SITE SPECIFICITY IN 1,3-DIPOLAR CYCLOADDITIONS TO A POLYCYCLIC POLYENE INDUCED BY COMPLEXATION WITH TRICARBONYLIRON#

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Abstract - Treatment of dimethyl tricyclo[4.2.2.$0^{2,5}$]deca-3,7,9-triene-7,8-dicarboxylate (**1**) with nonacarbonyldiiron led to dimethyl 7-10-tetrahapto-tricyclo[4.2.2.$0^{2,5}$]deca-3,7,9-triene-7,8-dicarboxylate tricarbonyliron (**12**). This derivative reacted smoothly with several 1,3-dipoles (nitrones, nitrile oxides, nitrile imines and diazoalkanes) at the cyclobutene double bond to give adducts from which the tricarbonyliron group could be easily removed by oxidative decomplexation with trimethylamine *N*-oxide. Thus, a formal site specific attack of 1,3-dipoles to **1** was achieved.

INTRODUCTION

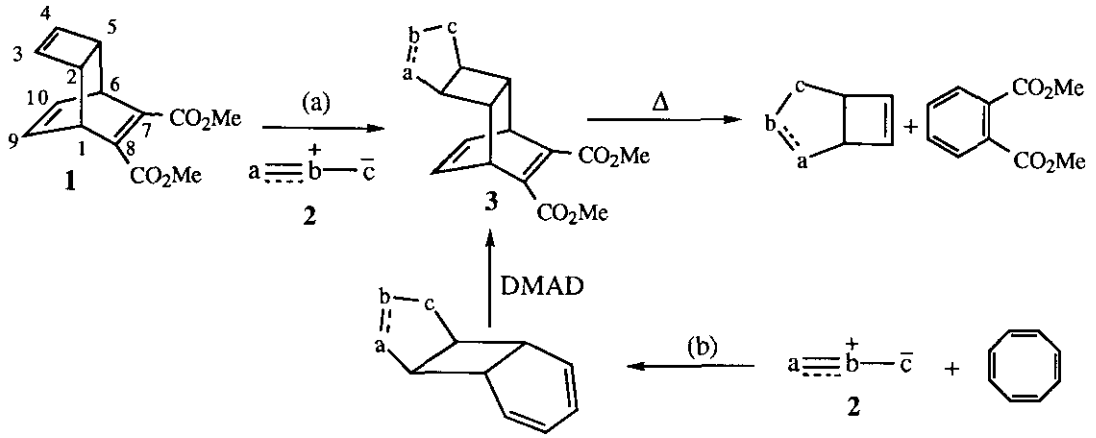
We have previously demonstrated that adducts of 1,3-dipoles (**2**) to the cyclobutene double bond of dimethyl tricyclo[4.2.2.$0^{2,5}$]deca-3,7,9-triene-7,8-dicarboxylate (**1**) (i.e., **3**) lend themselves as appealing starting products for the synthesis of cyclobutenes fused to a heterocyclic nucleus through a Diels-Alder cycloreversion (Scheme1).[1-3] Compound (**3**) can be obtained from the 1,3-dipolar cycloaddition of **2** to **1** [*via* (a), Scheme 1] as well as from the cycloaddition of **2** to cyclooctatetraene followed by a Diels-Alder reaction with DMAD [*via* (b)].[1-4]

We report here some further data on the limits of these two routes and illustrate a new pathway to **3** which corresponds to a formal site specific attack by 1,3-dipoles to **1**.

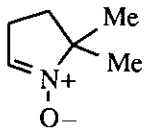
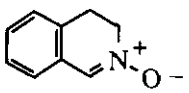
RESULTS

The cyclobutene double bond of tricyclic polyene (**1**) should be somewhat activated by angle strain with a resultant enhancement of its reactivity in 1,3-dipolar cycloadditions.[5] However, it is not reactive enough to clearly win over the other two double bonds present in the molecule. Actually in the reaction of **1** with *t*-butyl nitrone (**2a**) and 5,5-dimethylpyrroline *N*-oxide (**2b**) there is a dominance of compound (**3**) over

#Dedicated to Dr. Bernhard Witkop on the occasion of his 80th birthday.



Scheme 1

	2	3	4	5	Reference
a	$CH_2=\overset{t\text{-Bu}}{\overset{|}{\underset{|}{N^+}}}-O^-$	77	23	-	This paper
b		74	26	-	This paper
c		53	47	-	2
d	$ArC\equiv\overset{+}{N}-\overset{-}{O}$	23	77	-	1
e	$PhC\equiv\overset{+}{N}-\overset{-}{N}Ph$	21	58	21	3
f	$N\equiv\overset{+}{N}-\overset{-}{C}Me_2$	-	-	100	This paper
g	$N\equiv\overset{+}{N}-\overset{-}{N}Ar$	-	100	-	This paper

Adduct relative yields of the reactions of 1,3-dipoles (**2**) with **1**. Total yields ≥ 80%. For sake of simplicity numbering is the same (atom "a" is given a lower locant than atom "c") for all the heterocyclic derivatives

Scheme 2

compound (**4**) but in the case of the reaction of 3,4-dihydroisoquinoline *N*-oxide almost equimolecular amounts of these two adducts were formed.[2] Even more there is a reversal of site selectivity in the reaction of nitrile oxides (e.g. **2d**, Ar = Ph)[1] with **1** and attack at the cyclohexadiene double bond is now prevalent. All the three double bonds of **1** compete with each other in the reaction of diphenylnitrile imine (**2e**).[3]

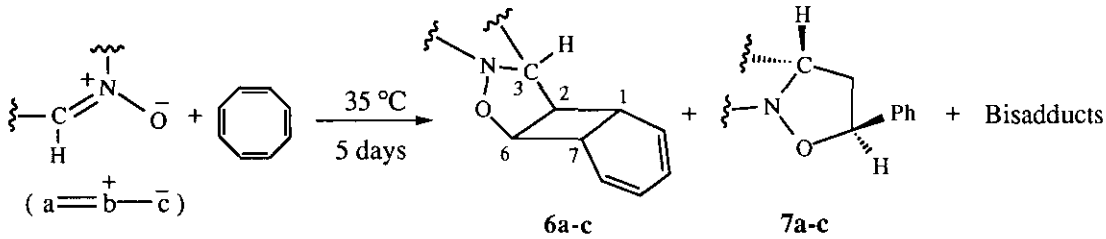
All the reported reactions were carried out in the presence of a large excess of **1** in order to avoid formation of bisadducts.

