**Mapping out the key carbon-carbon bond forming steps in manganese-catalysed C–H functionalisation.**

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**Abstract**

Detailed understanding of the mechanistic processes that underpin transition metal-catalysed reactions allows for the rational and *de novo* development of complexes with enhanced activity, efficacy and wider substrate scope. Directly observing bond cleaving and forming events underpinning a catalytic reaction is non-trivial as the species that facilitate these steps are frequently short-lived and present at low concentrations. Here we describe how the photochemical activation of a manganese precatalyst, [Mn(ppy)(CO)4], results in selective loss of a carbonyl ligand simulating entry into the catalytic cycle for Mn-promoted C–H bond functionalisation. Time-resolved infra-red spectroscopy (ps-ms timescale) allows direct observation of the species responsible for the essential carbon-carbon bond formation step and an evaluation of the factors affecting its rate. The mechanistic information prompted discovery of a new photochemically initiated manganese-promoted coupling of phenylacetylene with 2-phenylpyrindine. This study provides unique insight into the mechanistic pathways which underpin catalysis by an Earth-abundant metal, manganese.

**Introduction**

Transition metal-catalysed reactions play a central role in modern synthetic chemistry. A key advantage of such reagents is that detailed mechanistic investigations and/or structure/activity relationships permit the proposal of catalytic cycle(s) that can be subsequently used to rationally optimise catalyst structure, typically through judicious ligand selection and substrate matching. Studies which correlate ligand parameters with reaction kinetics, complemented with the observation of catalyst resting states, isotopic labelling and quantum chemical calculations (often using Density Functional Theory, DFT) are highly informative. The missing information is often the direct observation of the actual metal complexes involved within a catalytic cycle. A quantification of their behaviour can provide a precise understanding of the interplay between the different steps underpinning a given reaction, in addition highlighting subtle differences between substrates and co-ligands, specifically the balance between them. Such an approach is fraught with difficulty as the observation of the short-lived key states within the catalytic cycle is, by definition, challenging. Furthermore, the individual steps within a catalytic process are likely to occur over different timescales, with, for example, substrate coordination occurring at a markedly different rate to subsequent C-C bond forming events.

Time-resolved multiple-probe spectroscopy, TRMPS,1 permits the direct observation of molecular events over a wide timescale range, typically femto-second to micro-second. This is made possible using a synchronised 1 kHz pump and 10 kHz probe lasers together with integrated electronic and translational control over time delay. Photochemically initiated time-resolved spectroscopy enables observation of short-lived and fundamentally important species, *e.g.* alkane -complexes,2 enabling rationalisation of organometallic mechanistic processes.3, 4, 5, 6 However, with an appropriate choice of catalyst system, TRMPS has the potential to permit monitoring of a photo-initiated catalytic cycle by time-resolved infra-red spectroscopy (TRIR) over nine orders of magnitude in time. Conducting the experiment in the presence of an appropriate substrate would enable the interaction between the ligand and the photo-activated catalyst to be observed, allowing insight into the nature and fate of catalytically relevant states to be obtained.

To demonstrate the feasibility of the proposed approach, manganese-catalysed C-H bond functionalisations were selected as the first exemplar of this methodology. Transition-metal catalysed direct functionalisation of carbon-hydrogen bonds offers rapid and atom-efficient methods for structural elaboration.7 Following the key developments in C—H functionalisation methods using Platinum Group Metals (PGMs), notably ruthenium,8 rhodium9, 10 and palladium,11 there is an increasing desire to translate these synthetic methods to more sustainable Earth-abundant metals, such as manganese.12, 13, 14, 15 Simple precursors such as [MnBr(CO)5] or [Mn2(CO)10] may be employed to catalyse the formal insertion of unsaturated substrates (such as alkynes,16, 17, 18, 19, 20, 21, 22,23{Zhou, 2013 #618} alkenes,24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34 allenes,35, 36, 37, 38 isocyanates39 and carbonyl40, 41, 42, 43 compounds) into the C-H bond of heteroaromatic substrates (Figure 1a).44, 45, 46 The heteroatom, typically nitrogen, plays a central role in the initial coordination of this substrate to the metal and directing the site of C—H functionalisation.

The generally proposed mechanistic picture of Mn-catalysed C—H functionalisation reactions (Figure 1b, which uses 2-phenylpyridine as an exemplar substrate) involves cyclomanganation to give [Mn(ppy)(CO)4], **1**. Subsequent loss of a carbonyl ligand results in the initial formation of solvent complex **I**: coordination of the unsaturated substrate to the metal gives **II**. This is followed by insertion of the unsaturated substrate (E=CRn) into the Mn—C bond resulting in the formation of metallocycle **III**. Protonation liberates the product and restarts the catalytic cycle. In a recent study, we demonstrated how low-temperaturephotolysis of **2**, which is structurally related to **1**, can be used to generate metallocycle **IV** (Figure 1c).47 Complex **IV** may undergo reductive elimination to give **V** or liberate the alkenylated product **VI**, thus acting as a branching point in the reaction. Complex **1** was also successfully employed as a pre-catalyst, supporting its proposed role in catalysis.16



**Figure 1 Summary of Mn-catalysed C-H functionalisation reactions**. **a,** Exemplar synthetic transformations **b,** Mechanistic steps proposed to underpin the catalytic cycle. **c**, Observation of a manganacycle intermediate which acts as a branching point in catalysis to give either reductive elimination product **V** or, in the presence of alkyne, the product expected from a C-H functionalisation reaction **VI** analogous to a(i). **d**, metal complexes employed in this study, including the molecular structures of **3** and **4** determined by single crystal X-ray diffraction.

Photolysis of **1** would result in photo-ejection of a CO ligand from the manganese, simulating the formation of **II** and entry into the catalytic cycle (Figure 1b). The subsequent changes in the coordination environment at manganese will be reflected in the frequency and symmetry of the metal carbonyl stretch modes in the infra-red spectrum (2100-1850 cm-1). Difference spectra acquired using TRMPS will therefore provide quantitative and qualitative insight into the nature of ligand binding and the kinetics of carbon-carbon bond formation steps within the catalytic cycle.

The successful implementation of this strategy is now reported. The nature of the binding of alkynes (*e.g.* PhC≡CH), alkenes (*e.g.* H2C=CHCO2nBu), hexylisocyanate and benzaldehyde to manganese are successfully demonstrated, with n-butyl acrylate showing an unexpected competition between 1(O) and 2(C=C) binding modes. The kinetics of the subsequent C—C bond formation steps to give metallacycles related to **III** provide insight into the effect of different unsaturated substrates and cyclometallated ligands. The effects of the cyclometallated ligand on the insertion reaction has been further probed by substituting the 2-phenylpyridyl ligand in **1** for 4-(2'-pyridyl)-6-methyl-2-pyrone, **2**, *N*-benzyl-4-(2’-pyridyl)-6-methylpyridin-2-one, **3** and 1-(pyridine-2-yl)-1H-indole, **4**, (Figure 1d), allowing electronic perturbations to be probed in the ring-system which contains the C—H bond undergoing activation and functionalisation.

