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Chemistry and Synthetic Utility of Cobalt-Complexed Propargyl Cations

KENNETH M. NICHOLAS

Department of Chemistry, University of Oklahoma, Norman, Oklahoma 73019

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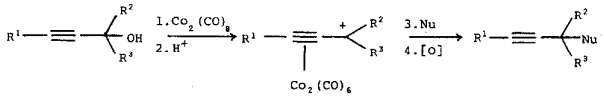
The dramatically enhanced stability of carbocations flanked by π-coordinated organic moieties is a phenomenon that sparked much interest and some controversy in the fledgling field of organotransition-metal chemistry.[1] This effect is manifested in many ways, as illustrated by the following: (1) (benzyl chloride)-$Cr(CO)_3$ undergoes hydrolysis some 10^5 times faster than benzyl chloride itself;[2] (2) the pK_{R^+} values (reflecting thermodynamic stabilities of carbocations) of α-ferrocenyl carbocations rival those of the remarkably stable aromatic cyclopropenium ions;[3] and (3) several of these metal-stabilized carbocations are isolable as crystalline shelf-stable salts suitable for X-ray structure determination.[4,5] Other metal-stabilized carbocations that have been identified include those flanked by α-$(C_4H_3)Fe(CO)_3$,[4] $-(C_5H_4)Cr(CO)_2NO$,[6] $-C[Co_3(CO)_9]$,[7] and $-(RCC)M_2(CO)_4(C_5H_5)_2$ (M = Mo, W)[8] groups.

Much of the interest in these systems centered on the mode of stabilization provided by the metal, with little thought given to the potential for synthetic exploitation of this effect. A spectacular exception to this generalization is provided by Ugi's use of optically active α-ferrocenyl derivatives in the asymmetric synthesis of peptides[9] which takes advantage of both the facility and stereospecificity of substitution at the α-carbon.

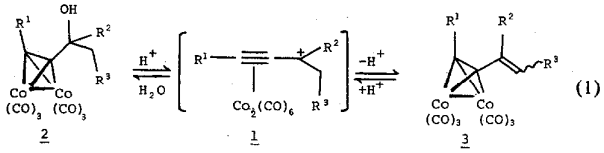
My interest in metal-stabilized carbocations was first aroused while investigating the use of the dicobalt hexacarbonyl ($-Co_2(CO)_6$) unit as a protecting group for the C–C triple bond.[10] During the course of this work

Kenneth M. Nicholas was born in Jamaica, NY, in 1947. He received his B.S. at the State University of New York at Stony Brook and Ph.D at the University of Texas in Austin under the guidance of Rowland Pettit. Following a postdoctoral position with Myron Rosenblum at Brandeis University, he joined the faculty at Boston College in 1973. He relocated to the University of Oklahoma in 1984 as Professor of Chemistry. Professor Nicholas was an Alfred P. Sloan Fellow during 1980–1984. The major theme in his work has centered on the reactivity of species coordinated to transition metals with emphasis on applications in organic synthesis and catalysis.

Scheme I



we discovered the ready acid-promoted hydration/dehydration equilibrium connecting the complexes of propargyl alcohols and 1,3-enynes (eq 1) which sug-



(1)

gested that the likely intermediates, (propargyl)$Co_2(CO)_6^+$ cations (1), possessed considerable stability.[11] Indeed, dissolution of either alcohol **2** ($R^1 = R^3 = H$; $R^2 = Me$) or enyne **3** ($R^1 = H$; $R^2 = R^3 = Me$) in trifluoroacetic-*d* acid produced cation **1** ($R^1 = R^3 = H$; $R^2 = Me$), observable by ^1H NMR. At about the same time Seyferth's group reported the facile, regiospecific

(1) Reviews: Cais, M. *Organomet. Chem. Rev.* **1966**, *1*, 435. Haynes, L.; Pettit, R. In *Carbonium Ions*; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley: New York, 1976; Vol. 5.
(2) Holmes, J. O.; Jones, D. A. K.; Pettit, R. *J. Organomet. Chem.* **1965**, *4*, 324.
(3) Hill, E. A.; Wiesner, R. *J. Am. Chem. Soc.* **1969**, *91*, 510.
(4) Davis, R. E.; Simpson, H. D.; Conte, N.; Pettit, R. *J. Am. Chem. Soc.* **1971**, *93*, 6688.
(5) Lupan, S.; Kapon, N.; Cais, M.; Herbstein, F. H. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 1025.
(6) Rausch, M. D.; Mintz, E. A.; Macomber, D. W. *J. Org. Chem.* **1980**, *45*, 689.
(7) Review: Seyferth, D. *Adv. Organomet. Chem.* **1976**, *14*, 97.
(8) Sokolov, V. I.; Barinov, I. V.; Reutov, O. A. *Izv. Akad. Nauk SSR, Ser. Khim.* **1982**, 1922.
(9) Ugi, I. *Rec. Chem. Prog.* **1969**, *80*, 289.
(10) Nicholas, K. M.; Pettit, R. *Tetrahedron Lett.* **1971**, *37*, 3475.
(11) Nicholas, K. M.; Pettit, R. *J. Organomet. Chem.* **1972**, *44*, C21.

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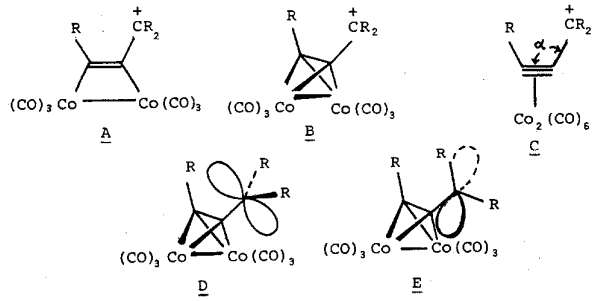
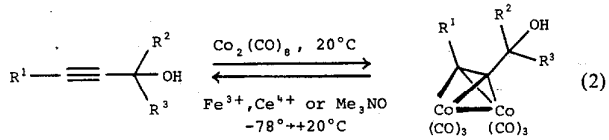


Figure 1.