Site specificity is observed in the reaction of dimethyldiazomethane (**2f**) and aryl azides (**2g**, Ar = *p*-CNC_6H_4 and *p*-$NO_2C_6H_4$). However, in the case of the reaction of electron rich **2f** the attack occurs only at the tetrasubstituted double bond, activated by the two electron withdrawing methoxycarbonyl groups, while the electron poor aryl azides (**2f**) attack only the disubstituted (C_9C_{10}) cyclohexadiene double bond.

Compounds (**3**) can also be prepared by the reaction of 1,3-dipoles with a very large excess (to avoid as far as possible formation of bisadducts) of cyclooctatetraene at room temperature to give adducts (**6**) which easily enter a Diels-Alder cycloaddition with dimethyl acetylenedicarboxylate (Scheme 1 and Scheme 3). This protocol works relatively well with nitrile oxides[1] and nitrile imines[3] and can also be used in the case of dimethyldiazomethane.[6]

The reaction of nitrones with cyclooctatetraene is however very sluggish.[2] One could hope to overcome this problem by carrying out the reaction in cyclooctatetraene as solvent with long reaction times and at temperatures somewhat higher than room temperature. However, commercial cyclooctatetraene contains small amounts of styrene which is much more reactive than cyclooctatetraene. As a result similar amounts, both in low yield, of adducts to cyclooctatetraene (**6**) and to styrene (**7**) are, for example, obtained in the reaction of t-butyl nitrone and 5,5-dimethylpyrroline *N*-oxide.

We did not manage to isolate triazoline derivatives from the reaction of azides with cyclooctatetraene.



2a-c **6a-c** **7a-c**

Scheme 3

As for structures of the new adducts reported above, structures of compounds (**3**) follow unequivocally from their syntheses starting from **1** and from cyclooctatetraene, respectively, as well as from **12** (see below). In agreement with their structure, ^{1}H NMR spectra of adducts (**3**) display the signals of two olefinic protons (H-12 and H-13) as complex multiplets. Also compounds (**4**) exhibit the signals of two olefinic protons either as slightly broadened singlets (when H-9 and H-10 accidentally resonate at the same field) or as doublets ($J \approx 2.5$ Hz). The coupling constant between these two cylobutene protons and their vicinal protons (H-8 and H-11) is lower than 0.5 Hz. Signals of both cyclobutene and cyclohexadiene

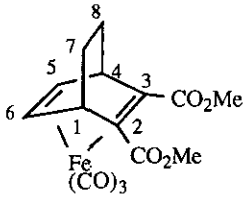
protons are obviously present in the ^{1}H NMR spectra of adducts (**5**). In assigning stereochemistry to both **4** and **5** we assumed that attack occurs from the bottom, i.e., on the sterically less hindered face of C_9C_{10} and C_7C_8 double bond, respectively.

Interest in compounds (**3**) led us to seek alternative ways to produce them. We reasoned that it could be possible to cause the 1,3-dipolar cycloaddition to **1** to be site specific by protecting the two double bonds of the "bottom" 1,4-cyclohexadiene moiety in **1** with the easily removable tricarbonyliron group.

It was known that a 1,4-cyclohexadiene moiety (as that in norbornadiene) can be complexed by the tricarbonyliron group.[7] This observation was further confirmed by us through the preparation of the beautiful orange crystalline complexes (**8**)[8] and (**9**) in high yields by treatment of the corresponding dienes with $Fe_2(CO)_9$ in refluxing ether.

However, in the case of **1** complexation can also involve, in addition to the "bottom" cyclohexadiene moiety, either the sole cyclobutene bond or the cyclobutene bond and one of the cyclohexadiene bonds.

The former possibility is strongly supported by the observation by Grimme *et al.*[9] who obtained the η^2 tetracarbonyliron complex (**10**) as the exclusive product from the reaction of the corresponding polyene



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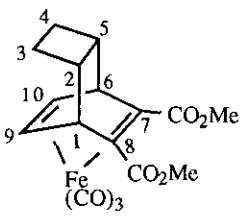

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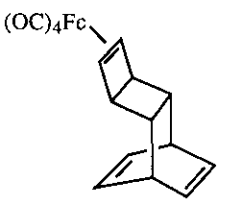

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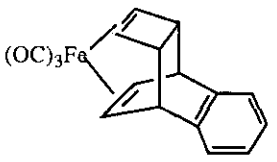

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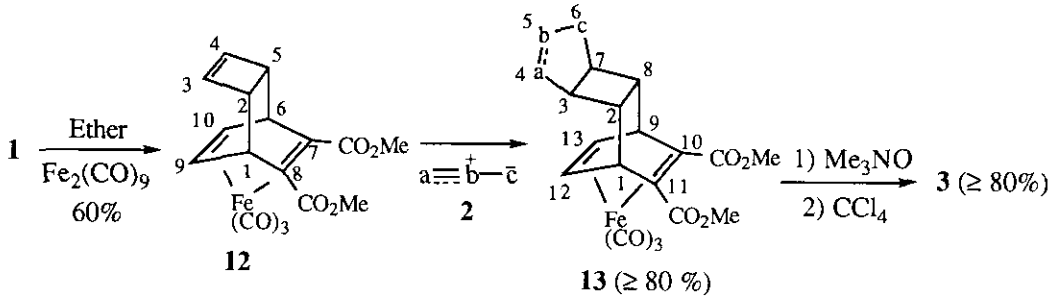

Scheme 4

with $Fe_2(CO)_9$ in hexane at 50 °C (40%) while the latter possibility is suggested by the synthesis of **11** by treatment of the corresponding polyene in hexane/benzene with $Fe_2(CO)_9$ at 55 °C (60%).[10]

