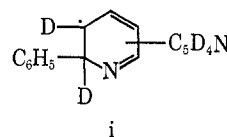


In the reaction of nitrobenzene with unlabeled pyridine, the mol wt 230, 231, 232, and 233 correspond to terphenyl, diphenylpyridine, phenylbipyridine, and terpyridine, respectively. Of these, diphenylpyridine is formed in greatest amount. Therefore, in the reaction with pyridine- d_5 , we would expect a major proportion of species of mol wt 234, 235, and 236, corresponding to tri-, tetra-, and pentadeuterated diphenylpyridine and pyridylbiphenyl, the latter being derived from phenylpyridine by phenyl-radical attack at the benzene ring. This is indeed the case, as shown by the data in Table VIII. The d_5 material, of mol wt 237, must of necessity involve intermolecular hydrogen exchange.

Phenylbipyridine from pyridine- d_5 should contain seven deuterium atoms, and indeed a significant amount of such product, of mol wt 239, appears in Table VIII. The formation of as much phenylbipyridine- d_8 indicates again the tendency for the radical intermediate^{1a}



i to aromatize as readily by loss of protium as of deuterium. Terpyridine from pyridine- d_6 should have mol wt 244, and this is so shown in Table VIII.

We have studied the reactions of nitrobenzene and nitrobenzene- d_5 with thiophene. These, as well as the relative reactivities of phenyl radicals in the gas phase at 600° to benzene, pyridine, and thiophene, is described in the following publication.¹⁷

Registry No.—Nitrobenzene, 98-95-3; nitrobenzene- d_5 , 4165-60-0; pyridine, 110-86-1; pyridine- d_5 , 7291-22-7.

Acknowledgment.—We acknowledge with thanks the assistance of D. K. Albert of the American Oil Co. in gas chromatographic analyses.

(17) E. K. Fields and S. Meyerson, *J. Org. Chem.*, **35**, 67 (1970).

Arylation by Aromatic Nitro Compounds at High Temperatures. VII. Reactions of Nitrobenzene and Nitrobenzene- d_5 with Thiophene

ELLIS K. FIELDS

Research and Development Department, Amoco Chemicals Corporation, Whiting, Indiana 46394

SEYMOUR MEYERSON

Research and Development Department, American Oil Company, Whiting, Indiana 46394

Received May 19, 1969

Nitrobenzene with thiophene at 600° gives 2- and 3-phenylthiophenes, ca. 3:1, and bithiophenes. The reaction is relatively clean, and, at a 1:20 mole ratio of nitrobenzene to thiophene, results in high product yields. It has been used to prepare phenyl- d_5 -thiophenes easily and efficiently. Isomer distributions of phenylthiophenes and phenylpyridines are almost identical in the reaction of thiophene and pyridine with phenyl radical from nitrobenzene and benzyne from phthalic anhydride. In competitive arylations, at 600°, the relative reactivity to phenyl radicals has been determined as follows: benzene, 1; pyridine, 2.3; thiophene, 5.

Earlier papers in this series have described the reactions at high temperatures of nitrobenzene, alone and with benzene and benzene- d_6 ,^{1a} with aromatic fluorine derivatives;^{1b} with toluene and toluene- d_3 ;^{1c} and with pyridine.^{1d} This paper concerns the reactions of nitrobenzene and nitrobenzene- d_5 with thiophene; a few details were mentioned in a preliminary communication.^{1e}

Experimental Section

Equipment and procedures are fully described in ref 1c.

Materials.—With the exception of labeled compounds and analytical standards, all chemicals were reagent grade.

Nitrobenzene- d_5 was prepared in 50 mol % yield by nitrating benzene- d_6 with nitrogen pentoxide in carbon tetrachloride according to Haines and Adkins.² Its isotopic composition was 96.9% d_6 and 3.1% d_4 .

