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Authors

Li, Zhi

Wu, Guang

Ford, Peter C

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The Dinuclear PhotoCORM $(\text{CO})_3(\text{bpy})\text{ReMn}(\text{CO})_5$. Formation of a Luminative Product upon CO Uncaging by MMLCT Excitation[†]

Zhi Li, Guang, Wu, Peter C. Ford*

Department of Chemistry and Biochemistry, University of California, Santa Barbara, Santa Barbara, CA, 93106 USA

Abstract: We report a photochemical investigation of the dinuclear metal carbonyl complex $(\text{CO})_3(\text{bpy})\text{ReMn}(\text{CO})_5$, where bpy = 2,2'-bipyridine. This investigation follows an earlier study of the photo-activated carbon monoxide release as the result of long-wavelength visible and near-infrared excitation of a several different $(\text{CO})_5\text{ReMn}(\text{CO})_3(\text{LL})$ complexes in aerobic media. These dinuclear species all show a strong metal–metal-bond (σ_{MM})-to-ligand (π_{L}^*) charge-transfer (MMLCT) bands as the lowest energy absorptions in their respective optical spectra. Photolysis of the MMLCT band leads to homolysis of the metal-metal bond to give mononuclear metal radicals that can be trapped with dioxygen. The species formed from the manganese carbonyl radical fragments undergo CO release via secondary reactions, while the mononuclear product(s) formed from the $\bullet\text{Re}(\text{CO})_3(\text{bpy})$ radical is luminescent. In these contexts, we discuss potential applications of such dinuclear compounds as photoactivated CO-releasing moieties.

Keywords: Photochemistry, Carbon Monoxide, PhotoCORM

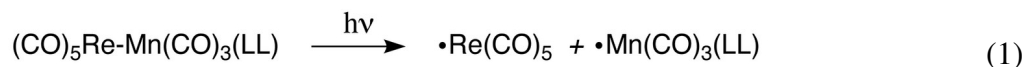
Introduction

Carbon monoxide is produced endogenously in mammals by heme oxygenase enzymes,¹ and recent studies identify CO as a signaling molecule with various physiological roles.²⁻⁴ Exogenous CO application also reduces organ graft rejection,⁵ promotes wound healing⁶ and protects against ischemia/reperfusion injury.⁷ In addition, there is continuing interest in the anti-microbial activity⁸ of this diatomic molecule, which is better known for its action as a toxic gas. While CO toxicity to mammals is often attributed to the blocking O₂ transport via carboxyhemoglobin formation, it is notable that blood Hb(CO) levels can approach 20% with limited adverse effects.² Thus, Hb's affinity for CO may serve as a buffer against even more toxic effects at the cellular level.^{2,9} However, this buffering function also makes it necessary to develop methods for CO delivery to physiological targets to avoid the Hb pool in the blood stream.

Potential therapeutic applications have been addressed by using CO releasing moieties (CORMs) designed to uncage CO under specific physiological conditions.^{2,3,7,10} Alternatively, one can photo-active CO release from otherwise stable compounds,^{11,12} species that have been dubbed "photoCORMs".^{11a} The use of light as an uncaging trigger offers exquisite temporal-spatial control. However, owing to the poor transmission of UV and shorter visible wavelengths through tissue,¹³ it is important to develop delivery systems that can be activated by more penetrating, red or near-infrared (NIR) light. In this context, we have previously employed upconverting nanoparticles (UCNPs)¹⁴ and simultaneous two photon excitation (TPE)¹⁵ in order to trigger CO release with NIR light, but these non-linear approaches to photo-uncaging may be compromised by scattering of the excitation beam by heterogeneous structures in real tissue.

Another strategy to extending the response of photoCORM systems to longer wavelengths was reported by Zhi Li et al from this laboratory in 2017.¹⁶ In short, this approach utilized direct single photon excitation of the metal-metal bond to ligand ($\sigma_{MM} \rightarrow \pi_L^*$) charge transfer (MMLCT) transition characteristic of certain dinuclear complexes to generate reactive intermediates that release CO upon subsequent reaction(s). MMLCT excitation of the dinuclear rhenium-manganese carbonyl compounds (CO)₅ReMn(CO)₃(LL) (LL = a bidentate diimine heterocycle including 2,2'-bipyridine (bpy), 1,10-phenanthroline (phen), 2,2'-biquinoline or 1,10-phenanthroline-4-carboxaldehyde) led to homolytic cleavage of the Re-Mn bond by deep red and/or NIR light to give

mononuclear metal radicals (e.g., eq. 1). In the absence of trapping agents, the radicals reform metal-metal bonds, but in aerobic solution, they are trapped by O₂. The resulting intermediates from the Mn radicals undergo further oxidation leading to CO uncaging.¹⁶ However, the rhenium radicals did not lead to CO release, perhaps because the rhenium carbonyl fragment may be resistant to further oxidation by dioxygen.



Notably, certain Re^I tricarbonyl complexes of the type Re(CO)₃(LL)X have been reported to have theranostic activity, namely that they may have therapeutic value, for example, in cancer chemotherapy, while also being luminescent, thus bioimagingable.¹⁷ Several have been shown to be photoCORMs¹⁸ but are primarily responsive to shorter wavelength excitation. Here we describe the synthesis and a brief photochemical investigation of the dinuclear complex (CO)₅MnRe(CO)₃(bpy) (**D1**). This compound was prepared with the expectation that photolysis of the MMLCT band in aerobic media would play dual roles. Photofragmentation of the Re-Mn bond would facilitate CO delivery via subsequent reactions of the photogenerated •Mn(CO)₅ radical with O₂ while formation of a luminescent Re^I fragment would allow optical imaging of the photoreaction site

Here we describe the photochemistry of compound **D1** in the context of the above goals.