The complexation reaction of **1** was carried out in refluxing ether in the presence of a large excess of $Fe_2(CO)_9$ and the stable η^4 complex (**12**) as orange prisms was isolated in fair yield (60%). Structure (**12**) rests firmly on elemental analysis, IR and ^{1}H NMR spectra and on its behavior in 1,3-dipolar cycloadditions. In particular, the ^{1}H NMR spectrum of **12** displays a broad singlet attributable to the two

cyclobutene protons at δ ($CDCl_3$) 5.96 [δ ($CDCl_3$) 6.06 in **1**] while the two protons of the complexed double bond (H-9 and H-10) experience the well known upfield shift[7a,11] and resonate at δ ($CDCl_3$) 3.69 [δ ($CDCl_3$) 6.13 in **1**]. Small changes are observed in the chemical shift of other protons on passing from **1** to **12** [e.g. H-1 and H-6 resonate at δ ($CDCl_3$) 3.85 in **1** and δ ($CDCl_3$) 3.97 in **12**].

The observed selectivity in the complexation reaction of **1** can be explained by assuming that i) the presence of the two methoxycarbonyl groups increases the propensity of the "bottom" 1,4-diene to coordinate the tricarbonyliron group enhancing the stability of the resulting complex ii) as a consequence the "front" 1,5-diene system (and, may be, also the cyclobutene bond) can not compete efficiently with the 1,4-diene system iii) either the cyclobutene double bond of compound (**12**) does not react further with $Fe(CO)_4$ or, more probably, the resulting bis-complex is so unstable towards an oxidative degradation that it reverts back to **12** simply under the action of atmospheric oxygen. Actually a better yield of **12** was obtained when the complexation reaction mixture was stirred for 24 h (after the complete disappearance of **1**) at room temperature in the presence of air.

Complex (**12**) reacted smoothly with nitrones (**2a-c**), nitrile oxides (**2d**((Ar = Ph and Ar = 2,6-$Cl_2C_6H_3$), diphenylnitrile imine (**2e**), and dimethyldiazomethane (**2f**) (an excess of 1,3-dipole was always used) to give the corresponding adducts (**13a-f**) in high yields. The tricarbonyliron group was easily removed from these compounds by treatment with trimethylamine *N*-oxide in acetonitrile. The fastest step of the decomplexation reaction is the oxidative removal of one carbonyl group to give a coordinatively unsaturated system that coordinates a molecule of acetonitrile.[12] Further oxidation is much slower. However, we have previously shown that treatment of the reaction mixture, after completion of the first step, with carbon tetrachloride leads to the final product in a clean and fast process.[12] In the case of compounds (**13**), trimethylamine *N*-oxide was added to an acetonitrile solution of **13** and the resulting reaction mixture was either left for five days at room temperature or treated with carbon tetrachloride after 24 h. With both protocols good yields of **3** were obtained.

Only azides proved unreactive with **12**, thus confirming their high reluctancy, already emphasized[5b,13] but unexplained yet, to add to cyclobutene double bonds.

In conclusion we have shown that it is possible to selectively protect with $Fe(CO)_3$ the 1,4-cyclohexadiene moiety of **1** to afford **12** whose cyclobutene double bond smoothly enters a 1,3-dipolar cycloaddition with several 1,3-dipoles. The tricarbonyliron group of the resulting cycloadducts can be easily removed oxidatively thus achieving a formal site specific attack on the polyene (**1**).

This reaction pathway provides a useful alternative for the synthesis of compounds (**3**) even if the fair yield of the complexation step makes it less appealing than was our hope.

EXPERIMENTAL

Melting points are uncorrected and were measured with a Büchi 535 apparatus. Elemental analyses were made on a Carlo Erba CHN analyzer, model 1106. IR spectra were recorded as either Nujol suspensions or films on a Perkin-Elmer 881 spectrophotometer. ^1H NMR spectra were recorded on a Bruker AE 300

(operating at 300.13 and 75.47 MHz, respectively) spectrometer with tetramethylsilane as internal standard at 20 °C for $CDCl_3$ solutions. ^1H NMR spectra were evaluated as first order spectra.

TLC were done on plates precoated with silicagel 60 GF_{254} (Merck). Spots were visualized either by spraying with 3% chromic oxide in sulfuric acid (50%) followed by heating at 120 °C or under UV light. Column chromatography was performed with silica gel 60 (70-230 mesh) Merck eluting with cyclohexane/ethyl acetate (in particular cyclohexane/ethyl acetate = 9:1- 7:3) mixtures.

1,3-Dipoles (**2**) were prepared according to standard literature procedures. Commercial cyclooctatetrene (COT) was freshly distilled prior to use.

Reaction of dimethyl tricyclo[4.2.2.0^{2,5}]deca-3,7,9-triene-7,8-dicarboxylate (1) with nitrones (2a,b). A solution of **1**[1] (0.738 g, 3.00 mmol) and **2a** or **2b** (1.00 mmol) in benzene (15 mL) was heated under reflux for 16 h. TLC analysis [cyclohexane/ethyl acetate (8:2) as eluant] of both reaction mixtures showed the presence of two adducts in addition to unreacted **1**. The spot of the higher Rf product was about three times as intense as that of the lower Rf one. Column chromatography allowed isolation of pure adducts: **3a/4a** = 69%:21% and **3b/4b** = 61%:21%.

