geometry of their anchoring sites, dynamics, and reactivity in zeolite Y.

Conclusions

The key points to emerge from this study are summarized in point form below: (i) $M(CO)_6$-$M'_{56}Y$ samples have the hexacarbonylmetal(0) guest anchored to two α-cage extraframework cations (or Brønsted protons) via the oxygen end of two trans bonded carbonyl ligands, with a saturation loading of 2M-$(CO)_6/\alpha$-cage. (ii) $M(CO)_6$-$M'_{56}Y$ have the hexacarbonylmetal(0) guest confined to the internal surface of the zeolite with an essentially homogeneous distribution running throughout the zeolite crystals. (iii) A Mo and Rb EXAFS structure analysis of $8\{Mo(CO)_6\}$-$Rb_{56}Y$ shows that the structural integrity of the $Mo(CO)_6$ guest is maintained in the α-cage of zeolite Y with some evidence for anchoring via extraframework Rb^+ cations. (iv) Rapid ^{13}CO intrazeolite thermal and photoinduced ligand exchange occurs for $M(^{12}CO)_6$-$M'_{56}Y$ to yield $M(^{12}CO)_m(^{13}CO)_{6-m}$-$M'_{56}Y$ the extent of which depends on the ^{13}CO loading. (v) $M(CO)_3$-$M'_{56}Y$ can be cleanly generated via the mild vacuum thermal decarbonylation of $M(CO)_6$-$M'_{56}Y$, the tricarbonyl stoichiometry of which is unequivocally established from its observed and calculated diagnostic $M(^{12}CO)_n(^{13}CO)_{3-n}$-$M'_{56}Y$ vibrational isotope patterns. (vi) Intrazeolite reactions of $M(CO)_3$-$M'_{56}Y$ with large and small arenes, trienes and phosphines, cleanly yield the respective intrazeolite six-coordinate complexes (shown to be identical with the products of direct vapor phase impregnation of the latter complexes) thereby supporting the tricarbonylmetal(0) assignment as well as pinpointing the location of the $M(CO)_3$-$M'_{56}Y$ tricarbonylmetal(0) moiety on the internal surface of the zeolite. (vii) Cation effects in the mid/far-IR and optical reflectance spectra of $M(CO)_3$-$M'_{56}Y$ indicate that the supercage confined $M(CO)_3$ moiety is anchored to an oxygen framework six-ring site (B) rather than to an extraframework cation site via the metal (A) or oxygen end of the carbonyls (C). (viii) A Mo and Rb EXAFS structure determination for $8\{Mo(CO)_3\}$-$Rb_{56}Y$ confirms the oxygen framework anchoring site model B. (ix) The occurrence and origin of an observed C_{3v} regular trigonal-pyramidal to C_s distorted trigonal-pyramidal structural change amongst the 15 $M(CO)_3$-$M'_{56}Y$ samples can be rationalized with a second-order Jahn-Teller (SOJT) effect. (x) EXAFS data for the controlled thermal decomposition of $8\{Mo(CO)_3\}$-$Rb_{56}Y$ demonstrates the formation of molybdenum atoms statistically distributed in the zeolite lattice.

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Supplementary Material Available: Experimental details and tables of observed νCO stretching frequencies and bond lengths and kinetic diameters and figures as described in the text (28 pages). Ordering information is given on any current masthead page.

Transition-State Stabilization and Molecular Recognition: Acceleration of Phosphoryl-Transfer Reactions by an Artificial Receptor

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Abstract: An artificial receptor that is complementary to the proposed trigonal-bipyramidal intermediate for phosphoryl-transfer reactions has been designed. Kinetic measurements with ^{31}P NMR methods show that the receptor causes up to a 10-fold acceleration in the aminolysis of phosphorodiamidic chloride derivatives, proceeding via an associative mechanism.

Introduction

Enzyme catalysis depends upon the preferential complexation and stabilization of transition states over their corresponding starting materials and products.[1] An important goal in the development of artificial enzymes must, therefore, involve the construction of synthetic receptors that are complementary to the electrostatic and spatial features of transition-state structures.[2] Such receptors would be expected to show substantial rate accelerations of those reactions with complementary transition states.[3] The success of this approach depends on the precise

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(1) Pauling, L. *Chem. Eng. News* **1946**, *24*, 1375. For more recent discussions, see: Schowen, R. L. *Transition States in Biochemical Processes*; Gandour, R. D., Schowen, R. L., Eds.; Plenum Press: New York, 1978; pp 77-114. Kraut, J. *Science (Washington, D.C.)* **1988**, *242*, 533-540.

(2) For an illuminating discussion of these goals, in general, and phosphoryl transfer reactions, in particular, see: Boger, J.; Knowles, J. R. *Ciba. Found. Symp. Mol. Interact. Act. Proteins* **1978**, *60*, 225-242.

