Molybdenum/Quinone-Catalyzed Deoxygenative Coupling of Aromatic Carbonyl Compounds

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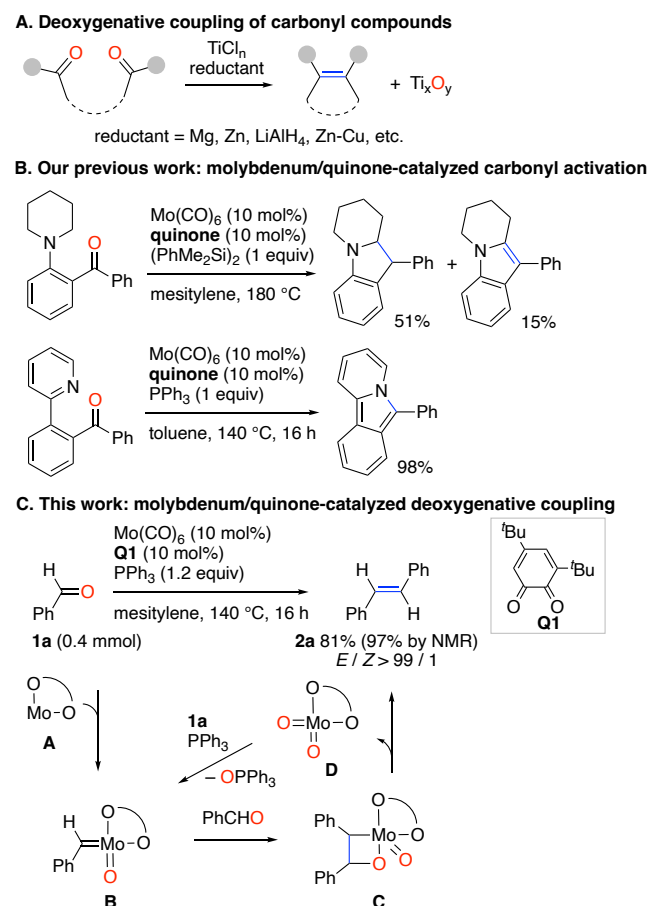
ABSTRACT: A catalytic amount of Mo(CO)$_6$ and an *ortho*-quinone ligand, in the presence of triphenylphosphine as a mild reductant enables the intermolecular reductive coupling of aromatic aldehydes and the intramolecular coupling of aromatic ketones to produce functionalized alkenes. Diaryl- and diheteroaryl alkenes are synthesized typically with high (*E*)-selectivity and with a tolerance of bromide, iodide, and steric hindrance. Intramolecular coupling of 1,6-diketones under similar conditions affords 9,10-disubstituted phenanthrenes.

The reductive coupling of two carbonyl compounds to produce an alkene,[1] typically in the presence of *in situ*-generated low-valent titanium (Tyrlik–Mukaiyama–McMurry reaction),[2] has found numerous applications for the synthesis of natural products, macrocyclic compounds, conjugated molecules, etc.[3] However, most of these reactions require a stoichiometric amount of a titanium salt and a metal reductant (Scheme 1A), resulting in chemoselectivity and reproducibility issues, and a significant decrease in popularity in recent years. Despite a pioneering early report on titanium-catalyzed deoxygenative cyclization to produce indole derivatives in the presence of metallic Mn and chlorotrimethylsilane,[4] probably because of the stability of the titanium oxo species, catalytic reactions have remained scarce[3h,5] and synthetically less attractive. For example, previous reports require metallic reductants such as Yb,[6] photochemical conditions prone to olefin isomerization,[7] or preconversion to hydrazone intermediates.[8] We report herein that a catalytic amount of inexpensive and easy-to-handle Mo(CO)$_6$ and *o*-quinone ligand, in the presence of essentially 1 equiv of triphenylphosphine as a mild reductant, enables the intermolecular reductive coupling of aldehydes and the intramolecular coupling of ketones to produce functionalized alkenes. Various di(hetero)arylalkenes, including sterically demanding ones, can be synthesized in high yields and with high (*E*)-selectivity. The mild reaction conditions tolerate halides such as bromide and iodide. The intramolecular coupling of 1,6-diketones produces 9,10-disubstituted phenanthrenes.

