BUTTERWORTH HEINEMANN

Polymer Vol. 36 No. 15. pp. 3045–3049. 1995
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0032-3861/95/$10.00 + 0.00

Characterization of sulfobetaine monomers by nuclear magnetic resonance spectroscopy: a note

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(Received 11 November 1994; revised 9 February 1995)

A set of zwitterionic monomers bearing the 3-ammoniopropanesulfonate moiety is analysed in $CDCl_3$, CD_3OD and D_2O by one- and two-dimensional ^1H n.m.r. and ^{13}C n.m.r. spectroscopy. Absolute and relative positions of the n.m.r. signals are determined depending on the solvent used; the refined assignments of the signals in the vicinity of the ammonium group deviate from previously proposed assignments based on standard n.m.r. shift tables. Still, there is no convincing evidence for a special ring current effect due to a six-membered ring conformation of the betaine moiety.

(Keywords: characterization; sulfobetaine monomers; n.m.r. spectroscopy)

Truly zwitterionic monomers and their polymers have seldom been studied up to now, and hence reliable reference data for their characterization are scarce. Recently, Lee and Tsai have investigated the ^1H spectra of 3-[*N*, *N*-dimethyl-*N*-(acrylamidopropyl)-ammonio]propanesulfonate **1** and 3-[*N*, *N*-dimethyl-*N*-(methacrylamidopropyl)ammonio]propanesulfonate **2** in water[1]. By comparison with cationic analogues, they concluded that the protons of α-methylene ammonium group of the sulfopropyl moiety (see *Figure 1*, protons N) were more strongly downfield shifted than expected from standard nuclear magnetic resonance (n.m.r.) shift tables[2], thus showing larger chemical shifts than the protons of α-methylene ammonium group of the 3-amidopropyl moiety (see *Figure 1*, protons P). The unusually large chemical shifts were attributed to a ring-current effect due to a six-membered ring conformation of the 3-ammoniopropanesulfonate moiety[1].

Applying double resonance experiments with saturation of the signals at 2.08 ppm and 3.2 ppm, we could confirm the proposed assignment for methacrylamide **2**. This result is in good agreement with previously reported assignments in the ^1H n.m.r. spectrum[3] of the analogously substituted sulfonamide sulfobetaine **3**, where the signals were assigned by double resonance experiments.

A few years ago[4], we synthesized and characterized the sulfobetaine surfactant monomers **4** and **5** bearing tertiary acrylamide moieties (*Figure 1*). The ^1H n.m.r. data of these monomers in $CDCl_3$ were attributed according to the shift increments of standard tables[2] and by comparison with the spectra of their precursors. Based on their observations for monomers **1** and **2**, Lee and Tsai postulated reassignments for the signals of the α-methylene ammonium protons for **4** and **5** (protons N and P, see *Figure 1*) differing from our original interpretation[1,4] (see Tables 1 and 2). In particular, the protons of the α-methylene ammonium groups of the sulfopropyl moiety (position N) were supposed to be more strongly downfield shifted than the α-methylene ammonium groups of the 2-amidoethyl moiety (position P).

Considering that: (i) compounds having propyl spacers between the amide and the ammonium groups are compared with those having ethyl spacers only, i.e. γ-effects are compared with β-effects; (ii) secondary amides are compared with tertiary ones; and (iii) spectra of ionic compounds in water are compared with those in $CDCl_3$, the postulated analogy of the n.m.r. spectra of **1** and **2** to **4** and **5** appeared to us to be disputable. Thus, we have revisited the n.m.r. spectra of **4** and **5** in more detail.

Detailed assignments for monomers **4** and **5** are complicated by a number of problems. Several signals are not well resolved in the standard ^1H n.m.r. spectra owing to the similarity of the chemical shifts (see *Figures 2* and *3*). In addition, the α-methylene ammonium protons exhibit complex coupling patterns. It should be kept in mind that compounds **5** and **6** bear ammonium groups with four different substituents, i.e. the nitrogens are chiral (even if racemates are used). Also, the tertiary amide groups tend to show distinguishable *cis–trans* conformers at ambient temperature, thus complicating the n.m.r. spectra even more[4] (see below).

