Aromatic Substitution. XXI. Kinetics of Nucleophilic Substitution of Some Bromopyridines and -picolines with Thiophenoxide Ion. Nature of Activation by ortho-Methyl Groups[1]

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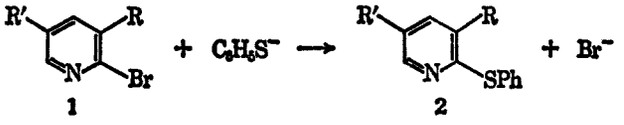
The rates and activation parameters were determined for the reaction of potassium thiophenoxide in methanol with 2-bromo-, 2-bromo-3-methyl-, 2-bromo-5-methyl-, 2,3-dibromo-, and 2,5-dibromopyridine. An *o*-methyl group accelerated the reaction, probably due to the combined effects of London forces and ion–dipole interactions. At 110°, $k_{o\text{-}CH_3}/k_{p\text{-}CH_3} = 5.0$, while $k_{o\text{-}Br}/k_{p\text{-}Br} = 2.5$. These results were compared with those obtained with methoxide ion in methanol. Substitutions with thiophenoxide ion in dimethyl sulfoxide were also studied. The increase in rate on going to this solvent was not as great as expected and is discussed. Thiophenol itself reacted faster in methanol than did the thiophenoxide ion due to a fast acid–base preequilibrium in which the bromopyridine was protonated and allowed to react as such with the thiophenoxide ion formed.

Quantitative studies[3] on orientation and reactivity in nucleophilic aromatic substitution of a hydride ion equivalent in the pyridine series by phenyllithium have brought to light the remarkable observation that a 3-methyl or a 3-ethyl group *activates* the 2 position of the pyridine nucleus toward this nucleophilic attack, the methyl substituent activating it more than ethyl. On the other hand, position 6 was normally deactivated, as expected from the electron-donating effect of the alkyl group. The relative rates were determined by the competitive technique and the total rate ratios and partial rate factors were: ${}^{Me}_{H}K = 1.30$, ${}^{Me}F_2 = 2.4$, ${}^{Me}F_6 = 0.13$ and ${}^{Et}_{H}K = 0.79$, ${}^{Et}F_2 = 1.4$, ${}^{Et}F_6 = 0.16$. In the Tschitschibabin reaction with sodamide, however, a 3-methyl group does not activate C-2 toward substitution although attack still takes place predominantly at the 2 rather than at the 6 position.[4] An ion–dipole attractive interaction of the 3-methyl group and the approaching amide ion might account for this observation.[5] Two possibilities were entertained to account for the results obtained in the phenyllithium reactions. (a) London dispersion forces acting between the 3-alkyl substitutent and the attacking nucleophile[6] could lower the energy of activation for attack at C-2 but not at C-6. The increase in the attractive force on going from the methyl to the more polarizable ethyl group would be counterbalanced by the increasing steric hindrance. (b) An alternative explanation invoked the existence of an electron-deficient type of bond between the 3-alkyl group and the organolithium compound which would facilitate attack at C-2. The ease of formation of such an electron-deficient bond would be expected to decrease as branching of the methyl substituent increased.[7] This type of bonding could be looked upon perhaps as a stronger version of an ion–dipole attraction.

In order to decide between the alternatives it was hoped to carry out kinetic studies on model systems and to get the required information from an analysis of the thermodynamic parameters. To this end, the reaction of 2-bromo-, 2-bromo-3-methyl-, and 2-bromo-5-methylpyridine with methoxide ion was studied under a variety of conditions.[8] The rates were in the order 2-bromo- > 2-bromo-3-methyl- > 2-bromo-5-methyl, and were dependent upon E_a. This order of reactivity parallels that found in the Tschitschibabin but not in the phenyllithium reaction. The lesser deactivation of the *ortho* then the *para* position by a 3-methyl group was attributed[8] to an ion–dipole attraction[9] between the methyl group and the attacking methoxide ion approaching the *ortho* position, this attraction overcompensating the greater inductive effect of the methyl substituent at the *ortho* than at the *para* position, and any steric hindrance by the 3 substituent to approach.[10] Release of steric compression between the bromine and methyl groups and the solvation shell around the lone pair of electrons on nitrogen in the ground state of 2-bromo-3-methylpyridine on going to the transition state, but not of 2-bromo-5-methylpyridine, may also play a minor role.

