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A CONVENIENT ENTRY INTO MULTIFUNCTIONAL SYSTEMS UTILIZING THE STEPWISE ADDITIONS OF A CARBON ELECTROPHILE AND A CARBON NUCLEOPHILE TO THE DOUBLE BOND OF VINYLACETYLENE

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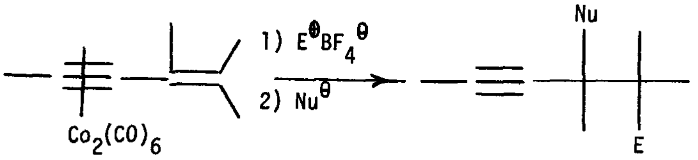
Abstract. The stepwise addition of carbon electrophiles and carbon nucleophiles to the double bond of vinylacetylene has been developed as an efficient method to assemble multifunctional molecules.

The synthetic potential of the Ad_E- process can be greatly enhanced if the reaction is performed as a stepwise and independent addition of a carbon electrophile and a carbon nucleophile to double or triple bonds.[1] Here we present what we believe to be the first example showing the viability of this concept for the addition to the double bond of vinyl acetylene.

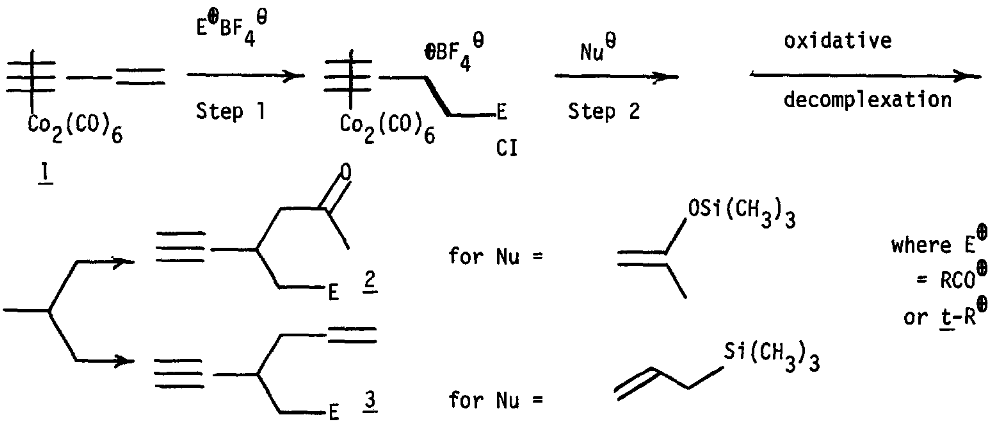
The methodology of the approach is based on the previously observed two step Ad_E-reaction of various cationoid electrophiles and some O-centered nucleophiles to the double bond of dicobalt hexacarbonyl complexes (DCHC) of conjugated enynes as outlined below.[2,3]

This concept has now been successfully extended to the addition of carbon electrophiles and carbon nucleophiles to the ene unit of the DCHC complexes of vinyl acetylene (1) to produce, in a single stage (via the formation of cationoid intermediate CI) structures of type 2 and 3.[4] These results are summarized in Table 1.



