

## Construction of Fused Bicyclo-[5.3.0]decane and -[5.4.0]undecane Ring Skeletons via Sequential Additions of Nucleophiles to Tricarbonyltropyliumchromium Tetrafluoroborate

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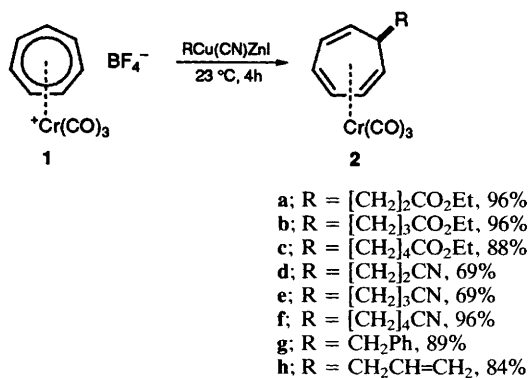
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The addition of a variety of the highly functionalized zinc-copper reagents  $\text{RCu}(\text{CN})\text{ZnI}$  to the title cation gives  $(\eta^6\text{-cyclohepta-1,3,5-triene})\text{Cr}(\text{CO})_3$  complexes with a functionalized side chain at the C-7 position of the ring: intramolecular cyclisation of ester-substituted adducts using lithium diisopropylamide generates fused bicyclo-[5.3.0]decane and -[5.4.0]undecane derivatives.

Seven-membered carbocycles are often used in the construction of complicated natural products.<sup>1</sup> Specially, the perhydroazulene or bicyclo[5.3.0]decane ring system is the most commonly encountered of the cycloheptane derived structure in natural occurring biologically-active compounds.<sup>2</sup> Recently, tropone has been shown to be a versatile building block for the synthesis of a variety of sesquiterpenes with the bicyclo[5.3.0]decane ring skeleton.<sup>3</sup> Normally, several steps starting from the 1,8-addition of a protected functionalized three-carbon chain to tropone are needed to construct the bicyclo[5.3.0]decane ring skeleton. However, bicyclo[5.3.0]decane and -[5.4.0]undecane derivatives may be available easily *via* sequential additions of nucleophiles to [(tropylium)Cr(CO)<sub>3</sub>] cation **1**. This method allows the formation of 5,7- and 6,7-*cis*-fused bicyclic systems which cannot be generated by sequential additions of nucleophiles to

$(\eta^5\text{-pentadienyl})\text{Fe}(\text{CO})_3$ .<sup>4</sup> Prior to our investigation, several classes of nucleophiles such as hydrides, methoxides and hydrogen sulfides had been shown to add to cation **1** to produce 7-*exo*-substituted  $(\eta^6\text{-cyclohepta-1,3,5-triene})\text{Cr}(\text{CO})_3$  complexes.<sup>5</sup> However, the addition of an excess of sodium diethylmalonate or lithium cyclopentadienide to **1** provided the ring contraction product  $[\text{C}_6\text{H}_6\text{Cr}(\text{CO})_3]$ <sup>6</sup> and the reaction of cyanide with **1** led by reductive coupling to a mixture of bi(cycloheptadienyl)Cr<sub>2</sub>(CO)<sub>6</sub> and bi(cycloheptadienyl)Cr(CO)<sub>3</sub>.<sup>7</sup> Moreover, phenyl lithium failed to react with **1**. Surprisingly, reports on the addition of organocopper derivatives to cation **1** are lacking. We now report that the highly functionalized zinc-copper reagents  $[\text{RCu}(\text{CN})\text{ZnI}]$ <sup>4,8</sup> add efficiently to **1** to afford  $(\eta^6\text{-cyclohepta-1,3,5-triene})\text{Cr}(\text{CO})_3$  complexes **2a-h** with a functionalized side chain at the C-7 position of the ring. The reactions are performed in the expectation that further manipulation of the resulting complexes will then be possible after the initial additions.

