sulfides in some solvents evidently represents another example of the $\alpha$ effect.[53]

Finally, it has been observed[54–56] that asymmetric induction, which is solvent dependent, obtains in systems related to the present study. Further work in this area should aid in the elucidation of solvent effects in rates of peroxide oxidation, since the optical induction can potentially give information on the solvation of the transition state.

**Registry No.**—*p*-Nitrodiphenyl sulfide, 952-97-6; *p*-nitrodiphenyl sulfoxide, 955-45-3; cyclohexene, 110-83-8.

**Acknowledgments.**—Generous support of this work by the Italian National Research Council (C. N. R., Rome) is gratefully acknowledged. One of us (J. O. E.) is grateful to Guggenheim Memorial Foundation for a fellowship, to Brown University for sabbatical leave, and to the University of Rome, Italy, for kind hospitality. We also wish to thank Professor F. Montanari (University of Milano, Italy) for helpful discussions.

(53) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962).

(54) R. C. Ewins, H. B. Henbest, and M. A. McKervey, *Chem. Commun.*, 1085 (1967).

(55) U. Folli, D. Iarossi, F. Montanari, and G. Torre, *Boll. Sci. Fac. Chim. Ind. Bologna*, **25**, 159 (1967); U. Folli, Abstracts, X Congresso Nazionale della Societa Chimica Italiana, Padova, Italy, June 1968, pp p XIII-43.

(56) H. B. Henbest, *Chem. Soc., Spec. Publ.*, No. 19, 83 (1965).

---

# The Alkaline Hydrolysis of Polynuclear Methyl β-Arylacrylates[1]

MICHAEL K. HOFFMAN[2] AND ERNST BERLINER[3]

*Department of Chemistry, Bryn Mawr College, Bryn Mawr, Pennsylvania 19010*

*Received August 5, 1969*

The rates of hydrolysis of 12 *trans*-methyl β-arylacrylates, $ArCH{=}CHCOOCH_3$, with Ar ranging from phenyl to 9-anthryl, were determined in 75% (by volume) aqueous acetone at 25°. The rates of seven of these compounds were also measured in 85% aqueous methanol. The compounds in which the side chain is attached to an unhindered position show only small differences in reactivity, whereas the rates of those compounds with the side chain in *peri* or *meso* positions increase with an increase in the size of Ar. The results are explained in terms of a combination of resonance and field effects. The correlation of rates with various Hückel molecular orbital reactivity parameters, as well as with parameters which express the electron-attracting field effect of aryl groups, is discussed.

Previous studies of side-chain reactivities of aromatic hydrocarbon systems, and the comparison of these reactivities with various theoretical parameters, have been hampered by the lack of exact information about the relative contributions of resonance, inductive, and steric effects. In particular, the last two effects appear to be of varying importance in determining reactivity, but neither can at present be expressed in terms of any of the available quantitative parameters.

We now wish to report data on the alkaline hydrolysis of *trans*-methyl β-arylacrylates, $ArCH{=}CHCOOMe$. This system was chosen because the reaction site is three carbons removed from the aromatic nucleus. On the basis of studies of the effect of *ortho* substituents on the dissociation constants of cinnamic acids[4] and the rates of saponification of *ortho*-substituted ethyl cinnamates,[5] it was thought that the methyl arylacrylate systems would be free, or almost free, from the steric effects of the *peri* hydrogen (the 1-naphthalene effect) which have influenced the work on other systems. On the other hand, in the arylacrylate system, the reaction site remains conjugated with the aromatic nucleus in the absence of steric effects, and the conjugation effects of the ring systems should be passed through the ethylenic side chain qualitatively unchanged and only slightly diminished. For this reason, the study of this system was anticipated to provide information concerning the relative importance of inductive and resonance effects of polynuclear aromatic hydrocarbon systems.

## Results and Discussion

The rates of hydrolysis of 12 *trans*-methyl β-arylacrylates in 75% by volume aqueous acetone were measured at 25°. Average rate constants are listed in Table I, in addition to rate constants for seven of the compounds which were also studied in 85% by volume aqueous methanol. The relationship between the rate constants in one solvent plotted against those obtained in the second is almost linear. The reaction is faster in the more aqueous solvent. This is due not only to the greater water content of the solvent, but also to the alkoxide–hydroxide ion equilibrium, which decreases the effective concentration of the hydroxide ions in the alcoholic solvent.[6]

In order to assess the effect of the polynuclear substituents on the rate of hydrolysis of methyl arylacrylates, it will be helpful to decide first which effects might be expected, and to what extent they manifest themselves in similar, but less complex, systems.

