Nitrogen Magnetic Resonance Spectroscopy. Correlation of Methylaniline Chemical Shifts with INDO Molecular Orbital Parameters

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Electron densities have been calculated for aniline, the toluidines, and the xylidines using the INDO method. Nitrogen chemical shifts reported earlier for these compounds correlate with total and σ electron densities; an apparent deviation induced by a *p*-methyl substituent disappears in a correlation with 2s orbital density. Electron densities at each ring carbon alternate in sign relative to aniline; the polarization is larger in the π than in the σ system. A substantial electron donation to the aromatic ring as well as to the nitrogens is shown to arise by withdrawal from the methyl hydrogens, whose electron densities correlate with the nitrogen shifts. Values for a given carbon in a xylidine are approximated by the sums of the corresponding values in the appropriate toluidines. The nitrogen chemical shifts of 3,4-xylidine and of aniline as a function of dilution are reported; the change in the aniline shift is smaller than the substituent effect.

Recently, Lichter and Roberts reported the ^{15}N chemical shifts of aniline, the toluidines, and all the xylidines except 3,4-xylidine.[1] The study exploited the inherently narrow line width of ^{15}N resonances and the resultant ability to measure small differences in line position precisely. In contrast to the deshielding effect which alkyl substituents exert in aliphatic amines, methyl substitution consistently induces small upfield shifts of the aniline nitrogen resonance position, whose magnitudes are comparable in the ortho and para positions and are smaller but still upfield in the meta position. Comparison with the effect of conjugatively interacting substituents[2] suggested that the influence of the methyl group is transmitted in an alternating unattenuated fashion through the carbon skelton to the nitrogen but in a different manner from that of the other substituents.

In order to gain some insight into the nature of the methyl electronic effect, and to determine whether the nitrogen chemical shift can serve as a probe of electron distribution, we have carried out molecular orbital calculations in the INDO approximation. We have also determined the ^{15}N shift of 3,4-xylidine and investigated the influence of dilution on the resonance position of aniline. We deemed the latter experiment necessary in order to exclude the possibility that the experimental trends[1] are a fortuitous consequence of different types of specific complexation in the highly associated pure liquids.

Experimental Section

Commercial samples of 3,4-xylidine and aniline were purified by distillation. The xylidine was run as a saturated solution in benzene at room temperature and as a melt at 50°. Dilution effects on the aniline resonance position were determined by adding an equal volume of solvent to the pure liquid and to each successive solution. No quantitative investigation was undertaken. Chemical shifts were measured in 10-mm tubes with respect to a sealed 2-mm capillary containing a 2.9 *M* solution of enriched ammonium chloride (96%, obtained from Thompson-Packard, Inc.) in 1 *M* HCl. Under these conditions, proton irradiation induces an optimum nuclear Overhauser effect.[3,4] Proton-decoupled spectra were determined by Fourier-transform techniques at the natural-abundance level of ^{15}N on a JEOL PS/PFT-100 spectrometer operating at 10.14 MHz in the external deuterium lock mode. Several hundred transients were accumulated over a 5-kHz range with a 30° pulse width at a 1.1-sec repetition rate using 8K words of memory. Chemical shifts are believed accurate to ±0.15 ppm. Figure 1 displays a typical spectrum.

Method of Calculation

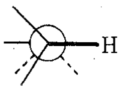
The CNINDO program was kindly provided by Professor David Beveridge of this department and uses parameters previously described.[5] Bond lengths were those of aniline and toluene. The pyramidal nitrogen geometry demonstrated for aniline[6] was approximated by using tetrahedral geometry at nitrogen in all the molecules; the plane of the NH_2 group was assumed to maintain a zero degree dihedral angle with respect to the ring plane in order to optimize electronic interactions with the π system. This conformation has been shown by *ab initio* calculations to be the most favorable.[7] Because the compounds are structurally and electronically very similar, the geometries were not optimized on the assumption that trends would not be critically affected. The values used are summarized in Table I.

