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Selectivities of Aromatic Methyl Metalation.[1] Unexpectedly Strong Interactions of Carbanions with Aromatic Rings

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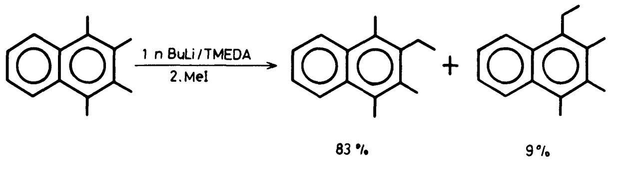
The site selectivities of the metalation reactions of dimethylnaphthalenes and dimethylanthracenes followed by MeOD quenching were investigated experimentally and theoretically. The 2(3)-methyl groups were found to be more effectively metalated than expected from the LUMO amplitudes of the aromatic rings. The MNDO calculations suggested that the naphthylmethyl and anthrylmethyl anions are not the aromatic rings perturbed by the carbanions, but the significantly different conjugated rings doubly bonded to the exocyclic carbon atoms. The unexpectedly strong interactions of the carbanion centers with the aromatic rings can account for the discrepancies between the selectivities and the LUMO amplitudes.

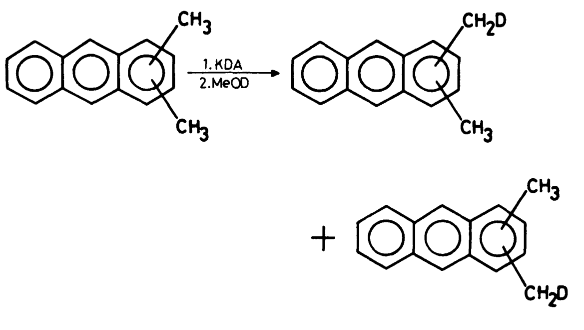
Aromatic compounds react with electrophiles (electron acceptors) and with nucleophiles (electron donors) at the positions where the HOMO and LUMO amplitudes are large, respectively. A similar expectation can be made for relative stabilities of aromatic compounds substituted by electron-releasing and -withdrawing groups. For example, aromatic compounds with an anionic center directly attached to the ring are expected to be stable when the LUMO amplitude is large on the substituted carbon atom. In fact, the acid dissociation constants[2] of isomeric naphthols and anthrols support the expectation: pK_a (H_2O, 20 °C)=9.85 for 1-naphthol and 9.93 for 2-naphthol; 9.88 for 1-anthrol and 9.92 for 2-anthrol. The LUMO of naphthalene and anthracene has greater extension at the 1- than 2-position (Fig. 1). However, the site-selectivity of the methyl metalation reactions of 1,2,3,4-tetramethylnaphthalenes observed by Dunkelblum and Hart[3] is opposite to the prediction based on the LUMO amplitudes. The metalation by butyllithium/*N,N,N′,N′*-tetramethylethylenediamine (*n*-BuLi/TMEDA) complex base preferentially occurs on the 2-methyl group (Eq. 1).



(1)

The anomaly was proposed[3] to come from steric origin: the C_2-methyls are closer to coplanarity with the naphthalene ring than the C_1-methyls, and *n*-BuLi/TMEDA, which is relatively large base, may attack the C_2-methyl to avoid the large steric interactions at the peri positions. A few years before, Kronzer and Sandel[4] estimated the kinetic parameters for the methylene rotation of the 1- and 2-naphthylmethyl (NM) organometallic compounds by the NMR spectroscopy. No appreciable difference was observed between the two isomers in the free energy of activation: ΔG^*(kcal mol^{-1}, 0 °C)=12.9±0.3 for 1-NM lithium and 12.8±0.5 for 2-NM lithium. In addition, Drakenberg et al.[5] reported the rotational barrier for the naphthoyl radicals. The barrier (ΔG^*) is lower for 1-naphthoyl radical (6.4 kcal mol^{-1}) than for 2-naphthoyl radical (8.2 kcal mol^{-1}). These rotational barriers throw a doubt on the steric explanation of the selectivity, rather than lend support to it.