Results and Discussion

The dinuclear compounds (CO)₅ReMn(CO)₃(LL) (LL = various bidentate diamine ligands) previously studied in this laboratory do not display photoluminescence under ambient conditions nor do their photo products.¹⁶ These dimers undergo fast photo-activated metal-metal bond cleavage upon irradiation of the MMLCT band, but the expected Re(CO)₅X products only emit at low temperature.¹⁹ By placing the diamine ligand on the rhenium center of (CO)₅MnRe(CO)₃(bpy) (**D1**), it was anticipated that the (•Re(CO)₃(bpy)) radical formed upon MMLCT excitation would be trapped by O₂ to form (eventually) a luminative species, while similar oxidative trapping of the •Mn(CO)₅ radical would lead to CO release.

Synthesis: The dinuclear complex **D1** was prepared from Re(CO)₃(bpy)Cl (**M1**) and Mn(CO)₅Br by a procedure similar to that reported by Stufkens and coworkers.²⁰ The key

difference was that the Re(I) monomer that was first reduced by Na(Hg) (Supporting Information Scheme S1) rather than the manganese component. After purification by column chromatography, **D1** was characterized by ^1H NMR and IR spectroscopy and by mass spectrometry (see Experimental Section and Supporting Information Figs. S1 and S2). The X-ray crystal structure presented in Figure 1 shows the three carbonyls on Re in *facial* configuration and a Re-Mn bond length of 3.010 Å. The absorption spectrum in acetonitrile (Fig. 2) displayed a strong absorption band with a λ_{max} at 483 nm ($\epsilon_{\text{max}} = 5.1 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$) which, in analogy to earlier studies,^{16,20} was assigned to a MMLCT absorption.

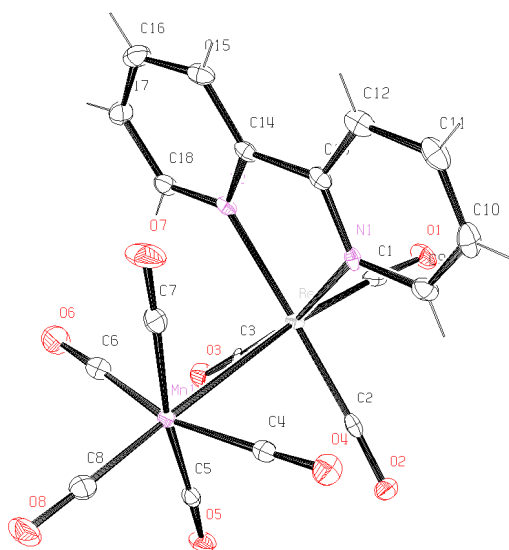


Figure 1. ORTEP drawing of the structure of $(\text{CO})_5\text{MnRe}(\text{CO})_3(\text{bpy})$ (**D1**) shown with 50% thermal ellipsoids.

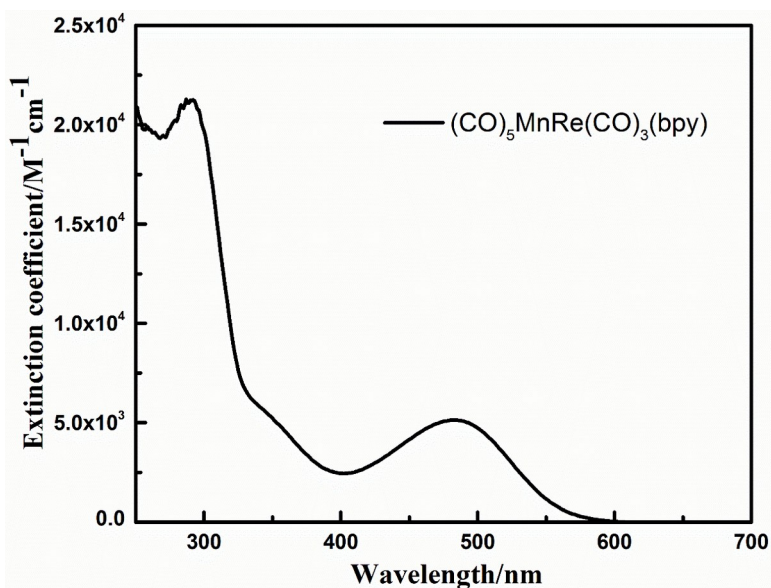
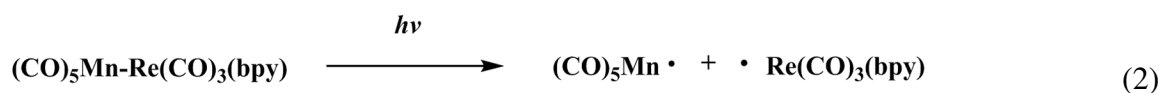


Figure 2. Optical spectrum of **D1** in ambient temperature MeCN solution. λ_{max} occur at 287 nm ($\epsilon = 2.12 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$) 341 nm (sh, $5.8 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$) and 483 nm ($5.1 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$)

An interesting side-product of this synthetic scheme was the bis(2,2'-bipyridine) dimer $[\text{Re}(\text{CO})_3(\text{bpy})]_2$ (**D2**) which was isolated in low yield and characterized by determining the X-ray crystal structure.²¹ The same compound had previously been reported by Fujita and Muckerman²² and structurally characterized by Benson and Kubiak.²³ The latter researchers isolated **D2** as a side product formed upon KC_8 reduction of **M1**.

Photolysis of D1: The excitation source was a green LED with output centered at 532 nm, where **D1** has an extinction coefficient of $2.4 \times 10^3 \text{ M}^{-1} \text{ cm}^{-1}$. Photolysis of aerobic acetonitrile solutions of **D1** led to bleaching of the MMLCT absorption (SI Fig. S3) as would be expected from photo-induced homolytic cleavage of the Mn-Re bond (eq. 2), followed by O_2 trapping of the resulting metal radicals. In contrast, analogous solutions of **D1** when kept in the dark proved to be quite stable with the absorbance at 483 nm decreasing less than 8% over a period of 16 h at 37 °C. The residual absorbance at 483 nm after exhaustive photolysis suggests that one or more photoproducts display absorbance in this spectral region, most likely due to metal-to-ligand charge transfer (MLCT) transition of a $\text{Re}^{\text{I}}(\text{bpy})$ moiety. The quantum yield (Φ_{dis}) for disappearance of the MMLCT absorbance of **D1** was determined to be 0.31 ± 0.01 from the linear plot of moles of complex reacted vs Einsteins of photons absorbed (SI Fig. S4).



