CHEMISTRY LETTERS, pp. 241-244, 1987.

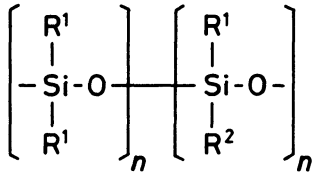
Unusual Effect of Methylation of a Benzene Ring on the Strength of Phenyl—Phenyl Interaction‡

Masato M. ITO,† Jun-ichi KATO, Ichiro TAKAMURA, Kyoko WAKATSUKI, and Tadashi ENDO*

College of Science and Engineering, Aoyama Gakuin University, Chitosedai, Setagaya-ku, Tokyo 157

Gas-chromatographic studies have shown that the strength of the weak interaction between a phenyl group in a stationary liquid and a benzene molecule in a sample alters most greatly when, among various substituents examined (e.g., Me, Et, Cl, and OMe), a methyl group —— a "simple" nonpolar group —— is introduced into a benzene ring in the sample.

It has been suggested that an aromatic—aromatic interaction has a marked influence on molecular conformations[1] and chemical reactivity,[2] this interaction being other than the well-known charge-transfer interaction.[3] Very little is known, however, about the effect of a substituent introduced into an aromatic ring on the aromatic—aromatic interaction. We have been studying the specificity of weak interactions associated with a phenyl (Ph) group using gas-chromatographic method,[4] and report here that a phenyl—phenyl interaction varies most greatly when a methyl group as a substituent is introduced into a benzene ring.



1 R^1 = Ph, R^2 = Me

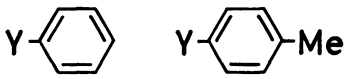
2 R^1 = R^2 = Me

As stationary liquids we used a pair of silicone oils (**1** and **2**)[5] with and without a Ph group. The

‡ Dedicated to Professor Teruaki Mukaiyama on the occasion of his 60th birthday.

† Present address: Department of Chemical Engineering, Faculty of Engineering, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113.

samples employed are a variety of monosubstituted (3) and para-disubstituted benzenes (4). The relative retention (α_x) was defined as the ratio of the retention time[6] for a sample (3 or 4) to that for n-hexane (5) as the reference, where x = 1 or 2, depending on the stationary liquid used (1 or 2).



3 4

The α_1 and α_2 values were measured at various temperatures. Plots of ln α_x against T^{-1} showed a straight line for each sample examined. Since the relationship ln $\alpha_x = -\Delta\Delta H_x/RT + C$ holds, where $\Delta\Delta H_x$ is the difference in molar heat of solution between samples 3 (or 4) and 5 in liquid x [e.g., $\Delta\Delta H_x = \Delta H_x(3) - \Delta H_x(5)$],[4,7] the slope of the plots yields $-\Delta\Delta H_x/R$. Though the $\Delta\Delta H_x$ itself involves the difference in heat of vaporization between 3 (or 4) and 5, the difference is cancelled by subtracting $\Delta\Delta H_2$ from $\Delta\Delta H_1$.[4] Thus, the $\Delta\Delta H^t$ (= $\Delta\Delta H_1 - \Delta\Delta H_2$) can be regarded as a measure of the difference in the weak interaction of the Ph group in 1 between 3 (or 4) and 5 —— as a measure, though not strict, of a phenyl—(substituted) phenyl interaction.

In Fig. 1, $\Delta\Delta H^t$ values for a variety of monosubstituted benzenes 3 are plotted against the structures of substituent Y. The difference between the $\Delta\Delta H^t$ values for benzene and a monosubstituted benzene becomes largest when Y = Me. It is interesting to note that, in the case of alkylbenzenes, the $\Delta\Delta H^t$ value reaches a maximum for toluene and that the introduction of substituents (i.e., Me, Cl, and OMe) at a benzylic carbon atom decreases the $\Delta\Delta H^t$.