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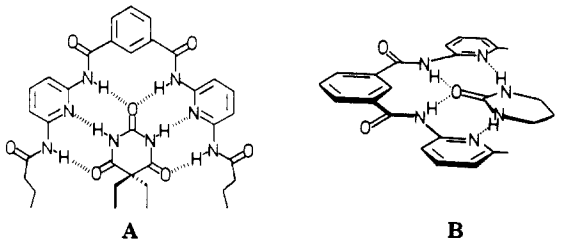
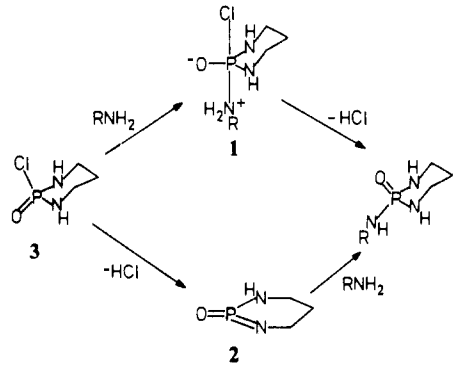


A **B**

Figure 1. Hydrogen-bonding arrangement in the barbiturate–**4** complex.

Scheme I



positioning of binding groups (e.g., hydrogen bonding,[4] electrostatic centers,[2,5] or metal centers[6]) in a receptor to bind more strongly to the transition state than the substrate. This will be most easily achieved for those reactions in which there are substantial changes in both geometry and electronic distribution on going from ground state to transition state. In this paper, we report the acceleration of a phosphoryl-transfer reaction with an artificial, hydrogen-bonding receptor that was designed to be complementary to the postulated transition state.[7]

Results and Discussion

Phosphoryl-transfer reactions are among the most studied in organic chemistry.[8] We have chosen the aminolysis of phosphorodiamidic derivatives as a target reaction since its mechanism has been intensely studied[9,10] and provides a model for biochemically important phosphoryl-transfer reactions. Furthermore, the NH groups of the substrate offer potential sites to which binding interactions can be directed. Two general mechanisms have been suggested for these reactions. These involve (Scheme I) either in-line displacement[9] via a trigonal-bipyramidal intermediate **1** or elimination–addition[10] through a metaphosphorodiimidate species **2**. In both cases, the reaction involves three substituents on phosphorus (O, NH, NH) moving from a pyramidal to a planar-trigonal arrangement in the reactive intermediate (**1** or **2**). Thus, selective stabilization of **1** and **2**, or the transition states for their formation, should be achieved by a synthetic receptor with complementary binding groups in a corresponding trigonal position.

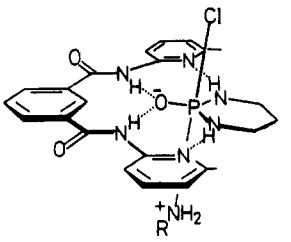


Figure 2. Proposed hydrogen-bonding stabilization of trigonal-bipyramidal intermediate.

Table I. Pseudo-First-Order Rate Constants for the Aminolysis of **3** in $CDCl_3$[13]

receptor	$k_{obs} \times 10^4$ (s^{-1})	receptor	$k_{obs} \times 10^4$ (s^{-1})
none	1.55 (±0.6)	**4** (0.007 M)	6.73 (±0.7)
4 (0.03 M)	15.4 (±0.8)	**4** (0.0158 M)	10.7 (±0.7)
5 (0.014 M)	1.50 (±0.6)	**4** (0.0245 M)	13.4 (±0.7)
4 (0.007 M) + barbital (**6**) (0.015 M)	1.46 (±0.2)	**7** (0.007 M)	8.14 (±0.7)
		8 (0.007 M)	4.66 (±0.1)

We have recently shown[11] that synthetic receptors formed from the reaction of 2,6-diaminopyridine and isophthaloyl dichloride (e.g., **4**) form strong complexes (Figure 1A) with urea substrates (barbiturates, propyleneurea, etc.). An X-ray structure of a complex with barbital shows a trigonal binding environment formed by four hydrogen bonds from the phthalimide NH and pyridine N sites to the carbonyl lone pairs and urea NH's,[12] as in Figure 1B. This planar arrangement of binding groups is well-suited to bind to the oxyanion and two NH substituents occupying the trigonal plane of reactive intermediate **1**, as shown in Figure 2. In both the starting material and products of the reaction (Scheme I), the binding groups are in a pyramidal orientation and, thus, are less disposed to interact strongly with the planar binding region on the receptor. This selective complexation and stabilization of the trigonal-bipyramidal intermediate should result in an acceleration of the phosphoryl-transfer reaction.