$E^{\oplus} = R^{\oplus}, RCO^{\oplus}, ArS^{\oplus}, NO_2^{\oplus}$

$Nu^{\ominus} = OH^{\ominus}, OCH_3^{\ominus}$



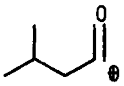
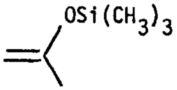
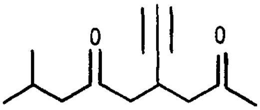
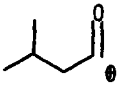
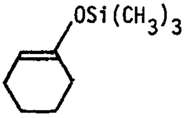
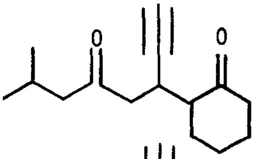
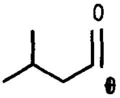
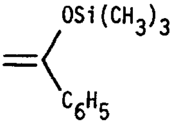
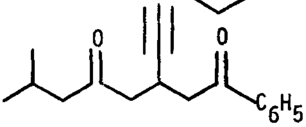
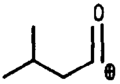
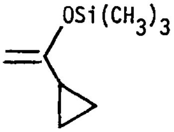
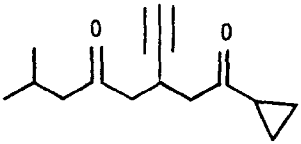
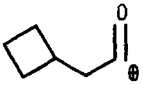
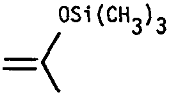
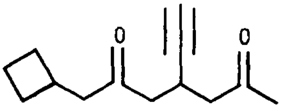
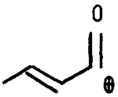
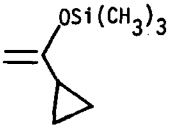
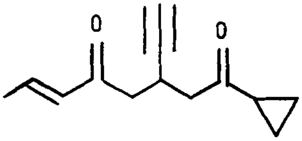
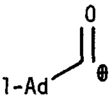
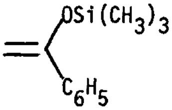
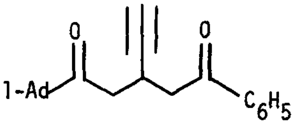
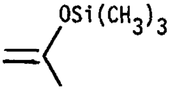
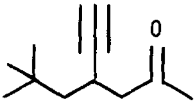
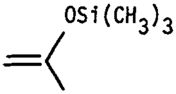
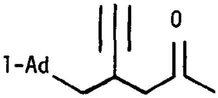
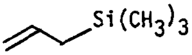
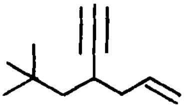
A typical experimental procedure runs as follows: To a well-stirred solution of isovaleryl tetrafluoroborate (3.6 mmol, prepared in situ by the interaction of isovaleryl fluoride with boron trifluoride) in CH_2Cl_2 (20 ml) at -78°C was added the solution of 1 (0.4 g, 1.18 mmol) in CH_2Cl_2-CH_3NO_2 (10 ml, 1:1). After 5-10 minutes a solution of cyclohexene (0.2 g, 2.42 mmol)[6] in CH_2Cl_2 (2 ml) was added and after an additional 10 minutes a solution of the trimethylsilyl enol ether of methylcyclopropyl ketone (0.94 g, 6 mmol) in CH_2Cl_2 (5 ml) was added. The reaction mixture was kept at -78°C for 20 minutes, then neutralized by aqueous $NaHCO_3$, and extracted with ether. After ether removal the residue was purified by TLC on SiO_2. The DCHC complex of 1-cyclopropyl-3-ethynyl-7-methylocta-1,5-dione was isolated as a dark red oil (0.52 g, yield 87% R_f = 0.32, C_6H_6); PMR (60MHz, CCl_4 δ, TMS): 0.98 m, 11 H; 1.93m, 1H CH-CO; 2.25 d, 2H at C_6; 2.6 and 2.78, 2 H doublets at C_2 and C_4; 3.85 pentet, 1H at C_3; 5.98 s, 1H C≡CH. Decomplexation of this product, with ceric ammonium nitrate according to a reported procedure,[5] produces the corresponding dione (yield 85%) as a colorless liquid PMR (60 MHz, CCl_4, δ, TMS): 0.93 m, 12H; 1.94 d, 1H C≡CH; 2.23 d, 2H at C_6; 2.5 and 2.73, 2H m at C_2 and C_4; 3.22 m, 1H at C_3, $C_{14}H_{20}O_2$; Calc, % C, 76.33: H 9.15: Found, % C 76.20; H 9.42. $M^{\oplus}$ 220.