**Results**

**Photochemically induced loss of CO from 1**

Photolysis of **1** with a pump wavelength of 355 nm results in ultra-fast (< 0.5 ps) dissociation of a CO ligand and formation of *fac*-[Mn(ppy)(CO)3(S)], where S is the solvent used for the experiment. Initial experiments were performed in neat unsaturated substrate, *e.g.* alkyne, alkene or isocyanate, ensuring that following initial loss of CO from **1** only a single coordination event to MnI was viable. The resulting changes to the vibrational modes of the metal carbonyl region (1800-2200 cm-1) are diagnostic for the structural changes at the metal, although the high concentration of unsaturated substrate saturates the regions in the IR spectrum where it absorbs, precluding the use of any diagnostic bands of the organic reagents to probe metal-ligand interactions. The difference spectra acquired after photolysis exhibited strong negative peaks corresponding to those for the ground state of **1** at *ca.* 1940, 1978, 1992 and 2075 cm-1 (Figure 2b). This indicated loss of the precursor and excluded any interference from a background thermal reaction in the TRMPS experiment. Positive carbonyl stretching bands in the difference spectra indicate the generation of photoproducts which, as evidenced by the change from four to three carbonyl bands, indicated that CO-dissociation had occurred. In all cases a high energy band was observed at *ca.* 2000 cm-1 corresponding to the symmetric stretching mode of the three CO ligands whereas two asymmetric stretching modes were observed at lower energy as expected for *fac*-coordinated tricarbonyl compounds.48 The experiments performed in neat substrate all displayed a similar pattern – at short timescales (< 250 ps) following the pump pulse, unselective ligand binding, *e.g*. through an alkyl chain or arene, to MnI occurs. These species then underwent a rearrangement to a thermodynamically preferable binding mode and, in certain cases, a subsequent insertion reaction was observed, the rate of which depends on the unsaturated substrate and cyclometallated ligand employed. Structural assignments were made based on comparisons to reference systems and predicted spectral changes from Density Functional Theory (DFT).

**Observation of alkyne binding to manganese and insertion into Mn—C bonds**

TRIR spectra of **1** recorded using TRMPS in neat PhC≡CH exhibited intense negative bands corresponding to bleaches of the carbonyl stretching vibrations of the ground state of **1**, Figure 2b, and evidence was obtained for the formation of three different species over the timescale of the experiment (Figure 2b). An initial photoproduct **A** with bands at 1907 and 2004 cm-1 was formed over the course of *ca.* 5 ps. Photoproduct **A** exhibited an exponential decay, *k* = (3.83 ± 0.73) × 109 s-1 to give **B** with bands at 1909, 1941 and 2008 cm-1; **B** then converted to **C** (bands at 1897, 1917 and 2006 cm-1; *k* = (1.35 ± 0.04) × 105 s-1).



**Figure 2** TRIR data for the reaction between **1** and PhC≡CH.

**Figure 2 Caption**

**a**, reaction scheme showing the proposed structures for intermediates **A**, **B** and **C**. **b**, TRIR data in the metal carbonyl region, the y-axis is change in absorbance, the negative peaks correspond to the bleach of the bands for **1**, the positive bands show the growth and change of intermediates. Data were acquired in a sealed flow system under ambient conditions. Spectra with pump-probe delays of 10 ps corresponding to **A**, ▼, (bands at 1907, and 2004 cm-1), 1 ns corresponding to **B**, ⚫, (bands at 1909, 1941 and 2008 cm-1,) and at 50 s for **C**, ▲, (bands at 1897, 1917 and 2006 cm-1). The bottom spectrum is the ground state spectrum of **1** in toluene solution. **c** TRIR data for **1** in a toluene/phenylacetylene solution (0.5 % *v/v*) recorded with pump-probe delays of 10 ps corresponding to [Mn(ppy)(CO)3(toluene) (bands at 1907 and 2004 cm-1), 1 ns corresponding to **B**, ⚫, (bands at 1909, 1940 and 2008 cm-1,) and at 50 s for **C**, ▲, (bands at 1990, 1917 and 2006 cm-1). The bottom spectrum is a TRIR experiment performed on **1** in pure toluene solution (bands at 1907 and 2004 cm-1). **d** Kinetic plots for the reactions in neat phenylacetylene (left) (fits to exponential fits in dotted lines). Experimental data for **B**, ⚫, (band at 1941 cm-1, *k* = (1.67 ± 0.28) × 105 s-1) and **C** , ▲, (band at 1900 cm-1, *k* = (1.35 ± 0.09) × 105). Kinetic plots for the reactions in toluene/phenylacetylene solution (0.5 % *v/v*) (right). (fits to exponential growth-and-decay for **B** and exponential function **C**). Experimental data for **B** , ⚫, (band at 1941 cm-1, *k* = (1.67 ± 0.31) × 105 s-1) and **C** , ▲,(band at 1900 cm-1, *kg* = (3.85 ± 0.63) × 106 s-1, *kd* = (1.78 ± 0.21) × 105 s-1).

These data are consistent with a pathway where the photo-ejection of CO from **1** results in an initial unselective binding of the alkyne to the metal. In a related study we have shown that photolysis of **1** in solvents such as THF or nBu2O can result in the initial binding as a C-H -complex,49 toluene appears to bind to MnI through its -system. Comparison with the data obtained in toluene (*q.v.*) indicates that initial binding of PhC≡CH through the arene occurs: this is followed by isomerisation to the thermodynamically more stable -bound alkyne form **B**.50 The blue shift in the IR stretching bands for **B** compared to **A** is consistent with the presence of an 2-(C≡C)-bound alkyne within the coordination sphere of MnI. The alkyne is an additional -acceptor which will reduce back-bonding to the three remaining carbonyl ligands, hence the observed shift in stretching frequency for **B**. The formation of **C** corresponds to the insertion of the alkyne into the Mn-C bond, with the red shift in the IR spectra consistent with the conversion of the -accepting alkyne ligand to the seven-membered metallacycle in **C**. The rate of the insertion (**B** → **C**) at 298 K corresponds to a free energy of activation of 44 kJ mol-1, which is in good agreement with that calculated by DFT (32 kJ mol-1).

Repeating the experiment using an 0.5 % *v/v* solution of PhC≡CH (Figure 2c) in toluene provides additional support for the interpretation of the data. In this instance, the initial photoproduct shows bands at 1907 and 2000 cm-1 which corresponds to a -bound toluene complex.49 The bands for **B** were then observed to grow in intensity, *kobs* = (3.85 ± 0.63) × 106 s-1, with a subsequent conversion to **C**:the rate of this latter process is statistically identical to the experiment performed in neat PhC≡CH (Figure 5a), supporting the interpretation that this process is unimolecular in nature and does not arise from reactions with an additional molecule(s) of alkyne. Consistent with this explanation, an experiment performed at an intermediate concentration of PhC≡CH (6 % *v/v* in toluene, Supplementary Figure 18) showed accelerated formation of **B**, *kobs* = (1.77 ± 0.55) × 107 s-1,with a similar rate of conversion of **B** to **C** observed(Figure 5a).

