to detect some of the products was not due to failure to extract them into the CH_2Cl_2 phase.

For ethylene, all three saturated esters were separated from the reaction mixtures by distillation, use being made of the solubility of the monoacetate in a water–acetic acid mixture as opposed to the organic solubility of the diacetate and chloroacetate. They were identified by physical properties, and by infrared and vpc retention times, which were identical with those of authentic samples.

For propylene, only the chloro acetate, which was mainly 1-chloro-2-acetoxypropane, determined by nmr,[23] was isolated by distillation. Standards of the mono- and diacetate esters of 1,2-propylene glycol, of 1,3-propylene glycol, and of 1-chloro-3-acetoxypropane were prepared, and the remainder of the unknowns were identified by vpc retention times.

The following butane standards were prepared by the acetylation of the corresponding glycol or chlorohydrin: 2,3-diacetate; 1,3-diacetate; 1,4-di- and 1,4-chloro acetates; and the 1,2-di- and 1,2-chloro acetates. The 2,3-chloro acetate was prepared by the reaction of the diacetate with HCl to make the chlorohydrin,[24] followed by acetylation of the chlorohydrin. The 1,3-chloro acetate was prepared by the method of Meltzer and King.[25] The 1,2-chloro acetate was prepared by reaction of 1,2-epoxybutane with concentrated aqueous HCl followed by acetylation.

3-Acetoxy-1-butene and crotyl acetate were prepared by acetylating the corresponding alcohols. 2-Acetoxy-2-butene was prepared by treating 2-butanone with acetic anhydride.[26] The 2,3-dichlorobutane was purchased from K & K Laboratories.

The treatment of 1,3-butanediol with acetyl chloride has been shown[27] to give a 60:40 mixture of 1-chloro-3-acetoxybutane and 1-acetoxy-3-chlorobutane. Vpc analysis of the reaction mixture showed that two materials were present in about this ratio. The assignment of structure of the two isomers was confirmed by the nmr of samples collected by preparative vpc. The structure assignment by nmr is based on the known chemical shifts of the methylene carbons attached to chlorine as opposed to those of the methylene carbons attached to acetate. This same procedure was used to assign the configurations of the two 1,2-chloro acetate isomers.

All products from oxidation of the butenes were identified by vpc retention times on two different columns. The identities of all the 1,3- and 2,3-di- and 1,3- and 2,3-chloro acetates were confirmed by collecting samples by preparative vpc and comparison of nmr with those authentic samples. The 1,2-diacetate and 1,2-chloro acetates were identified in the same way.

Quantitative analyses were made by comparing peak areas with the areas of standards of known concentration. Most of the values in the tables are the averages of at least two runs. Variation between runs was about 10%.

In all cases the products identified accounted for over 95% of the materials found by vpc. However, small amounts of unidentified materials, usually higher boiling, were detected. They were most likely formed by further oxidation of the initial products. One such product from the 2-butene reactions was collected by preparation vpc. Its nmr was consistent with the structure of 2-acetoxy-3-monochloroacetoxybutane.

Registry No.—Palladium(II) chloride, 7647-10-1; copper(II) chloride, 7447-39-4; acetic acid, 64-19-7; *cis*-2-butene, 590-18-1; *trans*-2-butene, 624-64-6; 1-butene, 106-98-9; ethylene, 74-85-1.

Acknowledgment.—The author gratefully acknowledges helpful discussions with Dr. H. G. Tennent and Professors S. Winstein and H. Taube and is also grateful for the assistance of Mr. John Jackson and Mr. Alan Jones with experimental work. The nmr spectra were obtained and analyzed by Dr. Mary Anderson and Dr. George Ward.

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[23] Standards of both the 1-chloro-2-acetoxy- and 1-acetoxy-2-chloropropane were prepared. The nmr of the unknown indicated that it consisted of about 90% of the former with the remainder being the secondary chloride.

[24] H. J. Lucas and C. W. Gould, *J. Am. Chem. Soc.*, **63**, 2541 (1941).

[25] R. L. Meltzer and J. A. King, *ibid.*, **75**, 1355 (1955).