3a: colorless prisms from petrol ether, mp 100-101 °C (Anal. Calcd for $C_{19}H_{25}NO_5$: C, 65.7; H, 7.25; N, 4.0. Found: C, 65.9; H, 7.1; N, 4.0.); ^1H NMR δ ($CDCl_3$) 1.09 (s, t-Bu), 2.13 (ddd, H-2, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 3.2 Hz and $J_{2,8}$ = 8.5 Hz), 2.37 (br ddd, H-3, $J_{2,3}$ = 3.2 Hz, $J_{3,4\text{-exo}}$ = 6.0 Hz and $J_{3,7}$ = 6.0 Hz), 2.42 (br dd, H-4-exo, $J_{3,4\text{-exo}}$ = 6.0 Hz and $J_{4\text{-endo},4\text{-exo}}$ = 6.0 Hz), 2.46 (br ddd, H-8, $J_{2,8}$ = 8.5 Hz, $J_{7,8}$ = 2.2 Hz and $J_{8,9}$ = 4.5 Hz), 2.72 (d, H-4-endo, $J_{4\text{-endo},4\text{-exo}}$ = 6.0 Hz), 3.76 (s, 6 H, two OMe), 3.79 (dd, H-7, $J_{3,7}$ = 6.0 Hz and $J_{7,8}$ = 2.2 Hz), 4.10 (ddd, H-1, $J_{1,2}$ = 4.0 Hz, $J_{1,12}$ = 5.5 Hz and $J_{1,13}$ = 2.6 Hz), 4.15 (ddd, H-9, $J_{8,9}$ = 4.5 Hz, $J_{9,12}$ = 2.5 Hz and $J_{9,13}$ = 5.5 Hz) and 6.47 (m, H-12 and H-13).

4a: colorless oil (Anal. Calcd for $C_{19}H_{25}NO_5$: C, 65.7; H, 7.25; N, 4.0. Found: C, 65.8; H, 7.2; N, 4.2.); ^1H NMR δ ($CDCl_3$) 1.04 (s, t-Bu), 2.51 (br m, 1 H, H-3-endo), 2.72 (dd, H-11, $J_{1,11}$ = 4.1 Hz and $J_{8,11}$ = 4.6 Hz), 2.78 (dd, H-8, $J_{7,8}$ = 4.5 Hz and $J_{8,11}$ = 4.6 Hz), 3.03 (br m, H-3-exo), 3.08 (br m, H-2), 3.22 (dd, H-1, $J_{1,2}$ = 2.1 Hz and $J_{1,11}$ = 4.1 Hz), 3.55 (m, H-7, $J_{6,7}$ = 3.5 Hz and $J_{7,8}$ = 4.5 Hz), 3.78 and 3.82 (two s, two OMe), 4.38 (dd, H-6, $J_{2,6}$ = 7.5 Hz and $J_{6,7}$ = 3.5 Hz), 6.33 and 6.38 (two d, H-9 and H-10, $J_{9,10}$ = 2.7 Hz).

3b: colorless prisms from petrol ether, mp 94-96 °C (Anal. Calcd for $C_{20}H_{25}NO_5$: C, 66.8; H, 7.0; N, 3.9. Found: C, 66.6; H, 6.8; N, 3.8.); ^1H NMR δ ($CDCl_3$) 1.10 and 1.35 (two s, two Me), 1.37, 1.52, 1.94 (three m, 4 H), 2.22 (m, 1 H), 2.34 (dd, H-3, $J_{2,3}$ = 2.5 Hz and $J_{3,7}$ = 6.2 Hz), 2.57 (m, 1 H), 3.53 (dd, H-4, J = 7.0 and 9.5 Hz), 3.73 and 3.74 (two s, two OMe), 3.92 (dd, H-7, $J_{3,7}$ = 6.2 Hz and $J_{7,8}$ = 2.4 Hz), 4.12 (m, H-1 and H-9), 6.48 (m, H-12 and H-13).

4b: colorless prisms from petrol ether, mp 69-70 °C (Anal. Calcd for $C_{20}H_{25}NO_5$: C, 66.8; H, 7.0; N, 3.9. Found: C, 66.8; H, 7.1; N, 4.0.); ^1H NMR (80 MHz) δ ($CDCl_3$) 1.10 (s, 6 H, two Me), 1.3-2.1 (m, 4 H), 2.40-2.80 (m, H-2, H-8 and H-11), 3.27 and 3.50 (two m, H-1, H-3 and H-7), 3.78 and 3.80 (two s, two OMe), 4.52 (dd, H-6, $J_{2,6}$ = 8.5 Hz and $J_{6,7}$ = 3.5 Hz), 6.38 and 6.42 (two d, H-9 and H-10, $J_{9,10}$ = 2.5 Hz).

Reaction of (1) with dimethyldiazomethane (2f). The reaction of **1** (0.246 g, 1.00 mmol) with excess **2f** (≈ 0.2 g, ≈ 3 mmol) in ether (50 mL) went to completion in less than 1 h. Adduct (**5f**) was isolated in quantitative yields by evaporation of the solvent.

5f: colorless prisms from petrol ether, mp 124-126 °C (Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.5; H, 6.4; N, 8.9. Found: C, 64.8; H, 6.4; N, 8.7.); ^{1}H NMR δ ($CDCl_3$) 1.28 and 1.62 (two s, two Me), 2.54 (dd, 2 H, J = 3.2 and 4.2 Hz), 3.01 (ddd, 1 H, J = 2.0, 3.5 and 6.0 Hz), 3.74 and 3.76 (two s, two OMe), 3.75 (m, 1 H), 3.80 (m, 1 H, J = 2.5, 3.0 and 6.0 Hz), 5.71 and 5.89 (two d, H-9 and H-10, $J_{9,10}$ = 2.5 Hz), 5.77 (m, H-12 and H-13).

Reaction of (1) with aryl azides (2g). A solution of *p*-cyanophenyl azide or *p*-nitrophenyl azide (1.00 mmol) and **1** (0.492 g, 2.00 mmol) in toluene (10 mL) was kept at 35 °C for 6 days. The precipitated solid was filtered off (≈ 95%) and consisted of pure adduct (**4g**). Tlc analysis of the mother liquor showed the presence of the sole **4g** in addition to unreacted **1**.