Friedel–Crafts acylation of (arylacetylene)$Co_2(CO)_6$,[12] again pointing to a special stability for carbocations α to the (alkynyl)cobalt unit.

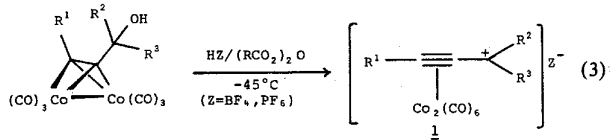
These initial findings stimulated us to ponder more deeply the unique structural aspects and potential reactivities of the complexed carbocations. The bimetallic nature of this system raises a number of interesting structural questions, including (1) what is the orientation of the alkyne axis relative to the metal–metal axis[13] (e.g., A vs. B, Figure 1), (2) what is the deformation angle (α) of the coordinated propargyl unit (C),[15] and (3) what is the orientation of the substituents at the carbenium ion center relative to the Co atoms (e.g., D vs. E)? Answers to these questions would provide crucial insight into the origin of the extraordinary stability of the cobalt-complexed propargyl cations and have important synthetic implications as well (vide infra).

We were even more intrigued by the synthetic prospects for these compounds, especially the possibility that they could be employed as electrophilic propargyl synthons, as in Scheme I. The practical importance of this concept lies, on one hand, in its potential for introducing the synthetically versatile C–C triple bond[7] and, on the other, for improving the poor regioselectivity generally associated with coupling reactions of conventional propargyl synthons, both electrophilic and nucleophilic.[18-21] Could the special affinity of the $-Co_2(CO)_6$ unit for the C–C triple bond deter formation of unwanted allenic isomers? As desired for full synthetic implementation, we (and others) had already demonstrated the ease and efficiency of introduction/removal of the metal moiety under mild conditions[10,12,22] (eq 2). Although other attempts have been made to overcome the propargyl/allenyl problem, e.g., using carbanions derived from 1-trialkylsilylpropyne,[23] until our studies no successful methods of broad generality were available.

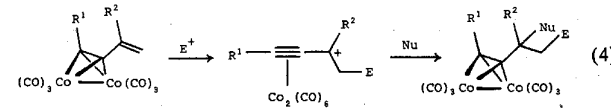


Synthetic Studies

Isolation and Properties of (propargyl)$Co_2(CO)_6^+$ Salts. Motivated by these considerations, we sought to isolate stable salts of cations 1 for structural characterization and reactivity testing. These were soon found to be readily obtained as dark red, thermally stable solids upon protonation of the carbinol complexes with acids of noncoordinating anions (eq 3).[24,25] In the



solid state the salts are stable in dry air for long periods and can be stored indefinitely at 0 °C under N_2; hydrolysis (back to the carbinol complexes) in solution is essentially instantaneous, requiring the use of dry solvents for solution-phase studies. Not surprisingly, IR and ^1H NMR spectral data indicate the positive charge to be highly delocalized in the cations,[26] extending onto the carbonyl ligands. Their thermodynamic stability (established by pK_{R^+} measurements) was found to be comparable to triarylmethyl (Ar_3C^+) carbenium ions![27] Besides protonation of the precursor alcohols, treatment of the corresponding ethers or acetates with Lewis acids (eq 3; X = OR, OAc) has proven useful, especially for use in in situ reactions of the cationic complexes. Alternatively, Smit and Caple have exploited the addition of electrophiles to 1,3-enyne complexes (eq 4)[28] as a means of generating α,β-functionalized cations which can then be employed in further reactions (vide infra).

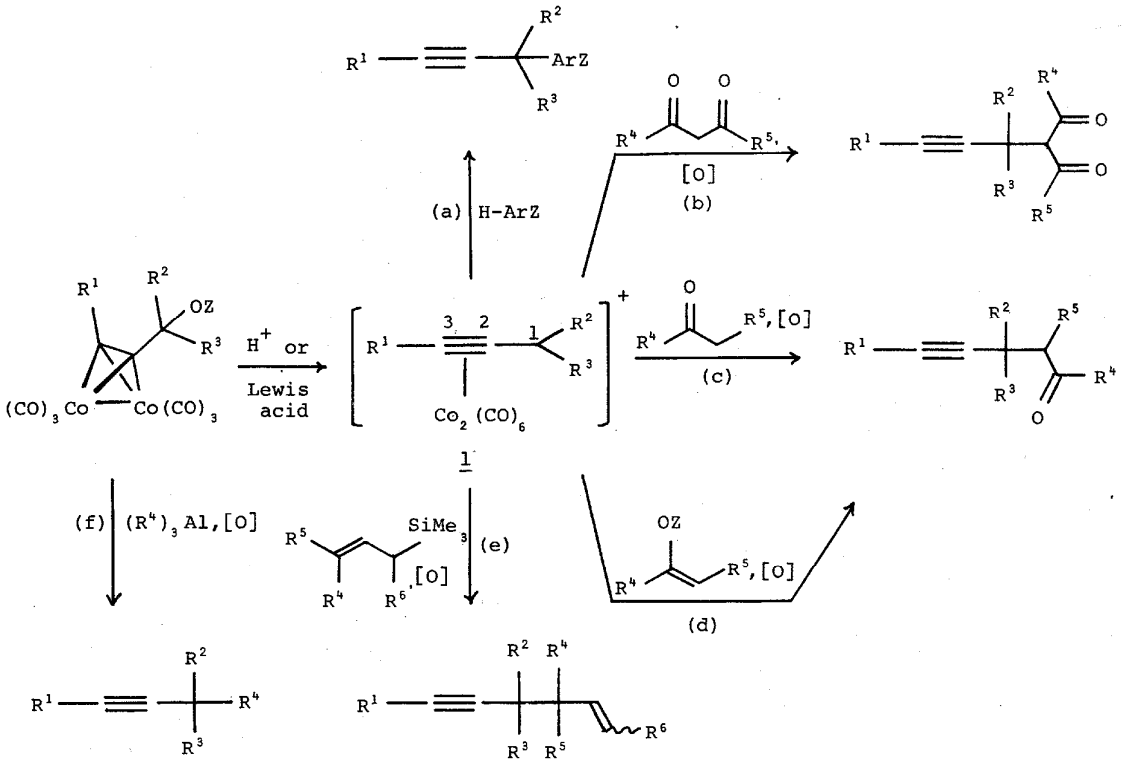


Reactions with Nucleophiles. The reactions of the parent (propargyl)$Co_2(CO)_6^+$ complexes (isolated or generated in situ) have been explored with a wide variety of carbon-centered nucleophiles (Scheme II). In all cases studied to date, attack by nucleophile occurs exclusively at the propargylic carbon (C1), providing a versatile propargylation method when followed by mild oxidative demetalation.

