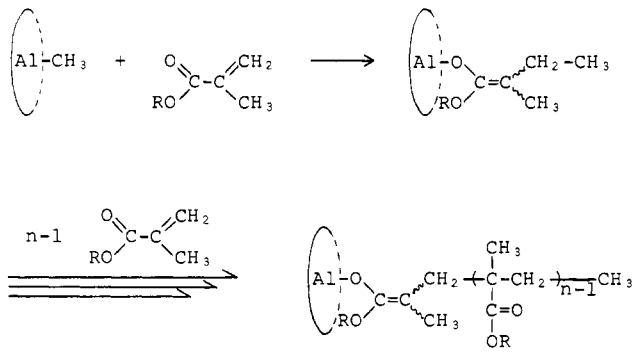
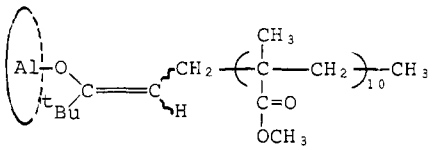
Scheme I



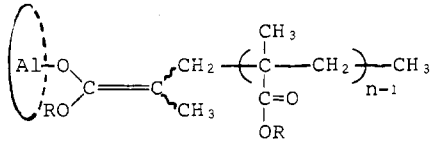
II

of methyl methacrylate. It is particularly noteworthy that moderate but definite acceleration by visible light was observed also in the block copolymerization reaction (Figure 2). In the block copolymerization of butyl methacrylate initiated from the living poly(methyl methacrylate) ($\bar{M}n$ = 9100) prepared with (TPP)AlMe (100/100/1) at 15 °C for 12 h, the conversion was 75% for the light reaction while 54% in the dark reaction; corresponding to this, $\bar{M}n$ = 17 800 ($\bar{M}w/\bar{M}n$ = 1.11) and $\bar{M}n$ = 16 000 ($\bar{M}w/\bar{M}n$ = 1.10), respectively.

In order to obtain further insight into the nature of the reactive species in polymerization, the reaction mixture (living polymer) was subjected to NMR spectral analysis, which can provide very useful information about the group bound to the metal in a porphyrin ring by the virtue of its strong shielding effect. In the reaction of 5 molar equiv of *tert*-butyl methacrylate and (TPP)AlMe in C_6D_6 at 30 °C for 72 h under irradiation, the signal due to Al-CH_3 (δ -5.8 ppm in C_6D_6) disappeared.[5] Among the new signals, a strong singlet at -0.3 ppm (-0.8 ppm in $CDCl_3$) was the most characteristic, the intensity relative to pyrrole-β proton of porphyrin being 8.4:8. In the reaction of the living poly(methyl methacrylate) with 5 molar equiv of *tert*-butyl vinyl ketone, a characteristic signal was observed at -1.5 ppm in $CDCl_3$, which is assigned to *tert*-butyl group of a (porphinato)aluminum enolate I.[6] Therefore, the signal observed at -0.8 ppm in the



I



II

former reaction is considered due to an aluminum enolate II, R = *t*-Bu derived from *tert*-butyl methacrylate.[7] These observations indicate that the active species of this polymerization is a (porphinato)aluminum enolate II (see Scheme I). The polymerization probably proceeds via the concerted mechanism, where the approach (coordination) of methacrylate to the aluminum atom and the conjugate addition of methyl or enolate group simultaneously take place.

Thus, not only the addition of (TPP)AlMe to alkyl methacrylate (initiation) but also the addition of (TPP)Al enolate to the methacrylate (every step of propagation) is accelerated by visible light, though to different extents.[8] Aluminum-alkyl or aluminum-enolate bonds cannot be directly excited by visible light but are considered to be activated indirectly by excitation of the porphyrin ring. Thus, the present reaction is a novel type of photocatalysis with metalloporphyrin.

(5) Quantitative incorporation of the methyl group into the terminal of poly(methyl methacrylate) was confirmed by ^{13}C NMR (δ 8.4 ppm in $CDCl_3$).

(6) For (TPP)Al—O—C[C(CH_3)$_3$]=CH—CH_2—Et, formed by the reaction of (TPP)AlEt and *tert*-butyl vinyl ketone, δ -1.46 ppm in $CDCl_3$: Murayama, H.; Inoue, S. *Chem. Lett.* **1985**, 1377.

