Kinetics, Isomer Distribution, and Additivity in the Bromination of the Dimethylnaphthalenes[1]

Jean B. Kim,[2] Christina Chen,[3a] Jeanne K. Krieger,[3b] Karan R. Judd,[3c] Candace C. Simpson,[3d] and Ernst Berliner[4]

*Contribution from the Marion Edwards Park Laboratory,
Bryn Mawr College, Bryn Mawr, Pennsylvania 19010.*
Received June 23, 1969

Abstract: Rate constants for bromination of the two methylnaphthalenes and nine dimethylnaphthalenes by molecular bromine were determined in aqueous acetic acid at 25°. The major bromination products were also determined for the reaction of the methyl- and eight of the dimethylnaphthalenes. Partial rate factors were calculated, and these were used to check the additivity principle in the naphthalene system. The experimental partial rate factors were also compared with various approximate MO parameters which utilize the "inductive model" of the methyl group. The correlation of the approximate MO parameters and experimental data is better for a transition state model of substitution than for a model of the isolated molecule.

The basic assumption of the additivity principle is that substituents on an aromatic ring act independently of each other and that their effects are additive in the free energies of activation.[5] The ability to predict reaction rates and isomer distribution by the additivity principle has been utilized quite widely for reactions of substituted benzenes but has been tested for only a limited series of compounds. Most of the more successful correlations have been made on reactions of polymethylated benzene derivatives, probably because the electronic effects of methyl groups are weak and their conjugative interactions small. Even though early correlations on the halogenation of methylbenzenes were quite successful,[6] further studies indicated limitations of the applicability of the principle in such reactions as halogenation,[7] mercuration,[8] nitration,[9] acetylation,[10] benzoylation,[11] and desilylation.[12] Corrections had to be introduced, mainly to allow for steric effects, such as in substitution *ortho* to two methyl groups, but differential solvation,[13] steric acceleration,[12] and other factors have also been invoked to account for the discrepancies.[14]

Data concerning the effects of substituents on the reactivity of naphthalene derivatives is not nearly as extensive as that for benzene derivatives. Calculation of partial rate factors for the bromination of the mono- and dimethylnaphthalenes from experimental rates and product distribution affords an opportunity to test the validity of the additivity principle in the naphthalene series, in addition to providing new quantitative data for reactions of substituted naphthalenes.

The rates of bromination by molecular bromine of naphthalene, 1- and 2-methylnaphthalene, and all of the dimethylnaphthalenes, except 1,7-dimethylnaphthalene, were measured in aqueous acetic acid. Some of the data had been reported previously in connection with other work.[15,16]

It has previously been shown that in aromatic bromination in aqueous acetic acid, in the presence of an excess of bromide ion, the brominating species is free molecular bromine, and the rate expression is $-\mathrm{d}(\mathrm{Br_2})_\mathrm{T}/\mathrm{d}t = k_\mathrm{obsd}(\mathrm{Br_2})_\mathrm{T}(\mathrm{ArH})$, where $(\mathrm{Br_2})_\mathrm{T}$ is the total titratable bromine.[17] Under these conditions the relation $k_\mathrm{obsd} = kK/(K + \mathrm{Br^-})$ (eq 1) holds, where K is the dissociation constant of the tribromide ion. Reactions were conducted at different bromide ion concentrations and at a constant ionic strength, and k, the rate constant for bromination by free, uncomplexed bromine, is then the slope of the straight line obtained when k_obsd is plotted against $K/(K + \mathrm{Br^-})$. This is a more reliable procedure than to conduct all the brominations at only one bromide ion concentration and use eq 1 directly.[18] In all cases here reported relationship 1 is followed; that is, the first step in the reaction is rate controlling, except in the case of 1,5-dimethylnaphthalene, where carbon–hydrogen bond breaking partly determines the rate as shown by different kinetics.[16] This change in mechanism has been discussed separately

---

[1] Relative Reactivities of Polynuclear Aromatic Systems. V.

[2] Taken in part from the Ph.D. Dissertation of J. B. Kim, Bryn Mawr College, May 1968; National Science Foundation Cooperative Fellow, 1965–1966; United States Steel Fellow in Chemistry, 1966–1967.

[3] (a) M. A. Thesis, Bryn Mawr College, 1963. (b) National Science Foundation Undergraduate Summer Research Participant, 1965, Senior Honors Thesis, 1966. (c) National Science Foundation Undergraduate Summer Research Participant, 1966. (d) National Science Foundation Undergraduate Summer Research Participant, 1964, Senior Honors Thesis, 1965. Some preliminary work was done by Kathleen O'Donnell, National Science Foundation Summer Research Participant, 1960.

[4] To whom inquiries should be addressed.

[5] P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworths and Co., Ltd., London, 1959, Chapters 6, 10, 18.

[6] F. E. Condon, *J. Amer. Chem. Soc.*, **70**, 1963 (1948); *ibid.*, **74**, 2528 (1952).

[7] H. C. Brown and L. M. Stock, *ibid.*, **79**, 1421, 5175 (1957); L. J. Andrews and R. M. Keefer, *ibid.*, **78**, 4549, 5623 (1956).

[8] H. C. Brown and C. W. McGary, Jr., *ibid.*, **77**, 2310 (1955).

[9] A. Fischer, J. Vaughan, and G. J. Wright, *J. Chem. Soc., B*, 368 (1967).

[10] G. Marino and H. C. Brown, *J. Amer. Chem. Soc.*, **81**, 5929 (1959).

[11] H. C. Brown, B. A. Bolto, and F. R. Jensen, *J. Org. Chem.*, **23**, 417 (1958).

[12] R. A. Benkeser, R. A. Hickner, D. I. Hoke, and O. H. Thomas, *J. Amer. Chem. Soc.*, **80**, 5289 (1958); C. Eaborn and R. C. Moore, *J. Chem. Soc.*, 3640 (1959).

[13] H. V. Ansell and R. Taylor, *ibid.*, *B*, 526 (1968).

[14] R. Taylor, G. J. Wright, and A. J. Homes, *ibid.*, 780 (1967); R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier Publishing Co., New York, N. Y., 1965.

[15] E. Berliner, D. M. Falcione, and J. L. Riemenschneider, *J. Org. Chem.*, **30**, 1812 (1965).

[16] E. Berliner, J. B. Kim, and M. Link, *ibid.*, **33**, 1160 (1968).

[17] E. Berliner and M. C. Beckett, *J. Amer. Chem. Soc.*, **79**, 1425 (1957); E. Berliner and J. C. Powers, *ibid.*, **83**, 905 (1961); U. P. Zimmerman and E. Berliner, *ibid.*, **84**, 3953 (1962); E. Berliner and B. J. Landry, *J. Org. Chem.*, **27**, 1083 (1962).

[18] L. Altschuler and E. Berliner, *J. Amer. Chem. Soc.*, **88**, 5837 (1966).

