

TRANSFORMATION OF ORGANOIRON COMPLEXES OF SYNTHETIC AND CHEMICAL INTEREST

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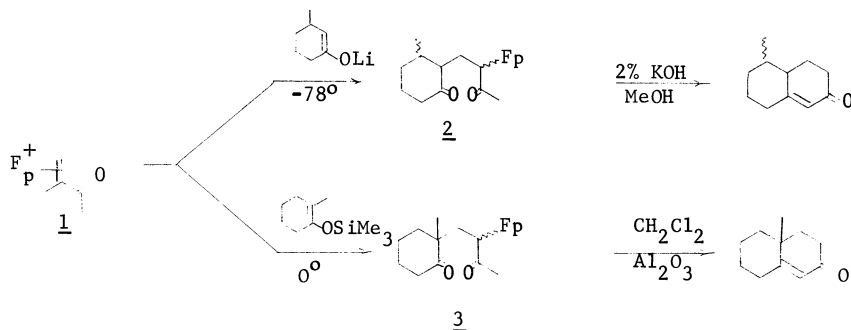
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Abstract - Cationic organometallic complexes derived by complexation of vinyl ethers with the dicarbonyl cyclopentadienyliron cation (F_p^+) are readily prepared, highly reactive reagents. These substances have been shown to function as vinyl cation equivalents for the vinylation of ketones, and for the synthesis of α -methylene- γ -lactones and dihydrofurans. Similar complexation of propiolic esters gives a reactive species, which functions as a β -acrylic ester cation equivalent and yields cyclobutenes, 1,3-dienes and dihydro- α -pyrones with olefins and cinnamic esters with aromatic systems.

Although carbonium ions constitute important reaction intermediates, few are sufficiently stable to be isolated. By contrast, isolable cationic organo-transition metal complexes with significant charge localization on the ligands are relatively commonplace species.¹ Their use as reagents in organic synthesis has become a focus of increasing interest, and it is my purpose to review here some of the synthetic options provided by the $C_5H_5Fe(CO)_2$ cation (F_p^+) and its olefin and acetylene complexes.

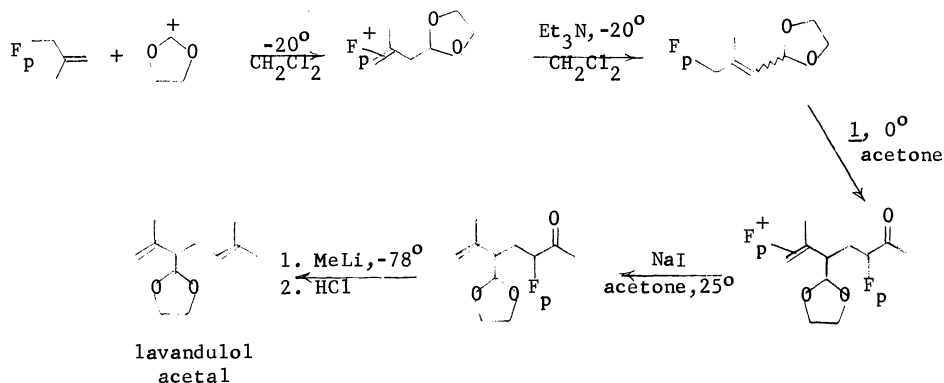
It is well recognized that olefin complexation by F_p^+ labilizes the ligand toward nucleophilic attack.² But such activation, especially for carbon nucleophiles, may be complicated by poor regioselectivity.

The use of complexes derived from α,β -unsaturated carbonyl compounds provides a class of electrophile which is both more reactive and highly regioselective in its reactions with a wide range of nucleophiles. The methyl vinyl ether complex 1 reacts readily with both cyclohexanone lithium enolate or the related silyl ether to give only the Michael adducts 2 and 3, and these may in turn be converted to the octalones, with concurrent loss of the F_p group, by the action of base.³

