tained at 134–135° (10 mm.), n^{25}_D 1.5136. *Anal.* Calcd. for $C_{15}H_{23}N$: C, 82.89; H, 10.67; N, 6.45. Found: C, 83.15; H, 10.46; N, 6.40. Since this compound appeared to be stable to acid at room temperature it was hydrolyzed by boiling with 10% aqueous hydrochloric acid for one hour. The benzaldehyde was extracted into ether, the ether evaporated, and the residual oil converted to the 2,4-dinitrophenylhydrazone. After recrystallization from aqueous ethanol a 65% yield of orange plates which melted at 235–236° was obtained (lit. m.p. 238–239°).

Supplementary Experiments.—In the experiment using 8.0 g. of U. O. P. nickel the standard conditions were used except that a magnetic stirrer was employed throughout to prevent violent bumping. A 114% yield of water was collected in about 8 hours. In the usual fashion 16.7 g. of N-benzylaniline hydrochloride and 1.2 g. of benzoic acid were isolated. The ether layer remaining after the usual acid extraction had a strong benzaldehyde odor and gave a precipitate with 2,4-dinitrophenylhydrazine. Upon shaking the ether layer for one hour with 100 ml. of saturated sodium bisulfite solution a solid precipitated. After filtering, washing and drying this bisulfite addition product of benzaldehyde weighed 12.7 g.

In the experiment to test whether nickel was needed at high temperatures 0.750 mole of benzyl alcohol, 0.375 mole of aniline and 0.12 mole of potassium were used with no solvent. After refluxing for 50 minutes at 189 to 227° the reaction was stopped; the volume of the aqueous layer was 5.9 ml. In order to facilitate separation of the layers in the Dean–Stark trap the lower part of the trap was immersed in a water-bath held at about 90°. In the usual fashion 77.1 g. of N-benzylaniline hydrochloride was isolated. It seems probable that at these higher temperatures less potassium and a smaller excess of alcohol could be used without lowering the yield.

In the series of three experiments using added benzalaniline equivalent to 2.5, 10 and 40% of the amount of aniline the amounts of benzyl alcohol and aniline were decreased correspondingly. Thus for example when 0.0125 mole (10%) of benzalaniline was employed 0.2375 mole of benzyl alcohol and 0.1325 mole of aniline were used. No nickel was employed and the standard procedure was followed in other respects. The yields of N-benzylaniline hydrochloride were 94, 95 and 93% while the yields of water were 111, 90 and 98%, respectively. The times required for a "50% yield of water" to collect, determined by adding the percentage of benzalaniline used to the percentage of water collected were 792, 203 and 8 minutes while the times required for a "90% yield of water" were 1201, 306 and 43 minutes, respectively.

In the two experiments that were quenched when a 25 and a 75% yield of water had collected the standard conditions were used, but the scale was quadrupled in order to facilitate the required separations. The reactions were quenched at the desired point by cooling rapidly and by adding water and ether. After the benzoic acid was obtained from the aqueous layers in standard fashion the combined organic layers were dried and the ether, xylene, aniline and benzyl alcohol removed by distillation up to a final temperature of 115° at 15 mm. N-Benzylaniline was removed from the residue by thoroughly shaking an ether solution with 10% aqueous hydrochloric acid and filtering. The filtrate containing benzaldehyde from the hydrolysis of the anil was washed with water until neutral and stirred 2 hours with 400 ml. of a saturated aqueous solution of sodium bisulfite. The washed and dried precipitate of the sodium bisulfite addition product of benzaldehyde amounted to 0.017 mole for the experiment stopped at a 25% yield of water and the precipitate amounted to 0.049 mole for the experiment stopped when a 75% yield of water had collected.

In an experiment exactly like the reference experiment except that sodium was used in place of potassium a 75% yield of water collected in 526 minutes (the corresponding time with potassium was 395 minutes) and water evolution stopped at 92% after a large amount of alkoxide suddenly precipitated. A 57% yield of N-benzylaniline hydrochloride was isolated in the standard fashion. If the extensive precipitation of alkoxide could be avoided, possibly by using less sodium along with higher temperatures to speed up the reaction, it appears probable that the yield could be raised. The slow conversion of sodium to the alkoxide is, however, another point against its use.

COLLEGE PARK, MD.

[CONTRIBUTION FROM THE MARION EDWARDS PARK LABORATORY OF BRYN MAWR COLLEGE]

Relative Rates of Iodination of *p*-Alkylanilines

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RECEIVED MAY 26, 1954

The rates of iodination of *p*-alkylanilines in aqueous methanol indicate the predominant operation of the inductive effect by the alkyl groups at the *meta* positions. The order of electron release by alkyl groups is discussed in terms of the nature of the substituting agent.

In a previous communication it was shown that *p*-alkylphenols are iodinated *meta* to the alkyl groups in an order which indicates the predominant operation by the alkyl groups of the general inductive effect.[2] We now report the similar iodination of *p*-alkylanilines, which is free from the complication which might be caused by the ionization of the phenols, because the anilinium ion forms appreciably only at low *p*H, and, unlike free phenol, it cannot be considered a serious participant in aromatic halogenation at moderately high *p*H. The substitution of the free amines should therefore give a more unambiguous indication of the power of direction of the *meta* alkyl groups in direct iodination.

p-Toluidine has been iodinated by elementary iodine before and only substitution *ortho* to the amino group has been recorded (Fig. 1).[3] The higher *p*-alkylanilines have not been iodinated directly, but their acetyl derivatives have been brominated and nitrated,[4] and no isomers other

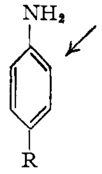

Fig. 1.

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[1] Presented in part before the Fourth Conference on Reaction Mechanisms, Bryn Mawr College, Bryn Mawr, Penna., September 10–13, 1952.

[2] E. Berliner, F. Berliner and I. Nelidow, THIS JOURNAL, **76**, 507 (1954).