Cation **1** was prepared in two steps from cyclohepta-1,3,5-triene and  $\text{Cr}(\text{CO})_3(\text{MeCN})_3$  (85% overall yield).<sup>9</sup> Finally, our synthesis of C-7-substituted  $(\eta^6\text{-cyclohepta-1,3,5-triene})\text{Cr}(\text{CO})_3$  complexes **2** involved the slow addition of a THF solution of the highly functionalized zinc-copper reagents  $\text{RCu}(\text{CN})\text{ZnI}$  (1.2 equiv.) to a stirred suspension of cation **1** in THF at 0 °C under nitrogen. The addition was carried out for 5 h at 23 °C followed by workup with saturated aqueous ammonium chloride and diethyl ether extraction. After purification by flash column chromatography on silica gel, complexes **2a-h** were obtained as the major products and in good yields (69–96%, Scheme 1). The *trans* relationship between the nucleophile and the metal moiety of complexes **2** was assigned based upon comparison of their <sup>1</sup>H NMR spectra [ $\delta$  5.95 (2H, br.s)] with the spectra of known 7-*exo*-( $\eta^6\text{-cyclohepta-1,3,5-triene})\text{Cr}(\text{CO})_3$  complexes.<sup>10</sup> Further manipulation of the resulting complexes **2** was demonstrated as follows. Treatment of **2b** with lithium diisopropylamide (LDA, 1.2 equiv.) in THF and hexamethylphosphoramide (HMPA, THF-HMPA = 3:1) at -78 °C for 1 h followed by quenching the reaction mixture with TFA (10 equiv.) produced a mixture of perhydroazulene derivatives **3a** and **3b** in a 1:1 ratio in 77% total yield. The formation of bicyclo[5.3.0]decane derivatives **3a** and **3b** agrees closely with the mechanism proposed for the intermolecular addition of nucleophiles to  $(\eta^6\text{-arene})\text{Cr}(\text{CO})_3$ .<sup>11</sup> Deprotonation of **2b** using LDA at -78 °C in THF-HMPA would result in the formation of the kinetic ester enolate.<sup>4,12</sup> *Anti* addition of the ester enolate to the terminal position of the triene ligands gave  $(\eta^5\text{-cycloheptadienyl})\text{Cr}(\text{CO})_3$  anion complex **4** ( $n = 1$ , Fig. 1). Electrophilic quenching of **4** with TFA afforded bicyclo[5.3.0]decane derivatives **5a** and **5b**. However, diene migration occurred and produced thermally more stable isomers **3a** and **3b** under the reaction conditions. Treatment of **2c†** with LDA (1.2 equiv.) in THF-HMPA (3:1) under atmosphere of CO at -78 °C for 1 h followed by quenching the reaction mixture with iodomethane (5 equiv.; CO; 25 °C; 2 h), and then iodine (4 equiv.; 25 °C; 4 h) generated the bicyclo[5.4.0]undecane derivative **6†** as the only diastereo-



