Oxidation of Methylmalonic Acid by Cerium(IV). Evidence for Parallel Reaction Pathways

Per Olav Kvernberg,[†] **Eddy W. Hansen,**[‡] **Bjørn Pedersen,**[†] **Asbjørn Rasmussen,**[†] **and Peter Ruoff*,**[§]

Department of Chemistry, University of Oslo, P.O. Box 1033 Blindern, N-0315 Oslo, Norway, SINTEF Oslo, P.O. Box 124 Blindern, N-0314 Oslo, Norway, and School of Technology and Science, Stavanger College, P.O. Box 2557 Ullandhaug, N-4004 Stavanger, Norway

Received: October 24, 1996; In Final Form: January 21, 1997[⊗]

The reaction between methylmalonic acid (MeMA) and Ce(IV) ion in 1 M sulfuric acid/D_2SO_4 has been studied by means of ^{1}H- and ^{13}C-NMR. When MeMA is in excess, acetic acid, hydroxymethylmalonic acid, and pyruvic acid are formed as stable end products. When Ce(IV) is in stoichiometric excess, acetic acid is the only product. Approximately 70−80% of the MeMA forms rapidly acetic acid with hydroxymethylmalonic acid and pyruvic acid as reactive intermediates. The remaining MeMA reacts along parallel pathways and forms two intermediates, which slowly convert to hydroxymethylmalonic acid and pyruvic acid, respectively.

Introduction

Ce(IV) compounds are important oxidants in many fields of chemistry.[1−5] In the Belousov[6]−Zhabotinsky[7] (BZ) reaction,[8] Ce(IV) oxidation of aliphatic organic substrates that contain a reactive C−H bond, as in malonic acid and derivatives, is a necessary component process for obtaining sustained concentration oscillations. While the inorganic mechanism for the oscillatory BZ reaction is well established[9,10] and has successfully been modeled by the Oregonator[11] and related models,[12] still little is known about the reactions of the organic subset. Considerable "detective work" is necessary to identify the various components in this subset.[13,14]

The methylmalonic acid (MeMA) BZ reaction[15] has shown a variety of unusual dynamical behaviors such as excitabilities of oxidized and reduced steady states and even bistability in a closed system.[16] A kinetic study of the reaction between MeMA and Ce(IV) has been performed by Ruoff and Nevdal[17] mainly by using initial rates and UV spectroscopy. Although the stoichiometry of the Ce(IV)−MeMA reaction is expected to be

$$CH_3CH(COOH)_2 + 6Ce(IV) + 2H_2O \rightarrow$$
$$CH_3COOH + 6Ce(III) + 6H^+ + 2CO_2 \quad (R1)$$
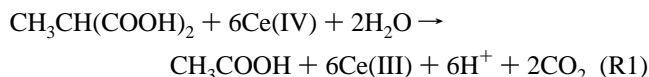
iodometric analysis showed that during a 20 h period only 4.7 mol of Ce(IV) were consumed per mole of MeMA.[17] Ruoff and Nevdal also found that under certain conditions a precipitate appeared, while the recorded ^{1}H-NMR spectrum of the reaction mixture showed an unidentified product together with pyruvic acid as a probable intermediate.

Earlier NMR investigations on MeMA−BZ systems and subsystems[18,19] encouraged us to study in further detail the MeMA−Ce(IV) system. In this paper we report new results where intermediates and products of the MeMA−Ce(IV) reaction were followed quantitatively with different initial concentrations. It was found that most of the MeMA (∼70−80%) reacts rapidly to form acetic acid (HOAc). For this main pathway NMR spectra indicate the presence of small amounts of hydroxymethylmalonic acid (MeMAOH) and pyruvic acid (Pyr), as reactive intermediates. The remaining MeMA reacts

by another route, where two additional intermediates form. These intermediates react slowly by first-order processes to form respectively MeMAOH and Pyr with half-lives of 6−8 h.

