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REACTIONS OF (ARENE)TRICARBONYLCHROMIUM STABILIZED CARBOCATIONS WITH AROMATICS AND β-DICARBONYL COMPOUNDS

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Summary

Primary and secondary benzylic carbocations, stabilized by a tricarbonylchromium group, gave coupling products with several aromatics or β-dicarbonyl compounds in good yield and this reaction presents a new synthetic method for carbon–carbon bond formation. The chromium complexes of tertiary benzyl alcohols gave dehydrated products without carbon–carbon coupling products under similar conditions.

The enhanced stability of carbocations adjacent to organotransition metal moieties has been demonstrated for a number of systems [1], and the origin and the magnitude of this stabilization receive continuous interest in organometallic chemistry. Attempts [2] to isolate a tricarbonylchromium-stabilized benzylic carbocation species [3] gave only decomposition products in acidic media, where carbon monoxide was liberated. However, stabilized benzylic carbocations have been easily trapped, in situ, with ROH, H_2O, RCN and RSH [4]. We have been interested in the synthetic potential of the stabilized carbocations particularly with respect to their function as benzyl electrophiles in carbon–carbon bond forming reactions. We, as did Reetz et al., reported the stereoselective alkylations of (η^6-arene)tricarbonylchromium complexes of benzylic acetates with silyl enol ethers [5], trialkylaluminums [6] and allyltrimethylsilanes [7] with high yields. To explore the scope and further use in synthesis of these electrophilic benzyl synthons, we have studied the reactions of these stabilized carbocations with other carbon nucleophiles such as aromatic and β-dicarbonyl compounds.

Results and discussion

Patin's and Jaouen's groups previously reported that the reactions of the tricarbonylchromium complexed tertiary benzyl alcohols with electron-richer arenes

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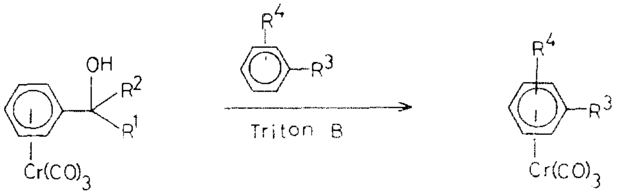
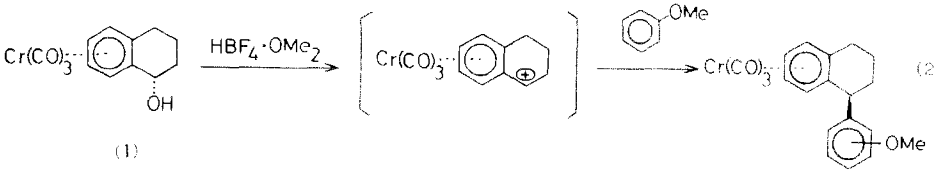
and 2-methyl-1,3-cyclopentadione in the presence of Triton B gave rise to transfer of the tricarbonylchromium group to the electron-richer arenes without carbon–carbon bond formation [8] (eq. 1). Although the mechanism of this ligand exchange reaction is uncertain, a bimolecular process or liberation of an active $Cr(CO)_3$ fragment via the stabilized carbocation has been proposed. In order to search the above transfer of the tricarbonylchromium group under our conditions, and to make sure the necessary complexation in the arene specified for the natural product synthesis, we have examined the reaction of chromium-complexed benzyl alcohols with aromatics or β-dicarbonyl compounds in the presence of a Lewis acid instead of Triton B.



(1)

Simple addition of $HBF_4 \cdot OMe_2$ to a solution of tricarbonyl(1-*endo*-tetralol)chromium (**1**) and anisole in methylene chloride at 0°C under argon resulted in a rapid reaction. Aqueous workup followed by silica gel chromatography gave an unseparable mixture of the *ortho*- and *para*-methoxyphenyl compound **2** in 52% yield, in which the methoxyphenyl group was introduced at the benzylic position of the tetralinchromium complex in an *exo*-fashion [9] without transfer of the $Cr(CO)_3$ group (eq. 2).



(1)

(2)

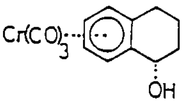
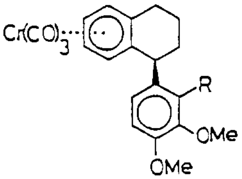
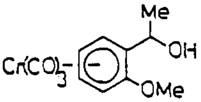
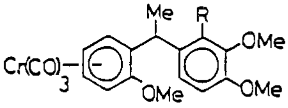
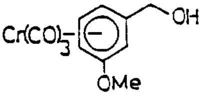
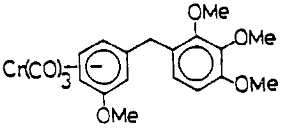
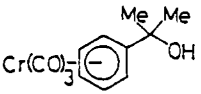
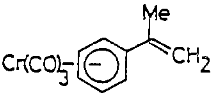
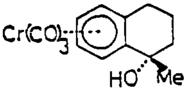
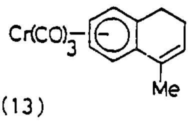
(2)

