Tetrahedron Vol. 41, No 18, pp. 3683 to 3688, 1985
Printed in Great Britain.

0040-4020/85 $3.00 + .00

WATERLESS MICROEMULSIONS - IV : DIELS-ALDER REACTION OF CYCLOPENTADIENE AND METHYLACRYLATE AS A PROBE OF FORMAMIDE MICROEMULSIONS

A. AHAMD-ZADEH SAMII, A. de SAVIGNAC, I. RICO and A. LATTES *

Laboratoire des IMRCP, UA n°470 CNRS Université Paul Sabatier
118, route de Narbonne, 31062 TOULOUSE CEDEX FRANCE

(*Received in France* 13 *December* 1984)

Abstract - The use of the Diels-Alder reaction between methyl acrylate and cyclopentadiene as a chemical probe has demonstrated two distinct zones in the formamide microemulsion system. Good selectivity and high yields can be obtained from Diels-Alder reactions in formamide.

INTRODUCTION

There have been a large number of studies of aqueous microemulsions over the last few years [1]. Microemulsions have been used as reaction media [2], although their more widespread use has often been limited by inadequate substrate solubility in water.

Recently, we have reported that it is possible to prepare microemulsions by replacing water with the highly structured solvent, formamide. Physicochemical studies of such media have been published [3].

We report here the first use of such non-aqueous microemulsions as reaction media. We carried out a Diels-Alder addition of methyl acrylate to cyclopentadiene in various formamide microemulsions. This type of reaction, which is highly sensitive to the polarity of the medium[4], can be used as a chemical probe of microemulsiuon.

RESULTS

Preparation of the reaction media : monophasic areas of formamide microemulsions

We replaced water with formamide, and we used a visual transparency criterion to determine the phase diagram[5]. The spontaneity of the change between milky emulsion and transparent solution conformed to FRIBERG's definition[6]. All the microemulsions prepared were stable for many months.

An ionic system was used with isooctane as oil, 1-butanol as cosurfactant and cetyltrimethylammonium bromide (CTAB) as surfactant.

Figure 1 shows the pseudo ternary phase diagram for (formamide/CTAB = 2, 1-butanol, isooctane) mixtures.

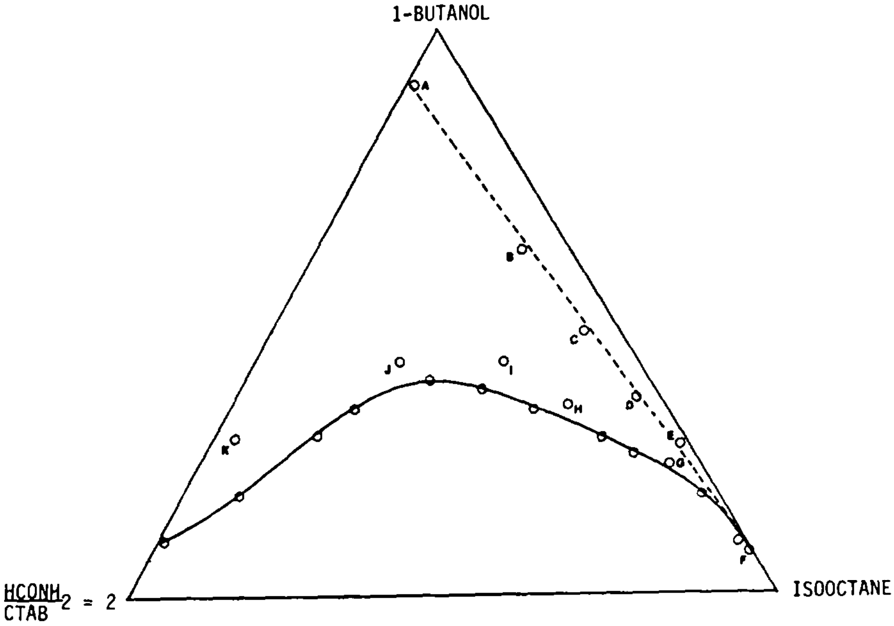
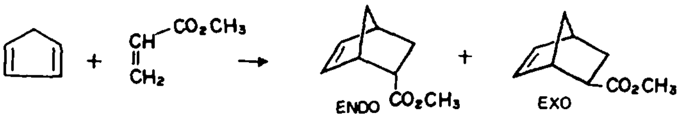