Molybdenum is the most abundant transition metal in seawater,[9] and it is an essential trace element for all life forms; but, arguably, the use of molybdenum for catalysis has been underexplored to date.[10] During our studies on the use of molybdenum catalysts in organic synthesis,[11] we found that a molybdenum/quinone complex, readily generated *in situ* from Mo(CO)$_6$ and an *o*-quinone, reacts with a carbonyl group to generate a putative molybdenum carbene, which was exploited

for intramolecular C–H bond functionalization and C–N bond-forming cyclization (Scheme 1B).[12]

Scheme 1. Strategies for deoxygenative coupling.

A. Deoxygenative coupling of carbonyl compounds

reductant = Mg, Zn, LiAlH$_4$, Zn-Cu, etc.

B. Our previous work: molybdenum/quinone-catalyzed carbonyl activation

C. This work: molybdenum/quinone-catalyzed deoxygenative coupling

Others later applied this molybdenum/quinone species for deoxygenative cyclopropanation,[13] and a related molybdenum catalyst for the cross-coupling of benzyl alcohols.[14] Importantly, the molybdenum oxo species could be reduced by a disilane or a phosphine to regenerate the molybdenum active species and complete a catalytic cycle.[12] We envisioned that a similar molybdenum/quinone complex (**A** in Scheme 1C) may activate a carbonyl compound (**1**) to generate a molybdenum carbene species (**B**), and this species may react with another carbonyl group to produce an alkene (**2**) via metallaoxocyclobutane **C**;[15] then, the resulting molybdenum oxide species (**C**) may be reduced by a phosphine[16] or silane to regenerate the active species and complete the catalytic cycle (Scheme 1C). According to this hypothesis,[17] we reacted benzaldehyde (**1a**) in the presence of 10 mol% of Mo(CO)$_6$/3,5-di-*tert*-butyl-1,2-benzoquinone (**Q1**) and 1.2 equiv of triphenylphosphine as the reductant at 140 °C for 16 h, and we obtained *trans*-stilbene (**2a**) in 81% yield after isolation by silica gel column chromatography (97% by ^{1}H NMR analysis of the crude reaction mixture). The product was obtained exclusively as the *trans* isomer; the *cis* isomer was not observed at all, even in the early stages of the reaction, as confirmed by GC and ^{1}H NMR analysis (see the SI for the kinetic profile of the reaction). The reaction was clean, and we did not observe any side products; a trace amount of the starting material was recovered. The formation of triphenylphosphine oxide was observed by GC analysis of the crude mixture, suggesting a catalytic turnover.

In Table 1 we show the effect of several key reaction parameters on the reaction of benzaldehyde (**1a**) to produce stilbene (**2a**). Among the *o*-quinone ligands investigated, **Q1** and *ortho*-chloranil (**Q2**) gave high yields (entries 1 and 2), whereas 9,10-Phenanthrenequinone (**Q3**) gave a much lower yield (entry 3). In the absence of a quinone ligand (entry 4), the product was not obtained, and the material balance was poor. Triphenylphosphine was the optimal reductant; a diphosphine such as dppe was also effective, albeit it gave a lower yield (entry 5). By contrast, triphenyl phosphite was completely ineffective (entry 6). A silane such as tris(trimethylsilyl)silane could also be used as a reductant (entry 7), but triethoxysilane was inefficient (entry 8). In the absence of a reductant, the reaction did not proceed at all (entry 9). However, a reaction using a larger amount (50 mol% or 100 mol%) of molybdenum/*o*-quinone in the absence of a reductant proceeded in 55% and 65% yield, respectively (SI).[15] The catalyst loading could be decreased to 5 mol%, without a significant decrease in yield (entry 10). The reaction temperature was important: after generation of the active molybdenum/quinone species at 140 °C, conducting the reaction at 100 °C resulted in a large decrease in yield (entry 11). We speculate that the high temperature is required not only to remove carbonyl ligands from molybdenum and generate the active species, but also for other steps such as ligand exchange to coordinate the carbonyl substrate or the reduction of the molybdenum oxide species generated during the catalytic cycle. The reaction was not complete after 8 h (entry 12). The yield was largely proportional to the amount of reductant (entry 13). The reaction was uniquely catalyzed by Mo/quinone; other metal carbonyl complexes such as Cr(CO)$_6$, W(CO)$_6$,[15] Mn$_2$(CO)$_{10}$, and Re$_2$(CO)$_{10}$ were ineffective (SI).

