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LETTERS

Biphasic manganese carbonyl reactions: a new approach to making carbon–carbon bonds

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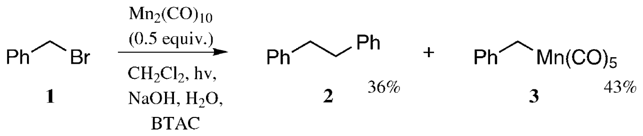
Abstract—A new, mild and practical biphasic method for conducting manganese carbonyl reactions, which lead to the formation of carbon–carbon bonds, has been developed: the mechanisms of these reactions can involve radical and/or ionic pathways.

Free-radical reactions, particularly cyclisations, have been extensively studied over the past 20 years and by far the most common method of initiation involves reaction of organohalide (or related) precursors with tributyltin hydride.[1] However, this method is far from ideal and the toxicity and difficulty of removing tin-containing by-products has led to the development of alternative reagents for radical generation.[2] Recent examples include silylated cyclohexadienes,[3] hypophosphorous acid (and its salts)[4] and phosphites,[5] although the use of tributyltin hydride still dominates. As part of a programme to develop alternative and more versatile free-radical initiators we have recently investigated the use of dimanganese decacarbonyl [$Mn_2(CO)_{10}$] in organic synthesis. This work has shown that photolysis of $Mn_2(CO)_{10}$ generates $^{\bullet}Mn(CO)_5$, which reacts with organohalides in CH_2Cl_2 to efficiently initiate a variety of radical coupling[6] and cyclisation reactions under mild conditions.[7]

For these reactions the manganese halide byproducts [of type $XMn(CO)_5$] can be removed by treating the crude reaction mixture with excess DBU; this forms a polar manganese complex, which can be separated from organic products by column chromatography. For polar organic compounds removal of excess DBU and/or the manganese–DBU complex can be problematic and so we sought to develop an alternative method, which involves carrying out the reactions in the presence of an aqueous solution of sodium hydroxide and the phase-transfer catalyst benzyltriethylammonium chloride (BTAC). Under these conditions, it was anticipated that the manganese halide byproducts would react with hydroxide to form water-soluble manganese complexes [e.g. $Et_3(Bn)N^+Mn_2(CO)_9Br^-$, $Et_3(Bn)N^+Mn(CO)_5^-$].[8]

Our first experiments centred on the preparation of bibenzyl **2** from benzyl bromide **1** (Scheme 1). Hence photolysis of **1** with $Mn_2(CO)_{10}$ (0.5 equiv.) in dichloromethane in the presence of aqueous sodium hydroxide and BTAC gave the desired dimer **2** in 36% yield.[9,10] This reaction also produced benzylmanganese pentacarbonyl **3** in 43% yield, which was unexpected as this compound was not formed when the same reaction was carried out solely in dichloromethane.[6] Similar biphasic reactions using different amounts of $Mn_2(CO)_{10}$ also gave both **2** and **3** (e.g. using 1 equivalent of $Mn_2(CO)_{10}$ gave **2** and **3** in 81 and 19% yield, respectively) although the yield of **2** generally increased (and **3** decreased) with reaction times of >2 h. This represents an exceptionally mild method of forming **3**, which is traditionally prepared from reaction of $Mn_2(CO)_{10}$ with Na/Hg and benzyl bromide (or chloride) in anhydrous diethyl ether.[11] Indeed, in the absence of photolysis, **3** is the major compound [e.g.



Scheme 1.

Keywords: manganese and compounds; radicals and radical reactions; cyclisation; coupling reactions.

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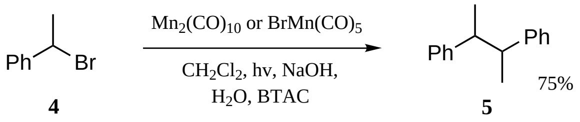
after 2 h, **3** was isolated in 30% yield (or 96% based on recovered **1**)] and only trace amounts of **2** are formed.

The most likely route to compound **3** involves nucleophilic substitution of bromide **1** by the manganese pentacarbonyl anion $^{-}Mn(CO)_5$. Benzylmanganese pentacarbonyl **3** could then react with bromide **1** to form **2**, in a second nucleophilic substitution reaction, or alternatively, the manganese radical $^{\bullet}Mn(CO)_5$ could abstract a bromine atom from **1** to form the benzyl radical which dimerises: the formation of the benzyl radical was confirmed by carrying out photolysis experiments in the presence of TEMPO, which led to the formation of 1-benzyloxy-2,2,6,6-tetramethylpiperidine (in 30–37% yield). It should also be noted that the benzyl radical could be formed on homolysis of the weak Mn–C bond in **3** ($\sim$105 kJ mol^{-1})[11,12], although attempts to convert **3** to **2** (using the same photolysis conditions as shown in Scheme 1) were unsuccessful.

