In similar thermolysis studies carried out at 370 °C, we have observed 12–15% isomerization of the *E* and *Z* isomers of 1. When *E*- or *Z*-**1** is generated under flash-vacuum pyrolysis conditions at 550 °C, complete randomization of stereochemistry occurs and identical product mixtures are obtained for either isomer.[12]

We are currently carrying out carefully controlled thermolyses at a series of temperatures aimed at determining the activation energy (and thus the Si=C π bond energy) for the isomerization.

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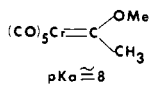
Diels–Alder Reactions of Fischer Carbene Complexes

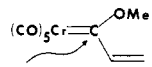
William D. Wulff* and Dominic C. Yang

Searle Chemistry Laboratory, Department of Chemistry
The University of Chicago, Chicago, Illinois 60637
Received June 2, 1983

The heteroatom-stabilized carbene complexes of the group 6 transition metals (Fischer carbene complexes[1]) were the first to be prepared[2] and are among the most stable of all transition-metal carbene complexes.[3] The chemical and physical properties of these complexes have been interpreted in terms of a polarized chromium–carbon bond with the carbon bearing an appreciable positive charge.[4,5] An example is the tremendous thermodynamic acidity of the α protons ($pK_a \simeq 8$) in the complex **1**.[6] With this



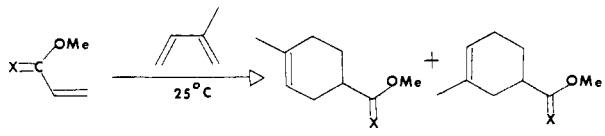
1



5

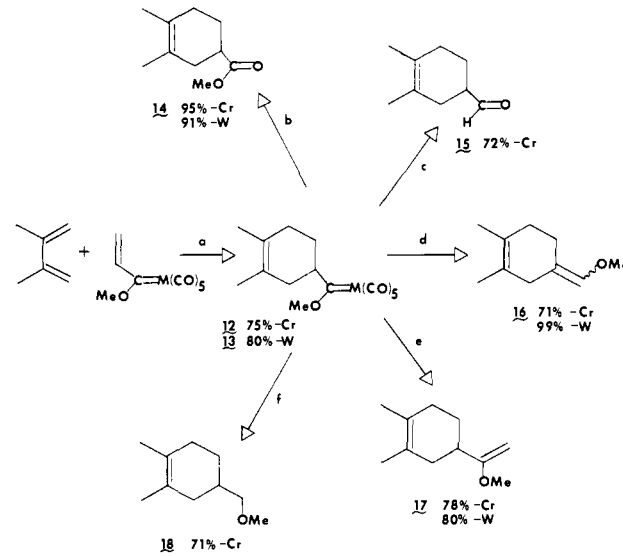
in mind and in an effort to find alternatives to or synthons for the Diels–Alder reaction, we were led to examine the dienophilicity of α,β-unsaturated complexes such as **5**.[7]

The vinyl-substituted complexes **5**–**7**[8] react with a variety of dienes with rate accelerations of greater than 10^4 over that of methyl acrylate, their closest carbon analogue. The comparative data for isoprene is presented in Table I. Methyl acrylate has previously been observed to react with isoprene in 7 months at 25 °C to give a 54% yield of a 70:30 mixture of the "para" and "meta" isomers **8** and **9**.[9] The chromium complex **5** on the other



8 **9**

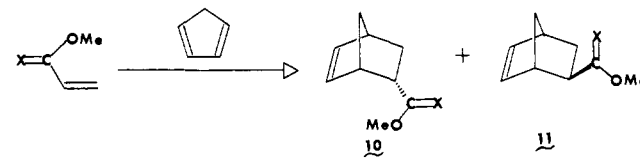
Scheme I



[a] (a) C_6H_6, 25 °C, 1.5 h; (b) Me_2SO, 3.5 h, 25 °C; (c) 10^{-3} M in CH_2Cl_2, 1 equiv of HBr, −78 → 25 °C, 1 equiv of HBr, −78 → 25 °C; (d) 1.1 equiv of pyridine, THF ↓, 5 h; (e) excess CH_2N_2 in Et_2O, 25 °C, 5 min; (f) 69 atm H_2/hexane, 170 °C, 48 h.

