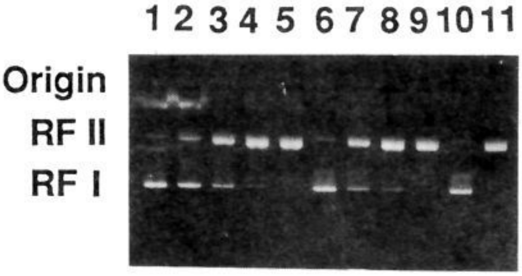

Figure 2. DNA single strand breaks induced by NPYR-dpT (and NPYR-pA) and UVA. Detection of DNA strand breaks was carried out with phage M13mp2 RF DNA using agarose gel electrophoresis as reported previously.[17] A change from form RFI to RFII is the indication for single strand breaks. The double-stranded covalently closed circular DNA (RFI) was prepared according to the literature.[18] DNA (10 ng/μL) in 20 mM sodium phosphate buffer (pH 7.4) was incubated with the reagents in a 96-well microtiter plate at 24 °C under UVA irradiation at 6.7 μW/mm^2. The volume of the reaction mixture was 40 μL. After a 3-h irradiation, aliquots (9 μL) were electrophoresed in 1% agarose gel with the running buffer, 89 mM Tris–89 mM boric acid–2.5 mM disodium EDTA, pH 8.3. Lane 1, no addition (DNA only); lane 2, UVA only; lanes 3–5, UVA + NPYR-pA, 0.05 mM, 0.25 mM, 0.75 mM, respectively; lane 6, NPYR-pA 0.75 mM only; lanes 7–9, UVA + NPYR-dpT, 0.05 mM, 0.25 mM, 0.75 mM, respectively; lane 10, NPYR-dpT 0.75 mM only; lane 11, a positive control: NPYR (1 mM) + UVA.[5]

tography and paper electrophoresis. After the acid or phosphodiesterase treatment, the solution became positive in the Bandrowski aldehyde test.[9] It has been suggested that 2-butenal is formed upon degradation of α-acetoxy-NPYR.[10] We found that NPYR-dpT (in an 8 mM aqueous solution at pH 6) can also be decomposed by UVA irradiation (320–400 nm, 6 μW/mm^2, 3 h, without appreciable changes in the pH) to give dpT.

We have prepared the NPYR phosphoesters from other deoxyribonucleoside 5′-phosphates and ribonucleoside phosphates. A dideoxynucleotide, dpCpT, was also derivatized. The preparation and properties of these derivatives are summarized in Table I.[11] All of these NPYR nucleotides are direct-acting mutagens, showing activities toward *Salmonella typhimurium* TA1535, a tester strain for base change mutations.[12] Their mutagenic potencies were similar to that of α-acetoxy-NPYR.[13]

DNA single strand breaks were caused by NPYR-pA and NPYR-dpT on UVA irradiation. Either the NPYR nucleotide alone or UVA alone was without the effect (Figure 2). The reaction seems to be mediated by active oxygen radicals, possibly $^{\bullet}$OH, because the breaks were inhibited by formate, thiourea, and cysteamine, which are scavengers of hydroxyl radical;[14] superoxide dismutase did not inhibit the strand break (data given in the supplementary material).

The NPYR moiety may be incorporated into oligonucleotides having terminal phosphomonoester groups. Such oligonucleotides would be useful in specific cleavage of nucleic acids[15] and in targeted gene-manipulation. This new class of nucleotide derivatives may also be useful in studies of mutagenesis and carcinogenesis mechanisms of *N*-nitrosodialkylamines. 2-Butenal, an α,β-unsaturated aldehyde generated on cleavage of the NPYR moiety from the NPYR nucleotides, should be reactive not only to DNA but also to nucleophilic groups in proteins and other biological substances.[16]

Acknowledgments. This work was supported in part by a Grant-in-Aid for Cancer Research from the Ministry of Education, Science, and Culture, Japan. We thank Dr. U. L. RajBhandary of the Massachusetts Institute of Technology for his gift of a protected dinucleotide from which the dpCpT used was prepared. Dr. B. N. Ames of the University of California at Berkeley is thanked for his gift of *Salmonella typhimurium* TA1535.

