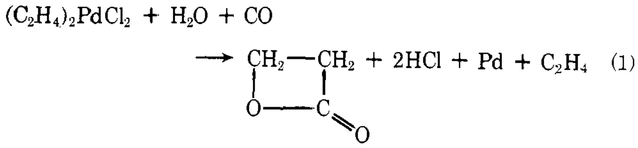
The reaction of bis(ethylene)palladium(II) chloride[12] in water–acetonitrile at −20 to −25 °C in the presence of carbon monoxide (3 atm) gave β-propiolactone **2** in a 72% yield[13] (eq 1). The direct catalytic conversion of ethylene to β-propiolactone could also be effected from a 2:1 ethylene–carbon monoxide charge (total 3 atm) using catalytic amounts of palladium, provided equivalent amounts of copper(II) chloride and sodium acetate (buffer) were present (eq 2). Although

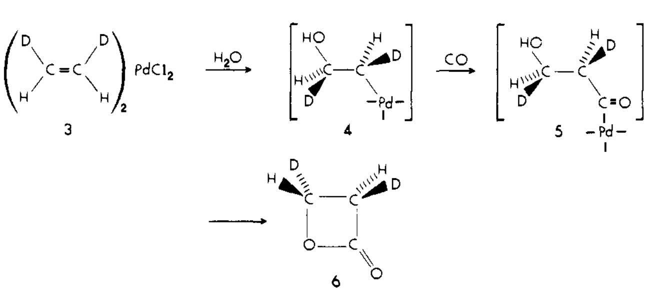


2

$$2CuCl_2 + CH_2{=}CH_2 + H_2O + CO \xrightarrow{PdCl_2} \mathbf{2} + Cu_2Cl_2 + 2HCl \quad (2)$$

carbon monoxide is rapidly oxidized to carbon dioxide under these conditions, the low reaction temperature apparently slows down this oxidation relative to the hydroxypalladation, and a 37% conversion of ethylene to β-propiolactone is realized. Since copper(I) can be reoxidized to copper(II) by air, this represents a unique catalytic synthesis of β-lactones from olefin, carbon monoxide, and water.

The stereochemistry of the hydroxypalladation step was determined by using the bis(ethylene)palladium(II) chloride complex **3** obtained from *cis*-1,2-dideuterioethylene.[14] Thus, the reaction in water–acetonitrile in the presence of carbon monoxide afforded *trans*-2,3-dideuterio-β-propiolactone (**6**): ^{1}H NMR ($CDCl_3$ δ 4.3 (d, J = 4 Hz), 3.8 (d, J = 4 Hz).[15] The insertion of carbon monoxide into a carbon–palladium σ bond (**4** → **5**) is known[16] to proceed with retention of configuration at carbon; therefore, the hydroxypalladation step (**3** → **4**) must proceed with trans stereochemistry.



These results for the stereochemistry of hydroxypalladation are consistent with those reported[17] for the reaction of *trans*-1,2-dideuterioethylene under the conditions of the Wacker process. The formation of *threo*-1,2-dideuterio-2-chloroethanol also requires trans hydroxypalladation. Thus, the attack of water on the ethylene–palladium complex is from outside the coordination sphere, and the addition of OH and palladium is trans.