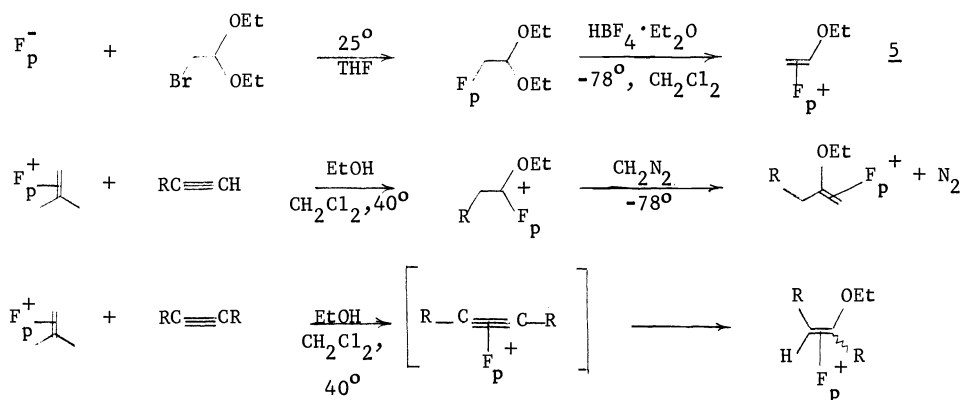


Even comparatively mild carbon nucleophiles such as (η^1 -allyl) F_p 4 condense with 1, and since simple (allyl) F_p complexes may be functionalized by successive electrophile addition and deprotonation, more complex, polyfunctional systems may be elaborated.

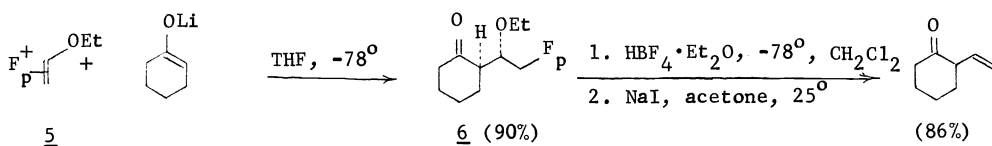




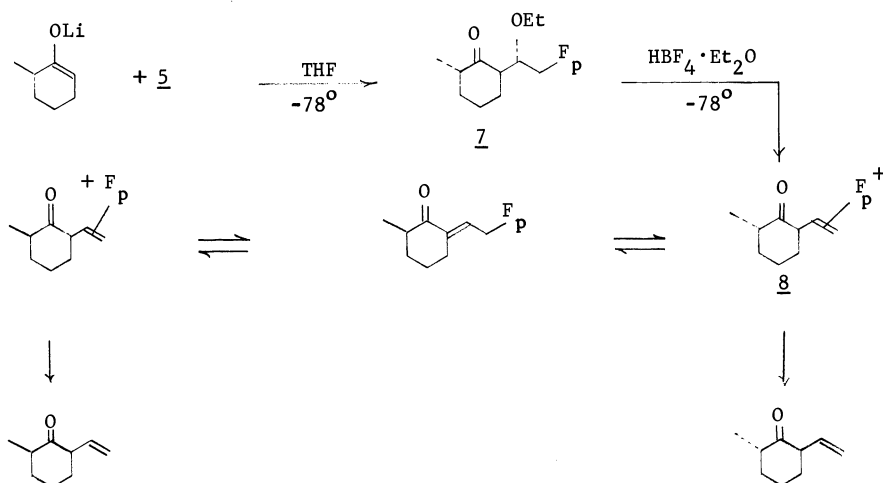
A second general solution to the problem of regioselectivity is provided by the use of vinyl ether complexes. These substances, readily available from simple starting materials, by a number of routes, have been shown to be useful vinyl cation equivalents⁴ for the vinylation of cyclohexanone enolates.⁵



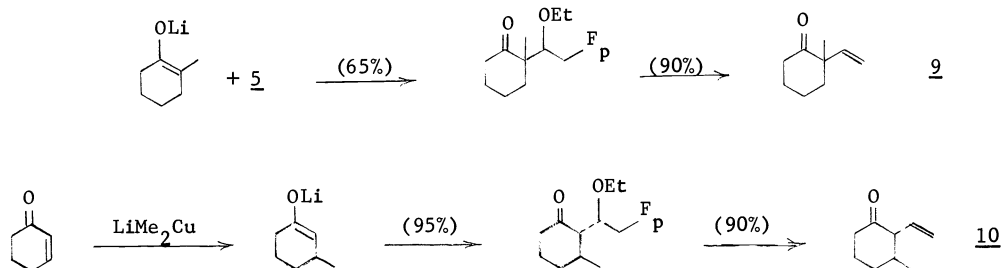
Addition of $F_p(\eta^2\text{-ethyl vinyl ether})BF_4$ 5 to cyclohexanone lithium enolates takes place rapidly at -78° , and the adduct 6 is readily transformed, under mild conditions, in high yield to 2-vinylcyclohexanone