Experimental Section

MeMA was purchased from Fluka (>99%) and dissolved in 1 M H_2SO_4 (Merck) or D_2SO_4/D_2O solution (Norsk Hydro). The purity of MeMA was checked by ^{1}H-NMR. Reacting solutions were made by dissolving $(NH_4)_2Ce(NO_3)_6$ (Merck, analytical quality) in H_2SO_4 or D_2SO_4 and adding a corresponding solution of MeMA. The reaction volume was 5 mL.

^{1}H- and ^{13}C-NMR spectra were recorded on a Varian XL 300 spectrometer. Sixty four scans were accumulated with a sweep width of 4000 Hz, a repetition time of 3.752 s, and a pulse angle of 17°. All NMR measurements were performed at 23 ± 2 °C. Because the chemical shifts are affected by the presence of paramagnetic Ce(III) ions, peaks were identified by adding the compound in question to the solution and observing a corresponding increase in the peak intensity. Partly overlapping peaks were resolved with the program PEAKFIT.[20]

In the experiments reported here we have not excluded atmospheric oxygen from the reaction solution. A test where oxygen was removed by Ar-bubbling through initial reagent solutions and through the reaction mixture during a NMR run showed very similar kinetics of the same intermediates and final products as under aerobic conditions. Although this indicates that oxygen probably has little effect on the Ce(IV)−MeMA reaction, more detailed studies are necessary to look for possible oxygen effects.

MeMAOH was synthesized using the method by An et al.[21] The purity of the MeMAOH was tested with ^{1}H- and ^{13}C-NMR.

The presence of Ce(III) in a formed precipitate was found by electron-emission spectroscopy using a Philipps 515 scanning electron microscope.

Simulation calculations were done by using the programs FACSIMILE/CHECKMAT[22] and the FORTRAN subrouine LSODE.[23]
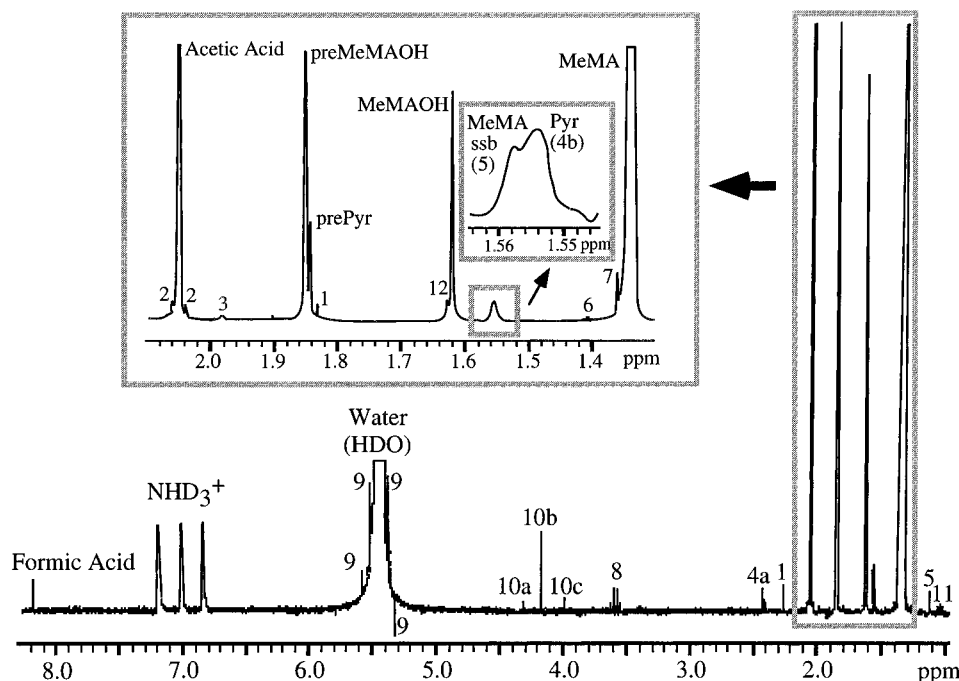
Experimental Observations

Stoichiometric Excess of MeMA. In a Ce(IV)−MeMA solution the main product is acetic acid (HOAc). Besides HOAc two new intermediates "preMeMAOH" and "prePyr" have been found (Figure 1). After about 1.5 h ([Ce(IV)]$_0$ = 0.2 M,

---

[†] University of Oslo.
[‡] SINTEF Oslo.
[§] Stavanger College.
[⊗] Abstract published in *Advance ACS Abstracts,* March 1, 1997.

