material. Also, oxidation products, if any, were not quantitatively evaluated, and tars were observed in some runs.

Analysis was carried out by means of a Hewlett-Packard 5750 analytical gas chromatograph equipped with a flame-ionization detector. Most of the neutral product fractions and a few of the acid fractions were examined by using a Model 4000 Finnigan GC/MS system as well. Most of the analyses were carried out by using a 240-cm, 2-mm internal diameter, 0.1% SP-1000 on Carbopack C (Supelco) column, which provided satisfactory separation of the isomers of cresol, of the isomeric dimethyldiphenyl ethers mentioned in this paper, and of isomeric halotoluenes, with the exception that certain isomer pairs, namely, *o*- and *m*-bromotoluene and *o*- and *m*-iodotoluene, were not separated. Other columns used contained OV-1, OV-101, OV-17, UC-98, SE-54, and polyphenyl ether liquid phases. Assignment of peaks was done on the basis of comparison of retention times and mass spectra with those of true samples. Internal standards used were bromobenzene or *p*-bromotoluene for the halotoluenes, xylene for toluene, and *p*-chlorophenol for phenol and the cresols. *o*-Cresol was used as internal standard for the phenolic products up to run 110. In these cases, analytical error due to *o*-cresol formed in the reaction was considered negligible. Integration was carried out by cut-and-weigh techniques or by using a Spectra Physics Minigrator electronic integrator.

Analysis for metal purities was done by using a Varian Techtron AA 6 atomic absorption spectrometer and suitable standards from Varian Analytical Instruments.

Experiments To Test the Homogeneity of Reaction Mixtures. Four heavy-walled Pyrex glass reaction tubes were charged respectively with 1.00, 2.05, 2.99, and 3.98 mmol of pIT as well as with 25 mL of 1.0 M aqueous NaOH. The atmosphere within the tubes was air. The tubes were sealed and heated in the usual way to a maximum temperature of 303 °C, with the tubes being rocked for 44 min, corresponding approximately to the time the bomb interior was hotter than 260 °C. The only reaction product determined was iodide ion, by potentiometric titration. Iodide ion was formed in yields of 15.9, 14.5, 15.2 and 12.5%, respectively.

Further Data. Supplementary experiments are summarized in appendices A, B, C, and D of chapter I of the dissertation of M.Z.[2]

Acknowledgment. We thank the National Science Foundation for financial support and Professor A. T. Bottini for discussions and for making available to us unpublished notes and reports from his earlier work on this topic.

Registry No. pIT, 624-31-7; pBrT, 106-38-7; pClT, 106-43-4; $CuSO_4$, 18939-61-2; Fe, 7439-89-6; Cd, 7440-43-9; Mn, 7439-96-5; Ni, 7440-02-0; benzene, 71-43-2; Cu_2O, 1317-39-1; NMM, 109-02-4; oIT, 615-37-2; mIT, 625-95-6; CuCl, 7758-89-6; KCl, 7447-40-7; KI, 7681-11-0; 4-methylbenzyne, 5849-21-8; NaOH, 1310-73-2; K_2CO_3, 584-08-7; NaOAc, 127-09-3; Na_2CO_3, 497-19-8; KOH, 1310-58-3; H_2O, 7732-18-5.

Reactivities of Several Nucleophiles toward 4-Methylbenzyne in Very Hot Water[1]

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By means of competition experiments, the relative rates of reaction of several nucleophiles with 4-methylbenzyne in aqueous solution at temperatures up to 318 °C have been determined. The relative nucleophilicities vs. chloride ion are as follows: PhS^-, 46; I^-, 6.2; piperidine, 3.0; Br^-, 1.7; aniline, 1.3; Cl^-, (1.0); PhO^-, 1.0; ammonia, 0.55; F^-, 0.20. For all but PhS^-, piperidine, and iodide, the p/m product ratio is 0.83 ± 0.02. In the cases of PhS^- and piperidine a competing mechanism of ipso substitution, probably involving catalysis by copper ions, caused the observed p/m ratios to be high and variable. Our experimental design precluded determination of the p/m ratio for iodide ion. Because of chemical complications, only rough estimates could be made of the nucleophilicities of nitrite and benzenesulfinate ions.

The addition of nucleophiles is one of the prominent modes of reaction of arynes. Assessing the relative addition reactivity of various nucleophiles is of obvious interest.

Among studies of relative nucleophilicity by means of competition experiments, an early one by Scardiglia and Roberts[3] served to rank several reagents in reactivity toward benzyne in ammonia as follows: $PhS^- > PhC{\equiv}C^- > PhO^- > RO^-, I^-, CN^-$, the last three giving no detectable addition. Wittig and Hoffmann[4] determined the halide ion reactivity ratios ($I^-:Br^-:Cl^- = 65:8:1$) against benzyne in ethanol. Huisgen, Mack, and Möbius[5] explored the relative reactivities of the lithium salts PhSLi, PhLi, lithium piperidide, and PhOLi, as well as of piperidine, vs. 9-phenanthryne in diethyl ether, but it is unclear whether they took into account effects of aggregation of the lithium salts in ether. These and other studies are summarized by Hoffmann.[6]

We mention also determination of the relative reactivities of CH_3O^- vs. CH_3OH in methanol[7] and of NH_2^- vs. NH_3 in ammonia[8] in addition to 4-chlorobenzyne. These determinations were made by the method of ad eosdem competition.

We are unaware of any previous determination of nucleophilicities toward any aryne in water.

In the present work, we generated 4-methylbenzyne (1) by the action of aqueous NaOH or KOH on *p*-bromo-

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(1) Based in part on ref 2.

