changes and NMR chemical shifts indicate (work in progress) that both enantiomers must bind to DNA. Cur binding studies with homopolymers (Table I) do not detect any significant biphasic binding which suggests that both enantiomers must have approximately the same binding constant with DNA. Model building studies also indicate that both enantiomers could form a hydrogen bond in the minor groove with the thymine C-2 carbonyl oxygen or with an associated water molecule. Preliminary studies with achiral carboxamide and ester analogues of **1–3** indicate binding interactions with DNA similar to **1–3**, and this also suggests that enantiomeric recognition is not an important factor in the binding of the hydroxy compounds with DNA.

Experimental Section

Materials. DNA samples were sonicated, filtered, phenol and ether extracted, ethanol precipitated, dialyzed into PIPES buffer (0.01 M PIPES, 10^{-3} M EDTA, pH 7.0), and characterized as previously described.[26] Samples for binding and viscosity studies were sonicated for shorter periods and had an average length of 500–600 base pairs. Samples for NMR experiments were sonicated for longer times and had an average length of 150–200 base pairs. All sonications were done with application of pulse power at near 0 °C in PIPES buffer with 0.5 M NaCl added. Closed circular supercoiled Col E_1 DNA was prepared as previously described.[20] The compounds **1–3** were synthesized with use of methods previously worked out;[18,19,35] the details of their synthesis will be published elsewhile.[36]

Spectrophotometric Studies. Absorbance measurements in the UV–visible region were made on a Cary 219 spectrophotometer interfaced to an Apple IIe microcomputer through a bidirectional digital communications port. Cell holders were thermostated with use of a Haake circulating water bath. Wavelength scans and extinction coefficient measurements were made in cells from 1 to 10 cm pathlength at the wavelength range appropriate for the compound being investigated. Extinction coefficients of compounds bound to DNA were determined at the same wavelength as the extinction coefficient measurements of the free compound, but a larger molar excess of DNA was present ([DNA-P]/[compound] > 100). The Cary 219 was also used in spectrophotometric binding studies. To remove some of the random error, for each absorbance measurement in the absence or presence of DNA, the microcomputer calculated the average of 100 acquired absorbance readings at the preselected wavelength for the compound under study. These averaged absorbance values were converted by the microcomputer to ν (moles of compound bound/mole of DNA base pairs) and free ligand concentrations using the free and bound extinction coefficients for the compound. At the end of a titration, the computer plotted the digitized data which was in the fraction bound range 0.2 to 0.8. Any binding results outside of this range are subject to large systematic errors as a result of experimental errors in extinction coefficients. The computer then calculated nonlinear least-squares best fit K and n values from the site exclusion method of McGhee and von Hippel[29] as defined in eq 1.

Thermal Melting. Denaturation experiments were also conducted on the Cary 219 spectrophotometer. The data were directly plotted on the Cary 219 chart paper as absorbance vs. temperature. The data were also sent to the Apple IIe computer, absorbance averaged as described above, and stored on disk for more accurate Tm analysis if desired. Melting experiments were conducted in 1-cm cells in the five chamber temperature control unit of the Cary 219. Temperature was increased at 0.5 °C per min during the melting experiment by a Haake A81 programmable temperature bath and Haake PG20 programmer unit.

NMR. Proton spectra were obtained at 270.05 MHz on a JEOL GX-270 spectrometer by using the Redfield 21412 pulse sequence under the following conditions: typically 15000 scans; 0.5-s pulse repetition rate; 4-Hz line broadening; carrier frequency at 13.5 ppm; 8K data points; TSP reference; 10000 Hz spectral width; 9% D_2O in H_2O–PIPES 00 buffer; 20 mM DNA phosphate molarity; and 0.825-mL sample volume in a 5-mm NMR tube.