The saponification of ethyl cinnamates in 85% aqueous ethanol has a $\rho$ value of 1.242.[7] Electron-withdrawing substituents favor the reaction. Because of the separation of the ring and reaction site by the ethylenic bridge, the effect of substituents is compressed by a factor of about two, compared with the alkaline hydrolysis of ethyl benzoates under similar conditions ($\rho = 2.558$).[7]

Because of the greater electronegativity of sp$^2$ carbon compared with sp$^3$, aryl groups attached to

---

(1) Relative Reactivities of Polynuclear Aromatic Systems. VI.

(2) Taken from the Ph.D. Thesis of M. K. Hoffman, Bryn Mawr College, May 1968.

(3) To whom inquiries should be addressed.

(4) G. Kortüm, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworth and Co. Ltd., London, 1961; J. F. J. Dippy, *Chem. Rev.*, **25**, 151 (1939).

(5) B. Jones and J. G. Watkinson, *J. Chem. Soc.*, 4064 (1958).

(6) M. L. Bender and W. A. Glasson, *J. Amer. Chem. Soc.*, **81**, 1590 (1959).

(7) Taken from K. Bowden, *Can. J. Chem.* **41**, 2781 (1963).

TABLE I

RATE CONSTANTS FOR THE ALKALINE HYDROLYSIS OF METHYL *trans*-$\beta$-ARYLACRYLATES AT 24.9°[a]

| Ar in $ArCH{=}CHCOOCH_3$ | Registry no. | $k_2 \times 10^4$ in acetone | $k_2 \times 10^4$ in methanol | $N_r$ | $\Delta E'$ [b] | $\Sigma\, 1/(r_{ij})^2$ $(1/r^2_{benzene})$ |
|---|---|---|---|---|---|---|
| *p*-Tolyl | 20754-20-5 | 0.927 | 2.53 | | | |
| 4-Biphenylyl | 22837-75-8 | 1.52 | | 1.167 | 0.431 | 3.317 |
| 3-Phenanthryl | 22837-76-9 | 1.58 | | 1.162 | 0.430 | 3.605 |
| Phenyl | 1754-62-7 | 1.59 | 3.94 | 1.206 | 0.424 | 2.917 |
| 2-Naphthyl | 22837-78-1 | 1.59 | 4.04 | 1.176 | 0.428 | 3.331 |
| 2-Phenanthryl | 22837-79-2 | 1.77 | 4.75 | 1.154 | 0.427 | 3.543 |
| 2-Anthryl | 22837-80-5 | 1.85 | | 1.132 | 0.431 | 3.504 |
| 1-Naphthyl | 22837-81-6 | 2.54 | 6.18 | 1.114 | 0.446 | 3.647 |
| 1-Pyrenyl | 22837-82-7 | 2.73 | | 1.032 | 0.454[c] | 4.081 |
| 9-Phenanthryl | 22844-32-2 | 2.97 | 8.05 | 1.112 | 0.446 | 4.061 |
| 7-Benzanthryl | 23043-02-9 | 3.64 | | 0.978 | 0.465[c] | 4.623 |
| 9-Anthryl | 22844-33-3 | 4.11 | 11.7 | 0.942 | 0.476 | 4.377 |

[a] Rate constants are in l. mol$^{-1}$ sec$^{-1}$. [b] $\Delta E' = \Delta E_\pi(ArCH{=}CH_2) - \Delta E_\pi(ArH)$. Computed from data in A. Streitwieser, Jr., and J. I. Brauman, "Supplemental Tables of Molecular Orbital Calculations," Pergamon Press, New York, N. Y., 1965. [c] A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley & Sons, Inc., New York, N. Y., 1961, Chapter 4, eq 35.

aliphatic carbon are electron attracting.[8] This is amply documented by examples taken from dissociation constants of appropriate acids[9] and the rates of hydrolysis of their esters. For instance, phenylacetic acid is a stronger acid than acetic acid,[4] and ethyl phenylacetate is hydrolyzed faster than ethyl acetate.[10] If this were the decisive factor, the arylacrylates should hydrolyze faster as the size of the aromatic systems and the number of rings increase.

