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Malodorogenic Sensing of Carbon Monoxide

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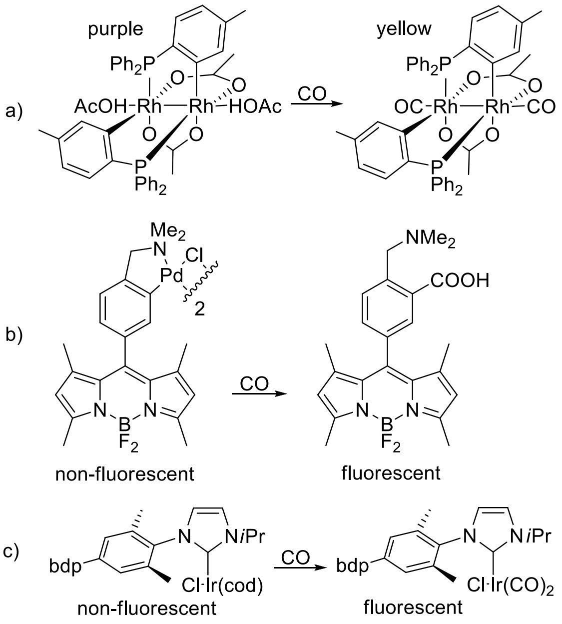
Dedicated to the memory of Dr. K. J. Wannowius

Abstract: *A thin film of poly-([IrCl(cod)(NHC-onbe)]$_n$-(propyl-onbe)$_m$) (onbe= oxanorbornene) coated on filter paper reacts quantitatively with CO to yield 1,5-cyclooctadiene, whose unpleasant smell can be detected by the human olfactory system with very high sensitivity. Odorless, but toxic CO is thus "translated" into the distinct smell of 1,5-cyclooctadiene. Based on malodorogenic sensing it is possible to smell the presence of CO.*

Carbon monoxide is a colorless, odorless and tasteless gas, liberated upon incomplete combustion of carbon containing materials.[1] The high toxicity of CO and its facile (accidental) generation in everyday life pose a serious health threat.[2] The risks associated with CO poisoning are aggravated due to the absence of highly characteristic symptoms.[3] Victims are treated with pure O_2 to compensate for the reduced oxygen uptake capacity and to displace hemoglobin-bound CO. Based on its toxicity the threshold limit value of CO during extended exposure (8 h) has been set to 25 ppm.[4] Higher levels of around 100 ppm result in headaches within a few hours, whereas prolonged exposure of up to 500 ppm carbon monoxide leads to severe poisoning, resulting in circulatory failure, brain damage, and finally death.[5] Consequently, a large number of CO-sensitive devices for the measurement of air quality are known.[6] From a commercial point of view solid state devices such as metal oxide based semiconductors[7] and electrochemical sensors are by far the most successful ones.[8] Colorimetric CO-detection is utilized in modern multichannel pulse oximetry and basically relies on the prominent deoxy-myoglobin assay.[9] More recently molecular probes for the detection of CO were developed, in which a chemical reaction with CO leads to a change in the color or the fluorescence signal.[10] The chromogenic rhodium complexes developed by Martinez-Máñez represented a breakthrough for the simple detection of CO (scheme 1a) in the critical concentration range of 50-100 ppm. [11] Fluorogenic reactions for CO-detection were also reported, in which the presence of CO leads to a pronounced increase in the fluorescence level (scheme 1b, 1c).[12] This is also relevant with a view to the intracellular detection, since CO is an important biogenic signaling molecule.[13]

We want to present here an entirely new approach for the detection of CO, which relies on the chemical translation of this toxic gas into a smellable compound. The well-known reaction of [MCl(cod)(NHC)] (M= Rh, Ir; NHC= *N*-heterocyclic carbene) with two equivalents of CO produces the carbonyl complex [MCl$(CO)_2$(NHC)] in almost quantitative yields.[14] The other product of this reaction, 1,5-cyclooctadiene, is normally ignored.[15] However, the human nose is extremely sensitive to the unpleasant smell of 1,5-cyclooctadiene[16] and the odor threshold was determined to be 0.00087 ppm[17] (triangle odor bag method).[18][19] The reaction of CO with [MCl(cod)(NHC)] can thus be viewed as a chemical translation of odorless CO into smelly 1,5-cyclooctadiene. Based on this reaction, the human olfactory system acquires the ability to smell the presence of toxic CO. The unpleasantness of 1,5-cyclooctadiene smell serves as an additional warning. We propose the term "malodorogenic sensing" for this new detection concept. This approach directly addresses our sense of smell and is quite different from an electronic nose.[20] The concept reported here can be considered as a special indicator displacement assay.[21]



Scheme 1. Chromogenic and fluorogenic CO-responsive reactions (bdp= bodipy fluorophore).