Figure 1. ^{1}H-NMR spectrum of a 0.1 M MeMA and 0.2 M Ce(IV) reaction solution in 1 M D_2SO_4 taken 7.7 h after the start of reaction. Peak identification: (1) HOAc satellites caused by $^{13}CH_3{}^{12}COOH$ coupling; (2) HOAc satellites caused by $^{12}CH_3{}^{13}COOH$ coupling; (3) HOAc spinning sidebands; (4a) Pyr (keto-form); (4b) Pyr (diol-form) superimposed on MeMA satellite; (5) MeMA satellite due to $^{13}CH_3{}^{12}CH(COOH)_2$ coupling; (6) MeMA spinning sidebands; (7) one of the doublet peaks of nondeuterated MeMA ($CH_3CH(COOH)_2$); (8) quartet caused by nondeuterated MeMA ($CH_3CH(COOH)_2$); (9) spinning sideband of the water peak; (10, 11, 12) unidentified peaks.
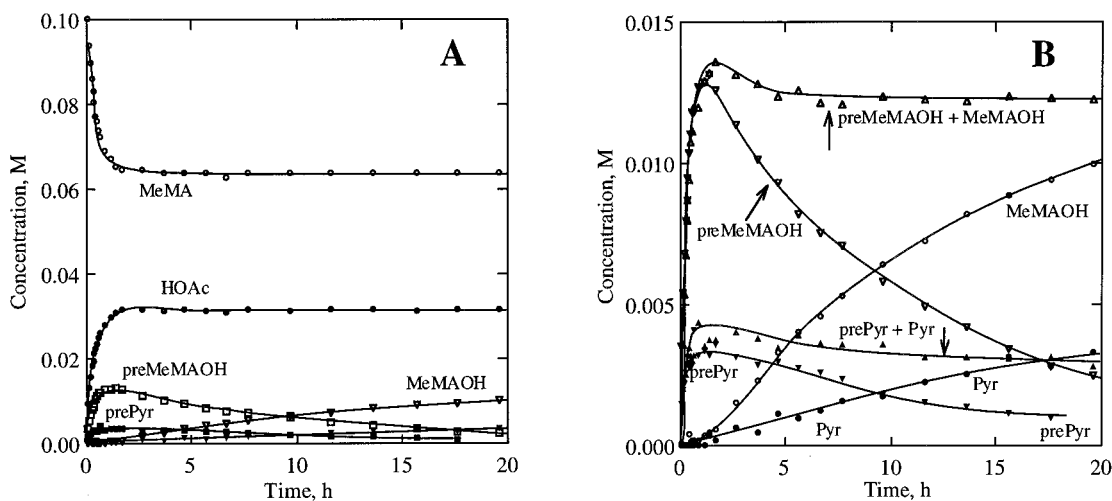

Figure 2. (A) Concentration profiles of a 0.1 M MeMA and 0.2 M Ce(IV) reaction solution in 1 M D_2SO_4 recorded during the first 20 h. (B) Concentration changes in preMeMAOH, MeMAOH, prePyr, Pyr, preMeMAOH + MeMAOH, and prePyr + Pyr for the same system as in A. Note that preMeMAOH + MeMAOH and prePyr + Pyr remain practically constant after the respective maxima of preMeMAOH and prePyr have been reached.

[MeMA]$_0$ = 0.1 M) the HOAc and MeMA concentrations reach constant values, indicating that all Ce(IV) has been consumed. At this point preMeMAOH and prePyr concentrations reach their maxima (Figure 2), and then they decay slowly, by first-order processes, to MeMAOH and pyruvic acid (Pyr), respectively (Figure 3). A quantitative analysis shows that the sums of preMeMAOH + MeMAOH concentrations and prePyr + Pyr concentrations are practically constant, indicating that the "preforms" are indeed precursors of MeMAOH or Pyr (Figure 2B). After approximately 40 h preMeMAOH and prePyr disappeared and the system reached equilibrium. When MeMA is in stoichiometric excess, the only products are HOAc, MeMAOH, and Pyr. Small amounts of formic acid have been observed to appear rapidly in the beginning of the reaction (Figure 1). However, once formed, the formic acid concentration remains unchanged until the end of the reaction.

