

Surfactant-assisted specific-acid catalysis of Diels–Alder reactions in aqueous media

Egid B. Mubofu^{1*} and Jan B.F.N. Engberts²

¹Chemistry Department, University of Dar es Salaam, Dar es Salaam, Tanzania

²Physical Organic Chemistry Unit, Stratingh Institute, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

Received 16 March 2007; revised 4 June 2007; accepted 9 June 2007

ABSTRACT: Surfactant-assisted specific-acid catalysis (SASAC) for Diels–Alder reactions of dienophiles **1** and **4** with cyclopentadiene **2** in aqueous media at 32 °C was studied. This study showed that acidified anionic surfactants (pH 2) such as sodium dodecyl sulfate (SDS) and linear alkylbenzene sulfonic acid (LAS) accelerate Diels–Alder reactions. Conversely, under similar reaction conditions (pH 2) these reactions are inhibited by (acidified) cationic surfactants such as dodecyltrimethylammonium bromide (DTAB), dodecylmethylammonium bromide (DDAB), and dodecylmethylammonium bromide (DMAB). A modest rate acceleration resulting from the surfactant hydrogen-bonding capacity is also recorded for the Diels–Alder reaction of naphthoquinones (**6**) with cyclopentadiene (**2**) in aqueous media at 32 °C. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: specific-acid catalysis; Diels–Alder reaction; surfactant-type Brønsted acid; micellar catalysis; micellar inhibition

INTRODUCTION

Diels–Alder reactions provide important and useful methods for the synthesis of six-membered ring compounds including versatile synthetic intermediates and natural products.¹ The reaction involves the stereospecific [4+2] cycloaddition of a dienophile and a conjugated diene. The reaction is accelerated when performed in water² and is catalyzed by both Lewis-acid^{3–5} and specific-acid catalysts.^{6–8} Generally, the use of micellar and vesicle-forming surfactants as catalysts is common for Diels–Alder and other types of cycloaddition reactions in aqueous solution.⁹ More interestingly, the combination of water-stable Lewis-acids such as scandium triflate and anionic surfactant (e.g. sodium dodecyl sulfate (SDS)), gives remarkably efficient Lewis-acid catalysts for some organic reactions in water.¹⁰ The use of scandium tris(dodecyl sulphate), Sc(DS)₃, for example, has been successfully applied to the three-component Mannich-type reaction of aldehydes, amines, and silyl enolates in water.¹¹ Furthermore, the use of copper salt of 5,5-di-*n*-dodecyl-2-hydroxyl-1,3,2-dioxaphosphorinan-2-one, Cu(dDP)₂¹² and copper bis(dodecyl sulphate), (Cu(DS)₂),¹³ have shown an excellent rate acceleration for Diels–Alder reactions in water.

Combined Lewis-acid surfactant catalysts form stable colloidal dispersions with organic substrates and hence are effective Lewis-acid catalysts. Combined Brønsted-acid surfactant catalysts in water have also been employed in a number of organic reactions in water.^{14–16} However, these catalysts have not been studied on Diels–Alder reactions in water. The aggregation of long-chain hydrocarbontails (C₁₀–C₂₀) in water results in the semi-ordered structures of micelles with ionic groups protruding into the aqueous phase whereas the aliphatic chains are brought to close proximity in the core of the aggregate excluding water. This means that when organic compounds are introduced in an aqueous micellar solution, dipolar and hydrophobic interactions will cause binding of these compounds to the micelles.^{17,18} The properties of the binding site will strongly depend on the nature and concentration of the solubilize and the nature of the surfactant used. It is therefore reasonable to assume that surfactant-assisted specific-acid catalysis (SASAC) for Diels–Alder reactions in water should occur depending on the type of the surfactant and the overall influence of hydrophobic effects, electrostatic interactions, and the accompanying medium effects. It is anticipated that for anionic surfactant molecules, the headgroups will concentrate the protons near the surface of the aggregates. In this solution, hydrophilic dienophiles are expected to reside near the surface of the micellar aggregates and hence will be in close proximity to the bound protons and as a result an enhancement of the rate of the Diels–Alder