4g (Ar = *p*-CNC_6H_4): colorless prisms, mp 185-189 °C (decomp) (Anal. Calcd for $C_{21}H_{18}N_4O_4$: C, 64.6; H, 4.65 ; N, 14.35. Found: C, 64.8; H, 4.5; N, 14.1.); ^{1}H NMR δ ($CDCl_3$) 2.82 (dd, 1 H, J ≈ 4.5 and 4.5 Hz), 2.87 (dd, 1 H, J = ≈ 4.5 and 4.5 Hz), 3.48 and 3.76 (two s, two OMe), 3.89 (dd, H-7, $J_{6,7}$ = 2.9 Hz and $J_{7,8}$ = 4.5 Hz), 4.15 (dd, H-1, $J_{1,2}$ = 3.1 Hz and $J_{1,11}$ = 4.5 Hz), 4.19 (dd, H-6, $J_{6,7}$ = 2.9 Hz and $J_{2,6}$ = 10.9 Hz), 4.99 (dd, H-2, $J_{1,2}$ = 3.1 Hz and $J_{2,6}$ = 10.9 Hz), 7.31 and 7.61 (4H, aromatic protons).

4g (Ar = *p*-$NO_2C_6H_4$): yellow needles, mp 210 °C (decomp) (Anal. Calcd for $C_{20}H_{18}N_4O_6$: C, 58.5; H, 4.4; N, 13.65. Found: C, 58.2; H, 4.4; N, 13.6.); ^{1}H NMR δ ($CDCl_3$) 2.85 (dd, 1 H, J ≈ 4.5 and 4.5 Hz), 2.91 (dd, 1 H, J = ≈ 4.5 and 4.5 Hz), 3.49 and 3.79 (two s, two OMe), 3.94 (dd, H-7, $J_{6,7}$ = 2.9 Hz and $J_{7,8}$ = 4.5 Hz), 4.18 (dd, H-1, $J_{1,2}$ = 3.1 Hz and $J_{1,11}$ = 4.5 Hz), 4.23 (dd, H-6, $J_{6,7}$ = 2.9 Hz and $J_{2,6}$ = 11.0 Hz), 5.03 (dd, H-2, $J_{1,2}$ = 3.1 Hz and $J_{2,6}$ = 11.0 Hz), 7.35 and 8.11 (4H, aromatic protons).

Reaction of nitrones (2a) and (2b) with cyclooctatetraene. A solution of *t*-butyl nitrone (0.435 g, 4.31 mmol) in cyclooctatetraene (8.2 g, 78.8 mmol) was left at 35 °C for 5 days. Cyclooctatetraene was evaporated off under reduced pressure and the oily residue column chromatographed [cyclohexane/ethyl acetate (7:3) as eluant] to afford, in order of elution, adduct (**6a**) (62 mg, 7%), adduct (**7a**) (84 mg, 9.5%) and two bisadducts [higher R_f: 160 mg; lower R_f: 106 mg].

Compound (**7a**) was obtained (85% yield) as the exclusive product from the reaction of **2a** with excess styrene at rt.

The two bisadducts were also obtained in the same ratio from the reaction of **2a** with **6a**.

6a: colorless prisms from petrol ether, mp 41-42 °C (Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.3; N, 6.8. Found: C, 75.9; H, 9.1; N, 6.6.); ^{1}H NMR δ ($CDCl_3$) 1.10 (s, t-Bu), 2.35 (dd, H-3-endo, J = 6.0 and 9.0 Hz), 2.50-3.35 (m, 4 H), 4.35 (dd, H-6, $J_{3,6}$ = 7.0 Hz and $J_{6,7}$ = 3.0 Hz), 5.68 (m, 4 H, olefinic protons).

7a: colorless oil (Anal. Calcd for $C_{13}H_{19}NO$: C, 76.05; H, 9.3; N, 6.8. Found: C, 76.3; H, 9.2; N, 6.9.).

Higher R_f bisadduct: colorless prisms from petrol ether, mp 70-72 °C (Anal. Calcd for $C_{18}H_{30}N_2O_2$: C, 70.55; H, 9.9; N, 9.1. Found: C, 70.4; H, 10.0; N, 8.9.); the ^{1}H NMR spectrum ($CDCl_3$) of this product

displays two singlets at δ 1.10 and 1.15 for the two t-Bu groups and a broad signal for the two olefinic protons at δ 5.77.

Lower R_f bisadduct: colorless prisms from petrol ether, mp 72-73 °C (Anal. Found: C, 70.6; H, 9.8; N, 9.3.); the ^{1}H NMR spectrum ($CDCl_3$) of this product displays two singlets at δ 1.10 and 1.15 for the two t-Bu groups while the two olefinic protons absorb at δ 5.70 (br d, J = 11.0 Hz) and 5.88 (dd, J = 4.0 Hz and J = 11.0 Hz), respectively.

Likewise, a solution of 5,5-dimethylpyrroline *N*-oxide (510 mg, 4.51 mmol) in cyclooctatetraene (8.00 g, 76.9 mmol) was set aside for 14 days at 35 °C. Column chromatography of the oily residue, obtained after evaporation of COT from the reaction mixture, led to isolation of **6b** (56 mg, 6%) and **7b** (79 mg, 8%) in order of elution [cyclohexane/ethyl acetate (7:3) as eluant].

Compound (**7b**) was isolated as the sole adduct from the reaction of **2b** with excess styrene at rt.

6b: colorless prisms from petrol ether, mp 65-66 °C (Anal. Calcd for $C_{14}H_{19}NO$: C, 77.4; H, 8.8; N, 6.45. Found: C, 77.7; H, 8.9; N, 6.3.) ; ^{1}H NMR δ ($CDCl_3$) 1.15 and 1.39 (two s, two Me), 1.40, 1.53, 1.93 and 2.05 (four m, 4 H), 2.82 (m, 1 H), 3.18 (m, 1 H), 3.21 (ddd, H-2, $J_{1,2}$ = 4.5 Hz, $J_{2,6}$ = 6.7 Hz and $J_{2,7}$ = 1.0 Hz), 3.68 (dd, H-3, J = 7.0 and 9.1 Hz), 4.53 (dd, H-6, $J_{2,6}$ = 6.7 Hz and $J_{6,7}$ = 3.0 Hz), 5.62 and 5.73 (two m, 4 H, olefinic protons).

