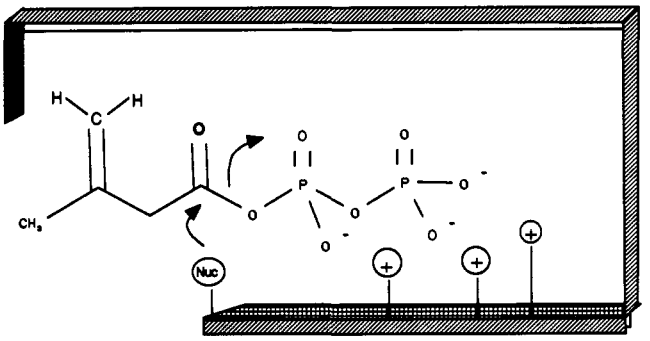
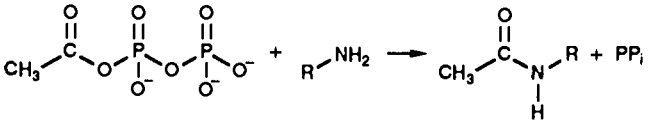


Figure 1. Schematic model for the binding of an acyl pyrophosphate as a substrate analogue.

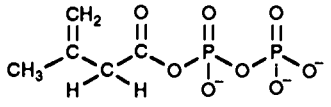
Amines and thiols are acylated by acyl pyrophosphates in organic solvents and in aqueous solution.



Reaction of acyl pyrophosphates (50 mM) with carboxyl-terminal-protected amino acid esters (250 mM) in phosphate buffer (200 mM) at pH 7.0 produces N-acylated amino acid esters (63% yield after workup and purification of reaction of valine ethyl ester and phenylacetyl pyrophosphate). Lysine ethyl ester is preferentially acylated at the ϵ-amino group under these conditions.

Acyl pyrophosphates hydrolyze in wet organic solvents or in water to form inorganic pyrophosphate and the corresponding acids. Inorganic pyrophosphate does not incorporate ^{18}O from the hydrolysis of 0.25 M isopentenoyl diphosphate in 0.75 M pH 7.0 HEPES buffer at 37 °C containing 25% $H_2{}^{18}O$ (^{31}P NMR ^{18}O analysis[16-18]). Thus, the hydrolysis occurs by acylation of water with pyrophosphate as the intact leaving group. Between pH 3.0 and 7.0, the hydrolysis of phenylacetyl pyrophosphate follows first-order kinetics (monitored by ^{31}P NMR), $k_{obsd} = 2.7 \pm 0.5 \times 10^{-5}$ s^{-1}, pH 6.2, 37 °C, 0.5 M potassium maleate buffer ($t_{1/2}$ = 7.2 h).

As a test of the ability of an acyl pyrophosphate to inactivate an enzyme that utilizes a related substrate, farnesyl synthetase from yeast (EC 2.5.1.1) was incubated with 0.25 mM isopentenoyl pyrophosphate.



isopentenoyl pyrophosphate

This enzyme is likely to contain nucleophilic groups in its substrate binding site.[15] Activity was monitored by using an acid lability assay with geranyl pyrophosphate and [1-^{14}C]isopentenyl pyrophosphate.[19] The enzyme lost all activity during a 2-min preincubation at 37 °C (the kinetics of the process were not determined due to the complexity of the assay). Activity could not be recovered by addition of excess substrate. Preincubation with large amounts of substrate protects the enzyme from inactivation. A schematic model for the inactivation reaction is shown in Figure 1.

Addition of the hydrolysis products of isopentenoyl pyrophosphate, isopentenoic acid, and inorganic pyrophosphate under the same conditions gave no inactivation, although competitive inhibition (due to the pyrophosphate[19]) was observed. The specificity of inhibition is further demonstrated by our observation that acetyl pyrophosphate does not inactivate the enzyme (concentrations up to 5 mM).

These results indicate that acyl pyrophosphates can be conveniently prepared and possess reaction patterns that permit them to be used as enzyme inactivators. Detailed evaluations of these materials are necessary to determine their potential for specific applications.[20]

Acknowledgment. We thank Professor C. D. Poulter for kindly providing the enzymes used in this study and Dr. Alex Young for mass spectra. Our work is supported by the Natural Sciences and Engineering Research Council of Canada and the PENCE project of the Medical Research Council.