Table I
Input Geometrical Parameters for INDO Calculations

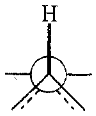
	Bond lengths, Å		Bond angles, deg
N—H[a]	0.998	H—N—C	109.47125
C—N[a]	1.431	H—N—H	109.47125
C═C[b]	1.397	H—C—H (methyl)	109.47125
═C—H[b]	1.084	All other angles	120.00000
C—CH_3[b]	1.390		
C—H[b]	1.090		

[a] Reference 6. [b] L. E. Sutton, Ed., "Tables of Interatomic Distances and Configurations in Molecules and Ions," The Chemical Society, London, 1958.

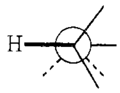
Perturbation of the electron distribution by the methyl group is small and, as quickly became apparent, very much dependent on methyl group conformation in ortho-disubstituted compounds[7,8] where considerable rotational barriers are expected. Accordingly, calculations were carried out on each molecule while varying the dihedral angle θ between a reference methyl C–H bond and the plane of the benzene ring, as shown in **1a–d**. In those structures, the dashed lines represent the two N–H bonds lying below the ring plane. In order to keep the number of calculations at a reasonable level, only the staggered conformations shown were considered for each methyl group, and all unique combinations of methyl rotation were taken for the dimethyl compounds. Symmetrical molecules with two or more equivalent conformations were appropriately weighted.



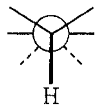
1a
$\theta = 0°$



1b
$\theta = 90°$



1c
$\theta = 180°$



1d
$\theta = 270°$

The coordinate system was such that the aromatic ring was in the x–z plane. Hence in the discussion below the $2p_y$ orbital electron density in the charge density–bond order matrix is defined as the π density, and the difference between this value and the total electron density is defined as the σ density.

Results

Chemical Shifts. The nitrogen chemical shifts of 3,4-xylidine and aniline are reported in Table II, where it is apparent that the shifts depend to some extent on the degree of molecular association.[9] The aniline dilution shift of ~1.5 ppm is outside experimental error but is still smaller than the *o*- and *p*-methyl substituent effect.[1] Those values were determined under an internally consistent set of experimental conditions (neat liquids, ~50°), where association effects are likely to be comparable; hence the chemical shifts are expected to reasonably reflect the influence of methyl substitution. The solvent dependence exhibited by 3,4-xylidine is well outside experimental error. To put its chemical shift on the same scale as the other anilines,[1] the value in the molten state was compared with that of aniline at the same temperature. The difference, 3.61 ± 0.2 ppm, is within experimental error of that (3.32 ± 0.3 ppm) calculated from the reported[1] substituent constants.

Electron Densities. The values obtained for each conformation were treated in three ways: (1) all conformations were weighted equally, to give an arithmetic average;[10] (2) the conformations were weighted according to the Boltzmann distribution with the assumption that the calculated total energy for each conformation was an accurate reflection of the actual energy; (3) only the lowest energy conformation was taken. Severe assumptions are inherent in each of the approximations, some of which will be discussed below, but the general relationships do not depend on the particular approach. Excess σ, π, 2s, and total electron densities are given in Table III, together with the corresponding nitrogen chemical shifts. Figures 2–5 display plots of the nitrogen shifts *vs.* the various electron densities.

Table II
Nitrogen Chemical Shifts of 3,4-Xylidine and Aniline

Compound	δ_N, ppm[a]
3, 4-Xylidine	
Saturated solution in benzene	29.86
Melted, T = 55°	27.81
Aniline	
Pure liquid, 22°	31.54
Pure liquid, 55°	31.42
~50% in benzene	30.82
~25% in benzene	30.34
~12% in benzene	29.98
~25% in CCl_4	30.94

[a] Downfield from external $^{15}NH_4Cl$; see text. Estimated error ±0.15 ppm.

