Alkylation of Arylacetic Esters by Phase-Transfer Catalysis and Sodium Hydride: Activation and Stereochemical Effects of the Chromium Tricarbonyl Group

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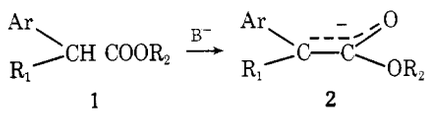
Received March 31, 1977

Methyl arylacetate–chromium tricarbonyl complexes and related compounds can be readily alkylated either by phase-transfer catalysis or by sodium hydride in *N,N*-dimethylformamide. The electron-withdrawing character of the $Cr(CO)_3$ group has a significant influence on the generation of the ester carbanion, and on its subsequent reaction with an alkyl halide. Alkylation of cyclic ester complexes is stereospecifically exo (with respect to the $Cr(CO)_3$ group), while acyclic analogues undergo alkylation with considerable stereoselectivity.

There has been considerable interest, particularly from a pharmacological viewpoint, in the alkylation of arylacetic esters (**1**) and related compounds.[1,2] Alkylation is generally



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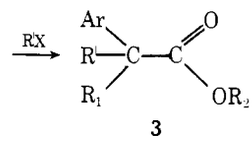

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effected by generation of an enolate anion (**2**) from the ester, followed by reaction with an alkyl halide. Strong bases are required for enolate anion formation, including sodamide (in liquid ammonia)[3] and lithium *N*-cyclohexyl-*N*-isopropylamide (tetrahydrofuran, −78 °C).[4] Due to the sensitivity of methyl esters (**1**, $R_2 = CH_3$) toward alkaline hydrolysis,[5] only the tertiary butyl esters [**1**, $R_2 = C(CH_3)_3$] can be alkylated by phase-transfer catalysis.[5]

We now report[6] that these alkylation reactions can be greatly improved by the use of the chromium tricarbonyl [$Cr(CO)_3$] moiety as a temporary complexing group of the aromatic ring.[7] Complexation of arylacetic esters can be readily effected using $Cr(CO)_6$, often giving high yields of arene chromium tricarbonyl complexes (see Experimental Section). Furthermore, liberation of the arene ligand from the complex is simple and quantitative, either by chemical[7a] or photochemical[8-10] oxidation.

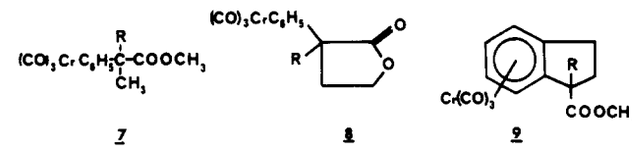
Both electronic and steric effects of the $Cr(CO)_3$ group are useful in the alkylation reactions. The former enhances the acidity of the esters, allowing a facile alkylation of methyl esters, with different alkylating agents [either by phase-transfer catalysis or by sodium hydride in *N,N*-dimethylformamide (DMF)]. Steric effects may induce stereospecific alkylations, some examples of which are given below.

Electronic Activation

Several studies have indicated the substantial electron-withdrawing influence of the $Cr(CO)_3$ group when attached to a benzene ring.[11] This effect is also significant in the phase-transfer-catalyzed methylation of some diarylacetic esters (Table I). Compounds **4–6** were each methylated by treatment with 50% sodium hydroxide, cetyltrimethylammonium bromide (CTAB, 40% of the ester concentration) as the catalyst, a stoechiometric amount of methyl iodide, and stirring 45 min at room temperature.

Clearly, the kinetic acidity of arylacetic esters, which is important in phase-transfer catalysis, is greatly enhanced by complexation of one or both arene sites. Evidence for the operation of a phase-transfer system rather than a micellar catalysis in these reactions comes from a study of the effect of the catalyst concentration on the alkylation of **6** (Table II): as the ratio of CTAB/**6** increases, the yield of alkylated material increases. Here the CTAB concentration covers a range of approximately 10^{-3}–10^{-2} M, higher than its critical micellar concentration ($\simeq 10^{-3}$ M at 25 °C).[12]

Several other related ester complexes (**7–9**, R = H) were



7 **8** **9**

subjected to phase-transfer-catalyzed alkylation, and the yields are listed in Table III. In all but one instance, alkylation of **7–9** is faster than hydrolysis. Further hydrolysis of the alkylated compounds is negligible, due to the increased steric hindrance of the ester or lactone groups. *None* of the noncomplexed analogues of **7–9** (R = H) could be alkylated by phase-transfer catalysis, since hydrolysis is more facile than alkylation.