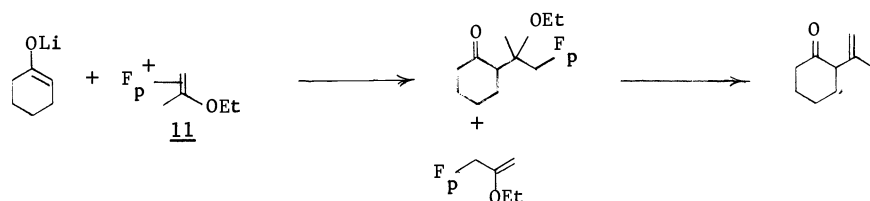
With 6-methylcyclohexanone lithium enolate, the adduct formed by reaction with 5 is shown to be only the trans 2,6-substituted cyclohexane 7, consistent with an axial approach of the complex cation to the enolate. However, low temperature conversion of this adduct to the olefin complex 8 and decomplexation with sodium iodide in acetone was found to give a 1:1 mixture of stereoisomeric 2-methyl-6-vinylcyclohexanones. This is apparently due to equilibration, through proton transfer from 8 to the solvent. However, decomplexation of 8 by simply warming in acetonitrile solution avoids this problem and gives the thermodynamically unstable trans-2-methyl-6-vinylcyclohexanone as the sole product.



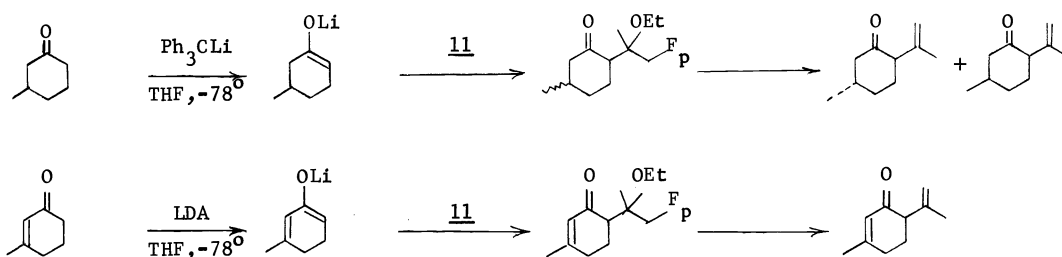
Analogous vinylation of 2- and 3-methylcyclohexanone enolates gives the cyclohexane derivatives 9 and 10 in high yield.



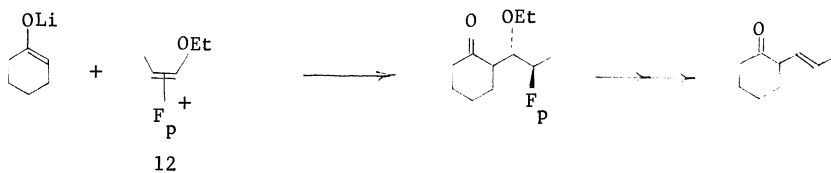
The isopropenyl group, a common structural element in many terpenes, may also be introduced in cyclohexanones through use of complex 11 as a vinyl cation equivalent.⁶ However, with this synthon, a competing side reaction involving proton transfer, especially with more hindered enolates, may intervene.



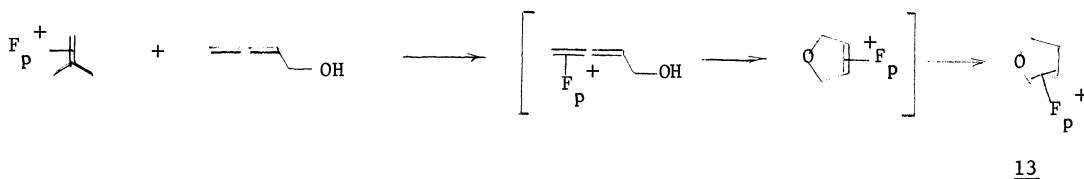
This reaction, which is a minor side reaction with cyclohexanone enolate, becomes the major mode of reaction with 2- and 3-methylcyclohexanone enolates. However, the kinetic enolates derived from 3-methylcyclohexanone and 3-methylcyclohexenone may be converted to their isopropenylated derivatives, isopulegone, isoisopulegone and isopiperitenone in good yield.