Phosphorus spectra were obtained at 109.25 MHz with a JEOL GX-270 spectrometer under the following conditions: typically 3000 scans; 45° pulse width with a pulse repetition time of 2.5 s; 4 Hz line broadening; broad band bilevel decoupling; 2K data points zero filled to 8K data points; trimethyl phosphate reference; 2000 Hz spectral width; 9% D_2O in H_2O–PIPES 00 buffer; 20 mM DNA phosphate molarity; and 1.50-mL sample volume in a 10-mm NMR tube. Temperature in ^{31}P NMR experiments was monitored by using the ^{31}P "thermometer" method described by Gorenstein and co-workers.[37]

Viscometric Measurements. Viscometric titrations of both sonicated calf thymus and closed circular superhelical Col. E_1 DNA were conducted in Cannon Ubbelohde semimicro dilution viscometers at 28 °C in PIPES buffer as previously described.[20]

Acknowledgment. This work was supported by NSF grant PCM83-09575 and the Georgia State University Research Fund. WDW is a recipient of an American Cancer Society Faculty Research Award.

(35) Duncan, W. G.; Colwell, W. T.; Scott, C. R.; Henry, D. W. *J. Med. Chem.* **1968**, *11*, 1221–1223.
(36) Kusuma, S.; Wilson, W. D.; Boykin, D. W. *J. Heterocycl. Chem.*, in press.
(37) Gorenstein, D. G.; Luxon, B. A.; Goldfield, E. M.; Lai, K.; Vegeais, D. *Biochemistry* **1982**, *21*, 580–589.

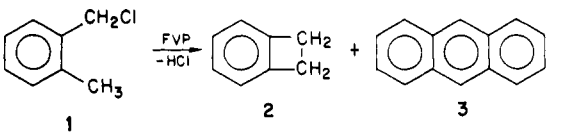
Communications to the Editor

Formation of Anthracenes in the Flash Vacuum Pyrolysis of Benzocyclobutenes and Dimers of *o*-Quinodimethanes

Walter S. Trahanovsky* and Bruce W. Surber

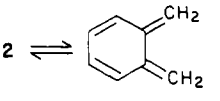
Ames Laboratory and the Department of Chemistry
Iowa State University, Ames, Iowa 50011
Received July 31, 1984

The Flash Vacuum Pyrolysis (FVP) of **1** gives, in addition to the major product benzocyclobutene (**2**),[1] varying amounts of a high molecular weight (MW) material. We have found this material to be primarily anthracene (**3**). Anthracene (**3**) has also been reported as a minor product in the later stages of the static gas-phase pyrolysis of **1** at 430 °C,[2] and **3** and dihydroanthracene



1 **2** **3**

have been obtained in low yields from the FVP of 1,2-bis[(phenylseleno)methyl]benzene, another precursor of **2**.[3] We proposed that these unusual routes to **3** involve the dimerization of *o*-quinodimethane (**4**) followed by loss of two carbon atoms and six



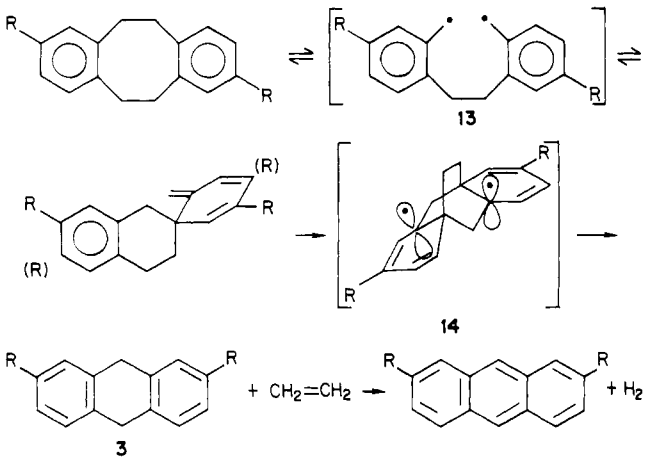
4

hydrogen atoms from the dimer or dimers of **4**. Compound **4** is formed by the thermal opening of the cyclobutene ring of **2** and

(1) Morello, M. J.; Trahanovsky, W. S. *Tetrahedron Lett.* **1979**, 4435 and references cited therein.
(2) Loudon, A. G.; Maccoll, A.; Wong, S. K. *J. Am. Chem. Soc.* **1969**, *91*, 7577–7580.
(3) Higuchi, H.; Sakata, Y.; Misumi, S. *Chem. Lett.* **1981**, 627–630.