To clarify the individual chemical shifts, we performed various ^1H double resonance experiments, and recorded two-dimensional heteronuclear (^1H, ^{13}C) correlated spectra which allowed the unambiguous assignment of all signals in the solvents $CDCl_3$, CD_3OD and D_2O. The results are listed in *Tables 1* and *2*, together with some ^{13}C data in *Table 3*. *Table 4* presents for comparison n.m.r. data of the acrylate **6**, which is the ester analogue to acrylamide **5**.

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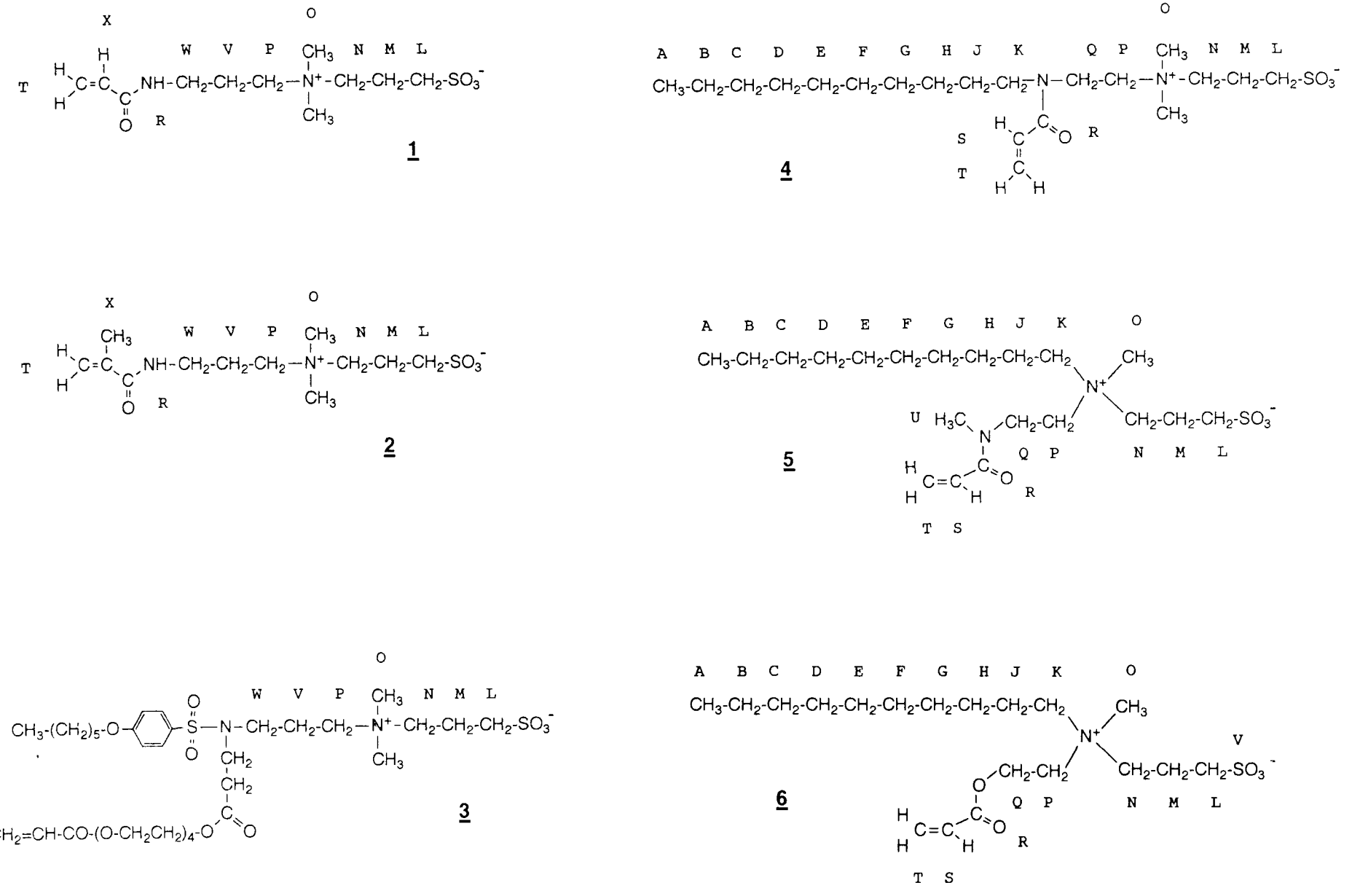

