylbiphenyl (VIII) was accomplished with sulfuryl chloride in the presence of benzoyl peroxide by following the procedure of Ott and Smith[4b] for the chlorination of 4-chloro-2-methylbiphenyl. The yield of IX was 1.98 g. (55.7%), b.p. 84–88° (0.18 mm.).[24]

**(3-Fluoro-2-biphenylyl)-acetic-1-$C^{14}$ acid (X)** was prepared from 1.98 g. (8.98 mmoles) of 2-chloromethyl-3-fluorobiphenyl (IX) by carbonation of the intermediate Grignard reagent with radioactive carbon dioxide by the procedure of Ott and Smith[4b] for the preparation of (4-chloro-2-biphenylyl)-acetic-1-$C^{14}$ acid. The light tan crude product weighed 0.82 g. (39.7% yield). Recrystallization from benzene–petroleum ether (b.p. 30–60°) gave 0.609 g. (29.4% yield) of white crystals, m.p. 101.5–102.5°. Sublimation of 16.9 mg. of this material at 60–70° (0.1 mm.) gave 5.2 mg. (30.7% recovery) of white product, m.p. 102.5–103°.

*Anal.* Calcd. for $C_{14}H_{11}O_2F$: C, 73.03; H, 4.82. Found: C, 72.89; H, 4.77.

**1-Fluoro-9-phenanthryl-9-$C^{14}$ acetate (XI)** was prepared in two separate runs by cyclization of 0.1636 g. (0.711 mmole) and 0.4280 g. (1.86 mmoles) of X in a zinc chloride–acetic anhydride solution[25] according to the procedure described by Ott and Smith[4b] for the 2-chloro analog. The light tan crude product (0.1790 g., 0.5766 g.)[26] was recrystallized from methanol and gave 0.0847 g. (46.9% yield) of XI, m.p. 134–136°, and 0.2751 g. (58.2% yield), m.p. 135–136°. Sublimation of 20.5 mg. of material from the latter run gave 12.3 mg. (60.0% recovery) of white crystals, m.p. 135–136°, for analysis.

*Anal.* Calcd. for $C_{16}H_{11}O_2F$: C, 75.59; H, 4.36. Found: C, 75.41; H, 4.50.

**1-Fluorophenanthrenequinone-9-$C^{14}$ (XII).**—Samples of compound XI from two runs, 0.0847 g. (0.333 mmole) and 0.2546 g. (1.002 mmoles), were dissolved separately in acetic acid and oxidized with chromium trioxide by the method reported by Ott and Smith[4b] for 2-chlorophenanthrenequinone-9-$C^{14}$. The yields of crude orange product were 80.1 and 136.7 mg., respectively. After two recrystallizations from acetic acid, bright orange needles, m.p. 236–238°, weighing 9.7 mg. (12.9% yield) and 33.9 mg. (15.0% yield) were obtained. Radioactivities are recorded in Table V.

*Anal.* Calcd. for $C_{14}H_7O_2F$: C, 74.33; H, 3.12. Found: C, 74.13, 74.33; H, 3.16, 3.31.

The combined mother liquors from the first and second recrystallizations in each run were treated separately with charcoal, filtered hot through Celite on sintered glass and concentrated before cooling; yields, 22.2 mg. (42.3%) and 50.2 mg. (22.1%), samples XIIa and XIIb, respectively, of bright orange crystals, m.p. 234–236°.

**1-Fluoro-9-fluorenone-9-$C^{14}$ (XIV).**—1-Fluorophenanthrenequinone-9-$C^{14}$ was rearranged in 8.5% potassium hydroxide solution (27.5 ml. for each mmole of XII). Duplicate runs, using products XIIa and XIIb, were made at room temperature (25–30°, shaking for 3 days) and on a steam-bath (stirring for 2 hr.). For the experiments at each temperature, the total reaction time exceeded by about one-third that necessary to cause the disappearance of the characteristic transient purple color. The final tan solution, in each case, was filtered, acidified with hydrochloric acid and extracted five times with ether. A light brown oil remained after concentrating the ether solution, and it solidified to a light tan product. This crude biphenyleneglycolic acid, XIII, was not purified further, but it was converted to XIV by oxidative decarboxylation with chromium trioxide in acetic acid (0.5 g. of chromium trioxide in 7.5 ml. of acetic acid and 3.0 ml. of water for each mmole of XII).[4a] After heating the green reaction mixture on a steam-bath for one hour, it was diluted with water (6.25 ml. for each mmole of XII); the resulting yellow precipitate was extracted three times with ether (2.5 ml. for each mmole of XII for each extraction). The ether solution was washed two times with water, twice with 10% sodium hydroxide solution and once with water; then it was treated with charcoal and anhydrous magnesium sulfate before filtration through Celite on sintered glass into a tared flask. Evaporation of the ether solution left a yellow residue of XIV (approximately 80% yield), which was recrystallized twice from methanol-water to give light yellow needles, m.p. 114–115°; the product so obtained was used for radioactivity analysis. (A third recrystallization of the product from the largest of the four runs did not change the melting point.)