In a continuation of efforts to find a system amenable to kinetic study which would reporduce the order of reactivities observed with phenyllithium, attention was turned to the reaction of 2-bromopyridine derivatives (**1**) with thiophenoxide ion, since the latter is much more polarizable than methoxide ion, which could lead to greater London attractive forces between the *o*-methyl group and the attacking nucleophile.[6] Preliminary studies of relative reactivities were carried out using the competitive technique in which equimolar mixtures of 2-bromo- and 2-bromo-3-methylpyridine, 2-bromo- and 2-bromo-5-methylpyridine, and 2-bromo-3-methyl- and 2-bromo-5-methylpyridine were allowed to react with a small amount of potassium thiophenoxide in methanol. The products were analyzed by gas chromatography and the total rate ratios and partial rate factors calculated. Authentic samples



1 **2**

of the 2-thiophenoxypyridines (**2**) were prepared for comparison with the reaction products. When an

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TABLE I

KINETIC DATA FOR THE REACTION OF 2-BROMOPYRIDINE DERIVATIVES WITH THIOPHENOXIDE ION IN METHANOL

Pyridine	10^5k_2[a], l. mol^{-1} sec^{-1} (temp, °C)	E_a, kcal/mol	$\Delta S^\ddagger$,[b] eu
2-Br	2.14 (110), 6.85 (123), 19.3 (136.8)	26.0	−13.5
2-Br-3-Me	3.0 (110), 3.64 (111), 7.35 (121), 14.3 (129.2), 27.4 (136.8)	24.0	−18.5
2-Br-5-Me	0.255 (101.5), 0.61 (110), 1.34 (120), 4.29 (133.5)	27.0	−13.5
2,3-Br_2	48.4 (99.5), 107 (110), 151 (114.5), 222 (120.5), 426 (130)	21.2	−19.0
2,5-Br_2	43.4 (110), 105.5 (121.2), 217.8 (131.2)	23.5	−14.0

[a] [PhS^-] = [bromopyridine] = 0.3075 N ≡ 0.0046125 mol of reactants. [b] Experimental errors are ±0.2 kcal in E_a and ± 1eu in $\Delta S^\ddagger$.

excess of potassium methoxide in methanol over thiophenol was used a substantial amount of the 2-methoxypyridines was formed in addition to **2**, and an analysis of the recovered starting materials indicated that, under these conditions, the rate of consumption of bromopyridines was in the order 2-bromo- > 2-bromo-3-methyl- > 2-bromo-5-methyl. This is due to the greater reactivity of 2-bromopyridine with methoxide ion compared with the methyl derivatives.[8] If, however, equimolar amounts of potassium methoxide and thiophenol were used in the preparation of thiophenoxide no competition from methoxide ion (which would be present in small amounts due to the equilibrium $C_6H_5S^- + MeOH \rightleftharpoons C_6H_5SH + MeO^-$) was observed and no methoxypyridines could be detected by gas chromatography. Under these conditions the sought-for order of reactivities was finally encountered: 2-bromo-3-methyl- > 2-bromo- > 2-bromo-5-methylpyridine; ${}^{o\text{-}Me}_{H}K = 2.46$ and ${}^{p\text{-}Me}_{H}K = 0.63$; *ortho*:*para* ratio (at 80°) = 3.85.

Kinetic measurements were now carried out with the bromopyridines and thiophenoxide ion in methanol. The results are summarized in Table I.

