Molecular Recognition of Amphiphilic Di(dodecyl)barbituric Acid with Long-Chain Alkylated Adenine and Thymine Derivatives

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The interaction of didodecylbarbituric acid with 9-hexadecyladenine or 1-hexadecylthymine through molecular recognition of their complementary moieties is investigated in aprotic solvents and in the bulk. In solution, complex formation was established by NMR spectroscopy while their association constants were determined in heptane by UV spectroscopy at low concentrations in contrast to the determination with NMR or infrared spectroscopy which requires higher concentrations. Intermolecular hydrogen bonding complexation was investigated in the bulk phase, by FT-IR spectroscopy, as a function of the temperature. Due to the bulkiness of the adenine derivative, 1:1 complexation occurs with barbituric acid derivative although the latter possesses two binding sites. The complex formed is stable within a broad temperature range, viz., from room temperature to the second endothermic transition, associated with the complete melting of the interacting mixture. Thymine derivative, on the contrary, forms with alkylated barbituric acid both 1:1 and 1:2 hydrogen-bonded complexes which are stable even at temperatures exceeding second phase transition attributed again to the completion of the sample melting.

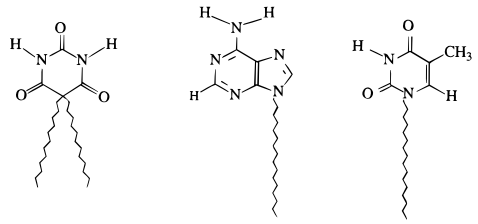
Introduction

Barbituric acid derivatives have been extensively employed in molecular recognition experiments in the bulk,[1] in solution,[2−5] and organized at interfaces.[6−11] The presence in barbituric acid and its derivatives of two recognition sites (O═C−NH−C═O), which are susceptible to hydrogen-bonding interaction by molecules bearing complementary functionalities, could be responsible, in principle, for the formation of a multiplicity of products. Depending on the nature of complementary molecules, barbituric acid or its derivatives either are encased in a cavity[4,5] or are interacting forming oligomeric or polymeric products.[1,7−9] The latter complexes are formed when the interacting complementary molecule also bears two hydrogen-bonding active moieties.

In the present study the amphiphilic-type di(*n*-dodecyl)-barbituric acid was synthesized and subsequently interacted with the complementary alkylated nucleobases, viz, with 9-hexadecyladenine (A-C_{16}) and 1-hexadecylthymine (T-C_{16}), Scheme 1, in melt or in solution for the formation of the respective association complexes. The determination of the binding constants of the complexes in solution and establishment of their structures in the melt are the main objectives of this investigation.

In living organisms an analogous interaction between barbiturates and nucleic acids may lead to destruction of hydrogen bonds between complementary nucleobases. From this aspect the interactions investigated could be useful as models of important biological reactions. The introduction of the long aliphatic chains in nucleobases and barbituric acid renders these molecules sufficiently soluble in nonpolar solvents, where hydrogen bonding between complementary moieties is favored and stacking is avoided as it is the case in aqueous solutions.[12] It is interesting to note that the commonly employed nonpolar solvents, such as chloroform or dichloromethane, form hydrogen bonds with the associating molecules acting in this way antagonistically with the interacting substrates and leading to drastically reduced association constants.[13] Furthermore, interactions that were not even detected in $CHCl_3$ were quantitatively measured in noninteracting solvents.[14]

SCHEME 1



Experimental Section

Synthesis of Ethyl Di(*n*-dodecyl) Malonate. To a completely dried flask 1.55 g (0.067 mol) of sodium metal was reacted with about 25 mL of absolute alcohol. The solution of sodium ethoxide that was obtained was allowed to reach room temperature and subsequently reacted with 5.0 g (0.03 mol) of ethyl malonate at 80 °C for ca. 15 min. The mixture was cooled down to room temperature, and 15.95 g (0.064 mol) of dodecyl bromide was slowly added. The mixture was heated at 210−220 °C for several hours (72 h). Most of the alcohol was distilled off, and to the remaining material water was added; subsequently, the mixture was extracted with ethyl ether. The ethereal solution was washed with water, and the ether extract was dried with magnesium sulfate. Ether was distilled off, and from the remaining oil unreacted dodecyl bromide was removed by distillation under vacuum (3−4 mm Hg) at 54 °C. The remaining oil was purified by oiling out from methanol.