Table I. Rates of Bromination of Methyl- and Dimethylnaphthalenes in Aqueous Acetic Acids at 25°

Compound	k, l. mol^{-1} sec^{-1}	Solvent, % acetic acid[a]	Rate relative to benzene	
			Obsd	Calcd
Benzene[b]	2.74×10^{-6}	50	1	
Naphthalene[b,c]	0.341	50	1.24×10^{5}	
	1.26×10^{-2}	75		
1-Methylnaphthalene[c]	1.97	75	1.95×10^{7}	1.99×10^{7}
2-Methylnaphthalene[c]	1.84	75	1.82×10^{7}	1.85×10^{7}
1,2-Dimethylnaphthalene[d]	0.597	90	7.34×10^{7}	6.53×10^{7}
1,3-Dimethylnaphthalene[d]	55.0	90	6.76×10^{9}	1.11×10^{10}
1,4-Dimethylnaphthalene[e]	1.10	75	1.09×10^{7}	3.66×10^{6}
1,5-Dimethylnaphthalene[f]	0.374	90	4.60×10^{7}	9.39×10^{7}
1,6-Dimethylnaphthalene[g]	10.5	90	1.29×10^{9}	6.13×10^{8}
1,8-Dimethylnaphthalene[g]	1.71	90	2.10×10^{8}	6.39×10^{8}
2,3-Dimethylnaphthalene[f]	0.810	90	9.96×10^{7}	1.19×10^{8}
2,6-Dimethylnaphthalene[h]	9.12	75	9.02×10^{7}	9.00×10^{7}
	0.733	90		
2,7-Dimethylnaphthalene[g]	4.88	90	6.00×10^{8}	5.87×10^{8}
1,7-Dimethylnaphthalene				9.20×10^{7}

[a] By volume, before mixing. [b] Reference 17. [c] Reference 3a. [d] Reference 3b. [e] Reference 3c. [f] Reference 16. [g] Reference 3d. [h] Reference 15.

and has been ascribed to steric crowding in the transition state, which is caused by a methyl group *peri* to the site of substitution. This is known to be a factor in making the decomposition of the σ-complex partly rate controlling.[19] The same deviation has since been found in the bromination of 1,4-dimethylnaphthalene, in which the methyl groups are also *peri* to the reaction site. From the kinetics of the reactions of both of these compounds it is possible to obtain k, the rate constant for the first step.

The values of all the rate constants and the solvents in which brominations were conducted are listed in Table I. Because of the great range of reactivity encompassed by these compounds, and the necessity of comparing rate constants to that of benzene, the slowest of all compounds, acetic acid with varying amounts of water had to be utilized as the solvent. In order to compare rate constants obtained in the different solvents, naphthalene was brominated in 50 and 75% aqueous acetic acid, and 2,6-dimethylnaphthalene in 75 and 90% acetic acid. The factors calculated for the ratio of rates (27.1 in the former and 12.4 in the latter case) were then used to refer all rates to 50% aqueous acetic acid.[18] These factors were assumed to be the same for all compounds studied. This assumption is probably not strictly true and introduces some uncertainty into the final values, but the consistency of the data and a check with several compounds makes it seem likely that the error is not a great one, particularly since all dimethylnaphthalenes, with the exception of the 1,4-isomer, were studied in 90% acetic acid. The rates relative to benzene, all referred to 50% aqueous acetic acid, are also listed in Table I.

Isomer Distribution and Partial Rate Factors

Isomer distributions were determined by gas-chromatographic analysis of the product mixtures obtained from reactions carried out under the kinetic conditions. Each of the mono- and dimethylnaphthalenes was also brominated on a preparative scale in carbon disulfide or carbon tetrachloride. For each of the hydrocarbons the main bromination product was isolated and its vpc retention time and infrared spectrum compared to those of the kinetic bromination products.

Preparative bromination of the monomethyl- and of many of the dimethylnaphthalenes has been reported previously. The major position of substitution in 1-methylnaphthalene[20] and in 1,2-[21] and 1,8-dimethylnapththalene[22] is reported to be the 4 position, and in 2-methylnaphthalene,[23] 2,3-,[24] 2,6-,[25] and 2,7-dimethylnaphthalene[26] the 1 position. Retention times and infrared spectra of these isomers prepared by literature procedures, demonstrated that these are also the major positions of substitution in these compounds under kinetic conditions. No bromo substitution products of 1,5- and 1,3-dimethylnaphthalene had previously been reported. Two pure monobromo substitution products of 1,5-dimethylnaphthalene were isolated and shown to be the 4-bromo and the 2-bromo compounds, and a small amount of an unidentified third product is very probably the 3 isomer.[16] Bromination of 1,3-dimethylnaphthalene, both under kinetic conditions and in carbon disulfide, afforded only one product, a monobromo compound, which was assumed to be the 4-bromo derivative (1-bromo-2,4-dimethylnaphthalene). This compound did not form a stable picrate. A similar observation was made with 2-bromo-1,5-dimethylnaphthalene,[16] and this behavior may be typical of picrates of compounds in which a bromine atom is *ortho* to a methyl group.

The only major discrepancy with the literature was found in the case of 1,6-dimethylnaphthalene. It has been reported that the only product isolated in bromination in carbon disulfide is the 4-bromo compound (1-bromo-4,7-dimethylnaphthalene).[27] In the present study, under both preparative and kinetic conditions, a mixture of two major products in almost equal amounts was obtained. In numerous other substitution reactions,

---

(19) H. Zollinger, *Helv. Chim. Acta*, **38**, 1597, 1617, 1623 (1955); E. Berliner, *Progr. Phys. Org. Chem.*, **2**, 253 (1964).

(20) R. D. Topsom and J. Vaughan, *J. Chem. Soc.*, 2842 (1957).

(21) C. L. Hewett, *ibid.*, 293 (1940).

(22) W. J. Mitchell, R. D. Topsom, and J. Vaughan, *ibid.*, 2526 (1962).

(23) R. Adams and L. O. Binder, *J. Amer. Chem. Soc.*, **63**, 2773 (1941).

(24) R. T. Arnold and R. W. Liggett, *ibid*, 64, 2875 (1942).

(25) V. Vesely and F. Sturša, *Collect. Czech. Chem. Commun.*, 4, 21 (1932).

(26) E. Clar and H. D. Wallenstein, *Chem. Ber.*, **64**, 2076 (1931).

(27) E. de B. Barnett and J. W. Cook, *J. Chem. Soc.*, 22 (1933).

Table II. Isomer Distribution and Partial Rate Factors in the Bromination of the Methyl- and Dimethylnaphthalenes[a]

