Dalton Transactions

PAPER

View Article Online
View Journal

Cite this: DOI: 10.1039/c6dt01709f

Solution or solid – it doesn't matter: visible light-induced CO release reactivity of zinc flavonolato complexes†

Stacey N. Anderson, Michael T. Larson and Lisa M. Berreau*

Received 1st May 2016,
Accepted 23rd August 2016

DOI: 10.1039/c6dt01709f

www.rsc.org/dalton

Two types of zinc flavonolato complexes ([(6-Ph_2TPA)Zn(flavonolato)]ClO_4 and Zn(flavonolato)$_2$) of four extended flavonols have been prepared, characterized, and evaluated for visible light-induced CO release reactivity. Zinc coordination of each flavonolato anion results in a red-shift of the lowest energy absorption feature and in some cases enhanced molar absorptivity relative to the free flavonol. The zinc-coordinated flavonolato ligands undergo visible light-induced CO release with enhanced reaction quantum yields relative to the neutral flavonols. Most notable is the discovery that both types of zinc flavonolato derivatives undergo similar visible light-induced CO release reactivity in solution and in the solid state. A solid film of a Zn(flavonolato)$_2$ derivative was evaluated as an *in situ* CO release agent for aerobic oxidative palladium-catalyzed alkoxycarbonylation to produce esters in ethanol. The CO release product was found to undergo ester alcolysis under the conditions of the carbonylation reaction.

Introduction

Delivery of controlled amounts of carbon monoxide (CO) is of significant current interest both in biology and synthetic chemistry. In humans, CO is produced endogenously *via* the enzyme-catalyzed breakdown of heme.[1] Studies of the effects of CO have demonstrated its potential to produce a variety of beneficial health outcomes including anti-inflammatory, anti-apoptotic, vasodilation, and anti-bacterial effects.[2,3] To explore the biology of CO and its possible uses as a therapeutic, CO-releasing molecules (CORMs) have been developed for the delivery of controlled amounts of CO.[4] To date, the majority of CORMs investigated have been metal carbonyl compounds (MCCs), with the most extensively studied being [Ru(CO)$_3$(glycinate)Cl] (CORM-3).[5] This compound coordinates to histidine residues of proteins and spontaneously releases CO *via* ligand exchange.[6–8] Other MCC CORMs release CO *via* enzyme-induced reactivity,[9,10] magnetic heating,[11] or *via* visible light-induced reactivity (photoCORMs).[12–14] CORMs that can be controlled in terms of their CO release reactivity are especially attractive as they offer the opportunity for localized release of CO at specific sites for biological studies or therapeutic purposes.

To address issues of solubility and concerns regarding the use of redox-active and heavy metals in MCCs, efforts to encapsulate these compounds in micelles, dendrimers, and solid supports have been reported.[11,15–19] Efforts to develop metal-free organic photoCORMs have also advanced.[20–23] The development of organic photoCORMs holds significant promise as standard approaches employed in medicinal chemistry for tuning and targeting could be possible.[24–26]

CO-releasing molecules are also of significant current interest for applications in synthetic organic chemistry. Due to the health hazards of handling CO gas, efforts in recent years have focused on the development of molecules that release CO on demand for synthetic applications, such as palladium-catalyzed carbonylation reactions.[27–32] The majority of the CO release compounds currently being used in synthetic organic applications either are used in an *ex situ* fashion or are used *in situ* but require the introduction of additional reagents, microwave irradiation, or heating to induce CO release. *Ex situ* approaches require either the use of specialized two-chamber glassware to separate the CO-generation process from the substrate reaction chamber,[27–31] or manual transfer of the gas (*e.g. via* a balloon).[32] *In situ* sources for CO have also been previously reported. These include metal carbonyls (*e.g.* Mo(CO)$_6$), which can serve as *in situ* CO release agents for palladium-catalyzed carbonylations, albeit not at a stoichiometric level with respect to CO.[33–43] When metal carbonyls are used, additional reagents, high temperatures and/or microwave assistance are generally needed for CO release. It is also important to note that low valent metal carbonyls typically cannot be used *in situ*

Department of Chemistry & Biochemistry, Utah State University, 0300 Old Main Hill, Logan, UT 84322-0300, USA. E-mail: lisa.berreau@usu.edu

† Electronic supplementary information (ESI) available: Spectra and additional experimental details. See DOI: 10.1039/c6dt01709f

for substrates containing functional groups that can be reduced (*e.g.* $-NO_2$ derivatives) due to the reducing nature of the low valent metal complex.[34–40,44] Two chamber systems can be used to address this issue.[45] Formamides[46] (including *N*-formylsaccharin[47,48]), formates and formic acid[49,50] derivatives, as well as $CHCl_3$,[51] and diethylpyrocarbonate[52,53] have been recently investigated as *in situ* CO release agents at near stoichiometric levels. However, all of these CO release compounds require either significant heat (formamides and formic acids, diethylpyrocarbonate), or the presence of additional reagents (*e.g.* *N*-formylsaccharin, mild base or KF); formates (mild base); formic acid (strongly acidic conditions); $CHCl_3$ (metal hydroxide) to induce CO release.

An area that has seen little development is that of solid compounds capable of visible light-induced CO release. Such compounds could offer the possibility of CO release materials that could have tremendous advantages for both biological and synthetic applications. Mascharak recently reported two visible light-induced MCC photoCORMs that undergo solid-state CO release.[54] However, the quantity of CO released and the byproducts of this reactivity have not been reported.

Our laboratory is developing visible light-induced CO release compounds based on the 3-hydroxy-4-flavone moiety found in naturally occurring flavonols. Prior to our work, metal flavonolato species were well known to undergo dioxygenase-type degradation to release CO *via* either enzyme catalysis[55] or thermal reactivity[56] involving O_2 activation. However, reports of light-driven CO release reactivity involving O_2 activation with either free or metal-coordinated flavonols were scarce.[57] We recently reported a new family of neutral flavonol derivatives (**1–4**, Fig. 1) that undergo dioxygenase-type visible light-induced quantitative CO release when dissolved in organic solvents or organic/aqueous mixtures.[58] As shown in Table 1, members of this class of compounds exhibit CO release under aerobic and/or anaerobic conditions. These flavonol derivatives are fluorescent and therefore trackable in cells. Compound **1** has been demonstrated to penetrate cells and then undergo CO release upon exposure to visible light. The structural framework in **1–4** also offers the opportunity for chelation to a metal center as a means of tuning the reactivity of the CO-releasing moiety. In the studies reported herein, we have used a supporting ligand structural template from our laboratory that has been employed in studies of other metal flavonolato compounds[59–61] to evaluate how zinc stabilization of **1–4** affects CO release reactivity. Key findings include that zinc coordination: (1) red shifts the absorption spectral features of the compounds, with some being in the therapeutic window (>650 nm), (2) significantly enhances the quantum yield for visible light-induced CO release, and (3) enables solid-state CO release activity that is identical to the reactivity seen in solution. The discovery of visible light-induced solid-state CO release reactivity is particularly significant as it suggests that CO release materials based on a zinc flavonolato motif could be developed. Building on this discovery, we sought to design zinc flavonolato derivatives that are insoluble in organic solvents, which could facilitate their use as *in situ* light-driven CO release agents in synthetic organic processes. Our experience with simple Zn(II) bis-flavonolato compounds ($Zn(flavonolato)_2$) suggested that such compounds could exhibit the desired minimal solubility.[59] Therefore derivatives of this type using **1–4** were synthesized, characterized, and evaluated as solid-state CO release agents. As outlined herein, we have found that a member of this family can be used in aerobic oxidative palladium-catalyzed carbonylation processes that employ O_2 as the sole oxidant and are performed under very mild conditions.[62] Overall, our results suggest that the structural motif in **1–4** is a highly versatile CO release unit that can be developed for various CO release applications.

Table 1 Properties of **1–4**

Compound	λ_{max} [a] (nm) ε (M^{-1} cm^{-1})	Aerobic CO release[b]	Φ[c]	Anaerobic CO release
1	409 (16 600)	Yes	0.007(3)	No
2	442 (51 000)	Yes	0.006(1)	No
3	478 (36 700)	Yes	0.43(3)	No
4	544 (85 500)	Yes	[d]	Yes

[a] Most red-shifted absorption feature. [b] Measured in acetonitrile in the presence of air. [c] Average of three independent trials; values in parenthesis represent standard error. [d] Quantum yield for CO release not reported due to concurrent aerobic and anaerobic CO release reactions.

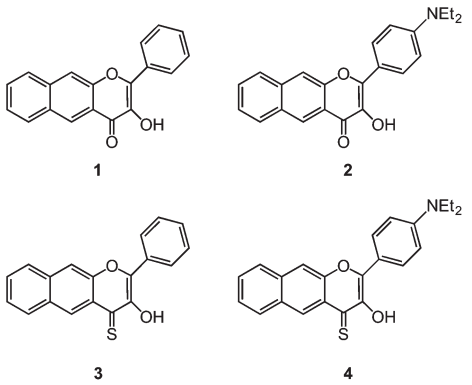


Fig. 1 Structures of flavonol-based CO-releasing molecules.