As compared with the preceding method, alkylation of noncomplexed analogues of **7–9** (R = H) using NaH/DMF is a poor reaction. Complexes **7–9** (R = H) are very reactive toward NaH/DMF, rapidly affording stable enolates in quantitative yields at room temperature, and alkylation of these formed enolates with different halides (RX = CH_3I, $PhCH_2Br$, $CH_2{=}CHCH_2Br$, $HC{\equiv}CCH_2Br$, $BrCH_2COOCH_3$) is also fast (<5 min) and quantitative at room temperature. The complexed enolate anions are, in fact, weaker nucleophiles than the corresponding noncomplexed species. This point was demonstrated by competitive reaction of equal amounts of a complexed and noncomplexed anion with a limited amount of methyl iodide (Table IV). The uncomplexed anion, in both instances, was alkylated to a greater extent than the complexed anion, the dicomplexed anion not undergoing any methylation. These results are principally due to the electron-attracting influence of the $Cr(CO)_3$ group, rather than to the steric bulk of this group: as noted below the R of RX becomes attached to the enolate on the side opposite to that of the $Cr(CO)_3$ group.

Using an appropriate substrate, the stereochemistry of the phase-transfer and NaH/DMF methods could be compared. Generation of the anion of **10** by phase-transfer catalysis and subsequent reaction with 1,4-dibromopentane gives **11** and **12** in a ratio of 72:28 (total yield 45%). A 76:24 ratio of **11**/**12** (total yield 100%) resulted with the use of NaH/DMF. These results are consistent with literature data[13] indicating the similarity between phase-transfer catalysis and S_N2 reactions

Table I. Methylation of Diarylacetic Esters

Reactant	Yield (%)
$Ph_2CHCOOCH_2$ (4)	2.5
$(CO)_3CrC_6H_5CHCOOCH_3$ (5)	60
Ph	
$[(CO)_3CrC_6H_5]_2CHCOOCH_3$ (6)	100

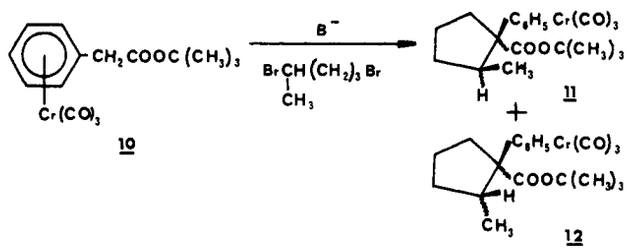
Table II. Effect of CTAB Concentration on Alkylation of 6

CTAB/6, %	5	10	20	30	40
Methylation %	25	30	60	80	100

Table III. Alkylation of 7–9

RX	7–9, R =	% Yield[a] 7	8	9
CH_3I	CH_3	70 (30)	40 (60)	100
$PhCH_2Br$	$PhCH_2$	100	60 (40)	100
CH_2=CHC-H_2Br	CH_2=CH-CH_2	100	90 (10)	100
$HC{\equiv}CCH_2Br$	$HC{\equiv}CCH_2$	100	100	100

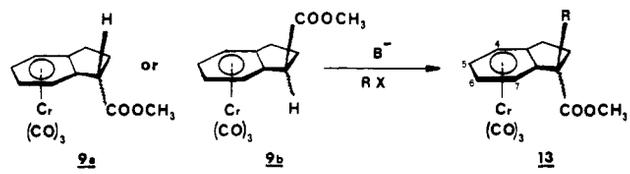
[a] Yields given using stoichiometric quantities of RX. Yields in brackets are for hydrolysis of starting materials.



conducted in a dipolar aprotic solvent; in both instances, few tight ion pairs exist between the carbanion and the counterion. Note that **10**, without the $Cr(CO)_3$ group, does not undergo cyclization with 1,4-dibromopentane by phase-transfer catalysis.

Stereochemical Effects

A. The Carbanionic Carbon Is Part of a Ring. In addition to the electronic effects noted above, the $Cr(CO)_3$ group may act as a stereodirecting unit when complexation of the arene site is diastereogenic. For example, complex **9** exists in two isomeric forms **9a** and **9b**, and alkylation should give two isomers **13**. In fact, the reaction is stereospecifically exo,



whatever the alkylating agent or the process used to effect alkylation.