The situation is different when the aromatic groups are directly attached to the carboxyl group. Conjugation of the aryl system with the carboxyl group stabilizes the initial state of acids or esters, but the conjugation is less important in the anion and is completely lost in the transition state for ester hydrolysis. This results, as has often been discussed,[9] in an apparent electron-releasing effect of aryl groups, which imparts on the aryl group an acid-weakening effect. Consequently, formic acid is a stronger acid than benzoic acid, and ethyl formate is hydrolyzed much faster than ethyl benzoate. This effect should make the rates of hydrolysis decrease with increasing conjugation of the aryl systems. Any loss of conjugation should enhance the rates. If the *peri* hydrogens were to interfere with coplanarity of ring and side chain, the inductive effect might become predominant. There is considerable evidence taken from the area of *ortho*-substituted benzoic acids and appropriate ethylenic acids that loss of conjugation increases acidity.[9,11] These views have been strengthened by a recent LCAO–HMO treatment of the acidity of unsaturated acids.[12] It must be expected, then, that in the absence of steric effects both conjugation and field effects will be present, but their extent is uncertain.

The data in Table I do not show a monotonous trend of increase or decrease which depends solely on the size of the aromatic system and which might have been expected if one or the other of the effects predominated. Instead, as has now been observed so frequently, the data divide themselves into two groupings. Those compounds which contain the 1-naphthalenelike structure exhibit greater difference in reactivity than those where the side chain is in a "benzenelike" unhindered position. In the latter group, there is very little difference among the unhindered compounds. The kinetic results are consistent with the possibility that the relative reactivities are a combination of the two opposing effects. In the unhindered compounds, the effects are about evenly balanced, although in the 2-phenanthryl and 2-anthryl compounds the electronegativity effects begin to be felt. In the hindered *peri* and *meso* compounds the electronegativity effects are predominant. The results on these compounds contrast with the original expectation that the ethylenic side chain would prevent interference of the *peri* hydrogens. Recent proton and $^{13}C$ nmr studies on substituted styrenes show that *ortho* methyl groups produce a small amount of deshielding, while two *ortho* methyl groups produce significantly more deshielding.[13] This has been interpreted in terms of reduced conjugation between the aromatic ring and the vinylic side chain. If *ortho* methyl groups prevent coplanarity, it is likely that *peri* hydrogens would also interfere. Space-filling models show that the side chain in the unhindered esters may lie in either of two strain-free conformations. In the *peri* compounds, steric interactions between the *peri* and the $\alpha$ hydrogens ($\alpha$ to the carboxyl group) in one of the conformations may prevent coplanarity of the ring and the side chain. In the other conformation, the interaction with the $\beta$ hydrogen is less severe but still present. The *meso* or bi-*peri* compounds will have the same unfavorable interaction in both conformations. Although the extent of the deviation is uncertain, any deviation from coplanarity will decrease the importance of the electron-donating resonance effect and will increase the importance of the electron-decreasing field effect. The increase in rate observed for the *peri* and *meso* compounds is consistent with this possibility. This increased rate need not necessarily be the result of steric loss of conjugation. In these particular compounds the field effect may by far outweigh the resonance effect, even in the absence of steric interference.

---

[8] A. D. Walsh, *Disc. Faraday Soc.*, **2**, 18 (1947).

[9] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter 13; H. C. Brown, D. H. McDaniel, and O. Häfliger in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, Chapter 14.

[10] K. Kindler, *Justus Liebigs Ann. Chem.*, **452**, 90 (1927).

[11] E. A. McCoy and L. L. McCoy, *J. Org. Chem.*, **33**, 2354 (1968).

[12] M. T. Reetz, *Tetrahedron Lett.*, No. 36, 3549 (1967).

[13] Gurudata, J. B. Stothers, and J. D. Talman, *Can. J. Chem.*, **45**, 731 (1967), and references cited therein.

If both field and conjugation effects are important in the above reactions, the results should not lend themselves to a consistent interpretation in terms of the usual MO reactivity parameters.[14] Yet some interesting aspects of such correlations emerge. The comparisons with reactivity parameters for the isolated molecule, the self-polarizabilities and free valencies, give single correlation lines with probable errors in the least-square slopes of 7.6 and 6.0%. The correlation with $\pi_{rr}$, typical of others, is shown in Figure 1. The 9-anthryl compound is predicted to be the fastest, as found, and the correlations show some of the features discussed qualitatively above. A parameter whose physical meaning is similar to that of the conjugation parameter $\Delta M$ is Dewar's reactivity number, $N_r$.[15] We used the butadienylaryl system ArCH=CHCH=CH$_2$ as a model for the methyl arylacrylate system, and $N_r$ can then be calculated from the coefficients of the nonbonding molecular orbitals of ArCH=CHCH$_2$. As in similar correlations with $N_r$, the compounds with the smallest $N_r$ react the fastest, and the correlation line has a least-square error of 7.7%.[16]

We have also calculated a parameter $\Delta E' = \Delta E_\pi$(ArCH=CH$_2$) $-$ $\Delta E_\pi$(ArH), which represents the additional stabilization energy caused by an ethylenic side chain. These values are available in the literature[17] or can be readily calculated.[14] The correlation shows that the greater the additional stabilization, the greater the reactivity (the error in the slope is 6.5%).