[26] D. Y. Curtin and M. J. Hurwitz, *ibid.*, **74**, 5381 (1952).

[27] S. Searles, Jr., K. A. Pollart, and F. Block, *ibid.*, **79**, 952 (1957).

Substituent Effects of Positive Poles in Aromatic Substitution. II. The Nitration of Sulfonium and Selenonium Salts[1a]

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Nitration of dimethylphenylsulfonium methyl sulfate and dimethylphenylselenonium methyl sulfate with concentrated HNO_3 in concentrated H_2SO_4 results in 3.6% *ortho*, 90.4% *meta*, and 6.0% *para* and 2.6% *ortho*, 91.3% *meta*, and 6.1% *para* substitution, respectively. Dimethylnitrophenylsulfonium and -selenonium salts are dealkylated with sodium methoxide at low temperatures. Since the resulting isomeric methyl nitrophenyl sulfides and selenides can be analyzed gas chromatographically, a convenient analysis of isomeric dimethylnitrophenylsulfonium and -selenonium salts has been accomplished.

Substituent effects of positive poles in aromatic nitration have been extensively investigated and found to be predominantly, if not completely, *meta* directing.[2,3] Recent work by Ridd[4–7] and Nesmeyanov[8] indicated that in some cases considerable *para* nitration also occurred. In fact, the anilinium ion is nitrated more rapidly in the *para* position than the *meta* position and is known as a *meta–para* director,[5] while the triphenyloxonium ion is nitrated almost entirely in the *para* position.[8] These results prompted us to reinvestigate the nitration of sulfonium[1a] and selenonium salts which have been reported to nitrate exclusively in the *meta* position.[8,9]

All positive poles involving elements of groups V and VI exhibit a strong $-I$ effect.[10,11] The $-I$ effect is most effective in the *ortho* position and least effective

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[1] (a) For part I, see H. M. Gilow and G. L. Walker, *Tetrahedron Letters*, No. 48, 4295 (1965). (b) National Science Foundation Undergraduate Research Participant.

[2] P. B. D. De La Mare and J. H. Ridd, "Aromatic Substitution—Nitration and Halogenation," Butterworth and Co. Ltd., London, 1959, Chapter 6.

[3] R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier Publishing Co., Amsterdam, The Netherlands, 1965, Chapter 2.

[4] M. Brickman, S. Johnson, and J. H. Ridd, *Proc. Chem. Soc.*, 228 (1962).

[5] J. H. Ridd and J. H. P. Utley, *ibid.*, 24 (1964).

[6] M. Brickman and J. H. Ridd, *J. Chem. Soc.*, 6845 (1965).

[7] M. Brickman, J. H. P. Utley, and J. H. Ridd, *ibid.*, 6851 (1965).

[8] N. N. Nesmayanov, T. P. Tolstaya, L. S. Isaeva, and A. V. Grid, *Dokl. Akad. Nauk SSSR*, **133**, 602 (1960).

[9] J. W. Baker and W. G. Moffitt, *J. Chem. Soc.*, 1722 (1930).

[10] S. G. Cohen, A. Streitwieser, Jr., and R. W. Taft, "Progress in Physical Organic Chemistry," Vol. 2, Interscience Publishers, Inc., New York, N. Y., 1964, p 334.

[11] F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 87 (1965).

in the most distant *para* position. This appears to be an important effect in the nitration of anilinium and methylanilinium salts as is suggested by the observed yields of *para* product ranging between 38 and 11%. That no *ortho* substitution is observed is apparently due to the strong $-I$ effect.[7] The recent observation of Nesmeyanov and co-workers[8] indicating that the oxonium group is 100% *para* directing appears to be the result of a strong $-I$ effect and a conjugative electron release from the positive pole.[3]

The sulfonium and selenonium poles have strong $-I$ effects,[11] have filled p orbitals which can interact with the aromatic π electrons activating the aromatic ring toward electrophilic substitution, and have empty d and s orbitals available that can interact with the aromatic π electrons deactivating the aromatic ring toward electrophilic substitution. These effects and others must be taken into consideration when considering the substituent effects of the sulfonium and selenonium groups.