Quantitative GC-TCD analysis of the gas phase after exhaustive photolysis at 532 nm of an aerobic MeCN solution of **D1** (3.18 mM in 4.0 mL, 0.0127 mmol) in a Schlenk cuvette²⁰ determined that the amount of CO released was 0.0117 mmol, which corresponds to 0.92 moles of CO per mole of **D1** depleted. The quantum yield of CO (Φ_{CO}) release under these conditions was measured independently as 0.27 ± 0.02 by measuring CO released at several time points during the photolysis (SI Fig. S5). The ratio between Φ_{CO} and Φ_{dis} is 0.87, consistent with release of 0.92 CO/**D1** consumed. In addition, the GC-TCD analysis found that the amount of CO_2 generated was 0.0107 mmol, that is, 0.85 moles of CO_2 released per mole of **D1** depleted. These results were surprising given the expectation that multiple CO's should be available for release upon oxidation of the manganese fragment $\cdot\text{Mn}(\text{CO})_5$. The relatively low quantum yield for CO release may be

partially due to dimerization of $\bullet\text{Mn}(\text{CO})_5$ radicals to form $\text{Mn}_2(\text{CO})_{10}$, a reaction known to occur at a nearly diffusion limited rate.²⁴ The latter product would be photo-inert to the 532 nm excitation used in the present experiment. (Based on our earlier studies,¹⁶ the Re moiety was not expected to release CO).

The dinuclear compound **D2** also proved to be quite photoactive when irradiated at 532 nm;²¹ however, this reaction was not probed quantitatively.

*Luminescence of **D1** and its photoproduct(s):* Figure 3 displays the luminescence spectra of **D1** in aerobic MeCN solution. The solution appeared to be very weakly emissive with a broad maximum centered at 555 nm ($\lambda_{\text{ex}} = 380$ nm). However, since compound **D1** has a quite high photo-fragmentation quantum yield under these conditions ($\Phi_{\text{dis}} = 0.31$), it is quite plausible that even this weak emission was the result of photoreaction triggered by the fluorimeter excitation source. To evaluate this possibility, the temporal emission intensity at 555 nm was recorded while using the continuous 380 nm excitation source of the PTI fluorimeter (Fig. 3 inset). Notably, the emission intensity increased nearly linearly with time. Extrapolation back to the starting time showed that **D1** is not emissive at all or at most very weakly emissive under these conditions and that even the residual emission seen in Figure 3 is indeed from photoproduct(s). Figure 4 displays the emission and excitation spectra of an exhaustively photolyzed aerobic MeCN solution of **D1**. Clearly, the photoproducts show a strong emission with $\lambda_{\text{max}} = 555$ nm with the excitation spectrum having a λ_{max} at 346 nm.

The temporal emission from the products after exhaustive photolysis of **D1** were recorded using a custom-built instrument at several monitoring wavelengths (λ_{mon}) over the range 450 - 600 nm. At each λ_{mon} , the decay was fit to simple exponential (SI Fig. S6). Although signal intensity was, as expected, a function of λ_{mon} across the emission spectrum, the lifetime at ambient temperature in each case was the same, $\tau_{\text{em}} = 135$ ns, suggesting that the photoproducts include only one emissive species which we will designate as **P1**.

*Further characterization of the **D1** photoproducts.* The ^1H NMR spectrum of the solution after **D1** was photolyzed at 532 nm in aerobic CD_3CN displays broadened proton resonances in the aromatic region ($\delta = 9.02, 8.48, 8.29, 7.72$ ppm) consistent with a bipyridine complex but different from those for **D1** (Fig. 5). The resulting peak broadening is a likely due to formation of a

paramagnetic species such as Mn^{2+} . The IR spectral changes recorded during photolysis (Fig. 6) show the disappearance of the strong ν_{CO} bands at 1890, 1945, 1997 and 2055 cm^{-1} characteristic of **D1** in MeCN

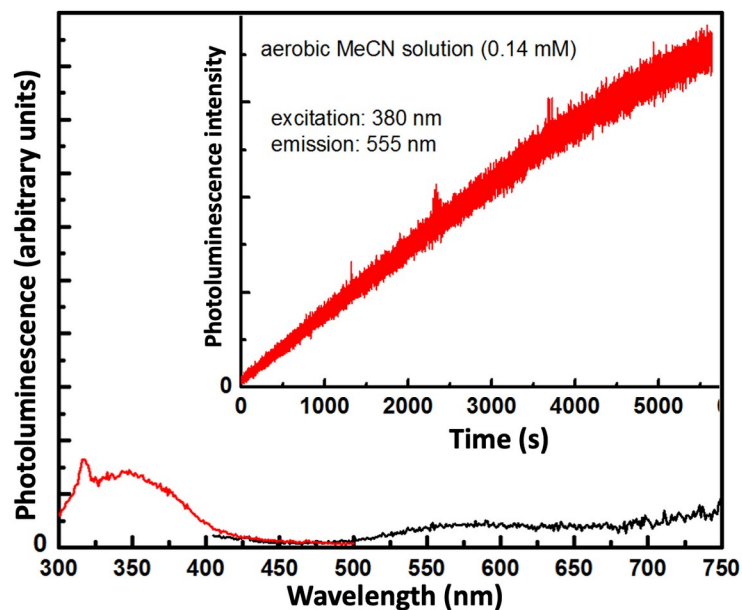


Figure 3. *Black:* Emission spectrum of **D1** in aerobic MeCN (0.165 mM) with $\lambda_{\text{ex}} = 380$ nm measured with a fresh solution. *Red:* The excitation spectrum of the same solution with the emission monitored at $\lambda_{\text{mon}} = 555$ nm. **Inset:** Temporal emission intensity at 555 nm of a solution initially containing **D1** (0.140 mM) in aerobic MeCN under 380 nm excitation in the fluorescence spectrometer.