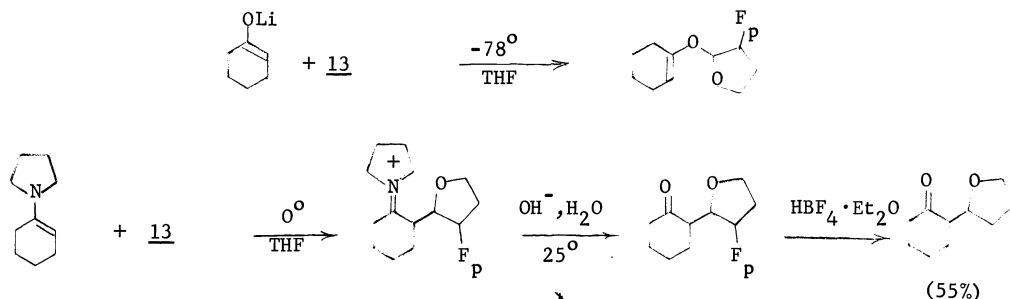
A final variant of this class of vinyl cation equivalent is provided by $F_p(\eta^2\text{-cis-propenyl ethyl ether})BF_4$ 12, which allows the trans-propenylation of enolates. The stereochemistry of the reaction follows from successive trans addition of enolate to 12 and trans F_p assisted elimination of ethanol.



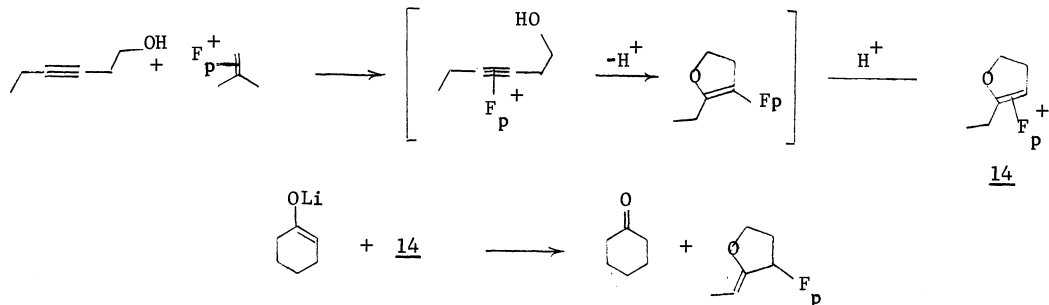
$F_p(\eta^2\text{-vinyl ether})BF_4$ salts incorporating additional functionality provide a further, synthetically valuable elaboration of this chemistry. The simplest members of this class are complexes of cyclic ethers, such as 13, in which the ether function also serves to mask an hydroxyl group in the vinyl cation. Complex 13, a nicely stable yellow solid, is readily obtained by exchange complexation of the allenyl alcohol.



The reaction of 13 with cyclohexanone lithium enolate gives only the O-alkylation product, but the less reactive enamine affords the C-alkylated product, which undergoes demetallation on treatment with acid.

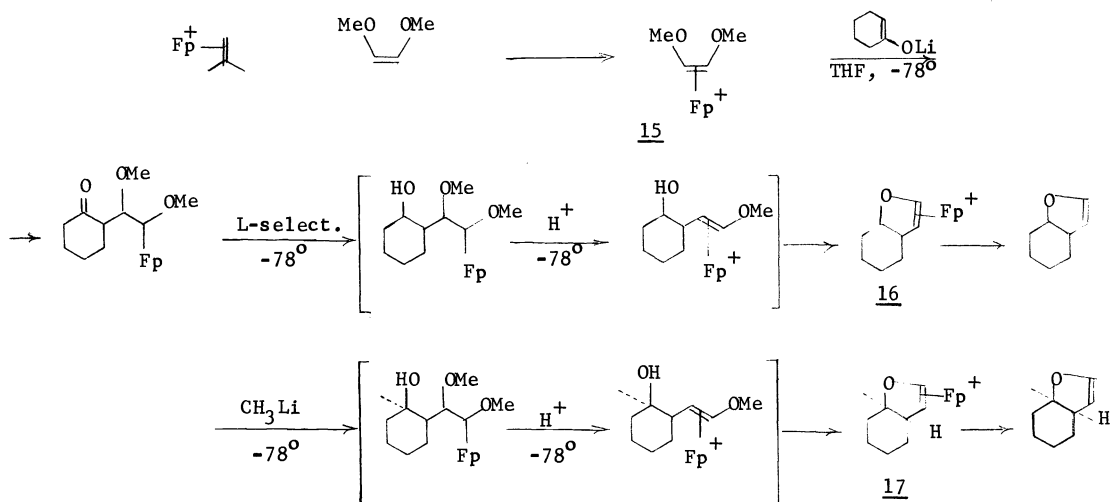


The homologous complex 14, prepared from 3-hexyne-1-ol, behaves differently with cyclohexanone enolate, and affords only the products of proton transfer. The reactions of 14 with enamines have not as yet been examined.