TABLE V

SUMMARY OF REARRANGEMENTS OF 1-FLUOROPHENANTHRENEQUINONE-9-$C^{14}$

| Starting compound | Amount rearranged (mmole) | Rearrangement conditions | Purified product XIV, yield | M.p., °C.[a] | Radioactivity of product XIV, μc./mmole |
|---|---|---|---|---|---|
| XIIa[b] | 10.7 mg.<br>(0.0474) | A[d] | 5.3 mg.<br>(56.5%) | 113–114 | 0.0193<br>.0198 |
| | 11.5 mg.<br>(0.0508) | B[e] | 3.3 mg.<br>(32.7%) | 114–115 | .0275<br>.0233 |
| XIIb[c] | 16.7 mg.<br>(0.0738) | A | 5.7 mg.<br>(38.9%) | 113–114 | .0202<br>.0160 |
| | 33.5 mg.<br>(0.148) | B | 9.4 mg.<br>(32.0%) | 114–115 | .0302<br>... |

[a] The melting points listed are those of samples obtained after two recrystallizations from methanol. [b] M.p. 234–236°; radioactivity: 0.123, 0.113, μc./mmole. [c] M.p. 234–236°; radioactivity: 0.113, 0.103, μc./mmole. [d] Shaking at room temp., 3 days. [e] Stirring on steam-bath, 2 hr.

*Anal.* Calcd. for $C_{13}H_7OF$: C, 78.78; H, 3.56. Found: C, 78.87, 78.75; H, 3.62, 3.78.

Data from the four separate rearrangements are summarized in Table V.

**Synthesis and Rearrangement of 3′-Fluorobenzil-α-$C^{14}$ (XVII). (*m*-Fluorophenyl)-acetic-1-$C^{14}$ Acid (XV).**—This acid was prepared from 75 mmoles (9.0 g.) of *m*-fluorobenzyl chloride,[27] b.p. 78–84° (20–21 mm.), by the method described earlier for the preparation of (3-fluoro-2-biphenylyl)-acetic-1-$C^{14}$ acid (X). A 73.5% yield (8.48 g.) of light yellow crude product was obtained (m.p. 44–45°)[28]; this product was used directly in the next step.

*Anal.* Calcd. for $C_8H_7O_2F$: C, 62.30; H, 4.58. Found: C, 62.23; H, 4.57.

**2-(*m*-Fluorophenyl)-acetophenone-1-$C^{14}$ (XVI).**—By standard procedure,[29] compound XV (8.47 g., 55 mmoles) was converted—through the acid chloride—to radioactive *m*-fluorophenylacetophenone. The yield (8.69 g.), based on unrecovered acid, was 75.2%; m.p. 45–47°. (Sublimation of a small sample of the product for analysis gave white crystals, m.p. 46.5–47°.)

*Anal.* Calcd. for $C_{14}H_{11}OF$: C, 78.49; H, 5.18. Found: C, 78.71; H, 5.49.

**3′-Fluorobenzil-α-$C^{14}$ (XVII).**—A mixture of 4.00 g. (18.7 mmoles) of XVI and 2.06 g. (18.7 mmoles) of freshly sublimed selenium dioxide in 25 ml. of glacial acetic acid was heated under reflux for 3 hours; there was no apparent change after the first hour. The reaction mixture was

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(23) D. G. Ott, Thesis, Washington State University, 1953.

(24) Compound IX was not analyzed. This type of compound has been reported as difficult to purify by distillation.

(25) L. F. Fieser and E. B. Hershberg, THIS JOURNAL, **59**, 1028 (1937).

(26) For the two syntheses of XI and XII, data from the smaller of the two are cited first.

(27) This compound was prepared in 72.3% yield from *m*-fluorotoluene (Eastman 2968) by the method described above for the chlorination of 3-fluoro-2-methylbiphenyl (VIII).

