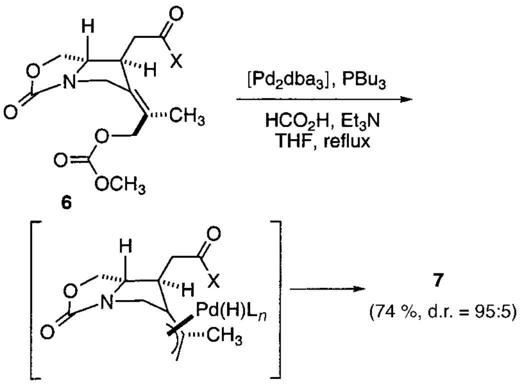

Scheme 4. Palladium-catalyzed reductive transposition.

The above strategy should provide simple variation of the C-4 substituent of allokainic acid simply by selection of a more complex organoaluminum or organozinc reagent. In addition, the introduction of chirality in sequential operations provides the opportunity for modification of the above strategy to allow preparation of the epimeric series of kainoids typified by kainic acid itself through a late-stage common intermediate.[11]

Experimental Section

5: Trimethylaluminum (2.0 M in hexanes, 1.44 mmol) was added dropwise to a solution of [Ni(cod)$_2$] (13.2 mg, 0.05 mmol) in THF (1.5 mL) at 0 °C. After 5 min, the mixture was transferred to a solution of **4** (210 mg, 0.48 mmol) at 0 °C in THF (3 mL) by cannula, and stirring was continued for 40 min at 0 °C. The reaction was quenched with NH_4Cl/NH_4OH pH 8 buffer, extracted with EtOAc (four times), dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (EtOAc/hexanes 1/1) afforded **5** (160 mg, 0.35 mmol, 73 %) in a 97:3 diastereomeric ratio: $[\alpha]_D^{25} = -90.9$ ($c = 0.5$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 4.64$ (dd, $J = 4.5$, 3.5 Hz, 1 H), 4.41–4.48 (m, 2 H), 4.01–4.09 (m, 4 H), 3.73 (dt, $J = 8.0$, 4.5 Hz, 1 H), 3.59 (d, $J = 15$ Hz, 1 H), 3.36 (d, $J = 16$ Hz, 1 H), 2.91–3.02 (m, 2 H), 1.68 (s, 3 H), 1.58 (s, 3 H), 1.55 (s, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.0$, 161.1, 154.0, 132.8, 130.2, 75.4, 70.5, 65.1, 64.8, 60.5, 48.5, 44.2, 41.1, 25.9, 24.85, 24.81, 18.3, 16.3, –5.3, –5.4; IR (film): $\tilde{\nu} = 2928$, 1772, 1695, 1396, 1311; HRMS: *m/z*: calcd. for $C_{18}H_{27}N_2O_6Si$ 395.1639, found 395.1642 $[M - C(CH_3)_3^+]$.

7: Tributylphosphane (6.1 mg, 0.03 mmol) was added to a solution of [Pd$_2$(dba)$_3$] (6.4 mg, 0.007 mmol) in THF (0.3 mL) at 0 °C. Formic acid (4.83 mg, 0.1 mmol) and triethylamine (10.6 mg, 0.1 mmol) were added neat, followed by carbonate **6** (25 mg, 0.06 mmol) in THF (0.3 mL), and the reaction mixture was refluxed (bath temperature 80–85 °C) for 3 h. The mixture was filtered through florisil, and the solvent was removed. Flash chromatography (EtOAc/hexanes 1/1) afforded **7** (15 mg, 0.05 mmol, 74 %) in a 95:5 diastereomeric ratio: $[\alpha]_D^{25} = -22.4$ ($c = 1.45$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 4.87$ (br. s,1 H), 4.85 (t, $J = 1.5$ Hz, 1 H), 4.45–4.49 (m, 2 H), 4.02 (s, 2 H), 3.74 (m, 1 H), 3.47 (dd, $J = 8.5$, 11.0 Hz, 1 H), 3.38 (dd, $J = 9.5$, 11.5 Hz, 1 H), 3.20 (dd, $J = 17.0$, 4.0 Hz, 1 H), 2.75 (m, 2 H), 2.25 (dq, J = 9.5, 4.0 Hz, 1 H), 1.70 (s, 3 H), 1.54 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.4$, 160.7, 154.0, 141.6, 114.7, 75.3, 68.0, 64.8, 60.6, 54.9, 48.6, 42.9, 38.2, 24.7, 24.6, 18.2; IR (film): $\tilde{\nu} = 1774$, 1696, 1381, 1308; HRMS (EI): *m/z*: calcd for $C_{16}H_{22}N_2O_5$ 322.1529, found 322.1535 [M^+].