The substrate phosphorodiamidic chloride **3** was formed from phosphoryl trichloride and diaminopropane. The aminolysis reactions were carried out in $CDCl_3$ at 25 °C under pseudo-first-order conditions, with the initial concentration of *n*-butylamine at 0.11 M and that of **3** at 7×10^{-3} M. The kinetics were followed by monitoring the change in the integral of the ^{31}P NMR resonances of **3** (at ~17 ppm) and the product phosphoryltriamide (at ~13 ppm). A representative example of the ^{31}P kinetics experiment is shown in Figure 3. The reactions were continued through 3–4 half lives, and rate constants were obtained by nonlinear regression analysis of the integration ratio versus time. The pseudo-first-order rate constants from different concentrations of receptor **4** were based on the average of two or three runs and are collected in Table I.

These results show that receptor **4** causes a 10-fold acceleration in the rate of reaction between **3** and *n*-butylamine. The reaction follows Michaelis–Menten kinetics with an increase in rate as the concentration of **4** increases.[13] That this rate enhancement is due to the special hydrogen-bonding environment provided by **4** was shown by the absence of an effect with the half-receptor 2,6-dibutyramidopyridine (**5**). Furthermore, barbital (**6**) binds strongly to **4**,[11] with an association constant (K_a) of 8.4×10^4 M^{-1} in $CDCl_3$.[14] This compares to 2.2×10^2 M^{-1} for the complex between phosphoryltriamide (**3**) and **4**.[16] Thus, barbital acts as

(3) A series of nonenzyme, protein-based receptors with complementarity to transition states has been developed using antibody technology and shown to be effective catalysts. Tramontrano, A.; Janda, K.; Nappa, A. D.; Benkovic, S. J.; Lerner, R. A. *Cold Spring Harbor Symp. Quant. Biol.* **1987**, *52*, 97. Schultz, P. *Acc. Chem. Res.* **1989**, *22*, 287–294.

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(5) Springs, B.; Haake, P. *Tetrahedron Lett.* **1977**, 3223–3226.

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(12) Chang, S. K.; Van Engen, D.; Hamilton, A. D., to be submitted for publication.

(13) Kinetic studies at concentrations of **4** greater than 0.03 M were not possible due to its limited solubility in $CDCl_3$.

(14) Measured by nonlinear regression analysis[15] of ^1H NMR titration data in $CDCl_3$.

(15) Cowart, M. S.; Sucholeiki, I.; Bukownik, R. R.; Wilcox, C. S. *J. Am. Chem. Soc.* **1988**, *110*, 6204–6210.

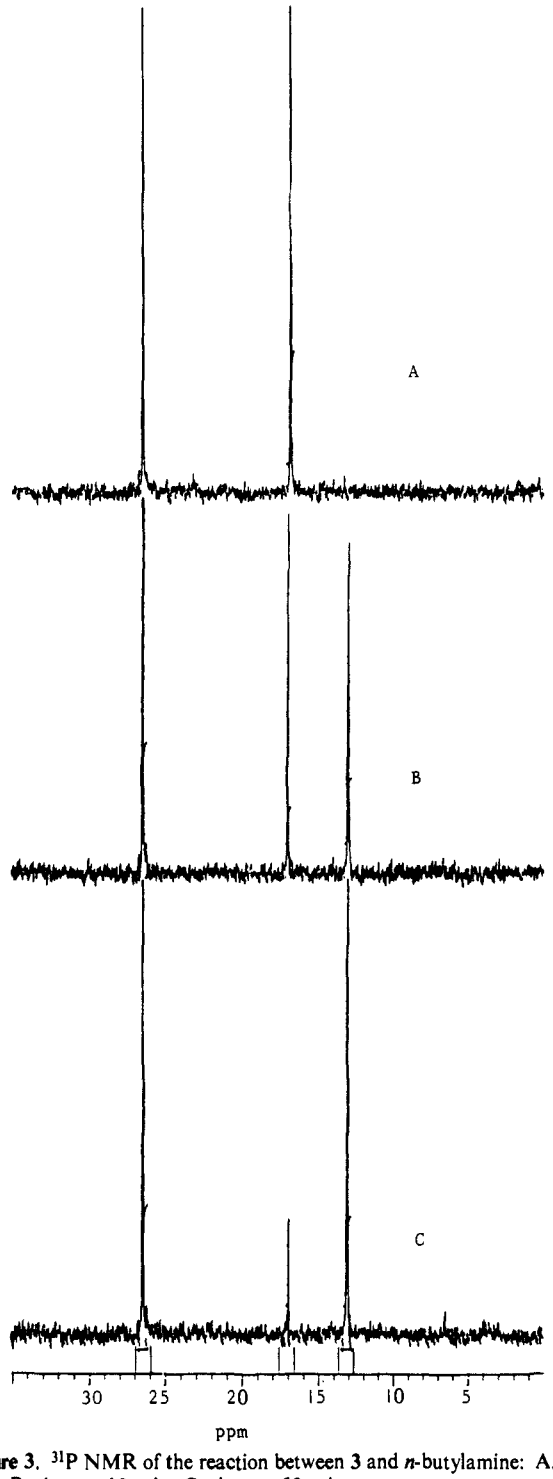


Figure 3. ^{31}P NMR of the reaction between **3** and *n*-butylamine: A, time = 0; B, time = 12 min; C, time = 30 min.

