ELSEVIER

Journal of Molecular Catalysis A: Chemical 156 (2000) 127–132

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

Influence of amphiphile concentration on the enantioselectivity in the rhodium-catalyzed reduction of unsaturated substrates in water

Fabien Robert [a], Günther Oehme [b], Ingrid Grassert [b], Denis Sinou [a,*]

[a] *Laboratoire de Synthèse Asymétrique, Associé au CNRS, CPE Lyon, Université Claude Bernard Lyon 1, 43, Boulevard du 11 novembre 1918, 69622 Villeurbanne Cedex, France*

[b] *Institut für Organische Katalyseforschung an der Universität Rostock, Buchbinderstrasse 5-6, 18055 Rostock, Germany*

Abstract

The enantioselectivity of the asymmetric hydrogenation of some unsaturated amino acid precursors with [Rh(COD)(**1**)]BF_4 and [Rh(COD)(**2**)]ClO_4 as catalyst is influenced by the presence of amphiphiles. Performing the reduction in water, both the activity and the enantioselectivity are enhanced significantly in the presence of surfactants. The determination of the CMC of some surfactants, as well as the reduction in mixtures of water/methanol in the presence of amphiphiles, give some evidence for the importance of micelles formation in these enhancements.

Keywords: Asymmetric hydrogenation; Rhodium; Surfactants; CMC

1. Introduction

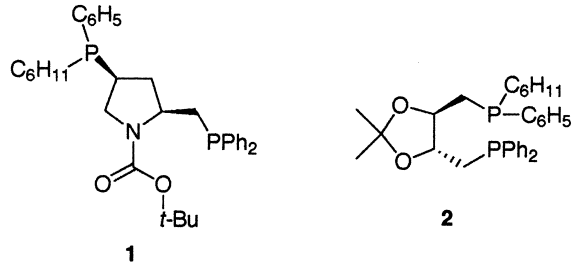
The homogeneous asymmetric hydrogenation of amino acid precursors in the presence of optically active rhodium or ruthenium complexes is now a well used methodology, in the laboratory or on a technical scale [1–4]. Very high enantioselectivities have been obtained when performing the reaction in methanol or ethanol. Although catalytic reactions in aqueous micelles have been an interesting research field in organic chemistry [5–7], it is only recently that Oehme et al. showed that the reduction of non-water-soluble unsaturated substrates could also be performed using the same rhodium complexes in water in the presence of surfactants [8–16]. Generally, the activity and enantioselectivity were increased in this aqueous medium.

We recently described the preparation of two new chiral ligands **1** and **2** (Scheme 1), analogues of BPPM and DIOP, and their use, in association with rhodium, in the asymmetric hydrogenation of some prochiral substrates [17]. In this paper, we describe the use of these ligands in the reduction of unsaturated amino acid precursors in the presence of various surfactants, and give some new evidence for the

* Corresponding author. Tel.: +33-4-72446263; fax: +33-4-72448160.

E-mail address: sinou@univ-lyon1.fr (D. Sinou).

1381-1169/00/$ - see front matter
PII: S1381-1169(99)00422-7



Scheme 1.

importance of micelles formation to obtain higher enantioselectivity and activity.

2. Experimental

The enantiomeric excess (% ee, $\pm 0.5\%$) was determined by glc on the methyl ester of alanine or phenylalanine with a 10-m capillary column coated with XE-60-L-valine-*tert*-butylamide. All detergents: sodium dodecyl sulfate (SDS), sodium dodecylsulfonate ($C_{12}H_{25}SO_3Na$), cetyltrimethylammonium hydrogen sulfate ($CTAHSO_4$), decaoxyethylene-dodecyl ether (Brij 35),polyoxyethylenesorbitane monopalmitate (Tween 40), *N*-decyl-*N*,*N*-dimethyl-3-ammonio1-propanesulfonate (DeDAPS), *N*-dodecyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (DDAPS), and *N*-hexadecyl-*N*,*N*-dimethyl-3-ammonio-1-propanesulfonate (HDAPS), are from commercial sources and used as obtained.