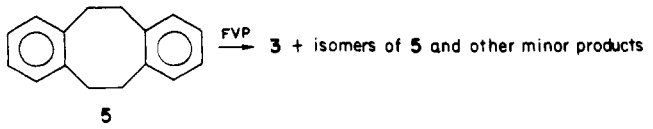
0002-7863/85/1507-4995$01.50/0

Scheme I



is known to dimerize extremely rapidly.[4] In this paper we report the results of a study of the formation of anthracenes in the FVP of benzocyclobutenes and dimers of *o*-quinodimethanes.

FVP of **5**, the [4 + 4] dimer of **4**,[5] gave a moderate yield of anthracene (**3**), several isomers of **5**, and two compounds resulting from the overall loss of CH_4 from **5** (MW = 192).[6] The product

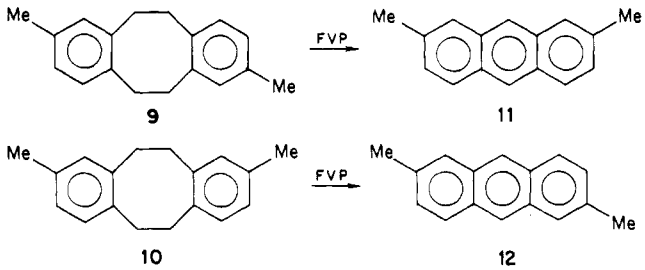


mixture[7] obtained at 900 °C was 9.5% recovered **5**, 25% **3**, a total of 27%, 1–9% each, of six isomers of **5**, and 1% and 8% of two compounds with a MW of 192. At 980 °C, no **5**, 33% **3**, and a total of 19% of the other eight compounds were obtained. At the higher temperatures, **3** is clearly the major product. No evidence for phenanthrene, benzocyclobutene (**2**), or styrene, the major product of the pyrolysis of **2**,[8] was obtained.

Anthracene (**3**) can also be obtained from benzocyclobutene (**2**) by pyrolyzing it rapidly to maximize bimolecular reactions in the hot zone. Rapid pyrolysis of **2** at 770 °C gave many "dimeric" compounds, ones having approximately but not necessarily exactly twice the molecular weight of **2**, in addition to styrene, the major product, and other low molecular weight compounds including ethylene. All the major "dimeric" products from the FVP of **5** were also obtained from the FVP of **2** in comparable relative yields; **5** (5.5%) and **3** (6.4%) were obtained in greatest yield. This is consistent with **3** coming from *o*-quinodimethane dimers formed during the reaction. However, the additional "dimeric" products from the FVP of **2** and the "monomeric" products such as styrene indicate that other reactions involving unimolecular rearrangements and dimerizations of **2** and isomers of **2** must be occurring during the FVP of **2**.

To test the generality of this conversion, 1,2-naphthocyclobutene (**6**)[9] was pyrolyzed at 890 °C. A solid condensed just outside the hot zone which was shown by ^1H NMR[10] and GC/MS analysis to be a 1:1 mixture of dibenz[*a*,*h*] anthracene (**7**) and dibenz[*a*,*j*]anthracene (**8**).

As a probe into the mechanism of the formation of **3** in the FVP of **5**, it was decided to determine the regiochemistry of the reaction by studying the pyrolysis of the dimethyl derivatives **9** and **10**;[12] **9** gave primarily **11** and **10** gave primarily **12**.[17] These results



show that the conversion of [4 + 4] dimers of *o*-quinodimethanes to anthracenes is highly regiospecific and proceeds by a mechanism in which one of the aromatic rings of the starting material is flipped 180° relative to the other. The regiospecificity of the reaction indicates that the dimer is not reverting to the corresponding *o*-quinodimethane or benzocyclobutene.

A mechanism for this conversion which accounts for the regiospecificity is presented in Scheme I.[21] The [4 + 2] dimer is an attractive intermediate because half of the ring flip takes place in going from the [4 + 4] to the [4 + 2] dimer. The proposed diradical **14** should be relatively stable, having two delocalized radicals and no severely strained bonds, and accounts for the facile loss of ethylene because the C–C bonds that undergo cleavage are almost parallel with the π-orbitals of the radical sites. Also, the loss of ethylene from **14** should be favorable since ethylene is a small stable molecule and aromatic rings are generated. Loss of hydrogen from dihydroanthracene is a well-known facile thermal reaction.[22] Although diradicals **13** and **14** are reasonable in-

(4) (a) Tuschka, T.; Naito, K.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 70–76 and references cited therein. (b) Ito, Y.; Nakatsuka, M.; Saegusa, T. *J. Am. Chem. Soc.* **1982**, *104*, 7609–7622. (c) Hersh, W. H.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 6992–6994.

