and H-3a (2.8); MS, m/z (rel intensity) 160 (M^+, 58), 145 (100), 131 (42), 117 (66), 105 (69), 91 (83), 77 (49), 65 (35).

(*Z*)-**10**: ^{1}H NMR (obtained on a 2:3 mixture of (*Z*)-**10** and (*E*)-**10** in C_6D_6; some coupling constants uncovered by homonuclear proton decoupling) δ 5.99 (d, ^3J = 5.5 Hz, 1 H, H-2), 5.8–5.6 (m, 2 H, H-6, H-7), 5.48 (d, ^3J = 5.5 Hz, 1 H, H-3), 5.33 (q, ^3J = 6.9 Hz, 1 H, =C*H*CH$_3$), 3.01 (m, 1 H, H-7a), 2.0–1.2 (m, 4 H, H-4, H-5), 1.65 (d, ^3J = 6.9 Hz, 3 H, =CHC*H*$_3$), 1.03 (s, 3 H, bridgehead CH$_3$); 1D NOE (C_6D_6, 25 °C), simultaneous irradiation of vinyl CH$_3$ and the H-4, H-5 protons, all of similar chemical shift, afforded NOEs (%) to H-7a (2.1), =C*H*CH$_3$ (4.3), H-3 (2.4), bridgehead CH$_3$ (2.4), and to overlapping resonances for H-6, H-7 of (*Z*)-**11** and to H-3, H-6, H-7 of (*E*)-**11** (total of 4.2% as referenced to the vinyl CH$_3$ resonances in both (*Z*)-**10** and (*E*)-**10**); MS, m/z (rel intensity) 160 (M^+, 40), 145 (100), 131 (33), 117 (50), 105 (30), 91 (67), 77 (35), 65 (28).

(*E*)-**10**: ^{1}H NMR (obtained on a mixture of (*Z*)-**10** and (*E*)-**10** in C_6D_6; some coupling constants uncovered by homonuclear proton decoupling) δ 6.30 (d, ^3J = 5.7 Hz, 1 H, H-2), 5.8–5.6 (m, 3 H, H-3, H-6, H-7), 5.12 (q, ^3J = 6.7 Hz, 1 H, =C*H*CH$_3$), 2.74 (m, 1 H, H-7a), 2.0–1.2 (m, 4 H, H-4, H-5), 1.64 (dd, ^3J = 6.7 Hz, $^5J_{CH_3,7a}$ = 1.5 Hz, 3 H, =CHC*H*$_3$), 1.02 (s, 3 H, bridgehead CH$_3$); 1D NOE (C_6D_6, 25 °C), simultaneous irradiation of vinyl CH$_3$ and H-4, H-5 protons, all of similar chemical shift, afforded NOEs (%) to H-2 (3.2), =C*H*CH$_3$ (4.2), bridgehead CH$_3$ (1.4), and to overlapping resonances for H-3, H-6, H-7 of (*E*)-**11**, and to H-6, H-7 of (*Z*)-**11** (total of 4.2% as referenced to the vinyl CH$_3$ resonances in both (*Z*)-**11** and (*E*)-**11**); MS, m/z (rel intensity) 160 (M^+, 40), 145 (100), 131 (33), 117 (50), 105 (30), 91 (67), 77 (35), 65 (28).

(B) **Analytical Scale on Separated Allenes 8a and 8b.** Approximately 1.5 μL (1.4 mg) of *syn*-allene **8a** was injected neat on the preparatory GC (oven temperature 215 °C, injector temperature 310 °C, detector temperature 175 °C, flow rate 20 mL/min), and all the eluted material (retention time 15–36 min following injection) was collected and analyzed by capillary GC. The analysis showed 5.4% of **8a** remaining, and trienes (*Z*)-**9**, (*E*)-**9**, (*Z*)-**10**, and (*E*)-**10** in a percentage ratio of 2.7, 61.1, 29.2, and 1.6, respectively. (Approximate product percentage ratio 3:64:31:2.) When a solution of approximately 0.5 mg of *syn*-allene **8b** in 150 μL of acetone-d_6 was injected under the same conditions, capillary GC analysis of the collected material (retention time 15–36 min following injection) showed 22.5% of **8b** remaining, and trienes (*Z*)-**9**, (*E*)-**9**, (*Z*)-**10**, and (*E*)-**10** in a percentage ratio of 49.5, 2.5, 0.8, and 28.3, respectively. (Approximate product percentage ratio 59:3:1:37.) Similar results were obtained when **8a** was injected as a solution in hexane and **8b** as solution in $CDCl_3$; only the percent of **8a** and **8b** remaining changed; however, the stereoselectivity of the rearrangement remained approximately the same. Approximately 0.75 μL of a 2:3 mixture of *anti*-allenes **12a** and **12b** was also injected neat on the preparatory GC under the conditions described above. Capillary GC analysis of all eluted material showed only starting material (**12a**/**12b**) in approximately the original 2:3 ratio.

Acknowledgment. Supported in part by a M. J. Murdock Charitable Trust Grant of Research Corporation and by a M. J. Murdock Charitable Trust Grant to Lewis and Clark College for which we are most grateful. Also supported by research grants awarded to R.T.H. and K.S.K. by the Student Academic Affairs Board (SAAB) of Lewis and Clark College. We are also grateful to the National Science Foundation (ILI 88-51627) for providing the funds for the purchase of a G.E. QE-300, 300-MHz NMR spectrometer system. We are indebted to Dr. David Peyton of Portland State University for his knowledgeable assistance in setting up, executing, and evaluating the experiments in NOE difference spectroscopy. The authors also thank Lewis and Clark College students, Cheryl Longfellow, Doris Meade, and Lêna Nouth for working out some of the experimental details and Mr. Loren Isabelle of the Oregon Graduate Institute for obtaining all of the mass spectra for us.

Host Properties of Cyclodextrins toward Anion Constituents of Antigenic Determinants. A Thermodynamic Study in Water and in *N*,*N*-Dimethylformamide

Angela F. Danil de Namor,*,† Rafic Traboulssi,† and David F. V. Lewis‡

Contribution from the Departments of Chemistry and Biochemistry, University of Surrey, Guildford, Surrey, GU2 5XH England. *Received March 19, 1990*

Abstract: Thermodynamic data for the transfer of α, β-, and γ-cyclodextrins from water to *N*,*N*-dimethylformamide derived from solution data in the two solvents are reported. Transfer data are characterized by rather small free energy values as a result of enthalpy (large and favorable) being largely compensated by entropy (large and negative) data. Data for cyclodextrins are not characteristic of those observed for the transfer of nonelectrolytes from water to the same reaction media and suggest a strong cyclodextrin–*N*,*N*-dimethylformamide interaction. Thermodynamic parameters for the complexation process involving *p*-hydroxyphenyl and substituted (*p*-hydroxyphenylazo)benzoate (hapten) anions and cyclodextrins in water and in *N*,*N*-dimethylformamide have been determined. The data suggest that two different types of complexation occurs as a result of a change in the reaction medium. In water, inclusion or axial type complexes are formed. In *N*,*N*-dimethylformamide, these anions interact with the hydroxyl groups of the cyclodextrin molecule and equatorial or lid type complexes are formed. A detailed explanation of the complexation process in water and *N*,*N*-dimethylformamide is given. Single ion free energy values for the transfer of the complexed anions from water to *N*,*N*-dimethylformamide show that no significant changes in solvation occurs, in both the anion and the ligand upon complexation. The free energy values are the result of a compensation effect between enthalpy and entropy data. These are the first data ever reported on the transfer of cyclodextrins and their adducts from water to a nonaqueous medium.