Authentic 2- and 3-phenylthiophenes for gas chromatographic standards were synthesized by the method of Melles and Backer.³ The preparation of 2- and 3-phenyl- d_5 -thiophenes has been described elsewhere⁴—both isomers by reaction of nitrobenzene- d_5 with thiophene, and the 2 isomer also by reaction of

2-nitrothiophene with benzene- d_6 and by the photochemical reaction of 2-iodothiophene with benzene- d_6 .^{5a,b} The nmr spectra of all the labeled products agreed closely enough with the appropriate published spectra^{5b} to establish that the principal component in every case is the phenyl- d_5 -thiophene. In view of our isotopic analysis, however, the literature report^{5b} of the photochemical preparation and nmr spectra of the two phenyl- d_5 -thiophenes is in error in that it failed to recognize d_6 components in the products. The authors of that report have since found other isotopic components.^{5c}

Analyses.—Mass spectra were measured on a modified Consolidated Model 21-103 instrument at 70 eV, operating in the nonfocused mode, with the sample-introduction system and ionization chamber both at 250°. Isotopic compositions were derived from low-voltage measurements, in which possible isotope effects on sensitivity were ignored. Spectra were measured at the conventional 70 eV and at low voltage—7.5 eV, uncorrected. For the low-voltage measurements, the repellers were maintained at an average potential of 3 V, the exact values being selected to give maximum sensitivity. Relative intensities in the low-voltage (7.5 eV, uncorrected) mass spectra of product mixtures were taken as a first approximation to relative concentrations.^{1a-c} In any case, the use of relative intensities is perfectly valid for intercomparison of concentration ratios of identical components in separate samples⁶ within the limits of reproducibility of the low-voltage data.

(1) (a) E. K. Fields and S. Meyerson, *J. Amer. Chem. Soc.*, **89**, 3224 (1967); (b) *J. Org. Chem.*, **32**, 3114 (1967); (c) *ibid.*, **33**, 2315 (1968); (d) *ibid.*, **35**, 62 (1970); (e) *J. Amer. Chem. Soc.*, **89**, 724 (1967).

(2) L. B. Haines and H. Adkins, *J. Amer. Chem. Soc.*, **47**, 1419 (1925).

(3) J. L. Melles and H. S. Backer, *Rec. Trav. Chim. Pays-Bas*, **72**, 325, 491 (1953).

(4) S. Meyerson and E. K. Fields, *Org. Mass Spectrom.*, **1**, 263 (1968).

(5) (a) N. Wolf and N. Kharasch, *J. Org. Chem.*, **26**, 283 (1961); (b) R. M. Kellogg and H. Wynberg, *J. Amer. Chem. Soc.*, **89**, 3495 (1967); (c) R. M. Kellogg, personal communication.

(6) S. Meyerson and E. K. Fields, *Chem. Commun.*, 275 (1966).

Analyses were also performed with a directly coupled gas chromatograph-mass spectrometer combination⁷ employing a 21-103 instrument with an electron multiplier in place of the Faraday-cup detector, and by gas chromatography, usually on a column of polyethylene glycol sebacate on Chromosorb W. Other types of columns were used in special analyses.

Results and Discussion

The products of reaction of nitrobenzene at 600° with thiophene at four different mole ratios are shown in Table I. At a 1:1 mol ratio, aniline, phenol, and biphenyl are relatively high in concentration; these are also formed in the pyrolysis of nitrobenzene alone. The biphenyl concentration goes down rapidly as the concentration of nitrobenzene is reduced; thiophene is readily arylated by the phenyl radical.

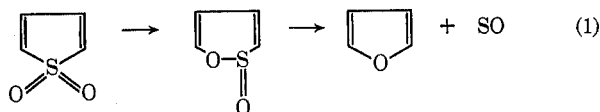
TABLE I
PRODUCTS FROM THE REACTION OF
NITROBENZENE WITH THIOPHENE^a

Products	Rel intensity ^b			
	Mol ratio of nitrobenzene/thiophene			
	(wt. g)			
	1:1 (36)	1:5 (39)	1:10 (65)	1:20 (69)
Aniline	17	9	8	10
Phenol	57	7	4	12
Biphenyl	22	4	2	1
Phenylthiophene	100	100	100	100
Bithiophene	10	23	30	35
Diphenylthiophene	27	9	6	4

^a Conditions: 600°; contact time, 15 sec; 0.5 mol of nitrobenzene. ^b Relative intensities in the low-voltage (7.5 eV, uncorrected) mass spectrum normalized to phenylthiophene = 100.

The total product yield, which reflects increasing amounts of dimerization products, did not increase as much as in the reaction of nitrobenzene with pyridine as the mole ratio of nitrobenzene to reagent was reduced from 1:1 to 1:20—1.9-fold for thiophene *vs.* 3.5-fold for pyridine. The difference may be caused by consumption of an appreciable amount of NO₂ or nitrobenzene in oxidation of the thiophene sulfur.