Compound	Position	% substitution	Partial rate factor Obsd	Partial rate factor Calcd
Benzene			1	
Naphthalene	1	99	1.84×10^5	
	2	1	1.86×10^3	
1-Methylnaphthalene	4	98.6 ± 0.30	1.15×10^8	1.15×10^8
	(5)	0.88 ± 0.12	1.08×10^6	3.04×10^6
	(2)	0.50 ± 0.18	5.85×10^5	1.08×10^8
2-Methylnaphthalene	1	98.2 ± 0.40	1.07×10^8	1.07×10^8
	(8)	1.00 ± 0.20	1.09×10^6	3.04×10^6
	(4)	0.51 ± 0.10	5.56×10^5	6.03×10^5
	(5)	0.27 ± 0.06	2.94×10^5	4.47×10^5
1,2-Dimethylnaphthalene	4	100.0	4.40×10^8	3.77×10^8
	(5)			7.38×10^6
1,3-Dimethylnaphthalene	4	100.0	4.06×10^{10}	6.68×10^{10}
	(5)			5.00×10^7
1,5-Dimethylnaphthalene[b]	2	19.2 ± 1.2	2.65×10^7	2.63×10^6
	(3)	7.7 ± 2.3	1.06×10^7	1.01×10^5
	4	72.6 ± 2.7	1.00×10^8	2.79×10^8
1,6-Dimethylnaphthalene	4	40.5 ± 0.20	3.13×10^9	1.90×10^9
	(5)	57.2 ± 1.50	4.43×10^9	1.76×10^9
	(2)	2.3 ± 1.20	1.78×10^8	1.78×10^7
1,8-Dimethylnaphthalene[c]	4	97.3 ± 0.30	6.13×10^8	1.90×10^9
	(2)	2.70 ± 0.30	1.70×10^7	1.78×10^7
2,3-Dimethylnaphthalene	1	97.4 ± 1.0	2.91×10^8	3.51×10^8
	(5)	2.60 ± 1.0	7.77×10^6	7.38×10^6
2,6-Dimethylnaphthalene	1	96.1 ± 0.90	2.60×10^8	2.60×10^8
	(4)	3.90 ± 0.90	1.06×10^7	9.96×10^6
2,7-Dimethylnaphthalene	1	98.6 ± 0.70	1.77×10^9	1.76×10^9
	(4)	1.40 ± 0.10	2.52×10^7	1.47×10^6
1,4-Dimethylnaphthalene	(2)			3.54×10^6
	(5)			7.38×10^6
	(6)			7.46×10^4
1,7-Dimethylnaphthalene	(4)			2.79×10^8
	(8)			2.60×10^8
	(5)			9.96×10^6

[a] Reference 2. [b] Reference 16. [c] See also ref 33.

notably various Friedel–Crafts reactions,[28,29] only one isomer has been reported, which has always been considered to be the 4 isomer, although structure proofs are often missing. The bromination product reported in the literature had been converted through the acid to cadalene (4-isopropyl-1,6-dimethylnaphthalene), and the assigned structure is therefore certainly correct for one of the products of bromination of 1,6-dimethylnapthalene. We carried out an independent synthesis of this 4-bromo compound starting with the known 4-acetyl derivative.[28] The acetyl compound was converted into the amine by a Schmidt reaction and thence to the 4-bromo compound. The picrate had a mp of 120.1–121.5° (lit. 114°).[27] The retention time of this 4-bromo compound was identical with that of the isomer formed in 47.9% yield in preparative bromination of 1,6-dimethylnaphthalene in carbon disulfide. The second major isomer in the preparative bromination, formed in 48.7% yield, was assumed to be the 5-bromo compound (1-bromo-2,5-dimethylnaphthalene) but was not synthesized independently. No assignment was made of the structure of the third isomer which was obtained in 3.4% yield, but which is probably the 2 isomer. Under kinetic conditions, the per cent of 4-bromo, assumed 5-bromo, and the unassigned isomer are 40.5, 57.2, and 2.3%, respectively.

The assignment of the bromine in the second major isomer to the 5 position was based largely on the additivity principle and the knowledge that a 1-methyl group has about the same effect on the reactivity at the 4 position as a 2-methyl group has on the 1 position. Both kinds of interactions are present in 1,6-dimethylnaphthalene. In only one other reaction of 1,6-dimethylnaphthalene have two isomers been isolated. Although in an earlier chloromethylation of 1,6-dimethylnaphthalene only the formation of the 4 isomer had been reported,[30] in later work almost equal amounts of 4- and 5-chloromethyl compounds were isolated and were unambiguously identified by conversion to trimethylnaphthalenes.[31] Our assignment is therefore a very reasonable one, and our results indicate that 5 substitution, possibly in significant amounts, probably occurs in most of the other substitution reactions of 1,6-dimethylnaphthalene recorded in the literature.[32]

Except for 1,2- and 1,3-dimethylnaphthalene, more than one monobromination product was detected by vpc for all compounds studied.[33] These minor isomers were not identified, but applicability of the additivity

---

(28) (a) F. Feist, *J. Prakt. Chem.*, **139**, 261 (1934); (b) N. P. Buu-Hoi, R. Royer, M. Hubert-Habart, and P. Mabille, *J. Chem. Soc.*, 3584 (1953).

(29) N. P. Buu-Hoi and G. Saint-Ruf, *Bull. Soc. Chim. Fr.*, 2307 (1963); J. W. Cook, *J. Chem. Soc.*, 489 (1931); L. F. Fieser and M. Fieser, *J. Amer. Chem. Soc.*, **55**, 3342 (1933); L. E. Hinkel, E. E. Ayling, and J. H. Beynon, *J. Chem. Soc.*, 339 (1936).

(30) N. P. Buu-Hoi and P. Cagniant, *Rev. Sci.*, 81, 173 (1943); *Chem. Zentr.*, *II*, 316 (1944).

(31) W. Ried and H. Bodem, *Chem. Ber.*, **91**, 1354 (1958).

(32) See also N. P. Buu-Hoi, and R. Daudel, *Rec. Trav. Chim.*, **65**, 730 (1946).

(33) In the older literature only the formation of one isomer has been noted in the bromination of the dimethylnaphthalenes. Recently I. K. Lewis, R. D. Topsom, J. Vaughan, and G. J. Wright (*J. Org. Chem.*, **33**, 1497 (1968)) reported the formation of 4.4% of 2-bromo-1,8-dimethylnaphthalene in the bromination of 1,8-dimethylnaphthalene in acetic acid, in addition to the 4 isomer. We are grateful to Professor Vaughan for telling us of these results prior to publication.

principle permits prediction of the positions of substitution. The per cent of substitution at the major position of reaction and the partial rate factor for this position in each of the mono- and dimethylnaphthalenes are listed in Table II. The per cents of minor isomers and the partial rate factors for their formation are listed in parentheses. The chromatographic method of analysis does not ensure detection of a few per cent of a minor isomer which may be hidden under the peak of the major component. The possibility of failure to detect a minor isomer therefore exists, and the assignments of these isomers remain tentative.

Additivity in the Naphthalene Series

In order to calculate predicted rate factors, it is necessary to determine the effect that a methyl group in a particular position will have on the reactivity at the other positions of naphthalene. Unlike the benzene series, the different reactivities at the 1 and 2 positions of naphthalene also have to be taken into account.