Figure 4 shows equilibrium concentrations of HOAc, MeMAOH, Pyr, and MeMA when the initial MeMA concentration is 0.05 M with varying initial Ce(IV) concentrations. Solid lines show the results of model computations (see below). It was found that as long as the initial MeMA concentration is in stoichiometric excess, the number of moles of consumed Ce(IV) per mole MeMA lies in the range 4.5–5.0. Interestingly, this value is in the same range as found previously (4.7)[17] by iodometric analysis when Ce(IV) was in 10-fold molar excess over MeMA.

Excess of Ce(IV). When more than 6 equiv of Ce(IV) are present, all MeMA reacts to form HOAc. However, also in this case we see the buildup and decay of preMeMAOH and prePyr, but now only very small equilibrium concentrations of MeMAOH or Pyr could be detected. Also here traces of formic acid appear early in the reaction and remain constant until
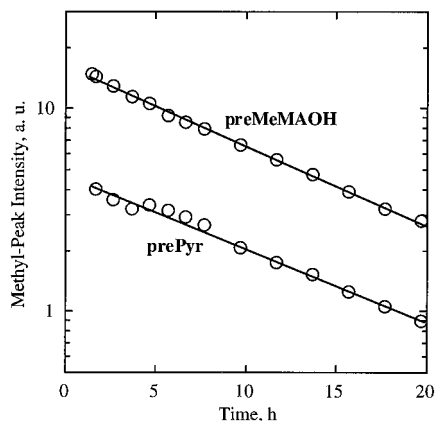
Figure 3. Intermediates preMeMAOH and prePyr show a first-order decay after they have reached their maximum at the end of the Ce(IV) consumption period. Decay constants: $k_{preMeMAOH} = 0.091$ h^{-1} ($r = 0.9982$), $k_{prePyr} = 0.084$ h^{-1} ($r = 0.9892$).
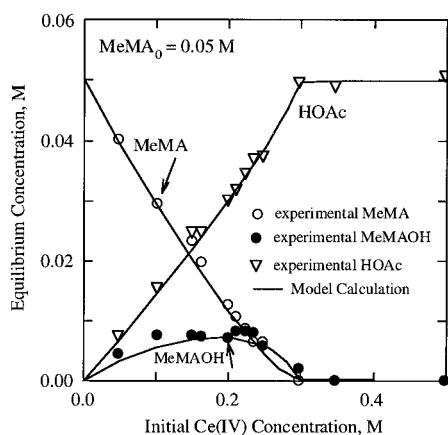
Figure 4. Experimental and computed equilibrium concentrations. Initial MeMA concentration is 0.05 M. Solid lines combine calculated equilibrium concentrations with [Ce(IV)]$_0$ increments of 0.05 M. Near [Ce(IV)]$_0 = 0.3$ M the increment was 0.01 M. Model (Scheme 4) computations were performed using the same rate constant values as in Figure 8.
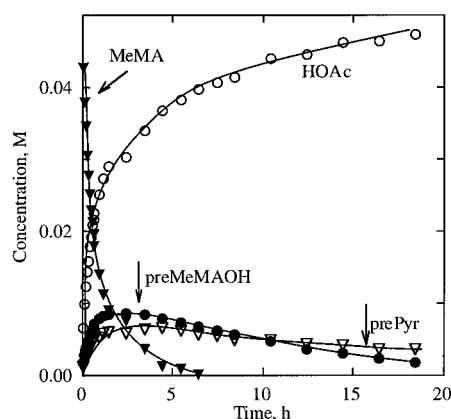