an inhibitor of the reaction, binding strongly to **4** and preventing access of **3** into the cavity.

These preliminary observations of binding-induced rate enhancement prompt several key questions.

First, which mechanism, associative[9] or dissociative,[10,17] is being influenced by **4**? The mechanistic features of the uncatalyzed control reaction appear to be complex. The simple reaction between **3** and *n*-butylamine shows a first-order dependence in amine. This rules out a possible preassociation dissociative mechanism, which has been shown by Freeman and Harger[17] to be second-order in amine for related phosphonamidic chlorides. A key distinction between the two mechanisms in Scheme I should be their discrimination between different nucleophiles. The bimolecular associative route should be strongly dependent on the nucleophilicity of the amine, whereas the dissociative pathway should be little affected. Nucleophile discrimination was assessed by carrying out competitive reactions between *n*-butylamine and the bulkier *tert*-butylamine. The product ratio was 2.6 (*n*-$BuNH_2$:*t*-$BuNH_2$) for the uncatalyzed control reaction and 17.8 for the accelerated one, measured for a concentration of **4** twice that of **3**. The relatively low selectivity of the uncatalyzed reaction toward competing nucleophiles indicates that, under these experimental conditions, both associative[9] and dissociative[10] mechanisms (Scheme I) are competing.[18] However, the accelerated reaction is much more selective than the uncatalyzed one toward different nucleophiles, and this strongly suggests that the bimolecular associative mechanism, via intermediate **1**, is favored by the binding properties of the catalyst.

Second, what is the origin of the catalytic effect of receptor **4**? Substrate binding into the receptor causes a downfield shift in the ^{31}P resonance, the size of the shift being proportional to the association constant. This implies that hydrogen bonding to the isophthalamide H's leads to a polarization of the P=O group.[19] Also, k_{obs} (measured for different concentrations of **4** as well as structural analogues **7** and **8**) increases with the size of the downfield shift. This suggests that the accelerating effect of **4** may be due to a combination of stronger binding to the oxyanionic transition state as well as hydrogen-bonded activation of the P=O group toward nucleophilic attack.

In summary, we have shown, using readily available synthetic receptors, that provision of a simple H-bonding environment that bears closer complementary to the transition state than the ground state of phosphoryl-transfer reactions can lead to modest rate accelerations. We are presently both increasing the rigidity of and introducing a metal center into the receptor to maximize substrate polarization and transition-state stabilization.

Experimental Section

General Methods and Materials. Melting points are uncorrected. ^1H NMR spectra were recorded with a Bruker AF300 spectrometer operating at 300.13 MHz, and chemical shifts are reported relative to internal Me_4Si. ^{31}P NMR spectra were recorded at 202 MHz with a Bruker AM 500 spectrometer, and the chemical shifts are given vs a solution of H_3PO_4 (80%) in D_2O as external standard. *n*-Butylamine and *tert*-butylamine were Aldrich products and were distilled before use.

Kinetics. Kinetic studies were performed by following the time evolution of the proton-decoupled ^{31}P NMR spectra (100–200 acquisitions) of a mixture of substrate, receptor, *n*-butylamine, and triphenylphosphine oxide as internal standard. In a typical experiment, 0.5 mL of a $CDCl_3$ solution of **3** (7×10^{-3} M), catalyst (7×10^{-3}–3×10^{-2} M), and triphenylphosphine oxide (7×10^{-3} M) was poured into a 5-mm NMR tube. The tube was allowed to thermally equilibrate in the ^1H NMR probe (thermostated at 298 K) for 30 min, and the reaction was started by addition of 50 μL of a $CDCl_3$ solution of *n*-butylamine (1.21 M). The kinetics were followed through 3–4 half-lives by monitoring the variation of the integral of the ^{31}P resonances of **3** (~17 ppm) and product triamide (~13 ppm) against that of triphenylphosphine oxide (~26 ppm). The rate constants were obtained by nonlinear regression analysis of the integral ratio versus time (with the software package ENZFITTER by Leatherbarrow, R. J., Elsevier: Amsterdam, 1987). The reported rate constants are the average of duplicate or triplicate runs.

