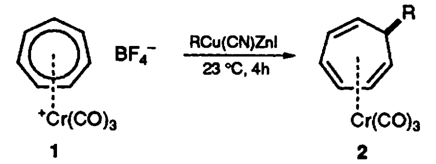
Construction of Fused Bicyclo-[5.3.0]decane and -[5.4.0]undecane Ring Skeletons *via* Sequential Additions of Nucleophiles to Tricarbonyltropyliumchromium Tetrafluroborate

Ming-Chang P. Yeh* and Chong-Nan Chuang

Department of Chemistry, National Taiwan Normal University, 88, Sec. 4, Ding-Jou Road, Taipei, Taiwan, Republic of China

The addition of a variety of the highly functionalized zinc–copper reagents RCu(CN)ZnI to the title cation gives (η^6-cyclohepta-1,3,5-triene)Cr(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.[1] 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.[2] 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.[3] 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)$_3$] 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 (η^5-pentadienyl)Fe(CO)$_3$.[4] 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 (η^6-cyclohepta-1,3,5-triene)-Cr(CO)$_3$ complexes.[5] However, the addition of an excess of sodium diethylmalonate or lithium cyclopentadienide to **1** provided the ring contraction product [C$_6$H$_6$Cr(CO)$_3$][6] and the reaction of cyanide with **1** led by reductive coupling to a mixture of bi(cycloheptadienyl)Cr$_2$(CO)$_6$ and bi(cycloheptadienyl)Cr(CO)$_3$.[7] 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 [RCu(CN)ZnI][4,8] add efficiently to **1** to afford (η^6-cyclohepta-1,3,5-triene)-Cr(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.



a; R = [CH$_2$]$_2$CO$_2$Et, 96%
b; R = [CH$_2$]$_3$CO$_2$Et, 96%
c; R = [CH$_2$]$_4$CO$_2$Et, 88%
d; R = [CH$_2$]$_2$CN, 69%
e; R = [CH$_2$]$_3$CN, 69%
f; R = [CH$_2$]$_4$CN, 96%
g; R = CH$_2$Ph, 89%
h; R = CH$_2$CH=CH$_2$, 84%

Scheme 1

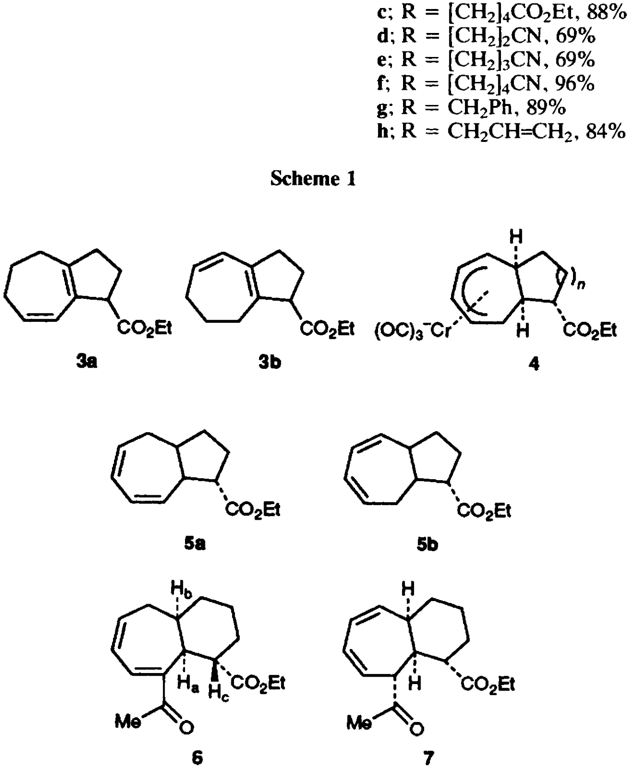


Fig. 1

Cation **1** was prepared in two steps from cyclohepta-1,3,5-triene and Cr(CO)$_3$(MeCN)$_3$ (85% overall yield).[9] Finally, our synthesis of C-7-substituted (η^6-cyclohepta-1,3,5-triene)-Cr(CO)$_3$ complexes **2** involved the slow addition of a THF solution of the highly functionalized zinc–copper reagents RCu(CN)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 ^{1}H NMR spectra [δ 5.95 (2H, br.s)] with the spectra of known 7-*exo*-(η^6-cyclohepta-1,3,5-triene)Cr(CO)$_3$ complexes.[10] 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 (η^6-arene)Cr(CO)$_3$.[11] Deprotonation of **2b** using LDA at −78 °C in THF–HMPA would result in the formation of the kinetic ester enolate.[4,12] *Anti* addition of the ester enolate to the terminal position of the triene ligands gave (η^5-cycloheptadienyl)Cr(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 at 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 diastereoisomer 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**[13] 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 kinectically controlled reaction conditions.[4] ^{1}H NMR studies provided the initial evidence for support of the structural assignments. The ^{1}H NMR spectrum of compound **6** exhibited a doublet of doublets, centred at δ 3.2, J = 12.0, 2.8 Hz, assigned to H_a. The coupling constant of H_a–H_b (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_a–H_c (J_{ac}) of 2.8 Hz agrees with the 3.2 Hz coupling constant observed for the similarly disposed *trans* hydrogens.[14]

We thank the National Science Council of the Republic of China for financial support.

Received, 6th December 1993; Com. 3/07188J

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† *Spectroscopic data* for: **2c**: ^{1}H NMR (CDCl$_3$) δ 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); ^{13}C NMR (CDCl$_3$) δ 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$_2$Cl$_2$, solution) ν/cm^{-1} 3067w, 2992w, 1977s, 1910s, 1879s, 1728w, 1620, 1424m and 1252m; mass (EI) m/z 357 (M$^+$, 27%), 328 (8), 300 (5), 272 (73), 254 (11), 194 (46), 180 (100); high resolution, calc. for $C_{17}H_{20}O_5Cr$ 356.0710; found m/z 356.0712. For **6**: ^{1}H NMR (CDCl$_3$) δ 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); ^{13}C NMR (CDCl$_3$) δ 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$_2$Cl$_2$, solution) ν/cm^{-1} 3072w, 2995m, 1723s, 1659s, 1601m, 1427m, 1375m and 1182s cm^{-1}; mass (EI) m/z 262 (M$^+$, 77%), 216 (23), 188 (37), 145 (100), 105 (9), 91 (17); high resolution, calc. for $C_{16}H_{22}O_3$ 262.1563; found m/z 262.1567.

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