[3] H. L. Wheeler and L. M. Liddle, *Am. Chem. J.*, **42**, 441 (1909); K. Elbs and H. Volk, *J. prakt. Chem.*, [2] **99**, 269 (1919).

[4] For instance: J. R. Johnson and L. T. Sandborn, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 111; C. Gelzer, *Ber.*, **20**, 3253 (1887); E. C. Sterling and M. T. Bogert, *J. Org. Chem.*, **4**, 20 (1939); M. Crawford and F. H. C. Stewart, *J. Chem. Soc.*, 4443 (1952); H. J. B. Biekart, P. E. Verkade and B. M. Wepster, *Rec. trav. chim.*, **71**, 340 (1952).

than those *meta* to the alkyl groups have been reported, or would be expected. The assumption is therefore justified that the relative values here reported refer only to *meta* iodination. Isolation as the acetyl derivative of a 70% yield of pure 3-iodo-4-aminotoluene in the iodination of *p*-toluidine under the kinetic conditions confirms the supposition.

Results.—The iodination reactions were carried out in 30% (by volume) methanol in the presence of phosphate buffers and at a constant ionic strength. The concentration of the amines and iodine was 0.008 and 0.001 *M*, respectively, the concentration of potassium iodide 0.05 *M* at the beginning of each run. As in the aqueous iodination of aniline[5] the reaction shows strong buffer catalysis. Instead of conducting all runs at a single buffer concentration, it seemed of interest to obtain separately the relative rate constants for both the catalyzed and uncatalyzed reactions to see if the relative rates of the two reactions are affected similarly by alkyl groups. Consequently, the reactions for *p*-toluidine and for *p*-*t*-butylaniline, as well as for aniline, were run at a constant buffer ratio (*p*H 7.73), but at four different buffer concentrations, while for *p*-ethyl- and *p*-isopropylaniline only one concentration was chosen. From the slopes of the least square plots of the rate constants against the Na_2HPO_4 concentration, the rate constants for the catalyzed reactions were obtained; the intercepts at zero buffer concentration yielded the values for the uncatalyzed reaction.[6]

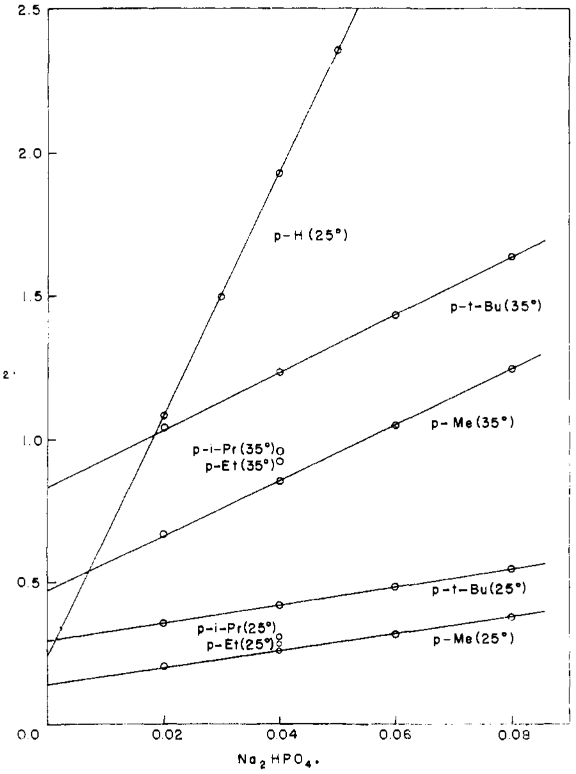

Fig. 2.—Rates of iodination of *p*-alkylanilines.

In Fig. 2 are shown these plots, and in Tables I and II are reported all the results at 25 and 35°. At every buffer concentration and at both temperatures the *p*-*t*-butyl compound reacts faster than the *p*-methyl compound, and for the uncatalyzed reaction the ratio of the relative rates of the two compounds is 2.09 ± 0.03 at 25° and 1.76 ± 0.02 at 35°. *p*-Ethyl and *p*-isopropylaniline react at intermediate rates at a 0.04 *M* concentration of Na_2HPO_4 at both temperatures, and their uncatalyzed reactions would presumably do likewise. In spite of the small differences in rate constants, the activation energies are surprisingly different, *i.e.*, 19.1 ± 0.2 kcal. for *p*-*t*-butylaniline and 22.2 ± 0.3 kcal. for *p*-toluidine. It is recognized that the activation energies were obtained from measurements at two temperatures only and over a narrow temperature range, which limits the interpretation, but it is probably safe to conclude that the order of the rate constants is exclusively determined by differences in activation energies, as is generally the case in electrophilic aromatic substitution. However, the log *PZ* factors and activation entropies are not constant, but parallel the activation energies; other examples of the same phenomenon have been cited frequently.[7] In the present case, the *p*-*t*-butyl compound reacts faster because of a lower activation energy and in spite of an appreciable lowering of the activation entropy. Whether this entropy effect might be due to a "freezing" of the larger alkyl group or to other causes can only be decided when more examples of this effect become available. In the present case the differences in rate constants would have been appreciably larger had the activation entropies been constant. It seems likely that the reactions of the *p*-ethyl and *p*-isopropyl compounds would also show significant differences in activation energies, because at the one buffer concentration the ratio k_{35}/k_{25} for the four compounds, *p*-Me, *p*-Et, *p*-*i*-Pr and *p*-*t*-Bu are 3.35, 3.23, 3.13 and 2.91. Neither the values for the activation energies nor those for the entropies are absolute, because they contain the heat changes involved in the formation of the substituting agent and the ionization of the buffer constituents. The rates of iodination decrease with an increase in alcohol content, but they show the same relative order. In 40% (by volume) methanol and at one single buffer concentration (Na_2HPO_4 0.05 *M*, KH_2PO_4 0.005 *M*) the rate constants for the same four compounds are 0.149, 0.155, 0.173 and 0.206.