Figure 1 : Pseudo ternary phase diagram of the system-formamide/CTAB = 2, 1-butanol, isooctane.

It should be pointed out that the microemulsions at the phase boundary could be obtained by addition of the detergent to biphasic mixtures of formamide, 1-butanol and isooctane. They are not, therefore, three component solvent mixtures, but are true microemulsions.

Probe reaction

We chose the Diels-Alder addition reaction of methyl acrylate to cyclopentadiene :



It is known that the endo/exo selectivity increases with increasing polarity of the solvent[4]. We carried out a preliminary study of the influence of the various constituents of the microemulsion on the reaction.

Effect of microemulsion components on the probe reaction

Table I summarises the results obtained in different solvents.

Table I ENDO/EXO product ratios in organic media and in water.

Solvent	Dielectric constant ε (20-25°C)	Concentration of diene and dienophile (M)	ENDO/EXO [a]
Isooctane	2.0	0.15	2.3
1-butanol	17.1	0.15	5.0
Water	78.5	0.15	7.4 (9.2[b])
Water	78.5	0.30	5.3 (5.9[b])
Formamide	109.0	0.07	6.9
Formamide	109.0	0.15	6.7
Formamide	109.0	0.30	6.7
N-Methyl acetamide	183.0	0.15	4.7

a. Determined by vapour phase chromatography. We carried out the reaction at 20°C (30°C for N-methyl acetamide due to its high melting point = 24°C)

b. Results from ref. 10b. The difference could be due to different experimental conditions. These authors gave no details on the procedure used, especially with respect to conditions of shaking, or product extraction from the aqueous medium.

We also included results obtained in water and N-methyl acetamide for comparison.

The use of water as a reaction medium for Diels-Adler type additions has been previously reported [7-11]. For exemple, BRESLOW et al.[10] and GRIECO at al.[11] have shown that high endo/exo selectivities can be obtained under these conditions. LASZLO et al.[12] have recently shown that high selectivities can also be achieved for Diels-Alder reactions carried out in the presence of clay.

Our results suggest the following comments :

i. In agreement with BERSON's explanation,[4] the solvents with the highest dielectric constant (most polar) favour formation of the endo isomer. This can explain the high stereoselectivity in both water and formamide.

ii. Nevertheless, the above parameter alone cannot fully explain the stereoselectivities observed. For example, in N-methyl acetamide (ε = 182.0) the endo/-exo selectivity was less than in water or formamide. As suggested by BRESLOW [10c] "solvophobic" type interactions would seem to play an important role. Therefore in formamide, which is highly structured, the stereoselectivity was similar to that observed in water, whereas in N-methyl acetamide which is less structured than water, the selectivity fell to that found in alcoholic solvents such as 1-butanol.

Overall, our results confirm BRESLOW et al's explanation for the stereoselectivity of Diels-Alder reactions. For high endo/exo selectivity, "solvophobic" interactions (and to a lesser extent solvent polarity) are fundamental.

Formamide, which strongly favours solvophobic interactions[3,13] would seem, therefore, to be an excellent medium for Diels-Alder reactions, especially at high concentrations. By using formamide, we have obtained considerably improved stereoselectivities at high concentrations, over those obtained by BRESLOW [10b] (for C = 0.30 mole/l, ENDO/EXO = 5.3 for water, and 6.7 for formamide). It is interesting that contrary to the results in water, where the reaction takes place in a heterogeneous medium, concentration effects were not observed in formamide. The same stereoselectivity was obtained whatever the substrate concentration. This is probably due to the fact that in formamide the reaction takes place in a homogeneous medium.

