Molecular Complexes, 8 [1]

Formation Constants and Topology of Complexes of Tetramethyluric Acid. An ^1H NMR Reinvestigation Based on the AUS Concept and on the Shift Difference Method. A Revised Complex Topology

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Dedicated to Professor Joachim Knabe on the occasion of his 65th birthday

Z. Naturforsch. **41b**, 1461–1470 (1986); received July 14, 1986

Formation Constants of Molecular Complexes, Face-to-Face Complexes, Tetramethyluric Acid Complexes, Arenes, ^1H NMR Spectra

The complexation of tetramethyluric acid (TMU) with the donors (D) benzene (B), biphenyl (BP), naphthalene (N), and phenanthrene (P) in CCl_4 is investigated by ^1H NMR shift measurements relative to an external reference in a series of solutions containing a constant concentration of TMU and varying concentrations of D under conditions of a great excess of D. Reduction of data according to the AUS concept (additional nonspecific shielding) provided formation constants K (in l/mol) and Icpt/K as approximations of the complex shifts. The increase in K from .17 (TMU-B) to .75 (TMU-N) to 2.08 (TMU-P) is compatible with a face-to-face complexation and with a preferred contact between the donor and TMU along the area of positive charge in the TMU molecule. The estimated Icpt/K figures indicate the centers of the complexes to lie between N-3 and N-9 of TMU, quite in the center of the positive charge area of TMU. K and Icpt/K figures for TMU-BP indicate this complex to have the same topology as TMU-B, the second ring of BP rotating in plane around the complexing ring of BP. The previous rejection of a face-to-face topology for such complexes was based on a misinterpretation of the ring current calculations. Deviating complex parameters in the previous report are shown to be caused by a solvent effect (CDCl_3) and in part by methodical errors.

Introduction

We are interested in molecular complexes of caffeine and related acceptors [2–4] because of their potential pharmaceutical and medicinal importance. The present work is the third paper [2, 3] in a series on complexes of such acceptors with aromatic donors in a non-polar medium. We use the terms acceptor and donor for convenience although we suspect that charge transfer (CT) from the donor D to the acceptor A does not play an essential role in these complexes. The ^1H NMR technique applied in our studies of such complexes does not depend on the presence of CT. Our method is in principle the well-known measurement and analysis of the chemical shift dependence Δ of an A signal on the concentration $[\text{D}_0]$ of D when the latter is present in a large excess.

A second aim of our work concerns validity and scope of the AUS concept [2, 3, 5] that considers the additional magnetic shielding of protons in A by non-complexing "collisions" with an aromatic D. Joint

measurements of chemical shifts for different protons of A and separate reduction of their data including separate AUS corrections [2, 3] provide a suitable test for these purposes. Consistent complex parameters, in particular identical formation constants K , from different signals are a good criterion whose reliability is the better the more signals contribute to it. Caffeine has three sharp methyl singlets and a weak quadruplet (8-H) [2]. Tetramethyluric acid (TMU) gives four sharp methyl singlets and can be expected to complex with an aromatic D in a manner that deviates topologically from the respective caffeine complex owing to a different charge distribution in the two A molecules.

A third reason for studying the complexation of TMU with aromatic donors arises from the topology of the TMU-benzene complex deduced in a previous study [6]. The proposed skewed topology is difficult to rationalize, since it cannot take an optimal profit from a dipole-quadrupole attraction of a T shaped complex nor from the various forces which can contribute to the stability of a face-to-face complex when the molecular planes of A and D lie parallel. Our reinvestigation of such complexes will differ method-

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ically from the previous report (1) by change of the solvent CDCl_3 to the less polar CCl_4 , (2) by using an external reference, and (3) by performing the AUS correction in the reduction of the data.

On presenting our results for the complexes of TMU with benzene (B), biphenyl (BP), naphthalene (N), and phenanthrene (P) in CCl_4 , we shall demonstrate the importance of the AUS correction decreasing or even vanishing when K becomes large and/or when the complex shift is large. As a consequence of the refined model introduced by the AUS concept, the true complex shift $\Delta_{\text{AD},00}$ cannot be evaluated precisely. In place of $\Delta_{\text{AD},00}$ an approximation, usually a good one, is obtained in the form of Icpt/K [2, 3, 5] whose precise meaning is given below in eq. (1). This formal difference does not give these "approximations" a lower rank than the "classic" $\Delta_{\text{AD},00}$. K is defined as usual by $[\text{AD}]/([\text{A}][\text{D}])$ where the square brackets indicate the concentration of the complex AD and of non-complexed A and D, respectively. The latter two concentrations have to be distinguished from the total concentrations of A and D that will be marked with the subscript zero:

$$[\text{A}_0] = [\text{A}] + [\text{AD}] \text{ and } [\text{D}_0] = [\text{D}] + [\text{AD}]$$

As previously described [2, 3], the AUS correction is performed by substituting $\Delta_0 - m_2[\text{D}_0]$ for Δ_0 in one of the known methods for the reduction of data as is shown for the Scatchard-Foster-Fyfe method (ScFF) in eq. (1).