Competitive Reactions. An equimolar $CDCl_3$ solution of *n*-butylamine and *tert*-butylamine (50 μL, 1.21 M in each amine) was added to a $CDCl_3$ solution of **3** (0.5 mL, 7×10^{-3} M) or **3** and **4** (0.5 mL, [**3**] = 7×10^{-3} M, [**4**] = 1.5×10^{-2} M). When the reaction was complete, the proton-decoupled ^{31}P NMR spectrum of the reaction mixture was recorded and the ratio of products was deduced directly from the relative areas of the peaks; i.e., it was assumed that because of their similarity the two products do not differ significantly in their ^{31}P NMR response.

(16) The increased polarity of the reaction mixtures (i.e., 0.11 M amine in $CDCl_3$) was expected to lead to a drop in K_a for **3**–**4**. The corrected K_a value was estimated to be 50 M^{-1}.

(17) Freeman, S.; Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 2* **1988**, 81–90.

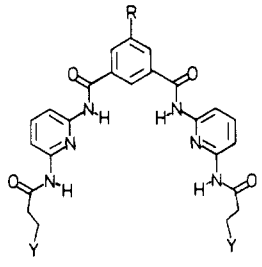
(18) A very similar competition between the two mechanisms has been proposed for a related system. See: Freeman, S.; Harger, M. J. P. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1399–1406.

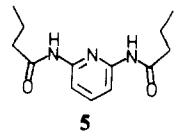
(19) Tebby, J. C. *Phosphorus 31 NMR Spectroscopy in Stereochemical Analysis*; Verkade, J. G., Quin, L. D., Eds.; VCH Publishers: Deerfield Beach, FL, 1987; p 27.

The peaks were assigned with the aid of pure samples of both possible triamide products.[20]

2-Chloro-2-oxo-1,3,2λ⁵-diazaphosphorinane (3). To a solution of freshly distilled $POCl_3$ (0.1 mL, 1 mmol) in dry CH_2Cl_2 (5 mL) was added 1,3-diaminopropane (0.18 mL, 2 mmol). The reaction mixture was stirred overnight at room temperature under argon. A white precipitate was then removed by filtration and washed with CH_2Cl_2. The organic fractions were combined and concentrated under reduced pressure to afford a white solid that was recrystallized from CH_2Cl_2–hexane to give 0.115 g (75%) of 2-chloro-2-oxo-1,3,2λ⁵-diazaphosphorinane (**3**): mp 117.5–118.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.72 and 1.95 (2 m, 2 H, $HNCH_2CH_2CH_2NH$), 3.33 (m, 4 H, $NHCH_2CH_2CH_2NH$), 3.59 (br s, 2 H, NH); mass spectrum, $C_3H_8N_2OP^{35}Cl$ requires 154.0063, observed 154.0064, *m/e* 154 (25%), 126 (25%), 119 (100%), 112 (10%), 98 (22%), 91 (20%), 72 (55%), 64 (24%), 56 (40%).

1,3-Bis[[[6-(1-propionylamino)pyrid-2-yl]amino]carbonyl]-5-(heptyloxy)benzene (4). To a suspension of 5-(*n*-heptyloxy)isophthalic acid (0.150 g, 0.54 mmol) in dry CH_2Cl_2 (10 mL) were added oxalyl chloride (0.5 mL) and 1 drop of DMF. The slurry was stirred at room temperature under an inert atmosphere until the diacid was completely dissolved (≈2 h). The solvent was then evaporated under reduced pressure, and





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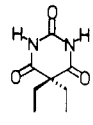

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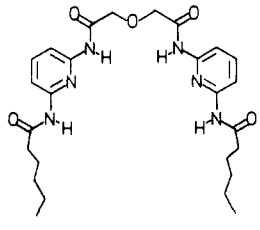
4: R = OC_7H_{15}, Y = H
7: R = NO_2, Y = CH_3