Figure 5. Concentration profiles of a 0.05 M MeMA and 0.4 M Ce-(IV) reaction solution in 1 M D$_2$SO$_4$ recorded during the first 20 h. The first-order decay constants for preMeMAOH and prePyr are $k_{preMeMAOH} = 0.039$ h^{-1} ($r = 0.9423$); $k_{prePyr} = 0.105$ h^{-1} ($r = 0.9888$).

equilibrium is reached. We consider formic acid to originate rapidly from small malonic acid impurities in the MeMA.[24]

Figure 5 shows the concentration profiles of a reacting system with initial concentrations of 0.05 M MeMA and 0.4 M Ce(IV). In such a system even after 20 h significant amounts of preMeMAOH and prePyr are still present.

SCHEME 1
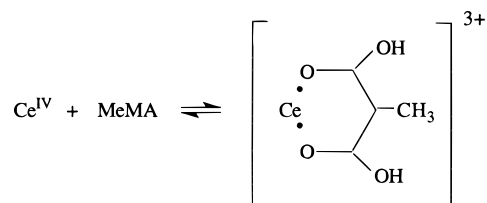
Other Reactions. We have tried to follow the reactions between Ce(IV) and MeMAOH or Pyr by NMR, but these reactions are too fast and were finished before the sample could be inserted into the spectrometer.

As reported earlier,[17] the formation of a white precipitate was observed, especially at an initial [MeMA]$_0$/[Ce(IV)]$_0$ ratio of 1:4. Sometimes, instead of an insoluble solid matrix,[17] crystals are observed. Electron-emission spectroscopy of the precipitate showed unequivocally the presence of Ce, indicating a Ce(III) compound, which we consider to be Ce(NH$_4$)SO$_4$.

Unidentified Peaks. We have not been able to identify peaks 10, 11, and 12 (Figure 1), but corresponding intermediates/products must be present in quite small amounts.

Discussion and Model Calculations

Comparison with Iodometric Results. Ruoff and Nevdal[17] have studied the stoichiometry of process R1 by measuring the amount of consumed Ce(IV) during an approximately 20 h reaction period when Ce(IV) was in 10-fold molar excess over MeMA. It was found that only 4.7 mol of Ce(IV) reacted for each mole of MeMA. An explanation of the discrepancy between the previous[17] findings and the present observation that under stoichiometric excess of Ce(IV) all MeMA reacts to HOAc is that a 20 h period is not sufficient (Figure 5) for process R1 to reach equilibrium.

Kinetic Considerations. The previous studies[17] also showed that the Ce(IV)−MeMA reaction, in analogy with the corresponding malonic acid reaction,[25] follows a sequential mechanism with probably an initial complexation between Ce(IV) and methylmalonic acid (Scheme 1).[5,26−28]

In an earlier proposed reaction scheme[17] it was assumed that MeMAOH originates from methylmalonyl radicals only. The present findings (Figure 2B) clearly show that also preMeMAOH is a precursor of MeMAOH. However, the rather long half-life of preMeMAOH makes it unlikely that this compound is related to any radical species!

In view of the above results, we propose the existence of parallel reaction pathways from MeMA to acetic acid (Figure 6). The main route forms rapidly HOAc via MeMAOH and Pyr as reactive intermediates. The remaining MeMA reacts by separate pathways via preMeMAOH and prePyr.

Further support for this interpretation can be obtained by analyzing the initial rates forming HOAc, preMeMAOH, and prePyr. In the case of parallel reaction channels "i" with identical or similar reaction orders in Ce(IV) and MeMA, the quotients of reaction velocities v_i/v_k should be constant. In other words, there should be an intrinsic proportionality between concentrations of produced species for each channel. Figure 7 shows that this is in fact the case: a plot of [preMeMAOH] and [prePyr] against [HOAc] gives two straight lines as long as HOAc, preMeMAOH, and prePyr are produced.

