Inverse-Electron Demand [$_\pi$2 + $_\sigma$2 + $_\sigma$2] Cycloaddition Reaction of Dimethyl Oxaquadricyclane-2,3-dicarboxylate with Cyclooctyne

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Dedicated to the memory of Professor Raymond N. Castle

A first example of an inverse-electron demand [$_\pi$2 + $_\sigma$2 + $_\sigma$2] cycloaddition reaction of dimethyl oxaquadricyclane-2,3-dicarboxylate was reported: cyclooctyne underwent cycloaddition with dimethyl oxaquadricyclane-2,3-dicarboxylate to afford the corresponding adducts one of whose structure was confirmed by a single crystal X-ray analysis.

Cyclooctyne is the smallest cyclic alkyne that is stable at room temperature and has been prepared by a number of methods that either start from cyclooctene or from cyclooctanone [1-5]. In spite of high strain and high reactivity of cyclooctyne as well as the synthetic potential of its cycloadditions, relatively few examples of cycloaddition reactions have been reported. Specifically, its cycloadditions and subsequent ring enlargement have been elegantly utilized for construction of the medium and large ring compounds [6]. Since the reaction of dimethyl oxaquadricyclane-2,3-dicarboxylate with electron-deficient alkynes and alkenes is known to proceed *via* carbonyl ylide [7a] and the subsequent cycloaddition has been established to take place in *exo* fashion with alkene such as maleic anhydride [5b], we envisaged that the cycloadditions of cyclooctyne with oxaquadricyclane might proceed *via* an inverse-electron demand *1,3-dipolar cycloaddition* [8]. However, this was not indeed the case and is the subject of the present communication.
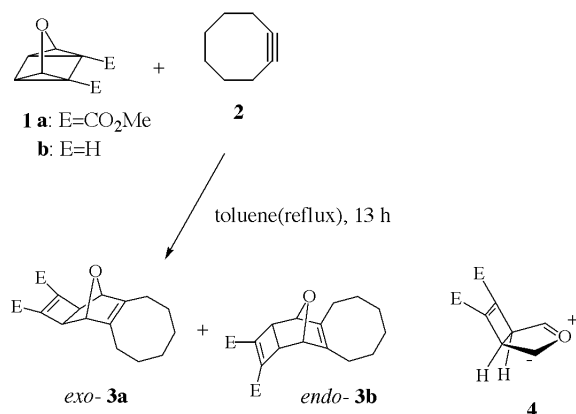
Reaction of dimethyl oxaquadricyclane-2,3-dicarboxylate (**1a**) with cyclooctyne (**2**) in refluxing toluene for 7 hours gave a mixture of colorless crystals and an oil after separation by silica gel chromatography. They have proven to be 1:1 adducts based upon their mass and elemental analyses. Initially, from consideration of their ^{1}H and ^{13}C nmr spectra (see Experimental), we thought, as shown in Scheme 1, one of the adduct (solid) had structure **3a,** the other one (oil) **3b** which are formed by cycloaddition of Prinzbach's carbonyl

Table 1

Crystal Data for **2a**

Formula	$C_{18}H_{22}O_5$
Crystal dimensions(mm)	0.22 x 0.42 x 0.94
M(amu)	318.37
Monoclinic space group	P2$_1$/n (no. 14)
a(Å)	7.838(6)
b(Å)	30.02(1)
c(Å)	7.759(7)
β(degree)	113.18(6)
U(Å^3)	1678(2)
Z	4
Dc(g cm^{-3})	1.260
μ(cm^{-1})	0.85
F(000)	680
Radiation Mo-Kα	λ=0.71069 Å
Diffractometer	Rigaku AFC5S
Orienting reflections, range	25, 35.20°<2θ<39.00°
T(K)	295
Scan method	ω
Data collection range	6.0°<2θ<55.0°
No. unique reflections	3936
No. of observed reflections with I>2σ(I)	1669
No. of parameters	208
R[a]	12.2%
Rw[b]	14.4%
Largest shift/esd, final cycle	0.03
Largest positive peak(e Å^{-3})	0.42
Largest negative peak(e Å^{-3})	-0.52

[a] R=[Σ|*Fo*| - |*Fc*||/Σ|*Fo* |; [b] R$_W$={[Σw(|*Fo*| - |*Fc*|)^2]/[Σw(|*Fo*|)^2]}$^{1/2}$; Weighting scheme: w=4*Fo*^{2}/σ^2(*Fo*^{2}).