The results clearly indicate the activation of the 2-bromopyridine by an *o*-methyl group and the expected deactivation by a *p*-methyl group. The *ortho* effect arises from a decrease in the energy of activation (ΔE_a = 2 kcal/mol) of the substitution process. This could be due either (i) to London dispersion attractive forces,[6] or (ii) to an ion–dipole attraction,[9,11] either of which should be large enough to overcome the electronic deactivation by the *o*-Me group ($\gtrsim$1 kcal/mol) and the steric hindrance to approach by the nucleophile. An examination of the *o*-Me:*p*-Me and *o*-Br:*p*-Br reaction rate ratios of benzyl chlorides with MeO^-, $C_6H_5S^-$, and I^- and calculations of the magnitude of London forces operating in the transition state led to the suggestion[12] that the differences in rate ratios could be assigned to these forces. This was questioned by Sisti and his coworkers who pointed out[11] that comparison of the *o*-CH_3:*p*-CH_3 and *o*-Br:*p*-Br rate ratios, with the same reagents, showed trends contrary to those expected from London interactions alone (*i.e.*, charged nucleophiles gave higher *ortho*:*para* ratios with the less polarizable methyl group than with the more polarizable bromo group). Also, in the reaction of substituted phenacyl chlorides with various nucleophiles, it was shown[9] that the highly polarizable iodide ion gave $k_{o\text{-}CH_3}/k_{p\text{-}CH_3} = 1.06$ and $k_{o\text{-}Br}/k_{p\text{-}Br} = 0.23$, *i.e.*, a higher *ortho*:*para* ratio with the less polariable substituent, while this trend was reversed when the nucleophile was a neutral species, *i.e.*, pyridine: $k_{o\text{-}CH_3}/k_{p\text{-}CH_3} = 0.79$ and $k_{o\text{-}Br}/k_{p\text{-}Br} = 1.17$. It was proposed that such results were more in accord with favorable Coulombic interactions of the ion–dipole type between the *ortho* substituents and the nucleophile since the dipoles of the $\overleftarrow{C\text{–}CH_3}$ and $\overrightarrow{C\text{–}Br}$ groups are in opposite directions. Ho, Miller, and Wong[13] reported that the reactivity of thiomethoxide ion with *p*-halogenonitro- and 1-halogeno-2,4-dinitrobenzene in methanol showed a high value of the ratio F/I similar to that found for a nucleophile of low polarizability such as methoxide ion, and felt that there was no support for the suggestion that polarizability effect enhanced reactivity in such reactions. On the other hand, Di Nunno and Todesco[14] found that the rates of the reactions of *p*-halogenonitrobenzene and 2-halogenobenzothiazoles with thiomethoxide and methoxide ions fitted well a linear relationship between the logarithm of the ratio of the reaction rates of a pair of nucleophiles (one polarizable and the other poorly so) and the polarizability of the leaving group,[15] thus confirming the relevance of polarizability factors in determining nucleophilic reactivity.

In order to decide between the two alternative explanations for the *ortho*:*para* ratio observed here, the kinetics of the reactions of 2,3- and 2,5-dibromopyridine with thiophenoxide ion in methanol were studied. The choice of bromine as the substituent was guided by the fact that it is much more polarizable than methyl and has the opposite polarity, but is similar in size to Me.[6] It would then be expected that if only London dispersion forces were at work that a larger *ortho*:*para* ratio would have been observed with the β-bromo substituent than with the β-methyl. If, on the other hand, only ion–dipole interactions were involved then an *ortho*:*para* ratio <1 would have been predicted for attack by PhS^-. For the sake of comparison, the rates and Arrhenius parameters for the reactions of the same compounds with MeO^- in MeOH are given in Table II.

TABLE II

RATE CONSTANTS AND ARRHENIUS PARAMETERS FOR REACTIONS OF 2-BROMOPYRIDINE DERIVATIVES WITH POTASSIUM METHOXIDE IN MEOH

Pyridine	10^5k_2, l. mol^{-1} sec^{-1} (at 110°)	E_a, kcal/mol	$\Delta S^\ddagger$, eu
2-Br[c]	9.44	26.6_3	−10.5
2-Br-3-Me[c]	2.39	27.8_7	−10.0
2-Br-5-Me[c]	1.54	28.9_3	−7.8
2,3-Br_2[a]	155	23.83	−11.4
2,5-Br_2[b]	152	24.75	−9.5

[a] 10^5k_2 at temperatures in parentheses: 63.5 (99.5°), 221 (114.5°), 359 (120.5°), 705 (130°); log A = 10.78. [b] 10^5k_2 at temperatures in parentheses: 29.5 (91.5°), 395.3 (121.5°); log A = 11.35. [c] See ref 8.