(28) G. P. Hoger and E. B. Starkey, *J. Am. Pharm. Assoc.*, **32**, 44 (1943), reported that this compound was an oil.

(29) C. F. H. Allen and W. E. Barker, in A. H. Blatt, Ed., "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 156.

cooled slightly, treated with bone charcoal and filtered through Celite on sintered glass. The filtered acetic acid solution was cooled in a refrigerator. On seeding the solution with crystals of non-radioactive *m*-fluorobenzil, three dimensional star crystals were formed. The first crop of light yellow crystals weighed 3.04 g. (71.4% yield), m.p. 100.5–101.5°. Sublimation of 0.25 g. of the crude product at 85–90° (0.050 mm.) gave 0.24 g. (96% recovery) of dense yellow crystals, m.p. 100.5–101°, radioactivity 0.1230 $\mu$c./mmole.

*Anal.* Calcd. for $C_{14}H_9O_2F$: C, 73.68; H, 3.97. Found: C, 73.50; H, 4.13.

**3-Fluorobenzilic-*carboxy*-$\alpha$-$C_2^{14}$ Acid (XVIII).**—Rearrangement of XVII was as follows: 2.0 g. (8.8 mmoles) of *m*-fluorobenzil was dissolved in a solution of 1.90 g. of potassium hydroxide in 4 ml. of 95% ethanol and 4 ml. of water which was allowed to shake at room temperature overnight. The rearrangement was followed by the initial appearance and final disappearance of the characteristic transient purple color. The final reaction mixture was concentrated on a steam-bath, then diluted with water and finally extracted with ether. The aqueous layer was treated with charcoal and filtered through Celite before acidification. The precipitated acid was recovered and gave 2.03 g. (94% yield), m.p. 105–108°. Recrystallization from chlorobenzene and petroleum ether (b.p. 60–90°) gave 1.28 g. (59% yield) of white crystals, m.p. 107.5–108°.

*Anal.* Calcd. for $C_{14}H_{11}O_3F$: C, 68.29; H, 4.50. Found: C, 68.28; H, 4.73.

**3-Fluorobenzophenone-*carbonyl*-$C^{14}$ (XIX).**—Compound XVIII (0.246 g., 1.0 mmole) was converted by oxidative decarboxylation to the corresponding benzophenone by a procedure reported for the oxidation of *p*-methoxybenzilic acids.[4a] Sublimation of the crude product yielded 0.190 g. (95%) of white crystals, m.p. 52–53°, radioactivity 0.0919 $\mu$c./mmole. (Sublimation of a small sample of the product for analysis gave white crystals, m.p. 52.5–53°.)

*Anal.* Calcd. for $C_{13}H_9OF$: C, 77.99; H, 4.53. Found: C, 78.13; H, 4.65.

**Synthesis and Rearrangement of 4′-Fluorobenzil-$\alpha$-$C^{14}$ (XXII). (*p*-Fluorophenyl)-acetic-1-$C^{14}$ Acid (XX).**—This compound was prepared from 9.0 g. (75 mmoles) of *p*-fluorobenzyl chloride[30] (b.p. 84–85° (30 mm.)) in 33% yield by the method used for the preparation of the *m*-fluoro isomer XV. The melting point of the creamy-white, crude product (3.81 g.) was 83.5–84.5°.[31] This product was used directly in the next step. (Sublimation of a small sample gave white crystals which melted sharply at 86°.[31])

**2-(*p*-Fluorophenyl)-acetophenone-1-$C^{14}$ (XXI).**—Compound XX (3.85 g., 25 mmoles) was converted to 2-*p*-fluorophenylacetophenone by the procedure described above for the preparation of the *m*-fluoro isomer XVI. The yield (4.57 g.), based on unrecovered acid, was 91%; m.p. 108.5–110°. (Sublimation of a small sample for analysis gave white crystals, m.p. 110–110.5°.)

*Anal.* Calcd. for $C_{14}H_{11}OF$: C, 78.49; H, 5.18. Found: C, 78.64; H, 5.21.

**4′-Fluorobenzil-$\alpha$-$C^{14}$ (XXII).**—Compound XXI (4.60 g., 21.5 mmoles) was oxidized to the corresponding benzil by the procedure described for the oxidation of the *m*-fluoro isomer XVI. The product weighed 4.43 g. (90.5% yield), m.p. 62–63°. Sublimation of a small sample gave yellow crystals, m.p. 63.5–64.5°, radioactivity 0.306 $\mu$c./mmole.