In addition, the use of formamide as a homogeneous reaction medium significantly improves yield. For water, the yields of product (after extraction) do not exceed 40 %, whereas in formamide, the yields are quantitative whatever the initial concentrations of the reactants. The yields of isolated product (after extraction) are then close to 85 %.

We are carrying out further investigations on the use of formamide in other preparative Diels-Alder reactions.

Diels-Alder reactions in formamide microemulsions

As opposed to results obtained for the same type of reaction in aqueous microemulsions without surfactant (only studied in the continuous oil phase) [14], we have been able to exploit the high solubility of substrates in formamide to investigate the complete microemulsion phase diagram (continuous oil phase and continuous formamide phase).

Representative points of the microemulsions studied are shown on figure 1. The microemulsion compositions and reaction selectivities are shown in table II.

Table II : microemulsion compositions (by weight) of the system (1-butanol, formamide/CTAB = 2, isooctane) and selectivity of the Diels-Alder probe reaction ($C_{substrate}$ = 0.15 M).

MICROEMULSION	% ISOOCTANE	FORMAMIDE		% BUTANOL 1	% CTAB	ENDO/EXO[b]
		%	Ø[a]			
A	1	6	0.07	90	3	4.50
B	32	5	0.04	60.5	2.5	4.50
C	48	4	0.03	46	2	4.27
D	62	3	0.02	34.5	1.5	3.87
E	72	1	0.01	26.5	0.5	3.16
F	92	0.2	0.003	7.7	0.1	2.85
G	72	4	0.03	22	2	3.76
H	54	10	0.08	31	5	3.96
I	38	14	0.15	41	7	4.09
J	20	26	0.28	41	13	4.12
K	3	46	0.51	28	23	4.55

a. Ø = volumic fraction calculated from the relative densities of formamide and the microemulsions,

b. determined by vapour phase chromatography. We carried out the reaction at 20°C over a 3 days period, as for the pure solvents. Product yields could not be determined accurately since product was lost during the extraction procedure. We did check though, that the extraction process did not alter the ENDO/EXO ratios (see experimental section).

DISCUSSION

The results demonstrated the presence of two zones in the microemulsions studied :

- a zone of relatively low selectivity in the oil rich part of the diagram
- a much wider zone of higher selectivity.

Good agreement between the changes in conductivity and endo/exo selectivity are found along the lines AF and FK (demixtion line) on a plot of these changes as a function of the formamide volumic fraction Ø (figures 2 and 3).

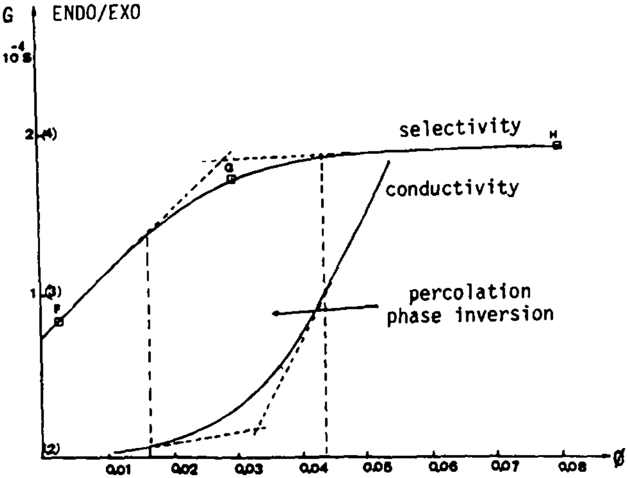


Figure 2 : Plot of conductivity and endo/exo ratios as a function of the formamide volumic fraction Ø, along the demixtion line.