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References and Notes

(1) P. M. Henry, *J. Am. Chem. Soc.*, **86**, 3246 (1964); **88**, 1595 (1966).
(2) J. K. Stille and R. A. Morgan, *J. Am. Chem. Soc.*, **88**, 5135 (1966).
(3) (a) W. A. Whitla, H. M. Powell, and L. M. Venanzi, *Chem. Commun.*, 310 (1966); (b) C. Panattoni, G. Bombieri, E. Forsellini, B. Crociani, and U. Belluco, *ibid.*, 187 (1969).
(4) P. M. Henry, *Adv. Chem. Ser.*, No. 70, 151 (1968); *Div. Pet. Chem. Prepr., Am. Chem. Soc.*, **14**, F17 (1969).
(5) R. F. Heck, *Fortschr. Chem. Forsch.*, **16**, 221 (1971).
(6) M. Green and R. F. Hancock, *J. Chem. Soc. A*, 2054 (1967).
(7) B. L. Shaw, *Chem. Commun.*, 464 (1968); *Div. Pet. Chem., Prepr., Am. Chem. Soc.*, **14**, F17 (1969).
(8) F. R. Hartley, *Nature (London)*, **223**, 615 (1969).
(9) J. K. Stille, D. E. James, and L. F. Hines, *J. Am. Chem. Soc.*, **95**, 5062 (1973).
(10) T. Majima and H. Kurosawa, *J. Chem. Soc., Chem. Commun.*, 610 (1977).
(11) J. K. Stille and D. E. James, *J. Am. Chem. Soc.*, **97**, 674 (1975); *J. Organomet. Chem.*, **108** 401 (1976).
(12) M. S. Kharasch, R. C. Seyler, and W. Frank, *J. Am. Chem. Soc.*, **60**, 382 (1938).
(13) The IR and NMR spectra were superimposable with those of an authentic sample: IR ($CHCl_3$) 1820 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.4–4.2 (m, OCH_2), 3.6–3.3 (m, CH_2CO).
(14) P. O. Nicholas and R. T. Carroll, *J. Org. Chem.*, **33**, 2345 (1968).
(15) (a) Calculated coupling J_{AB}(cis) = 7.2 Hz; J_{AB}(trans) = 3.7 Hz; M. Karplus, *J. Am. Chem. Soc.*, **85**, 2870 (1963). (b) Coupling constants for 2,3-diphenylpropiolactone are J_{AB}(cis) = 7.0 Hz, and J_{AB}(trans) = 4.5 Hz: O. L. Chapman and W. R. Adams, *J. Am. Chem. Soc.*, **90**, 2333 (1968).
(16) L. F. Hines and J. K. Stille, *J. Am. Chem. Soc.*, **94**, 485 (1972).
(17) J. E. Bäckvall, B. Åkermark, and S. O. Ljungren, *J. Chem. Soc., Chem. Commun.*, 264 (1977).

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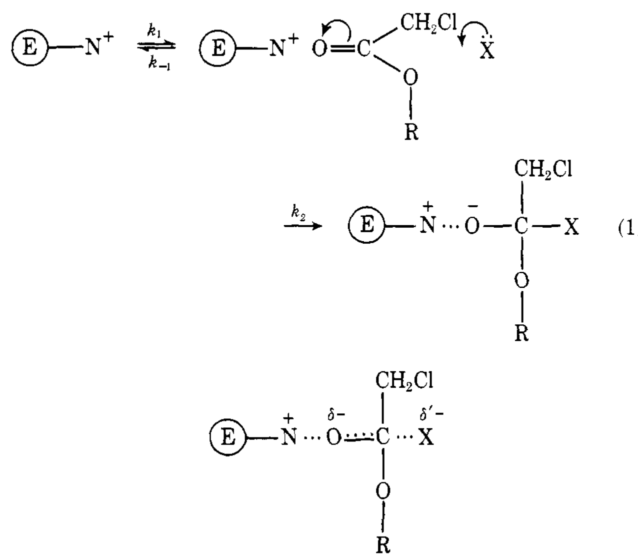
Specific Catalysis of Ester Hydrolysis by A New Water-Soluble Heterocyclophane

Sir:

Substrate specificity in enzymic reactions is understood to indicate that a specific substrate has a "best fit" to a unique array of binding site residues and that the spatial arrangement of atoms relevant to the catalysis is particularly favorable for the stabilization of the transition state.[1] Among the variety of ways in which such stabilization can arise, electrostatic stabilization is very important since most enzymic reactions involve various charged transition states. In an active site, cationic residues of protonated basic amino acids such as Lys or Arg can stabilize an anion generating in the transition state of an enzyme-catalyzed reaction.[2] For example, in ribonuclease action it is hypothesized that electrostatic stabilization of a dianionic pentacoordinate intermediate is provided by a cationic residue (probably protonated lysine).

In a previous communication we reported that certain water-soluble macrocyclic heterocyclophanes are excellent inclusion hosts toward organic substrates.[3a,b] In this communication we wish to report evidence supporting the formation of markedly stabilized transition state complexes of aromatic ester substrates with a new member of the group of water-soluble heterocyclophanes, II, leading to remarkably effective catalysis. The observed substrate specificity is shown herein



quasi-tetrahedral
transition state

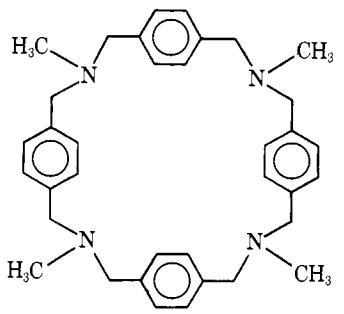
Table I. Catalytic Action of Heterocyclophane II on Hydrolyses of Aromatic Esters[a,b]