Several articles dealing with the properties of cyclodextrins can be found in the literature.[1-9] An enormous amount of effort has been devoted to explore their applications based on the ability of cyclodextrins to form complexes with a large number of substrates. An account on the uses of cyclodextrins in research and industry has been given by Saenger.[5] The pharmaceutical applications of

† Department of Chemistry.
‡ Department of Biochemistry.

(1) French, D. *Adv. Carbohydr. Chem.* **1957**, *12*, 189.
(2) Thoma, J. A.; Stewart, L. *Starch: Chemistry and Technology*; Whilster, R. L., Paschall, E. F. Eds.: Academic Press: New York, 1965: Vol. 1, p 209.

0002-7863/90/1512-8442$02.50/0

cyclodextrins have been discussed by Ukahama.[10] In recent years, a number of papers have been published on the interactions of cyclodextrins with biological membrane components.[11,12] Thermodynamic and kinetic studies on complexation of cyclodextrins with a number of substrates have been reported by several workers.[13-21] Most of these data refer to water as the reaction medium. Complexation studies involving cyclodextrins in nonaqueous media are very scarce. The first set of data on dissociation constants of β-cyclodextrin–substrate complexes in dimethyl sulfoxide were reported by Siegel and Breslow in 1975.[22] More recent studies on cyclodextrins in nonaqueous media are those by Harada and Takahaski,[23] Matsui et al.,[24] Martre et al.,[25] and Kobayashi.[26]

Thermodynamic parameters of complexation of cyclodextrins and substrates in nonaqueous media are almost nonexistent. No data are found in the literature on transfer parameters of cyclodextrins and their complexes from water to nonaqueous media. Transfer parameters are a measure of the differences in solvation of a given ion or molecule between two solvents. Therefore, these parameters are useful in determining some of the factors controlling complex formation in processes involving cyclodextrins and guest species in different reaction media.

Cyclodextrins have been extensively used as models for enzymatic specificity.[27-30] Therefore, it is not surprising to find that the aqueous medium has been selected for these studies. However, thermodynamic studies in nonaqueous media are useful since some aspects relating the complex nature of water as a reaction medium are eliminated by the use of a nonaqueous medium.

Thermodynamic data have been successfully applied in the interpretation of complexation processes involving metal cations and macrocyclic ligands (cryptands) in water and in dipolar aprotic media.[31-34] Therefore, we thought that solution thermodynamic studies involving cyclodextrins would not only provide an interesting extension of our current research but would also contribute further to the present knowledge on cyclodextrin–substrate complexation reactions, particularly in nonaqueous media. Antibodies (as cyclodextrins) are able to form inclusion complexes with antigenic determinants. On the basis Cramer[13,35] put forward the suggestion that cyclodextrins could serve as models for antibodies. Interactions which contribute to the formation of stable complexes between an antibody and an antigenic determinant are the same as those involved in the stabilization of the configuration of proteins or the complexation of macrocyclic ligands and substrates.[36] Therefore, it is particularly important to explore this possibility by selecting a group of anions which are known to be constituents of antigenic determinants (haptens). Given that cyclodextrins are able to interact with azo dyes,[13,15] the *p*-hydroxyphenylazo and substituted (*p*-hydrophenylazo)benzoate (p-$OHPhN_2$)B^- anions were selected as a prior step to our research program on thermodynamics of binding of monoclonal antibodies against (*p*-hydroxyphenylazo)benzoate haptens.

The solution properties of electrolytes containing *p*-hydroxyphenylazo and substituted (*p*-hydroxyphenylazo)benzoate anions in water, methanol, and *N,N*-dimethylformamide (DMF) have been the subject of three recent publications from our groups.[37-39] For this study three cyclodextrins are selected. These are α-, β-, and γ-cyclodextrins (CD) whose cavity sizes are 6.0, 7.0, and 8.5 Å, respectively.[2]

The aims of this study are as follows: (a) To gain some understanding on the solvation of α-, β-, and γ-cyclodextrins in water and in *N,N*-dimethylformamide from the interpretation of their transfer parameters. (b) To investigate the complexing abilities of cyclodextrins toward *p*-hydroxyphenylazo and substituted (*p*-hydroxyphenylazo)benzoate anions in water and in *N,N*-dimethylformamide and whenever possible to obtain thermodynamic data for complex formation in these two solvents. (c) To derive single-ion thermodynamic data for anion–cyclodextrin complexes from water to *N,N*-dimethylformamide in order to get information regarding the state of solvation of both the host and guest anion in the complex.

Experimental Section

The salts [*o*-(*p*-$OHPhN_2$)NaB, *m*-(*p*-$OHPhN_2$)NaB, *p*-(*p*-$OHPhN_2$)NaB, 5Cl2(*p*-$(OHPhN_2)$NaB, 6Cl2(*p*-$OHPhN_2$)NaB, 2Cl4-(*p*-$OHPhN_2$)NaB, and 4Cl2(*p*-$OHPhN_2$)NaB] were prepared and purified as described elsewhere.[37]

α-, β-, ad γ-cyclodextrins were purchased from Sigma Chemicals Ltd. and further dried under vacuum at temperature between 60 and 70 °C for several days before use. Microanalyses on the samples were carried out. *N,N*-Dimethylformamide (BDH 98%) was first dried over BaO for several hours. The solvent was then purified by fractional distillation and carried out under vacuum at temperature between 60 and 80 °C. Only the middle fraction distilled solvent was collected and used. The water content of the solvent was checked by gas–liquid chromatography and by Karl Fisher titration and was found to be less than 0.05%.

Heats of solution of cyclodextrins in water and *N,N*-dimethylformamide at 298.15 K were measured by using the TRONAC 450 calorimeter. The reliability of the equipment was tested by determining the heat of reaction of tris(hydroxymethyl)aminomethane (THAM) with 0.1 mol dm^{-3} of HCl as suggested by Irving and Wadsö.[40] A value of −29765