2.1. Hydrogenation

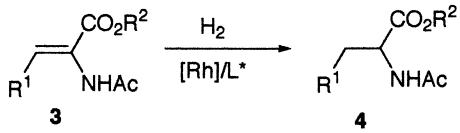
Hydrogenations were performed under normal pressure and at 25°C. The solvent, the substrate, the surfactant, the rhodium complex, and the phosphine were placed in a deaerated hydrogenation flask and stirred for 15 min in an argon atmosphere. Then, argon was changed against hydrogen and the reaction was followed by a volumetric measurement at 25°C. When the reaction was complete, the mixture was extracted with chloroform in the case of the methyl ester and the enantioselectivity controlled by glc. In the case of the acid, the solvent was evaporated and the residue, dissolved in ethanol was esterified with diazomethane; then the enantioselectivity was measured by glc.

3. Results and discussion

We first investigated the reduction of methyl-(*Z*)-2-acetamidocinnamate **3a** (Scheme 2) in the presence of the rhodium complex prepared in situ from $[Rh(COD)_2]BF_4$ and ligand **1** (Table 1). Reduction in methanol gave high enantioselectivity [ee = 93% (*R*)] and activity (Table 1, entry 1). Water alone is a poor solvent for both the catalyst and the substrate and gave lower activity and enantioselectivity (Table 1, entry 2). However, the addition of a surfactant, which could be anionic (Table 1, entry 3), cationic (Table 1, entry 4), or non-ionic (Table 1, entry 5), gave all high activities and enantioselectivities, and up to 95% ee in the presence of $CTAHSO_4$. A similar behaviour was previously observed using BPPM as the chiral ligand [9].

The use of the zwitterionic surfactants HDAPS, DDAPS, and DeDAPS (Table 1, entries 6–8) gave quite different results. Although high enantioselectivities (up to 94% ee) and activities were obtained in the presence of DDAPS and HDAPS, DeDAPS led to lower enantioselectivity (83% ee) and activity.

We then turned our attention to the reduction of **3a** catalyzed by the rhodium complex



a $R^1 = C_6H_5$, $R^2 = CH_3$
b $R^1 = C_6H_5$, $R^2 = H$
c $R^1 = H$, $R^2 = CH_3$

Scheme 2.

Table 1
Effect of amphiphiles on the hydrogenation of **3a** with the catalytic system [Rh(COD)(**1**)]BF_4[a]

Entry	Solvent	Amphiphile	$t_{1/2}$ (min)	ee (%) (configuration)[b]
1	CH_3OH	–	3	93(*R*)
2	H_2O	–	45	78(*R*)
3	H_2O	SDS	4	91(*R*)
4	H_2O	$CTAHSO_4$	3.7	95(*R*)
5	H_2O	Brij 35	4	94(*R*)
6	H_2O	DeDAPS	43	83(*R*)
7	H_2O	DDAPS	6.5	93(*R*)
8	H_2O	HDAPS	8	93(*R*)

[a]Reaction conditions: 25°C; 0.1 MPa H_2; 7.5 ml solvent; [substrate] = 67 mmol l^{-1} (0.5 mmol per experiment); [substrate]:[catalyst] = 100; [amphiphile]:[catalyst] = 20; $t_{1/2}$ is the time necessary to consume half of the theoretical amount of hydrogen.

[b]Determined by glc with a 10-m capillary column coated with XE-60-L-valine-*tert*-butylamide.

[Rh(COD)(**2**)]ClO_4 in the presence of various surfactants (Table 2). In methanol as the solvent, methyl (*S*)-*N*-acetylphenylalaninate was obtained in 24% ee within 1.7 min (Table 2, entry 1); however, the (*R*) enantiomer was obtained in H_2O in 7% ee within 45 min (Table 2, entry 2). The addition of surfactants such as SDS, $C_{12}H_{25}SO_3Na$, $CTAHSO_4$, Brij 35, or Tween 40 (Table 2, entries 3–7), increased the activity in all cases and the enantioselectivity only in the first two cases, the (*S*) enantiomer being always obtained. Although DDAPS and HDAPS also gave the (*S*) enantiomer in 10% ee within 5 min (Table 2, entries 9–10), the amphiphile DeDAPS gave the (*R*) enantiomer with lower ee (5%) and also lower activity (Table 2, entry 8).

