Synthetic Photochemistry. XXXIX.[1] Sensitized-Photooxygenation of 2-Benzyltropone, 2-[Hydroxy(4-nitrophenyl)methyl]tropone, and 2-(1-Hydroxy-2-oxo-2-phenylethyl)tropone. A Quenching Effect of Hydroxyl Group in the Vicinity of the Reaction Site

Akira Mori,* Hiroshi Suizu,† and Hitoshi Takeshita*
Research Institute of Industrial Science, 86, Kyushu University, Kasuga-koen, Kasuga, Fukuoka 816
†Graduate School of Engineering Sciences, 39, Kyushu University, Kasuga-koen, Kasuga, Fukuoka 816

(Received April 24, 1987)

Synopsis. Singlet-oxygen oxidation of 2-[hydroxy(4-nitrophenyl)methyl]tropone gave 6,7-dioxabicyclo[3.2.2]-nona-3,8-dien-2-one derivatives in good yields. A change of regioselectivity of the oxygenation with a remarkable rate of enhancement (23 times) in deuteriomethanol vs. methanol could be best explained in terms of the quenching of singlet oxygen by the free hydroxyl group in the vicinity of the reaction site. Similarly studied were 2-(1-hydroxy-2-oxo-2-phenylethyl)tropone and 2-benzyltropone. The stereochemistry of the oxygen adducts was elucidated by a ^{1}H NMR chemical-shift comparison.

Sensitized photooxygenation of tropones is a useful method for preparing 2,5-dihydroxytropones which are important starting materials for functionalized troponoids such as *p*-tropoquinones.[2] Among those, tropone (**1**)[3] and 2-methoxytropone (**2**)[4] gave corresponding single endoperoxides, 6,7-dioxabicyclo[3.2.2]-nona-3,8-dien-2-one and its 1-methoxy derivative (**3** and **4**), while 2-aryltropones (**5**) gave two regioisomers, 1- and 3-aryl derivatives (**6** and **7**), the former of which was predominant (ca. 2.3 : 1).[5] Thus, the oxygenation takes place predominantly at electron-rich 2,5-positions rather than less-hindered 4,7-positions. Contrary to the previous cases, 2-[hydroxy-(4-nitrophenyl)methyl]tropone (**8**)[6] and 2-(1-hydroxy-2-oxo-2-phenylethyl)tropone (**9**),[7] have now been found to react predominantly at the 4,7-positions, while 2-benzyltropone (**10**) reacted at both positions in a 1 : 1-ratio. Herein, we describe the findings.

First of all, **10** gave a 1 : 1-mixture of photooxygenation products (**11** and **12**) upon irradiation with a tungsten lamp in the presence of a sensitizer, hematoporphyrin (HMP), under an oxygen atmosphere. The reaction rate was considerably larger than those of the other substrates taken in this study. The structures of **11** and **12** were elucidated by a ^{1}H NMR analysis to be 3-benzyl-6,7-dioxabicyclo[3.2.2]nona-3,8-dien-2-one and 1-benzyl-6,7-dioxabicyclo[3.2.2]nona-3,8-dien-2-one, respectively; in **11**, there were three vinylic proton signals together with the five-proton singlet for the phenyl group, and in **12**, there were four vinylic proton signals together with rest of signals which closely resembled those of **11**. No other product was detectable in spite of the careful check of every chromatographic fraction.

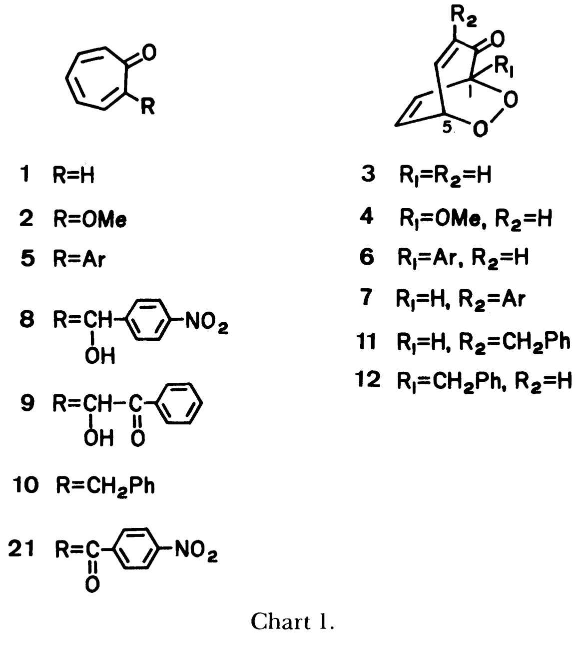

Chart 1.