$$\begin{aligned} (\Delta_0 - m_2[\text{D}_0])/[\text{D}_0] = \\ -K(\Delta_0 - m_2[\text{D}_0]) + \text{Icpt} \end{aligned} \quad (1)$$

where

$$\text{Icpt} = K(\Delta_{\text{AD},00} + (m_1 - m_2)/K)$$

and

$$m_1 = a_1 + b$$

$$m_2 = a_2 + b$$

b is the correction for the susceptibility change within the experimental series, a_1 is the AUS coefficient for A and a_2 is the AUS coefficient for AD. The reason for using the subscripts for the observed relative chemical shifts Δ and the complex shifts Δ_{AD} is given in ref. [5].

Experimental

Materials

TMU, the trimethyluric acids, and BP were purchased from Fluka, Switzerland, N from Riedel-

de-Haen, Germany, and P from Aldrich, Europe. Uvasol qualities of CCl_4 , CDCl_3 (99.8% deuterated), C_6D_6 (= B, 99.5% deuterated), D_2O (99.95% deuterated) were purchased from E. Merck, Darmstadt, West Germany, as well as TSPNa ($\text{Me}_3\text{SiCD}_2\text{CD}_2\text{CO}_2\text{Na}$).

Procedure

Preparation of solutions, external and internal references, precision sample tubes, precision capillaries, lock of spectrometer, and recording of ^1H NMR spectra on a Bruker HX 90-E spectrometer at 90 MHz are described in ref. [2].

Experimental details

The temperature was 37 °C. The number of scans was 200–500. Data acquisition and Fourier transformation were performed with 16 K data points (32 K for the series with B and BP) resulting in a precision of shift measurements of .122 Hz (.061 Hz for the series with B and BP).

Calculations

For the calculation of K various basic methods are known (compare ref. [2, 3] and the lit. cited therein), of which the method first described by Creswell and Allred (CA) proved to be least sensitive to experimental errors. The method of Scatchard transformed for NMR technique by Foster and Fyfe (Sc or ScFF) is nearly as good as CA. Therefore, in principle all computations in the present paper were performed both in the CA and in the Sc mode, usually in the programs CA-AUS and Sc-AUS [2, 3].

Results

If not otherwise stated, throughout this paper concentrations are given in mol l^{-1} , K in l mol^{-1} , shift values in Hz (at 90 MHz), m_2 and a_2 in Hz l mol^{-1} .

Since the correct assignment of the four methyl singlets of TMU is of prime importance for the determination of the topology of the complexes we checked the published [6] assignment by shift comparisons with three trimethyluric acids (Table I in D_2O for solubility reasons). The formula of TMU is given below (Fig. 2).

We prefer CCl_4 as solvent on principle in our investigations. The often used polar CDCl_3 tends to undergo specific interactions with the acceptor and with the donor, *e.g.* by hydrogen bonding with the oxygen atoms of TMU or with the π cloud of an aromatic donor. However, in the present case the

Table I. Assignment of ^1H NMR signals of TMU by comparison with trimethyluric acids (TriMU). Chemical shifts in Hz (at 90 MHz) in D_2O relative to internal $\text{Me}_3\text{SiCD}_2\text{CD}_2\text{CO}_2\text{Na}$.

	1-Methyl	7-Methyl	3-Methyl	9-Methyl
TMU	297.7	315.2	327.5	336.4
1,3,7-TriMU	299.1	311.4	313.0	
1,3,9-TriMU	300.6		325.8	337.5
3,7,9-TriMU		315.6	327.7	332.8

low solubility of TMU in CCl_4 has the disadvantage of a low signal-to-noise ratio (SNR) as consequence. Because of the experience of various operators we found it best to complete the experiments for one series within one day. This sets a time limit for data acquisition and correspondingly also for the SNR. A second problem with TMU was already noticed by the Italian group [6], namely signal crossing when $[\text{D}_0]$ increases. In some experimental probes with small $[\text{D}_0]$ in each of our TMU series the signal of 3-methyl or of 9-methyl overlaps more or less with the signal of 7-methyl or with the signal of 1-methyl, making the respective shift measurements less reliable.