Results and Discussion

The orientation results of the nitration of dimethylphenylsulfonium methyl sulfate (**1**) and dimethylphenylselenonium methyl sulfate (**2**) in concentrated H_2SO_4 and HNO_3 are listed in Table I along with the results of nitration of other salts in groups V and VI.

TABLE I

ISOMER DISTRIBUTION OBTAINED IN NITRATION OF AROMATICS HAVING POSITIVE POLES[a]

Aromatic	*ortho*, %	*meta*, %	*para*, %
$C_6H_5N(CH_3)_3{}^{+}$ [b]	0	89	11
$C_6H_5P(CH_3)_3{}^{+}$ [b]	0	97	3
$C_6H_5As(CH_3)_3{}^{+}$ [b]	0	96	4
$C_6H_5O(C_6H_5)_2{}^{+}$ [c]	0	0	100[d]
$C_6H_5S(CH_3)_2{}^{+}$	3.6 ± 0.2	90.4 ± 0.3	6.0 ± 0.2
$C_6H_5Se(CH_3)_2{}^{+}$	2.6 ± 0.2	91.3 ± 0.3	6.1 ± 0.2

[a] Nitrations were carried out in H_2SO_4 and HNO_3. [b] Reference 5. [c] Reference 8. [d] Using nitromethane as solvent and NO_2BF_4 as nitrating agent, 95% *para* and 5% *ortho* substitution was observed.

Considering the fact that the phenyloxonium ion is nitrated exclusively in the *para* position in concentrated H_2SO_4 and HNO_3, it is surprising that the phenylsulfonium ion yields only 6% of the *para* product. The oxonium group would be expected to have a larger $-I$ effect than the sulfonium group. The $-I$ effect coupled with the availability of the p electrons on oxygen to promote *para* substitution results in only *para* substitution. In the case of the sulfonium ion, an additional factor, π(d–p) interaction, is also possible. Considerable evidence for π(d–p) interaction in sulfonium salts is available[12-15] and appears to be a factor in contributing to the relatively small amount of *para* substitution.

Ridd and Utley have observed that positive poles involving elements of group V may be regarded as being *meta–para* directing as a result of strong electrostatic deactivation of the *ortho* position. π(d–p) interaction ($-M$ effect) may be regarded as being *ortho–meta* directing similar to the nitro group. A combination of these two effects results in the strong *meta*-directing effect of the phosphonium and arsonium groups. A small amount of *para* but no *ortho* substitution was also observed.[5] These two effects also cause the sulfonium and selenonium groups to be principally *meta* directing. The dimethylsulfonium and dimethylselenonium groups direct *para* and to a smaller extent also *ortho*. *ortho* substitution is not observed in the case of positive poles of group V elements.

Another factor, π(p–p) interaction, needs to be considered. Possibly the first example of π(p–p) interaction involving a positive pole is the oxonium ion which yields only the *para* product in a nitration reaction using concentrated H_2SO_4 as a solvent and HNO_3 as the nitrating agent. If π(p–p) interaction is important in the case of the sulfonium ion, *ortho* and *para* substitution are expected.[3] The strong $-I$ effect would lead to a small *ortho*/*para* ratio. Since an appreciable amount of *ortho* nitration of the sulfonium salt is observed (3.6%, *ortho*/*para* ratio of 0.43), π(p–p) interaction is a possible explanation, although it might be predicted to yield more *para* substitution than was actually obtained. The fact that an appreciable amount of *ortho* nitration is observed indicates that resonance interaction of the sulfonium group does occur. It is not clear whether this is a π(d–p) and/or a π(p–p) interaction.

The nitration results of the selenonium salt **2** are very similar to the sulfonium salt **1** and hence what was said about the sulfonium salt is also true of the selenonium salt with slight modifications. The selenium atom is larger than the sulfur atom; hence there is more steric inhibition toward *ortho* substitution, less resonance interaction with the π system, and a slightly smaller $-I$ effect in the case of the selenonium than the sulfonium ion. The small differences in isomer distribution of the selenonium and sulfonium salts seem to indicate that the importance of each individual effect changes, but that the over-all system is such that the isomer distribution is approximately the same. It was observed that the selenonium salt reacted more rapidly than the sulfonium salt.