7b: colorless oil (Anal. Calcd for $C_{14}H_{19}NO$: C, 77.4; H, 8.8; N, 6.45. Found: C, 77.4; H, 8.8; N, 6.6.) ; ^{1}H NMR (80 MHz) δ ($CDCl_3$) 1.12 and 1.39 (two s, two Me), 2.45 (m, 2 H, H-4), 4.05 (complex m, H-3), 4.95 (dd, H-5, $J_{4,5}$ = 8.0 and ≈ 8.0 Hz), 7.20 (m, 5 H, aromatic protons).

The minor product cited in our previous study of the cycloaddition of **2c** with COT (see experimental part of reference 2) corresponds to **7c**.

Compounds (**6a**) (0.256 g, 1.25 mmol) and (**6b**) (0.271 g, 1.25 mmol), respectively, were reacted with excess dimethyl acetylenedicarboxylate (0.355 g, 2.50 mmol) in benzene (10 mL) at rt for three d. Evaporation of the solvent and column chromatography afforded compounds (**3a**) and (**3b**), respectively, in ≈ 80% yield.

Synthesis of 8, 9 and 12. To a solution of dimethyl bicyclo[2.2.2]octa-2,5-diene-2,3-dicarboxylate (0.555 g, 2.50 mmol) and, respectively, dimethyl tricyclo[4.2.2.$0^{2,5}$]octa-3,7-diene-7,8-dicarboxylate[14] (0.620 g, 2.50 mmol) in ether (30 mL) $Fe_2(CO)_9$ (1.82 g, 5.0 mmol) was added and the resulting mixture heated under reflux until complete disappearance of the starting diene as judged by TLC (5 h). Insoluble materials were filtered off and the solvent evaporated to give a brown-orange oily residue which was column chromatographed to afford pure **8** (0.498 g, 55%) and **9** (0.747 g, 77%), respectively.

8: orange plates from cyclohexane, mp 113-115 °C (decomp) (Anal. Calcd for $C_{15}H_{14}O_7Fe$: C, 49.8 ; H, 3.9. Found: C, 50.0 ; H, 3.8.); IR ν_{max} (Nujol) 2028, 1981, 1952, 1710 and 1695 cm^{-1}; ^{1}H NMR δ ($CDCl_3$) 1.17 (m, 2 H), 1.59 (m, 2 H), 3.69 (s, 6 H, two OMe), 3.88 (br s, H-1, H-4, H-5 and H-6). .

9: orange prisms from petrol ether, mp 104-105 °C (decomp) (Anal. Calcd for $C_{17}H_{16}O_7Fe$: C, 52.6; H, 4.2. Found: C, 52.7; H, 4.3.); IR ν_{max} (Nujol) 2037, 1990, 1964, 1720 and 1690 cm^{-1}; ^{1}H NMR δ ($CDCl_3$)

1.55 (m, 2 H), 1.96 (m, 2 H), 2.48 (m, H-2 and H-5), 3.68 (s, 6 H, two OMe), 3.82 (m, H-1 and H-6), 4.06 (m, H-9 and H-10).

Complexation of **1** (0.615 g, 2.50 mmol) was carried out under the same conditions as those used for preparation of **8** and **9** but with a larger excess of $Fe_2(CO)_9$ (2.73 g, 7.5 mmol) and heating under reflux for 12 h. TLC analysis showed the presence, aside from **12**, of a further yellow product which however disappeared when the reaction mixture was stirred in the presence of air (12 h). Inorganic products were filtered off and the solvent evaporated to leave a yellow-orange oily residue which was purified by column chromatography [cyclohexane/ethyl acetate (95:5) as eluant, 60% yield (0.579 g) of **12**].

12: orange prisms from petrol ether, mp 94-95°C (decomp) (Anal. Calcd for $C_{17}H_{14}O_7Fe$: C, 52.9; H, 3.65. Found: C, 52.8; H, 3.5.); IR ν_{max} (Nujol) 2040, 1991, 1959, 1722 and 1683 cm^{-1}; ^1H NMR δ ($CDCl_3$) 2.82 m, H-2 and H-5), 3.69 (m, H-9 and H-10), 3.70 (s, 6 H, two OMe), 3.97 (m, H-1 and H-6), 5.96 (br s, H-3 and H-4). For comparison the ^1H NMR spectrum ($CDCl_3$) of **1** is as follows: δ 2.72 (m, H-2 and H-5), 3.78 (s, 6 H, two OMe), 3.85 (m, H-1 and H-6), 6.06 (s, H-3 and H-4) and 6.13 (m, H-9 and H-10).

Reaction of dimethyl 7-10-tetrahapto-tricyclo[4.2.2.$0^{2,5}$]deca-3,7,9-triene-7,8-dicarboxylate (12) with nitrones (2a-c). A solution of **12** (0.193 g, 0.50 mmol) and of nitrones (**2a-c**) (1.00 mmol), respectively, in benzene (5 mL) was kept at 35 °C under nitrogen in the dark for 10 d. TLC analysis showed the disappearance of **12** and formation of only one product, i.e., **13**, which was separated from the excess nitrone by column chromatography [cyclohexane/ethyl acetate (7:3) as eluant; **13a**, 83%; **13b**, 88%; **13c**, 80%].

13a: yellow prisms from petrol ether, mp 129-130 °C (Anal. Calcd for $C_{22}H_{25}NO_8Fe$: C, 54.2; H, 5.2; N, 2.9. Found: C, 53.95; H, 5.35; N, 3.0.); IR ν_{max} (Nujol) 2050, 1991, 1950, 1720 and 1680 cm^{-1}; ^1H NMR (80 MHz) δ ($CDCl_3$) 1.10 (s, t-Bu), 2.00-2.87 (m, 5 H), 3.73 (s, 6 H, two OMe), 4.00 (m, 5 H).