Supplementary Material Available: Figure showing the gel electrophoresis of antioxidant inhibition of DNA single strand breaks induced by NPYR-dpT and UVA (2 pages). Ordering information is given on any current masthead page.

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Preparation and Characterization of Singly Oxidized Metalloporphyrin Dimers: $[M(OEP^{\cdot/2})]_2SbCl_6$, M = Cu, Ni. Photosynthetic Special Pair Models

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Received July 6, 1992

We report the preparation and physical characterization (X-ray, UV–visible–near IR, IR, EPR, magnetic susceptibility) of two new metalloporphyrin π-cation radical derivatives formally analogous to the radical cation of the photosynthetic reaction center special pair.[2] The complexes are $[M(OEP^{\bullet/2})]_2^+$ (M = Ni or Cu),[3] and they possess a single electron hole per *pair* of porphyrin rings; both form discrete dimers in the solid state. The absence of an obvious covalent bond in these dimers distinguishes them from all previously characterized "partially oxidized" bis(porphyrin) systems.

Oxidation of [M(OEP)] in CH_2Cl_2 with 0.5 equiv of $[(4\text{-}BrPh)_3N]SbCl_6$ yields $[M(OEP^{\bullet/2})]_2SbCl_6$, which shows the empirical, porphyrin ring oxidation IR marker band.[4,5] The nickel

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(1) (a) University of Notre Dame. (b) Permanent address: University of New South Wales, Kensington, NSW, Australia. (c) University of Southern California. (d) CENG, Grenoble.

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(3) Abbreviations: Ct, center of porphyrin ring; N_p, porphinato nitrogen; RC, photosynthetic reaction centers; OEP, TPP, TnPrP, and P, dianions of octaethyl-, tetraphenyl- tetra-*n*-propylporphyrin, and a generalized porphyrin, respectively; π-cation radical derivatives are indicated with a raised dot in the formula (i.e., $OEP^{\bullet}$).

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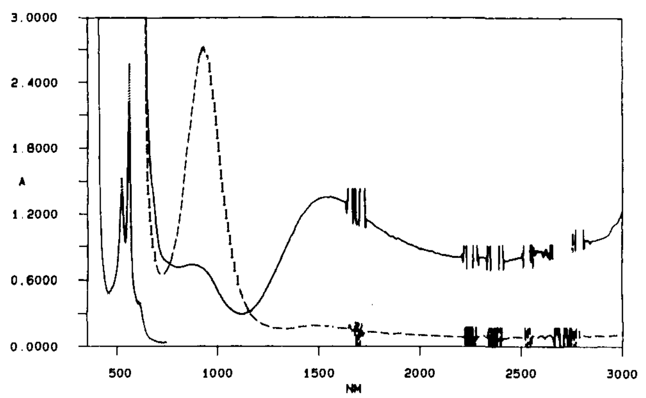

Figure 1. Sum of the spectra (3000–750 nm) of equimolar (2.80 × 10^{-3} M) CH_2Cl_2 solutions of [Cu(OEP)] and [Cu(OEP$^{\bullet}$)]$^+$ held in the two compartments of a quartz mixing cell (spectrum a (- - -)). Spectrum b (—) is obtained after the two solutions are mixed; this spectrum is virtually identical to that of pure [Cu(OEP$^{\bullet/2}$)]$_2^+$. The oscillations at wavelengths greater than 1600 nm result from interference of CH_2Cl_2. The spectra at the left (750–350 nm) are from equimolar solutions (1.75 × 10^{-4} M) of [Cu(OEP)] and [Cu(OEP$^{\bullet}$)]$^+$: (···) before mixing, (—) after mixing.