We undertook experimental studies (Eq. 2) by employing 1,3-dimethylnaphthalene (DMN) and some dimethylanthracenes (DMA). The selectivity of the metalation reactions of the aromatic methyls was not always found to be in agreement with the LUMO amplitudes. The methyl metalations at the 2-positions of naphthalene and anthracene were shown to occur more preferentially than expected. The MNDO calculations suggested that methylnaphthalene and -anthracene, especially 2-methyl derivatives, might undergo more drastic structural change in the aromatic rings on metalation, which may account for the failure of the prediction based on the LUMO amplitudes.



(2)

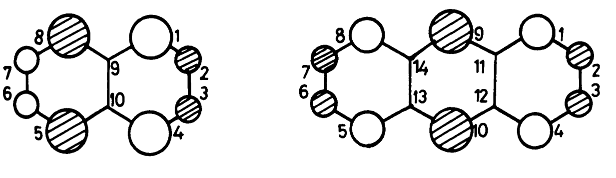


Fig. 1. The LUMO's of naphthalene and anthracene.

Results and Discussion

Selectivity. The metalation of 1,3-DMA preferentially occurred at the 3-methyl group, irrespective of the molar ratio of bases to the substrate (Fig. 2) and the reaction time (Fig. 3), although the LUMO amplitude is the smallest on C_3. For 1,10-DMA the 10-methyl metalation was preferred (Fig. 4). The LUMO amplitude is greater at the 9(10)-position(s). The selectivity is such as expected from the LUMO. The reactions of 2,9-DMA were not selective (Fig. 5), while the LUMO amplitude is much greater at the 9(10)-position(s). The absence of the selectivity is incompatible with the LUMO.

The reactions of 1,3-DMN were compared with 1,3-DMA. The 3-methyl metalation was preferred (Fig. 6). The selectivity is in good agreement with the observation by Dunkelblum and Hart.[3]

The selectivity consistent with the LUMO amplitude of the aromatic rings is only for 1,10-DMA. The other DMN and DMA examined here exhibited the opposite or inconsistent selectivities. The results present a striking contrast to the relative acidities of the isomeric naphthols and anthrols which can be explained in terms of the LUMO amplitudes.

MO Study. Molecular orbital study was undertaken to investigate the selectivity. Geometries of naphthylmethyl (NM) and anthrylmethyl (AM) carbanions were optimized by the MNDO molecular orbital calculations.[6] The relative stabilities of the isomeric anions are listed in Table 1.

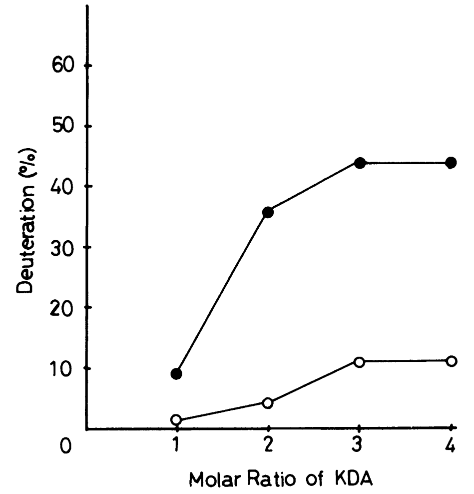


Fig. 2. The site selectivity of the metalation reactions of 1,3-dimethylanthracene (1,3-DMA). ○: 1-methyl, ●: 3-methyl.

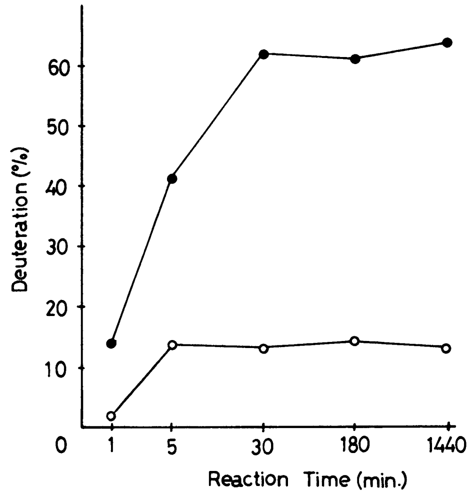


Fig. 3. The dependence of the selectivity on the reaction time for 1,3-dimethylanthracene (1,3-DMA). ○: 1-methyl, ●: 3-methyl.