The $^{-}Mn(CO)_5$ could arise from reaction of $Mn_2(CO)_{10}$ and/or $BrMn(CO)_5$ with hydroxide.[8,13] To clarify the mechanism, bromide **1** was reacted under the same conditions with $BrMn(CO)_5$ (2 equiv.) in place of $Mn_2(CO)_{10}$.[14] This produced bibenzyl **2** and benzylmanganese pentacarbonyl **3** in 60 and 34% yield, respectively, which points to the formation of the $^{-}Mn(CO)_5$ anion from $BrMn(CO)_5$. However, the formation of $^{\bullet}Mn(CO)_5$ cannot be completely discounted from this reaction as photolysis of $BrMn(CO)_5$ is known to generate $Mn_2(CO)_{10}$ and this was confirmed by both TLC and IR analysis of the crude reaction mixture.[15]

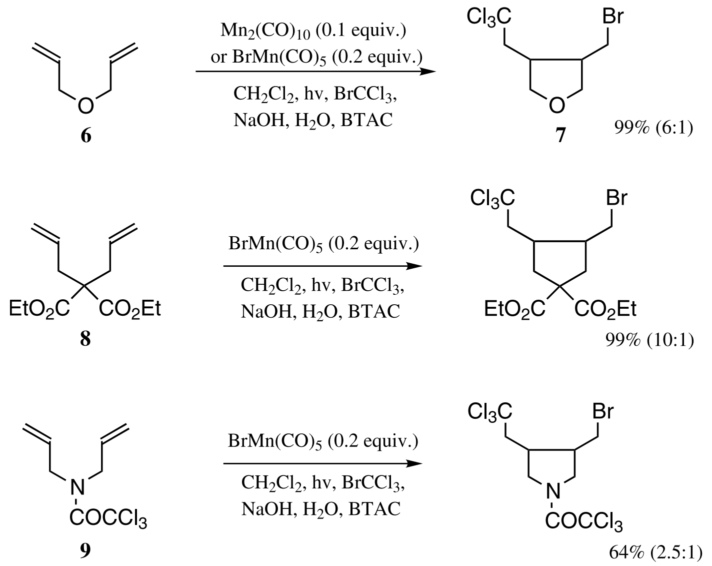


Scheme 2.

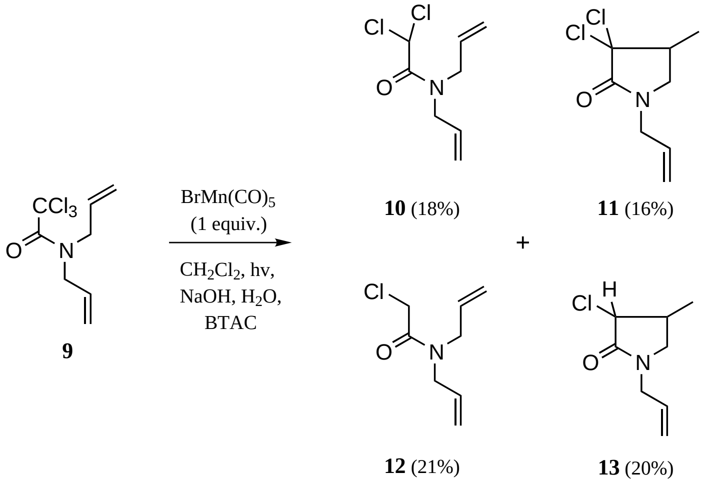
The pronounced effect of employing biphasic conditions was also apparent for reactions involving secondary bromide **4** (Scheme 2). Whereas only unreacted starting material was isolated on photolysis of **4** with $Mn_2(CO)_{10}$ in CH_2Cl_2, the same reaction in the presence of aqueous hydroxide and BTAC produced dimer **5** (as a 1:1 mixture of diastereomers) in 75% yield. When $BrMn(CO)_5$ was used in place of $Mn_2(CO)_{10}$ in the biphasic reaction, dimer **5** was isolated in the same yield (75%).[16] It is therefore likely that **5** is formed via reaction of bromide **4** with $^{-}Mn(CO)_5$ rather than $^{\bullet}Mn(CO)_5$.

