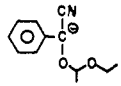
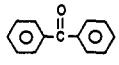
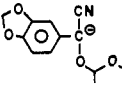
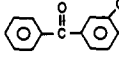


Table I. Reactions of π -(Chlorobenzene)chromium Tricarbonyl with Carbanions

Anion	Product	% yield
$-\text{C}(\text{CH}_3)_2\text{CN}$	$\text{PhC}(\text{CH}_3)_2\text{CN}$	85–90 ^a
$-\text{C}(\text{CH}_3)_2\text{CO}_2\text{Et}$	$\text{PhC}(\text{CH}_3)_2\text{CO}_2\text{Et}$	71
$-\text{C}(\text{CH}_3)_2\text{CO}_2^-$	$\text{PhC}(\text{CH}_3)_2\text{CO}_2\text{H}$	63 ^b
$-\text{CH}(\text{CO}_2\text{Et})_2$	$\text{PhCH}(\text{CO}_2\text{Et})_2$	51 ^c
		88 ^d
		90 ^{d,e}

^a This yield is from quantitative glpc analysis; a representative isolated yield is ca. 70%. ^b The acid was isolated as the methyl ester. ^c The solvent is hexamethylphosphoric triamide instead of tetrahydrofuran. ^d After the usual iodine oxidation, the cyanohydrin-acetal unit was removed by sequential treatment with acid and base: G. Stork and L. Maldonado, *J. Amer. Chem. Soc.*, **93**, 5286 (1971). ^e The product has mp 55–56°, lit. mp 55° (W. Borsche, *Ann.*, **526**, 1 (1936)) and 57° (Ramart-Lucas and J. Hoch, *Bull. Soc. Chim. Fr.*, **5**, 987 (1938)).

lithium salts of 1,3-dithiane, 2-methyl-1,3-dithiane, *tert*-butyl acetate, acetophenone, 5,6-dihydro-2,4,4,6-tetramethyl-4*H*-1,3-oxazine, and acetonitrile. We suspect that primary and secondary carbanions are less efficient because the postulated product chromium complex (parallel with **3**) bears relatively acidic protons (benzylic)¹² and protonates the starting carbanion. With certain of the substrates tested, this process would undoubtedly lead to rapid self-condensation.

The anion of diethyl malonate reacts only slowly with complex **1** in tetrahydrofuran. Raising the temperature to reflux leads to serious side reactions, apparently from decomposition of **1** or an intermediate. However, polar aprotic solvents such as hexamethylphosphoric triamide (HMPA) have an accelerating effect on the reaction and lead to generally simpler product mixtures. With HMPA as solvent, diethyl malonate anion reacts to completion with **1** after 24 hr at 50°, and diethyl phenylmalonate is obtained in 51% yield.

Preliminary results indicate that the dependence of reactivity on leaving group for the series of different π -(halobenzene)chromium tricarbonyl complexes is similar to that observed in classical nucleophilic aromatic substitution.¹³ As displayed in Table II, π -(iodobenzene)chromium tricarbonyl¹⁴ shows no reaction toward malonate anion under conditions where complex **1** reacts to a small extent and π -(fluorobenzene)chromium tricarbonyl¹⁵ is nearly completely converted. The higher reactivity of the fluoro complex (**5**) leads to much higher yields than can be obtained from **1**, with malonate anion, for example (entries 2 and 6, Table II). The anion of *tert*-butyl α -methylthiopropionate reacts only very slowly with **1** at 25° in THF but reacts to completion within 15 hr at 25° with complex **5**. In this case, the reaction mixture (after

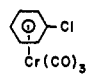
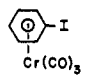
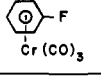
(12) W. S. Trahanovsky and R. J. Card, *J. Amer. Chem. Soc.*, **94**, 2897 (1972).

(13) Cf., J. F. Bunnett, *Quart. Rev., Chem. Soc.*, **12**, 1 (1958).

