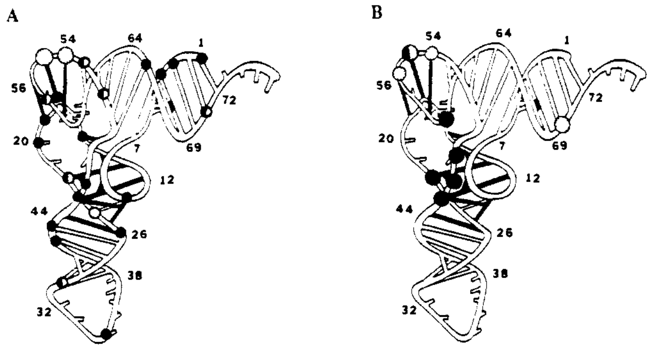

Figure 2. Cleavage data for the metal complexes mapped onto the three-dimensional structure[1] of tRNA^{Phe}. All bases involved in non-Watson–Crick base pairing, indicative of tertiary interactions, are shown by black lines. (A) Cleavage by Ru(phen)$_3^{2+}$ and Ru(TMP)$_3^{2+}$. Guanine residues cut by both Ru(phen)$_3^{2+}$ and Ru(TMP)$_3^{2+}$ are indicated by black circles. Guanine residues cleaved only by Ru(phen)$_3^{2+}$ are indicated by half black/white circles. Stippled circles indicate other (non-guanine) residues cleaved by Ru(phen)$_3^{2+}$. G24, protected from cleavage by both Ru(phen)$_3^{2+}$ and Ru(TMP)$_3^{2+}$, in indicated by the white circle. (B) Specific cleavage by Rh(phen)$_2$phi^{3+} (black circles) and Rh(DIP)$_3^{3+}$ (shaded circles). Note the correspondence between shaded regions where tertiary interactions are found and the Rh(phen)$_2$phi^{3+} cleavage sites.

Under denaturing conditions,[19] no cleavage is observed at these sites, indicating that the native structure is required for interaction. These sites do not correspond to regions that are purely helical or single-stranded. Instead, the major cleavage sites are located in the D and T loops and within the variable loop, a uniquely organized and structured region of the molecule. In particular, cutting is found at G22, G45, and m^{7}G46 (weaker), bases that are involved in triple interactions, in which normal Watson–Crick base pairs interact with a third base in the major groove. Cutting at U47, directly above these sites, and U59 is likely also a function of binding at these same positions. *No other reagents specifically target these regions of tRNA.* The selective targeting of these positions by Rh(phen)$_2$phi^{3+} is in fact consistent with its recognition pattern on DNA, where cleavage is seen at sites that are open in the major groove to permit intercalation by the bulky complex.[12] In double-helical regions of RNA, the A-like conformation limits access to its deep major groove. As is evident from the crystal structure,[1] however, the addition of a third base distorts the groove from the usual A-like helix, now facilitating intercalative stacking with this third base by the rhodium complex.[20] Rh(phen)$_2$phi^{3+} may more generally target such triply bonded positions in folded RNA molecules.[21]

In conclusion, transition-metal complexes developed in our laboratory show a distinctive diversity in site-selective cleavage of tRNA. Photocleavage by the complexes parallels reactions on DNA, both in terms of products formed and patterns of recognition. In particular, Rh(phen)$_2$phi^{3+}, an important shape-selective probe of DNA, appears to target triply bonded sites in tRNA. Given the uniqueness of sites cleaved, these probes should be valuable in assessing the structural integrity of new tRNAs.[22] More generally, these complexes may become extremely useful in deducing the major secondary and even tertiary structural features of other RNA molecules.

Acknowledgment. We are grateful to the NIH for their financial support of this research.

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[19] Conditions for the denaturation experiment were identical with those described in Figure 1 except that irradiations were conducted at 80 °C.

[20] In contrast, MPE–Fe(II), which likely intercalates from the minor groove, shows a high affinity for double-stranded, helical regions of tRNA. See: Kean, J. M.; White, S. A.; Draper, D. E. *Biochemistry* **1985**, *24*, 5062–5070. Intercalation in A-like helices from the minor groove is not sterically hindered.

[21] Of the three triply bonded sites in the tRNA (G45-m^{2}G10-C25, A9-A23-U12, and m^{7}G46-G22-C13, which are adjacent to one another), only the central A9-A23-U12 site shows no cleavage, but here, owing to the folding of the strand, the sugars are not accessible to attack from the major groove.