Aniline is formed in only trace amounts in the pyridine reaction at 1:20 mole ratio, but ten times as much is formed in thiophene under the same conditions. No obvious oxidation products of thiophene appear; however, thiophene dioxide would probably not survive at 600°. Benzofuran and phenylfuran, found at about the 0.4 mol % level by both mass spectrometry and gas chromatography, may well arise by the rearrangement demonstrated to occur in the sulfones derived from dibenzothiophene,^{8a,b} benzothiophene,^{8c,d} 2,3-dihydrobenzothiophene,^{8c} thianthrene,^{8d,e} and phenothioxin^{8d} (eq 1).



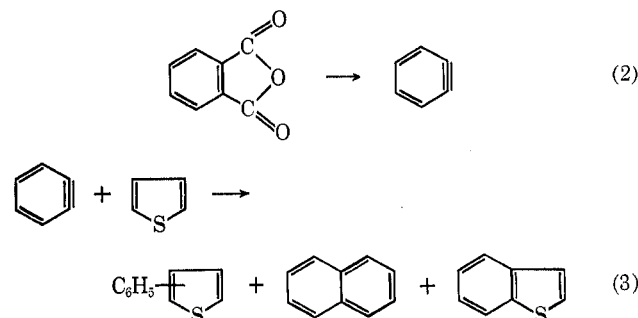
(7) R. S. Gohlke, *Anal. Chem.*, **31**, 535 (1959); L. P. Lindeman and J. L. Annis, *ibid.*, **32**, 1742 (1960); J. T. Watson and K. Biemann, *ibid.*, **36**, 1135 (1964).

(8) (a) E. K. Fields and S. Meyerson, *J. Amer. Chem. Soc.*, **88**, 2836 (1966); (b) J. H. Bowie, D. H. Williams, S. D. Lawesson, C. Nolde, and G. Schroll, *Tetrahedron*, **22**, 3515 (1966); (c) Q. N. Porter, *Aust. J. Chem.*, **20**, 103 (1967); (d) J. Heiss, K. P. Zeller, and P. Zech, *Tetrahedron*, **24**, 3255 (1968); (e) S. Meyerson and E. K. Fields, unpublished results.

The ratio of bithiophene to phenylthiophene increased from 0.1 to 0.35 over the 20-fold change in reactant concentrations, whereas the corresponding values for bipyridine to phenylpyridine were 0.17 and 1.18^{1d}—the increase was 3.5-fold and 7-fold for thiophene and pyridine, respectively. This difference, coupled with the absence of hydroxythiophenes from the products at all concentrations, further supports the suggestion that the NO₂ group tends to react with the thiophene sulfur atom as well as to abstract hydrogen.

The ratio of 2- to 3-phenylthiophene remained almost constant over the 20-fold change of concentration in reactants, 2.73 at 1:1 and 2.91 at 1:20. Studies of homolytic phenylation of thiophene in the liquid phase gave these ratios of 2- to 3-phenylthiophene (phenyl source, ratio): nitrosoacetanilide, 19;⁹ phenylazotriphenylmethane in air, 6.6;¹⁰ phenylazotriphenylmethane in nitrogen, 1.7;¹⁰ iodobenzene, 11.5.¹⁰ 2-Arylthiophenes were the only reported isomers in Gomberg arylations of thiophenes;¹¹ also, phenylation of thiophene by benzoyl peroxide gave only 2-phenylthiophene.¹⁰ The yields of phenylthiophene in the most recent study¹⁰ were low; the highest was only 3.75%, which contrasts sharply with our yield of 50 mol % at 1:20 mole ratio of nitrobenzene to thiophene.

Phenylthiophenes are also formed by the reaction of benzyne from phthalic anhydride at 690° with thiophene, along with naphthalene and thianaphthene¹² (eq 2 and 3). Similarly, phthalic anhydride with pyri-



dine at 690° gives phenylpyridines, as well as naphthalene and quinoline.¹²

Isomer distribution of phenylthiophenes and phenylpyridines from nitrobenzene and phthalic anhydride are shown in Table II. The isomer distributions are

TABLE II
ISOMER DISTRIBUTION IN PHENYLATION OF
THIOPHENE AND PYRIDINE

Phenylating agent	Phenylthiophene		Phenylpyridine		
	isomer, %	isomer, %	isomer, %	isomer, %	isomer, %
Nitrobenzene ^a	74	26	62	29	9
Phthalic anhydride ^b	75	25	59	33	8

^a At 600°; mol ratio of nitrobenzene/reagent, 1:10; contact time, 15 sec. ^b At 690°; mol ratio of phthalic anhydride/reagent, 1:10; contact time, 20 sec.