Experimental section

General

Chemicals and reagents. All chemicals and reagents were obtained from commercial sources and used as received unless otherwise noted. The synthesis of the extended flavonols **1–4** proceeded as previously reported.[58] The 6-Ph_2TPA (*N*,*N*-bis((6-phenyl-2-pyridyl)methyl)-*N*-((2-pyridyl)methyl)amine) ligand was prepared and purified as previously described.[63]

Physical methods. Anaerobic procedures were performed in a Vacuum Atmospheres glovebox under N_2. Solvents for glovebox use were dried according to published methods and dis-

tilled under N_2.[64] UV-vis spectra were recorded at room temperature using a Hewlett-Packard 8453A diode array spectrophotometer. Fluorescence emission spectra were collected using a Shimadzu RF-530XPC spectrometer in the range of 400–800 nm with the excitation wavelength corresponding to the most red shifted absorption maximum of the compound. Infrared spectra were recorded using a Shimadzu FTIR-8400 as KBr pellets. Water was present in the KBr used for all IR samples. ^{1}H NMR spectra (in ppm) are referenced to the residual solvent peaks in acetonitrile-d_3 or pyridine-d_5. J values are given in Hz. Mass spectral data was collected at the Mass Spectrometry Facility, University of California, Riverside. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA, or by Robertson Microlit Laboratories, Ledgewood, NJ. Photochemical experiments were performed using a Luzchem photoreactor equipped with RPR-4190A, RPR-5750A, or Sylvania cool white lamps. Carbon monoxide quantification was performed by gas chromatography as previously described.[61] Quantum yields were determined by potassium ferrioxalate or potassium reineckate actinometry using an integrative analysis method.[65–67] The output measured during the quantum yield determination for **5** was 1.46091×10^{17} photons per s when illuminated with RPR-4190A lamps and for **6**, **7**, and **8** was 6.87824×10^{15} photons per s when illuminated with white light lamps equipped with 546 nm cut off filters.

Caution! Perchlorate salts of metal complexes with organic ligands are potentially explosive. Only small amounts of material should be prepared, and these should be handled with great care.[68]

Synthesis of 5–8

In a N_2-filled glovebox, a methanolic solution (2 mL) of Zn$(ClO_4)_2{\cdot}6H_2O$ (0.0500 g, 0.134 mmol) was added to solid 6-Ph$_2$TPA (0.0594 g, 0.134 mmol) and the resulting mixture was stirred until all of the chelate ligand dissolved. The solution was then added to a methanolic solution (2 mL) containing **1**, **2**, **3**, or **4** (0.134 mmol) and $Me_4NOH{\cdot}5H_2O$ (0.0243 g, 0.134 mmol). The mixture was allowed to stir for 4 hours at ambient temperature. The solvent was then removed under reduced pressure and the residual solid was dissolved in CH_2Cl_2. The solution was then filtered through a Celite/glass-wool plug and the final product was precipitated by the addition of excess hexanes. Each solid product was dried under reduced pressure.

[(6-Ph$_2$TPA)Zn(1$^-$)]ClO$_4$ (5). Orange solid (89%). ^{1}H NMR (CD_3CN, 300 MHz) δ 8.62 (d, J = 5.1 Hz, 1H), 8.27 (d, J = 6.0 Hz, 2H), 8.21 (s, 1H), 8.14 (s, 1H), 8.07–7.99 (m, 2H), 7.96 (t, J = 7.5 Hz, 1H), 7.78 (t, J = 7.8 Hz, 2H), 7.67–7.35 (m, 9H), 7.33 (d, J = 7.8 Hz, 2H), 7.18–7.09 (m, 4H), 7.06–6.85 (m, 6H) 4.92 (d, J = 14.7 Hz, 2H), 4.57 (d, J = 14.7 Hz, 2H), 4.43 (s, 2H) ppm. FTIR (KBr, cm^{-1}) 1094 (ν_{ClO_4}), 622 (ν_{ClO_4}). UV-vis (CH_3CN) nm (ε, M^{-1} cm^{-1}) 480 (6300), 384 (1700). ESI/APCI-MS, m/z (relative intensity) 793.2152, calc. 793.2157 ([M − ClO$_4$]$^+$, 34%). Anal. Calc. $C_{49}H_{37}N_4O_7ClZn{\cdot}0.7CH_2Cl_2$: C, 62.56; H, 4.06; N, 5.87. Found: C, 62.62; H, 4.26; N, 6.16. The presence and quantity of dichloromethane in the elemental analysis sample was confirmed through integration of the CH_2Cl_2 resonance in the ^{1}H NMR spectrum.

[(6-Ph$_2$TPA)Zn(2$^-$)]ClO$_4$ (6). Orange-red solid (93%). ^{1}H NMR (CD_3CN, 300 MHz) δ 8.50 (d, J = 4.8 Hz, 1H), 8.31 (d, J = 9.3 Hz, 2H), 8.22 (s, 1H), 8.09 (s, 1H), 8.05–7.93 (m, 2H), 7.85 (t, J = 7.8 Hz, 1H), 7.78 (t, J = 7.5 Hz, 2H), 7.64–7.45 (m, 4H), 7.44–7.34 (m, 3H), 7.31–7.21 (m, 5H), 7.11 (t, J = 7.5 Hz, 2H), 7.01 (t, J = 7.5 Hz, 4H), 6.80 (d, J = 9.0 Hz, 2H), 4.93 (d, J = 14.4 Hz, 2H), 4.54 (d, J = 14.4 Hz, 2H), 4.37 (s, 2H), 3.51 (q, J = 7.2 Hz, 4H), 1.24 (t, J = 7.2 Hz, 6H) ppm. FT-IR (KBr, cm^{-1}) 1088 (ν_{ClO_4}), 618 (ν_{ClO_4}). UV-vis (CH_3CN) nm (ε, M^{-1} cm^{-1}) 524 (80 000). ESI/APCI-MS, m/z (relative intensity) 864.2887, calc. 864.2882 ([M − ClO$_4$]$^+$, 7%). Anal. Calc. $C_{53}H_{46}N_5O_7ClZn{\cdot}3H_2O$: C, 62.42; H, 5.14; N, 6.87. Found: C, 62.20; H, 4.65; N, 6.94. The presence and quantity of water in the elemental analysis sample was confirmed through integration of the H_2O resonance in the ^{1}H NMR spectrum.

[(6-Ph$_2$TPA)Zn(3$^-$)]ClO$_4$ (7). Dark red solid (93%). ^{1}H NMR (CD_3CN, 300 MHz) δ 8.80 (s, 1H), 8.47–8.39 (m, 2H), 8.38–8.30 (m, 2H), 8.13 (d, J = 9.0 Hz, 1H), 8.05 (d, J = 9.0 Hz, 1H), 7.85 (t J = 7.8 Hz, 1H), 7.79 (t, J = 7.8 Hz, 2H), 7.64 (t, J = 6.6 Hz, 1H), 7.60–7.52 (m, 4H), 7.43 (t, J = 6.6 Hz, 5H), 7.28 (d, J = 6.9 Hz, 5H), 7.08 (t, J = 7.2 Hz, 2H), 6.99 (t, J = 7.2 Hz, 4H), 4.82 (bd, J = 14.4 Hz, 2H), 4.49 (bd, J = 14.4 Hz, 2H), 4.41 (s, 2H) ppm. FT-IR (KBr, cm^{-1}) 1086 (ν_{ClO_4}), 619 (ν_{ClO_4}). UV-vis (CH_3CN) nm (ε, M^{-1} cm^{-1}) 550 (9300), 396 (7200). ESI/APCI-MS, m/z (relative intensity) 809.1930, calc. 809.1923 ([M − ClO$_4$]$^+$, 25%). Anal. Calc. $C_{49}H_{37}N_4O_6ClSZn{\cdot}0.5H_2O{\cdot}1CH_2Cl_2$: C, 59.77; H, 4.01; N, 5.58. Found: C, 59.29; H, 3.51; N, 5.57. The presence and quantity of water and dichloromethane in the elemental analysis sample was confirmed through integration of the respective resonances in the ^{1}H NMR spectrum.

[(6-Ph$_2$TPA)Zn(4$^-$)]ClO$_4$ (8). Dark blue solid (91%). ^{1}H NMR (CD_3CN, 300 MHz) δ 8.69 (s, 1H), 8.58 (d, J = 9.3 Hz, 2H), 8.43 (d, J = 5.4 Hz, 1H), 8.21 (s, 1H), 8.10 (d, J = 8.1 Hz, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.89–7.77 (m, 3H), 7.64–7.42 (m, 10H), 7.38 (t, J = 7.2 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 7.24–7.17 (m, 2H), 7.16–7.07 (m, 4H), 6.86 (d, J = 9.3 Hz, 2H), 4.83 (d, J = 13.8 Hz, 2H), 4.49 (d, J = 13.8 Hz, 2H), 4.41 (s, 2H), 3.54 (q, J = 7.2 Hz, 4H), 1.23 (t, J = 7.2 Hz, 6H) ppm. FT-IR (KBr, cm^{-1}) 1084 (ν_{ClO_4}), 622 (ν_{ClO_4}). UV-vis (CH_3CN) nm (ε, M^{-1} cm^{-1}) 600 (111 700). ESI/APCI-MS, m/z (relative intensity) 880.2659, calc. 880.2658 ([M − ClO$_4$]$^+$, 15%). Anal. Calc. $C_{53}H_{46}N_5O_6ClSZn{\cdot}H_2O$: C, 63.67; H, 4.84; N, 7.00. Found: C, 63.37; H, 4.57; N, 6.75. The presence and quantity of water in the elemental analysis sample was confirmed through integration of the H_2O resonance in the ^{1}H NMR spectrum.