Method of Analysis

p-Nitrodimethylphenylsulfonium methyl sulfate (**5**) undergoes very rapid S_N reactions with methoxide ion, indicating that in this case the dimethylsulfonium group is an excellent leaving group.[16] It has also been found that at room temperature *o*-nitrodimethylphenylsulfonium methyl sulfate (**3**) as well as *o*- (**6**) and *p*-nitrodimethylphenylselenonium methyl sulfates (**8**) react rapidly with dilute solutions of sodium methoxide in methanol to form the corresponding nitroanisoles. *m*-Nitrodimethylphenylsulfonium methyl sulfate (**4**) and *m*-nitrodimethylphenylselenonium methyl sulfate (**7**) form only a small amount of *m*-nitroanisole under the same conditions. Baker and Moffitt's[9] procedure for the isolation of the nitrosulfonium and -selenonium salts from the strongly acidic reaction involved neutralization was dilute sodium hydroxide at room tem-

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[12] R. W. Taft and J. W. Rakshys, Jr., *J. Am. Chem. Soc.*, **87**, 4387 (1965).

[13] C. C. Price and S. Oae, "Sulfur Bonding," Ronald Press Co., New York, N. Y., 1962, Chapter 5.

[14] F. G. Bordwell and P. J. Bouton, *J. Am. Chem. Soc.*, **78**, 87 (1965).

[15] D. P. Craig, *J. Chem. Soc.*, 997 (1959).

[16] B. A. Bolto and J. Miller, *Australian J. Chem.*, **9**, 74 (1965).

perature. This could have converted the *o*- and *p*-nitrosulfonium and -selenonium salts to the corresponding nitrophenols, leaving only the *meta* isomers.

A methanolic solution of **3**, **4**, **5**, **6**, **7**, or **8** cooled to the temperature of Dry Ice in methanol yields only the dealkylated product upon treatment with sodium methoxide. That is **3**, **4**, and **5** yield only the corresponding methyl nitrophenyl sulfides and **6**, **7**, and **8** the corresponding methyl phenyl selenides. Gas chromatographic analysis indicated less than 0.5% nitroanisoles which would have resulted from displacement of the dimethylsulfonium or -selenonium group by methoxide. This so-called abnormal reaction has been observed previously using SCN^- as the dealkylating agent,[17] but to our knowledge it has not been observed with the methoxide ion on groups which are activated toward S_N reactions.

$$ArY(CH_3)_2SO_4CH_3 + NaOCH_3 + CH_3OH \longrightarrow ArYCH_3$$

1, Y = S; Ar = phenyl
2, Y = Se; Ar = phenyl
3, Y = S; Ar = *o*-nitrophenyl
4, Y = S; Ar = *m*-nitrophenyl
5, Y = S; Ar = *p*-nitrophenyl
6, Y = Se; Ar = *o*-nitrophenyl
7, Y = Se; Ar = *m*-nitrophenyl
8, Y = Se; Ar = *p*-nitrophenyl

Each individual nitrosulfonium and nitroselenonium salt was dissolved in nitric and sulfuric acid and treated in a manner identical with conditions for the nitration of dimethylphenylsulfonium (**1**) and dimethylphenylselenonium (**2**) methyl sulfate. Gas chromatographic analysis of the dealkylated salts indicated no rearrangement.

Known mixtures of **3**, **4**, and **5** were treated in the same manner as the nitration of **1**. The results in Table II indicate good agreement with the percentage calculated from the gas chromatographic analysis and the calculated values. No dinitration was observed.

TABLE II

GAS CHROMATOGRAPHIC ANALYSIS OF KNOWN MIXTURES OF *o*-, *m*-, AND *p*-NITRODIMETHYLPHENYLSULFONIUM METHYL SULFATE

	ortho, %	*meta*, %	*para*, %
Calculated	6.44	85.22	8.34
Gas chromatographic analysis[a]	6.2 ± 0.2	85.3 ± 0.3	8.5 ± 0.2
Calculated	2.65	91.21	6.14
Gas chromatographic analysis	2.5 ± 0.3	91.3 ± 0.3	6.2 ± 0.2

[a] Each value is an average of five gas chromatographic analyses.