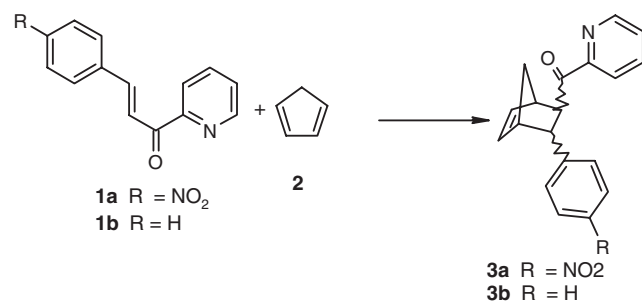
*Correspondence to: E. B. Mubofu, Chemistry Department, University of Dar es Salaam, P.O. Box 35061, Dar es Salaam, Tanzania.
E-mail: mubofu@chem.udsm.ac.tz

reaction is expected. On the contrary however, it is anticipated that the cationic surfactants will repel the protons from the Stern region of the micelle and hence inhibit the Diels–Alder reactions. Consequently, Diels–Alder reactions would efficiently be accelerated in the specific-acid/anionic surfactant combination and will be retarded in the specific-acid/cationic surfactant combination. To our knowledge, SASAC of Diels–Alder reactions in aqueous media has not been reported previously. In this study, we present kinetic data that illustrate the catalytic efficiency of SASAC for Diels–Alder reactions. The hydrogen-bond donor capacity of surfactants has also been applied to increase the reactivity of these cycloaddition reactions in aqueous media.

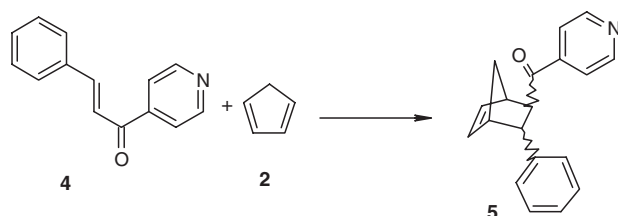
RESULTS AND DISCUSSION

Diels–Alder reactions in the presence of SDS and acidified SDS

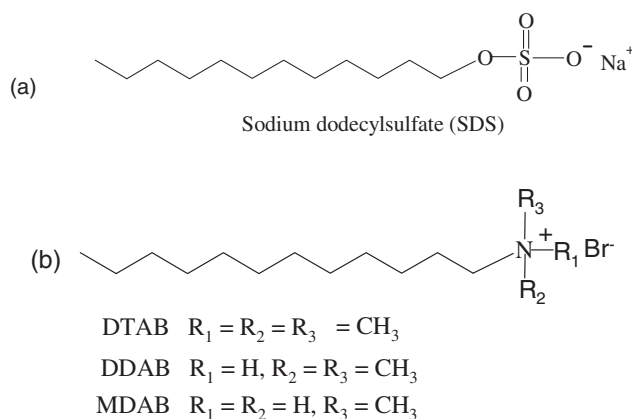
SASAC has been examined for the Diels–Alder reactions of substituted 3-phenyl-1-(2-pyridyl)-2-propen-1-one **1** and 3-phenyl-1-(4-pyridyl)-2-propen-1-one **4** with cyclopentadiene **2** (Schemes 1 and 2). First, the reaction of dienophile **1a** with cyclopentadiene **2** was carried out in SDS solutions in water. The presence of SDS (Scheme 3a) afforded reaction rates higher than those for the same reaction in water under similar reaction conditions. At the critical micelle concentration (cmc) of SDS, the acceleration reaches a maximum of almost 40 times faster than the uncatalyzed reaction rates under similar reaction



Scheme 1



Scheme 2



Scheme 3

conditions (Table 1). It is reasonable to assume that the rate acceleration in the presence of SDS in water is due to concentration of diene and dienophile in the micellar reaction volume.^{19,20} Upon acidification of the surfactant solution with hydrochloric acid up to pH 2, the reaction rates are further improved (Fig. 1). At the cmc of SDS (8.38 mM)²¹ at 32 °C, the apparent second-order rate constant of the reaction is increased from 0.26 to 0.57 s⁻¹ M⁻¹. Above the surfactant cmc, a gradual decrease in the reaction rate occurs due to the dilution effect upon increasing the surfactant concentration.

We suggest that the increased concentration of protons near the surfactant headgroups leads to the reaction rate enhancements for the Diels–Alder reaction. The rate increase upon acidification of the SDS solution suggests that the combination of hydronium ions and anionic surfactant leads to a more effective specific-acid catalyst for this Diels–Alder reaction. This observation serves as an indirect proof that this type of bimolecular Diels–Alder reaction occurs near the surface of the micellar headgroups. Even if the precise preferred location of the less hydrophobic dienophile is uncertain, these observations suggest that it is close to the micellar surface while that of the hydrophobic reactant (i.e. cyclopentadiene) is probably deeper in the micelle.