Anal. Calcd for $C_{31}H_{60}O_4$: C, 74.95; H, 12.17. Found: C, 74.85; H, 12.51.

Synthesis of Di(*n*-dodecyl)barbituric Acid. To 0.34 g (0.0148 mol) of sodium, 20 mL of absolute alcohol was added. When sodium had reacted, 3.00 g (0.006 mol) of ethyl didodecylmalonate and 0.48 g (0.008 mol) of urea were added.

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The mixture was heated at 80 °C for 24 h, and subsequently alcohol was distilled off. The temperature was raised to 120 °C and maintained at this level for about 16 h. After the mixture was cooled, dilute sulfuric acid was added, and the material was stirred for several hours. The mixture was filtered, and the solid was recrystallized from hexane: mp 105 °C.

Anal. Calcd for $C_{28}H_{52}O_3N_2$: C, 72.07; H, 11.23; N, 5.98. Found: C, 72.0; H, 11.39; N, 5.66.

Synthesis of Alkylated Nucleobases. The synthesis of 1-hexadecylthymine and 9-hexadecyladenine has recently been described.[15]

Formation of Complexes in the Bulk. One molar equivalent of the barbituric acid derivative was mixed with 1 or 2 equiv of the alkylated nucleobases, and each mixture was heated under vacuum at 130 °C for about 3 min. The materials obtained were used for the subsequent characterization.

Characterization. Difference absorption spectra were recorded on a Cary 210 spectrophotometer. All spectra were obtained in 5 or 10 cm path cells at 21 ± 1 °C using extensively dried chromatography grade heptane. The didodecylbarbituric acid concentration ranged from approximately the concentration of the adenine or thymine derivative employed up to its 10-fold. Since the receptor that was added was dissolved in the solution of the substrate, the total concentration of the substrate remained constant throughout the titration. The experiments are performed at a concentration range of the receptor where Beer's law is obeyed.

FT-IR spectra were obtained with a Nicolet Magna 550 FT-IR spectrometer at a resolution of 2 cm^{-1} combined with the Variable Temperature cell VLT-2 (Research & Industrial Instruments Company). Over 200 scans were signal averaged and stored for subsequent processing.

Optical microscopy studies were performed with a Reichert polarizing microscope equipped with a Linkam TMS 91 controller and a hot stage.

For the DSC experiments a Perkin Elmer DSC 7 calorimeter was employed coupled with a TAC 7/3 Controller at a cooling rate of 10 °C/min.

Proton NMR spectra were obtained employing a Bruker AC 250 spectrometer operating at 250 MHz. Solutions of 10^{-2} M in chloroform-*d* were used, and chemical shifts were measured relative to tetramethylsilane.

Determination of Association Constants of the Complexes in Solution. For the determination of the binding constants with UV absorption the mathematical treatment is essentially the same as that previously described.[14,16,17] According to the assumptions of Lancelot[14] the concentration of the receptor should be very high compared to the concentration of the substrate. Also the receptor must not absorb at the wavelength of interest. The first assumption is not always possible due to solubility limitations and additionally is not acceptable according to the guidelines proposed by Wilcox.[18] The second assumption restricts the application of this method to nonabsorbing receptors. However, with the currently employed computer programs, adherence to the above mentioned assumptions can be avoided, provided of course that the extinction coefficient of the receptor is not large compared to the extinction coefficient of the complex formed.

As a first approximation, the self-association of adenine or thymine derivatives was neglected in the models used, since this self-association is expected to modify the free concentrations of the substrates by less than 0.5%.[14] It is not therefore surprising that in a recent study by Pistolis et al.[13] it was shown that the elaboration of more complex models, with the incorporation of adenine dimers, led to essentially the same value for the association constant as that derived from simpler models in which this dimerization was not taken into account.

For the mathematical description of complex formation, it was assumed that the association leads to the formation of only a 1:1 complex having an association constant K according to the following general equation

$$A + B \rightleftharpoons AB$$

The self-association of the receptor is also taken into account

$$B + B \rightleftharpoons B_2$$

having a self-association constant of K_D.