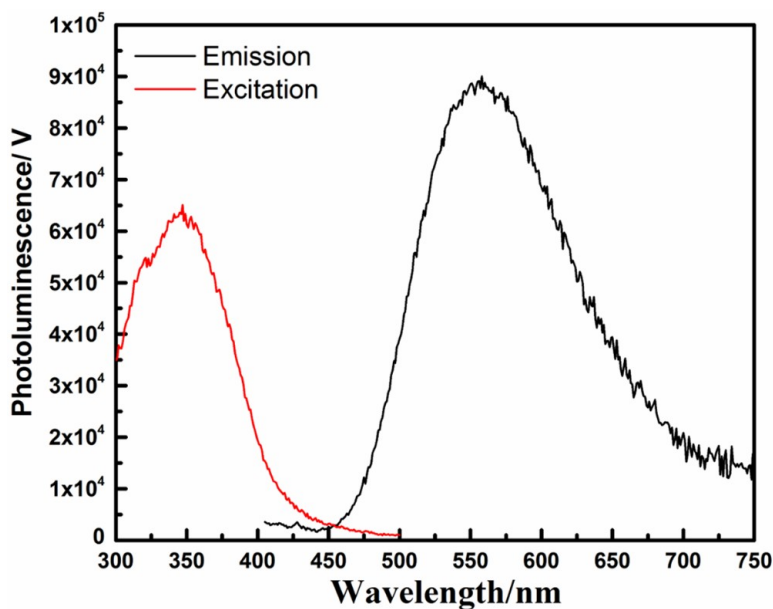


Figure 4. Emission spectrum ($\lambda_{\text{ex}} = 380$ nm) (black) and excitation spectrum ($\lambda_{\text{mon}} = 555$ nm) (red) after exhaustive photolysis at 532 nm of an aerobic MeCN solution of **D1** (initially 0.140 mM).

and the appearance of new bands at 1880, 1910, 1935, 2010 and 2040 cm^{-1} attributed to the photoproducts. The ESI+ mass spectrum of the product solution (SI Fig. S7) displayed strong signals consistent with the rhenium(I) fragments $\text{Re}(\text{CO})_3(\text{bpy})^+$ and $\text{Re}(\text{CO})_3(\text{bpy})(\text{CH}_3\text{CN})^+$.

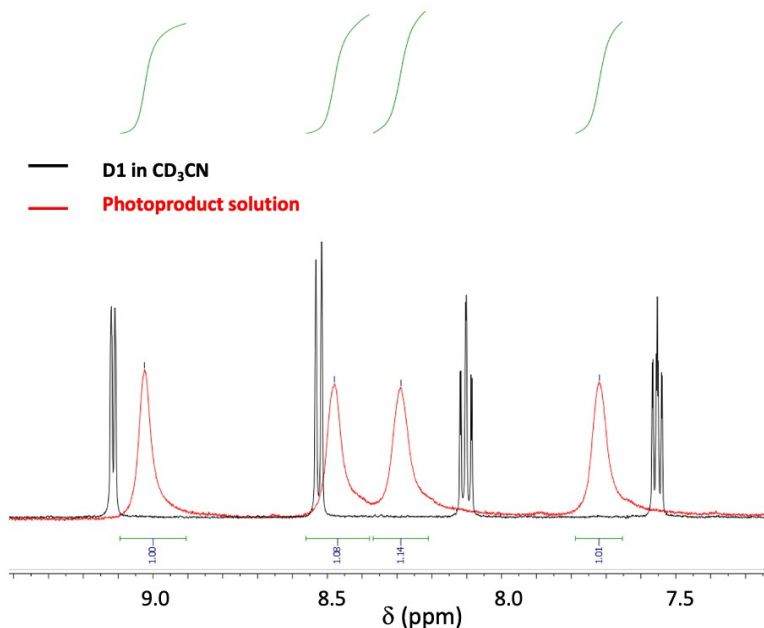
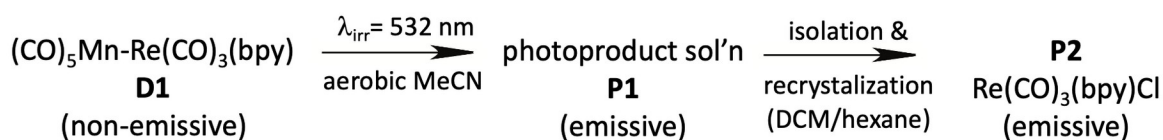


Figure 5. Black: ^1H NMR (500 MHz, CD_3CN) spectra of compound **D1**. Red: ^1H NMR of the photoproduct solution (**P1**) after exhaustive photolysis of **D1** in aerobic acetonitrile- d_3 ($\delta = 9.02, 8.48, 8.29, 7.72$ ppm).

Possible isolation and further characterization of the emissive photoproduct **P1** used chromatography with an activated alumina column. Crystallization was attempted by diffusing hexane into a dichloromethane (DCM) solution of isolated product. However, the overall result of this procedure was conversion of **P1** into another emissive species **P2** (Scheme 1), which was shown to have ^1H NMR and IR spectra consistent to those of synthesized *fac*- $\text{Re}(\text{CO})_3(\text{bpy})\text{Cl}$ (**M1**, SI Figs. S8 and S9),²³ the DCM presumably being the chloride source. Comparison of the ^1H NMR and IR spectra of **P1** to literature examples leads to the conclusion that **P1** is neither $[\text{Re}(\text{CO})_3\text{bpy}(\text{CH}_3\text{CN})]^+$ nor the dimer $[\text{Re}(\text{CO})_3\text{bpy}]_2$.^{23,25} However, although the $\text{Re}(\text{CO})_3(\text{bpy})$ moiety apparently remains intact, the exact identity of **P1** remains uncertain.



Scheme 1 Steps leading to photoproduct **P1** and to **P2** from **D1**.

