REACTION OF SINGLET OXYGEN WITH α,β-UNSATURATED ALDIMINES: NOVEL FORMATION OF 3-AMINO-4-METHYLENE-1,2-DIOXOLANES[1]

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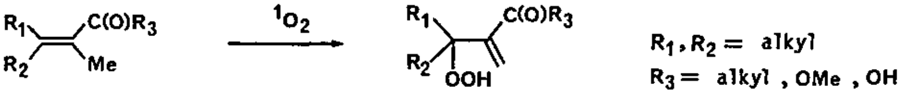
Abstracts - The reaction of singlet oxygen with several α,β -unsaturated aldimines (N-1-(2-alkylidene)-t-butylamines, 1a-c) gave the novel unsaturated hemiperacetal derivatives (3-amino-4-methylene-1,2-dioxolanes, 2a-c) of the hydroperoxy aldimines (3). α,β-Unsaturated aldimine (1e) which was held in the s-trans conformation failed to react with singlet oxygen. The mechanistic implications are also discussed.

The reaction of singlet oxygen ($^1O_2$) with alkenes has been extensively studied because of its synthetic utility[2] and mechanistic interest.[3] Despite this intense investigation, there are few examples of the oxidation of alkenes which are substituted with electron-withdrawing groups.[4] Since $^1O_2$ has been shown to be weakly electrophilic,[5] the fact that electron-deficient olefins are unreactive toward $^1O_2$ is not surprising. Photooxygenation of α,β-unsaturated ketones,[4a-c] esters[4d] and carboxylic acids[4e] has been reported to afford the corresponding allylic hydroperoxides. In all cases, the regioselectivity of $^1O_2$ reactions has been observed;[6] these reactions show preferential abstraction of allylic hydrogens geminal to the carbonyl group (Scheme I). As a part of our continuing synthetic and mechanistic interest in $^1O_2$ reaction of imine compounds,[7] we have investigated the reaction of $^1O_2$ with α,β-unsaturated aldimines (N-1-(2-alkylidene)-t-butylamines). The compounds which prefer the s-cis conformation are rapidly oxidized by $^1O_2$ to give the hemiperacetal derivatives (3-amino-4-methylene-1,2-dioxolanes) of the corresponding hydroperoxy aldimines, whereas the other compound which has the s-trans conformation does not react at all.

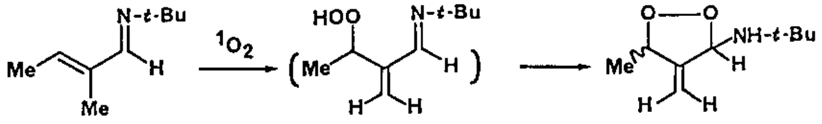
Scheme I



RESULTS AND DISCUSSION

In a typical experiment, photooxygenation of N-1-(2-methyl-2-butenylidene)-t-butylamine (1a) at -40°C in tetrahydrofuran with tetraphenylporphine (TPP) as sensitizer gave 3-(N-t-butylamino)-4-methylene-5-methyl-1,2-dioxolane (2a) in a yield of 71% (Scheme II). Dioxolane 2a was isolated by preparative gas chromatography and its structure was readily assigned on the basis of spectroscopic data. Dimethyl sulfide added to the reaction mixture after photooxygenation was not oxidized to the sulfoxide at all. Conducting the reaction of 2a with lithium aluminum hydride led to a complex mixture of products. 2a readily liberated iodine from an aqueous alcohol solution of potassium iodide, and was unstable in halogenated solvents such as chloroform and methylene chloride. Very similar results were obtained with α,β-unsaturated aldimines, 1b and 1c, under the same conditions as shown in Table. Compound 2 might be formed by cyclization of the hydroperoxy aldimines 3. That the cyclization is spontaneous and does not occur during separation, has been demonstrated by spectroscopic examination of the crude reaction mixture after photooxygenation. The photolysis in the absence of sensitizer does not give any product. Moreover, the photooxygenation is inhibited by addition of 1,4-diazabicyclo [2.2.2.]octane, a $^1O_2$ quencher.[8] These results clearly demonstrate that $^1O_2$ is the active oxygen species responsible for the photooxygenation.