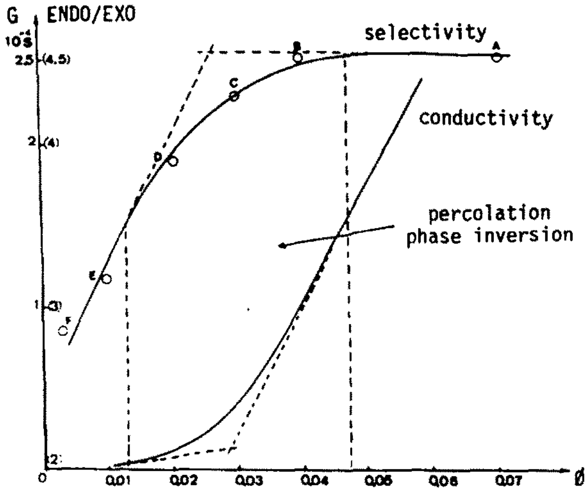


Figure 3 : Plot of conductivity and endo/exo ratios as a function of the formamide volumic fraction Ø, along the line AF.

The abrupt changes in selectivity and conductivity around C on line AF, and around G on the demixtion line can be attributed to phase inversion from reverse micelles (formamide in oil) to direct micelles (oil in formamide).

Conductivity changes

This type of change in conductivity has been demonstrated, for aqueous microemulsions, to be due to percolation, in which there is a concatenation of reverse micelles of water in oil, followed almost immediately by a phase inversion from reverse (low conductivity zone) to direct micelles (higher conductivity zone).[15]

Selectivity change

Reverse micelles

In the continuous oil phase of microemulsion G, it appears that the reaction takes place in the continuous phase. The endo/exo ration (= 2.85 - Table II) is close to that obtained for pure isooctane (= 2.3 - Table I).

Direct micelles

On the other hand, in the formamide rich zone, the endo/exo ration (= 4.5) obtained in microemulsion K is virtually the same as that found in the alcohol rich microemulsion A (table II). This value is also close to that found in pure butanol (= 5.0 - table I). It would seem that the reaction takes place at the micelle interface in the continuous formamide phase.

CONCLUSION

This Diels-Alder reaction is a valuable probe reaction for the study of formamide microemulsions. It is able to discriminate the continuous oil phase from the continuous structured phase (formamide or alcohol rich).

We are carrying out kinetic studies of this reaction in the constituent solvents of the microemulsions. This should enable us to localise the reaction site at the microscopic level, in this heterogenous medium. We intend, in the first instance, to study the reaction in pure formamide, which appears to be an excellent medium for Diels-Alder reactions.

EXPERIMENTAL

Methyl acrylate was purchased from ALDRICH (99% min. pure) and cyclopentadiene was obtained by distillation of dicyclopentadiene (ALDRICH, 95% min. pure) at atmospheric pressure (BP_{760}= 40°C).

The microemulsion conctituents were used as supplied : formamide (Merck analytic, 99.7% min. pure), 1-butanol (Merck spectroscopic, 99.7% min. pure), isooctane (Merck spectroscopie, 99% min. pure), cetyltrimethylammonium bromide (Merck, 99% min. pure).

We carried out the reaction at 20°C in 50 ml solvent with magnetic agitation. In the case of water, the concentrations are formal since the reaction medium was heterogenous. The reactions were analysed after they had gone to completion (3 days).

The yields were determined after direct extraction into ether for the water reaction, and after ether extraction and several water washes for the formamide reaction. The endo/exo selectivities were determined by vapour phase chromatography (6' 0.25", 8 carbowax 1500 on chromosorb column) :

i. directly for the organic solvents
ii. after ether extraction in the case of water
iii. after CCl_4 extraction, and several water washes to remove the surfactant, for the microemulsions.

N.B. we checked by double extraction that the endo/exo ratios were not altered by the extraction procedures.

Conductivity measurements were carried out at 25°C using a TACUSSEL CD6N-G conductimeter as described in references 3a and 3b.