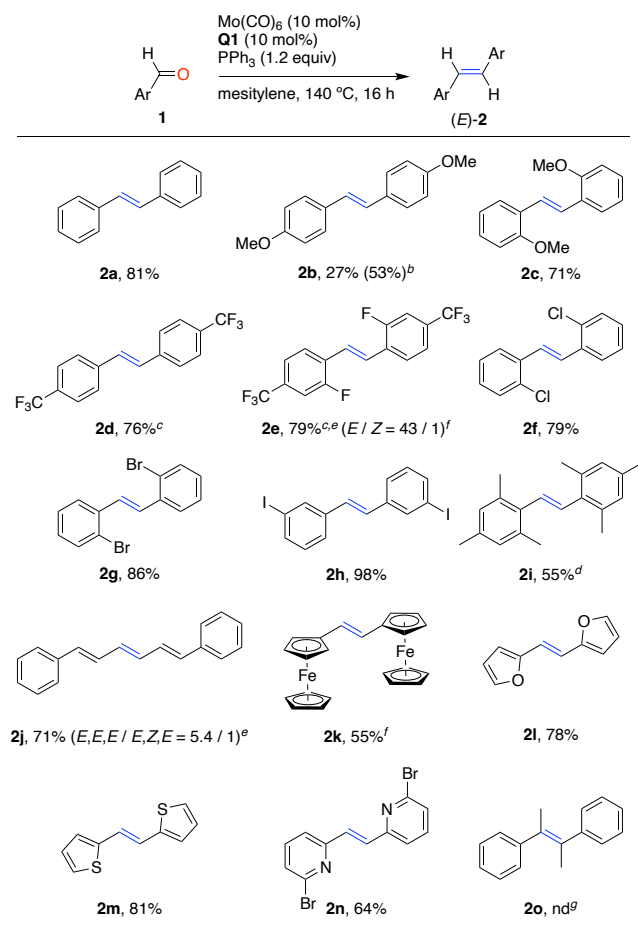**Table 1. Effect of the key reaction parameters on the deoxygenative coupling of benzaldehyde (1a)^a**

Entry	*o*-Quinone	Reductant	x	2a (%)^b	1a (%)^b
1	**Q1**	PPh$_3$	1.2	91	<5
2	**Q2**	PPh$_3$	1.2	85	<5
3	**Q3**	PPh$_3$	1.2	29	17
4	none	PPh$_3$	1.2	<5	35
5	**Q1**	dppe^c	0.6	50	7
6	**Q1**	P(OPh)$_3$	1.2	nd	nd
7	**Q1**	(Me$_3$Si)$_3$SiH	1.2	59	<5
8	**Q1**	(EtO)$_3$SiH	1.2	nd	<5
9	**Q1**	none	—	nd	30
10^d	**Q1**	PPh$_3$	1.2	77	<5
11^e	**Q1**	PPh$_3$	1.2	14	18
12^f	**Q1**	PPh$_3$	1.2	72	6
13	**Q1**	PPh$_3$	0.6	64	9

^{a}Reactions were conducted with benzaldehyde (**1a**, 0.40 mmol), Mo(CO)$_6$ (10 mol%), *o*-quinone (10 mol%), and reductant (n equiv) in mesitylene (0.40 mL) at 140 °C for 16 h. ^{b}The yield was determined using GC in the presence of tridecane as an internal standard, after calibration. nd = not detected. ^{c}dppe = 1,2-diphenylphosphinoethane ^{d}5 mol% of Mo(CO)$_6$ and 5 mol% of **Q1** was used. ^{e}The active molybdenum/quinone species was generated at 140 °C for 15 min, then **1a** and reductant were added at rt, and then the reaction was conducted at 100 °C. ^{f}The reaction time was 8 h.