complex has a narrow EPR band (~4 G, peak to peak) at g = 2.003; the copper complex has a broader band at g = 2.05 (width >80 G). For each, frozen solution (CH_2Cl_2) and solid-state EPR spectra are similar. The magnetic susceptibility[6] of M = Ni is that of a simple $S = {}^1/_2$ paramagnet; M = Cu shows μ_{eff} = 3.2 μ_B from an essentially uncoupled $S = {}^1/_2, {}^1/_2, {}^1/_2$ system at 300 K, decreasing to 1.9 μ_B at 10 K because of modest antiferromagnetic coupling ($J \approx -19$ cm^{-1}).

[M(OEP$^{\bullet/2}$)]$_2^+$ displays a broad near-IR band at ~1536 nm, which tails far into the infrared[7] and which is not observed in either [M(OEP)] or [M(OEP$^{\bullet}$)]$SbCl_6$. This near-IR band is similar to the ~1300-nm band in photooxidized *R. viridis* reaction centers which is uniquely associated with the oxidized primary donor of bacterial reaction centers.[8] However, we do not cleanly observe the broad, discrete peak in the IR (at ~2700 cm^{-1}) that has been recently[9] reported for photooxidized RCs although, as noted, the 1536-nm^{-1} peak does tail into this region. Similar near-IR bands are found for oxidized metal(III) and metal(IV) bis(porphyrin) complexes.[10] It is presumed that all such near-IR bands arise from transitions between new MOs arising from the substantial porphyrin–porphyrin interaction.[10d,11] Figure 1 presents results of mixing experiments. An equilibrium process like [Cu(OEP)] + [Cu(OEP$^{\bullet}$)]$^+$ $\rightleftharpoons$ [Cu(OEP$^{\bullet/2}$)]$_2^+$ clearly pertains in which the equilibrium is predominantly to the right. [Ni(OEP$^{\bullet/2}$)]$_2^+$ has similar spectra and equilibria.

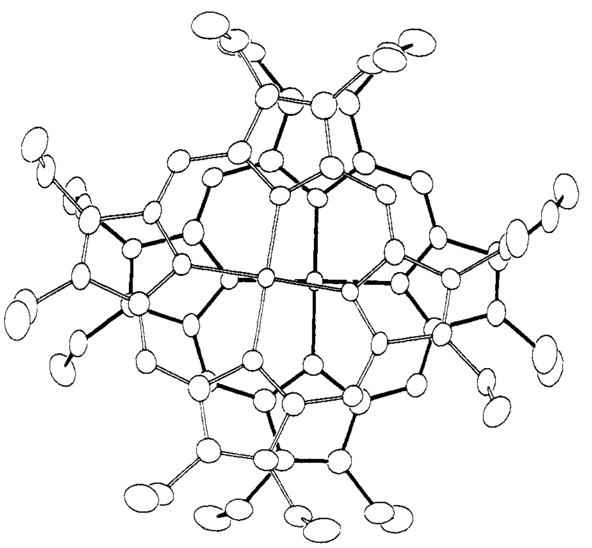

Figure 2. ORTEP diagram of the [Ni(OEP$^{\bullet/2}$)]$_2^+$ cation. The mean plane of the bottom porphyrin ring is parallel to the plane of the paper. The Ni···Ni separation is 3.425(2) Å, the Ct···Ct separation is 3.466 Å, the lateral shift is 0.83 Å, and the mean plane separation is 3.36 Å. Values in the copper complex are 3.375(1), 3.435, 1.05, and 3.27 Å, respectively.