(5) Jensen, F. R.; Coleman, W. E.; Berlin, A. J. *Tetrahedron Lett.* **1962**, 15–16.

(6) These products were analyzed by GC/MS.

(7) Absolute yields were determined by GC using biphenyl as an internal standard.

(8) (a) Baron, W. J.; DeCamp, J. R. *Tetrahedron Lett.* **1983**, 4225. (b) Berman, M. R.; Comita, P. B.; Moore, C. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 5692–5694. (c) Swenson, K. E.; Trahanovsky, W. S. *J. Org. Chem.* **1981**, *46*, 2984–2985. (d) Chapman, O. L.; Tsou, U.-P. E. *J. Am. Chem. Soc.* **1984**, *106*, 7974–7976. (e) Trahanovsky, W. S.; Scribner, M. E. *J. Am. Chem. Soc.* **1984**, *106*, 7976–7978.

(9) Ewing, G. D.; Boekelheide, V. *Synthesis* **1979**, 427.

(10) Compounds **7** and **8** have very characteristic signals in the region downfield from δ 8.0.[11]

(11) (a) Memory, J. D.; Wilson, N. K. "NMR of Aromatic Compounds"; Wiley: New York, 1982; p 43. (b) Martin, R. H.; Defay, N.; Geerts-Evrard, F.; Delavarenne, S. *Tetrahedron* **1964**, *20*, 1073–1090.

(12) A 45:55 mixture of the corresponding carbomethoxy derivatives was prepared by heating 4-carbomethoxybenzocyclobutene in Ph_2O to reflux.[5] After the mixture was purified, the two isomers were separated by fractional crystallization. Analysis by 300-MHZ ^1H NMR allowed positive identification of both isomers: the dibenzyl linkages of the 2,8 isomer[13] showed an AA'BB' signal (δ 2.71–2.60) and those of the 2,9 isomer[13] showed two singlets (δ 2.67 and 2.64). Each diester was converted[14,15] to the corresponding dimethyl derivative, **9** or **10**. Compounds **9**[13,16] and **10**[13,16] could not be distinguished by ^1H NMR, ^{13}C NMR, or GC. There are slight differences in the mp's (**9**, 141.5–144.5 °C; **10**, 130.5–134 °C) and IR spectra. The isomeric purity of each compound was assumed to be the same as that of the diester from which it was obtained (**9**, >99% pure; **10**, 92% pure, 8% **9**).

(13) Satisfactory ^1H NMR, IR, and mass spectra, including an exact mass determination, were obtained for this compound.

(14) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, pp 582–586.

(15) Small, G. H.; Minnella, A. E.; Hall, S. S. *J. Org. Chem.* **1975**, *40*, 3151–3152.

(16) A satisfactory ^{13}C NMR was obtained for this compound.

(17) FVP of **9** at 920 °C gave a product mixture that was similar by GC to that from the parent system except that the retention times were longer. The anthracene products were separated by preparative TLC. ^1H NMR analysis showed it to be **11** and **12** in 96:4 mol ratio[18] and another minor product. FVP of **10** (92% pure) gave primarily **12**. Anthracenes **11** and **12** were distinguishable by the NMR signals of their 9- and 10-protons:[18] **11**, two singlets at δ 8.30 and 8.20; **12** one singlet at δ 8.25. They are also distinguishable by ^{13}C NMR since **11** gave eight aromatic carbon signals and **12** gave only seven. The mp's[19] and IR spectra[20] of **11** and **12** after recrystallization agreed with literature values.

(18) Banerji, J.; Bhaduri, N.; Rej, R. N.; Shoolery, J. N.; Mukherjee, S.; Bhattacharya, S. *Indian J. Chem., Sect B* **1980**, *19B*, 341–345.