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Acrylate-Assisted Arene–Chromium Bond Cleavage: Generation of a [Cr(CO)$_2$] Fragment under Mild Conditions[**]

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Patrick Romanens

Ligand exchange is a key reaction in stoichiometric and catalytic applications of transition metal compounds. It is instrumental in the coordination of a substrate and, following metal-mediated reactions, in the release of the product. Therefore the rate of these processes often determines the efficiency of the overall transformation. Acceleration of ligand exchange and the increase in selectivity that results

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are prime objectives in the use of metals in synthesis.[1, 2] Herein we report the results of a study aimed at the labilization of a metal–benzene bond.

Thermal arene–metal bond cleavage in [(η^6-benzene)Cr(CO)$_3$] (**1**) requires quite harsh conditions (PnBu$_3$: 135 °C, pyridine: reflux in neat pyridine, 2 h).[3, 4] Likewise, arene exchange reaction in **1** and analogous compounds is not a routinely useful method for the synthesis of functionalized arene complexes because of the high temperatures required (> 140 °C).[5, 6] [(η^6-naphthalene)Cr(CO)$_3$] (**2**) is an exception in this respect. Complex **2** is a convenient source of the Cr(CO)$_3$ fragment and has found application in catalysis and in the synthesis of functionalized [(arene)Cr(CO)$_3$] complexes.[5, 7, 8] Reasons for the faster ligand exchange in **2** compared to that in **1** are a weaker arene–metal bond and a lower energy pathway to arene displacement.[9] The arene–metal bond in **2** is labile because the haptotropic ring slippage ($\eta^6 \rightarrow \eta^4$) that is postulated to initiate arene displacement is far easier for naphthalene than for benzene.[3, 6b, 10]

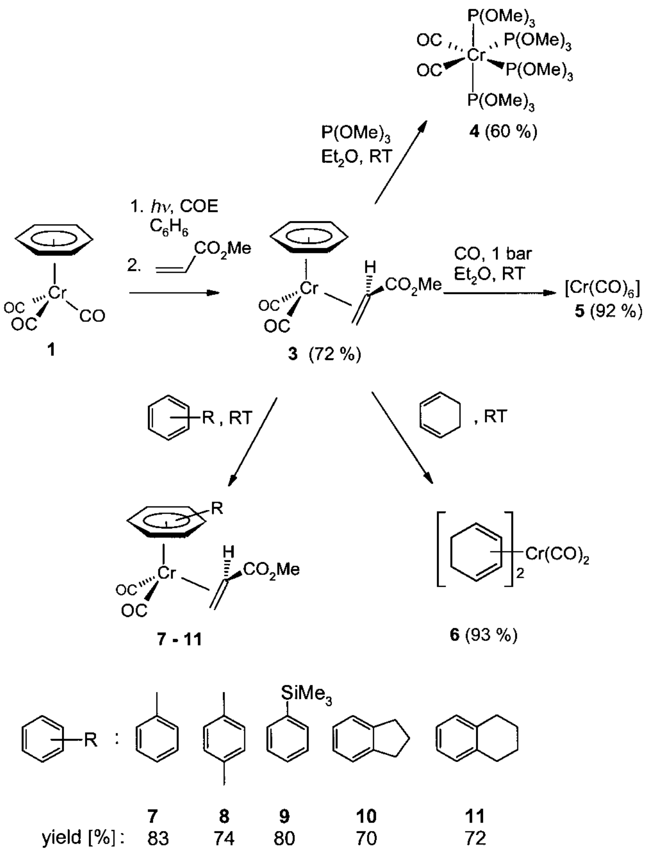
We here show that facile slippage leading to arene displacement is not limited to Cr(CO)$_3$ complexes of condensed aromatic compounds but can be induced even in the normally rather inert benzene complex. The key to this is substitution of one of the three CO ligands in **1** for an acrylate ligand.