The effect of a methyl group in the 1 position on reactivity in the 4 position will be designated $\mathrm{Me}_{1,4}$. This effect is equal to the ratio of the partial rate factor at the 4 position of 1-methylnaphthalene to that for reaction at the 1 position in naphthalene itself, $f_4^{1-\mathrm{Me}}/f_1^{\mathrm{naph}} = 625$. Experimental rate factors for the position of the major substitution for each of the compounds studied were used to calculate the interaction factors between various positions as shown: $\mathrm{Me}_{1,4} = f_4^{1-\mathrm{Me}}/f_1^{\mathrm{naph}} = 1.15 \times 10^8/1.84 \times 10^5 = 625$; $\mathrm{Me}_{2,1} = f_1^{2-\mathrm{Me}}/f_1^{\mathrm{naph}} = 1.07 \times 10^8/1.84 \times 10^5 = 581$; $\mathrm{Me}_{3,1} = f_1^{2,3}/f_1^{2-\mathrm{Me}} = 2.91 \times 10^8/1.07 \times 10^8 = 2.72$; $\mathrm{Me}_{3,1} = f_4^{1,2}/f_4^{1-\mathrm{Me}} = 4.40 \times 10^8/1.15 \times 10^8 = 3.83$; $\mathrm{Me}_{2,8} = f_1^{2,7}/f_1^{2-\mathrm{Me}} = 1.77 \times 10^9/1.07 \times 10^8 = 16.5$; $\mathrm{Me}_{2,8} = f_4^{1,6}/f_4^{1-\mathrm{Me}} = 3.13 \times 10^9/1.15 \times 10^8 = 27.2$; $\mathrm{Me}_{2,5} = f_1^{2,6}/f_1^{2-\mathrm{Me}} = 2.60 \times 10^8/1.07 \times 10^8 = 2.43$; $\mathrm{Me}_{1,5} = f_4^{1,8}/f_4^{1-\mathrm{Me}} = 6.13 \times 10^8/1.15 \times 10^8 = 5.33$; $\mathrm{Me}_{1,5} = f_5^{1,6}/f_1^{2-\mathrm{Me}} = 4.43 \times 10^9/1.07 \times 10^8 = 41.4$; $\mathrm{Me}_{1,4} = f_4^{1,3}/f_1^{2-\mathrm{Me}} = 4.06 \times 10^{10}/1.07 \times 10^8 = 379$; and $\mathrm{Me}_{2,1} = f_4^{1,3}/f_4^{1-\mathrm{Me}} = 4.06 \times 10^{10}/1.15 \times 10^8 = 353$.

These data provide some duplicate values, and in order to minimize the amount of experimental data necessary to derive the interaction factors, some data were eliminated and some assumptions had to be made. Data derived for the 1,4- and 2,1-interactions from the reaction of 1,3-dimethylnaphthalene were not used, because in benzene derivatives in which two or more methyl groups are *meta* to each other, rates calculated from reactivity data of toluene are invariably higher than observed.[7,14] This saturation effect also leads to too high a prediction for the rate of reaction of this dimethylnaphthalene. Data obtained from 1,8-dimethylnaphthalene also were not used. There is ample evidence that, because of the two methyl groups *peri* to each other, the molecule is strained, and the methyl groups are presumably distorted, so that the overall rate of bromination of this compound is not a true indication of the activating effect of the methyl groups. Strain in this molecule has been discussed in connection with the p*K*'s of various related acids, chemical shifts, and the X-ray crystallographic study of its 3-bromo derivative.[34] Because of the change in mechanism in the reaction of 1,5-dimethylnaphthalene,[16] the interaction factors derived from its reaction were also discarded.

The following values were chosen as the most reliable. The 1,4-methyl interaction was taken as 625, the 2,1-interaction as 581, and this was assumed to be equal to the 1,2-interaction. Although this is probably not strictly true, because of steric hindrance in the 1 position, it probably is not seriously in error. The *meta* interactions in the same ring were taken as 3.28, the average of the two values listed above, and the nonconjugated interactions in two different rings (2,5; 2,7; 1,6; 1,8) were given the value 2.43. All conjugated interactions between the rings were assigned the same value 16.5, obtained from substitution in the 1 (8) position of 2,7-dimethylnaphthalene (see below). A value for the 2,3-interaction cannot be obtained from our data, but because of the well known lack of reactivity of the 3 position in 2-substituted naphthalenes, a fraction of the 2,1-interaction was chosen. One per cent (5.81) seemed a reasonable choice, in view of the value determined from detritiation[35] of the methylnaphthalenes and similar data. However, the calculated overall rates are not sensitive to that choice, and values for the 2,3-interaction varying from 581 to 5.81 predict the same major isomers within 1% and do not change the partial rate factors, although they make a difference in the calculated amounts of minor isomers in the 3 position next to a 2-methyl group.

The factors thus derived can be employed to predict partial rate factors, isomer distribution, and overall reaction rates. For instance, for 2,3-dimethylnaphthalene, the calculation of partial rate factors, overall rate relative to benzene, and isomer distribution is shown: $f_1^{2,3} = f_4^{2,3} = f_1^{\mathrm{naph}} \times \mathrm{Me}_{1,2} \times \mathrm{Me}_{1,3} = 1.84 \times 10^5 \times 581 \times 3.28 = 3.51 \times 10^8$; $f_5^{2,3} = f_8^{2,3} = f_1^{\mathrm{naph}} \times \mathrm{Me}_{2,5} \times \mathrm{Me}_{2,8} = 1.84 \times 10^5 \times 2.43 \times 16.5 = 7.38 \times 10^6$; $f_6^{2,3} = f_7^{2,3} = f_2^{\mathrm{naph}} \times \mathrm{Me}_{2,6} \times \mathrm{Me}_{2,7} = 1.86 \times 10^3 \times 16.5 \times 2.43 = 7.46 \times 10^4$; rate relative to benzene = sum of rate factors/6 = $7.17 \times 10^8/6 = 1.19 \times 10^8$; per cent of 1 isomer = $3.51 \times 10^8 \times 2 \times 100/7.17 \times 10^8 = 97.91\%$; per cent of 5 isomer = $7.39 \times 10^6 \times 2 \times 100/7.17 \times 10^8 = 2.06\%$; and per cent of 6 isomer = $7.46 \times 10^4 \times 2 \times 100/7.17 \times 10^8 = 0.02\%$. According to this calculation, the minor isomer found by vpc analysis of the product mixture of bromination of 2,3-dimethylnaphthalene is the 5 isomer. The observed amount of minor isomer, not identified, is 2.60%. The predicted overall rate, relative to benzene, is 1.19×10^8, in good agreement with the observed value of 9.96×10^7. In Tables I and II the calculated values for overall rates and partial rate factors are compared with those determined experimentally. With the exceptions noted below, the rates and partial rate factors calculated for the major substitution products agree well with those observed.

The greatest deviation in overall rates between calculated and observed rates, a factor of three, occurs in 1,8-dimethylnaphthalene, probably for the reason already mentioned. In 1,5-dimethylnaphthalene the differences between calculated and observed values in both partial rate factors and overall rates are due to a

---

(34) A. Fischer, W. J. Mitchell, J. Packer, R. D. Topsom, and J. Vaughan, *J. Chem. Soc.*, 2892 (1963); J. Packer, J. Vaughan, and E. Wong, *J. Amer. Chem. Soc.*, **80**, 905 (1958); M. B. Jameson and B. R. Penfold, *J. Chem. Soc.*, 528 (1965); C. MacLean and E. L. Mackor, *Mol. Phys.*, **3**, 223 (1960); B. A. Nagasampagi, R. C. Pandey, V. S. Pansare, J. R. Prahlad, and S. Dev, *Tetrahedron Lett.*, 411 (1964).

(35) C. Eaborn, P. Golborn, R. E. Spillett, and R. Taylor, *J. Chem. Soc., B*, 1112 (1968).

