of a pretransition in the DDAB bilayer and argues against the presence of smaller vesicles as contaminant in this fraction.

Concluding Remarks

The results described in this study indicate that disturbance in the hydrophilic region of the bilayer causes anion-induced fusion of large DDAB vesicles. The inability of DPA^{2-} to perturb the head group packing in the small vesicles *prior to aggregation* and the resistance of such vesicles to fusion[3] further support the conclusion that the observed initial changes induced in the bilayer interface of the large vesicles are essential for fusion to occur. Since the actual fusion susceptibility was evidently conferred to vesicles within the aggregated state, prior dehydration and subsequent head group packing alterations would thus constitute a necessary though not sufficient prerequisite for the induction of fusion. Thus, an additional process must take place. As a likely possibility, we suggest a further tightening of adjacent vesicles via formation of a specific "trans" complex between anions and amphiphiles in apposed vesicles, very similar to that proposed for cation-induced fusion of negatively charged phospholipid vesicles.[6a] Prior dehydration of the vesicle surface will allow the apposed membranes to come into sufficiently close proximity for such a complex to be formed.[6b,25] It is interesting to note that such a sequence of events is fully consistent with observations previously reported on the effect of the dehydrating agent polyethylene glycol on cation-induced fusion of phosphatidylserine vesicles.[6b]

Several possibilities may explain the highly resistant properties of small vesicles toward fusion: (i) the strongly bound water surrounding the head groups was only partially removed, preventing the bilayers from coming into sufficiently close, i.e., fusion susceptible, contact; (ii) as a result, and analogous to phospholipid systems (e.g., the interaction between Mg^{2+} and phosphatidylserine[6a]), the ability of forming a trans-anion complex will be abolished; (iii) the low cooperativity in head group packing alterations, compared to that observed in the large vesicles, could be indicative for molecular areas formed too small for allowing stable fusion contact sites to be created.

Modification of either the head group structure or the aliphatic chain may allow further insight into the physical properties of the bilayer interface and the dynamic behavior of these surfactant vesicles to be obtained. Such experiments are currently in progress.

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Unusual Selectivities of Radical Reactions by Internal Suppression of Fast Modes

Hanns Fischer

Contribution from the Institute of Physical Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland.

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Abstract: Radical reactions involving two or more intermediates and many mutual reaction channels may lead to the specific formation of (ideally) only one product if one species is more persistent than the others and if persistent and transient species are generated with equal rates. This is caused by an initial buildup of the persistent intermediate which thereafter steers the system to follow (ideally) a single path. A kinetic analysis explains recent data on the photochemistry of nitrosamines and cobalamine. The effect is a likely reason for the high selectivities observed in many photoreactions involving NO as intermediate, e.g., the Barton reaction or the photooxidation of alkanes by NOCl.

Reactions involving two and more free radical intermediates have been reported which exhibit unusually high selectivities of product formation though no chain processes are involved: Gas-phase photolysis of dimethylnitrosamine in the $n\pi^*$-transition region leads to cleavage with a quantum yield of unity.[1]

$$(CH_3)_2N\text{-}NO \rightarrow (CH_3)_2N\cdot + NO\cdot \qquad (1)$$

During continuous photolysis in inert atmospheres the only reaction of the radicals appears to be cross-termination.

$$(CH_3)_2N\cdot + NO\cdot \rightarrow (CH_3)_2N\text{-}NO \qquad (2)$$

Thus, the nitrosamine exhibits an apparent high photostability under inert conditions. Similarly, the photolability of methylcobalamine in aqueous solution is drastically reduced in the absence of free radical traps.[2] Photolysis in the presence of 0.03 M CO leads to acetylcobalamine with high yield (≅70%). The mechanism

$$CH_3\text{–cob} \xrightarrow{h\nu} \cdot CH_3 + \cdot\text{cob} \qquad (3)$$

$$\cdot CH_3 + \cdot\text{cob} \rightarrow CH_3\text{–cob} \qquad (4)$$

$$\cdot CH_3 + CO \rightarrow CH_3\dot{C}O \qquad (5)$$

$$CH_3\dot{C}O + \cdot\text{cob} \rightarrow CH_3CO\text{–cob} \qquad (6)$$

was suggested.[2] If the mechanisms are correct the selectivity for the cross-terminations 2, 4, and 6 is surprising. The reactions involve radicals ($(CH_3)_2N\cdot$, $\cdot CH_3$, $CH_3\dot{C}O$) which are known to self-terminate with high rate constants,[3] and one would intuitively

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[1] Geiger, G.; Huber, J. R. *Helv. Chim. Acta* **1981**, *64*, 989.