(9) J. Degani, M. Pallotti, and A. Tundo, *Ann. Chim. (Rome)*, **51**, 434 (1961).

(10) C. E. Griffin and K. R. Martin, *Chem. Commun.*, 154 (1965).

(11) M. Gomberg and W. E. Bachmann, *J. Amer. Chem. Soc.*, **46**, 2339 (1924); N. P. Buu-Hoi and N. Hoan, *Rec. Trav. Chim. Pays-Bas*, **69**, 1455 (1950); P. A. S. Smith and J. H. Boyer, *J. Amer. Chem. Soc.*, **73**, 2626 (1951).

(12) E. K. Fields and S. Meyerson, *Advan. Phys. Org. Chem.*, **6**, 1 (1968).

almost identical in the reactions of phenyl radical from nitrobenzene and benzyne from phthalic anhydride. Evidently the insertion of benzyne into a C-H bond has a good deal of the character of a radical reaction. This has previously been suggested by the work of Kampmeier and Rubin,¹³ who generated benzyne by unimolecular elimination of iodine from 2-iodophenyl radicals.

Labeled phenylthiophenes for a separate study of the behavior of phenylthiophenes under electron impact⁴ were made by reaction of nitrobenzene-*d*₅ with thiophene at 600°, and separating the 2- and 3-phenyl-*d*₅-thiophenes by gas chromatography. The combined yield was 42 mol %. 2-Phenyl-*d*₅-thiophene was also prepared from 2-nitrothiophene and benzene-*d*₆ at 600° in 29 mol % yield. Isotopic compositions were as shown in Table III.

TABLE III
ISOTOPIC COMPOSITION OF PHENYLTHIOPHENES

No. of deuterium atoms	Mol wt	2-Phenyl ^a	2-Phenyl ^b	3-Phenyl ^c
0	160	0.4	0.1	0.5
1	161	0.1	0.1	0.1
2	162	0.1	0.04	0.1
3	163	0.8	0.03	0.8
4	164	10.4	4.8	10.6
5	165	75.2	68.7	75.7
6	166	11.7	21.5	11.6
7	167	1.0	3.8	0.6
8	168	0.3	0.7	0.05

^a From nitrobenzene-*d*₅ and thiophene. ^b From 2-nitrothiophene and benzene-*d*₆.

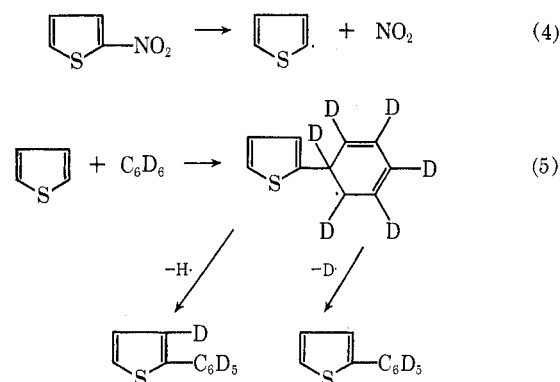
Some intermolecular H-D exchange took place at the high temperatures of the nitrobenzene-*d*₅-thiophene reaction; however, the extent of such exchange at 600° was far lower than that found in earlier work at 690°.¹⁴ Recovered nitrobenzene was 91% *d*₅ and 9% *d*₄, compared with the initial composition of 96.9% *d*₅ and 3.1% *d*₄.

The reaction at about 50% conversion of the nitrobenzene-*d*₅ was remarkably clean. Other than deuterated phenylthiophene, there were formed only about 25% bithiophene isomers and some diphenylthiophene-*d*₈, -*d*₉, and a little -*d*₁₀. The products from 2-nitrothiophene and benzene-*d*₆ included some phenylbithiophene-*d*₄ and -*d*₅ and a small amount of terthiophene.

There was obviously some scrambling of deuterium and protium. Although these were not so severe as to invalidate our mass spectral analyses of the isolated phenylthiophenes, we tried to prepare a more nearly isotopically pure 2-phenyl-*d*₅-thiophene by photolysis of 2-iodothiophene in benzene-*d*₆ (3.6% *d*₅, 96.4% *d*₆).⁴ The temperature was that of refluxing benzene, some 520° lower than our pyrolysis; even so, the 2-phenylthiophene separated by preparative gas chromatography had the isotopic composition of 2.9% *d*₄, 81.1% *d*₅, 14.0% *d*₆, 1.6% *d*₇, and 0.4% *d*₈.