[22] See, for example: Sampson, J. R.; Uhlenbeck, O. C. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 1033. Sampson, J. R.; DiRenzo, A. B.; Behlen, L. S.; Uhlenbeck, O. C. *Science* **1989**, *243*, 1363. Hou, Y.-M.; Schimmel, P. *Nature* **1988**, *333*, 140. Behlen, L.; Sampson, J. R.; DiRenzo, A. B.; Uhlenbeck, O. C. *Biochemistry*, in press.

[23] England, T. E.; Uhlenbeck, O. C. *Nature* **1978**, *275*, 5680.

[24] Peattie, D. A. *Proc. Natl. Acad. Sci. U.S.A.* **1979**, *76*, 1760–1764.

(1-Oxidoalkylidene)pentacarbonylchromium Anion [R(O$^-$)C=Cr(CO)$_5$] ↔ Acylpentacarbonylchromate [Acyl–Cr$^-$(CO)$_5$] Chemistry: In Situ Preparation and Reactions with Alkynes and Enynes

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Received July 13, 1989

Some of our recent studies have shown that differences in heteroatom "X" donor ability in the neutral chromium carbene complexes (CO)$_5$Cr=C(X)R can significantly alter their reactivity patterns.[2] Addition of carbanions to metal carbonyls produces acyl metallates (e.g., **1′**), which can also be viewed as carbene complexes bearing a particularly electron rich donor atom (e.g., **1**). The robust nature of some of these anions [lithium salts (e.g., **1** ↔ **1′a**) are stable in aqueous solution,[3a] and the tetramethylammonium salt **1** ↔ **1′b** can be purchased[3b]] led us to examine their reactivity with some substrates typically used as reaction partners with carbene complexes.

Whereas simple alkynes react with the neutral carbenes (CO)$_5$Cr=C(X)R to give various annulated products,[4] reaction of the *anion* **1** ↔ **1′a** with hexyne gave butenolide **2a** as the sole isolable product (Table I, entry 1, notes *a* and *b*). Although butenolide formation is unprecedented in group-VI metal carbene chemistry, such a process has been observed for isoelectronic acylpentacarbonyl manganese species.[5]

Possible mechanistic interpretations for this outcome (Scheme I, brackets) include an intramolecular addition of the anionic oxygen in the vinylcarbene intermediate **3** (or vinylogous acylate **3′**) to a CO ligand to generate the anionic bis(carbene) complex[6] **4** (or carbene-"acylate" **4′**) which might collapse[7] to an anionic furan complex like **5** (or the related η^4-species). Alternatively,

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[1] Fellow of the Alfred P. Sloan Foundation, 1985–1989.

[2] (a) Korkowski, P. F.; Hoye, T. R.; Rydberg, D. B. *J. Am. Chem. Soc.* **1988**, *110*, 2676. (b) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1989**, *8*, 2070.

[3] (a) Fischer, E. O.; Maasböl, A. *Chem. Ber.* **1967**, *100*, 2445. (b) Aldrich Chemical Co.

[4] For example, phenols and/or cyclohexadienones [2:1 adducts from (CO)$_5$Cr=C(OMe)R^{4a} and (CO)$_5$Cr=C(NR$_2$)R^{4b}]; naphthols^{4c} and/or indenes^{4d} [from (CO)$_5$Cr=C(OMe)Ar]; indanones^{4e} [from (CO)$_5$Cr=C(NR$_2$)Ar]; cyclopentenones^{4f,g} [from (CO)$_5$Cr=C(OMe)cyclopropyl]; or cyclobutenones^{4a} [from (CO)$_5$Cr=C(OMe)R]. (a) Wulff, W. D.; Kaesler, R. W.; Peterson, G. A.; Tang, P.-C. *J. Am. Chem. Soc.* **1985**, *107*, 1060. (b) (1-Pyrrolidinoethylidene)pentacarbonylchromium reacts with 1-hexyne to give the 2:1 adduct 2,4-dibutyl-6-methylphenol: Rehberg, G. M., unpublished observation. (c) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 644. (d) Wulff, W. D.; Tang, P. C.; Chan, K. S.; McCallum, J. S.; Yang, D. C.; Gilbertson, S. R. *Tetrahedron* **1985**, *41*, 5813. (e) Yamashita, A. *Tetrahedron Lett.* **1986**, *27*, 5915. (f) Herndon, J. W.; Tumer, S. U.; Schattner, W. F. K. *J. Am. Chem. Soc.* **1988**, *110*, 3334. (g) Herndon, J. W.; Tumer, S. U. *Tetrahedron Lett.* **1989**, *30*, 295.