TABLE I

RATES OF IODINATION OF *p*-ALKYLANILINES

Concn. of Na_2HPO_4	0.02	0.04	0.06	0.08	0.02	0.04	0.06	0.08
R in *p*-$RC_6H_4NH_2$	k_2 (25°)[a]				k_2 (35°)[a]			
Me	0.202	0.255	0.316	0.377	0.671	0.855	1.049	1.244
Et		.286				.925		
i-Pr		.307				.960		
t-Bu	0.358	.421	0.484	0.548	1.043	1.225	1.431	1.636
H[b]	1.088	1.499	1.928	2.359				

[a] Rate constants in liters $mole^{-1}$ $min.^{-1}$. [b] For aniline the Na_2HPO_4 concentrations are 0.02, 0.03, 0.04 and 0.05 *M*.

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[5] E. Berliner, THIS JOURNAL, **72**, 4003 (1950).

[6] The rate constants for the catalyzed reactions contain also a term contributed by the much weaker base KH_2PO_4, but this term is so much smaller (by a factor of about 100 in water[5]) than catalysis by Na_2HPO_4 that it was neglected.

[7] For instance: E. W. Timm and C. N. Hinshelwood, *J. Chem. Soc.*, 862 (1938); I. Meloche and K. J. Laidler, THIS JOURNAL, **73**, 1712 (1951); E. Berliner and L. H. Altschul, *ibid.*, **74**, 4110 (1952).

TABLE II[a]

R in p-$RC_6H_4NH_2$	Methyl	t-Butyl	Hydrogen
k_0(25°)	0.141 ± 0.002	0.294 ± 0.001	0.234 ± 0.008
k_0(35°)	0.476 ± .003	0.838 ± .007	
k_{cat}(25°)	2.93 ± .04	3.18 ± .004	42.42 ± 0.22
k_{cat}(35°)	9.57 ± .06	9.93 ± .1	
E_0 (kcal.)	22.2 ± .3	19.1 ± .2	
log A_0[b]	13.66 ± .26	11.71 ± .12	
ΔS_0 (e.u.)	+1.96 ± 1.2	−6.94 ± .55	
E_{cat} (kcal.)	21.6 ± 0.3	20.8 ± .2	
log $A_{cat.}$[b]	14.53 ± .26	13.97 ± .15	
$\Delta S_{cat.}$ (e.u.)	+5.97 ± 1.2	+3.38 ± .69	

[a] Rate constants in liters mole^{-1} min.$^{-1}$. The subscript zero refers to the uncatalyzed reactions. [b] In liters mole^{-1} sec.$^{-1}$.

The rate constants for the catalyzed reactions are much closer than those for the uncatalyzed reactions, the slopes for *p-t*-butylaniline and *p*-toluidine being almost parallel (Fig. 2). The *p-t*-butyl compound is still faster, but the ratio $k(t\text{-Bu})/k(\text{Me})$ is only 1.08 ± 0.015 at 25° and 1.04 ± 0.012 at 35°. The activation energies are also closer, 20.8 and 21.6 kcal. for the catalyzed iodination of *p-t*-butylaniline and *p*-toluidine, respectively.

Aniline was included in the comparison in order to obtain some measure of the extent of activation by a *m*-alkyl group. To obtain an exact value, the exact amount of *ortho* iodination in aniline has to be known. No *ortho* iodination in aniline has actually ever been reported, but in reference 8 a maximum yield of 85% of pure *p*-iodoaniline is obtained.[8] Taking 10–15% as the maximum amount of *ortho* iodination in aniline, the partial rate factors for the uncatalyzed iodination of aniline and two *p*-alkylanilines are represented in Fig. 3, and it can be seen that a methyl group activates a *meta* position by factors of at least 4–6, which agrees with factors of 3 and 5 that have been reported for nitration[9] and chlorination.[10] Because of the uncertainty in the estimation of *ortho* iodination in aniline, these values must be considered tentative.

Discussion.—The *p*-alkyl groups activate aniline toward electrophilic iodination in the order *t*-Bu > (*i*-Pr > Et) > Me. This is also then the order of electron release by the alkyl groups, and therefore the difference in rates of iodination of the *p*-alkylanilines is determined by the predominant operation of the general inductive effect. Similar results were obtained in the iodination of *p*-alkylphenols.[2] Furthermore, these differences are determined by corresponding differences in activation energies.

Two reasons can be offered for the operation of the inductive effect in the iodination of *p*-alkylanilines and *p*-alkylphenols. The first, and more obvious, one immediately suggests itself as follows: it is quite generally agreed, and is an integral part of all contemporary theories of aromatic substitution, that the resonance effect, *i.e.*, hyperconjugation, is distributed preferentially to the *ortho*/*para* positions of the benzene ring.[11] Contributing structures involving direct transmission to the *meta* position must be of much higher energy content than structures involving the *ortho*/*para* positions. Although *meta* structures may contribute some and cannot be completely ruled out,[12] they cannot be concerned to an appreciable extent as a primary mechanism for polar transmission. Brown and Dewar[13] have recently shown on the basis of molecular orbital calculations that such *meta* interactions in pyridine and substituted benzenes are unimportant and that the resonance integrals between pairs of *meta* carbon atoms can be neglected in calculating both energy levels and charge densities. A resonance effect also can be relayed to the *meta* position without direct *meta* interaction, first by conjugation to the *ortho* and *para* positions and then by a secondary inductive relay to the seat of reaction in the *meta* position.[11] One or both of these mechanisms may be necessary to account for some phenomena, such as the slight activation of the benzene ring by a *meta* methoxyl group in bromination.[14] The smallness of such an effect is indicated by the observation that the difference in activation of the *ortho*/*para vs.* the *meta* positions is of the order of 10^8 in bromination.[14] In general, a substituent in the *meta* positions can therefore be considered primarily to operate through an inductive effect—in any case, much more so than when it is situated *ortho* or *para*. The operation of the inductive effect in the reaction under discussion can then be considered a normal and expected behavior of *m*-alkyl groups; in addition, the inductive effect of the alkyl groups is enhanced, relative to *p*-alkyl groups, by the greater proximity of the substituents to the reaction site.

