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Molybdenum(II)-Catalyzed Alkylation of Electron-Rich Aromatics with Allylic Acetates

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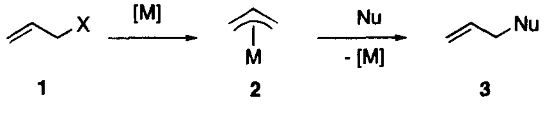
Abstract: The molybdenum(II) complex $[Mo(CO)_4Br_2]_2$ has been found to catalyze allylic substitution with aromatic ethers, e.g., anisole (**7**), as nucleophiles. The reaction is remarkably *para*-selective (e.g., **7** + **8** → **11**). © 1997 Elsevier Science Ltd.

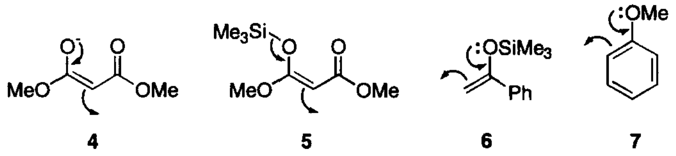
The Pd(0)-catalyzed allylic substitution, that occurs via the intermediate η^3-complexes **2** (Scheme 1), has been primarily developed to construct C-C bonds,[1] although formation of the C-H, C-O, and C-N bonds has also been reported.[2] Recently, Sinou[3] has demonstrated that phenols and naphthols can be used as *O*-nucleophiles to produce aryl allyl ethers **3** (Nu = OAr), provided that carbonates **1** (X = OCO_2Et), rather than acetates, are employed as allylic substrates. Under modified conditions, the latter reaction could also be directed to give a *C*-allylation, as exemplified by the reaction of β-naphthol with cinnamyl acetate.[3]

Scheme 1



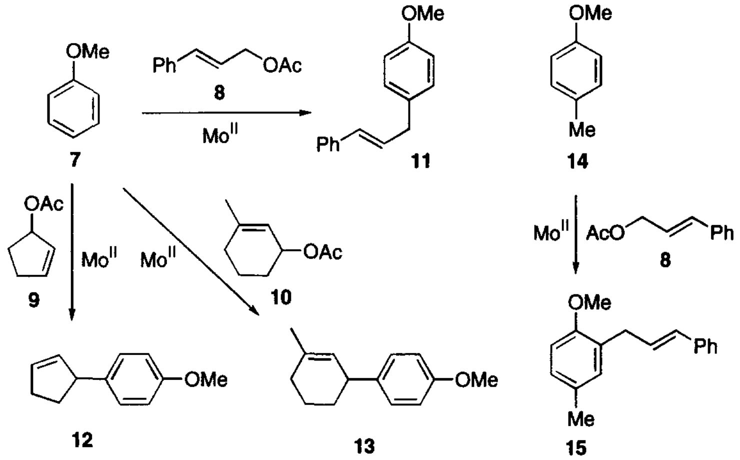
As a C-C bond-forming strategy, allylic substitution catalyzed by Pd(0) is usually confined to β-dicarbonyl enolates as nucleophiles, e.g., **4**.[1,4] We have shown in the adjacent paper,[5,6] that the new catalyst $Mo^{II}(CO)_5(OTf)_2$ accommodates a wider range of nucleophiles, including silyl enol ethers derived not only from β-dicarbonyls (e.g., **5**) but also from selected ketones, such as **6** (Scheme 2).[5] In view of the latter example, we were curious to determine whether or not aromatic ethers, e.g., anisole (**7**), would mimic the behavior of **5** and **6** and afford allylation products under the same, mild conditions. Since the initial experiments with $Mo^{II}(CO)_5(OTf)_2$ proved fruitless, we have focused on another Mo(II) complex, namely $[Mo^{II}(CO)_4Br_2]_2$, which is also known to have a weakly coordinated ligand (CO in this case rather than TfO).[7] Herein, we describe the behavior of the latter complex, readily prepared by bromination of $Mo(CO)_6$,[7] as a new catalyst for the Friedel-Crafts-type[8] allylation of aromatics.

Scheme 2



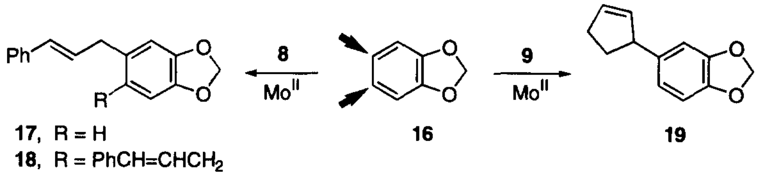
In order to explore the potential reactivity of electron-rich aromatics as nucleophiles in allylic substitution, we employed anisole (**7**) as the prime model compound, $[Mo(CO)_4Br_2]_2$ as the catalyst, and selected allylic acetates (Scheme 3). The first attempt, namely the treatment of **7** with cinnamyl acetate (**8**) in CH_2Cl_2 at rt with 2 mol% of the catalyst for 1 h, turned out to be highly successful, affording solely the *p*-cinnamylanisole **11** in 68% isolated yield.[9,10] Under the same conditions, the cyclic allylic acetates **9** and **10** gave the respective *para*-substituted products **12** (40%) and **13** (50%). Surprisingly, no *ortho*-isomer has been detected in either of the crude product mixtures. On the other hand, blocking the *p*-position, as in *p*-methylanisole (**14**), resulted in the formation of the *o*-product **15** (30%).[10] However, in this instance the reaction turned out to be slower and the yield not as good as in the case of anisole, clearly demonstrating the strong preference for the attack at the *p*-position.

