calculated asymmetry, but of course, the geometric conformation that we have assumed for the reaction center of *R. viridis is* influenced by the protein and all its polar groups.[27] No doubt specific interactions can change the observed kinetics, but we might speculate that the primary influence of these specific interactions arises from changes in the geometry of the reaction center, itself. Considering only thermodynamics, a difference in energy of 890 cm^{-1} between $P \rightarrow H_L$ and $P \rightarrow H_M$ excitations translates into a factor of 70:1 favoring the L side at room temperature, to be compared with experimental values of about 100:1 to 200:1.[28-30]

These calculations do not specifically include the nearby hydrogen bonding or aromatic amino acid residues that may be important in electron transfer.[31] Also this simple solvent model is correct only through first order in the CI. We do not attempt to demonstrate highly accurate agreement with experiment. Rather we wish to show that consideration of the protein as a polarizable medium can play a significant role in lowering the energies of the $P \rightarrow H_{L,M}$ CT states relative $P \rightarrow B_{L,M}$, placing them vibrationally accessible to the lowest excited state of the RC. Our calculations also demonstrate the preference for CT along the L branch as well as supplying a rationale for the absence of an active participation of the auxiliary BChl.[32]

Acknowledgment. This work was supported in part through a grant from the Office of Naval Research (N00014-90-J-1608).

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An Unprecedented and Reversible Cobalt-to-Carbon Alkyl Bond Rearrangement in the Coenzyme B_{12} Model Complex $C_6H_5CH_2Co^{III}[C_2(DO)(DOH)pn]I$

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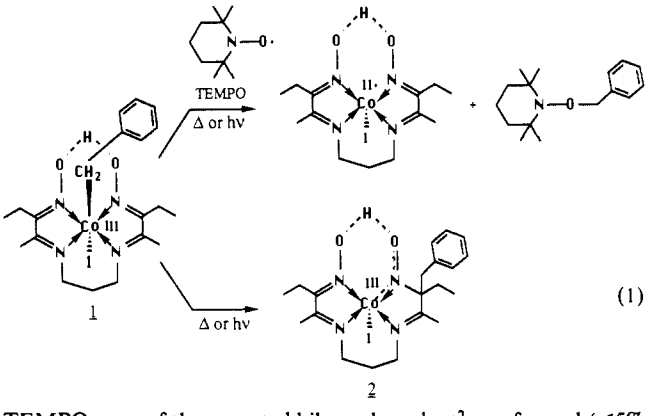
Previously,[2] in developing the now widely used[3-5] nitroxide radical-trapping method for studying cobalt–carbon[3,4] and other metal–carbon[3,5] bond homolyses, we examined the thermolysis of the orange-brown benzyl coenzyme B_{12} model complex[6] $C_6H_5CH_2Co^{III}[C_2(DO)(DOH)pn]I$ (**1**), both with and without the nitroxide TEMPO, eq 1. Surprisingly, in the absence of



(1)

TEMPO none of the expected bibenzyl product[2] was formed (<5% by NMR).[2c] Instead, a curious blood-red product, **2** (λ_{max} = 525 nm), is produced that initially appeared to be similar to paramagnetic, red $Co^{II}[C_2(DO)(DOH)pn]I$ (λ_{max} = 522 nm). However, ^1H NMR (vide infra) indicates that **2** is in fact diamagnetic and *still contains the benzyl group in what is a low-symmetry* (C_1) *structural isomer of* **1**.

Herein we report the required clean, high-yield photochemical synthesis of **2**, the first definitive characterization of **2** (by X-ray