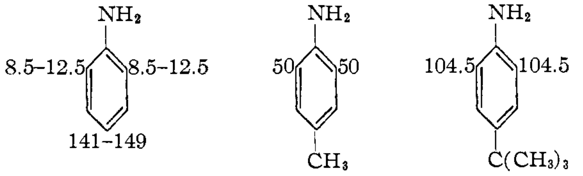

Fig. 3.

Another possible explanation of the activating effect of *meta* alkyl groups focuses attention not so much on the position of the alkyl groups on the benzene ring, as on the nature of the substituting agent. Chlorination[15] and bromination[15,16] of alkylbenzenes in the *para* position by elementary halogen, when the substituting agents are molecular chlorine or bromine, follow a hyperconjugation order. Any doubt that the fall-off in rate on going from toluene to *t*-butylbenzene may be due to steric hindrance in the *ortho* position of the larger alkylbenzenes recently has been removed by a determination of the *o*/*p* ratios in bromination.[17] On the other hand, *para* nitration by nitric acid in acetic acid, where the substituting agent is $+NO_2$,[11]

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[8] R. Q. Brewster, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 347.

[9] H. Cohn, E. D. Hughes, H. H. Jones and M. G. Peeling, *Nature*, **169**, 291 (1952); C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *J. Chem. Soc.*, 1959 (1931).

[10] F. E. Condon, THIS JOURNAL, **70**, 1963 (1948).

[11] For instance see: C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter IV.

[12] C. G. Overberger, L. H. Arond, D. Tanner, J. J. Taylor and T. Alfrey, THIS JOURNAL, **74**, 4848 (1952).

[13] D. A. Brown and M. J. S. Dewar, *J. Chem. Soc.*, 2406 (1953).

[14] P. B. D. de la Mare and C. A. Vernon, *ibid.*, 1764 (1951); see also ref. 12.

[15] P. B. D. de la Mare and P. W. Robertson, *ibid.*, 279 (1943); P. W. Robertson, *ibid.*, 1267 (1954).

[16] E. Berliner and F. Berliner, THIS JOURNAL, **71**, 1195 (1949).

[17] P. W. Robertson, P. B. D. de la Mare and B. E. Swedlund, *J. Chem. Soc.*, 782 (1953).

follows the general order of the inductive effect of alkyl groups,[9] and isopropylation, where the substituting agent is similar to nitration in that it is an electronically deficient entity, distinguishes very little among the alkylbenzenes.[18] In iodination, the substituting agent is either I+ or (H_2OI)+,[5] and therefore analogous to the nitrating agent and, as in *para* nitration, an inductive order is obtained, although the attack is *meta* to the alkyl groups. An explanation for these varying orders might most profitably be looked for in the difference in the substituting agents and the substitution processes. Such explanations have been offered in the recent past by de la Mare, Robertson and coworkers,[19] and independently by Brown and Nelson.[20] De la Mare points out that in nitration by $+NO_2$, as in the Hofmann elimination, the electrostatic field of the positive ion will provoke the development of an electrostatic effect in the substituent. Bromination by molecular bromine in acetic acid involves an intermediate of greater stability than that in nitration (as indicated by the kinetically higher order of bromine participation), which causes a greater development of the time-variable electromeric hyperconjugation effect. Bromination is therefore a "more powerfully electron-demanding process than nitration." Support for this view has also come from the difference in nitration and bromination of halobenzenes. In a similar way, although arrived at by different reasoning, Brown and Nelson have pointed out that bromination is a more electron-demanding process than nitration and, stressing particularly the relation between reactivity and selectivity of the substituting agent, that bromination is more selective than nitration. While we agree essentially with these explanations, some additional remarks are suggested, particularly as they pertain to the problem at hand, and also because the problem of the effect of the substituting agent on substituent effects has received only scant attention in the past, when all considerations were focused on the substituent only. The way in which the various substituents respond to the substituting agents is, however, an important aspect in aromatic substitution, and one to which more attention will have to be paid in the future.

That the nitronium ion, $+NO_2$, should behave as it does can be explained and seems plausible *post factum*, but it is doubtful that such behavior could have been predicted. On the contrary, one could have reasoned that the positive ion should have been the most effective in promoting any kind of electron release, including hyperconjugation. The following represents a possible explanation for the difference in nitration and bromination. The nitronium ion, wherever it has been found to be involved in aromatic substitution, is formed prior to the substitution process and its formation does not depend on the aromatic compound.[11] Once formed, it need not evoke large additional polarities in the alkyl groups and, because of its immediate availability for an attack and its powerful electrophilic character, does not require particularly activated positions in the benzene ring. It can utilize the positions of high electron density already present in the benzene ring, as revealed for instance by the permanent dipoles.[19] For that reason, as Brown and Nelson have pointed out,[20] the $+NO_2$ is not selective, it does not differentiate much between methyl and hydrogen nor between the various positions in toluene. To that can be added that it does not differentiate much between methyl and *t*-butyl. In bromination, however, the actual entity that enters the benzene ring is not present prior to reaction; it has to be torn away from the bromine molecule in the transition state, splitting out a bromide ion at the same time and thus exerting a much greater pull on the electrons of the aromatic system. This can only happen in the transition state if an extensive flow of electrons is available and compensates for the breaking of the bromine–bromine bond. The process of bromination must therefore be a much more difficult one than nitration and a much more electron-demanding one (as was derived by both groups of workers), as well as one that will be much more dependent on the aromatic substrate than nitration. Bromination will bring about and require the greatest possible temporary electron release by the alkyl groups in the transition state, which appears to be provided by release through hyperconjugation.