A similar behaviour was observed in the reduction of (*Z*)-2-acetamidocinnamic acid **3b**. When the reduction was performed in water in the presence of SDS, $CTAHSO_4$, Brij 35, or DDAPS (Table 2, entries 13–15 and 17), the (*S*)-*N*-acetylphenylalanine was obtained with higher enantioselectivities and activities than those observed in water alone (Table 2, entry 12). Again, DeDAPS gave the (*S*)-*N*-acetylphenylalanine with very low activity and enantioselectivity, quite close to those observed in water alone (Table 2, entry 16).

The reduction of methyl-2-acetamidoacrylate **3c** gave quite similar results. Noteworthy, the reduction in water gave the methyl (*R*)-*N*-acetylalaninate with 6% ee within 12 min (Table 2, entry 19), and performing the reaction in methanol gave the (*S*) enantiomer within 1.3 min with 20% ee (Table 2, entry 18). Again, although the enantioselectivity was very low, DDAPS gave the (*S*) enantiomer (< 1% ee) within 1.5 min (Table 2, entry 24), and DeDAPS the (*R*) enantiomer (4% ee) within 12 min (Table 2, entry 23).

Table 2
Effect of amphiphiles on the hydrogenation of different unsaturated amino acid precursors with the catalytic system [Rh(COD)(**2**)]ClO_4[a]

Entry	Substrate	Amphiphile	$t_{1/2}$ (min)	ee (%)[b]	Configuration
1	**3a**	without in CH_3OH	1.7	24	(*S*)
2	**3a**	without in H_2O	45	7	(*R*)
3	**3a**	SDS	4.5	16	(*S*)
4	**3a**	$C_{12}H_{25}SO_3Na$	8.5	16	(*S*)
5	**3a**	$CTAHSO_4$	5	5	(*S*)
6	**3a**	Brij 35	6	8	(*S*)
7	**3a**	Tween 40	9	2	(*S*)
8	**3a**	DeDAPS	40	5	(*R*)
9	**3a**	DDAPS	5	11	(*S*)
10	**3a**	HDAPS	5	10	(*S*)
11	**3b**	without in CH_3OH	2.5	47	(*S*)
12	**3b**	without in H_2O	180	20	(*S*)
13	**3b**	SDS	9	34	(*S*)
14	**3b**	$CTAHSO_4$	7	45	(*S*)
15	**3b**	Brij 35	7	45	(*S*)
16	**3b**	DeDAPS	150	22	(*S*)
17	**3b**	DDAPS	10.5	43	(*S*)
18	**3c**	without in CH_3OH	1.3	20	(*S*)
19	**3c**	without in H_2O	12	6	(*R*)
20	**3c**	SDS	3	2	(*R*)
21	**3c**	$CTAHSO_4$	6	4	(*R*)
22	**3c**	Brij 35	4.5	5	(*S*)
23	**3c**	DeDAPS	12	4	(*R*)
24	**3c**	DDAPS	1.5	< 1	(*S*)

[a]Reaction conditions: 25°C; 0.1 MPa H_2; 7.5 ml solvent; [substrate] = 67 mmol l^{-1} (0.5 mmol per experiment); [substrate]:[catalyst] = 100; [amphiphile]:[catalyst] = 20; $t_{1/2}$ is the time necessary to consume half of the theoretical amount of hydrogen.

[b]Determined by glc with a 10-m capillary column coated with XE-60-L-valine-*tert*-butylamide.