Table 1. The apparent second-order rate constants for the Diels–Alder reaction of **1a** with cyclopentadiene **2** in different reaction media at 32 °C

Medium	k (M ⁻¹ s ⁻¹)	Relative to the uncatalyzed reaction in water
Uncatalyzed reaction in water	0.0067	1
SDS (10 mM in water))	0.259	37
SDS (10 mM in water, pH 2)	0.57	81
Hydrochloric acid (0.01 M)	0.141	21
LAS (0.8 mM)	1.16	173

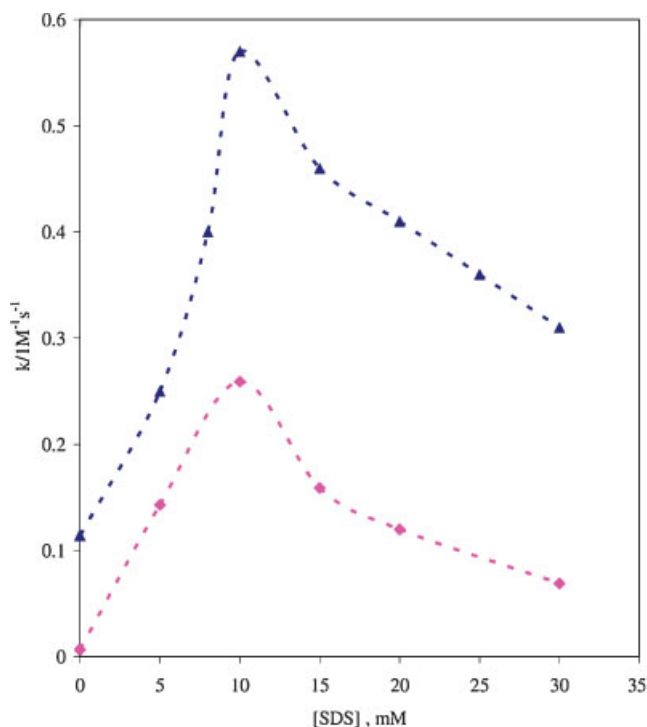
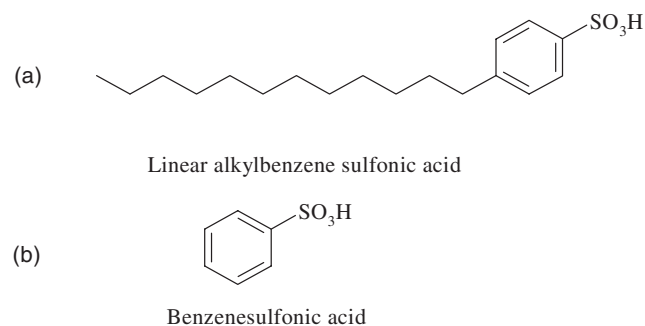


Figure 1. Catalysis of the Diels–Alder reaction of 3-(4-nitrophenyl)-1-(2-pyridyl)-2-propen-1-one (**1a**) with cyclopentadiene (**2**) using SDS (◆) and acidified SDS (▲)

Diels–Alder reactions using linear alkylbenzene sulfonic acid (LAS)

The catalysis of Diels–Alder reactions with linear LAS, an examined micelle-forming surfactant (Scheme 4a), was also examined. Figure 2 shows the apparent second-order rate constants for these reactions. They are larger than those obtained when the reaction was performed in aqueous acidified SDS (Table 1).

The Diels–Alder reaction of 4-nitrophenyl-1-(2-pyridyl)-2-propen-1-one **1a** with cyclopentadiene **2** in linear LAS is about 170 times faster than the uncatalyzed reaction under similar reaction conditions. The maximum apparent second-order rate constant in linear LAS is almost eightfold faster than that in aqueous 0.01 M HCl and it



Scheme 4

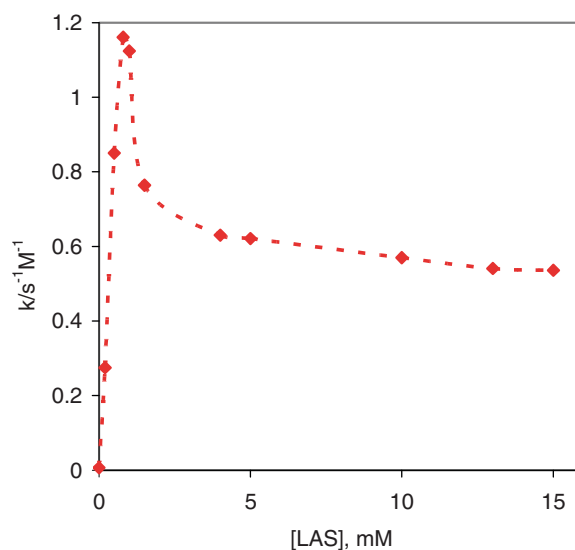


Figure 2. The influence of linear alkylbenzene sulfonic acid (LAS) on the apparent second-order rate constants for the Diels–Alder reaction of 3-(4-nitrophenyl)-1-(2-pyridyl)-2-propen-1-one (**1a**) with cyclopentadiene (**2**)

is twice faster than that in SDS solution at pH 2. The maximum catalytic efficiency of LAS is found to be at relatively low acid strength (pH 3) and at a concentration of 0.8 mM. The activity then drops drastically even though the acid strength increases (Table 2). This demonstrates that the catalytic efficiency of LAS depends on both the surfactant properties of LAS and its specific-acid strength. Dilution of diene and dienophile on more micelles is in competition with an increase in acid concentration.