The sulfonium salt **1** and selenonium salt **2** were dissolved in the nitrating mixture and immediately treated with sodium methoxide in the normal fashion. Gas chromatographic analysis indicated only methyl phenyl sulfide or methyl phenyl selenide (<0.5% methyl *m*-nitrophenyl sulfide and methyl *m*-nitrophenyl selenide). This indicated that there was no substitution occurring during the work-up of the reaction mixture.

Methyl phenyl sulfide and methyl phenyl selenide were also nitrated under the same conditions as were **1** and **2**. Gas chromatographic analysis of the reaction mixture, after the normal work-up procedure, indicated the absence of any of the methyl nitrophenyl sulfides or methyl nitrophenyl selenides. This indicated that, if **1** or **2** were contaminated with the corresponding sulfide or selenide, they would not interfere with the analysis. These control experiments indicated no rearrangement during the reaction or the work-up and that methyl phenyl sulfide and methyl phenyl selenide, if present, did not interfere with the analysis.

Experimental Section[18]

Dimethylphenylsulfonium Methyl Sulfate (1).—Methyl phenyl sulfide (Aldrich Chemical Co.) (12.4 g, 0.1 mole) and dimethyl sulfate (13.6 g, 0.108 mole) were heated in an oil bath at 95° for 3 hr. Upon cooling the viscous solution crystallized. The crystalline product was ground in a mortar under acetone, rapidly filtered, and crystallized from isopropyl alcohol. After two crystallizations, the pure hygroscopic sulfonium salt was obtained (21.2 g, 84% yield), mp 81–82°. *Anal.* Calcd for $C_9H_{14}S_2O_4$: C, 43.18; H, 5.64. Found: C, 43.38; H, 5.56.

Dimethylphenylselenonium Methyl Sulfate (2).—Benzeneselenol[19] (15.7 g, 0.10 mole), dimethyl sulfate (15.1 g, 0.10 mole), and 40 ml of 20% sodium hydroxide solution were heated on a water bath for 30 min. The selenide was extracted with ether, dried over sodium sulfate, and distilled. The yield of methyl phenyl selenide was 13.3 g (78%), bp 46–47° (2 mm). Methyl phenyl selenide (13.3 g, 0.077 mole) and dimethyl sulfate (11.3 g, 0.09 mole) were heated in an oil bath at 90° for 30 min. Upon cooling the viscous solution crystallized. The crystalline product was ground in a mortar under acetone, filtered, and crystallized from isopropyl alcohol. After two crystallizations, the pure selenonium salt was obtained (21.0 g, 92% yield), mp 107–108°. *Anal.* Calcd for $C_9H_{14}SSeO_4$: C, 36.33; H, 4.75. Found: C, 36.69; H, 4.90.

Nitration of 1 and 2.—Sulfonium salt **1** (1 g) was added to a mixture of 3 ml of concentrated H_2SO_4 (reagent grade, meets ACS specifications, sp gr 1.84, 95.5–96.5%) and 2 ml of concentrated HNO_3 (reagent grade, meets ACS specifications, sp gr 1.42, 70–71%) at room temperature and stirred until in solution. The reaction mixture was then placed in an oil bath at 60° for 2 hr and then analyzed. The time of the reaction was varied from 1 to 8 hr and the temperature of the reaction up to 80° with no noticeable change in results. Under these conditions, no evidence for disubstitution or starting material was obtained. The nitration of the selenonium salt **2** was carried out in a similar manner except that the temperature of the reaction was kept at 25° for 30 min.

Analysis of Reaction Mixture.—The nitration reaction mixture was added to 200 ml of methanol and cooled to the temperature of Dry Ice in methanol. A concentrated solution of sodium methoxide in methanol (~10%) was added dropwise with stirring until the solution was basic to litmus paper. After the mixture came to room temperature, it was filtered; the filtrate was evaporated to a small volume on a rotary evaporator, and analyzed gas chromatographically. An F & M Model 700 gas chromatograph was used with a 6-ft, $^1/_8$-in. copper column. The column packing consisted of 5% 2,4,7-trinitro-9-fluorenone on 60–80 mesh Chromosorb W (nonacid washed).