There is a reasonably good correlation between various HMO parameters and the logarithmic rates of hydrolysis. The deviations, in terms of conventional least-square correlation lines, are not worse than is usually encountered in such comparisons. Since the MO parameters are all interrelated mathematically, it is not surprising that similarly good correlations are obtained with all, if they are obtained with one.

Yet the situation is not satisfactory, and the goodness of the fit cannot be taken at face value. If conjugation parameters were decisive, the correlation between MO parameters and rates should indeed hold, but they should all be in the opposite direction with slopes opposite to those actually obtained. This is derived from the qualitative discussion given earlier which is based on generally accepted concepts. In the hydrolysis of ethyl arylcarboxylates, ArCOOEt[18] (but not the p$K$'s of polynuclear acids),[19] the expected order is in fact almost obtained, *i.e.*, ethyl 9-anthrylcarboxylate has the slowest rate, and this was explained in terms of conjugation effects. The interpretation, however, is obscured by the possible intervention of classical steric effects, because the esters which react the slowest are also those most susceptible to steric hindrance in ester hydrolysis.[20,21]

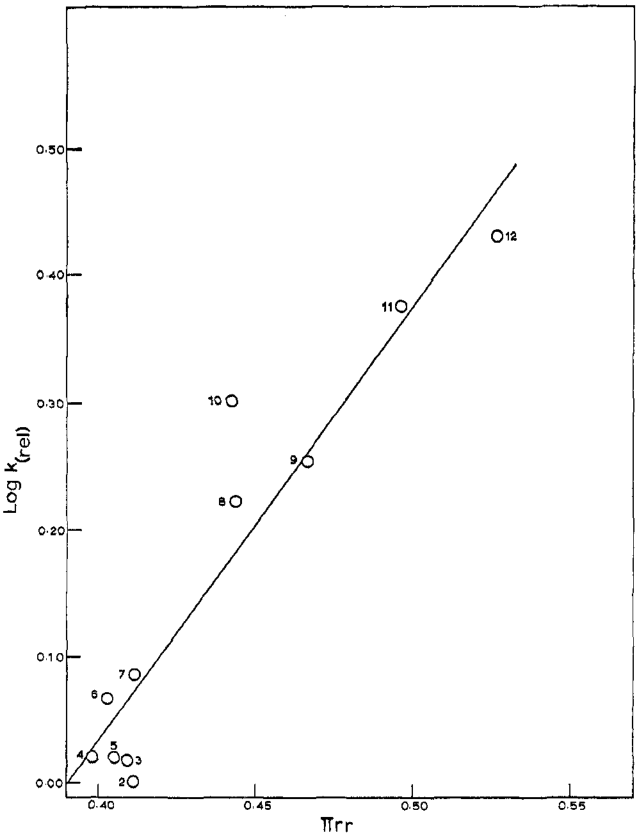


Figure 1.—Correlation of rates of hydrolysis of methyl $\beta$-arylacrylates in 75% aqueous acetone with self-polarizabilities. The numbers refer to the compounds in the order in which they appear in Table I.

One is therefore led to the conclusion that the correlations are either fortuitous in spite of their acceptable fit, or that there is in this particular system a factor, as yet unidentified, which causes an increase in conjugation energy to be responsible also for an increase in rate in ester hydrolysis. The latter is contrary to what is generally accepted.

A closer inspection of the graphs reveals that the correlations are not so satisfactory as they appear. The unhindered esters are all lumped together at the lower reactivity end. These are the compounds which behave normally in the usual correlations with side-chain reactivities. It is the compounds which usually behave abnormally which define the line. This anomalous situation is best accounted for by assuming that in the abnormal compounds the field effect, which is not encompassed in the conventional MO parameters, has become decisive, and this increases the rate.

