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# THE GAUCHE INTERACTION IN *trans*-1,2-DIMETHYLCYCLOHEXANE

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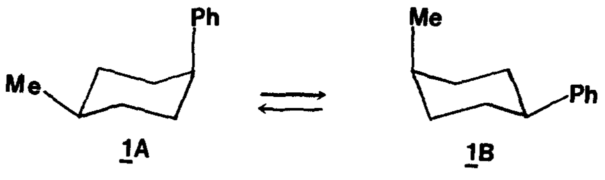
*Abstract.* The gauche interaction in the diequatorial conformation of *trans*-1,2-dimethylcyclohexane is found to be 0.74±0.09 kcal/mol (3.10±0.38 kJ/mol).

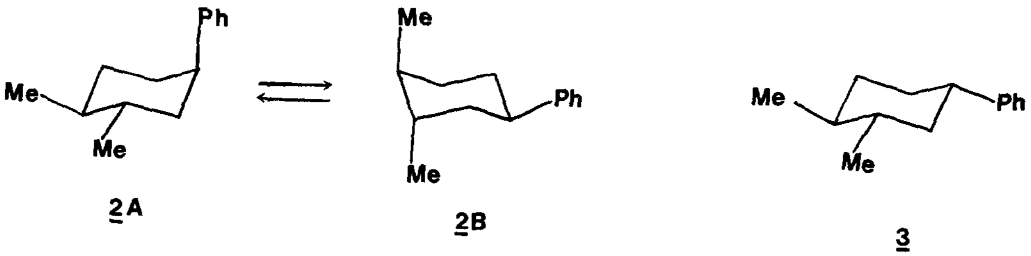
One of the important parameters in conformational analysis is the gauche interaction of the methyl groups in *trans*-1,2-dimethylcyclohexane. Its magnitude enters into the calculation of the cis/trans 1,2-dimethylcyclohexane equilibrium, a classical stereochemical problem.[1] Nevertheless there are only two earlier experimental determinations[2-4] of this quantity in the literature, neither of them explicit. The first is based on the difference in enthalpy between *trans*-1,2-dimethylcyclohexane on one hand and the *cis*-1,3 or *trans*-1,4 isomers (which are devoid of this interaction) on the other. The pertinent enthalpies of formation have been determined with great accuracy by Rossini *et al.*[2] as -43.02, -44.16 and -44.12 kcal/mol in the vapor and -52.18, -53.29 and -53.17 kcal/mol in the liquid phase, respectively. Assuming that the *only* difference between the 1,2 isomer on one hand and the 1,3 and 1,4 compounds on the other is the Me/Me gauche interaction in the former, and averaging values for the 1,3 and 1,4 compounds, one obtains a value of 1.12 kcal/mol in the vapor and 1.05 kcal/mol in the liquid phase for the gauche interaction. These values are not only contingent on the assumption stated but also, being small differences between large numbers, have quite large standard errors. A more precise determination of the Me/Me gauche interaction comes from the comparison of conformational equilibria in *trans*-2-hydroxy-*cis*-4-isopropylcyclohexyl-*r*-1-amine and *trans*-2-hydroxy-*cis*-4,-*trans*-5-dimethylcyclohexyl-*r*-1-amine assessed by $pK_a$ measurements.[3] Taking up-to-date values of 2.21 kcal/mol for the conformational energy of isopropyl[5] and 1.74 kcal/mol for methyl,[6] this allows one to deduce 0.61 kcal/mol for the Me/Me gauche interaction. Usually, however, this interaction has been *assumed* to be equal either to one-half the syn-axial methyl/H interaction in axial methylcyclohexane[7] (½ x 1.74 kcal/mol) or to the Me/Me gauche interaction in the gauche form of *n*-butane. The latter parameter has been determined numerous times and the best values for it appear to be 0.5-0.7 kcal/mol in the liquid or solution phase and 0.88-0.96 kcal/mol in the gas phase.[8]

The recent determination of the *cis*-1-phenyl-4-methylcyclohexane (Scheme 1, **1**) equilibrium[9] has allowed us to use the phenyl group as a counterpoise to measure conformational equilibria. We report here on the conformational equilibrium of *r*-1-phenyl-*trans*-3,*cis*-4-dimethylcyclohexane (Scheme 2, **2**) and its use in the determination of the Me/Me gauche interaction when the two methyl groups are equatorial.