The effect of methylation on the weak interaction was further examined

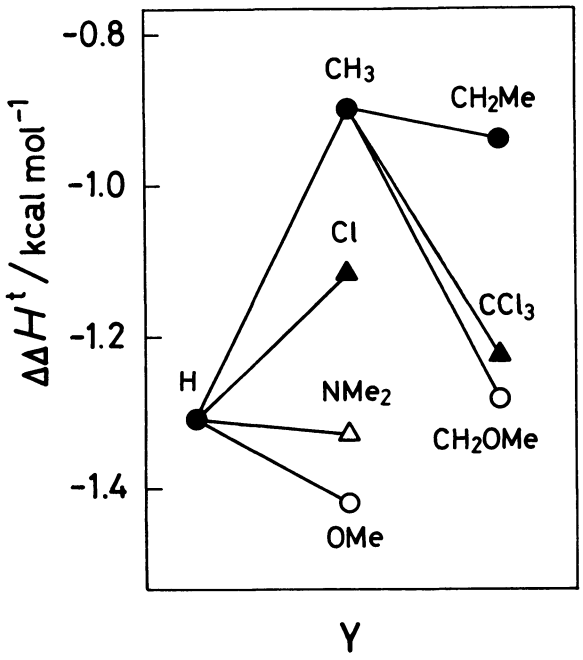


Fig. 1. Plot of $\Delta\Delta H^t$ for 3 against the structures of Y. The $\Delta\Delta H^t$ value for n-propylbenzene is -1.00 ± 0.12 kcal/mol, the value slightly more negative than that for ethylbenzene.[8] The experimental errors (standard deviation) range from ± 0.04 to ± 0.07 kcal/mol for Y = H, Me, Et, Cl, OMe, and CH_2OMe, and from ± 0.10 to ± 0.12 kcal/mol for Y = NMe_2 and CCl_3. 1 cal = 4.184 J.

using substituted benzenes and toluenes as samples. Figure 2 plots the $\Delta\Delta H^t$ for the two sets of samples against substituent Y. Regardless of the structures of Y, methylation of benzene rings has proved to increase the $\Delta\Delta H^t$ by ca. 0.3—0.4 kcal mol^{-1}.[9]

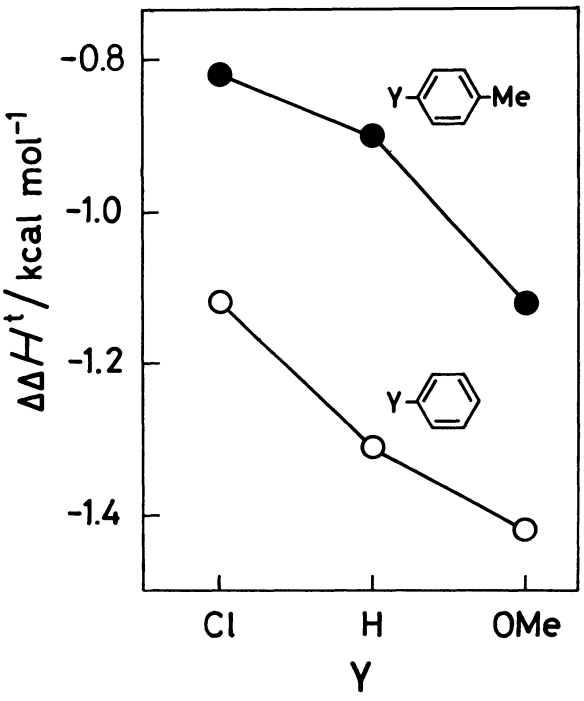


Fig. 2. Plot of $\Delta\Delta H^t$ for 3 and 4 against the structures of Y. The experimental errors (standard deviation) for 3 and 4 (Y = Cl) range from ± 0.04 to ± 0.07 kcal/mol, that for 4 (Y = OMe) being ± 0.11 kcal/mol.