Substrate	pH	Buffer[c]	k_0 (10^3 s^{-1})[d]	k_{cat} (10^3 s^{-1})[e]	K_m, mM[f]	k_{cat}/k_0
β-NpClA (IVc)	8.10	p	0.77 ± 0.01	19.2 ± 2.4	0.54 ± 0.05	25
		b	0.51 ± 0.05	9.7 ± 0.8	0.90 ± 0.04	19
	6.96	p	0.10 ± 0.01	1.85 ± 0.08	2.23 ± 0.22	18
		b	0.12	2.12	1.89	17
p-NpClA (IVa)	8.10	p	5.54	14.6	0.51	2.6
		b	6.01	10.5	0.91	1.7
	6.96	p	2.55 ± 0.06	6.0	0.90	2.4
		b	0.89	1.6	2.4	1.8
α-NpClA (IVb)	8.10	p	0.82 ± 0.01	3.53 ± 0.26	0.14 ± 0.04	4.3
	6.96	p	0.16 ± 0.01	1.7 ± 0.1	0.60 ± 0.02	10.6

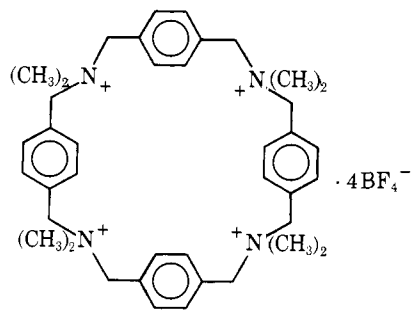
[a] Average of at least three independent kinetic runs, 20.2 ± 0.2 °C. [b] CTAB micellar catalysis, IVc: k_{cat}, 5.9×10^{-3} s^{-1}; K_m = 0.03 mM; k_{cat}/k_0, = 6.8. IVb: $k_{cat} = 4.5 \times 10^{-3}$ s^{-1}; K_m = 0.024 mM; k_{cat}/k_0 = 5.6. [c] Abbreviations p and b refer to phosphate (1/15 M) and borate (1/15 M) buffers, respectively. [d] Uncatalyzed rate constant. [e] See ref 6b. [f] Michaelis constant defined by $K_m = (k_{-1} + k_{cat})/k_1$.

to be the result of differences in the ease of stabilization of the transition state (eq 1).

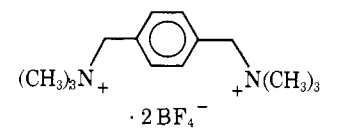
A new water-soluble heterophane (II) was prepared by the action of Et_3OBF_4[4] on *N,N',N'',N'''*-tetramethyl-2,11,20,29-tetraaza[3.3.3.3]paracyclophane (I).[5] II: mp 273–277 °C dec (CH_3CN–CH_3OH = 1:1); IR (KBr) 3020, 2960, 1480, 1300, 1130, and 1040 cm^{-1}; NMR (DMSO-d_6) δ 3.18 (24 H, CH_3–N), 3.96 (16 H, –CH_2–), 7.30 (16 H, aromatic). Anal. Calcd for $C_{40}H_{56}N_4B_4F_{16}\cdot 2H_2O$: C, 49.08; H, 6.15. Found: C, 49.22; H, 5.78.



I



II

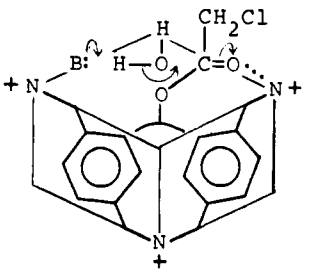


III

The kinetics of the catalytic action of the heterocyclophane II in hydrolyses of chloroacetates[6a] $ClCH_2CO_2R$ (IV) (R = *p*-nitrophenyl (IVa), α-naphthyl (IVb), β-naphthyl (IVc)) were analyzed by use of the Lineweaver-Burk equation[6b,c] (Table I). It is evident from Table I that the heterocyclophane catalyst (II) accelerates the hydrolysis rate of each substrate, while much smaller catalytic effects were observed for III, an open-chain analogue of the catalyst ($k_{cat}/K_m = 0.5$ s^{-1} M^{-1}, for IVc at pH 8.10). Therefore, the rate accelerations seen with II are due not just to simple electrostatic catalysis, but also to inclusion-electrostatic catalysis. The hypothesis that a productive inclusion complex was formed was also supported by the drastic fluorescence change of a substrate analogue,[3] 1,8-ANS, in a separate experiment, where the observed K_m was 2.6 mM.