(19) Morgan, G. T.; Coulson, E. A. *J. Chem. Soc*, **1929**, 2203–2214.

(20) Vodehnal, J.; Stepän, V. *Coll. Czech., Chem. Commun.* **1971**, *36*, 3980–3991.

(21) As shown in Scheme I, for 2,8-disubstituted derivatives, two [4 + 2] dimers but only one diradical **13** and one diradical **14** are possible. For 2,9-disubstituted derivatives, two of each of these species are possible but they both lead only to **12**.

(22) (a) Voronkov, M. G.; Deryagina, E. N.; Shagun, L. G. *Zh. Org. Khim.* **1982**, *18*, 902. (b) Gajewski, J. J. "Organic Chemistry"; Wasserman, H. H., Ed.; Academic Press: New York, 1981; Vol. 44, pp 128–130.

termediates, concerted reactions involving no intermediates cannot be excluded.

Preliminary experiments in our laboratory indicate that the fragmentation involved in the conversion of **5** to **3** may be quite general. Results of these and other related studies will be reported soon.

Acknowledgment. This work was supported by U.S. Department of Energy, Office of Basic Energy Sciences, Chemical Sciences Division, under Contract W-7405-ENG-82. We thank Leslie Campbell Hanson for assistance with the early experimental work.

Registry No. 2, 4026-23-7; **3**, 120-12-7; **5**, 1460-59-9; **6**, 32277-35-3; **7**, 53-70-3; **8**, 224-41-9; **9**, 69978-58-1; **9** (carbomethoxy derivative), 96394-19-3; **10**, 69978-57-0; **10** (carbomethoxy derivative), 96411-82-4; **11**, 782-23-0; **12**, 613-26-3; 4-carbomethoxybenzocyclobutene, 93185-60-5.

High Lithium Selectivity in Competitive Alkali-Metal Solvent Extraction by Lipophilic Crown Carboxylic Acids

Richard A. Bartsch,* Bronislaw P. Czech, Sang Ihn Kang, Louis E. Stewart, Wladyslaw Walkowiak, Witold A. Charewicz, Gwi Suk Heo, and Byungki Son

Department of Chemistry, Texas Tech University Lubbock, Texas 79409

Received October 26, 1984

Selectivity for lithium complexation by 13-crown-4,[1] benzo-13-crown-4,[2] 14-crown-4,[1,3] and dibenzo-14-crown-4[4] compounds has recently been reported for extractions of alkali-metal picrates from aqueous solutions into organic media[1,2] and for responses of polymeric membrane electrodes to alkali-metal cations.[3,4] These findings suggest that incorporation of such crown ether units into lipophilic crown ether carboxylic acids[5] might provide novel reagents for the solvent extraction of lithium from aqueous solutions. For solvent extraction, such ionizable crown ethers would have the special advantage that concomitant transfer of an aqueous phase anion is not required for extraction of a lithium cation into the organic solvent.[6]

The lipophilic crown ether carboxylic acids **1–10** with 12-, 13-, 14-, and 15-membered macrocyclic rings and four ring oxygens were synthesized[7–9] from the corresponding crown ether alcohols.[1,8] Competitive solvent extractions of aqueous solutions of lithium, sodium, potassium, rubidium, and cesium chlorides (0.25 M in each) with 0.050 M solutions of the lipophilic crown ether carboxylic acids were conducted by the previously reported method.[6] Results are recorded in Table I.

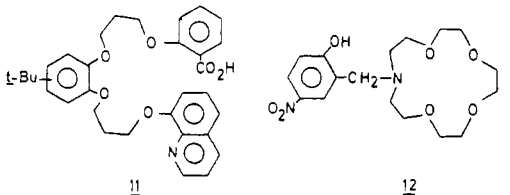
Table I. Competitive Extraction Selectivity Orders and Li^+/Na^+ Ratios