(2) Zoratti, M. Ph.D. Dissertation, University of California, Santa Cruz, CA, June 1979.

(3) Scardiglia, F.; Roberts, J. D. *Tetrahedron* **1958**, *3*, 197.

(4) Wittig, G.; Hoffmann, R. W. *Chem. Ber.* **1962**, *95*, 2729.

(5) Huisgen, R.; Mack, W.; Möbius, L., quoted by: Huisgen, R.; Sauer, J. *Angew. Chem.* **1960**, *72*, 91.

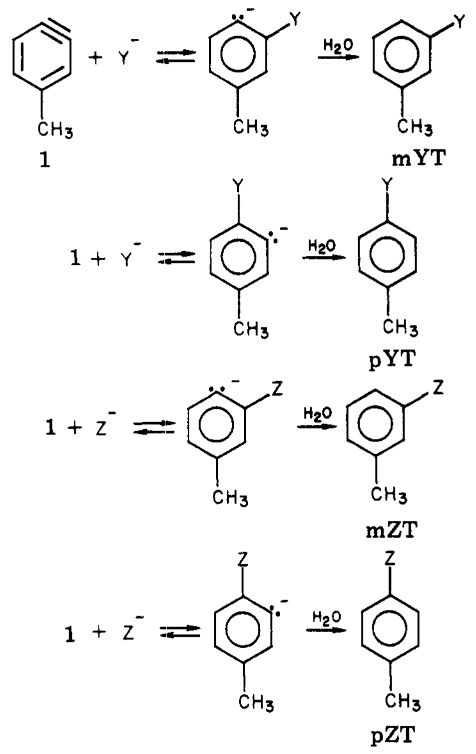
(6) Hoffmann, R. W. "Dehydrobenzene and Cycloalkynes"; Academic Press: New York, 1967.

(7) Bunnett, J. F.; Pyun, C. *J. Org. Chem.* **1969**, *34*, 2035.

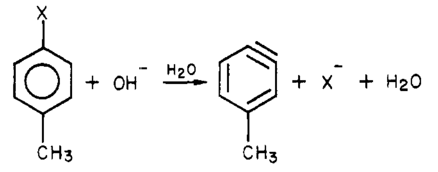
(8) Bunnett, J. F.; Kim, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 2254.

0022-3263/80/1945-1776$01.00/0

Scheme I



toluene (pBrT) or *p*-iodotoluene[9] (pIT) in sealed Pyrex glass tubes[10] at temperatures up to about 318 °C (eq 1).



(1)

pBrT, X = Br
pIT, X = I
1

Various other nucleophiles were present, usually in pairs, and their addition (with ensuing protonation) afforded meta- and para-substituted toluenes whose yields were measured by GLC. The reactions of 4-methylbenzyne are depicted in Scheme I, in which Y^- and Z^- represent two nucleophiles. We note that neutral nucleophiles may also add to 1.

The system employed is not suitable for evaluation of the relative nucleophilic reactivity of hydroxide ion. One reason is that hydroxide ion is partially consumed in reaction with the glass of the sealed tubes. Another is that *m*- and *p*-hydroxytoluenes (mHOT and pHOT) are probably formed in part by addition of the water solvent to 1.

Results

Inasmuch as aqueous solutions at, say, 310 °C develop high pressures, we placed the sealed glass reaction tubes in a bomb reactor containing outside the tubes essentially the same materials as inside, for the purpose of equalizing internal and external pressures on the glass walls of the tubes. Experiments of this sort require careful attention to certain aspects of experimental procedure, as we have discussed elsewhere.[10] One noteworthy precaution is rinsing the tubes before use with aqueous ammonia solution. Such a rinse largely removes traces of copper ions that may contaminate the glass walls and thereby serves to minimize complications arising from copper-catalyzed reactions of pBrT or pIT with nucleophiles.

In order for determinations of relative nucleophilicity in this type of system to be valid, certain conditions must be satisfied. The nucleophiles must be stable in aqueous alkali at the temperatures employed. The products of nucleophilic addition to 4-methylbenzyne must also be stable under the reaction conditions. Also, these products must be formed uniquely by addition to that aryne and not by any alternative mechanism.

Two of the nucleophiles that we investigated failed, either totally or substantially, to satisfy the requirement of nucleophile stability. One of these was cyanide ion, which underwent hydrolysis to formate ion; no tolunitrile, toluamide, or toluic acid product could be detected. The other was benzenesulfinate ion; from experiments involving it we were able to obtain significant amounts of *m*- and *p*-tolyl phenyl sulfones, but they were accompanied by large amounts of benzene from decomposition of the nucleophile.[11] We were therefore able to make only rough estimates of the addition reactivity of benzenesulfinate ion.

As to the stability of the nucleophile addition products, control experiments showed that the diaryl ethers, diaryl sulfides, fluorotoluenes, and chlorotoluenes were essentially stable under the conditions utilized in our experiments. A control experiment involving typical reaction conditions indicated *p*-bromotoluene to react to the extent of about 6%. We therefore believe that our measurements somewhat underestimate the reactivity of bromide ion, but only by a few percent.

Conceivably the products of addition of ammonia and aniline to 4-methylbenzyne, namely, toluidines and *N*-phenyltoluidines, might undergo further addition to the aryne.[12] We were, however, unable to find any of the diarylamine or triarylamine products that would result from such further addition. Inasmuch as tertiary amines have been observed to add to arynes, in more complex processes,[13] we also sought to find products that might be attributed to further reactions of the *N*-tolylpiperidines, but we found none.