ΔG° = −1.13 ± 0.06 kcal/mol

Scheme 1



ΔG°= − 0.13 ± 0.03 kcal/mol

Scheme 2

Compound **2** was synthesized by addition of phenylmagnesium bromide to *trans*-3,4-dimethylcyclohexanone (Wiley Organics) followed by dehydration ($H_2SO_4/CH_3CO_2H$) and catalytic hydrogenation (10% Pt/C, 95% EtOH, r.t., 40 psi). The resulting mixture of diastereomers (phenyl *cis* or *trans* to Me-3) was inseparable in our hands but the signals in its 62.89 MHz C-13 nmr spectrum could be readily assigned - by parametric assignment in the case of the *c*-3-Me isomer (**3**, Scheme 2) and by the finding that the signals decoalesced at -100°C in the case of the *t*-3-Me isomer (**2**). (Shift parameters for phenyl are:[9] $\alpha_e$ 17.6, $\beta_e$ 7.5, $\gamma_e$ -0.1, $\delta_e$ -0.85, $\alpha_a$ 8.2, $\beta_a$ 3.0, $\gamma_a$ -6.0, $\delta_a$ 0.0; for methyl the standard shift parameters[10] were used with the assumption of zero for vicinal $Me_a/Me_a$). The experimental and calculated shifts at room temperature and (in the case of **2**) at -100°C are shown in Table 1 and the area ratios for resolved signals in **2** at -100°C are shown in Table 2.

Table 1 - Chemical Shifts[a]

| Cpd. | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | Me-3 | Me-4 | C-*ipso* | C-*o* | C-*m* | C-*p* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **3**,r.t. | 45.0 | 43.9 | 39.8 | 39.2 | 36.3 | 34.8 | 20.4 | 20.4 | 148.1 | 127.1 | 128.6 | 126.0 |
| **3**,calc'd[b] | 44.5 | 43.6 | 39.5 | 38.7 | 36.0 | 34.4 | 20.5 | 20.5 | 148.0 | 126.8 | 128.3 | 125.8 |
| **2**,r.t. | (38.1) | 36.2 | 34.5 | (37.1) | 29.1 | 29.6 | (20.1) | (19.9) | 147.1 | 127.6 | 128.3 | 125.7 |
| **2**,calc'd[c] | 37.3 | 36.0 | 34.0 | 35.6 | 28.3 | 29.1 | 20.2 | 19.9 | 146.6 | 127.4 | 127.7 | 125.8 |
| **2**A | 36.3 | 38.5 | 33.8 | 39.6 | 30.6 | 29.8 | 20.5 | 20.4 | 144.5 | 127.7 | 128.3 | 125.3 |
| **2**A,calc'd[b] | 35.1 | 39.1 | 33.6 | 39.6 | 30.1 | 29.9 | 20.5 | 20.5 | d | d | d | d |
| **2**B | 38.2 | 33.9 | (34.3) | (32.3) | 26.5 | 28.5 | 20.0 | 19.5 | 148.4 | 127.1 | 127.3 | 126.1 |
| **2**B,calc'd[b] | 38.4 | 33.6 | 33.9 | 33.2 | 26.1 | 28.2 | 19.5 | 19.5 | 148.5 | 127.2 | 128.6 | 126.2 |

[a] Chemical shifts in ppm in TMS in $CD_2Cl_2$. Parenthesized values may be interchanged. [b] Parametric calculation. [c] Calculated from low-temperature shifts, by the equation[11] $\delta = n_A\delta_A + n_B\delta_B$ assuming 45% **2**A, 55% **2**B and disregarding effect of temperature on shifts. [d] No basis for calculation.