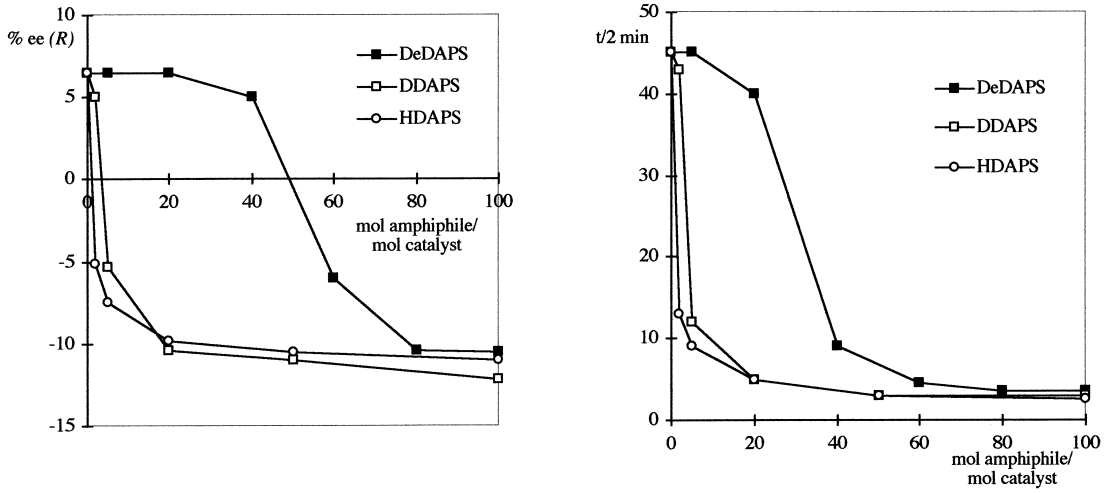


Fig. 1. Influence of amphiphiles on the enantioselectivity (left) and the activity (right) in the hydrogenation of **3a** with [Rh(COD)(**2**)]ClO_4 in water. For conditions, see Table 2, footnote [a].

In order to have a better understanding of the different behaviour of the zwitterionic amphiphiles DeDAPS, DDAPS, and HDAPS, we studied the influence of the relative concentration of the amphiphile both on the enantioselectivity and the activity of this latter catalyst on the hydrogenation of **3a** (Fig. 1). We observed that at low concentration in amphiphiles, the (*R*) enantiomer was predominantly obtained, and the (*S*) enantiomer at higher concentration; the same behaviour was observed for the half-life. However, the hydrogenation of **3a** needed higher concentration in amphiphile in the case of DeDAPS compared with DDAPS or HDAPS for equivalent activities.

It was previously noticed by Grassert et al. [9] that the change in activity and enantioselectivity was maximal near the CMC. The formation of micelles depends on the structure of the amphiphile, and particularly on its hydrophobic–hydrophilic balance. Since one explanation of these different behaviours could be the different CMC values, we determined the CMC values of DeDAPS and HDAPS using the methodology of Furton and Norelus [18]. We obtained the values of 14 and 0.15 mmol l^{-1} for the CMC of DeDAPS and HDAPS, respectively, and 1.1 mmol l^{-1} for DDAPS, close to the value of 1.2 found in the literature [5].

With these values in hands, we performed some more hydrogenations of **3a** by changing the amphiphile concentration near the CMC (Fig. 2). We effectively observed that the inversion of the configuration of the obtained amino acid occurred around 2.5 mmol l^{-1} in DDAPS and 19 mmol l^{-1} for DeDAPS. These values are slightly higher than the CMC of these amphiphiles; however, the presence of the substrate and the catalyst have not been taken into account in the CMC determinations, and they could influence the latter [19].

In order to see if this reversal in configuration was general, hydrogenation of **3a** was performed in the presence of various amounts of SDS (CMC = 8.1 mmol l^{-1}) and $CTAHSO_4$ (CMC = 0.92 mmol l^{-1}). In the case of SDS, the (*S*) enantiomer was obtained in 16% ee using a ratio [amphiphile]/[rhodium] = 20, corresponding to [amphiphile] = 13.3 mmol l^{-1} accordingly higher to the CMC, and the enantioselectivity was 6% in the (*R*) enantiomer by decreasing the ratio [amphiphile]/[rhodium] to 5, corresponding to [amphiphile] = 3.3 mmol l^{-1}, thus, lower to the CMC. For $CTAHSO_4$,

