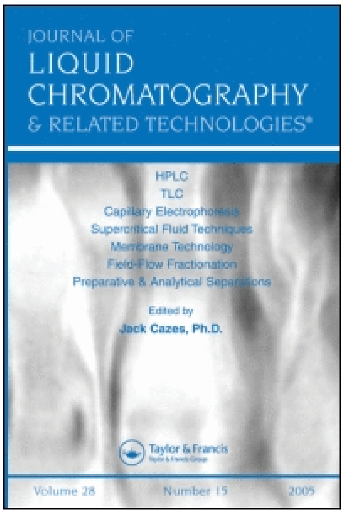


Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

Separation by Permeation Effect in High Performance Liquid Chromatographic Studies of Selected Dithia[3.3]Cyclophanes and Thia[3.2]Cyclophanenes

Y. -H. Lai[a]; S. -G. Ang[a]
[a] Department of Chemistry, National University of Singapore, Kent Ridge, Republic of Singapore

To cite this Article Lai, Y. -H. and Ang, S. -G.(1994) 'Separation by Permeation Effect in High Performance Liquid Chromatographic Studies of Selected Dithia[3.3]Cyclophanes and Thia[3.2]Cyclophanenes', Journal of Liquid Chromatography & Related Technologies, 17: 6, 1219 — 1230

To link to this Article: DOI: 10.1080/10826079408013757

URL: http://dx.doi.org/10.1080/10826079408013757

JOURNAL OF LIQUID CHROMATOGRAPHY, 17(6), 1219-1230 (1994)

SEPARATION BY PERMEATION EFFECT IN HIGH PERFORMANCE LIQUID CHROMATOGRAPHIC STUDIES OF SELECTED DITHIA[3.3]CYCLOPHANES AND THIA[3.2]CYCLOPHANENES

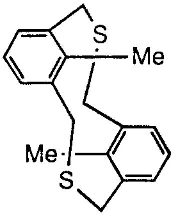
YEE-HING LAI* AND SIAU-GEK ANG
Department of Chemistry
National University of Singapore
Kent Ridge
Republic of Singapore 0511

ABSTRACT

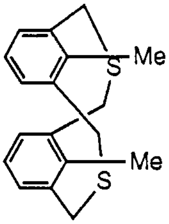
The retention order of a series of conformationally mobile dithia[3.3]cyclophanes **3** - **7** was investigated by means of reversed-phase high performance liquid chromatography. By means of the "slot model", the conformational behavior of these dithiacyclophanes, which governs the extent of their interactions with the bonded phase, correlates well with the observed retention order. Another series of conformationally rigid bridge-annelated thia[3.2]cyclo-phanenes **8** - **14** were also similarly investigated. The *anti* conformation allows the whole annelated cyclophanene molecule to slide readily into the "slot" resulting in stronger interactions between the cyclophanene and the bonded phase. The *syn* conformation however has the cyclophane and polycyclic benzenoid moieties held almost perpendicular so that each moiety could not possibly permeate deep into the "slot" independently. Based on the rigid stereochemistries of **8** - **14**, the "slot model" again explains the observed retention order.

---

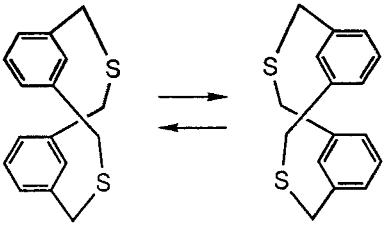
* Author to whom correspondence should be addressed.



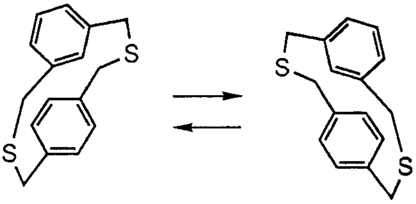
anti - (1)



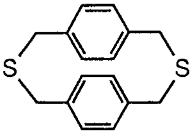
syn - (2)



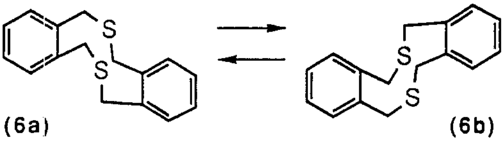
(3a) (3b)