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the residue was redissolved in dry THF (10 mL). To this solution were added 2,6-diaminopyridine (0.470 g, 4.3 mmol) and triethylamine (0.150 mL). After the solution was stirred overnight at room temperature under an inert atmosphere, the solvent was evaporated, the residue was extracted into CH_2Cl_2, and the organic phase was washed several times with a saturated solution of sodium bicarbonate. Evaporation of the dried (Na_2SO_4) organic solvent afforded 0.240 g (97%) of 1,3-bis[[(6-aminopyrid-2-yl)amino]carbonyl]-5-(heptyloxy)benzene: mp 196–197 °C; ^{1}H NMR ($CDCl_3$) δ 0.931 (t, J = 6.96 Hz, 3 H, $(CH_2)_6CH_3$), 1.39 (m, 6 H, $(CH_2)_3(CH_2)_3CH_3$), 1.46 (m, 2 H, $(CH_2)_2CH_2(CH_2)_3CH_3$), 1.81 (q, J = 6.78 Hz, 3 H, $CH_2CH_2(CH_2)_4CH_3$), 4.06 (t, J = 6.78 Hz, 2 H, $CH_2(CH_2)_5CH_3$), 4.37 (br s, 4 H, NH_2), 6.30 (d, J = 7.98 Hz, 2 H, H_5Py), 7.51 (t, J = 7.98, 2 H, H_4Py), 7.60 (s, 2 H, $H_{2,6}$Ph), 7.69 (d, J = 7.98 Hz, 2 H, H_3Py), 7.93 (s, 1 H, H_4Ph), 8.93 (br s, 2 H, NH(C=O)); mass spectrum, $C_{25}H_{30}N_6O_3$ requires 462.2375, observed 462.2376, *m/e* 462 (1%), 398 (2%), 369 (2%), 354 (2%), 159 (4%), 136 (30%), 109 (100%), 82 (30%).

To a solution of the above diamine (0.120 g, 0.26 mmol) and triethylamine (80 μL, 0.57 mmol) in dry THF (10 mL) was added propionyl chloride (50 μL, 0.57 mmol). After it was stirred at room temperature for 1 h, the solution was concentrated under reduced pressure and the residue partitioned between CH_2Cl_2 and a saturated solution of $NaHCO_3$. The organic phase was washed with water and dried (Na_2SO_4) and the solvent evaporated to dryness. The crude product was purified by crystallization from THF–hexanes (1:1) to give the title compound as a pale yellow solid: 0.122 g, 82%, mp 109–110 °C; ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 6.6 Hz, 3 H, $(CH_2)_6CH_3$), 1.27 (t, J = 7.5 Hz, 3 H, $COCH_2CH_3$), 1.32 (m, 6 H, $(CH_2)_3CH_3$), 1.48 (m, 2 H, $O(CH_2)_2CH_2$), 1.83 (m, 2 H, OCH_2CH_2), 2.46 (q, J = 7.5 Hz, $COCH_2CH_3$), 4.08 (t, J = 6.8 Hz, 2 H, OCH_2), 7.62 (s, 2 H, $H_{2,6}$Ph), 7.69 (br s, 2 H, CH_2CONH), 7.78 (t, J = 7.9 Hz, 2 H, H_4Py), 7.95 (s, 1 H, H_4Ph), 7.98 (d, J = 7.9 Hz, 2 H, H_3Py), 8.04 (d, J = 7.9 Hz, 2 H, H_5Py), 8.40 (br s, 2 H, PhCONH); mass spectrum, $C_{31}H_{38}N_6O_5$ requires 574.2904, observed 574.2902, *m/e* 574 (2%), 545 (5%), 439 (2%), 410 (2.5%), 354 (1.5%), 221 (25%), 165 (30%), 109 (100%).

1,3-Bis[[[6-(1-butyrylamino)pyrid-2-yl]amino]carbonyl]-5-nitrobenzene (7). To a suspension of 5-nitroisophthalic acid (0.43 g, 2 mmol) in CH_2Cl_2 were added oxalyl chloride (0.57 mL, 6 mmol) and 1 drop of DMF. The reaction mixture was stirred overnight during which time all the acid went into solution. The volatile materials were then removed under reduced pressure, and the solid diacid chloride was redissolved in CH_2Cl_2 (10 mL). This solution was added dropwise to a stirred solution of diaminopyridine (2.18 g, 20 mmol) and triethylamine (0.7 mL, 5 mmol) in THF (40 mL) under an atmosphere of argon. The solution was stirred for 2 h and then evaporated to dryness. The solid was suspended in water, filtered, washed with water, and dried under reduced pressure. Purification by column chromatography (alumina, THF) gave 1,3-Bis-[[(6-aminopyrid-2-yl)amino]carbonyl]-5-nitrobenzene (0.59 g, 75%) as a white solid: mp 271.5–273 °C; ^{1}H NMR (CD_3OD–$CDCl_3$, 4:1) δ 6.35 (dd, J = 1.7, 7.0 Hz, 2 H, H_5Py), 7.44 (dd, J = 1.7, 7.0 Hz, 2 H, H_3Py), 7.47 (t, J = 7.6 Hz, 2 H, H_4Py), 8.87 (d, J = 1.4 Hz, 1 H, H_4Ph), 8.95 (d, J = 1.4 Hz, 2 H, $H_{2,6}$Ph; mass spectrum, $C_{18}H_{15}N_7O_4$ requires 393.1185, observed 393.1190. Anal. Calcd for $C_{18}H_{15}N_7O_4$: C, 54.96; H, 3.84; N, 24.93. Found: C, 54.72; H, 3.91; N, 24.46.