The η^2-methyl acrylate complex **3** was obtained by photolytic CO substitution for cyclooctene (COE) followed by alkene exchange.[11] Structural assignment of **3** is based on spectroscopic and analytical data and on comparison with literature data of η^2- and η^4-acrylate transition metal complexes.[12, 13] We next probed the propensity of **3** to undergo arene substitution and arene exchange reactions. The results are shown in Scheme 1.

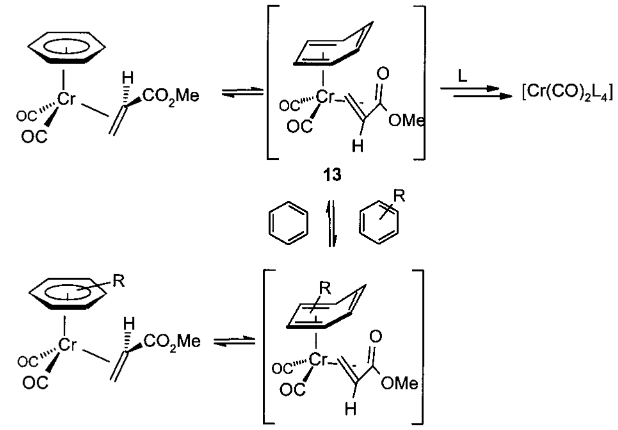
Treatment of **3** with P(OMe)$_3$ at ambient temperature led to the *cis*-dicarbonyl complex **4**.[14] Reaction of **3** with CO afforded a near quantitative yield of [Cr(CO)$_6$] (**5**), and dissolving **3** in cyclohexadiene presented a high-yield route to the recently reported complex bis(η^4-cyclohexadiene)dicarbonylchromium (**6**).[15] The reactions leading to **4**–**6** showed that both the arene–chromium and the acrylate–chromium bonds are labile. Surprisingly, the arene was displaced first. Had this not been the case, the products of the reactions with P(OMe)$_3$ and with CO would have been [Cr(benzene)(CO)$_2${P(OMe)$_3$}] (**12**) and [Cr(benzene)(CO)$_3$] (**1**), respectively. Neither **12** nor **1** undergo arene displacement reactions under the above conditions. Reaction of **3** with arenes resulted in arene exchange to give the arene complexes **7**–**11** in 70–83 % yield. The arene exchange reactions are reversible and to drive the reaction to a single product they are best carried out in neat arene; albeit in some cases (e.g. **8**) the yield was higher when ether was used as solvent. Generally, the analogous arenetricarbonylchromium complexes of **7**–**11** were secondary products formed in these reactions and were isolated in 10 to 20 % yield.

The ease of arene–chromium bond cleavage in **3** is not due to a weakening of the arene–metal bond. Other complexes with a Cr(CO)$_2$L fragment, where L is either a stronger electron acceptor (e.g. maleic anhydride (vide infra), CS) or a stronger electron donor (e.g. P(OMe)$_3$, PPh$_3$) than methyl acrylate, do not undergo these reactions. Scheme 2 shows a tentative rationalization for the observed reactivity and for the labilization effect of the methyl acrylate on the metal–arene bond. It is based on the ability of the acrylate ligand π system to coordinate in a η^2 or in a η^4 fashion to a transition metal. Haptotropic $\eta^2 \rightarrow \eta^4$ rearrangement of the acrylate in **3** would induce a $\eta^6 \rightarrow \eta^4$ rearrangement of the coordinated arene to give intermediate **13**.[16] Arene substitution and arene exchange in **13** would then follow low-activation energy pathways.

