Table II. ν_{CO} of Sterically Hindered and Unhindered CO Hemes[a]

compd	medium	$\nu^{12}CO$	$\nu^{13}CO$
Fe-Cu-4	neat *N*-MeIm	1960	1915
	0.1 M *N*-Ph_3CIm in CH_2Br_2	1967	1924
FeSP-13	neat *N*-MeIm	1962	
	0.1 M *N*-Ph_3CIm in CH_2Br_2	1967	
heme 5	neat *N*-MeIm	1955	1910
	0.1 M *N*-Ph_3CIm in CH_2Br_2	1966	1922

[a] Spectra were obtained by using a Perkin-Elmer 283B Spectrometer interfaced with computer.

binding results of Traylor.[34] Since it has previously been shown that CO and O_2 association rates are nearly independent of medium and heme electronic effects and that the O_2 off rates are very much affected by the local polarity of the ligand binding site,[28,29] it is futile to directly compare the O_2/CO affinity ratio (*M*) of different model compounds. However, when we compare only the association rate data we find, relative to chelated mesoheme, for FeCu-5 or FeSP-15 a CO reduction of 90-fold while O_2 is reduced by 30 (a reduction ratio of 3) and for FeCu-4 a CO reduction of 400-fold with O_2 being reduced by 100 (a reduction ratio of 4). This unequal reduction of CO and O_2 association rates may be considered as an evidence for the steric differentiation of O_2 and CO. This steric selectivity nonetheless does not explain why we cannot obtain the degree of differentiation observed for Mb, i.e., chelated protoheme or R-Hb vs. Mb has a reduction ratio of at least 5, even though our model compounds have more steric hindrance built into them than does Mb, as reflected by CO on rates. Neither can we reconcile the fact that there is essentially no change in the on rate reduction ratio nor the *M* value going from FeCu-5 to FeCu-4 while the structural data as well as the CO on rates indicate clearly that the FeCu-4 has a tighter gap than FeCu-5. If the bending of CO is responsible for the differentiation, it would have to show in the 4 to 5 comparison. One possibility is that the differentiation is not proportional to the steric hindrance; it reaches a maximum and then decreases as the steric effect becomes too great. Unfortunately, in the present study we found it is difficult to have a system whose CO on rate is in the neighborhood of $5 \times 10^5\ M^{-1}\ s^{-1}$, to compare with Mb. Cofacial diporphyrins with longer linkages, e.g., FeCu-6 and FeCu-7 exhibit kinetic rates similar to FeCu-5 since the two porphyrin rings have a tendency to assume a slipped conformation and maintain a tight gap, as shown by X-ray studies;[35] thus these compounds offered no insight. On the other hand, hemes equipped with longer straps tend to form 6-coordinate hemochromes with the excess base.

Although the present study does not provide a definitive answer as to whether or not steric bulk at the ligand binding site can selectively reduce the *affinity* of CO vs. O_2, surely the kinetic results imply that models which bind CO 2–3 orders of magnitude slower than Mb should decisively indicate whether there is any relation between ligand affinity and ν_{CO}. Table II summarizes the ν_{CO} of some of the synthetic compounds measured in different solvents. It is evident that the influence of medium is far greater than the steric effect. *There is no correlation between ν_{CO} and the ligand affinity.*[30] While it is unclear whether ν_{CO}, which is a function of the bond order between C and O, should be sensitive to slight distortion at the C–Fe bond, the lack of any significant change in ν_{CO} suggests that the bond nature in hindered hemes is not very different from those in a normal octahedral geometry. The unequal reduction of the CO and O_2 association rates by the steric bulk implies that such differentiations must be related to the bond-forming processes. Szabo[31] has suggested that CO-heme transition state resembles product while O_2 heme has a more reactant-like transition state. That is to say since the Fe–CO bond formation requires shorter contact, the CO molecules must be in closer proximity than O_2 to attain transition state. Any steric barricade at the heme binding site therefore would hinder CO coordination more than O_2 coordination.

The present study also indicates that it would be a unique synthetic challenge to prepare heme models[36] that match Mb's kinetic behavior. So long as we showed that bending of CO cannot be solely responsible for the large differentiation observed in Mb, other factors such as the basicity of the proximal base, preequilibrium of the heme conformation inside the protein pocket, etc., have to be taken into consideration.[37] The synthesis of other sterically hindered, 5-coordinate hemes is under way.