Figure 1 Formulae and attributions of sulfobetaines 1–6

Table 1 ^{1}H n.m.r. data of monomer **4** in various solvents at room temperature (data given only for the major conformer, integrals are approximate values ±10%)

$CDCl_3$				CD_3OD		D_2O	
Signal	Assignment ref. 4	Assignment ref. 1	Correct assignment	Signal	Assignment	Signal	Assignment
0.86 t, 3H	A		A	0.94 t, 3H	A	0.83 t, 3H	A
1.2–1.35 m, 14JH	B–H		B–H	1.25–1.5 m, 14H	B–H	1.15–1.40 m, 14H	B–H
1.56 m, 2H	J		J	1.68 m, 2H	J	1.57 m, 2H	J
2.25 m, 2H	M		M	2.28 m, 2H	M	2.24 m, 2H	M
2.88 t, 2H	L		L	2.92 t, 2H	L	2.93 t, 2H	L
3.24 s, 6H	O	O	O	3.23 s, 6H	O	3.19 s, 6H	O
3.44 t, 3H	K	K	K	3.54 m, 4H	K + P	3.4–3.65 m, 6H	K + N + P
3.56 m, 2H	Q	Q	P		(δK ≈ δP)		(δK < δN < δP)
3.7–3.9 m, 4H	N + P	N + P	N + Q	3.62 m, 2H	N		
		(δP < δN)	(δN < δQ)	3.89 m, 2H	Q	3.85–3.95 m, 2H	Q
5.72 m, 1H	T_{trans}		T_{trans}	5.83 m, 1H	T_{trans}	5.71 m, 1H	T_{trans}
6.30 m, 1H	T_{cis}		T_{cis}	6.34 m, 1H	T_{cis}	6.26 m, 1H	T_{cis}
6.4–6.6 m, 1H	S		S	6.78 m, 1H	S	6.60 m, 1H	S

Table 2 ^{1}H n.m.r. data of monomer **5** in various solvents at room temperature (data given only for the major conformer, integrals are approximate values ±10%)

$CDCl_3$				CD_3OD		D_2O	
Signal	Assignment ref. 4	Assignment ref. 1	Correct assignment	Signal	Assignment	Signal	Assignment
0.85 t, 3H	A	A	A	0.94 t, 3H	A	0.86 t, 3H	A
1.2–1.35 m, 14H	B–H	B–H	B–H	1.25–1.5 m, 14H	B–H	1.15–1.45 m, 14H	B–H
1.73 m, 2H	J	J	J	1.86 m, 2H	J	1.78 m, 2H	J
2.22 m, 2H	M	M	M	2.25 m, 2H	M	2.24 m, 2H	M
2.88 t, 2H	L	L	L	2.92 t, 2H	L	2.96 t, 2H	L
3.15 s, 3H	O	O	O	3.17 s, 3H	O	3.13 s, 3H	O
3.2–3.3 m, 5H	K + U	K + ?	K + U(δU < δK)	3.26 s, 3H	U	3.20 s, 3H	U
				3.40 m, 2H	K	3.37 m, 2H	K
3.5–3.6 m, 1H	N + Q	P + Q	N + P	3.53 m, 2H	P	3.6–3.8 m, 4H	N + P
3.6–3.8 m, 3H		(δQ < δP)	($\delta P_1 < \delta N_1 \approx \delta P_2 < \delta N_2$)	3.61 m, 2H	N		(δP ≈ δN)
3.87 m, 2H	P	N	Q	3.91 m, 2H	Q	3.85–4.0 m, 2H	Q
5.72 m, 1H	T_{trans}	T_{trans}	T_{trans}	5.84 m, 1H	T_{trans}	5.84 m, 1H	T_{trans}
6.28 m, 1H	T_{cis}	T_{cis}	T_{cis}	6.31 m, 1H	T_{cis}	6.22 m, 1H	T_{cis}
6.55 m, 1H	S	S	S	6.80 m, 1H	S	6.74 m, 1H	S