Scheme 1

1 a: E=CO₂Me
  b: E=H

2

toluene(reflux), 13 h

exo- **3a** *endo-* **3b** **4**
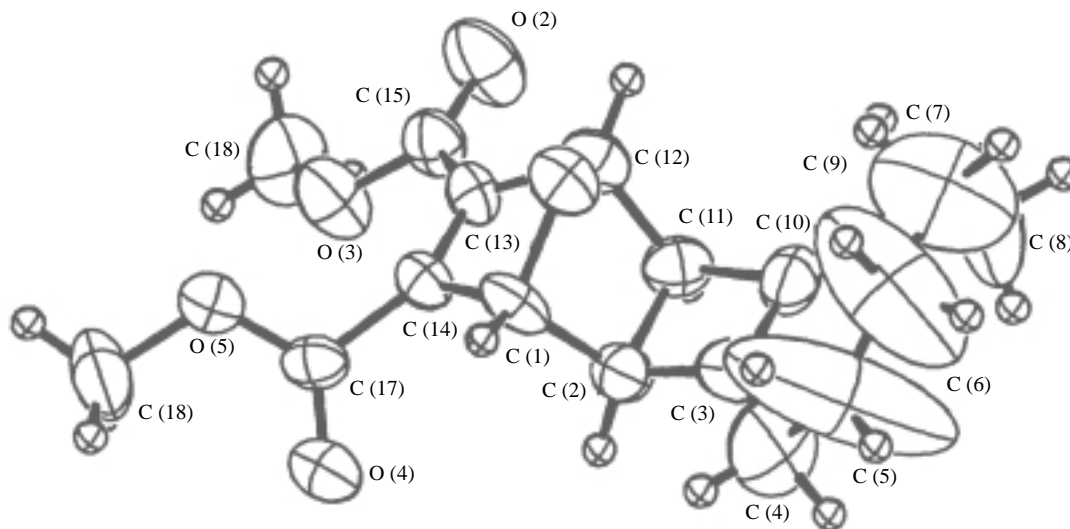
Figure 1. ORTEP Drawing of **5a**.

Table 2

Bond Lengths(Å) and Bond Angles(deg)

O(1)-C(1)	1.43(1)	C(6)-H(8)	0.988
O(1)-C(12)	1.48(1)	C(7)-C(8)	1.47(2)
O(2)-C(15)	1.18(1)	C(7)-H(9)	1.037
O(3)-C(15)	1.34(1)	C(7)-H(10)	0.939
O(3)-C(16)	1.43(1)	C(8)-C(9)	1.45(1)
O(4)-C(17)	1.18(1)	C(8)-H(11)	0.946
O(5)-C(17)	1.31(1)	C(8)-H(12)	1.035
O(5)-C(18)	1.45(1)	C(9)-C(10)	1.48(1)
C(1)-C(2)	1.56(1)	C(9)-H(13)	0.966
C(1)-C(14)	1.51(1)	C(9)-H(14)	0.963
C(1)-H(1)	0.975	C(10)-C(11)	1.52(1)
C(2)-C(3)	1.50(1)	C(11)-C(12)	1.49(1)
C(2)-C(11)	1.57(1)	C(11)-H(15)	0.979
C(2)-H(2)	0.965	C(12)-C(13)	1.51(1)
C(3)-C(4)	1.53(2)	C(12)-H(16)	0.962
C(3)-C(10)	1.34(2)	C(13)-C(14)	1.33(1)
C(4)-C(5)	1.33(2)	C(13)-C(15)	1.48(1)
C(4)-H(3)	0.966	C(14)-C(17)	1.50(1)
C(4)-H(4)	1.009	C(16)-H(17)	1.009
C(5)-C(6)	1.33(3)	C(16)-H(18)	0.943
C(5)-H(5)	1.145	C(16)-H(19)	0.946
C(5)-H(6)	0.836	C(18)-H(20)	0.939
C(6)-C(7)	1.39(3)	C(18)-H(21)	0.976
C(6)-H(7)	0.986	C(18)-H(22)	0.968
C(1)-O(1)-C(12)	96.4(6)	H(11)-C(8)-H(12)	102.99
C(15)-O(3)-C(16)	118.1(8)	C(8)-C(9)-C(10)	119(1)
C(17)-O(5)-C(18)	117.1(7)	C(8)-C(9)-H(13)	104.49
O(1)-C(1)-C(2)	102.1(7)	C(8)-C(9)-H(14)	110.63
O(1)-C(1)-C(14)	100.4(7)	C(10)-C(9)-H(13)	107.20
O(1)-C(1)-H(1)	114.59	C(10)-C(9)-H(14)	107.90
C(2)-C(1)-C(14)	105.1(6)	H(13)-C(9)-H(14)	107.13
C(2)-C(1)-H(1)	116.39	C(3)-C(10)-C(9)	137.4(8)
C(14)-C(1)-H(1)	116.11	C(3)-C(10)-C(11)	93.5(8)
C(1)-C(2)-C(3)	115.8(6)	C(9)-C(10)-C(11)	128.9(9)
C(1)-C(2)-C(11)	100.4(7)	C(2)-C(11)-C(10)	85.4(7)
C(1)-C(2)-H(2)	114.86	C(2)-C(11)-C(12)	102.4(8)