To determine the addition reactivity of iodide ion, we generated 4-methylbenzyne from pIT in the usual way, in the presence of known amounts of chloride, iodide, and (in two of three experiments) bromide ion. Presumably all three halide ions added in the usual way to form the halotoluenes mClT, pClT, mBrT, pBrT, mIT, and pIT. All six were detected, but inasmuch as reactions were conducted for a very short time, most of the pIT was unreacted starting material, and it is uncertain how much of it resulted from addition of I^- to the aryne. Because only a small percentage of the pIT reacted, it was assumed that only a small percentage of the mIT formed underwent further reaction. The yield of mIT, relevant to the yields of the other products, was used to reckon the addition reactivity of iodide ion to the 2-position of 4-methylbenzyne. Similar experiments starting from mIT, which would enable evaluation of addition reactivity at the 1-position, were not performed.

From the reaction of pIT, aqueous KOH, and sodium nitrite, we obtained large amounts of tars, some *m*-nitro-

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[9] Bottini, A. T.; Roberts, J. D. *J. Am. Chem. Soc.* **1957**, *79*, 1458.

[10] Zoratti, M.; Bunnett, J. F. *J. Org. Chem.*, preceding paper in this issue.

[11] Cf.: Johnson, P. Y.; Koza, E.; Kohrman, R. E. *J. Org. Chem.* **1973**, *38*, 2967.

[12] Cf.: Bergstrom, F. W.; Wright, R. E.; Chandler, C.; Gilkey, W. A. *J. Org. Chem.* **1936**, *1*, 170.

[13] Lepley, A. R. *J. Am. Chem. Soc.* **1969**, *91*, 1237.

toluene, but no *p*-nitrotoluene. Control experiments showed that both of these nitrotoluenes react with aqueous KOH under our conditions to give intractable orange tars and that *p*-nitrotoluene was consumed faster than its meta isomer. The small amount of *m*-nitrotoluene that we obtained from the nitrite addition reaction is therefore of little quantitative significance.

The addition of each nucleophile afforded both a meta- and a para-substituted toluene (see Scheme I). For most nucleophiles, the *p*/*m* product ratio was about 0.83. Substantial deviation from this ratio, e.g., *p*/*m* variable and as high as 9.6 with thiophenoxide ion, was taken as evidence of a complication. The exceptionally high *p*/*m* ratios observed with PhS^- and piperidine are due, we believe, to the competing operation of another mechanism, one that effects only ipso substitution. In such cases, only the yields of the meta products were considered in evaluating relative nucleophilicites.

For evaluation of relative nucleophilicities, we used a standard expression for treatment of data from direct competition experiments.[14] The treatment involves assumptions that the addition reaction is first order in the aryne and in each of the participating nucleophiles.

Data from our principal experiments are presented in Table I. Each of these experiments involved two or three nucleophiles besides the hydroxide ion necessary to generate the aryne and the water solvent. Yields of the products of addition of the participating nucleophiles to 4-methylbenzyne and of certain byproducts are tabulated. Most of the experiments involved chloride ion as one of the nucleophiles.

In Table II we present the *p*/*m* product ratios observed from addition of several nucleophiles to the aryne, as well as the nucleophilicity of each relative to chloride ion as a standard. Each of the relative nucleophilicity values in Table II derives from direct comparison with chloride ion in the experiments of Table I. These values are corroborated by additional measurements of ours reported elsewhere.[2] Furthermore, several experiments in Table I provide comparisons of various pairs of nucleophiles, other than chloride ion, with each other and furnish evaluations of relative nucleophilicity within such pairs consistent with the values tabulated in Table II.

In the case of ammonia as nucleophile, we had to take into account the possibility that enough of it might have been in the gas phase to diminish appreciably the concentration of ammonia in the aqueous phase. A computation based on data of Jones,[15] detailed elsewhere,[2] furnished an estimate that only 6% of the ammonia was in the vapor phase under the conditions of our experiments. This small correction was taken into account in reckoning the relative nucleophilicity of ammonia listed in Table II.

Discussion

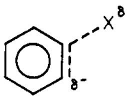
Two features of our principal results, which are summarized in Table II, are of immediate interest. One is that for all cases in which it could be measured, the *p*/*m* product ratio for addition of a nucleophile to 4-methylbenzyne is within experimental error the same, namely, 0.83. The other is that the differences in reactivity among the several nucleophiles are relatively small; the greatest difference, between thiophenoxide and fluoride ions, is only 230-fold.

***p*/*m* Ratio.** The *p*/*m* ratio for addition of hydroxide ion to 4-methylbenzyne is also 0.83 within experimental error.[10] In comparing this ubiquitous ratio with those measured by other workers,[6] we must take into account the effect of temperature. If the difference in reactivity of the 1- and 2-positions of 4-methylbenzyne stems entirely from differences in enthalpy of activation, a *p*/*m* ratio of 0.83 at 305 °C corresponds to a *p*/*m* of 0.70 at 25 °C or 0.64 at −33 °C. Inasmuch as the *p*/*m* ratios for addition of several nucleophiles to this aryne, as tabulated by Hoffmann,[6] range from 0.54 to 0.9 and inasmuch as most of them were measured at temperatures much lower than those that prevailed in our experiments, our *p*/*m* ratio may be considered to fall within the usual range.

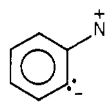
Nucleophilicities. The fact that differences in reactivity among the nucleophiles studied are relatively small can at least in part be ascribed to the relatively high temperature of our reactions. For example, consider the PhS^-/PhO^- reactivity ratio of 46.5 at ca. 305 °C (Table II). If this difference in reactivity is wholly of enthalpic origin, it corresponds to a PhS^-/PhO^- reactivity ratio of 1700 at 25 °C or 10300 at −33 °C. It is not surprising that earlier investigators[3,5] were unable to detect at lower temperatures much if any addition of PhO^- to arynes in competition with PhS^-.