The observation of alkyne coordination to MnI, coupled with the resulting insertion process in toluene solution, provides confidence that the results are pertinent to the catalytic systems. Furthermore, the data indicate that in reactions that are thermally promoted the coordination of the alkyne occurs extremely rapidly (s timescale), following the initial loss of a CO ligand from **1**.

To ascertain the factors controlling the rate of alkyne insertion into the Mn-C bond, analogous experiments in neat PhC≡CH with compounds **2**, **3** and **4** were conducted (Supplementary Figures 20, 22 and 24 respectively). Complex **4** is of particular interest as the indole-substituted substrate has been employed in a range of different Mn-catalysed reactions.20, 21, 22, 23, 29, 34, 38, 39, 42 Spectral analysis demonstrated that the rate of alkyne insertion into the Mn-C bond decreased in the sequence **3** > **2** > **1** > **4** a trend in behaviour that was predicted by DFT (Figure 5a). The behaviour of HC≡CCH2CO2Ph (a substrate which can also be used in Mn-catalysed C-H functionalisations)16 mirrored the observations for PhC≡CH (Supplementary Figure 26). Initial binding to the phenyl group of the alkyne was seen, followed by migration to the 2-C≡C-bound form: subsequent C-C bond formation by alkyne insertion occurs at a similar rate as that for PhC≡CH (Figure 5a), consistent with the prediction from DFT. These data demonstrate that it is possible to use TRMPS to directly activate MnI-carbonyl complexes and observe subsequent substrate binding and C—C bond formation steps which underpin the catalytic cycle.

**Observation of alkene binding to manganese and insertion into Mn—C bonds**

In addition to alkynes, polarised (activated) alkenes are viable unsaturated substrates for MnI-catalysed C—H functionalisations (Figure 1a, reaction ii).24, 25 The presence of the carbonyl group connected to the alkene is vital; substrates such as styrene are not viable.24 Probing complexes **1** - **3** in n-butyl acrylate and **1** in ethyl acrylate, using TRMPS, provided new insight into the key interactions between the MnI and the substrates. The resulting spectra for **1** in neat n-butyl acrylate are presented in Figure 3b.

Spectra recorded with short delays (< 10 ps) exhibited broad features which sharpened (presumably as a result of vibrational cooling)50 to give bands at 1909 and 2006 cm-1. Based on the similarity of these bands with those of the -alkane complex [Mn(ppy)(CO)3(heptane)],49 generated from the

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**Figure 3**. TRIR data for the reaction between **1** and H2C=CHCO2nBu.

**Figure 3 Caption**

**a**, reaction scheme showing the proposed structures for intermediates **D**, **E**, **F** and **G**. **b**, TRIR data in the metal carbonyl region, the y-axis is change in absorbance, the negative peaks correspond to the bleach of the bands for **1**, the positive bands show the growth and change of intermediates. Data were acquired in a sealed flow system under ambient conditions. Spectra recorded with pump-probe delays of 10 ps corresponding to **D**, ▼, (bands at 1894, 1910, and 2007 cm-1), 1 ns corresponding to **E**, ⚫, (bands at 1890, 1903 and 1997 cm-1,) **F**, ◼, (bands at 2021 cm-1) and at 100 s for **G** ▲, (bands at 1907, 1921 and 2008 cm-1). Reference spectra for complexes **H** and **I** prepared from the photolysis of **1** in neat ethylacetate and styrene respectively with pump-probe delays of 1 ns. **c**, kinetic plots showing the change in absorbance due to the loss of **E** and **F** (⚫, 1997 cm-1 and ◼, 2021 cm-1 respectively) and the growth of **G** (▲, 2008 cm-1). The dashed lines are fits to a kinetic model **E** → **F** → **G** with rate constants of **E** → **F** = (3. 21 ± 0.01) × 104 s-1 and **F** → **G** = (3.62 ± 0.01) × 104 s-1 **d**. Structures of complexes **H**-**J** and DFT-calculated potential energy surface for the insertion of butyl acrylate into the Mn-C bond. Energies are Gibbs energies at 298.15 K at the D3-pbe0/def2-TZVPP//bp86/sv(p) level with COSMO solvent correction and are relative to **E**.

photolysis of **1** in neat heptane, this initial photoproduct was assigned as -complex, **D**. Over the course of 100 ps these stretching bands decreased in intensity to be replaced by those for **E** (1890, 1903 and 1997 cm-1) and **F** (2017 cm-1): additional peaks for **F** may be obscured either by those of **E** or the bleach bands. The observed rate constants for the growth of **E** (2.89 ± 0.55) × 1010 s-1 and **F** (2.72 ± 0.79) × 1010 s-1 were statistically identical (Supplementary Figures 28 and 29).

Insight into the nature of **E** and **F** was obtained from control experiments with ethyl acetate and styrene. Photolysis of **1** in neat ethyl acetate gave **H** (Figure 3d), which showed bands essentially identical to **E**. Hence the ligand was assigned an 1(O)-substrate binding mode in both cases. The significant blue shift observed in the spectrum of **F** (2017 cm-1) is consistent with the introduction of a good -acceptor ligand into the coordination sphere of MnI. Hence the n-butyl acrylate ligand was assigned an 2-C=C -bonding mode in **F**. A smaller, but still significant, blue shift was observed in the 2-C=C complex, **I**, obtained on photolysis of **1** in neat styrene (bands at 1911, 1943, 2006 cm-1). The smaller shift compared to **F** is expected as the more electron-deficient butyl acrylate is expected to be a better -acceptor than styrene.51

A related study into the photochemical reaction between **1** and ethyl acrylate demonstrated that the formation of analogous species of **E** and **F** from the corresponding -complex was more rapid, *k* = (5.95 ± 0.51) × 1010 s-1 and (4.96 ± 0.71) × 1010 s-1 respectively (Supplementary Figures 31 and 32). This is consistent with the initial binding of the manganese at the alkyl group of the acrylate before chain-walking to either the oxygen atom or alkene group. Presuming that the chain-walking is stochastic in nature, this would occur more rapidly in ethyl acrylate when compared to the n-butyl analogue, due to the greater number of C-H bonds in the latter, as was observed.52

Over the course of 100 s the bands for both **E** and **F** decreased in intensity to be replaced by those for a single new species **G** (1907, 1921 and 2008 cm-1). Kinetic modelling (Figure 3c and Supplementary Discussion) of the resulting data indicated that a mechanistic process **E** → **F** → **G** was feasible, with the rate constants of both steps being similar.

These data allowed us to propose the mechanistic pathway for alkene insertion shown in Figure 3a. A critical observation is that competitive 1(O) and 2(C=C) binding of the n-butyl acrylate is viable, but only the latter leads to the product. This is consistent with DFT calculations that indicate there is a small difference in energy between **E** and **F** and the barrier to alkene insertion from **F** is greater than that for PhC≡CH. A transition state for C-C bond formation from **E** could be located (**TSEJ**, Figure 3d), although the barrier was found to be too high (+118 kJ mol-1) for the resulting process to be observed on the timescale of the experiments.