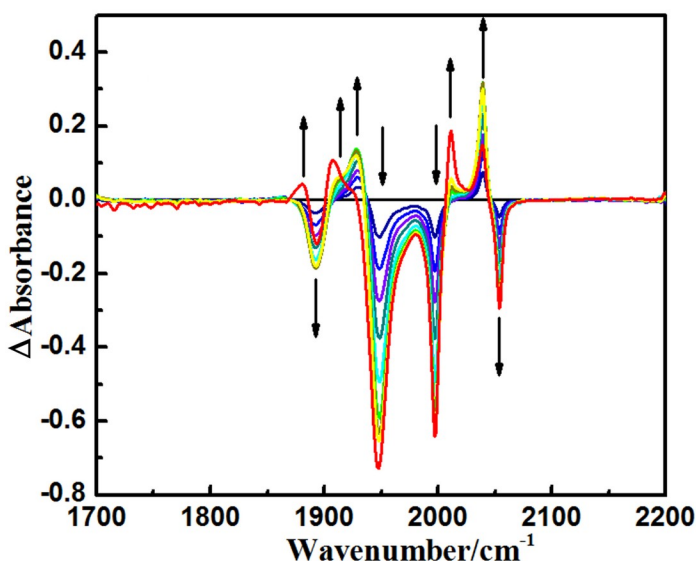


Figure 6. Difference IR spectral changes recorded during 532 nm photolysis of **D1** (4.2 mM) in aerobic MeCN in a 0.1 cm pathlength KBr cell. The negative peaks represent the consumption of **B** while positive peaks represent the formation **P1**.

Summary:

This study is a proof of principle example showing that compounds similar to **D1** can be theranostic, in this case undergoing photolysis-induced carbon monoxide release (i.e. is a photoCORM) while serving as a turn-on luminescent indicator of the photochemical event. In order to address possible biomedical applications of compounds such as **D1**, several issues need to be addressed. The first is biocompatibility, both in terms of being deliverable to targeted sites and of potential toxicity of the dimeric photoCORM. One may also be concerned with toxicity of the photoproducts, but in anti-cancer or anti-bacterial applications, photoproduct toxicity may be desirable. Another issue is the excitation wavelength needed to trigger cleavage of the metal-metal bond. While photolysis at 532 nm would be sufficient to deliver CO at a subcutaneous site, it would be inefficient with a deep tissue target such as a solid tumor owing to the relatively poor transmission of green light through mammalian tissue.¹³ Thus, it would be desirable to tune the MMLCT band to longer wavelengths into the phototherapeutic window. This task should be easily accomplished by

replacing the bpy of **D1** with a more conjugated diimine ligand or one with electron-withdrawing substituents.^{16,20}

Another issue would be developing a mechanism for delivery of theranostic compounds to the appropriate biological target(s). Implantation of a device based on some type of biocompatible polymer infused with the photoCORM would be a simple approach. This could be attached to an optical fiber so that the CO photo release could be activated upon demand.²⁶ An advantage of this method is that it would not be limited by the transmission properties of tissue. A less invasive approach would be to attach pendant groups to the dimers that enhance the solubility in biological media and target specific cellular types. Example of the latter are certain sugars and peptides that target tumors.^{17b,27} A third strategy would be to use a cellular Trojan Horse such as macrophage immune cells to carry a payload such as photoCORM loaded polymer microcarriers into tumor structures.²⁸ Like the first approach, the photoCORM would not need to be soluble in biological fluids but like the second strategy, activation by longer red or near-IR wavelengths would be highly desirable. Dinuclear photoCORMs of the type described here, and previously, would appear to be promising candidates for such approaches.

EXPERIMENTAL SECTION

Materials: Bromidopentacarbonylmanganese(I) ($\text{Mn}(\text{CO})_5\text{Br}$, 98%) and dirhenium decacarbonyl ($\text{Re}_2(\text{CO})_{10}$, 98%), were purchased from Strem Chemicals and used without further purification. The 2,2'-bipyridine (bpy, 99%) was purchased from Aldrich Chemicals and used without further purification.

Analytical Instrumentation: Solution optical absorption spectra were recorded in 1.0 cm path length quartz cells using Shimadzu dual beam UV-2401 PC spectrophotometer. Infrared spectra of solutions were recorded using a Mattson Research Series FTIR spectrometer. Solution NMR spectra were recorded using a Varian Unity Inova 500 MHz spectrometer or a 400 mHz Agilent 400-MR DD2 spectrometer using a 5 mm OneNMR broadband probe with pulsed field gradients. Exact molecular masses were measured using a Waters (Milford, Mass.) GCT Premier time-of-flight mass spectrometer with field desorption (FD) ion sources. Carbon monoxide release

was quantified using an Agilent 6890 gas chromatograph with a thermal conductivity detector (GC-TCD) as previously described.^{10c} The structures of solid-state single crystals were determined by X-ray diffraction on a Kappa Apex II single-crystal diffractometer. The X-ray structural data are summarized in the Supporting Information (SI Table S1).

Photochemical/photophysical procedures: Photolysis experiments were carried out using light emitting diodes (LEDs) from LUXEON Rebel as the excitation sources. Incident photon flux during irradiation was measured using Newport optical power/energy meter Model 8442 PE with a silicon photodiode Model 884-UVR detector. Irradiation time was controlled by shutter drive/timer UniBlitz Model SD-1000.

Photolyses were carried out on solutions contained in a custom-made Schlenk cuvette consisting of 1.0 cm square quartz cuvette fused to glass tubing and stopcocks designed for attachment to a vacuum line for degassing and for introducing or withdrawing gas samples.^{11a} Solutions for anaerobic experiments were degassed by freeze–pump–thaw (3x) procedures, after which the Schlenk cuvette was backfilled to 1.0 atm with purified argon. After photolysis, the gas was sampled by removing an aliquot with a gastight syringe and analyzing by GC–TCD. The overall CO released was calculated by taking into account the cell and solution volumes and CO solubility in the solvent.

Quantum yield (Φ) measurements followed the procedure described previously.¹⁶ Plots of molecules (or moles) reacted (N_{reacted} , calculated from absorption changes) vs photons (or Einsteins) absorbed (N_{abs} , calculated from the incident photon flux and the solution absorbance at λ_{irr}) were linear (SI Fig. S4). The Φ values were determined from the slopes of these N_{reacted} versus N_{abs} plots, corrected for dark reactions, which were very small.