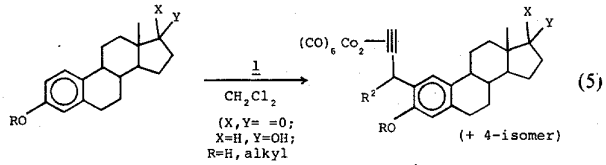
Aromatics. Electron-rich aromatic compounds including anisole (Z = OMe), phenol (Z = OH), *N*,*N*-dimethylaniline (Z = NMe_2), and 1,2,4-trimethoxybenzene[29,30] react at room temperature or below with

(12) Seyferth, D.; Wehman, A. *J. Am. Chem. Soc.* **1970**, *92*, 5520.
(13) In the precursor (alkyne)$Co_2(CO)_6$ complexes the alkyne axis is perpendicular to the Co–Co axis (ref 14).
(14) Sly, W. G. *J. Am. Chem. Soc.* **1959**, *81*, 18. Gregson, D.; Howard, J. A. K. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1983**, *C39*, 1024.
(15) Coordinated alkynes are characteristically bent (ref 13). In the (alkyne)$Co_2(CO)_6$ complexes α is typically ca. 140–150° (ref 16).
(16) Review: Ittel, S. D.; Ibers, J. A. *Adv. Organomet. Chem.* **1976**, *14*, 33.
(17) Review: Fuks, E.; Viehe, M. In *Chemistry of Acetylenes*; Marcel Dekker: New York, 1969; pp 477–508.
(18) Wotiz, J. In *Chemistry of Acetylenes*; Viehe, H. G., Ed.; Marcel Dekker: New York, 1969; pp 365–424.
(19) Shiner, V.; Humphrey, J. S. *J. Am. Chem. Soc.* **1967**, *89*, 622.
(20) Saucy, G.; Marbet, R. *Helv. Chim. Acta* **1967**, *50*, 1158.
(21) Wotiz, J.; Palchack, R. *J. Am. Chem. Soc.* **1951**, *73*, 1971.
(22) Sternberg, H. W.; Greenfield, H.; Friedel, R. H.; Wotiz, J.; Markby, R.; Wender, I. *J. Am. Chem. Soc.* **1965**, *76*, 1457. Dickson, R. S.; Fraser, P. J. *Adv. Organomet. Chem.* **1974**, *12*, 323.
(23) (a) Corey, E. J.; Kirst, H. A. *Tetrahedron Lett.* **1968**, 5041. (b) Corey, E. J.; Rucker, C. *Tetrahedron Lett.* **1982**, *23*, 719.
(24) Connor, R. E.; Nicholas, K. M. *J. Organomet. Chem.* **1977**, *125*, C45.
(25) Saha, M.; Varghese, V.; Nicholas, K. M. *Org. Synth.*, in press.
(26) ROH → R^+, $\Delta\nu$(MC≡O) ca. +40 → +60 cm^{-1}; $\Delta\delta$(CHOH→CH^+) ca. +0.7 (ref 24).
(27) Deno, N. C.; Jarurelski, J. J.; Schriesheim, A. *J. Am. Chem. Soc.* **1955**, *77*, 3044.
(28) Schegolev, A. A.; Smit, W. A.; Kalyan, Y. B.; Krimer, M. Z.; Caple, R. *Tetrahedron Lett.* **1982**, 4419.

Scheme II.
Carbon–Carbon Bond Formation with (propargyl)$Co_2(CO)_6^+$ Complexes



complexes 1 to produce, after demetalation, good to excellent yields of C-propargylated aromatic derivatives (Scheme II, eq a). Recent collaborative efforts with Prof. G. Jaouen and co-workers have focused on "labeling" the A-ring of aromatic steroids with the (propargyl)$Co_2(CO)_6$ unit and then using FT IR as a tool in receptor binding studies (eq 5).[31] The ready attack by cations 1 on most nucleophilic carbon and heteroatomic sites offers exciting prospects for widespread use of the complexes in tagging biomolecules as an alternative to radioactive assays.



(5)

Pauson's group has shown that heteroaromatic substrates, including substituted furans and thiophenes, may also be alkylated efficiently at the 2-position.[32] Such reactions have been used in the synthesis of prostaglandin analogues.

β-Dicarbonyls. Complexes 1, as isolated salts or generated in situ with HBF_4 or $TiCl_4$, react easily (−78 → 0 °C) with β-diketones and β-keto esters, presumably via attack on the electron-rich double bond of the enol tautomer, affording mono-C-propargylated products in good yields[33] (Scheme II, eq b). This selectivity probably reflects the ready reversibility of the coupling reaction (C-alkylation being thermodynamically favored) and the steric bulk of the (propargyl)$Co_2(CO)_6$ group; it is noteworthy because more conventional enolate/propargyl halide reactions suffer from dialkylation, O-alkylation, and allenic by-product formation.[19,34] Although not yet examined thoroughly, the stereoselectivity of these reactions is very interesting. Reactions of chiral complexes with prochiral β-diketones (Scheme II, eq b; $R^2 \neq R^3$, $R^4 \neq R^5$) were found to proceed with diastereoselectivities of 2:1 to 15:1 (the latter at −78 °C, short reaction time).