Wang and co-workers24 have proposed that coordination of the ester functionality underpins the successful implementation of acrylates in the catalytic reaction (Figure 1a, reaction ii). While it may be conjectured that our data show that the C-C bond formation occurs at a *fac-*Mn(CO)3 complex, rather than the dicarbonyl complexes proposed by Wang, it is evident that that the ester group plays a central role in coordination to the metal. Styrene is not a viable substrate for the catalytic reaction. Indeed, no insertion into the Mn-C bond from 2(C=C) bound complex **I** was observed reflecting the higher predicted barrier for this process (55 kJ mol-1) when compared to n-butyl acrylate (41 kJ mol-1, Figure 5a).

**Observation of isocyanate and benzaldehyde binding to MnI and insertion into Mn—C bonds**

The insertion of isocyanates into an Mn—C bond has been proposed to be a key step in manganese-catalysed aminocarbonylation (Figure 1A, reaction iv).39 The resulting TRIR study of **1** in hexylisocyanate demonstrated the sequential formation of four photoproducts **K**, **L** , **M** and **N** (Figure 4a). At short timescales (*ca.* 10 ps) both **K** and **L** were present (Figure 4b). Subsequently **K** converted to **L** (*k* = (1.89 ± 0.26) × 1010 s-1) and the pathway **L** → **M** → **N** was observed with the rate constant of the last step *k* = (4.38 ± 0.02) × 103 s-1. Complex **K** was assigned as a C-H -complex based on its similarity to the spectrum of **D**. Product **N** was assigned as arising from insertion of the isocyanate into the Mn—C bond based on theobserved blue shift in the three carbonyl bands (1919, 1945, 2028 cm-1), mirroring those predicted computationally (Supplementary Table 1). The



**Figure 4** TRIR data for the reaction between **1** and HexNCO**.**

**Figure 4 Caption**

**a**, reaction scheme showing the proposed structures for intermediates **K**, **L**, **M** and **N**. **b**, TRIR data in the metal carbonyl region, the y-axis is change in absorbance, the negative peaks correspond to the bleach of the bands for **1**, the positive bands show the growth and change of intermediates. Data were acquired in a sealed flow system under ambient conditions. Spectra recorded with pump-probe delays of 10 ps corresponding to **K**, ▼, (bands at 1907 and 2007 cm-1) and **L**, ⚫, (bands at 1897, 1907 and 2002 cm-1), 1 ns corresponding to **M**,◼, (bands at 1894, 1911 and 1999 cm-1), and at both 50 s and 600 s for **M**, ◼,and **N**, ▲, (bands at 1918, 1944 and 2027 cm-1). **c**, double y plot showing the change in absorbance due to the loss of **M** (◼ 2000 cm-1, left-hand axis) and the growth of **N** (▲, 2027 cm-1, right-hand axis). The dashed lines are fits to exponential growth (**N**) and decay (**M**) functions. The data for **N** have been corrected for flow-effects (see E.S.I.) **d**. reaction scheme showing the proposed structures for intermediates **O**, **P** and **Q**.

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| Complex | Substrate | *kinsert* / s-1 | G‡298 / kJ mol-1 | DFT-Predicted G‡298 / kJ mol-1 | DFT-Predicted G298 / kJ mol-1 |
| **1** | HC≡CPh | (1.35 ± 0.09) × 105 | 44 | 34 | -95 |
| **1** | HC≡CPh [a] | (1.63 ± 0.18) × 105 | 43 | 34 | -95 |
| **1** | HC≡CPh [b] | (1.78 ± 0.21) × 105 | 43 | 34 | -95 |
| **2** | HC≡CPh | (1.04 ± 0.15) × 106 | 39 | 26 | -77 |
| **3** | HC≡CPh | (7.46 ± 1.28) × 106 | 34 | 20 | -87 |
| **4** | HC≡CPh | (2.00 ± 0.08) × 104 | 48 | 42 | -88 |
| **1** | HC≡CCH2CO2Ph | (1.79 ± 0.49) × 105 | 43 | 35 | -102 |
| **1** | H2C=CHPh | N.O. | N.O. | 55 | -11 |
| **2** | H2C=CHPh | N.O. | N.O. | 53 | +7 |
| **3** | H2C=CHPh | N.O. | N.O. | 46 | -4 |
| **1** | H2C=CHCO2nBu | (3.62 ± 0.01) × 104 | 47 | 41 | -47 |
| **1** | HexCNO | (4.38 ± 0.02) × 103 | 52 | 39 | -57 |
| **1** | PhC(O)H | N.O. | N.O. | 48 | -11 |

** Figure 5** Analysis of experimental and DFT-calculated reaction kinetics.

**Caption** (a) Tabulated rates of insertion, free energies of activation at 298 K and DFT-calculated free energies of activation. (b) DFT-calculated structures of complexes II, TSII-III and III for the reaction of 1 with PhC≡CH, H2C=CHCO2nBu and HexCNO. Selected bond lengths (Å) are given.In the case of PhC≡CH **II** and **III** correspond to the experimentally observed species **B** and **C**, for nBuO2CCH=CH2,**F** and **G** and for HexNCO **M** and **N** respectively. [a] 6 % *v/v* PhC≡CH in toluene solution [b] 0.5 % v:v PhC≡CH in toluene solution. N. O. no insertion reaction was observed. DFT-calculated energies are at the D3-pbe0/def2-TZVPP//bp86/sv(p) level with COSMO solvent correction and are relative to the appropriate complex **II**, in the case of the acrylate complexes, this is the *O*-bound form.

assignment of structures **L** (*O*-bound isocyanate) and **M** (*N*-bound isocyanate) was made on the basis that (1) **M** it predicted to be at lower energy than **L** (G298 **L-M** = -12 kJ mol-1), hence **M** would not convert to **L** and (2) an appropriate transition state for the conversion of **M** to **N** could be located at an energy (G298‡**M-N** = +39 kJ mol-1), consistent with the observed rate of reaction (Figure 5a). The predicted IR stretching modes for **L** and **M** are similar, as are the experimental spectra, hence they could not be used to distinguish between the two binding modes.

The conversion of **M** to **N** was proposed by Ackermann *et al.*39 to be the rate-limiting step in manganese-catalysed aminocarbonylation and, although our data do not currently allow for a direct comparison with the rates of C-H activation, the insertion of the hexyl isocyanate is slower than PhC≡CH and acrylate substrates. A TRMPS experiment on the reaction between **1** and benzaldehyde (Supplementary Figure 33) was performed to mirror the manganese-catalysed insertion of an aldehyde into a C-H bond (Figure 1a, reaction iii).41,43 In the same manner as the experiments conducted with PhC≡CH, a short-lived complex corresponding to the aryl-bound aldehyde photoproduct **O** was formed. Complex **O** then isomerised to **P** in which the benzaldehyde was assignedan 1(O)-binding mode based on the spectral similarity of both **E** and **H**. In these experiments an additional band at 1819 cm-1, assigned to the benzoyl radical [PhCO]●,53 was observed, both in the presence and absence of **1**, consistent with this being a photoproduct of benzaldehyde (Supplementary Figure 33). Complex **P** remained unchanged for the experiment duration (850 s), indicating that any insertion into the Mn-C bond to give **Q** (Figure 4) must be much slower than the experiment timescale. This deduction is supported by DFT calculations that show a larger barrier to insertion of benzaldehyde into the Mn-C bond (48 kJ mol-1)when compared to PhC≡CH, butyl acrylate and hexylisocyanate.