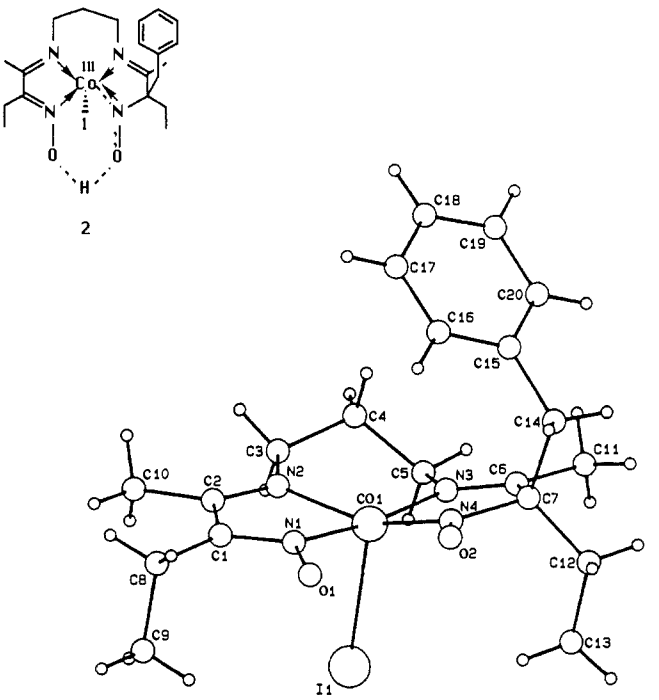


Figure 1. X-ray crystallographically determined molecular structure of the cobalt-to-carbon alkyl migration product **2**, (*SP*-5-15)-[2-[[3-[[2-(hydroxyamino)-1-methyl-2-(phenylmethyl)butylidene]amino]propyl]imino]-3-pentanone oximato(2-)-*N,N',N'',N'''*]iodocobalt(III).

(1) Undergraduate research associates.
(2) (a) Finke, R. G.; Smith, B. L.; Mayer, B. J.; Molinero, A. A. *Inorg. Chem.* **1983**, *22*, 3677-3679. (b) Smith, B. L. Ph.D. Dissertation, University of Oregon, 1982. (c) Aromatic solvents were used[2a,b] since formation of $PhCH_3$ by $H^\bullet$ abstraction from the solvent cannot, and does not,[2a,b] occur.
(3) (a) The nitroxide method has subsequently proven to be the method of choice for B_{12} alkyls[3b-d] [including coenzyme B_{12} itself,[4a,b] AdoCbi$^+$ (base-free B_{12}),[4c] MeB_{12},[4d] and neopentyl-B_{12}[4e]] as well as non-B_{12} systems.[5] (b) Bakac, A.; Espenson, J. H. *J. Am. Chem. Soc.* **1984**, *106*, 5197-5202. Blau, R. J.; Espenson, J. H. *J. Am. Chem. Soc.* **1985**, *107*, 3530-3533. (c) Geno, M. K.; Halpern, J. *J. Am. Chem. Soc.* **1987**, *109*, 1238-1240. Geno, M. K.; Halpern, J. *J. Chem. Soc., Chem. Commun.* **1987**, 1052-1053. (d) Gamelkoorn, H. J.; de Bolster, M. W. G.; Bait, S. *Inorg. Chem.*, submitted for publication.
(4) (a) For coenzyme B_{12}'s thermolysis and associated BDE, see: Finke, R. G.; Hay, B. P. *Inorg. Chem.* **1984**, *23*, 3041-3043. (b) Full paper: Hay, B. P.; Finke, R. G. *Polyhedron* **1988**, *7*, 1469-1481. (c) AdoCbi$^+$ thermolysis and BDE: Hay, B. P.; Finke, R. G. *J. Am. Chem. Soc.* **1987**, *109*, 8012-8018. (d) MeB_{12} thermolysis and BDE: Martin, B. D.; Finke, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 2419-2420. (e) Neopentyl-B_{12} thermolysis and BDE: Waddington, M.; Finke, R. G., manuscript in preparation.
(5) Collman, J. P.; McElwee-White, L.; Brothers, P. J.; Rose, E. *J. Am. Chem. Soc.* **1986**, *108*, 1332.
(6) (a) Finke, R. G.; Smith, B. L.; McKenna, W. A.; Christian, P. A. *Inorg. Chem.* **1981**, *20*, 687-693. (b) The $[CoC_2(DO)(DOH)pn]$ or equivalently[14b] [Co(EMO)(EMOH)pn] "modified-Costa"[6a] B_{12} model is shown in eq 1 and Figure 1. The $C_2(DOH)_2pn$ ligand therein is 2,10-diethyl-3,9-dimethyl-1,4,8,11-tetraazaundeca-1,3,8,10-tetraene-1,11-diol. The IUPAC nomenclature for **2** is given in the caption for Figure 1.