Table II presents the parameters for the system TMU/B obtained with CA-AUS [2, 3] and Sc-AUS [2, 3], respectively, from two experimental series with n data points from n solutions with the donor concentration going from $[\text{D}_0]_1$ to $[\text{D}_0]_n$. According to eq. (1) the essential principle of the AUS correction is a linearization of a non-linear correlation of data. This correction consists in a search for the best m_2 that gives the smallest least squares sum SDDQ for eq. (1). This correction and therefore the finally estimated complex parameters depend strongly on an usually slight curvature of plotted data points in the Scatchard-Foster-Fyfe plot [2, 3, 5], particularly when Icpt/K is small as for 1-methyl and 7-methyl. In other words, the correction is rather sensitive to outlying points. Therefore, when necessary, one or two data points with the largest squared deviation DDO were omitted out of 16 data points as indicated in Table II. This omission procedure was introduced and discussed in ref. [3]. It gives a better congruence between K from different signals and different series as well as between Icpt/K from different series as well as between results from CA-AUS and from Sc-AUS. It is justified by a decrease in the magnitude of the relative least squares sum SDDQ/n , *i.e.* the least

Signal or $(\Delta_\alpha - \Delta_\beta)$	Series	Data points i omitted ^b	K	Icpt/K^c	m_2^c
1	I		.164 [.170]	13.4 [12.9]	4.3 [4.3]
	II		(.192)	(14.2)	(4.2)
	II	8, 10	.163 [.164]	16.8 [16.7]	4.1 [4.1]
3	I		.160 [.161]	143.6 [142.9]	5.3 [5.3]
	II		.166 [.165]	141.5 [142.1]	5.3 [5.3]
7	I		(.152)	(17.2)	(4.6)
	I	2, 7	.167 [.139]	16.0 [19.0]	4.7 [4.6]
	II		(.144)	(21.7)	(4.4)
	II	12, 1	.169 [.162]	18.5 [19.2]	4.5 [4.5]
9	I		.165 [.165]	144.3 [144.3]	5.5 [5.5]
	II		.164 [.163]	145.3 [146.1]	5.4 [5.4]
$(\Delta_3 - \Delta_1)$	I		.160 [.160]	130.2 [130.2]	1.0 [1.0]
	II		.163 [.165]	127.6 [128.7]	1.1 [1.0]
$(\Delta_3 - \Delta_7)$	I		.162 [.165]	126.6 [124.0]	.6 [.7]
	II		.170 [.170]	120.0 [120.1]	.9 [.9]
$(\Delta_9 - \Delta_1)$	I		.165 [.164]	130.9 [131.6]	1.2 [1.2]
	II		.161 [.160]	131.4 [132.3]	1.2 [1.1]
$(\Delta_9 - \Delta_7)$	I		.166 [.169]	127.3 [125.5]	.9 [.9]
	II		.168 [.167]	123.8 [124.0]	1.0 [1.0]

Table II. Complex parameters obtained with CA-AUS [Sc-AUS] for TMU/B from series I^a and II^a. Values in round brackets are obtained before omission of outlying points.

^a Ser. I: n 16; $[\text{A}_0]$.00125; $[\text{D}_0]$.91–11.27; saturation fraction 0.13–0.65; Ser. II: n 16; $[\text{A}_0]$.00070; $[\text{D}_0]$ 2.07–9.98; saturation fraction 0.25–0.62;

^b data points are numbered $i = 1, \dots, n$ in the sequence of increasing $[\text{D}_0]$;

^c or the respective differences between signal α and signal β .

squares sum divided by the number n of data points. The purpose of this omission procedure is twofold. Besides finding the best K and the best values for the various Icpt/K (that are important for the complex topology), a failure to obtain, within experimental precision, the same K from different signals can be taken as evidence that the pure AD model (1:1 model) is insufficient. For instance, work in our laboratory [7] confirmed in this way the conclusions on the picrylacetone/benzene system by Foster's group (1:1 and 1:2 complexes) [8]. By the same procedure Strumm [7] found, contrary to the latter group, the complexing of picrylacetone with the larger donor naphthalene to be compatible with the pure 1:1 model.

The results of the shift difference method [3], shown in the lower part of Table II, are perhaps even more important for the correctness of our data processing as a whole as well as in detail. This method calculates complex parameters from shift differences $\Delta_\alpha - \Delta_\beta$ of two A signals α and β . It is completely independent of any possible reference or susceptibility problems. However, this difference method as well as the direct method (upper part of Table II) yield unreliable results when Icpt/K (direct method) or the corresponding difference $\text{Icpt}_\alpha/K - \text{Icpt}_\beta/K$ is too small. Therefore the shift differences $\Delta_7 - \Delta_1$ and $\Delta_9 - \Delta_3$ are not included in Table II.

The congruence in K is good both for the direct method and for the shift difference method as Table II shows. The results are thus in good accord with the 1:1 model. The shift difference method works well in this case due to large differences $\text{Icpt}_\alpha - \text{Icpt}_\beta$ but it implicates also small AUS coefficients in the form of the differences $m_{2,\alpha} - m_{2,\beta}$. Since the influence of the AUS effect vanishes when a_2 approaches zero, reduction of data without AUS correction should lead to approximately correct values in the shift difference method. Indeed, K determined in this way ranged from .133 to .145 (CA computation). These figures steadily increased up to the range of 0.145–0.152 when the data of the highest $[\text{D}_0]$ were stepwise omitted until the number of data points was 8.

In the same manner as described above, Table III shows the complex parameters for TMU/BP. The reliability of investigating a complexation depends among other factors on the saturation fraction $[\text{AD}]/[\text{A}_0]$ [9]. The latter should extend over as large a range as possible lying between 0.2 and 0.8 [10].