Luminescence spectra were obtained using a Photon Technology International fluorimeter with an 814 PMT detection system at 1 nm resolution. This system is equipped a UV-Vis-NIR tunable excitation source and NIR emission can also be detected. Emission lifetimes were measured on a custom-built time-resolved optical spectroscopy instrument using a Spectra Physics Quanta-Ray Nd:YAG Q-switched laser operated at the third harmonic (355 nm) as the excitation source and a Hamamatsu model 1P28 PMT coupled to a LeCroy Waverunner LT 342 500MHZ oscilloscope for detection.

*Syntheses of the mononuclear complex $\text{Re}(\text{CO})_3(\text{bpy})\text{Cl}$: **M1*** was prepared from dirhenium decacarbonyl (1.000 g, 1.53 mmol) and bpy (0.716 g, 4.59 mmol) by refluxing in 2-chloroethanol (120 mL) for 18 h under argon. After removing the solvent under vacuum, the solid residue was dissolved in dichloromethane (50 mL) and washed with water (50 mL $\times$ 3). After removing the solvent under vacuum, the resulting yellow solid was dried in vacuum oven at 60 °C for 12 h. Yield: 1.085 g (76.8%). The ^1H NMR spectrum agreed with the literature²⁹ (500 MHz, CDCl_3 , ppm) δ = 9.08 (d, $J(\text{H,H})$ = 5.4 Hz, 2H), 8.20 (d, $J(\text{H,H})$ = 8.1 Hz, 2H), 8.09 (td, $J(\text{H,H})$ = 7.9, 1.6 Hz, 2H), 7.56 (ddd, $J(\text{H,H})$ = 7.5, 5.5, 1.2 Hz, 2H) (SI Fig. S1).

*Syntheses of the dinuclear complex $(\text{CO})_5\text{MnRe}(\text{CO})_3(\text{bpy})$: **D1*** was previously prepared by Stufkens and coworkers²⁰ from the reaction of the $\text{Mn}(\text{CO})_5^-$ anion with the mononuclear $\text{Re}(\text{I})$ complex *fac*- $\text{Re}(\text{CO})_3(\text{bpy})\text{Cl}$. However, in our hands, this procedure gave a low yield (~1%). Therefore, the alternative pathway shown in SI Scheme S1 was initiated, where the $[\text{Re}(\text{CO})_3(\text{bpy})^-]$ anion first prepared by the Na(Hg) reduction of **M1** (0.324 mmol) in tetrahydrofuran (THF) under argon. After 4 h, the resulting solution was transferred via cannula to a round bottom flask containing $\text{Mn}(\text{CO})_5\text{Br}$ (0.100 g, 0.365 mmol) dissolved in 35 mL of dry THF. The resulting solution was allowed to stir under argon in the dark at 40 °C for 12 h during which time the color changed from bright yellow to orange. The solvent was then removed under vacuum, and the residue was purified by flash chromatography over activated alumina. The column was washed with one column volume of pure hexanes, then eluted with a gradient of DCM/hexanes (0%-50% DCM). The main component from the column chromatography purification was collected and was further purified by recrystallization from DCM by slow vacuum evaporation of solvent giving a crystalline product (**D1**) with a yield of 43 mg (15%).

The NMR spectrum (500 MHz) of **D1** in acetonitrile- d_3 displayed proton resonances at δ (ppm) 9.12 (d, $J(\text{H,H})$ = 5.6 Hz, 2H), 8.52 (d, $J(\text{H,H})$ = 8.3 Hz, 2H), 8.10 (td, $J(\text{H,H})$ = 8.2, 1.5 Hz, 2H), 7.56 (ddd, $J(\text{H,H})$ = 7.1, 5.7, 1.2 Hz, 2H) (Fig. S1) and the ATR-IR spectrum of solid **D1** displayed ν_{CO} bands at 2053(s), 1984(s), 1949(s), 1922(s), 1875(s), 1860(s). The molar mass of **D1** was determined as 621.87 m/z by FD+ mass spectrum (calculated: 621.92 m/z) (Fig. S2). The UV-visible spectrum (Fig. 2) in MeCN solution displays an absorption band at λ_{max} 483 nm attributed to a MMLCT ($\sigma_{\text{MM}} \rightarrow \pi\text{L}^*$) transition in analogy to related dinuclear complexes.¹⁶ X-ray

suitable crystals were grown by diffusing hexane vapor into an MeCN solution of **D1**. The crystals are monoclinic. Complete parameters including bond lengths and angles are listed in the SI (Table S1)

Associated Content

Supporting Information: nine figures; a table presenting the crystal structure data for compound **D1**; scheme illustrating the synthesis of **D1**.

Author Information

Corresponding Author: Peter C. Ford
email: pcford@ucsb.edu
ORCID: Peter C. Ford: 0000-0002-5509-9912

Author: Zhi Li
email: lizhi86chem@gmail.com
ORCID: Zhi Li: 0000-0002-8799-0283

Author: Guang Wu
email: wuucsb@ucsb.edu

Author Contributions:

P. C. Ford helped conceive of the project, provided funding, and wrote the final draft. Z. Li also contributed to planning the experiment, carried out the bulk of the experimental studies, and wrote the first draft. G. Wu carried out the X-ray crystal structure studies. All authors read the final draft and approved of it.

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Author contributions:

Conflict of interest statement: The authors have no conflict of interest to declare.