[2] Kräutler, B. *Helv. Chim. Acta* **1984**, *67*, 1053.

[3] $(CH_3)_2N\cdot$ and $\cdot CH_3$ self-terminate in liquids with rates close to diffusion control.[4] The rate constant for self-termination of $CH_3\dot{C}O$ in liquids is nearly equal[5] to that of $(CH_3)_3\dot{C}$ which is diffusion controlled.[4] $2k$ for $(CH_3)_2N\cdot$ in the gas phase seems unknown, but the constant is high[6] for $H_2N\cdot$ at pressures similar to those used in ref 1.

[4] *Radical Reaction Rates in Liquids*; Fischer, H., Ed.; Springer: Berlin, 1983; Landolt-Börnstein, New Series, Group II, Vol. a and c.

[5] Vollenweider, J. K.; Fischer, H.; Hennig, J.; Leuschner, R. *Chem. Phys.* **1985**, *97*, 217.

[6] *Handbook of Bi- and Termolecular Gas Reactions*; Kerr, J. A., Moss, S. J., Eds.; CRC-Press: Boca Raton, 1981.

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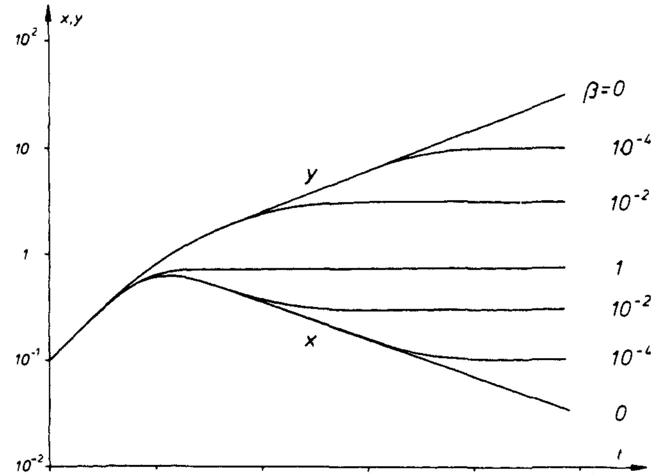

Figure 1. Time dependence of the reduced concentrations of intermediates R_1 and R_2 for equal rates of generation ($r = 1$). $2k_1 = k_c$ ($\alpha = 1$) and various values of $2k_2/2k_1 = \beta$.

expect that the formation of their self-termination products competes effectively with the cross-terminations. A possible explanation has been suggested to the author by K. U. Ingold.[7] In the photolyses 1 and 3 persistent radicals (NO· and ·cob) are formed together with the transient species.[8] If some self-termination of the latter takes place, the concentrations of the persistent species will increase in time to high levels and steer the systems toward cross-termination. In effect, the self-termination of the transient species (a fast process) will be suppressed by the slow self-termination of the persistent species.[9]

To check the validity of this explanation for realistic conditions, we have analyzed the kinetics of simple reaction systems relevant to the cases mentioned before. Consider the mechanism

$$S_1 \rightarrow R_1 \quad \text{rate } I_1 \tag{7}$$

$$S_2 \rightarrow R_2 \quad \text{rate } I_2 \tag{8}$$

$$2R_1 \rightarrow P_1 \quad \text{rate constant } 2k_1 \tag{9}$$

$$R_1 + R_2 \rightarrow P_c \quad \text{rate constant } k_c \tag{10}$$

$$2R_2 \rightarrow P_2 \quad \text{rate constnat } 2k_2 \tag{11}$$

where the intermediates R_1 and R_2 are formed continuously with time-independent rates I_1 and I_2 and may self- ($2k_1$, $2k_2$) and cross-terminate (k_c). Use of $\tau = (2k_1I_1)^{-1/2}$ as a unit of time and $\overline{[R_1]} = (I_1/2k_1)^{1/2}$ as a unit of concentration leads to the kinetic equations for the reduced concentrations $x = [R_1]/\overline{[R_1]}$ and $y = [R_2]/\overline{[R_1]}$.