We next investigated the reaction of various aromatic aldehydes under the optimized reaction conditions (Table 2). The reaction proceeded with a variety of electron-rich, electron-deficient, and bulky aromatic aldehydes and afforded the corresponding *trans*-stilbene derivatives with high (*E*)-selectivity. A notable feature of the reaction is the tolerance of organic halides[18] such as chloride (**2f**), bromide (**2g**, **2n**), and iodide (**2h**) – valuable handles for further functionalization. A sterically demanding alkene bearing mesityl groups (**2i**), could be synthesized in moderate yield. *trans*-Cinnamaldehyde gave a triene product **2j** in high yield, but with the erosion of stereoselectivity, as previously observed.[6] Ferrocenecarboxaldehyde (**1k**) reacted with a moderate yield, but with high (*E*)-selectivity. Heteroaromatic aldehydes such as 2-furancarboxaldehyde (**1l**), 2-thiophenecarboxaldehyde (**1m**), and 6-bromo-2-pyridinecarboxaldehyde (**1n**) gave the corresponding (*E*)-alkenes with high yield and selectivity. Ketone substrates, such as acetophenone (**1o**), did not react under these conditions and the starting material was recovered. Several other unsuccessful substrates are shown in the SI.

Table 2. Molybdenum/*o*-quinone-catalyzed deoxygenative coupling of aromatic aldehydes (1).[a]

2a, 81%

2b, 27% (53%)[b]

2c, 71%

2d, 76%[c]

2e, 79%[c,e] (E / Z = 43 / 1)[f]

2f, 79%

2g, 86%

2h, 98%

2i, 55%[d]

2j, 71% (E,E,E / E,Z,E = 5.4 / 1)[e]

2k, 55%[f]

2l, 78%

2m, 81%

2n, 64%

2o, nd[g]

[a]Reaction conditions: aromatic aldehyde (**1**, 0.40 mmol), Mo(CO)$_6$ (10 mol%), **Q1** (10 mol%), PPh$_3$ (0.48 mmol) in mesitylene (0.40 mL) at 140 °C for 16 h. The yields of the isolated (*E*)-alkenes **2** are reported. [b]Determined by ^{1}H NMR in the presence of 1,1,2,2-tetrachloroethane as an internal standard. [c]5 mol% of Mo(CO)$_6$, 5 mol% of **Q1**, and 1.0 equiv of PPh$_3$ were used. [d]**1h** was recovered in 22% (^{1}H NMR). [e]Yield of the isolated major isomer. The isomer ratio of the crude reaction mixture determined by GC analysis. [f]Reduced product (1,2-diferrocenylethane) was also obtained in 21% yield. [g]nd = not detected. **1o** was recovered in 95% (GC).

The intramolecular reaction of an aromatic 1,6-diketone gave 9,10-diphenylphenanthrene (**4a**) in high yield (Scheme 2). An aliphatic ketone reacted with a lower yield to give 9,10-diethylphenanthrene (**4b**). Previously reported catalytic routes to these compounds include rhodium-catalyzed cyclization of bis(*N*-tosylhydrazones),[8a] ruthenium-catalyzed metathesis of bis(alkenes),[19] and iron-catalyzed carbonyl–olefin metathesis,[20] but these reactions require preparation of the corresponding substrates from carbonyl precursors.

Scheme 2. Molybdenum/*o*-quinone-catalyzed deoxygenative coupling of 1,6-diketones.

4a, R = Ph 85%
4b, R = Et   45%
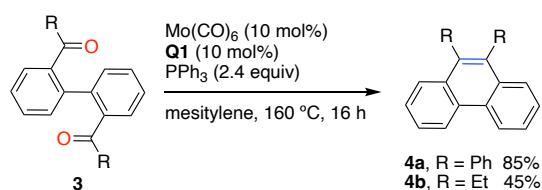
In summary, we found that a molybdenum species generated from Mo(CO)$_6$ and an *o*-quinone promotes the deoxygenative coupling of aldehyde and ketones. Furthermore, in the presence of a reductant such as triphenylphosphine or a silane derivative, the reaction becomes catalytic. These findings are particularly significant for the development of catalytic deoxygenative coupling to synthesize functionalized olefins,[21] a reaction that has typically relied on stoichiometric amounts of a transition metal and a strong reductant, and also for the development of new molybdenum catalytic species for organic synthesis. Efforts toward a mechanistic understanding and synthetic applications are ongoing in our laboratory.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Experimental details, characterization data, and NMR spectra (PDF).

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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