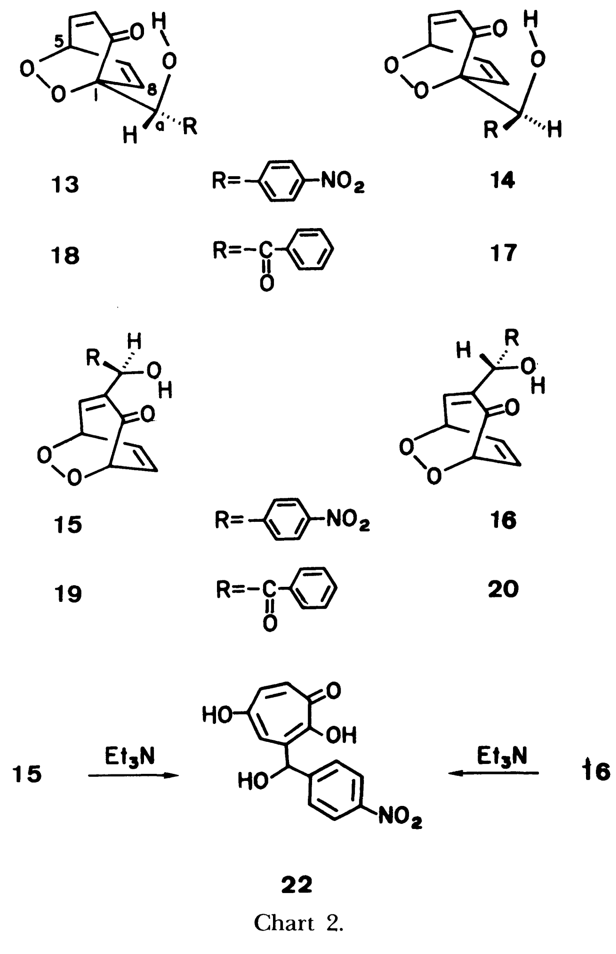

Chart 2.

Table 1. The ^{1}H NMR Chemical Shifts[8] of Photoproducts

Compd	H-C$_1$	H-C$_3$	H-C$_4$	H-C$_5$	H-C$_8$	H-C$_9$	H-C$_a$	Aryl-H
11	—	6.02	6.94	4.96	6.06	6.90	3.07, 3.40	7.1—7.4(5H)
12	5.05	—	a)	5.00	a)	a)	3.57(2H)	a)
13	—	6.02	7.02	4.96	6.42	6.97	5.22	7.66(2H), 8.17(2H)
14	—	6.02	6.98	5.03	6.26	7.05	5.31	7.70(2H), 8.21(2H)
15	5.02	—	7.12	5.19	6.50	7.02	5.58	7.56(2H), 8.18(2H)
16	5.00	—	7.09	5.17	6.54	7.04	5.73	7.56(2H), 8.20(2H)
17	—	5.95	6.92	5.02	6.73	7.05	5.24	7.4(3H), 8.0(2H)
18	—	5.95	6.92	4.96	6.65	7.05	5.62	7.4(3H), 8.0(2H)
19	b)	—	7.18	b)	6.43	6.84	5.68	7.4(3H), 8.0(2H)
20	b)	—	7.03	b)	6.47	6.91	5.84	7.4(3H), 8.0(2H)
3	5.00	6.00	7.06	5.00	6.50	7.02		

a) Appeared as overlapped signals at 6.4—6.7(2H) and 6.9—6.3(6H). b) Appeared as overlapped signals at 4.9.

The oxygenation of **8** gave four endoperoxides **13**—**16** in good yields. They were all of the possible [4+2] cycloadducts, and their structures were easily identified by the ^{1}H NMR spectroscopy; the less polar **13** and **14** were 1-substituted 6,7-dioxabicyclo[3.2.2]nona-3,8-dien-2-ones, while the more polar **15** and **16** were 3-substituted derivatives.

Similarly, **9** gave diastereomeric mixtures of 1-substituted products **17** and **18** and 3-substituted products **19** and **20**. Their stereostructure was deduced by chemical-shift comparisons; i.e., one can assume that the preferential conformer of each product must possess the internally-hydrogen-bonded structure for the C-2 carbonyl and the benzylic hydroxyl groups. As a result, one of the isomers should have the up-field shifted C-8 proton signal and a low-field shifted C-a proton signal, depending on the relative geometry to the anisotropic phenyl group. The cases were two pairs of 1-substituted derivatives: **13** and **14** and **17** and **18**. In the 3-substituted derivatives, the chemical shifts of the a-protons led to an assignment of their orientation as depicted in Chart 2.

