Tetrahedron Letters, Vol.31, No.24, pp 3385-3388, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

TRICARBONYL(TROPONE)IRON AS A USEFUL FUNCTIONALIZED ENONE EQUIVALENT

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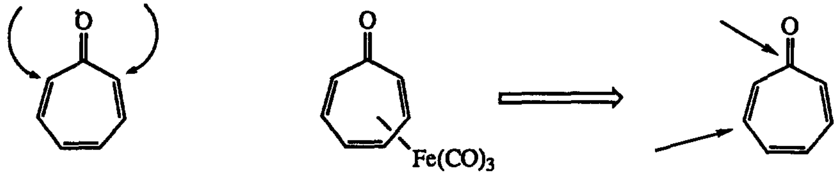
Summary: Tricarbonyl(tropone)iron has been shown to undergo reactions that are characteristic of an isolated enone.

2, 4, 6-Cycloheptatriene-1-one(tropone)(1) is a highly functionalized and reactive species that has been exploited extensively as a building block for the assembly of complex natural products.[1] Although this compound has proven to be a versatile substrate from which to elaborate a wide-range of important structural features, its reactivity profile, depicted in Figure 1, is rather limited. Facile bond formation at additional locations around the tropone periphery would substantially expand the synthetic utility of this readily accessible molecule. Of particular appeal from a synthetic perspective would be to express this enhanced reactivity in the form of an enone which would display the normal array of reactions associated with that important functionality. We wish to report that tricarbonyl[(2,3,4,5-η)-2,4,6-cycloheptatrien-1-one]iron(2) displays reactivity that parallels that of a normal enone in nearly every respect.

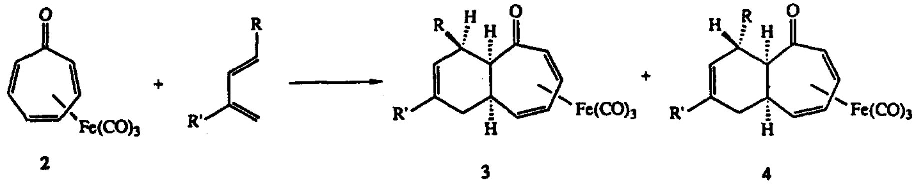


1 2

Figure I

While a few studies on the reactions of complex 2 have been reported, it is interesting to note that in most instances the uncomplexed double bond has participated as an electron rich reaction partner.[2,3] For example, the C_2 position in complex 2 can be acylated under standard Friedel-Crafts conditions[3a] and inverse electron demand cycloadditions appear to proceed smoothly across the free unsaturation.[3b] Nucleophilic additions to C_3 have been achieved only through the intermediacy of either an O-protonated or O-alkylated cation complex.[3c,d] In contrast, the potential for the uncomplexed double bond in 2 to undergo reactions characteristic of an electron deficient enone has been virtually unexplored.[4]

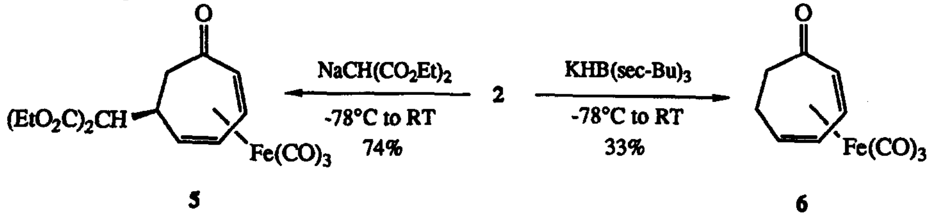
Table I. High-Pressure Diels-Alder Reactions of Complex 2.[a]



	Diene	Pressure(kbar)	3:4	Yield(%)[b]
a	R=OTMS, R'=H	10	3:1	96
b	R= 3,5-dinitrobenzoate, R'=H	12	4:3[c]	74
c	R=H, R'=OTMS	8	1:0	47
d	R=OAc, R'=H	12	1:1	75

[a] All new compounds exhibit spectral(^1H NMR, ^{13}C NMR, IR) and analytical data (HRMS) consistent with the assigned structures. [b] Refers to the combined isolated yields of products after chromatography. [c] Structure was established by X-ray crystallographic analysis of the major isomer (3b). Other stereochemical assignments based on chemical correlation with compounds 3a,b.

