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Estimation of magnetic anisotropy in polycyclic aromatics

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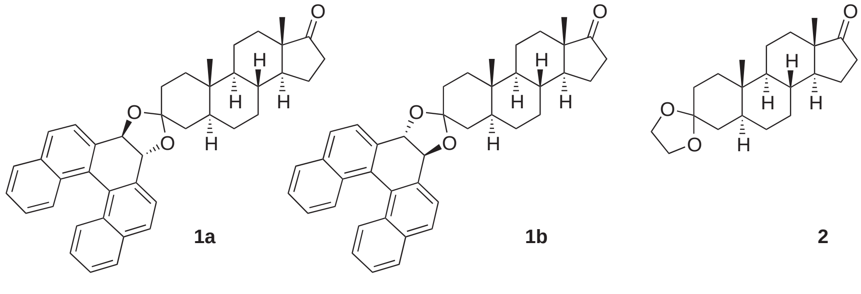
Abstract—Dihydro-dibenzophenanthrene derivatives **1a** (**1b**) were synthesised in order to obtain the NMR shielding parameters for naphthalene ring. The ^{1}H NMR assignment of **1a** and substituent-induced shifts (SIS) from the corresponding androstanone ethylene ketal (**2**) are presented. A simple sum of the magnetic shielding of benzene rings can satisfactorily reproduced the observed SIS values due to the naphthalene ring of **1**. © 2001 Elsevier Science Ltd. All rights reserved.

It is well known that NMR chemical shifts reflect molecular structure. Thus, variation in the local environment affects chemical shieldings, and changes the chemical shift of nuclei with respect to a nearby substituent.[1] The conformational analysis of flexible macrocyclophanes[2] have been carried out successively with the chemical shift changes caused by secondary induced magnetic fields due to aromatic ring currents.[3] However, the quantification of such shielding effects[4] has been rather limited, and this situation has restricted the broad application of the technique. In our previous papers, we have reported parameters associated with the shielding effect of a polar functional group[5] and by using them succeeded in the determination of the preferred conformation of a flexible macrocyclophane.[6]



1a **1b** **2**

In order to extend the applicability of the method of chemical shift simulation to polycyclic aromatic compounds, it is necessary to obtain the shielding parameters for other functionalities such as the naphthalene ring. To obtain the reliable shielding parameters for this group, the steroid skeleton and 7,8-dihydro-dibenzophenanthrene were chosen because of its rigidity and well defined geometry. Hence, we synthesised androstanone derivatives (**1a**, **1b**), and the chemical shifts of the protons in **1a** were compared with those of the corresponding reference compound (**2**).

The synthesis of compound **1** is shown in Scheme 1. Thus, acetalization of androstane-3,17-dione (**3**) with racemic (7*R**,8*R**)-7,8-dihydro-dibenzophenanthrene-7,8-diol[7] (**4**) under acidic condition yielded the corresponding mixture of acetal **1a** and **1b**. HPLC separation of the mixture afforded targets **1a** and **1b** in a 1:1 ratio. The preparation of the reference compound (**2**) was carried out by the selective mono acetalization of **3** with ethylene glycol. The structure of **1a** was confirmed by X-ray crystallographic analysis (Fig. 1).[8] Assignments of the ^{1}H NMR signals for **1a** and **2** in $CDCl_3$ solution were made using a combination of COSY, NOESY, HMBC, HMQC, and phase-sensitive DQF-COSY experiments. The observed substituent-induced shift (SIS), which is defined as the change in chemical shift of a proton produced by the substituent, can be obtained by the chemical shift differences between **1a** and **2**.

Keywords: substituent-induced shift; magnetic anisotropy; polycyclic conjugate system.

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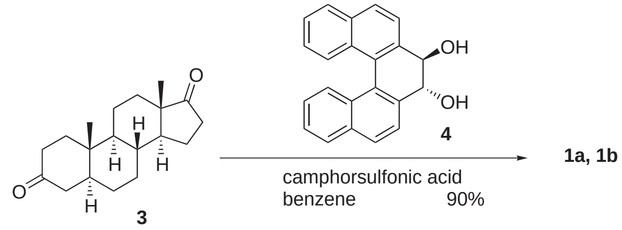

Scheme 1.

The observed SIS values can be reproduced by calculation if the correct set of shielding parameters and relative geometry of the protons with respect to the substituent are known and in the present case the precise geometrical factors associated with these protons were obtained from the molecular mechanics calculation[9,10] (AMBER* force field as encapsulated in MacroModel[11] ver. 6.5). The ring current induced shift was estimated using the calculated structure.