Possible Chemical Nature of preMeMAOH and prePyr. Compared with MeMAOH and Pyr, the increased chemical shifts of the methyl group in preMeMAOH and prePyr (Figure 1) suggest the presence of electron-withdrawing groups. A possibility may be that Ce(IV) in complexes like in Scheme 1
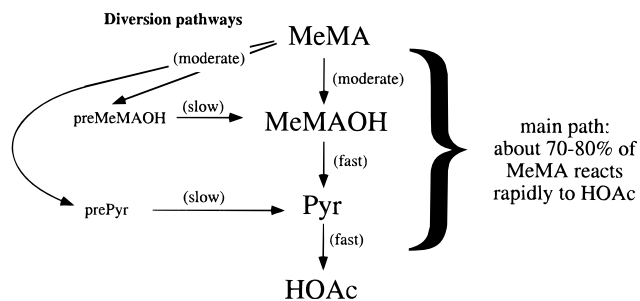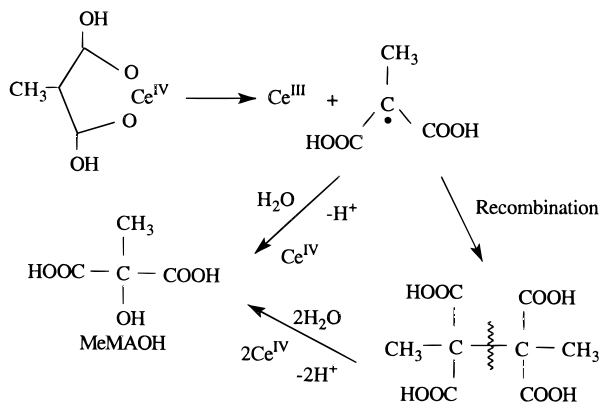
Figure 6. Proposed diversions from the main reaction path in the Ce(IV) oxidation of MeMA.
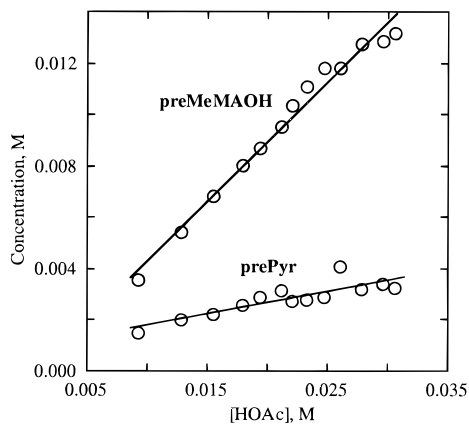
Figure 7. Concentrations of formed preMeMAOH and prePyr in relation to formed HOAc during the first 1.5 h of the reaction shown in Figure 2. The linear relationship suggests an additional parallel path from MeMA forming preMeMAOH and prePyr.
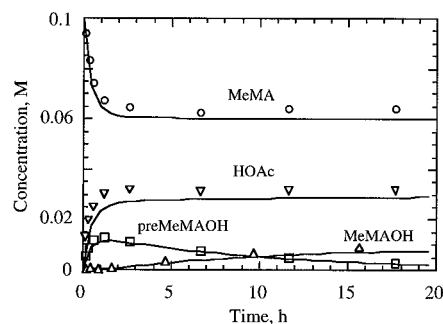
SCHEME 2

leads to an increase in the chemical shift of the methyl group and that preMeMAOH and prePyr may correspond to less reactive Ce(IV) complexes of MeMAOH or Pyr.

The work of Gao et al.[13] and Sirimungkala et al.[14] have identified a variety of possible radical recombination products in the Ce(IV)−malonic acid reaction. Similarly, preMeMAOH and prePyr may be related to analogous recombination products. In the case of preMeMAOH the deviation pathway may be due to methylmalonyl radical recombination. The main pathway is assumed to be the hydrolysis of methylmalonyl radicals forming MeMAOH (Scheme 2). For the "prePyr pathway" the deviation may occur in a similar manner, where the one-electron oxidation of $CH_3C^\bullet(OH)COOH$ radicals represents the main path (Scheme 3).