The observation of 1,5-cyclooctadiene smell depends on the chemical substitution of the cod ligand with CO and on the physical transfer of the liberated 1,5-cyclooctadiene from the surface into the gas phase and into the human olfactory system.[22] Malodorogenic reactions should be carried out in the absence of solvents to facilitate the transfer of 1,5-cyclooctadiene into the gas phase and to prevent masking the smell of the olefin. For a preliminary test of the malodorogenic concept, the behavior of several powdered metal complexes containing cod ligands (figure 1) were investigated. Between (0.1 – 0.9) $\cdot 10^{-6}$ mol of the respective complex were physisorbed on a small piece of Linters paper by evaporation of a $CHCl_3$ solution of the respective complex. First the smell of these samples after exposure to ambient air during 5- 120 min was tested. None of the complexes produced smellable quantities of 1,5-cyclooctadiene. Obviously, the constituents of ambient air do not lead to false positives. Next, the samples were exposed to air containing between 800 – 1600 ppm of CO for 5 min. Following this treatment most of the complexes transpire a strong smell of 1,5-cyclooctadiene.

The reaction of dissolved [MCl(cod)(NHC)] complexes with CO is known to be very fast.[12d] In order to obtain reliable data on the CO uptake, the solid-gas reactions of 13 Rh and Ir complexes with CO were tested (Figure 1).[23] Powdered sample of the complex were exposed to CO (500 ppm CO in N_2) and the ratio of the respective [(MCl(cod)(NHC)] and [(MCl(CO)$_2$(NHC)] complexes determined by ^{1}H-NMR spectroscopy. Significant differences in the reaction rates with CO were observed. In general, iridium complexes react faster with CO than rhodium complexes, as had been observed before for the solution reactions.[12d] The nature of the NHC ligand also has a significant influence, notably the reaction of the CAAC –based NHC Ir complex **2** is very slow.

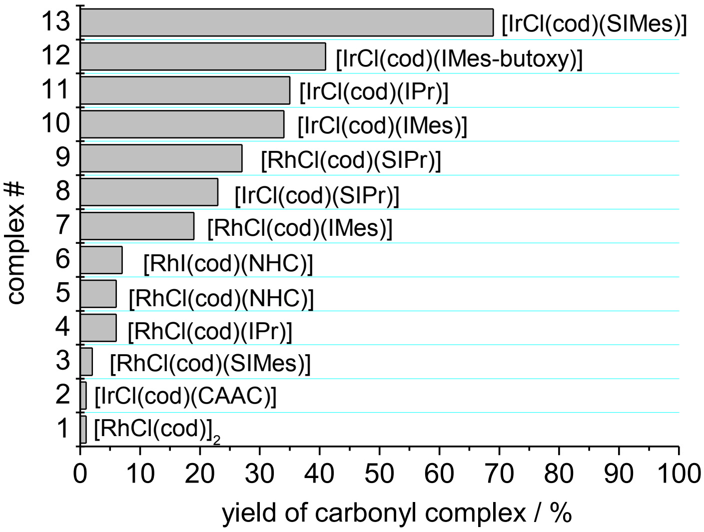


Figure 1. Conversions for the solid-gas reactions of [MCl(cod)(NHC)] (M= Rh, Ir) complexes with CO (CO-for-cod substitution) after 4 h to give [MCl(CO)$_2$(NHC)] (IPr= 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene, SIPr= 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene, IMes= 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene, SIMes= 1,3-bis(2,6-trimethylphenyl)imidazolidin-2-ylidene, CAAC= cyclic alkylamino carbene, NHC in complex **5**= 1,3-diisopropyl,-4,5-dichloro-imidazol-2-ylidene, NHC in complex **6**= 1,4-diphenyl-1,2,3-triazol-5-ylidene)(for a full list of complexes studied, see supporting information).

The release of cod from different [MCl(cod)(NHC)] complexes upon exposition to a CO containing atmosphere of ambient air was monitored via EI-mass spectrometry (figure 2). Filter paper strips were impregnated with solutions of the respective complex. After evaporation of the solvent, the paper strips were exposed to a CO-containing atmosphere. Aliquots of the atmosphere close to the impregnated paper were periodically transferred into the mass spectrometer via a capillary located close to the samples. The transfer rate of 1,5-cyclooctadiene into the gas phase shows a significant spread for the different metal complexes (figure 2). The ordering of the transfer rates for the various [MCl(cod)(NHC)] complexes is qualitatively correlated with the ordering of the CO-for-cod substitution reactions (see figure 1).[24] Based on this observation, it seems that the physical process of 1,5-cyclooctadiene release from the solid residue following the CO-for-cod substitution reaction appears to be relatively independent of the nature of the starting complex.