In contrast to the reactions involving alkyne and activated alkene substrates, the Mn-catalysed addition of benzaldehyde to cyclometallated heteroaromatic stubstrates rely on the use an additive. 41, 43 For example, as shown in Scheme 1a(iii), the coupling of 1-methyl-2-phenyl-1*H*-imidazole requires the use of a silane to trap the product. The DFT-calculated change in free energy for the formation of **Q** from **P** is the smallest in this study (G298 = -11 kJ mol-1), demonstrating that these is only a small thermodynamic driving force for the C-C bond formation step which may explain the requirement for the silane. Furthermore, ZnBr2 is required to promote the coupling of 2-phenylpyridine with benzaldehyde and it is proposed that the Lewis acid assists with the insertion step by increasing the electrophilicity of the aldehyde. Our data indicate that this insertion step would be certainly be slower than that of alkynes and activated alkenes and provide some support for this hypothesis.

**A photochemically promoted alkenylation reaction**

Given that the photodissociation of CO occurs readily at wavelengths of either 355 or 400 nm49 and, for substrates such as PhC≡CH, the C-C bond formation is occurring on a sub-millisecond timescale, it was reasoned that the formation of the alkenylated product **5** from **1** could be initiated by light. Reaction optimisation (Figure 6) demonstrated that LED irradiation (400 nm) of a room temperature nBu2O solution of **1** for 3 hr in the presence of PhC≡CH (2 equivalents) and PhCO2H (1 equivalent) leads to 59 % conversion to **5**: extending the irradiation to 48 hr resulted in 81 % conversion. No product was observed under the same conditions in the absence of LED irradiation, demonstrating the potential for a room temperature photochemically induced manganese-promoted alkenylation reaction. The discovery of what is the mildest MnI-prompted alkenylation was driven by the mechanistic information unearthed from this TRIR study.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | | | |
| Entry | Solvent | Additive | Time / h | Conversion to **5** / % |
| 1 | Bu2O | None | 3 | 21 |
| 2 | Bu2O | PhCO2H | 3 | 59 |
| 3 | Bu2O | PhCO2H | 16 | 67 |
| 4 | Bu2O | PhCO2H | 48 | 81 |
| 5 | Bu2O | EtCO2H | 3 | 45 |
| 6 | Toluene | PhCO2H | 3 | 50 |
| 7a | Bu2O | PhCO2H | 16 | 0 |
| 8 b | Bu2O | PhCO2H | 3 | 0 |

**Figure 6 Photochemical generation of (*E*)-2-(2-styrylphenyl)pyridine, 5, from 1 and PhC≡CH.** a. reaction performed in the absence of **1**. b Reaction performed without irradiation.

**Discussion**

The kinetic data for the insertion steps for all the reactions studied are presented in Figure 5a, along with the DFT-predicted values for G‡298 and G298. There is a direct correlation between the experimentally determined values for G‡298 and those predicted by DFT. These data demonstrate that the barrier to insertion into the Mn-C bond of **1** increase in the series PhC≡CH ≈ HC≡CCH2OCOPh < H2C=CHCO2nBu ≈ HexNCO << PhC(O)H < H2C=CHPh: in the case of PhC≡CH the insertion increases in the series **3** < **2** < **1** < **4**.

As shown in Figure 5a, the DFT calculations reveal a common pathway for C—C bond formation in this series of complexes. Prior to C—C bond formation (State **II**, Figure 5b) the unsaturated ligand (alkyne, alkene or isocyanate) is ligand aligned along the M-C axis of the 2-phenylpridine ligand. In the calculated transition state structures for C—C bond formation, (**TSII-III**) for the alkyne and alkene examples, the Mn-Cb bond lengthens, as does the Cb—Cc bond, however, the Mn—Cc shortens. Similar effects are seen in the HexNCO example, with a shortening of the Mn—Nc bond and bending of the isocyanate ligand. In all three cases, the phenyl group of the 2-phenylpyridyl group deviates from planarity in the transition state and there is a notable lengthening of the Mn—Ca bond. Therefore, our experimental and computational data indicate a common low-energy pathway for C—C bond formation in these Mn-catalysed reactions which is probably best viewed as a migratory insertion reaction supported by a low-spin d6 Mn(CO)3 fragment.

These experiments permitted the direct observation of C—C bond formation by insertion of unsaturated substrates into the MnI—C bond, within the coordination sphere of cyclometallated *fac*-Mn(CO)3 complexes, indicating that it is a viable mechanistic pathway underpinning manganese-catalysed C-H functionalisation reactions. The effect of different substrates and co-ligands within the coordination sphere of the metal have been quantified. Detailed information about substrate binding to MnI, *e.g.* an unexpected 1(O)-binding mode observed for acrylate substrates and the reactions performed in toluene solution with PhC≡CH, have provided information about the kinetics of the coordination step of the cycle. Central to the success of this unique approach to the study of individual steps within a catalytic cycle is the versatility of TRMPS, which permits the observation of processes occurring over a wide range of timescales and of short-lived states that have only previously been predicted computationally.

**Author Contributions**

J.M.L. and I.J.S.F. conceived the experimental programme with input on project direction from A.R.. L.A.H, J.M.L., I.J.S.F., I.P.C. and I.V.S. conducted the TRIR experiments on instrumentation set-up and built by M.T. Compounds **1** and **2** were prepared by L.A.H., F.C. prepared compound **3**, S. M. prepared compound **4**. J.M.L. performed and analysed the DFT calculations. TRIR data were analysed by J.M.L., L.A.H., I.J.S.F., I.P.C. and M.T.. J.M.L. wrote the paper with input from all authors.

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**Competing interests:**

The authors declare no competing interests

**Data availability:**

All data supporting this study are available by request from the University of York's York Research Database http://dx.doi.org/10.15124/46f25600-736a-408a-b498-8b7f6a5f3f2e.

**Methods**

**Sample Preparation**

Compounds **1**54 and **2**47 were prepared by literature methods. The syntheses and characterisation of **3** and **4** are described in the Supplementary Methods. Substrates were purchased from Sigma Aldrich and used as supplied. Solutions of the manganese complexes were prepared at a concentration of *ca.* 1.88 mM in the appropriate substrate and flowed through a Harrick cell for the duration of the TRIR experiment.