Acknowledgment. This work was supported by NSF Grant CHE-7815285. The PE 283 B IR spectrometer was purchased by USDA Grant 59-2261-0-1-437-0. C.K.C. is an Alfred P. Sloan Fellow, 1980–1984, and a Camille and Henry Dreyfus Teacher–Scholar, 1980–1985.

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A New Mechanism for Photosubstitution of Organometallic Complexes. Generation of Substitutionally Labile Oxidation States by Excited-State Electron Transfer in the Presence of Ligands

David P. Summers, John C. Luong, and Mark S. Wrighton*

*Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139*

Received April 20, 1981

Photosubstituion remains one of the most important reactions of inorganic and organometallic complexes.[1,2] Photosubstitution occurs by dissociative and associative pathways[1–4] involving loss of a ligand from the excited state or ligand addition to the excited state as the key step. By either of these mechanisms the quantum yield for substitution can be no greater than 1. We wish to report results that establish a new mechanism for light-induced ligand substitution where quantum yields can, and do, exceed 1. Photoinitiated substitution via the generation of substitution labile, metal-centered radicals by cleavage of metal–metal bonds can also lead to substitution with quantum yields that exceed 1.[5] The basis of our new mechanism is that a unit change in the oxidation state of the metal can have profound consequences on the substitution lability. Classic examples include the pairs of complexes derived from Cr^{3+}/Cr^{2+} and $Co^{3+/2+}$ where the 2+ oxidation states yield labile complexes, and the 3+ states yield inert complexes.[6] Accessing substitution labile oxidation states of metal complexes by ligand-to-metal charge transfer is known (eq 1), but the net

$$Co(NH_3)_5Br^{2+} \xrightarrow[H_2O]{h\nu} Co^{2+} + 5NH_4^+ + Br^- \qquad (1)$$

result is not substitution on the original complex.[2] We now describe results that show that excited-state electron transfer can

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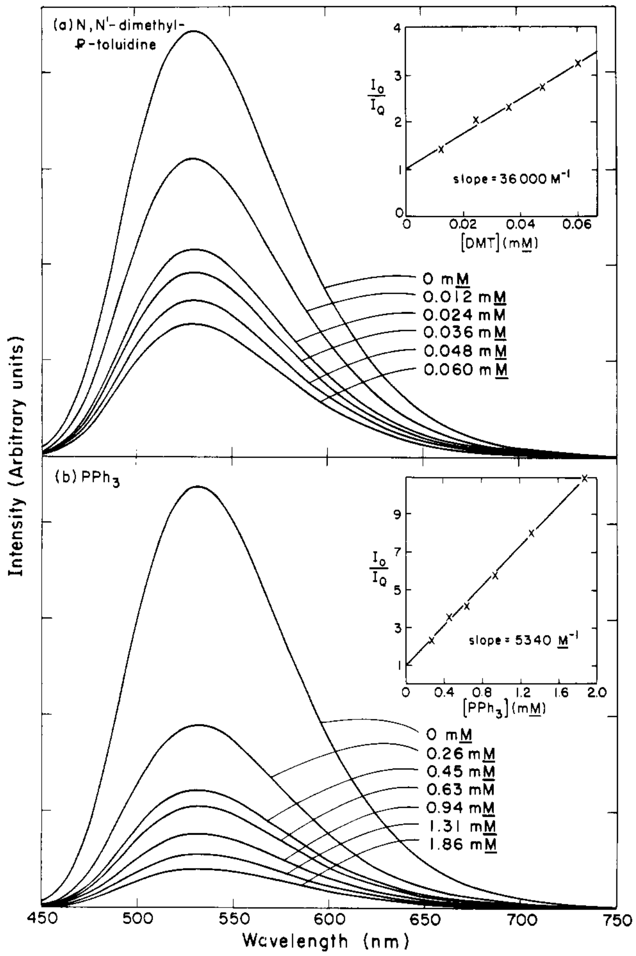

Figure 1. Stern–Volmer quenching by (a) N,N'-dimethyl-p-toluidine and (b) PPh_3. The Stern–Volmer constants (slope) gives $k_q = 1.5 \times 10^{10}$ M^{-1} s^{-1} for N,N'-dimethyl-p-toluidine and $k_q = 2.2 \times 10^9$ M^{-1} s^{-1} for PPh_3 for an excited-state lifetime in the absence of quencher of 2.4×10^{-6} s.

yield substitution labile oxidation states where the net result is a substitution product, not a redox product.