The tables show that neither our original assignments[4] for **4** and **5** nor the proposed revised ones[1] are fully correct. Whereas the largest chemical shifts are always found for the protons in the α-position to the amide nitrogen (position Q), the relative positions of the α-methylene ammonium protons depend on the solvent used. The α-methylene ammonium protons of the propylsulfonate moiety (position N) exhibit stronger chemical shifts in $CDCl_3$ and in CD_3OD than the α-methylene ammonium proton signals of the acrylamidoethyl moiety (position P). However, this is not true in D_2O where the signal sequence is reversed in the case of monomer **4**. The differences of the chemical shifts are often small, and the relative positions of the signals become clear only in double resonance experiments, as otherwise the signals are superposed to produce complex multiplets. Still, it is obvious that for these compounds the γ-effect of the sulfonate group is comparable to or even stronger than the β-effect of the amide group. This result is rather unexpected, paralleling the findings for monomers **1**–**3**. It should be noted that for the analogous acrylate **6**, although the relative positions of the n.m.r. signals are the normal ones (i.e. the γ-effect of the sulfonate group is weaker than the β-effect of the ester group), the absolute value of the chemical shift of protons N is virtually identical with the values observed in the case of the amides, and is thus much larger than expected.

There is another noteworthy feature in the spectrum of **5** which is present only in $CDCl_3$ (*Figure 3*): whereas the α-methylene ammonium protons of the decyl group (position K) apparently produce one signal, the α-methylene ammonium protons of the propylsulfonate moiety (position N) and of the amidoethyl moiety

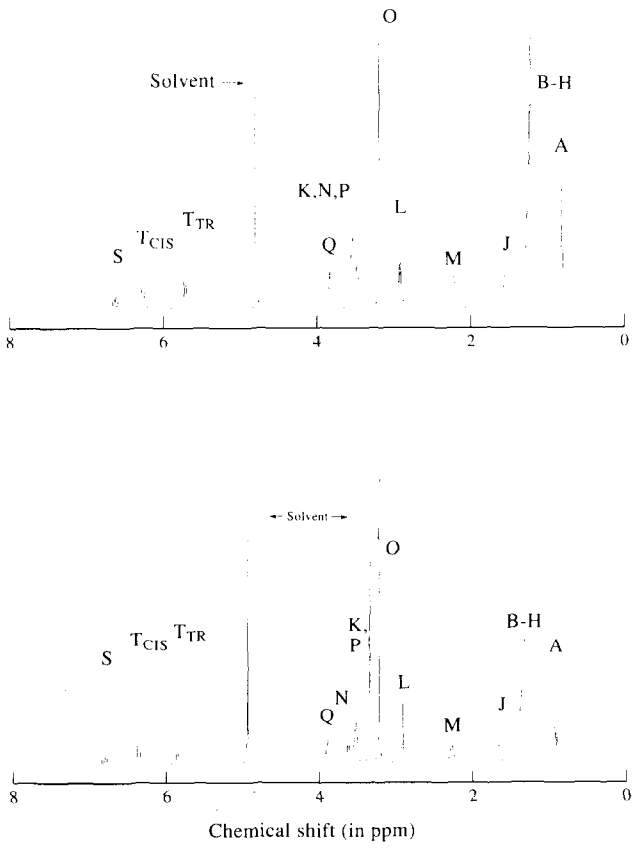

Figure 2 ^{1}H spectrum of monomer **4** in D_2O (top) and in CD_3OD (bottom) at room temperature (frequency 400 MHz, concentration 20 mg l^{-1})