**TRIR Measurements**

The TRIR measurements were performed at the ULTRA55 facility using the Time-Resolved Multiple Probe Spectroscopy mode of operation,1 (hereafter TRMPS) at the Central Laser Facility (STFC Rutherford Appleton Laboratories, Oxfordshire, UK). The experiments were driven by a 10 kHz repetition rate Ti:Sapphire amplifier (Thales) as a probe source, producing 40 fs pulses at 800 nm. The Ti:Sapphire laser output was used to pump an Optical Parametric Amplifier (TOPAS, Light Conversion Ltd.) followed by a AgGaS Difference Frequency Mixing stage which produced tuneable mid-IR probe beam of ~ 500 cm-1 useable bandwidth. The IR probe beam was split to form reference and probe beams, which were passed through spectrographs onto MCT array detectors (IR Associates). The probe beam spot size at sample was ca. 80x80 μm2. High speed data acquisition systems (Quantum Detectors) allowed 10 kHz acquisition and processing of the probe and reference pulses to generate a pump-on pump-off infrared absorption difference signal. The excitation source for the TRIR experiments was the output of the 1 kHz titanium sapphire amplifier (Spectra Physics Spitfire XP, 100 fs pulse length) equipped with another TOPAS OPA, pulse energy at sample attenuated down to 1 μJ and focused down to ca. 150 × 150 μm2 spot). Both ULTRA amplifier and Spitfire amplifier were optically synchronised by sharing the same seed from 68 MHz Ti:Sapphire oscillator. The seed beam was delayed with an optical delay line before the 1 kHz amplifier to accommodate for the 100 fs – 14.7 ns time delays between pump and probe. To go beyond 14.7 ns and up to 100 μs, subsequent seed pulses are selected from the 68 MHz seed pulse train accompanied by the appropriate setting of the optical delay line. The polarisation of the excitation beam at sample was set to be at 54.7° with respect to the probe.

Data were collected with pump-probe delays from 0.5 ps to 850 µs. Datasets were acquired with the pump laser on (pump-on) and also under essentially identical conditions with the pump laser off (pump-off). Subtraction of the pump-off data from the pump-on allowed for a number of artefacts from electrical noise to be eliminated. The resulting data were then manipulated by firstly subtracting the reference data to obtain a difference spectrum and then a first- or second-order polynomial fitting to the baseline was performed. The data were then exported as comma-separated variable files and imported into Origin. Spectral calibration was then performed with a 190 m polystyrene standard allowing for detector pixels to be allocated to specific frequencies. The overlap in detection frequency between the two detectors was then removed manually. Kinetic data were obtained by fitting the intensities of selected peak maxima to appropriate functions within Origin. In the cases in which kinetic process were occurring over long pump-probe delays (e.g. greater than 1 s) then only the data with pump-probe delays of greater than 1 ms were typically considered. In addition, for the analysis of more rapid processes (< 1 ms) then only the data at short pump-probe delays were employed.

**Data Analysis**

Spectra were initially processed to perform subtraction of reference spectra and baseline correction, the resulting data were then analysed in Origin and kinetic fits performed with the *ExpGro*, *ExpDec* and *ExpGroDec* functions. Quoted errors are 95 % confidence limits. Rate constants, *k*, were converted to free energies of action G‡ using the Eyring equation where T was taken as 298 K and the transmission coefficient,  of unity.

**Computational Chemistry**

All calculations were performed using the TURBOMOLE V6.4 package using the resolution of identity (RI) approximation.56, 57, 58, 59, 60, 61, 62, 63

Initial optimisations were performed at the (RI-)BP86/SV(P) level, followed by frequency calculations at the same level. Transition states were located by initially performing a constrained minimisation (by freezing internal coordinates that change most during the reaction) of a structure close to the anticipated transition state. This was followed by a frequency calculation to identify the transition vector to follow during a subsequent transition state optimisation. A final frequency calculation was then performed on the optimised transition-state structure. All minima were confirmed as such by the absence of imaginary frequencies and all transition states were identified by the presence of only one imaginary frequency. Dynamic Reaction Coordinate analysis confirmed that transition states were connected to the appropriate minima. Single-point calculations on the (RI-)BP86/SV(P) optimised geometries were performed using the hybrid PBE0 functional and the flexible def2-TZVPP basis set. The (RI-)PBE0/def2-TZVPP SCF energies were corrected for their zero point energies, thermal energies and entropies (obtained from the (RI-)BP86/SV(P)-level frequency calculations). No symmetry constraints were applied during optimisations. Solvent corrections were applied with the COSMO dielectric continuum model64 and dispersion effects modelled with Grimme’s D3 method.65, 66 Energies, xyz coordinates and the first 50 lines of the vibrational spectra are presented in Supplementary Data 1.

**References**

1. Greetham G. M., Sole D., Clark I. P., Parker A. W., Pollard M. R., Towrie M. Time-resolved multiple probe spectroscopy. *Rev. Sci. Instrum.*, **83**, 103107 (2012).

2. Calladine J. A., Torres O., Anstey M., Ball G. E., Bergman R. G., Curley J.*, et al.* Photoinduced N2 loss as a route to long-lived organometallic alkane complexes: A time-resolved IR and NMR study. *Chem. Sci.*, **1**, 622-630 (2010).

3. Ford P. C. From curiosity to applications. A personal perspective on inorganic photochemistry. *Chem. Sci.*, **7**, 2964-2986 (2016).

4. Jackson S. A., Hodges P. M., Poliakoff M., Turner J. J., Grevels F. W. Infrared spectroscopic studies on the photocatalytic hydrogenation of norbornadiene by Group 6 metal carbonyls. 1. The role of H2 and the characterization of nonclassical dihydrogen complexes, (η4-norbornadiene)M(CO)3(η2-H2). *J. Am. Chem. Soc.*, **112**, 1221-1233 (1990).

5. Hodges P. M., Jackson S. A., Jacke J., Poliakoff M., Turner J. J., Grevels F. W. Infrared spectroscopic studies on the photocatalytic hydrogenation of norbornadiene by Group 6 metal carbonyls. 2. The role of the diene and the characterization of (η4-norbornadiene)(η2-norbornadiene)M(CO)3 complexes. *J. Am. Chem. Soc.*, **112**, 1234-1244 (1990).

6. Guan J., Wriglesworth A., Sun X. Z., Brothers E. N., Zarić S. D., Evans M. E.*, et al.* Probing the Carbon–Hydrogen Activation of Alkanes Following Photolysis of Tp′Rh(CNR)(carbodiimide): A Computational and Time-Resolved Infrared Spectroscopic Study. *J. Am. Chem. Soc.*, **140**, 1842-1854 (2018).

7. Wencel-Delord J., Glorius F. C-H bond activation enables the rapid construction and late-stage diversification of functional molecules. *Nat Chem*, **5**, 369-375 (2013).

8. Arockiam P. B., Bruneau C., Dixneuf P. H. Ruthenium(II)-Catalyzed C–H Bond Activation and Functionalization. *Chem. Rev.*, **112**, 5879-5918 (2012).

9. Song G., Wang F., Li X. C-C, C-O and C-N bond formation via rhodium(iii)-catalyzed oxidative C-H activation. *Chem. Soc. Rev.*, **41**, 3651-3678 (2012).