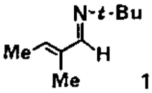
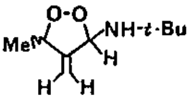
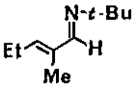
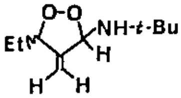
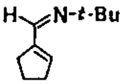
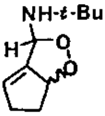
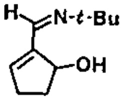
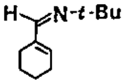
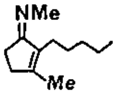
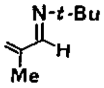
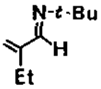
Scheme II



1a 3a 2a

To delineate the limitation and scope of the photooxygenation of α,β-unsaturated aldimines, a series of aldimines (1d-g) were also submitted to reaction with $^1O_2$ (Table). As shown, the electronic and/or conformational effects may be important in accounting for the differences in reactivity of aldimines. The β-values as a measure of reactivity of the aldimines toward $^1O_2$ are also shown in the Table.[2] In the oxidation of α,β-unsaturated ketones,[4c,d] it has been reported that there is no correlation between ionization potential of the ketones and reactivity toward $^1O_2$, and that electronic effects are not important.[4c] The one-electron oxidation potentials (Ep vs. SCE) of the aldimines (1a-g) are over +2.2V in 0.1M $n\text{-}Bu_4NClO_4/CH_3CN$ solution. Since it is well known that a good linear relationship exists between frequencies for charge-transfer absorptions in complexes of tetracyanoethylene (TCNE) with electron-donors and ionization potentials of the donors,[9] we measured the charge-transfer frequencies in complexes of TCNE with

Table. Reaction of Singlet Oxygen with α,β-Unsaturated Aldimines

Reactant	β-value	ν_{max}(cm^{-1}) of CT complex with TCNE	Products and Yields(%)[a]
 1a	2.5	23,500	 2a (71)
 1b	1.0	23,600	 2b (78)
 1c	2.3	24,000	 2c (19)  4 (29)
 1d	>180	23,800	N.R.[b]
 1e	>180	23,600	N.R.[b]
 1f	>180	23,500	N.R.[b]
 1g	>180	23,500	N.R.[b]

a) Yields were determined by gas chromatography.

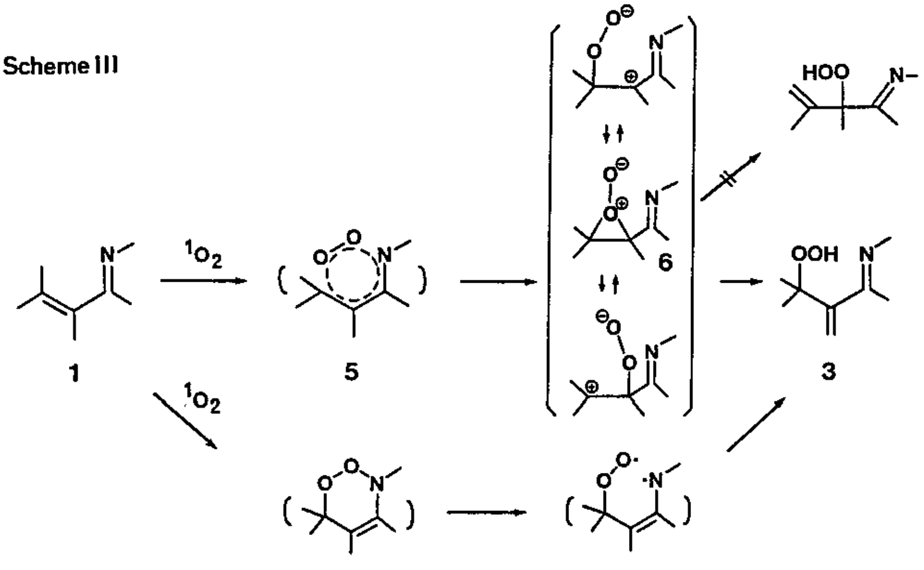
b) Reactant was recovered unchanged after prolonged photooxygenation.

the aldimines (Table) and found that in the oxidation of α,β-unsaturated aldimines, there is no correlation between ionization potential and reactivity toward ${}^1O_2$, and that electronic effects do not influence reactivity.

The explanation for the data presented in the table accounts for the large differences in the values for s-cis- and s-trans-α,β-unsaturated aldimines and the preference for the formation of the oxidation products. Trialkyl substituted aldimine 1e, which is structurally confined to the s-trans conformation, failed to react with ${}^1O_2$. This means that the oxidation arises from reaction of the s-cis conformer of the aldimines with ${}^1O_2$.[4c] An alternative explanation which involves preferential physical quenching of ${}^1O_2$ by s-trans aldimines appears unlikely since the addition of 1e (final concentration of 2.2×10^{-1} M) to a solution of 1a (7.2×10^{-2} M) or 1b in the tetrahydrofuran did not affect the rate of oxidation. 6-Membered aldimine 1d was characteristically unreactive toward ${}^1O_2$. The sizable difference in reactivity toward ${}^1O_2$ between the 5- and 6-membered rings of aldimines (1c and 1d, k_{rel}=1 for 1c and 0.01 for 1d) is presumably due to the α-carbon-hydrogen bond having better sigma-Pz overlap with the cationic center and greater accessibility to the peroxide group, similar to the case of 1-methylcycloalkenes (k_{rel}=1 for 1-methylcyclopentene and 0.1 for 1-methylcyclohexene) reported by Jefford et al.[10] 1f and 1g, presumably having s-cis conformation, were not photooxygenated, which indicates that monoalkyl substituted α,β-unsaturated aldimines may be inert toward ${}^1O_2$, as is true of 1,1-disubstituted alkenes.[3a]

