Difference in Directive Power among Strong Activating Groups in the Benzene Ring[1]

VIJA KESE AND GABRIEL CHUCHANI[2]

Department of Chemistry, Instituto Venezolano de Investigaciones Científicas, Caracas, Venezuela

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The results of systematic intermolecular competition between monosubstituted benzenes with strong activating substituents for a triphenylmethyl carbonium ion imply the sequence $—N(CH_3)_2 > —NHCH_3 > —NH_2 > —OH$ in directive power.

This work continues the investigation of aromatic electrophilic substitution through tritylation reactions.[3-5] The reagent used for the intermolecular competition of the monosubstituted benzenes was triphenylmethyl perchlorate, a true "carbonium salt." Reaction conditions were similar to those recently reported,[4c,5] and the comparative results may be observed in Table I.

TABLE I

COMPETITION WITH TRIPHENYLMETHYL PERCHLORATE

		Separation by Chromatography				
		Yield (%)				
		Position taken by $(C_6H_5)_3C$[a]				
Compounds	Temp.	$4(N(CH_3)_2 = 1)$	$4(NHCH_3 = 1)$	$4(NH_2 = 1)$	$4(OH = 1)$	$(C_6H_5)_3CH$
N,*N'*-Dimethylaniline and *N*-methylaniline	90–100°	32.8	27.4			22.5
	140–145°	29.5	27.4			24.2
	Reflux	2.8	...			77.5
N,*N'*-Dimethylaniline and aniline	90–100°	54.5		...		20.8
	140–145°	54.5		...		24.2
	Reflux	...		...		79.2
N-Methylaniline and aniline	90–100°		62.8	...		16.7
	140–145°		62.2	...		23.3
	Reflux		...	...		85.0
N,*N'*-Dimethylaniline and phenol	90–100°	50.5			...	22.5
	140–145°	34.0			1.2	37.5
	Reflux	1.1			...	89.2
N-Methylaniline and phenol	90–100°		70.3		...	15.0
	140–145°		45.6		...	35.0
	Reflux		...		...	87.5
Aniline and phenol	90–100°			88.0[b]	...	...
	140–145°			81.0[b]	...	...
	Reflux			83.0[b]	...	...

[a] Products were identified by mixed melting point. [b] Data taken from M. L. Cortés and G. Chuchani, *J. Org. Chem.*, **27**, 125 (1962).

These systematic results are of qualitative significance only, and apparently indicate that the sequence in directive influence among these strong groups is as follows:

$$—N(CH_3)_2 > —NHCH_3 > —NH_2 > —OH$$

With the exception of one case, all competition reactions also gave triphenylmethane as a byproduct. The formation of triphenylmethane was favored by an increase in temperature and the reasons for its formation require a more detailed study.

The results of several publications covering substituent effects in aromatic systems are comparable although the experimental methods are very different. According to theoretical viewpoints, the replacement of the hydrogen atoms of amines by alkyl groups increases their basic strength, if steric factors are not significant.[6] This view extends to the aromatic amines as well, since the alkyl groups cause a relative increase in the induction of electrons towards the ring. The basic strength of aniline derivatives has been studied by a number of authors.[7-12] The reinforcement in the basicity

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[2] To whom inquiries should be addressed.

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due to alkyl groups will hold, as in this case, provided the predominant factor resides in electronic effects and not in steric effects.

Dipole moment values[13-15] were reviewed for the different monosubstituted benzenes under study, and the semiquantitative measurements do not reveal a correlation with the orientation problem, or at least do not seem to be conclusive in this respect.

The NMR data of the $—NH_2$, $—NHCH_3$, and $—N(CH_3)_2$ substituents[16] show that these have large negative (downfield) shifts for all ring protons, which is a good indication of their directive power. Yet, their relative differences in electron densities in the activated aromatic nucleus are not determinant enough as to establish a definite sequence. However, the cited NMR evidence substantiates the generalization $N > O$ in orientational control.

The rate constants and σ-values deduced from a study of nucleophilic displacement in the benzene series[17] suggest a different order of activation for the substituents. However, subsequent work includes values of certain relative rate constants[18] and Hammett σ-values based on ionization of substituted benzoic acids[19] ($—N(CH_3)_2$ -0.83; $—NHCH_3$ -0.84; $—NH_2$ -0.66; $—OH$ -0.37) and these agree partly with the order of activation obtained in this work.