(7) Other signals at high magnetic field are observed at δ -0.1 to -0.2 ppm and at δ -1.8 to -1.9 ppm (in $CDCl_3$), which are considered due to either =C—CH_2— or =C—CH_3, respectively.

(8) Although there are the examples of photoinduced addition polymerization, light is effective only for the generation of the initiating species. For the example of the initiation with organoaluminum compound: Allen, P. E. M.; Bateup, B. O.; Casey, B. A. *J. Organomet. Chem.* **1971**, *29*, 185.

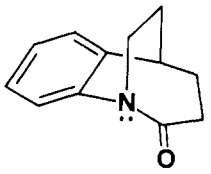
Hydrolysis of a Distorted Amide Facilitated by Diacids: A Phenomenological Model for the Aspartate Proteinases

V. Somayaji and R. S. Brown*

Department of Chemistry, University of Alberta Edmonton, Alberta, Canada T6G 2G2

Received January 28, 1987

The aspartate proteinases (APases) are hydrolytic enzymes containing two essential aspartate residues.[1] X-ray crystallographic structures of various members have shown close similarity of the active site regions,[2] but the mechanism by which they cleave proteins is said to be[1c] among the most obscure of any protease,[3,4] partly because there exist no satisfactory simple chemical models for precedent.[5] Two possible mechanisms, nucleophilic or general acid/general base, have been proposed.[1-4] Current thinking favors the latter, primarily because experimental detection of covalent intermediates (required in the nucleophilic route) have proven unsuccessful. We have recently presented the synthesis and hydrolysis kinetics of amide I[6a] as well as its x-ray crystal structure



I

and reactivity with β-amino alcohols.[6b] I also shows a striking reactivity toward hydrolysis promoted by certain dicarboxylic acids. Several lines of evidence indicate that the hydrolysis proceeds via the formation of anhydrides as shown in the Scheme I. Firstly, from Table I diacids geometrically capable of forming

(1) (a) *Aspartic Proteinases and Their Inhibitors*; Proceeding of FEBS advanced course no. 84/07; Kosta, V., Ed.; Walter de Gruyer: Berlin, 1985. (b) *Acid Proteases, Structure, Function, and Biology*; Tang, J., Ed.; Plenum Press: New York, 1977; p 95. (c) Fersht, A. *Enzyme Structure and Mechanism*; W. H. Freeman and Co.: New York, 1985: pp 422-426. (d) Fruton, J. P. *Adv. Enzymol.* **1966**, *44*, 1-36.

(2) (a) Hsu, I.-N.; Delbaere, L. T. J.; James, M. N. G.; Hofmann, T. *Nature (London)* **1977**, *266*, 140-145. (b) Subramanian, E.; Swan, I. D. A.; Liu, M.; Davies, D. R.; Jenkins, J. A.; Tickle, I. J.; Blundell, T. L. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 556-559. (c) Jenkins, J. A.; Tickle, I. J.; Sewell, T.; Ungaretti, J.; Wollmer, A.; Blundell, T. In *Acid Proteases, Structure, Function and Biology*; Tang, J., Ed.; Plenum Press: New York, **1977**; pp 43-60. (d) Andreeva, N. S.; Zdanov, A. S.; Gustchina, A. E.; Fedorov, A. A. *J. Biol. Chem.* **1984**, *259*, 11 353-11 365. (e) Bott, R.; Subramanian, E.; Davies, D. R. *Biochemistry* **1982**, *21*, 6956-6962. (f) James, M. N. G.; Sielecki, A. R. *Biochemistry* **1985**, *24*, 3701-3713, and references therein.

(3) For a review of the current status of thinking on the mechanism, see: appendix of Hofmann, T.; Dunn, B. M.; Fink, A. L. in ref 4.

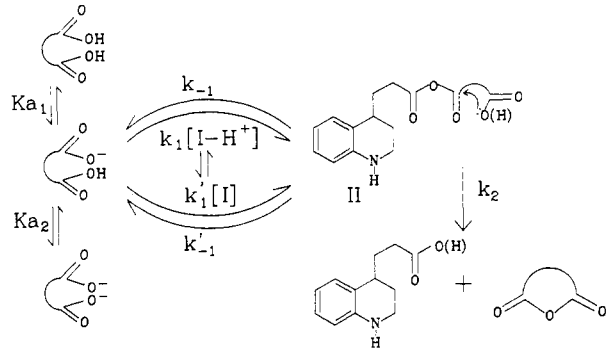
(4) Hofmann, T.; Fink, A. L. *Biochemistry* **1984**, *23*, 5247-5256.