The system chosen for study is represented by eq 2. The

$$[(CH_3CN)Re(CO)_3phen]^+ \xrightarrow[L\,=\,py,\,PPh_3]{h\nu} [LRe(CO)_3phen]^+ + CH_3CN \quad (2)$$

$[(CH_3CN)Re(CO)_3phen]^+$ (phen ≡ 1,10-phenanthroline) complex has been previously synthesized and characterized.[7] The thermally inert complex has a lowest excited state associated with a Re → phen CT transition in absorption [λ_{max} ~360 nm (ϵ ~6400 M^{-1} cm^{-1}) in CH_3CN] that is emissive [λ_{max} ~532 nm, τ ~ 2.4×10^{-6} s) in fluid solution at 25 °C (Figure 1). Generally, it has been found that such MLCT excited states do not lead to quantum-efficient ligand substitution.[8-11] Indeed, 436-nm irradiation (~10^{-7} einstein/min) of $[(CH_3CN)Re(CO)_3phen]^+$ in CH_3CN containing 2 M pyridine yields no substitution;[12] the quantum yield for disappearance of the starting complex is ≪10^{-3}, and the emission properties are the same as in CH_3CN containing no pyridine.

The first important finding relating to the new mechanism for light-induced subsititution is that 436-nm irradiation of $[(CH_3CN)Re(CO)_3phen]^+$ in CH_3CN containing 0.2 M PPh_3 and 0.1 M $[n\text{-}Bu_4N]PF_6$ yields clean and quantum-efficient substitution to yield $[(Ph_3P)Re(CO)_3phen]^+$ (Figure 2). Note that quantum yields for substitution far exceed 1 (Table I). The photoproduct was characterized spectroscopically by infrared absorption and was compared to an authentic sample prepared independently.[13] As shown in Figure 1, PPh_3 quenches the emission of $[(CH_3CN)Re(CO)_3phen]^+$ according to Stern–Volmer kinetics; the associated quenching constant, k_q, is 2.2×10^9 M^{-1} s^{-1}. The quenching is logically associated with the electron-transfer process represented by eq 3 where Q = PPh_3, since the oxidizing

$$([(CH_3CN)Re(CO)_3phen]^+)^* + Q \xrightarrow{k_q} [(CH_3CN)Re(CO)_3phen]^0 + Q^+ \quad (3)$$

power of the excited complex is ~+1.5 V vs. SCE,[14] exceeding

Table I. Light- and Electroreduction-Induced Formation of $[LRe(CO)_3phen]^+$ from $[(CH_3CN)Re(CO)_3phen]^+$ [a]

A. Light-Induced Substitution (436 nm, 1×10^{-7} einstein/min)

L, M	Q, M	% conv[b]	Φ ± 10%[c]
PPh_3, 0.2	PPh_3, 0.2	8	8
		22	11
		27	12
		52	22
		53	21
		60	21
		62	19
		93	24
pyridine, 2.0	N,N'-dimethyl-p-toluidine, 0.005	7.0	0.22
		11.7	0.32
		23.5	0.58
		28.9	0.65
		33.9	0.70
		39.3	0.74

B. Electroreduction-Induced Substitution

L, M	mol electrons passed,[d] $\times 10^8$	% conv[b]	Coulomb efficiency[e]
PPh_3, 0.2	106	4.1	16
	210	5.5	11
	364	15	16
	520	24	18
	714	84	45
pyridine, 2.0	137	2.3	6.4
	347	15	16
	697	53	30
	1068	61	23

[a] All experiments carried out by using 0.016 M $[(CH_3CN)Re(CO)_3phen]^+$ in dry CH_3CN solvent containing 0.1 M $[n\text{-}Bu_4N]ClO_4$ or $[n\text{-}Bu_4N]PF_6$. In every case the solutions are deoxygenated. Photochemical experiments involved the use of 3.0 mL of sample freeze-pump-thaw degassed in four cycles, in hermetically sealed ampules. The electrochemical experiment was carried out in a two compartment cell with 25.0 mL of catholyte. [b] % conv refers to percent of $[(CH_3CN)Re(CO)_3phen]^+$ compound. The yield of $[LRe(CO)_3phen]^+$ is >90% based on the amount of starting material consumed. [c] Quantum yield is the number of $[LRe(CO)_3phen]^+$ molecules formed per 436-nm photon adsorbed. [d] Number of electrons passed in external circuit. [e] Number of $[LRe(CO)_3phen]^+$ molecules produced per electron passed in external circuit.