Thus, the photooxygenation reaction of **10** yielded a 1 : 1-mixture of **11** and **12**. However, the hydroxyl-carrying substrates all produced the 3-substituted products preferably, and retardations in the rates of the oxygenation were recognized to some extent. This would be due to a quenching effect of the hydroxyl group to singlet oxygen. This has been confirmed when the photooxygenation of **9** was carried out in methanol-d_4: the rate was much improved, as large as 23 times that in methanol; the product distribution, the ratio of (**17**+**18**) : (**19**+**20**), was changed to 44:56. The rate enhancement in deuterio solvent is interpreted in terms of an increased lifetime of the singlet oxygen; the degree of the rate-enhancement effect by the medium was theoretically estimated as being ca. 8—10.[9] The present figure is, therefore, attributable to not only the medium effect, but also a quenching effect of the hydroxyl group in the vicinity of the reaction site.[10] This is related to the inversed ratio of the formation of **19** and **20** vs. **17** and **18**. The results are cited in Table 2.

2-(4-Nitrobenzoyl)tropone (**21**) gave no photooxygenation product after prolonged irradiation; this is parallel to the general tendency of the reaction with singlet oxygen, e.g., an introduction of the electron-withdrawing substituent into tropones retarded the oxygenetion.[11]

Table 2. The Product Distributions of the Photooxygenation of **9**

Solv.	Yield/%		Recovery
	(**19**+**20**)	(**17**+**18**)	
Acetone	64	36	
CH$_3$OH	5.7	7.3	87
CD$_3$OD	51	40	9

A mild base treatment of **15** and **16** gave 5-hydroxytropolone derivative **22** quantitatively; unfortunately, its attempted conversion to the tropoquinone derivative has not yet been successful.[2]

Experimental

Sensitized Photooxygenation of 2-Benzyltropone (10). Formation 11 and 12. An acetone solution of **10** (114.8 mg) was oxygenated with HMP (10.5 mg) by a 500-W tungsten lamp under oxygen stream. After 4 h, the mixture was chromatographed on a silica-gel column to give **11** [a yellow oil, 43 mg; 32%. Found: C, 73.41; H, 5.29%; *m/z*, 228.0745 (M$^+$). Calcd for C$_{14}$H$_{12}$O$_3$: C, 73.67; H, 5.30%; M, 228.0787. ^{13}C NMR δ[8]= 37.8, 74.8, 90.3, 126.0, 127.1, 128.5 (2C), 130.9 (2C), 131.7, 134.8, 139.0, 142.8, and 195.7. IR ν: 3040, 1680, 1495, 1450, 1240, 1005, 965, 825, 750, and 700 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 208 ($\varepsilon$=13900), 241 (1400, sh), and 383 (1000)] and **12** [a yellow oil, 41.2 mg; 31%. Found: C, 73.74; H, 5.40%; *m/z* 228.0787 (M$^+$). ^{13}C NMR δ=36.3, 75.5, 85.8, 123.5, 126.7, 128.8 (2C), 129.4 (2C), 138.1, 138.8, 140.7, 142.1, and 195.5. IR ν: 3025, 1675, 1490, 1450, 1365, 1220, 960, 790, 730, and 695 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 206 nm ($\varepsilon$=13900, sh) and 260 (2200)].