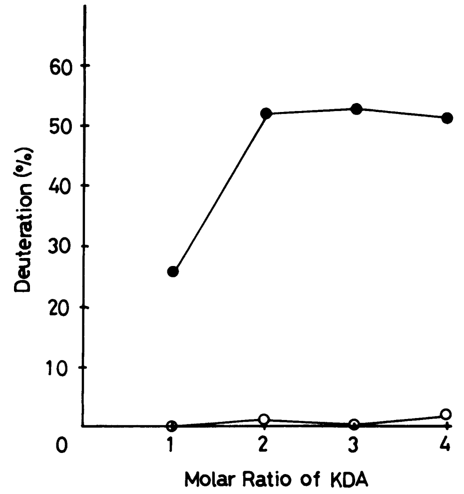


Fig. 4. The selectivity of the metalation reactions of 1,10-dimethylanthracene (1,10-DMA). ○: 1-methyl, ●: 10-methyl.

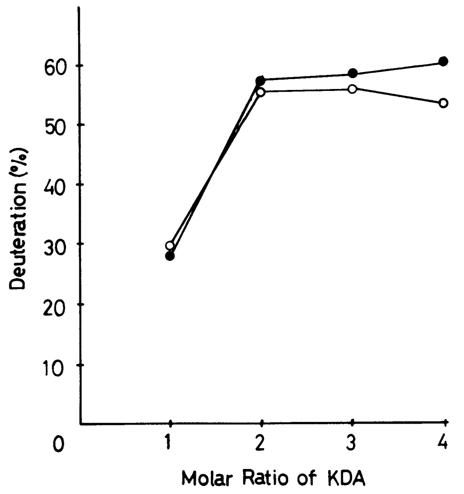


Fig. 5. The selectivity of the metalation reactions of 2,9-dimethylanthracene (2,9-DMA). ○: 2-methyl, ●: 9-methyl.

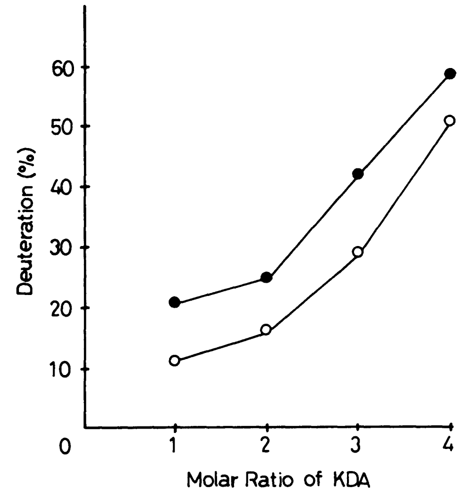


Fig. 6. The selectivity of the metalation reactions of 1,3-dimethylnaphthalene (1,3-DMN). ○: 1-methyl, ●: 3-methyl.

Table 1. Relative Energies[a] of Naphthylmethyl (NM) and Anthrylmethyl (AM) Anions

1-NM	2-NM	1-AM	2-AM	9-AM
0.0	−0.77	0.0	−0.29	−2.44

a) The results of the MNDO calculations in kcal mol^{-1}.

Although the calculated energy differences between 1- NM and 2-NM and between 1-AM and 2-AM anions are small, the relative stabilities are unexpectedly compatible with the observed selectivities of 1,3-DMN and 1,3-DMA. The 9-AM anion was shown to be the most stable. This result is in agreement with the prediction based on the LUMO amplitude and with the preferential C_{10} methyl metalation of 1,10-DMA. However, the result conflicts with the comparable extents of the C_2 and C_9 methyl metalations of 2,9-DMA. As a result, the 2-methyl metalation was concluded to occur more preferentially than expected from the calculated relative stabilities of the intermediate carbanions and the LUMO amplitudes of the aromatic rings.