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TABLE III

RATE RATIOS FOR REACTIONS OF 3-R- OR 5-R-2-BROMOPYRIDINES WITH POTASSIUM METHOXIDE AND POTASSIUM THIOPHENOXIDE IN MeOH AT 110°

R	k_{o-R}/k_{p-R}	$(k_{PhS^-}:k_{MeO^-})_R/(k_{PhS^-}:k_{MeO^-})_H$	$(k_{PhS^-}:k_{MeO^-})_{o-R}/(k_{PhS^-}:k_{MeO^-})_{p-R}$
CH_3	5.0 (PhS^-), 1.6 (MeO^-)	5.5 (*o*-Me), 1.7 (*p*-Me)	3.2
Br	2.5 (PhS^-), 1.0 (MeO^-)	3.1 (*o*-Br), 1.3 (*p*-Br)	2.4

The *ortho*:*para* ratios can be looked at in a number of ways. The rate ratios k_{o-R}/k_{p-R} can be compared directly for a given nucleophile and are very instructive. They do not, however, take into account differences in nucleophilicities when the behaviors of different reagents are compared. Two approaches have been used to cancel out nucleophilicity differences between reagents PhS^- and MeO^-. Reinheimer and Bunnett[6] used an expression such as eq 1 for this purpose, except

$$\frac{(k_{o-R}/k_H)_{PhS^-}}{(k_{o-R}/k_H)_{MeO^-}} \equiv \frac{(k_{PhS^-}/k_{MeO^-})_{o-R}}{(k_{PhS^-}/k_{MeO^-})_H} \quad (1)$$

that hydroxide ion (and not methoxide ion) was chosen as the basis for comparison because of its low polarizability and small size. On the other hand, it was felt by Sisti and Lowell[11] that eq 2 was a better way of adjusting the rate ratio to cancel out the nucleophilicity differences. All three of these ratios are given in Table III.

$$\frac{(k_{o-R}/k_{p-R})_{PhS^-}}{(k_{o-R}/k_{p-R})_{MeO^-}} \equiv \frac{(k_{PhS^-}/k_{MeO^-})_{o-R}}{(k_{PhS^-}/k_{MeO^-})_{p-R}} \quad (2)$$

A different way of looking at this "*ortho* effect" to take into account the difference in nucleophilicities of the two reagents is to consider the differences in Arrhenius parameters in these reactions as a function of the nature and position of the substituent. These data are given in Table IV from which it may be seen that

TABLE IV

DIFFERENCES IN ARRHENIUS PARAMETERS

	Substituent in 2-bromopyridine				
	H	3-CH_3	5-CH_3	3-Br	5-Br
ΔE_a ($\equiv E_{MeO^-} - E_{PhS^-}$)	0.6	3.9	1.9	2.6	1.3
$\Delta\Delta S^{\ddagger}_{(MeO^- - PhS^-)}$	3.0	8.5	5.7	7.6	4.5

ΔE_a for a 3-methyl substituent is larger than that for a 5-methyl substituent ($\Delta\Delta E_a = 2.6$). If the polarizability of sulfur is not taken into account the thiophenoxide ion is undoubtedly larger than methoxide and an unfavorable steric effect should have led to a trend in ΔE_a in the opposite direction. On the other hand, ΔE_a for 3-Br is not that much larger than ΔE_a for 5-Br ($\Delta\Delta E_a = 1.3$), and had only polarizability factors been involved this difference should have been greater than that for the β-methyl group.

Irrespective of which rate ratios are considered (Table III), the data are not consistent with either the involvements of pure London dispersion forces or of pure ion–dipole interactions to account for the observed "*ortho* effect," since the *ortho*:*para* ratio for a β-bromo substituent was not less than unity, but neither was it larger than the *ortho*:*para* ratio for a β-methyl group. It would seem reasonable to suggest a combination of these two factors to account for the observed results. Since these would act in opposition in the case of the 3-bromo derivative it appears that the polarizability factor is somewhat more important than the Coulombic interaction in this case. Such a situation may also well obtain in the substitutions of 3-picoline by phenyllithium and by sodium amide. In the former case, a combination of attractive interactions could explain the net activation of C-2; in the Tshitschibabin reaction, on the other hand, an ion–dipole attractive interaction would account for the observed high *ortho*:*para* ratio (10:1), but alone would not be strong enough to lead to an activation of C-2 by the 3-methyl group. Whether or not the activation of C-2 by a 3-methyl group in the reaction of 2-bromopyridine with theophenoxide ion is indeed due in large measure to polarizability effects or whether a heavy-nucleophile effect[13] is important is now under investigation using phenoxide and thiomethoxide ions with the above substrates.