Scheme 1

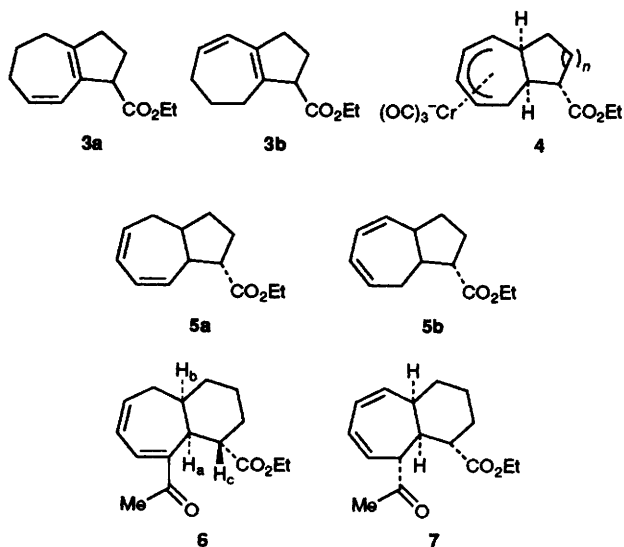


Fig. 1

isomer isolated in 63% yield. Reaction of **4** ( $n = 2$ ) with iodomethane under an atmosphere of CO would give the bicyclo[5.4.0]undecane derivative **7**<sup>13</sup> which isomerized to provide the highly conjugate dienone **6**. The *cis* stereochemistry at the ring juncture of **6** is fixed by *anti* addition of the ester enolate to the terminal position of the triene ligand (to give **4**,  $n = 2$ ) and the ester group assigned as *exo* was resulted from the formation of the kinetic ester enolate under the kinetically controlled reaction conditions.<sup>4</sup> <sup>1</sup>H NMR studies provided the initial evidence for support of the structural assignments. The <sup>1</sup>H NMR spectrum of compound **6** exhibited a doublet of doublets, centred at  $\delta$  3.2,  $J = 12.0$ , 2.8 Hz, assigned to H<sub>a</sub>. The coupling constant of H<sub>a</sub>-H<sub>b</sub> ( $J_{ab}$ ) of 12.0 Hz agrees closely with the 12.7 Hz coupling constant observed for the *cis* fused bicyclo[5.4.0]undecanone and the coupling constant of H<sub>a</sub>-H<sub>c</sub> ( $J_{ac}$ ) of 2.8 Hz agrees with the 3.2 Hz coupling constant observed for the similarly disposed *trans* hydrogens.<sup>14</sup>

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#### Footnote

† Spectroscopic data for **2c**: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  5.95 (2H, brs), 4.77 (2H, brs), 4.10 (2H, q,  $J$  7.2 Hz), 3.70 (2H, t,  $J$  8.6 Hz), 2.90 (1H, m), 2.17 (2H, t,  $J$  7.3 Hz), 1.39 (2H, m), 1.23 (3H, t,  $J$  7.2 Hz), 1.06 (2H, m) and 0.25 (2H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  231.9, 173.4, 98.9, 97.8, 67.7, 60.2, 38.6, 35.9, 34.0, 24.3, 23.2 and 14.2; IR (CH<sub>2</sub>Cl<sub>2</sub>, solution)  $\nu$ /cm<sup>-1</sup> 3067w, 2992w, 1977s, 1910s, 1879s, 1728w, 1620, 1424m and 1252m; mass (EI)  $m/z$  357 (M<sup>+</sup>, 27%), 328 (8), 300 (5), 272 (73), 254 (11), 194 (46), 180 (100); high resolution, calc. for C<sub>17</sub>H<sub>20</sub>O<sub>5</sub>Cr 356.0710; found  $m/z$  356.0712. For **6**: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  6.84 (1H, d,  $J$  7.8 Hz), 6.14 (1H, dd,  $J$  10.7, 8.3 Hz), 5.91 (1H, m), 4.14 (2H,  $J$  6.8 Hz), 3.26 (1H, dd,  $J$  12.0, 2.8 Hz), 2.71-2.61 (2H, m), 2.44 (1H, m), 2.34 (3H, s), 2.12 (1H, m) and 1.82-1.23 (9H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  199.4, 174.3, 144.8, 139.5, 133.7, 122.8, 60.0, 47.3, 41.8, 34.8, 27.8, 27.6, 26.1, 25.5, 21.8 and 14.1; IR (CH<sub>2</sub>Cl<sub>2</sub>, solution)  $\nu$ /cm<sup>-1</sup> 3072w, 2995m, 1723s, 1659s, 1601m, 1427m, 1375m and 1182s cm<sup>-1</sup>; mass (EI)  $m/z$  262 (M<sup>+</sup>, 77%), 216 (23), 188 (37), 145 (100), 105 (9), 91

(17); high resolution, calc. for C<sub>16</sub>H<sub>22</sub>O<sub>3</sub> 262.1563; found  $m/z$  262.1567.

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