The configurations of **9a** and **9b** were previously determined by Jackson and co-workers.[14] The spectral properties of **9a**, **9b**, and **13** display some interesting trends. An infrared (IR) study of the ester carbonyl absorption showed the presence of two such bands for **9a** and for **13** in CCl_4, a nonpolar solvent (Table V). Complex **9b**, containing the ester function exo to the $Cr(CO)_3$ group, shows only one absorption band in CCl_4. In the more polar solvent $CHCl_3$, only one broad ester carbonyl absorption was observed for **9a**, **9b**, or **13**.[15] The nuclear magnetic resonance (NMR) spectra of complexes **9a** and **13** gave a doublet signal for H_7 in the region of δ 5.62–6.11, which is deshielded relative to H_4, H_5, and H_6 (see Experimental Section). The relative abundances of the principal peaks in the mass spectra of **9a** and **13** (R = CH_3) are similar (Table VI), but distinct from those of **9b**.

Table IV. Competitive Alkylation of Enolate Anions by CH_3I

Enolate pair	% yield
$Ph_2\bar{C}COOCH_3$	38
Ph, $\bar{C}COOCH_3$, $(CO)_3CrC_6H_5$	2
$Ph_2\bar{C}COOCH_3$	32
$[(CO)_3CrC_6H_5]_2\bar{C}COOCH_3$	0

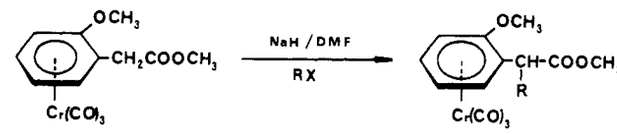
Table V. IR Ester Carbonyl Stretching Bands

Compd	$\nu_{C=O}$, cm^{-1} CCl_4	$CHCl_3$
9a	1755, 1739	1751
9b	1748	1741
13, R = CH_3	1748, 1738	1738
13, R = $PhCH_2$	1752, 1737	1738
13, R = $CH_2CH{=}CH_2$	1751, 1737	1741
13, R = $CH_2C{\equiv}CH$	1751, 1738	1738

Table VI. Mass Spectra Data for 9a, 9b, and 13 (R = CH_3)

	% Rel abundance 9b	9a	13
$M\cdot^+$	22.29	13.25	12.21
$(M - CO)^+\cdot$	0	2.41	3.49
$(M - 2CO)^+\cdot$	1.20	6.02	5.81
$(M - 3CO)^+\cdot$	100	100	100
$(M - COOCH_3)^+\cdot$	1.80	2.41	2.33

B. The Carbanionic Carbon Is Part of a Chain. The readily available complex **14** was chosen for this study. Here,



monoalkylation of **14** by phase-transfer catalysis proved tedious. Efficient methylation of **14** by NaH/DMF and methyl iodide gave two diastereoisomers (**15a**, **15b**, R = CH_3) in a 82:18 ratio. With $PhCH_2Br$, only one of the two diastereoisomers was produced. Only one stereoisomer, **16**, was obtained by treatment of either **15** (**a** or **b**, R = CH_3) with NaH/DMF and $PhCH_2Br$, or **15** (**a** or **b**, R = CH_2Ph) with NaH/DMF and CH_3I. These alkylation reactions are quite stereoselective. The stereochemical assignments were more difficult to establish for **15a,b** than for **9a**, **9b**, or **13**, but NMR provided useful structural information. When deuteriochloroform is used as the solvent for the NMR spectral determinations, the chemical shifts of the two methoxy groups (ester

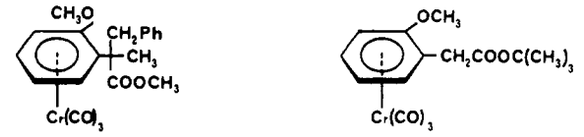


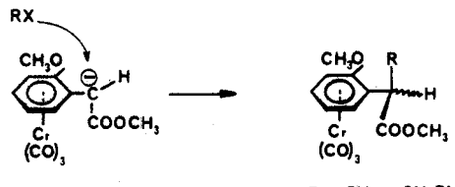
Table VII. Chemical Shifts for Complexes 14–17