A more satisfactory correlation must therefore be sought in parameters which express the electronegativity of aryl groups or in experimental data in which this

---

(14) A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley & Sons, Inc., New York, N. Y. 1961, Chapters 11 and 12.

(15) M. J. S. Dewar and R. J. Sampson, *J. Chem. Soc.*, 2789 (1956).

(16) The value for $\beta_{eff}$ obtained from this correlation is 2.2 kcal/mol. For the meaning of $\beta_{eff}$ see ref 15 and M. J. S. Dewar and R. J. Sampson, *J. Chem. Soc.*, 2946 (1957).

(17) A. Streitwieser, Jr. and J. I. Brauman, "Supplemental Tables of Molecular Orbital Calculations," Pergamon Press, New York, N. Y., 1965.

(18) M. Adam-Briers, P. J. C. Fierens, and R. H. Martin, *Helv. Chem. Acta*, **39**, 2021 (1955).

(19) H. Schenkel, *Experientia*, **4**, 383 (1948). The author showed that there is a relation between the p$K$'s of the acids and calculated "$\pi$-electron densities" of ArH. Actually, the theoretical figures used were the free valencies calculated by the valence-bond method.

(20) A similar order of reactivity, 9-anthryl < 9-phenanthryl < 1-naphthyl < phenyl, has been reported by Ono and Uehara for the saponification of the ethyl arylacrylates in 50% aqueous ethanol: S. Ono and M. Uehara, *Bull. Univ. Osaka Prefect., Ser. A*, **6**, 167 (1958); *Chem. Abstr.*, **53**, 1902 (1959). The authors used a glycine–NaOH buffer at pH 13 and followed the rates polarographically. They explained their results in terms of an S$_N$1 mechanism of hydrolysis. We cannot explain the discrepancy between their results and ours. However, Price and Dudley found that ethyl $\beta$-(1-naphthyl)acrylate is hydrolyzed faster than ethyl cinnamate in 70% aqueous dioxane, which is similar to our result: C. C. Price and E. A. Dudley, *J. Amer. Chem. Soc.*, **78**, 68 (1956).

(21) In the methanolysis of aryl acid chlorides, ArCOCl, the results are more similar to those obtained here: G. Geuskens, M. Planchon, J. Nasielski, and R. H. Martin, *Helv. Chim. Acta*, **42**, 522 (1959).

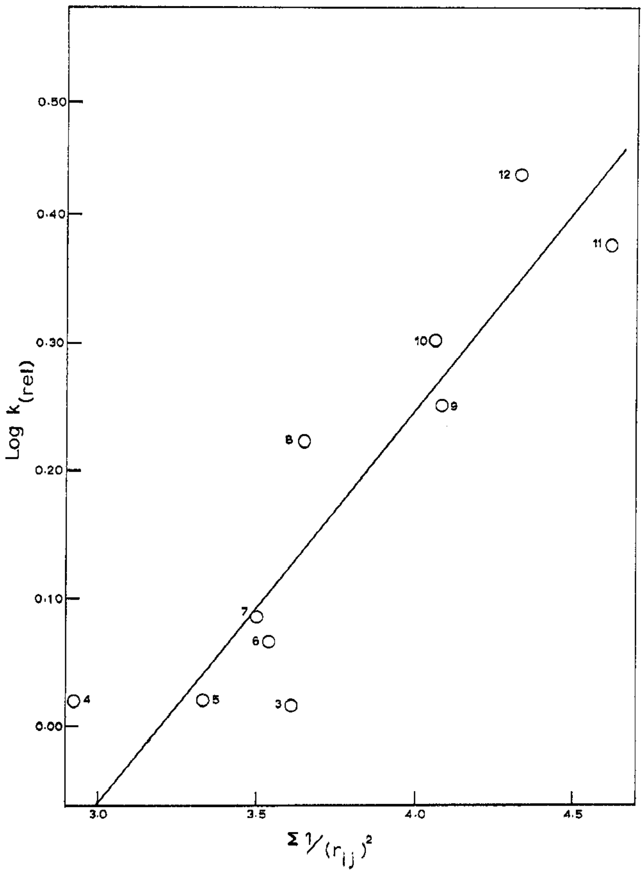


Figure 2.—Correlation of rates of hydrolysis of methyl $\beta$-arylacrylates in 75% aqueous acetone with the parameter $\Sigma\ 1/(r_{ij})^2$. The numbers refer to the compounds in the order in which they appear in Table I.

effect is known to predominate. The kinetic data qualitatively correlate well with the chemical shifts for the $^{13}C$ carbonyl in methyl aryl ketones.[22] Correlation of this sort indicates the importance of electron density at the carbonyl carbon in the methyl arylacrylates, and furthermore, the correlation is in the right direction. The carbonyl carbon in the 9-anthryl compound is the most deshielded (9-anthryl > 9-phenanthryl > 1-naphthyl > 2-naphthyl ≅ phenyl ≅ 3-phenanthryl), and the rates of hydrolysis parallel the order of deshielding.