The necessity of tearing away a Br+ from bromine in the transition state seems to us the reason for the fact that bromination by molecular bromine is highly electron demanding, rather than that Br_2 is a neutral molecule and NO_2+ a positively charged ion. The complexity of the problem is indicated by the fact that the diazonium ion and the nitrosonium ion[11] both also carry a unit positive charge and yet both are very poor substituting agents and very selective, and unlike the nitronium ion attack only the most activated aromatic molecules. The diazonium ion is a weak substituting agent perhaps because in its most stable form it is not electron deficient, and only becomes so through a minor contributing structure, but the same cannot be said of the nitrosonium ion. Both diazo-coupling and nitrosation might therefore be expected to go through transition states more similar to molecular halogenation than nitration. The arguments outlined above refer strictly only to bromination and nitration, about which most is known. However, if one were to generalize to other substitution reactions, it could be said that a substitution process involving an attacking reagent of low electrophilic character (like molecular bromine) will go through a transition state which is more highly electron demanding than that obtained from a reagent of greater electrophilic character (such as the nitronium ion).

In view of these explanations it would seem that the operation of the inductive effect in the iodination of *p*-alkylanilines by positive iodine or the conjugate acid of hypoiodous acid is the expected behavior, enhanced perhaps by the fact that the alkyl groups are also in the *meta* position, but not conditioned by it. The substituting agent in iodina-

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(18) F. E. Condon, THIS JOURNAL, **70**, 2265 (1948).

(19) P. B. D. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 100 (1948); de la Mare, *ibid.* 2871 (1949); P. B. D. de la Mare, A. D. Ketley and C. A. Vernon, *Research*, Vol. 6, No. 2 (1953); ref. 17.

(20) H. C. Brown and K. L. Nelson, THIS JOURNAL, **75**, 6292 (1953).

tion is electronically similar to the nitrating agent, and, unlike molecular chlorine and bromine but like the nitrating agent, it causes the operation of the electrostatic inductive effect.[21]

This argument can only stand if cases can be produced where *m*-alkyl groups can also cause a hyperconjugation order to be followed. There are not many cases in which *m*-alkyl groups have been studied systematically. However, in the chlorination by molecular chlorine of various *p*-alkylphenol ethers, Bradfield and Jones[22] observed the order Me > *t*-Bu. Here, too, the attack is *meta* to the alkyl group, but the order is that of the hyperconjugation effect. (The other alkyl groups do not fall within a well-spaced series, the over-all order being Me:Et:*n*-Pr:*t*-Bu-*t*-Am = 100:121:93:49:41.) In fact, in this chlorination the methyl compound is numerically just about as much faster than the *t*-butyl compound as it is slower in iodination. A hyperconjugation order is also observed in the S_N1 solvolysis of both *p*- and *m*-alkylphenyldimethylcarbinyl chlorides in 90% acetone at 25°.[23] Both reactions are known to be highly electron demanding: chlorination for the reasons outlined before, and the S_N1 solvolysis because of the formation of a carbonium ion in the rate-determining step.[24] On the other hand, the dissociation of alkyltriphenylmethyl chlorides in liquid SO_2, investigated by Lichtin and Bartlett,[25] is an equilibrium reaction which measures only the differences in polarities between initial and final states. No additional polarities of the time-variable type are evoked beyond those present in the ground states, and the *m*- as well as the *p*-alkyl groups affect the equilibrium constants in accordance with their inductive effects. The spacing is considerably compressed in the *para* series, because of an appreciable hyperconjugation contribution to the ground states. The conclusion, applicable to the present case, is that in reactions going through highly electron-demanding transition states a hyperconjugation effect will be transmitted even through the *meta* positions—whatever the mechanism of such transmission may be—while in less highly electron-demanding reactions the permanent inductive effect must be considered to provide sufficient activation. There is an indication of a hyperconjugation contribution in the iodination of the anilines, in spite of the over-all inductive effect order that is observed. The spacing of the *p*-Me, *p*-Et and *p*-*i*-Pr compounds is much more compressed and there is a larger interval between the *t*-Bu and the *i*-Pr compounds than between any of the other pairs. This can be accounted for by assuming contribution from hyperconjugation by those alkyl groups containing α-hydrogens; the effect would work in the opposite direction and account for the uneven spacing.

The above reasoning can be applied to explain the observation that the catalyzed reactions of *p*-toluidine and *p*-*t*-butylaniline differ only very little in their respective rate constants. Their ratio is only 1.08 at 25°, as compared to 2.09 for the uncatalyzed reactions. In the catalyzed reaction the rate has been shown to be proportional to (HOI) (acid), which in phosphate buffers becomes $(HOI)(H_2PO_4^-)$.[5] This reflects an important difference in the substituting agent as compared to the uncatalyzed reaction, where the corresponding expression is (I^+) or $(HOI)(H^+)$. It is not positively charged and may be considered to be more similar to the brominating agent in molecular bromination than to the iodinating entity in uncatalyzed molecular iodination. If that is so, the operation of the hyperconjugation effect will become more pronounced and, although not important enough to reverse the order, it suffices to bring the rate differences closer together and to make the rates almost identical.[26]

The catalyzed reaction of aniline is much faster than that for the *p*-alkylanilines (see Table II). This may be the result of a large amount of steric hindrance for the catalyzed reaction in the *ortho* position, because of the bulkier substituting agent, and in aniline almost all catalyzed substitution may occur in the unhindered *para* position, which is not possible with the *p*-alkylanilines.