Sensitized Photooxidation of 8. An acetone solution (50 cm^3) of **8** (617 mg) was irradiated for 8.5 h with HMP (22 mg) under an O$_2$ stream. The reaction mixture was evaporated in vacuo and the residue was chromatographed on a silica-gel column to give **13**[pale yellow needles, mp 110—114 °C, 87.2 mg; 14%. Found: C, 58.00; H, 3.85; N, 5.10%. Calcd for C$_{14}$H$_{11}$NO$_6$: C, 58.13; H, 3.83, N, 4.84%. ^{13}C NMR δ=71.1, 75.8, 89.2, 122.6, 123.1 (2C), 128.8 (2C), 131.3, 139.9, 144.3, 144.5, 147.6, and 197.5. IR ν: 3480, 3080, 1660, 1600, 1515, 1400, and 1345 cm^{-1}; UV $\lambda_{\max}^{\mathrm{MeOH}}$: 214 nm ($\varepsilon$=15200), 268 (11300), 344 (2900), and 388 (2500)], **14** [pale yellow needles, mp 129—131 °C, 113.4 mg; 18%. Found: C, 58.25; H, 3.89; N, 5.14%. ^{13}C NMR δ=75.1 (2C), 89.9, 123.5 (2C), 123.8, 129.8 (2C), 131.7, 140.3, 143.3, 144.5, 148.1, and 197.2. IR ν: 3580, 3070, 1680, 1600, 1510, and 1345 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 213 nm ($\epsilon$=14300), 268 (11300), and 340 (1100)], **15** [pale yellow needles, mp 131—134 °C, 127 mg; 21%. Found: C, 57.84; H, 3.88; N, 5.09%. ^{13}C NMR δ=72.0, 75.3, 85.7, 123.5 (2C), 123.9 (2C), 127.4 (2C), 138.6, 141.9, 142.4, 148.5, and 195.6. IR ν: 3550, 1675, 1600, 1505, and 1340 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 211 nm ($\varepsilon$=14700) and 273 (11600)], and **16** [pale yellow needles, mp 127—130 °C, 162.6 mg; 26%. Found: C, 58.25; H, 3.87; N, 5.14%. ^{13}C NMR δ=70.8, 75.3, 85.6, 123.5, 123.7, 124.0 (2C), 127.9 (2C), 138.7, 140.8, 142.7, 148.0, and 195.5. IR ν: 3500, 1655, 1600, 1510, and 1345 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 214 nm ($\varepsilon$=14700) and 271 (12500)], together with recovered **8** [70.2 mg; 11%].

Sensitized Photooxygenation of 9. An acetone solution (10 cm^3) of **9** (160 mg) was oxygenated similarly. The reaction mixture was heated in vacuo to remove the solvent, and chromatographed on a silica-gel column to give a 4:1-mixture of **17** and **18** [a yellow oil, 54.5 mg; 30%. Found: *m/z*, 272.0688 (M$^+$). Calcd for $C_{15}H_{12}O_5$: M, 272.0684. ^{13}C NMR δ=73.8, 75.2, 90.0, 124.2, 128.7 (2C), 129.4 (2C), 131.5, 133.8, 135.9, 139.0, 141.3, 195.9, and 196.5 for **17**; δ=73.8, 75.2, 90.0, 123.6, 128.7 (2C), 129.4 (2C), 131.1, 133.8, 135.2, 138.6, 143.5, 195.9, and 196.5 for **18**. IR ν: 3400, 1680, 1665, 1595, 1575, 1450, 1370, and 1335 cm^{-1} UV $\lambda_{\max}^{\mathrm{MeOH}}$: 247 nm ($\varepsilon$=15200) and 345 (900)] and a 2:1-mixture of **19** and **20** [a yellow oil, 97.6 mg; 54%. Found: *m/z*, 272.0641 (M$^+$). ^{13}C NMR δ=71.5, 75.2, 85.5, 123.5, 129.4 (4C), 133.7, 134.4, 138.2, 140.7, 144.7, 193.8, and 198.0 for **19**; δ=70.9, 75.2, 85.5, 123.5, 129.0 (4C), 133.7, 134.4, 138.2, 140.5, 144.7, 194.3, and 198.4 for **20**. IR ν: 3450, 1690, 1600, 1580, 1450, and 1380 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 246 nm ($\varepsilon$=13300) and 292 (1200)].

Sensitized Photooxygenation of 9 in CD_3OD. An anhydrous CD_3OD solution (0.5 cm^3) of **9** (13.3 mg) was irradiated by a 500-W tungsten lamp in the presence of HMP (1.4 mg) under an O_2 stream for 3 h. The rate of the oxygenation was ca. 23 times larger than in MeOH. The ratio of (**17**+**18**) and (**19**+**20**) was analyzed to be 44:56 according to ^{1}H NMR spectrometry.

Sensitized Photooxygenation of 9 in CH_3OH. An MeOH solution (0.5 cm^3) of **9** (13.3 mg) was irradiated in the presence of HMP (1.3 mg) under an O_2 stream for 10 h. The ratio of (**17**+**18**) : (**19**+**20**) was analyzed to be 56 : 44.