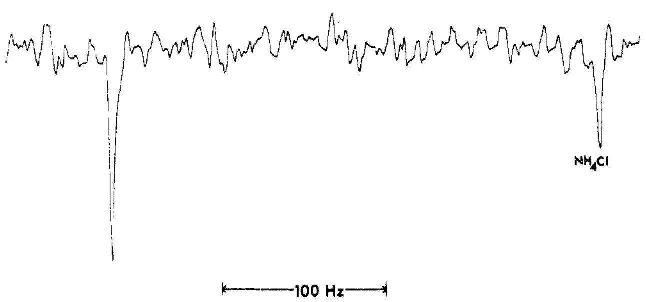


Figure 1. Pulsed Fourier-transform ^{15}N spectrum of 3,4-xylidine at 55°, obtained in natural abundance. Total accumulation time for the 1400 transients was 25 min. The inverted phase was arbitrarily set to represent the consequences of the expected nuclear Overhauser effect.

Discussion

From Table III and Figures 2–4 it is apparent that while there is considerable scatter, the nitrogen shifts increase with total and σ electron density. Dependence on total density has been suggested for benzamide and benzonitrile chemical shifts on the basis of empirical correlations with Hammett σ values.[11a] Both ^{14}N[11b] and ^{15}N[2] shifts of anilines substituted in the para position with conjugatively interacting substituents have been interpreted in terms of changes in nitrogen π electron density. That this cannot explain the methylaniline results is apparent from the present data: methyl substitution decreases the nitrogen π density, and the upfield shifts arise because of larger increases in the nitrogen σ density. This behavior difference is consistent with the different correlation that the *o*- *m*, and *p*-methyl substituent chemical shifts display with Hammett σ values compared to the conjugatively electron-donating halogens and alkoxy substituents.[1] The inductive effect of the latter groups, which is expected to be transmitted

Table III
Nitrogen INDO Electron Densities (×10⁴) of Methylanilines[a]

	$\Delta q^{av\,c}$				$\Delta q^{Boltz\,d}$				$\Delta q^{min\,e}$				
Compd[b]	Δq_{tot}	Δq_σ	Δq_π	Δq_{2s}	Δq_{tot}	Δq_σ	Δq_π	Δq_{2s}	Δq_{tot}	Δq_σ	Δq_π	Δq_{2s}	δ_N, ppm[f]
o-Toluidine	24	41	−17	24	12	38	−25	20	9	38	−29	19	2.31
m-Toluidine	5	13	−8	0	5	13	−8	0	4	13	−9	0	0.89
p-Toluidine	−5	2	−7	6	−5	2	−7	6	−5	2	−7	6	2.59
2, 3-Xylidine	32	55	−23	25	28	49	−21	22	13	34	−21	13	3.66
2, 4-Xylidine	23	42	−19	29	16	36	−20	25	3	21	−18	18	4.88
2, 5-Xylidine	33	54	−21	24	25	48	−23	20	13	33	−20	12	3.10
2, 6-Xylidine	48	83	−35	46	27	65	−38	33	16	58	−42	29	5.55
3, 4-Xylidine	0	11	−11	4	−1	11	−12	5	−1	11	−12	5	3.61[g]
3, 5-Xylidine	10	25	−15	0	10	25	−15	0	9	26	−17	1	1.56

[a] Relative to aniline: $\Delta q_i = q_i - q_{aniline}$. Positive values denote higher electron density than in aniline. [b] Registry numbers are respectively 95-53-4, 108-44-1, 106-49-0, 87-59-2, 95-68-1, 95-78-3, 87-62-7, 95-64-7, 108-69-0. [c] Arithmetic average value, all conformations weighted equally. [d] Conformations weighted according to Boltzmann distribution. [e] Lowest energy conformation. [f] Upfield from aniline, ref 1. [g] This work.