While this requirement is well met in Table II, this is not so in Table III for solubility reasons. In spite of this experimental disadvantage the results for TMU/BP are fair. K estimated from the shift difference method without AUS correction ranges from .44 to .48 (CA results), *i.e.* it is only slightly smaller than the average of Table III.

Table IV gives the computed results for TMU/N showing a good congruence in K . Even when computed from the shift differences without AUS correction, K was found too low by only about 5% with a concomitant increase in $\text{Icpt}_\alpha/K - \text{Icpt}_\beta/K$ by maximal 11%. A comparison with the figures given above for TMU/B and TMU/BP makes clear, how the dispensability of the AUS correction depends on the magnitude of K in addition to the discussed influence of a vanishing AUS coefficient and a large complex shift (or its approximation). As can be expected for a simple linear correlation, reduction of data without AUS correction is much less sensitive to outlying points than with inclusion of the AUS correction, so that there was no need to omit data points. The good compliance with Deranleau's criterion [10] in the four series of TMU/N is weakened by an increased problem of signal crossing. With high $[\text{D}_0]$ the signals of 3-methyl and 9-methyl come rather close to one another. The same applies to the TMU/P series below.

The results for TMU/P are collected in Table V. Here the agreement in K is very good throughout the Table although the computations from shift differences were performed without AUS correction only, except $\Delta_9 - \Delta_7$ of series II. Even the direct method applied without AUS correction provided deviations that were only small for 3-methyl (and 9-methyl): $K = 1.93 - 1.96$ (1.94–2.06), $\Delta_{\text{AD}} = 204 - 206$ (211–219).

Discussion

The mean values for K and for the various Icpt/K (from the direct method only) as extracted from Tables II–V are shown in Table VI and compared with published [6] values for K and Δ_{AD} . These literature values, that will be discussed later, reveal in their general trends much similarity with our parameters.

There is clearly the expected increase in K with the number of rings in the donor molecule. A plot of $\log K$ vs. the ionization potential of the donors gives a

Signal or ($\Delta_\alpha - \Delta_\beta$)	Series	Data points i omitted ^b	K	Icpt/K ^c	m ₂ ^c
1	I		(.506)	(35.6)	(5.4)
	I	6	.496 [.505]	36.3 [35.3]	5.3 [5.5]
	II		(.461)	(44.0)	(3.6)
	II	11	.509 [.501]	38.4 [39.2]	4.5 [4.4]
3	I		(.516)	(135.2)	(8.9)
	I	6	.507 [.486]	137.4 [146.2]	8.6 [7.1]
	II		(.436)	(177.8)	(1.8)
	II	11, 1	.513 [.499]	142.2 [147.2]	7.4 [6.7]
7	I		(.512)	(39.4)	(5.6)
	I	6	.505 [.505]	39.9 [39.9]	5.6 [5.6]
	II		(.443)	(47.7)	(4.5)
	II	11	.508 [.521]	39.4 [38.2]	5.9 [6.1]
9	I		(.500)	(146.8)	(7.0)
	I	6, 7	.507 [.470]	140.5 [157.2]	8.6 [5.7]
	II		(.451)	(170.1)	(3.9)
	II	11	.503 [.493]	146.0 [149.7]	7.8 [7.2]
($\Delta_3 - \Delta_1$)	I		(.518)	(100.1)	(.3)
	I	6	.511 [.478]	101.2 [111.4]	3.3 [1.5]
	II		(.428)	(134.0)	(-1.8)
	II	11, 1	.515 [.502]	103.6 [107.1]	2.9 [2.4]
($\Delta_3 - \Delta_7$)	I		(.516)	(96.0)	(3.2)
	I	6	.509 [.477]	97.1 [106.6]	3.2 [1.5]
	II		(.434)	(129.9)	(-2.7)
	II	11, 1	.517 [.500]	102.3 [106.6]	1.1 [1.0]
($\Delta_9 - \Delta_1$)	I		(.498)	(111.3)	(1.6)
	I	6, 7	.514 [.465]	103.3 [119.6]	3.6 [.7]
	II		(.447)	(126.2)	(.3)
	II	11	.502 [.490]	107.4 [110.8]	3.3 [2.8]
($\Delta_9 - \Delta_7$)	I		(.496)	(107.4)	(1.4)
	I	6, 7	.507 [.450]	101.3 [120.7]	2.9 [-0.4]
	II		(.454)	(122.3)	(-0.6)
	II	11	.501 [.482]	106.5 [112.0]	1.9 [1.1]

Table III. Complex parameters obtained with CA-AUS [Sc-AUS] for TMU/BP from series I^a and II^a. Values in round brackets are obtained before omission of outlying points.