The electronic distribution in the benzene derivatives,[20] deduced from the reactivity parameters reflects the sequence $—N(CH_3)_2 > —NH_2 > —OH$. The parameters represent a set of values obtained from the relative net charge releasing effect and from Hammett σ-values.

Several spectroscopic studies[21-23] correlate the relative change in electron distribution in the benzene molecules dependent on the substituent present, and at least do show that $—NH_2 > —OH$ in electron releasing power.

The literature gives a number of references[24-36] which indicate that molecular association takes place for systems of an aniline and phenol, while there are a few others[29, 37, 38] indicating that no such combinations occur. There may be a certain degree of molecular association or hydrogen bonding, but not strong enough to affect the activating power of each group. The authors are inclined to believe that no actual proton transfer is involved, since it would result in the formation of phenolate and anilinium ions, of which the latter deactivate the ring, and would allow the former to control the orientation in the aromatic nucleus. Such a phenomenon implies a sequence different from the one given above. The feasibility of a solvent effect due to the phenolic proton was questioned in a previous publication.[5] In a number of experimental reactions described below, two anilines were competed for the trityl reagent; the absence of the phenolic proton in these cases eliminated the possibility of its participation in the dissociation of the trityl reagent. Moreover, it leads us to support the view[5] that the polarity of the media may favor the dissociation of the "carbonium salt."

Experimental[39]

Triphenylmethyl Perchlorate.—The compound was prepared as described by Dauben, Honnen, and Harmon.[40]

I. Competition of *N*,*N*-Dimethylaniline and *N*-Methylaniline. Method A.—*N*,*N'*-Dimethylaniline (0.05 mole), *N*-methylaniline (0.05 mole), and triphenylmethyl perchlorate (0.005 mole) were heated at 90–100°. In this case as well as all the following ones, the reaction time was 4 hr. and during this time the reaction was protected from light. The reaction mixture was diluted with water and concd. hydrochloric acid added until no further precipitate formed. The solid was filtered off and washed until the filtrate gave no acid reaction. The crude product was dried, dissolved in a small amount of chloroform, and the compounds separated by column chromatography. The columns were packed with acid alumina (50 g. Woelm, grade 1) and eluted with a mixture of benzene–chloroform (2:1 by volume). In most cases this mixture eluted all the tritylated reaction products as well as the triphenylmethane, while further elution with chloroform and finally acetone removed small amounts of unidentified oily material. Tritylated products were crystallized from petroleum ether and the triphenylmethane washed with methanol. This procedure was followed throughout the experiments, and each compound obtained was checked by mixed melting point with the corresponding authentic sample.

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The mixture of benzene–chloroform eluted: triphenylmethane, m.p. 92–93°, unchanged on admixture with an authentic sample[3]; *p*-trityl-*N*,*N*-dimethylaniline, m.p. 210–211°, not depressed with an authentic sample[3] and *p*-trityl-*N*-methylaniline, m.p. 211–212°, unchanged with the pure compound.[3] Yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 32.8%; *p*-trityl-*N*-methylaniline, 27.4%; and triphenylmethane, 22.5%.

Method B.—With the same procedure as in A, but when heated at 140–145°, the yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 29.5%; *p*-trityl-*N*-methylaniline, 27.4%; and triphenylmethane, 24.2%.

Method C.—As in A, but when refluxed under nitrogen, the yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 2.8%, and triphenylmethane, 77.5%.

II. Competition of *N*,*N'*-Dimethylaniline and Aniline. Method A.—*N*,*N'*-Dimethylaniline (0.05 mole), aniline (0.05 mole), and triphenylmethyl perchlorate (0.005 mole) were heated at 90–100°. The reaction mixture was treated in the same way as in (IA) and the crude product passed through a column of alumina with the benzene–chloroform mixture as indicated. The separation gave: *p*-trityl-*N*,*N'*-dimethylaniline, 54.5%; and triphenylmethane, 20.8%.

Method B.—As in A, but when heated at 140–145°, the yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 54.5%; and triphenylmethane, 24.2%.