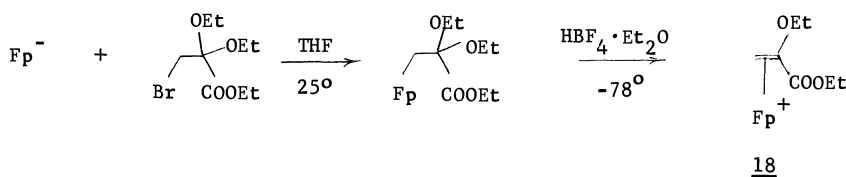


Exchange complexation of *cis*-1,2-dimethoxyethylene yields vinyl ether complex 15, which may be used as a 1,2-vinyl dication equivalent. With cyclohexanone enolate addition, reduction and acid catalyzed conversion may be effected in a one pot reaction yielding the dihydrofuran complex 16. Alternatively treatment of the initial adduct with methyllithium yields

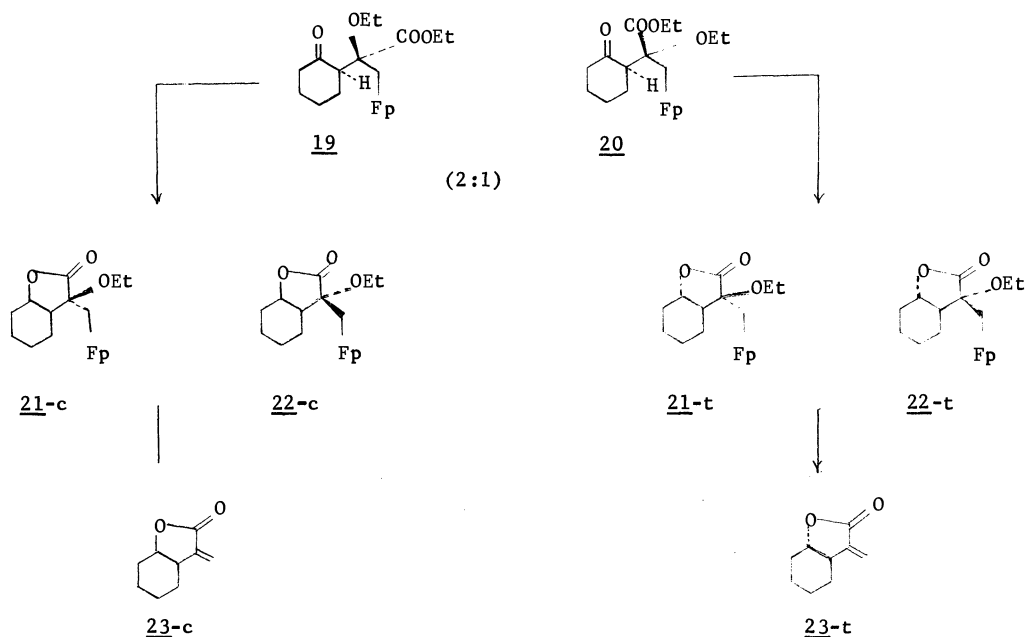
17. The free dihydrofurans are liberated from 16 and 17 by treatment with iodide.