General synthetic method for zinc bis(flavonolato) compounds (9–12)

A 500 mL round bottom flask, protected from light with aluminum foil, was charged with the flavonol (21 mmol), $Me_4NOH{\cdot}5H_2O$ (21 mmol), and MeOH (50 mL) and the resulting mixture was stirred at room temperature for 2 hours. Zinc triflate (10.3 mmol) was then transferred to the flask using

MeOH (15 mL). This mixture was stirred overnight after which time the product was collected by filtration, washed with water and dried *in vacuo*.

Zn(1$^-$)$_2$·4H$_2$O (9). 88% yield. Orange solid. ^{1}H NMR (pyridine-d_5, 300 MHz) 9.35 (d, J = 7.8 Hz, 4H), 8.86 (s, 2H), 8.07 (s, 2H), 7.89 (d, J = 8.4 Hz, 2H), 7.80–7.77 (m, 6H), 7.54–7.39 (m, 4H), 7.27 (t, J = 7.2 Hz, 2H). UV-vis (pyridine), nm (ε, M^{-1} cm^{-1}) 483 (23 300), 375 (7600), 306 (25 700). UV-vis (pyridine) nm (ε, M^{-1} cm^{-1}) 479 (23 300). LIFDI-MS, m/z (relative intensity) 638.0710, calc. 638.0702 ([M]$^+$, 100%). Anal. Calc. $C_{38}H_{22}O_6Zn{\cdot}4H_2O$: C, 64.10; H, 4.25. Found: C, 63.48; H, 4.08. The presence and quantity of water present in the solid sample was confirmed through integration of the water peak in the ^{1}H NMR spectrum.

Zn(2$^-$)$_2$·2H$_2$O (10). 86% yield. Red solid. ^{1}H NMR (pyridine-d_5, 300 MHz) 9.37 (d, J = 8.7 Hz, 4H), 9.03 (s, 2H), 8.10 (s, 2H), 7.91 (d, J = 8.1 Hz, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.46 (t, J = 8.7 Hz, 2H), 7.34 (t, J = 8.1 Hz, 2H), 6.94 (d, J = 8.7 Hz, 4H), 3.30 (q, J = 7.2 Hz, 8H), 1.08 (t, J = 7.2 Hz, 12H) ppm. UV-vis (pyridine) nm (ε, M^{-1} cm^{-1}) 525 (92 500), 402 (17 600). LIFDI-MS, m/z (relative intensity) 780.2163, calc. 780.2172 ([M]$^+$, 100%). Anal. Calc. $C_{46}H_{40}N_2O_6Zn{\cdot}2H_2O$: C, 67.52; H, 5.42; N, 3.42. Found: C, 67.30; H, 5.29; N, 3.50. The presence and quantity of water present in the solid sample was confirmed through integration of the water peak in the ^{1}H NMR spectrum.

Zn(3$^-$)$_2$·2H$_2$O (11). 92% yield. Purple solid. ^{1}H NMR (pyridine-d_5, 300 MHz) 9.48 (d, J = 7.5 Hz, 4H), 9.45 (s, 2H), 8.26 (s, 2H), 8.10 (d, J = 8.7 Hz, 2H), 8.01 (d, J = 8.4 Hz, 2H), 7.70 (t, J = 7.5 Hz, 4H) 7.56–7.43 (m, 6H) ppm. UV-vis (pyridine) nm (ε, M^{-1} cm^{-1}) 564 (31 700), 405 (27 500). LIFDI-MS, m/z (relative intensity) 670.0259, calc. 670.0246 ([M]$^+$, 72%). Anal. Calc. $C_{38}H_{22}O_4S_2Zn{\cdot}2H_2O$: C, 64.45; H, 3.70. Found: C 64.21; H: 3.73. The presence and quantity of water present in the solid sample was confirmed through integration of the water peak in the ^{1}H NMR spectrum.

Zn(4$^-$)$_2$·2H$_2$O (12). 91% yield. Blue solid. ^{1}H NMR (pyridine-d_5, 300 MHz) 9.55 (d, J = 9.3 Hz, 4H), 9.44 (s, 2H), 8.16 (s, 2H), 8.05 (d, J = 8.1 Hz, 2H), 7.95 (d, J = 8.7 Hz, 2H), 7.55–7.37 (m, 4H), 6.91 (d, J = 6.9 Hz, 4H), 3.33 (q, J = 6.9 Hz, 8H), 1.09 (t, J = 6.9 Hz, 12H) ppm. UV-vis (pyridine) nm (ε, M^{-1} cm^{-1}) 609 (189 750). LIFDI-MS, m/z (relative intensity) 812.1711, calc. 812.1715 ([M]$^+$, 100%). Anal. Calc. $C_{46}H_{40}N_2O_4S_2Zn{\cdot}2H_2O$: C, 64.97; H, 5.22; N, 3.29. Found: C, 65.75; H, 5.08; N, 3.27. The presence and quantity of water present in the solid sample was confirmed through integration of the water peak in the ^{1}H NMR spectrum.

Photoinduced reactivity of 5–8 in CH$_3$CN

Illumination of aerobic CH_3CN solutions of **5–8** using visible light (**5**: 419 nm; **6**, **7**, **8**: >546 nm) results in the release of one equivalent of CO (Table 2) and the formation of the carboxylato derivatives [(6-Ph$_2$TPA)Zn(carboxylato)]ClO$_4$ (**13–16**) which were characterized by ^{1}H NMR, IR, and ESI/MS.

[(6-Ph$_2$TPA)Zn(((3-benzoyl)oxy)-2-naphthoate)]ClO$_4$ (13). ^{1}H NMR (CD_3CN, 300 MHz) δ 8.22 (d, J = 4.5 Hz, 1H), 8.14–7.99 (m, 3H), 7.93–7.78 (m, 4H), 7.66 (d, J = 7.5 Hz, 2H), 7.64–7.51 (m, 6H), 7.50–7.37 (m, 5H), 7.34–7.23 (m, 2H), 7.20–7.05 (m, 9H), 4.58–4.26 (m, 6H) ppm. FT-IR (KBr, cm^{-1}) 1724 ($\nu_{C=O}$). ESI/APCI-MS, m/z (relative intensity), 797.2113, calc. 797.2201 ([M − ClO$_4$]$^+$, 35%).

[(6-Ph$_2$TPA)Zn(3-((4-(diethylamino)benzoyl)oxy)-2-naphthoate)]ClO$_4$ (14). ^{1}H NMR (CD_3CN, 300 MHz) δ 8.24 (d, J = 5.4 Hz, 1H), 8.15–7.97 (m, 3H), 7.88–7.77 (m, 2H), 7.68 (t, J = 9.0 Hz, 4H), 7.61–7.50 (m, 4H), 7.49–7.39 (m, 3H), 7.34–7.24 (m, 2H), 7.21–6.84 (m, 9H), 6.60 (d, J = 9.0 Hz, 2H), 4.65–4.27 (m, 6H), 3.41 (q, J = 7.2 Hz, 4H), 1.15 (t, J = 7.2 Hz, 6H) ppm. FT-IR (KBr, cm^{-1}) 1722 ($\nu_{C=O}$). ESI/APCI-MS, m/z (relative intensity), 868.2870, calc. 868.2836 ([M − ClO$_4$]$^+$, 3%).

[(6-Ph$_2$TPA)Zn(3-((benzoyloxy)naphthalene)-2-carbothiolate)]ClO$_4$ (15). ^{1}H NMR (CD_3CN, 300 MHz) 8.46 (d, J = 5.4 Hz, 1H), 8.15–7.84 (m, 6H), 7.83–7.74 (m, 3H), 7.70 (t, J = 7.5 Hz, 1H), 7.65–7.32 (m, 13H), 7.27 (t, J = 7.8 Hz, 4H), 7.09 (d, J = 7.8 Hz, 3H), 4.60–4.16 (m, 6H) ppm. FT-IR (KBr, cm^{-1}) 1742 ($\nu_{C=O}$). ESI/APCI-MS, m/z (relative intensity), 813.1889, calc. 813.1872 ([M − ClO$_4$]$^+$, 100%).