(14) G. A. Razuvaev, G. G. Petruchoy, A. N. Artemov, and N. I. Sirotkin, *J. Organometal. Chem.*, **37**, 313 (1972).

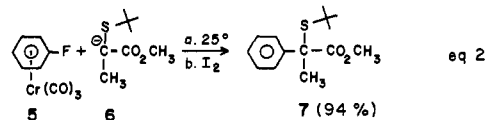
(15) Prepared according to the general method reported in ref 7, but using the recycling technique of Strohmeier (ref 6) and longer reaction times (15–30 hr), the yield of complex **5** raised to 60%.

Table II. Reactions of Diethyl Sodiomalonate with π -(Halobenzene)chromium Tricarbonyl Complexes

Complex	Entry	Conditions ^a	% phenylmalonate yield ^b
 (1)	1	25°, 48 hr	5
	2	50°, 24 hr	51
	3	25°, 48 hr	0 (very low conversion)
 (5)	4	25°, 48 hr	63
	5	50°, 0.5 hr	72
	6	50°, 20 hr	>95

^a All reactions are run in HMPA using 2 molar equiv of diethyl sodiomalonate. ^b All yields are by quantitative glpc.

oxidation with iodine) contains two products in approximately equal amounts, *tert*-butyl 2,2-diphenylpropionate and *tert*-butyl 2,2-bis(methylthio)propionate. With the related anion **6**, reaction with complex **5** proceeds smoothly to give (after oxidation), methyl α -phenyl- α -(*tert*-butyl)propionate (**7**) in 94% yield (eq 2).



Experiments to further define the scope and limitations of the chromium tricarbonyl unit as an activating group in "phenylation" of anions are under study; the mechanism¹⁶ of the reaction appears more complicated than that for classical nucleophilic aromatic substitution and may lead to unique applications.¹⁷

(16) M. F. Semmelhack and H. T. Hall, *J. Amer. Chem. Soc.*, **96**, 7092 (1974).

(17) We wish to thank Professor T. Traylor for making us aware of the results in ref 7 and gratefully acknowledge support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society.

(18) Fellow of the Alfred P. Sloan Foundation (1972–1974) and recipient of the Camille and Henry Dreyfus Teacher-Scholar Grant (1973–1978).

M. F. Semmelhack,*¹⁸ H. T. Hall

Baker and Olin Laboratories of Chemistry, Cornell University
Ithaca, New York 14850

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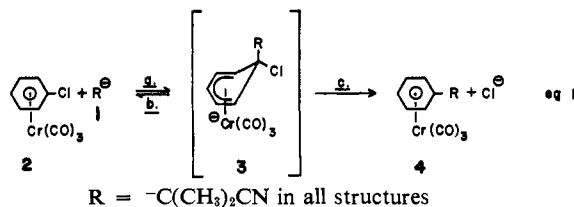
Intermediates in the Reaction of Carbanions with π -(Chlorobenzene)chromium Tricarbonyl

Sir:

In the preceding paper, we reported the phenylation of carbanions *via* π -(halobenzene)chromium tricarbonyl complexes.¹ As illustrated by the specific example of isobutyronitrile anion (**1**) and π -(chlorobenzene)chromium tricarbonyl (**2**), a plausible pathway for the reactions is attack by the carbanion to form a π -(alkylcyclohexadienyl)chromium tricarbonyl anion (*i.e.*, **3**) followed by irreversible loss of halide anion to

(1) M. F. Semmelhack and H. T. Hall, *J. Amer. Chem. Soc.*, **96**, 7091 (1974).

produce a π -(alkylbenzene)chromium tricarbonyl complex (*i.e.*, **4**; eq 1). Analogy for this pathway exists



in the classical mechanism for nucleophilic aromatic substitution² and in the observations of π -cyclohexadienyl metal species from attack of cyanide anion on π -benzenemanganese tricarbonyl cation³ and from *n*-butyllithium with bis- π -benzeneiron dication.⁴ Evidence from monitoring of the reaction by pmr and quenching the reaction at low conversion leads to the conclusion that the actual pathway is somewhat more complicated than is suggested by eq 1 and presents the possibility of unanticipated applications in synthesis. It is now clear that (1) steps a and b in eq 1 are very fast compared to step c, (2) attack can occur at several positions on the chlorobenzene ligand, and (3) addition of a proton to an intermediate can lead to dihydrobenzene derivatives.