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crystallography) as the novel cobalt-to-carbon (*not* the purported cobalt-to-nitrogen)[7] alkyl rearrangement product[8,9] (Figure 1), and evidence that the rearrangement of **1** to **2** is thermally reversible. Kinetic and mechanistic studies are in progress and will be reported elsewhere.[10] These findings provide the first firm precedent from which to interpret scattered reports since 1975 of generally ill-characterized anaerobic photolysis or thermolysis products in B_{12} model systems.[7]

A key to our success was the development of a high-yield, reliable synthesis of **2**. Initially both photolysis and thermolysis of **1** were investigated, but only photolysis led to quantitative yields of **2** as conveniently judged by the clean isosbestic point in the visible spectrum at 466 nm as **1** (λ_{max} = 416 nm) is converted into **2** (λ_{max} = 525 nm). ^{1}H NMR is also convenient for following the quantitative conversion of **1** to **2** (complete replacement of the –O···H···O– peak at δ 20.24 by a δ 17.47 peak for **2**). A detailed synthetic procedure, a satisfactory elemental analysis, mass spectral data, and the ^{1}H and ^{13}C NMR data and peak assignments for **2** [supported by COSY and APT (attached proton test) experiments] are provided in a footnote.[11]

Once a clean sample of **1** was available, control experiments revealed why thermolysis of **1** fails to yield 100% of **2**. Starting with either **1** *or with* **2**, the *same equilibrium mixture* is reached, 40 (±2)% **1** and 60 (±2)% **2**, K_{eq} = 1.5 ± 0.1 (at 69 °C in benzene). That is, the conversion of **1** to **2** is thermally (but not photochemically) reversible (the photostability of **2** follows from, and is a key to, its high-yield photosynthesis).

Single-crystal X-ray crystallography provided an unequivocal structural characterization of **2**.[12] The crystallographic analysis reveals an unprecedented cobalt-to-*carbon* migration of the benzyl group as **1** is converted to **2** (not the widely proposed but unsubstantiated migration to nitrogen).[7] Specifically, the benzyl group has migrated from an axial coordination site on Co(1), trans to the axial I(1), to the atom C(7) adjacent to the oxime nitrogen atom N(4), Figure 1. It remains on the side of the ring system opposite from I(1).

The chelate ring Co(1)–N(1)–C(1)–C(2)–N(2) is planar to within 0.08 Å. The Co(1)–N(1) (oxime) and Co(1)–N(2) (imine) bond lengths are respectively at the lower and upper limits of the ranges observed in related complexes.[13,14] *Both* the N(4)–Co(1) and the N(4)–O(2) bond lengths [1.78 (1) and 1.28 (1) Å] are significantly shorter than their "normal" counterparts N(1)–Co(1) and N(1)–O(1) [1.86 and 1.38 (1) Å], *indicating the increased bonding between these pairs of atoms*. The O(1)···O(2) distance, 2.47 (1) Å, is at the upper end of the range of values found in related Co complexes.[13,14] The hydrogen atom of the intramolecular –O···H···O– hydrogen bond (detectable by ^{1}H NMR) could not be located crystallographically. The phenyl ring is placed so as to hinder access or solvent coordination to the vacant coordination site on Co(1), thereby giving rise to a relatively rare 5-coordinate,[15a,b] *formally*[15c] Co(III) complex and to distinctive chemical shifts for the phenyl aromatic hydrogens,[11] but the shortest C(phenyl)–Co distance [C(16), 3.79 (2) Å] is far too long for significant bonding. There are no short intermolecular contacts.

The significance of this work is severalfold: (1) it suggests a reexamination of the literature[7,8a,b] proposing cobalt-to-N or other migrations; (2) it extends the growing body of such alkyl migrations in other metal–macrocycle ring systems;[8,9] (3) it suggests, especially when combined with the cobaloxime literature,[7] the existence of similar products in the burgeoning literature employing alkylcobaloximes as alkyl radical precursors in organic synthesis;[16] and perhaps most importantly, (4) it raises the question of the possible existence,[17] and if so the implications,[17d] of analogous chemistry in B_{12} itself.