Experimental Part

Materials.—Methanol was fractionated from magnesium methoxide.[27] The 30% (by volume) solvent was prepared by diluting 300 ml. of absolute methanol to one l. in a volumetric flask, while thermostating at 25°. Iodine, potassium iodide, sodium chloride and the buffer constituents were best Reagent Grade chemicals, used without further purification. The amines were all prepared from their solid acetyl derivatives which had been crystallized repeatedly in bulk from ethanol or aqueous ethanol (benzene–ligroin for the *p*-ethyl compound). *p*-Acetotoluidide was a commercial sample and *p*-*t*-butylacetanilide was made directly from acetanilide, *t*-butyl chloride and aluminum chloride according to the patent literature.[28] If the directions are followed exactly and the solvents dried carefully, yields ranging from 50–70% of once crystallized product are obtained. Several more crystallizations were necessary to obtain a product of the desired purity, but the procedure seemed simpler than the usual one, which involves nitration of butylbenzene. *p*-Cumidine was obtained by catalytic hydrogenation of the nitro compound[29] with Raney nickel in ethanol. *p*-Ethylaniline[30] and *p*-cumidine were acetylated in benzene solution.[31] All samples of *p*-ethylacetanilide melted first at 90.2–90.7°, but on retake at 94.4–95.0°. The purified acetamides were hydrolyzed by refluxing 50 g. in a mixture of 500 ml. of water and 115 ml. of concd. sulfuric acid until a clear solution was obtained. The amines were isolated as the sulfates, from which the free bases were obtained by adding sodium hydroxide to the suspension of the sulfate in water. They were then distilled twice from zinc dust *in*

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[21] That halogenation by molecular halogen is different from halogenation by a positive halogen entity, and that the latter is more like nitration, has been pointed out by de la Mare, Ketley and Vernon (ref. 19), who have shown that in halogenation by $(HOBr)(H^+)$ the compounds toluene, benzene and fluorobenzene react in the ratio 20:1:0.25 compared with the values 24:1:0.15 in nitration and 350:1:1.2 in chlorination by Cl_2.

[22] A. E. Bradfield and B. Jones, *Faraday Soc.*, **37**, 726 (1941).

[23] H. C. Brown, Fourth Conference on Reaction Mechanisms, Bryn Mawr College, Bryn Mawr, Pa., September 10–13, 1952. We are greatly indebted to Professor Brown for making available to us the data prior to publication.

[24] E. D. Hughes, C. K. Ingold and N. A. Taher, *J. Chem. Soc.*, 949 (1940).

[25] N. N. Lichtin and P. D. Bartlett, THIS JOURNAL, **73**, 5530 (1951).

[26] This interpretation of the rate differences in the catalyzed reaction was suggested by Dr. P. B. D. de la Mare.

[27] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 360.

[28] French Patent 811,832, *Chem. Zentr.*, **108**, 1267 (1937).

[29] C. Hansch and G. Helmkamp, THIS JOURNAL, **73**, 3080 (1951).

[30] We are indebted to Dr. W. B. Hardy of the American Cyanamid Co., Calco Chemical Division, Bound Brook, N. J., for a generous sample of *p*-ethylaniline.

[31] Reference 27, p. 398.

vacuo and stored in brown bottles. *p*-Toluidine was crystallized first from ligroin and then several times from petroleum ether. Because it readily forms a hydrate in contact with air, it has to be put in a desiccator for several days in order to obtain a constant-melting product. The liquid amines slowly darkened on standing and were always redistilled from zinc dust before use. They were then completely colorless. Aniline was a sample used before,[5] and was redistilled before use.[32]

CONSTANTS OF ACETANILIDES AND FREE AMINES

R in *p*-$RC_6H_4NH_2$	M.p. of acetanilides, °C	B.p. (mm.) of amines, °C.
Me	148–148.6, lit.[33] 155 (146)	76–76.5 (8–9) m.p. 42.7–43.7 lit.[33] 44.5–45
Et	90.2–90.7 (ret. 94.4–95), lit.[33] 94	88 (8)
i-Pr	105.7–106.5, lit.[33] 102.5	90–90.5 (2)
t-Bu	171.5–172.3, lit.[33] 169–170	98.5–99 (3)

Kinetic Measurements.—The kinetic runs were conducted as described before.[2] The exact amounts of buffers (Na_2HPO_4 to KH_2PO_4 = 4 to 1), amines, NaCl and iodine in KI were separately dissolved in the solvent in such concentrations that dilution of an appropriate volume to 100 ml. gave a solution of the desired concentrations. The ionic strength was 0.28 throughout all the runs, except those 0.08 *M* in Na_2HPO_4, when it was 0.31 (mole per liter). Solutions containing the amines were made up shortly before each run because the methanolic solutions of the amines developed some impurity which caused reactions to be faster, although the rate constants in the faster runs showed no trend. This acceleration was least observed with *p*-*t*-butylaniline and may be connected with the α-hydrogens. Direct sunlight was avoided and runs were conducted in a dimmed-out room. All runs were conducted at least in triplicate, and the rate constants in Table I are averages of these triplicate runs. Rate constants were calculated from the integrated form of the second-order rate equation. The average deviations in the rate constants within each individual run were 1–2%, although rarely larger than 1.5%, and in the averages listed in Table I they were never larger than 1.5%. Activation energies and log *A* factors were calculated from the Arrhenius equation and activation entropies from the expression relating log *A* to the activation entropy[34] (at 25°). Errors in the activation energies (Table II) were estimated from the "error in the quotient" of the rate constants and errors in log *A* and the activation entropies similarly, by considering the largest and smallest possible values, corresponding to the errors in rate constants. Errors in the intercepts (k_0) and the slopes are the probable errors of the least square constants, and the errors in the ratios of rate constants are the "probable errors in the quotients."[35] The results of two kinetic runs are recorded in Table III. Through blank determinations a correction factor was established, which was apparently due to vaporization of iodine as the reaction progressed. The blank increased as successive samples were withdrawn, but was only about 1–2% of the initial titer for the last three points of a run and less for the first five. For the much faster reaction of aniline no blank correction was necessary. The thiosulfate titers listed below are corrected for the blank.