We have found that there was an additivity associated with the SIS values of two moieties that are interacting electronically.[12] Coulson reported that π-electron ring susceptibility of polycyclic conjugated systems was partitioned into a sum of individual contributions from each of its constituent ring.[13] So we calculated the SIS values of protons in compound **1a** assuming that there are four individual benzene rings in the compound (Table 1).[14] The correlation analysis [a set of 21 data (range of the observed data 0.03–0.29 ppm) $\Delta\delta_{\text{obs}}=a\cdot\Delta\delta_{\text{calc}}+b$; $a=1.039$, $b=-0.009$, $R^2=0.950$ (Fig. 2)] of the observed and calculated SIS values clearly shows that the shielding effect of the naphthalene ring is a simple sum of those due to the two fused benzene rings. Since we applied the line current model[3c,d] for the estimation of the ring current of benzene, the simple sum of the line current of the two fused six-membered rings exactly cancelled out the current through the fused bond. Thus the magnetic anisotropy of the naphthalene can be reasonably approximated by a loop current through the 10 π peripheral bonds.

Acknowledgements

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Table 1. ^{1}H NMR chemical shifts for compounds **1a** and **2** together with their observed and calculated SIS values

Position	1a	2	Obs. SIS	Calc. SIS
1α	1.47	1.20	0.27	0.23
1β	1.76	1.67	0.09	0.11
4α	1.59	1.39	0.20	0.21
4β	1.81	1.56	0.25	0.23
5	1.70	1.42	0.28	0.29
6β	1.33	1.26	0.07	0.09
7α	1.07	0.99	0.08	0.10
7β	1.82	1.78	0.04	0.05
8	1.61	1.53	0.08	0.07
9	0.90	0.77	0.13	0.15
11α	1.73	1.66	0.07	0.08
11β	1.34	1.30	0.04	0.07
12α	1.30	1.24	0.06	0.08
12β	1.86	1.79	0.07	0.04
14	1.33	1.25	0.08	0.09
15α	1.96	1.93	0.03	0.04
15β	1.52	1.48	0.04	0.04
16α	2.10	2.06	0.04	0.05
16β	2.47	2.43	0.04	0.03
18	0.89	0.85	0.04	0.04
19	0.93	0.83	0.10	0.12

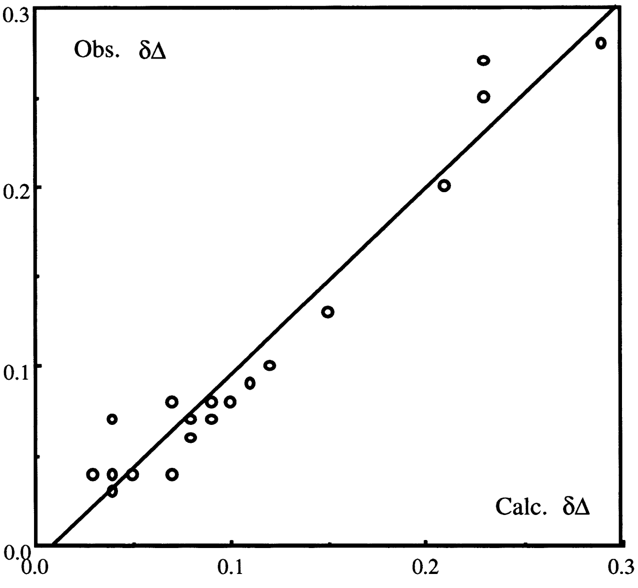

Figure 2. Plot of observed and calculated SIS values of **1a**.

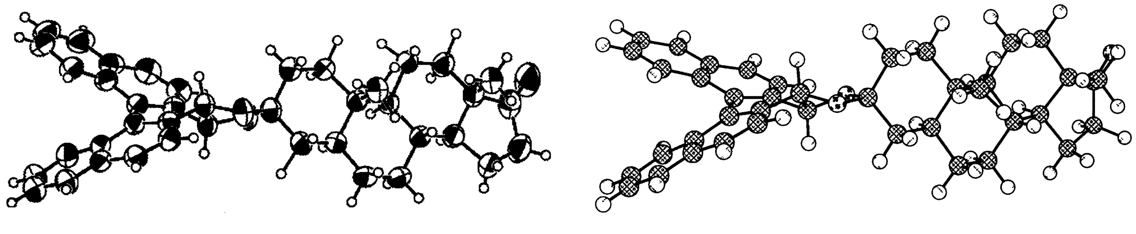

Figure 1. ORTEP drawing of **1a** (left) and the calculated structure of **1a** (right).