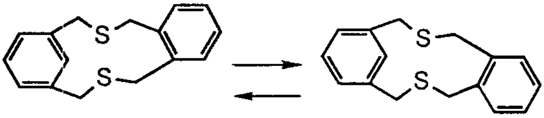
(4a) (4b)



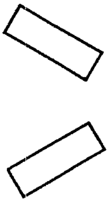
(5)



(6a) (6b)



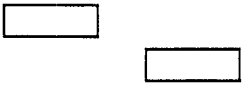
(7a) (7b)



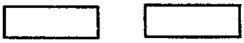
(I)

(II)

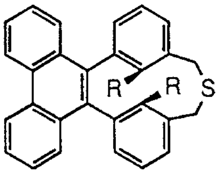
(III)



(IV)

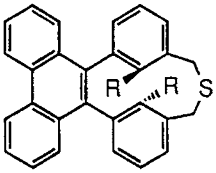


(V)



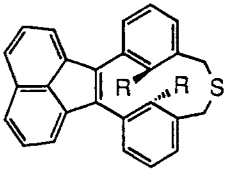
syn

(8) R = H
(9) R = CH_3



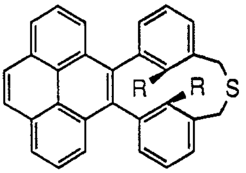
anti

(10) R = CH_3



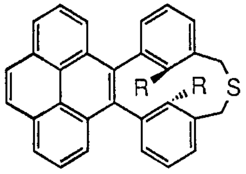
anti

(11) R = H
(12) R = CH_3



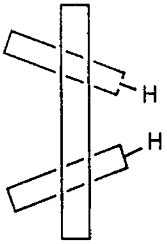
syn

(13) R = CH_3

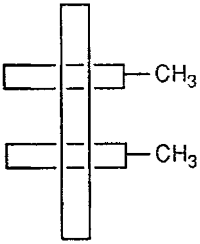


anti

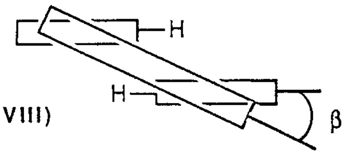
(14) R = CH_3



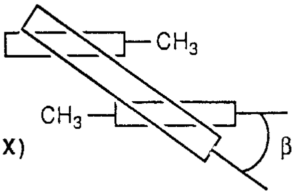
(VI)



(VII)



(VIII)



(IX)

INTRODUCTION

The syntheses, physicochemical properties and stereochemical aspects of cyclophanes have been of particular interest over the last three decades.[1] Whereas the conformational behavior of mobile cyclophanes could be studied[2] readily by dynamic ^{1}H NMR spectroscopy, some rigid conformers of cyclophanes such as **1**[3] and **2**[3] could in fact be separated. Literature on chromatographic studies of cyclophanes is however limited. Chromatographic separation[4] of a series of rigid naphthalenophanes and optical resolution[5] of selected metacyclophanes have been achieved by high performance liquid chromatography (HPLC). Data on thin layer chromatography (TLC)[6] and HPLC[7] separation of some dithia[3.3]cyclo-phanes have also been reported. There is however no detailed description on the correlation of the retention order of these cyclophanes with their structural properties. There is extensive literature on the dependence of retention of polycyclic aromatic compounds (PACs) on various factors in HPLC studies. Since cyclophanes form a unique family of novel aromatic compounds, we wish to report results from the HPLC studies on the series of dithia[3.3]cyclophanes **3**,[3,8] **4**,[9] **5**,[10] **6**,[11] **7**,[12] and thia[3.2]cyclophanenes **8**,[13] **9**,[14] **10**,[15] **11-14**,[16] and correlate their retention behavior with their structural features.

EXPERIMENTAL

Dithiacyclophanes **3** - **7** and thiacyclophanenes **8** - **10** were prepared according to reported procedures.[3-15] Syntheses[16] of compounds **11** - **14** have been achieved in our laboratory and will be published elsewhere.