The unprecedented cobalt-to-carbon alkyl rearrangement of

(7) Anaerobic photolysis of cobaloxime and related B_{12} models is purported to yield ligand–N–R products, despite their inadequate characterization or quantitation, see: Gianotti, G.; Merle, G.; Fontaine, C.; Bolton, J. R. *J. Organomet. Chem.* **1975**, *91*, 357–362. Gianotti, G.; Merle, G.; Bolton, J. R. *J. Organomet. Chem.* **1975**, *99*, 145–156. Gianotti, G.; Bolton, J. R. *J. Organomet. Chem.* **1976**, *110*, 383–388. Maillard, P.; Massot, J. C.; Gianotti, G. *J. Organomet. Chem.* **1978**, *159*, 219–227. LeHoang, M. D.; Robin, Y.; Devynck, J.; Bied-Charreton, C.; Gaudemer, A. *J. Organomet. Chem.* **1981**, *222*, 311.

(8) Several interesting and thorough studies of possibly related reactions are available, but these generally involve unstable intermediates whose unequivocal structural characterization has also not proven possible: (a) C–R or N–R intermediates are acknowledged, but the latter are favored, in the reactions of R–cobaloximes with R′• free radicals: McHatton, R.; Espenson, J.; Bakac, A. *J. Am. Chem. Soc.* **1986**, *108*, 5885–5890. Note that R′ = benzyl does *not* yield an R–CH_2Ph product in this study. (b) A SALEN ligand–N–R intermediate is proposed in the following: Samsel, E. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 4790–4804. (c) Following $IrCl_6^{2-}$ oxidation, benzylcobaloxime produces a N–CH_2Ph (or possibly O–CH_2Ph) containing ligand-fragment by NMR and mass spectroscopy: Abley, P.; Dockal, E.; Halpern, J. *J. Am. Chem. Soc.* **1972**, *94*, 659. (d) Ligand–O–R intermediates are proposed following electrochemical oxidation of RCo(SALEN) and RCo(SALPHEN) complexes: Vol'pin, M. E.; Levitin, I. Y.; Sigan, A. L.; Halpern, J.; Tom, G. M. *Inorg. Chim. Acta* **1980**, *41*, 271. (e) See also p 1674 of the following: Seeber, R.; Marassi, R.; Parker, W. O., Jr.; Marzilli, L. G. *Organometallics* **1988**, *7*, 1672.

(9) Lead references to the extensive literature of metalloporphyrin alkyl-migration reactions: (a) *Cytochrome P-450: Structure, Mechanism, and Biochemistry*; Ortiz de Montellano, P. R., Ed.; Plenum Press: New York, 1986; Chapter 8 and references therein. (b) Lavalle, D. K. *The Chemistry and Biochemistry of N-Substituted Porphyrins*; VCH Publishers: New York, 1987; Chapter 7 and references therein.

(10) Daikh, B.; Finke, R. G., manuscript in preparation.