$$\dot{x} = 1 - \alpha xy - x^2 \tag{12}$$

$$\dot{y} = r - \alpha xy - \beta y^2 \tag{13}$$

Here, $\alpha = k_c/2k_1$, $\beta = 2k_2/2k_1$, and $r = I_2/I_1$. Without loss of generality we set $\beta \leq 1$, so that R_2 is the more persistent species. Cross-terminations between transient and persistent radicals often have rate constants which are similar to the self-termination constants of the transients,[4] so that $\alpha \cong 1$ will hold for many cases. For $\alpha = \beta = 1$ and the initial condition $x(0) = y(0) = 1$ the analytic solution of eq 12 and 13 is $y(t) = rx(t) = r(1 + r)^{-1/2} \tanh{(1 + r)^{1/2}t}$. The selectivity of formation of the cross-reaction product is $q_c = [P_c]/([P_1] + [P_2]) = 2r/(1 + r^2)$ and reflects a purely statistical pattern for this case ($r = 1$, $[P_1]:[P_c]:[P_2] =$ 1:2:1). For other sets of α and β the equations were integrated numerically, and some typical results are shown in Figures 1 and 2. Obviously, for $r = 1$, $\alpha = 1$, and $\beta < 1$ the system *orders in time* to produce dominantly the cross-reaction product by elimination of the more transient species. For stationary states ($\dot{x} = \dot{y} = 0$), eq 12 and 13 are easily solved to give the concentrations x_s and y_s. Linear stability analysis[9,10] reveals that for most cases (x_s, y_s) is an asymptotically stable node in the phase plane and yields two relaxation constants by which the stationary state is approached after small excursions. Various calculations of x_s, y_s, q_{cs}, and the relaxation constants λ and their dependencies on the internal parameters α, β, and the external variable r were carried out, and some results are shown in Figures 3 and 4. In brief they are summarized as follows: (1) If $\beta = 0$ and $\alpha \neq 0$ the r-dependence shows a region of finite x_s, y_s, g_{cs}, λ_1, and λ_2 ($r < 1$; $x_s = (1 - r)^{1/2}$, $y_s = r/x_s$, $q_{cs} = 2r/(1 - r)$) which is sharply divided by a dynamic critical point $r = 1$ from the region $r \geq 1$ where no steady state exists, and $x \rightarrow 0$, $y \rightarrow \infty$, $q_c \rightarrow \infty$ for $t \rightarrow \infty$ (curves $\beta = 0$ in Figures 3 and 4). For $r \rightarrow 1$, $\lambda_1 \rightarrow \infty$, and associated with x, and $\lambda_2 \rightarrow 0$, associated with y. (2) For 0 <

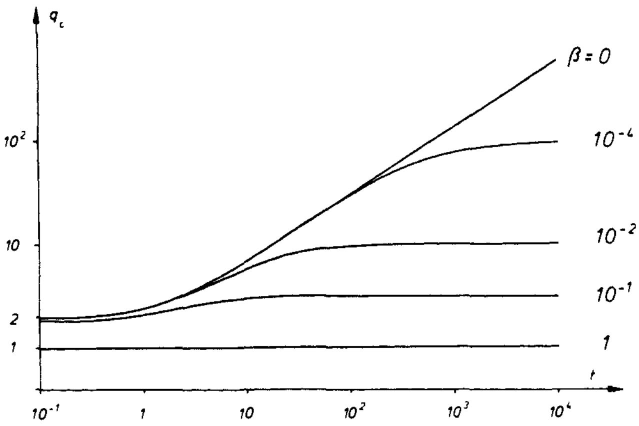

Figure 2. Time dependence of the selectivity of formation of the cross-reaction product of R_1 and R_2. Parameters as in Figure 1.