Compd	δ Cr(CO)$_3$ArOCH$_3$			δ OCH$_3$ ester		
	$CDCl_3$	C_6D_6	Δ	$CDCl_3$	C_6D_6	Δ
14	3.85	3.03	0.82	3.85	3.45	0.4
17	3.88	3.00	0.88			
15a, R = CH_3	3.95[a]	3.18	0.77	3.96[a]	3.75	0.21
15b, R = CH_3	3.83[a]	3.05	0.78	3.88[a]	3.38	0.50
15a, R = CH_2Ph	3.88	3.01	0.87	3.88	3.66	0.22
15b, R = CH_2Ph	3.88	3.00	0.88	3.88	3.25	0.63
16	3.83	3.05	0.78	3.83	3.63	0.20

[a] Signals too close to be ascertained.

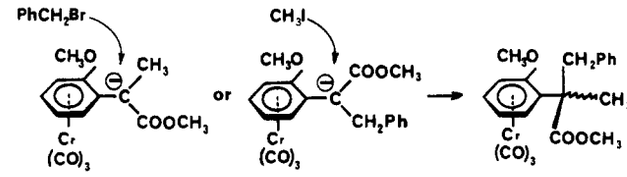
and aromatic) of **14–16** are very similar, if not identical. Differentiation of the two methoxy groups can be made by use of a strong anisotropic solvent such as benzene-d_6. Complex **17**, the *tert*-butyl analogue of **14**, displays only one methoxy signal, but at quite different chemical shifts in C_6D_6 (δ 3.00) and $CDCl_3$ (δ 3.88), i.e., $\Delta(CDCl_3 - C_6D_6) = 0.88$.

Similar pronounced solvent effects were observed for **14–16** (Table VII). The solvent effect is not as great for the ester methoxy group, and in three cases (**15a**, R = CH_3; **15a**, CH_2Ph; **16**) $\Delta(CDCl_3 - C_6D_6)$ was 0.22 or less. For **15b** (R = CH_3, CH_2Ph), $\Delta(CDCl_3 - C_6D_6)$ was considerably larger (0.5–0.63). Therefore, it is proposed that **15a** (R = CH_3, CH_2Ph) and **16** are of one configuration, while **15b** (R = CH_3, CH_2Ph) are of another. This assignment is consistent with exo attack of RX on the enolate (previously demonstrated with **9**), the enolate being in a stable conformation. The most stable conformation of the enolate derived from **14** should be **18**, where the ortho



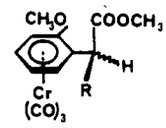
18 **15a** R = CH_3, CH_2Ph

effect is minimized by placing the smallest group attached to the carbanionic carbon near the aromatic methoxy group (H for **18**, CH_3 for **19**, $COOCH_3$ for **20**). The most likely structure



19 **20** **16**

for **15b** has the carbomethoxy group on the "top" of the mol-



15b; R = CH_3, CH_2Ph

ecule, permitting closer contact with the anisotropic solvent than in **15a**, and consequently a larger $\Delta(CDCl_3 - C_6D_6)$.

Experimental Section

General. All melting points were determined on a Kofler bank and are uncorrected. NMR spectra were recorded on a Varian A60A spectrometer. Chemical shifts are given as δ units, Me_4Si being used as internal standard (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet). Precise IR data were determined with a Beckman IR 12 spectrophotometer on diluted solutions. UV analyses were made with a Beckman DK2 apparatus. Mass spectra were recorded on a Varian MAT 311 spectrometer; the energy of the electronic beam was 70 eV.

Starting materials were commercially available or prepared according to literature methods (2-phenylpropanoic acid,[16] 2-phenylbutyrolactone,[17] 1-indancarboxylic acid[18a–c]). Chromium hexacarbonyl was purchased from Strem Inc. and used as received.

Complexes 5–10, 14, and 17. The following procedure for (methyl 1-indancarboxylate) chromium tricarbonyl is typical (previously prepared by a slightly different process).[14] A mixture of methyl 1-indancarboxylate (2 g, 0.011 mol), $Cr(CO)_6$ (3 g, 0.013 mol), heptane (70 mL), hexane (20 mL), and di-*n*-butyl ether (70 mL) was heated under N_2 for 3 days at 127 °C in a Strohmeir[19] type apparatus. After filtration of the solution and evaporation in vacuo, the crude product was chromatographed on silica gel. Elution with ether–petroleum ether (ratio 3:7) first gave **9a** (1.46 g, 42%) followed by **9b** (1.69 g, 49%). The complexes were recrystallized from ether–petroleum ether. Yields and physical and analytical data are in Table VIII.