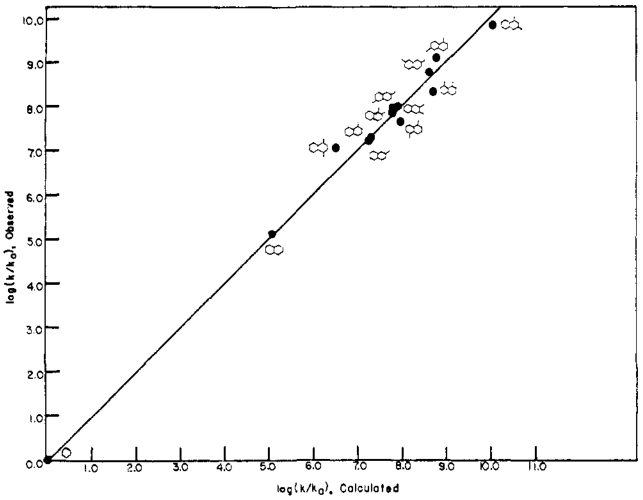


Figure 1. Observed and calculated relative rates of bromination of the mono- and dimethylnaphthalenes.

change in mechanism, and the calculated partial rate factors do not accurately reflect the reactivity in these positions, as was discussed earlier.[16] The same change also causes the poor correlation in the bromination of 1,4-dimethylnaphthalene. The predicted value for 1,3-dimethylnaphthalene is too high because of the unreliable prediction in compounds with *meta*-methyl groups.[7-9,14]

The value chosen for conjugated interactions between rings (16.5) causes serious discrepancies only in the case of 1,6-dimethylnaphthalene. Actually, bromination of this compound allows calculation of the two different conjugated interactions, the 2,8 (7,1) and 1,5 interactions, for which it affords values of 27.2 and 41.4, respectively. Although the differences are relatively small, it is of some interest to know if all conjugated interactions in naphthalene have different values. In particular, we found no way to decide if a 1,5 interaction should be generally higher than a 1,7-, 2,8-, or 2,6-interaction. Literature data are rather conflicting on this point. In a recent detritiation study on the methylnaphthalenes, 1,7-interactions were found to be superior to 1,5-interactions in a variety of substituted compounds,[35] but in other situations the reverse seems to hold, for instance in nitration.[36] An MO calculation on the two methylnaphthalenes, using the hyperconjugation model for the methyl groups, indicates the 1,5-interaction to be less than the other conjugated interactions, which are all equal.[37] We considered the possibility that the 1,5-interactions in 1,6-dimethylnaphthalene might be different from all other conjugated interactions in bromination. When all rate constants were recalculated with a value of 41.5 for the 1,5-interaction and 21.8 for all other conjugated interactions (the average of 16.5 and 27.2), only data calculated for 1,6-dimethylnaphthalene were improved; almost all others became worse.

A plot of calculated against observed overall rates is shown in Figure 1. Because of the large difference in reactivity, data are plotted logarithmically. The slope of the least-squares line has a value of 1.01 ± 0.02 and the intercept is −0.05 ± 0.15. In a similar correlation of calculated with observed partial rate factors for all the compounds isolated the slope is 1.00 ± 0.02 and the intercept −0.05 ± 0.18. Considering that the compounds encompass differences in reactivity of more than ten powers of ten, the agreement must be considered good, and the results correlate satisfactorily with the additivity principle.

It is noted that conjugated interactions between the rings, no matter which values are chosen, are only a few per cent of the conjugated interactions in the same ring, and that the unconjugated interactions are less than 1% of the latter. This is clearly a consequence of the very high selectivity and large ρ value for bromination. It is also the reason why in most cases, except in 1,6-dimethylnaphthalene, the major product of bromination is formed in over 95% yield.[38]

In general, the relative order of the interaction factors found in bromination agrees qualitatively with that found in the nitration[36] and detritiation[35] of the methylnaphthalenes and the dedeuteration of the dimethylnaphthalenes,[39] but there are also differences, caused presumably by the different ρ values for these reactions and different steric requirements of the various reagents, and a detailed discussion of the similarities and differences does not seem warranted. With the interaction factors derived above the order of reactivity in the bromination of 2-methylnaphthalene is calculated to be $1 > 8 > 4 > 5 > 6 > 3 > 7$; the order found experimentally in detritiation[35] is $1 > 8 > 4 > 6 > 5 > 3 > 7$ and in nitration[36] in acetic acid $1 > 8 > 4 > 5 > 6$ (> 3 and 7).

Correlations of Results with MO Parameters

A rigorous calculation of MO parameters by the Hückel method not only requires the introduction of additional parameters for the methyl group but also the decision as to what model to use for this group.[40] We have, instead, used the usual perturbation approximations, which have proved quite successful in various calculations for substituted aromatic compounds.[40,41] Parameters for both the isolated molecule and the transition state using the "inductive" model for the methyl group were calculated and tested.

The simplest "isolated molecule" model assumes that the property which determines the site of reaction is the relative change in electron density of the molecule produced by a hetero atom or a substituent (eq 2). Since

$$q_s' = q_s + \pi_{rs}\delta\alpha_r \qquad (2)$$

q_s is unity for all alternant hydrocarbons, the net charge at atom s induced by a substituent at atom r, δq_s, is equal to $\pi_{rs}\delta\alpha_r$. Values for π_{rs}, the mutual atom polarizabilities, have been tabulated for naphthalene[40,42] and if

---

[36] P. G. E. Alcorn and P. R. Wells, *Aust. J. Chem.*, 18, 1377 (1965).

[37] J. M. Bonnier, M. Gelus, and P. Nounou, *J. Chim. Phys.*, 62, 1191 (1965).

[38] However, with the interaction factors derived above, the bromination of 1,4-dimethylnaphthalene is predicted to afford 32.20, 67.12, and 0.68% of 2-, 5-, and 6-bromo-1,4-dimethylnaphthalene, and the bromination of 1,7-dimethylnaphthalene 50.57, 1.80, and 47.13% of 4-, 5-, and 8-bromo-1,7-dimethylnaphthalene, respectively. Because of the change in mechanism, this prediction and the one in Table II are likely to be in error for 1,4-dimethylnaphthalene.

[39] G. Dallinga, P. J. Smit, and E. L. Mackor, *Mol. Phys.*, 3, 130 (1960).

[40] A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," John Wiley & Sons, Inc., New York, N. Y., 1961, Chapters 4, 5, 11.

[41] L. Salem, "The Molecular Orbital Theory of Conjugated Systems," W. A. Benjamin, Inc., New York, N. Y., 1966, Chapters 1, 6.

[42] C. A. Coulson and H. C. Longuet-Higgins, *Proc. Roy. Soc.* London), A192, 16 (1947).

one further assumes additivity of the effects of methyl groups, δq_s can be calculated.

This procedure was used by Dallinga, Smit, and Mackor to correlate rates of deuterium exchange in all symmetrical dimethylnaphthalenes.[39] We have calculated δq_s values with $\delta\alpha_r = -0.3$, -0.4, and -0.5β. A plot of log k_s/k_n, where k_n refers to the 1 and 2 positions of naphthalene, against δq_s with $\delta\alpha_r = -0.5\beta$ is shown in Figure 2. Only rate factors for the major bromination products are used and that for 1,5-dimethylnaphthalene was not included in the calculation.[43] The agreement is only fair; the least-squares line has a probably error of 27.3% with $\delta\alpha_r = -0.3\beta$, and 30.7% when $\delta\alpha_r$ is -0.5β.[44] One of the major discrepancies when this parameter is used is that a 1-methyl substituted naphthalene is predicted to have a greater reactivity in the 2 position than in the 4 position, while, for instance, the bromination of 1-methylnaphthalene leads to 98.6% bromination in the 4 position.