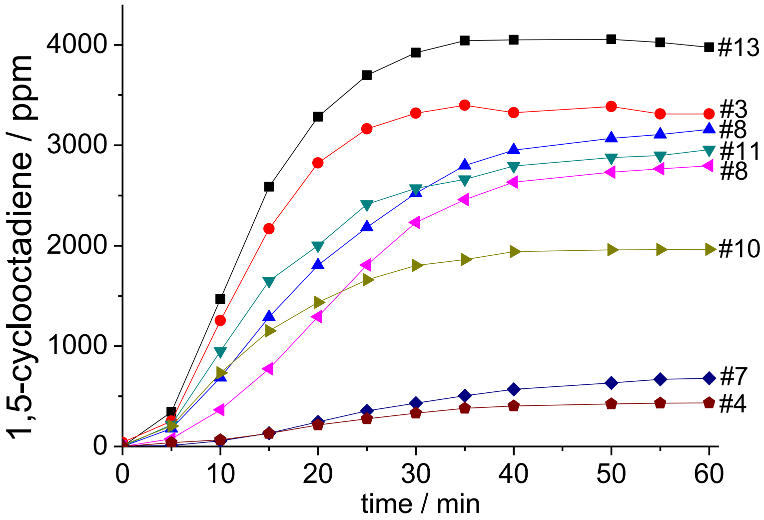


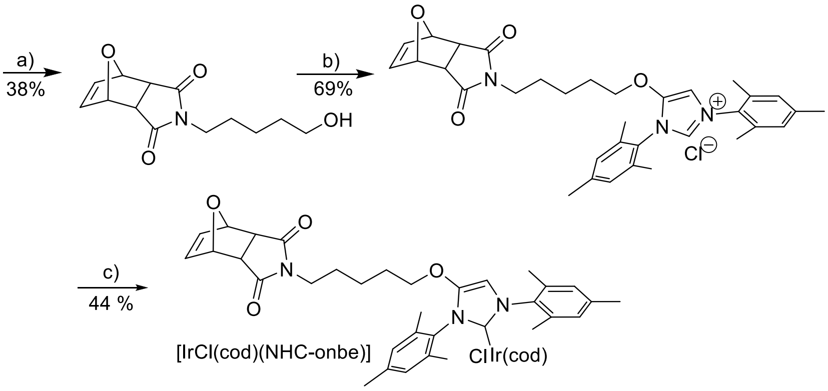
Figure 2. Release of 1,5-cyclooctadiene from [MCl(cod)(NHC)] (M= Rh, Ir for complexes **3**, **4**, **7**, **8**, **9**, **10**, **11**, **13**) into the gas phase as monitored via EI-MS.

When trying to directly probe the rate of CO uptake of the organometallic complexes adsorbed on filter paper using ATR-IR spectroscopy, we experienced reproducibility problems. It seems the organometallic complexes are easily lost from the paper surface by mechanical abrasion during handling of the samples. This facile loss of complex from the paper is problematic for the potential application of malodorogenic sensing, since the accidental intake of transition metal containing particles while smelling cod must be avoided.

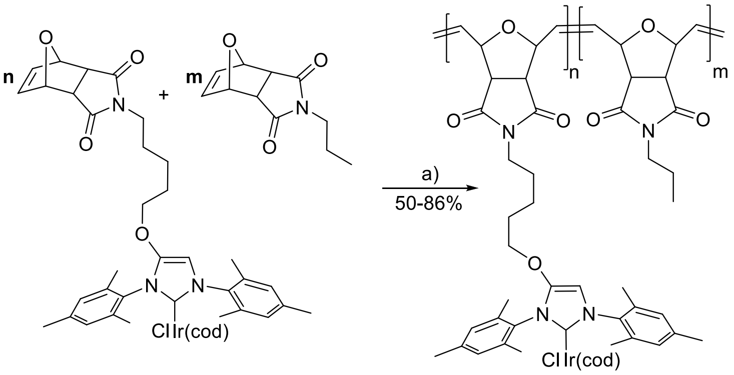
To overcome this problem, analogous polymeric [IrCl(cod)(NHC)] complexes were synthesized. This approach was based on the expectation, that thin polymer films firmly stick to the paper surface and are characterized by fast CO penetration and rapid evaporation of 1,5-cyclooctadiene.