A similar calculation converts the previously measured[4] Br^-/Cl^- reactivity ratio of 7.7, for addition to benzyne in ethanol at ca. 15 °C, to a ratio of 2.8 at 305 °C. The difference between that and the ratio of 1.7 that we determined might be attributed either to a solvent effect or to an entropic contribution.

Although the relative nucleophilicities of Cl^-, Br^-, and I^- vs. benzyne in ethanol have previously been measured,[4] our study provides the first measurement or even observation of the addition reactivity of fluoride ion as well as the first comparison of the halide ions with other anionic nucleophiles. It is interesting that the halide ions compete so well. One factor contributing to their reactivity is the very strong influence of ortho halogen atoms in stabilizing aryl anions.[6,16] The transition state for addition of a halide ion to an aryne (e.g., **2**) has partial *o*-haloaryl anion character and benefits energetically therefrom.



2



3

The high nucleophilicity of iodide ion accounts for the formation of small amounts of mIT and oHOT as byproducts (see Table I). Iodide ion released by reaction of pIT with hydroxide ion can add to the 2-position of 4-methylbenzyne to form, after acquisition also of a proton, mIT. We have demonstrated that such addition of iodide ion can occur; see above. Further reaction of mIT with hydroxide ion, via 3-methylbenzyne, can form, in part, oHOT.

For the addition of a nucleophile to 4-methylbenzyne, either the nucleophile-addition step or the proton-acquisition step might in principle be rate limiting (see Scheme I). For the reactions of iodide, bromide, and probably chloride ion, the addition step must be at least partially reversible and the protonation step, at least in part, rate limiting. For PhO^- and PhS^-, the addition step is doubtless rate determining. For the amine nucleophiles, it is quite possible that the initial addition to form a zwitterion (e.g.,

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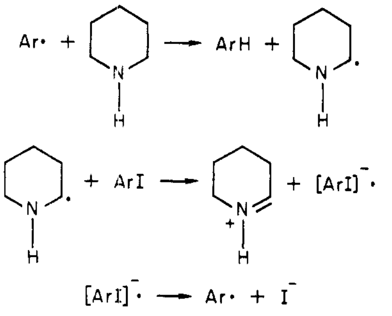
[14] Bunnett, J. F. In "Investigations of Rates and Mechanisms of Reactions", 3rd ed.; Lewis, E. S., Ed.; Wiley-Interscience: New York, 1974; Part I, p 159; eq 4.84.

[15] Jones, M. E. *J. Phys. Chem.* **1963**, *67*, 1113.

[16] Bunnett, J. F. *Acc. Chem. Res.* **1972**, *5*, 139.

Scheme II. Propagation Cycle for a Conceivable Radical-Chain Mechanism for Hydrodeiodination of *p*-Iodotoluene by the Action of Piperidine



3) is rate limiting, being followed by rapid proton removal from nitrogen and protonation at carbon.

Side Reactions. A recurring complication, already mentioned, was the incursion of a competing ipso substitution mechanism, most prominently with thiophenoxide ion and piperidine nucleophiles. These are excellent nucleophiles in $\mathrm{S_NAr}$ reactions,[17] and piperidine has been observed to participate in $\mathrm{S_NAr}$ reactions with unactivated aryl halides.[18] Another possibility is the radical chain $\mathrm{S_{RN}1}$ mechanism.[19] Thiophenoxide ion is known to be a good nucleophile in $\mathrm{S_{RN}1}$ reactions. Attempts to suppress the exalted *p*/*m* product ratios obtained in $\mathrm{PhS^-}$ reactions by using tetraphenylhydrazine (a radical trap[20]) and azobenzene (an electron acceptor[21]) were unsuccessful. However, the possibility of a radical process is not wholly excluded.

A more likely hypothesis is that the observed direct displacement was due to catalysis by traces of some extraneous substance, possibly copper ions. Copper is well-known to catalyze nucleophilic aromatic substitution reactions.[22] Support for this hypothesis is derived from the erratic nature of the phenomenon: isomer ratios (para/meta) varied from 1.5 to 2.0 for piperidine and from 1.2 to 9.6 for thiophenoxide. Also, formation of direct-substitution products was often accompanied by formation of an excess of pHOT, a behavior attributed to the presence of metallic impurities.[10]

If this interpretation is correct, our observations suggest that the effectiveness of copper catalysis in our system roughly follows the order $\mathrm{PhS^-}$, piperidine > $\mathrm{Br^-}$, $\mathrm{PhO^-}$ > $\mathrm{Cl^-}$, $\mathrm{NH_3}$, aniline, fluoride. By comparison, Bacon and Hill[23] found that aromatic nucleophilic sustitution by piperidine, aniline, $\mathrm{OH^-}$, and $\mathrm{F^-}$ was not catalyzed by cuprous oxide suspended in polar aprotic solvents at 150–200 °C, a system in which thiophenoxide ion and phenoxide ion were particularly effective, and $\mathrm{Br^-}$ and $\mathrm{Cl^-}$ also reacted readily.