Table 2 - Relative Signal Areas and Calculation of ΔG°

| Carbon | Relative Area | | K | -ΔG° cal/mol |
|---|---|---|---|---|
| | **2**B | **2**A | | |
| $C_{ortho}+C_{meta}$ | 50 | 32 | 1.56 | 154 |
| C-1 | 21 | 14.5 | 1.45 | 127 |
| C-5 | 20 | 13 | 1.54 | 148 |
| C-6 | 19 | 15 | 1.27 | 81 |
| Average | | | 1.46±0.13 | 128±33 |

From Schemes 1 and 2 it may be deduced that, in terms of free energy, **2**A = **1**A + X and **2**B = **1**B + (1.74±0.06) where X is the desired Me/Me gauche interaction (not present in **1**A) and 1.74 is the extra Me-axial[6] in **2**B (compared to **1**B). Since **2**A-**2**B = (0.13±0.03) and **1**A-**1**B = (1.13±0.06)[9] it follows that the Me/Me gauche interaction X = **2**A-**1**A = [**2**B + (0.13±0.03)]-[**1**B + (1.13±0.06)] = [**1**B + (1.74±0.06) + (0.13±0.03)]-[**1**B + (1.13±0.06)] = 0.74±0.09 kcal/mol.

This value, which refers to the liquid phase, is, as expected, somewhat larger than the *n*-butane-gauche and somewhat less than ½ the axial methylcyclohexane interaction, presumably because the ability of the methyl groups to move away from each other by torsion is greatest for gauche-butane, intermediate for e,e-*trans*-1,2-dimethylcyclohexane and least for axial methylcyclohexane. The value is also compatible (within the error limits) with the two values previously determined.[2,3]

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## *References and Footnotes*

1. E.L. Eliel, N.L. Allinger, S.J. Angyal and G.A. Morrison, "Conformational Analysis" Reprinted by the American Chemical Society, Washington, DC (1981), pp. 52-56.

2(a) E.J. Prosen, W.H. Johnson and F.D. Rossini, *J.Res.Natl.Bur.Std.*, **39**, 173 (1947).

(b) J.E. Kilpatrick, H.G. Werner, C.W. Beckett, K.S. Pitzer and F.D. Rossini, *J.Res.Natl.Bur.Std.*, **39**, 523 (1947). See also calculations of N.L. Allinger, J.A. Hirsch, M.A. Miller, I.J. Tyminski and F.A. Van-Catledge, *J.Am.Chem.Soc.*, **90** 1199 (1968).

3(a) M. Tichy, S. Vasickova, S.V. Arakelian and J. Sicher, *Collect.Czech.Chem.Commun.*, **35**, 1522 (1970).

(b) M. Tichy, *Collect.Czech.Chem.Commun.*, **38**, 3631 (1973).

4. *Tabulation:* E.J. Corey and N.F. Feiner, *J.Org.Chem.*, **45**, 765 (1980).

5. H. Booth and J.R. Everett, *J.Chem.Soc.Perkin Trans.2*, 255 (1980).

6. H. Booth and J.R. Everett, *J.Chem.Soc.Chem.Commun.*, 278 (1976).

7. H.R. Buys and E. Havinga, *Tetrahedron Letters*, 3759 (1968).

8. L. Rosenthal, J.F. Rabolt and J. Hummel, *J.Chem.Phys.*, **76**, 817 (1982). See also P.B. Woller and E.W. Garbisch, Jr., *J.Am.Chem.Soc.*, **94**, 5310 (1972).

9. E.L. Eliel and M. Manoharan, *J.Org.Chem.*, **46**, 1959 (1981).

10. G.C. Levy, R.L. Lichter and G.L. Nelson, "Carbon-13 Nuclear Magnetic Resonance Spectroscopy" 2nd ed., John Wiley & Sons, New York (1980), p. 57.

11. E.L. Eliel, *Chem.Ind.(London)*, 568 (1959). See also reference 1, pp. 47-48.

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