[5] DeShong, P.; Sidler, D. R.; Rybczynski, P. J.; Slough, G. A.; Rheingold, A. L. *J. Am. Chem. Soc.* **1988**, *110*, 2575.

[6] For examples of group VI metal bis(carbene) complexes, see: (a) Fischer, E. O.; Kreissl, F. R.; Winkler, E.; Kreiter, C. G. *Chem. Ber.* **1972**, *105*, 588. (b) Casey, C. P.; Anderson, R. L. *J. Chem. Soc., Chem. Commun.* **1975**, 895. (c) Fischer, E. O.; Röll, W.; Schubert, U.; Ackerman, K. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 611. (d) Fischer, E. O.; Röll, W.; Huy, N. H. T.; Ackerman, K. *Chem. Ber.* **1982**, *115*, 2951. (e) Huy, N. H. T.; Pascard, C.; Dau, E. T. H.; Dötz, K. H. *Organometallics* **1988**, *7*, 590, and ref 7b.

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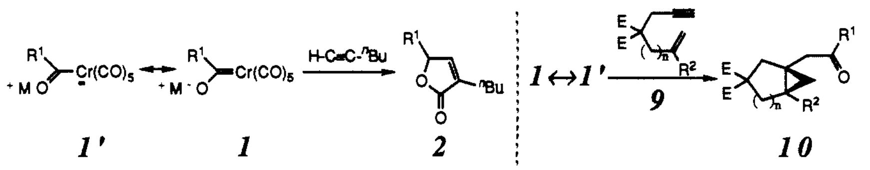
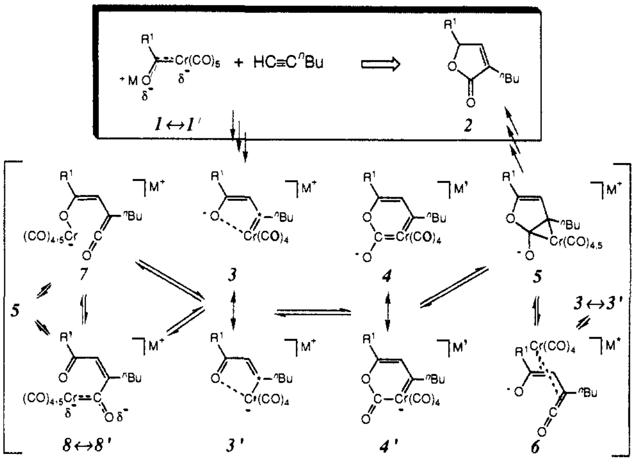
Table I. Reaction[a] of Anions **1** ↔ **1′**[b] with 1-Hexyne (Entries 1–6) or Enynes **9** (Entries 7–12) To Give Butenolides **2**[c] or Bicyclic Cyclopropanes **10**[d]



entry	**1** ↔ **1′**	M⁺	R¹	**2**	yield,[e] %	entry	**1** ↔ **1′**	M⁺	R¹	R²	*n*	**10**	yield,[e] %
1	**a**	Li	Me	**a**	58	7	**b**	Me_4N	Me	H	1	**a**	87
2	**b**	Me_4N	Me	**a**	54	8	**a**	Li	Me	H	1	**a**	79
3	**c**	MgI	Me	**a**	56	9	**c**	MgI	Me	H	1	**a**	68
4	**d**	MgCl	allyl	**b**	46	10	**a**	Li	Me	Me	1	**b**	74
5	**e**	MgCl	benzyl	**c**	54	11	**g**	Li	Ph	H	1	**c**[c]	66
6	**f**	MgBr	Et	**d**	41	12	**a**	Li	Me	H	2	**d**	76

[a] Isolated or in situ generated **1** ↔ **1′** in tetrahydrofuran (~0.7 M) was refluxed under N_2 in the presence of 1-hexyne or **9** (1.3 equiv) for 12 h. [b] Addition of ethereal MeLi, PhLi, or MeMgI or THF solutions of $CH_2{=}CHCH_2MgCl$, $PhCH_2MgCl$, or EtMgBr to $Cr(CO)_6$ (1.0 equiv) suspended in THF (RLi fast at room temperature or RMgX for 1 h at ~40 °C) gave brown to black solutions of **1** ↔ **1′**. [c] See supplementary material. [d] See refs 2a,b. [e] Material after MPLC on SiO_2.