^a Ser. I: n 16; [A_o] .00138; [D_o] 0.093–1.01; saturation fraction 0.05–0.34; Ser. II: n 16; [A_o] .00125; [D_o] 0.105–1.62; saturation fraction 0.05–0.43;

^b data points are numbered $i = 1, \dots, n$ in the sequence of increasing [D_o];

^c or the respective differences between signal α and signal β .

fairly good straight line with the figures from our work. As will be discussed below, this linear dependence is also reconcilable with another donor property that parallels more or less the ionization potential, but it is hard to reconcile with a T shaped or a skewed [6] complex topology. In particular, how can such non-parallel topologies provide an explanation for the great strength of the TMU-P complex and for the large difference in strength between the TMU complexes with P and BP? For TMU-BP a simple statistical consideration would lead to a doubling in K of TMU-B, but we found three times the figure of TMU-B and twelve times this figure for TMU-P. The conformation of the two phenyl rings of BP may be planar (like the BP part of P), orthogonal, or skewed, the energy differences being very small [11]

thus allowing the BP molecule to adopt that conformation that would be favorable for any type of complexation. As will be shown later, the main argument [6] against a parallel topology of the TMU-B complex does not hold.

One point is certain from both investigations. The center of the complex must always be close to N-9 and N-3 of the TMU molecule as indicated by the largenesses of Icpt/K or Δ_{AD} , respectively. One of the most remarkable details emerges from a pairwise comparison of the various Icpt/K of TMU-B with those of TMU-BP. In spite of the difference in K, the situation at the center of the two complexes seems to be precisely the same, while the peripheral two methyls 1 and 7 in the complex are magnetically shielded in TMU-BP more than in TMU-B, indeed,

Signal or ($\Delta_\alpha - \Delta_\beta$)	Series	Data points i omitted ^b	K	Icpt/K ^c or Δ_{AD} ^c	m_2^c
1	I		(.718)	(31.1)	(3.1)
	I	4	.744 [.760]	30.1 [29.7]	3.2 [3.3]
	II		(.704)	(27.0)	(4.2)
	II	10, 8	.752 [.755]	24.9 [24.8]	4.6 [4.7]
	III		.749 [.746]	23.6 [24.1]	5.1 [5.0]
3	IV		.698 [.715]	26.9 [26.3]	4.5 [4.6]
	I		(.872)	(155.5)	(11.0)
	I	1, 5	.760 [.763]	179.3 [178.6]	6.1 [6.2]
	II		(.796)	(169.6)	(8.2)
	II	14, 3, 2	.760 [.747]	178.2 [181.8]	6.5 [5.7]
7	III		.757 [.753]	174.8 [175.8]	6.9 [6.7]
	IV		.746 [.749]	180.5 [179.8]	6.3 [6.4]
	I		(.861)	(28.3)	(4.9)
	I	2	.752 [.759]	32.4 [32.2]	4.1 [4.1]
	II		(.737)	(29.1)	(5.2)
9	II	1, 10	.757 [.769]	28.2 [27.7]	5.4 [5.5]
	III		.750 [.732]	28.4 [29.1]	5.4 [5.3]
	IV		(.831)	(26.3)	(5.7)
	IV	8	.774 [.771]	28.4 [28.5]	5.3 [5.3]
	I		(.862)	(169.4)	(10.8)
$(\Delta_3 - \Delta_1)$	I	1, 6	.746 [.748]	197.3 [196.9]	5.0 [5.1]
	II		(.817)	(178.2)	(9.1)
	II	3, 2, 16	.753 [.769]	196.6 [192.2]	4.8 [5.8]
	III		.758 [.751]	191.0 [192.9]	5.4 [5.0]
	IV		.745 [.751]	193.2 [191.7]	6.5 [6.8]
$(\Delta_3 - \Delta_1)$	I		.716 [.726]	162.0 [160.7]	no AUS correction
	I		(.903)	(125.6)	(7.8)
	I	1, 4	.787 [.788]	144.8 [144.6]	3.7 [3.7]
	II		.741 [.746]	159.9 [159.3]	no AUS correction
	II		(.810)	(143.2)	(3.9)
$(\Delta_3 - \Delta_7)$	II	14, 16	.774 [.770]	151.7 [152.9]	1.8 [1.6]
	III		.723 [.724]	159.4 [159.3]	no AUS correction
	III		.757 [.754]	151.1 [151.8]	1.8 [1.7]
	IV		.716 [.719]	162.7 [162.3]	no AUS correction
	IV		.753 [.754]	153.8 [153.8]	1.7 [1.7]
$(\Delta_3 - \Delta_7)$	I		.722 [.731]	175.0 [173.9]	no AUS correction
	I		(.874)	(127.2)	(6.1)
	I	1	.746 [.748]	149.6 [149.1]	1.6 [1.6]
	II		.753 [.762]	172.1 [170.9]	no AUS correction
	II		(.807)	(140.7)	(3.0)
$(\Delta_9 - \Delta_1)$	II	14, 16	.771 [.765]	149.1 [150.6]	.9 [.6]
	III		.752 [.751]	168.8 [169.0]	no AUS correction
	III		.758 [.756]	146.4 [146.9]	1.5 [1.4]
	IV		.712 [.716]	176.6 [176.1]	no AUS correction
	IV		.730 [.734]	154.7 [153.8]	.5 [.7]
$(\Delta_9 - \Delta_1)$	I		.726 [.735]	155.8 [154.8]	no AUS correction
	I		(.889)	(139.4)	(7.6)
	I	1	.798 [.799]	155.1 [155.0]	4.3 [4.4]
	II		.753 [.755]	153.4 [153.0]	no AUS correction
	II		(.833)	(152.1)	(4.7)
$(\Delta_9 - \Delta_7)$	II	3	.810 [.809]	156.9 [157.2]	3.7 [3.6]
	III		.729 [.730]	153.3 [153.1]	no AUS correction
	III		.757 [.751]	167.4 [169.0]	.3 [.0]
	IV		.718 [.721]	157.3 [157.1]	no AUS correction
	IV		.752 [.756]	166.5 [165.7]	2.0 [2.1]
$(\Delta_9 - \Delta_7)$	I		.732 [.739]	168.9 [168.0]	no AUS correction
	I		(.862)	(141.1)	(5.9)
	I	1	.753 [.753]	162.0 [161.9]	1.7 [1.7]
	II		.764 [.771]	165.6 [164.7]	no AUS correction
	II		(.831)	(149.5)	(3.8)
$(\Delta_9 - \Delta_7)$	II	11	.809 [.808]	154.5 [154.8]	2.7 [2.6]
	III		.759 [.757]	162.7 [162.9]	no AUS correction
	III		.759 [.753]	162.6 [164.0]	.0 [-0.2]
	IV		.715 [.718]	171.3 [170.9]	no AUS correction
	IV		.730 [.738]	167.4 [165.7]	.8 [1.0]