Catalysis by LAS on the Diels–Alder reaction of dienophiles (**1b**, **4**) with cyclopentadiene **2** in water

LAS was also found to be the catalyst of choice for the Diels–Alder reaction of 3-phenyl-1-(2-pyridyl)-2-propen-1-one **1b** and 3-phenyl-1-(4-pyridyl)-2-propen-1-one **4** dienophiles with cyclopentadiene **2** in water at 32 °C

Table 2. Comparison of LAS and HCl for their catalytic activity on the Diels–Alder reaction of **1a** with **2** in water at 32 °C

pH of LAS in water	k_{LAS} (M ⁻¹ s ⁻¹)	pH of HCl in water	k_{H} (M ⁻¹ s ⁻¹)
1.37	0.52	1.37	0.20
2.08	0.54	2.00	0.14
2.35	0.63	2.42	0.09
2.99	1.12	2.90	0.04
3.10	1.16	3.00	0.034

Table 3. The apparent second-order rate constants for the Diels–Alder reaction of dienophiles **1** and **4** with cyclopentadiene **2** in 1 mM linear alkylbenzene sulfonic acid compared to the uncatalyzed reaction in water at 32 °C

Reaction	k_{LAS} ($\text{M}^{-1} \text{s}^{-1}$)	k_{w} ($\text{M}^{-1} \text{s}^{-1}$)	$k_{\text{LAS}}/k_{\text{w}}$
1a + 2	1.124	0.0067	168
1b + 2	0.1223	0.0049	25
4 + 2	0.0267	0.0041	6.5

(Table 3). The catalysis by LAS on these reactions shows that the bidentate character of the dienophile **1b** provides an advantage over the monodentate counterpart **4** (Fig. 3).

This behavior has been previously observed for these reactions when catalyzed by conventional aqueous hydrochloric acid under similar reaction conditions.²² This reactivity difference is caused by both hydrogen-bonding interactions and electronic effects. The proton at the pyridyl nitrogen of **1b** may undergo intramolecular hydrogen-bonding with the oxygen atom of the carbonyl group. Consequently, this interaction will stabilize the lowest unoccupied molecular orbitals (LUMO) of **1b**, and thereby enhancing its reactivity. On the other hand, the proton attached at the pyridyl nitrogen of the dienophile **4** is at a too remote distance from the carbonyl oxygen for the intramolecular hydrogen-bonding. In addition, the intramolecular electrostatic interaction between the positive charge on the pyridyl nitrogen and the negative charge on the oxygen of the carbonyl carbon in dienophile **1b** is another possible reason of this reactivity difference between these dienophiles.

The catalytic activity of benzenesulfonic acid and that of linear LAS (Scheme 4a) on the Diels–Alder reactions of 3-(4-nitrophenyl)-1-(2-pyridyl)-2-propen-1-one dienophile

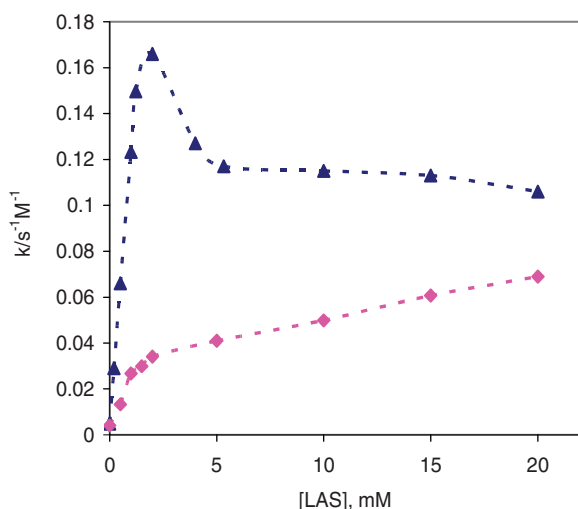


Figure 3. Comparison of the apparent second-order rate constants for the reaction of dienophile **1b** (▲) and dienophile **4** (◆) with cyclopentadiene **2** at 32 °C in aqueous linear alkylbenzene sulfonic acid