2-Iodo-4-*t*-butylacetanilide was prepared by iodination of *p*-*t*-butylanline with elementary iodine, as described for *p*-toluidine,[36] followed by acetylation. 2-Iodo-4-*t*-butylaniline was obtained as a brown oil in 88% yield by steam distillation from the reaction mixture. The structure of the product was not proved, but it was assumed that the iodine had entered the position *ortho* to the amino group. The acetyl derivative, crystallized five times from 95% ethanol, forms colorless lustrous plates, m.p. 153.4–154.3° (cor.). *Anal.* Calcd. for $C_{12}H_{16}ONI$: C, 45.44; H, 5.09. Found: C, 45.42; H, 5.24. 2-Iodo-4-*t*-butylbenzanilide, prepared by treating the iodoamine with benzoyl chloride and aqueous KOH, forms long colorless needles melting, after five crystallizations from 95% ethanol, at 145.7–147.2° (cor.). *Anal.* Calcd. for $C_{17}H_{18}ONI$: C, 53.84; H, 4.78. Found: C, 53.79; H, 4.94.

TABLE III

THE IODINATION OF *p*-TOLUIDINE AT 35° IN 30% METHANOL

p-Toluidine 0.008019 *M*, I_2 0.001 *M*, Na_2HPO_4 0.06 *M*, KH_2PO_4 0.015 *M*, KI 0.05 *M*, NaCl 0.035 *M*, μ = 0.28

Time, min.	0.02 *M* thiosulfate, ml.	k_2, liters mole^{-1} min.$^{-1}$
0	0.992	. . .
8	.927	1.039
17	.860	1.056
27	.793	1.048
38	.725	1.048
49	.664	1.045
61	.603	1.045
74	.551	1.022
88	.492	1.030

THE IODINATION OF *p*-*t*-BUTYLANILINE AT 25° IN 30% METHANOL

p-*t*-Butylaniline 0.008011 *M*, I_2 0.001 *M*, Na_2HPO_4 0.04 *M*, KH_2PO_4 0.01 *M*, KI 0.05 *M*, NaCl 0.1 *M*, μ = 0.28

Time, min.	0.02 *M* thiosulfate, ml.	k_2, liters mole^{-1} min.$^{-1}$
0	1.000	. . .
19	0.938	0.423
39	.877	.424
60	.818	.423
82	.762	.421
107	.700	.425
135	.640	.423
167	.575	.426
196	.521	.430

Isolation Runs. (A) ***p*-Toluidine.**—A run was conducted duplicating all the kinetic conditions except that the total volume was 4 l. When the iodine color had disappeared, the solution was extracted repeatedly with 100-ml. portions of benzene. The benzene extract was washed twice with very dilute HCl solution in order to remove the excess of *p*-toluidine. It was then washed with water containing a little sodium carbonate, again with water, dried and the benzene was evaporated. The residue was warmed with 2 ml. of acetic anhydride, followed by 5 ml. of water. There was obtained after filtration an 80.6% yield of crude product melting at 121–128°. After one crystallization from aqueous ethanol the product weighed 0.626 g. (67.2%), and another 0.02 g. (2.2%) was obtained from the mother liquor. The material melted at 130.5–131.5° (cor.), with very slight softening below. Mixed with an authentic sample[3] of m.p. 131.4–132.4°, the material melted at 130.5–132.3°. Since the yield in the acetylation was probably not quantitative, the percentage isolation was probably somewhat higher.

(B) ***p*-*t*-Butylaniline.**—This amine (0.0074 mole in one l.) was iodinated similarly, except that the ratio amine-to-iodine was 1:1 instead of 8:1, because of the difficulty of separating a large excess of *p*-*t*-butylaniline. The ether extract, containing the iodoaniline, was treated as above. One crystallization of the acetyl derivative afforded a 36.7% yield of product melting at 151.2–152.7°, 10.4% melting at 151.0–152.0° and 7.3% melting at 149.5–151.4°. On the basis of a maximum yield of 78.3% of once-crystallized material previously obtained in the acetylation of 2-iodo-4-*t*-butylaniline, the total product represents a 69.5% isolation of 2-iodo-4-*t*-butylaniline.

Acknowledgment.—Part of this work was carried out in the Chemistry Laboratories of University College, London, and we wish to express our thanks to Professor C. K. Ingold for the hospitality

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(32) We thank Miss Y. W. Chu for help in the preparation of some of the amines.

(33) I. M. Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1934.

(34) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., Inc., New York, N. Y., p. 417.

(35) O. F. Steinbach and C. V. King, "Experiments in Physical Chemistry," American Book Company, New York, N. Y., 1950, p. 8.

(36) H. L. Wheeler and L. M. Liddle, ref. 3.

shown to us. We also gratefully acknowledge the benefit derived from stimulating conversations with Professor C. K. Ingold, Professor E. D. Hughes, Dr. P. B. D. de la Mare, Mr. C. A. Vernon and other members of the staff of University College, and with Professor P. W. Robertson. In addition, we want to acknowledge the continuous help afforded by a Frederick Gardner Cottrell Grant of the Research Corporation.

BRYN MAWR, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INSTITUTE OF POLYMER RESEARCH, POLYTECHNIC INSTITUTE OF BROOKLYN]

Azo-bis Nitriles. XI.[1] Decomposition of Azo Compounds. Steric Factors

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RECEIVED MAY 28, 1954

The preparation and characterization of six new azo nitriles are described. Their rates of decomposition have been determined in solution. The results substantiate previous suggestions that steric requirements in the alkyl groups are responsible for differences in rates of decomposition.