Dimethylnitrophenylsulfonium Methyl Sulfate (3, 4, 5) and Dimethylnitrophenylsulfonium Methyl Sulfate (6, 7, 8).—The isomeric methyl nitrophenyl sulfides[20] were heated at 95° for 2 hr with a slight excess of dimethyl sulfate. The isomeric methyl nitrophenyl selenides[20,21] were heated for 30 min. The crystalline salts were ground in a mortar under acetone, filtered, and crystallized twice from methanol. The melting points and analytical data are given in Table III.

Verification of Analysis.—A number of experiments were run in order to verify as completely as possible the method of analysis used. The following is a description of the test experiments performed. Sulfonium salt **1** (1 g) was dissolved in 3 ml of

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[17] B. A. Bolto and J. Miller, *J. Org. Chem.*, **20**, 558 (1955).

[18] All melting points are uncorrected. Microanalyses were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn.

[19] D. G. Foster, "Organic Syntheses," Coll. Vol. III, E. C. Horning, Ed., John Wiley and Sons, Inc., New York, N. Y., 1955, p 771.

[20] A. J. Parker and D. Brody, *J. Chem. Soc.*, 4067 (1963).

[21] H. Rheinbolt, "Methoden Der Organischen Chemie," Houben-Weyl, Vierte Auglage, Vol. 9, E. Muller, Ed., VEB George Thieme Verlag, Stuttgart, 1955, pp 917–1209.

TABLE III

DIMETHYLNITROPHENYLSULFONIUM AND -SELENONIUM METHYL SULFATE SALTS

Compound	Yield, %	Mp, °C	Formula	Carbon, % Calcd	Carbon, % Found	Hydrogen, % Calcd	Hydrogen, % Found
Dimethyl-*o*-nitrophenylsulfonium methyl sulfate	85	160–162[a]	$C_9H_{13}NS_2O_6$	36.60	. . .	4.44	. . .
Dimethyl-*m*-nitrophenylsulfonium methyl sulfate	78	142–143[b]	$C_9H_{13}NS_2O_6$	36.60	36.85	4.44	4.62
Dimethyl-*p*-nitrophenylsulfonium methyl sulfate	92	157–158[c]	$C_9H_{13}NS_2O_6$	36.60	. . .	4.44	. . .
Dimethyl-*o*-nitrophenylselenonium methyl sulfate	63	156–158	$C_9H_{13}NSSeO_6$	31.58	31.38	3.83	3.83
Dimethyl-*m*-nitrophenylselenonium methyl sulfate	83	153–157	$C_9H_{13}NSSeO_6$	31.58	31.56	3.83	4.00
Dimethyl-*p*-nitrophenylselenonium methyl sulfate	93	163–165	$C_9H_{13}NSSeO_6$	31.58	31.72	3.83	4.00

[a] Lit. mp 155–157°, K. Brand and O. Stallmann, *Ber.*, **B54**, 1578 (1921). [b] Lit. mp 140–141°, K. Brand and H. W. Leyerzapf, *ibid.*, **B70**, 284 (1937). [c] Lit. mp 157–158.5°, F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 87 (1956).

concentrated H_2SO_4 and 2 ml of concentrated HNO_3 at room temperature. As soon as a homogeneous solution was obtained, the solution was analyzed in the normal fashion. Gas chromatographic analysis indicated methyl phenyl sulfide and a trace of methyl *m*-nitrophenyl sulfide (<0.5%). The selenonium salt **2** was treated in a similar manner except that the reaction mixture had to be cooled in Dry Ice since, at room temperature, a considerable amount of substitution occurred even with a short reaction time. Only methyl phenyl selenide was observed with a trace of methyl *m*-nitrophenyl selenide (<0.5%). This indicated that there was essentially no substitution occurring during work-up of the reaction mixture.