(11) Mildly air sensitive **2** is conveniently prepared by the following procedure. In an inert atmosphere (N_2) Vacuum Atmospheres drybox, 200 mg (0.37 mmols) of **1** was dissolved in 100 mL of benzene in a 300-mL round-bottom flask fitted with a Rodaviss ground-glass joint (Witeg). A magnetic stirbar was added to the solution, and the flask was sealed without grease and removed from the box. The flask was secured above a foil plate, 30 cm below a GE 275-W sunlamp. The flask was photolyzed for ca. 48 h while the solution was stirred by magnetic stirrer and room temperature air was blown over the surface of the flask. The benzene was removed by rotary evaporation outside the box (i.e., some exposure to air is acceptable), and the deep red microcrystalline product was scraped from the flask, placed in an amber vial under N_2, and placed in a −20 °C freezer. Yields, 100 ± 5% (by ^{1}H NMR), 110–197-mg (41–63%) isolated yields (six experiments). Elemental analysis [vacuum dried (6 h, 25 °C), benzene solvate-free sample]; calculated for $C_{20}H_{30}N_4O_2ICo$: C, 44.1; H, 5.5; N, 10.3. Found: C, 43.88; H, 5.47; N, 9.50. (Repeat analysis: C, 43.91; H, 5.46; N, 9.64). Mass spectrum: *m/e* (relative intensity; assignment) 544 (0.43; M^+, parent ion), 528 (0.40; M^+ – O), 453 (0.37; M^+ – benzyl), 91 (100; benzyl$^+$). ^{1}H NMR (benzene-d_6): δ 1.1 (m, 6 H), 1.2 (m, 3 H), 1.3 (m, 3 H), 1.6 (m, 2 H), 1.9 (d, 1 H), 2.6 (m, 2 H), 2.8 (m, 2 H), 2.9 (m, 2 H), 3.1 (m, 1 H), 3.3 (m, 1 H), 4.3 (t, 1 H), 6.1 (d, 2 H), 6.7 (m, 3 H), 17.5 (s, 1 H). ^{13}C NMR (benzene-d_6): δ 10.32 (C_9), 11.00 (C_{13}), 15.32 (C_{10}), 16.66 (C_{11}), 21.20 (C_{14}), 26.93, 30.14, and 38.08 (C_3 or C_4 or C_5), 49.84 (C_8), 50.37 (C_{12}), 126.44, 127.01, 129.29 (C_{15}–C_{20}), 161.74, 176.60 (C_1, C_2, C_6, and C_7). Atom subscript numbers refer to Figure 1.

(12) Red-black lath-shaped crystals of **2**·0.5C_6H_6 were grown from O_2-free benzene solution, washed with hexane, and dried on a glass frit under N_2 in a Vacuum Atmospheres drybox. They were sealed in capillaries outside the drybox. Crystal data: triclinic, space group $P\bar{1}$, a = 9.966 (1) Å, b = 16.514 (3) Å, c = 7.892 (3) Å, α = 101.42 (2)°, β = 90.66 (2)°, γ = 77.70 (2)°, V = 1243 (1) Å^2, Z = 2; Rigaku AFC6R diffractometer; crystal size 0.30 × 0.15 × 0.07 mm; 2258 independent reflections, $I \geq 3\sigma(I)$; solved by heavy-atom method; all non-H atoms of **2** anisotropic; R = 0.052, R_w = 0.061, S = 1.29. For details, see supplementary material.

(13) Calligaris, M. *J. Chem. Soc., Dalton Trans.* **1974**, 1628.

(14) (a) Parker, W., Jr.; Bresciani-Pahor, N.; Zangrando, E.; Randaccio, L.; Marzilli, L. *Inorg. Chem.* **1985**, *24*, 3908–3913. (b) Marzilli, L.; Bresciani-Pahor, N.; Randaccio, L.; Zangrando, E.; Finke, R. G.; Myers, S. *Inorg. Chim. Acta* **1985**, *107*, 139–145.

(15) (a) Marzilli, L. G.; Summers, M. F.; Bresciani-Pahor, N.; Zangrando, E.; Charland, J. P.; Randaccio, L. *J. Am. Chem. Soc.* **1985**, *107*, 6880. (b) Hay, B. P.; Finke, R. G. *J. Am. Chem. Soc.* **1987**, *109*, 8012. See footnote 25 and references therein. (c) Cobalt(II) and even cobalt(I) resonance forms for **2** can also be drawn and are probably more important than a cobalt(III) formulation.[10]

(16) Lead references: (a) Tada, M.; Okabe, M. *Chem. Lett.* **1980**, 201. Okabe, M.; Tada, M. *Chem. Lett.* **1980**, 831. (b) Branchaud, B.; Meier, M. S.; Malekzadeh, M. N. *J. Org. Chem.* **1987**, *52*, 212–217 and references therein. Note that these authors report (p 216) that 14–26% of uncharacterized products, "presumably derived from the ligand", are formed that adhere to silica gel as dark-colored material. (c) Bandaranayake, W. M.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1988**, 1179 and earlier references in this series. (d) Baldwin, J.; Li, C.-S. *J. Chem. Soc., Chem. Commun.* **1988**, 261; **1987**, 166.