It should be noted, that the two Ce(IV) equivalents needed to oxidize the radical recombination products to MeMAOH and Pyr (Schemes 2 and 3) must be incorporated in preMeMAOH and prePyr, because no further acetic acid is formed during the
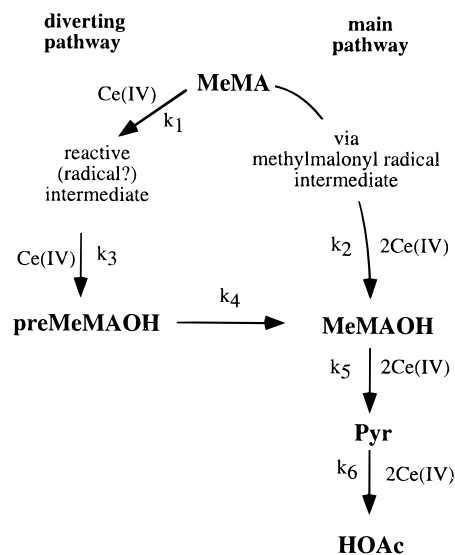

Figure 8. Model computations testing the kinetic behavior of the model (Scheme 4). Initial concentrations: $[MeMA]_0 = 0.1$ M, $[Ce(IV)]_0 = 0.2$ M. Rate constant values: $k_1 = 2.5$ M^{-1} h^{-1}, $k_2 = 3.1$ M^{-1} h^{-1}, $k_3 = 1000$ M^{-1} h^{-1}, $k_4 = 0.1$ h^{-1}, $k_5 = 500$ M^{-1} h^{-1}, $k_6 = 2000$ M^{-1} h^{-1}. Symbols indicate experimental results.

SCHEME 3
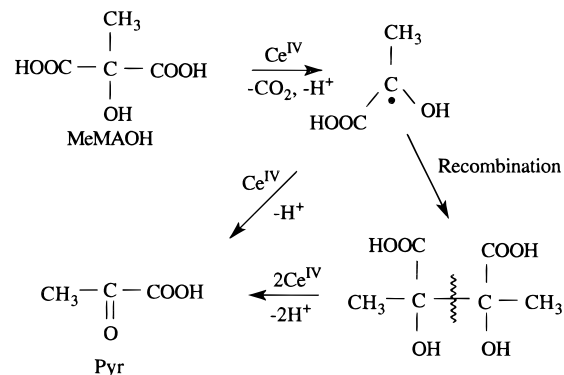
SCHEME 4

decay of the preforms to MeMAOH and Pyr. It may be possible that the preforms of MeMAOH and Pyr are complexes between two Ce(IV) ions and $(CH_3C(COOH)_2)_2$ (forming preMeMAOH) or two Ce(IV) and $(CH_3C(COOH)(OH))_2$ (forming prePyr). In the case of preMeMAOH each of the two Ce(IV) may interact with both sets of the adjacent carboxyl groups, analogous to the Ce(IV)−MeMA complex (Scheme 1). In prePyr, one Ce(IV) may bind to the two COOH groups, while the other Ce(IV) may form a complex with the OH groups.[29] Also recombinations between radical species $CH_3C^\bullet(COOH)_2$ (Scheme 2) and $CH_3C^\bullet(COOH)(OH)$ (Scheme 3) may be possible, and we wonder whether some of the unidentified peaks are related to "mixed" radical recombination products.

A Simple Model. To test the kinetic behavior of a parallel reaction pathway, we have, for the case of preMeMAOH, studied a simple model (Scheme 4). Because prePyr and Pyr are present in low concentrations, we have not included them in the calculations. All processes are assumed to be first-order in Ce(IV) and organic substrates, respectively.

To account for linear double-reciprocal plots,[17] a rapid equilibrium between complexed and uncomplexed MeMA has to be assumed (Scheme 1). Although complexed and uncomplexed MeMA could in principle be observed by NMR, a rapid equilibrium will result in only one "average" ^{1}H-methyl peak (as is observed). In the model we have so far not distinguished between uncomplexed and Ce(IV)-complexed MeMA and MeMAOH. The formation of Pyr and HOAc are rapid processes, while k_1, k_2, and k_4 are rate determining.

Practically quantitative agreement can be obtained between this simple model and experiments (Figure 4 and Figure 8) showing that the parallel reaction pathway gives an adequate description.