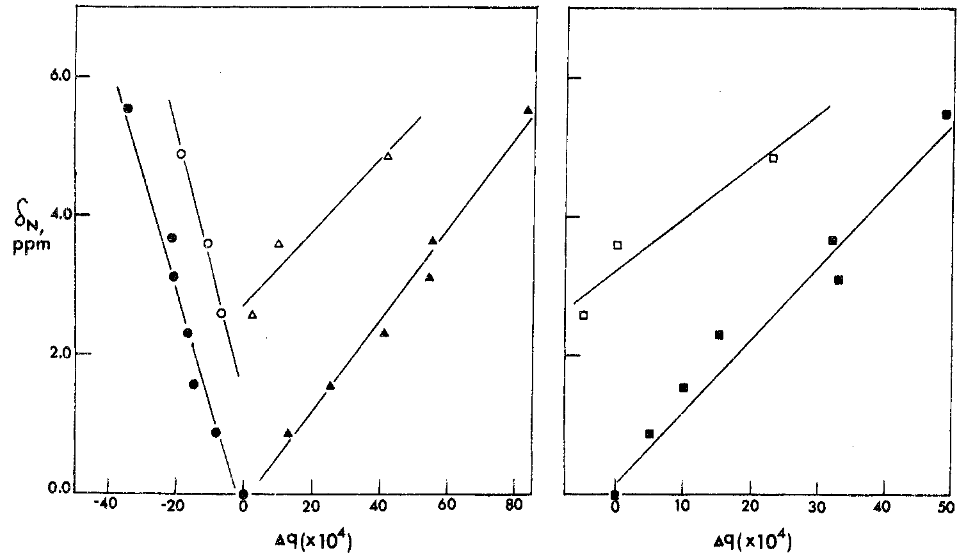


Figure 2. Plot of methylaniline nitrogen chemical shifts *vs.* average excess nitrogen electron densities. The open symbols represent compounds with *p*- methyl substituents: (●, ○) π density; (▲, △) σ density; (■, □) total density.

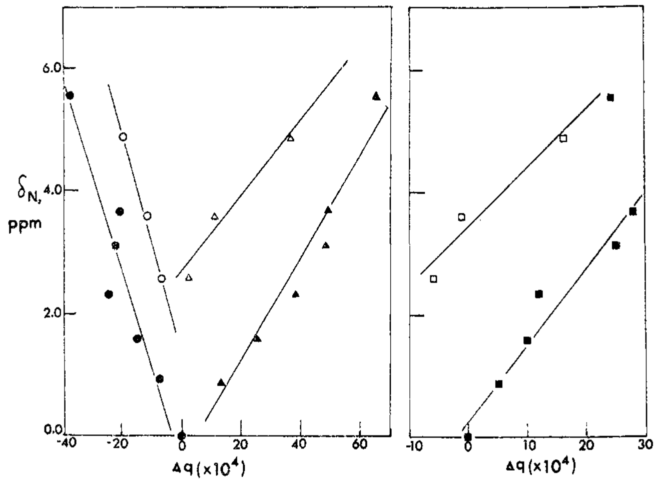


Figure 3. Plot of methylaniline nitrogen chemical shifts *vs.* Boltzmann excess nitrogen electron densities. The symbols have the same designations as in Figure 2.

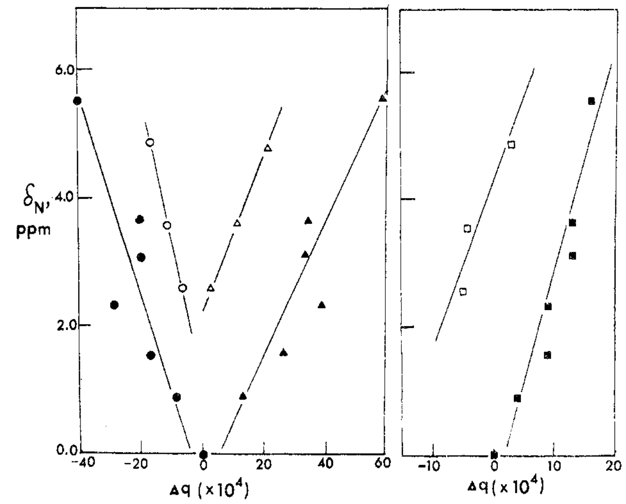


Figure 4. Plot of methylaniline nitrogen chemical shifts *vs.* lowest energy excess nitrogen electron densities. The symbols have the same designations as in Figure 2.