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(12) Typically, 0.016 M $[(CH_3CN)Re(CO)_3phen]Tf$ in CH_3CN solution is irradiated in the presence of various additives; 3.00-mL samples in Pyrex ampules prepared from 13- × 100-mm test tubes are freeze–pump–thaw degassed in at least four cycles and hermetically sealed. Samples are then irradiated at 436 nm (1×10^{-7} einstein/min) in a merry-go-round. Quantitative analysis was done by IR using a Perkin Elmer 180 IR spectrometer.

(13) The $[LRe(CO)_3phen]^+$ species are generally prepared by refluxing $[(CH_3CN)Re(CO)_3phen]Tf$ in THF containing excess L for ~2 h. After concentration by rotary evaporation, addition of anhydrous Et_2O precipitates the complex: Luong, J. C. Ph.D. Thesis, M.I.T., 1981.

the potential needed to oxidize PPh_3.[15] The lowest excited state of PPh_3 is too high in energy[16] for PPh_3 to quench the excited Re complex by energy transfer at a diffusion controlled rate. Various related Re complexes have been shown to be quenched by electron transfer.[17] Since 0.2 M PPh_3 is sufficient to quench virtually all excited Re complexes, substitution must occur subsequent to the quenching step that yields the one-electron reduced complex that is formally a 19-valence electron species. Substitution thus occurs at the 19-valence electron stage (eq 4). Quantum yields that

$$[(CH_3CN)Re(CO)_3phen]^0 + L \rightarrow [LRe(CO)_3phen]^0 + CH_3CN \quad (4)$$

exceed 1 are accommodated by the process represented by eq 5

$$[LRe(CO)_3phen]^0 + [(CH_3CN)Re(CO)_3phen]^+ \xrightarrow{k_5} [LRe(CO)_3phen]^+ + [(CH_3CN)Re(CO)_3phen]^0 \quad (5)$$

$$[LRe(CO)_3phen]^0 + Q^+ \xrightarrow{k_6} [LRe(CO)_3phen]^+ + Q \quad (6)$$

$$[(CH_3CN)Re(CO)_3phen]^0 + Q^+ \xrightarrow{k_7} [(CH_3CN)Re(CO)_3phen]^+ + Q \quad (7)$$

with eq 6 and 7 representing two sources of chain termination. The electron-transfer process represented by eq 5 is energetically possible, since the $[LRe(CO)_3phen]^+$ species are all reducible electrochemically at nearly the same potential in CH_3CN/0.1 M $[n\text{-}Bu_4N]ClO_4$, -1.2 ± 0.1 V vs. SCE.

Two additional sets of experiments confirm the electron-transfer mechanism for the substitution of CH_3CN of $[(CH_3CN)Re(CO)_3phen]^+$. First, the reduction of the $[(CH_3CN)Re(CO)_3phen]^+$ is only quasi-reversible at ~ -1.2 V vs. SCE. Controlled potential reduction of $[(CH_3CN)Re(CO)_3phen]^+$ at -1.1 V vs. SCE in CH_3CN/0.1 M $[n\text{-}Bu_4N]ClO_4$ containing L = pyridine or PPh_3 yields rapid formation of the substitution product $[LRe(CO)_3phen]^+$ (Table I).[18] The important result is that many molecules of the substitution product are obtained with only a small extent conversion to *net* reduction product. Indeed, the chemical yield of $[LRe(CO)_3phen]^+$ is quantitative within experimental error. Presumably electrochemical generation of $[(CH_3CN)Re(CO)_3phen]^0$ (eq 8) initiates the chain mechanism

$$[(CH_3CN)Re(CO)_3phen]^+ \xrightarrow[-1.1\text{V vs. SCE}]{+e^-} [(CH_3CN)Re(CO)_3phen]^0 \quad (8)$$

for substitution that results when the same species is generated by excited-state electron transfer, eq 3.