hand, reacts in 3 h at 25 °C to give after chromatographic purification on silica gel with hexane a 70% yield of **8** and **9** as a 92:8 mixture. A ratio of the rate constants gives a rate enhancement of 2.1 x 10^4, and as can be anticipated there is an associated increase in the regioselectivity. It is interesting to note that the increased reactivities in the reaction of these complexes with isoprene are comparable to those of the aluminum chloride catalyzed reaction of methyl acrylate and isoprene.[10]

The vinyl-substituted complexes **5** and **7** have been found to react with cyclopentadiene in a highly stereoselective fashion in accord with the Alder endo rule (Table II). The red vinyl chromium complex **5** reacts with cyclopentadiene in 3 min at 25 °C to give a 78% yield of the yellow endo and exo cycloadducts **10** and **11** in a ratio of 94:6 that is identical with the endo/exo



10 **11**

ratio obtained from the aluminum chloride catalyzed reaction of methyl acrylate and cyclopentadiene.[11] Given the substantial acidity of protons α to the carbene carbon in Fischer carbene complexes,[6] we have taken a mixture of **10** and **11** (X = $W(CO)_5$) that is enriched in the exo isomer **11** (5.1:1.0) and found that the composition of the mixture is unaffected by either exposure to the reaction conditions or by oxidation to the corresponding methyl esters. This indicates that the endo/exo ratios given in Table II represent kinetic values.

These metal-complexed cycloadducts can serve as synthons for a variety of organic functional groups by employing known reactions of Fischer carbene complexes.[12] We have examined a few of these methods for the chromium and tungsten adducts **12** and **13** (Scheme I). Esters can be obtained with a variety of oxidizing agents of which the mildest is perhaps dimethyl sulf-

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Table I. Regioselectivity with Isoprene

dienophile	X	catalyst	time	yield, %	8/9	rel rate[a]
2	O		7 mo[b]	54[b]	70:30[c,d]	1
2	O	$AlCl_3$	3 h	50[d]	95:5[d]	7.4×10^5 [e]
5	$Cr(CO)_5$		3 h	70[f]	92:8[g]	2.1×10^4 [h]
6	$Mo(CO)_5$		1 h	61[f]	94:6[g]	
7	$W(CO)_5$		2 h	87[f]	91:9[g]	2.6×10^4 [h]

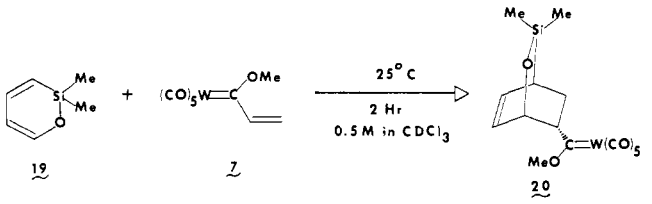
[a] Ratio of rate constants. [b] Reference 9. [c] Reference 21. [d] References 10 and 22. [e] Reference 23. [f] Yield of complexes isolated by flash chromatography. [g] Determined after oxidation to the known methyl esters. [h] Reaction followed with 0.05 M complex in benzene with 1.0 M isoprene at 25 °C; presuming a second-order reaction the rate constants are $4.9 \pm 0.4 \times 10^{-4}$ L mol^{-1} s^{-1} for **7** and $4.0 \pm 0.4 \times 10^{-4}$ L mol^{-1} s^{-1} for **5**.