The order of $\Delta\Delta H^t$ values for samples 3 (Fig. 1) does not agree with that of their ionization potentials [9.24 (benzene), 9.07 (chlorobenzene), 8.82 (toluene), and 8.22 eV (anisole)];[10] this indicates that the $\Delta\Delta H^t$ cannot be explained by the charge-transfer interaction, since the energy of this interaction depends on the ionization potential of a donor.[3] The $\Delta\Delta H^t$ (Fig. 1) tends to decrease with increasing molar polarization (P) [27 (benzene), 34 (toluene), 39 (ethylbenzene), 44 (n-propylbenzene), 58 (anisole), 62 (chlorobenzene), and 72 (N,N-dimethylaniline) cm^3 mol^{-1}][11] except for benzene and anisole; this suggests that the $\Delta\Delta H^t$ reflects the dispersion interaction to some extent. Electronic effect of Y also fails to account for the data in Fig. 1.[12] Thus, the reason for the observed effect of a substituent on the phenyl—phenyl interaction remains to be elucidated.

From the experimental results presented here, it seems reasonable to conclude that the introduction of a methyl group —— a "simple" nonpolar group —— into a benzene ring causes an unusual change in the strength of the phenyl—phenyl interaction. Experimental evidence is obtained to suggest that the change in the interaction by methylation markedly affects the selectivity in oxidation of a pair of associating thiols.[14]

This gas-chromatographic method will enable us to evaluate the strength of the weak interaction between a group other than the phenyl group and a sample

molecule by utilizing a pair of adequate stationary liquids.

References

1) a) R. M. Tel and J. B. F. N. Engberts, J. Chem. Soc., Perkin Trans. 2, 1976, 483; b) S. K. Burley and G. A. Petsko, Science, 229, 23 (1985).

2) A. K. Colter and M. R. J. Dack, J. Chem. Soc., Chem. Commun., 1977, 5.

3) R. S. Mulliken and W. B. Person, "Molecular Complexes," Wiley, New York (1969).

4) T. Endo, M. M. Ito, and T. Namiki, J. Chem. Soc., Chem. Commun., 1985, 933.

5) Silicone oils were used as the stationary liquids: 1, Silicone OV-25 (75% Ph and 25% Me); 2, Silicone OV-101 (100% Me). These were coated on acid-treated Celite 545 in a weight ratio of 1 to 5, and the stationary phases were packed in stainless-steel tubes (3 mm internal diameter × 2 m). The carrier gas was nitrogen with a flow rate of 20 ml min^{-1}.

6) Retention time was measured from the methane peak to correct for the free space in the system.

7) R. J. Laub and R. L. Pecsok, "Physicochemical Applications of Gas Chromatography," Wiley, New York (1978).

8) The energies of aromatic—aromatic interactions between the aromatic side chains in model peptides and proteins are reported to lie between -1 and -2 kcal mol^{-1} on the basis of nonbonded potential energy calculations.[1b)]

9) In this connection, $\Delta\Delta H^t$ values for benzene-d_6 and toluene-d_8 have been found to be equal to those for benzene and toluene, respectively.

10) Ref. 3, p. 135; K. Watanabe, J. Chem. Phys., 26, 542 (1957).

11) The P is proportional to the polarizability (α) ($P = (4/3)\pi N_A \alpha$, where N_A is Avogadro constant), upon which the dispersion interaction energy (E) depends [$E = -(3/2)(II'/(I+I'))(\alpha\alpha'/r^6)$, where I and I' are ionization potentials and r is intermolecular distance].

12) This is because the order of σ_p values for Y [0.33 (CCl_3), 0.23 (Cl), 0 (H), -0.17 (Me), -0.27 (OMe), and -0.83 (NMe_2)][13)] differs sharply from that of the corresponding $\Delta\Delta H^t$ values (Fig. 1).

13) C. Hansch, A. Leo, S. H. Unger, K. H. Kim, D. Nikaitani, and E. J. Lien, J. Med. Chem., 16, 1207 (1973).

14) T. Endo et al., unpublished results.

(Received August 13, 1986)