The absorbance, OD, measured at a certain wavelength, with the assumption that B does not absorb, is expressed as

$$OD = l([A]\epsilon_A + [AB]\epsilon_{AB})$$

where ϵ_A and ϵ_{AB} are the extinction coefficients of A and AB respectively, [A] and [AB] are their concentrations, and l is the path length, while the absorbance in the reference cell, OD_r, is expressed as:

$$OD_r = l[A_0]\epsilon_A$$

where $[A_0]$ is the total concentration of A.

Therefore the difference absorbance, Δ(OD), is expressed as

$$\Delta(OD) = l[AB](\epsilon_{AB} - \epsilon_A) \quad (1)$$

On the other hand, if it is assumed that B absorbs at the wavelength of interest the difference absorbance can easily be expressed as

$$\Delta(OD) = l([AB](\epsilon_{AB} - \epsilon_A - \epsilon_B) - [B_o]\epsilon_B) \quad (2)$$

where $[B_0]$ is the total concentration of B and ϵ_B is its extinction coefficient.

The concentration [AB] of the complex can be expressed as a function of the variable $[B_0]$, considering $[A_0]$, K, and K_D as constants, using mass and equilibrium equations.

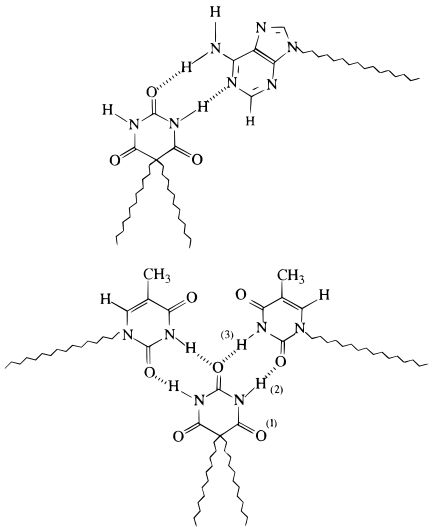
Minimization of the sum of squared deviations between the observed experimental data points and those calculated with the proposed model was performed employing the nonlinear least-squares fitting program Minsq (MicroMath Scientific Software) which is based on a modified Levenberg−Marquardt algorithm.

Results and Discussion

The structures that may be obtained in principle by the interaction of the barbituric acid derivative with the alkylated nucleobases are shown in Scheme 2, including dimeric and trimeric complexes. It has to be noted, however, that along with the complexes shown in this scheme, there is also the possibility of the formation of complexes with the nucleobases through hydrogen-bonding interactions at the 1- and 2-position of the barbituric acid derivative.

Complex Formation in Solution. Formation of complexes in solution between didodecylbarbituric acid and adenine or thymine derivatives was established by proton NMR. Thus, when A-C_{16} was dissolved in deuterated chloroform containing the barbituric acid derivative marked, downfield chemical shifts of the participating protons were observed. Thus for barbituric acid there is a shift from 8.30 down to 10.15 ppm, while the chemical shift for the N−H proton of the adenine derivative changes from 5.46 to 7.12 ppm. In the same manner and under identical experimental conditions for the barbituric acid deriva-

SCHEME 2



tive and T-C_{16} pair, the variation of the chemical shift for the first compound is from 8.30 down to 8.54 ppm and from 8.15 to 8.77 ppm for the N-H of the thymine derivative. Thus according to NMR experiments, the binding affinity is more effective between barbituric acid and adenine than it is for barbituric and thymine derivatives.

The determination of equilibrium constants in solution was primarily performed employing NMR and infrared methods.[2,3] However, the limited solubility in aprotic solvents of the alkylated derivatives in question renders attractive UV[14,16,17] or fluorescence spectroscopy[13,19] methods. In this case there is an advantage since the low concentrations employed justify the approximation of determining the true thermodynamic equilibrium constants which are based on activities. Another advantage is that it is easy to follow the "rules" put forward by Wilcox[18] regarding the optimum concentrations of the interacting molecules for obtaining a valid association constant.