X-ray structures[12] confirm the stoichiometry. The two rings of the dimers are crystallographically equivalent, consistent with the unpaired electron being delocalized over both rings of a dimer. Figure 2 shows one view of the [Ni(OEP$^{\bullet/2}$)]$_2^+$ dimer. The two rings are related by a crystallographic twofold axis, while in the copper complex the two are related by an inversion center. These discrete dimeric complexes are distinctly different from those of a number of other partially oxidized porphyrin and phthalocyanine species which form one-dimensional stacks.[13] The average value of the Ni(Cu)–N_p bond distance is 1.950(3) (1.984(6)) Å, both are within the range found for neutral four-coordinate nickel(II) and copper(II) porphyrinates.[14] Deviations from exact planarity in the unique porphyrin core of [Cu(OEP$^{\bullet/2}$)]$_2^+$ are small but nonzero, while the cores in the [Ni(OEP$^{\bullet/2}$)]$_2^+$ cation display S_4 ruffling. Ni(II) (Cu(II)) is displaced 0.04(0.07) Å out of its 24-atom plane toward the other ring.

The inter-ring geometry of strongly associated porphyrins is conveniently described by the mean plane separation, the Ct···Ct distance, and the lateral shift of the two rings.[15] Dimers formed by *neutral* metalloporphyrin derivatives are found to have lateral

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(5) The marker band is observed at ~1570 (Ni) or ~1548 cm^{-1} (Cu) and, while similar to that of the respective [M(OEP$^{\bullet}$)]$^+$ derivative, is significantly broadened.

(6) Magnetic susceptibilities measurements (6–300 K) were performed on ground, compressed samples (~30 mg) prepared from large single crystals. Measurements for the nickel complex were made on a SHE VTS 905 susceptometer at Grenoble; those for the copper complex were made on a SHE Model 905 SQUID susceptometer at USC.

(7) As judged by the anomalously high background, this band extends to ~1400 cm^{-1}.

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(15) See Figure 7 of ref 16 for pictorial definitions.

shifts clustered at ~1.5 or ~3.4 Å[16] and with mean plane separations of 3.30 Å upwards. Dimeric $[M(OEP^{\bullet})]_2^{2+}$ systems[17-19] are completely overlapped (zero lateral shift) and have mean plane separations of 3.25-3.35 Å.[20] The $[M(OEP^{\bullet/2})]_2^{+}$ derivatives have lateral shift values (0.8-1.0 Å) and inter-ring Ct⋯Ct distances that are about halfway between those of the oxidation extremes. These structural data, along with the recent observation of Le Mest et al.[21] that only certain dimeric, covalently linked, cofacial porphyrin systems can be electrochemically oxidized by 1 equiv per two rings, suggest that there are particular inter-ring geometries that stabilize the partially oxidized species and that are distinctly different from either the neutral or fully oxidized analogs. The importance of the inter-ring geometry in stabilizing a "special pair" is an intriguing question that is being further explored in these laboratories. Whether oxidation-reduction rates are also affected by the inter-ring geometry remains a question to be explored.

Acknowledgments. We thank the National Institutes of Health for support of this research (Grant GM-38401 to W.R.S. and GM-23851 to C.A.R.). W.R.S. thanks Dr. J. Fajer for helpful discussions on the spectra of photooxidized reaction centers.

Supplementary Material Available: Tables (SI-SIV) of atomic coordinates, bond distances, and bond angles for $[M(OEP^{\bullet/2})]_2SbCl_6$ (M = Ni, Cu) (8 pages); observed and calculated structure amplitudes (×10) (26 pages). Ordering information is given on any current masthead page.

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Chemoselective Functionalization of More Hindered Aldehyde Carbonyls with the Methylaluminum Bis(2,6-diphenylphenoxide)/Alkyllithium System