Scheme I



CO insertion into the Cr=C(*) bond in **3** ↔ **3′** could provide either a ketene complex (**6** or **7**) or the new carbene ↔ acylate **8** ↔ **8′**, any of which could then proceed to **5**.[8] We do not know the origin of the proton that ultimately quenches the intermediate butenolide anions.[9]

The lithium salt **1** ↔ **1′a** could be used either after isolation (Et_2O removal) and storage (<0 °C) or, more conveniently, directly upon in situ generation. Grignard reagents are rarely used in the synthesis of group VI Fischer carbenes. However, in situ preparation of the magnesium salts **1** ↔ **1′c–f** followed by reaction with 1-hexyne gave the butenolides **2a–d** in yields similar to those with the lithium or tetramethylammonium anions **1** ↔ **1′a,b**. It is significant that this in situ anionic methodology also allows, for the first time, the use of a β,γ-unsaturated carbene complex (**1d**) which, as its neutral analogue $(CO)_5Cr{=}C(OMe)CH_2CH{=}CH_2$, suffers the expected complications from ready isomerization to the α,β-unsaturated, 2-butenylidene complex because of the high kinetic acidity of its α-protons.[10]

Because of our familiarity with the reactivity of neutral carbene complexes with the 1,6- and 1,7-enynes **9**,[2] the anions **1** ↔ **1′** were also reacted with **9** (Table I, entries 7–12). The previously observed bicyclic cyclopropanes **10a–d** were obtained in superior yields,[2] and these reactions gave none of the ketene-derived byproducts that had before accompanied the use of the neutral methoxy analogues.[2a]

In conclusion, this work demonstrates (i) the synthetic utility and operational benefits of the in situ generated carbene complex procedure; (ii) a protocol for efficient use of infrequently used, yet often advantageous, Grignard reagents in carbene complex generation; and (iii) that new reaction pathways can be discovered when "old" substrates are exposed to *anionic* 1-oxidoalkylidene complexes. Additional new processes[11] as well as attempts to find other anions compatible with this strategy are under study.

Acknowledgment. This investigation was supported by Grant GM-38854 awarded by the DHHS and by an award from the Alfred P. Sloan Foundation.

Supplementary Material Available: Complete spectral and characterization data for compounds **2a–d** and **10c** and a detailed general experimental procedure (3 pages). Ordering information is given on any current masthead page.

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(7) For examples of carbene complex dimerizations to olefins, see: (a) Fischer, E. O.; Heckl, B.; Dötz, K. H.; Müller, J.; Werner, H. *J. Organomet. Chem.* **1969**, *16*, P29. (b) Macomber, D. W.; Hung, M.-H.; Verma, A. G.; Rogers, R. D. *Organometallics* **1988**, *7*, 2072. (c) O'Connor, J. M.; Pu, L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1989**, *111*, 4129.

(8) Other studies that bear on the mechanistic nuances in Scheme I include: (a) Rudler, H.; Parlier, A.; Yefsah, R.; Denise, B.; Daran, J. C.; Vaissermann, J.; Knobler, C. *J. Organomet. Chem.* **1988**, *358*, 245. (b) Hegedus, L. S.; Miller, D. B., Jr. *J. Org. Chem.* **1989**, *54*, 1241. (c) Aumann, R.; Ring, H.; Krüger, C.; Goddard, R. *Chem. Ber.* **1979**, *112*, 3644. (d) Annis, G. D.; Ley, S. V.; Self, C. R.; Sivaramakrishnan, R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 270. (e) Casey, C. P.; Polichnowski, S. W. *J. Am. Chem. Soc.* **1978**, *100*, 7565. (f) Raubenheimer, H. G.; Kruger, G. J.; Lotz, S.; Coetzer, J. *J. Chem. Soc., Chem. Commun.* **1976**, 732. (g) Raubenheimer, H. G.; Kruger, G. J.; Viljoen, H. W.; Lotz, S. *J. Organomet. Chem.* **1986**, *314*, 281. (h) Raubenheimer, H. G.; Kruger, G. J.; Viljoen, H. W. *J. Organomet. Chem.* **1987**, *319*, 361.

(9) When the reaction mixture of **1** ↔ **1a** with 1-hexyne was quenched with DOAc, only protio-**2a** was isolated.

(10) (a) Parlier, A.; Rudler, M.; Rudler, H. *J. Organomet. Chem.* **1987**, *323*, 353. (b) Unpublished observations by P. F. Korkowski in our laboratory.

(11) An initial experiment (**1** ↔ **1′a** + 3-hexyne → 2,3-diethyl-4-methyl-2-butenolide, 64%) suggests that internal alkynes will also generate butenolides.