Ketones and Enol Derivatives. In the course of testing the suitability of acetone as an NMR solvent for the cation salts, we made the surprising and important discovery that acetone and other ketones with α-hydrogens react at <0 °C with the cations to give excellent yields of α-(propargyl)$Co_2(CO)_6$ derivatives (Scheme II, eq c).[35] The regioselectivity of these reactions with unsymmetrical ketones is striking: attack by the cationic complexes occurs exclusively (>95%) at the more substituted α-carbon. This observation, coupled with the ready alkylation of β-dicarbonyls (above), is consistent with a mechanism involving attack by the electrophilic complexes on the more substituted (and more prevalent[36]) enol tautomer. In order to obtain useful rates and high yields without a large excess of ketone, it is advantageous to use stoichiometric quantities of the corresponding enol acetates or trimethylsilyl enol ethers (Scheme II, eq d). In this way it is possible

(29) Lockwood, R. F.; Nicholas, K. M. *Tetrahedron Lett.* **1977**, *18*, 4163.
(30) Hodes, H. D.; Nicholas, K. M., unpublished results, 1982.
(31) Top, S.; Gruselle, M.; Jaouen, G.; Varghese, V.; Nicholas, K. M. *Appl. Organomet. Chem.*, in press.
(32) Jaffer, H. J.; Pauson, P. L. *J. Chem. Res. Synop.* **1983**, 244.
(33) Hodes, H. D.; Nicholas, K. M. *Tetrahedron Lett.* **1978**, *19*, 4349.
(34) Crombie, L.; McKenzie, G. *J. Chem. Soc.* **1958**, 4417.
(35) Nicholas, K. M.; Mulvaney, M.; Bayer, M. *J. Am. Chem. Soc.* **1980**, *102*, 2508.
(36) House, H. O. In *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: New York, 1972; Chapters 8–10.

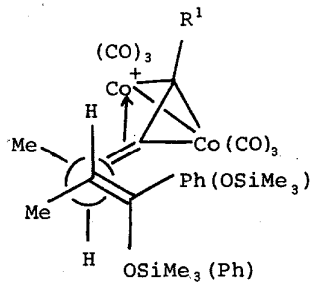
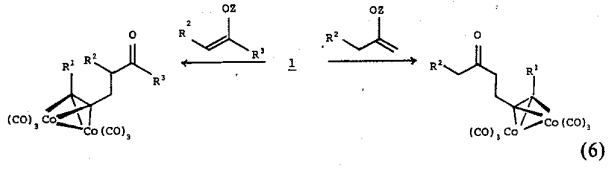


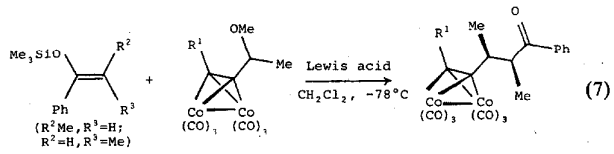
Figure 2.

to control the regioselectivity via the kinetic or thermodynamic enol derivatives (eq 6).



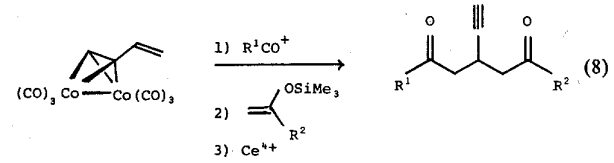
(6)

Furthermore, a recent report by Schreiber and coworkers has demonstrated that excellent syn diastereoselectivities accompany the Lewis-acid-promoted reactions of chiral propargyl ether complexes with enol silyl ethers (and allylsilanes) (eq 7).[7,37] Interestingly, the highest stereoselectivities were obtained with bulky substituents R at the acetylenic carbon, an effect which was accounted for in a proposed transition state shown in Figure 2.



(7)

In a further adaptation of the trimethylsilyl enol ether coupling reaction Caple and Smit[38] have reported trapping the cations formed by electrophilic addition to 1,3-enyne complexes with trimethylsilyl enol ethers (and allylsilanes) according to eq 8. Such metal-directed Ad_E reactions afford a promising method for the construction of highly functionalized acetylenes, especially where both the electrophilic and nucleophilic components are carbon-centered.

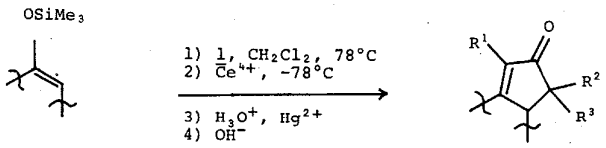


(8)

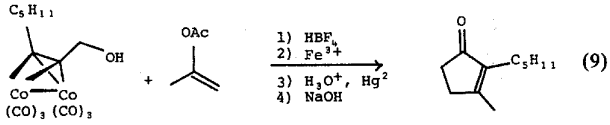
The γ-keto acetylenes which are obtained (after demetalation) from reactions of cations 1 with enol derivatives are very useful synthetic intermediates in part because of their regioselective convertibility to 1,4-diketones[39] and, subsequently, to cyclopentenones. In order to provide a broader perspective on the potential synthetic utility of the cobalt-complexed propargyl cations, we have coupled enol alkylations by 1 with the sequence demetalation, hydration, and base-catalyzed

(37) Schreiber, S. L.; Sammakia, T.; Crowe, W. E. *J. Am. Chem. Soc.* **1986**, *108*, 3128.
(38) Mikaelian, G. S.; Gybin, A. S.; Smit, W. A.; Caple, R. *Tetrahedron Lett.* **1985**, *26*, 1269.
(39) Borch, R.; Stork, G. *J. Am. Chem. Soc.* **1964**, *84* 935.

Scheme III



cyclization to provide a new and efficient process (Scheme III) for cyclopentenone annulation.[40] This methodology was first applied to the synthesis of dihydrojasmone[41] and, more recently, the guaiane sesquiterpene cyclocolorenone[42] and its relative isocyclocolorenone[43] (eq 9 and 10). The high stereoselectivities observed for the key alkylation step by 1 (R^1 = Me, R_2 = R_3–H) in the latter two syntheses (6:1, >20:1) are particularly noteworthy.