Base-Catalyzed Isomerization of 15. A benzene solution (7 cm^3) of **15** (21.5 mg) was stirred in the presence of Et_3N (1 mg) for 2 d at room temperature. The precipitates were filtered off and washed with benzene to give **22** [yellow powders, 20.2 mg; 93%. Found: *m/z*, 289.0621 (M$^+$). Calcd for $C_{14}H_{11}NO_6$: M, 289.0586. ^{1}H NMR (CD_3OD) δ=6.36 (1H, s), 6.95 (1H, dd, *J*=11, 3 Hz), 7.26 (1H, d, *J*=11 Hz), 7.66 (2H, d, *J*=9 Hz), 7.79 (1H, d, *J*=3 Hz), and 8.10 (2H, d, *J*=9 Hz). ^{13}C NMR (CD_3OD) δ=71.7, 123.9, 124.1, 124.5 (2C), 127.2, 129.0 (2C), 145.9, 148.8, 152.4, 160.4, 165.8, and 169.9. IR ν: 3600—3200, 1590, 1510, 1400, and 1345 cm^{-1}. UV $\lambda_{\max}^{\mathrm{MeOH}}$: 219 nm ($\varepsilon$=19100), 241 (22500), 266 (13300, sh), 340 (8300), 380 (8500, sh), and 394 (8800)].

Base-Catalyzed Isomerization of 16. A benzene solution (13 cm^3) of **16** (38.0 mg) was similarly treated with Et_3N (1 mg) at room temperature for 2 d to give **22** [35.0 mg; 94%], which was identical with the sample prepared from **15**.

Attempted Oxygenation of 21. An acetone solution (2 cm^3) of **21** (16.2 mg) and HMP (2 mg) was photooxygenated under an O_2 stream at room temperature for 15 h. The silica-gel column chromatogram of the mixture gave **21** quantitatively.

Attempted DDQ-Dehydrogenation of 22. An acetone solution (5 cm^3) of **22** (52.5 mg) and DDQ (74.2 mg) was stirred at room temperature for 1.5 h. The thin-layer chromatography of the mixture confirmed that no reaction occurred.

We wish to thank The Ministry of Education, Science and Culture for a financial assistance through a Grant-in-Aid for Scientific Research to A. M. (No. 60470025).

References

1) Part XXXVIII: A. Mori and H. Takeshita, *Bull. Chem. Soc. Jpn.*, **60**, 3037 (1987).

2) S. Itô, Y. Shoji, M. Hirama, H. Takeshita, and K. Takahashi, *Tetrahedron Lett.*, **1975**, 1075; H. Takeshita, T. Kusaba, and A. Mori, *Chem. Lett.*, **1982**, 701; **1983**, 1371; *Bull. Chem. Soc. Jpn.*, **55**, 1659 (1982); H. Takeshita, A. Mori, Y. Isayama, and T. Kusaba, *Kyushu Daigaku Sogo Rikogaku Kenkyuka Hokoku*, **6**, 185 (1985); H. Takeshita, A. Mori, and Y. Isayama, *Bull. Chem. Soc. Jpn.*, **58**, 1678 (1985).

3) M. Oda and Y. Kitahara, *Tetrahedron Lett.*, **1969**, 3295.

4) E. J. Forbes and J. Griffiths, *J. Chem. Soc.*, **1968**, 575.

5) T. Tezuka, R. Miyamoto, T. Mukai, C. Kabuto, and Y. Kitahara, *J. Am. Chem. Soc.*, **94**, 9280 (1972).

6) H. Takeshita, A. Mori, and H. Suizu, *Chem. Lett.*, **1986**, 593.

7) H. Takeshita, A. Mori, and H. Suizu, *Bull. Chem. Soc. Jpn.*, **60**, 1429 (1987).

8) The NMR spectra were measured in $CDCl_3$ unless otherwise stated, and the chemical shifts were expressed in δ unit.

9) D. R. Kearns, "Singlet Oxygen," ed by H. H. Wassermann and R. W. Murray, Academic Press, New York (1979), p. 115.

10) A change of life-time of $^1O_2$ by the deuteration of the solvent in bulk may not cause an inversed change in the product distributions. And a change of hydroxyl- to deuteroxyl group on the ethereal substituents of 2-alkoxytropones is least likely to alter the steric effect or electronic properties of the reactant tropones. It is true that the reactivity of $^1O_2$ is known to decrease by introducting oxygen functions; e.g., 3-hydroxyalkenes. A duallity due to the cyclic structures in present cases verified this in terms of the product distributions.

11) I. Saito and T. Matsuura, "Singlet Oxygen," ed by H. H. Wassermann and R. W. Murray, Academic Press, New York (1979), pp. 511—574.