The hydrodehalogenation of iodotoluene in reactions run in the presence of piperidine is interesting. Hydrodehalogenations of aryl halides under aryne-forming conditions in the presence of alkylamides/-amines have been known for a long time[24] and have been the object of several studies.[18,25] All but one[26] of these studies were conducted with dialkylamine/-amide systems in amine or ether solvents. The mechanism of these reductions has generally been considered to involve a hydride shift from the α-carbon of the amide ion to either the aryl halide[25a,b] or the aryne,[25] the main alternative being an attack by the amide ion on the halogen, with displacement of a phenyl anion.[18] Such a process is unlikely to account for the formation of toluene in our system, in which piperidine would not be expected to be deprotonated.

Two other possibilities are a copper-catalyzed reaction[27] and a radical-chain process, presented in Scheme II. Reaction mechanisms analogous to Scheme II have been proposed for hydrodehalogenation reactions of aryl halides in basic methanol[28] and with sodium borohydride under irradiation in acetonitrile,[29] and of alkyl halides in alkaline 2-propanol[30] and with sodium borohydride in dimethylformamide.[31] Some support for the involvement of radicals in our experiments is provided by the formation of dimethylbiphenyl(s) (see entries 3, 7, and 14 in Table I).

As mentioned above, reaction of pIT with KOH and KCN gave no trace of tolunitrile or a hydrolysis product thereof. However, it did produce 29% of toluene, an unusually large amount. We suspect that formate ion, from hydrolysis of $\mathrm{CN^-}$, might be responsible for the deiodination. Indeed, we found that reaction of pIT with 1.0 M KOH and 0.4 M sodium formate at temperatures up to 308 °C afforded 44% of toluene. For this dehalogenation we also suspect a radical mechanism, similar to that in Scheme II, but with formate ion donating a hydrogen atom to the aryl radical in the first step and the $\mathrm{CO_2^-\cdot}$ radical anion donating an electron to pIT in the second.

Experimental Section

Procedure. Competition experiments were conducted in sealed Pyrex glass tubes by means of techniques described in the accompanying paper.[10] The reagents were placed into annealed, ammonium hydroxide washed tubes. The aqueous solution of potassium or sodium hydroxide was added, and the tubes were sealed. Ammonia, phenoxide ion, and thiophenoxide ion were loaded into the tubes in the form of ammonium chloride, phenol, and thiophenol, respectively. Four tubes at a time were heated in the reaction bomb to the desired temperature, kept at that temperature for a few minutes, and allowed to cool. The assembly was rocked for a period of about 70 min, centered roughly at the time the maximum temperature was attained. Reactions were therefore conducted over a range of temperatures.

Workup was similar to the procedure described in the accompanying paper. Acid, neutral, and, for reactions involving nitrogen nucleophiles, basic fractions were obtained by extraction techniques and analyzed separately. In the case of thiophenoxide ion, the ethereal acid fraction, containing any phenolic products and excess thiophenol, was shaken with an excess of $\mathrm{AgNO_3}$ in water; the silver thiophenoxide was then filtered off, and the remaining ether solution was used for analysis. Workup of thiophenol-containing reaction mixtures was carried out in air as rapidly as possible: only a trace of diphenyl disulfide was found to have formed in the runs reported in Table I. Whether this formed by reaction with traces of air during the reaction or during the workup is unclear.

Materials. *p*-Iodotoluene and *p*-bromotoluene were the products of Eastman Kodak and were used as received or after distillation. They were pure and isomer free by GLC. Sodium

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(22) Bacon, R. G. R.; Hill, H. A. O. *Q. Rev., Chem. Soc.* **1965**, *19*, 95.

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(25) See, for example: (a) Benkeser, R. A.; De Boer, C. E. *J. Org. Chem.* **1956**, *21*, 281. (b) Wittig, G.; Rentzea, C. N.; Rentzea, M. *Justus Liebigs Ann. Chem.* **1971**, *744*, 8. (c) Wittig, G.; Schmidt, H.; Renner, H. *Chem. Ber.* **1962**, *95*, 2377. (d) Biehl, E. R.; Smith, S. M.; Lapis, S.; Reeves, P. C. *J. Org. Chem.* **1972**, *37*, 3529; **1974**, *39*, 1900.

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Table I. Representative Experiments[a]