The kinetics of the reactions with thiophenoxide ion were studied briefly under two other sets of conditions. As expected, the reaction of 2-bromopyridine with potassium thiophenoxide in dimethyl sulfoxide was faster than that in methanol. While the same reaction with MeO^- proceeded 3×10^3 faster in DMSO than in MeOH,[8] that with PhS^- was only 100 times faster in the nonprotic solvent, this being due to a lower energy of activation (by 3.7 kcal/mol) in DMSO than in MeOH. The entropy of activation was about the same in both solvents for the PhS^- reaction. This contrast with $\Delta\Delta S^{\ddagger}_{(MeOH-DMSO)} = 7.6$ eu and $\Delta E_{(MeOH-DMSO)} = 8.7$ kcal/mol when MeO^- was used as the nucleophile.[8] This suggests that thiophenoxide, but not methoxide, ions are appreciably solvated in DMSO solution, perhaps due to the high polarizability of the thiophenoxide ion compared with methoxide, or perhaps to an equilibrium which would lower the reactivity of

$$(CH_3)_2SO + PhS^- \rightleftharpoons (CH_3)_2\overset{O^-}{\underset{|}{S}}SPh \quad (3)$$

the nucleophile and the entropy of the ground state. There do not appear to be any data in the literature to support the latter suggestion.

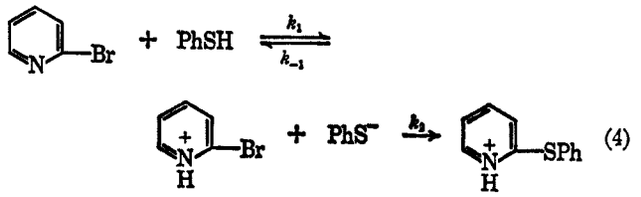
In early runs aimed at discouraging the intrusion of methoxide ions into the reactions, an excess of thiophenol over potassium methoxide was used so that both thiophenoxide ion and thiophenol were present in solution. The rate plots so obtained were unsatisfactory. Thus, at any one temperature and under identical conditions, the order of reactivity found was 3-CH_3 > H > 5-CH_3; but when an Arrhenius plot of the results at three temperatures was essayed a straight line could not be obtained. At the lower temperatures there was an initial rapid reaction, the extent of which appeared to depend on the time allowed for thermal equilibrium to be reached and on the amount of free thiophenol present. This suggested that the "free" thiophenol (always present in lesser quantities than the 2-bromopyridine) first protonated the pyridine nucleus, and that the initial fast reaction was due to an SNAr2 reaction of that fraction of the 2-bromopyridine present as the pyridinium ion with thiophenoxide ion (eq 4).[16]

(16) Presented by R. A. Abramovitch at the Gordon Conference on the Chemistry of Heterocyclic Compounds, New Hampton, N. H., July 4–8, 1966.

TABLE V

MISCELLANEOUS RUNS WITH 2-BROMOPYRIDINE

Nucleophile	Solvent	10^5k_2, l. mol^{-1} sec^{-1}	E_a, kcal/mol	$\Delta S^\ddagger$, eu
PhS^-	DMSO	5.89 (67.5°), 230 (110°)	22.3	−13.0
PhSH	MeOH	47.6 (110°), 150.1 (132°)	16.2	−10.8



(4)

In order to check this possibility the reaction of 2-bromopyridine with an equivalent amount of thiophenol in methanol (no methoxide added) was carried out at two temperatures (Table V). The product was shown to be 2-thiophenoxypyridine; no 2-methoxypyridine was detected by glc. Good second-order kinetics were observed. The activation parameters are uncertain to the extent that they were calculated from measurements at two temperatures only. The results are entirely consistent with a substitution proceeding *via* a pyridinium salt;[16] such salts are known to undergo nucleophilic substitution much faster than do the free bases.[17] The reaction with thiophenol itself proceeds 22.2 times faster at 110° than does that with thiophenoxy anion.