compd	ring type	selectivity order	max Li^+/Na^+ ratio
1	B12C4	$Li^+ > Na^+ > K^+ > Rb^+ > Cs^+$	1.8
2	B14C4	$Li^+ > Na^+ > K^+ > Rb^+$ (no Cs^+)	4.7
3	DB14C4	$Na^+ > Li^+ > K^+ > Rb^+ > Cs^+$	0.6
4	12C4	$Li^+ > Na^+ > K^+ > Rb^+, Cs^+$	1.7
5	13C4	$Li^+ > Na^+ > K^+ > Rb^+ > Cs^+$	2.3
6	13C4	$Li^+ > Na^+ > K^+ > Rb^+, Cs^+$	2.5
7	14C4	$Li^+ >> Na^+$ (no K^+, Rb^+, Cs^+)	20
8	14C4	$Li^+ >> Na^+$ (no K^+, Rb^+, Cs^+)	19
9	15C4	$Li^+ > Na^+ > K^+, Cs^+ > Rb^+$	3.5
10	13C4	$Li^+ > Na^+ > K^+ > Rb^+ > Cs^+$	1.6

[a] B = benzo, DB = dibenzo. [b] Reproducibility is ±5% of the listed value.

For extractions conducted with **1–10**, metal loading of the chloroform phase was strongly influenced by the pH of the contacted aqueous phase. Acidic or neutral pH's gave little or no extraction, whereas maximal extraction efficiency (85% or greater loading) was observed at pH 10–11. All compounds except **3** exhibited lithium selectivity.

For the monobenzo-12-crown-4 and -14-crown-4 compounds **1** and **2**, respectively, the modest Li^+/Na^+ ratio observed with the former is substantially enhanced for the latter. The Li^+/Na^+ selectivity of 4.7 obtained with **2** surpasses the selectivity of 3.4 reported[10] for competitive transport of alkali-metal cations across a chloroform membrane by the acyclic polyether carboxylic acid **11** and a selectivity of 4.1 calculated from single ion extraction



11 **12**

constants for extractions of lithium and sodium cations from water into 1,2-dichloroethane by the chromogenic azacrown **12**.[11] Surprisingly the lithium selectivity noted with **2** is completely lost with the dibenzo-14-crown-4 derivative **3**.

Compounds **4–9** are a series which possesses a common lipophilic carboxylic acid unit but has systematic variation of the crown ether ring size. All are lithium selective, but the degree of selectivity is a function of ring size. Thus the low Li^+/Na^+ ratio noted for the 12-crown-4 compound **4** is increased with the 13-crown-4 compounds **5** and **6**. Compared with **5**, compound **10** has the same crown ether ring system but a different lipophilic carboxylic acid group. The lower Li^+/Na^+ ratio observed with **10** indicates that the less rigid lipophilic carboxylic acid group in **10** diminishes selectivity. With the 14-crown-4 derivatives **7** and **8**, only Li^+ and Na^+ are extracted into the chloroform phase and the lithium selectivity is very high. *The Li^+/Na^+ ratios of 19–20 observed with 7 and 8 are the highest yet achieved in*

(1) Czech, B. P.; Babb, D. A.; Son, B.; Bartsch, R. A. *J. Org. Chem.*, in press.
(2) Olsher, U.; Jagur-Grodzinski, J. *J. Chem. Soc., Dalton Trans.* **1981**, 501–505.
(3) Kimura, K.; Kitazawa, S.; Shono, T. *Chem. Lett.* **1984**, 639–640.
(4) Olsher, U. *J. Am. Chem. Soc.* **1982**, *104*, 4007–4008.
(5) Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 2251–2253.
(6) Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 1894–1899.
(7) Structures of **1**, **2**, and **5–10** were verified by elemental analysis and ^1H NMR and IR spectra. Full details of the syntheses of **1**, **2**, and **5–10** will be reported separately.
(8) Bartsch, R. A.; Liu, Y.; Son, B.; Heo, G. W.; Hipes, P. G.; Bills, L. J. *J. Org. Chem.* **1983**, *48*, 4864–4869.
(9) Czech, B.; Son, B.; Bartsch, R. A. *Tetrahedron Lett.* **1983**, 2923–2926.
(10) Hiratani, K. *Chem. Lett.* **1982**, 1021–1024.
(11) Nakamura, J.; Sakka, H.; Takagi, M.; Ueno, K. *Chem. Lett.* **1981**, 1305–1306.

0002-7863/85/1507-4997$01.50/0