entry	run	ArX[v] (mmol)	medium[b]	t_{max}, °C	nucleophiles (mmol)[w]	atm	% X^- released	% yield					
								$PhCH_3$	PhOH	oHOT	mHOT	pHOT	mClT
1	118-1	pIT (2.3)	1.0 M KOH (35 mL)	312	KCl (4.01), Y = NaF (40.0)	air	58.7	0.41	2.6	0.23	18.6	13.0	3.0
2	123-2	pIT (2.32)	1.0 M KOH (39 mL)	310	KCl (27.06), Y = KBr (19.27), Z = $PhNH_2$ (9.33)	air	22	0.28	0.85		2.33	2.06	3.57
3	120-4	pIT (2.31)	1.0 M NaOH (25 mL)	318	KCl (15.04), Y = pip (5.75)	air	*i*	10.5	tr		4.17	4.37	5.61
4	135-2	pBrT (2.37)	0.95 M NaOH (40 mL)	298	Cl^- (21.94), Y = NH_3 (21.94), Z = PhO^- (20.19)	Ar	6.7	tr	*i*		1.5	2.2	1.75
5	135-3	pBrT (0.65)	1.05 M NaOH (40 mL)	298	NaCl (20.00), Y = PhS^- (5.24), Z = PhO^- (32.6)	Ar	26.3	0.05	*i*				0.354
6	121-2	pIT (2.3)	1.0 M KOH (25 mL)	308	KCl (4.00), Y = KBr (4.00), Z = NaF (16.02)	air	17.0	0.24	1.57	tr	2.88	0.88	1.67
7	123-1	pIT (4.64)	1.0 M KOH (39 mL)	310	KCl (26.86), Y = pip (10.98)	air	42	18.0	tr		1.47	1.83	2.33
8	123-3	pIT (2.4)	0.76 M NaOH (39 mL)	310	Cl^- (31.6), Y = KBr (18.18), Z = NH_3 (9.46)	air	20	3.47	0.4	tr	1.73	1.23	3.63
9	123-4	pIT (2.35)	0.80 M NaOH (39 mL)	310	KCl (27.43), Y = NH_3 (7.60), Z = $PhNH_2$ (10.38)	air	17	0.25	0.93		2.37	1.75	3.42
10	136-4	pBrT (0.70)	0.90 M NaOH (40 mL)	299	NaCl (19.71), Y = PhS^- (4.30)	Ar	18.6	tr					0.69
11	137-1	pIT (3.13)	1.0 M NaOH (25 mL)	296	NaCl (25.15), Y = PhO^- (25.16)	Ar	16.1	0.2	*i*	~0.1	1.45	2.3	3.11
12	137-2	pIT (2.46)	1.0 M NaOH (25 mL)	296	NaCl (25.03), Y = KBr (25.03), Z = NaOPh (24.76)	Ar	14.3	0.4	*i*	~0.1	0.83	1.8	2.08
13	138-2	pIT (3.06)	1.0 M NaOH (25 mL)	305	NaCl (25.14), Y = KBr (25.02), Z = NaOPh (25.07)	Ar	12.1	0.2	*i*	~0.2	0.61	1.63	1.40
14	138-3	pIT (3.20)	1.0 M NaOH (25 mL)	305	Cl^- (40.04), Y = NH_3 (40.04), Z = pip (17.40)	Ar	*i*	14.1		~0.1	0.57	1.56	1.61
15	138-4	pBrT (2.70)	1.0 M NaOH (25 mL)	305	NaCl (25.09), Y = NaOPh (25.05)	Ar	*i*	0.15		~0.1	0.53	0.9	1.41
16	140-1	pBrT (2.71)	1.29 M NaOH (40 mL)	307	Y = PhS^- (9.50), Z = PhO^- (99.01)	Ar	38.4	tr	*i*				
17	140-3	pIT (3.39)	0.93 M NaOH (40 mL)	307	Y = $PhNH_2$ (21.58), Z = PhONa (42.59)	Ar	29.7	tr	*i*	~0.1	1.8	7.1	
18	141-1	pIT (4.85)	1.0 M NaOH (40 mL)	288	KCl (40.52), Y = KI (39.77), Z = KBr (39.98)	Ar	*i*	0.09			tr	tr	0.146
19	142-1	pIT (3.17)	1.0 M NaOH (40 mL)	292	NaCl (27.74), Y = NaI (14.94), Z = NaBr (29.36)	Ar	*i*	0.22			tr	tr	0.214
20	142-2	pIT (4.18)	1.0 M NaOH (40 mL)	292	NaCl (39.78), Y = NaI (20.08)	Ar	*i*	tr			tr	tr	0.266

[a] Yields are based on the *p*-halotoluene reactant. [b] Base concentration is that after reaction with any acidic materials (phenol, thiophenol, or ammonium chloride). [c] mYT, mZT, pYT, and pZT are, respectively, the products of *m*- and *p*-tolylation of nucleophiles Y^- and Z^-. [d] Ditolyl ether(s), 3.2%. [e] Ca. 0.1% oFT and ca. 0.9% of an unknown side product also seen. [f] The figure listed is (PhOH + pHOT)/mHOT. [g] An unknown side product accounted for ca. 0.4% of pIT. [h] Dimethylbiphenyl(s) (0.8%) and ca. 0.2% of an unknown side product were also detected. [i] Not determined. [j] See text. [k] Based on ratio of meta isomers only. [l] Ratio calculated more accurately than product percentages.

hydroxide was the "Titrisol" product sold by EM Laboratories. Potassium hydroxide was the commercial product of Mallinckrodt Chemical Co. Water was from the Thimann Laboratories deionized water system, distilled in an all-glass apparatus before use. Sodium fluoride and sodium and potassium chlorides, bromides, and iodides were the products of Mallinckrodt and were used as received or were heated in an oven at 100–120 °C for several hours and allowed to cool in a desiccator. Ammonium chloride was the product of Mallinckrodt and was dried in a drying pistol overnight before use. Phenol was the product of Mallinckrodt, was pure by GLC analysis, and was used as received. Thiophenol was the product of Eastman Kodak and was frac-