The results of the other (arene)tricarbonylchromium complexes with some representative electron-rich aromatic compounds are presented in Table 1. While the primary and secondary benzylic hydroxyl groups of the (arene)tricarbonylchromium complexes could be easily replaced by the methoxyphenyl group, the tertiary benzylic alcohol complexes gave only dehydrated products under similar conditions without carbon–carbon bond formation (entries 6 and 7). These results are in contrast to the reactions of the same chromium complexes with trialkylaluminums [6] or allyltrimethylsilane [7] under the Lewis acid condition, in which the tertiary hydroxyl groups were smoothly replaced by the alkyl or allyl group. These differences could be explained by a lower nucleophilicity of aromatic compounds than that for the aluminum or silyl reagents.

Several important features of this type of carbon–carbon bond formation are noteworthy: (1) Since electron-rich arene rings can be directly introduced as nucleophiles stereoselectively at the benzylic position of the tetralin complexes, it could be utilized in the synthesis of natural products such as lignans; (2) The tricarbonylchromium group remains fixed at the original aromatic nucleus during the reaction, and consequently the original chromium-complexed aromatic part

TABLE 1

ADDITION OF (ARENE)TRICARBONYLCHROMIUM COMPLEXES WITH 1,2-DIMETHOXYBENZENE (A) AND 1,2,3-TRIMETHOXYBENZENE (B)

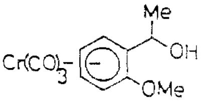
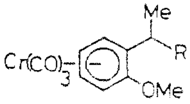
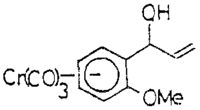
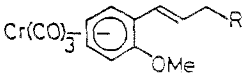
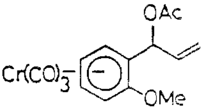
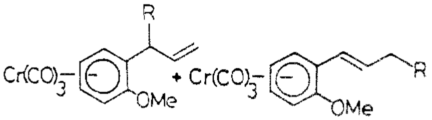
Entry	Complex	Nucleophile	Product	Yield (%)
1	 (1)	A	 (3) R=H	74
2	(1)	B	(4) R=OMe	80
3	 (5)	A	 (6) R=H	77
4	(5)	B	(7) R=OMe	80
5	 (8)	B	 (9)	86
6	 (10)	B	 (11)	90
7	 (12)	B	 (13)	90

could be further transformed to other useful intermediates by utilizing nucleophilic addition [10] or directed regioselective lithiation [11]; (3) The $Cr(CO)_3$ unit is efficiently removed by mild oxidation (air, I_2 etc.), and various metal-free substituted benzyl compounds could be easily obtained.

Next, β-dicarbonyl compounds were used as nucleophiles in this carbon–carbon bond forming reaction. Acetylacetone and methyl acetoacetate reacted readily to

TABLE 2

REACTION OF ACETYLACETONE (A), METHYL ACETOACETATE (B) AND 1,2,3-TRIMETHOXYBENZENE (C) WITH SOME SELECTED CHROMIUM COMPLEXES

Entry	Complex	Nucleophile	Product	Yield (%)
				
1	(5)	A	(14) $R = CH(COMe)_2$	73
2	(5)	B	(15)[a] $R = CH(COMe)CO_2Me$	81
				
3	(16)	C	(17) $R = 2,3,4\text{-}(OMe)_3\text{-}C_6H_3$	37
4	(16)	A	(18) $R = CH(COMe)_2$	61
				
5	(19)	Me_3Al[b]	(20) R = Me (3 : 1)	62
6	(19)	Et_3Al[b]	(21) R = Et (1 : 1)	58

[a] Diastereomeric mixture. [b] Without Lewis acid.

give chromium complexes substituted at the benzylic position in a similar way (Table 2). However, diethyl malonate afforded no coupling product.

We further examined the reaction of tricarbonylchromium complexes of 1-arylallyl alcohol, such as **16** and **19**, with the same nucleophiles. These types of chromium complexes are interesting, since they have two reactive sites, the benzylic position and the terminal position by double bond migration. The reaction of complex **16** and the corresponding acetoxy complex **19** gave as expected, products substituted at the terminal position with 1,2,3-trimethoxybenzene or acetylacetone in the presence of $HBF_4 \cdot OMe_2$. The geometry of the internal double bond resulting from isomerization is *trans* (J 16 Hz). The free hydroxy complex **16** afforded no coupling product with trialkylaluminum. However, the corresponding acetoxy complex **19** gave a regioisomeric mixture of products that reacted at the internal and external positions (entries 5 and 6). No evidence was observed for the tricarbonylchromium transfer to an electron-richer aromatic nucleus in this series of reactions.