In previous papers[3] the importance of steric effects on the rates of decomposition of azo nitriles of the type RR'C(CN)N=N(CN)CR'R has been emphasized. In particular, steric interaction between the two halves of a *trans* symmetrical azo compound has been of prime importance,[3a] especially with alkyl groups with branching in the β-position (R = isobutyl). This paper reports the preparation and decomposition of azo nitriles which have increased branching in the alkyl groups R = CH_3, R' = $CH_2C(CH_3)_3$; R = CH_3, R' = *n* = C_5H_{11}; R = R' = $CH_2—CH(CH_3)_2$; R = R' = $CH(CH_3)_2$; R = C_2H_5, R' = $CH(CH_3)_2$ and correlates their decomposition rate with previous mechanistic suggestions.

A. Preparation of Azo Compounds

(1) **Discussion.**—The azo compounds from methyl neopentyl, methyl *n*-amyl, diisobutyl, diisopropyl and ethyl isopropyl ketone were prepared according to previously described procedures.[3] Both stereoisomers, the *dl*- and *meso*-forms of the substituted hydrazine and the azo nitrile from methyl neopentyl ketone were isolated and characterized. Ethyl isopropyl ketone was prepared from isobutyronitrile and ethylmagnesium bromide in 65% yield and this method is a useful procedure for its synthesis. The synthesis is of interest because reactions of aliphatic nitriles with aliphatic Grignard reagents usually give poor yields. The branching in the isobutyl group probably prevents the competing reaction of self condensation with the Grignard reagent functioning as the base.

(2) **Experimental.**[4] **2-2'-Azo-bis-2,4,4-trimethylvaleronitrile** **(2,2'-Azo-bis-2-cyano-4,4-dimethylpentane).**—Methyl neopentyl ketone was prepared by the oxidation of commercial diisobutylene with sodium dichromate and sulfuric acid according to the procedure of Mosher and Cox.[5]

The azine was prepared by refluxing 57.0 g. (0.50 mole) of methyl neopentyl ketone with 8.0 g. (0.25 mole) of anhydrous hydrazine for three days. The aqueous layer was separated, the crude ketazine dried over anhydrous magnesium sulfate and distilled through a short center-tube column to yield 44.2 g. (79%) of a pale yellow oil, b.p. 113–114° (10 mm.), n^{25}_D 1.4590, d^{25}_4 0.8340, together with 5.5 g. (9.7%) of recovered starting ketone.

Anal.[6] Calcd. for $C_{14}H_{28}N_2$: N, 12.49. Found: N, 12.72.

A solution of 40.4 g. (0.36 mole) of the ketazine in 65 ml. (*ca.* 1.6 moles) of liquid hydrogen cyanide was allowed to stand at room temperature for four days. The reaction mixture was then poured into water and the resulting waxy solid removed by filtration. After trituration with dilute sodium hydroxide solution and several water rinses, the crude product was dissolved in ether; cooling yielded 11.0 g. (22%) of disubstituted hydrazine, m.p. 104–107° dec. Recrystallization from ether raised the melting point to 108.5–110° dec.

Anal. Calcd. for $C_{16}H_{30}N_4$: C, 69.01; H, 10.86; N, 20.12. Found: C, 69.10; H, 10.77; N, 19.96.

The stereoisomeric disubstituted hydrazine was obtained by concentrating the mother liquors after separation of the high melting disubstituted hydrazine and cooling the solution in Dry Ice. The crude product was recrystallized from petroleum ether (b.p. 60–68°) to give 18.9 g. (38%) of material, m.p. 81–83.5° dec. Further recrystallization raised the melting point to 86–87.5° dec.

Anal. Calcd. for $C_{16}H_{30}N_4$: C, 69.01; H, 10.86; N, 20.13. Found: C, 69.12; H, 10.83; N, 20.07.

Both hydrazine compounds were thermally unstable and prolonged refluxing during recrystallization markedly reduced the amount of product obtained.

The azo nitriles were prepared by oxidation of the individual hydrazines.

From 4.8 g. (0.0173 mole) of the hydrazine isomer melting at 108.5–110° and 4 g. (0.025 mole) of bromine in 50–50 ethanol–water solution, 4.1 g. (85%) of azo nitrile melting at 65–67° was obtained. Recrystallization from petroleum ether (b.p. 28–36°) raised the melting point to 66.5–68.5° dec. (65°, a 29% yield of both isomers is reported, no analysis given[7]).

Anal. Calcd. for $C_{16}H_{28}N_4$: C, 69.52; H, 10.21; N, 20.27. Found: C, 69.49; H, 10.19; N, 20.20.

The lower melting hydrazine, 7.8 g. (0.0281 mole), and 5 g. (0.031 mole) of bromine in the ethanol-water solution gave 5.7 g. (73%) of azo nitrile, m.p. 88–91°. Recrystallization from chloroform–ether brought the melting point to 94.5–95.5° dec. (102–103°[7]).

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[1] This is the eleventh in a series of articles concerned with the decomposition of azo compounds. For the tenth paper in the series, see C. G. Overberger and Alexander Lebovits, THIS JOURNAL, **76**, 2722 (1954).

[2] This paper contains portions of theses presented by Warren F. Hale in partial fulfillment of the requirements for the degree of Master of Science and by M. B. Berenbaum in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

[3] (a) C. G. Overberger, M. T. O'Shaughnessy and H. Shalit, THIS JOURNAL, **71**, 2661 (1949); (b) C. G. Overberger and M. B. Berenbaum, *ibid.*, **73**, 2618 (1951); (c) **73**, 4883 (1951); (d) C. G. Overberger H. Biletch, A. B. Finestone, J. Lilker and J. Herbert, *ibid.*, **75**, 2078 (1953).

[4] All melting points are corrected.

[5] W. A. Mosher and J. C. Cox, Jr., THIS JOURNAL, **72**, 3701 (1950).

[6] Analyses by Drs. Weiler and Strauss, Oxford, England; Dr. K. Ritter, Basel, Switzerland; Dr. F. Schwarzkopf, New York, N. Y.

[7] J. A. Robertson, U. S. Patent 2,586,995 (Feb. 26, 1952).