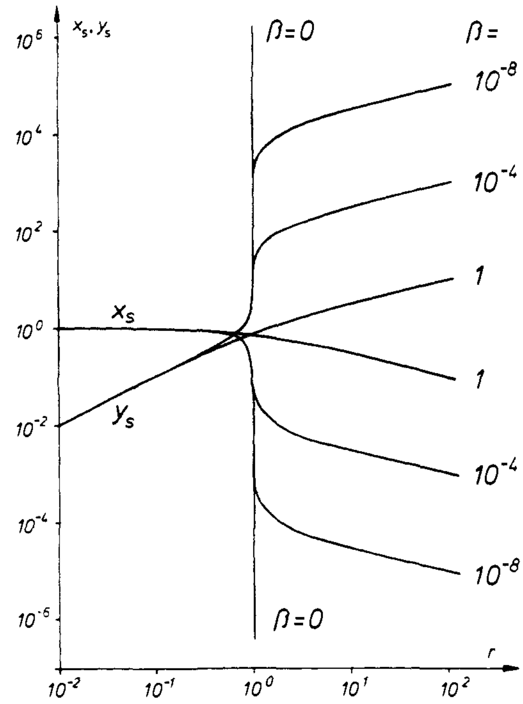

Figure 3. Stationary state reduced concentrations of intermediates R_1 and R_2 for $2k_1 = k_c$ ($\alpha = 1$) and various values of $2k_2/2k_1 = \beta$ as functions of the relative rate of generation $I_2/I_1 = r$.

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[7] Ingold, K. U., private communication.

[8] For the self-termination of NO· log $k/\mathrm{M^{-1}s^{-1}} \cong 10 - 260$ kJ/mol/2.3 *RT*, ref 6. ·cob is likely to be rather persistent due to charge at the central Co and the bulky corrin residue.

[9] The idea that significant differences in homocoupling rate constants will produce larger than statistical fractions of cross-coupling product has also been put foreward by P. J. Wagner to explain solvent effects on photoreduction ratios (Wagner, P. J., submitted to *J. Am. Chem. Soc.*, private communication).

[10] Hirsch, H. W.; Smale, S. *Differential Equations, Dynamical Systems and Linear Algebra*; Academic Press: New York, 1974.

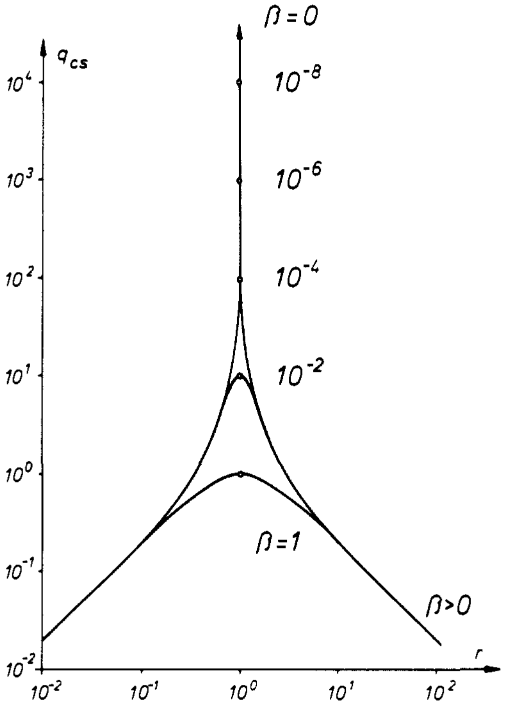

Figure 4. Selectivity of formation of the cross-reaction product of R_1 and R_2 in the stationary state for $2k_1 = k_c$ ($\alpha = 1$) and various values of $2k_2/2k_1 = \beta$ as a function of the relative rate of generation $I_2/I_1 = r$.

$\beta < 1$ and $\alpha < \beta^{1/2}$ (strong coupling) much of the transition behavior at $r = 1$ is retained. At this point x_s drops, y_s and λ_1 increase, and q_{cs} and λ_2 peak sharply as r is increased.[11] For $r = 1$, $q_{cs} = \alpha/\beta^{1/2}$, $y_s = (\beta + \alpha\beta^{1/2})^{-1/2}$, and $x_s = \beta^{1/2}y_s$. These relations show that even for a moderate difference in the self-termination constants of $k_1/k_2 = 100$ and for $k_c = 2k_1$ a fair selectivity of 91% P_c is predicted while the radical concentrations differ by factors of 3 from those attained for $\beta = 1$ (curves $\beta = 10^{-2}$ in Figures 1–4). (3) For $0 < \beta < 1$ and $\alpha \leq \beta^{1/2}$ (weak coupling) the transition from $r < 1$ to $r > 1$ does not lead to spectacular changes of the dependent variables. The curves resemble those for $\beta = 1$ in Figures 3 and 4. The cross-termination ansatz[12] $\alpha = \beta^{1/2}$ yields $q_cs = 2r/(1 + r^2)$ as for $\alpha = \beta = 1$.