References:

1. T. Sjöstrand, *Scand. J. Clinical and Laboratory Investigation* **1**, 201–214 (1949); *Nature* **164**, 580-581 (1949).
2. (a) R. Motterlini, L.E. Otterbein. *Nat. Rev. Drug Discov.* **9**, 728–743 (2010). (b) D. Babu, R. Motterlini, R. A. Lefebvre. *Brit. J. Pharmacol.* **172**, 1557-1573 (2015). (c) N. Bauer, Q. Y. Mao, A. Vashistha, A. Seshadri, Y. C. N. Du, L. Otterbein, C. L. Tan, N. P. de Caestecker, B. H. Wang. *Med. Res. Rev.* **45**, 1275-1301(2025).
3. (a) J. M. Fukuto, S. J. Carrington, D. J. Tantillo, J. G. Harrison, L. J. Ignarro, B. A. Freeman, A. Chen, D. A. Wink. *Chem. Res. Toxicol.* **25**, 769–793 (2012). (b) Z. Yaun, L. K. De La Cruz, X. Yang, B. H. Wang. *Pharmacol. Rev.*, **74**, 823-873 (2022). (c) Z. Li, Y. Wang, M. Liu, Y. Pan, Z. Ni, Q. Min, B. Wang, H. Ke, X. Ji. *J. Med. Chem.* **66**, 14583-14596 (2023). (d) A. M. Mansour, R. M. Khaled, O. R. Shehab. *Dalton Trans.* **53**, 19022-19057 (2024).
4. (a) I. Nassour, B. Kautza, M. Rubin, D. Escobar, J. Luciano, P. Loughran, H. Gomez, J. Scott, D. Gallo, J. Brumfield, L. E. Otterbein, B. S. Zuckerbraun. *Shock*. **43**, 166-171 (2015). (b) C. C. Romão, S. S. Mendes, C. Rebelo, S. M. Carvalho, L. M; Saraiva. *Dalton Trans.*, **53**, 11009-1102 (2024). (c) S. Bansal, D. N. Liu, Q. Y. Mao, N. Bauer, B. H. Wang. *J. Medicinal Chem.* **67**, 9789-9815 (2024).
5. (a) L. E. Otterbein, B. S. Zuckerbraun, M. Haga, F. Liu, R. Song, A. Usheva, C. Stachulak, N. Bodyak, R. N. Smith, E. Cszmadia, S. Tyagi, Y. Akamatsu, R. J. Flavell. T. R. Billiar, E. Tzeng, F. H. Bach. A. M. K. Choi, M. P. Soares. *Nat Med.* **9**, 183–190 (2003). (b) T. Obara, H. Yamamoto, T. Aokage, T. Igawa, T. Nojima, T. Hirayama,

