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CYCLOADDITION OF SINGLET OXYGEN AND 4-METHYL-1,2,4-TRIAZOLINE-3,5-DIONE (MTAD) TO METHOXYCYCLOOCTATETRAENE (MCOT)

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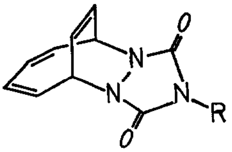
SUMMARY: The endoperoxides 6 and 7, respectively 9-methoxy- and 1-methoxy-7,8-dioxabicyclo[4.2.2]deca-2,4,7-trienes, and the urazoles 8 and 9, respectively 9-methoxy- and 2-methoxy-7,8-diazatricyclo[4.2.2]deca-2,4,9-trien-N-methyl-7,8-dicarboximide, were obtained in the cycloaddition of singlet oxygen and 4-methyl-1,2,4-triazoline-3,5-dione (MTAD) to methoxycyclooctatetraene (MCOT).

Although cyclooctatetraene (COT) reacts readily with 1,2,4-triazoline-3,5-dione (TAD) to give the [4+2]-cycloadducts 1 (minor product) and 2 (major product)[1], singlet oxygen is reportedly[2] inert towards COT. However, under persistent conditions singlet oxygenation of COT can be achieved[3], leading exclusively to the bicyclic endoperoxide 3 and none of the tricyclic endoperoxide 4 [4]. It was, therefore, of interest to see whether electron-rich cyclooctatetraenes, e.g. methoxycyclooctatetraene (MCOT), would undergo cycloaddition with singlet oxygen sufficiently well[5] in order to explore:
a) the product distribution between tricyclic and bicyclic endoperoxides 3 and 4, respectively and b) the regioselectivity of $^1O_2$ within each type of adduct. Presently we report our preliminary results on this investigation.



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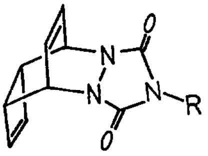

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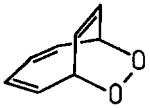

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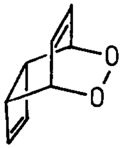

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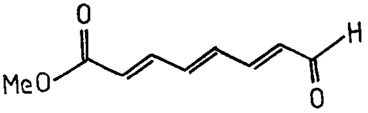
Methoxycyclooctatraene (MCOT), prepared in 77% yield according to literature[6], was submitted to the usual photosensitized oxygenation conditions[7], using tetraphenylporphyrin (TPP) as sensitizer in methylene chloride (10^{-4} M) at -20°C. After 24 h of singlet oxygenation, TLC on silica gel and ^{1}H-NMR monitoring indicated complete consumption of MCOT. The reaction mixture was roto-evaporated (0°C at 12 torr), the residue[8] triturated four times with warm 12:1 cyclohexane-ethanol, and the triturates cooled to 0°C, upon which the aldehyde-ester 5 crystallized out, mp 132-133°C from ethyl acetate (lit.[7] mp 128-130°C). The combined filtrates were roto-evaporated (0°C at 12 torr) and chromatographed on silica gel (50:1 adsorbant to substrate) at -27°C eluting with CH_2Cl_2.

As first and second fractions the bicyclic endoperoxides 6 and 7 eluted,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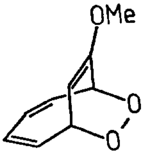
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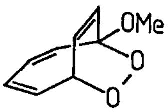
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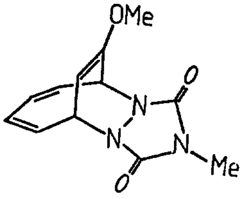
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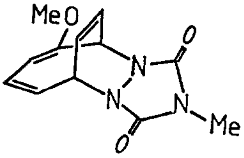
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respectively with R_F values of 0.39 and 0.32. The yields, physical constants and the spectral data are collected in Table I. Both materials gave satisfactory elemental compositions for $C_9H_{10}O_3$ by combustion analysis.

On the basis of the spectral data alone it was not possible to assign the location of the methoxy substituents in 6 and 7 unambigously. Since no adequate crystals of the endoperoxides 6 and 7 could be grown for X-ray analysis[8], we opted for investigating the cycloaddition of MCOT with 4-methyl-1,2,4-triazoline-3,5-dione (MTAD), in the hope that a structure determination of the resulting urazoles would prove useful in elucidating the structures of the endoperoxides 6 and 7.

The reaction of MCOT with MTAD in methylene chloride (10^{-4}M) at 20°C was completed within 4h. Roto-evaporation (20°C at 12 torr) of the solvent and silica gel chromatography (10:1 adsorbant to substrate) afforded the two urazoles 8 and 9. The yields, physical constants and spectral data are summarized in Table I. Both urazoles gave satisfactory elemental compositions for $C_{12}H_{13}N_3O_3$ by combustion analysis. Fortunately, it was possible to confirm the proposed structures of the urazoles 8 and 9 with the help of X-ray[9].