Phase-Transfer Alkylation of 5–10, 11, 12, and 14. Into a 25-mL Erlenmeyer flask (N_2 atmosphere) was placed 50% aqueous NaOH (5 mL), benzene (5 mL) or CH_2Cl_2 for **8**, complex (0.25 mmol), alkylating agent RX (0.25 mmol), and CTAB (36 mg). The reaction

Table VIII. Complexed Starting Materials, Yields, and Analytical and Physical Data[a]

Registry no.	Compd	% yield	Mp, °C	NMR data, δ ($CDCl_3$)
63703-98-0	**5**	41[b]	80	3.8 (s, 3 H, OCH_3), 4.7 (s, 1 H, CH), 5.1–6 (m, 5 H, $PhCr(CO)_3$), 7.45 (s, 5 H, Ph)
63703-99-1	**6**	17[b]	201	3.85 (s, 3 H, OCH_3), 4.15 (s, 1 H, CH), 5.1–6 (m, 10 H, $PhCr(CO)_3$)
63704-00-7	**7** (R = H)	71	26	1.5 (d, 3 H, CH_3, J = 7 Hz), 3.36, 3.46, 3.6, 3.73 (q, 1 H, CH), 5.6 (s, 5 H, $PhCr(CO)_3$)
63704-01-8	**8** (R = H)	54	121	2.2–3.2 (m, 2 H), 4.3–4.8 (m, 2 H, CH_2CH_2O), 3.5–3.9 (q, 1 H, CH), 5.6 (s, 5 H, $PhCr(CO)_3$)
12215-81-5	**9a**	42[b]	87	2.1–2.75 (m, 4 H, CH_2CH_2), 3.6 (s, 3 H, OCH_3), 3.7 (t, 1 H, CH), 4.75–5.70 (m, 4 H, $C_6H_4Cr(CO)_3$)
12215-80-4	**9b**	49[b]	70	2.15–2.45 and 2.6–2.95 (m, 4 H, CH_2CH_2), 3.5 (s, 3 H, OCH_3), 3.5 (t, 1 H, CH), 4.9–5.45 (m, 4 H, $PhCr(CO)_3$)
63704-02-9	**10**	66	63	1.5 (s, 9 H, $C(CH_3)_3$), 3.38 (s, 2 H, CH_2), 5.52 (s, 5 H, $PhCr(CO)_3$)
63704-03-0	**14**	73	69	2.7, 3.3, 3.62, 3.92 (q, 2 H, CH_2), 3.03 (s, 3 H, $ArOCH_3$), 3.45 (s, 3 H, $COOCH_3$), 4.3 (t), 4.83 (t), 5.18 (d, 4 H, $PhCr(CO)_3$)[c]
63704-04-1	**17**	70	81	

[a] Satisfactory analytical data (±0.3% for C and H) for all compounds (except as noted) were submitted for review. Exception, compound **10**: calcd C, 54.90; H, 4.87; found C, 54.29; H, 4.78. [b] **5** and **6** were obtained from one starting material in the same experiment, and then separated by TLC as described above; the same for **9a** and **9b**. [c] Solvent C_6D_6.

Table IX. Alkylated Products from 7, 8 (R = H), and 9: Analytical and Physical Data[a]