Chromatographic studies were performed on a Shimadzu LC-6A Binary Gradient Liquid Chromatograph equipped with a Shimadzu SPD-6AV UV-Vis Spectrophotometric (254 nm) Detector and a Shimadzu SCL-6A System Controller. A CHROMPACK reversed-phase C_{18} column (25 cm x 4.9 mm I.D) was used for chromatographic separations. HPLC grade acetonitrile was

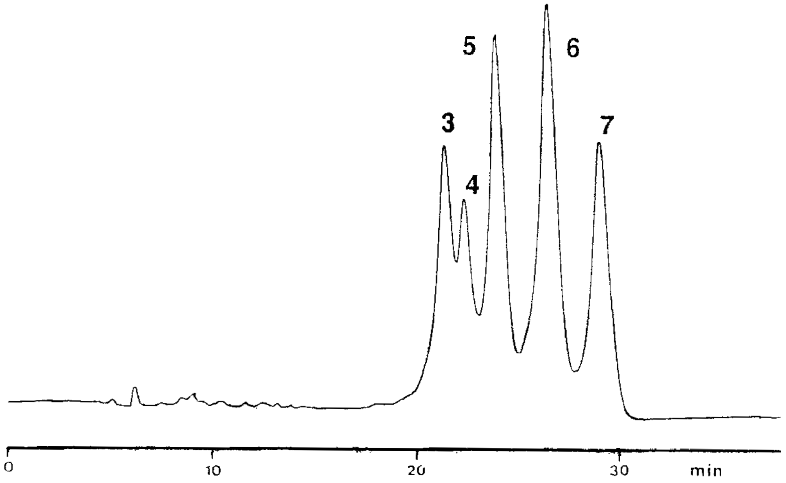


Figure 1. High-performance liquid chromatograms of a mixture of **3** - **7**.

purchased from Fisher Scientific. Water was purified with a Milli-Q system (Millipore, Bedford, MA, USA).

Isocratic chromatographic conditions were employed using 60% (Figure 1) or 80% (Figure 2) acetonitrile in water with 0.1% trifluoroacetic acid at a flow rate of 0.5 ml/min at a maximum pressure of 500 kgf/cm^2.

RESULTS AND DISCUSSION

Dithiacyclophanes 3 - 7.—Reversed-phase HPLC studies of the cyclophane systems **3** - **7** were attempted using various solvent systems. The best resolution of these compounds was achieved using a mixture of acetonitrile and water. Further improvement was obtained with the addition of 1% of trifluoroacetic acid.[17] The order of ease of elution in our work was shown to be **3** > **4** > **5** > **6** > **7** (Figure 1). This however does not correspond to a reversed order to that observed in the TLC studies[6] of the same series of dithiacyclophanes. The conformational behavior of the dithiacyclophanes **3**,[8b]

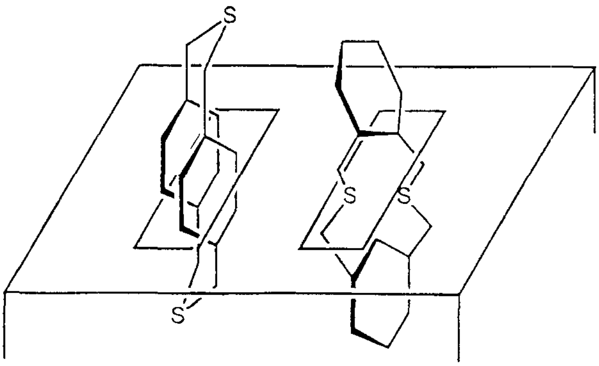


Figure 2. Representation of the slot model of retention based on the permeation effect of the cyclophanes.

4,[9] **6**[11] and **7**[12] at room temperature are known to involve different ring flipping processes as shown. The diagrammatic representations of the averaged relative positions of benzene rings could then be depicted as **I**, **II**, **IV** and **V** respectively. For dithiacyclophane **5**,[10] inversion processes of the bridges are possible but free rotation of the benzene rings is considered unlikely. Thus the two benzene rings in **5** are held more or less parallel to each other as represented by **III**.

