**Large-Scale Rearrangement of 1-Adamantyl Benzyl Ether.**—A solution of 2.40 g. (0.01 mole) of the ether in 20 ml. of tetrahydrofuran was treated with 18 ml. of 1.1 $M$ methyllithium (0.02 mole) in tetrahydrofuran. The reaction mixture was hydrolyzed and worked up after 48 hr. Chromatography of the crude product over alumina, with petroleum ether–ether (3:1) as eluent, led to the isolation of 1.29 g. (54%) of pure phenyl-1-adamantylcarbinol (X), identical by infrared with an authentic sample.

**Preparation of n-Butyl o-Methoxybenzyl Ether.**—The reaction of equimolar quantities (0.30 mole) of o-methylanisole and N-bromosuccinimide in refluxing carbon tetrachloride, in the presence of a trace of benzoyl peroxide, afforded o-methoxybenzyl bromide in 66% yield, b.p. 113–115°/10 mm. (reported,[36] b.p. 115°/10 mm.).

Twenty grams (0.10 mole) of the above bromide was slowly added to 400 g. of n-butyl alcohol containing 0.25 mole of sodium n-butoxide. A white precipitate began to form almost immediately. After 3 hr. of reflux, the reaction mixture was cooled and then poured into water. The product was taken up in ether, washed with salt solution, dried over sodium sulfate, and distilled through an 8-in. Vigreux column, yielding 10.7 g. (55%) of product, b.p. 129–130°/5 mm.

*Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.20; H, 9.32.

(36) O. Brunner, E. Mullner, and G. Weinwurm, *Monatsh.*, **83**, 1477 (1952).

**Cleavage and Attempted Rearrangement of n-Butyl o-Methoxybenzyl Ether.**—The procedure of Gilman, *et al.*,[37] was used. Into a nitrogen-flushed, three-neck flask equipped with Herschberg stirrer, reflux condenser, and addition funnel, was placed 2.5 g. (0.35 g.-atom) of lithium ribbon, cut into small pieces, and 60 ml. of ether. To the cooled (−10°), stirred mixture was slowly added 5.0 g. (0.025 mole) of n-butyl o-methoxybenzyl ether, dissolved in 50 ml. of ether. The mixture was allowed to warm to room temperature and after 2 hr. a 10-ml. aliquot of the reddish brown solution was removed, hydrolyzed with dilute hydrochloric acid, washed with salt solution, and dried. Evaporation of the ether solution, followed by vapor phase chromatographic analysis revealed ca. 90% o-methylanisole and 10% starting material. After 48 hr., the entire reaction mixture was worked up in the usual manner, together with the previously isolated product, giving 2.60 g. (86%) of o-methylanisole, whose infrared spectrum was superimposable on that of an authentic sample. No o-ethylphenol was present, according to vapor phase chromatographic analysis.

(37) H. Gilman, H. A. McNinch, and D. Wittenberg, *J. Org. Chem.* **23**, 2044 (1958).
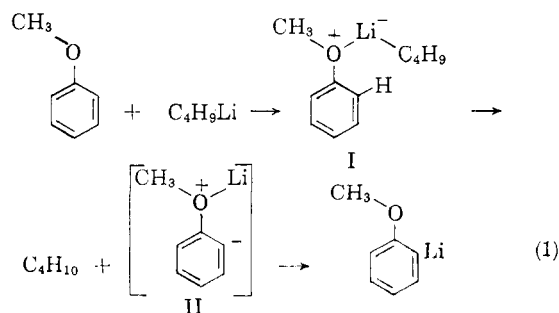
---

# The Metalation of Methoxynaphthalenes[1]

RODERICK A. BARNES AND LOUIS J. NEHMSMANN

*School of Chemistry, Rutgers, The State University, New Brunswick, N. J.*

The molecular orbital procedure has been used for calculating the distribution of the π-electrons in the mono- and dimethoxynaphthalenes. These data together with an estimation of the inductive effect has been used in an attempt to predict the relative reactivities of these substances toward metalation with a reagent such as butyllithium. The predictions agree with the experimental data which is available. However, contrary to a previous report 1-methoxynaphthalene has been found to metalate most rapidly at the 8-position with the initial product undergoing rearrangement of the lithium atom to the 2-position.

The metalation reaction is rather unique among aromatic substitution reactions in that the π-electron system of the molecule is essentially undisturbed in the process. Thus, the metalation of anisole is represented by equation 1.



$$ \text{(1)} $$

It has been suggested[2] that the inductive effect is most important in determining the course of the reaction. However, previous results with 1,7-dimethoxynaphthalene[3] indicate that, at least for this molecule, resonance effects are of prime importance.