The α -ethoxyacrylic ester complex 18 serves as an α -acrylic ester cation equivalent, and is a particularly useful synthon for the construction of α -methylene- γ -lactones from enolates.⁷ This cation may be prepared from ethyl α -bromopyruvate diethyl ketal, but unlike all of the other vinyl ether complexes described, which are sufficiently stable to isolate and store, 18 must be prepared at low temperature and used directly

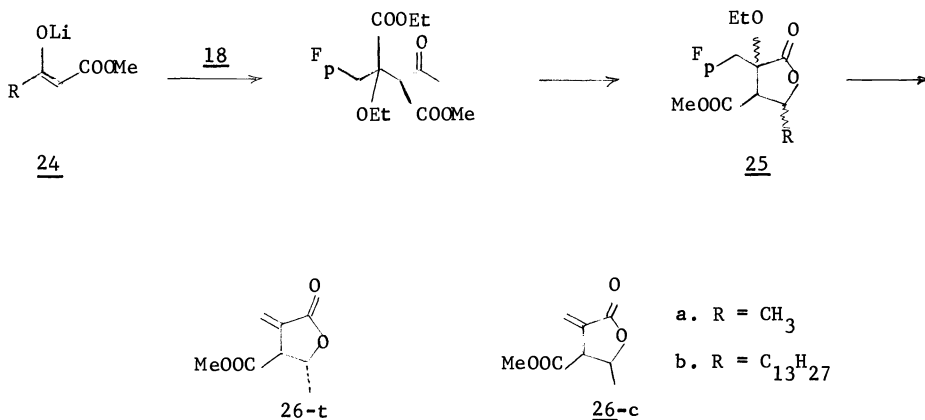


With cyclohexanone lithium enolate and 18, a mixture of diastereomeric adducts 19 and 20 are obtained, which are reduced with L-selectride to give the cis-lactones 21-c, 22-c or with sodium borohydride to give predominantly the corresponding trans-lactones 21-t and 22-t. Each of these substances have been transformed, either individually or as a mixture of diastereomers to the corresponding cis- or trans- α -methylene- γ -lactones 23-c and 23-t.



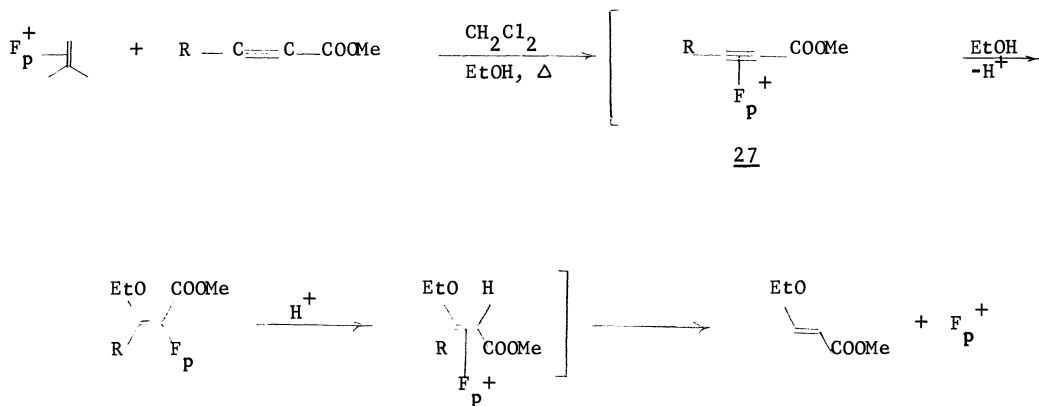
The ketone function in the minor adduct 20 is evidently more hindered compared with its diastereomer 19 since L-selectride or sodium borohydride reduction proceeds more slowly and the latter reagent is not stereospecific with 20 as it is with 19.

The condensation of 18 with β -ketoesters has also been examined.⁸ With methyl acetoacetate enolate, the adduct 24a is obtained in 85% yield, and this on direct reduction with L-selectride gives lactone 25a as a 9:1 mixture of C_{4,5}-cis and trans isomers 26a-c,t. The same sequence carried out on the long chain ketoester 24b gave protolichesterinic acid ester 26b-t as the exclusive product, but the overall yield (15%) is reduced because the lithium enolate of 24b undergoes O-alkylation principally with 18, even in toluene suspension.