Streitwieser and Lawler[23] have devised a field-effect parameter, $F_j = \Sigma_j 1/r_{ij}$, in which $r_{ij}$ denotes the distance between the reaction site or the ring position to which the side chain is attached and every carbon in the aromatic ring system. This parameter takes account of the size of the ring system and can be justified by the fact that the skeleton carbon atoms are in nodal planes of the aromatic $\pi$ electrons and therefore are electron attracting. The correlation of this parameter with the hydrolysis data shows a least-square error of 19%, somewhat poorer than was obtained in the correlation with hydrogen isotope exchange in arenes (4.8%)[23] and the hydrolysis of unhindered ethyl arylacetates (6.2%).[24]

A parameter $F_j' = \Sigma_j 1/(r_{ij})^2$ has been calculated for the various aryl systems. This parameter, which involves the inverse square of the distance and is characteristic of the electrostatic field of a dipole,[25] exhibits equally good correlations with the two aforementioned reactions (errors of 6.1 and 4.6%), as well as a better correlation with the hydrolysis of the methyl arylacrylates (Figure 2, 4.6% error). The improvement in fit is probably accidental because the unhindered esters still differ from prediction owing to the contribution of the resonance effect to their reactivity.

The results of the ester hydrolysis must be explained as a combination of the resonance and nonresonance effects, which have opposing influences upon rates. They are in agreement with the observation that the field and resonance effects of the phenyl group may make about equal contributions in appropriate situations.[26] They reinforce the view[23,24] that electron-attracting field effects cannot be neglected in discussions of the reactivity of polynuclear aromatic systems. In the present system field effects are of greater importance than the resonance effect, although the latter predominates in many other situations.

## Experimental Section

**Materials.**—All arylacrylic acids were prepared by the Knoevenagel synthesis from the corresponding aldehydes, malonic acid, pyridine, and piperidine. The yield of crude product was almost quantitative in most cases. Decarboxylation was spontaneous except in three cases. The crude substituted malonic acid obtained from 9-anthraldehyde was decarboxylated by heating at 180–190° for 30 min, whereas the reaction mixture from the preparation of 1-pyreneacrylic acid was heated to 150° for 10 min to complete decarboxylation. In the synthesis of $\beta$-(7-benzanthryl)acrylic acid, the dibasic acid was refluxed in boiling 1-chloronaphthalene for 1 hr. The yellow acid was recrystallized three times from glacial acetic acid and afforded yellow needles of *trans*-$\beta$-(7-benzanthryl)acrylic acid, mp 259.1–260.4°.[27]

*Anal.*[28] Calcd for $C_{21}H_{14}O_2$: C, 84.54; H, 4.73. Found: C, 84.32; H, 4.81.

Cinnamic and *p*-methylcinnamic acid were commercial samples. The aldehydes which were not available commercially, or could not be obtained by direct formylation, were prepared by the useful method of Staskun and Backeberg,[29] involving reduction of the nitrile with moist Raney nickel catalyst. The yield of crude aldehyde, prepared by this method, was 75–88%. The cyanides were synthesized from the acids (which had been obtained from the methyl ketones by hypochlorite oxidation) through the amides, which were treated with $P_2O_5$ or $POCl_3$.

All methyl esters were made by direct esterification with methanol and concentrated $H_2SO_4$ and were recrystallized from methanol–methyl acetate to constant melting point. The methyl *trans*-$\beta$-arylacrylates had the following melting points: phenyl, 34.8–35.1° (lit.[30] 36.5°); *p*-tolyl, 56.7–57.4° (lit.[31] 57–58°); 4-biphenylyl, 147.4–148.0° (*Anal.* Calcd for $C_{16}H_{14}O_2$: C, 80.64; H, 5.92. Found: C, 80.66; H, 5.99); 1-naphthyl, bp 123–124° (0.1 mm) [lit.[32] bp 167–170° (3 mm)] (this material solidified in the refrigerator after long standing; the melting point was not recorded but is *ca.* 22°); 2-naphthyl, 93.0–93.5° (lit.[33] 93.0–93.5°); 2-anthryl, 205.4–206.5° (*Anal.*

---

(22) K. S. Dhami and J. B. Stothers, *Can. J. Chem.*, **43**, 479, 498 (1965).