[(6-Ph$_2$TPA)Zn(3-((4-diethylamino)benzoyl)oxy)naphthalene-2-carbothiolate)]ClO$_4$ (16). ^{1}H NMR (CD_3CN, 300 MHz) 8.46 (d, J = 5.1 Hz, 1H), 8.00–7.88 (m, 4H), 7.85–7.75 (m, 2H), 7.65 (d, J = 9.3 Hz, 2H), 7.61–7.52 (m, 4H), 7.48–7.35 (m, 7H), 7.25 (t, J = 7.8 Hz, 4H), 7.10 (d, J = 7.5 Hz, 4H), 6.68 (d, J = 9.3 Hz, 2H), 4.62–4.28 (m, 6H), 3.51 (q, J = 6.9 Hz, 4H), 1.25 (t, J = 6.9 Hz, 6H) ppm. FT-IR (KBr, cm^{-1}) 1739 ($\nu_{C=O}$). ESI/APCI-MS, m/z (relative intensity), 884.2641, calc. 884.2607 ([M − ClO$_4$]$^+$, 50%).

Table 2 Absorption and CO release properties of **5–12**

Compound	λ_{max} [a] (nm) ε (M^{-1} cm^{-1})	Solution CO release (eq. CO)[d]	Φ[g]	Solid-state CO release (eq. CO)
5	480[b] (6300)	0.94(4)[b,e]	0.651(2)[h]	0.96[j]
6	524[b] (80 000)	0.98(1)[b,e]	0.583(4)[i]	0.93[j]
7	550[b] (9300)	0.92(3)[b,e]	0.951(4)[i]	0.97[j]
8	600[b] (111 700)	0.97(2)[b,e]	0.947(7)[i]	0.94[j]
9	479[c] (23 300)	1.86(2)[c,f]		1.77(4)[k]
10	525[c] (92 500)	1.91(4)[c,f]		1.63(2)[k]
11	564[c] (31 700)	1.89(3)[c,f]		No
12	609[c] (189 750)	1.95(4)[c,f]		No

[a] Most red-shifted absorption feature. [b] Compound dissolved in acetonitrile in the presence of O_2. [c] Compound dissolved in pyridine in the presence of O_2. [d] Determined using GC; average of three independent measurements. [e] CO quantification performed by GC after illumination with 419 nm lamps (**5**) or white light lamps equipped with 546 nm cut off filters (**6**, **7**, **8**) for 24 h. [f] Illuminated with white compact fluorescent (CFL) bulbs for 48 h. Compounds **9** and **10** will also undergo CO release using blue CFL bulbs in 48 h. [g] Average of three independent trials; values in parenthesis represent standard error. [h] Φ obtained for solution (CH_3CN) CO release *via* illumination using 419 nm lamps and potassium ferrioxalate actinometer. [i] Φ obtained for solution (CH_3CN) CO release *via* illumination with white light lamps equipped with 546 nm cut off filters and potassium reineckate actinometer. [j] Powdered compound in the presence of O_2. CO quantification performed by GC after illumination with 419 nm light (**5**) or white light lamps equipped with 546 nm cut off filters (**6**, **7**, **8**) for 48 h. Average CO release of two independent samples. [k] Illuminated with white CFL bulbs for 4 days; average of three independent measurements.

Photoinduced reactivity of 9–12 in pyridine

Solutions of **9–12** (~0.01 mmol) in pyridine-d_5 (~0.7 mL) were placed in NMR tubes under air. Each was then placed in a Luzchem photoreactor equipped with 419 nm or white light lamps and illuminated until the reaction was determined to be complete by ^{1}H NMR. The solvent was then removed under reduced pressure and an FT-IR spectrum was obtained.

Zinc bis((3-benzoyl)oxy)-2-naphthoate) (17). Beige solid. ^{1}H NMR (pyridine-d_5, 300 MHz) δ 9.14 (s, 2H), 8.48 (d, J = 6.9 Hz, 4H), 7.94–7.82 (m, 6H), 7.56–7.37 (m, 10H) ppm. FT-IR (KBr, cm^{-1}) 1728 ($\nu_{C=O}$).

Zinc bis(3-((4-(diethylamino)benzoyl)oxy)-2-naphthoate) (18). Beige solid. ^{1}H NMR (pyridine-d_5, 300 MHz) δ 9.11 (s, 2H), 8.47 (d, J = 7.2 Hz, 4H), 8.00–7.75 (m, 6H), 7.51–7.26 (m, 4H), 6.71 (d, J = 7.2 Hz, 4H), 3.19 (q, J = 6.9 Hz, 8H), 0.99 (t, J = 6.9 Hz, 12H) ppm. FT-IR (KBr, cm^{-1}) 1714 ($\nu_{C=O}$).

Zinc bis(3-(benzoyloxy)naphthalene-2-carbothiolate) (19). Beige solid. ^{1}H NMR (pyridine-d_5, 300 MHz) δ 9.14 (s, 2H), 8.36 (d, J = 8.6, 4H), 7.97 (d, J = 8.1, 2H), 7.84 (d, J = 8.1, 2H), 7.79 (s, 2H), 7.55–7.35 (m, 10H) ppm. FT-IR (KBr, cm^{-1}) 1739 ($\nu_{C=O}$).

Zinc bis(3-((4-(diethylamino)benzoyl)oxy)naphthalene-2-carbothiolate) (20). Beige solid. ^{1}H NMR (pyridine-d_5, 300 MHz) δ 9.06 (s, 2H), 8.36 (d, J = 7.5, 4H), 8.00–7.65 (m, 6H), 7.57–7.29 (m, 4H), 6.73 (d, J = 7.5, 4H), 3.26 (q, J = 6.9, 8H), 1.04 (t, J = 6.9, 12H) ppm. FT-IR (KBr, cm^{-1}) 1713 ($\nu_{C=O}$).

Dark control reactions for 5–8

Solutions of **5–8** (~10 mM) in acetonitrile-d_3 were prepared in air under minimal red light and placed in NMR tubes. The tubes were then covered with aluminum foil and illuminated with white light for 24 hours. Evaluation of each solution by ^{1}H NMR indicated that no reaction had occurred which provides evidence that light is required for the O_2 activation chemistry leading to CO release.

Dark control reactions for 9–12

Solutions of **9–12** (~2 mM) in pyridine-d_5 were prepared in air under minimal red light and each was placed in a NMR tube. Each NMR tube was then covered in foil, placed in a photoreactor, and illuminated using 419 nm (**9** and **10**) or white light lamps (**9–12**) for 24 hours. Evaluation of each solution by ^{1}H NMR indicated that no reaction had occurred.

Anaerobic control reactions for 5–8

Solutions of **5–8** (~10 mM) in acetonitrile-d_3 were prepared in a Vacuum Atmospheres glovebox under N_2 and placed in NMR tubes. The caps of the NMR tubes were wrapped securely with parafilm and the tubes were illuminated with white light lamps for 24 hours. Evaluation of the samples by ^{1}H NMR indicated that no reaction had occurred which provides evidence that O_2 is required for CO release reactivity.

Anaerobic control reactions for 9–12

Solutions of **9–12** in pyridine-d_5 were prepared, each was placed in a NMR tube, and N_2 was bubbled through each solution for ~5 minutes. Each NMR tube was then placed in a photoreactor and illuminated with 419 nm (**9** and **10**) or white light lamps (**9–12**) for 24 hours. Evaluation of each solution by ^{1}H NMR indicated that no reaction had occurred.

CO release quantification of 5–12 in solution

50 mL round bottom flasks were loaded with **5–8** (*ca.* 10 mg) dissolved in acetonitrile (5.0 mL). The flask was then sealed with a septum, purged with O_2 for 45 seconds, and illuminated with white light for 24 hours, which resulted in bleaching of each solution to colorless. A sample (10 mL) of the headspace gas was then analyzed by gas chromatography and the area of the peak associated with CO applied to a calibration curve created specifically for reactions done in acetonitrile. The solvent was then removed under reduced pressure and the residual solid was analyzed by ^{1}H NMR for completeness of reaction.

Photoreactivity of 5–8 as powdered solids

Compounds **5–8** (*ca.* 10 mg) were loaded into 50 mL round bottom flasks under O_2. Exposure of solid **5–8** to white light for 48 hours results in clean conversion to **13–16** as determined by ^{1}H NMR of the final product. Additionally, the color of the solid compounds changed to beige (Fig. 3).

Photoreactivity of 9–12 as powdered solids

Compounds **9–12** were placed in 50 mL round bottom flasks as powdered solids. Each flask was then sealed with a septum, gently purged with O_2 for 1 minute, and placed in a photoreactor with 419 nm (**9** and **10**) or white light lamps (**9–12**) for 72 hours. The head space gas of the flask was then analyzed by gas chromatography for the production of CO. Compounds **9** and **10** as powdered solids produced two equivalents of CO per equivalent of compound when illuminated with 419 nm or white light lamps. Compounds **11** and **12** did not produce CO upon illumination with white light lamps. The residual solid in the flask was then dissolved in pyridine-d_5 and the solution evaluated by ^{1}H NMR, indicating **9** and **10** had fully converted to the photoproducts **17** and **18**, while no reaction occurred for **11** and **12**.

Photoreactivity of 9 as a film deposit

Powdered compound **9** (52.6 μmol, 33.7 mg) was placed in a round bottom flask and dissolved in pyridine (*ca.* 10 mL). The solvent was then removed *via* rotary evaporator using the highest rpm setting to deposit the compound on the vessel walls as a film. The flask was sealed with a septum and placed in a photoreactor with 419 nm or white light lamps and illuminated for 48 hours. Complete conversion to **17** was determined by ^{1}H NMR.