The binding of didodecylbarbituric acid with alkylated nucleobases can be treated in an analogous fashion. Didodecylbarbituric acid absorbs in the wavelength of interest ($\epsilon = 20$ at 277 nm and $\epsilon = 80$ at 293 nm), and therefore eq 2 is being used. In the present study the dimerization of alkylated barbituric acid is neglected, as it is also the case with the alkylated nucleobases. In fact, continuous dilution of a solution of this barbiturate in heptane, at the concentration range of interest, revealed a linear decrease of absorption, and therefore it was not possible to estimate the dimerization constant and the molar absorptivity of the complex. This is also needed for the complete description of the model. Certainly this does not imply that dimerization does not occur. The constant is anticipated in the order of a few hundreds (as in adenine and thymine derivatives), and therefore higher concentrations should be used[18] to measure the self-association constant. Unfortunately due to the low solubility of this derivative (ca 2×10^{-4} M), this constant cannot be measured. If dimerization of didodecylbarbiturate is, however, included in the model with the additional assumption that its molar absorptivity is zero at the wavelength of interest, a dimerization constant of 245 ± 112 is derived. This is a reasonable value if it is considered that cyclohexyluracil is estimated to have an association constant of 472 mol^{-1} in cyclohexane at 10 °C.[14] By using this model, the association constant between adenine and barbituric derivative is found to be 7300 ± 100 instead of the value of 8930 ± 280 mol^{-1} (Table 1) which is determined if self-dimerization is not taken into consideration.

TABLE 1: Experimentally Determined Association Constants (K) and Molar Absorptivities (ϵ) at Wavelength λ of Complexes Formed between Didodecylbarbituric Acid and Alkylated Adenine and Thymine Derivatives in Heptane at 21 °C

	K (M^{-1})	ϵ (M^{-1} cm^{-1})	λ (nm)
9-hexadecyladenine	8930 ± 280	8360 ± 100	276
1-hexadecylthymine	5560 ± 670	1230 ± 30	293

Previous results[2] had determined the binding constants between adenine and barbituric acid derivatives in $CHCl_3$. It was not, however, possible to determine the binding constant of barbituric acid derivatives with thymine or uracil derivatives due to solvent perturbation in the complex formation. However, by using IR spectroscopy, evidence was given[2,20] that such complexes do form in solution.

In this connection and in order to justify the relatively low association constants that were obtained between barbituric acid derivative and these nucleobases, it has to be noted that molecular recognition interactions are equilibria processes, which according to recent results[21] are affected by participating secondary forces stabilizing the intermolecular complexes. In order for these secondary forces to be comparatively more effective for this stabilization, most or all of the acceptor moieties must be located on one of the interacting molecules while donors are located on the other. In this respect, it has to be noted that the secondary forces associated with barbituric acid and its derivatives are not very strong since the system "acceptor−donor−acceptor" is a characteristic feature of their structure.

Complex Formation in the Melt. Recognition experiments were performed in the melt phase. The method was preferred over the one performed by slow evaporation from solution in order to avoid the destructive effect of the remaining solvent on the complexes.

For the hydrogen-bonded complexes under investigation, segregation of the central, heterocyclic-based polar segment from the lipophilic aliphatic chains occurs. In principle, therefore, structural conditions are encountered for the formation in the bulk of complexes with organizational characteristics.[22−25] The formation of these complexes was established by FT-IR spectroscopy. It is, however, appropriate before proceeding to infrared studies to investigate the thermal behavior of the complexes with DSC and optical microscopy. FT-IR spectra were obtained within a broad temperature range and in between the observed phase transitions. In this manner the formation itself and the type of complexes existing between these phase transitions were investigated.

Thermal Studies. The DSC trace (Figure 1) of the 1:1 mixture of adenine−barbituric acid derivatives shows a weak broad exothermic peak and two endothermic peaks. The exothermic peak is centered at approximately 70 °C and is attributed to a crystallization transition. This is presumably due to the geometry of the interacting molecules in the melt during the preparation of the complex, which on cooling produce metastable crystals. Similar results have been obtained for the interaction of alkylated adenine and thymine derivatives.[15] The onsets of the two endothermic transitions were observed at 80 and at 116 °C. For comparison, the barbituric and adenine derivatives melt at 105 and 123 °C, respectively. Therefore, the first endothermic transition can be the result of a eutectic behavior, while the second rather broad transition may be primarily attributed to the melting of the complex affected by a small amount of unbound adenine. A small shoulder at approximately 103 °C is most probably due to the presence of a small fraction of uncomplexed barbituric derivative.