The rapidity of step a is best observed by pmr where the characteristic doublet (δ 5.48) of **2** (in THF-*d*₆) disappears within a few minutes when a solution of anion **1** in THF-*d*₆ is added at 25°. New peaks appear as complex multiplets (at δ 4.2–5.2, 2.3–2.9, and 1.0–1.6) and as a strong singlet (δ 0.85). The solution is kinetically active, with rapid appearance of a singlet at δ 5.44 and slower changes to give eventually (25–36 hr, 25°) a spectrum reflecting the presence of π -[(2-cyano-2-propyl)benzene]chromium tricarbonyl (**4**) as the major product. The singlet at δ 5.44 reaches a maximum intensity after 1.5 hr and does not diminish with time. The identity of the compound responsible for the singlet and evidence for intermediates in the reaction were obtained by quenching the reaction mixture at an early stage.

For example, when water was added to the reaction of complex **2** and anion **1** (0.5 mol equiv) after 3.0 hr at 0° in THF, a mixture of π -arene complexes was isolated from the THF solution. At 80° (0.005 Torr), a mixture sublimed which contained unreacted **1** (25%), complex **4** (5%),¹ and π -benzenechromium tricarbonyl (**5**, 10%, singlet at δ 5.44).⁵ Oxidation with iodine gave a mixture of the free ligands: chlorobenzene, benzene, and phenylisobutyronitrile. With equimolar quantities of **1** and **2** (the usual preparative conditions), the yield of **5** is *ca.* 10%.

More revealing is the array of products obtained by addition of an electrophile to the reaction system of **1** and **2**, followed immediately by addition of iodine to separate the organic ligands from the chromium.

(2) (a) J. F. Bunnett, *Quart. Rev., Chem. Soc.*, **12**, 1 (1958); (b) R. Sauer and R. Huisgen, *Angew. Chem.*, **72**, 294 (1960); (c) A. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963).

(3) (a) P. J. C. Walker and R. J. Mawby, *Inorg. Chem.*, **10**, 404 (1971); *J. Chem. Soc., Dalton Trans.*, 632 (1973).

(4) J. F. Helling and D. M. Braitsch, *J. Amer. Chem. Soc.*, **92**, 7207 (1970).

(5) Complex **5** has mp 166–170° dec; B. Nicholls and M. C. Whiting *J. Chem. Soc.*, 551 (1959), report mp 165.5–166.5°.

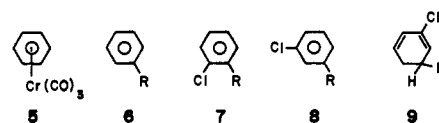
Among the products are chlorobenzene (from unreacted **2**), phenylisobutyronitrile (**6**), *o*- and *m*-chloro-(2-cyano-2-propyl)benzene (**7** and **8**), and a series of dihydro analogs of **7** and **8**, at least five isomers with the major one being tentatively identified as **9** (pmr, mass spectra).⁶ Table I displays the results of a series

Table I. Interruption of the Reaction of Complex **2** with Anion **1**

Entry	Reaction conditions ^c	Quenching sequence ^d	Products (% yield) ^a				
			PhCl	6	7	8	9 ^b
1	20 hr, 25°	a. Water, 25° b. Iodine	0	85	0	0	0
2	3 hr, 0°	a. Water, 25° b. Iodine	18	40	10	2	12
3	3 hr, 0°	a. CH ₃ I, 25°, 3 hr b. Iodine	88	4	0	0	0
4	3 hr, 0°	a. CF ₃ CO ₂ H, –78° b. Iodine	0	39	19	4	22
5	3 hr, 0°	a. Iodine	0	19	56	12	0