(23) A. Streitwieser, Jr., and R. G. Lawler, *J. Amer. Chem. Soc.*, **85**, 2854 (1963); **87**, 5388 (1965).

(24) N. Acton and E. Berliner, *ibid.*, **86**, 3312 (1964).

(25) M. J. S. Dewar and P. J. Grisdale, *ibid.*, **84**, 3541 (1962), have discussed the question as to whether the field effect should vary with the inverse first or second power of the distance and decided in favor of the former. See also ref 23.

(26) B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, **71**, 1159, 1171 (1952).

(27) Melting points below 220° are corrected; those above 220° were taken on an aluminum block and are uncorrected.

(28) All analyses were by Galbraith Laboratories, Inc., Knoxville, Tenn.

(29) B. Staskun and O. G. Backeberg, *J. Chem. Soc.*, 5880 (1964).

(30) F. M. Jaeger, *Z. Anorg. Chem.*, **101**, 1 (1917).

(31) G. R. Ramage, *J. Chem. Soc.*, 397 (1938).

(32) S. Ono and M. Uehara, *Bull. Univ. Osaka Prefect., Ser. A*, **5**, 139 (1957); *Chem. Abstr.*, **51**, 16146 (1957).

(33) V. M. Rodionov and B. I. Kurtev, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 113 (1952); *Chem. Abstr.*, **47**, 2157 (1953).

Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.37; H, 5.49); 9-anthryl, 109.7–110.5° (lit.[34] 112–113°); 2-phenanthryl, 104.0–104.7° (lit.[35] 104.5–105.5°); 3-phenanthryl, 105.7–106.8° (lit.[35] 106.0–107.0°); 9-phenanthryl, 106.9–108.0° (lit.[35] 108.0–109.0); 1-pyrenyl, 143.8–144.7° (lit.[36] 146°); 7-benzanthryl, 130.9–131.6° (*Anal.* Calcd for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.41; H, 5.16). All of the esters, as well as the acids from which they were derived, showed infrared absorptions in the region 970–960 $cm^{-1}$, indicative of the C–H bending of a *trans*-disubstituted alkene. No absorption was observed for the C–H bending of a *cis*-disubstituted alkene (*ca.* 690 $cm^{-1}$).[37] The Knoevenagel synthesis appears to result in the formation of the *trans* acids only. See, for instance, the paper by Jensen, *et al.*[38]

The solvents used in the kinetic determinations were purified by literature procedures. The aqueous solvents were prepared by mixing appropriate amounts of thermostated solvent and distilled and boiled-out water. The 85% aqueous methanol (by volume before mixing) had $n^{25}\text{D}$ 1.3357 (lit.[24] $n^{25}\text{D}$ 1.3354) and 75% aqueous acetone had $n^{25}\text{D}$ 1.3436.

**Kinetic Determinations.**—The method was similar to that described before.[24] The hydrolyzing solutions were prepared daily as described.[24] For reasons of solubility, seven of the compounds were studied at concentrations of *ca.* 0.01 *M*, four at 0.05 *M*, and one at 0.001 *M*. The second-order rate constants were found to be independent of the concentration, as shown by the following data: 1-methyl naphthylacrylate (in aqueous acetone), 0.01028 *M*, $k_2$ (in l. $mol^{-1}$ $sec^{-1}$) 0.0254; 0.01024 *M*, $k_2$ = 0.0248; 0.0050 *M*, $k_2$ = 0.0260; 2-methyl phenanthrylacrylate, 0.01027 *M*, $k_2$ = 0.0180; 0.01019 *M*, $k_2$ = 0.0177; 0.00113 *M*, $k_2$ = 0.0175. The reaction temperature was 24.89 ± 0.02°. Rate constants were obtained graphically from the integrated form of the second-order rate equation for equal concentrations. A least-square computer program was used for the final calculations.[39] The probable errors for rate constants in individual runs did not exceed 1.2%. Runs were conducted at least in duplicate, and reproducibility between duplicate runs was *ca.* 2%. The rate constants in Table I are average values of duplicate runs.

**Acknowledgment.**—This work was supported by National Science Foundation Grant GP-4986, which is gratefully acknowledged.

---

[34] J. W. Cook, R. S. Ludwiczak, and R. Schoental, *J. Chem. Soc.*, 1112 (1950).