REFERENCES

1. A.M. BELLOCQ, J. BIAIS, P. BOTHOREL, B. CLIN, G. FOURCHE, P. LALANNE,B. LEMAIRE, B. LEMANCEAU and D. ROUX, Advances in Colloid and Interface Science, 20, 167 (1984) and cited refs.
2. a. R.A. MACKAY, Advances in Colloid and Interface Science, 15, 131 (1981)
   b. D.G. WHITTEN, J.C. RUSSELL and R.H. SCHMEHL, Tetrahedron, 38, 2455 (1982)
   c. I. RICO, M.T. MAURETTE, E. OLIVEROS, M. RIVIERE and A. LATTES, Tet. Lett., 48,4795 (1978)
   d. R. FARGUES, M.T. MAURETTE, E. OLIVEROS, M. RIVIERE and A. LATTES, Nouveau J. de Chim. 3, 487 (1979)
   e. I. RICO, M.T. MAURETTE, E. OLIVEROS, M. RIVIERE and A. LATTES, Thetrahedron, 36,1779 (1980)
   f. R. FARGUES-SAKELLARIOU, E. OLIVEROS, M.T. MAURETTE, M. RIVIERE and A. LATTES, J. Photochem., 18, 101 (1982)
   g. R. FARGUES-SAKELLARIOU, M.T. MAURETTE. E. OLIVEROS, M.RIVIERE and A. LATTES, Tetrahedron, 40, 2381 (1984)
   h. H. AMAROUCHE, C. de BOURAYNE, M. RIVIERE and A. LATTES, C.R. Ac. Sci., 298, 121 (1984)
3. a. I. RICO, A. LATTES, Nouveau J. de Chim., 8, 429 (1984)
   b. I. RICO, A. LATTES, J. Coll. Int. Sci., 102, 285 (1984)
4. J.A. BERSON, Z. HAMLET and W.A. MUELLER, J. Am. Chem. Soc., 84,297 (1962)
5. J.L. CAYIAS, R.S. SCHECHTER and W.H. WADE, J. Coll. Int. Sci., 59, 31 (1977)
6. S.E. FRIBERG, Colloids and Surfaces, 4, 201 (1982)
7. R.B. WOODWARD, H. BAER, J. Am. Chem. Soc., 70, 1161 (1948)
8. H. HOPFF, C.W. RAUTENSTRAUCH, U.S. Patent 2, 262, 002 (C.A., 36, 1046 (1942)
9. D.D. STERNBACH, D.M. ROSSANA. J. Am. Chem. Soc., 104, 5853 (1982)
10. a. R.C. RIDEOUT, R. BRESLOW, J. Am. Chem. Soc., 102, 7816 (1980)
    b. R. BRESLOW, U. MAITRA, D. RIDEOUT, Tet. Lett., 24, 1901 (1983)
    c. R. BRESLOW, U. MAITRA, Tet. Lett., 25, 1239 (1984)
11. a. P.A. GRIECO, P. GARNER, K. YOSHIDA, M.C. HOFFMAN, Tet. Lett., 24, 3807 (1983)
    b. P.A. GRIECO, K. YOSHIDA, P. GARNER, J. Org. Chem., 48, 3139 (1983)
    c. P.A. GRIECO, P. GARNER, Z.M.HE, Tet. Lett., 24, 1897 (1983)
12. P. LASZLO, J. LUCCHETI, Tet. Lett., 25, 1567 (1984)
13. B. ESCOULA, H. HAJJAJI, I. RICO, A. LATTES, J.C.S. Chem. Comm., 18, 1233 (1984)
14. A. GONZALEZ, SL.L. HOLT, J. Org. Chem. 47, 3186 (1982)
15. a. M. LAGUES, R. OBER and C. TAUPIN, J. Phys . Lett., 39, 487 (1978)
    b. M. LAGUES, C. SAUTEREY, J. Phys. Chem., 84, 3503 (1980)