The extreme selectivity for $r = 1$ and $\beta \ll 1$ (Figures 2 and 4) explains the reported photostability of dimethylnitrosamine very well. For $r = 1$, $\alpha = 1$, and $\beta = 0$ and an assumed $2k_1 = 10^9$ M^{-1} s^{-1} for $(CH_3)_2N\cdot$ one calculates with $I_1 = I_2 = 8 \times 10^{-9}$ M^{-1} s^{-1} a conversion to self-termination products of $(CH_3)_2N\cdot$ of only 0.15% after 20 h of photolysis.[1] This may well have escaped detection. The total turnover of $(CH_3)_2N{-}NO$ corresponds to 150%, however.

Extension of the mechanism 7–11 to the cobalamine case ($R_1 = \cdot CH_3$, $R_2 = \cdot cob$) involves the addition of[13]

$$R_1 \rightarrow R_3 \qquad \text{rate constant } k_a \qquad (14)$$

and of the self- and cross-termination constants of $R_3(CH_3\dot{C}O)$. For equal self- and cross-termination constants of all reactions except the self-termination of the persistent $R_2(\cdot cob)$, calculations showed that selectivities for the cross-reaction 6 exceeding 10 reached for $r = 1$ if $\beta \leq 10^{-4}$ and $k_a\tau \geq 1$. With the time of reaction specified in ref 2 and from the rate constant[14] for reaction 5 one estimates $k_a\tau > 1$ for [CO] = 0.03 M, i.e., the observed selectivity seems plausible.

Apart from the two examples treated here a large variety of known reactions with high specificities for the formation of cross-coupling products follows very likely the same kinetic scheme. Obvious cases are photoreactions involving NO as persistent intermediate as of nitrite esters RONO, including the Barton reaction,[15] of many *N*-nitrosoamines[16] R_2NNO and *N*-nitrosoamides[17] $R_1CO(R_2)NNO$. The high yields of the photooxidation reaction[18] of alkanes by NOCl can also be explained by the persistence of NO and does not require the postulation of a cage process.[18a]

Furthermore, the high yields of nitro compounds during photoreactions of nitrosoamines under oxygen[1,16b] appear natural now. There the initial cleavage 1 is followed by

$$2NO + O_2 \rightarrow 2NO_2 \qquad (15)$$

which transforms the persistent NO to the also persistent NO_2 radical which then cross-terminates with the aminyl radical or its equivalent.

In general, high yields of the cross-reaction product are expected from two intermediates with markedly different self-termination constants if they are generated with equal rates and if the rate constant for the cross-reaction is larger than the geometric mean of the self-reaction rate constants.[19] If the less persistent intermediate is transformed by some reaction to another transient and if this can react with the presistent reactant, again high yields for that reaction are achievable. The same holds if the persistent species transforms to another persistent intermediate. Since many types of persistent radicals are known and since other radicals can be made persistent by proper substitution (steric or electrostatic hindrance of self-termination), the principle of internal suppression of fast reactions may be of future synthetic use in radical chemistry, but the treatment given above is valid for other chemical intermediates as well.

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(11) Numerical integrations of eq 12 and 13 show that rapid switching of r from $r < 1$ to $r > 1$ causes x to attain the new x_s immediately. On the other hand, switching from $r > 1$ to $r < 1$ leads to an induction period for x.

(12) Kerr, J. F.; Trotman-Dickenson, A. F.; Progr. *React. Kinet.* **1961**, *1*, 129.

(13) In general, reaction 14 may represent a first- or pseudo-first-order process.

(14) Watkins, K. W.; Word, W. W. *Int. J. Chem. Kinet.* **1974**, *6*, 855.

(15) (a) Akhtar, M. *Adv. Photochem.* **1964**, *2*, 263. (b) Rieke, R. D.; Moore, N. A. *J. Org. Chem.* **1972**, *37*, 413. (c) Suginome, H.; Osada, A. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1963 and references therein.

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(18) (a) Müller, E. *Pure Appl. Chem.* **1968**, *16*, 153. (b) Mosher, M. W.; Bunce, N. J. *Can. J. Chem.* **1971**, *49*, 28.

(19) Replacement of the second-order self-termination terms in eq 12 and 13 by terms linear in x and y does not change the behavior of the system in a qualitative sense.