The second set of experiments concerns the light-induced substitution of CH_3CN using pyridine as the entering group, but employing Q = *N,N'*-dimethyl-*p*-toluidine as the electron-transfer quencher to produce $[(CH_3CN)Re(CO)_3phen]^0$ (eq 3). Figure 1 shows that *N,N'*-dimethyl-*p*-toluidine is an efficient quencher, and as for Q = PPh_3, the process is likely electron transfer (eq 3). While no substitution using pyridine occurs without an electron-transfer quencher, vide supra, clean, quantum-efficient substitution to yield $[(pyridine)Re(CO)_3phen]^+$ occurs when the solution contains 2.0 M pyridine *and* the electron-donor quencher (Figure 2 and Table I). This result is consistent with the electroreduction-induced substitution described above. Note, however, that the Coulombic efficiencies for the electroreduction for L = PPh_3 or pyridine are qualitatively the same, whereas the quantum efficiency for L = PPh_3, Q = PPh_3 is qualitatively higher than for L = pyridine, Q = *N,N'*-dimethyl-*p*-toluidine. In the electroreduction-induced substitution the chain termination cannot be due to the processes represented by eq 6 and 7, since Q^+ is not generated. Rather, radical coupling and impurities (O_2, H_2O, trace peroxides, etc.) are the sources of chain termination. Thus, in the electroreduction qualitatively similar Coulombic efficiencies for L = PPh_3 and pyridine are reasonable. The discrepancy in the quantum yields is likely due to the fact that processes 6 and 7 are more important for Q = *N,N'*-dimethyl-*p*-toluidine than for Q = PPh_3, since the oxidation of PPh_3 is not chemically reversible under the conditions employed. Thus, PPh_3^+ is effectively unavailable after cage escape of the primary products formed from excited-state electron transfer. The *N,N'*-dimethyl-*p*-toluidine, by way of contrast, is chemically and kinetically reversible, $E^0(Q^+/Q) = +0.7$ V vs. SCE, under the conditions employed.

Since the rate constants k_6 and k_7 likely approach the diffusion controlled limit, it would appear that the 19-valence electron species is very substitution labile. The substitution itself is likely dissociative in character owing to the fact that the 19-valence electron complex can be regarded as already super coordinatively saturated. The extra electron density is likely mainly localized on phen with some leakage into a σ-antibonding level with respect to the Re–$NCCH_3$ bond.[19] Future studies will concern the elaboration of these findings and the measurement of the substitution lability of the 19-valence electron species.

The results described herein add a new mechanistic pathway to light-induced substitution of metal complexes. Further, the results add to the important reactions that can be visible-light induced by bimolecular excited-state electron transfer of long-lived excited complexes,[17,20-26] though similar kinds of reactivity have been observed in certain organic molecules such as aromatic halides.[27,28] Substitution quantum yields that exceed 1 may have

(14) The E^0 for the excited-state oxidation is only approximate since the Re(I)/Re(0) couple is not reversible and the excited-state energy is taken to be 2.7 ± 0.1 eV. The Re(I)/Re(0) couple is ~ -1.2 V vs. SCE, giving an excited-state potential [Re(I)*/Re(0)] of +1.5 V vs. SCE.

(15) We observe an irreversible PH_3 oxidation wave at +1.3 V vs. SCE in CH_3CN/0.1 M $[n\text{-}Bu_4N]ClO_4$ under Ar. Even at a scan rate of 50 V/s the cyclic voltammetry shows the oxidation to be irreversible.

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(18) Electroreduction was carried out in a two compartment cell with the two compartments separated by an ultrafine glass frit. The working cathode was Pt, and the cathode compartment contained the Ag^+/Ag reference. The potential was controlled to -1.1 V vs. SCE (-1.5 V vs. Ag^+/Ag) by using a PAR 173 potentiostat and a 175 programmer. The catholyte was dry CH_3CN/0.1 M $[n\text{-}Bu_4N]ClO_4$ containing 2 M pyridine or 0.2 M PPh_3 and 0.016 M $[(CH_3CN)Re(CO)_3phen]^+$. All electrochemistry was done under Ar; aliquots were withdrawn from the cathode component for analysis by IR spectroscopy as a function of coulombs passed. There are other examples of electron-transfer induced substitiution that results in chain substitution: Rieger, P., private communication. Bezems, G. J.; Rieger, P. H.; Visco, S. *J. Chem. Soc., Chem. Commun.*, **1981**, 265.

