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DIELS-ALDER REACTIONS ON LINEAR POLYENES, SELECTIVELY PROTECTED AS THEIR TRICARBONYL-IRON COMPLEXES.

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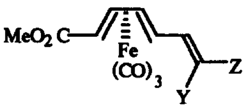
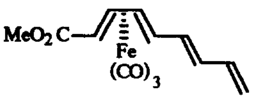
Abstract : The first examples of Diels-Alder reactions using dienophiles or a diene bearing butadiene-tricarbonyliron moieties are described. These highly stereoselective reactions are useful for the synthesis of polycyclic derivatives via tandem cycloadditions.

The selective complexation of dienes or linear polyenes by $Fe(CO)_3$ has already proved to be extremely useful in asymmetric organic synthesis [1]. In the field of cycloadditions many examples using carbenes, ketenes or 1,3 dipoles have been described. However, no example of a successful Diels-Alder reaction has been described though unsuccessful attempts have been reported [1,2]. It was thus of interest to study the possibilities and limits of these reactions which would be especially useful for the selective synthesis of polycyclic derivatives via successive (or "tandem") cycloadditions. The purpose of this note is to establish that highly electrophilic olefins such as 1 are, indeed, dienophiles ; to describe in the case of 1b, a very efficient catalysis by $TiCl_4$; and, finally to report the cycloaddition of the complexed tetraene 2 with N-methylmaleimide.

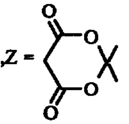


1



2

a : Y,Z =



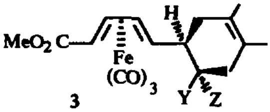
b : Y = Z = CO_2Me

c : Y = Z = CN

d : Y = CN, Z = CO_2Me

I - Diels-Alder reactions with the selectively complexed dienophiles 1

Meldrum's acid derivative **1a** [3] reacts with 5 equivalents of 2,3 dimethyl butadiene in refluxing THF for 12 hours to give the adduct **3a** as a single isomer in 70 % yield. As expected from previous results [1], the addition of the diene occurs from the face anti to the $Fe(CO)_3$ moiety as has been clearly established by X-ray analysis of **3a** [4].



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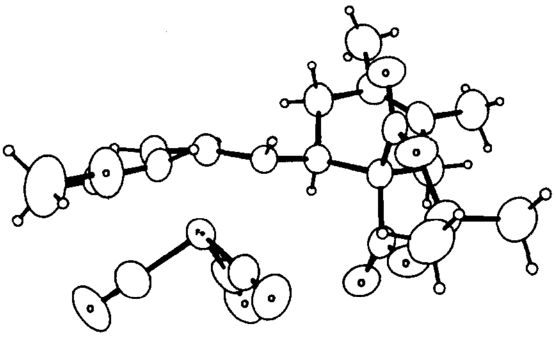
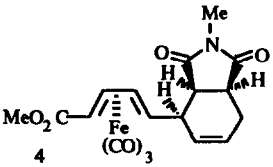


The other gem-diactivated olefins **1b-1d** also react with 2,3 dimethylbutadiene under the same conditions to give the corresponding cycloadducts **3**. In each case only one isomer is obtained but yields are low (8-10 %) even after several days at reflux. The monosubstituted derivative **1e** (Y = H,Z = CO_2Me) does not react under these conditions.

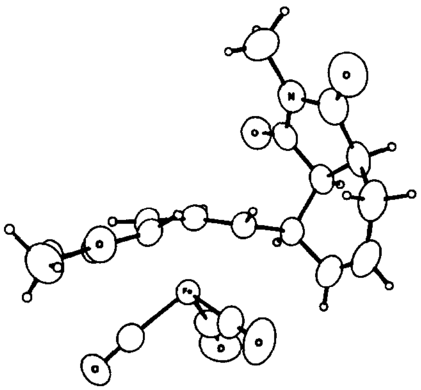
Using **1b** as substrate, one equivalent of $TiCl_4$ in CH_2Cl_2 was found to be an efficient catalyst for cycloaddition and adduct **3b** is obtained in excellent yield (≥ 95 %) after only 3 hours at 0°C. The quantity of $TiCl_4$ is important since the reaction is slower when less than one equivalent of the Lewis acid is used and degradation products are obtained with more than one equivalent of $TiCl_4$. However, this catalysis appears to be rather specific since other Lewis acids like BF_3. Et_2O or $AlCl_3$ are not effective with **1b** and no Lewis acid catalysis has thus far been observed with olefins **1c** or **1d**.

II - Diels-Alder reactions with the selectively complexed diene 2

The easily accessible diene **2** [5] reacts readily with N-methylmaleimide (3 eq. for 4 hours in refluxing THF) to give a 70 % yield of **4**, as a single adduct. An X-ray analysis of this compound established the stereochemistry unambiguously. Several points relating to this reaction are worthy of note :