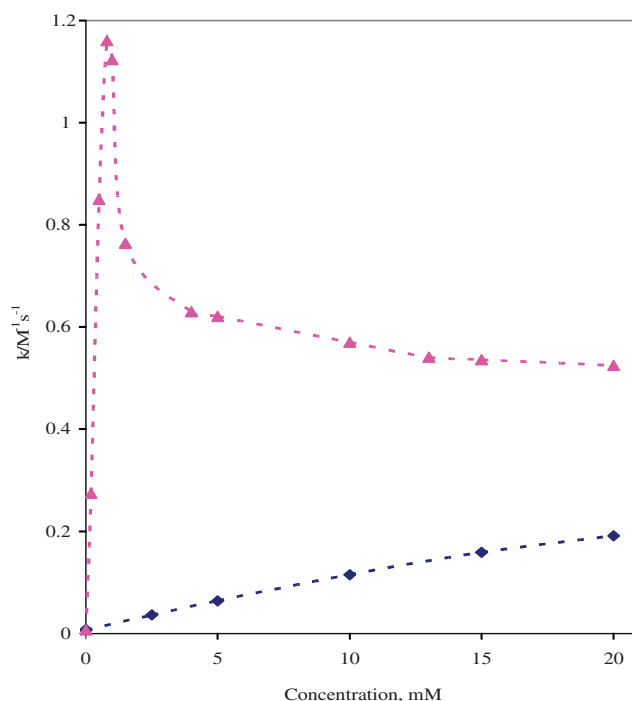


Figure 4. Apparent second-order rate constants for the Diels–Alder reaction of 3-(4-nitrophenyl)-1-(2-pyridyl)-2-propen-1-one dienophile (**1a**) with cyclopentadiene (**2**) in the presence of benzenesulfonic acid (◆) and linear alkylbenzene sulfonic acid (▲) at 32 °C in aqueous solution

phile **1a** with cyclopentadiene **2** was also studied so as to establish the influence of the hydrophobic alkyl moiety of LAS on the catalysis of this reaction. The kinetic results clearly indicate that the use of benzenesulfonic acid, which lacks the hydrophobic alkyl moiety, under similar reaction conditions led to much less effective catalysis (Fig. 4).

Inhibition of Diels–Alder reactions in the presence of cationic surfactants

After the successful acceleration of the Diels–Alder reactions with acidified anionic surfactants, the study was extended to acidified cationic surfactants (Scheme 3). Our hypothesis was that cationic surfactants will repel the protons from the Stern region of the micelles and thereby inhibit the Diels–Alder reactions. Indeed, the Diels–Alder reaction of 3-(4-nitrophenyl)-1-(2-pyridyl)-2-propen-1-one dienophile (**1a**) with cyclopentadiene (**2**) at 32 °C, showed inhibition by dodecyltrimethylammonium bromide (DTAB) and dodecylmethylammonium bromide surfactants at pH 2 (Fig. 5). The inhibition begins immediately after the cmc of these surfactants which is consistent with the notion that binding of **1a** to the micelles hampers specific-acid catalysis.

The inhibition was also observed when the reaction of 3-phenyl-1-(4-pyridyl)-2-propen-1-one dienophile (**4**)

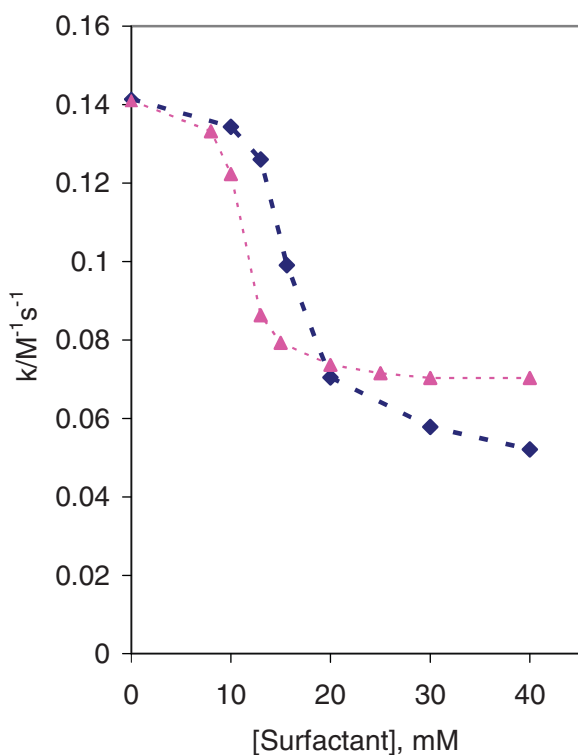


Figure 5. Apparent second-order rate constants for the Diels–Alder reaction of 3-(4-nitrophenyl)-1-(2-pyridyl)-2-propen-1-one dienophile (**1a**) with cyclopentadiene (**2**) at 32 °C inhibited by dodecyltrimethylammonium bromide (◆) and dodecylmethylammonium bromide (▲) surfactants at pH 2

with cyclopentadiene (**2**) was performed in dodecyltrimethylammonium bromide (DDAB) cationic surfactant at pH 2 at 32 °C (Fig. 6).