Table IV. Complex parameters obtained with CA-AUS [Sc-AUS] for TMU/N from series I–IV^a. Values in round brackets are obtained before omission of outlying points.

^a Ser. I: n 15; $[A_o]$.00090; $[D_o]$ 0.50–1.64; saturation fraction 0.27–0.55; Ser. II: n 16; $[A_o]$.00101; $[D_o]$ 0.14–1.40; saturation fraction 0.10–0.51; Ser. III: n 12; $[A_o]$.00120; $[D_o]$ 0.46–1.37; saturation fraction 0.26–0.51; Ser. IV: n 13; $[A_o]$.00085; $[D_o]$ 0.46–1.85; saturation fraction 0.25–0.58;

^b data points are numbered $i = 1, \dots, n$ in the sequence of increasing $[D_o]$;

^c or the respective differences between signal α and signal β .

Signal or ($\Delta_\alpha - \Delta_\beta$)	Series	Data points i omitted ^b	K	Icpt/K ^c or Δ_{AD} ^c	m_2^c
1	I		(1.853)	(48.8)	(3.7)
	I	4	2.001 [2.022]	45.6 [45.1]	5.0 [5.2]
	II		(2.471)	(38.0)	(8.8)
	II	2	2.116 [2.073]	44.4 [45.3]	5.2 [4.8]
3	I		(2.185)	(180.1)	(14.8)
	I	15	2.125 [2.131]	186.3 [185.8]	10.1 [10.4]
	II		(2.247)	(174.6)	(17.2)
	II	2	2.052 [2.060]	191.8 [191.0]	7.8 [8.2]
7	I		(1.729)	(60.0)	(1.1)
	I	3, 4	2.092 [2.072]	50.2 [50.7]	5.4 [5.2]
	II		(2.359)	(44.9)	(8.0)
	II	2	2.091 [2.087]	50.7 [50.8]	4.7 [4.7]
9	I		2.106 [2.128]	200.0 [198.0]	10.0 [10.9]
	II		(3.146)	(135.5)	(48.0)
	II	2, 1	2.089 [2.050]	201.2 [205.0]	8.7 [6.9]
($\Delta_3 - \Delta_1$)	I		2.038 [2.056]	150.4 [149.7]	no AUS correction
	II		1.998 [2.021]	151.2 [150.3]	no AUS correction
($\Delta_3 - \Delta_7$)	I		2.043 [2.059]	162.9 [162.3]	no AUS correction
	II		2.134 [2.293]	158.2 [152.2]	no AUS correction
($\Delta_9 - \Delta_1$)	I		2.040 [2.062]	144.3 [143.5]	no AUS correction
	II		1.994 [2.017]	145.7 [144.8]	no AUS correction
($\Delta_9 - \Delta_7$)	I		2.046 [2.065]	156.9 [156.1]	no AUS correction
	II		2.134 [2.300]	152.6 [146.7]	no AUS correction
	II	1, 2	2.101 [2.052]	149.6 [153.0]	4.4 [2.8]
	II				

Table V. Complex parameters obtained with CA-AUS [Sc-AUS] for TMU/P from series I^a and II^a. Values in round brackets are obtained before omission of outlying points.