2-Phenylthiophene-*d*₅ from benzene-*d*₆ by pyrolysis with 2-nitrothiophene and by photolysis with 2-iodothiophene presumably arises by the same mechanism

invoked in the reaction of nitrobenzene with benzene-*d*₆^{1a} to give biphenyl-*d*₆ as well as biphenyl-*d*₅ (eq 4 and 5).



The two reactions, although initiated by different means, evidently involve a common intermediate.

Competitive Phenylations.—To determine the relative reactivity of benzene, pyridine, and thiophene toward phenyl radicals, nitrobenzene was treated with mixtures of these reagents at 600° in the ratio of 0.05 mol of nitrobenzene to 0.25 mol of each reagent. The results are shown in Table IV.

TABLE IV
PRODUCTS FROM COMPETITIVE PHENYLATIONS^a

Products	Rel intensity ^b			
	Reactants (product wt, g)			
	Benzene and pyridine (7.8)	Benzene and thiophene (6.25)	Pyridine and thiophene (6.8)	Benzene, pyridine, and thiophene (9.1)
Phenol	7	7	11	6
Biphenyl, total	36	25	2	19
By process a ^c	2	3	2	2
By process b ^c	16	10	...	8
By process c ^c	18	12	...	9
Phenylpyridine	36	...	15	17
Bipyridine	7	...	5	4
Terphenyl	6	3	0.3	1
Diphenylpyridine	8	...	0.7	1
Phenylthiophene	...	52	37	36
Bithiophene	...	6	8	3
Diphenylthiophene	...	7	3	3
Pyridylthiophene	18	9

^a Conditions: 0.05 mol of nitrobenzene; 0.25 mol of each other reagent; 600°; 12 sec. ^b Ion per cent in the low-voltage (7.5 eV, uncorrected) mass spectra, ignoring distinctly minor components. ^c See text.

The order of reactivity to phenyl radical is evidently thiophene > pyridine > benzene. Numerical values may be calculated with certain assumptions. Phenylation products from pyridine and thiophene are easily distinguished from the dimers, bipyridine and bithiophene. Biphenyl, however, arises by three processes: (a) dimerization of phenyl radical from nitrobenzene; (b) phenylation of benzene; and (c) dimerization of benzene. The amount formed in the first process is shown in the third column of Table IV. Estimates of biphenyl from phenylation and dimerization can be derived by examining the relative amounts of each product in other reactions (Table V). The ratio of phenylation to dimerization does not differ appreciably in the reactions of nitrobenzene with benzene-*d*₆, fluorobenzene, and chlorobenzene. By correcting the amount of biphenyl by that shown in the third column

(13) J. A. Kampmeier and A. B. Rubin, *Tetrahedron Lett.*, 2853 (1966).

(14) E. K. Fields and S. Meyerson, *J. Amer. Chem. Soc.*, **88**, 21 (1966).

of Table IV and using the average of 47% for phenylation and 53% for dimerization, we arrived at the estimates of biphenyl formed in the two processes b and c shown in Table IV.

TABLE V

Source of R	Phenylation C ₆ H ₅ R, %	Dimerization R-R, %
C ₆ D ₆ ^a	44	56
C ₆ H ₅ F ^b	47	53
C ₆ H ₅ Cl ^c	47	53

^a Reference 1a. ^b Reference 1b. ^c Unpublished results.

Relative reactivities to phenyl radical from nitrobenzene at 600°, derived from the benzene-pyridine and benzene-thiophene product distributions, follow: benzene, 1; pyridine, 2.3; thiophene, 5. Calculated from the data in the fourth column of Table IV, the corresponding values are 1, 2.1, and 4.6. The agreement between the two sets of figures is quite good, especially as the concentration of nitrobenzene in the

reaction with the mixture of all three reagents differs somewhat from that in the other reactions.

We are presently surveying the relative reactivities of a variety of aromatic and heteroaromatic compounds to phenyl and substituted phenyl radicals derived from nitrobenzene and substituted nitrobenzenes at 600°. As shown in the fourth column of Table IV, the total yield of phenylation and dimerization products increased appreciably when a mixture of all three reagents was allowed to react with nitrobenzene. In our present studies we find even more pronounced yield increases in the reactions of nitrobenzene with certain mixtures of more than one reagent, and we are exploring the cause.