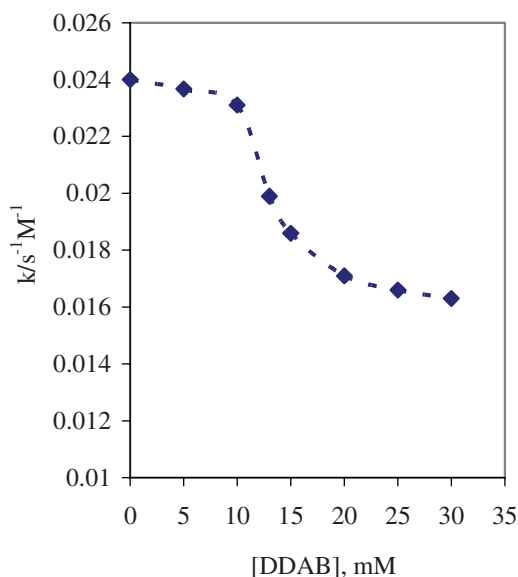
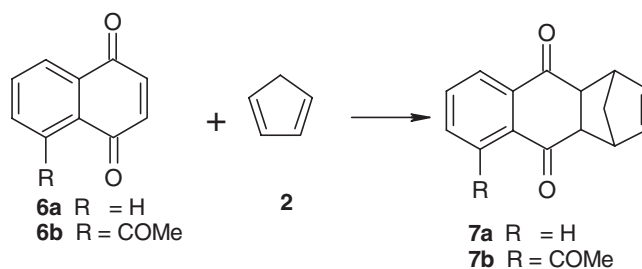


Figure 6. Apparent second-order rate constants for the Diels–Alder reaction of 3-phenyl-1-(4-pyridyl)-2-propen-1-one dienophile (**4**) with cyclopentadiene (**2**) at 32 °C inhibited by dodecyltrimethylammonium bromide (DDAB) surfactant at pH 2

The hydrogen-bond interaction effect of cationic surfactants on the Diels–Alder reaction of **6** with **2**

The extent to which water can affect a reaction through hydrogen-bond interactions depends on the number and the hydrogen-bond-accepting capability of the substituents in the substrates. We therefore extended our study to an examination of the hydrogen-bonding influence of cationic surfactants on the Diels–Alder reactions of naphthoquinones **6** with cyclopentadiene **2** (Scheme 5). The use of DDAB, and DTAB surfactants gave different reaction rates (Fig. 7). The apparent second-order rate constants for the Diels–Alder reaction of **6a** with **2** in the presence of a surfactant with a higher hydrogen-bond donating capacity are slightly higher than those for a structurally similar surfactant with a lower hydrogen-bond donating capacity. This indeed suggests that there is a kinetic effect due to hydrogen-bond interaction between the surfactant ammonium hydrogen atom and the activated complex.



Scheme 5

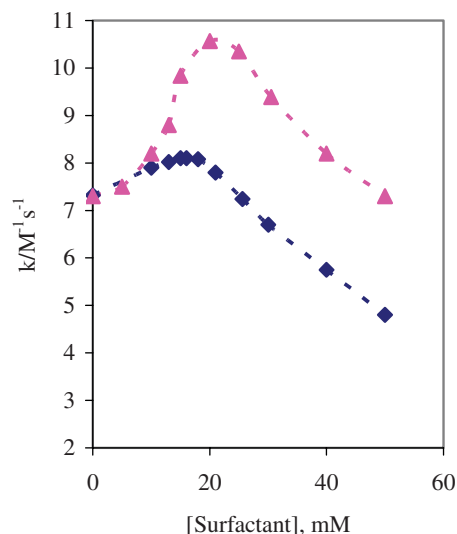


Figure 7. The influence of the surfactant hydrogen-bonding capacity on the second-order rate constants for the Diels–Alder reaction of naphthoquinone (**6a**) with cyclopentadiene (**2**) at 32 °C using surfactants DTAB (◆) and DDAB (▲)

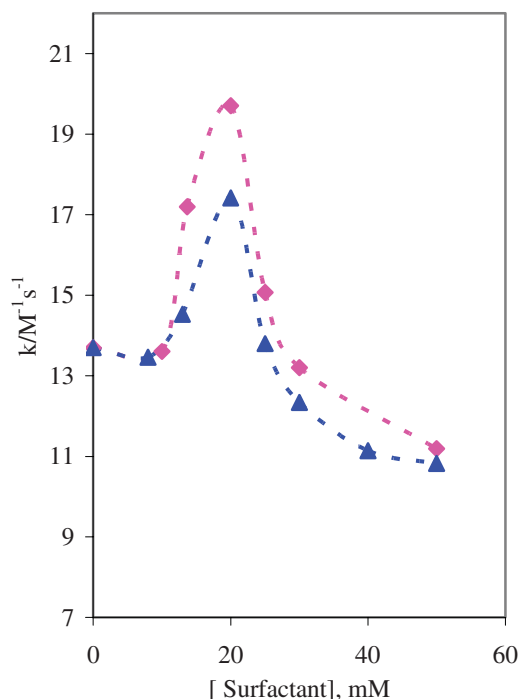


Figure 8. The influence of the surfactant hydrogen-bond donating capacity on the second-order rate constants for the Diels–Alder reaction of 5-acetyl-2,4-naphthoquinone (**6b**) with cyclopentadiene (**2**) at 32 °C using surfactants DDAB (▲) and MDAB (◆)