Similar observations have been reported in more extensive studies by Illuminati, Linda, and Marino,[18] who found the noncatalyzed reaction of a chloroquinoline with *p*-toluenethiol in methanol solution is faster than the reaction involving either the aryl sulfide or the chloroquinoline ion with the non-ionized form of the other reactant. In the present case, we believe the fast reaction taking place is that between the pyridinium *salt* and the thiophenoxide *ion* produced in eq 4. The reaction of the free base with thiophenoxide is known to be much slower and that between the pyridinium salt and unionized thiophenol is expected to be slow.[18] Assuming the preequilibrium in eq 4 is fast compared with the substitution process, a steady-state treatment will lead to eq 5 and, if $k_{-1} \gg k_2$ and $K = k_1/k_{-1}$,

$$\text{rate} = \frac{k_1k_2}{k_{-1} + k_2}[\text{PhSH}][\text{PyBr}] \qquad (5)$$

this reduces to eq 6 in accord with the observed second-order kinetics. The same result was obtained by Illuminati[18] in the chloroquinoline series.

$$\text{rate} = k_2K[\text{PhSH}][\text{PyBr}] \qquad (6)$$

Experimental Section

Materials.—Thiophenol (Eastman) was fractionally distilled, the cut bp 166–168° (740 mm) being used. The purification of dimethyl sulfoxide, methanol, 2-bromo-, 2-bromo-3-methyl- and 2-bromo-5-methylpyridine was as previously reported,[8] as was the preparation of solutions of potassium methoxide in methanol. 2,5-Dibromopyridine (Aldrich) was recrystallized from ethanol and had mp 94° (lit.[19] mp 94°).

Solutions of potassium thiophenoxide in methanol were prepared by adding an equivalent amount of potassium methoxide in methanol to a weighed amount of thiophenol.

Solutions of potassium thiophenoxide in dimethyl sulfoxide were prepared by dissolving solid potassium thiophenoxide in pure dimethyl sulfoxide and storing the solutions under nitrogen. These could be standardized either by direct titration with hydrochloric acid or by the addition of excess hydrochloric acid and back-titration with baryta (bromocresol green–methyl red indicator). Potassium thiophenoxide itself was prepared by the addition of slightly less than the equivalent amount of potassium methoxide solution to a solution of thiophenol in methanol. The solution was evaporated to near dryness, thiophenol (1–2 ml) was then added, and the solution taken completely to dryness to give the white salt.

2,3-Dibromopyridine.—A mixture of 3-bromo-2-pyridone[20] (4.0 g) and phosphorus oxybromide (20 g) was heated to near reflux for 2.5 hr. The mixture was then poured into ice–water, neutralized with potassium carbonate and extracted with ether. The solid residue after the evaporation of the ether was recrystallized from aqueous alcohol to give 2,3-dibromopyridine (4.0 g, 65%): mp 59° (lit.[19] mp 58–59°); nmr (CCl_4) τ 1.75 (H-6, quartet $J_{5,6} = 4.5$ cps, $J_{4,6} = 1.5$ cps), 2.16 (H-4, quartet, $J_{4,5} = 8$ cps), 2.87 (H-3, quartet).

Reaction Products.—These were obtained by a preparative reaction of the appropriate 2-bromopyridine with potassium thiophenoxide in methanol under a dry nitrogen atmosphere under the conditions of the kinetic runs. 2-Thiophenoxypyridine had bp 121–122° (1 mm) [lit.[21] bp 160–162° (8 mm)]. The picrate (from water) had mp 142–143°.

3-Methyl-2-thiophenoxypyridine had bp 142–144° (2 mm) (72.7% yield).

Anal. Calcd for $C_{12}H_{11}NS$: C, 70.70; H, 5.47. Found: C, 70.21; H, 5.47.

The picrate (from benzene) had mp 158–159°.

Anal. Calcd for $C_{12}H_{11}NS$, $C_6H_3N_3O_7$: C, 50.20; H, 3.25. Found: C, 50.48; H, 3.45.

5-Methyl-2-thiophenoxypyridine had bp 148–150° (2 mm) (78.5% yield).

Anal. Calcd for $C_{12}H_{11}NS$: C, 70.70; H, 5.47. Found: C, 70.34; H, 5.51.

The picrate (from benzene) had mp 174–175°.

3-Bromo-2-thiophenoxypyridine was purified by gas chromatography on a 6 ft × 0.25 in. 20% SE 30 on Chromosorb column. It gave a picrate, mp 129–130° (from methanol).

Anal. Calcd for $C_{11}H_8BrNS$, $C_6H_3N_3O_7$: C, 41.23; H, 2.24. Found: C, 41.28; H, 2.30.