(17) (a) An interesting report (among others)[17b,c] in this regard is one describing the "incipient homolysis" of coenzyme B_{12} following photolysis in a frozen H_2O/propylene glycol matrix at −193 to −73 °C: Lowe, D. J.; Joblin, K. N.; Cardin, D. J. *Biochim. Biophys. Acta* **1978**, *539*, 398–401. (b) Ramakirshna Rao, D. N.; Symons, M. C. R. *J. Chem. Soc., Chem. Commun.* **1982**, 954. (c) Ramakrishna Rao, D. N.; Symons, M. C. R. *J. Chem. Soc., Perkin Trans. 2* **1983**, 187. (d) The possible implications for B_{12} chemistry, and the evidence for or against them, will be discussed in a full paper.[10]

1 to **2** also provides a clean, definitively characterized system in which to probe several additional questions, notably, the origin of the rearrangement's driving force,[18] its detailed mechanism, and the carbon–benzyl (C–CH_2Ph) bond energy (BDE)[19,20] in **2**, apparently *about 24 kcal/mol*—roughly one-third that of a normal C–CH_2Ph BDE—based on preliminary studies.[19] The needed studies are nearing completion and will be reported in due course.[10]

Acknowledgment. Support from NIH Grant DK 22614, and especially the support of this undergraduate research project[1] as one component of that grant, is gratefully acknowledged. B.E.D. thanks Dr. Bruce Martin for valuable advice and assistance during Dr. Martin's postdoctoral appointment at the University of Oregon.

Supplementary Material Available: Details of the X-ray structural analysis of **2**·0.5C_6H_6 including an ORTEP diagram, tables of refined atomic coordinates, bond lengths and angles, and tables of calculated hydrogen atom coordinates, and anisotropic thermal parameters (12 pages); listing of observed and calculated structure factors (16 pages). Ordering information is given on any current masthead page.

(18) The overall driving force ΔG must be small, since $K_{eq}(69°C) = 1.5$, but the ΔH and ΔS components are of interest.[10]

(19) Initial work thermolyzing **2** with TEMPO, under conditions first order in **2** and zero order in TEMPO, gives a $\Delta H^{\ddagger} = 26 \pm 2$ kcal/mol in benzene and thus a C–CH_2Ph BDE *estimate* (once radical-cage effects are taken into consideration)[20] of 24 kcal/mol.

(20) (a) Koenig, T. W.; Hay, B. P.; Finke, R. G. *Polyhedron* **1988**, *7*, 1499–1516. (b) Koenig, T. K.; Finke, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 2657.

Ionically Cross-Linkable Polyphosphazene: A Novel Polymer for Microencapsulation

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Synthetic polymers are used increasingly in medical science due to the chemist's ability to incorporate specific properties such as strength, hydrogel characteristics, permeability, or biocompatibility, particularly in fields like cell encapsulation and drug delivery where such properties are often prerequisites. However, harsh conditions, e.g., heat or organic solvents, are always used when encapsulating with these polymers,[1] often causing difficulties in encapsulating sensitive entities, e.g., proteins, liposomes, and mammalian cells. At the opposite extreme, a natural polymer, alginate, extracted from seaweed, has been widely used for cell encapsulation.[2] This polymer can be ionically cross-linked in water to form hydrogels that fulfill many of the above requirements. However, natural polymers display variable biocompatibility and some properties can be reproduced only with difficulty.[1b]

Until now, no synthetic polymer has existed that can encapsulate sensitive entities under mild conditions. Here we report the development of a polyphosphazene that forms gel matrices by simply adding divalent cations in water at room temperature and can encapsulate mammalian cells, liposomes, and proteins.