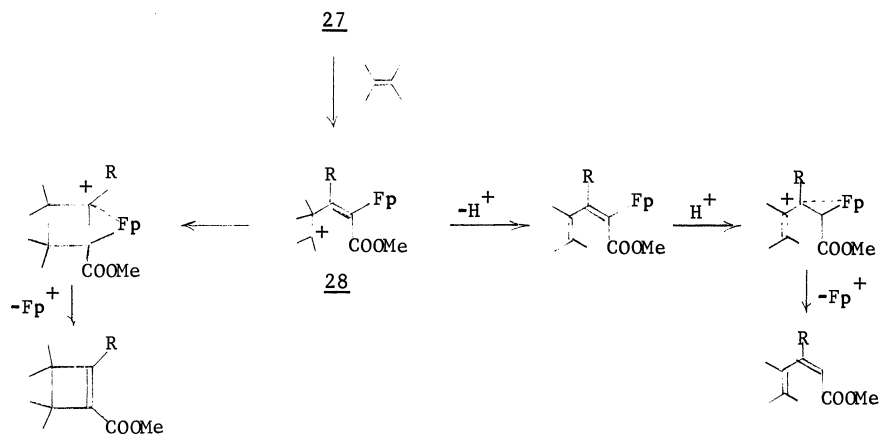


β -Acrylic ester cation equivalents are derived not from vinyl ethers but from acetylene esters. F_p complexes of α,β -acetylenic esters are, like F_p(acrylic ester) complexes, not obtainable by an exchange reaction with F_p(isobutylene)BF₄, since these complexes are thermally unstable, owing to the poor π -donor capacity of the acetylene bond.

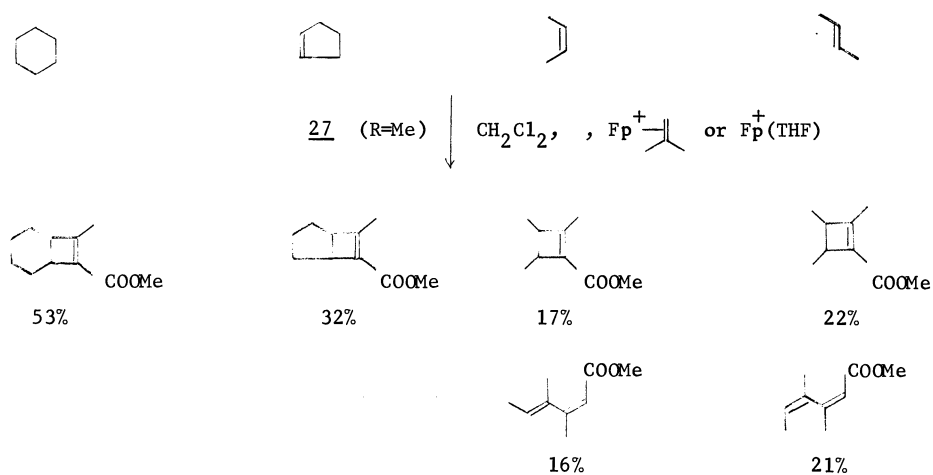
Nevertheless, evidence for the transient existence of species such as 27 may be inferred from the observation that F_p(isobutylene)BF₄ catalyzes the addition of ethanol to methyl propiolate.



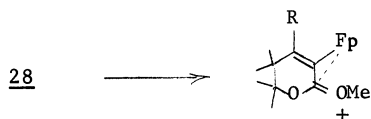
Complex 27 is a powerful electrophile, which initiates condensation with olefins as well.⁹ The course of the reaction depends on the degree and form of olefin substitution. With acyclic and cyclic 1,2-disubstituted olefins the principal products are cyclobutenes and dienes formed stereospecifically in reactions which are mildly catalytic in F_p(isobutylene)BF₄. A plausible sequence of events which accounts for these observations is shown below. The intermediate cation 28, generated by reaction of 27 with olefin, is converted by proton transfer to a diene with concurrent regeneration of F_p⁺. Alternatively 28 may cyclize to the cyclobutane cation, promoted by stabilization of charge by the adjacent F_p group. Loss of F_p⁺ yields product and regenerates the catalyst.