The nmr spectrum ($CDCl_3$) of free base showed τ 1.99 (1 H quartet, H-5), 1.20–1.60 (5 H multiplet), 1.16 (1 H doublet, H-4), 0.64 (1 H doublet, H-6).

5-Bromo-2-thiophenoxypyridine was similarly purified by glpc and the picrate, mp 111° (from methanol), was analyzed.

Anal. Calcd for $C_{11}H_8BrNS$, $C_6H_3N_3O_7$: C, 41.23; H, 2.24. Found: C, 41.35; H, 2.10.

The nmr spectrum ($CDCl_3$) of free base showed τ 3.28 (1 H doublet, H-3), 2.40–2.70 (6 H multiplet, H-4 and C_6H_5), 1.59 (1 H singlet, H-6).

Competitive Reactions.—The procedure used is illustrated by means of a typical run using 2-bromo- and 2-bromo-3-methylpyridine. A solution of 2-bromopyridine (0.3119 g), 2-bromo-3-methylpyridine (0.3285 g), and thiophenol (0.0530 g) in methanol was treated with 0.13 *N* potassium methoxide in methanol solution (1 ml) and heated in a sealed tube under dry oxygen-free nitrogen in a thermostat at 80° for 24 hr. The reaction mixture was analyzed by glpc using a 2.5 ft × 0.25 in. column packed with precipitated asphalt on Chromosorb W (15% w/w) operated at 163° and a helium inlet pressure of 40 psi. Standard calibration curves were plotted between concentration of authentic products and peak areas. The total rate ratios were calculated using the Ingold–Shaw equation (eq 7),[22]

$$x^YK = \log\left[1 - \frac{Z_0}{Y_0}R/(1 + R)\right] \Big/ \log\left[1 - \frac{Z_0}{X_0}1/(1 + R)\right] \qquad (7)$$

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where X_0 = initial concentration of 2-bromopyridine, Y_0 = initial concentration of the substituted 2-bromopyridine, Z_0 = initial concentration of the nucleophilic reagent, and R = ratio of the isomers formed. Similar runs were carried out using mixtures of 2-bromo- and 2-bromo-5-methylpyridine and a ternary mixture of 2-bromo-, 2-bromo-3-methyl-, and 2-bromo-5-methylpyridine.

Kinetic Procedures. A. Potassium Thiophenoxide in Methanol.—The runs were carried out in sealed tubes under nitrogen using 15-ml portions of solution containing equimolar (≡0.00461 mol) proportions of potassium thiophenoxide and the 2-bromopyridine. Aliquots were quenched in halide-free nitric acid and the solution was allowed to stand for 24 hr in air so that the unreacted thiophenol which was liberated was oxidized and did not interfere with the titration. Liberated bromide ion was titrated against silver nitrate. To check this procedure an aliquot was also quenched with hydrochloric acid and back-titrated with baryta to determine the amount of thiophenoxide consumed; data indicating that halide liberated is equivalent to thiophenoxide consumed [time in hours, titer for bromide determination *vs.* 0.0202 *N* $AgNO_3$ (a = 12.1 ml), titer for thiophenoxide determination after addition of aliquot of HCl *vs.* 0.0312 *N* $Ba(OH)_2$ (a = 18.72 ml)]: 0, 0.02, 11.00; 7.6, 0.78, 11.55; 24, 2.03, 12.25; 48, 3.42, 13.24; 73, 4.38, 13.95; 100, 5.40, 14.52; k_2 (from Br^- determination) = 4.853×10^{-5} l. mol^{-1} sec^{-1}; k_2 (from acid–base titration) = 4.942×10^{-5} l. mol^{-1} sec^{-1}.

B. Thiophenol in Methanol.—Equimolar amounts of the 2-bromopyridine and thiophenol in methanol were sealed in glass tubes under nitrogen. The rates were initially followed by pouring the reaction mixture into halide-free nitric acid, extraction with two portions of chloroform and then the addition of a few drops of hydrogen peroxide. After a few hours the solution was extracted with ether, the ether layer washed with water and the aqueous extracts combined and analyzed for bromide ion. This did not lead to consistent titration values, and the method was abandoned in favor of that of Bevan and Hirst.[23] The contents of the sample tube were added to 25 ml of 1 *N* hydrochloric acid, to which solid potassium iodide was added followed by a known volume of standard potassium iodate. The excess iodine was titrated against sodium thiosulfate solution.