(3) Griffiths, D. W.; Bender, M. L. *Adv. Catal. Relat. Subj.* **1973**, *23*, 209.
(4) Bender, M. L.; Komiyama, M. *Cyclodextrin Chemistry*; Springler-Verlag: Berlin, 1978.
(5) Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344.
(6) Breslow, R. *Adv. Chem. Ser.* **1980**, *191*, 1.
(7) Tabushi, I. *Acc. Chem. Res.* **1982**, *15*, 66.
(8) Saenger, W. *Inclusion Compounds*; Atwood, J. L., Davies, J. E., MacNicol, D. D., Eds.; Academic Press: New York, 1984; Vol. 2, p 231.
(9) D'Souza, V. T.; Bender, M. L. *Acc. Chem. Res.* **1987**, *20*, 146.
(10) Uekama, K. *J. Pharm. Soc., Jpn.* **1981**, *10*, 857.
(11) Komiyama, M. *Chem. Lett.* **1988**, 689; *Makromol. Chem., Rapid Commun.* **1988**, 453.
(12) Okahata, Y.; Te, X. *J. Chem. Soc., Chem. Commun.* **1989**, 1147.
(13) Cramer, F.; Saenger, W.; Spatz, H. Ch. *J. Am. Chem. Soc.* **1967**, *89*, 14.
(14) Lewis, E. A.; Hansen, L. D. *J. Chem. Soc., Perkin Trans. II* **1973**, 2081.
(15) Machida, K.; Kagita, A.; Matsui, Y.; Date, Y. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3703.
(16) Uekama, K.; Otagiri, M.; Kanie, Y.; Tanaka, S.; Ikeda, K. *Chem. Pharm. Bull.* **1975**, *23*, 1421.
(17) Otagiri, M.; Miyaji, T.; Uekama, K.; Ikeda, K. *Chem. Pharm. Bull.* **1976**, *24*, 1146.
(18) Nakajima, T.; Suganawa, M.; Hirohashi, T.; Fujioka, K. *Chem. Pharm. Bull.* **1984**, *32*, 383.
(19) Tagaki, S.; Kimura, T.; Maeda, M. *Thermochim. Acta* **1985**, *88*, 247.
(20) Cromwell, W. C.; Byström, K.; Eftink, M. R. *J. Phys. Chem.* **1985**, *89*, 326.
(21) Briggner, L. E.; Ni, X. R.; Tempesti, F.; Wadsö, I. *Thermochim. Acta* **1986**, *109*, 139.
(22) Siegel, B.; Breslow, R. *J. Am. Chem. Soc. Soc.* **1975**, *97*, 6869.
(23) Harada, A.; Takahashi, T. *Chem.* Lett. **1984**, 2089.
(24) Matsui, T.; Akiba, U.; Suzufuji, K.; Osa, T. *Denki Kagaku* **1985**, *53*, 508.
(25) Martre, A. M.; Mousset, G.; Pouillen, P.; Dauphin, G. *Bull. Soc. Chim. Fr.* **1988**, *3*, 489.
(26) Kobayashi, N. *J. Chem. Soc., Chem. Commun.* **1989**, 1126.
(27) Bender, M. L. *Proceedings of the First International Symposium on Solution Behaviour. Theoretical and Practical Aspects*; Mittal, K. J. L., Fendler, E. J., Eds.; Plenum Press: New York, 1982; Vol. 2.
(28) Van Etten, R. L.; Sebastian, J. F.; Cloves, G. A.; Bender, M. L. *J. Am. Chem. Soc.* **1967**, *89*, 3242.
(29) Straub, T. S.; Bender, M. L. *J. Am. Chem. Soc.* **1972**, *94*, 8896.
(30) Komiyama, M.; Bender, M. L. *J. Am. Chem. Soc.* **1978**, *100*, 2260.
(31) Danil de Namor, A. F.; Ghousseini, L. *J. Chem. Soc., Faraday Trans I* **1985**, *81*, 781.
(32) Danil de Namor, A. F. *J. Chem. Soc., Faraday Trans. I* **1988**, *84*, 2441.
(33) Danil de Namor, A. F.; Fernandez Salazar, F. *J. Chem. Soc., Faraday Trans. I* **1988**, *84*, 3539.
(34) Danil de Namor, A. F.; Ritt, M. C.; Schwing-Weill, M. J.; Arnaud-Neu, F. *J. Chem. Soc., Faraday Trans. I* **1990**, *86*,(*1*), 87.
(35) Cramer, F. *Einschlussverbindungen*; Springer-Verlag: Heidelberg, 1954.
(36) Steward, M. W. *Antibodies. Their Structure and Function*; Chapman and Hall: 1984.
(37) Danil de Namor, A. F.; Traboulssi, R.; Salomon, M. *J. Chem. Soc., Faraday Trans. I* **1990**, *86*(*3*), 501.
(38) Danil de Namor, A. F.; Traboulssi, R.; Marquardt, F. H. *J. Chem. Soc., Faraday Trans. I* **1990**, *86*, 1067.
(39) Danil de Namor, A. F.; Traboulssi, R.; Salomon, M. *J. Chem. Soc., Faraday Trans. I* **1990**, *86*, 2193.
(40) Irving, R. J.; Wadsö, I. *Acta Chim. Scand.* **1964**, *18*, 195.

Table I. Solubilities and Thermodynamic Parameters of Solution of α-, β-, and γ-Cyclodextrins in Water and *N,N*-Dimethylformamide at 298.15 K and Derived Thermodynamic Parameters of Transfer from Water

	α-cyclodextrin		β-cyclodextrin		γ-cyclodextrin	
	H_2O	DMF	H_2O	DMF	H_2O	DMF
solubility, mol dm^{-3}	1.49×10^{-1} [a]	$(7.38 \pm 0.25) \times 10^{-2}$	1.63×10^{-2} [a]	$(9.08 \pm 2) \times 10^{-2}$	1.79×10^{-1} [a]	$(9.56 \pm 1.7) \times 10^{-2}$
$\Delta G°_s$, kJ mol^{-1}	4.72	6.46	10.21	5.95	4.26	5.82
$\Delta H°_s$, kJ mol^{-1}	−62.69	−107.03	−75.52	−125.56	−96.31	−156.10
$\Delta S°_s$, J K^{-1} mol^{-1}	−224.7	−380.6	−287.5	−441.1	−337.3	−543.1
	$H_2O \rightarrow$ DMF		$H_2O \rightarrow$ DMF		$H_2O \rightarrow$ DMF	
$\Delta G°_t$, kJ mol^{-1}	1.74		4.26		1.56	
$\Delta H°_t$, kJ mol^{-1}	−44.34		−50.04		−59.79	
$\Delta S°_t$, J K^{-1} mol^{-1}	−155.9		−153.6		−205.8	

[a] Reference 1.

± 28 J mol^{-1} (−7114 ± 9 cal·mol^{-1}) which is in excellent agreement with the literature value of −29757 ± 9 J mol^{-1} (−7112 ± 2 cal mol^{-1}) was obtained. All heats of solution were corrected from ampoule breaking in *N,N*-dimethylformamide. The heat of breaking of empty ampoules in this solvent was found to be 0.0518 ± 0.0025 J (average of seven measurements).

The heat of complexation of cyclodextrins and salts in water and in *N,N*-dimethylformamide was measured by using an isoperibol titration calorimeter (The Hart Scientific 5021). The reliability of the calorimeter was checked by carrying out measurements of the heat of protonation of TRIS in 0.1 mol dm^{-3} of HCl. A value of −47.54 kJ mol^{-1} was obtained. This value is in agreement with the value reported by Öjelund and Wadsö[41] (−47.49 ± 0.04 kJ mol^{-1}). In addition, the heat of ionization of water was determined. The value obtained (−56.13 ± 0.46 kJ mol^{-1}) is in good agreement with the value reported by Vanderzee and Swanson[42] ($\Delta H°$ = −55.80 kJmol^{-1}), Hale et al.[43] ($\Delta H°$ = −55.79 kJ mol^{-1}), and Hansen and Lewis ($\Delta H°$ = −55.70 kJ mol^{-1}).[44]

Analysis of the calorimetric titration data was carried out by using a least-squares method. This involves a simultaneous determination of the equilibrium constant (log *K*) and the enthalpy of complexation, $\Delta H°_c$. The procedure of calculation is based on the program KAFORI developed by Karlsson and Kullberg,[45] kindly provided by Professor Wadsö and M. Bastos, Chemical Center, University of Lund, Sweden.