The bonded phase of the reversed-phase column is an orderly structure made up of sheets of octadecyl-methyl polysiloxane projecting out of the derivatised silica packing. The retention of any of the dithiacyclophanes will depend on the interaction between the cyclophane and the bonded phase. Each polysiloxane moiety however is large enough to hinder the movement and arrangement of the other moieties and thus a slotted structure[13] is formed (Figure 2). The better the cyclophane fits into the "gaps" or "slots" between the polysiloxane sheets, the stronger the interaction between the cyclophane and the bonded phase and thus the higher the retention time of the cyclophane on the column. The dithiacyclophanes **3** (**I**) and **4** (**II**) have the benzene rings held at an angle and thus would be unable to fit deep into the slots. The more perpendicular stereochemistry in **II** would allow the 1,3-bridged ring to permeate better into the slots consistent with its observed longer retention time (Figure 1). The conformationally more rigid dithiacyclophane **5** have the benzene rings held parallel and both rings could somewhat squeeze into the slots (Figure 2) thus increasing the interaction between **5** and the bonded phase. The dithiacyclophane **6** exhibits a conformational equilibrium between "chair" conformers **6a** ⇌ **6b** (represented by **IV**) while **7** displays a pendulum behavior between **7a** ⇌ **7b** with averaged linear positions of the benzene rings as shown in **V**. Both **IV** and **V** are expected to permeate most deeply into the slots of the bonded phase (Figure 2) among the five dithiacyclophanes studied, with **V** being the most ideal molecule to slide readily in between the polysiloxane sheets. The above argument based on the permeation effect clearly correlates well the observed order of retention with the conformational behavior of the respective dithiacyclophanes.

Thiacyclophanenes 8 - 12. As discussed earlier, the interactions between dithiacyclophanes **3**, **4**, **6** and **7** with the bond phase may be affected by their conformational mobilities. In order to investigate whether the above slot model could be applied to other cyclophane systems, HPLC studies of conformationally rigid thiacyclophanenes **8** - **12** were carried out under similar conditions. With reference to *anti*-**1** and *syn*-**2**, thiacyclophanenes **8**[13] (**VI**), **9**[14] (**VII**) and **13**[16] (**VII**) were found to exist in rigid syn conformation whereas anti conformers of **10**[15] (**IX**), **11**[16] (**VIII**), **12**[16] (**IX**) and **14**[16] (**IX**) have also been isolated.

The increasing retention order of the thiacyclophanenes studied (Figures 3a - 3c) was found to be **8** < **9** < **11** < **12** < **10**,**13** < **14**. Earlier reports[19,20] on the reversed-phased HPLC studies of PACs show an increasing order of acenaphthylene < phenanthrene < pyrene. Our results (Figure 3a - 3c) indicate a random order if the retention behavior of these compounds depends solely on the nature of the respective PAC moieties. The phenanthrocyclophanenes **8** and **9** were eluted faster but **10** slower than the acenaphthylenocyclophanes **11** and **12** (Figure 3c); whereas phenanthrocyclophane **10** and pyrenocyclophane **13**

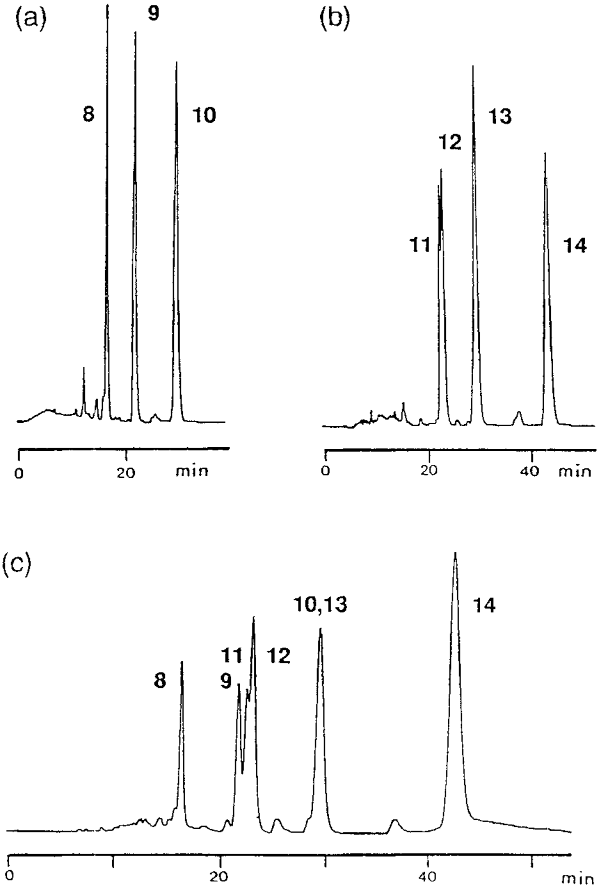


Figure 3. High-performance liquid chromatograms of (a) a mixture of **8** - **10**; (b) a mixture of **11**- **14**; and (c) a mixture of **8** - **14**.