*Anal.* Calcd. for $C_{14}H_9O_2F$: C, 73.68; H, 3.97. Found: C, 73.59; H, 3.94.

**4-Fluorobenzilic-*carboxy*-$\alpha$-$C_2^{14}$ Acid (XXIII).**—Rearrangement of 2.0 g. (8.8 mmoles) of XXII was carried out at room temperature (about 25°) by the procedure described for rearrangement of the *m*-fluoro isomer XVII. Recrystallization of the crude product from chlorobenzene and petroleum ether (b.p. 60–90°) gave 1.00 g. (46% yield) of very light tan crystals, m.p. 113–114°.

*Anal.* Calcd. for $C_{14}H_{11}O_3F$: C, 68.29; H, 4.50. Found: C, 68.25; H, 4.43.

**4-Fluorobenzophenone-*carbonyl*-$C^{14}$ (XXIV).**—Compound XXIII (0.246 g., 1.0 mmole) was oxidized quantitatively to the corresponding benzophenone by the procedure used for oxidation of the *m*-fluoro isomer XVIII. The crude product weighed 0.20 g. (100% yield), m.p. 43.5–45.5°. Sublimation of 0.18 g. of this product gave 0.16 g. (88% recovery) of white crystals, m.p. 46.5–47.5°,[32] radioactivity 0.158 $\mu$c./mmole.

*Anal.* Calcd. for $C_{13}H_9OF$: C, 77.9; H, 4.53. Found: C, 78.04; H, 4.69.

**Rearrangement of 2′-Fluorobenzil-$\alpha$-$C^{14}$. 2-Fluorobenzilic-*carboxy*-$\alpha$-$C_2^{14}$ Acid (XXV).**—Rearrangement of a 2.0-g. (8.8 mmoles) sample of radioactive *o*-fluorobenzil[33,34] at 25° according to the procedure used with *m*-fluoro isomer gave 0.18 g. (83% yield) of radioactive *o*-fluorobenzilic acid, m.p. 166–167°,[35] radioanalysis 1.375 $\mu$c./mmole.

**2-Fluorobenzophenone-*carbonyl*-$C^{14}$ Oxime (XXVI).**—Oxidative decarboxylation of XXV (0.246 g., 1.0 mmole), according to the procedure described for the same reaction of the *m*-fluoro isomer XVIII, gave the related benzophenone as a light yellow oil which could not be crystallized. The oxime XXVI melted at 114–115°,[36] radioactivity 0.932 $\mu$c./mmole.

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PULLMAN, WASH.

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[30] This compound was prepared in 87.0% yield from *p*-fluorotoluene (Eastman 2969) by the method described above for the chlorination of 3-fluoro-2-methylbiphenyl (VIII).

[31] J. F. J. Dippy and F. R. Williams, *J. Chem. Soc.*, 1466 (1934), reported m.p. 86°.

[32] M. S. A. Koopal, *Rec. trav. chim.*, **34**, 157 (1915), reported m.p. 52°; E. Bergman, H. Hoffman and H. Meyers, *J. prakt. Chem.*, **135**, 257 (1932), reported m.p. 45–47°; R. D. Dunlop and J. H. Gardner, THIS JOURNAL, **55**, 1665 (1933), reported m.p. 48.2–48.7.°

[33] This compound was prepared by R. B. Casebier, Senior research problem, Washington State University, 1955.

[34] G. G. Smith and R. B. Casebier, unpublished work, reported m.p. 56–57°. *Anal.* Calcd. for $C_{14}H_9O_2F$: C, 73.68; H, 3.98. Found: C, 73.96; H, 3.97.

[35] G. G. Smith and R. B. Casebier, *ibid.*, reported m.p. 166.5–168°. *Anal.* Calcd. for $C_{14}H_{11}O_3F$: C, 68.29; H, 4.50. Found: C, 68.31; H, 4.4.

[36] G. G. Smith and R. B. Casebier, *ibid.*, reported m.p. 112°. *Anal.* Calcd. for $C_{13}H_{10}NOF$: C, 72.55; H, 4.68. Found: C, 72.81; H, 4.84. E. Bergman and A. Bondi, *Ber.*, **64**, 1474 (1931), reported m.p. 126°, dimorphous crystals—needles or octahedrals—that decompose to a yellow oil on standing.