Registry no.	Compd, R =	Mp, °C	NMR data, δ ($CDCl_3$)
58482-52-3	7, CH_3	55	1.6 (s, 3 H, CH_3), 3.8 (s, 3 H, OCH_3), 5.2–6 (m, 5 H, $PhCr(CO)_3$)
63704-05-2	7, CH_2Ph	100	1.45 (s, 3 H, CH_3), 2.95, 3.18, 3.45, 3.68 (q, 2 H, CH_2), 3.9 (s, 3 H, OCH_3), 5.2–6.2 (m, 5 H, $PhCr(CO)_3$), 7–7.6 (m, 5 H, Ph)
63704-06-3	7, $CH_2CH{=}CH_2$	61	1.55 (s, 3 H, CH_3), 2.2–3.2 (m, 2 H, CH_2), 3.9 (s, 3 H, OCH_3), 4.8–6.1 (m, 8 H, $CH{=}CH_2$ and $PhCr(CO)_3$)
63704-07-4	7, $CH_2C{\equiv}CH$	65	1.70 (s, 3 H, CH_3), 2.10 (s, 1 H≡CH), 2.75–3.1 (m, 2 H, CH_2), 3.9 (s, 3 H, OCH_3), 5.2–6 (m, 5 H, $PhCr(CO)_3$)
63704-08-5	7, CH_2COOCH_3	100	1.68 (s, 3 H, CH_3), 2.58, 2.85, 3.13, 3.40 (q, 2 H, CH_2), 3.7 (s, 3 H, OCH_3), 3.8 (s, 3 H, OCH_3), 5–5.9 (m, 5 H, $PhCr(CO)_3$)
63704-09-6	8, CH_3	128	1.7 (s, 3 H, CH_3), 2.2–3.1, 4.3–4.8 (m, 4 H, CH_2CH_2O), 5.2–6.2 (m, 5 H, $PhCr(CO)_3$)
63703-90-2	8, CH_2Ph	206	Insoluble in usual solvents
63703-91-3	8, $CH_2CH{=}CH_2$	106	2.3–2.9 (m, 4 H, $2CH_2$), 4.2–4.8 (m, 2 H, CH_2O), 5.0–6.6 (m, 8 H, $CH{=}CH_2$ and $PhCr(CO)_3$)
63703-92-4	8, $CH_2C{\equiv}CH$	152	2.0–3.0 (m, 5 H, $2CH_2$ and ≡CH), 4.5–4.9 (m, 2 H, CH_2O), 5.3–6.5 (m, 5 H, $PhCr(CO)_3$)
63703-93-5	8, CH_2COOCH_3	142	2.85 (m), 4.7 (m, 4 H, CH_2CH_2O), 3.1 (s, 2 H, CH_2Ph), 3.85 (s, 3 H, OCH_3), 5.3–6.4 (m, 5 H, $PhCr(CO)_3$)
57628-76-9	13, CH_3	86	1.4 (s, 3 H, CH_3), 1.6–2.75 (m, 4 H, CH_2CH_2), 3.6 (s, 3 H, OCH_3), 4.75–5.25 (m, 3 H), 5.65 (d, 1 H, J = 6 Hz, $C_6H_4Cr(CO)_3$))
61168-83-0	13, CH_2Ph	98	2.0–3.4 (m, 6 H, $PhCH_2$ and CH_2CH_2), 3.87 (s, 3 H, OCH_3), 5.1–5.8 (m, 3 H), 6.11 (d, 1 H, J = 6 Hz, $C_6H_4Cr(CO)_3$)), 7.0–7.6 (m, 5 H, C_6H_5)
63730-30-3	13, $CH_2CH{=}CH_2$	65	1.9–3.0 (m, 6 H, CH_2 and CH_2CH_2), 3.8 (s, 3 H, OCH_3), 4.85–5.85 (m, 6 H), 5.95 (d, 1 H, J = 6 Hz, $C_6H_4Cr(CO)_3$ and $CH{=}CH_2$)
63730-31-4	13, $CH_2C{\equiv}CH$	112	1.9–3 (m, 5 H, ≡CH and CH_2CH_2), 3.87 (s, 3 H, OCH_3), 5.00–5.60 (m, 3 H), 5.90 (d, 1 H, J = 6 Hz, $C_6H_4Cr(CO)_3$)
63730-32-5	13, CH_2COOCH_3	80	1.80–3.4 (m, 6 H, CH_2 and CH_2CH_2), 3.8 (s, 3 H, OCH_3), 4.0 (s, 3 H, OCH_3), 5.1–5.85 (m, 3 H), 6.10 (d, 1 H, J = 6 Hz, $C_6H_4Cr(CO)_3$)

[a] Satisfactory analytical data (±0.4% for C and H) for all compounds were submitted for review.