10. Colby D. A., Bergman R. G., Ellman J. A. Rhodium-Catalyzed C−C Bond Formation via Heteroatom-Directed C−H Bond Activation. *Chem. Rev.*, **110**, 624-655 (2010).

11. Lyons T. W., Sanford M. S. Palladium-Catalyzed Ligand-Directed C−H Functionalization Reactions. *Chem. Rev.*, **110**, 1147-1169 (2010).

12. Pototschnig G., Maulide N., Schnürch M. Direct Functionalization of C−H Bonds by Iron, Nickel, and Cobalt Catalysis. *Chem.-Eur. J.*, **23**, 9206-9232 (2017).

13. Su B., Cao Z.-C., Shi Z.-J. Exploration of Earth-Abundant Transition Metals (Fe, Co, and Ni) as Catalysts in Unreactive Chemical Bond Activations. *Acc. Chem. Res.*, **48**, 886-896 (2015).

14. Moselage M., Li J., Ackermann L. Cobalt-Catalyzed C–H Activation. *ACS Catalysis*, **6**, 498-525 (2016).

15. Shang R., Ilies L., Nakamura E. Iron-Catalyzed C–H Bond Activation. *Chem. Rev.*, **117**, 9086–9139 (2017).

16. Zhou B., Chen H., Wang C. Mn-Catalyzed Aromatic C–H Alkenylation with Terminal Alkynes. *J. Am. Chem. Soc.*, **135**, 1264-1267 (2013).

17. He R., Huang Z.-T., Zheng Q.-Y., Wang C. Manganese-Catalyzed Dehydrogenative [4+2] Annulation of N-H Imines and Alkynes by C-H/N-H Activation. *Angew. Chem. Int. Ed.*, **53**, 4950-4953 (2014).

18. Shi L., Zhong X., She H., Lei Z., Li F. Manganese catalyzed C-H functionalization of indoles with alkynes to synthesize bis/trisubstituted indolylalkenes and carbazoles: the acid is the key to control selectivity. *Chem. Commun.*, 7136-7139 (2015).

19. Lu Q. Q., Gressies S., Cembellin S., Klauck F. J. R., Daniliuc C. G., Glorius F. Redox-Neutral Manganese(I)-Catalyzed C-H Activation: Traceless Directing Group Enabled Regioselective Annulation. *Angew. Chem. Int. Ed.*, **56**, 12778-12782 (2017).

20. Lu Q. Q., Gressies S., Klauck F. J. R., Glorius F. Manganese(I)-Catalyzed Regioselective C-H Allenylation: Direct Access to 2-Allenylindoles. *Angew. Chem. Int. Ed.*, **56**, 6660-6664 (2017).

21. Ruan Z. X., Sauermann N., Manoni E., Ackermann L. Manganese-Catalyzed C-H Alkynylation: Expedient Peptide Synthesis and Modification. *Angew. Chem. Int. Ed.*, **56**, 3172-3176 (2017).

22. Wang H., Pesciaioli F., Oliveira J. C. A., Warratz S., Ackermann L. Synergistic Manganese(I) C-H Activation Catalysis in Continuous Flow: Chemoselective Hydroarylation. *Angew. Chem. Int. Ed.*, **56**, 15063-15067 (2017).

23. Lu Q., Cembellin S., Gressies S., Singha S., Daniliuc C. G., Glorius F. Manganese(I)-Catalyzed C-H (2-Indolyl)methylation: Expedient Access to Diheteroarylmethanes. *Angew. Chem. Int. Ed.*, **57**, 1399-1403 (2018).

24. Zhou B., Ma P., Chen H., Wang C. Amine-accelerated manganese-catalyzed aromatic C-H conjugate addition to α,β-unsaturated carbonyls. *Chem. Commun.*, **50**, 14558-14561 (2014).

25. Liu W., Zell D., John M., Ackermann L. Manganese-Catalyzed Synthesis of cis-β-Amino Acid Esters through Organometallic C-H Activation of Ketimines. *Angew. Chem. Int. Ed.*, **54**, 4092-4096 (2015).

26. Cai S. H., Ye L., Wang D. X., Wang Y. Q., Lai L. J., Zhu C.*, et al.* Manganese-catalyzed synthesis of monofluoroalkenes via C-H activation and C-F cleavage. *Chem. Commun.*, **53**, 8731-8734 (2017).

27. Liang Y. F., Muller V., Liu W. P., Munch A., Stalke D., Ackermann L. Methylenecyclopropane Annulation by Manganese(I)-Catalyzed Stereoselective C-H/C-C Activation. *Angew. Chem. Int. Ed.*, **56**, 9415-9419 (2017).

28. Liu S. L., Li Y., Guo J. R., Yang G. C., Li X. H., Gong J. F.*, et al.* An Approach to 3-(Indo1-2-yl)succinimide Derivatives by Manganese Catalyzed C-H Activation. *Org. Lett.*, **19**, 4042-4045 (2017).

29. Meyer T. H., Liu W. P., Feldt M., Wuttke A., Mata R. A., Ackermann L. Manganese(I)-Catalyzed Dispersion-Enabled C-H/C-C Activation. *Chem. Eur. J.*, **23**, 5443-5447 (2017).

30. Ni J. B., Zhao H. C., Zhang A. Manganese(I)-Catalyzed C-H 3,3-Difluoroallylation of Pyridones and Indoles. *Org. Lett.*, **19**, 3159-3162 (2017).

31. Wang H., Lorion M. M., Ackermann L. Air-Stable Manganese(I)-Catalyzed C-H Activation for Decarboxylative C-H/C-O Cleavages in Water. *Angew. Chem. Int. Ed.*, **56**, 6339-6342 (2017).

32. Zell D., Dhawa U., Muller V., Bursch M., Grimme S., Ackermann L. C-F/C-H Functionalization by Manganese(I) Catalysis: Expedient (Per)Fluoro-Allylations and Alkenylations. *ACS Catalysis*, **7**, 4209-4213 (2017).

33. Liu W., Richter S. C., Zhang Y., Ackermann L. Manganese(I)-Catalyzed Substitutive C-H Allylation. *Angew. Chem. Int. Ed.*, **55**, 7747-7750 (2016).

34. Lu Q., Klauck F. J. R., Glorius F. Manganese-catalyzed allylation via sequential C-H and C-C/C-Het bond activation. *Chem. Sci.*, **8**, 3379-3383 (2017).

35. Chen S. Y., Han X. L., Wu J. Q., Li Q. J., Chen Y. Y., Wang H. G. Manganese(I)-Catalyzed Regio- and Stereoselective 1,2-Diheteroarylation of Allenes: Combination of C-H Activation and Smiles Rearrangement. *Angew. Chem. Int. Ed.*, **56**, 9939-9943 (2017).

36. Chen S. Y., Li Q. J., Wang H. G. Manganese(I)-Catalyzed Direct C-H Allylation of Arenes with Allenes. *J. Org. Chem.*, **82**, 11173-11181 (2017).