^a The yields were determined by quantitative glpc on the organic extract after washing with aqueous sodium thiosulfate and aqueous acid solutions. Each run was repeated at least once; agreement between runs was generally within 10%. ^b This column represents the combined yield of **9**. ^c The reactions were carried out by addition of isobutyronitrile to lithium diisopropylamide in THF followed by a solution of complex **2** in THF. ^d A large excess of the indicated reagents was added.

of quenching experiments using different electrophiles. The isomers **7** and **8** were isolated separately and the spectral data (ir, pmr, mass spectral) were compared with those from samples of **7** and **8** prepared by a conventional route.⁷ The mixture of dihydro isomers (**9**



and about four others) is converted slowly to a mixture of **7** and **8** upon air oxidation, but not by iodine at 25°. An authentic sample of *p*-chloro(2-cyano-2-propyl)benzene was prepared and shown to be absent (<2%) in all reaction mixtures.

When D₂O is used in place of H₂O for a quenching experiment parallel with entry 2 in Table I, no deuterium (<3%) appears in products **7** and **8**, while the dihydro isomers (**9**, *et al.*) are labeled (*ca.* 60% *d*₁) and the phenylisobutyronitrile (**6**) is labeled (*ca.* 30% *d*₁).⁸

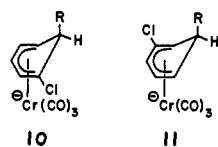
The results of this preliminary study can be accounted for by assuming attack on the π -chlorobenzene ligand in **2** at each of the ring carbons (except para). Attack at the carbon bearing chlorine (eq 1) leads to **6**, reaction at the ortho and meta positions produces intermediates (**10** and **11**, respectively) which can be trapped by proton

(6) The isomers of **9** are incompletely separated by glpc. Rapid scanning GC-MS verified that all of the components in the group accompanying **9** are isomers of molecular weight 181.

(7) Alkylation of the appropriate chlorophenylacetone nitriles using sodium amide and excess methyl iodide provided the ortho (**7**), meta (**8**), and para isomers of chloro(2-cyano-2-propyl)benzene.

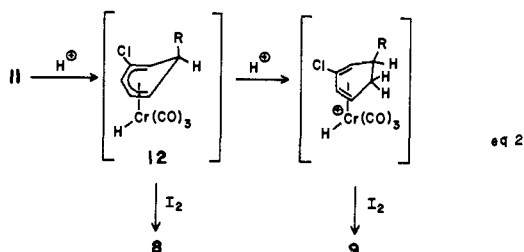
(8) The percentage of deuterium incorporation was obtained by mass spectrometry using the parent ions. Inspection of the abundance of appropriate fragment ions of labeled and unlabeled samples of **6** and **9** indicated that the deuterium was exclusively at ring positions.

donors (water, trifluoroacetic acid) but which are in rapid equilibrium with the starting materials, **1** and **2**. Addition of methyl iodide to the dynamic mixture of **1**, **2**, **3**, **10**, and **11** leads to selective reaction of **1** (to



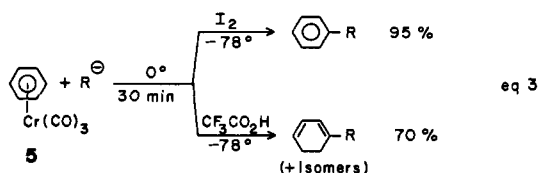
form pivaloylnitrile) and a shift in the equilibrium back to **2**, consistent with efficient recovery of chlorobenzene (entry 3, Table I).

The nature of the intermediates produced by protonation is not completely clear; a possible scheme is suggested in eq 2 using intermediate **11** as an example.



This pathway is consistent with the very low incorporation of deuterium into **8** (and **7**) when D_2O is used as the quenching agent. The dihydro analogs of **7** and **8** then arise by protonation on the carbon ligand in **12** to give intermediates which react with iodine to produce **9**, consistent with high incorporation of deuterium into **9** and with the higher proportion of **9** (and isomers) formed when a strong acid is used as quenching agent (entry 4, Table I).