happen to have identical retention times (Figure 3c). The retention order of these cyclophanenes clearly depends also on the stereochemistry of the cyclophane moieties to a significant extent. The presence of methyl groups in **9**, **10**, **12** and **14** will also indirectly affect the overall results (see later discussion).

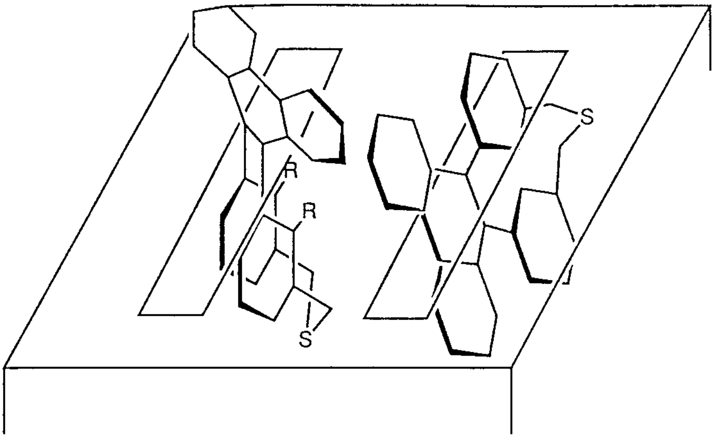


Figure 4. Representation of the slot model of retention based on the permeation effect of the *syn* and *anti* cyclophanenes.

The stereochemistry of the three anti cyclophanenes **10**, **12** and **14** could in general be represented by **IX**. The PAC and cyclophane moieties in each case could interact with the bonded phase independently or more likely the whole annelated cyclophanene molecule could slide readily into the slots (Figure 4). The cyclophane moiety is common among the three compounds and thus their retention order of **12** < **10** < **14** follows that observed for acenaphthylene < phenanthrene < pyrene. Going from **12** (**IX**) to **11** (**VIII**), the small spatial requirement of the two "internal" hydrogen atoms in **11** is expected to result in an outward slide of the two stepped benzene rings leading to a smaller angle β as shown in **VIII**. Such a sliding phenomenon has been described for other related cyclophane systems.[21] Our results (Figure 3b) however show that **11** was eluted before **12** indicating that the smaller angle β in **11** (**IX**) does not increase appreciably its permeability compared with that of **12**. On the other hand the stronger interaction between the two "toluene" units in **12** and the bonded phase could account for its slightly longer retention time.

A comparison of the relative retention order of each pair of syn and anti isomers, namely **9** and **13** against **10** and **14** respectively (Figures 3a and 3b), shows that the syn isomer is always eluted significantly faster than the anti isomer. The two syn cyclophanenes **9** and **13**, as represented by **VII**, have the PAC and cyclophane moieties held almost perpendicularly. The two moieties thus could not possibly permeate deep into the slots independently (Figure 4). The large difference in the retention time of each pair of syn and anti isomers therefore further supports the fact that the stepped stereochemistry of the anti isomers allows the whole molecule to slide readily in between the polysiloxane sheets thus significantly increasing their interaction with the bonded phase.

Of the two cyclophanenes **9** and **13** having the same stereochemistry as represented by **VII**, their retention order of **9** < **13** follows that expected of phenanthrene < pyrene. Going from **9** (**VII**) to **8** (**VI**), the small spatial requirement of the "internal" protons is again expected to result in a change in the molecular geometry of the cyclophane moeity as indicated. The tilting of the two rings is encouraged to minimize their π-π interaction. With the phenanthrene moiety common in both **8** and **9**, their retention order of **8** < **9** depends solely on the nature of their respective cyclophane moieties which resemble those of **3** (**I**) and **5** (**III**) discussed earlier. In addition the "toluene" units in **9** are also expected to interact more strongly with the bonded phase as described in the comparison of **11** and **12**.