The idea of an auxiliary inductive parameter (AIP)[45] assumes that the Coulomb integrals of the atom adjacent to the substituted carbon are changed by some fraction of $\delta\alpha_r$. We have assumed that a similar procedure is permissible in the perturbation methods. Values were calculated with $\delta\alpha_r$ equal to -0.3 and -0.5β, and AIP of 0.1 and 0.3 $\delta\alpha_r$. The use of AIP improves the agreement in several cases. In all cases the higher value for AIP predicts that a 1-methyl group activates the 4 position more than the 2 position, but only the lower value correctly predicts the almost equal reactivity in the 4 and 5 positions of 1,6-dimethylnaphthalene. A plot of log k_s/k_0 (relative to benzene) with $\delta\alpha_r = -0.3\beta$ and AIP 0.1 $\delta\alpha_r$ has a least-squares error of 24%.

Greenwood and McWeeny[46] noted that the ground-state electron distribution as calculated from eq 2 does not accurately predict the position of nitration in quinoline and that a better agreement is obtained when eq 3 is used

$$q_s'' = q_s' + \pi_{ss}\delta\alpha_s \qquad (3)$$

Here q_s' is the ground-state distribution (eq 2) which involves the mutual atom polarizabilities, π_{ss} is the self-atom polarizability[40,42] at atom s, and $\delta\alpha_s$ is the change in Coulomb integral at this atom resulting from the approach of the reagent. This treatment has the advantage of introducing the self-polarizabilities and of thus making the 1 and 2 positions in naphthalene different. Electron distributions for all the methylated naphthalenes as polarized by the electrophile were calculated for various combinations of values of $\delta\alpha_r$ and $\delta\alpha_s$. In general, an increase in $\delta\alpha_s$ relative to $\delta\alpha_r$ improves the agreement between prediction and observation for the order of positional reactivities. The values which qualitatively agree best are those for which $\delta\alpha_r = -0.3\beta$ and $\delta\alpha_s = 1.0\beta$. That is, the approach of the bromine molecule polarizes the positions over three times more strongly than does a methyl substituent. A plot of rate factors against electron densities using the above values has a least-squares error of 22.5%; with $\delta\alpha_r = -0.3\beta$ and $\delta\alpha_s = 0.7\beta$ the error is 19.9%.

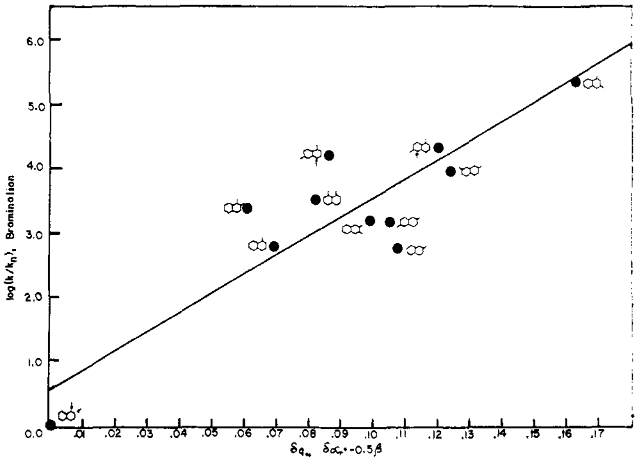


Figure 2. Correlation of rates of bromination with charge densities δq_s (eq 2).

Localization approximations for methylated hydrocarbons have often been utilized.[40] They can be calculated from the NBMO coefficients in the residual molecule, which in turn are easily obtained.[47] Since the nonbonding molecular orbital coefficients are zero at the unstarred positions,this approximation predicts that substituents affect the rates only if they are in starred positions in the residual ion, which are positions conjugated with the reaction site. Consequently, this treatment results in the prediction that many of the rate factors will be the same, for instance, the 1 positions in 2-methyl,2,6- and 2,3-dimethylnaphthalene, and the 4 positions in 1-methyl, 1,5-, and 1,2-dimethylnaphthalene all have $L^+ = -2.19\beta$. It is encouraging, however, that even this oversimplified treatment gives a better agreement with observed rates than the isolated molecule approximation, and a log plot of rate constants (relative to benzene) against L^+ has an error of only 15.7%. It correctly predicts that the 4 position will be more reactive than the 2 position in 1-methylnaphthalenes, and that the 4 and 5 positions of 1,6-dimethylnaphthalene are of equal reactivity.

We have corrected for the lack of interaction between nonconjugated positions by assigning a value of 0.1 $\delta\alpha$ to each carbon bonded to a substituted carbon. The justification for the treatment, which is similar to the AIP treatment, is that it results in a small increase in nonconjugated interactions. The errors in the least-squares plots are now reduced to 14.7% ($\delta\alpha = -0.3\beta$ and AIP = 0.1 $\delta\alpha$) and 13.2% ($\delta\alpha = -0.5\beta$ and AIP = 0.1$\delta\alpha$).

Finally, one can utilize published data on the π energies of naphthalenes substituted with a conjugating group, *i.e.*, ArCH$_2\pm$, and the π energies of all possible residual systems resulting from attack in the 1 and 2 positions of naphthalene.[48,49] Because the reference

---

[43] Because the point for benzene invariably falls below the line in all correlations with the MO parameters, benzene has also been omitted in the subsequent least-squares correlations, although it is shown on the graphs.

[44] A. Streitwieser, Jr., and P. M. Nair, *Tetrahedron*, **5**, 149 (1959).

[45] G. W. Wheland and L. Pauling, *J. Amer. Chem. Soc.*, **57**, 2086 (1935); M. J. S. Dewar, *J. Chem. Soc.*, 463 (1949); R. D. Brown, *Quart. Rev.* (London), **6**, 63 (1952); ref 40.

[46] H. H. Greenwood and R. McWeeny, *Advan. Phys. Org. Chem.*, **4**, 73 (1966).

[47] H. C. Longuet-Higgins, *J. Chem. Phys.*, **18**, 265, 275 (1950); M. J. S. Dewar, *J. Amer. Chem. Soc.*, **74**, 3345 (1952); see L. Salem, ref 41, pp 316–321.

[48] A. Streitwieser, Jr., and J. I. Brauman, "Supplemental Tables of Molecular Orbital Calculations," Pergamon Press, New York, N. Y., 1965.

[49] We are grateful to Dr. A. Fischer of the University of Canterbury, Christchurch, New Zealand, for suggesting this type of calculation.