However, further work will be needed to understand in more detail the chemistry of the radical and nonradical interactions and their significance in the dynamic behavior of MeMA−BZ systems.

References and Notes

(1) Willard, H. H.; Young, P. *J. Am.Chem. Soc.* **1930**, *52*, 132.

(2) Smith, G. F. *Cerate Oxidimetry*; The G. Frederick Smith Chemical Co.: Columbus, OH, 1942.

(3) Richardson, W. H. In *Oxidation in Organic Chemistry;* Wiberg, K. G., Ed.; Academic Press: New York, 1965.

(4) Ho, T.-L. *Synthesis* **1973**, 347.

(5) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*; Interscience: New York, 1972.

(6) Belousov, B. P. In *Oscillations and Traveling Waves in Chemical Systems*; Field, R. J., Burger, M., Eds.; Wiley: New York, 1985.

(7) Zhabotinsky, A. M. In *Oscillations and Traveling Waves in Chemical Systems*; Field, R. J., Burger, M., Eds.; Wiley: New York, 1985.

(8) Noyes, R. M. *J. Phys. Chem.* **1990** *94*, 4404.

(9) Field, R. J.; Körös, E.; Noyes, R. M. *J. Am. Chem. Soc.* **1972**, *94*, 8649.

(10) Ruoff, P.; Varga, M.; Körös, E. *Acc. Chem. Res.* **1988** *21*, 326.

(11) Field, R. J.; Noyes, R. M. *J. Chem. Phys.* **1974**, *60*, 1877.

(12) Tyson, J. J. In *Oscillations and Traveling Waves in Chemical Systems*; Field, R. J., Burger, M., Eds.; Wiley: New York, 1985.

(13) Gao, Y.; Försterling, H.-D.; Noszticzius, Z.; Meyer, B. *J. Phys. Chem.* **1994**, *98*, 8377.

(14) Sirimungkala, A.; Försterling, H.-D.; Noszticzius, Z. *J. Phys. Chem.* **1996**, *100*, 3051.

(15) Ruoff, P.; Schwitters, B. *Z. Phys. Chemie (Wiesbaden)* **1983**, *135*, 171.

(16) Ruoff, P.; Noyes, R. M. *J. Phys. Chem.* **1985**, *89*, 1339.

(17) Ruoff, P.; Nevdal, G. *J. Phys. Chem.* **1989**, *93*, 7802.

(18) Hansen, E. W.; Gran, H. C.; Ruoff, P. *J. Phys. Chem.* **1985**, *89*, 682.

(19) Hansen, E. W.; Ruoff, P. *J. Phys. Chem.* **1989**, *93,* 2696.

(20) *PEAKFIT ver 2.0*; Jandel Scientific Europe, P.O.B. 4107, D-40688 Erkrath, Germany, 1989.

(21) An, Z.; Rino, A.; Venturello, C. *Synthesis (Stuttgart)* **1992**, *March issue*, 273.

(22) *FAKSIMILE/CHECKMAT*; Harwell Laboratory Computer Science and System Division: Oxfordshire, Oxon OX11 0RA, England, 1988.

(23) Hindmarsh, A. C. *ACM-SIGNUM Newslett.* **1980** *15*, 10.

(24) (a) Willard, H. H.; Young, P. *J. Am. Chem. Soc.* **1930**, *52*, 132. (b) Senguptya, K. K.; Aditya, S. *Z. Phys. Chem. (Frankfurt am Main)* **1963**, *38*, 25.

(25) Kasparek, G. J.; Bruice, T. C. *Inorg. Chem.* **1971**, *10*, 382.

(26) Brusa, M. A.; Perissinotti, L. J.; Colussi, A. J. *J. Phys. Chem.* **1985**, *89*, 1572.

(27) Brusa, M. A.; Perissinotti, L. J.; Colussi, A. J. *Inorg. Chem.* **1988**, *27*, 4474.

(28) Hanson, R. W. *J. Chem. Educ.* **1987**, *67*, 591.

(29) Young, I. B.; Trahanovsky, W. S. *J. Am. Chem. Soc.* **1969**, *91*, 5060.