[35] W. E. Bachmann and M. C. Kloetzel, *J. Amer. Chem. Soc.*, **59**, 2207 (1937).

[36] E. Bergmann and E. Borgrachov, *ibid.*, **62**, 3016 (1940).

[37] We thank Mr. Waldemar Palaitis of the University of Pennsylvania for his assistance with some of the infrared spectral determinations.

[38] K. A. Jensen, A. Kjaer, and S. C. Linhoft, *Acta Chem. Scand.*, **6**, 180 (1952).

[39] We gratefully acknowledge the help of Dr. Ingeborg Schuster in the design of the least-square computer program.

---

# Biologically Oriented Organic Sulfur Chemistry. IV. Synthesis and Properties of 1,2,5-Trithiepane, a Model for Study of Sulfide and Disulfide Moieties in Proximity[1a,b]

LAMAR FIELD AND CHARLES H. FOSTER[1c]

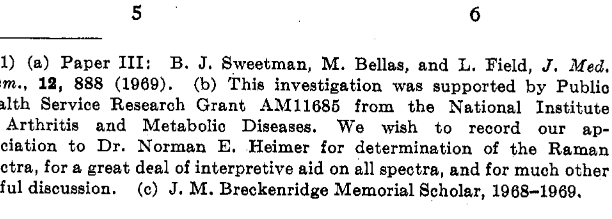
*Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203*

*Received July 8, 1969*

1,2,5-Trithiepane (**2**) was synthesized by oxidation of bis(2-mercaptoethyl) sulfide (**1**) with ferric chloride in 55% yield; attempted use of *p*-toluenesulfonyl chloride and dimethyl sulfoxide failed. Compound **2** was a liquid with properties quite different from any of three previously reported compounds tentatively or definitely considered to be **2**. Structural evidence for **2** included nmr, Raman, uv, and mass spectra, and molecular weight determination in solution. The trithiepane **2** formed a solid salt **3** with methyl iodide, and oxidation with 1 molar proportion of sodium metaperiodate gave a sulfoxide (**4**), showing that selective reactions of a cyclic sulfide are possible in the presence of a disulfide moiety. Comparative reactivities of **2**, **3**, **4**, and **6** (1,2-dithiepane), as adjudged by polymerization and cleavage with cyanide ion, and the uv spectra of **2**, **3**, **4**, and **6** suggest that interactions between the sulfide functions and disulfide bonds are not marked, a point which seems biochemically relevant.

1,2,5-Trithiepane, compound **2** in Scheme I, has been reported, or at least alluded to, three times in the literature. Rây assigned the name "diethylene trisulfide," presumably signifying **2**, to a solid, mp 96°, formed as a by-product of the reaction of "dithioethylene glycol" with benzylidene chloride.[2] Fromm and Jörg, seeking a synthesis of **2**, obtained a solid, mp 74–75°, from the reaction of bis(2-chloroethyl) disulfide with sodium sulfide;[3] in an effort to confirm the structure as that of **2**, they obtained a solid, also believed to be **2**, from the reaction of bis(2-chloroethyl) sulfide with sodium disulfide. Westlake and coworkers suggested that a colored liquid, $n^{20}\text{D}$ 1.5746, obtained as one product from the reaction of ethylene and sulfur might be **2**.[4]

SCHEME I



It was desirable to synthesize **2** in order to determine which, if any, of the previous reports were correct. A further objective was to provide a model for study of the chemistry of sulfide and disulfide moieties held in close proximity and thereby to afford information on the possibility of selective reactions and of interaction.

---

[1] (a) Paper III: B. J. Sweetman, M. Bellas, and L. Field, *J. Med. Chem.*, **12**, 888 (1969). (b) This investigation was supported by Public Health Service Research Grant AM11685 from the National Institute of Arthritis and Metabolic Diseases. We wish to record our appreciation to Dr. Norman E. Heimer for determination of the Raman spectra, for a great deal of interpretive aid on all spectra, and for much other useful discussion. (c) J. M. Breckenridge Memorial Scholar, 1968–1969.

[2] P. C. Rây, *J. Chem. Soc.*, **125**, 1141 (1924).

[3] E. Fromm and H. Jörg, *Ber.*, **58**, 304 (1925).

[4] H. E. Westlake, Jr., M. G. Mayberry, M. H. Whitlock, J. R. West, and G. J. Haddad, *J. Amer. Chem. Soc.*, **68**, 748 (1946).