The reaction of **6b** with cyclopentadiene **2** was expected to show higher reaction rates in these media because the presence of another carbonyl group could further enhance the hydrogen-bond stabilizing effect. The reaction of **6b** with cyclopentadiene **2** at 32 °C in DDAB and dodecylmethylammonium bromide (DMAB) surfactants solution are compared in Fig. 8.

As expected, the second-order reaction rate constant is increased by increasing the hydrogen-bond donating capacity of the dienophile.

CONCLUSIONS

SASAC using acidified anionic surfactant and linear LAS of Diels–Alder reactions in water has been investigated by kinetic measurements. The catalysis is enhanced by the acidification of the anionic surfactant and the reaction rate is enhanced by about 40 times for SDS while it is enhanced by about 170 times for LAS. When the reactions are performed using acidified cationic surfactants, rate inhibition is found. The results serve as an indirect indication that bimolecular Diels–Alder reactions occur close to the micellar surface (Stern region). Moreover, the reactions are faster in these surfactant media than in aqueous hydrochloric acid under similar reaction conditions. Furthermore, we have established

that a bidentate dienophile reacts faster than a structurally related monodentate dienophile when catalyzed by LAS.

EXPERIMENTAL

Materials

Naphthoquinone (Aldrich), ethanol (Merck), 4-acetylpyridine (Aldrich), 2-acetylpyridine (Aldrich), benzaldehyde (Aldrich), ether (Merck), acetonitrile (Aldrich), *N,N*-dimethyldodecylamine (Aldrich), *N*-methyl-dodecylamine (Aldrich), and DTAB (Aldrich) were of the highest purity available. Technical grade (96%) linear alkylbenzene sulfonic acid, which comprised of a mixture of linear LAS with molecular weight 304, was employed. Cyclopentadiene was cracked from its dimer (Merck) immediately before use. Dimineralized water was double distilled in a quartz distillation unit. The solvents were used as received without further purification. Dienophiles **1b** and **4** were prepared by aldol condensation of 2- and 4-acetylpyridine with the corresponding substituted benzaldehyde using documented procedures.^{3,23} Dienophile **1a** was purified from the stock sample prepared before in the group.²³

1b and **4**: To 100 ml of water cooled to 5 °C, 16.5 mmol of the appropriate benzaldehyde and 17 mmol of the appropriate acetylpyridine were introduced. The mixture was thoroughly shaken to obtain a finely dispersed emulsion. This was followed by the addition of 10 ml of 10% NaOH. The mixture was once again shaken and left undisturbed overnight at 4 °C. The product which was oil-like solidified upon shaking and was filtered and washed with water giving good yields: **1b**, 93%, **4**, 77%. The products were crystallized from ethanol to afford pure products with melting points for **1b**, 74.8–75.5 °C (lit. 74.5–75.3 °C,²³ 74 °C²⁴ and **4**, 89.5–90.0 °C (lit. 89.0–89.2 °C,²³ 87–88 °C²⁵). The ¹H NMR spectra of these products were checked and were consistent with the previously reported results.²³

Kinetic measurements

Rate constants were determined by UV–VIS spectroscopy (Perkin Elmer $\lambda 2$, $\lambda 5$, or $\lambda 12$ spectrometer). The disappearance of the absorption of the dienophile at an appropriate wavelength was monitored for at least four half-lives. The dienophile was introduced into a 1 cm path length quartz cuvet containing 3.5 ml of the appropriate surfactant solution. After equilibration, 10–25 μ l of a concentrated stock solution of cyclopentadiene in acetonitrile was added. The pseudo-first-order rate constants were obtained using a fitting program. The apparent second-order rate constant was then calculated by dividing the observed pseudo-first-order rate constant by the initial concentration of cyclopentadiene. Typical

concentrations employed were $[\text{diene}] = 1 \times 10^{-3}$ – 2×10^{-3} M and $[\text{dienophile}] = 1 \times 10^{-5}$ M. The rate constants were measured at least three times and the reported rate constants are an average of three runs. The rate constants were reproducible to within 3%.