- M. Seya, M. Ishikawa-Aoyama, A. Nakao, R. Motterlini, H. Naito. *Transplantation*, **106**, 1365-1375 (2022).
6. (a) M. H. Norahan, S. C. Pedroza-Gonzalez, M. G. Sanchez-Salazar, M. M. Alvarez, G. Trujillo de Santiago, *Bioactive materials*, **24**, 197-235 (2023). (b) Y. Duan, L. Li, J. Hu, B. Zheng, K. He, *Chembiochem*, **26**, e202400790 (2025)
 7. (a) S. W. Ryter, D. Morse, A. M. K. Choi. *Am. J. Respir. Cell Mol. Biol.* **36**, 175-182 (2007). (b) J. Ma, Y. Tian, Y. B. Chen, X. D. Zhang, C. Y. Ding, Z. Y. Lin. *Colloid Interfac. Sci. Commun.* **65**, 100820 (2025)
 8. (a) J. L. Wilson, H. E. Jesse, R. K. Poole, K. S. Davidge. *Curr. Pharm. Biotechnol.* **13**, 760-768 (2012). (b) P. V. Simpson, C. Nagel, H. Bruhn, U. Schatzschneider. *Organometallics*. **34**, 3809–3815 (2015). (c) L. S. Nobre, H. Jeremias, C. C. Romão, L. M. Saraiva. *Dalton Trans.* **45**, 1455–1466 (2016). (d) S. McMahon, A. Rajagopal, S. Amirjalayer, Y. Halpin, D. Fitzgerald-Hughes, W.J. Buma, J. Wybren, S. Woutersen, C. Long, M. T. Pryce. *J. Inorg. Biochem.* **208**, 111071 (2020). (e) J. Cheng, J. M. Hu. *ChemMedChem*. **16**, 3628-3634 (2021). (f) L. Wang, W. Zhong, B. Liu, D. Pranantyo, M. B. Chan-Park. *ACS Appl. Mater. Interfaces* **15**, 41772–41782 (2023). (g) Y. R. Lai, L. Wang, H. B. Ma, Z. Chen, W. R. Wu, G. Q. Wen, X. Wu, B. L. Yu, D. Li, G. T. Yuan, H. Y. Huang, P. Y. Zhang. *J. Am. Chem. Soc.* **147**, 19353-19363 (2025)
 9. B. Chance, M. Erecinska, M. Wagner. *Ann. N. Y. Acad. Sci.* **174**, 193–204 (1970).
 10. (a) C. C. Romão, W. A. Blaettler, J. D. Seixas, G. J. L. Bernardes. *Chem. Soc. Rev.* **41**, 3571-3583 (2012). (b) U. Schatzschneider. *Br J Pharmacol.* **172**, 1638–1650 (2015). (c) A. L. Amorim, M. M. Peterle, A. Guerreiro, A. L. Amorim, M. M. Peterle, A. Guerreiro, D. F. Coimbra, R. S. Heying, G. F. Caramori, A. L. Braga, A. J. Bortoluzzi, A. Neves, G. J. L. Bernardes, R. A. Peralta. *Dalton Trans.* **48**, 5574-5584 (2019). (d) J. A. Barrett, Z. Li, E. Wien, J. V. Garcia, D. Zheng, C. Hunt, L. Ngo, L. Sepunaru, A. V. Iretskii, P. C. Ford. *Royal Society Open Science* **8**, 211022 (2021). (correction: *Royal Society Open Science* **10**, 231206 (2023)). (e) X. Ning, X. Zhu, Y. Wang, J. Yang. *Bioactive Materials* **37**, 30–50 (2024).
 11. (a) R. D. Rimmer, H. Richter, P. C. Ford. *Inorg. Chem.* **49**, 1180–1185 (2010). (b) R. D. Rimmer, A. E. Pierri, P. C. Ford. *Coord. Chem. Rev.* **256**, 1509–1519 (2012). (c) A. E. Pierri, D. A. Muizzi, A. D. Ostrowski, P. C. Ford. *Struct. Bond.* **165**, 1-45 (2015). (d) P. C. Ford. *Coord. Chem. Rev.* **376**, 548-564 (2018).
 12. (a) U. Schatzschneider. *Inorg. Chim. Acta.* **374**, 19–23 (2011). (b) I. Chakraborty, S. J. Carrington, P. K. Mascharak. *Acc. Chem. Res.* **47**, 2603-2611 (2014). (c) L. S. Lazarus, A. D. Benninghoff, L. M. Berreau. *Acc. Chem. Res.* **53**, 2273-2285 (2020). (d) M. N. Pinto, P. K. Mascharak. *J. Photochem. Photobiol. C--Photochem Rev.* **42**, 100341 (2020). (e) M. F. Wang, K. Murata, Y. Koike, G. Jonusauskas, A. Furet, D. M. Bassani, D. Saito, M. Kato, Y. Shimoda, K. Miyata, K. Onda, K. Ishii, *Chem. Europ. J.* **28**, e202200716 (2022) (f) P. K.; Singh, R. Mengji, S. Kumar, A. K. Singh, A. Jana, S. P. Singh. *ACS Applied Bio Materials* **6**, 3778-3789 (2023). (g) M. X.; Hu, H. F. Zhou, Z. X. Wang, Y. Q. Du, Y. W.; Wang, C. Eerdun, B. H. Zhu. *J. Coord. Chem.* **76**, 61-75 (2023). (h) J. M. Wang, J. Y. Li, X.H. Shi, Z. G. Wang, L. Zeng, D.W. Pang, L. Huang, S. L. Liu. *J. Am. Chem. Soc.* **147**, 5459-5471 (2025).
 13. (a) K. König. *J. Microscopy.* **200**, 83–104 (2000). (b) A. Alabugin, *Photochem. Photobiol.* **96**, 722-732 (2019).
 14. A. E. Pierri, P-J. Huang, J. V. Garcia, J. G. Stanfill, M. Chui, G. Wu, N. Zheng, P. C. Ford. *Chem. Commun.* **51**, 2072-2075 (2014).
 15. Q. Jiang, Y. Xia, J. Barrett, A. Mikhailovsky, G. Wu, D. Wang, P. Shi, P. C. Ford. *Inorg. Chem.* **58**, 11066-11075 (2019).
 16. Z. Li, A. E. Pierri, P-J. Huang, G. Wu, A. V. Iretskii. *Inorg. Chem.* **56**, 6094-6104 (2017) (Correction: *Inorg. Chem.* **57**, 6191 (2018)).
 17. (a) J. J. Wilson. *Adv. Inorg. Chem.*, **80**, 35-94 (2022). (b) L. C-C. Lee, K. K-W. Lo. *Adv. Inorg. Chem.* **80**, 35-94 (2022).
 18. (a) S. C. Marker, S. N. MacMillan, W. R. Zipfel, Z. Li, P. C. Ford, J. J. Wilson. *Inorg. Chem.* **57**, 1311-1331(2018). (b) G.-X. Xu, E. C.-L. Mak, K. K.-W. Lo. *Inorg. Chem. Frontiers*, **8**, 4553-4579 (2021). (c) C. C. Romão, S. S. Mendes, C. Rebelo, S. M. Carvalho, L. M. Saraiva. *Dalton Trans.* **53**, 11009-11020 (2024).
 19. M. S. Wrighton, D. L. Morse, H. B. Gray, D. K. Ottesen. *J. Am. Chem. Soc.* **98**, 1111–1119 (1976).
 20. J. W. M. Van Outersterp, F. Hartl, D. J. Stufkens. *Organometallics* **14**, 3303–3310 (1995).
 21. S. Kulkarni, M.S. Thesis, University of California, Santa Barbara (2023)
 22. E. Fujita, J. T. Muckerman. *Inorg. Chem.* **43**, 7636-7647 (2004).

23. E. E. Benson, C. P. Kubiak, *Chem. Commun.* **48**, 7374–7376 (2012).
24. J. L Hughey, C. P. Anderson, T. J. Meyer. *J. Organomet. Chem.* **125**, C49-C52 (1977)
25. A. Woźna, A. Kapturkiewicz, *Phys. Chem. Chem. Phys.* **17**, 30468–30480 (2015).
26. (a) J. B. Wolinsky, Y. L. Colson, M. W. Grinstaff. *J. Controlled Release* **159**, 14–26 (2012). (b) B. P. Timko, M. Arruebo, S. A. Shankarappa, J. B. McAlvin, O. S. Okonkwo, B. Mizrahi, C. F. Stefanescu, L. Gomez, J. Zhu, A. Zhu, J. Santamaria, R. Langer, D. S. Kohane. *Proc. Natl. Acad. Sci. USA* **111**, 1349–1354 (2014).
27. (a) K. N. Sugahara, T. Teesalu, P. P. Karmali, V. R. Kotamraju, L. Agemy, O. M. Girard, D. Hanahan, R. F. Mattrey, E. Ruoslahti. *Cancer Cell*, **16**, 510–520 (2009). b) E. S. Levy, D. P.; Morales, J. V. Garcia, N. O. Reich, P. C. Ford, *Chem. Commun.* **51**, 17692–17695 (2015).
28. (a) M. M. C. Kwan, N.B.Day, I. R. Konigsberg, E. Thoresen, A. G. Harrell, C. E. Busch, E. J. Davidson, I. V. Yang, C.W. Shields. *Adv. Healthcare Mat.* (2025) 10.1002/adhm.202501348. (b) M.A. Evans, P.-J. Huang, Y. Iwamoto, K.N. Ibsen, E.M. Chan, Y. Hitomi, P.C. Ford, S. Mitragotri. *Chemical Science* **9**, 3729-3741 (2018).
29. X. Yi, J. Zhao, J. Sun, S. Guo, H. Zhang. *Dalton Trans.* **42**, 2062–2074 (2013).

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