In the present work it has been assumed that the metalation is a rate-controlled process and that the slow step is the removal of the hydrogen atom by the butyl carbanion (conversion of I to II). If this idea is correct the most acidic hydrogen should be removed most rapidly. The relative acidities of the hydrogen atoms at the various positions can, in turn, be estimated from the charge density on the carbon atom to which each hydrogen is bonded. The problem is thus resolved into one of calculating the charge at positions which may be available for metalation.

(2) J. D. Roberts and D. Y. Curtin, *J. Am. Chem. Soc.*, **68**, 1658 (1946).

(3) R. A. Barnes, and W. M. Bush, *J. Am. Chem. Soc.*, **81**, 4705 (1959).

The LCAO molecular orbital procedure[4] has been used to calculate the distribution of the $\pi$-electrons over the aromatic system. In previous molecular orbital calculations the value used for coulomb integral of the oxygen atom ($\alpha_O = \alpha_C + h_O\beta$) has varied with $h_O$ having a value between 1 and 2. There have been even greater variations in the resonance integral ($\beta_{C-O} = k\ \beta_{C-C}$).[5] In the present work it was assumed[6] that the lower value of $h_O$ was more likely to be correct. Therefore, starting with $h_O = 1$ and using 1,3-dimethoxybenzene as a trial molecule the dipole moment was calculated using various values for the resonance integral. As indicated in Table I, parameter set 2 gave the best agreement with the experimental dipole moment (1.58 D).

TABLE I

| | $h_O$ | $k_{C-O}$ | $\pi$-Moment | Total moment[a] |
|---|---|---|---|---|
| 1 | 1.00 | 1.00 | 2.23 | 1.01 |
| 2 | 1.00 | 1.20 | 3.13 | 1.91 |
| 3 | 1.00 | 1.40 | 3.97 | 2.75 |
| 4 | 1.50 | 1.20 | 3.71 | 2.49 |
| 5 | 0.75 | 1.20 | 2.10 | 0.88 |

[a] The moment was calculated to be 1.22 D, see C. P. Smyth, "Dielectric Behaviour and Structure," McGraw-Hill Book Co., Inc., New York, 1955, pp. 253, 330.

Although further adjustment of the parameters would have given even closer agreement, it was considered to be unnecessary for the present purposes. It may be worthwhile to note that the resonance integral obtained in this way is not greatly different from that derived in various other ways.[5,7]

The auxiliary inductive parameter ($h_{C\alpha} = \delta h_X$) used for atoms adjacent to heteroatoms was evaluated with $\delta = 1/5$. This is essentially a median value among those previously employed.[8]

The results of calculations are summarized in Table II. It was not necessary to calculate the charges at all atoms of the aromatic system, but these were automatically obtained by the computational method used and have been included in the table.

The inductive effect is more difficult to evaluate. The bond moment for a carbon-oxygen bond is usually about 1.2 D and for the systems under consideration it is necessary to assign charges to adjacent carbon atoms as well as to the oxygen. If the bond lengths are 1.4 Å. and the angles 120°, this moment could result from the charge distribution

(4) C. A. Coulson, "Valence," Oxford University Press, Amen House, London, E. A. 4, 1952, pp. 238–256.

(5) A. Streitwieser, "Molecular Orbital Theory for Organic Chemists," John Wiley and Sons, New York, 1961, p. 123.

(6) This assumption was in part by analogy with the nitrogen atom where better correlation with experimental values is observed when the older value of $h_N = 2$ is replaced by 0.5. See R. A. Barnes, J. Am. Chem. Soc., **81**, 1935 (1959), and references quoted therein.

(7) A very much lower value, $k_{C-O} = 0.1$ to 0.3 has recently been used for the furan molecule by F. L. Pilar and J. R. Morris, J. Chem. Phys., **34**, 389 (1961). The application of this value to other systems has not yet been reported.

(8) Ref. 5, pp. 128–129 points out that $\delta$ has varied between 1/10 and 1/3.