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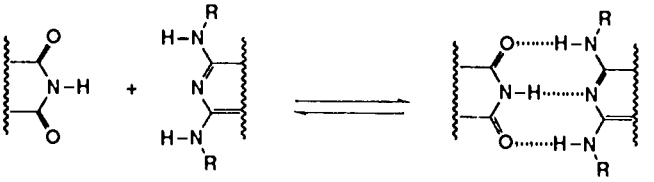
New Molecular Complements to Imides. Complexation of Thymine Derivatives

Tae Kyo Park, Joseph Schroeder, and Julius Rebek, Jr.*

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received February 15, 1991

Molecular recognition of imides (Scheme I) is of interest in

Scheme I



chromatographic resolutions,[1] thymine receptors,[2] liquid crystals,[3] and molecular tapes and sheets,[4] as well as theoretical[5] and experimental[6] evaluations of secondary effects in hydrogen bonding. We describe here new systems for base-pairing to thymines which offer unusual affinities and promise for the catalysis of reactions involving thymines.

The receptors are prepared from the readily available xanthene-1,8-dicarboxylic acid **1**, and they resemble those derived from Kemp's triacid[7] but have more spacious interiors.[8] Esterification with phenol (DCC, CH_2Cl_2, 0 °C) or naphthylethanol gave the mono esters[9] **2** (Scheme II). Activation ($SOCl_2$) and then coupling with suitable amines gave the amide esters **3a-c** (not shown), which were heated with biguanide (2 equiv) in ethanol to give the receptors **4a-c** (30-40% overall from **1**).[9] The ester **4d** was prepared from **2a** by sequential treatment with $SOCl_2$ and

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(9) All new compounds were characterized by high-resolution NMR and MS and IR spectra. Mp (°C) (**4a**) 284-285, (**4b**) >310, (**4c**) 168-169, (**4d**) 238-2390, (**4e**) 283-285, (**9**) 163-164, (**10**) 222-223.

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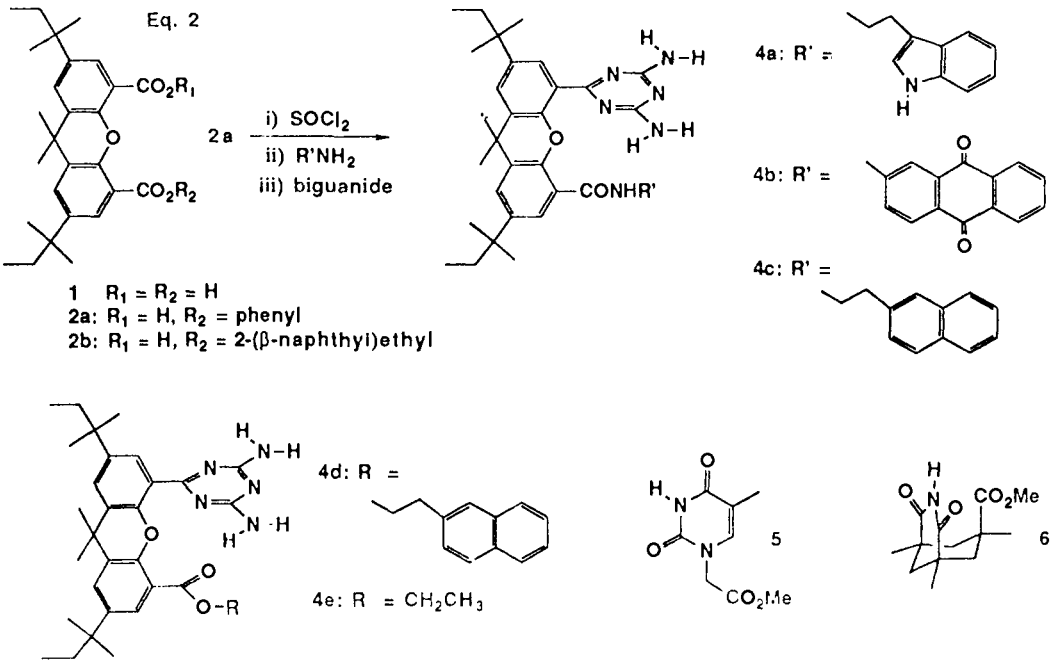
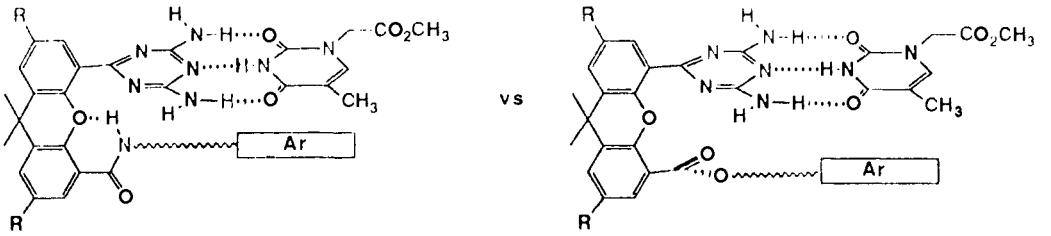
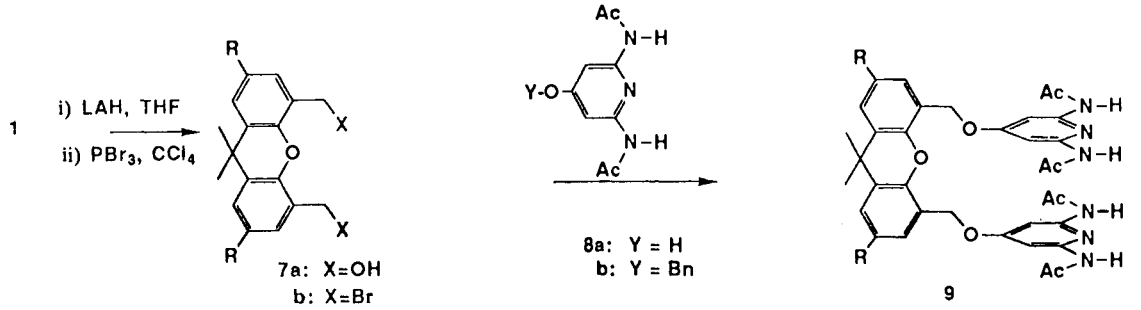
Scheme II