The foregoing diamine (0.197 g, 0.5 mmol) was dissolved in THF (30 mL) and triethylamine (0.2 mL, 1.4 mmol), and a solution of butyryl chloride (0.128 mL, 1.2 mmol) in CH_2Cl_2 (5 mL) was added with stirring. After it was stirred further for 30 min, the reaction mixture was evaporated to dryness, redissolved in CH_2Cl_2, and washed with dilute aqueous $NaHCO_3$. The organic phase was dried over Na_2SO_4 and evaporated to dryness. The product was purified by crystallization from THF–heptane to give **7** as buff needles: 0.255 g, 96%; mp 160–162 °C; ^{1}H NMR ($CDCl_3$) δ 1.02 (t, J = 7.4 Hz, 6 H, CH_3), 1.78 (m, 4 H, CH_2CH_3), 2.39, (t, J = 7.4 Hz, 4 H, $COCH_2$), 7.63 (s, 2 H, CH_2CONH), 7.82 (t, J = 8.1 Hz, 2 H, H_4Py), 8.01, 8.03 (2 d, J = 8.1 Hz, 4 H, $H_{3,5}$Py), 8.44 (s, 2 H, PhCONH), 8.79 (d, J = 1.3 Hz, 1 H, H_4Ph), 8.91 (d, J = 1.3 Hz, 2 H, $H_{2,6}$Ph); mass spectrum, $C_{26}H_{27}N_7O_6$ requires 533.2023, observed 533.1993, *m/e* 533 (14%), 516 (29%), 490 (100%), 460 (28%), 420 (94%), 255 (23%), 169 (27%), 136 (51%), 109 (54%), 71 (87%).

Bis[[[[6-(1-hexanoylamino)pyrid-2-yl]amino]carbonyl]methyl] Ether (8). To a suspension of diglycolic acid (0.750 g, 5.6 mmol) in dry CH_2Cl_2 (25 mL) were added oxalyl chloride (2 mL) and 1 drop of DMF. The slurry was stirred under argon at room temperature until all the solid had gone into solution (≈2 h). After evaporation of the solvent, the residue was redissolved in dry THF (20 mL). To this solution were added 2,6-diaminopyridine (6.1 g) dissolved in dry THF (100 mL) and triethylamine (1.5 mL). The resulting solution was stirred overnight at room temperature under an inert atmosphere, the solvent was then evaporated, and the residue was dissolved in CH_2Cl_2 and washed with a saturated solution of sodium bicarbonate until the excess diaminopyridine was completely removed from the organic phase (10 times). The CH_2Cl_2 solution was dried over Na_2SO_4, filtered and evaporated to dryness to afford 1.52 g (86%) of bis[[[(6-amino-pyrid-2-yl)amino]carbonyl]methyl] ether that was used without further purification: mp 160.5–161.5 °C; ^{1}H NMR ($CDCl_3$) δ 4.24 (s, 4 H, OCH_2), 4.36 (br s, 4 H, NH_2), 6.29 (d, J = 7.8 Hz, 2 H, H_5Py), 7.49 (t, J = 7.8 Hz, 2 H, H_4Py), 7.56 (d, J = 7.8 Hz, 2 H, H_3Py), 8.53 (br s, 2 H, NHC(=O)); mass spectrum, $C_{17}H_{16}N_6O_3$ requires 316.1284, observed 316.1284, *m/e* 316 (50%), 207 (20%), 181 (20%), 151 (100%), 136 (90%), 122 (40%), 109 (97%), 93 (55%), 81 (30%), 66 (40%). The crude diamide above (0.190 g, 0.6 mmol) was dissolved in dry THF (25 mL), and hexanoyl chloride (0.185 mL, 1.3 mmol) and triethylamine (0.185 mL) were added. After the solution was stirred overnight at room temperature under an inert atmosphere, the solvent was evaporated and the residue was extracted into CH_2Cl_2 and then washed with a saturated solution of $NaHCO_3$. Evaporation of the dried solvent gave a crude product that was chromatographed on silica gel (eluent, CH_2Cl_2–CH_3OH (5%)) and recrystallized from CH_2Cl_2–hexanes to give **8**: 0.11 g, 36%; mp 173.5–174 °C; ^{1}H NMR ($CDCl_3$) 0.91 (t, J = 7.23 Hz, 6 H, $(CH_2)_6CH_3$), 1.38 (m, 8 H, $(CH_2)_2(CH_2)_2CH_3$), 1.79 (q, J = 7.35 Hz, 4 H, $CH_2CH_2(CH_2)_2CH_3$), 2.40 (t, J = 7.35 Hz, 4 H, $CH_2(CH_2)_4CH_3$), 4.29 (s, 4 H, OCH_2), 7.74 (t, J = 8.01 Hz, 2 H, H_4Py), 7.93 and 7.98 (2 d, J = 8.01 Hz, 4 H, $H_{3,5}$Py), 8.00 (s, 2 H, $NHC(=O)C_5H_{11}$), 8.56 (s, 2 H, $OCH_2C(=O)NH$); mass spectrum, $C_{26}H_{33}N_6O_5$ requires 512.26, observed 513 ($M + H^+$).