Table 2 (continued)

Bond Lengths(Å) and Bond Angles(deg)

C(3)-C(2)-C(11)	85.9(7)	C(2)-C(11)-H(15)	116.33
C(3)-C(2)-H(2)	117.12	C(10)-C(11)-C(12)	117.1(6)
C(11)-C(2)-H(2)	118.40	C(10)-C(11)-H(15)	116.03
C(2)-C(3)-C(4)	126(1)	C(12)-C(11)-H(15)	115.08
C(2)-C(3)-C(10)	95.2(8)	O(1)-C(12)-C(11)	102.6(7)
C(4)-C(3)-C(10)	138.2(9)	O(1)-C(12)-C(13)	99.0(7)
C(3)-C(4)-C(5)	119(1)	O(1)-C(12)-H(16)	114.48
C(3)-C(4)-H(3)	109.72	C(11)-C(12)-C(13)	106.7(7)
C(3)-C(4)-H(4)	107.23	C(11)-C(12)-H(16)	115.82
C(5)-C(4)-H(3)	115.64	C(13)-C(12)-H(16)	116.18
C(5)-C(4)-H(4)	99.42	C(12)-C(13)-C(14)	106.3(7)
H(3)-C(4)-H(4)	103.54	C(12)-C(13)-C(15)	122.1(8)
C(4)-C(5)-C(6)	141(2)	C(14)-C(13)-C(15)	131.1(7)
C(4)-C(5)-H(5)	92.96	C(1)-C(14)-C(13)	106.0(7)
C(4)-C(5)-H(6)	114.33	C(1)-C(14)-C(17)	122.3(8)
C(6)-C(5)-H(5)	88.26	C(13)-C(14)-C(17)	130.8(7)
C(6)-C(5)-H(6)	103.84	O(2)-C(15)-O(3)	122.4(8)
H(5)-C(5)-H(6)	101.98	O(2)-C(15)-C(13)	124.9(7)
C(5)-C(6)-C(7)	132(2)	O(3)-C(15)-C(13)	112.6(8)
C(5)-C(6)-H(7)	114.72	O(3)-C(16)-H(17)	109.21
C(5)-C(6)-H(8)	100.24	O(3)-C(16)-H(18)	113.23
C(7)-C(6)-H(7)	103.26	O(3)-C(16)-H(19)	113.06
C(7)-C(6)-H(8)	97.96	H(17)-C(16)-H(18)	105.25
H(7)-C(6)-H(8)	103.61	H(17)-C(16)-H(19)	105.04
C(6)-C(7)-C(8)	121(2)	H(18)-C(16)-H(19)	110.42
C(6)-C(7)-H(9)	104.32	O(4)-C(17)-O(5)	125.3(8)
C(6)-C(7)-H(10)	113.87	O(4)-C(17)-C(14)	121.1(8)
C(8)-C(7)-H(9)	101.98	O(5)-C(17)-C(14)	113.5(7)
C(8)-C(7)-H(10)	109.37	O(5)-C(18)-H(20)	112.34
H(9)-C(7)-H(10)	103.34	O(5)-C(18)-H(21)	110.24
C(7)-C(8)-C(9)	121(1)	O(5)-C(18)-H(22)	111.23
C(7)-C(8)-H(11)	112.89	H(20)-C(18)-H(21)	108.14
C(7)-C(8)-H(12)	104.58	H(20)-C(18)-H(22)	108.81
C(9)-C(8)-H(11)	109.72	H(21)-C(18)-H(22)	105.83
C(9)-C(8)-H(12)	103.43		