The synthesis of the new organometallic polymer[25] was conducted as follows (scheme 2, scheme 3): A polymerizable oxanorbornene unit was covalently attached to an azolium salt containing a nucleofuge.[26] This NHC precursor was converted into [IrCl(cod)(NHC-onbe)] (onbe = oxanorbornene) according to standard procedures.[27] The polymerizable Ir-complex is closely related to complex **12** (figure 1), which stood out for fast CO-for-cod substitution reactions. Treatment of the onbe-tagged complex with a ROMP catalyst[28] provided the respective homopolymer, albeit in modest yields (ca.

50%), which turned out to be unsuitable for film formation. The properties of the polymer and the polymer yield were significantly improved by synthesizing copolymers of the organometallic monomer and a closely related propyl-terminated monomer (scheme 3). The copolymers are produced in yields of 73-86% with M_n= 35.000 g/mol and PDI = 2.3 (for 1:2 polymer). Notably, the ROMP catalyst selectively polymerizes the oxanorbornene unit. The metal bound 1,5-cyclooctadiene does not react.



Scheme 2. Synthesis of polymerizable [IrCl(cod)(NHC-onbe)] complexes for malodorogenic sensing. Reagents and conditions: a) 3a,4,7,7a-tetrahydro-4,7-epoxyisobenzofuran-1,3-dione, 5-aminopentan-1-ol, neat, 80 °C; b) methanesulfonyl chloride, Et_3N, CH_2Cl_2, 0 °C and 5-hydroxy-1,3-dimesityl-1*H*-imidazol-3-ium chloride, KI, K_2CO_3, acetone, 60 °C; c) $[IrCl(cod)]_2$, K_2CO_3, acetone reflux.



Scheme 3. Polymerization of organometallic and organic monomers via ROMP to the organometallic homopolymer (m= 0, yield: 50%) or statistical copolymers (yield: 73-86%) with n:m= 1:2, 1:5 and 1:10. Reagents and conditions: a) OPh-Grubbs-Hoveyda complex,[28] CH_2Cl_2, r.t., polymer precipitated with MeOH.

A solution of poly-($[IrCl(cod)(NHC\text{-}onbe)_1]\text{-}(propyl\text{-}onbe)_2$) in $CHCl_3$ was used for spin-coating the polymer onto a quartz disc. Thin films of the metallopolymer with an average thickness of 5-10 μm were produced. The CO-for-cod substitution reaction and the liberation of 1,5-cyclooctadiene was studied using a quartz crystal microbalance (QCB) (figure 3). The admission of a nitrogen atmosphere containing 500 ppm of CO at *t*= 213 s leads to a pronounced increase in the signal due to the uptake of CO by the film and the substitution of cod by two molecules of CO. The reaction with CO appears to be very fast and is followed by the evaporation of 1,5-cyclooctadiene from the polymer film. This process was accelerated significantly at *t*= 600 s by allowing a gentle nitrogen flow through the sample chamber. To prove that this frequency change is due to a CO-for-cod substitution reaction, a similar experiment using a poly-([IrCl(CO)$_2$(NHC-onbe)]-(onbe-propyl)) film was done. In this experiment the admission of CO gas did not result in significant changes in the resonance frequency of the quartz disc.

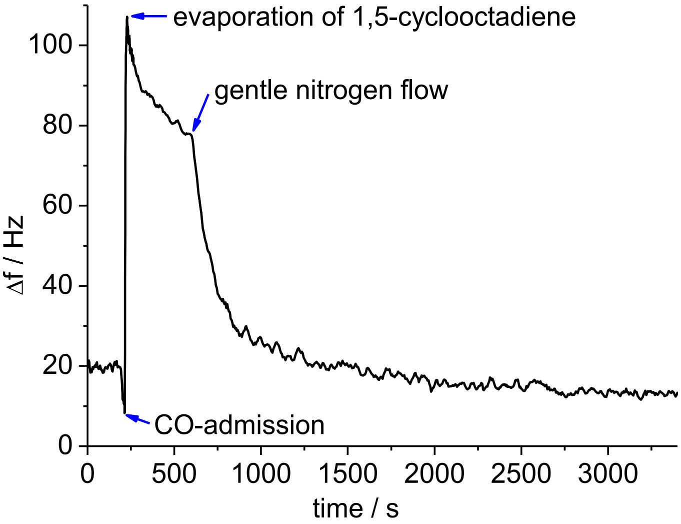


Figure 3. CO-uptake and release of 1,5-cyclooctadiene by the thin film of poly-([IrCl(cod)(NHC-onbe)]-(onbe-propyl)) monitored by quartz crystal microbalance. Exposure to CO atmosphere (500 ppm) in nitrogen starting at *t*= 213 s, gentle flow of nitrogen over the sample starting at *t*= 600 s.