In conclusion, (arene)tricarbonylchromium complexes possessing a hydroxyl group at the benzylic position could easily react with aromatics or β-dicarbonyl compounds to give coupling products via the tricarbonylchromium stabilized-benzylic carbocations, generated by the action of $HBF_4 \cdot OMe_2$. Applications of these reactions to natural product synthesis is in progress.

Experimental

All melting points are uncorrected and were determined on a Yanagimoto Model MPJ-2 micro melting apparatus. IR spectra were recorded in $CHCl_3$ solution by a JASCO Model A-102 spectrometer, and ^1H NMR spectra were measured on JEOL Model PS and FX at 100 MHz in $CDCl_3$ solution. NMR chemical shifts are given in ppm downfield from Me_4Si, and coupling constants are given in Hertz.

The tetrafluoroboric acid dimethyl ether complex was purchased from Aldrich Chemical Company. Tricarbonyl(1-*endo*-tetralol)chromium (**1**) and tricarbonyl(1-*exo*-methyl-1-*endo*-tetralol)chromium (**12**) were prepared from tricarbonyl(1-tetralone)chromium by treatment with $LiAlH_4$ or MeLi, respectively [11]. The chromium complexes **5** and **8** were obtained by direct complexation from hexacarbonylchromium and the parent arenes. The complexes **10** and **16** were synthesized by the reaction of tricarbonyl(acetophenone)chromium and MeLi, or tricarbonyl(*ortho*-methoxybenzaldehyde)chromium and vinylmagnesium bromide.

Reaction of tricarbonyl(1-endo-tetralol)chromium (1) with anisole

$HBF_4 \cdot OMe_2$ (0.05 ml, 0.30 mmol) was added to a solution of the chromium complex **1** (85 mg, 0.30 mmol) and anisole (40 μl, 0.36 mmol) in dry methylene chloride (5 ml) at 0°C under argon. The reaction mixture was stirred at 0°C for 3 h and quenched with saturated aqueous $NaHCO_3$. The mixture was extracted with methylene chloride, and the extract was washed with brine and dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by silica gel chromatography with ether/petroleum ether to give complex **2** (59 mg, 52%) as a yellow liquid. The ratio of *ortho*- and *para*-isomers were determined by the area of aromatic H in ^1H NMR (*ortho/para* 1/5). ν_{max} 1960, 1880 cm^{-1}; δ(ppm) 1.44–1.86 (4H, m), 2.58–2.76 (2H, m), 3.78 (3H, s), 3.80–3.90 (1H, br), 4.99–5.26 (4H, m, Cr–ArH), 6.79 (d, $J = 8$) and 7.00 (d, $J = 8$) (ArH of *para*-isomer), 6.81–6.88 (m, Ar*H* of *ortho*-isomer); *m/e* (relative intensity) 394 (M^+, 3), 290(17), 266(29), 182(87), 53(100).

The reaction of other chromium complexes with aromatics or *β*-dicarbonyl compounds except trialkylaluminums was achieved in a similar way as described above. Physical and spectral data of the reaction products are as follows.

3: m.p. 161°C; ν_{max} 1950, 1880, 1510 cm^{-1}; δ(ppm) 1.13–1.88 (4H, m), 2.68–2.80 (2H, m), 3.84 (3H, s), 3.85 (3H, s), 3.85–3.96 (1H, br), 5.02–5.29 (4H, m), 6.48–6.62 (2H, m), 6.78 (1H, d, *J* = 8). Anal. Found: C, 62.37; H, 4.98. $C_{21}H_{20}O_5Cr$ calcd.: C, 62.08; H, 5.02%.

4: yellow liquid; ν_{max} 1960, 1880 cm^{-1}; δ(ppm) 1.19–1.95 (4H, m), 2.63–2.75 (2H, m), 3.73 (3H, s), 3.83 (3H, s), 3.85 (3H, s), 3.86–3.92 (1H, br), 5.00–5.28 (4H, m), 6.10 (1H, d, *J* = 8), 6.65 (1H, d, *J* = 8); *m/e* 434 (M^+, 7), 350(34), 298(70), 130(100).

6: m.p. 244°C; ν_{max} 1960, 1870, 1510 cm^{-1}; δ(ppm) 1.54 (3H, t, *J* = 7), 3.78 (3H, s), 3.86 (3H, s), 3.90 (3H, s), 4.23 (1H, q, *J* = 7), 4.68 (1H, t, *J* = 6), 4.98 (2H, t, *J* = 6), 5.42 (1H, d, *J* = 6), 6.89–7.00 (3H, m). Anal. Found: C, 58.76; H, 4.96. $C_{20}H_{20}O_6Cr$ calcd.: C, 58.82; H, 4.94%.