37. Wang C. M., Wang A., Rueping M. Manganese-Catalyzed C-H Functionalizations: eHydroarylations and Alkenylations Involving an Unexpected Heteroaryl Shift. *Angew. Chem. Int. Ed.*, **56**, 9935-9938 (2017).

38. Zhu C., Schwarz J. L., Cembellin S., Gressies S., Glorius F. Highly Selective Manganese(I)/Lewis Acid Cocatalyzed Direct C-H Propargylation Using Bromoallenes. *Angew. Chem. Int. Ed.*, **57**, 437-441 (2018).

39. Liu W., Bang J., Zhang Y., Ackermann L. Manganese(I)-Catalyzed C–H Aminocarbonylation of Heteroarenes. *Angew. Chem. Int. Ed.*, **54**, 14137-14140 (2015).

40. Zhou B. W., Hu Y. Y., Liu T., Wang C. Y. Aromatic C-H addition of ketones to imines enabled by manganese catalysis. *Nature Communications*, **8**, 1169 (2017).

41. Kuninobu Y., Nishina Y., Takeuchi T., Takai K. Manganese-Catalyzed Insertion of Aldehydes into a C-H Bond. *Angew. Chem. Int. Ed.*, **46**, 6518-6520 (2007).

42. Liang Y.-F., Massignan L., Liu W., Ackermann L. Catalyst-Guided C=Het Hydroarylations by Manganese-Catalyzed Additive-Free C−H Activation. *Chem.-Eur. J.*, **22**, 14856-14859 (2016).

43. Zhou B., Hu Y., Wang C. Manganese‐Catalyzed Direct Nucleophilic C(sp2)-H Addition to Aldehydes and Nitriles. *Angew. Chem. Int. Ed.*, **54**, 13659-13663 (2015).

44. Liu W., Ackermann L. Manganese-Catalyzed C-H Activation. *ACS Catalysis*, **6**, 3743-3752 (2016).

45. Wang C. Y. Manganese-Mediated C-C Bond Formation via C-H Activation: From Stoichiometry to Catalysis. *Synlett*, **24**, 1606-1613 (2013).

46. Hu Y., Zhou B., Wang C. Inert C–H Bond Transformations Enabled by Organometallic Manganese Catalysis. *Acc. Chem. Res.*, **51**, 816-827 (2018).

47. Yahaya N. P., Appleby K. M., Teh M., Wagner C., Troschke E., Bray J. T. W.*, et al.* Manganese(I)-Catalyzed C−H Activation: The Key Role of a 7-Membered Manganacycle in H-Transfer and Reductive Elimination. *Angew. Chem. Int. Ed.*, **55**, 12455-12459 (2016).

48. Farrell I. R., Matousek P., Towrie M., Parker A. W., Grills D. C., George M. W.*, et al.* Direct Observation of Competitive Ultrafast CO Dissociation and Relaxation of an MLCT Excited State:  Picosecond Time-Resolved Infrared Spectroscopic Study of [Cr(CO)4(2,2‘-bipyridine)]. *Inorg. Chem.*, **41**, 4318-4323 (2002).

49. Aucott B. J., Duhme-Klair A.-K., Moulton B. E., Clarke I. P., Sazanovich I. V., Towrie M.*, et al.* Manganese carbonyl compounds reveal ultra-fast metal-solvent interactions. *Manuscript in preparation*, (2018).

50. Shanoski J. E., Payne C. K., Kling M. F., Glascoe E. A., Harris C. B. Ultrafast Infrared Mechanistic Studies of the Interaction of 1-Hexyne with Group 6 Hexacarbonyl Complexes. *Organometallics*, **24**, 1852-1859 (2005).

51. Moulton B. E., Duhme-Klair A. K., Fairlamb I. J. S., Lynam J. M., Whitwood A. C., Moulton B. E.*, et al.* A rationale for the linear correlation of aryl substituent effects in iron(0) tricarbonyl complexes containing α,β-unsaturated enone (chalcone) ligands. *Organometallics*, **26**, 6354-6365 (2007).

52. Shanoski J. E., Glascoe E. A., Harris C. B. Ligand Rearrangement Reactions of Cr(CO)6 in Alcohol Solutions:  Experiment and Theory. *J. Phys. Chem. B*, **110**, 996-1005 (2006).

53. Neville A. G., Brown C. E., Rayner D. M., Lusztyk J., Ingold K. U. First direct detection of transient organic free radicals in solution by time-resolved infrared spectroscopy. Kinetic studies on some acyl radicals. *J. Am. Chem. Soc.*, **113**, 1869-1870 (1991).

54. Bruce M. I., Goodall B. L., Matsuda I. Cyclometallation reactions .13. reactions of phenyl-substituted heterocyclic nitrogen-donor ligands. *Aust. J. Chem.*, **28**, 1259-1264 (1975).

55. Greetham G. M., Burgos P., Cao Q., Clark I. P., Codd P. S., Farrow R. C.*, et al.* ULTRA: A Unique Instrument for Time-Resolved Spectroscopy. *Appl. Spectrosc.*, **64**, 1311-1319 (2010).

56. Császár P., Pulay P. Geometry optimization by direct inversion in the iterative subspace. *J. Mol. Struct.*, **114**, 31-34 (1984).

57. Ahlrichs R., Bär M., Häser M., Horn H., Kölmel C. Electronic structure calculations on workstation computers: The program system turbomole. *Chem. Phys. Lett.*, **162**, 165-169 (1989).

58. Deglmann P., Furche F., Ahlrichs R. An efficient implementation of second analytical derivatives for density functional methods. *Chem. Phys. Lett.*, **362**, 511-518 (2002).

59. Deglmann P., May K., Furche F., Ahlrichs R. Nuclear second analytical derivative calculations using auxiliary basis set expansions. *Chem. Phys. Lett.*, **384**, 103-107 (2004).

60. Eichkorn K., Treutler O., Öhm H., Häser M., Ahlrichs R. Auxiliary basis sets to approximate Coulomb potentials. *Chem. Phys. Lett.*, **240**, 283-290 (1995).

61. Eichkorn K., Weigend F., Treutler O., Ahlrichs R. Auxiliary basis sets for main row atoms and transition metals and their use to approximate Coulomb potentials. *Theor. Chem. Acc.*, **97**, 119-124 (1997).

62. Treutler O., Ahlrichs R. Efficient molecular numerical integration schemes. *J. Chem. Phys.*, **102**, 346-354 (1995).

63. von Arnim M., Ahlrichs R. Geometry optimization in generalized natural internal coordinates. *J. Chem. Phys.*, **111**, 9183-9190 (1999).

64. Klamt A., Schuurmann G. COSMO: a new approach to dielectric screening in solvents with explicit expressions for the screening energy and its gradient. *J. Chem. Soc., Perk. Trans. 2*, 799-805 (1993).

65. Grimme S., Antony J., Ehrlich S., Krieg H. A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H-Pu. *J. Chem. Phys.*, **132**, 154104 (2010).

66. Grimme S., Ehrlich S., Goerigk L. Effect of the damping function in dispersion corrected density functional theory. *Journal of computational chemistry*, **32**, 1456-1465 (2011).