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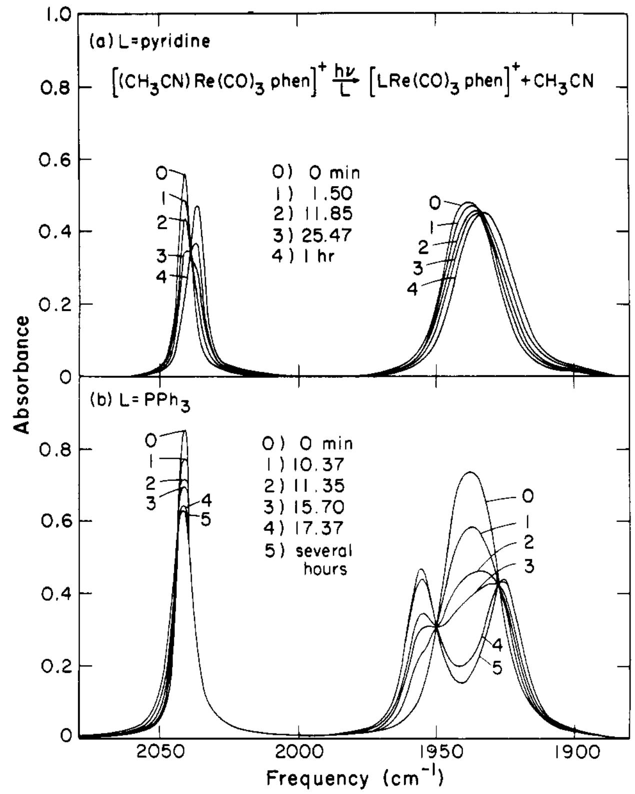


Figure 2. Infrared spectral changes accompanying light-induced formation of $[LRe(CO)_3phen]^+$ from $[(CH_3CN)Re(CO)_3phen]^+$ for (a) L = pyridine and (b) L = PPh_3.

relevance in imaging, since many metal complexes undergo significant optical spectral changes upon ligand substitution.

Acknowledgment. We thank the National Science Foundation for support of this research.

(*R*)-1-Acetamido-2-phenylethaneboronic Acid. A Specific Transition-State Analogue for Chymotrypsin

Donald S. Matteson* and Kizhakethil M. Sadhu

Department of Chemistry, Washington State University Pullman, Washington 99164

Gustav E. Lienhard*

Department of Biochemistry, Dartmouth Medical School Hanover, New Hampshire 03755

Received March 30, 1981

We report the synthesis of (*R*)-1-acetamido-2-phenylethaneboronic acid (**5a**), the boronic acid analogue of *N*-acetyl-L-phenylalanine, by the unambiguous route outlined in Scheme I, and its potent competitive inhibition of chymotrypsin, with a dissociation constant of 2.1×10^{-6} M at 25.0 °C and pH 7.5.

Aryl and arylalkylboronic acids bind strongly to the serine proteases chymotrypsin[1,2] and subtilisin.[2,3] The reason for this affinity is that the boronic acid group reversibly forms a tetrahedral adduct with the active site serine hydroxyl group, and the adduct crudely resembles the transition state for ester or amide hydrolysis.[2,4] It was anticipated that boronic acids corresponding to the specific amino acid substrates for these proteases would be even more potent inhibitors than the compounds tested to date, which only partially satisfy the specificity requirements of the enzymes. Previous attempts to synthesize α-amino or α-amido boronic acids have been unsuccessful, except for the alkylated amino series $R_2NCH_2B(OR')_2$ and $R_3N^+\!-\!CH_2B(OR')_2$.[5,6] Esters and amides of *N*-acetyl-L-phenylalanine are specific substrates for chymotrypsin,[7] and the compound described herein provides the first example of a transition-state analogue of the boronic acid type corresponding to a specific substrate for a serine protease.