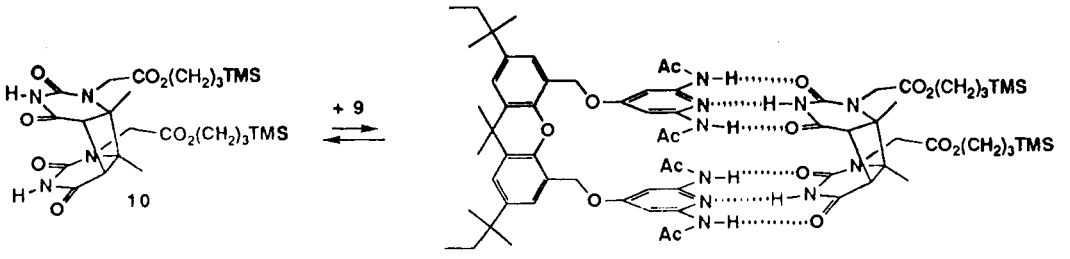
Scheme III



Scheme IV



Scheme V



biguanide, while the ethyl ester triazine **4e** was prepared by treatment of **1** with $SOCl_2$ and then biguanide in EtOH. The imides used were the thymine-derived methyl ester **5** and the saturated imide **6** obtained from Kemp's triacid.[10]

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The affinities were determined by titrations in $CDCl_3$ using NMR; the results are given in Table I. Stacking can contribute up to an order of magnitude in binding affinities at room temperature. The amides are especially well suited for this as the intramolecular hydrogen bonds bring the side chains (bearing the aryl surfaces) close to the site of base-pairing (Scheme III).

Ditopic systems are also available. Reduction of **1** (LAH/THF) gave the diol **7a**, from which the dibromide **7b** was obtained by

Table I. Association Constants

receptor	guest	K_a	receptor	guest	K_a
4a	5	2500	**4d**	5	1100
4b	5	6700	**4e**	5	670
4c	5	2000	**4e**	6	340

treatment with PBr_3 in CCl_4. Condensation with 2,6-bis(acylamino)-4-pyridone **8a**[2,11] (K_2CO_3, DMF) gave **9** (Scheme IV). Binding to **5** gave a 2:1 complex,[12] while the thymine photodimer **10**[13] gave a 1:1 complex (K_a = 4800 M^{-1}). Model studies for the photolyase system[14] and template synthesis of thymine derivatives are currently underway.

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this research.

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An η^4-Benzene Species Mediates Acetylene Cyclotrimerization

Claudio Bianchini,*[†] Kenneth G. Caulton,*[‡]
Catherine Chardon,[§] Odile Eisenstein,*[§] Kirsten Folting,[‡]
Todd J. Johnson,[‡] Andrea Meli,[†] Maurizio Peruzzini,[†]
David J. Rauscher,[‡] William E. Streib,[‡] and Francesco Vizza[†]

Department of Chemistry and Molecular Structure Center
Indiana University, Bloomington, Indiana 47405
Istituto per la Studio della Stereochimica ed
Energetica dei Composti di Coordinazione
CNR Via Nardi 39, 50132 Florence, Italy
Laboratoire de Chimie Théorique, Bâtiment 490
Université de Paris-Sud, 91405 Orsay, France