through the σ framework, is opposed by a dominant π donation of the substituent lone pair, which is expected to inhibit delocalization of the nitrogen lone pair. In the methylanilines inductive electron withdrawal to the amine nitrogen appears to be enhanced by the methyl group, probably because the latter's polarizability is larger than that of hydrogen. The parallel decrease in π density at nitrogen may owe to the increase in σ density; this type of "σ–π" repulsion has been noted for the para carbon of monosubstituted benzenes and for the fluorine-bearing carbon of para substituted fluorobenzenes.[12] Indeed, an inverse correlation exists between the corresponding σ and π densities at nitrogen.

Our inference that σ polarization effects and nitrogen electron densities dominate the nitrogen shifts is at variance with other studies for fluorine,[12] carbon,[10,13] and nitrogen shifts,[11b] where π polarization and electron density changes appear to dominate. However, in all these cases substituents have been capable of direct conjugative interaction with the observed nucleus, which is not possible in the methylanilines; hence it is reasonable that a different electronic mechanism should ensue.

Closer examination of Figures 2–4 reveals that the ani-

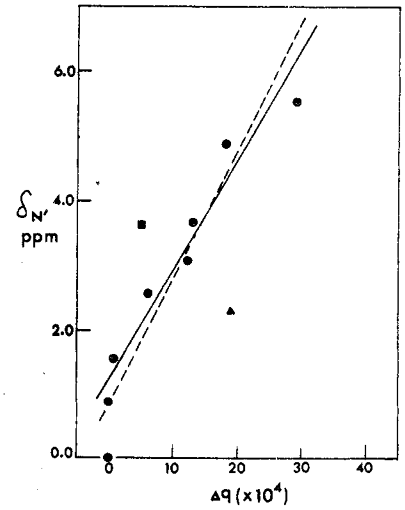


Figure 5. Plot of methylaniline nitrogen chemical shifts *vs.* lowest energy excess 2s orbital electron densities. The solid line is the least-squares fit (r = 0.90) calculated with exclusion of *o*-toluidine, while the dashed line is that (r = 0.95) calculated with exclusion of both *o*-toluidine and 3,4-xylidine: (▲) *o*-toluidine; (■) 3,4-xylidine.

Table IV
Excess INDO Electron Densities (×10⁴) of Methylaniline Ring Carbons[a]

	Δq_{C_1}	Δq_{C_2}	Δq_{C_3}	Δq_{C_4}	Δq_{C_5}	Δq_{C_6}	$\Sigma\Delta q$
o-Toluidine							
σ	−42	26	−53	75	−35	49	20
π	229	−316	261	261	136	−108	78
Total	187	−290	208	−49	101	−59	98
m-Toluidine.							
σ	67	−66	47	−56	62	−47	7
π	−114	272	−289	269	−113	151	176
Total	−47	206	−242	213	−51	104	183
p-Toluidine							
σ	−38	66	−47	47	−48	71	51
π	124	−129	249	−305	249	−124	64
Total	86	−63	202	−258	201	−53	115
2,3-Xylidine							
σ	19	−26	4	8	31	8	44
π	118	−51	−40	142	18	37	224
Total	137	−77	−36	150	49	45	268
2,4-Xylidine							
σ	−76	102	−109	115	−89	121	64
π	356	−436	527	−427	383	−236	167
Total	280	−334	418	−312	294	−115	231
2,5-Xylidine							
σ	30	−12	14	14	10	−11	45
π	113	−175	139	128	−161	167	211
Total	143	−187	153	142	−151	156	256
2,6-Xylidine							
σ	−83	83	−93	140	−93	86	40
π	473	−418	396	−251	395	−418	177
Total	390	−335	303	−111	302	−332	217
3,4-Xylidine							
σ	29	0	9	4	9	23	74
π	10	153	−44	−49	133	14	217
Total	39	153	−35	−45	142	37	291
3,5-Xylidine							
σ	133	−109	115	−121	110	−114	14
π	−218	414	−395	540	−393	426	374
Total	−85	305	−280	419	−283	312	388

[a] Lowest energy conformation only. Values are with respect to corresponding carbons in aniline.