Solubility data were obtained by adding an excess of solute to the solvent. The mixtures were left to equilibrate for several days at 298.15 K. Aliquots were taken and analyzed calorimetrically. Solvate formation was checked according to the method described before.[37] No solvate formation was observed.

Thermodynamic Parameters of Solution of Cyclodextrins in Water and in *N,N*-Dimethylformamide and Their Transfer from Water at 298.15 K. Table I lists solubilities and thermodynamic parameters of solution of cyclodextrins in water and in *N,N*-dimethylformamide at 298.15 K. Solution free energy data ($\Delta G°_s$) of α-, β-, and γ-cyclodextrins were calculated from solubility measurements of these compounds in water and in *N,N*-dimethylformamide at 298.15 K. Standard enthalpies of solution ($\Delta H°_s$) of cyclodextrins in these solvents are the result of heats of solution of these compounds in water and in *N,N*-dimethylformamide carried out by the calorimetric technique. Standard entropies of solution ($\Delta S°_s$) were calculated from corresponding free energy and enthalpy data at 298.15 K. A striking feature of these results is the compensation effect observed between entropies and enthalpies of solution of α-, β-, and γ-cyclodextrins in water and in *N,N*-dimethylformamide. In fact, a plot of solution entropy data against solution enthalpy data in these solvents gives a straight line of slope 307 ± 9 K. This is known as the compensation temperature.[46] A correlation coefficient of 0.998 was calculated.

The solvation process may be best interpreted by considering thermodynamic data for the transfer ($\Delta G°_t$, $\Delta H°_t$, and $\Delta S°_t$) of cyclodextrins (CD) from water to *N,N*-dimethylformamide. These data reported in Table I are referred to the process described by

$$\text{CD } (H_2O) \rightarrow \text{CD (DMF)} \qquad (1)$$

where both solvents are in their pure state. Transfer thermodynamic data are characterized by rather small $\Delta G°_t$ values as a result of a compensation effect between favorable enthalpy data ($\Delta H°_t$ values are large and negative) and unfavorable entropy data ($\Delta S°_t$ values are large and negative). It must be stressed that these data do not follow the pattern usually observed in terms of enthalpy and entropy for the transfer of nonelectrolytes from water to dipolar aprotic media. In fact, data for the transfer of cyclodextrins from water to *N,N*-dimethylformamide are just opposite in sign to those observed for the transfer of other macrocyclic ligands in their transfer from water to the same reaction medium. A typical example is cryptand 222. The small $\Delta G°_t$ value observed for this ligand is the result of large and positive values for the transfer enthalpy and entropy from water to nonaqueous media.[31] The results shown in Table I indicate that this is not the case for cyclodextrins. As far as these ligands are concerned, cyclodextrins are enthalpically more stable in *N,N*-dimethylformamide than in water (negative $\Delta H°_t$ values). For the latter solvent, 2, 8, and 12 mol of water, respectively, are known to be included in the cavities of α-, β-, and γ-cyclodextrins. It is not known whether or not *N,N*-dimethylformamide may be included in the cavity of cyclodextrins. However, the results in Table I suggests that this may be the case. A definite size effect is reflected in the transfer enthalpies of cyclodextrins among these two solvents. Indeed, an increase in stability (in enthalpic terms) as the size of the ligand increases is observed. In fact, a linear relationship is observed between $\Delta H°_s$ values in water with corresponding data in *N,N*-dimethylformamide. The same linear relationship is observed in terms of $\Delta S°_s$.

Complex Formation of Cyclodextrins and Anions in Water and in *N,N*-Dimethylformamide. It is well established that the complexation process involving cyclodextrins and substrates in aqueous media is enthalpically controlled. Therefore, titration calorimetry was the technique chosen to detect complex formation of (*p*-hydroxyphenylazo)benzoate and substituted (*p*-hydroxyphenylazo)benzoate anions and cyclodextrins in water and in *N,N*-dimethylformamide. Provided that stability constants are not very large, this technique offers the advantage that all thermodynamic parameters of complexation ($\Delta G°_c$, $\Delta H°_c$, and $\Delta S°_c$) can be derived from calorimetric data. Seven anions were considered for complex formation with α-, β-, and γ-cyclodextrins in water and in *N,N*-dimethylformamide. These are *o*-, *m*-, and *p*-(*p*-hydroxyphenylazo)benzoate (Figure 1) and chlorosubstituted (*p*-hydroxyphenylazo)-benzoate [5Cl2(*p*-$OHPhN_2$)B^-, 6Cl2(*p*-$OHPhN_2$)B^-, 2Cl4(*p*-$OHPhN_2$)B^-, and 4Cl3(*p*-$OHPhN_2$)B^-]. Three out of the seven anions considered [*m*-(*p*-$OHPhN_2$)B^-, *p*-(*p*-$OHPhN_2$)B^-, and 2Cl4(*p*-$OHPhN_2$)B_2] were found to form 1:1 complexes with α-cyclodextrin in water. In addition, the 4Cl3(*p*-$OHPhN_2$)B^- anion was also found to form a 1:1 complex with γ-cyclodextrin in this solvent. The relatively low solubility of β-cyclodextrin in water did impede accurate detection as to whether or not complexation of β-cyclodextrin and these anions takes place in water.

As far as *N,N*-dimethylformamide is concerned five out of seven anions considered are able to form 1:1 complexes with α- and γ-cyclodextrins. Complexation was not observed for any of these two ligands and 5Cl2(*p*-$OHPhN_2$)B^- and 6Cl2(*p*-$OHPhN_2$)B^- anions in this solvent. These two anions and *o*-*p*-$OHPhN_2$)B^- are unable to complex with β-cyclodextrins in *N,N*-dimethylformamide. Therefore, the number of anions capable of complexation with β-cyclodextrin in *N,N*-dimethylformamide is reduced from five (α and γ) to four.