Indeed, the ^{1}H- and C^{13}-NMR spectra of the urazole 8 and endoperoxide 6 were so similar that by analogy the 9-methoxy-7,8-dioxabicyclo[4.2.2]deca-2,4,9-triene structure was assigned to endoperoxide 6. However, comparison of the spectra of endoperoxide 7 with those of urazole 9 clearly revealed that the methoxy substituents had distinct locations in these cycloadducts. Since the endoperoxide 7 exhibited only one bridgehead carbon resonance as a doublet at the expected δ72.0 ppm, the resonance at δ100.5 ppm (singlet) was assigned to the methoxy-substituted bridgehead.

With respect to our initially posed questions, clearly both dienophiles $^1O_2$ and MTAD afford only bicyclic cycloadducts, i.e. endoperoxides **6** and **7** and urazoles **8** and **9**, quite analogous to tetracyanoethylene (TCNE)[10]. Apparently, similar to cycloheptatriene[11] the electron-donating methoxy substituent shifts the cyclooctatraene-bicyclo[4.2.0]octa-2,4,7-triene equilibrium still further to the side of the monocyclic valence tautomer so that no tricyclic products such as **2** and **4** are formed[12]. However, in regard to the regioselectivity, while MTAD and TCNE behave identically, $^1O_2$ gives the bridgehead-substituted cycloadduct **7** instead of substitution in the butadiene bridge. Experiments are in progress to elucidate the mechanistic origin of this divergent dienophilic behavior of $^1O_2$ versus MTAD.

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REFERENCES AND FOOTNOTES

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≠ Diplomarbeit, University of Würzburg, April 1981.

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5. It is well known that alkoxy substituents activate alkenes towards singlet oxygenation, e.g. cf. A. A. Frimer, *Chem. Rev.*, **79**, 359 (1979).
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8. CAUTION! On several occasions we observed that the dry residue would spontaneously ignite with detonation. All safety precautions should be exercised.
9. Details will be published in the full report of this study.
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TABLE I: Yields, physical constants and spectral data of the endoperoxides and urazoles.

Product	Yield (%)[a]	mp. (°C)	IR ($CDCl_3$) ν(cm^{-1})	^1H-NMR ($CDCl_3$, TMS)[b]				^{13}C-NMR ($CDCl_3$, TMS)		
				type	no	δ, ppm	pattern	type	δ, ppm	pattern[c]
(6)	6[d]	51-52.5	3040	OCH_3	3	3.59	s	OCH_3	54.8	
			2975	1	1	4.92	td	1	72.8	
			2960	6	1	4.98	dt	6	75.0	
			2920	10	1	5.08	dd	10	90.3	
			2850	4	1	5.95	dd	2	125.5	
			1675	5,2,3	3	5.92-6.18	m	3	129.4	
			1365					4	131.1	
			1225					5	134.7	
								9	152.9	
(7)	5[d]	50-51.5	3025	OCH_3	3	3.3	s	OCH_3	51.2	q
			2970	6	1	4.7-4.8	dd	6	72.0	d
			2940	9,10	2	5.8-5.9	d	1	100.5	s
			2840	2,3,4,5	4	5.9-6.3	m	9	121.0	d
			1685					10	121.5	d
			1480					4	125.4	d
			1230					3	129.3	d
								5	130.5	d
								2	135.9	d
(8)	22	3	3020	NCH_3	3	3.06	s	N-CH_3	25.3	
			2940	OCH_3	3	3.59	s	1	47.0	
			2840	1,10	2	5.03	dd	6	51.2	
			1760	6	1	5.13	d	OCH_3	55.4	
			1700	3	1	5.89	dd	10	88.9	
			1660	4	1	6.01	dd	2	125.3	
			1475	5	1	6.13	dd	3	127.7	
			1400	2	1	6.25	dd	4	131.4	
			1180					5	134.3	
			1000					2xC=O	150.1 u. 150.3	
								9	150.9	
(9)	4[e]	158	3060	NCH_3	3	3.05	s			
			3010	OCH_3	3	3.65	s			
			2950	3	1	5.00	t			
			2840	1,6	2	5.11	dd			
			1760	4,5,9,10	4	5.83-6.04	m			
			1700							
			1630							
			1590							
			1475							
			1400							
			1210							

a. Isolated yields of pure product.

b. The ^1H-NMR spectra were taken at 400, 270 and 500 MHz, respectively for 6, 7 and 8 and 9.

c. Of endoperoxide 6 and urazoles 8 and 9 insufficient material was available for off-resonance spectra.

d. By ^1H-NMR total yield of endoperoxides 6 and 7 was ca. 30%; ca. 10% of 5 and ca. 60% of polymeric peroxide were observed.

e. By ^1H-NMR total yield of urazoles 8 and 9 was ca. 56%; ca. 40% of polymeric material was observed.

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