^a Ser. I: n 16; [A_o] .00095; [D_o] 0.12–0.73; saturation fraction 0.20–0.61; Ser. II: n 16; [A_o] .00108; [D_o] 0.11–0.62; saturation fraction 0.19–0.56;
^b data points are numbered $i = 1, \dots, n$ in the sequence of increasing [D_o];
^c or the respective differences between signal α and signal β . See text.

Table VI. Mean values of K (L/mol) and Icpt/K or Δ_{AD} (both in Hz), respectively, estimated in this work using CA-AUS [Sc-AUS]. Comparison with literature values.

K	TMU-B this work .17 [.16]	lit. ^a .16	TMU-BP this work .51 [.50]	lit. ^a –	TMU-N this work .75 [.75]	lit. ^a .39	TMU-P this work 2.08 [2.07]	lit. ^a .79
Signal								
1	15 [15]	15	37 [37]	–	26 [26]	32	45 [45]	59
7	17 [19]	20	40 [40]	–	29 [29]	35	51 [51]	61
3	143 [143]	104	140 [147]	–	178 [179]	167	189 [188]	206
9	145 [145]	107	143 [154]	–	195 [193]	182	201 [202]	221

^a Ref. [6]; mean values of K (in CDCl₃) after transformation of molalities into molarities by division with the density ρ (1.501) of CDCl₃. Δ_{AD} values after transformation from 100 MHz [6] to 90 MHz (this work).

even more than in TMU-N although all remaining parameters of the latter are distinctly larger than in TMU-BP. All these details can simply and easily be rationalized in a face-to-face complexation with one phenyl ring of BP in the same mean position as B in the TMU-B complex and with an in-plane rotation of

the planar BP molecule. This rotation would lead (a) to a stronger shielding of the peripheral protons through an interval shielding by the second phenyl ring (Fig. 1) and (b) to an increase of K beyond the statistical doubling *e.g.* by an increased contribution from dispersion forces.

Fig. 1. Schematic drawing of the TMU-BP complex showing the proposed rotation.

Fig. 2. Schematic charge distribution in TMU according to ref. [14]. Thick bonds indicate the area of positive charge. Centers of negative charge are indicated by open spheres.

The major contribution to the stability of a T shaped or skewed TMU-arene complex should come from the dipole moment of TMU (*cf.* ref. [6]). However, a comparison of the dipole moments of caffeine and uric acid [12] is not compatible with the strength of the respective complexes, since the caffeine complex is always distinctly weaker than the corresponding TMU complex [13]. On the other hand, according to the calculated [14] charge distribution for uric acid there exists a continuous area of positive charge in the TMU molecule extending from N-1 to C-2 to N-3 to C-4 to N-9 to C-8 to N-7 (Fig. 2). The greatest partial charges are calculated for N-9 and for N-3, quite in accord (a) with the chemical shifts of the N-methyl groups in TMU and (b) with the discussed mean center of the TMU complexes. Considering Coulombic repulsion by the oxygens at position 2 and 8, the positive area in the TMU molecule usable for an interaction with the π cloud of the donor will extend from C-2 to C-8 only. So it seems reasonable to suppose that one major contribution to the stabilization of face-to-face TMU complexes comes from an interaction of this area with the "face" of the donor molecule. A rough calculation of the contact areas on this basis with inclusion of the methyl groups of TMU gives a fairly straight line when these areas are plotted *vs.* $\log K$ of TMU-B, TMU-N, and TMU-P. A similar analysis has previously been performed by Connors group [15] for other complexes. The relatively large area in the present acceptor provides a simple explanation for the strong increase in K within the series TMU-B, TMU-N, TMU-P. The proposed face-to-face topologies of the four TMU complexes find support from the topologies of crystalline TMU-arene complexes [16].

How can this topology be reconciled with the calculated [6] magnetic shielding (I_{cpt}/K or Δ_{AD}) of the four methyl groups in TMU? Using the ring current

data of Johnson and Bovey [17] a recalculation of the proposed topology shows that the rejection of the face-to-face model was based on a probably very common misinterpretation. The ring current calculations comprise exclusively the true ring current effect and do not comprise the magnetic anisotropy of the basic non-delocalized olefinic double bonds. This emerges clearly from the primary publications [17, 18]. Experimentally however, the complex shifts or their approximations are the result of the total magnetic anisotropy of the donor, to say nothing of possible other effects of the complexation, *e.g.* changes of partial charges in A or disturbances of the above-and-below-plane orbital symmetry in A and D. So, the shielding calculated from the true ring current effect alone is too small, probably much too small. Therefore, we see no reason to question the compatibility of a face-to-face complexation with the estimated figures of the TMU-B complex, even with our figures for 3-methyl and 9-methyl that are larger than the published complex shifts.