% yield								product ratios						
pClT	mYT^c	pYT^c	mZT^c	pZT^c	mXT	pXT	other	pHOT/ mHOT	pClT/ mClT	pYT/ mYT	pZT/ mZT	k_Y/ k_{Cl}	k_Z/ k_{Cl}	k_Y/ k_Z
2.45	5.97	5.01			1.3	35.2	*d*, *e*	0.84^f	0.82	0.84		0.20		
2.92	4.22	3.49	1.51	1.24	0.4	77.1	*g*	1.25^f	0.82	0.83	0.82	1.66	1.23	1.35
4.60	6.0	9.0			0.3	30.3	*h*	1.05	0.82	1.5^j		2.80^{j-l}		
1.48	0.88	0.72	1.55	1.58	0.1	87.8		1.47	0.85	0.82	1.02^n	0.53^m	0.96^k	0.56^{k,m}
0.294	4.43	16.7	0.62	0.85	0.03	61.8			0.83	3.8^{j,n}	1.4^{j,n}	47.8^k	1.07^k	44.4^k
1.44	2.66^q	2.22^o	1.37	1.11	0.4	72.8	*i*	0.85^f	0.86	0.83	0.81	1.57^o	0.20	0.13^o
1.93	3.0^q	5.8^n			0.4	53.5	*p*	1.24^n	0.83	1.93^n		3.15^k		
2.95	3.50	2.86	0.54^q	0.36^q	0.3	83.2		0.94^n	0.81	0.82	0.67^q	1.71	0.49^m	3.5^{m,q}
2.80	0.59	0.50	1.78	1.49	0.3	80.4	*r*	1.13^n	0.82	0.85	0.84	0.67^m	1.39	0.48
0.59	6.5	12.3				70.1			0.85	1.9^n		43.2^k		
2.70	2.98	2.56			0.25	86.9		1.59^n	0.87	0.86		0.95		
1.66	3.26	2.86	2.01	1.68	0.2	80.9		2.17^n	0.80	0.88	0.84	1.64^s	1.00	1.64^s
1.16	2.27	1.97	1.35	1.19	0.2	78.5		2.67^n	0.83	0.87	0.88	1.66^s	0.99	1.68
1.34	0.81	0.64	2.11	4.2	0.24	60.6	*t*	2.7^n	0.83	0.79	2.0^n	0.52^m	3.0^k	6.0^k
1.24	1.38	1.14			tr	85.4		1.7^n	0.88	0.83		0.95		
	3.99	38.3	0.91	1.82		54.1				9.6^n	2.0^n			48.6^u
	3.26	2.70	5.11	5.53	0.4	75.8		3.9^n		0.83	1.08^n			1.26^k
0.149	0.925	*j*	0.254	0.232	*j*	91.2			1.0^n		0.91^n	6.45^k	1.76^k	3.66^k
0.196	0.721	*j*	0.397	0.809	*j*	87.0			0.92^n		2.0^n	6.26^k	1.76^k	3.56^k
0.232	0.811	*j*			*j*	98.0			0.87			6.03^k		

[m] Based on an estimate that 6% of the ammonia was in the gas phase. [n] Some nonbenzyne ipso substitution took place. [o] Significant hydroxydebromination of bromotoluene products may have occurred. [p] Dimethylbiphenyl (0.6%) and ca. 0.4% of an unidentified side product were also formed. [q] Less precise than most values. [r] An unidentified side product accounted for ca. 0.9% of pIT. [s] Not corrected for hydroxydebromination of bromotoluene. [t] Ca. 1.8% dimethylbiphenyl(s) was also formed. [u] Based on ratio of meta isomers only, on the assumption that the effective average of PhS$^-$ during the reaction was 8.93 mmol. [v] Aryl halide. [w] Piperidine abbreviated as pip.

tionally distilled shortly before use. Aniline was the product of Matheson Coleman and Bell (MCB) and was fractionally distilled. Piperidine was the product of MCB; it was refluxed over sodium and distilled under nitrogen. Sodium benzenesulfinate was the product of Aldrich and was used as received or was recrystallized from ethanol. Sodium formate and sodium nitrite were "Baker Analyzed" (J. T. Baker Chemical Co.) reagents and were used as received. Potassium cyanide was the product of MCB and was used as received.

Analysis. Analysis was carried out with use of a Hewlett-Packard Model 5750 research gas chromatograph equipped with a flame-ionization detector. Most reaction mixtures were also

Table II. Isomer Ratios and Realtive Nucleophilicities toward 4-Methylbenzyne[a]

Y	products	no. of expts	p/m product ratio	relative nucleophilicity
F^-	fluorotoluenes	2	0.82 ± 0.02	0.20
NH_3	toluidines	4	0.81 ± 0.02	0.55 ± 0.08[b]
Cl^-	chlorotoluenes	15	0.82 ± 0.03	(1.00)[c]
PhO^-	phenyl tolyl ethers	8	0.84 ± 0.02	0.99 ± 0.05
$PhNH_2$	phenyltolylamines	3	0.83 ± 0.01	1.31 ± 0.08
Br^-	bromotoluenes	7	0.83 ± 0.02	1.7 ± 0.1[b,d]
piperidine	*N*-tolylpiperidines	3	*e*	3.0 ± 0.2[b,f]
I^-	*m*-iodotoluene	3	*e*	6.2 ± 0.2[b,f]
PhS^-	phenyl tolyl sulfides	3	*e*	46 ± 2[b,f]
$PhSO_2^-$	phenyl tolyl sulfones	2	ca. 0.8	>1.6[b,f]
NO_2^-	*m*-nitrotoluene	2	*d*	>0.5[b]

[a] Error estimates are based on variability between determinations. Isomer ratios and relative nucleophilicity values are the average of at least two determinations, chosen as the most reliable. [b] See text for a discussion of this value. [c] By definition. [d] The measured values of k_{Br}/k_{Cl} average 1.68 ± 0.06. [e] Could not be determined (see text). [f] Ratio for attack at the 2-position of 4-methylbenzyne only.

examined by means of a Model 4000 Finnigan GC/MS system. Most analyses were carried out with the use of a 240-cm, 2-mm internal diameter, 0.1% SP-1000 on Carbopack C (Supelco) column, which provided satisfactory separation of the meta and para isomers of all the reaction products. For the diaryl sulfones, the retention times were extremely long on this column, and a 240-cm, 3% OV-101 on Chromosorb W column was used instead. Other columns used contained OV-17 or UC-98 liquid phases. Assignment of peaks was done on the basis of comparison of retention times and of mass spectra with those of true samples. For comparison purposes, the following compounds were prepared as indicated. 3- and 4-methylphenyl ethers were prepared by following the method of Bacon and Stewart.[32] 3- and 4-methylphenyl sulfides were prepared in 90% yield by reaction of thiophenoxide with *m*- or *p*-iodotoluene in a basic solution containing copper sulfate in the Monel metal bomb (maximum temperature 304 °C). The corresponding sulfones were prepared by oxidation with $KMnO_4$ in acetic acid. *N*-(*m*- and *p*-tolyl)-piperidines were prepared by the method of Sommers and Aaland.[33]