CO quantification for solid samples of 9 and 10

A GC calibration curve for the quantification of CO was created using sodium bicarbonate as an inert solid in a 50 mL round bottom flask. Each flask was sealed with a septum, evacuated, and varying volumes of O_2 and CO were injected. The inte-

grated area of the CO peak was plotted against the number of moles of CO calculated to be in the flask. Following a similar set up procedure, followed by illumination of solid samples of **9** or **10** for 96 h, GC analysis was performed using 10 mL of the head space gas to determine the amount of CO released.

Aerobic oxidative palladium-catalyzed carbonylation reactions

The general reaction conditions were as follows. Compound **9** was deposited as a film in a 50 mL round bottom flask as described above. The flask was then loaded with phenyl boronic ester (52.6 μmol, 10 mg), $PdCl_2(PPh_3)_2$ (2.63 μmol, 1.8 mg), NEt_3 (105.2 μmol, 15 μL), and ethanol (5 mL, 190 proof). The flask was then sealed with a septum and placed in an oil bath pre-heated to 40 °C. Each reaction mixture was illuminated with two CFL blue bulbs set at an average distance of 5 cm from the flask for 24 hours. The flask was removed from the oil bath and allowed to cool to room temperature. The reaction mixture was then passed through a short silica plug (*ca.* 600 mg). 2 μL of the filtrate was then analyzed by GC-MS. The remaining filtrate from the reactions was then brought to dryness under reduced pressure and analyzed by ^{1}H NMR.

GC-MS parameters

GC-MS spectral data was collected on a Shimadzu GCMS-QP5000 equipped with an EC-5 column that is 5% phenyl : 95% methylpolysiloxane with a fused silica coating. The column is 30 m in length with a 0.25 μm coating and 0.25 mm diameter. The injection temperature was 185 °C with an interface temperature of 250 °C. The column initial temperature was 70 °C with a final temperature of 250 °C and a ramp rate of 12 °C per minute. The column inlet pressure was 43.5 kPa with a column flow of 0.8 mL min^{-1} and a linear velocity of 32.8 cm s^{-1} for a total flow of 35.4 mL min^{-1}.

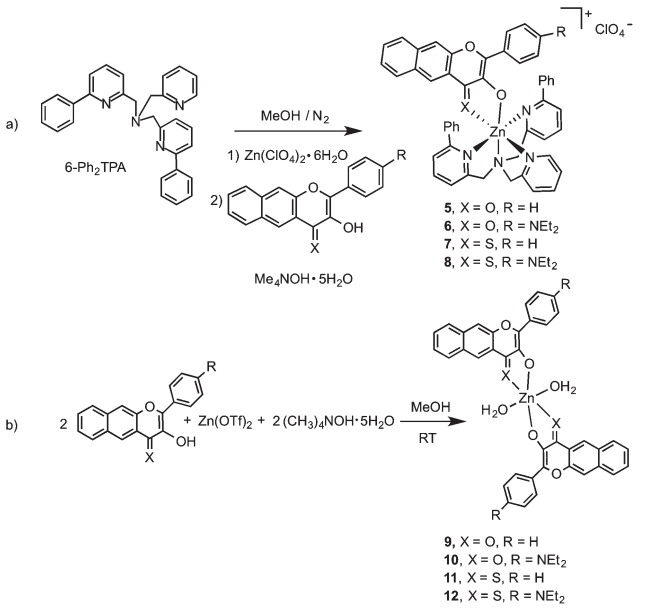
Evaluation of CO release reactivity of 9 (film deposit) in the presence of ethanol

A film deposit of **9** in a 50 mL round bottom flask was generated as outlined above. To this flask was added ethanol (5 mL). The flask was then sealed with a septum and placed in an oil bath pre-heated to 40 °C. The flask was illuminated with two CFL blue bulbs set at an average distance of 5 cm from the flask for 24 hours. The flask was removed from the oil bath and allowed to cool to room temperature. The ethanol solution was passed through a short silica plug (*ca.* 600 mg). The filtrate was then analyzed by GC-MS, which revealed the formation of ethyl benzoate. The remaining filtrate was then brought to dryness under reduced pressure and analyzed by ^{1}H NMR.

Results

The development of CO-releasing structural motifs that can be easily prepared and tuned *via* multiple strategies (*e.g.* organic synthesis and/or metal coordination) offers advantages toward the generation of compounds that can be applied in biology and synthetic chemistry. Our approach focuses on the use of extended 3-hydroxy-4-pyrone based frameworks, which are easily structurally modified to modulate spectroscopic and CO release properties. The presence of the 3-hydroxy-4-pyrone unit also offers the possibility of metal coordination. The chelate ligand-supported **5–8** were prepared *via* the approach shown in Scheme 1(a). Each was obtained in high yield as an analytically pure solid following precipitation from hexanes. Although X-ray quality crystals could not be obtained for any member of this family of compounds, the ^{1}H NMR spectral features of **5–8** (Fig. S1, S6, S11, and S16†) suggest a mononuclear pseudo-octahedral Zn(II) center with the flavonolato ligand positioned between the phenyl-appended pyridyl donors of the 6-Ph_2TPA ligand. Evidence for this type of structure comes from the ^{1}H NMR features of the benzylic hydrogens, which are consistent with C_s (mirror plane) symmetry in the cation. When dissolved in CH_3CN, each compound exhibits a molecular ion consistent with the proposed mononuclear formulation (Fig. S5, S10, S15, and S20†). The outer sphere ClO_4^- is evidenced in the solid state IR spectra of the compounds (Fig. S2, S7, S12, and S17†).

Each compound **5–8** exhibits a ~60–90 nm red-shift of the lowest energy absorption feature relative to neutral **1–4** (Tables 1 and 2; Fig. S3, S8, S13, S18†). While **5** and **7** exhibit lower molar absorptivity values for the lowest energy absorption band than the neutral flavonols, those of the NEt_2-substituted **6** and **8** are enhanced relative to the neutral flavonols. In terms of previously reported photoCORMs, the molar absorptivity values of **6–8** at >500 nm exceed those exhibited by molecular metal carbonyl photoCORMs that absorb above 500 nm.[12] Compounds **6** and **8** have molar absorptivity values at >500 nm that exceed all organic photoCORMs,[20–23] including recently reported BODIPY derivatives.[20] Illumination into the lowest energy absorption band of **5–8** produces a fluorescent emission with a Stokes shift of 30–72 nm (Fig. S4, S9, S14, and



Scheme 1 Synthesis of (a) **5–8** and (b) **9–12**.

S19†). The sulfur-containing **7** and **8** exhibit smaller Stokes shifts relative to the oxygen analogs.

Mixing of **1–4** with $Zn(OTf)_2$ in MeOH in the presence of base yielded precipitates of the analytical formulation [Zn(flavonolato)$_2$]·nH$_2$O (**9**, n = 4; **10–12**, n = 2; Scheme 1(b)). All exhibit poor solubility in common organic solvents except pyridine. Each compound was characterized as a solid using elemental analysis and FTIR. ^{1}H NMR, LIFDI-MS, UV-vis and emission spectra for **9–12** were obtained in pyridine (Fig. S21–S36†). The ^{1}H NMR features are consistent with equivalent flavonolato ligands, suggesting possible *trans* water ligands (Scheme 1(b)) in a pseudo-octahedral structure. As shown in Fig. 2, the absorption features of **9–12** in pyridine (Table 2) span the visible region from ~400–650 nm. The NEt_2-containing derivatives **14** and **16** have high extinction coefficients. These features are generally similar to those exhibited by **5–8** albeit with increased molar absorptivity values, which is consistent with the presence of two flavonolato ligands.