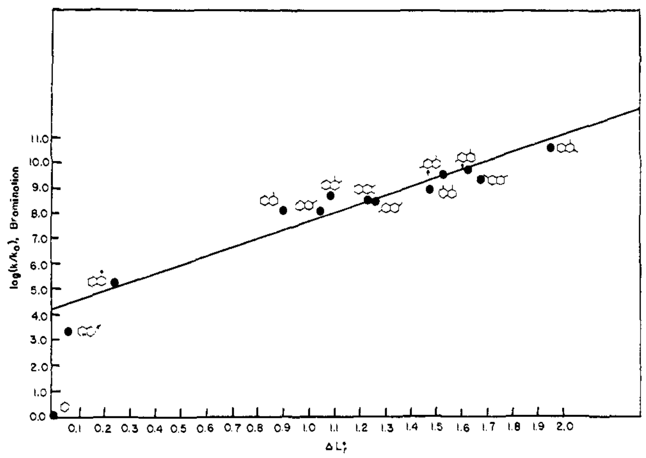
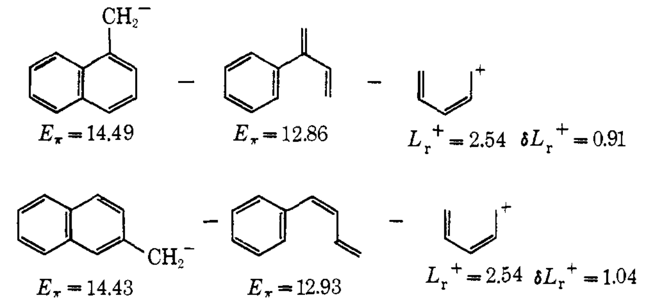


Figure 3. Correlation of rates of bromination with the localization energies ΔL_r^+.

compounds are odd alternant hydrocarbon systems, here approximated by an anion, the residual π systems for electrophilic attack are neutral species, either molecules or formally diradicals.[50] This calculation of the approximate localization energy, relative to that of benzene, is shown below for the 1 position of 1,3-dimethylnaphthalene ($\Delta L^+ = 1.95$). This is tantamount to treating the methyl group as a group capable of conjugation with the ring. A plot of ΔL^+ for the most reactive positions against the rate factors now has a probable error of 13.5% (Figure 3).

Scheme I



therefore $\Delta L_1^+ = 1.95\beta$

Both qualitative comparisons of orders of reactivity and graphical treatment indicate that localization calculations correlate better than isolated molecule treatments, which should be so, because the former provide a superior model of the transition state. It should particularly be so in bromination, where the transition state is assumed to come rather late on the reaction coordinate, as inferred from its large ρ value.[18,51] It is noteworthy, however, that with unsubstituted aromatic hydrocarbons the choice of MO parameters does not appear to affect the correlations significantly,[18] although it does in the present case of the methyl substituted naphthalenes. The deviations from the least-squares slopes are about 30% when the ground-state charge distribution is used to predict reactivity, and they are reduced to about 24% when an AIP is added. A model of the polarized ground state decreases the error to about 20%, and a further improvement to about 14% results when the σ complex is taken as the model for the transition state. The general agreement demonstrates at least a qualitative validity for the additivity principle of the effect of methyl groups, because this assumption was utilized in order to calculate the reactivity parameters.

Experimental Section

Materials. Inorganic reagents used in the kinetic determinations and the glacial acetic acid were as described before.[15,16] The solid dimethylnaphthalenes used in the kinetic determinations, in addition to those described earlier,[15,16] were recrystallized three times, and had the following mp:[52] 2,7-dimethylnaphthalene, 95.3–96.2°; 1,8-dimethylnaphthalene, 63.4–63.6°. The liquid 1,3- and 1,4-dimethylnaphthalenes (Chemical Samples Co., Columbus, Ohio) were over 99% pure and were distilled *in vacuo;* 1,6-dimethylnaphthalene was purified through the picrate (mp 111.5–112.5°) and had bp 95.9–96.9° (2.5 mm), and 1,2-dimethylnaphthalene (bp 96.2–97.2° (2.5 mm)) was 97.9% pure by vpc. For determination of products under kinetic conditions solid hydrocarbons were recrystallized to greater than 99.5% purity, and liquid hydrocarbons were purified to greater than 99% purity. The known bromo compounds were prepared according to literature procedures and had the following mp: 1-bromo-2,3-dimethylnaphthalene, 61.8–62.8° (lit.[24] 63°), 1-bromo-2,6-dimethylnaphthalene, 27.8–28.6° (lit.[25] 33–34°), 1-bromo-2,7-dimethylnaphthalene 47.1–47.9° (lit.[26] 48°), 1-bromo-4,5-dimethylnaphthalene, 31.6–32.2° (lit.[22] 30.5°), 1-bromo-3,4-dimethylnaphthalene, purified through the picrate of mp 108.2–109.8° (lit.[21] 108–109°), 37.8–38.4° (lit.[21] 39–40°). They were recrystallized until vpc analysis indicated at least 99.9% purity. The columns and instrument used in vpc analysis of the hydrocarbons and their bromo derivatives were the same as described earlier.[16]

1-Bromo-2,4-dimethylnaphthalene. A sample of 1,3-dimethylnaphthalene (Chemical Samples Co., Columbus, Ohio) was brominated with Br_2 in CS_2. The product was distilled *in vacuo* (118–121° (0.5 mm)) and had a mp of 16–17°. A mp of 20° was obtained in one determination, but this could not be reproduced. *Anal.*[53] Calcd for $C_{12}H_{11}Br$: C, 61.29; H, 4.72. Found: C, 61.49; H, 4.80. The picrate had mp 124.2–124.8° but could not be obtained analytically pure. The 1,3,5-trinitrobenzene derivative had mp 135–139°, which could not be improved on further recrystallizations. The 2,4,7-trinitro-9-fluorenone derivative, after two recrystallizations from ethanol, melted at 148.4–149.2°. *Anal.* Calcd for $C_{18}H_{14}BrN_3O_7$ (picrate): C, 46.57; H, 3.04. Found: C, 47.67; H, 3.05. Calcd for $C_{25}H_{16}BrN_3O_7$ (trinitrofluorenone): C, 54.46; H, 2.93. Found: C, 54.63; H, 3.08.

1-Bromo-4,7-dimethylnaphthalene. Preparative bromination of 1,6-dimethylnaphthalene was first carried out according to the literature procedure[27] on a 15-g scale. Three monobromination products, in the order of their retention times, were formed in 3.4, 47.9, and 48.7% yield. Recrystallization from ethanol of the first crop of picrate yielded a mixture containing 69% of the isomer second in retention time and 31% of the third isomer, but further crystallization of the picrate did not significantly concentrate either isomer. The pure 4 isomer was then prepared as follows. 1-Acetyl-4,7-dimethylnaphthalene[54] of mp 41.1–42.6° (lit.[28a] 43°) was converted to N-acetyl-4,7-dimethyl-1-naphthylamine by a Schmidt reaction in trichloroacetic acid as described for a similar compound.[55] The product was recrystallized from ethanol and had mp 175.8–177.3° (60%). *Anal.* Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.64; H, 7.25. The benzoyl

---

(50) See also J. D. Roberts and A. Streitwieser, Jr., *J. Amer. Chem. Soc.*, 74, 4723 (1952).

(51) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, 1, 35 (1963).

(52) All melting points are corrected.

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

(54) In the synthesis of this compound, 17.2% of the solid 4-acetyl-1,6-dimethylnaphthalene of 94.8% purity was formed after the first recrystallization from petroleum ether. The remaining oil contained 4.6 and 38.9% of presumably the 2 and 5 isomers, and 53.6% of the 4 isomer, so that in the Friedel-Crafts reaction a mixture of 4 and 5 isomers is also formed. See text. The pure 4-acetyl compound was oxidized with hypochlorite, and the resulting 1,6-dimethyl-4-naphthoic acid had mp 191.8–192.7°. The literature value for the acid obtained from the literature 4-bromo compound is 188–189° (L. E. Hinkel, *et al.*, ref 29). This provides a connection between Feist's 4-acetyl compound (ref 28a) and the bromo compound isolated on direct bromination in ref 27.