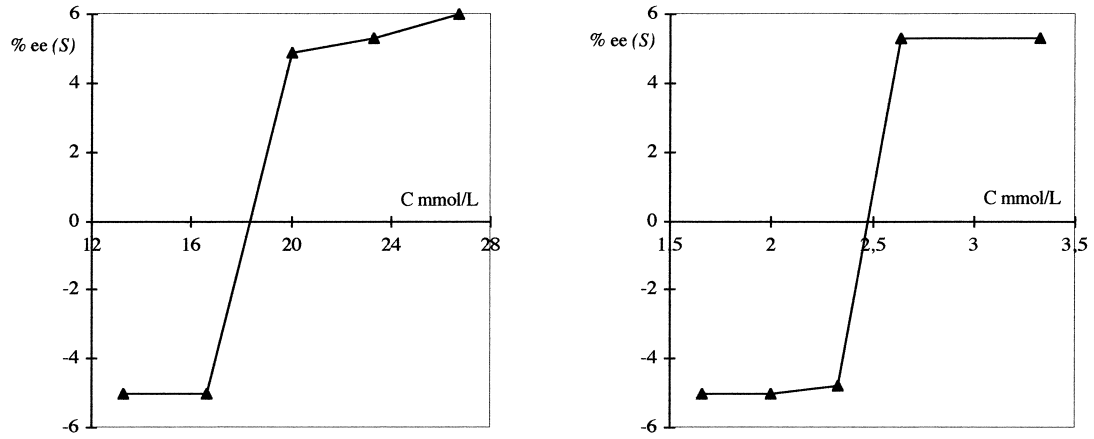


Fig. 2. Influence of the concentration of DeDAPS (left) and DDAPS (right) on the enantioselectivity in the hydrogenation of **3a** with [Rh(COD)(**2**)]ClO_4 in water. For conditions, see Table 2, footnote [a].

the (*S*) enantiomer was obtained in 5% ee using a ratio [amphiphile]/[rhodium] = 5 corresponding to [amphiphile] = 3.3 mmol l^{-1} and the enantioselectivity was 6% in the (*R*) enantiomer by using a ratio [amphiphile]/[rhodium] = 1, corresponding to [amphiphile] = 0.67 mmol l^{-1}. All these experiments show clearly that the reversal in configuration, shifting on the (*R*)–(*S*) scale in the (*S*) direction, occurred at a concentration in amphiphiles slightly higher than the CMC. This is a further argument for the importance of micelle formation on the enhancement of the enantioselectivity.

To confirm the importance of micelle formation in the enhancement of enantioselectivity in the rhodium-catalyzed reduction of **3a**, we performed some experiments in water/methanol mixtures (Fig. 3). It is effectively known that the ability of amphiphiles such as SDS or $CTAHSO_4$ to form micelles decreases as the

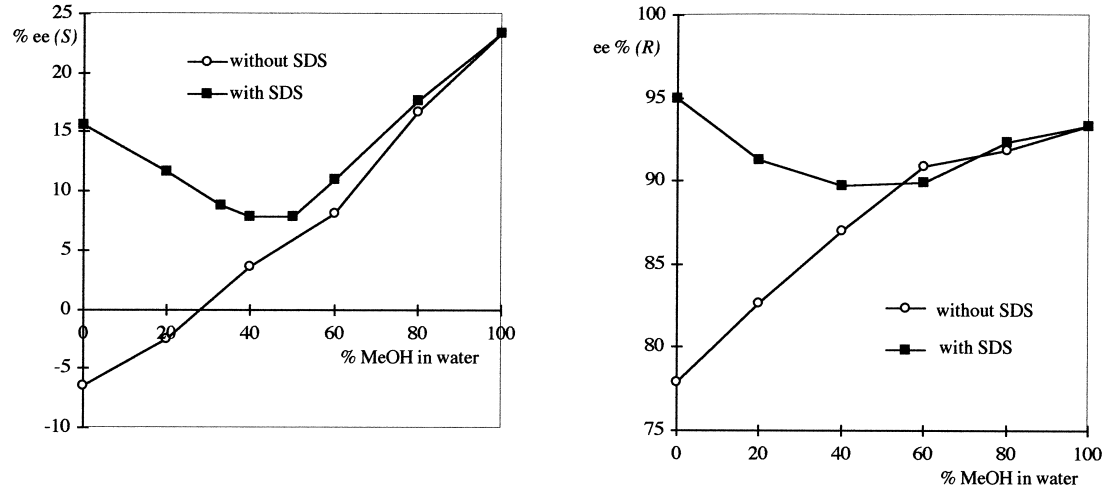


Fig. 3. Influence of varying amounts of methanol in water on the enantioselectivity in the hydrogenation of **3a** with [Rh(COD)(**2**)]ClO_4 (left) and [Rh(COD)(**1**)]BF_4 (right). For conditions, see Table 2, footnote [a].

percentage of methanol in water/alcohol mixture increases [20]. Indeed, using [Rh(COD)-(**2**)]ClO_4 as the catalyst and without added SDS, we observed a continuous increase in enantioselectivity, and an inversion of configuration of the amino acid obtained at a ratio water/MeOH = 70/30. In the presence of SDS, we obtained in neat water the (*R*) enantiomer with ee of up to 16%. This enantioselectivity decreased with increasing amounts of methanol in water. However, this enantioselectivity decrease stops at 50% methanol content, when it reaches the curve without SDS. At higher amount of methanol, the enantioselectivies obtained in the presence or not of SDS are quite similar.