Some interesting features were found in the optimized geometries (Fig. 7). The exocyclic bonds are surprisingly among the shortest in each species. These structures are not regarded as the aromatic rings perturbed by the methyl anions, but as entirely different conjugated rings doubly bonded to the methyl carbon atoms. The unexpected structural features can account for the failure in predicting the selectivity on the basis of the frontier orbital theory. The interactions of the carbanion centers with the naphthalene and anthracene rings are suggested to be too strong to be treated by the perturbation approach. The discrepancy between the LUMO amplitudes and the selectivities of the aromatic methyl metalations (the relative stabilities of the arylmethyl anions) is not necessarily incompatible with the success in explaining the relative acidities of the naphthols and anthrols. The oxy anions have n-orbitals at a lower energy level than the carbanions. The energy gaps between the n-orbitals and the LUMO of the aromatic rings are greater for the oxy anions. The frontier orbital interaction is weak enough to treat the

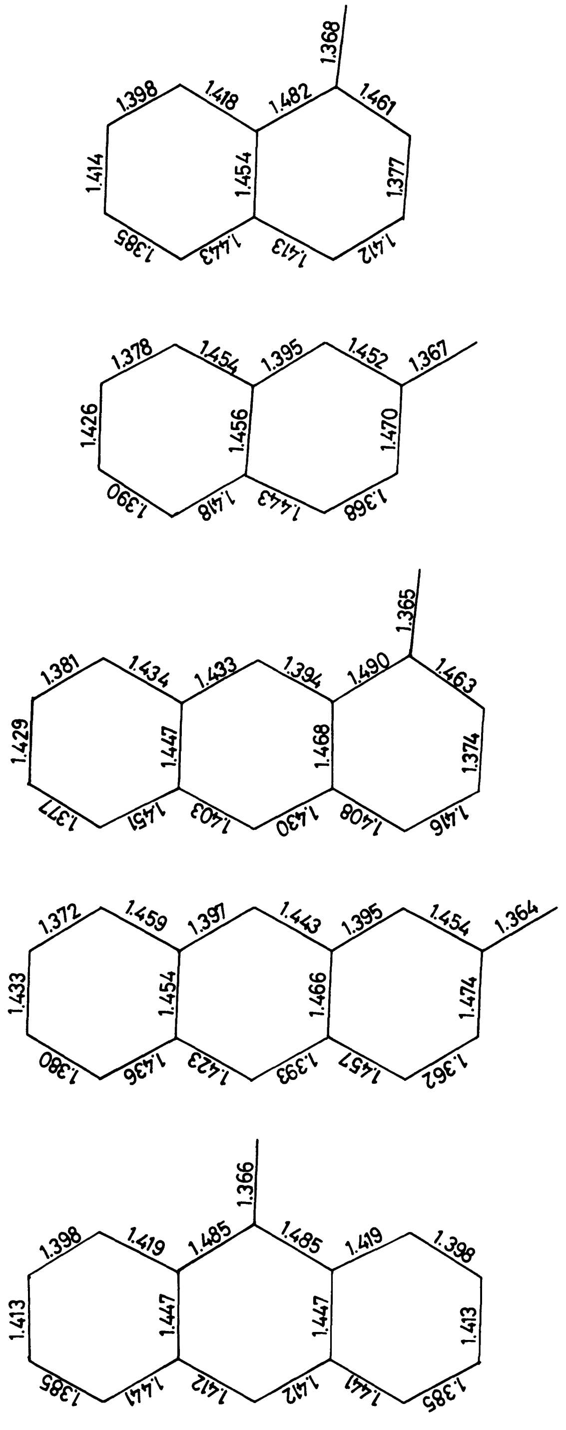


Fig. 7. The MNDO-optimized geometries of the naphthylmethyl (NM) and anthrylmethyl (AM) anions.

interactions of the oxy anions with the aromatic rings by the perturbational approach.

The bond alternations are remarkable all over the aromatic rings of the 2-NM and 2-AM anions. On the other hand, no appreciable bond alternation was found in the unsubstituted rings of the 1-NM, 1-AM, and 9-AM anions. The contrast was expected to give a clue to interpreting the preference of the 2-methyl metalation. Unfortunately, the explicit relation between the structural peculiarities and the selectivities still remains open to question.