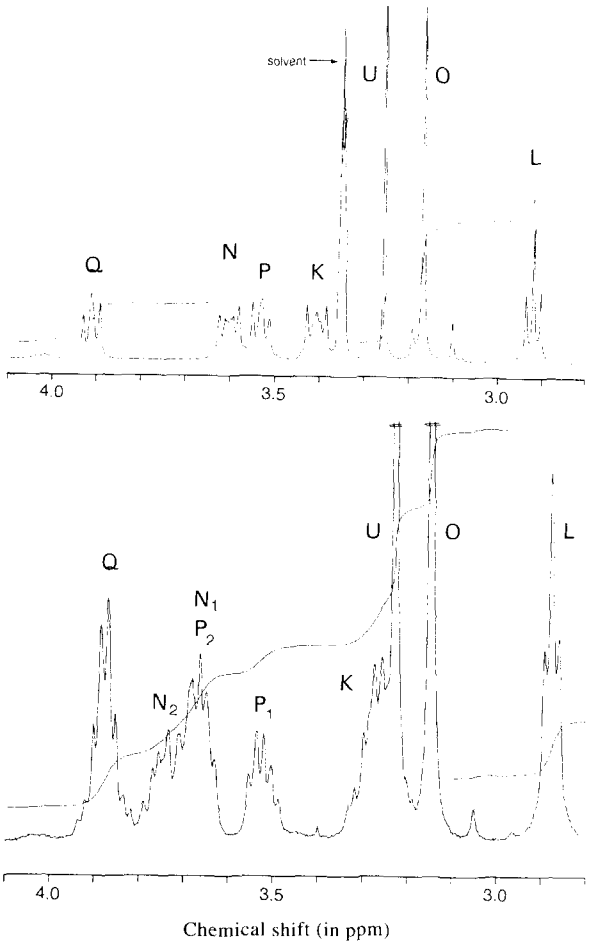

Figure 3 Details of the ^{1}H spectrum of monomer **5** in CD_3OD (top, 400 MHz) and in $CDCl_3$ (bottom, 500 MHz) at room temperature (concentration 20 mg l^{-1})

Table 3 ^{13}C n.m.r. data of monomers **4–6** in CD_3OD at room temperature

Monomer **4**		Monomer **5**		Monomer **6**	
Signal	Assignment	Signal	Assignment	Signal	Assignment
14.4	A	14.4	A	14.4	A
20.0	M	19.6	M	19.7	M
		23.1	J	23.2	J
23.7	B	23.7	B	23.6	B
27.6	H	27.4	H	27.4	H
30.35, 30.4, 30.5, 30.6, 30.7	D–G, J	30.2, 30.3, 30.6*	D–G	30.2, 30.3, 30.5*	D–G
33.0	C	33.0	C	33.0	C
		36.6	U		
41.6	Q	43.0	Q		
48.5	L	48.5	L	48.7	L
50.0	K				
51.7	O	49.1	O	49.4	O
				58.7	Q
61.2	P	58.1	P	61.3	P
64.5	N	62.0	N	62.3	N
		63.6	K	64.0	K
128.6	S	128.6	S	128.7	S
129.5	T	129.4	T	132.8	T
168.9	R	169.2	R	166.6	R

* Relative intensity 1 : 1 : 2

Table 4 ^{1}H n.m.r. data of monomer **6** in various solvents at room temperature