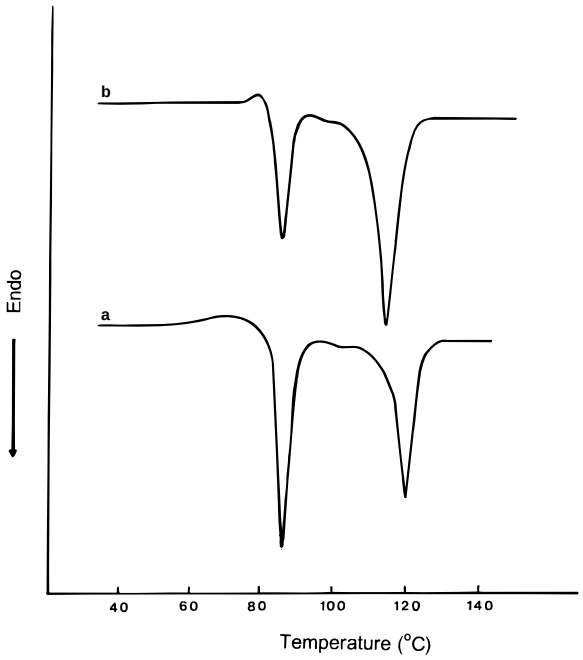


Figure 1. DSC traces of (a) 1:1 and (b) 2:1 mixtures of adenine−barbituric derivatives.

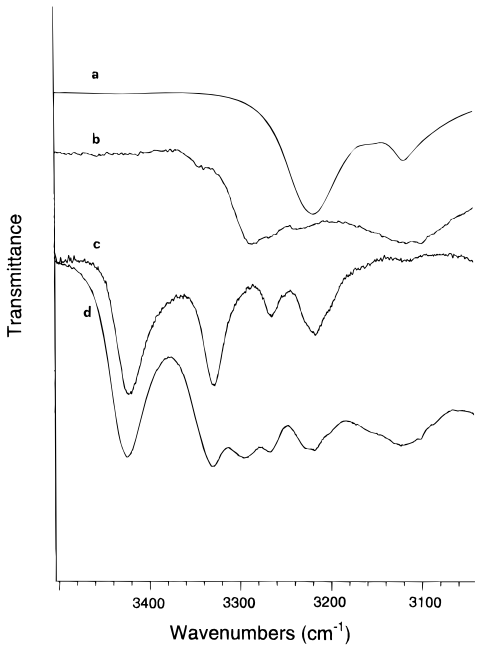


Figure 2. FT-IR spectra of (a) barbituric and (b) adenine derivatives as well as of their (c) 1:1 and (d) 1:2 mixtures.

For the mixture adenine−barbituric derivatives (2:1), a small exothermic peak (Figure 1) is observed at approximately 78 °C and two endothermic transitions are seen at 81 and 109 °C. The second peak is now of higher intensity due to the existence of significant amount of uncomplexed adenine, in agreement with FT-IR spectra, while the small peak attributed to uncomplexed barbituric is small and shown at approximately 100 °C.

The DSC trace of the 1:1 mixture of thymine−barbituric derivatives shows a small exotherm at approximately 80 °C and only one peak at 93 °C. For comparison the thymine derivative melts at 122 °C. For the 2:1 mixture an exothermic peak centered at 88 °C and an endothermic peak at 93 °C were again observed. A rather small broad peak in the region of 105−120 °C can be assigned to the uncomplexed thymine. It is therefore clear that only a small quantity of the added thymine is not participating in the complex formation.

The phase transitions observed with polarized microscope confirm the transitions observed in DSC experiments. The melts produced do not exhibit textures characteristic of any known liquid crystalline phase, these textures being attributed to tiny crystals of high-melting materials floating within the melted phase of the low-temperature melting material.