CONCLUSION

Our results have demonstrated that the respective retention orders of related dithia[3.3]cyclophanes and another series of bridge-annelated thia[3.2]cyclophanenes could be correlated qualitatively to the conformational behavior of the cyclophane systems based on the permeation effect in a slot model. We believe that the results observed in this work would be valuable in future related investigations on analytical and conformational studies of cyclophanes by HPLC.

ACKNOWLEDGEMENT

The authors thank the National University of Singapore for financial support (*RP860606 and RP880603*).

REFERENCES

1. (a) Cyclophanes, edited by P. M. Keehn and S. M. Rosenfeld, Vol. I and II. Academic Press, New York (1983); (b) Cyclophanes I, edited by F. Vögtle, Top. Curr. Chem. 113, 1-182 (1983); (c) Cyclophanes II, edited by F. Vögtle, Top. Curr. Chem. 115, 1-150 (1985).

2. (a) R. H. Mitchell, Adv. in Theoret. Interesting Molec. 1, 135 (1989); (b) Y.-H. Lai, Heterocycles 16, 1739 (1981).

3. R. H. Mitchell and V. Boekelheide, J. Am. Chem. Soc. 96, 1547 (1974).

4. A. Deege, B. Heinecke and G. Schomburg, Chromatographia 15, 65 (1982).

5. K. Meurer, A. Aigner and F. Vögtle, J. Inclusion Phenom. 3, 51 (1985).

6. (a) P. Kuś, J. Chromatogr. 436, 338 (1988); (b) P. Kuś, J. Chromatogr. 442, 378 (1988).

7. J. Śliwiok, P. Kuś and M. Sajewicz, J. Chromatogr. 472, 314 (1989).

8. (a) T. Sato, M. Wakabayashi, K. Hata and M. Kainosho, Tetrahedron 27, 2737 (1971); (b) W. Anker, G. W. Bushnell and R. H. Mitchell, Can. J. Chem. 57, 3080 (1979).

9. (a) F. Vögtle, Chem. Ber. 102, 3077 (1969); (b) V. Boekelheide, P. H. Anderson and T. A. Hylton, J. Am. Chem. Soc. 96, 1558 (1964).

10. (a) J. Bruhin and W. Jenny, Tetrahedron Lett., 1215 (1973); (b) F. Vögtle, Chem. Ztg. 94, 313 (1970).

11. (a) D. W. Allen, P. N. Braunton, J. T. Millar and J. C. Tebby, J. Chem. Soc. C, 3454 (1971); (b) Y.-H. Lai and M. Nakamura, J. Org. Chem. 53, 2360 (1988); (c) T. Okajima, Z.-H. Wang, Y. Fukazawa, Tetrahedron Lett. 30, 1551 (1989).

12. F. Vögtle, Tetrahedron 25, 3231 (1969).

13. Y.-H. Lai and S.-M. Lee, J. Org. Chem. 53, 4472 (1988).

14. Y.-H. Lai and P. Chen, J. Org. Chem. 54, 4586 (1989).

15. Y.-H. Lai, J. Am. Chem. Soc. 107, 6678 (1985).

16. Y.-H. Lai, P. Chen and T.-G. Peck, unpublished results.

17. J. L. Meek and Z. L. Rossetti, J. Chromatogr. 211, 15 (1981).

18. S. A. Wise and L. C. Sander, J. High Resolut. Chromatogr. Chromatogr. Commun. 8, 248 (1985).

19. S. A. Wise, W. J. Bonnett and W. E. May, in Polynuclear Aromatic Hydrocarbons: Chemistry and Biological Effects; A. Bjørseth and A. J. Dennis, eds., Battelle Press, Columbus, Ohio (1980).

20. Y.-H. Lai, S.-G. Ang and H.-C. Li, J. Chromatogr. 606, 251 (1992).

21. R. H. Mitchell, J. S. H. Yan and T. W. Dingle, J. Am. Chem. Soc. 104, 2551 (1982).

Received: September 28, 1993
Accepted: October 8, 1993