Based on these observations, the following mechanism is proposed in which ${}^1O_2$ might react with α,β-unsaturated aldimines to give an exciplex intermediate 5, similar to the case of phenyl-

Scheme III



substituted alkenes,[11] followed by formation of a zwitterionic intermediate 6, forcing geminal hydrogen abstraction (Scheme III). An alternative intermediate such as a trioxene intermediate (7)[4c] may be conceivable. Formation of trioxene 7, followed by rupture of the N-O bond, might lead to intermediate 8, forcing geminal hydrogen abstraction. This reaction path is similar to that proposed by Ensley et al. in the oxidation of α,β-unsaturated ketones.[4c] Based on the comparison of bond energy of N-O and O-O bond (53 and 34 kcal/mol, respectively),[12] however, this pathway may be unlikely. In conclusion, the present results show the first ene-type reaction of $^{1}O_2$ with α,β-unsaturated aldimines to afford a new type of dioxolanes, α-amino substituted ones.[13]

EXPERIMENTAL

Ir spectra were recorded with a Hitachi 26-50 infrared spectrophotometer, ^{1}H-nmr spectra recorded with a JEOL JNM-PMX60SI spectrometer, ^{13}C-nmr recorded with a JEOL JNM-FX100 spectrometer (solvent, deuteriochloroform and deuteriobenzene; tetramethylsilane as an internal standard), and uv spectra with a Shimadzu UV365 spectrophotometer. Mass spectral data were obtained on a Hitachi RMU-6M mass spectrometer and exact mass data on a JEOL LMS-D300 mass spectrometer. Gas chromatography was done on an Ohkura 802 gas chromatograph equipped with a tcd detector, 8 mm x 1 m glass column, and 3% OV-1 on Uniport HP. The light source was two 500-W tungsten-halogen lamps. Irradiations were carried out in Pyrex tubes at -40°C while oxygen was passed through. Tetrahydrofuran was distilled twice in the presence of lithium aluminum hydride before use. Dichloromethane was washed with water, dried over calcium chloride and then distilled. Meso-tetraphenylporphine (TPP, STREM CHEMICALS) was used as received. 1,4-Diazabicyclo[2.2.2]octane was used after purification by sublimation. TCNE was recrystallized from chlorobenzene and sublimed at 125°C/4mmHg. Aldimines 1, except 1e, were prepared from the corresponding aldehyde and t-butylamine according to the procedure reported previously.[14] 1e was prepared by the reaction of dihydrojasmone with heptamethyldisilazane in the presence of Zn-Cd.[15] 1b: bp 74 °C/23mmHg; ir(NaCl) 1640 cm^{-1}; ^{1}H-nmr($CDCl_3$) δ 7.79(s,1H), 5.72-5.92(m,1H), 2.10-2.40(m,2H), 1.83(brs,3H), 1.20(s,9H), 1.04(t,J=4.9Hz,3H); ^{13}C-nmr($CDCl_3$) δ 159.7(d), 142.28(d), 136.14(s), 56.40(s), 29.89(q), 29.72(q), 21.76(t), 13.63(q); exact mass: Calcd for $C_{10}H_{19}N_1$: 153.1518. Found:153.1529. 1c: bp 85°C/25mmHg; ir(NaCl) 1650 cm^{-1}; ^{1}H-nmr($CDCl_3$) δ 8.0(s,1H), 6.0(m,1H), 2.27-2.73(m,4H), 1.67-2.27(m,2H), 1.13(s,9H); ms: m/z 151(M^{+}); exact mass: Calcd for $C_{10}H_{17}N_1$: 151.1359. Found: 151.1349. 1e: 118-119°C/15mmHg; ir(NaCl) 1640 cm^{-1}; ^{1}H-nmr(CCl_4)δ3.15(s,3H), 2.32-2.54(m,2H), 1.92-2.10(m,4H), 1.67(s,3H), 1.12-1.48(m,6H), 0.89(t,J=6.4Hz,3H); ^{13}C-nmr(CCl_4)δ 178.18(s), 151.30(s), 140.44(s), 40.10(q), 33.70(t), 32.47(t), 28.65(t), 25.95(t), 24.48(t), 23.01(t), 15.50(q), 14.33(q); ms: m/z 179(M^{+}); exact mass: Calcd for $C_{12}H_{21}N_1$: 179.1672. Found: 179.1655.