13b: yellow prisms from petrol ether, mp 148-149 °C (Anal. Calcd for $C_{23}H_{25}NO_8Fe$: C, 55.3; H, 5.05; N, 2.8. Found: C, 55.0; H, 4.8; N, 2.7.); IR ν_{max} (Nujol) 2053, 1990, 1975, 1720 and 1690 cm^{-1}; ^1H NMR δ ($CDCl_3$) 1.09 and 1.33 (two s, two Me), 1.33, 1.51 and 1.95 (three m, 4 H), 2.26 (ddd, H-2, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 4.0 Hz and $J_{2,8}$ = 9.0 Hz), 2.51 (br ddd, H-8, $J_{2,8}$ = 9.0 Hz, $J_{7,8}$ = 2.4 Hz and $J_{8,9}$ = 4.0 Hz) 2.65, (dd, H-3, $J_{2,3}$ = 4.0 Hz and $J_{3,7}$ = 6.2 Hz), 3.55 (dd, H-4, J = 7.0 and 9.0 Hz), 3.68 and 3.70 (two s, two OMe), 4.00 (m, 3 H), 4.21 (dd, H-7, $J_{3,7}$ = 6.2 Hz and $J_{7,8}$ = 2.4 Hz).

13c yellow prisms from methanol, mp 186-188 °C (decomp) (Anal. Calcd for $C_{26}H_{23}NO_8Fe$: C, 58.55; H, 4.35; N, 2.6. Found: C, 58.6; H, 4.5; N, 2.45.); IR ν_{max} (Nujol) 2042, 1990, 1954, 1715 and 1687 cm^{-1}; ^1H NMR δ ($CDCl_3$) 2.48 (m, 1 H), 2.56 (m, 2 H), 2.91 (dd, H-3, $J_{2,3}$ = 3.5 Hz and $J_{3,7}$ = 6.5 Hz), 3.09 (m, 1 H), 3.22 (m, 1 H), 3.62 (m, 1 H), 3.66 and 3.67 (two s, two OMe), 3.95 (m, 3 H), 4.03 (m, 1 H), 4.06 (m, 2 H), 4.32 (s, H-4), 7.0-7.3 (4 H, aromatic).

Reaction of (12) with nitrile oxides (2d). Benzonitrile oxide (**2d**, Ar = Ph) was generated *in situ* from benzohydroximic acid chloride (0.156 g, 1.00 mmol, in 10 mL of benzene) by slowly (4 h) adding triethylamine (0.106 g, 1.05 mmol) in the presence of **12** (0.193 g, 0.50 mmol) under stirring. The reaction mixture was stirred at rt in the dark under nitrogen for further 24 h. Then the reaction mixture was diluted with dichloromethane, washed with water and dried with anhydrous sodium sulfate. After evaporation of the solvent pure **13d** (Ar = Ph, 0.207 g, 82%) was obtained by column chromatography (cyclohexane/ethyl acetate (7:3) as eluant).

Compound (**12**) (0.100 g, 0.259 mmol) also reacted with the stable 2,6-dichlorobenzonitrile oxide (**2d**, Ar = 2,6-$Cl_2C_6H_3$) (0.095 g, 0.505 mmol added portionwise during two days) in methanol (5 mL) at rt (in the dark and under nitrogen). After 5 d the solvent was evaporated and the yellow residue column chromatographed [cyclohexane/ethyl acetate (8:2) as eluant] to give pure **13d** (Ar = 2,6-$Cl_2C_6H_3$, 0.141 g, 95%).

13d (Ar = Ph): yellow needles from methanol, mp 162-164 °C (decomp) (Anal. Calcd for $C_{24}H_{19}NO_8Fe$: C, 57.05 ; H, 3.8; N, 2.8. Found: C, 57.1; H, 3.5; N, 2.8.); IR ν_{max} (Nujol) 2042, 1990, 1954, 1715 and 1687 cm^{-1}; ^1H NMR δ ($CDCl_3$) 2.61 (m, 1 H), 2.74 (m, 1 H), 3.62 and 3.68 (two s, two OMe), 3.78 (br d, H-3, $J_{3,7}$ = 8.0 Hz), 4.10 (m, 2 H), 4.15 (m, 1 H), 4.22 (m, 1 H), 4.78 (br d, H-7, $J_{3,7}$ = 8.0 Hz), 7.35-7.65 (5 H, aromatic protons).

13d (Ar = 2,6-$Cl_2C_6H_3$): yellow needles from methanol, mp 162-164 °C (decomp) (Anal. Calcd for $C_{24}H_{17}NO_8Cl_2Fe$: C, 50.2; H, 3.0; N, 2.4. Found: C, 50.0; H, 2.8; N, 2.5.); IR ν_{max} (Nujol) 2052, 2005, 1970, 1724 and 1688 cm^{-1}; ^1H NMR δ ($CDCl_3$) 2.87 (m, H-2 and H-8), 3.68 and 3.72 (two s, two OMe), 3.86 (dd, H-3, $J_{2,3}$ = 1.5 Hz and $J_{3,7}$ = 7.5 Hz), 4.06 (m, 3 H), 4.20 (m, 1 H), 4.87 (dd, H-7, $J_{3,7}$ = 7.5 Hz and $J_{7,8}$ = 1.5 Hz), 7.2-7.5 (3 H, aromatic protons).

Reaction of (12) with diphenylnitrile imine (2e). To a solution of **12** (0.100 g, 0.259 mmol) and *N*-α-chlorobenzylidene-*N'*-phenylhydrazine (0.115 g, 0.500 mmol) in acetonitrile (10 mL) excess triethylamine (0.101 g, 1.00 mmol) was added. The reaction mixture was stirred at rt in the dark under nitrogen for 4 d. Then the reaction mixture was diluted with benzene and washed with water. The organic layer was dried with anhydrous sodium sulfate and the solvent evaporated to give a brown yellow solid residue. Column chromatography [benzene/etyl acetate (95:5) as eluant] allowed isolation of pure **13e** in 82% yield (0.123 g).