Table V
Total Methyl and Hydrogen Electron Densities of Toluidines and Xylidines[a]

	Δq_{CH_3}	Δq_{H_3}
o-Toluidine	363	379
m-Toluidine	210	198
p-Toluidine	314	366
2,3-Xylidine	569	597
2,4-Xylidine	635	708
2,5-Xylidine	607	654
2,6-Xylidine	684	727
3,4-Xylidine	535	600
3,5-Xylidine	406	404

[a] With respect to toluene CH_3, ×10⁴.

lines bearing a *p*-methyl substituent can be separated from the remaining ones. The straight lines shown in the figures are the least-squares fit of the data within each group. Moderate to good correlations (r = 0.90–0.99) are obtained, although the Boltzmann analysis results in the least satisfactory fit. This is probably because the calculated total energies do not properly estimate the actual energies and rotational isomer population differences. It is not clear whether the division of the *p*-methyl compounds into a separate group arises from an unrecognized contribution to the chemical shift which is not reflected in the calculations, whether it is an artifact of the computational method, or whether the assumption of toluene geometry is invalid for *p*-methyl substitution.[14] However, an improved correlation is obtained which includes these compounds when the total 2s orbital density is taken (Figure 5). The implication that, despite expectations based on the Ramsey formulation of the chemical shift, the diamagnetic term σ_d dominates the chemical shift expression is not supported by our (unreported) estimation of that term, which are at least two orders of magnitude too small. However, the paramagnetic term σ_p is a function of the average inverse cube of the 2p orbital radius, $\langle r^{-3}\rangle_{2p}$, which in turn depends on the effective nuclear charge Z^*. Thus, this term still may be influenced by changes in the 2s orbital density in that its estimation using Slater's rules may not be adequate within this family of compounds.[15]

It should also be noted that the geometrical constraints imposed on the amino group may not be appropriate in the ortho-substituted isomers, particularly 2,6-xylidine, where severe steric interactions may induce changes in the H–N–H bond angle as well as in the NH_2 conformation with respect to the ring plane. Some of the deviations noted above may be attributable to this.

Examination of the σ, π, and total electron densities at the ring carbons is instructive. The values given in Table IV are for the lowest energy conformations, but the same trends obtain for the other sets of values. A substantial polarization exists in both the σ and π frameworks, and in all cases there is a net donation of electron density to the ring relative to aniline. While in some cases the excess ring electron density is substantial, in all cases the magnitude of the σ density is smaller then that of the π. This accords with the increase in nitrogen σ density and is consistent with the suggestion above that the nitrogen exerts its influence primarily through the σ skelton. Furthermore, in agreement with previous CNDO[16] and *ab initio*[7] calculations, as well as with a very recent extended Hückel study of the effect of methyl substitution on an aromatic ring,[17] the effects are transmitted *via* an alternating polarization of intervening carbon electron densities relative to aniline. However, both the net increase in ring electron density and the polarization exhibited here are larger than that calculated for toluene, so it is apparent that the amino group must enhance the otherwise small donation of electrons by the methyl group. Examination of the net change in methyl electron density relative to toluene, obtained by summing the total carbon and hydrogen electron densities, reveals this effect (Table V), and these values display a very good correlation with the nitrogen chemical shifts (Figure 6, r = 0.90). Decomposition into the contributions from carbon and hydrogen shows that the bulk of the electron donation is contributed by the hydrogens (Figure 6). Thus the amino group appears to polarize the ring electron density, and this polarization is transmitted through the substituent carbons to the electropositive hydrogens. Hence it is reasonable that there is no correlation between the nitrogen shifts and any other electron density in the molecules. These results further suggest a relationship between the nitrogen shifts and