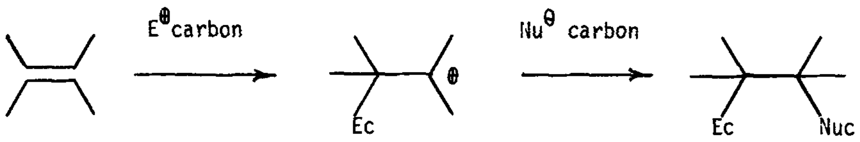
As can be seen from the Table, the nature of the acylating agent as the electrophile and trimethylsilyl enol ether as the nucleophile could be varied over rather broad limits. Thus the reaction shown appears to be a fairly general synthetic method for the preparation of an entire series of 3-ethynyl-1,5-dicarbonyl derivatives.[7] It is also to be noted that the carbonium ion intermediate (CI) produced by the addition of tert-alkyl cations could be successfully trapped by both enolsilyl ethers and allylsilane.[8]

At present a two-step Ad_N- reaction to double bonds in α,β-unsaturated systems is extensively used as a method for assembling multifunctional molecules from simpler precursors.[9] We believe that the results presented in this paper can serve as a good illustration showing the promise of the complementary approach to this problem via the use of the Ad_E-process to form two novel C-C bonds according to the following general scheme:

TABLE I

Products of Type 2 and 3 obtained in the Addition to 1

$E^{\oplus}$	$Nu^{\ominus}$	Product	Yield^5
			68
			44
			62
			74
			50
			69
			91
			92
1-Ad$^{\oplus}$			78
			76



ACKNOWLEDGMENT: We are indebted to the Research Corporation for financial assistance.

REFERENCES AND NOTES

1. To the best of our knowledge, no examples of such a reaction have been described. For earlier references to a step-wise Ad_E-process with the use of heteroatomic electrophiles (ArS^+ or $FeCp(CO)_2^+$) and various (heteroatomic and carbon) nucleophiles, see: a) ArS^+, M.A. Ibragimov, W.A. Smit, Tetrahedron Letters, 24, 961 (1983). b) $FeCp(Co)_2^+$, P. Lennon, A.M. Rosan, M. Rosenblum, J. Amer. Chem. Soc., 99, 8426 (1977).

2. K.M. Nicholas, M.O. Nestle, D. Seyferth, in "Transition Metal Organometallics in Organic Synthesis," ed. H. Alper, Vol. II, Ch.1, Academic Press, N.Y., 1978.

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4. The ability of DCHC complexes of propargyl cations to react with a number of C-nucleophiles described earlier (see ref. 2) did not necessarily imply that DCHC complexes of carbonium ions containing a β-carbonyl group (e.g., CI) would behave in a similar way (vide infra).

5. The yields (not optimized) are given for the purified products; the oxidative decomplexation was carried out with ceric ammonium nitrate[2] (yields 85%-98%). Correct elemental analysis and the expected patterns for the NMR spectra were obtained for all the compounds.

6. Cyclohexene was used as a quencher to remove excess acylium salt.

7. It is noteworthy that the incorporation of ethynyl groups into the β-position of carbonyl compounds is difficult to achieve by conventional methods; for example, 1,4-addition of ethynylmagnesium cuprate usually fails; c.f., P.F. Hudrlik, A.M. Hudrlik, in "The Chemistry of the Carbon-Carbon Triple Bond," Part 1, Ch. 7, S. Patai, ed., J. Wiley, N.Y., 1978.

8. Thus far we were unable to perform similar transformations with other enynes, such as isopropenyl acetylene. In the latter case the cationoid intermediates formed upon acylation (or alkylation step) failed to react with enolsilyl ethers or allylsilanes in the temperature range -78°C - 0°C.

9. J.C. Stowell "Carbanions in Organic Synthesis," Wiley-Interscience publication, N.Y., 1979.

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