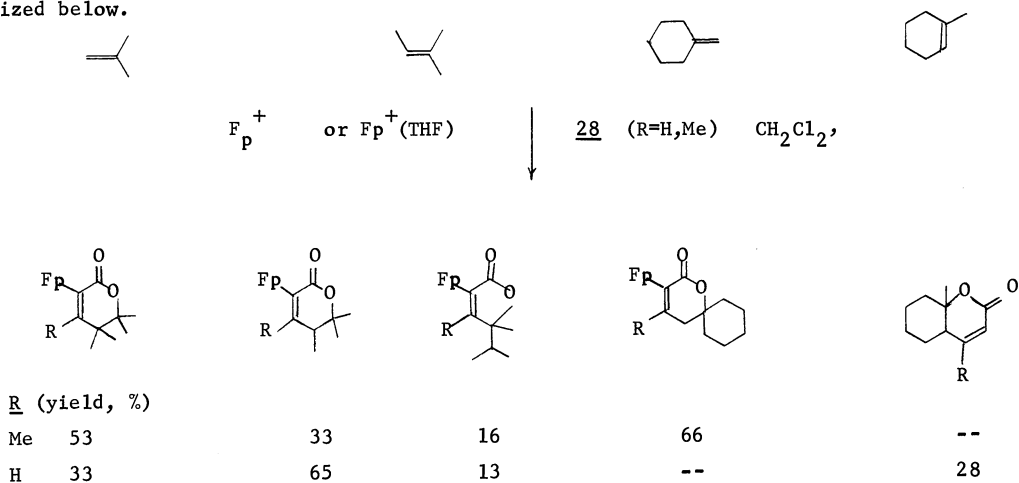
The condensation of cyclopentene, cyclohexene, and cis- and trans-2-butene with methyl tetrolate in the presence of either F_p (isobutylene) BF_4 or F_p (tetrahydrofuran) BF_4 exemplify those reactions.



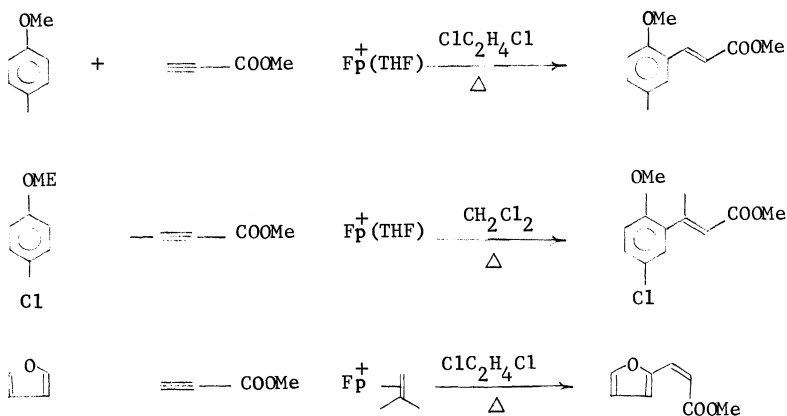
With 1,1-disubstituted olefins the principal reaction product is a methylated lactone salt, formed by reaction of the cationic center in 28 with the cis-ester function.



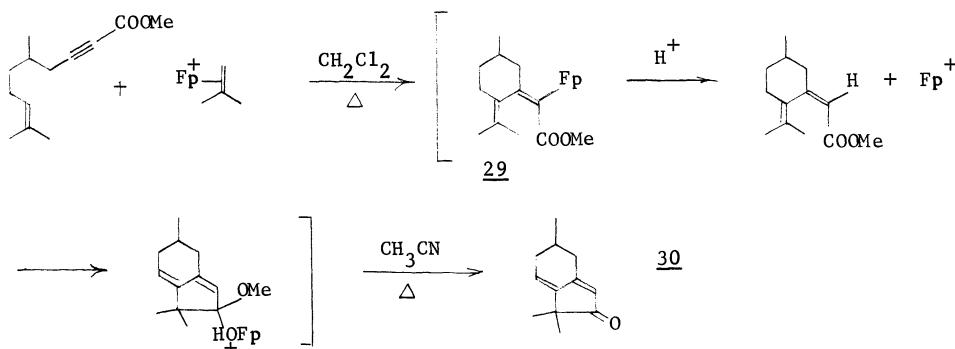
Demethylation of this salt is readily achieved by brief treatment with sodium iodide in acetone. Some examples of these reactions with propiolic and tetrolic esters are summarized below.



These reactions have now been extended to reactive aromatic systems which are observed to undergo carbomethoxy vinylation on treatment with acetylenic esters and a source of F_p^+ .



A final, intramolecular variant of these reactions gave a single product in high yield (87%) which is assigned structure 30. This substance is apparently formed by F_p^+ assisted cyclization of the dienonic ester 29, which, because of its mode of formation, possesses the requisite stereochemistry for such a transformation.



In conclusion, F_p complexes of vinyl ethers and acetylenes show promise as unique and synthetically useful vinyllating reagents. A further elaboration of this chemistry and its application in syntheses is being pursued.

It is a pleasure to acknowledge the contributions of my students and postdoctoral associates whose names appear as coauthors of this paper. This research has been supported by the National Science Foundation and in part by the National Institutes of Health.

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