Although the binding of *p*-nitrophenyl (K_m = 0.51 mM) and β-naphthyl (K_m = 0.54 mM) substrates by II was almost equally effective, the subsequent catalysis showed marked specificity and the rate constant enhancements observed, k_{cat}/k_0, were 25 for β-naphthyl and 3 for *p*-nitrophenyl in phosphate buffer at pH 8.10 and 20.2 °C. On the other hand, the CTAB micellar catalyst was found to be less effective and exhibited no substrate specificity, the ratio of k_{cat}/k_0 being 5.6 and 6.8 for α- and β-naphthyl substrates, respectively. It is concluded, therefore, that the spatial arrangement of the carbonyl group which is directed to the quaternary ammonium residue of the host (II) in the inclusion complex favors stabilization of the negatively charged quasi-tetrahedral transition state as proposed in eq 1. The α-naphthyl derivative (IVb) was the second best substrate.

When the buffer was changed from borate to phosphate, an appreciable increase in the k_{cat} value was generally observed (Table I), suggesting a possibility of general base catalysis by phosphate schematically shown in V. Also a drop in the pH from 8.10 to 6.96 resulted in an increase in the K_m values regardless of the substrate species, strongly suggesting competitive inhibition by the anion $H_2PO_4^-$ (K_I = ca. 10^{-2} M).[7]



V

The enzyme-like behavior of the ammonium residue of II, stabilization of the transition state, and provision of a base (or a nucleophile) offer the promise of further successes in the future in modelling hydrolase functions. The covalent introduction of effective functional groups on the heterocyclophane II may provide improved models of a variety of enzymes.

References and Notes

(1) (a) M. L. Bender, "Mechanism of Homogeneous Catalysis from Protons to Proteins", Wiley-Interscience, New York, N.Y., 1971, Chapter 19; (b) E. Zeffren and P. L. Hall, "The Study of Enzyme Mechanism", Wiley-Interscience, New York, N.Y., 1973, pp 128–129.
(2) D. Robertus, *Biochemistry*, **11**, 4293 (1972).
(3) (a) I. Tabushi, H. Sasaki, and Y. Kuroda, *J. Am. Chem. Soc.*, **98**, 5727 (1976); (b) I. Tabushi, Y. Kuroda, and Y. Kimura, *Tetrahedron Lett.*, 3327 (1976); (c)

previous work on ammonium substituted cyclophane catalyst: I. Tabushi and Y. Kuroda, *Catalyst*, **16**, 78 (1974).
(4) H. Meerwein, *Org. Syn.*, **46**, 120 (1966).
(5) See ref 3b and the references cited therein for our modified preparation of I.
(6) (a) Chloroacetates IV were chosen as the substrates in the present studies because the rates of spontaneous and catalyzed hydrolyses can be adequately compared under the condition. (b) The kinetics of the catalytic action of the heterocyclophane II in the hydrolyses of the ester substrates (IV) were analyzed, based on the following assumptions of hydrolysis mechanisms,

$$C + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CS \xrightarrow{k_{cat}} C + P \quad (2)$$

$$S \xrightarrow{k_0} P \quad (3)$$

where the eq 2 refers to the Michaelis–Menten type hydrolysis of the substrate (S) to the product (P) catalyzed by C, and eq 3 refers to the uncatalyzed (spontaneous) hydrolysis. (c) R. L. VanEtten, J. F. Sebastian, G. A. Clowes, and M. L. Bender, *J. Am. Chem. Soc.*, **89**, 3242 (1967).
(7) K_I constant was determined from pH dependence and phosphate concentration dependence of the apparent K_m value.

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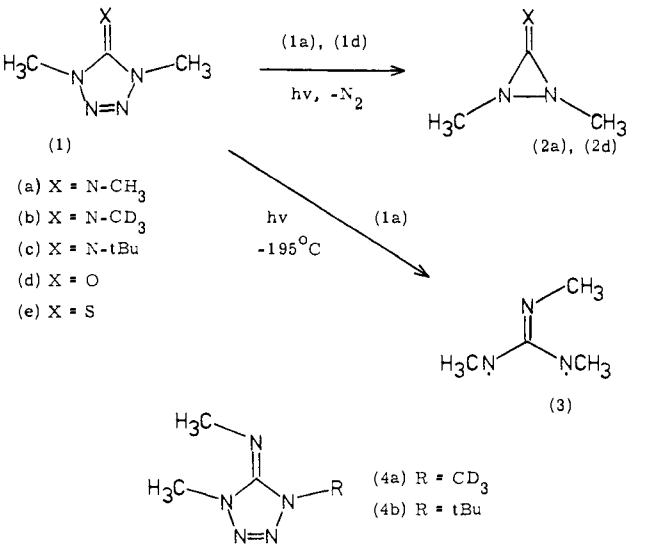
Tris(imino)methanes. An Electron Spin Resonance Identification of Nitrogen Analogues of Trimethylenemethane[1]