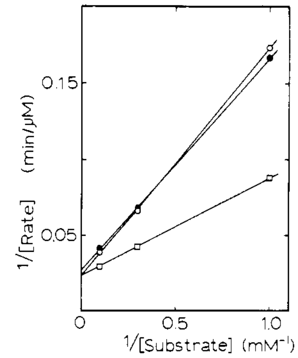
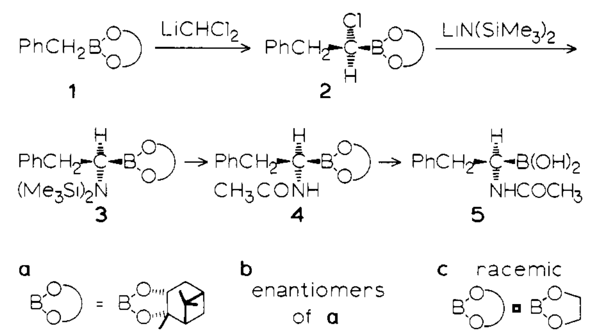


Figure 1. Inhibition of the chymotrypsin-catalyzed hydrolysis of methyl hippurate at pH 7.5 and 25.0 °C by 4×10^{-6} M (*R*)-1-acetamido-2-phenylethaneboronic acid (**5a**) (●) and 5×10^{-5} M *S* enantiomer (**5b**) (○). (□) Values obtained without inhibitor. The concentration of chymotrypsin, determined by active site titration of the stock solution,[23] was 2.8×10^{-6} M in each assay. The details of the assay are given in ref 1. Each rate of hydrolysis was constant for at least 5 min after initiation. The points give the averages of duplicate determinations, which agreed to within ±5%.

Scheme I



The recently reported homologation of ethylene glycol benzylboronate (**1c**) by (dichloromethyl)lithium to yield the 1-chloro-2-phenylethaneboronate (**2c**)[8] made this material easily available. The key to completion of the synthesis was the reaction of **2c** with lithiohexamethyldisilazane, which yielded 85% of the silylated amino boronic ester **3c**, a stable, distillable liquid that

(1) (a) Koehler, K. A.; Lienhard, G. E. *Biochemistry* **1971**, *10*, 2477–2483. (b) Rawn, J. D.; Lienhard, G. E. *Ibid.* **1974**, *13*, 3124–3130.

(2) Philipp, M.; Bender, M. L. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 478–480.

(3) Lindquist, R. N.; Terry, C. *Arch. Biochem. Biophys.* **1974**, *160*, 135–144.

(4) (a) Matthews, D. A.; Alden, R. A.; Birktoft, J. J.; Freer, S. T.; Kraut, J. *J. Biol. Chem.* **1975**, *250*, 7120–7126. (b) Robillard, G.; Shulman, R. G. *J. Mol. Biol.* **1974**, *86*, 541–558.

(5) Lindquist, R. N.; Nguyen, A. C. *J. Am. Chem. Soc.* **1977**, *99*, 6435–6437 reported the preparation of benzamidomethaneboronic acid and its inhibition of chymotrypsin. However, it now appears likely that the compound obtained by them was an isomer, $PhC(=NH)OCH_2B(OH)_2$ (probably with B–N chelation), from O-alkylation of the amide anion by the α-halo boronic ester, which has been observed by D.S.M. in analogous reactions. Their compound did not exhibit the expected pK of ~ 9 upon potentiometric titration.

(6) (a) Matteson, D. S.; Cheng, T. C. *J. Org. Chem.* **1968**, *33*, 3055–3060. (b) Matteson, D. S.; Jesthi, P. K. *J. Organomet. Chem.* **1976**, *114*, 1–7. (c) Matteson, D. S.; Majumdar, D. *Ibid.* **1979**, *170*, 259–264. (d) Matteson and Arne (Matteson, D. S.; Arne, K. *J. Am. Chem. Soc.* **1978**, *100*, 1325–1326) reported $PhCH_2CHIBO_2C_2(CH_3)_4$, which with ammonia yields 2-phenylethylamine. Matteson, D. S., unpublished.

(7) (a) Blow, D. M. *Enzymes, 3rd Ed.* **1971**, *3*, 185–212. (b) Hess, G. P. *Ibid.* **1971**, *3*, 213–248.

(8) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588–7590.

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