Preliminary experiments to test the above hypothesis have been carried out. By using the same route as for **3**, the

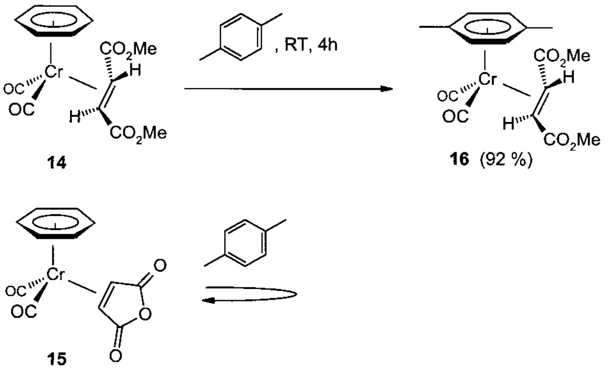


Scheme 1. Substitution and arene exchange reactions of complex **3** that occur at ambient temperature.



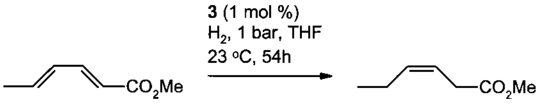
Scheme 2. Proposed mechanism for acrylate-assisted arene–metal bond cleavage.

fumarate complex **14** and the maleic anhydride complex **15**[17] were obtained in 15 and 63 % yield, respectively. The low yield of **14** was due to competitive reduction of the dimethyl fumarate to give dimethyl succinate.[18] Remarkably, the fumarate complex **14** shows the same behavior as **3** but the maleic anhydride complex **15** does not. In **15**, rearrangement to a *cisoid* oxadiene is not possible and arene displacement cannot be triggered. (Scheme 3).



Scheme 3. The fumarate complex **14** exhibits reactivity analogous to that of **3** but the maleic anhydride complex **15** does not react under these conditions.

The *cisoid* conformation of the respective diene is also a key requirement in the use of [(η^6-arene)Cr(CO)$_3$] complexes in the catalytic hydrogenation of conjugated dienes to (*Z*)-alkenes and in the reduction of enones to ketones.[7] The arene complex is a precatalyst for the hydrogenation and the first step is arene dissociation. Reaction conditions therefore reflect the ease of this process. Benzene and substituted benzene complexes require temperatures in excess of 120 °C, whereas the naphthalene complex **2** already reacts at 25 °C. Our preliminary data show that complex **3** readily generates a catalyst at ambient temperature that hydrogenates methyl sorbate (**17**) to *cis*-methyl 3-hexenoate (**18**; Scheme 4).



Scheme 4. Hydrogenation of methyl sorbate (**17**) catalyzed by **3**.

In conclusion, a new mild arene displacement reaction has been discovered. The thermally stable complexes **3** and **16** are precursors to the highly unsaturated [Cr(CO)$_2$(alkene)] and [Cr(CO)$_2$] fragments.

Experimental Section

3: A solution of [Cr(η^6-benzene)(η^2-*cis*-cyclooctene)(CO)$_2$] was prepared by photolysis (Philips, HPK 125) of **1** (0.642 g, 3 mmol) in a mixture of benzene (200 mL) and cyclooctene (16 mL), according to the method given in reference [11]. After completion of the irradiation, methyl acrylate (270 µL, 3 mmol) was added to the reaction mixture. After 16 h the mixture was filtered over Celite and volatiles were removed in vacuo. The residue was taken up in hexane/benzene (20:1) and recrystallized at −40 °C to give red-orange crystals of **3** (0.586 g, 72 %); m.p.: 82–83 °C; ^{1}H NMR (C_6D_6, 200 MHz): δ = 4.35 (s, 6 H, C_6H_6), 3.56 (s, 3 H, OCH_3), 2.93 (dd, $J = 11.3$, 7.7 Hz, 1 H, C=C*H*−CO$_2$Me), 2.76 (dd, $J = 11.3$, 0.8 Hz, 1 H, C*H*$_2$=C), 2.37 (dd, $J = 7.7$, 0.8 Hz, 1 H, C*H*$_2$=C); ^{13}C NMR (C_6D_6, 50 MHz): δ 246.6, 245.9, 177.2, 95.9, 50.1, 41.4, 38.6; IR (hexane): $\tilde{\nu} = 1948, 1896, 1704$; MS (*m*/*z*): 272 ([$M^+$],0.4), 186(4), 158(7), 130(18), 78(100), 52(65); C,H analysis calcd for $C_{12}H_{12}CrO_4$ (272.22): C 52.95, H 4.44; found: C 52.72, H 4.36.

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