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Registry No. 3, 129648-64-2; 4, 129648-66-4; 7, 129648-69-7; 8, 129678-22-4; $POCl_3$, 10025-87-3; 1,3-diaminopropane, 109-76-2; 5-(*n*-heptyloxy)isophthalic acid, 129648-65-3; oxalyl chloride, 79-37-8; 2,6-diaminopyridine, 141-86-6; 1,3-bis[[(6-aminopyrid-2-yl)amino]-carbonyl]-5-(heptyloxy)benzene, 129648-67-5; propionyl chloride, 79-03-8; 5-nitroisophthalic acid, 618-88-2; 1,3-bis[[(6-aminopyrid-2-yl)-amino]carbonyl]-5-nitrobenzene, 129648-68-6; butyryl chloride, 141-75-3; diglycolic acid, 110-99-6; bis[[[(6-aminopyrid-2-yl)amino]-carbonyl]methyl] ether, 129648-70-0; hexanoyl chloride, 142-61-0; *N*-butylamine, 109-73-9.

Ligand Dependence of Molybdenum-Catalyzed Alkylations. Molybdenum–Isonitrile Complexes as a New Class of Highly Reactive Alkylation Catalysts

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Abstract: A series of molybdenum complexes bearing α-diimine, *N,N'*-diarylideneethylenediamine, and isonitrile ligands have been prepared and evaluated for their ability to catalyze alkylations by using allyl acetates and especially allyl sulfones. $(bpy)Mo(CH_3CN)(CO)_3$ proved to be a very effective catalyst in contrast to $bpyMo(CO)_4$. The addition of isonitrile ligands to molybdenum hexacarbonyl generates the most effective molybdenum catalysts known to date. The reactive catalyst proved to be $Mo(RNC)_4(CO)_2$. With this new catalyst, a much broader range of substrates can be employed including many that failed or reacted very poorly by using molybdenum hexacarbonyl. The regioselectivity also differs from that obtained with molybdenum hexacarbonyl. The stereochemistry of the reaction proceeds with very clean net retention of configuration even under conditions that produced diastereomeric mixtures with molybdenum hexacarbonyl. A mechanistic rationale that accounts for the seemingly disparate complexes that are catalysts is presented.

Metal-catalyzed allylic alkylations for building molecular frameworks and for protecting group chemistry continues to enjoy explosive growth. Their attractiveness derives from their attributes of chemo-, regio-, and diastereoselectivity. Nevertheless, numerous opportunities exist to expand the scope of such processes. Many questions can be posed. What types of leaving groups at the allylic position suffice? Of special significance are those groups which normally do not participate in substitution reactions. Can regioselectivity of reactions with unsymmetrical allyl substrates be altered at will? While low valent palladium complexes have proven to be the most general and versatile catalysts,[1] will other less expensive low valent metal complexes[2,3] prove effective? To what extent can chiral metal complexes control absolute stereochemistry?[4] The beauty of metal-catalyzed reactions, in part, lies in the ability to broach these and other questions by "tuning" the catalyst via metal and ligand variation.

We have begun to seek solutions to a number of the questions posed above. While these questions can be approached individually, at times they overlap. For example, we sought to control regioselectivity by altering the low valent metal complex, especially by focusing on those derived from less expensive metals. Of these molybdenum catalysts, notably molybdenum hexacarbonyl, has proven especially interesting since it strongly promoted regioselective attack of malonate anion at the more substituted terminus of an unsymmetrical allyl system.[3] Our attempts to utilize this catalyst system to control regioselectivity of alkylation of allyl sulfones demonstrated a limitation since the reactions became almost stoichiometric in the molybdenum catalyst. We attributed a partial source of the problem to the facile disengagement of carbon monoxide which led to new molybdenum complexes that no longer functioned as catalysts. Earlier work noted that clearly ligand substitution was occurring under our alkylation conditions although we do not know the exact nature of the substitution. Therefore, we turned to the question of ligand choice.

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Part I. The Catalysts

Imine Ligands. Our early work demonstrated the feasibility of replacing several CO ligands of molybdenum hexacarbonyl with 2,2'-bipyridyl (bpy) and 1,2-bis(diphenylphosphino)ethane (dppe), but both complexes were significantly less reactive catalysts.[3a] The

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