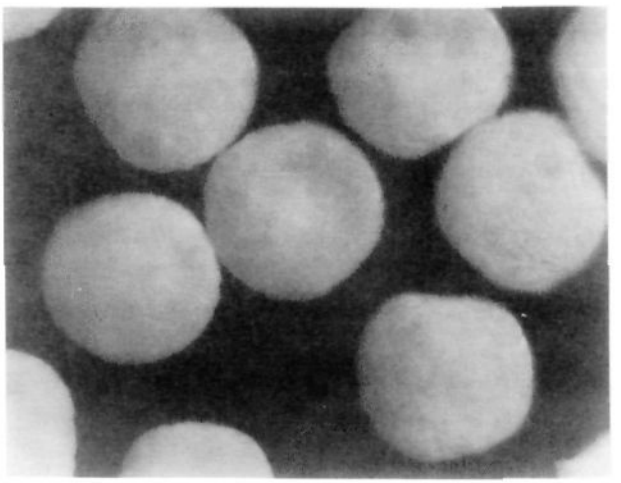
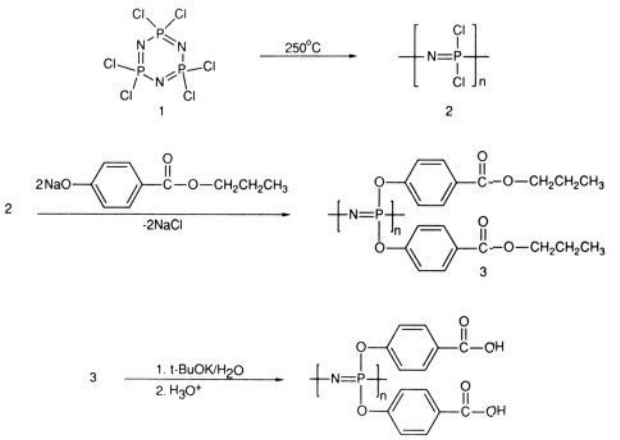


Figure 1. Ca-PCPP microspheres via phase contrast microscopy (magnification 1540×).[4a]

Scheme I. Poly[bis(carboxylatophenoxy)phosphazene] Synthesis



Poly[bis(carboxylatophenoxy)phosphazene] (PCPP (**4**)] (Scheme I) was prepared by first synthesizing poly(dichlorophosphazene) (**2**) by thermal bulk polymerization of hexachlorocyclotriphosphazene (**1**). Chlorine atoms were then replaced by carboxylate ester containing side groups, by reacting propyl *p*-hydroxybenzoate with **2**, forming poly[bis(aryloxy)phosphazene] ester **3**, followed by hydrolysis of ester groups to carboxylic acids (**4**).[3]

PCPP was insoluble in acidic or neutral solvents but soluble in basic solutions, e.g., sodium carbonate. The dissolution of 10% (w/v) PCPP in 30 mg/mL sodium carbonate caused a decrease in solution pH to 7.5–7.8 (due to polymer deprotonation), enabling mild encapsulation. When Ca^{2+} was added to PCPP, fast gelation occurred. Presumably, Ca^{2+} forms salt bridges between carboxylic groups of adjacent polymers, creating an ionically cross-linked matrix (Ca-PCPP).[3] Microspheres (Figure 1) were prepared by using a droplet-forming apparatus.[4a] Their shape and size depended on polymer and calcium ion concentrations, polymer extrusion rate, air flow, and needle diameter.[5]

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[‡] Department of Chemistry, The Pennsylvania State University.

[§] Department of Biology, Massachusetts Institute of Technology.

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(3) Allcock, H. R.; Kwon, S. *Macromolecules* **1989**, *22*, 75.

(4) (a) Microspheres were prepared by spraying aqueous PCPP (2.5% w/v) with FITC-BSA (20 mg; Sigma), or β-gal (1 mg; Sigma No. G-5635), or hybridoma cells (5 × 10^6 cells; ATCC HB123), into 7.5% w/v $CaCl_2$, using a droplet-forming apparatus.[2,5] Beads were hardened for 30 min and coated with 30 mL of 0.25% (w/v) PLL (MW 21.5 kDa; Sigma) for 30 min. (b) Release studies were performed at 37 °C, with gentle agitation, in vials containing 10 mL of phosphate-buffered saline (PBS) at pH 7.4, with 0.01% gentamicin sulfate as preservative. FITC-BSA and β-gal release was followed by absorbance at 495 nm and BCA protein assay (Pierce No. 23235), respectively. Hybridoma cell viability was followed by a trypan blue exclusion assay.

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