FT-IR Studies. The infrared spectrum of the 1:1 mixture of adenine−barbituric derivatives does not show the adenine bands in the NH_2 stretching region, i.e., at 3298, 3239, and 3110 cm^{-1}, attributed to polymeric structures of the adenine derivative[26] in the bulk phase. Similarly, the 3120 cm^{-1} band of the barbituric derivative attributed to the NH stretching mode is not detected, while three new bands at 3424, 3329, and 3267 cm^{-1} appear in the spectrum of the mixture (Figure 2). The bands at higher wavelengths, i.e., 3424 and 3329 cm^{-1}, are attributed to the existence of a non-hydrogen-bonded NH group of the adenine moiety[2,26,27] implying a 1:1 binding of barbituric and adenine moieties. In this respect one hydrogen of the NH_2 adenine group remains free, giving rise to the high-intensity symmetric and antisymmetric stretching vibration.[2,26] In the spectrum of the 2:1 mixture of adenine−barbituric derivatives, the three new bands that arise from the complexation of the two molecules are also present. However, the adenine bands at 3298 and at 3110 cm^{-1} are observed. Therefore, the additional adenine units are not bound to the barbituric acid derivative.

Similar results were obtained in the 1700−1600 cm^{-1} range of the spectra. For the 1:1 mixture, the adenine-bonded NH_2 scissoring mode at 1672 cm^{-1} and the 1705 and 1717 cm^{-1} ν(C═O) bands of the barbituric unit are not present. On the contrary, new bands at 1682, 1713, and 1647 cm^{-1} are observed. For the 2:1 mixture broad bands at 1680 and 1720 cm^{-1}, which probably is the sum of the 1:1 complex and the additional free adenine units, are observed.

It is therefore clear that only one adenine species can be bound to each barbituric moiety in the solid phase although there are two "binding sites" available, apparently due to the bulkiness of the adenine molecule. However, the tendency to bind adenine in 1:1 ratio is strong since we observe the breakage of the linear polymeric structure of adenine[26] in favor of the formation of a dimeric structure between the two units. This result is also in agreement with crystallographic studies of 9-ethyladenine-5,5-diethylbarbituric acid[28] where extended planar sequences of mutually hydrogen-bonded barbiturate and adenine rings were reported.

As the 1:1 mixture is heated, the 3424 cm^{-1} band shifts to higher wavelengths and decreases in intensity (Figure 3). After the first transition, above 80 °C, this band is shifted at 3430 cm^{-1}, while above the second transition, at temperatures above 120 °C, the band becomes weak and two new broad bands can be observed at 3490 and 3400 cm^{-1} which are attributed to the free NH_2 stretching mode.[20,26,27] Also the 3329 band decreases in intensity as well as the 3266 cm^{-1} band which in addition gradually shifts to 3262 cm^{-1}. The bands in the 1700−1600 cm^{-1} region also exhibit the same behavior, becoming broader and less intense above the second transition. In the 2:1 mixture a similar trend was again observed. The 3424 band shifts to 3432 cm^{-1} above the first transition, while above the second transition the free NH_2 band at 3488 cm^{-1} appears again. Similarly, all the new bands of the complex above the second transition decrease in intensity. It is therefore concluded that the second transition is associated with the destruction of the complex, while the first transition is basically associated with a small modification of the binding forces.

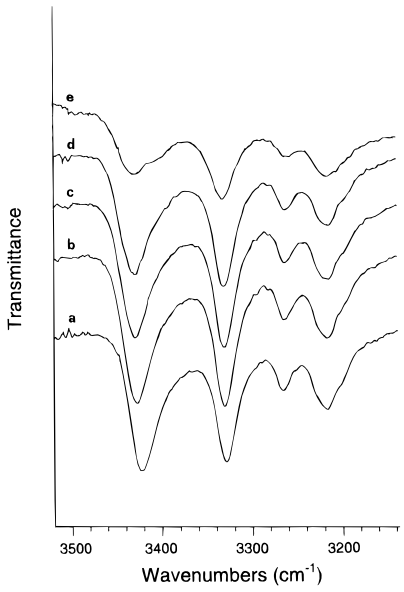


Figure 3. Survey FT-IR spectra of 1:1 adenine−barbituric derivatives as a function of temperature: (a) 25, (b) 75, (c) 95, (d) 110, and (e) 130 °C.