Internal standards used were as follows: bromobenzene for toluene and the halotoluenes; *p*-chlorophenol for phenol and the cresols; aniline and *o*-ethylaniline for the toluidines; diphenylamine for the methyldiphenylamines; diphenyl ether for the tolyl phenyl ethers, sulfides, and sulfones. Molar response factors were determined and used.

Analyses can generally be considered accurate to within a few percent of the values, except when they are stated to be approximate. Errors are probably larger for the heavier (diaryl) compounds than for the ones containing only one aromatic ring.

In the case of the tolylpiperidines, these compounds from run 120-4 (entry 3, Table I) were isolated from the reaction mixture by preparative GLC on a 10% UC-98 on Chromosorb P column, and their isomeric composition was determined by IR and NMR methods. Results were in agreement with those obtained by GLC.

Experiments Involving Benzensulfinate and Nitrite Ions as Nucleophiles. These were conducted in the usual manner, under air or argon, with maximum temperatures in the range 300–312 °C and with 1.0 M KOH solutions as media. The products obtained from two reactions (runs 117-3 and 118-4) of pIT (2.3 mmol) with 1.0 M KOH (25 mL) in the presence of Cl^- (8.0 mmol) and $PhSO_2^-$ (6.0 mmol) ions are reported (air atmosphere). Percentage yields, based on starting pIT for phenol and products containing methyl groups and on starting benzenesulfinate for the others, were as follows (percent in run 117-3/percent in run 118-4): toluene, 3.5/6.2; phenol, 1.5/3.8; oHOT, trace/0.1; mHOT, 6.3/10.5; pHOT, 5.3/5.6; mIT, 0.7/0.7; pIT, 49.6/27.5; mClT, 3.72/4.74; pClT, 2.83/3.99; phenyl *m*-tolyl sulfone, ca. 4.5/ca. 4.2; phenyl *p*-tolyl sulfone, ca. 3.9/ca. 2.8; methylbiphenyl(s), 2.3/3.4; phenyl tolyl sulfides, ca. 3.7/ca. 5 (p/m ratio of ca. 4/ca. 3.1). The ratio [phenyl *m*-tolyl sulfone][Cl^-]/[*m*-chlorotoluene][$PhSO_2^-$] was ca. 1.6 in 117-3 and ca. 1.2 in 118-4. These ratios represent a lower limit for the nucleophilicity ratio $k_{PhSO_2^-}/k_{Cl^-}$.

In two reactions (116-4 and 117-4) of pIT (2.3 mmol) with 1.0 M KOH in the presence of Cl^- (6.08 and 5.99 mmol, respectively) and NO_2^- (6.08 and 7.99 mmol, respectively), the following products were obtained (percent yield) besides orange tar (percent in run 116-4/percent in run 117-4): toluene, 0.5/0.5; phenol, 0/3.0; oHOT, 0/0.3; mHOT, 1/7; pHOT, 0/0.2; mIT, 0.9/1.3; pIT, 53.0/55.9; ditolyl ethers, 1.8/1.2; mClT, 3.21/3.70; pClT, 2.51/2.98; *m*-nitrotoluene, 1.56/2.07. The ratio [Cl^-][*m*-nitrotoluene]/[NO_2^-][*m*-chlorotoluene] was 0.49 in run 116-4 and 0.42 in run 117-4. These numbers represent a lower limit for the nucleophilicity ratio $k_{NO_2^-}/k_{Cl^-}$. In a control experiment, *m*- and *p*-nitrotoluene were heated with 1.0 M KOH; small amounts of phenol and *m*-cresol formed along with tar and traces of unidentified products. No *p*-cresol was observed. Thirty percent of *m*-nitrotoluene, but no *p*-nitrotoluene, was recovered from the reaction.

Further Data. Supplementary experiments and reckoning of the amount of ammonia in the vapor phase in certain experiments appear in appendices A, B, and C of Chapter II of the dissertation of M.Z.[2]

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Registry No. 1, 5849-21-8; pIT, 624-31-7; pBrT, 106-38-7; KCl, 7447-40-7; NaF, 7681-49-4; KBr, 7758-02-3; $PhNH_2$, 62-53-3; piperidine, 110-89-4; Cl^-, 16887-00-6; NH_3, 7664-41-7; PhO^-, 3229-70-7; NaCl, 7647-14-5; PhS^-, 13133-62-5; NaOPh, 139-02-6; KI, 7681-11-0; NaI, 7681-82-5; NaBr, 7647-15-6; F^-, 16984-48-8; Br^-, 24959-67-9; I^-, 20461-54-5; $PhSO_2^-$, 16722-50-2; NO_2^-, 14797-65-0; NaOH, 1310-73-2; KOH, 1310-58-3; ammonium chloride, 12125-02-9; phenol, 108-95-2; thiophenol, 108-98-5; sodium benzenesulfinate, 873-55-2; sodium nitrite, 7632-00-0; hydroxide ion, 14280-30-9; KCN, 151-50-8; CN^-, 57-12-5; sodium formate, 141-53-7; formate ion, 71-47-6.

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