ATR-IR measurements of the polymer film after CO exposure provide additional evidence for the formation of the iridium carbonyl complex. The typical carbonyl stretching absorbances are observed at 1974, 2056 cm^{-1} for CO ligands located cis and trans to the NHC ligand.[29] A large area (ca. 100 cm^2) polymer film of similar film thickness was prepared and exposed to CO (500 ppm in N$_2$). An NMR-spectrum of the dissolved film shows that the majority of polymeric Ir(cod) complex in the film was converted into the respective iridium carbonyl complex. Based on the mass balance of the CO-for-cod substitution and according to the Sauerbray equation[30] the frequency drop in the QCB experiments was expected to be more pronounced than observed. The NMR experiments and the asymptotic curve (figure 3) indicate, that the majority of the liberated 1,5-cyclooctadiene is removed from the polymer film. We therefore attribute the weaker than expected drop in the QCB frequency to changes in the film elasticity upon CO-for-cod substitution and inelastic mass oscillation in the soft polymer film.[30]

Thin films of the organometallic polymer on various substrates (filter paper, aluminum foil, glas) were prepared to optimize the detection sensitivity for a 100 ppm concentration of CO in ambient air. Based on our preliminary experiments, paper supports perform better than the other substrates. A smellable amount of 1,5-cyclooctadiene is produced within a few seconds after exposure to CO containing atmosphere when using as little as 0.2 mg of a polymer (iridium content 0.04 mg) is applied to a 1 cm^2 paper strip.[31]

In conclusion, the simple CO-for-cod substitution in complexes [IrCl(cod)(NHC)] leads to the rapid formation of 1,5-cyclooctadiene, which evaporates into the gas phase. The human nose is extremely sensitive to the distinct smell of 1,5-cyclooctadiene. The CO-for-cod substitution thus corresponds to a chemical translation of toxic, but odorless CO into smelly 1,5-cyclooctadiene. This approach is termed malodorogenic sensing. Thin films of polymeric iridium complexes are very useful for the highly sensitive indirect detection of CO.[32] With a view to the very small amounts of CO-sensitive polymer needed, the application of malodorogenous CO sensing appears to be a realistic target. The concept reported here is simple and cheap, it's application does not require special expertise or a sophisticated infrastructure. According to Whitesides simple paper-based analytical devices are suitable for applications everywhere in the world.[33]

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Keywords: carbon monoxide · sensing · iridium · quartz crystal microbalance · 1,5-cyclooctadiene

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[23] We tried to generate samples with similar particle size to suppress the potential effect of different surface morphology on the reaction rate with CO.

[24] All samples were prepared in the same manner, but it cannot be excluded, that different morphology of the samples has an influence on the cod release.

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[31] Preliminary experiments show, that from a sample size of eight people, all eight were able to smell the presence of 1,5-cyclooctadiene generated from this amount of polymer film.

[32] The amount of 1,5-cyclooctadiene contained in 0.2 mg of polymer is approximately 0.015 mg. The real intake of this compound while smelling should be significantly smaller. Based on the toxicity of 1,5-cyclooctadiene, this amount appears to be unproblematic.

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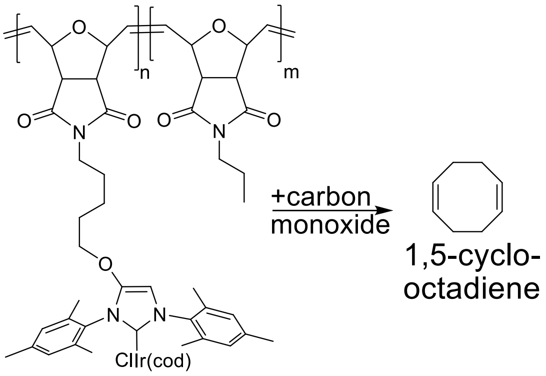
Malodorogenic Sensing of Carbon Monoxide



A rose by any other name would smell as sweet. A chemical reaction involving a thin film of an organometallic polymer and CO translates odorless, but toxic carbon monoxide into 1,5-cyclooctadiene. The human olfactory system is able to perceive the unpleasant smell of this olefin at concentrations below 0.001 ppm. Based on the malodorogenic approach humans are enabled to smell the presence of carbon monoxide.