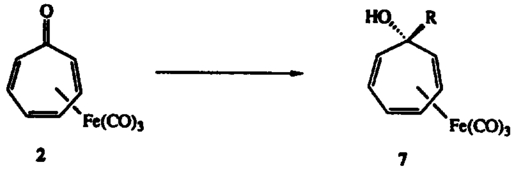
Initial efforts to induce 2 to react with a series of 1-oxygen substituted dienes under typical Diels-Alder conditions met with limited success. In contrast, the high-pressure variant (RT, CH_2Cl_2)of this process was found to occur without incident to provide the desired cycloadducts in good to excellent yields. The results of this study are compiled in Table I. It is most noteworthy that the only regioisomer formed in each case was that which is expected from a normal enone partner. This result is particularly intriguing in light of the regiochemical outcome of certain 1,3-dipolar cycloadditions which occur in the opposite sense to that observed for normal enones.[3e]

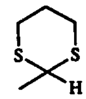


(1)

A further illustration of the enone character of complex 2 is the stereoselective conjugate addition that occurs with typical Michael nucleophiles. Treatment with sodio diethyl malonate (THF) gave adduct 5[5] as a single diastereoisomer in 74% yield[6] and the reaction of 2 with K-selectride (THF), which is known to deliver hydride in a 1,4-fashion to enones[7], provided dihydrotropone complex 6.[5] To date, attempted 1,4-additions with various organocopper reagents have been unsuccessful.

Table II. 1, 2-Addition of Nucleophiles to Complex **2**.

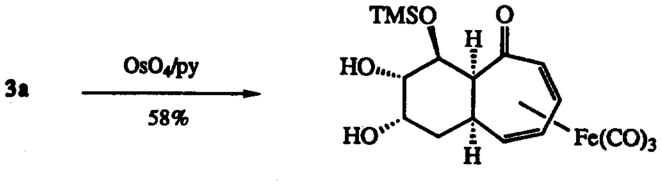


	Nucleophile	Conditions	Product[a]	Yield(%)[b]
a		THF, -78°C	R= 	30
b	NaBH$_4$/CeCl$_3$	MeOH, 0°C	R=H	89
c		THF, -30°C	R= 	50

[a]A single diastereoisomer was isolated in each case. [b]Based on isolated product after chromatography. [c]Extremely acid sensitive product, yield may reflect decomposition during purification.

Table II displays the results of 1,2-additions of various nucleophiles to **2**. Again each reaction resulted in the production of a single diastereomeric adduct. The assignment of product stereochemistry based on attack of the reagent from the face distal to the Fe(CO)$_3$ group is completely consistent with the known behavior of other diene iron tricarbonyl electrophiles[4a,8] and demonstrates the crucial role of the Fe(CO)$_3$ as a potent stereochemical control element in these transformations. Furthermore, the resultant η^4-Fe(CO)$_3$ diene complex can serve as a very effective protecting group for the dihydrotropone diene system allowing for selective manipulation at other regions of the molecule as evidenced by the production of diol **8**.[5]

The synthetic utility of the processes described herein is critically dependent on the convenient removal of the iron moiety under conditions sufficiently mild such that most functionalities can survive the operation intact. Numerous methods for accomplishing this task were explored. Cerium(IV) ammonium nitrate(CAN) emerged as the most generally useful reagent. It was viewed as being of paramount importance that the decomplexation protocol did not disturb the diene system[9] and, in the event, the reaction proceeded cleanly to give compounds 9 and 10.



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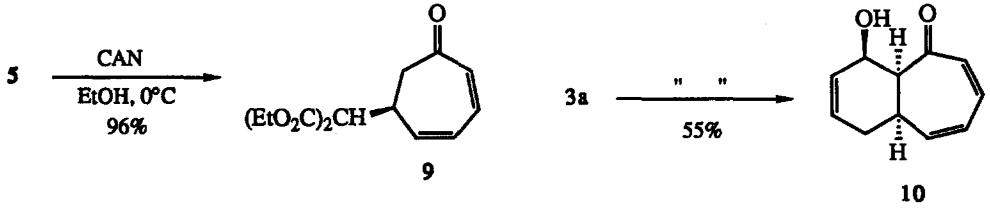
The capability of tricarbonyl(tropone)iron to serve as a convenient equivalent to tropone in which a portion of the conjugated system can function as an electron deficient enone solves a major, long-standing problem that until now has severely limited the full exploitation of tropone as a building block for natural product synthesis.



Acknowledgment. We thank the National Institutes of Health(CA-36543) and the National Science Foundation(CHE-8719185) for financial support and Dr. M.J. Heeg for the X-ray structural work.

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5. This compound exhibited spectral (^{1}H NMR, ^{13}C NMR, IR) and analytical (HRMS) date in complete accord with the assigned structure.

6. The formation of malonate adduct **5** was always accompanied by the production of a trace (<5%) of **6**.

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(Received in USA 28 March 1990)