$CDCl_3$		CD_3OD		D_2O	
Signal	Assignment	Signal	Assignment	Signal	Assignment
0.83 t, 3H	A	0.94 t, 3H	A	0.87 t, 3H	A
1.2–1.35 m, 14H	B–H	1.25–1.5 m, 14H	B–H	1.2–1.45 m, 14H	B–H
1.68 m, 2H	J	1.84 m, 2H	J	1.79 m, 2H	J
2.21 m, 2H	M	2.25 m, 2H	M	2.26 m, 2H	M
2.84 t, 2H	L	2.92 t, 2H	L	2.97 t, 2H	L
3.20 s, 3H	O	3.20 s, 3H	O	3.21 s, 3H	O
3.28 m, 2H	K	3.45 m, 2H	K	3.43 m, 2H	K
3.72 m, 2H	N	3.64 m, 2H	N	3.62 m, 2H	N
3.86 m, 2H	P	3.82 m, 2H	P	3.83 m, 2H	P
4.65 m, 2H	Q	4.67 m, 2H	Q	4.66 m, 2H	Q
5.88 m, 1H	T_{trans}	6.02 m, 1H	T_{trans}	5.99 m, 1H	T_{trans}
6.08 m, 1H	S	6.28 m, 1H	S	6.22 m, 1H	S
6.39 m, 1H	T_{cis}	6.50 m, 1H	T_{cis}	6.48 m, 1H	T_{cis}

(position P) present four individual signals. Monomer **4** does not exhibit a similar effect in $CDCl_3$. This splitting of the signals was originally misinterpreted by us as the coexistence of *trans* and *cis* conformers of the amide group in roughly equal amounts (as found for the tertiary amine precursors[4]), thus leading to an incorrect assignment. In fact, a close inspection of the spectra shows a weak additional set of signals which can be assigned to the protons close to the amide moiety, suggesting a partition between the two possible amide conformers in a ratio of between 10:1 and 20:1 depending on the solvent used.

We have no fully satisfactory explanation of the above-described 'irregularities' in the n.m.r. spectra of the sulfobetaine monomers. The non-equivalence of the individual methylene protons in positions N and position P could be easily explained by their vicinity to the chiral ammonium centre. However, the non-equivalence of these methylene protons close to the chiral nitrogen is observed only in the case of monomer **5** in $CDCl_3$ solution. In solvents other than $CDCl_3$, or in the case of other racemic compounds analogues to **5** even in $CDCl_3$ (such as the acrylate **6** or the methacrylate analogue[4]), the two methylene protons in positions N, P and K always appear to be equivalent.

Most probably, the conformation of betaine moiety deviates from the usually assumed all-*trans* conformation. In $CDCl_3$, the presumed formation of inverse micelles of the surfactants **4** and **5** may contribute to the stabilization of unusual conformations[5], which could account for the unconventional splitting behaviour of the signals of the α-methylene ammonium protons.

Whether the unusually large chemical shifts observed for the α-methylene ammonium protons of the propylsulfonate moiety (position N) are caused by a ring-current effect due to a six-membered ring conformation of the 3-ammoniopropanesulfonate moiety, as proposed by Lee and Tsai[1], cannot be decided. Their interpretation contrasts with previously detailed i.r. and n.m.r. studies of 3-(alkylammonio)propanesulfonate surfactants in water, in which a pairing of the ammonium and the sulfonate group was denied[6]. With decreasing the polarity of the solvent from water via methanol to chloroform, a pairing of the complementary ionic groups might be more likely. But considering the solvent effects observed on the absolute and the relative positions of signals of protons N and P (*Tables 1* and *2*), there is no clear indication for that. In any case, the effects causing the unusually large chemical shift of the protons in position N are not restricted to amide derivatives, but are also present in esters, as exemplified in *Table 3* for acrylate **6**, and as also found for the analogous methacrylates[1,4].

Experimental

Compound **2** was a gift of Raschig (Germany). The synthesis of compounds **4–6** was described previously[4]. N.m.r. spectra were recorded with a Varian Gemini (300 MHz), a Bruker Aspect 3000 (400 MHz) and a Bruker AM500 (500.13 MHz). For $^1H-^{13}C$ coupling experiments, the HETCOR pulse sequence[7] was applied.

Acknowledgement

Helpful discussions with H. Kolshorn (Mainz) are gratefully acknowledged.

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