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Received October 23, 1992

The chemoselective functionalization between two different carbonyl substrates is a synthetically useful operation and is closely related to the chemistry of molecular recognition.[1] The discrimination between two different aldehydes or between aldehydes and ketones is commonly achievable by using bulky organometallic reagents or bulky Lewis acids to discriminate the structural or electronic environment of the carbonyl group, in which the sterically less hindered or electronically more labile aldehyde is more easily functionalized.[2-4] For example, titanium reagents of the type $RTi(OPr^i)_3$ offer the most satisfactory results for this selective transformation.[2] However, the opposite selectivity, i.e., chemoselective functionalization of the sterically more hindered aldehyde carbonyl, seems quite difficult to attain in view of the high reactivity of the paired aldehydes toward nucleophiles, and hence it has not yet been realized in spite of long-standing concern.[5,6] Here we wish to disclose our initial results on this subject using certain modified organoaluminum reagents, featuring a Lewis acidic molecular cleft for recognition and stabilization of structurally similar aldehydes based on the selective Lewis acid-base complex formation (Scheme I).

Scheme I

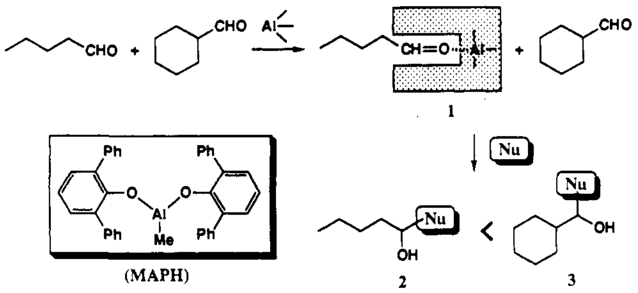
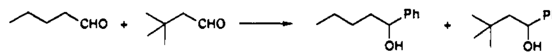
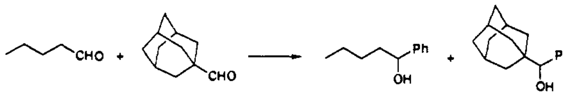
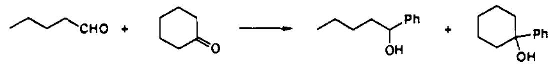


Table I. Chemoselective Functionalization between Two Different Carbonyl Substrates[a]

entry	reagent (equiv)	conditions (°C, h)	yield[b] (%)	ratio[c]
				
1	$BuTi(OPr^i)_3$ (1)	-40, 1; 28, 34	31	2.5 : 1
2	BuLi (1)	-78, 0.25	76	1 : 1.9
3	MAD (1)/BuLi (1)	-78, 0.3	41	1 : 1.4
4	MAPH (1)/BuLi (1)	-78, 0.3	76	1 : 6.5
5	MAPH (2)/BuLi (1)	-78, 0.3	45	1 : 14
				
6	$PhTi(OPr^i)_3$ (1)	-40, 1	60	3.3 : 1
7	MAPH (1)/PhLi (1)	-78, 0.5	80	1 : 4.3
8	MAPH (2)/PhLi (1)	-78, 0.5	60	1 : 10.8
				
9	$PhTi(OPr^i)_3$ (1)	-40, 2	80	10.1 : 1
10	MAPH (1)/PhLi (1)	-78, 0.5	60	1 : 2.9
11	MAPH (2)/PhLi (1)	-78, 1	58	1 : 24
				
12	$PhTi(OPr^i)_3$ (1)	-40, 1	83	>99 : 1
13	MAPH (1)/PhLi (1)	-78, 0.5	90	1 : 2.7
14	MAPH (2)/PhLi (1)	-78, 1	68	1 : 56

[a] The alkylation of two different carbonyl substrates (1 equiv each) was carried out in CH_2Cl_2. [b] Isolated yield. [c] Determined by capillary GLC and/or 200-MHz ^1H NMR analysis.

First, we examined the possibility of discriminating two different aldehyde carbonyls with the exceptionally bulky, oxygenophilic methylaluminum bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD), which was recently introduced for the selective reduction of one out of two different ketone carbonyls by combining certain hydride reagents.[7] Attempted treatment of a mixture of 1 equiv each of MAD, valeraldehyde, and cyclohexanecarboxaldehyde in CH_2Cl_2 at -78 °C with BuLi in hexane afforded two carbinols

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