TABLE II

DISTRIBUTION OF $\pi$-ELECTRONS IN METHOXYNAPHTHALENES, CHARGE AT EACH POSITION

| Position of Methoxyl Groups | Oxygen atoms | Carbon 1 | Carbon 2 | Carbon 3 | Carbon 4 | Carbon 5 | Carbon 6 | Carbon 7 | Carbon 8 | Carbon 9 | Carbon 10 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | +0.267[a] | +0.031[b] | −0.164[b] | +0.011 | −0.082 | −0.010 | +0.005 | −0.019 | +0.010 | −0.057 | +0.008 |
| 2 | +.260 | −.166 | +.029 | −.061 | +.019 | +.003 | −.028 | +.002 | −.020 | +.010 | −.048 |
| 1,2 | +.224 | −.076 | −.080 | −.073 | −.061 | −.006 | −.021 | −.023 | −.003 | −.068 | −.045 |
| 1,3 | +.251 | +.042 | −.242 | +.035 | −.231 | −.028 | +.007 | −.043 | +.012 | −.098 | +.017 |
| 1,4 | +.233 | −.026 | −.148 | −.148 | −.026 | +.003 | −.012 | −.012 | +.003 | −.049 | −.049 |
| 1,5 | +.261 | +.024 | −.158 | −.006 | −.070 | −.024 | +.158 | −.006 | −.070 | −.050 | −.050 |
| 1,6 | +.267, | +.024 | −.185 | +.014 | −.098 | −.173 | +.032 | −.083 | +.027 | −.110 | +.017 |
| 1,7 | +.259, | +.033 | −.167 | +.014 | −.078 | +.010 | +.059 | +.016 | +.150 | −.043 | −.044 |
| 1,8 | +.265, | +.019 | −.174 | +.016 | −.089 | −.089 | +.016 | +.174 | +.036 | −.125 | +.017 |
| 2,3 | +.260, | +.036 | −.007 | −.007 | −.171 | −.021 | +.027 | +.027 | −.021 | −.034 | −.034 |
| 2,6 | +.247, | −.171 | +.010 | −.059 | +.002 | −.163 | +.010 | −.059 | +.002 | −.036 | −.036 |
| 2,7 | +.261, | −.163 | +.030 | −.088 | +.021 | +.021 | −.088 | +.030 | −.187 | +.019 | −.096 |

[a] An oxygen atom with zero charge has exactly two $\pi$-electrons and the plus charges indicate the fraction of an electron which has been lost. [b] A carbon atom with zero charge has one $\pi$-electron and the plus charges indicate the loss and the minus charges, the gain of a fraction of an electron.

The oxygen atoms column second entries: +0.233, +.269, +.233, +.261, +.257, +.259, +.265, +.260, +.247, +.261,

illustrated by III, if it is also assumed that the inductive effect is transmitted from one carbon to its neighbors by a factor of one fifth. Somewhat larger values have been used previously for transmission of the inductive effect in aliphatic systems. However, in the absence of strong evidence to the contrary, the most logical assumption was that this be the same as the factor used in determining the auxiliary inductive parameter which applies to the distribution of $\pi$-electrons.



III          IV
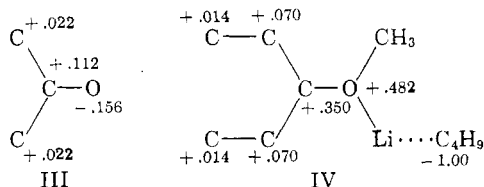
For 1,3-dimethoxybenzene, the sum of the $\pi$-electron distribution and the inductive effect illustrated by III gives a net charge distribution (V) which would indicate that metalation should take place at position 4 instead of at 2. The factor



V          VI
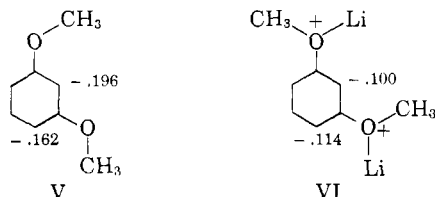
which has not been taken into account is the coordination of the metal atom with the oxygen of the methoxyl group. It seems reasonable to assume that coordination would involve the electron pair on the oxygen atom which is *not* a part of the $\pi$-electron system. The coulomb integral of the oxygen may be increased slightly by this process and hence the distribution of electrons would be modified.[9] However, it is believed that no serious error results by assuming that coordination has *no* effect on the $\pi$-electrons.

The partial positive charge on the oxygen atom resulting from such coordination should increase the inductive effect and hence the charges on the adjacent oxygen as is illustrated by IV. These values are somewhat arbitrary but were chosen so that the charges on the carbon atoms would be sufficient to make the 2-position of 1,3-dimethoxybenzene the more positive position (VI) and the one at which metalation should occur. It is interesting that in the range of fairly reasonable values for the inductive and resonance effects a correct prediction for 1,3-dimethoxybenzene is not obtained unless the species actually undergoing metalation has both oxygens coordinated with metal atoms.

(9) The calculations for 1,3-dimethoxybenzene show that an increase of the coulomb integral of the oxygen atom (parameter set 4 of Table I) does not appreciably change the difference in electronic charge between the 2- and 4-positions.