The same trends were observed using [Rh(COD)(**1**)]BF_4 as the catalyst. Without $CTAHSO_4$, a continuous increase in enantioselectivity was observed, going from 78% in neat water to 93% in pure methanol. In the presence of the amphiphile $CTAHSO_4$, starting with 96% ee (*S*) in water, a decrease in enantioselectivity was observed, which stops at approximatively 50% methanol content. Then the values obtained in the presence or not of $CTAHSO_4$ are again quite similar.

4. Conclusion

Different types of micelle-forming amphiphiles have been shown to have beneficial effect both on activity and enantioselectivity in the hydrogenation of some amino acid precursors. The results obtained in water in the presence of the surfactant are quite comparable to those obtained in pure methanol. The effect of surfactants seems to be directly connected with the formation of micelles since positive effects have been observed above the CMC. However, in the case of water/methanol mixtures, this positive effect decreased when the proportion of methanol in the solvent mixture is increased, and this is probably due to the destruction of the micelles.

Acknowledgements

We are grateful to the M.E.N.E.S.R (fellowship to F.B.) and the Région Rhône-Alpes for financial support. We also have to thank the Fonds der Chemischen Industrie.

References

[1] J.D. Morrison (Ed.), Asymmetric Synthesis Vol. 5 Academic Press, New York, 1985.
[2] R. Noyori, in: Asymmetric Catalysis in Organic Synthesis, Wiley, New York, 1994, p. 16.
[3] H. Takaya, T. Ohta, R. Noyori, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, Wiley, Weinheim, 1998, p. 1.
[4] M. Beller, C. Bolm (Eds.), Transition Metals for Organic Synthesis Vol. 2 Wiley, Weinheim, 1998, p. 1.
[5] J.H. Fendler, Membrane Mimetic Chemistry, Wiley, New York, 1982.
[6] C.A. Bunton, G. Savelli, Adv. Phys. Org. Chem. 22 (1986) 213.
[7] C.A. Bunton, Surfactant Sci. Ser. 38 (1991) 13.
[8] G. Oehme, E. Paetzold, R. Selke, J. Mol. Catal. 71 (1992) L1.
[9] I. Grassert, E. Paetzold, G. Oehme, Tetrahedron 49 (1993) 6605.
[10] A. Kumar, G. Oehme, J.P. Roque, M. Schwarze, R. Selke, Angew. Chem., Int. Ed. Engl. 33 (1994) 2197.
[11] I. Grassert, V. Vill, G. Oehme, J. Mol. Catal. A: Chem. 116 (1997) 231.
[12] I. Grassert, U. Schmidt, S. Ziegler, C. Fischer, G. Oehme, Tetrahedron: Asymmetry 9 (1998) 4193.
[13] G. Oehme, I. Grassert, S. Ziegler, R. Meisel, H. Fuhrmann, Catal. Today 42 (1998) 459.
[14] T. Dwars, U. Schmidt, C. Fischer, I. Grassert, R. Kempe, R. Fröhlich, K. Drauz, G. Oehme, Angew. Chem., Int. Ed. Engl. 37 (1998) 2851.
[15] R. Selke, J. Holz, A. Riepe, A. Börner, Chem.-Eur. J. 4 (1998) 769.
[16] S. Trinkhaus, R. Kadyrov, R. Selke, J. Holz, L. Götze, A. Börner, J. Mol. Catal. A: Chem. 144 (1999) 15.
[17] F. Robert, G. Oehme, D. Sinou, J. Mol. Catal. A: Chem. 139 (1999) 105.
[18] K.G. Furton, A. Norelus, J. Chem. Educ. 70 (1993) 254.
[19] M.J. Rosen, in: Surfactants and Interfacial Phenomena, Wiley, New York, 1989, p. 137.
[20] R. Zana, Adv. Colloid Interface Sci. 57 (1995) 1.