(55) A. Fischer, G. J. Sutherland, R. D. Topsom, and J. Vaughan, *J. Chem. Soc.*, 5948 (1965).

derivative had mp 254-256° (lit.[28b] 225-226°) and was analyzed because of the discrepancy with the literature value. *Anal.* Calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22. Found: C, 82.75; H, 6.22. 4,7-Dimethyl-1-naphthyl-*p*-toluenesulfonamide melted at 217.7-220.2° (lit.[28b] 218°). The amine obtained from the Schmidt reaction was converted to the bromo compound by the diazotization procedure of Newman and Wise.[56] 1-Bromo-4,7-dimethylnaphthalene was obtained in 31.9% yield as an oil which boiled at 120-125° (1.0 mm) (lit.[27] 171-172° (15 mm)) and did not solidify. The picrate melted at 120.1-121.5° (lit.[27] 114°). *Anal.* Calcd for $C_{18}H_{14}BrN_3O_7$: C, 46.57; H, 3.04. Found: C, 46.50; H, 2.99. The trinitrobenzene derivative has mp 153.8-155.2°. *Anal.* Calcd for $C_{18}H_{14}BrN_3O_6$: C, 48.23; H, 3.15. Found: C, 48.49; H, 3.40. Gas chromatography of the picrate mixture from the preparative bromination of 1,6-dimethylnaphthalene enriched with the above picrate, showed that this isomer is the one second in retention time of the three formed in preparative bromination.

Kinetic Determinations and Product Analysis. The kinetic determinations were carried out as described previously,[16] and all runs were conducted at least in duplicate. Rate constants were obtained graphically from the integrated form of the second-order rate equation by the method of least squares. The probable errors in the individual rate constants (k_{obsd}) and in the final rate constants, k (eq 1; Table I) were rarely greater than 2%. The kinetic runs were conducted over a period of several years, but with each new compound a previously determined one was usually checked to assure reproducibility of the technique, of the preparations of the solutions, etc.[3] The kinetics of bromination of 1,4-dimethylnaphthalene had the same characteristics as those found in the case of 1,5-dimethylnaphthalene.[16] In 75% acetic acid k_1 is 1.10 l. mol^{-1} sec^{-1}, and the ratio k_{-1}/k_2 has the value 5.93.

For product analysis of the kinetic runs, 100 ml of solution, 0.004 *M* in mono- or dimethylnaphthalene, 0.10 *M* in NaBr, 0.40 *M* in $NaClO_4$ and approximately 0.001 *M* in Br_2 was allowed to stand in brown bottles, thermostated at 25°, for at least ten half-lives of the reaction. Two isolation runs on 2,6-dimethylnaphthalene were also carried out with 0.5 *M* NaBr and no $NaClO_4$ (material balances 92.2 and 98.3%) and another two runs only with 0.1 *M* NaBr (material balances 94.0 and 97.8%). The variations in salt concentrations had no detectable effect on the composition of the product mixtures. The product mixtures were worked up by extraction with five 20-ml portions of petroleum ether, which were washed with four 20-ml portions of water, dried, and analyzed as described before.[2,16] At least two independent kinetic runs were analyzed for products, and between 3 and 8 chromatographs were recorded for each compound. The errors listed in Table II for the products are average deviations.

The results of the calculations of the MO parameters are contained in the Ph.D. dissertation of Kim.[2]

Acknowledgment. This work was supported by National Science Foundation Grant GP-4986, which is gratefully acknowledged. We also acknowledge stimulating discussions with Professor P. B. D. de la Mare.

---

(56) M. S. Newman and P. H. Wise, *J. Amer. Chem. Soc.*, **63**, 2847 (1941).

Enol Phosphates of β-Keto Acids. Synthesis and Hydrolysis of Ethyl β-Hydroxy-*trans*-cinnamic Acid Cyclic Phosphate[1]

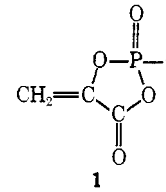
James F. Marecek and Dean L. Griffith

Contribution from the Department of Chemistry,
Case Western Reserve University, Cleveland, Ohio 44106.
Received July 2, 1969

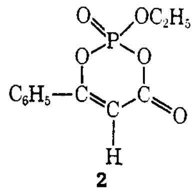
Abstract: The reaction of ethyl phosphoenol benzoylacetic acid (**6**) with N,N′-dicyclohexylcarbodiimide results in formation of the cyclic anhydride **2**. Hydrolysis of **2** in ^{18}O-enriched water indicated carbon-oxygen bond fission. The hydrolysis was subject to catalysis by hydroxide, by hydronium ion, and by general bases.

Since the investigations by Perkow in 1952,[2] a considerable amount of work has been done in the synthesis and reactions of enol phosphates.[3] A number of these enol phosphates have been found to be effective phosphorylating agents.[4,5] Enol phosphates obtained from keto acids, such as phosphoenol pyruvate,[6] are of particular interest, since they may fulfill important biological roles as phosphorylating agents.[7]

The reported[8] formation of an unstable cyclic anhydride of phosphoenol pyruvate (**1**) and its powerful phosphorylating ability led us to investigate the related compound, ethyl β-hydroxy-*trans*-cinnamic acid cyclic phosphate (**2**). Since the evidence for **1** was based primarily on its infrared spectrum, we hoped to produce a more stable compound of this type by taking advantage of the greater stability of six-membered cyclic phosphates.[9]



1



2

Prior to this work only one cyclic anhydride of this type had been reported. Salicoyl cyclic phosphate

---

(1) Aided by Grant No. IN57-F from the American Cancer Society.

(2) W. Perkow, K. Ullerich, and F. Meyer, *Naturwissenschaften*, **39**, 353 (1952).

(3) (a) F. W. Lichtenthaler, *Chem. Rev.*, **61**, 607 (1961); (b) T. C. Bruice and S. J. Benkovic, "Bioorganic Mechanisms," Vol. 2, W. A. Benjamin, Inc., New York, N. Y., 1966, pp 103-109.

(4) F. Cramer and K. Gartner, *Ber.*, **91**, 704 (1958); F. Cramer and R. Wittmann, *ibid.*, **94**, 328 (1961).

(5) H. H. Wasserman and D. Cohen, *J. Org. Chem.*, **29**, 1817 (1964).

(6) For a recent investigation of phosphoenol pyruvate and ethyl phosphoenol pyruvate see S. J. Benkovic and K. J. Schray, *Biochemistry*, **7**, 4090, 4097 (1968).

(7) V. M. Clark, D. W. Hutchinson, A. J. Kirby, and S. G. Warren, *Angew. Chem. Intern. Ed. Engl.*, **3**, 678 (1964); V. M. Clark and D. W. Hutchinson, *Progr. Org. Chem.*, **7**, 75 (1968).

(8) V. M. Clark and A. J. Kirby, *J. Amer. Chem. Soc.*, **85**, 3705 (1963).

(9) H. G. Khorana, G. M. Tenner, R. S. Wright, and J. G. Moffatt, *ibid.*, **79**, 430 (1957); J. R. Cox, R. E. Wall, and F. H. Westheimer, *Chem. Ind.* (London), 929 (1959); P. C. Haake and F. H. Westheimer, *J. Amer. Chem. Soc.*, **83**, 1102 (1961).