Scheme 3: $Mo^{II} = [Mo(CO)_4Br]_2, CH_2Cl_2$, rt



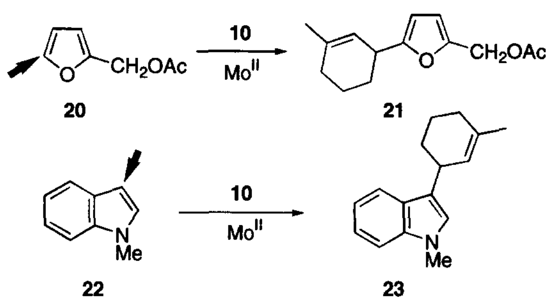
Increasing the electron density of the aromatic ring had a beneficial effect on the reactivity. Thus, **16** was readily allylated with **8** to give **17**, accompanied by the *bis*-allylation product **18**[11] (~4:1), in 70% yield. The cyclopentenyl derivative **19** was obtained under analogous conditions in 46% yield, with no *bis*-allylation observed. By contrast, aromatics having electron-withdrawing substituents (PhCl, $PhNO_2$, PhCOMe, and $PhCO_2Et$) were inert, which further demonstrates the nucleophilic role of the aromatic ring.[12]

Scheme 4: Conditions as in Scheme 3



Since allylation of the electron-rich anisole was successful, we selected the furan derivative **20** as a probe for the reactivity of heteroaromatics. Indeed, allylation of **20** with **10** did occur, affording exclusively **21** (65%). Similarly, *N*-methyl indole (**22**) furnished the β-allylated product **23** (85%).

Scheme 5: Conditions as in Scheme 3



In conclusion: We have developed a new, extremely mild method for allylation of electron rich aromatics and heteroaromatics, catalyzed by the known, readily available Mo(II) complex $[Mo(CO_4Br_2]_2$ that, in spite of its ready availability, has never been used as catalyst in organic synthesis before. The *para*-selectivity, observed with anisole (**7**) and its congeners **14** and **16**, is remarkable and will be the subject for further studies. Since the selected heteroaromatics, such as the furan and indole derivatives **20** and **22**, undergo the reaction as easily as the other aromatics (**7**, **14**, and **16**), this methodology is likely to open a new avenue in the Friedel-Crafts-type[8] allylation of aromatics under extremely mild conditions (≤ 2 mol% catalyst at rt for 30 min - 2 h, etc.).

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9. All yields refer to "isolated" yields rather than "GC yields". All new compounds gave satisfactory spectral and analytical data.
10. *Typical experiment:* To a stirred solution of anisole **7** (70 mg; 0.65 mmol) and the allylic acetate **8** (100 mg; 0.57 mmol) in CH_2Cl_2 (5 mL) at r.t. was added $[Mo(CO_4Br_2]_2$ (4 mg; 2 mol%). The mixture was stirred under nitrogen for 4 h (until the reaction was complete as revealed by TLC monitoring). The mixture was then diluted with ether (20 mL) and the ethereal solution thus obtained was washed successively with 5% aq. $NaHCO_3$ and water and dried with $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography on a silica gel column (15 x 2 cm) with a hexane-ethyl acetate mixture (9:1) to afford pure **11** (87 mg; 68%) as a colorless viscous oil: ^1H NMR δ (250 MHz, $CDCl_3$) 3.46 (d, $J = 6.0$ Hz, 2 H, CH_2), 3.76 (s, 3 H, CH_3O), 6.28 (dt, $J = 16.0$ and 6.0 Hz, 1 H, 2-H), 6.42 (d, $J = 16.0$ Hz, 1 H, 1-H), 6.84 (d, $J = 8.5$ Hz, 2 H, 3''-H, 5''-H), 7.14 (d, $J = 8.5$ Hz, 2 H, 2''-H, 6''-H), 7.17-7.35 (m, 5 H, C_6H_5); ^{13}C NMR δ (62.9 MHz, $CDCl_3$) 38.9 (t), 55.7 (q), 114.4 (d), 126.2 (d), 127.5 (d), 129.0 (q), 130.1 (d), 130.2 (d), 131.2 (d), 132.6 (s), 138.0 (s), 158.6 (s); MS (EI) *m/z* (rel. intensity) 224 ($M^{+\cdot}$, 100), 209 (14), 197 (21), 193 (20), 178 (10), 165 (9), 147 (7), 135 (15), 121 (49), 115 (31), 105 (10), 91 (22), 84 (44), 77 (19); HRMS (EI) calcd for $C_{16}H_{16}O$ requires M^+, 224.1201. Found: 224.1201.
11. The *bis*-allylated derivative **18** was characterized by NMR and MS spectra in a mixture with **17**.
12. During the preparation of this manuscript, two papers reporting on the Friedel-Crafts-type allylation of aromatics, such as toluene, xylene, and anisole, with allylic esters, chlorides, or alcohols have appeared.[13,14] However, neither $Mo(CO)_6$ (10 mol%)[13] nor $Cp^*RuCl(SPr^i)\text{-}Ru(OH_2)(SPr^i)Cp^*$ (5 mol%)[14] were as selective as our Mo(II) complex and the reaction condition were rather harsh (typically 80-140 °C for 6-72 h). Our isolated yields cannot be directly compared with the "GC yields" reported by the two groups.
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