C. Thiophenol in Dimethyl Sulfoxide.—DMSO liberated iodine from acid solutions of iodide and iodate so that this method of assaying was discarded. Equimolar amounts (0.00275–0.00500 mol) of the 2-bromopyridine and potassium thiophenoxide in DMSO were heated under nitrogen in sealed tubes. Aliquots were quenched in hydrochloric acid and the excess acid was back-titrated with baryta.

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Registry No.—Thiophenoxide ion, 13133-62-5; 2-bromopyridine, 109-04-6; 2-bromo-3-methylpyridine, 3430-17-9; 2-bromo-5-methylpyridine, 3510-66-5; 2,3-dibromopyridine, 13534-89-9; 2,5-dibromopyridine, 624-28-2; 2-thiophenoxypyridine (picrate), 19520-21-9; 3-methyl-2-thiophenoxypyridine, 19520-22-0; 3-methyl-2-thiophenoxypyridine (picrate), 19520-23-1; 5-methyl-2-thiophenoxypyridine, 19541-52-7; 5-methyl-2-thiophenoxypyridine (picrate), 19520-24-2; 3-bromo-2-thiophenoxypyridine, 19520-25-3; 3-bromo-2-thiophenoxypyridine (picrate), 19520-26-4; 5-bromo-2-thiophenoxypyridine, 19520-27-5; 5-bromo-2-thiophenoxypyridine (picrate), 19520-28-6.

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Electronic Absorption and Fluorescence of Phenylethynyl-Substituted Acenes

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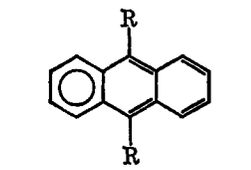
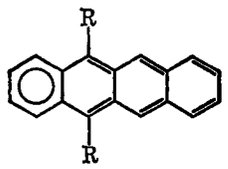
Substitution of acenes Ia, IIa and IIIa with the phenylethynyl group substantially increased quantum yields of fluorescence, and produced large shifts to longer wavelengths in the visible absorption and fluorescence spectra. A nearly constant displacement toward the red of 100 mμ in the fluorescence emission was observed for the *meso*-substituted bis(phenylethynyl)acenes Ib, IIb, and IIIb, when compared with the parent hydrocarbons. The spectral data indicate that the ethynyl group is a better conductor of electronic effects in the excited state than in the ground state.

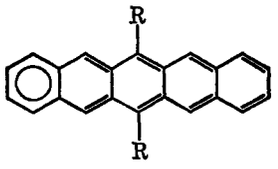
An extensive study of the fluorescence efficiencies of 9,10-disubstituted anthracenes has shown that the relative effectiveness of the phenyl group in intensifying fluorescence is considerably greater than that for such substituents as halo, hydroxy, alkoxy, alkyl, amino, acyl and nitro.[1] We have found that 9,10-bis(phenylethynyl)anthracene (Ib), a bright yellow-green fluorescer,[2] has an absolute fluorescence quantum yield (ϕ_F) = 0.96, which is even higher than ϕ_F = 0.84 for 9,10-diphenylanthracene (Ic). Thus the fluorescence efficiency of Ib is greater than any of the 9,10-disubstituted anthracenes previously reported. A comparison of the absorption and emission properties of Ib with those of the parent hydrocarbon, anthracene (Ia), shows that in addition to enhancing the fluorescence efficiency, the mild electron accepting phenylethynyl group[3] has also produced unusually large red shifts (see Table I).



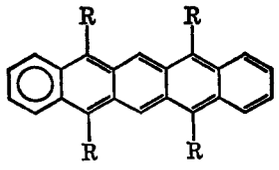
Ia, R = H
b, R = $-C{\equiv}CC_6H_5$
c, R = $-C_6H_5$
d, R = $-CH{=}CHC_6H_5$



IIa, R = H
b, R = $-C{\equiv}CC_6H_5$



IIIa, R = H
b, R = $-C{\equiv}CC_6H_5$



IVb, R = $C{\equiv}CC_6H_5$

To test the generality of the effect of phenylethynyl substitution on excited state behavior, phenylethynylacenes IIb, IIIb and IVb were prepared (see Table II for visible absorption spectra) and evaluated. 5,12-Bis(phenylethynyl)naphthacene (IIb), and 6,13-bis-

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