References

1. (a) ApSimon, J. W.; Craig, W. G.; Demarco, P. V.; Mathieson, D. W.; Saunders, L.; Whalley, W. B. *Tetrahedron* **1967**, *23*, 2339, 2357, and 2375; (b) ApSimon, J. W.; Demarco, P. V.; Mathieson, D. W.; Craig, W. G.; Karim, A.; Saunders, L.; Whalley, W. B. *Tetrahedron* **1970**, *26*, 119; (c) ApSimon, J. W.; Beierbeck, H. *Can. J. Chem.* **1971**, *49*, 1328; (d) ApSimon, J. W.; Beierbeck, H.; Todd, D. K. *Can. J. Chem.* **1972**, *50*, 2351; (e) Asakura, T.; Niizawa, Y.; Williamson, M. P. *J. Magn. Res.* **1992**, *98*, 646; (f) Osapay, K.; Case, D. A. *J. Am. Chem. Soc.* **1991**, *113*, 9436; (g) Sitkoff, D.; Case, D. A. *J. Am. Chem. Soc.* **1997**, *119*, 12262.
2. (a) Fukazawa, Y.; Ogata, K.; Usui, S. *J. Am. Chem. Soc.* **1988**, *110*, 8692; (b) Fukazawa, Y.; Ogata, K.; Usui, S. *J. Am. Chem. Soc.* **1988**, *110*, 8692; (c) Okajima, T.; Wang, Z.-H.; Fukazawa, Y. *Tetrahedron Lett.* **1989**, *30*, 1551; (d) Okajima, T.; Wang, Z.-H.; Fukazawa, Y. *Chem. Lett.* **1991**, 37; (e) Fukazawa, Y.; Deyama, K.; Usui, S. *Tetrahedron Lett.* **1992**, *33*, 5803; (f) Wang, Z.-H.; Usui, S.; Fukazawa, Y. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1239; (g) Fukazawa, Y.; Usui, S.; Tanimoto, K.; Hirai, Y. *J. Am. Chem. Soc.* **1994**, *116*, 8169.
3. (a) Waugh, J. S.; Fessenden, R. W. *J. Am. Chem. Soc.* **1957**, *79*, 846; **1958**, *80*, 6697; (b) Johnson, C. E.; Bovey, F. A. *J. Chem. Phys.* **1958**, *29*, 1012; (c) Longuet-Higgins, H. C.; Salem, L. *Proc. R. Soc. (London)* **1960**, *A257*, 445; (d) Mallion, R. B. *Mol. Phys.* **1973**, *25*, 1415.
4. (a) Zürcher, R. F. *Progr. NMR Spectrosc.* **1967**, *2*, 205; (b) Schneider, H.-J.; Buchheit, U.; Becker, N.; Schmidt, G.; Siehl, U. *J. Am. Chem. Soc.* **1985**, *107*, 7027.
5. Fukazawa, Y.; Yang, Y.; Hayashibara, T.; Usui, S. *Tetrahedron* **1996**, *52*, 2847.
6. Iwamoto, H.; Yang, Y.; Usui, S.; Fukazawa, Y. *Tetrahedron Lett.* **2001**, *42*, 49.
7. Ohmori, K.; Kitamura, M.; Suzuki, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 1226.
8. The crystal data for **1a** are as follows; **1a**: Orthorhombic; space group $P2_12_12_1$ with $a=8.020(1)$, $b=17.899(1)$, $c=21.842(1)$ Å, $V=3145.1(3)$ Å^3, and $z=4$; of 4101 total unique reflections, 3679 were considered observed at the level of $|F_o|>3.0\sigma|F_o|$. The structures were solved by the direct method (Sir 97). Full-matrix least squares refinements converged to a conventional R factor of 0.063, $wR^2=0.054$.
9. The structure found in the crystal of **1a** is heavily distorted by a crystal packing force as witnessed by the short interatomic C···C distance between 18- and 19-Me (4.292(7) Å). While the observed one is far shorter than the corresponding value of the undistorted skeleton (4.73(2) Å; average value of 14 androstan-17-one derivatives[10]), that of the calculated is quite reasonable (4.748 Å).
10. 3D search and research using the Cambridge Structural Database, Allen, F. H.; Kennard, O. *Chem. Des. Autom. News* **1993**, *8*, 1, 31.
11. Richards, N. G. H.; Guida, W. C.; Liskamp, T.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comp. Chem.* **1990**, *11*, 440.
12. Fukazawa, Y.; Haino, T.; Kondoh, Y. *Tetrahedron Lett.* **1999**, *40*, 3519.
13. Coulson, C. A.; Gomes, J. A. N. F.; Mallion, R. B. *Mol. Phys.* **1975**, *30*, 713.
14. The chemical shifts of 2α, 2β and 6α were omitted because assignment of these signals in reference compound **2** was not given.