13e: yellow prisms from methanol, mp 187-189 °C (decomp) (Anal. Calcd for $C_{30}H_{24}N_2O_7Fe$: C, 62.1; H, 4.2; N, 4.8. Found: C, 62.3; H, 4.3; N, 4.7.); IR ν_{max} (Nujol) 2049, 1998, 1973, 1708 cm^{-1}; ^1H NMR δ ($CDCl_3$) 2.58 (br s, 2 H), 3.62 (s, 6 H, two OMe), 3.71 (dd, H-3, $J_{2,3}$ = 3.0 Hz and $J_{3,7}$ = 9.5 Hz), 4.16 (m, 2 H), 4.22 (m, 2 H), 4.32 (dd, H-7, $J_{3,7}$ = 9.5 Hz and $J_{7,8}$ = 2.2 Hz), 6.70-7.70 (10 H, aromatic protons).

Reaction of (12) with dimethyldiazomethane (2f). Compound (**12**) (0.251 g, 0.650 mmol) was reacted with a large excess of dimethyldiazomethane in ether at rt in the dark. After 12 h the solvent evaporated and **13f** (0.240 g, 81%) purified by column chromatography.

13f: orange-yellow prisms from petrol ether, mp 112-115 °C (Anal. Calcd for $C_{20}H_{20}N_2O_7Fe$: C, 52.65; H, 4.4; N, 6.1. Found: C, 52.6; H, 4.2; N, 6.05.); IR ν_{max} (Nujol) 2055, 1997, 1970, 1710 cm^{-1}; ^1H NMR δ ($CDCl_3$) 1.09 and 1.51 (two s, two Me), 1.81 (dd, H-7, $J_{3,7}$ = 6.5 Hz and $J_{7,8}$ = 4.5 Hz), 2.14 (ddd, H-8, $J_{2,8}$ = 9.0 Hz, $J_{7,8}$ = 4.5 Hz and $J_{8,9}$ = 4.0 Hz), 2.28 (ddd, H-2, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 3.0 Hz and $J_{2,8}$ = 9.0 Hz), 3.65 and 3.68 (two s, two OMe), 3.95 (ddd, H-9, $J_{9,12}$ = 1.6 Hz, $J_{9,13}$ = 6.0 Hz and $J_{8,9}$ = 4.0 Hz), 3.99 (ddd, H-13, $J_{1,13}$ = 1.6 Hz, $J_{9,13}$ = 6.0 Hz and $J_{12,13}$ = 6.0 Hz), 4.08 (ddd, H-12, $J_{1,12}$ = 6.0 Hz, $J_{9,12}$ = 1.6 Hz and $J_{12,13}$ = 6.0 Hz), 4.13 (ddd, H-1, $J_{1,2}$ = 4.0 Hz, $J_{1,12}$ = 6.0 Hz and $J_{1,13}$ = 1.6 Hz).

Decomplexation reaction of compounds (13). To a solution of compound (**13**) (0.500 mmol) in acetonitrile (10 mL) an excess of trimethylamine *N*-oxide dihydrate (300 mg, 2.70 mmol) was added under stirring at rt. A strong odor of trimethylamine developed at once and after some hours TLC analysis showed, in addition to compound (**3**), the presence of a new yellow spot which exhibited a very low R_f. After four-five days the reaction mixture was diluted with dichloromethane and the solid precipitate filtered off. The organic layer was washed with water, dried and evaporated to leave compound (**3**) that was purified by column chromatography [**3a**, 95%; **3b**, 93%; **3c**, 85%; **3d** (Ar = Ph), 86%; **3d** (Ar = 2,6-$Cl_2C_6H_3$), 95%, **3e**, 81%; **3f**, 80%]. This compound was equal in every respect to adduct **3** obtained from the corresponding 1,3-dipolar cycloaddition of **2** to **1** (when formed) or from treatment by DMAD of the adduct of **2** with COT.

In an alternative procedure the acetonitrile solution after 24 h was diluted with carbon tetrachloride and the solid precipitate filtered off. The organic layer washed with water, dried and evaporated to give **3** (purified by column chromatography).

3d (Ar = 2,6-$Cl_2C_6H_3$): colorless prisms from EtOH, mp 169-171 °C (Anal. Calcd for $C_{21}H_{17}NO_5Cl_2$: C, 58.1; H, 3.95; N, 3.2. Found: C, 58.1; H, 4.2; N, 3.2.); ^1H NMR δ ($CDCl_3$) 2.74 and 2.78 (two m, H-2 and H-8), 3.57 (dd, H-3, $J_{2,3}$ = 3.4 Hz and $J_{3,7}$ = 7.6 Hz), 3.76 and 3.81 (two s, two OMe), 4.13 (ddd, H-9, $J_{8,9}$ = 3.8 Hz, $J_{9,12}$ = 2.4 Hz and $J_{9,13}$ = 5.4 Hz), 4.32 (ddd, H-1, $J_{1,2}$ = 3.8 Hz, $J_{1,12}$ = 5.4 Hz and $J_{1,13}$ = 2.4 Hz), 4.57 (dd, H-7, $J_{3,7}$ = 7.6 Hz and $J_{7,8}$ = 2.4 Hz), 6.56 (m, H-12 and H-13), 7.15-7.45 (3 H, aromatic protons).

3f: colorless prisms from cyclohexane, mp 110 °C (decomp) (Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.5; H, 6.4; N, 8.9. Found: C, 64.7; H, 6.5; N, 8.8.); ^1H NMR δ ($CDCl_3$) 1.11 and 1.52 (two s, two Me), 1.56 (dd, 1 H, H-7, $J_{3,7}$ = 6.5 Hz and $J_{7,8}$ = 4.0 Hz), 2.10 (ddd, H-8, $J_{2,8}$ = 8.5 Hz, $J_{7,8}$ = 4.0 Hz and $J_{8,9}$ = 4.0 Hz), 2.24 (ddd, H-2, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 3.0 Hz, $J_{2,8}$ = 8.5 Hz), 3.77 and 3.78 (two s, two OMe), 4.05 (ddd, 1 H, J = 2.0, J = 4.0 and J = 6.0 Hz), 4.30 (ddd, 1 H, J = 2.0, J = 4.0 and J = 6.0 Hz), 4.61 (dd, H-3, $J_{2,3}$ = 3.0 Hz and $J_{3,7}$ = 6.5 Hz), 6.52 and 6.59 (two m, H-12 and H-13).

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