Method C.—As in A, but refluxed under nitrogen. The first fraction eluted all the triphenylmethane reported and there were no other products, except a small amount of oily material removed by the acetone. The yield was: triphenylmethane, 79.2%.

III. Competition of *N*-Methylaniline and Aniline. Method A.—*N*-Methylaniline (0.05 mole), aniline (0.05 mole), and triphenylmethyl perchlorate (0.005 mole) were heated at 90–100°. Following the general procedure described in (IA) the products separated and identified were: *p*-trityl-*N*-methylaniline, 62.8%; and triphenylmethane, 16.7%.

Method B.—As in A, but at 140–145°. The yields were: *p*-trityl-*N*-methylaniline, 62.2%, and triphenylmethane, 23.3%.

Method C.—As in A, but refluxed under nitrogen. The yield was: triphenylmethane, 85.0%.

IV. Competition of *N*,*N'*-Dimethylaniline and Phenol. Method A.—*N*,*N'*-dimethylaniline (0.05 mole), phenol (0.05 mole), and triphenylmethyl perchlorate (0.005 mole) were heated at 90–100°. Following the procedure already described (IA), the resulting products were identified as indicated and the yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 50.5%; and triphenylmethane, 22.5%.

Method B.—As in A, but at 140–145°. The chloroform fraction eluted in this case some *p*-trityl phenol, identified by mixed melting point with an authentic sample of *p*-tritylphenol.[3] The yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 34.0%; *p*-tritylphenol, 1.2%; and triphenylmethane, 37.5%.

Method C.—As in A, but refluxed under nitrogen. Yields were: *p*-trityl-*N*,*N'*-dimethylaniline, 1.1%, and triphenylmethane, 89.2%.

V. Competition of *N*-Methylaniline and Phenol. Method A.—*N*-Methylaniline (0.05 mole), phenol (0.05 mole), and triphenylmethyl perchlorate (0.005) were heated at 90–100°. The chromatographic procedure described in (IA) gave: *p*-trityl-*N*-methylaniline, 70.3%; and triphenylmethane, 15.0%.

Method B.—As in A, but at 140–145°. The yields were: *p*-trityl-*N*-methylaniline, 45.6%; and triphenylmethane, 35.0%.

Method C.—As in A, but refluxed under nitrogen. The yield was: triphenylmethane, 87.5%.

Reactions of 2*H*,3*H*-Thieno[3,2-*b*]pyrrol-3-one. IV.[1,2] Benzylation

GERD W. MICHEL[3] AND H. R. SNYDER

William Albert Noyes Laboratory, University of Illinois, Urbana, Ill.

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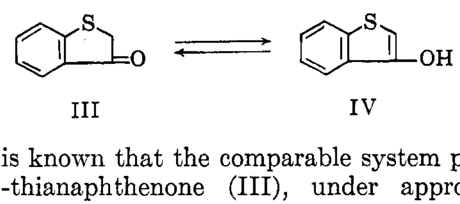
The heterocyclic ketone 2*H*,3*H*-thieno[3,2-*b*]pyrrol-3-one (I) reacts with benzyl chloride in the presence of sodium hydride to give the tribenzyl derivative Vd, in which nitrogen and carbon, but not oxygen, have been alkylated. Similar treatment of either the *N*-benzyl derivative (VIII) or the C-benzyl derivative (VII), prepared by other means, yields the same tribenzyl ketone Vd. Hydrogen peroxide in acetic acid attacks the sulfur atom of the tribenzyl ketone Vd, producing the dioxide. Preparations of the dioxides by similar oxidation of the parent ketone (I) and its benzylidene derivative (VI) also are described.

Past investigations in this laboratory have been concerned with the synthesis of substitution products of 2*H*,3*H*-thieno[3,2-*b*]pyrrol-3-one (I)[4,5] such as carbethoxy,[6] acetyl,[7] formyl-,[7,8] and arylidene[1] derivatives. In continuation of this program we have now studied the benzylation of this unique ketone.


I II III IV

It is known that the comparable system present in 3-thianaphthenone (III), under appropriate conditions, yields derivatives of both the keto and

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[1] For the preceding paper, see R. J. Tuite and H. R. Snyder, *J. Am. Chem. Soc.*, **82**, 4364 (1960).

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