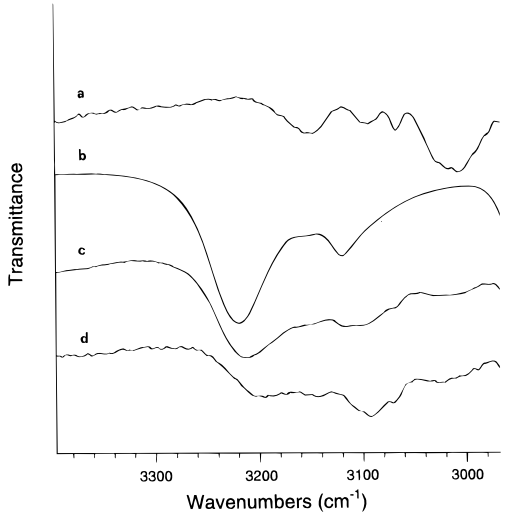


Figure 4. FT-IR spectra of (a) thymine and (b) barbituric derivatives as well as of their (c) 1:1 and (d) 1:2 mixtures.

The spectrum of the 1:1 mixture of thymine−barbituric derivative has a peak at 3215 cm^{-1} (Figure 4) instead of the expected one at 3220 cm^{-1} which is present in the barbituric derivative spectrum and also in the sum of the spectra of the two compounds. In the 2:1 thymine−barbituric derivatives spectrum, this peak is further shifted at 3200. Another new feature in the spectra of the two mixtures is a relatively strong band located at 3096 cm^{-1}. This band is more intense in the spectrum of the 2:1 mixture. This peak cannot originate from the uncomplexed thymine, which is absorbing in this region, as evidenced by the calculated sum of the spectra of pure compounds. In addition the intense peak of pure thymine at 3150 cm^{-1} is not as strong as expected in the spectra of the mixtures. Therefore, complexation in the solid phase between the thymine and the barbituric derivatives does take place and is more strong at a 2:1 ratio, indicating qualitatively that two thymine units bind to each barbituric moiety. This is not unexpected since the barbituric derivative has two binding sites available to associate with the thymine group.

Similar results can be obtained from the carbonyl stretching vibrations that are observed. The main band of the barbituric carbonyl group at 1705 cm^{-1} is shifted in the 1:1 complex at 1698 and at 1694 cm^{-1} in the 2:1 complex. The calculated sum of the two spectra exhibits two peaks at 1702 and at 1684 cm^{-1} which are much sharper than those of the mixture. The 1684 band of the pure thymine is also present in the 1:1 complex but is less strong than that expected from the calculated sum of the two spectra. Additionally this band in the 2:1 complex is less intense relative to the 1694 cm^{-1} peak, showing that added thymine strongly binds with barbituric units.

Upon increasing the temperature in the 1:1 thymine−barbituric spectra, we observe that the 3213 cm^{-1} band becomes broad above 100 °C, which corresponds to the first transition. Above the second transition a new band appears at 3407 cm^{-1}, while the 3096 cm^{-1} band becomes less intense and the 3210 cm^{-1} band broader. In the ν(C═O) region no change is observed up to the second transition. Above this temperature the 1698 cm^{-1} band becomes much broader. For the 2:1 thymine−barbituric mixture the 3195 cm^{-1} band is relatively stable up to the second transition. At higher temperatures it broadens and shifts to 3205 cm^{-1}. The new band at 3407 cm^{-1} is again observed. The changes of the other bands that arise from the thymine−barbituric complexation are similar to those of the 1:1 mixture. Therefore, the second transition is related to a partial destruction of the complexation as evidenced by the free NH band at 3407 cm^{-1}. However, the complexation is present even in the completely melted phase, i.e., when the small crystallites disappear, since bands originating from the association can be observed.

Concluding Remarks

Hydrogen-bonding interaction of didodecylbarbituric acid with 9-hexadecyladenine or 1-hexadecylthymine, through molecular recognition of their complementary moieties, is established by NMR in chloroform. The association constants of these complementary molecules in heptane were determined by UV spectroscopy, at low concentrations, in contrast to the determination with NMR or infrared spectroscopy which requires higher concentrations. In the bulk phase, FT-IR spectroscopy, in conjunction with thermal studies, was employed for the investigation of the intermolecular complexation between the same complementary molecules. Thus the adenine derivative within a broad temperature range, viz., from room temperature to its second endothermic transition, forms only an 1:1 complex with the barbituric acid derivative although the latter possesses two binding sites. The thymine derivative forms on the contrary, with alkylated barbituric acid, both 1:1 and 1:2 hydrogen-bonded complexes which are not completely destructed even at temperatures exceeding the second phase transition, where complete melting of the sample occurs.