Table II. Stereoselectivity with Cyclopentadiene

dieno-phile	X	catalyst	temp, °C	time	yield, %	10/11
2	O		30	7.5 h		78:22[a]
2	O	$AlCl_3$	30	1.0 h		94:6[a]
5	$Cr(CO)_5$		25	3 min	78[b]	94:6[b,c]
7	$W(CO)_5$		25	3 min	93[b]	93:7[b,c]

[a] Reference 11. [b] Yields of complexes isolated by flash chromatography. [c] Determined after oxidation to the known methyl esters.

Scheme II



oxide.[13] The methyl ester **14** is formed in excellent yields from either **12** or **13** by simple treatment with dimethyl sulfoxide at room temperature. The aldehyde **15** can be obtained in good yield from the reaction with hydrogen bromide.[14] The methyl vinyl ether **16** can be obtained by heating either **12** or **13** with pyridine.[16] Reaction with diazomethane[17] results in clean formation of the enol ether **17**, and thus **5** and **7** can serve as synthons for 2-methoxybutadiene as a dienophile. The metal can also be reductively removed by treatment with hydrogen where the metal center can serve to activate and deliver hydrogen thus allowing the double bond in **18** to survive intact.[18]

These results suggest that the combination of the high dienophilicity of Fischer carbene complexes and their relative stability to sensitive functionality[12] may be sufficient to allow for Diels–Alder reactions with the silapyran **19**.[19,20] Indeed, the tungsten complex **7** reacts with the silapyran **19** at 25 °C with clean formation of the cycloadduct **20** as evidenced by ^{1}H NMR (Scheme II). It can be further anticipated that Diels–Alder reactions of Fischer carbene complexes will have a broad range of applications in synthetic chemistry especially in combination with other reactions indigenous to organometallic compounds of the group 6 metals. We will report further on the scope of these and related cycloaddition reactions of Fischer carbene complexes and on their applications to natural product synthesis.

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Supplementary Material Available: Spectroscopic data and experimental details for compounds **5–20** (11 pages). Ordering information is given on any current masthead page.

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2-Carbomethoxy-3-tropinone: An Advanced Intermediate in the Biosynthesis of Cocaine

Edward Leete

Natural Products Laboratory[1]
Department of Chemistry, University of Minnesota
Minneapolis, Minnesota 55455

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It has recently been established that the tropane moiety of cocaine (**7**) is derived from ornithine[2] and acetic acid,[3,4] the latter presumably being incorporated via acetoacetate since [1-^{14}C]-acetate afforded cocaine with a preponderance of radioactivity at C-3 and C-9. These results are consistent with a biosynthetic route to cocaine, depicted in Scheme I. A condensation between acetoacetate, perhaps as its coenzyme A ester (**2**) and the *N*-methyl-Δ^1-pyrrolinium salt **1** (derived from ornithine), yields hygrine-1′-carboxylate. It is proposed that this β-keto ester is converted to its methyl ester (**3**) prior to the subsequent reactions which involve dehydrogenation to the iminium salt **5** and cyclization to 2-carbomethoxy-3-tropinone (**4**). A stereospecific reduction of this ketone yields methyl ecgonine (**6**), which on esterification with benzoic acid (derived from phenylalanine[3,5]) yields cocaine.

The intermediacy of **4** in this biosynthetic sequence has now been established by feeding this compound labeled with ^{13}C, ^{14}C, and ^{3}H to *Erythroxylon coca* plants. Reaction of 3-tropinone with [*carbonyl*-^{13}C,^{14}C,*O-methyl*-^{3}H]dimethyl carbonate[6] in the

(1) Contribution 189 from this Laboratory. Part 33 in the series "Chemistry of the Tropane Alkaloids". For Part 32, see: Leete, E. *Phytochemistry* **1983**, *22*, 933. Presented at the 2nd International Conference on the Chemistry and Biotechnology of Biologically Active Natural Products, Budapest, Hungary, Aug 15–19, 1983.
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