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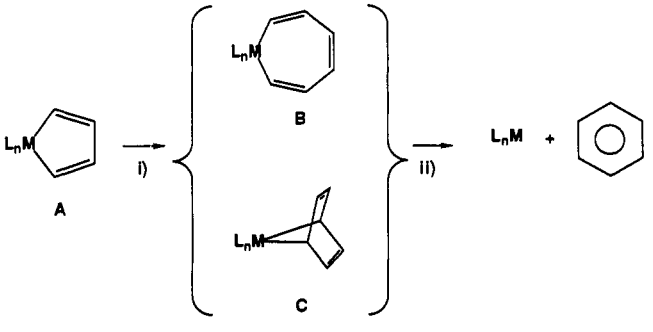
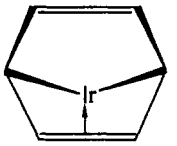
The mechanism of alkyne cyclotrimerization is widely discussed,[1-9] but most[10] experiments do not strongly distinguish between the generally considered two paths (via B and C) from metallacyclopentadiene (A) to free arene. We now report results



wherein systematic variation of M from Rh to Ir, with L_n = $MeC(CH_2PPh_2)_3$ (triphos), appears to eliminate intermediate B, yet C is a still an imperfect representation of the mechanism.

We reported earlier[11] that a species isolated and spectroscopically characterized as the complex (triphos)RhCl(η^2-C_4H_4) (Figure 1a)[12] is catalytically active for acetylene cyclotrimerization (6 turnovers/h at 1 atm of C_2H_2 and 25 °C). No additional intermediates were detected and, in particular, no experimental evidence was provided for distinguishing between paths B and C. However, when HCCH is passed through a THF solution of (triphos)IrCl(C_2H_4) at 25 °C in the presence of a chloride scavenger[13] ($TlPF_6$), solution ^1H and $^{31}P\{^1H\}$ NMR data show the production of (triphos)Ir(C_6H_6)$^+$, which can be isolated as its BPh_4^- salt. The structure[14] of this cation (Figure 1b) shows it to be an 18-electron species with η^4 coordination of the C_6H_6 ligand. The dihedral angle within the bent benzene is 134.8°. The nonbonded carbons, C50 and C51, have Ir/C distances longer than 2.97 Å, and they are connected by a localized double bond of length 1.36 (3) Å. The observed C-C bond lengths share with all previous η^4-benzene structures[15] the C/C bond length pattern shown in D. This is symptomatic of a large degree of backbonding,[16,17] which is appropriate for a 5d metal ligated by three electron-donating ligands (triphos).[18]



D

The variable-temperature $^{31}P\{^1H\}$ NMR spectra in $CDCl_3$ show (triphos)Ir(η^4-C_6H_6)$^+$ to be fluxional. The rapid-exchange spectrum (>313 K) shows a single line, which transforms at low temperature to an AM_2 pattern. Simulation (DNMR3) yields (253-313 K) $\Delta H^\ddagger$ = 10.9 ± 0.3 kcal/mol and $\Delta S^\ddagger$ = -25 ± 1 cal K^{-1} mol^{-1}. Variable-temperature ^1H NMR spectra in $CDCl_3$ show one broad resonance (5.18 ppm) for the C_6H_6 ring at 323

† Istituto per la Studio della Stereochimica ed Energetica dei Composti di Coordinazione.
‡ Indiana University.
§ Université de Paris-Sud.

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(12) Crystal data for $C_{45}H_{43}ClP_3Rh\cdot CH_2Cl_2\cdot 0.5C_7H_{16}$ (-155 °C): a = 10.133 (1) Å, b = 23.620 (4) Å, c = 18.682 (3) Å, β = 93.62 (0)° with Z = 4 in space group $P2_1/c$. $R(F)$ = 0.063 and $R_w(F)$ = 0.061 for 2038 reflections with $F > 3\sigma(F)$ and anisotropic thermal parameters on Rh, Cl, and P.
(13) $TlPF_6$ is not required for cyclotrimerization by the more labile rhodium analogue.
(14) Crystal data for $C_{71}H_{65}BrIrP_3\cdot C_5H_{10}O$ (-155 °C): a = 16.471 (6) Å, b = 17.126 (6) Å, c = 12.030 (4) Å, α = 101.22 (2)°, β = 93.61 (2)°, γ = 75.46 (1)°, with Z = 2 in space group $P\bar{1}$. $R(F)$ = 0.0845 and $R_w(F)$ = 0.0819 for 7211 absorption-corrected reflections with $F > 3\sigma(F)$ and anisotropic thermal parameters.
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(18) This pattern of C/C bond lengths is *not* seen in (triphos)M(butadiene)$^+$ species of group VIII metals and thus is specific to the η^4-benzene ligand in an electron-rich environment.

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