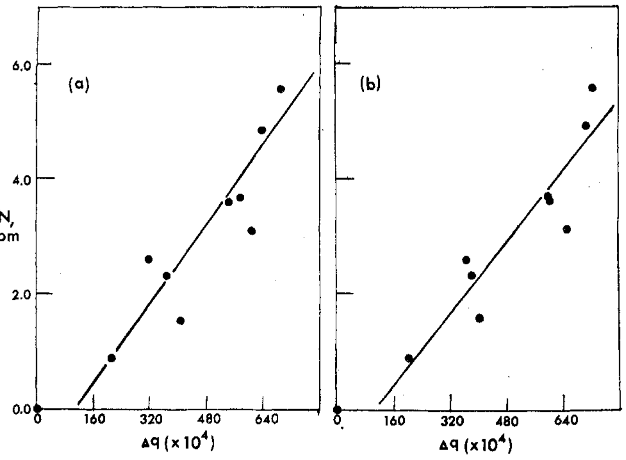


Figure 6. Plot of methylaniline chemical shifts *vs.* (a) excess total methyl electron densities and (b) excess methyl hydrogen electron densities. For (a) the values are the sum of the carbon and hydrogen electron densities of all the methyl groups, while for (b) only the hydrogen electron densities were taken. All values are given with respect to corresponding values in toluene. The least-squares lines (r = 0.924 and 0.939, respectively) were determined with all points included.

the methyl proton chemical shifts. This possibility is being explored.

It should be noted that the electron density at a given carbon of a disubstituted aniline is approximately the sum of the values at the corresponding carbons in the appropriate toluidine. This result is expected and indicates that there is no mutual electronic interaction between pairs of methyl groups.

It thus appears that even within the limitations of the INDO method and particularly the geometrical assumptions on which the calculations are based, the aniline nitrogen shifts depend on total electron density.

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Registry No.—Aniline, 62-53-3.

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The Mechanism of Equilibration of *cis*- and *trans*-2,3-Dimethyl-2,3-dihydrobenzofurans by Sulfuric Acid-d_2. Isomerizations Initiated by Oxonium Ions[1]

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Treatment of pure *trans*-2,3,4-trimethyl-5,7-dichloro-2,3-dihydrobenzofuran (**3**) with D_2SO_4 at room temperature gives the cis and trans equilibrium mixture **2** and **3**; these show deuterium uptake at the free aromatic position, slow uptake at C-2 and C-3, slower uptake on the 2- and 3-methyl groups, and none at the aromatic methyl. There is also formed in small amount at room temperature, and in larger amounts at 42°, the 2,2,4-trimethyl compound **4**, the product of methyl rearrangement. This compound can exchange all of its hydrogens for deuterium. The compound without a 2-methyl group, 2,3-dihydro-4-methyl-5,7-dichlorobenzofuran (**7**), shows only exchange of the aromatic hydrogen with D_2SO_4. Compound **7** could not be synthesized by the usual cyclization reactions of β-bromo- or β-hydroxyethyl phenyl ethers, presumably because of the steric effect of the *o*-methyl group (in **8d** and **8e**); it was synthesized by a procedure involving the intermediate 2-allyl-3-methyl-4,6-dichlorophenol (**9b**). Mechanisms for the isomerizations, exchange, and methyl rearrangements are discussed. The changes due to D_2SO_4 and H_2SO_4 on **2**, **3**, **4**, and **7** were followed by using vpc, nmr, and mass spectral methods.

It was shown[2] earlier that cyclization of the phenol **1a** or the methyl ether **1b** by concentrated H_2SO_4 gave a mixture of the *cis*- and *trans*-2,3-dimethyl-2,3-dihydrobenzofurans **2** and **3**; a small amount of the product of methyl rearrangement, the 2,2-dimethyl compound **4** was also isolated and identified.[2]

It was found that isomer **2** was formed under kinetic control of the cyclization, but at longer reaction times, the thermodynamically more stable trans form **3** was favored, the equilibrium favoring the trans form at room temperature by about 4:1. Treatment of the phenolic ether **1b** with ICl gave mainly the *trans*-iodomethyl compound **6**, which