It is indeed the lack of complexation of these anions in water which provides information on the likely site of interaction for those anions which are able to undergo complexation with cyclodextrins in this solvent. Unlike *m*, *p*-, and 2Cl4(*p*-$OHPhN_2$)B^-, complexation with *o*- and substituted *o*-(*p*-$OHPhN_2$)B^- anions and α- and γ-cyclodextrins does not occur in water. These observations lead to the suggestion that the *p*-$OHPhN_2$ group must be the active site for complexation between these anions and cyclodextrins in this solvent. This interpretation is supported by the results obtained from computer calculations by using a COSMIC package.[47] The structural conformation which corresponds to the minimum energy (higher stability) for the formation of inclusion (axial) type

(41) Öjelund, G.; Wadsö, I. *Acta Chim. Scand.* **1968**, *22*, 2691.
(42) Vanderzee, C. E.; Swanson, J. A. *J. Phys. Chem.* **1963**, *67*, 2608.
(43) Hale, J. D.; Izatt, R. M.; Christensen, J. J. *J. Phys. Chem.* **1963**, *67*, 2605.
(44) Hansen, L. D.; Lewis, E. A. *J. Chem. Thermodynamics* **1971**, *3*, 35.
(45) Karlsson, R.; Kullberg, L. *Chem. Scr.* **1976**, 54.
(46) Lumry, R.; Rajender, S. *Biopolymers* **1970**, *9*, 1125.
(47) Vinter, J. G.; Davis, A.; Saunders, M. R. *J. Comput. Aided Molecular Design* **1987**, *1*(1), 31.

complexes is that shown in Figure 2. These findings suggest that steric effects which may not be attributed to the position but also to the state of solvation of the substituent groups in the guest ion are likely to be responsible for the lack of complexation of α- and γ-cyclodextrins with *o*- and chlorosubstituted *o*-benzoate anions in water. It is of interest to observe that an increase in the cavity size of the ligand (from α to γ) results in complexation of 4Cl3(*p*-OHPhN$_2$)B$^-$ anion with γ-cyclodextrins in water. No complexation for this anion and α-cyclodextrin in water was observed.

Thermodynamic Parameters of Complexation of Anions and Cyclodextrins in Water and in *N,N*-Dimethylformamide at 298.15 K. Stability constant data for azobenzoate and substituted azobenzoate anions and cyclodextrins (α and γ) in water and in *N,N*-dimethylformamide (α, β and γ) at 298.15 K are listed in Table II. The standard deviations of the data are also included in the table. No significant differences are found among log K_s values for these anions and cyclodextrins in these solvents. Indeed, average values of 3.83 ± 0.27 (H_2O) and 3.49 ± 0.25 (DMF) are calculated for α-cyclodextrins against values of 4.13 ± 0.15 (H_2O) and 3.80 ± 0.35 (DMF) for γ-cyclodextrin. With β-cyclodextrin in *N,N*-dimethylformamide, the average log K_s value is 3.80 ± 0.26. These results analyzed in terms of the ligand, the guest molecule, and the solvent show the following: (a) Stability constants in water and in *N,N*-dimethylformamide are slightly higher for anions complexed with γ-cyclodextrin. (b) These ligands do not show any specificity for these anions. (c) The reaction media does not seem to have any significant effect on the stability constant data. Obviously, these statements can be extended to the free energies of complexation, $\Delta G°_c$, of these anions and cyclodextrins which are also included in Table II.

It must be emphasized that similar $\Delta G°_c$ values for the complexation process involving different ligands and anions in a given reaction medium are the result of (a) an equal value for the enthalpic and entropic contributions for the different complexes or (b) a compensation effect between enthalpy and entropy data.

Standard enthalpies, $\Delta H°_c$, and entropies, $\Delta S°_c$, for the complexation process involving *p*-OHPhN$_2$ benzoate and substituted *p*-OHPhN$_2$ benzoate anions in water and in *N,N*-dimethylformamide are shown in Table II. $\Delta H°_c$ vs $\Delta S°_c$ plot in water gives a straight line of intercept −23.52 ± 0.62 kJ mol^{-1}. The slope known as the compensation temperature is 305 ± 30K. A correlation coefficient of 0.99 was calculated. The same compensation effect is shown in *N,N*-dimethylformamide (intercept −21.22 ± 0.87 kJ mol^{-1}, slope 307 ± 46 K, correlation coefficient 0.89). The $\Delta H°_c - \Delta S°_c$ compensation effect in cyclodextrin complexes in water has been pointed out by several workers.[14,16-19] Some authors[14] have stated that this effect is limited to highly ordered and hydrogen-bonded solvents, such as water. The results obtained in this work demonstrate that as far as these anions and cyclodextrins are concerned the compensation effect is also found in *N,N*-dimethylformamide, a solvent which can neither be regarded as a hydrogen bonding nor a highly ordered solvent.[48]

Except for *p*-(*p*-OHPhN$_2$)B$^-$α-CD(DMF) and *p*-(*p*-OHPhN$_2$)B$^-$γ-CD(H_2O), two distinctive patterns are observed in terms of entropy. Unlike water, the complexation process between these anions and cyclodextrins is entropically favorable. For both solvents, this process is enthalpically controlled. In the complexation process involving ions and macrocyclic ligands, a significant role must be played by the solvated state of the anion and ligand. On this basis, a good solvating medium for the anion or indeed the ligand is unlikely to be a good solvating medium for anion–ligand interaction. In order to apply this criterion enthalpy and entropy data are analyzed in terms of the effect of both the ligand and the anion on the complexation process. In order to do so, their transfer data from water to *N,N*-dimethylformamide are considered.

Effect of Ligand on the Complexation Process. The effect of the ligand on the complexation process is reflected in the two different patterns shown by the thermodynamic parameters of complexation in water and in *N,N*-dimethylformamide. (a) In water, $\Delta H°_c$ and $\Delta S°_c$ values are ligand dependent. Thus, for a given anion, the following differences in terms of enthalpies or entropies of complexaion are found:

$$\Delta H°_c X^-\alpha CD - \Delta H°_c X^-\gamma CD = -8.6 \text{ kJ mol}^{-1}$$

$$\Delta S°_c X^-\alpha CD - \Delta S°_c X^-\gamma CD = -34.8 \text{ J K}^{-1} \text{ mol}^{-1}$$

These results suggest that, independently of the anion, substitution of the ligand (α for γ) results in an almost constant variation in $\Delta H°_c$ and $\Delta S°_c$ values, which may be attributed to the release of solvent (water) from the cavity of the ligand during the complexation process. (b) In *N,N*-dimethylformamide, no significant differences are observed in the $\Delta H°_c$ and $\Delta S°_c$ values for the complexation of a given anion and the various

Table II. Thermodynamic Parameters of Complexation of Cyclodextrins and *p*-Hydroxyphenyl and Substituted (*p*-Hydroxyphenylazo)benzoate Anions in Water and in *N,N*-Dimethylformamide at 298.15 K