Using the values given by IV for the inductive effects, the net charge may be calculated for positions on the naphthalene nucleus adjacent to a methoxyl group (Table III).

TABLE III

| Position of methoxyl groups | Position, charge | | |
|---|---|---|---|
| 1,6 | 2, −0.115; | 5, −0.103; 7, −0.013, 8, +0.041 | |
| 1,3 | 2, −.102; | 4, −.161; 8, +.026 | |
| 1 | 2, −.094; | 8, +.024 | |
| 1,4 | 2, −.064; | 8, +.017 | |
| 1,7 | 2, −.097; | 6, +.011; 8, −.066 | |
| 1,2 | *3,* +.011; | 8, +.011 | |
| 2,6 | 1, −.093; | 3, +.011 | |
| 2 | 1, −*.096*; | 3, +.009 | |
| 2,7 | 1, −.117; | 3, −.019 | |
| 1,5 | 2, −.088; | 4, −.056 | |
| 2,3 | 1, −.087 | | |
| 1,8 | 2, −.104 | | |

For each substance in Table III, the more positive value, which is underlined, indicates the position at which metalation should occur. The substances are arranged in order of decreasing ease of substitution. However considering the approximations involved in these calculations, the order for two substances could well be reversed where the differences in charge between the preferred positions are small.

The metalation of 1- and 2-methoxynaphthalene and of 1,7- and 2,7-dimethoxynaphthalene have been studied and the predictions of Table III are correct with the exception of 1-methoxynaphthalene. Sunthanker and Gilman[10] have reported that metalation followed by carbonation yields 1-methoxy-2-naphthoic acid (25%). Table III predicts that the 8-position should be metalated and although it is not a position *ortho* to the methoxyl group, the mechanism (equation 1) seems to require only that the hydrogen be sterically accessible to the butyl carbanion of the coordination complex.

These considerations led us to reinvestigate the metalation of 1-methoxynaphthalene. Preliminary experiments indicated that a mixture of substances resulted when the metalation product was carbonated and that the composition of the mixture was variable. The mixture was found to contain 1-methoxy-2-naphthoic acid (VII) and 1-methoxy-8-naphthoic acid (VIII). The latter substance was identified by cleaving the methoxyl group to yield acid IX and lactone X, previously known substances.



VIII          IX          X
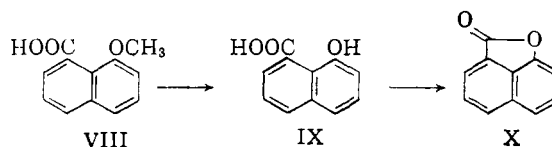
(10) S. V. Sunthanker and H. Gilman, *J. Org. Chem.,* **16**, 8 (1951).

In two separate experiments it was observed that toward the beginning of the metalation, carbonation of an aliquot yielded acid VIII as the major product and that as the reaction proceeded, the amount of acid VII increased. There was considerable variation with regard to the initial ratio of acid VIII to VII and the rate at which the ratio changed. The explanation for this may be that there were differences in the amount of some substance which tends to facilitate the conversion of the 8-metalated to the 2-metalated compound.

At least, these data support the idea that initially 8-metalation takes place most rapidly as is predicted by the calculations. Although one might be tempted to postulate that coordination (see XI) could stabilize an 8-metalated product, this evidence suggests that there is sufficient



XI
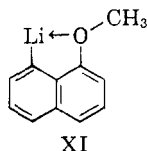
steric interaction between these two substituents in the 1- and 8-positions to make the 1,2-orientation thermodynamically preferred when conditions permit equilibration to occur.

By analogy, the other methoxynaphthalenes, which should metalate most rapidly at a peri position, would also be expected to rearrange to an unhindered orientation. Assuming that when rearrangement occurs it will be to the more positive position, excluding the peri positions, Table III indicates the following rearrangements to be likely: for 1,6-dimethoxynaphthalene the metal should rearrange to the 7-position and the 1,3- 1,4-, and 1,5- isomers should all rearrange to the 2-metalated products.

Some additional experiments are in progress to test further the validity of these predictions.

## Experimental[11]

**Calculations.**—The LCAO procedure described by Coulson was employed. The secular equations in matrix form were solved by the Jacobi procedure for determining the eigenvalues and eigenvectors of a real symmetric matrix. A program written for the IBM 650 computer was used,[12]

(11) Ultraviolet spectra were measured with a Cary recording spectrophotometer.