Sir:

Increasing numbers of both experimental[2] and theoretical[3] investigations center around trimethylenemethane. The triplet character of its ground state survives even rather severe perturbations by substituents.[2b] In contrast, virtually nothing is known experimentally about the influence of heteroatoms in the trimethylenemethane skeleton. Thus, attempts to detect oxyallyl, for which a triplet ground state has been predicted,[4] by ESR spectroscopy during low temperature photolysis of 1,3-cyclobutanediones have met with failure.[5] We report here the ESR spectra observed when the iminotetrazoline **1a** is irradiated at low temperatures. We assign the spectra to a nitrogen analogue of trimethylenemethane, i.e., the tris(imino)-methane **3**.

In the search for heteronuclear analogues of trimethylenemethane the tetrazolines **1** were designed as precursors,

Scheme I



since they readily lose nitrogen on photolysis, **1a** and **1d** thereby affording the diaziridine derivatives **2a** and **2d**, respectively, Scheme I.[6] When **1a**, at −195 °C in a butyronitrile matrix[7] degassed at 10^{-5} Torr, was irradiated inside the cavity of an ESR spectrometer,[8] a centrosymmetrical four-line spectrum, centered at 3286 ± 10 G (Figure 1), was observed after only 30 s. The spectrum persisted after the irradiation had been terminated and lost about half of its intensity on warming to −150 °C. Under the same conditions, very similar, but less intense, ESR spectra appeared in methylcyclohexane, 2,2-dimethylbutane/*n*-pentane (73:27), hexafluorobenzene, and perfluoromethylcyclohexane.

The four-line spectrum of Figure 1 can be assigned to the "parallel" (z) and "perpendicular" (xy) signals of randomly oriented triplet molecules having an axis of threefold or higher symmetry, i.e., $E/hc = \sim 0\ cm^{-1}$.[9] From $|D'| = 356 \pm 10$ G the zero-field splitting parameter is calculated as $|D/hc| = 0.033 \pm 0.001\ cm^{-1}$. The half-field ($\Delta m = 2$) transition which is a criterion of triplets was observed at 1644 ± 10 G. It exhibited a hyperfine structure of at least nine equidistant lines separated by 11.7 ± 0.5 G. The absorption near the center of the four-line high-field spectrum was produced by monoradicals generated during the irradiation.

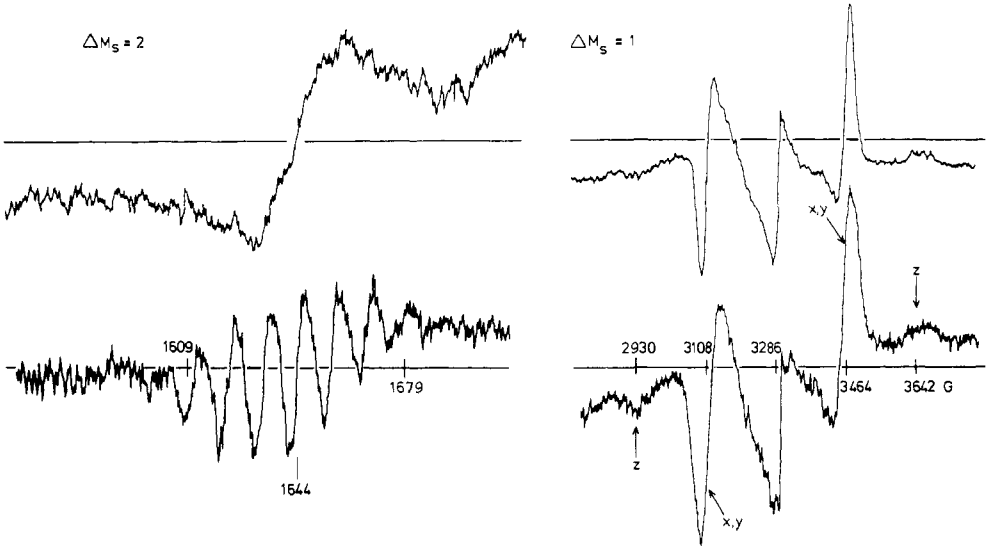


Figure 1. First derivative of the ESR absorption obtained during irradiation of the iminotetrazoline **1a** (lower trace) and the perdeuterated iminotetrazoline [D_9]-**1a**, respectively (upper trace), both in a butyronitrile matrix at −195 °C. Klystron frequency 9285 MHz, calculated from the resonance field of Fremy's salt.

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