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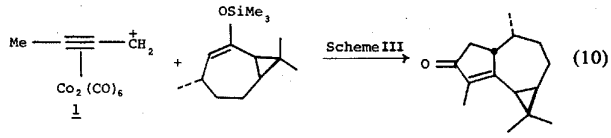
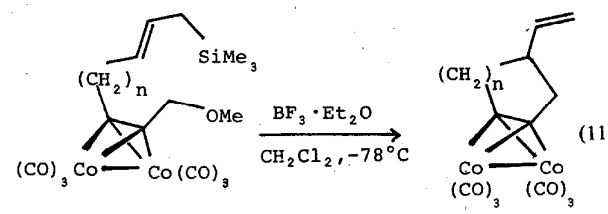


(10)

Allylsilanes. A final class of π-nucleophiles found to enter into efficient coupling with the propargyl complexes 1 are allylsilanes.[44] This reaction provides a novel and regiocontrolled route to 1,5-enynes, useful intermediates in terpenoid synthesis[45] (Scheme II, eq e). As is characteristic of allylsilane/electrophile reactions, the new C–C bond is formed specifically γ to the silicon;[46] even quaternary centers can be generated in this way with little or no competing elimination.

Schreiber's group has successfully developed an intramolecular variant of this reaction.[37] The endocyclic version produces the novel cycloalkyne complexes (eq 11, n = 2–4). The existence of such strained cycloalkyne derivatives is made possible by the severely bent geometry of coordinated alkynes,[14,16] which suggests a similar bending in the intermediate cationic complexes (op cit. question 2). An example of the exocyclic version (eq 12) proceeds with complete stereocontrol (trans), attesting once again to the powerful stereodirecting effect of the (alkyne)$Co_2(CO)_6$ group.



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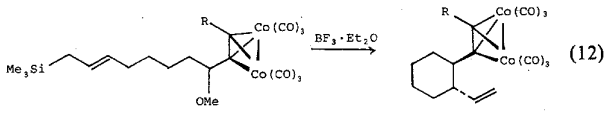
(40) Saha, M.; Nicholas, K. M. *Isr. J. Chem.* **1984**, *24*, 105.
(41) Padmanabhan, S.; Nicholas, K. M. *Synth. Commun.* **1980**, *10*, 503.
(42) Saha, M.; Bagby, B.; Nicholas, K. M. *Tetrahedron Lett.* **1986**, *27*, 915.
(43) Saha, M.; Muchmore, S.; van der Helm, D.; Nicholas, K. M. *J. Org. Chem.* **1986**, *51*, 1960.
(44) O'Boyle, J. E.; Nicholas, K. M. *Tetrahedron Lett.* **1980**, *21*, 1595.
(45) Corey, E. J.; Kirst, H. A. *Tetrahedron Lett.* **1968**, 5041. Corey, E. J.; Katzenellenbogen, J. A.; Gilman, N. W.; Roman, S.; Erickson, B. *J. Am. Chem. Soc.* **1968**, *90*, 5618. Corey, E. J.; Achiwa, K. *Tetrahedron Lett.* **1970**, 2245.
(46) Review: Colvin, E. In *Silicon in Organic Synthesis*; Butterworths: London, 1981; pp 104–117.

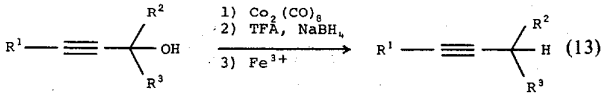


(12)

Other Organometallic Nucleophiles. We have sought to develop general methods for propargyl/hydrocarbyl coupling by examining reactions of **1** and appropriate precursors with nucleophilic σ-bonded organometallics. To date, we have found the combination of organoaluminum reagents, R_3Al, with the complexes of propargyl acetates to be most effective. The reactions with trialkylaluminums proceed rapidly even at −78 °C, giving moderate to excellent yields of coupled products depending on the nature of R = Me > Et > Pr ≫ *i*-Bu[47,48] (Scheme II, eq f). This methodology permits reasonably efficient generation of 3° and 4° centers and hence is superior to classical acetylide/alkyl halide routes in such cases. The facility of these reactions is ascribable to the special ability of the aluminum reagents to function as Lewis acids[49] coupled with the ability of the organocobalt unit to release electron density to the developing carbocationic center.

A particularly useful variation on this theme is the reaction of $(RC{\equiv}C)_3Al$ with the propargyl acetate complexes.[50] This alkynyl/propargyl coupling method provides a general route to 1,3-"skipped"-diynes, previously rather inaccessible, yet interesting compounds. Extension of this mixed-metal-mediated coupling methodology to effect propargyl/aryl, /vinyl, /propargyl, and /allenyl coupling is planned.

Miscellaneous Nucleophiles. Although not yet studied in a systematic fashion, several non-carbon-centered nucleophiles have also been combined with cations **1**. Perhaps most important among these is hydride. In collaboration with J. Siegel (Princeton University), we found that tertiary propargyl alcohols could be converted to the corresponding *sec*-alkylacetylenes via treatment of their $-Co_2(CO)_6$ complexes with $NaBH_4/CF_3CO_2H$ followed by demetalation in a one-pot sequence in good overall yields[51] (eq 13). This



(13)

process offers an attractive alternative to the direct acetylide/*sec*-alkyl halide coupling which is particularly inefficient.[52] Deuterium-labeled diisopropylacetylene prepared by this cobalt-mediated route has been used in the synthesis of (hexaisopropyl-d_6)benzene, a molecule which exhibits interesting correlated, hindered rotation of the six isopropyl groups.[53]

An interesting, albeit isolated and unoptimized, example of N-propargylation by cations **1** comes from

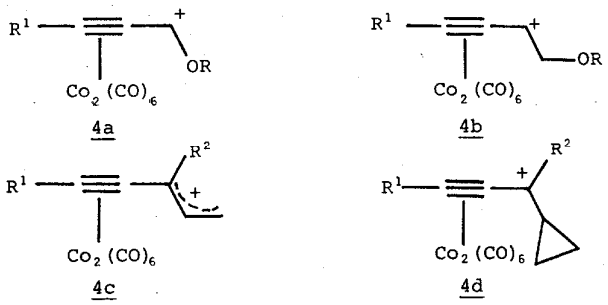
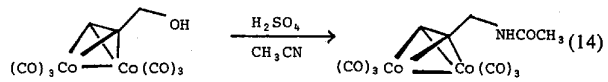


Figure 3. Second generation cations.

their inclusion in the Ritter reaction with acetonitrile (eq 14).[54] This reaction, in general, could afford a



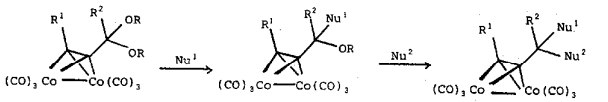
(14)

practical route to propargyl amines and amides which have important use as monoamine oxidase inhibitors and sedatives.[53]

Oxygen-centered nucleophiles (OH^-, MeO^- from H_2O, MeOH) have been utilized extensively by Smit and Caple[28,56] to intercept the cations generated by addition of electrophiles to 1,3-enyne cobalt derivatives (eq 4; Nu = OH^-, OR^-).