(5) (a) Aldersley, M. F.; Kirby, A. J.; Lancaster, P. W.; McDonald, R. S.; Smith, C. R. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1487-1495. (b) Kirby, A. J.; McDonald, R. S.; Smith, C. R. *Ibid.* **1974**, 1495-1504. (c) Kluger, R.; Chin, J. *J. Am. Chem. Soc.* **1982**, *104*, 2891-2897.

(6) (a) Somayaji, V.; Brown, R. S. *J. Org. Chem.* **1986**, *51*, 2676-2686. (b) Skorey, K. I.; Somayaji, V.; Brown, R. S.; Ball, R. G. *J. Org. Chem.* **1986**, *51*, 4866-4872.

0002-7863/87/1509-4738$01.50/0 © 1987 American Chemical Society

Scheme I[7,8]



stable cyclic anhydrides are ~1–2 orders of magnitude more reactive than acetate, malonate, or *trans*-1,2-cyclopropane dicarboxylic acid at pH 5.0 even after due account of disparities in [ionic species] is taken. In aqueous media (succinate buffers, μ = 0.3 M (KCl) T = 25 °C) succinate exhibits the simplest kinetic behavior. The pH vs. log (k_2^{obsd}) profile from pH 3.5–6.5 exhibits a plateau at low pH indicative of the dominance of the mono anionic form of succinate reacting with protonated I[7] (Table 1S, Supplementary Material). Under these conditions the reaction is driven by the closure of II to form succinic anhydride (k_2 in Scheme I), that process competing effectively with k_{-1} and k_{-1}'.[8] When the FTIR spectrum of 0.1 M I in CH_3CN containing equimolar $Et_3N^+H/O_2^-CCH_2CH_2CO_2H$ is periodically monitored,[9] the characteristic C=O stretches of succinic anhydride (1789 and 1862 cm^{-1}) are seen to grow at the expense of the overlapping C=O bonds of I and succinate. Bands characteristic of the linear anhydride II are not observed. After ~10 h in that medium, an equilibrium is established which, judging by peak intensities, favors succinic anhydride by a factor of ~2. A similar situation exists under the same conditions for glutarate monoanion, and after the establishment of equilibrium, mass spectrometric analysis of the product mixture shows prominent peaks characteristic of the amino acid of I (M^+ = 205). In the above experiments neither succinate (glutarate) alone nor in the presence of the authentic amino acid of I shows a tendency to form anhydrides. Finally, the FTIR spectrum of a CH_3CN solution containing 0.1 M I and equimolar $Et_3N^+H/O_2^-CCH_3$, monitored over a 24-h period, shows no detectable bands characteristic of an anhydride and no loss of I. However CH_3CN solutions containing 0.02 M I and 5 M $Et_3N^+H/O_2^-CCD_3$ produce an approximate 1:1 equilibrium mixture of I and its CD_3^- acetate derived open anhydride judging from ^1H NMR, and UV spectrophotometry. The presence of that anhydride is also verified by CI-MS spectrometry (M^+ = 251, $C_{14}H_{14}D_3NO_3 + H^+$). Importantly, when a 25-μL aliquot of the above solution is directly injected into 3 mL of an aqueous, pH 4.75, 0.3 M acetate buffered medium, an immediate regeneration of I is observed, along with its subsequent normal hydrolysis to the amino acid.[10] Hence k_{-1} in Scheme I must be much larger than $k_1[O^-Ac]$ so that nucleophilic attack of carboxylate alone cannot lead to significant hydrolysis of I in the absence of a suitably oriented second intramolecular carboxyl group.[11]

(7) UV kinetic procedures ar analogous to those reported for the hydrolysis of I.[6a,b] Second-order rate constants for succinate attack on I (k_2^{obsd}) were determined from the slopes of the pseudo-first-order rate constant, k_{obsd} vs. [succinate]$_t$ at various pH values with [succinate]$_t$ = 0.01–0.10 M. The experimental data are given as Supplementary Material. The fit of the kinetic data to Scheme I involving only I-H$^+$ and monoanion is unsatisfactory at higher pH. However, the fit is markedly improved by the inclusion of a term corresponding to the monoanion attacking I or its kinetic equivalent. This latter process is included in scheme I for completeness.