Table 3

Fractional Coordinates (x 10^5) and B(eq) (A^2) for **2a**

	X	Y	Z	B(eq)
O(1)	1.0658(7)	0.0894(2)	0.8885(7)	4.2(3)
O(2)	0.4845(8)	0.0763(3)	0.7010(9)	6.5(4)
O(3)	0.4952(8)	0.0600(2)	0.4268(8)	5.5(3)
O(4)	0.871(1)	0.0943(2)	0.2790(8)	6.1(3)
O(5)	0.8026(9)	0.0266(2)	0.3430(8)	5.0(3)
C(1)	1.065(1)	0.1017(3)	0.710(1)	4.0(4)
C(2)	1.025(1)	0.1526(3)	0.703(1)	3.7(4)
C(3)	1.157(1)	0.1794(4)	0.862(1)	5.6(5)
C(4)	1.353(2)	0.1935(5)	0.890(2)	8.5(7)
C(5)	1.485(2)	0.194(1)	1.061(2)	27(2)
C(6)	1.513(2)	0.1830(9)	1.236(2)	18(1)
C(7)	1.398(2)	0.1850(7)	1.336(2)	13(1)
C(8)	1.234(2)	0.2138(5)	1.275(2)	10.7(8)
C(9)	1.057(1)	0.1985(3)	1.139(1)	5.6(5)
C(10)	1.046(1)	0.1814(3)	0.957(1)	4.3(4)
C(11)	0.893(1)	0.1543(3)	0.811(1)	4.0(4)
C(12)	0.879(1)	0.1065(3)	0.854(1)	4.0(4)
C(13)	0.771(1)	0.0836(3)	0.669(1)	3.4(3)
C(14)	0.885(1)	0.0809(3)	0.581(1)	3.2(3)
C(15)	0.571(1)	0.0734(3)	0.607(1)	4.0(4)
C(16)	0.301(1)	0.0503(4)	0.347(1)	6.1(5)
C(17)	0.848(1)	0.0685(3)	0.382(1)	3.5(4)
C(18)	0.760(2)	0.0121(4)	0.152(1)	6.4(5)
H(1)	1.1758	0.0928	0.6900	4.8
H(2)	0.9829	0.1658	0.5797	4.2
H(3)	1.3868	0.1797	0.7949	10.6
H(4)	1.3486	0.2262	0.8592	10.6
H(5)	1.5391	0.1596	1.0449	25.9
H(6)	1.5754	0.2104	1.0735	25.9
H(7)	1.5829	0.1552	1.2815	20.0
H(8)	1.6020	0.2065	1.3060	20.0
H(9)	1.3398	0.1535	1.3196	16.7
H(10)	1.4633	0.1876	1.4659	16.7
H(11)	1.2176	0.2280	1.3759	11.9
H(12)	1.2671	0.2401	1.2068	11.9
H(13)	1.0236	0.1742	1.2016	6.4
H(14)	0.9641	0.2212	1.1154	6.4
H(15)	0.7744	0.1697	0.7476	4.9
H(16)	0.8378	0.1007	0.9540	5.0
H(17)	0.2294	0.0780	0.3502	7.4
H(18)	0.2568	0.0421	0.2198	7.4
H(19)	0.2658	0.0289	0.4165	7.4
H(20)	0.6608	0.0281	0.0639	7.6
H(21)	0.8680	0.0158	0.1204	7.6
H(22)	0.7303	-0.0194	0.1369	7.6