anion	α-cyclodextrin				β-cyclodextrin				γ-cyclodextrin			
	log K_s	$\Delta G°_c$, kJ mol^{-1}	$\Delta H°_c$, kJ mol^{-1}	$\Delta S°_c$, J K^{-1} mol^{-1}	log K_s	$\Delta G°_c$, kJ mol^{-1}	$\Delta H°_c$, kJ mol^{-1}	$\Delta S°_c$, J K^{-1} mol^{-1}	log K_s	$\Delta G°_c$, kJ mol^{-1}	$\Delta H°_c$, kJ mol^{-1}	$\Delta S°_c$, J K^{-1} mol^{-1}
					Solvent: Water							
m-(*p*-OHPhN$_2$)B$^-$	3.72 ± 0.03	−21.23	−33.35 ± 1.89	−40.6					3.94 ± 0.05	−22.49	−25.18 ± 0.25	−9.0
p-(*p*-OHPhN$_2$)B$^-$	3.63 ± 0.04	−20.72	−29.13 ± 0.43	−28.2					4.13 ± 0.09	−23.57	−20.44 ± 0.08	10.5
2Cl4(*p*-OHPhN$_2$)B$^-$	4.14 ± 0.06	−23.73	−36.96 ± 0.39	−44.7					4.30 ± 0.17	−24.55	−28.04 ± 0.77	−11.7
4Cl3(*p*-OHPhN$_2$)B$^-$									4.16 ± 0.02	−23.75	−34.84 ± 1.17	−37.2
					Solvent: *N,N*-Dimethylformamide							
o-(*p*-OHPhN$_2$)B$^-$	3.20 ± 0.04	−18.27 (−21.62)[a]	−9.29 ± 0.08 (−31.27)[a]	30.1 (−32.0)[a]					3.28 ± 0.06	−18.72 (−21.62)[a]	−10.24 ± 0.74 (−31.27)[a]	28.4 (−32.0)[a]
m-(*p*-OHPhN$_2$)B$^-$	3.47 ± 0.03	−19.81 (−20.07)[a]	−21.37 ± 0.23 (−21.18)[a]	−5.2 (−3.7)[a]	4.01 ± 0.03	−22.89 (−20.07)[a]	−17.47 ± 0.03 (−21.18)[a]	18.2 (−3.7)[a]	4.04 ± 0.01	−23.06 (−20.07)[a]	−22.05 ± 0.20 (−21.18)[a]	3.4 (−3.7)[a]
p-(*p*-OHPhN$_2$)B$^-$	3.77 ± 0.12	−21.52 (−25.36)[a]	−15.53 ± 0.93 (−19.30)[a]	20.8 (20.8)[a]	4.04 ± 0.09	−23.06 (−25.36)[a]	−17.17 ± 0.79 (−19.30)[a]	19.7 (20.8)[a]	4.15 ± 0.05	−23.69 (−25.36)[a]	−15.56 ± 2.20 (−19.30)[a]	27.3 (20.8)[a]
2Cl4(*p*-OHPhN$_2$)B$^-$	3.32 ± 0.18	−18.95	−14.49 ± 1.22	14.9	3.64 ± 0.05	−20.78	−12.94 ± 0.35	26.3	3.63 ± 0.07	−20.72	−14.82 ± 0.45	19.8
4Cl3(*p*-OHPhN$_2$)B$^-$	3.71 ± 0.04	−21.18	−19.27 ± 1.10	6.4	3.51 ± 0.14	−20.04	−20.05 ± 0.60		3.88 ± 0.02	−22.15	−18.73 ± 0.50	11.5

[a] Single ion ($\Delta G°_t$, $\Delta H°_t$, and $\Delta S°_t$) of *o*-, *m*-, and *p*-(*p*-OHPhN$_2$)B$^-$ anions from *N,N*-dimethylformamide to methanol. Data based on the Ph_4AsPh_4B convention.

(48) Criss, C. M. *J. Chem. Ed.* **1976**, *53*, 764.
(49) Fong, D. W.; Grunwald, E. *J. Phys. Chem.* **1969**, *73*, 3908.
(50) Danil de Namor, A. F.; Traboulssi, R. Unpublished results.

cyclodextrins. These findings lead to the suggestion that the cavity of the ligand is unlikely to provide the site of complexation for these anions in this solvent. Indeed, these results support the interpretation that the larger stability observed for cyclodextrins in DMF with respect to water ($\Delta H°_t$ large and negative, Table I) must be attributed to the inclusion of solvent molecules in the cavity of the ligand. Therefore, unless the energy requirements to remove the solvent from the cavity are met, the formation of inclusion complexes (axial) with these anions in this solvent is unlikely to occur.

Effect of the Anion upon Complexation with Cyclodextrins. The stability (in enthalpic terms) of these anions is greater in water than in *N,N*-dimethylformamide ($\Delta H°_t$ values are positive).[39] These data are referred to the transfer of the whole anion. To facilitate this discussion, the structure of the (*p*-hydroxyphenylazo)benzoate anion is divided into its constituent parts (i) the *p*-hydrophenylazo group and (ii) the benzoate or chlorosubstituted benzoate group.

The hydration or solvation of these constituent parts in water and in *N,N*-dimethylformamide is particularly relevant to this discussion. We have demonstrated before[36] that the *p*-$OHPhN_2$ group in meta and para positions with respect to the carboxylate group behave as a delocalized group. The importance of London dispersion forces between delocalized solutes and localized solvents have been discussed elsewhere.[49] These forces are expected to be greater in *N,N*-dimethylformamide than in water. In water the benzoate group is better solvated than the *p*-$OHPhN_2$ group, whereas the opposite is true for *N,N*-dimethylformamide. It is indeed the introduction of the *p*-$OHPhN_2$ group which makes the (*p*-$OHPhN_2$)NaB electrolyte soluble in *N,N*-dimethylformamide. (Sodium benzoate is much less soluble in this solvent than in water).[50] Therefore, the solvation of the constituent parts of these anions are likely to play a significant role in the process of complexation. Consequently, it cannot be assumed that the same type of complexes found in water (axial) will necessarily occur in *N,N*-dimethylformamide.

Interpretation of the Complexation Process in *N,N*-Dimethylformamide. In order to interpret the enthalpy and entropy data in *N,N*-dimethylformamide, the complexation process is visualized as the transfer of these anions from *N,N*-dimethylformamide to a rich alcohlic medium (the cyclodextrin molecule, constituted by an interior cavity and two open ends, the open ends surrounded on one side by primary hydroxyl groups and on the other by secondary hydroxyl groups) in which these anions are known to interact strongly. Indeed our recent work has shown that among the three solvents considered (H_2O, MeOH, DMF) methanol is the best and DMF the poorest solvator for these anions. Therefore, it is reasonable to assume that the (*p*-hydroxyphenylazo)benzoate anions poorly solvated in *N,N*-dimethylformamide (particularly the carboxylate group) are likely to interact with the hydroxyl groups of the cyclodextrins. Comparison between the complexation data ($\Delta H°_c$ and $\Delta S°_c$) for (*m*- and (*p*-hydroxyphenylazo)benzoate anions and cyclodextrins with transfer data ($\Delta H°_t$, $\Delta S°_t$) for these anions from *N,N*-dimethylformamide to methanol (see Table II, values in brackets) support this interpretation. In fact, a remarkable agreement is found between these two sets of data. As far as the chlorosubstituted azobenzoate anions are concerned, it is most unlikely that the chlorine atom could be an active site of interaction with cyclodextrins. Therefore, for the purpose of this interpretation, 2Cl4(*p*-$OHPhN_2$)B^- and 4Cl3(*p*-$OHPhN_2$)B^- are related to *p*- and *m*-(*p*-$OHPhN_2$)B^- anions, respectively. Again, this interpretation is supported by the results given in Table II.