Table X. Physical and Analytical Data for the Alkylated Complexes 11, 12, 15a, 15b (R = CH_3 or CH_2Ph), and 16[d]

Registry no.	Compd	Mp, °C	NMR data, δ ($CDCl_3$ or C_6D_6)
63703-94-6	11	86	0.75 (d, 3 H, CH_3, J = 7 Hz), 1.58 (s, 9 H, $C(CH_3)_3$), 1.6–2.9 (m, 7 H, $(CH_2)_3$ and ≡CH), 5.3–5.95 (m, 5 H, $PhCr(CO)_3$)[a]
63730-33-6	12	133	1.21 (d, 3 H, CH_3, J = 7 Hz), 1.45 (s, 9 H, $C(CH_3)_3$), 1.6–2.9 (m, 7 H, $(CH_2)_3$ and CH), 5.25–5.85 (m, 5 H, $PhCr(CO)_3$)[a]
63703-95-7	**15a** (R = CH_3)	98	1.32 (d, 3 H, CH_3, J = 7 Hz), 3.18 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 3.80, 3.92, 4.05, 4.17 (q, 1 H, CH), 4.2–4.5 (m), 5.08 (t), 5.9 (d, $C_6H_4Cr(CO)_3$)[b]
	15b (R = CH_3)	77	1.4 (d, 3 H, CH_3, J = 8 Hz), 3.05 (s, 3 H, OCH_3), 3.38 (s, 3 H, OCH_3), 3.9–4.45 (m), 4.9 (t) and 5.51 (d, $C_6H_4Cr(CO)_3$ and CH)[b]
63703-96-8	**15a** (R = CH_2Ph)	127	2.7, 2.92, 3.1, 3.32 (q, 2 H, CH_2), 3.01 (s, 3 H, OCH_3), 3.66 (s, 3 H, OCH_3), 4.1–4.65 (m), 4.95 (t), 6.15 (d, $C_6H_4Cr(CO)_3$), 7.25–7.60 (m, 5 H, Ph)[b]
	15b (R = CH_2Ph)	110	3.00 (s, 3 H, OCH_3), 3.25 (s, 3 H, OCH_3, CH_2,[c] 4.1–4.6 (m), 4.9 (t), 5.75, (d, $C_6H_4Cr(CO)_3$ and CH), 7.1–7.75 (m, 5 H, Ph)
63703-97-9	**16**	175	1.42 (s, 3 H, CH_3), 2.68, 3.0, 3.58, 3.8 (q, 2 H, CH_2), 3.05 (s, 3 H, OCH_3), 3.63 (s, 3 H, OCH_3), 4.00–4.30 (m), 4.98 (t), 5.42 (d, $C_6H_4Cr(CO)_3$), 7.48 (s, 5 H, Ph)[b]

[a] Solvent $CDCl_3$. [b] Solvent C_6D_6. [c] Quartet mixed with precedent signals. [d] Satisfactory analytical data (±0.3% for C and H) for all compounds were submitted for review.

mixture was stirred at room temperature and its progress was checked with TLC. After complete disappearance of starting material, a spectrophotometric titration at 407 nm on a diluted aliquot of organic layer was used to determine the yield of alkylated product (the spectrophotometer was previously standardized with a known solution of alkylated product). In those experiments alkylated products are easily isolated after drying and evaporation of the organic layer, and chromatographic purification on silica gel. In experiments given in Tables I and II, crude products were photochemically decomplexed according to ref 7e, and then analyzed by GC with an added internal standard [diphenylacetonitrile; column DEGS (diethylene glycol succinate) 3 m, T = 170 °C].

Alkylation of complex **10** with 1,4-dibromopentane needed 3 days of stirring, then giving **11** and **12**. Separation by TLC (eluent ether–petroleum ether 1:9) yields **11** (higher R_f, 34%) and **12** (lower R_f, 11%). The NMR spectra of the decomplexed ligands (according to ref 7e) were found consistent with those given in the literature for the corresponding acids:[20] ligand desired from **11**, δ_{CH_3} 0.60 (d, J = 7 Hz); from **12**, δ_{CH_3} 1.18 (d, J = 7 Hz).

Alkylation of Complexes 5–10, 11, 12, 14, 16 by NaH/DMF/RX System. The following procedure is typical. A mixture of anhydrous DMF (3 mL), complex **7** (R = H, 0.25 mmol), and an equivalent amount of NaH was stirred under N_2 for 10 min at room temperature. The alkyl halide was then added and the mixture was stirred for 5 min. The mixture was poured on ice, extracted several times with benzene, and worked up as previously described. If desired, the crude product may be purified on thick-layer chromatograph using silica gel, followed by recrystallization from petroleum ether, ether–petroleum ether, or benzene–heptane. Usually, "in situ" yields given by GC after decomplexation are quantitative. Due to the workup, yields of isolated

products are slightly lower. Ratios of stereoisomers 11 and 12, 72:28.