Concluding Remarks

The selectivities of the methyl metalations of some dimethyl derivatives of naphthalene and anthracene were carried out under the same experimental conditions in order to examine the relation with the LUMO amplitudes of the aromatic rings. The preferential 3-methyl metalation of 1,3-DMN and 1,3-DMA is in conflict with the prediction from the LUMO amplitudes. The nonselective metalation of 2,9-DMA cannot be explained in terms of the LUMO which has much greater extension at the 9-position. The preference of the 10-methyl metalation of 1,10-DMA is in agreement with the LUMO amplitude. These results suggest that 2(3)-methyl group is more effectively metalated than expected from the LUMO amplitudes. The failure in predicting the selectivities from the LUMO presents a striking contrast to the success in predicting the acidities of the isomeric naphthols and anthrols.

The MNDO calculations suggested the strong interactions of the carbanions with the aromatic rings and the resulting double bond formation between them. The strong interaction rather than perturbation may be associated with the failure in the LUMO predictions of the relative stabilities of the isomeric arylmethyl anions or the selectivities of the aromatic methyl metalations. The successful explanation of the relative acidities of naphthols and anthrols can be understood in terms of weak interactions of the oxy anions with the aromatic rings due to lower n-orbital energies of the oxy anions.

Experimental

Materials. 1,3-, 1,4-, and 2,3-DMA's were prepared[7-9] from the anthraquinones.[10] 2,9- and 1,10-DMA's were obtained by Grignard synthesis from the anthrones.[11]

Metalation Reactions follwed by MeOD Quenching. DMA or DMN (0.1 g) was added to the KDA solution[12] which was prepared by mixing of t-BuOK into equimolar LDA in 10 ml of hexane under nitrogen atmosphere. The reaction mixtures immediately colored dark green for DMA and dark violet for DMN. The mixtures were stirred for a given period of time, and then quenched by a large excess of MeOD. After washing with dilute hydrochloric acid the organic layer was extracted by benzene and dried over sodium sulfate. The mixture was separated on the TLC. The ratios of methyl protons were determined by the 270 MHz FT-NMR spectroscopy on the basis of the 9- and 10-protons (2.0) for 1,3-DMA, the 9-proton (1.0) for 1,10-DMA, and the 10-proton (1.0) for 2,9-DMA.

The MNDO molecular orbital calculations were carried out on a HITAC M-680H computer, at the Institute for Molecular Science. NMR spectra were recorded on a JEOL JNM-GX 270 spectrometer, at the Center of Instrumentation, Gifu University. This work was partially supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture.

References

1) Orbital Theory Provoked Experiments in Organic Chemistry: Part 4. Part 3: S. Inagaki, T. Okajima, and K. Tanaka, *Chem. Lett.*, **1988**, 1219.

2) K. Lauer, *Ber.*, **70B**, 1127 (1937).

3) E. Dunkelblum and H. Hart, *J. Org. Chem.*, **44**, 3482 (1979).

4) F. J. Kronzer and V. R. Sandel, *J. Am. Chem. Soc.*, **94**, 5750 (1972).

5) T. Drakenberg, J. Sandstörm, and J. Seita, *Org. Magn. Reson.*, **11**, 239, 246 (1978).

6) M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, **99**, 4899 (1977).

7) L. F. Fieser, "Organic Experiments," Maruzen, Tokyo (1964), p. 195.

8) J. V. Braum and O. Bayer, *Ber.*, **59**, 914 (1926).

9) F. Griendt and H. Cerfontain, *Tetrahedron*, **36**, 317 (1980).

10) V. Stepan and J. Vodehnal, *Collect. Czech. Chem. Commun.*, **36**, 3964 (1971).

11) E. B. Barnett and N. F. Goodway, *J. Chem. Soc.*, **1929**, 1754.

12) B. Renger, H. Hügel, W. Wykypiel, and D. Seebach, *Chem. Ber.*, **111**, 2630 (1978); S. Raucher and G. A. Koolpe, *J. Org. Chem.*, **43**, 3794 (1978).