Agreement between complexation and transfer data is not found for *o*-(*p*-$OHPhN_2$)B^- anion and cyclodextrins for which heats of complexation are relatively small. This must be attributed to a reduction in the number of the active sites of the anion which are able to interact with the hydroxyl groups of the ligand. This effect is even more pronounced for 5Cl2- and 6Cl2(*p*-$OHPhN_2$)B^- anions. These two anions are unable to interact with cyclodextrins in *N,N*-dimethylformamide. The proximity between the carboxylate and the *p*-$OHPhN_2$ groups in *o*-(*p*-$OHPhN_2$)B^- or chlorosubstituted is likely to inhibit (partially or totally) interaction with the hydroxyl groups of the ligand which (unlike methanol) must be in relatively fixed positions within the structure of the ligand.

Conclusions Regarding Complexation Data. The conclusions regarding complexation of these anions and cyclodextrins are summarized as follows: (a) In water, the complexation process between cyclodextrins and these anions takes place through the inclusion of the *p*-$OHPhN_2$ group in the cavity of the ligand and an axial type complex results as shown in Figure 2. Indeed, in water, $\Delta H°_c$ and $\Delta S°_c$ values (Table II) are ligand dependent. This is a strong indication that it is the cavity of the cyclodextrin which provides the site complexation for these anions in this solvent. These findings are in line with the results reported by previous workers on the complexation of cyclodextrins and azo dyes.[13,15] (b) In *N,N*-dimethylformamide, the conclusion to be drawn is based on thermodynamic data (complexation and transfer data for the anion and the ligand) originating from three independent sets of measurements. These

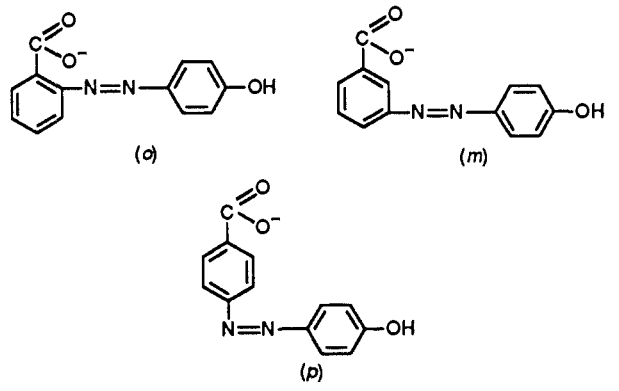

Figure 1. Structures of *o*-, *m*- and *p*-(*p*-hydroxyphenylazo)benzoate ions.

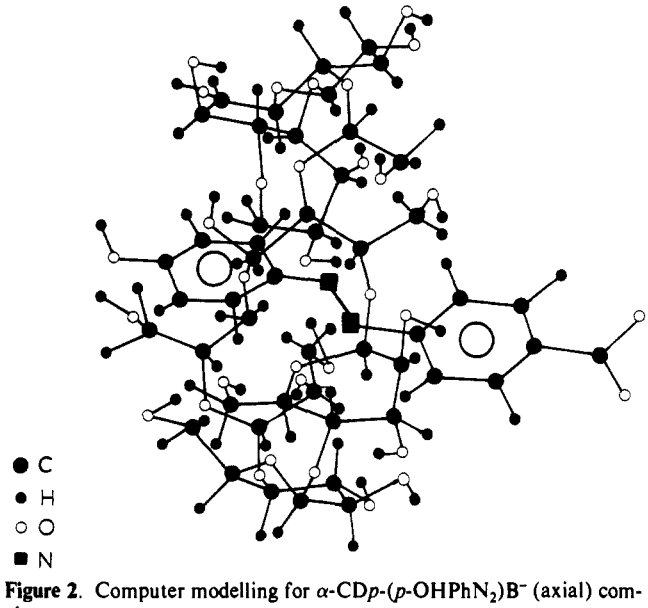

Figure 2. Computer modelling for α-CD*p*-(*p*-$OHPhN_2$)B^- (axial) complex.

parameters have been discussed separately throughout the paper. However, taking into account that this approach is novel in the study of cyclodextrin–substrate complexation reactions, these parameters are now collectively considered in order to draw some conclusions regarding the complexation reactions of cyclodextrin and these anions in *N,N*-dimethylformamide. Thus, the transfer data for cyclodextrins (Table I) shows a strong ligand–DMF interaction. The effect of the size of the cavity reflected on the $\Delta H°_t$ values of the various cyclodextrins is a substantial indication that the solvent is included in the cavity of the ligand. This is in accord with the data obtained for the complexation of these anions and cyclodextrins in DMF. Indeed, unlike water, $\Delta H°_c$ and $\Delta S°_c$ values do not reflect the effect of the ligand upon complexation with a given anion (in Table II). Thus, transfer and complexation data give strong indications that the cavity does not provide the site of complexation for these anions in *N,N*-dimethylformamide. Therefore, formation of inclusion complexes in this solvent is most unlikely to occur. Then, it is reasonable to consider that complexation of these anions with cyclodextrin takes place through the hydroxyl groups of the ligand (equatorial type complexes). On these bases, the complexation process is visualized as the transfer of these anions from DMF to a hydroxy rich environment (the cyclodextrins). This interpretation is supported by the agreement found between transfer data for these anions from DMF to methanol and complexation data (Table II). The structural conformation (obtained from computer calculations) which corresponds to the minimum energy (higher stability) for the formation of equatorial type complexes is that shown in Figure 3. Spectrophotometric (UV and NMR) studies are now in progress. It must be emphasized that formation of lid type complexes of cyclodextrins with cyclic monophosphates of ribonucleosides[51] and with *p*-nitrophenylacetate ions[52] has been recently reported.

Thermodynamic Parameters of Transfer of Anion Cyclodextrin Complexes. Availability of transfer data for the guest anion X^- and the

(51) Komiyama, M. *J. Am. Chem. Soc.* **1989**, *111*, 3046.
(52) Tee, O. S.; Hoeven, J. J. *J. Am. Chem. Soc.* **1989**, *111*, 8318.

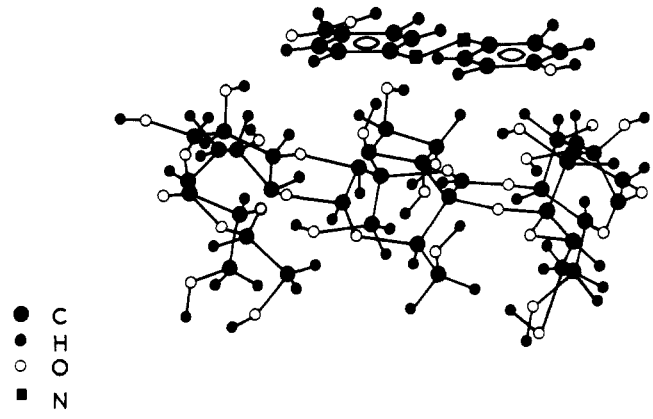

Figure 3. Computer modelling for α-CD*p*-(*p*-OHPhN$_2$)B$^-$ (equatorial) complex.

cyclodextrin ligand (CD) and data for the complexation of anions with α- and γ-cyclodextrin in water and in *N*,*N*-dimethylformamide permit the calculation of single ion transfer parameters ($\Delta P°_t = \Delta G°_t$, $\Delta H°_t$, or $\Delta S°_t$) of the anion–cyclodextrin complex (X$^-$CD) from water to *N*,*N*-dimethylformamide. For this purpose, the following thermodynamic cycle is used.

$$\begin{array}{ccc} X^-(H_2O) + CD(H_2O) & \xrightarrow{\Delta P°_c} & X^-CD(H_2O) \\ \downarrow \Delta P°_t(X^-) \quad \downarrow \Delta P°_t(CD) & & \downarrow \Delta P°_t(X^-CD) \\ X^-(DMF) + CD(DMF) & \xrightarrow{\Delta P°_c} & X^-CD(DMF) \end{array} \quad (2)$$

The data shown in Table III are the first reported on the transfer of cyclodextrin complexes from water to any nonaqueous solvent. The data are based on the Ph_4AsPh_4B convention. It must be emphasized that relative transfer data for anions are not dependent on any extrathermodynamic convention.