Registry No.—Nitrobenzene, 98-95-3; nitrobenzene-*d*₅, 4165-60-0; thiophene, 110-02-1.

Acknowledgment.—We acknowledge with thanks the assistance of D. K. Albert of the American Oil Co. in gas chromatographic analysis.

Kinetics of Reactions of Piperidine with Substituted Phenyl Ethers of 2,4-Dinitrophenol in 60% Dioxane-40% Water. Base Catalysis as a Function of the Group Displaced¹

J. F. BUNNETT AND C. F. BERNASCONI²

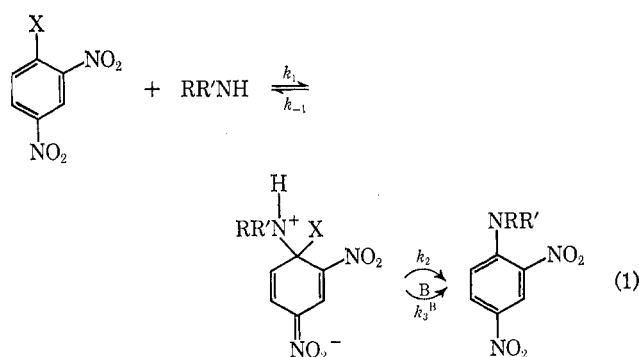
Metcalf Chemical Laboratories, Brown University, Providence, Rhode Island

Received June 20, 1969

The rates of reactions of piperidine with several 2,4-dinitrophenyl aryl ethers have been measured as functions of hydroxide ion and piperidine concentrations. The reactions of 2,4-dinitrophenyl 4-methoxyphenyl ether and of 2,4-dinitrophenyl 3,4,5-trimethylphenyl ether are strongly catalyzed by hydroxide ion, and plots of second-order rate coefficient (k_A) vs. base concentration are curvilinear, as observed for similar reactions in other studies. These reactions are also catalyzed by piperidine, the plot of k_A vs. piperidine concentration being linear. The reaction of 2,4-dinitrophenyl 4-nitrophenyl ether is weakly catalyzed by hydroxide ion, but no catalysis by piperidine has been detected. The effect of sodium hydroxide on the reaction of bis(2,4-dinitrophenyl) ether is very small and not considered to represent base catalysis. The partial rate coefficients k_1 and ratios k_2/k_{-1} , k_3^P/k_{-1} , and k_3^{OH}/k_{-1} were calculated. The k_1 values give a reasonable Hammett plot with $\rho = 1.15$. Incidentally, our measurements furnished rate coefficients (k_{OH}) for the reaction of NaOH with the various substrates.

The occurrence or absence of base catalysis in reactions of primary and secondary amines with 1-substituted 2,4-dinitrobenzenes, as well as the efficiency of base catalysis (*i.e.*, whether a large or a small acceleration is brought about by a given catalyst) depend among other things on the leaving group ability or "nucleofugicity"³ of the 1 substituent. Because this catalysis is associated with the second step of the intermediate complex mechanism (eq 1), rate accelerations by bases may be observed when $k_{-1} > (k_2 + \Sigma k_3^B[B])$, but not when $k_{-1} \ll (k_2 + \Sigma k_3^B[B])$. The first condition is generally fulfilled with poor (strongly or moderately basic) leaving groups X, the second with good (weakly basic) leaving groups. Incidentally, the occurrence or absence of base catalysis in a reaction series involving the same amine allows a crude classification of nucleofugicity in nucleophilic aromatic substitutions, if it is assumed that k_{-1} is

substantially independent of the leaving group. However, the ratios k_2/k_{-1} , which frequently can be determined experimentally, permit a more subtle ordering of such tendencies.



(1) (a) Supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is made to the donors of this fund. (b) Based in part on the Dissertation of C. F. B., Eidgenössische Technische Hochschule, Zürich, Switzerland, 1965.

(2) Address correspondence to either author at the University of California, Santa Cruz, Calif. 95060.

(3) J. Mathieu, A. Allais, and J. Valls, *Angew. Chem.*, **72**, 71 (1960).

These statements concerning the relationship between the incidence or extent of base catalysis and the relative magnitudes of k_{-1} and $(k_2 + \Sigma k_3^B[B])$ follow from qualitative consideration of the system of eq 1. Alternatively, these relationships emerge