What are then the reasons for the discrepancies in Table VI between the published results and the present results? K differs markedly for TMU-N and TMU-P while Δ_{AD} or its approximation deviate strongly for 3-methyl and 9-methyl of TMU-B only. Apparently the system TMU/B does not fit into the scheme of the other two systems. This divergence is caused mainly by the molality scale that falsifies the results for TMU/B much more than for the other systems because of the great difference in concentration ranges. With TMU/B the published experimental series [6] goes up to concentrations that contain more solute B than solvent CDCl_3 . We suspect that the authors felt somehow this concentration problem since there is no other reason to stop the increase in $[D_0]$ at the selected point and since at this point a curvature may have begun to become detectable

in the assumed linear dependence $1/\Delta = 1/K + 1/(K\Delta_{AD}[D_o])$. Using the molality scale for $[D_o]$ in place of molarity is justifiable for low concentrations only, for higher concentrations the simple linear transformation $K_{\text{molar}} = K_{\text{molal}} \varrho_{\text{solvent}}$ does not hold. For solutions of B in CDCl_3 the concentration 3.74 is the same for molality and molarity. At higher concentrations the molality figure is greater than the molarity figure, at lower concentrations the situation is reversed.

To analyze the discrepancies quantitatively, we run a further series of TMU/B in CDCl_3 relative to our usual external reference and simultaneously relative to internal tetramethylsilane like in ref. [6]. Fig. 3 shows the uncorrected ScFF plots, *i.e.* plots according to equation (1) when $m_1 = m_2 = 0$. The plot with triangles is from molality and internal reference, the plot with spheres from molarity and internal reference, and the plot with squares from molarity and external reference. Reduction of data (CA-AUS) of the first plot yielded practically the published parameters after making allowance for the different spectrometer frequencies. m_2 was close to zero for each signal. As already indicated in Table VI, transformation of the obtained figures for K from molality into molarity yields practically the same K as obtained by us when we used an external

reference and the solvent CCl_4 . This congruence comes into being because three methodical errors accidentally cancel each other in the published procedure [6]: use of the molality scale, use of internal TMS, and use of the solvent CDCl_3 that interacts with B. The influence of the first two errors is particularly great for B due to the necessary and experimentally possible large $[D_o]$ range (compare ref. [2]). For other donors, *e.g.* N, use of molality and internal TMS may be tolerable. So, in our CCl_4 series TMU/N–I (Table IV) with TMS present in the solutions, shifts relative to internal TMS provided results harmonizing more or less with Table IV depending on the computation. Reduction of data with CA-AUS gave good congruence from all signals, reduction of data with CA, *i.e.* without AUS correction, gave rather good congruence for 3-methyl and 9-methyl only, *i.e.* for the signals with large complex shifts.

Reduction of data (CA-AUS) of the third plot in Fig. 3 provided $K = 0$. We then considered competing formations of TMU-B and of a 1:1 solvent-D complex SD [19] that leaves one side of this solvent complexed D free for exerting the AUS effect. According to this concept we reduced $[D_o]$ usable for the formation of TMU-B by subtracting the concentration [SD] of SD and we reduced $[D_o]$ capable of

Fig. 3. Uncorrected Scatchard-Foster-Fyfe plots for TMU/B-Cl (TMU/B in CDCl_3). First plot (triangles): shifts relative to internal TMS; concentrations in mol/kg solvent. Second plot (spheres): shifts relative to internal TMS; concentrations in mol/l solution. Third plot (squares): shifts relative to an external reference; concentrations in mol/l solution.

exerting an AUS effect by subtracting $[SD]/2$. The required $[SD]$ s were calculated from SD formation constants .02, .04 *etc.* In this manner we obtained K for the TMU-B complex ranging from .15 to .18, *i.e.* in fair congruence with Table II, when the SD formation constant was .10. Homer and his group [20] reported for the $CHCl_3$ -B complex a formation constant between .1 and .2 depending on the solvent. H.-O. Strumm in our laboratory found .10 in CCl_4 [7].

Since the figures for I_{cpt}/K of TMU-B in the above described procedure were too great by 24–47 Hz, we assume hydrogen bonding to occur between solvent molecules and the three oxygens of TMU. Indeed, we found downfield solvent induced shifts $\delta_{CDCl_3} - \delta_{CCl_4}$ (external reference, susceptibility corrected shifts) of 3.9 Hz (1-methyl), 2.6 Hz (7-methyl), and 1.4 Hz (3-methyl and 9-methyl). This solvent complexation (or solvation) of TMU

does not seriously disturb the estimation of the TMU-B complex parameters apart from some effect on the complex shifts. It is well documented, that the concentration of the deficit component, usually A as here, has little influence on the computations.

We are thus able to sum up. Different results in the present and in previous [6] work are readily explained by solvent effects and in part by methodical errors. Strong arguments for a face-to-face topology of the TMU-arene complexes are presented, while the previous argument against this topology is shown to be untenable.

This work was supported by the Deutsche Forschungsgemeinschaft and by the Fonds der Chemischen Industrie. This support is gratefully acknowledged as well as the assistance by Professor Hans Suschitzky in writing the manuscript.

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