Second Generation Complexes. In addition to exploring a wide range of nucleophilic coupling partners for cations **1**, we have been interested in studying the chemistry of new classes of cations **4** possessing α- and β-conjugating substituents at the propargyl carbon (Figure 3) in order to probe further the stereoelectronic properties of the (alkynyl)$Co_2(CO)_6$ unit and to expand as well the synthetic utility made possible by its presence.

α-Alkoxy Cations (4a). We were first attracted to the complexes of acetylenic acetals because of their potential as propargyl dication synthons (eq 15). In-



(15)

deed, the α-alkoxy cations **4a** derived from these acetals are easily generated (and isolated if desired) and have been found to combine efficiently with *one* equivalent of most of the nucleophiles discussed in the previous section (e.g., enol derivatives, allylsilanes).[57] The π-donating ability of the attached oxygen atom appears to attenuate the reactivity of cations **4a** as indicated by their unreactivity toward anisole and 2,4-pentanedione. Recent preliminary experiments containing **5a** with trimethylsilyl enol ethers[58] have produced β-alkoxy ketone complexes with high (>10:1) diasteroselectivities. Our efforts to effect reaction with a second nucleophile largely have been thwarted by the facile acid-promoted loss of alcohol (producing substituted enyne complex) from most of the systems examined.

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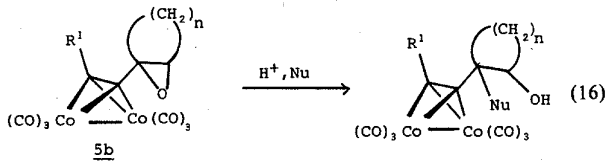
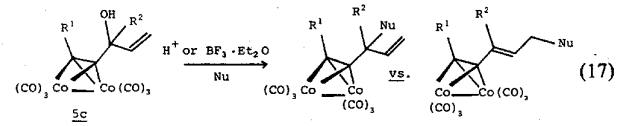
β-Alkoxy Cations (4b). Acid-promoted reactions of α,β-epoxyacetylene complexes **5b** with several nucleophiles have been investigated in order to assess the ability of the $-Co_2(CO)_6$ group to control the regio- and stereochemistry of ring opening (eq 16). This new class



(16)

of cobalt derivatives was found to be rather unstable, but if prepared at 5 °C and used in situ, they react with our full slate of nucleophiles, affording exclusively the products derived from cleavage of the C–O bond which places the developing positive charge on the carbon bearing the stabilizing (alkynyl)$Co_2(CO)_6$ unit[59] (i.e., via cations **4b**). The cyclohexene oxide complex **5b** (R = H, n = 4) offered an opportunity to compare directly the chemistry of the coordinated acetylene to that of the parent acetylene since previous studies of 1-substituted cyclohexene oxides have revealed an apparent correlation between product stereochemistry and the carbonium ion stabilizing ability of R with the cis/trans ratio increasing with increasing electron-releasing ability of R[59] (eq 16). As anticipated, the reactions of the complexed ethynylcyclohexene oxide (Nu = H_2O, MeOH, CCl_3CO_2H) led to greatly enhanced selectivity for the cis product (Nu relative to OH) compared to the free acetylene: for R = C≡CH, % cis = 1 (Nu = MeOH), 2 (Nu = H_2O), 42 (Nu = CCl_3CO_2H) vs. for R = (C≡CH)$Co_2(CO)_6$, % cis = 50, 59, >95.

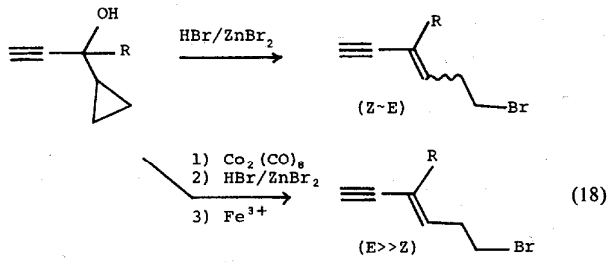
α-Vinyl Cations (4c). We have also generated the substituted allyl cations **4c** from complexes of vinyl ethynyl carbinols (**5c**) and have explored their reaction chemistry (eq 17). We were pleased to find that carbon



(17)

nucleophiles (anisole, allyl silanes, isopropenyl acetate) react (essentially irreversibly) specifically at the terminus remote from the organometallic substituent (B ≫ A) and with complete (E) stereoselectivity.[61] Interestingly, with EtOH as nucleophile the opposite regioisomer predominates, shown to be the result of thermodynamic control. The stereoselectivity of these reactions is also noteworthy since various acid-catalyzed and Claisen-type rearrangements of free en-yn-ols give (E), (Z) mixtures with only modest selectivity, consistent with a steric demand for the ethynyl group between that of Me and H.[62] Attachment of the $-Co_2(CO)_6$ group, therefore, exerts a dramatic steric effect in addition to the amply demonstrated electronic one. This cobalt-mediated route to (E)-1,3-enynes, intermediates of considerable importance in the preparation of insect phenomones,[63] vitamin A derivatives,[64] and carotenes[64] appears to hold much promise for the synthesis of complex natural products.