Preparation of the cationic surfactants

The alkylammonium surfactants were prepared by protonation of the respective amines. Due to solubility problems of these amines in aqueous systems, direct protonation using aqueous HBr/HCl was not feasible. The protonation was thus achieved by dissolving the amines in diethyl ether. This was followed by bubbling in hydrogen bromide gas until the surfactant salts precipitated out. The surfactant salts were then vacuum-dried at room temperature overnight. The cmc of each surfactant was determined by conductivity at 32 °C. The cmc were 13.01 and 11.58 mM for DDAB and DMAB.

Acknowledgements

The National Research School Combination Catalysis (NRSCC, Netherlands) is gratefully acknowledged for financial support. The University of Dar es Salaam (Tanzania) is acknowledged for a generous study leave to Egid B. Mubofu.

REFERENCES

- Corey EJ. *Angew. Chem. Int. Ed.* 2002; **41**: 1650.
- For organic reactions in aqueous media see: (a) Li C-J. *Chem. Rev.* 2005; **105**: 3095; (b) Li C-J, Chen L. *Chem. Soc. Rev.* 2006; **35**: 68–82; (c) Lindstrom UM (ed.). In *Organic Chemistry in Water*, Blackwell Publ: Oxford, UK, 2007.
- (a) Otto S, Engberts JBFN. *J. Am. Chem. Soc.* 1999; **121**: 6798; (b) Otto S, Bertocin F, Engberts JBFN. *J. Am. Chem. Soc.* 1996; **118**: 7702.
- Fringuelli F, Piermatti O, Pizzo F, Vaccaro L. *Eur. J. Org. Chem.* 2001; 439.
- Yates P, Eaton P. *J. Am. Chem. Soc.* 1960; **82**: 4436.
- Wassermann A. *J. Chem. Soc.* 1942; 623.
- Wassermann A. *J. Chem. Soc.* 1946; 1089.
- Rubin W, Steiner H, Wassermann A. *J. Chem. Soc.* 1949; 3046.
- (a) Tascioglu S. *Tetrahedron*, 1996; **52**: 11113; (b) Berezin IV, Martinek K, Yatsimirskii AK. *Russ. Chem. Rev.* 1973; **42**: 787.
- (a) Kobayashi S, Wakabayashi T, Nagayama S, Oyamada H. *Tetrahedron Lett.* 1997; **38**: 4559; (b) Kobayashi S, Busujima T, Nagayama S, Oyamada H. *Chem. Commun.* 1998; 19; (c) Tian H-Y, Wang Y-J, Zeng C-C, Li C-J. *Tetrahedron Lett.* 2000; **41**: 2529.
- Kobayashi S, Busujima T, Nagayama S. *Synlett* 1999; 545.
- Rispens T, Engberts JBFN. *Org. Lett.* 2001; **3**: 941.
- Otto S, Engberts JBFN, Kwak JCT. *J. Am. Chem. Soc.* 1998; **120**: 9517.
- (a) Manabe K, Mori Y, Kobayashi S. *Synlett.* 1999; 1401; (b) Manabe K, Mori Y, Kobayashi S. *Tetrahedron*, 2001; **57**: 2537; (c) Manabe K, Kobayashi S. *Org. Lett.* 1999; **1**: 1965; (d) Manabe K, Mori Y, Wakabayashi T, Nagayama S, Kobayashi S. *J. Am. Chem. Soc.* 2000; **122**: 7202.
- Akiyama T, Takaya J, Kagoshima H. *Tetrahedron Lett.* 1999; **40**: 7831.
- Akiyama T, Takaya J, Kagoshima H. *Synlett* 1999; 1426.
- (a) Abraham MH, Chadha HS, Dixon JP, Rafols C, Treiner C. *J. Chem. Soc., Perkin Trans. 2* 1995; 887; (b) Quina FH, Alonso EO, Farah JPS. *J. Phys. Chem.* 1995; **99**: 11708.
- Eriksson JC, Gillberg G. *Acta Chem. Scand.* 1966; **20**: 2019.
- Blokzijl W, Blandamer MJ, Engberts JBFN. *J. Am. Chem. Soc.* 1991; **113**: 4241.
- Otto S, Blokzijl W, Engberts JBFN. *J. Org. Chem.* 1994; **59**: 5372.
- Moroi Y, Nishikido N, Uechara H, Matuura R. *J. Colloid Interface Sci.* 1975; **50**: 254.
- Mubofu EB, Engberts JBFN. *J. Phys. Org. Chem.* 2004; **17**: 180.
- Otto S. Ph.D. thesis, University of Groningen, 1998.
- Tsukerman SV, Nikitchenko VM, Bugai AI, Lavrushin VF. *Khimstr. Svoistva Reaktivnost Org. Soedin.* 1969; 53 (Chem. Abstr. 1970, **73**, 45276t).
- Durinda J, Szucs L, Krasnec L, Heger J, Springer V, Kolena J, Keleti J. *Acta Fac. Pharm. Bohemoslov.* Chem. Abstr. **1968**, 68, 114494y.