7: m.p. 104°C; ν_{max} 1960, 1860, 1490 cm^{-1}; δ(ppm) 1.56 (3H, d, *J* = 7), 3.77 (3H, s), 3.85 (6H, s), 3.91 (3H, s), 4.35 (1H, q, *J* = 7), 4.89 (1H, d, *J* = 7), 5.34–5.47 (2H, m), 6.62 (1H, d, *J* = 7), 7.01 (1H, d, *J* = 7). Anal. Found: C, 57.43; H, 5.00; $C_{21}H_{22}O_7Cr$ calcd.: C, 57.53; H, 5.06%.

9: m.p. 99°C; ν_{max} 1960, 1870, 1500 cm^{-1}; δ(ppm) 3.66 (3H, s), 3.70–3.75 (2H, brs), 3.71 (3H, s), 3.72 (3H, s), 3.74 (3H, s), 4.79–5.13 (3H, m), 5.49 (1H, t, *J* = 7), 6.59 (1H, d, *J* = 8), 6.71 (1H, d, *J* = 8). Anal. Found: C, 56.88; H, 4.80; $C_{20}H_{20}O_7Cr$ calcd.: C, 56.61; H, 4.75%.

14: yellow liquid; ν_{max} 1960, 1880, 1710 cm^{-1}; δ(ppm) 1.29 (3H, d, *J* = 7), 2.08 (3H, s), 2.14 (3H, s), 3.77 (3H, s), 4.66–4.89 (2H, m), 5.64–5.98 (2H, m), 6.42–6.66 (2H, m).

15: yellow liquid; ν_{max} 1960, 1880, 1730, 1710 cm^{-1}; δ(ppm) 1.36 (3H, d, *J* = 7), 2.19 (3H, s), 3.64 and 3.68 (3H, s, diastereoisomer 2/3), 3.74 (3H, s), 4.77–4.98 (2H, m).

17: yellow liquid; ν_{max} 1960, 1880, 1490 cm^{-1}; δ(ppm) 3.46 (2H, d, *J* = 6), 3.77 (3H, s), 3.83 (3H, s), 3.86 (3H, s), 3.88 (3H, s), 4.91 (1H, t, *J* = 7), 5.07 (1H, dd, *J* = 1 and 7), 5.44 (1H, td, *J* = 1 and 7), 5.88 (1H, dd, *J* = 1 and 7), 6.16 (1H, dt, *J* = 6 and 16), 6.44 (1H, d, *J* = 16), 6.59 (1H, d, *J* = 8), 6.84 (1H, d, *J* = 8); *m/e* 450 (M^+, 15), 366(71), 351(28), 336(16), 314(100), 299(33).

18: m.p. 128°C; ν_{max} 3350, 1960, 1880, 1580 cm^{-1}; δ(ppm) 2.11 (6H, s), 3.11 (2H, d, *J* = 5), 3.73 (3H, s), 4.97 (1H, t, *J* = 7), 5.13 (1H, d, *J* = 7), 5.48 (1H, d, *J* = 7), 5.79 (1H, d, *J* = 7), 6.14 (1H, dt, *J* = 16 and 5), 6.40 (1H, s). Anal. Found: C, 56.55; H, 4.75; $C_{18}H_{18}O_6Cr$ calcd.: C, 56.41; H, 4.80%.

*Reaction of complex **19** with trimethylaluminum*

Me_3Al (1.3 ml of 0.9 *M* in hexane, 1.17 mmol) was added to a solution of the chromium complex **19** (100 mg, 0.29 mmol) in dry methylene chloride (5 ml) at −78°C under argon. The reaction mixture was stirred for 30 min at −78°C, and for 1 h at 0°C. The mixture was decomposed with saturated aqueous NH_4Cl and extracted with methylene chloride. The organic layer was dried over $MgSO_4$, and removed in vacuo. The residue was purified by silica gel chromatography to give a yellow unseparable regioisomeric mixture **20** (54 mg). ν_{max} 1960, 1880 cm^{-1}; δ(ppm) 1.05 (t, $J = 7$), 1.25 (d, $J = 7$), 1.33 (d, $J = 7$), 3.69 and 3.79 (3H, s), 4.73–5.44 (m).

21: ν_{max} 1960, 1880 cm^{-1}; δ(ppm) 0.92 (t, $J = 7$), 1.03 (d, $J = 7$), 3.67 (s, OCH_3) and 3.73 (s, OCH_3), 4.73–5.57 (m); *m/e* 312 (M^+, 5), 229(100), 201(50), 147(70).

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