Direct quenching with iodine (entry 5, Table I) again gives a mixture of **6**, **7**, and **8**, consistent with oxidation of the proposed intermediates **4**, **10**, and **11**, respectively; this reaction may be providing the best measure of the equilibrium mixture of early intermediates. In addition, the quenching with iodine provides a suggestion of a potentially useful synthetic reaction, where an aryl ring hydrogen is replaced by a nucleophile *via* coordination to chromium.⁹ Similarly, the substitution for hydrogen *with* reduction observed as a minor process during quenching with proton sources (entries **4** and **5**, Table I) points to potential applications in synthesis. For example, work in progress has shown that these processes are much more efficient for π -benzenechromium tricarbonyl (eq 3).¹⁰ Further ex-



(9) A related conversion involving *n*-butyl- and *tert*-butyllithium with complex **2** may also involve nucleophilic addition although the mechanism is obscure. Cf. R. J. Card and W. S. Trahanovsky, *Tetrahedron Lett.*, 3823 (1973).

(10) M. F. Semmelhack and H. T. Hall, to be submitted for publication.

amples of these processes and direct observation of the intermediates involved are currently under study.¹¹

(11) Support of this work by the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

(12) Fellow of the Alfred P. Sloan Foundation (1972-1974) and recipient of the Camille and Henry Dreyfus Teacher-Scholar Grant (1973-1978).

M. F. Semmelhack,*¹² H. T. Hall

Baker and Olin Laboratories of Chemistry, Cornell University
Ithaca, New York 14850

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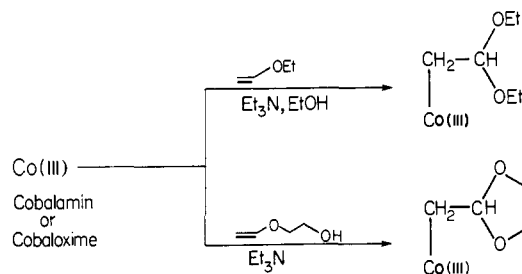
Reactions of Vinyl Ethers with Cobalamins and Cobaloximes

Sir:

We recently reported¹ that cobaloximes and cobalamins reacted with vinyl ethers, in the presence of alcohols, to give acetals containing cobalt-carbon σ -bonds. On the basis of these, and earlier² experiments, we suggested that the reactions proceeded *via* the intermediary of a Co(III)-olefin π -complex. Schrauzer, *et al.*,³ then reported that they were unable to confirm our results and concluded that the reactions we reported did not in fact take place. It was further concluded³ that the biochemical implications our reactions suggested were also invalid.

We wish to report, for a second time, that both cobaloximes and cobalamins react as their Co(III) complexes with vinyl ethers, in the presence of alcohols and bases, to give the corresponding cobalt(III) alkyl complexes (Scheme I). The experimental details,⁴ for

Scheme I



the reactions we reported in our earlier communication,¹ are given below.

Reaction between bromo(pyridine)cobaloxime and ethyl vinyl ether was accomplished as follows. To a deaerated solution of bromo(pyridine)cobaloxime (0.9 g, 2.0 mmol) in dry methylene dichloride (35 ml), over Drierite, was added triethylamine (0.31 g, 3.2 mmol, twice distilled from 1-naphthyl isocyanate), absolute ethanol (4.7 g, 100 mmol), and ethyl vinyl ether (7.53 g,

(1) R. B. Silverman and D. Dolphin, *J. Amer. Chem. Soc.*, **95**, 1686 (1973).

(2) R. B. Silverman, D. Dolphin, and B. M. Babior, *J. Amer. Chem. Soc.*, **94**, 4028 (1972).

(3) W. J. Michaely and G. N. Schrauzer, *J. Amer. Chem. Soc.*, **95**, 5771 (1973).

(4) We wish to thank Professor Alan Davison (MIT) for confirming our experimental procedures. After this confirmation, Professor Schrauzer informed us that he too had repeated the experiments and confirmed our observation we reported¹ for the reactions between cobaloximes and vinyl ethers.