Photoinduced O_2 reactivity of 5–12

Illumination of CH_3CN solutions of **5–8** with visible light under aerobic conditions results in the release of one equivalent of CO and the clean formation of a single zinc carboxylate compound (**13–16**; Scheme 2(a)) as determined by ^{1}H NMR, IR, and ESI-MS. The ^{1}H NMR spectra of **13–16** exhibit features that are consistent with mononuclear structures for the cationic component of each compound (Fig. S37, S41, S44, S47†). Infrared and ESI/APCI mass spectral data also support the proposed formulation of mononuclear carboxylato compounds that have resulted from dioxygenase-type reactivity and CO release (IR: Fig. S38, S42, S45, S48; ESI/APCI: Fig. S39, S43, S46, S49†). The incorporation of two oxygen atoms from

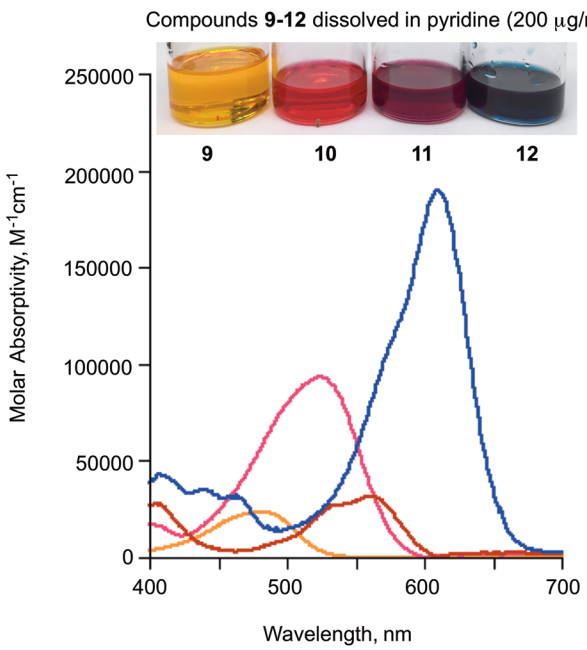
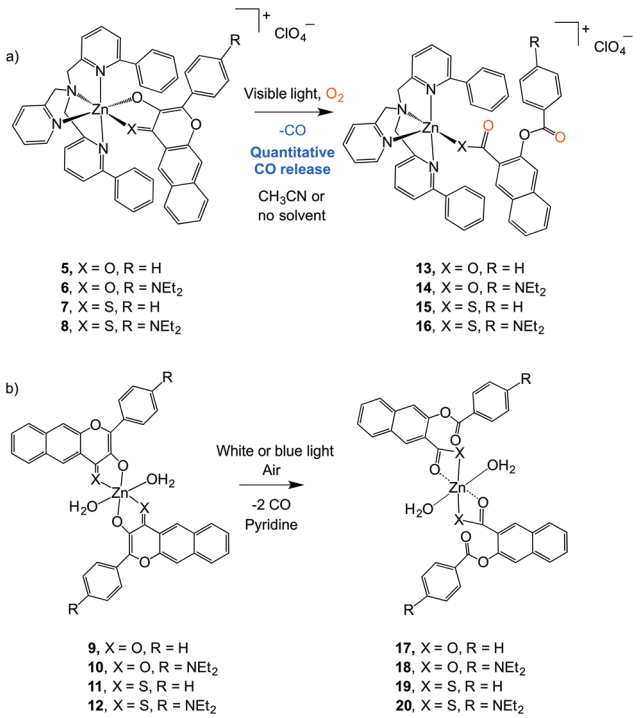


Fig. 2 Absorption spectral features of **9–12**.



Scheme 2 (a) Visible light induced CO release reactivity of **5–8** in CH_3CN or the solid state. (b) Visible light induced CO release reactivity of **9–12** in pyridine.

O_2 into the product is evidenced by the reaction of **5** in the presence of $^{18}O_2$, which yields **13** containing two labelled oxygen atoms (ESI/APCI MS Fig. S40†). The reaction quantum yields for CO release from **5–8** (Table 2) in CH_3CN significantly exceed those exhibited by the neutral flavonols **1–4**, metal carbonyl photoCORMs,[12] and all reported neutral organic photoCORMs.[20–23]

When dissolved in pyridine under aerobic conditions and illuminated with white (**9–12**) or blue light (**9** and **10**), the Zn(II) bis(flavonolato) compounds exhibit dioxygenase-type photoinduced release of two equivalents of CO (Table 2). The zinc-containing products (**17–20**, Scheme 2(b)) are bis-carboxylate derivatives based on ^{1}H NMR and IR spectral features (Fig. S50–S57†). Thus, both flavonolato ligands in **9–12** undergo light-induced CO release when dissolved in pyridine. We note that Tran and Cohen previously reported light-induced reactivity for a zinc bis(flavonothianoato) complex in $CHCl_3$ but did not report the nature of the products.[69]

Solid-state photoinduced CO release reactivity of 5–8

Light-induced CO release compounds offer the possibility of control over the temporal and spatial release of CO. To date, compounds developed for biological and *in situ* synthetic applications have focused on soluble species. However, solid-state materials or compounds that release CO upon introduction of visible light could also be very useful in various applications, including in medicine and for CO release within reaction mixtures. Visible and near infra-red light-driven

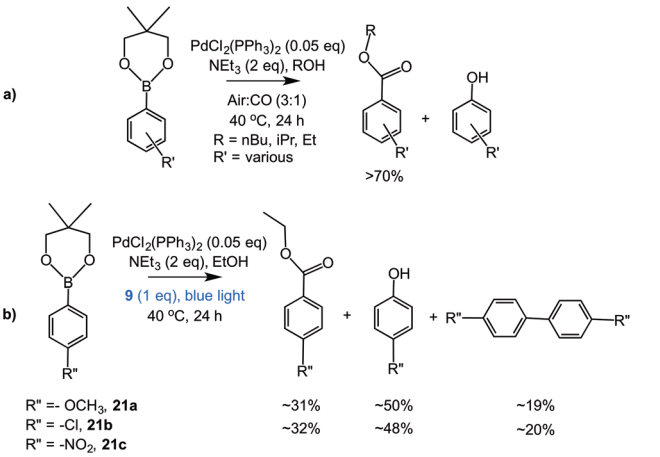
NO-releasing solid-state materials (photoNORMs) have been previously developed for biological applications.[70–78] A current limitation in terms of the development of photoCORM materials is the almost complete lack of availability of compounds that exhibit solid state CO release reactivity upon illumination with visible light. Recently, Mascharak *et al.* reported two Mn(I) tricarbonyl compounds that will release CO upon illumination of the crystals with microscope light. However, these compounds were not characterized in terms of the amount of CO released or the products remaining following CO release.[54]

Notably, we have discovered that exposure of powders of **5–8** to visible light in the presence of O_2 for 48 h results in quantitative CO release (Table 2). Analysis of the remaining beige powders (Fig. 3) following light illumination *via* ^{1}H NMR in CD_3CN indicates the clean formation of **13–16**. Thus, the same reactivity is observed for **5–8** both in solution and in the solid-state. It is important to note that the neutral flavonols **1–4** are unreactive as solids upon extended illumination (one week) with visible light. The zinc flavonolato derivatives (**5–8**) are unreactive as solids under anaerobic conditions.

In terms of the zinc bis(flavonolato) compounds, only **9** and **10** exhibit quantitative CO release (2 eq.) reactivity upon illumination with white light under air. The solid thiocarbonyl derivatives did not exhibit CO release even after extensive periods of illumination (1 week). These results demonstrate that there are factors that influence solid-state CO release reactivity within this family of compounds that remain to be determined. However, it is noteworthy that the pairs of compounds **5**/**9** and **6**/**10** demonstrate that solid-state CO release reactivity can be retained while the structure (*e.g.* supporting chelate ligand) can be tuned to adjust solubility.

Initial evaluation of 9 as a CO source for oxidative palladium-catalyzed carbonylation in ethanol

Building on the discovery of solid-state CO release reactivity for **9**, we performed initial studies to examine the possibility of using this compound as an *in situ* heterogeneous visible light-induced CO release agent for oxidative palladium-catalyzed alkoxycarbonylation processes such as the reactions outlined in Scheme 3(a). Liu *et al.* have previously reported that such reactions can be performed using air : CO (ratio 3 : 1–5 : 1) to give carbonylated products in >70% yield using various alcohols as the solvent.[62] Our initial screening reactions focused on the use of **9** at a near stoichiometric level in terms of available CO in reactions with boronic esters having various substituents (Scheme 3(b)). For each reaction, a 50 mL round bottom flask was coated with one equivalent of **9** (up to 2 eq. CO) as a film *via* rotary evaporation of a pyridine solution of the complex. The boronic ester, NEt_3, and $PdCl_2(PPh_3)_2$ were then added along with ethanol (5 mL). Each reaction mixture was heated under air at 40 °C using an oil bath and was illuminated with two blue CFL bulbs to initiate CO release. After 24 h of heating and illumination, the products of the reactions were evaluated using GC-MS and ^{1}H NMR. In the reactions of **21a** and **21b**, the desired carbonylation ester products are generated, along with phenol and biphenyl byproducts (Scheme 3; Fig. S58 and S59†). Generally similar results were obtained for the nitro derivative **21c** albeit no biphenyl product was identified (Fig. S60†). The production of significant amounts phenol and biphenyl byproducts indicates that the CO flux in the reaction mixture needs to be further optimized to limit the formation of these oxidation byproducts. However, this was not pursued in these reactions due to the additional identification of formation of ethyl benzoate in each reaction mixture. This ester is generated *via* the breakdown of the flavonol-based CO release product by ester alcoholysis (Scheme 4). Compound **9** releases ~1 eq. of CO after 24 h of illumination of the deposited film (Fig. S61†). Quantification (*via* GC-MS) of the ethyl benzoate generated in reaction mixtures shown in Scheme 3(b) after 24 h indicates that ~60–80% of the expected CO release product (1 eq.) has undergone ethanolysis to produce ethyl benzoate. Overall, these results indicate that while the starting heterogeneous zinc bis(flavonolato) complex is a viable source of CO for carbonylation reactivity, the ester functionality in the CO release product is reactive with alcohols. Minimizing this background alcoholysis reactivity is the subject of ongoing studies. Additionally, efforts to modify the reaction conditions to enhance selectivity for the ester product are in progress. We believe that such studies are justified by the combination of the low temperature reaction conditions, use of air as the sole oxidant, and the safe CO-handling present in these reactions.