References and Notes

(1) Lehn, J. M.; Mascal, M.; DeCian, A.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1990**, 479.
(2) Buchet, R.; Sandorfy, C. *J. Phys. Chem.* **1983**, *87*, 275.
(3) Buchet, R.; Sandorfy, C. *J. Phys. Chem.* **1984**, *88*, 3274.
(4) Hamilton, A. D. *J. Chem. Educ.* **1990**, *67*, 821.
(5) Chang, S. K.; Engen, D. V.; Fan, E.; Hamilton, A. D. *J. Am. Chem. Soc.* **1990**, *113*, 7640.
(6) Honda, Y.; Kurihara, K.; Kunitake, T. *Chem. Lett.* **1991**, 681.
(7) Ahuga, R.; Caruso, P.-L.; Mobius, D.; Paulus, W.; Ringsdorf, H.; Wildburg, G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1033.
(8) Bohanon, T. M.; Denziger, S.; Fink, R.; Paulus, W.; Ringsdorf, H.; Weck, M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 58.
(9) Kimizuka, N.; Kawasaki, T.; Kunitake, T. *J. Am. Chem. Soc.* **1993**, *115*, 4387.
(10) Motesharei, K.; Myles, D. C. *J. Am. Chem. Soc.* **1994**, *116*, 7413.
(11) Kimizuka N.; Kawasaki T.; Kunitake T. *Chem. Lett.* **1994**, 1399.
(12) Rebek, J., Jr. *Angew. Chem., Int. Engl. Ed.* **1990**, *29*, 245.

(13) Pistolis, G.; Paleos, C. M.; Malliaris, A. *J. Phys. Chem*. **1995**, *99*, 8896.
(14) Lancelot, G. *Biochimie* **1977**, *59*, 57.
(15) Michas, J.; Paleos, C. M.; Skoulios, A.; Weber, P. *Mol. Cryst. Liq. Cryst*. **1995**, *239*, 245.
(16) Long, J. D.; Drago, R. S. *J. Chem. Educ*. **1982**, *59*, 1037.
(17) Lancelot, G. *J. Am. Chem. Soc*. **1977**, *99*, 7037.
(18) Wilcox, C. S. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H. J., Durr, H. Eds.; VCH: Weinheim, 1991; p 123.
(19) (a) Aoki, I.; Harada, T.; Sakaki, T.; Kawahara, Y.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1341. (b) Aoki, I.; Kawahara, Y.; Sakaki, T.; Harada, T.; Shinkai S. *Bull. Chem. Soc. Jpn*. **1993**, *66*, 927. (c) Yoon, J.; Gzarnik, A. W. *J. Am. Chem. Soc.* **1992**, *114*, 5874.
(20) Buchet, R.; Sandorfy, C. *J. Phys. Chem*. **1984**, *88*, 3274.
(21) (a) Pranata, J.; Wierschke, S. G.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1991**, *113*, 2810. (b) Pranata, J.; Wierschke, S. G.; Jorgensen, W. L. *J. Am. Chem. Soc*. **1990**, *112*, 2008.
(22) Lehn, J. M. *Makromol. Chem. Macromol. Symp*. **1993**, *69*, 1.
(23) Brienne, M. J.; Galard, J.; Lehn, J. M.; Stibor, J. *J. Chem. Soc., Chem. Commun*. **1989**, 1868.
(24) Paleos, C. M. *Mol. Cryst. Liq. Cryst.* **1994**, *243*, 159.
(25) Paleos, C. M.; Tsiourvas, D. *Angew. Chem., Int. Engl. Ed*. **1995**, *34*, 1696.
(26) Kyogoku, Y.; Lord, R. C.; Rich, A. *J. Am. Chem. Soc.* **1967**, *89*, 496.
(27) Kyogoku, Y.; Lord, R. C.; Rich, A. *Nature* **1968**, *218*, 69.
(28) Voet, D. *J. Am. Chem. Soc.* **1972**, *94*, 8213.

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