Radical cyclisation reactions can also be carried out using biphasic conditions. For example, reaction of bromotrichloromethane with diene **6** and $Mn_2(CO)_{10}$ (0.1 equiv. w.r.t. $BrCCl_3$ or 0.3 equiv. w.r.t. diene **6**) or $BrMn(CO)_5$ (0.2 equiv. w.r.t. $BrCCl_3$) afforded tetrahydrofuran **7** in essentially quantitative yield (Scheme 3). The use of $BrMn(CO)_5$ is of particular interest because this is the first time that this reagent has been reported to initiate radical cyclisation reactions. A similar result was obtained using dienes **8** and **9**, and in all cases the crude products were not contaminated with any $BrMn(CO)_5$ as shown by the infrared spectra.

A more complex result was obtained on reaction of $BrMn(CO)_5$ [or $Mn_2(CO)_{10}$] with trichloroacetamide **9** in the absence of $BrCCl_3$ (Scheme 4). This gave rise to four products in a combined 75% yield. Each of the products **10**–**13** could be formed by radical reactions. For example, dichloroamide **10** could be formed by abstraction of a chlorine atom from **9** [by $^{\bullet}Mn(CO)_5$] followed by abstraction of a hydrogen atom (from, for example, CH_2Cl_2) by the intermediate dichloroamide radical. However, **10**–**13** could also be formed from intermediate organomanganese adducts of the type R–$Mn(CO)_5$. Thus, dichloroamide **10** could be prepared on hydrolysis of an intermediate organomanganese compound generated from reaction of **9** with



Scheme 3.



Scheme 4.

$^{-}$Mn(CO)$_5$. In order to distinguish these pathways, the same reaction [using BrMn(CO)$_5$] was carried out in D_2O rather than H_2O. Any incorporation of deuterium in the products would identify compounds derived from intermediate organomanganese adducts. Interestingly, monochlorinated products **12** and **13** showed complete deuteration of the CH_2Cl and CHCl groups adjacent to the amide carbonyl (by ^{1}H NMR spectroscopy). In comparison, dichloroamide **10** showed 50% incorporation of deuterium at the $CHCl_2$ position while cyclic dichloride **11** did not contain any deuterium. This suggests that initial organomanganese adducts are formed from reaction of **9** with $^{-}$Mn(CO)$_5$, which are then hydrolysed. The formation of pyrrolidinones **11** and **13** also indicates the generation of an α-amido radical, which on 5-*exo* cyclisation, forms a primary radical that abstracts a hydrogen atom from the solvent CH_2Cl_2. Indeed, the role of CH_2Cl_2 as a hydrogen atom donor in this reaction was confirmed by reacting **9** with BrMn(CO)$_5$ in CD_2Cl_2.

This work has shown, for the first time, that manganese carbonyl-mediated carbon–carbon bond forming reactions can be carried out in biphasic conditions. The incorporation of an aqueous alkaline solution and a phase transfer catalyst effectively removes BrMn(CO)$_5$ from organic products, which are retained in the dichloromethane layer. Indeed, this work has shown that BrMn(CO)$_5$ can be used in place of $Mn_2(CO)_{10}$ in coupling and cyclisation reactions. The use of $Mn_2(CO)_{10}$ or BrMn(CO)$_5$ in biphasic conditions can also lead to alternative products to those observed when using $Mn_2(CO)_{10}$ in dichloromethane. This can be explained by the formation of $^{-}$Mn(CO)$_5$, which can react with organohalides to produce organomanganese adducts. The formation of organomanganese adducts [e.g. BnMn(CO)$_5$] under such mild reaction conditions is of particular note and this method offers a flexible approach to these types of compounds, which have been shown to undergo synthetically important ionic and/or radical reactions.

Acknowledgements

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9. To a solution of $Mn_2(CO)_{10}$ (0.28 g, 0.73 mmol, 0.5 equiv.) in dichloromethane (10 cm^3) was added benzyl bromide **1** (0.25 g, 1.46 mmol, 1 equiv.) followed by an aqueous solution of sodium hydroxide (5 M, 10 cm^3) containing BTAC (0.04 g, 0.18 mmol). The mixture was then photolysed (using an ICL 302 UV xenon lamp, 300 W) under an atmosphere of nitrogen for 2 h. The organic phase was separated, washed with water, dried ($MgSO_4$) and evaporated under reduced pressure. Purification using column chromatography (silica) gave bibenzyl **2** (0.05 g, 36%) and benzylmanganese pentacarbonyl **3** (0.18 g, 43%) as solids.
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16. When the same reaction was carried out in the presence of diphenyl diselenide, the selenide $PhCH(CH_3)SePh$ was isolated in 71% yield.