Transfer Free Energy. Examination of $\Delta G°_c$ values in water and in *N*,*N*-dimethylformamide (Table II) leads to the suggestion that

$$\Delta G°_c(H_2O) \cong \Delta G°_c(DMF) \quad (3)$$

Therefore, taking into account (3) and the thermodynamic cycle (2), it emerges that

$$\Delta G°_t X^-CD(H_2O \rightarrow DMF) \cong \Delta G°_t X^-(H_2O \rightarrow DMF) + \Delta G°_t CD(H_2O \rightarrow DMF) \quad (4)$$

The $\Delta G°_t$ values given in Table III support this interpretation. An illustrative example is given by inserting in (2) transfer free energy data from $H_2O \rightarrow DMF$ for both *m*-(*p*-hydroxyphenylazo)benzoate anion[39] and the α-cyclodextrin ligand (Table I) and complexation data for the same anion and ligand in water and in *N*,*N*-dimethylformamide (Table II). $\Delta G°$ values are in kJ mol^{-1}.

$$\begin{array}{ccc} m\text{-}(p\text{-}OHPhN_2)B^-(H_2O) + \alpha\text{-}CD(H_2O) & \xrightarrow{-21.23} & m\text{-}(p\text{-}OHPhN_2)B^-\alpha\text{-}CD(H_2O) \\ \downarrow 8.90 \qquad\qquad \downarrow 1.74 & & \downarrow 12.06 \\ m\text{-}(p\text{-}OHPhN_2)B^-(DMF) + \alpha\text{-}CD(DMF) & \xrightarrow{-19.81} & m\text{-}(p\text{-}OHPhN_2)B^-\alpha\text{-}CD(DMF) \end{array} \quad (5)$$

As far as solvation is concerned, $\Delta G°_t$ is the most significant thermodynamic parameter. Therefore, we conclude that no significant change in solvation occurs in both the ligand and the anions upon complexation in this solvent system.

Table III. Single Ion Free Energies, Enthalpies, and Entropies of Transfer of Anion Cyclodextrin Complexes from Water to *N*,*N*-Dimethylformamide at 298.15 K on the Molar Scale[b]

complex anion (CDX$^-$)	$\Delta G°_t$, kJ mol^{-1} $H_2O \rightarrow$ DMF[a]	$\Delta H°_t$, kJ mol^{-1} $H_2O \rightarrow$ DMF[a]	$\Delta S°_t$, J K^{-1} mol^{-1} $H_2O \rightarrow$ DMF[a]
m-(*p*-OHPhN$_2$)B$^-$α-CD	12.06	−28.08	−136.0
p-(*p*-OHPhN$_2$)B$^-$α-CD	14.17	−28.34	−143.2
2Cl4(*p*-OHPhN$_2$)B$^-$α-CD	12.03	−7.41	−66.6
m-(*p*-OHPhN$_2$)B$^-$γ-CD	9.89	−52.38	−208.9
p-(*p*-OHPhN$_2$)B$^-$γ-CD	14.67	−52.51	−225.3
2Cl4(*p*-OHPhN$_2$)B$^-$γ-CD	11.00	−32.11	−144.6
4Cl3(*p*-OHPhN$_2$)B$^-$γ-CD	20.35	−47.79	−228.5

[a] Calculated by using eq 2, see text. Single ion transfer values for X$^-$($H_2O \rightarrow$ DMF) from ref 39. Transfer data for α- and γ-cyclodextrin from water to DMF (Table I) and complexation data (Table II) in water and DMF. [b] Data based on the Ph_4AsPh_4B convention.

Transfer Enthalpy and Entropy Data. The $\Delta G°_t$ values result from the contribution of $\Delta H°_t$ and $\Delta S°_t$ values. Therefore, a similar example to that given in terms of $\Delta G°$ is now presented in terms of $\Delta H°$ (kJ mol^{-1}).

$$\begin{array}{ccc} m\text{-}(p\text{-}OHPhN_2)B^-(H_2O) + \alpha\text{-}CD(H_2O) & \xrightarrow{-33.35} & m\text{-}(p\text{-}OHPhN_2)B^-\alpha\text{-}CD(H_2O) \\ \downarrow 4.28 \qquad\qquad \downarrow -44.34 & & \downarrow -28.08 \\ m\text{-}(p\text{-}OHPhN_2)B^-(DMF) + \alpha\text{-}CD(DMF) & \xrightarrow{-21.37} & m\text{-}(p\text{-}OHPhN_2)B^-\alpha\text{-}CD(DMF) \end{array} \quad (6)$$

and ΔS (JK^{-1} mol^{-1})

$$\begin{array}{ccc} m\text{-}(p\text{-}OHPhN_2)B^-(H_2O) + \alpha\text{-}CD(H_2O) & \xrightarrow{-40.6} & m\text{-}(p\text{-}OHPhN_2)B^-\alpha\text{-}CD(H_2O) \\ \downarrow -15.5 \qquad\qquad \downarrow -155.9 & & \downarrow -136.0 \\ m\text{-}(p\text{-}OHPhN_2)B^-(DMF) + \alpha\text{-}CD(DMF) & \xrightarrow{-5.2} & m\text{-}(p\text{-}OHPhN_2)B^-\alpha\text{-}CD(DMF) \end{array} \quad (7)$$

Enthalpy and entropy data for the transfer of the anion cyclodextrin complex are largely influenced by corresponding data for the transfer of the ligand and $\Delta H°_t$ values being largely compensated by $\Delta S°_t$ values as a result of the effect of solvent–solvent interactions taking place during the transfer process. It is remarkable to find that the same enthalpic and entropic contributions are observed for *m*- and *p*-(*p*-OHPhN$_2$)B$^-$CD anions. These data reflect that these two anions are likely to have the same groups exposed to solvation in the axial (water) and in the equatorial (DMF) complexes.

Final Remarks

From the results obtained in this work the following conclusions emerge: (a) Further research into the solvation properties of cyclodextrins in nonaqueous media is needed. Indeed, these studies are relevant in assessing whether or not cyclodextrins could serve as potential receptors in these media. (b) Transfer data for the guest species to a reaction medium containing functional groups common to receptors are important parameters in the interpretation of complexation processes involving cyclodextrins. In a more general context, this approach needs to be explored in molecular recognition processes.