The nitration of **1** and **2** was carried out in the normal fashion except that 0.3 g of methyl phenyl sulfide and methyl phenyl selenide, rspectively, were added to the reaction mixture. Analysis of the reaction mixture indicated no change in isomer distribution. Nitration of methyl phenyl sulfide and selenide under the nitration conditions of **1** and **2** yielded no methyl nitrophenyl sulfides or methyl nitrophenyl selenides.

Each individual dimethylnitrophenylsulfonium methyl sulfate (**3**, **4**, **5**) (0.5 g) and dimethylnitrophenylselenonium methyl sulfate (**6**, **7**, **8**) (0.5 g) was subjected to the normal nitration and analysis procedure. In all cases, only the corresponding methyl nitrophenyl sulfide or selenide was observed, indicating that there was no rearrangement under the conditions of the reaction and analysis. Two different known concentrations of the dimethylnitrophenylsulfonium methyl sulfate salts (**3**, **4**, **5**) were subjected to the normal nitration and analysis procedure. The results given in Table II indicate good agreement between the calculated and the actural percentages found. No dinitration was observed.

Registry No.—**1**, 6203-16-3; **2**, 13118-29-1; **3**, 13118-30-4; **4**, 13118-31-5; **5**, 13118-32-6; **6**, 13118-33-7; **7**, 13118-34-8; **8**, 13118-35-9.

The Effect of Intramolecular Hydrophobic Bonding on Partition Coefficients

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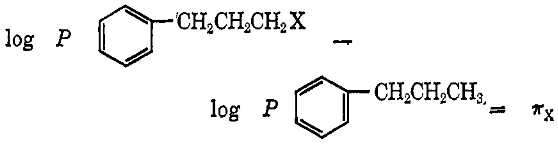
The 1-octanol–water partition coefficients are presented for 54 organic compounds. The additive–constitutive nature of the logarithm of partition coefficients is considered. It is postulated that intramolecular hydrophobic bonding can result in lower than expected values for partition coefficients in certain types of compounds.

Relatively few partition coefficients have been determined for simple neutral aliphatic compounds. While many studies have been made on simple aliphatic acids and bases, the difficulties involved in the problems of analysis of small concentrations of neutral molecules has not invited work in this area. The largest collection of such constants, although admittedly not very accurate, is that of Collander.[3]

In extending[4–7] the classical studies of Meyer and Overton on the use of partition coefficients for structure–activity correlations, we have used a relative constant π defined as $\pi = \log P_X - \log P_H$. P_H is the partition coefficient of the parent compound in a congeneric series and P_X is that of a derivative. We have shown that π and $\log P$ are additive–constitutive constants[8,9] and this property has now been confirmed by others.[10]

In our first studies[8] using aromatic compounds, we found the ultraviolet spectrophotometer to be a convenient tool for the determination of concentrations of the partitioned compounds. For the sake of analytical convenience, we decided to take advantage of the additive character of $\log P$ and π to obtain $\log P$ for aliphatic compounds. The approach given in eq 1 was used.



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[1] John Simon Guggenheim Fellow.

[2] Smith Kline and French research associate.

[3] R. Collander, *Physiol. Plantarum.*, **7**, 420 (1954).

[4] C. Hansch, R. M. Muir, T. Fujita, P. P. Maloney, F. Geiger, and M. Streich, *J. Am. Chem. Soc.*, **85**, 2817 (1963).

[5] K. Kiehs C. Hansch, and L. Moore, *Biochemistry*, **5**, 2602 (1966).

[6] C. Hansch and E. W. Deutsch, *Biochim. Biophys. Acta*, **126**, 117 (1966).

[7] E. W. Deutsch and C. Hansch, *Nature*, **211**, 75 (1966).

[8] T. Fujita, J. Iwasa, and C. Hansch, *J. Am. Chem. Soc.*, **86**, 5175 (1964).

[9] J. Iwasa, T. Fujita, and C. Hansch, *J. Med. Chem.*, **8**, 150 (1965).

[10] D. J. Currie, C. E. Lough, R. F. Silver, and H. L. Holmes, *Can. J. Chem.*, **44**, 1035 (1966).