(12) The assistance of the staff of the Computer Laboratory, University of Oklahoma, in locating this program and carrying out the initial runs is gratefully acknowledged. Most of the calculations were carried out at the Computation Center, Rutgers University, and the help of the staff in arranging for computing time is also acknowledged.

and the output from this computation was used as input for a program written for the special purpose of converting the eigenvectors into charged densities at each position.

The inductive effect of the methoxyl group was taken into account by increasing the coulomb integral of adjacent carbon atoms. Thus for 1-methoxynaphthalene: $\alpha_O = \alpha_C + 1.0\,\beta$; $\alpha_{C-1} = \alpha_C + 0.2\beta$; $\alpha_{C-2,C-9} = \alpha_C + 0.04\beta$; $\alpha_{C-3,C-8}$, etc. $= \alpha_C$. The resonance integral ($\beta_{C-C}$) usually employed for benzene is 1.0 $\beta$, but in the naphthalene series the bond orders and bond lengths are not all equal. Therefore for the bonds between carbons 1–2, 3–4, 5–6, and 7–8, $\beta_{C-C}$ was assumed to be 1.1 $\beta$ and for all other bonds it was 0.9 $\beta$.

**Metalation Procedure.**—In a typical experiment butyllithium was prepared by adding butyl chloride (25 g.) dropwise to a rapidly stirred suspension of finely cut lithium ribbon (6.0 g.) in dry ether (200 ml.) at reflux temperature. When the lithium had reacted, methoxynaphthalene (20 g.) was added and the mixture stirred and refluxed for 22 hr. Powdered Dry Ice was introduced quickly into the mixture and then after carbonation was complete, dilute acid was added. The ether layer was extracted with sodium bicarbonate solution. Acidification of this extract yielded the crude acids (15–21%) which melted over a range, usually at 100–130°.

**Identification and Separation of Acids VII and VIII.**—In one experiment acid VIII was obtained directly in nearly pure form. However, it may be separated from the usual mixture by extracting the crude material for several hours with 20% benzene in ligroin (b.p. 70–90°) using a Soxhlet apparatus. Acid VIII is relatively insoluble and remains in the extraction thimble. In one experiment 2.9 g. of acid VIII was obtained in this way from 5.5 g. of mixed acids.

Pure acid VIII melts at 159–160.5° (lit.,[13] m.p. 162–163°). As a further check on its identity, a sample (2 g.) was refluxed with acetic acid (20 ml.) and hydrobromic acid (20 ml.) for 5 hr. Dilution of the reaction mixture with water precipitated the lactone of 1-hydroxy-8-naphthoic acid (X) which melted at 106–107° after recrystallization from ligroin (lit.,[14] m.p. 108°). The aqueous filtrate after removal of the lactone was extracted with 50% ether–benzene. The residue from evaporation of the solvents was recrystallized from ligroin to yield 1-hydroxy-8-naphthoic acid (IX), m.p. 167–168° (lit.,[14] 168–169°).

It was somewhat difficult to obtain a pure sample of 1-methoxy-2-naphthoic acid by crystallization. However absorption on silica gel and elution with 3% ethyl acetate in chloroform yielded pure acid VII, m.p. 127–128° (Sunthanker and Gilman, ref. 6, report m.p. as 125–126°).

**Ultraviolet Spectral Procedure for Analysis of Mixed Acids.**—Pure acid VIII had $\lambda_{max}^{C_2H_5OH}$ 221 m$\mu$ (log $\epsilon$ 4.48) 299 m$\mu$ (log $\epsilon$ 3.76), 311 m$\mu$ (log $\epsilon$ 3.66), 324 m$\mu$ log $\epsilon$ 3.48, and acid VII had $\lambda_{max}^{C_2H_5OH}$ 231 m$\mu$ (log $\epsilon$ 4.62), 284 m$\mu$ (log $\epsilon$ 3.68), 296 m$\mu$ (log $\epsilon$ 3.61). The absorption peak located at 324 m$\mu$ was chosen for determination of the amount of acid VIII since at this wave length acid VIII had only minimal absorption. The procedure was checked by using known mixtures of the two acids. Aliquots of some of the metalation reactions were withdrawn at various time intervals and carbonated. The percentage of acid VIII in the acidic product was then determined: expt. 1—4.5 hr. (73%), 24 hr. (46%); expt. 2—10 min. (65%); expt. 3—30 min. (50%), 2 hr. (45%); 24 hr. (40%).

(13) E. Bretscher, H. G. Rule, and J. Spence, *J. Chem. Soc.*, 1500 (1928).

(14) A. G. Ekstrand, *Ber.*, **19**, 1138 (1886).