Scheme 3 (a) Aerobic palladium-catalyzed alkoxycarbonylation reactions. (b) The relative yields of the products generated for R'' = $-NO_2$ in could not be determined due to peak overlap in the GC-MS trace.

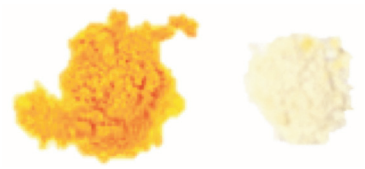
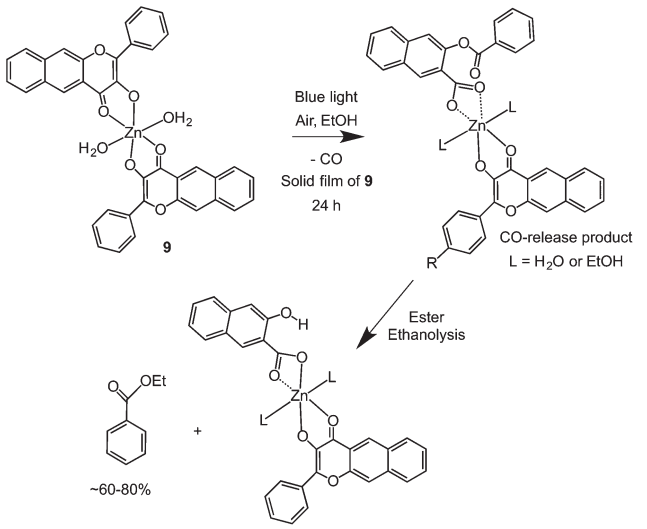


Fig. 3 Color change observed for solid **5** upon illumination with white light for 48 h at room temperature in the presence of O_2.



Scheme 4 Proposed ester aloholysis reactivity of CO release product.

Conclusions

The dioxygenase-type CO release chemistry of metal complexes of 3-hydroxy-4-pyrone derivatives (flavonols) has received considerable attention due to its relevance to quercetin dioxygenase enzymes.[56,79–85] Our discovery of light-induced CO release chemistry for divalent metal flavonolato compounds[60,61,67] has spurred us to further evaluate the light-induced CO release reactivity of flavonol and flavonolato species for applications as photoCORMs. Construction of the extended 3-hydroxy-4-pyrone derivatives **1–4** led to the discovery that unlike neutral 3-hydroxyflavone,[57] which undergoes multiple types of reactions upon illumination with UV light, the neutral extended flavonols undergo clean dioxygenase-type visible-light induced CO release in the presence of O_2.[58] In this contribution we have evaluated how stabilizing the flavonolato anion of **1–4** *via* zinc coordination affects the CO release chemistry. Importantly, we have discovered that zinc coordination results in a red-shift of the absorption features, with **8** exhibiting a large absorption feature that extends into the therapeutic window (>650 nm). The reaction quantum yields for CO release are enhanced in the flavonolato derivatives relative to the neutral flavonols, in some cases by two orders of magnitude. Most importantly, the flavonolato derivatives exhibit CO release both in solution and in the solid state. Overall, these results demonstrate that 3-hydroxy-4-pyrone (flavonol) derivatives are tunable using both organic and inorganic approaches for the development of light-driven CO-releasing molecules. The ease with which structural modifications can be made positions this family of CO release molecules to contribute to various current goals in the biology and chemistry of carbon monoxide. Specifically, the tunability of the quantum yield in flavanol/flavonolato derivatives suggests that such compounds could be used to deliver various fluxes of CO under site and temporal control. The discovery of light-induced solid-state CO release reactivity in **5–8** and **9–12** also opens up the opportunity for the development of metal flavonolato-based solid-state CO-releasing materials that can be triggered using visible light. As demonstrated herein, solid zinc bis(flavonolato) derivatives can be used as *in situ* CO release compounds in oxidative palladium-catalyzed carbonylation reactions albeit with some degradation of the CO release product. Further studies of the applications of these solids in carbonylation processes are currently in progress.

Acknowledgements

The authors thank the National Science Foundation (CHE-1301092) and USTAR (Utah Science and Research Technology Initiative) for funding. We thank Tatiana Soboleva for technical assistance.

References

1 R. Tenhunen, H. S. Marver and R. Schmid, *Proc. Natl. Acad. Sci. U. S. A.*, 1968, **61**, 748–755.
2 R. Motterlini and L. E. Otterbein, *Nat. Rev. Drug Discovery*, 2010, **9**, 728–743.
3 L. K. Wareham, R. K. Poole and M. Tinajero-Trejo, *J. Biol. Chem.*, 2015, **290**, 18999–19007.
4 B. E. Mann, *Top. Organomet. Chem.*, 2010, **32**, 247–285.
5 J. E. Clark, P. Naughton, S. Shurey, C. J. Green, T. R. Johnson, B. E. Mann, R. Foresti and R. Motterlini, *Circ. Res.*, 2003, **93**, e2–e8.
6 T. Santos-Silva, A. Mukhopadhyay, J. D. Seixas, G. J. L. Bernardes, C. C. Ramão and M. J. Ramão, *J. Am. Chem. Soc.*, 2011, **133**, 1192–1195.
7 M. Chaves-Ferreira, I. S. Albuquerque, D. Matak-Vinkovic, A. C. Coelho, S. M. Carvalho, L. M. Saraiva, C. C. Ramão and G. J. L. Bernardes, *Angew. Chem., Int. Ed.*, 2015, **54**, 1172–1175.
8 I. S. Albuquerque, H. F. Jeremias, M. Chaves-Ferreira, D. Matak-Vinkovic, O. Boutureira, C. C. Ramão and G. J. L. Bernardes, *Chem. Commun.*, 2015, **51**, 3993–3996.
9 N. S. Sitnikov, Y. Li, D. Zhang, B. Yard and H.-G. Schmalz, *Angew. Chem., Int. Ed.*, 2015, **54**, 12314–12318.
10 S. Romanski, B. Kraus, M. Guttentag, W. Schlundt, H. Rücker, A. Adler, J.-M. Neudörfl, R. Alberto, S. Amslinger and H.-G. Schmalz, *Dalton Trans.*, 2012, **41**, 13862–13875.
11 H. Meyer, F. Winkler, P. Kunz, A. M. Schmidt, A. Hamacher, M. U. Kassack and C. Janiak, *Inorg. Chem.*, 2015, **54**, 11236–11246.
12 I. Chakraborty, S. J. Carrington and P. K. Mascharak, *Acc. Chem. Res.*, 2014, **47**, 2603–2611.
13 U. Schatzschneider, *Br. J. Pharmacol.*, 2015, **172**, 1638–1650.
14 A. E. Pierri, A. Pallaoro, G. Wu and P. C. Ford, *J. Am. Chem. Soc.*, 2012, **134**, 18197–18200.
15 U. Hasegawa, A. J. van der Vlies, E. Simeoni, C. Wandrey and J. A. Hubbell, *J. Am. Chem. Soc.*, 2010, **132**, 18273–18280.