Scheme 2
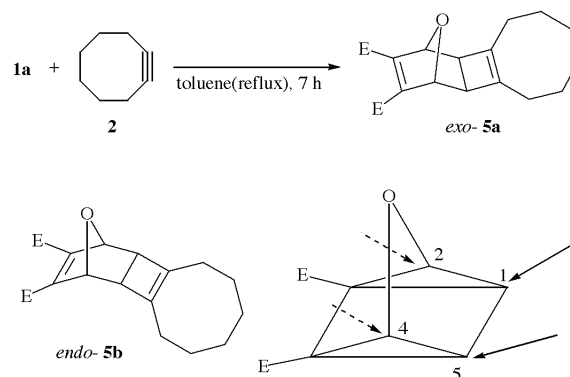
explained by a concerted $[_\pi 2 + _\sigma 2 + _\sigma 2]$ cycloaddition (1,5-attack) even in the reactions of heterosystems (Scheme 2). Teracyanoethylene (TCNE) having a very low-lying LUMO is reported to react with the parent oxaquadricyclane (**1b**) in a $[_\pi 2 + _\sigma 2 + _\sigma 2]$ fashion [10], but not to react with **1a** with a relatively lower-lying HOMO, whereas cyclooctyne (a high-lying HOMO) did react with **1a** (a low-lying LUMO), which is a first example of *an inverse-electron demand* $[_\pi 2 + _\sigma 2 + _\sigma 2]$ cycloaddition of oxaquadricyclanes. (Table 4)

Further studies are underway employing electron rich addends such as ynamines and enamines.

Table 4

HOMO and LUMO Energies (eV) of Oxaquadricyclanes (**1**), Cyclooctyne(**2**), and TCNE

	HOMO		LUMO	
	AM1	PM3	AM1	PM3
1a	-10.927	-10.984	0.437	0.408
1b	-10.209	-10.436	2.081	2.057
2	-9.997	-10.150	1.437	1.177
TCNE	-11.522	-11.402	-2.525	-2.680

EXPERIMENTAL

Spectroscopic and Analytical Data.

Dimethyl 15-Oxatetracyclo[10.2.1.0^{2,11}.0^{3,10}]pentadeca-$\Delta^{3,10}$, 13-diene-13,14-dicarboxylate (**5**).

Compound **5a** was obtained in 47% yield; mp 114.0-115.0 °C; ^{1}H nmr (deuteriochloroform): δ 4.78 (s, 2H), 3.82 (s, 6H), 2.51 (s, 2H), 2.17 (m, 4H), 1.65 (m, 4H), 1.55 (m, 4H); ^{13}C nmr (deuteriochloroform): δ 163.4, 143.4, 140.9, 77.8, 52.3, 44.0, 27.8, 26.4, 24.2. ir (potassium bromide): 2800, 2750, 1710, 1620, 1300 cm^{-1}; ms: m/z 318 (M$^+$).

Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.95; H, 6.87.

ylide **4** [7, 9] with **2**. However, a single crystal X-ray analysis of the solid product confirmed that one of the adduct had structure **5a** (*exo* adduct) which is also consistent with the ^{1}H and ^{13}C nmr spectra. Unfortunately, attempts to crystallize the other product failed, being an oil. Due to the close similarity between the NMR spectra of the solid product **5a** and that of the oil product, we believe that the oil product is the *endo* adduct **5b**. The formation of **5** can be

Compound **5b** was obtained in 41% yield as an oil; ^{1}H nmr (deuteriochloroform): δ 4.45 (s, 2H), 3.82 (s, 6H), 2.82 (s, 2H), 2.52-2.25 (m, 4H), 1.80-1.38 (m, 4H), 1.58 (m, 4H); ^{13}C nmr (deuteriochloroform): δ 161.4, 144.0, 140.0, 79.8, 51.9, 44.9, 26.5, 25.7, 24.5; ir (potassium bromide): 2820, 2770, 1720, 1600, 1300 cm^{-1}; ms: m/z 318 (M^+).

Anal. Calcd. for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.79; H, 6.82

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