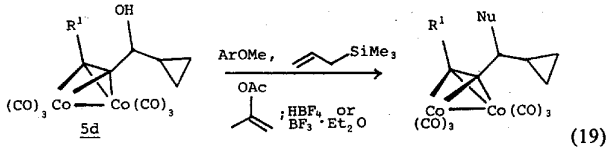
α-Cyclopropyl Cations (4d). The potential for homologous chemistry with cations **4d** derived from α-cyclopropyl carbinol complexes was first realized in an early report by Descoins and Samain (eq 18).[65] Here



(18)

again the contrast between the stereoselectivities of the free and complexed carbinols is striking—for R = H: % E(parent) = 48, 33; % E(complex) = 91, 98. Attachment of the bulky $-Co_2(CO)_6$ group not only greatly facilitates the reaction but also completely reverses the stereochemistry, providing a highly stereoselective route to functionalized (E)-1,3-enynes.

Our efforts to extend this reaction to carbon nucleophiles met with surprising results. Treatment of the carbinol complex with the usual nucleophiles in the presence of HBF_4·Me_2O or BF_3·Et_2O did give coupled products in good yields but without ring opening (eq 19).[66] Although we do not yet understand completely



(19)

this remarkable nucleophile effect, we have evidence (from control experiments) that it reflects, in part, the fact that the reactions with carbon nucleophiles are kinetically controlled (i.e., attack at C4 is faster and essentially irreversible), whereas the $HBr/ZnBr_2$ reactions operate under thermodynamic control.

Tandem Cobalt-Promoted Alkylation/Cyclization. In two recent reports the special abilities of the (alkynyl)$Co_2(CO)_6$ group to stabilize adjacent carbonium ion centers and to promote (2 + 2 + 2) cyclizations with olefins (Pauson–Khand reaction)[67] have been cleverly combined to provide a powerful methodology for constructing complex cyclopentanoid derivatives (eq 20). The Caple/Smit groups have utilized the stepwise

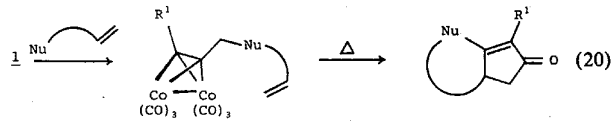


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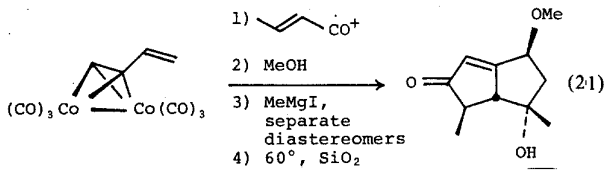
Table I.[65]
Carbon-13 NMR Parameters of (propargyl)$Co_2(CO)_6^+$ Cations in Sulfur Dioxide Solution[a]

cation	R^2	R^3	R^1	C(1)	C(2)	C(3)	CO	other
1a	H	H	H	79.5 (+14.5)[b]	122 (+23)	80 (+9)	192 (-7)	
1b	H	H	Me	79.5 (+17.5)	123 (+27)	109 (+17)	191 (-1)	Me(C(3)): 19.5 (0)
1c	Me	H	H	107 (+39.5)	117 (+17)	79.5 (+3.5)	193 (-2)	Me: 21 (-4.5)
1d	Ph	H	H	112.5 (+42.5)	107 (+7)	82 (+9)	192 (-6)	Ph: 112.5, 130.5,[c] 133,[c] 136.5[c] (-12)
1e	Me	Me	H	146 (+77)	110 (+4)	79.5 (+7.5)	192 (-9)	Me: 31;[d] 28, 34[e] (-2)
MeC≡CC$^+$Me$_2$ (**2**)				269 (+204)	111 (+26)	218 (+140)		Me(C(1)): 44 (+13); Me(C(3)): 14 (+11)

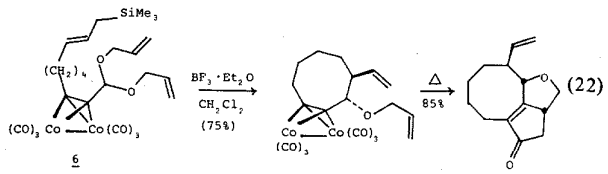
[a] Obtained at 20.0 MHz; chemical shifts are referenced to Me_4Si at 0 ppm; T = -30 °C except where noted otherwise. [b] $\Delta\delta$ value for alcohol → cation conversion; + indicates a downfield shift; - indicates an upfield shift. [c] Assignments of ortho, meta, para carbons uncertain. [d] T - 14 °C. [e] T - 40 °C.

Ad_E reactions of conjugated enyne complexes with either unsaturated nucleophiles or electrophiles to afford the enyne precursors for cyclization,[68,69] as in eq 21.



(21)

Schreiber and co-workers utilized the diallyl acetal **6** in an intramolecular alkylation leaving the pendant allyloxy group ready for subsequent Pauson–Khand cyclization (eq 22).[37] Variations of this reaction may



(22)

prove valuable in the synthesis of fusicoccin-type diterpenes which possess the same distinctive oxatricyclic core.

Structural Studies

Although the structure/bonding questions posed earlier led us into our investigations of the cobalt-complexed propargyl cations, the gratifying success of the initial and continuing synthetic studies diverted somewhat our attentions away from these issues. Obviously, the single most valuable probe of these questions would be X-ray crystallography. Unfortunately, our modest efforts to obtain diffraction quality crystals have been unsuccessful thus far. However, solution NMR studies and various features of their reaction chemistry do provide some insight into the structures of these interesting species.

The questions of the orientation of the C1 p orbital relative to the cluster core and the rotational barrier about the C1–C2 bond have been addressed by ^1H and ^{13}C NMR.[24,70] The most important observations/conclusions derived from these studies are (1) there is a rather small change in chemical shifts in passing from the complexed alcohols to the corresponding cations ($\Delta\delta(^1H)$ at C1 ca. +0.5–1.5 and $\Delta\delta(^{13}C)$ at C1 ca. +14–40), indicating tremendous charge dispersal in the cations, and (2) the C1–C2 rotaional barrier is markedly dependent on the nature of the C1 substituents—the parent complex **1a** ($R^1 = R^2 = R^3 = H$) exhibits a static structure (T = +25 → 70 °C) with nonequivalent propargylic hydrogens (from the ^1H NMR spectrum) whereas the dimethyl derivative **1e** ($R^1 = H$, $R^2 = R^3 = Me$) undergoes relatively facile C1–C2 rotation ($\Delta G^\ddagger$ = +12 kcal/mol), exhibiting nonequivalent methyl groups at low temperature (by ^{13}C NMR). The ^{13}C chemical shifts (Table I), which often qualitatively reflect charge distribution,[71] and the tool of increasing electron demand[72] offer a possible explanation for this interesting dependency of the rotational barrier on the substituents R_1 and R_2. In moving from complexes **1a** to **1b** to **1e** there is a substantial increase (30–40) in δ(C1), pointing to increasing positive charge at this carbon. This suggests that in the series there is increasing participation of the C1 substituents in charge dispersal and a corresponding decreasing involvement of the (alkynyl)$Co_2(CO)_6$ unit. Accordingly, rotation about the C1–C2 bond becomes more facile.