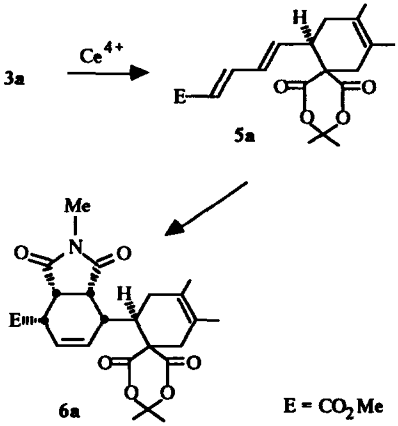


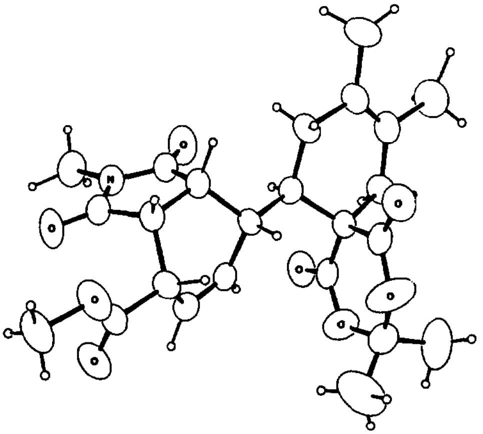
4



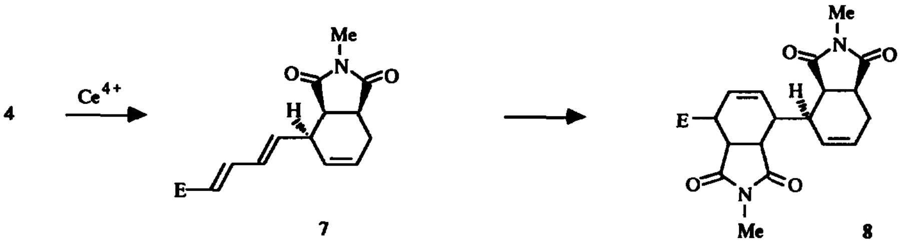
- There is no bond-shift of the $Fe(CO)_3$ unit along the tetraenic structure [7] before the cycloaddition.
- The dienophile again reacts from the face anti to $Fe(CO)_3$ and the expected endo-transition state is observed during the cycloaddition.
- Also, it was found that diene **2** would not react with dimethyl maleate or dimethyl fumarate under a variety of conditions.

Diels-Alder reactions can then be performed on linear polyenes selectively complexed by $Fe(CO)_3$. In spite of some limitations, these reactions are of interest for two main reasons. Firstly, they are highly stereoselective and, since the starting complexes are easily accessible in a chiral form [6], they can be of much use for the synthesis of optically active cycloadducts. Secondly, after decomplexation of the primary adducts, a new diene is obtained which can be utilized for a second cycloaddition thus opening a route to new polycyclic derivatives. This *tandem* [8] Diels-Alder approach is illustrated by reaction of **5a** with N-methyl maleimide giving **6a**, as the only isolated cycloadduct.





The X-ray analysis of **6a** establishes that the second cycloaddition occured, via an endo approach, from the least hindered side of **5a**.



In the same way, **7** reacts with N-methylmaleimide but this cycloaddition is only stereoselective giving a (7/3) mixture of adducts **8**. Extension of this methodology is under study in our laboratory.

References and notes

1 - Grée R., Synthesis, 1989, 341 and ref. therein.

2 - Johnson B.F.G., Lewis J., Parker D.G., Postle S.R., J. Chem. Soc. Dalton Trans., 1977, 794.

3 - Laabassi M., Grée R., Tetrahedron Lett., 1988, 29, 611.

4 - Atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre. The coordinates can be obtained from the Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CBZ 1EW, UK.

3a : $FeC_{22}H_{24}O_9$: Mr = 488.3, monoclinic, $P2_1/n$, a = 10.238(6), b = 16.852(8), c = 13.099(8) Å, β = 93.01(5), V = 2258(1) Å^{-3}, Z = 4, D_x = 1.44 Mg.m^{-3}, λ(MoKα) = 0.71069 Å, μ = 7.12 cm^{-1}, F(000) = 1016, T = 296 K. Sample studied on an automatic diffractometer CAD4 ENRAF-NONIUS. Structure solved with a Patterson map and refined by full-matrix least-square techniques with the resulting R = 0.032, R_ω = 0.029 and S_ω = 1.40 (residual $\Delta\rho \leq 0.26$ eÅ^{-3}).

4 : $FeC_{18}H_{17}O_7$: Mr = 415.2, monoclinic, $P2_1/n$, a = 9.953(2), b = 11.287(2), c = 16.445(3) Å, β = 93.01(2), V = 1844.9(8) Å^{-3}, Z = 4, D_x = 1.50 Mg.m^{-3}, λ(MoKα) = 0.71069 Å, μ = 8.53 cm^{-1}, F(000) = 856, T = 296 K. Sample studied on an automatic diffractometer CAD4 ENRAF-NONIUS. Structure solved with a Patterson map and refined by full-matrix least-square techniques with the resulting R = 0.027, R_ω = 0.026 and S_ω = 1.29 (residual $\Delta\rho \leq 0.22$ eÅ^{-3}).

6a : $C_{24}H_{29}O_8N$, C_2H_5OH : Mr = 505.6, monoclinic, $C2_1/c$, a = 38.641(9), b = 6.222(3), c = 22.113(5) Å, β = 110.35(2), V = 4985.(2) Å^{-3}, Z = 8, D_x = 1.40 Mg.m^{-3}, λ(MoKα) = 0.71069 Å , μ = 0.95 cm-1, F(000) = 2160, T = 296 K, final R = 0.063 for 2190 observations and 394 variables.

5 - Diene 2 is prepared (46 %, non optimized yield) by Wittig reaction of the known aldehyde (6) with the phosphorane prepared from allyltriphenylphosphonium bromide.

6 - Monpert A., Martelli J., Grée R., Carrié R., Tetrahedron Lett., 1981, 22, 1961.

7 - Thermally induced bond-shifts of $Fe(CO)_3$ in complexed polyenes are known : Whitlock Dr H.W., Markezich R.L., J. Am. Chem. Soc., 1971, 93, 5290.

8 - Tandem cycloadditions already proved to be useful in synthesis, see for instance : Denmark S.E., Moon Y.C., Senanayake C.B.W., J. Am. Chem. Soc., 1990, 112, 311 and ref. therein ; for *timed* Diels-Alder reactions, see Kraus G.A., Taschner M.J., J.J. Am. Chem. Soc., 1980, 102 1974.

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