16 P. Govender, S. Pai, U. Schatzschneider and G. S. Smith, *Inorg. Chem.*, 2013, **52**, 5470–5478.
17 C. Bohlender, S. Gläser, M. Klein, J. Weisser, S. Thein, U. Neugebauer, J. Popp, R. Wyrwa and A. Schiller, *J. Mater. Chem. B*, 2014, **2**, 1454–1463.
18 M. A. Gonzales, H. Han, A. Moyes, A. Radinos, A. J. Hobbs, N. Coombs, S. R. J. Oliver and P. K. Mascharak, *J. Mater. Chem. B*, 2014, **2**, 2107–2113.
19 A. E. Pierri, P.-J. Huang, J. V. Garcia, J. G. Stanfill, M. Chui, G. Wu, N. Zheng and P. C. Ford, *Chem. Commun.*, 2015, **51**, 2072–2075.
20 E. Palao, T. Slanina, L. Muchová, T. Solomek, L. Vítek and P. Klán, *J. Am. Chem. Soc.*, 2016, **138**, 126–133.
21 L. A. P. Antony, T. Slanina, P. Sebej, T. Solomek and P. Klán, *Org. Lett.*, 2013, **15**, 4552–4555.
22 D. Wang, E. Viennois, K. Ji, K. Damera, A. Draganov, Y. Zheng, C. Dai, D. Merlin and B. Wang, *Chem. Commun.*, 2014, **50**, 15890–15893.
23 P. Peng, C. Wang, Z. Shi, V. K. Johns, L. Ma, J. Oyer, A. Copik, R. Igarashi and Y. Liao, *Org. Biomol. Chem.*, 2013, **11**, 6671–6674.
24 S. García-Gallego and G. J. L. Bernardes, *Angew. Chem., Int. Ed.*, 2014, **53**, 9712–9721.
25 X. Ji, K. Damera, Y. Zheng, B. Yu, L. E. Otterbein and B. Wang, *J. Pharm. Sci.*, 2016, **105**, 405–416.
26 S. H. Heinemann, T. Hoshi, M. Westerhausen and A. Schiller, *Chem. Commun.*, 2014, **50**, 3644–3660.
27 P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp and T. Skyrdstrup, *J. Am. Chem. Soc.*, 2011, **133**, 6061–6071.
28 S. D. Friis, R. H. Taaning, A. T. Lindhardt and T. Skrydstrup, *J. Am. Chem. Soc.*, 2011, **133**, 18114–18117.
29 C. Lescot, D. U. Nielsen, I. S. Makarov, A. T. Lindhardt, K. Daasbjerg and T. Skrydstrup, *J. Am. Chem. Soc.*, 2014, **136**, 6142–6147.
30 S. D. Friis, T. Skrydstrup and S. L. Buchwald, *Org. Lett.*, 2014, **16**, 4296–4299.
31 S. D. Friis, A. T. Lindhardt and T. Skrydstrup, *Acc. Chem. Res.*, 2016, **49**, 594–605.
32 S. V. F. Hansen and T. Ulven, *Org. Lett.*, 2015, **17**, 2832–2835.
33 P. H. Gertz, V. Hirschbeck and I. Fleischer, *Chem. Commun.*, 2015, **51**, 12574–12577.
34 N.-F. K. Kaiser, A. Hallberg and M. Larhed, *J. Comb. Chem.*, 2002, **4**, 109–111.
35 J. Wannberg and M. Larhed, *J. Org. Chem.*, 2003, **68**, 5750–5753.
36 J. Georgsson, A. Hallberg and M. Larhed, *J. Comb. Chem.*, 2003, **5**, 350–352.
37 O. Lagerlund, M. L. H. Mantel and M. Larhed, *Tetrahedron*, 2009, **65**, 7646–7652.
38 A. Wieckowska, R. Fransson, L. R. Odell and M. Larhed, *J. Org. Chem.*, 2011, **76**, 978–981.
39 L. R. Odell, F. Russo and M. Larhed, *Synlett*, 2012, 685–698.
40 L. Akerbladh, P. Nordeman, M. Wejdemar, L. R. Odell and M. Larhed, *J. Org. Chem.*, 2015, **80**, 1464–1471.
41 M. Iizuka and Y. Kondo, *Chem. Commun.*, 2006, 1739–1741.
42 A. Begouin and M.-J. R. P. Queiroz, *Eur. J. Org. Chem.*, 2009, 2820–2827.
43 S. R. Borhade, A. Sandström and P. I. Arvidsson, *Org. Lett.*, 2013, **15**, 1056–1059.
44 S. Iyer and G. M. Kulkarni, *Synth. Commun.*, 2004, **34**, 721–725.
45 P. Nordeman, L. R. Odell and M. Larhed, *J. Org. Chem.*, 2012, **77**, 11393–11398.
46 Y. Wan, M. Alterman, M. Larhed and A. Hallberg, *J. Org. Chem.*, 2002, **67**, 6232–6235.
47 T. Ueda, H. Konishi and K. Manabe, *Angew. Chem., Int. Ed.*, 2013, **52**, 8611–8615.
48 T. Ueda, H. Konoshi and K. Manabe, *Org. Lett.*, 2013, **15**, 5370–5373.
49 H. Konishi and K. Manabe, *Synlett*, 2014, 1971–1986.
50 X. Qi, L.-B. Jiang, C.-L. Li, R. Li and X.-F. Wu, *Chem. – Asian J.*, 2015, **10**, 1870–1873.
51 S. N. Gockel and K. L. Hull, *Org. Lett.*, 2015, **17**, 3236–3239.
52 A. Liang, S. Han, L. Wang, J. Li, D. Zou, Y. Wu and Y. Wu, *Adv. Synth. Catal.*, 2015, **357**, 3104–3108.
53 X. Li, D. Zou, H. Zhu, Y. Wang, J. Li, Y. Wu and Y. Wu, *Org. Lett.*, 2014, **16**, 1836–1839.
54 S. J. Carrington, I. Chakraborty and P. K. Mascharak, *Dalton Trans.*, 2015, **44**, 13828–13834.
55 S. Fetzner, *Appl. Environ. Microbiol.*, 2012, **78**, 2505–2514.
56 J. S. Pap, J. Kaizer and G. Speier, *Coord. Chem. Rev.*, 2010, **254**, 781–793.
57 M. Sisa, S. L. Bonnet, D. Ferreira and J. H. Van der Westhuizen, *Molecules*, 2010, **15**, 5196–5245.
58 S. N. Anderson, J. M. Richards, H. J. Esquer, A. D. Benninghoff, A. M. Arif and L. M. Berreau, *ChemistryOpen*, 2015, **4**, 590–594.
59 K. Grubel, K. Rudzka, A. M. Arif, K. L. Klotz, J. A. Halfen and L. M. Berreau, *Inorg. Chem.*, 2010, **49**, 82–96.
60 K. Grubel, B. J. Laughlin, T. R. Maltais, R. C. Smith, A. M. Arif and L. M. Berreau, *Chem. Commun.*, 2011, **47**, 10431–10433.
61 K. Grubel, A. R. Marts, S. M. Greer, D. L. Tierney, C. J. Allpress, S. N. Anderson, B. J. Laughlin, R. C. Smith, A. M. Arif and L. M. Berreau, *Eur. J. Inorg. Chem.*, 2012, 4750–4757.
62 Q. Liu, G. Li, J. He, J. Liu, P. Li and A. Lui, *Angew. Chem., Int. Ed.*, 2010, **49**, 3371–3374.
63 M. M. Makowska-Grzyska, E. Szajna, C. Shipley, A. M. Arif, M. H. Mitchell, J. A. Halfen and L. M. Berreau, *Inorg. Chem.*, 2003, **42**, 7472–7488.
64 W. L. F. Armarego and D. D. Perrin, *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Boston, MA, 4th edn, 1996.
65 C. G. Hatchard and C. A. Parker, *Proc. R. Soc. London, A*, 1956, **235**, 518–536.
66 H. J. Kuhn, S. E. Baslavsky and R. Schmidt, *Pure Appl. Chem.*, 2004, **76**, 2105–2146.

67 K. Grubel, S. L. Saraf, S. N. Anderson, B. J. Laughlin, R. C. Smith, A. M. Arif and L. M. Berreau, *Inorg. Chim. Acta*, 2013, **407**, 91–97.
68 W. C. Wolsey, *J. Chem. Educ.*, 1973, **50**, A335–A337.
69 B. L. Tran and S. M. Cohen, *Chem. Commun.*, 2006, 203–205.
70 J. D. Mase, A. O. Razgoniaev, M. K. Tschirhart and A. D. Ostrowski, *Photochem. Photobiol. Sci.*, 2015, **14**, 775–785.
71 M. C. Frost, M. M. Reynolds and M. E. Meyerhoff, *Biomaterials*, 2005, **26**, 1685–1693.
72 D. A. Riccio, P. N. Coneski, S. P. Nichols, A. D. Broadnax and M. H. Schoenfisch, *ACS Appl. Mater. Interfaces*, 2012, **4**, 796–804.
73 S. Sortino, *Chem. Soc. Rev.*, 2010, **39**, 2903–2913.
74 J. Bordini, P. C. Ford and E. Tfouni, *Chem. Commun.*, 2005, 4169–4171.
75 J. T. Mitchell-Koch, T. M. Reed and A. S. Borovik, *Angew. Chem., Int. Ed.*, 2004, **43**, 2806–2809.
76 A. A. Eroy-Reveles, Y. Leung and P. K. Mascharak, *J. Am. Chem. Soc.*, 2006, **128**, 7166–7167.
77 A. A. Eroy-Reveles and P. K. Mascharak, *Future Med. Chem.*, 2009, **1**, 1497–1507.
78 E. Tfouni, F. G. Doro, A. J. Gomes, R. S. da Silva, G. Metzker, P. G. Z. Benini and D. W. Franco, *Coord. Chem. Rev.*, 2010, **254**, 355–371.
79 G. Baráth, J. Kaizer, G. Speier, L. Párkányi, E. Kuzmann and A. Vértes, *Chem. Commun.*, 2009, 3630–3632.
80 A. Y. S. Malkhasian, M. E. Finch, B. Nikolovski, A. Menon, B. E. Kucera and F. A. Chavez, *Inorg. Chem.*, 2007, **46**, 2950–2952.
81 A. Matuz, M. Giorgi, G. Speier and J. Kaizer, *Polyhedron*, 2013, **63**, 41–49.
82 Y.-J. Sun, Q.-Q. Huang, T. Tano and S. Itoh, *Inorg. Chem.*, 2013, **52**, 10936–10948.
83 Y.-J. Sun, Q.-Q. Huang and J.-J. Zhang, *Inorg. Chem.*, 2014, **53**, 2932–2942.
84 Y.-J. Sun, Q.-Q. Huang and J.-J. Zhang, *Dalton Trans.*, 2014, **43**, 6480–6489.
85 Y.-J. Sun, Q.-Q. Huang, P. Li and J.-J. Zhang, *Dalton Trans.*, 2015, **44**, 13926–13938.