Questions 2 and 3 posed earlier also have been addressed theoretically by Hoffmann and Schilling[73] using extended HMO calculations. They found a deep energy minimum for the bent geometry of the complexed propargyl ligand with $\alpha \sim 150°$, quite similar to established structures of the neutral (alkyne)$Co_2(CO)_6$ complexes.[14] This conclusion is consistent with the aforementioned ease of forming small-ringed cycloalkyne complexes (n = 6–8) via intramolecular nuleophilic trapping of the cobalt-stabilized carbocations.[37] Regarding the preferred conformation about C1–C2 in the parent complex **1a**, little difference in energy (ca. 2–4 kcal/mol) was found between the "horizontal" and "vertical" structures D and E (Figure 2), indicating virtually unrestricted rotation about the C1–C2 bond. This result is clearly at odds with the available ^1H and ^{13}C NMR data (vide supra).

Concluding Remarks

The extraordinary stabilization of carbocations provided by adjacent organotransition-metal groups has provided in the α-(alkynyl)$Co_2(CO)_6$ system the basis for a highly versatile method of carbon–carbon bond formation. The facile introduction and removal of the cobalt carbonyl moiety, the variety of suitable nucleophiles which couple with these complexes giving pro-

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pargylic products exclusively, together with the synthetic mutability of the triple bond combine to make this the method of choice for propargylation.

Many important aspects of this chemistry require additional attention. Perhaps most obviously, complete elucidation of the solution and solid-state structures of the cations 1 (questions 1–3) will give deeper insight into the mode of stabilization provided by the organocobalt group. On the synthetic front we forsee great opportunities for stereochemical control based on the special stereoelectronic properties of the –(alkynyl)-$Co_2(CO)_6$ unit. Additional tailoring of the characteristics, both steric and electronic, of the cluster core should be possible with various CO-substituted derivatives, e.g., (propargyl)$Co_2(CO)_5(PR_3)^+$. New coupling partners for the cations, "third generation" cation complexes, and developments along the lines envisioned above should result in significant new applications in the synthesis of natural and unnatural products. Another newly developing, exciting area of application for the (propargyl)$Co_2(CO)_6^+$ cations, and possibly other electrophilic metal π-complexes, is their use to "tag" biomolecules in receptor binding studies and immunology.[74]

One may wonder whether the stabilization of propargylium ions is the exclusive province of cobalt. Indeed, the answer is no! Reutov and co-workers have reported the isolation of propargylium derivatives of the $(C_5H_5)_2M_2(CO)_6$ (M = Mo, W) unit[8] which is isolobal[75] with the $-Co_2(CO)_6$ group. While these group VI (6)[76] complexes are inferior to their cobalt relatives in terms of preparative convenience, their reactions have not been examined and may provide new options for selectivity and synthetic utilization. Ultimately, systems for catalytic propargylation eventually may be developed through careful selection of reaction conditions, metal, and auxiliary ligand.

I am indebted to the enthusiastic efforts of the students, postdocs, and collaborators cited throughout the text. Financial support provided by the National Institutes of Health and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is greatly appreciated. Finally, special gratitude is due to the late Professor Rowland Pettit whose inspirational creativity planted the seed for this chemistry and whose benevolent latitude allowed me to pursue a tangent which ultimately led to the body of work described herein.

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Electron-Transfer-Induced Chain Reactions and Catalysis. Building Bridges† between Inorganic, Organic, and Organometallic Substrates

MICHEL CHANON

U.A. CNRS 126, Faculté des Sciences de Saint-Jérôme, 13397 Marseille Cedex 13, France

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The starting point of this presentation is the reaction

$$ArCH_2Cl + C(CH_3)_2NO_2^- \xrightarrow{} \begin{cases} ArCHO \\ ArCH_2C(CH_3)_2NO_2 \end{cases} \quad (1)$$

for which, in 1964, Kornblum[1] proposed that two concurrent pathways explained the formation of the observed products. The pathway leading to ArCHO is a classical S_N2 mechanism where the oxygen of the ambident[2] nitronate anion is the nucleophilic center. The second pathway involves an electron transfer from the nucleophile to $ArCH_2Cl$.[1] Kornblum's[3] and Russell's[4] groups defined this second pathway in 1966 by describing a chain mechanism initiated by an electron transfer. A good introduction to the purpose of this presentation may be found in a quotation taken from Kornblum's recent review:[5] "This novel type of substitution at a saturated carbon would constitute an interesting, but somewhat parochial phenomenon, if it were restricted to the alkylation of nitroparaffin salts. But in actuality, electron transfer chain substitutions turn out to be much more general than originally envisaged; new examples constantly are being discovered

Michel Chanon was born in Roannes, France, in 1940. He obtained a State Thesis from the University of Marseille (1967), entered CNRS, and did postdoctoral research on the gear effect in Lund (Sweden) with Professor J. Sandstrom. He was hired as Professor of Chemistry in the Ecole Normale Superieure de Tunis from 1973 to 1977. Since 1977, he has been Professor of Chemistry at the University of Aix Marseille III. His research topics are electron-transfer-induced reactions, comparison of mechanistic approaches in organic, organometallic, and inorganic reactivities, and computer aids to synthesis.

† We thank Professor R. Hoffmann for allowing us to borrow part of the title of one of his publications (ref 111a).

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