Photooxygenation of Aldimines

In a typical experiment, photooxygenation of 1a (7.2×10^{-2} M) was carried out in 30 ml of tetrahydrofuran with TPP (7.2×10^{-4} M) as a sensitizer. The oxygenated products were separated by preparative gas chromatography (column temperature 50°C). 2a was obtained in 71% yield. Photooxygenation of 1c yielded hydroxy aldimine 4 after addition of dimethyl sulfide to the reaction mixture. 2a: ir(NaCl) 3340 cm^{-1}; ^{1}H-nmr(C_6D_6) δ 7.16(s,2H), 5.45-5.56(m,2H), 5.01-5.08(m,2H), 4.54-4.65(m,2H), 4.42-4.51(m,2H), 1.15(d,J=6.4Hz,3H), 1.11(d,J=5.9Hz,3H), 1.06(s,9H), 1.03(s,9H); ^{13}C-nmr(C_6D_6) δ 158.87(s), 158.69(s), 106.21(t), 105.15(t), 90.59(s), 90.47(s), 79.26(d), 78.49(d), 50.26(s), 30.82(q), 18.38(q), 17.26(q); ms: m/z 171(M^+), 156, 98, 57; exact mass: Calcd for $C_9H_{17}N_1O_2$: 171.1257. Found: 171.1252; GC column temperature 50°C. The isomeric mixture was not separated but showed the expected ^{13}C-nmr spectrum and a 1 : 1 ratio. 2b: ir(NaCl) 3340 cm^{-1}; ^{1}H-nmr(C_6D_6)δ7.17(s,2H), 5.40-5.58(m,2H), 5.05-5.10(m,2H) 4.65-4.71(m,2H) 4.33-4.55(m,2H), 1.40-1.70(m,4H), 1.06(s,9H), 1.05(s,9H), 0.84-0.99(m,6H); ^{13}C-nmr(C_6D_6)δ 157.49(s), 157.37(s), 106.07(t), 105.71(t), 90.56(d), 90.45(d), 84.01(d), 83.54(d), 50.31(s), 30.83(q), 26.74(t), 26.56(t), 10.18(q), 9.54(q); exact mass: Calcd for $C_{10}H_{19}N_1O_2$: 185.1414. Found: 185.1402. GC column temperature 80°C. The isomeric mixture was not separated but showed a 1 : 1 ratio. 2c: ir(NaCl) 3360 cm^{-1}; ^{1}H-nmr(C_6D_6) δ 7.29(s,1H), 4.98-5.06(m,1H), 4.76(d,J=5.4Hz,1H), 3.18-3.26(m,1H), 1.65-1.98(m,4H), 0.91(s,9H); ^{13}C-nmr(C_6D_6) δ 158.21(d), 156.13(s), 73.51(d), 62.18(d), 57.51(s), 28.96(q), 28.84(t), 26.62(t); exact mass: Calcd for $C_{10}H_{17}N_1O_2$: 183.1258. Found: 183.1251; GC column temperature 60°C. 4: ir(NaCl) 1670 cm^{-1}; ^{1}H-nmr(C_6D_6) δ 7.87(s,1H), 5.74(brs,1H), 5.29-5.37(m,1H), 3.03-3.18(m,1H), 1.97-2.25(m,4H), 1.02(s,9H); ^{13}C-nmr(C_6D_6) δ 153.0(d), 145.64(s), 139.08(d), 76.75(d), 56.80(s), 32.71(t), 30.81(t), 29.54(q); exact mass: Calcd for $C_{10}H_{17}N_1O_1$: 167.1310. Found: 167.1328; GC column temperature 60°C.

Physical Properties of Aldimines

β-Values (kd/kr; kd=rate constant for solvent deactivation of $^{1}O_2$; kr=rate constant for chemical reaction of the substrate) were determined using linalool (β=0.18) as the standard by means of GC analysis and are listed in Table.

Uv measurements of formation of complexes between TCNE and aldimine were carried out as follows. To a methylene chloride solution of the aldimine (0.1 M) was added an equimolar amount of TCNE in methylene chloride under argon at room temperature. The resulting complexes were immediately analyzed by uv spectroscopy. Frequencies of charge-transfer complexes obtained are shown in Table.

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