(8) Scheme I is highly simplified since it does not explicitly consider tetrahedral intermediates, and there are kinetically equivalent pathways which at this time cannot be distinguished (e.g., dianion of succinate + I-H$^+$ is equivalent to monoanion + I). Also II, being a dibasic acid has four pH dependent forms. The k_{-1} and k_2 terms will be, respectively, suppressed when the amino and CO_2^- groups of II are protonated.

(9) FTIR spectra recorded in 0.1-mm cell every 10 min over a 16-h period.

(10) Hydrolysis k_{obsd} for I formed by reclosure = 1.64×10^{-3} s^{-1} while k_{obsd} for authentic I = 1.70×10^{-3} s^{-1} under identical conditions, pH 4.75, 0.3 M acetate, T = 25 °C.

Table I. Second-Order Rate Constants for Attack of Various Acids on Amide I[a]

acid	% monoanion	k_2^{obsd}[c] ($\times 10^3$ M^{-1} s^{-1})
acetic	74	2.0
succinic	60	250
glutaric	46	172
cis-cyclopropane-1,2-dicarboxylic[b]	85	114
trans-cyclopropane-1,2-dicarboxylic	27	3.1
malonic	55	2.3

[a] T = 25.0 °C, μ = 0.3 M (KCl), pH 5.0 (pK_a values at μ = 0.3 M given in Supplementary Material). [b] pH 5.05. [c] Error limits ±2% of value or better.

The striking feature of the process is a hydrolysis of I without water per se, since the latter's constituents are created stepwise by the conversion of a diacid into a cyclic anhydride. In this case, the driving force for the process obtains from the unique torsional destabilization of I.[6b] Interestingly, substrate distortion has been considered[12] as an important component for catalysis in the APases. While one cannot be certain this model is an accurate reflection of the enzymatic pathway, phenomenologically, the observation of amide hydrolysis promoted by diacids bears a relationship to the situation in the APases and merits continued investigation.

Acknowledgment. We gratefully acknowledge the financial assistances of the University of Alberta and Natural Sciences and Engineering Research Council of Canada as well as Jim Hoyle for technical assistance and Dr. Paul Street (University of Houston) for preliminary observations in this system.

Supplementary Material Available: Tables of kinetic data for succinate with I and pK_a values of various acids titrated at μ = 0.3 M (1 page). Ordering information is given on any current masthead page.

(11) The modest catalysis seen with acetate arises from general acid/base promotion of H_2O attack.[6a]

(12) (a) Sachdev, G. P.; Fruton, J. S. *Proc. Natl. Acad. Sci. U.S.A.* **1975**, *72*, 3424–3427. (b) Medzihradszky, K.; Voynick, I. M.; Medzihradszky-Schweiger, M.; Fruton, J. S. *Biochemistry* **1970**, *9*, 1154–1162. (c) Pearl, L. ref 1a, pp 189–195.

Titanium-Activated Carbon–Carbon Bond Formation by Reductive Head-to-Head Coupling of Carbon Disulfide: Synthesis of $[(\eta^5\text{-}C_5H_5)_2Ti]_2(C_2S_4)$ and Comparative Analysis of This Electron-Delocalized Tetrathiolene-Bridged Dititanium Complex with the Electronically Equivalent, Electron-Localized Oxalate- and Tetra-*p*-tolyloxalylamidine-Bridged Dititanium Complexes

Holly A. Harris, A. David Rae,[1] and Lawrence F. Dahl*

Department of Chemistry
University of Wisconsin—Madison
Madison, Wisconsin 53706

Received February 13, 1987

Metal-promoted reductive fixation of carbon disulfide to form the tetrathiooxalate (or ethylenetetrathiolate) anion has received much attention in recent years, partly due to problems encountered in obtaining tetrathiooxalate salts by electrochemical dimerization of CS_2.[2] Interest in developing new transition-metal tetrathio-

(1) On leave (Sept 1983–Feb 1984) from the School of Chemistry, University of New South Wales, Kensington, New South Wales 2033, Australia.

(2) Hoyer, E. *Comments Inorg. Chem.* **1983**, *2*, 261–270, and references cited therein.

0002-7863/87/1509-4739$01.50/0 © 1987 American Chemical Society