15a and 15b (R = CH_3) were obtained from complex 14, the alkylating agent being CH_3I, and separated on TLC (eluent ether–petroleum ether 1:7). The higher band gave pure 15a (63%). The lower band gave both 15b (14%) and 14 (23%). The best way to get 15b was found to epimerize pure 15a (NaH/DMF and further hydrolysis). Alkylation of 14 with benzyl bromide only gave one isomer 15a (R = CH_2Ph). 15b (R = CH_2Ph) was produced by epimerization of 15a as described above, and then was separated from 15a by TLC (eluent ether–petroleum ether 1:4). Ratio 15a/15b, 72:28.

Complex 16 was prepared starting from 15 (R = CH_3; benzyl bromide) or 15 (R = CH_2Ph; CH_3I) and then purified from ether, yield 70%.

Analytical and physical data are given in Tables IX and X.

Competitive Methylation of Enolates Shown in Table IV. Equivalent amounts of methyl diphenylacetate enolate and mono- (or di-) complexed enolate (from 5 or 6) were prepared in the usual way with equivalent amounts of NaH (completion of the reaction after 10 min can be checked in a side experiment by methylation with excess CH_3I). About 30–40% of the equivalent quantity of CH_3I vs. one enolate is injected with a syringe. After stirring for 10 min and usual workup, the crude mixture was separated on a thick-layer plate of silica gel (eluent: ether–petroleum ether 20:80). Two bands were observed: one contained a mixture of noncomplexed alkylated and nonalkylated products, while the other contained the same for complexed products. The later mixture was decomplexed according to literature methods.[7d] Every fraction was analyzed by GC after adding the same quantity of internal standard (diphenylacetonitrile) as described above.

Acknowledgment. We are indebted to Professor Alper, University of Ottawa, Canada, who kindly reviewed this manuscript.

Registry No.—4, 3469-00-9; NaH, 7646-69-7; $Cr(CO)_6$, 13007-92-6; CH_3I, 74-88-4; $PhCH_2Br$, 100-39-0; $CH_2{=}CHCH_2Br$, 106-95-6; $HC{\equiv}CCH_2Br$, 106-96-7; $BrCH_2COOCH_3$, 96-32-2; $PhMeACCO_2Me$, 31508-44-8; $PhCH_2COOC(Me)_3$, 16537-09-0; $MeOC_6H_4$-o-CH_2COOMe, 27798-60-3; $MeOC_6H_4$-o-$CH_2COOC(Me)_3$, 63730-75-6; methyl 1-indancarboxylate, 26452-96-0; 3-phenyldihydro-3H-furan-2-one, 6836-98-2.

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Stereochemistry and Absolute Configuration in Homoadamantane and Protoadamantane Derivatives[1]

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Received May 16, 1977

Double Favorskii rearrangement of (+)-3,6-dibromohomoadamantane-2,7-dione (6) eventually led to (+)-(1*S*,3*R*,6*R*,8*S*)-twist-brendane (4), assigning the (1*R*,3*S*,6*S*,8*R*) configuration to the (+)-dibromodione 6. (−)-Protoadamantane (tricyclo[4.3.1.$0^{3,8}$]decane) 3 was obtained by the sequence of reactions involving single Favorskii rearrangement of the (−)-dibromodione 6, and this correlation gave the (1*R*,3*S*,6*R*,8*R*) configuration to (−)-protoadamantane. Temperature-dependent circular dichroism spectrum analyses of (+)-homoadamantane-2,7-dione (15) and (+)-homoadamantan-2-one (23) suggested the C_{2v} untwisted conformation to the homoadamantane (tricyclo[4.3.1.$1^{3,8}$]undecane) (1) molecule.

On ring expansion of adamantane by one carbon atom, the high-symmetry T_d inherent to this molecule permits homoadamantane (1)[2] to emerge as a sole product. Although an inspection of the molecular model indicates a flexible structure, for convenience of discussion homoadamantane (1) will be regarded as a rigid molecule with C_{2v} symmetry until we shortly return to discuss this conformational complexity (vide infra) (Chart I).

In the C_{2v} molecular model 1, we can discern two sets of homotopic methylene groups: $C_2{=}C_7$ and $C_{10}{=}C_{11}$. Since the molecule possesses two planes of symmetry which contain the C_2 axis and are mutually perpendicular, these four methylene