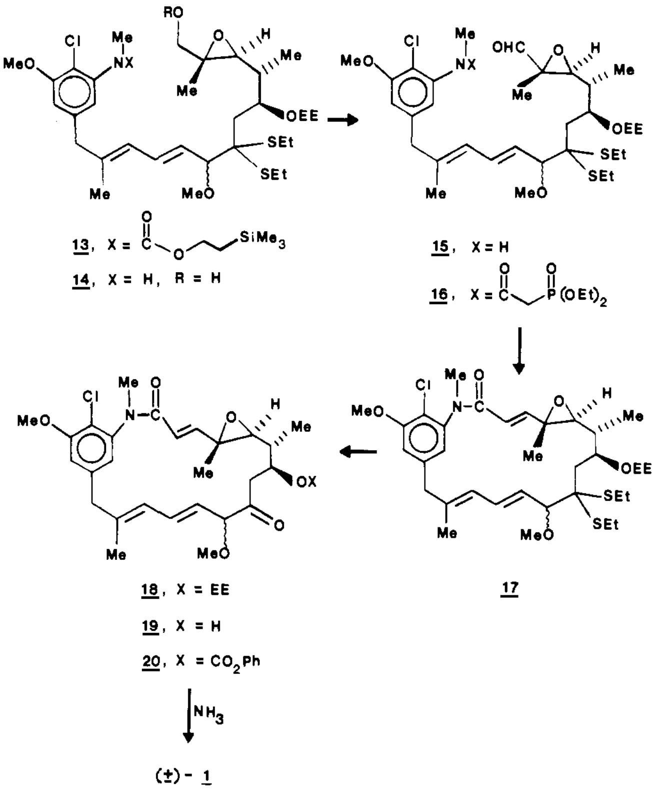
Scheme I



(concentration of **16**, 5×10^{-4} M), −78 to 25 °C, 10 h) and afforded the macrocycle **17** as the pure *E* isomer in 56% yield after PLC (IR (film) 1663 cm^{-1}). The thioacetal was cleanly removed (95%, 2.2 equiv of $HgCl_2$, 2.5 equiv of $CaCO_3$, 4:1 CH_3CN-H_2O) to the ketone **18** (IR (film) 1718, 1663 cm^{-1}) and the ethoxyethyl (EE) group was quantitatively removed (0.5 N HCl-THF, 0 °C) to the hydroxy ketone **19** (IR (film) 3420, 1720, 1660 cm^{-1}). The final synthetic step was carried out by in situ preparation (PhOCOCl, pyridine, Et_2O) of the mixed carbonate **20** (IR (film) 1754 cm^{-1}) and followed immediately with liquid ammonia at −78 °C. After warming to ambient temperature, workup and preparative layer chromatography (silica gel) gave a product (R_f 0.13, 20% benzene-ethyl acetate) which was identical, except for optical rotation, with an authentic sample of (−)- maysine:[1] IR (film) 1709, 1662, 1628, 1575, 1088 cm^{-1}; NMR ($CDCl_3$) of selected proton signals δ 1.00 (s, 3, C-4 CH_3), 1.26 (d, J = 6.1 Hz, C-6 CH_3), 1.64 (br s, C-14 CH_3), 2.62 (d, J = 9.6, C-5 H), 3.27 (s, C-10 CH_3O), 5.66 (d, J = 15.5 Hz, C-2 H), 6.38 (d, J = 15.5 Hz, C-3 H); mass spectrum (70 eV, 170 °C) m/e 546 (M^+), 528 ($M^+ - 18$), 485 ($M^+ - 61$, $-(H_2O + HNCO)$, base peak), 470 ($M^+ - 76$), 450 ($M^+ - 96$); UV (EtOH) λ 226, 242, 252, 280, 288 nm. High-pressure liquid chromatographic (Waters 244) comparison using a 4 mm × 30 cm μ-Porasil column and eluting with 50% ethyl acetate-chloroform (0.5% ethanol) at a flow rate of 5 mL/min gave identical peaks for synthetic and natural maysine at a retention time of 5.2 min.

Studies are continuing to reach additional members of this class of macrocycles and these will be described in future reports.

Acknowledgment. The authors are grateful to the National Institutes of Health (CA-16051) for financial support for this program. An NIH postdoctoral Fellowship to D. M. Roland and a travel grant from the Deutsche Forschungsgemeinschaft to R. Henning are also gratefully acknowledged. We thank Dr. Albert T. Sneden for his kind assistance and authentic samples of maysine, Dr. James Frye of the CSU Regional NMR Center for NMR spectra, and Dr. Phillip Ryan for the mass spectral data. Furthermore, it is a pleasure to acknowledge the technical assistance of Dr. Arthur Campbell and Mr. Curtis Gillespie.

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(4) Using various alkyl and acyl substituents on **6** gave epoxide mixtures as high as 10:1, but unfortunately rich in the wrong isomer, **7b**.

(5) Separation on a 10-g scale was carried out using a Waters 500 high-pressure LC system with 10% acetone-hexane. Retention times at 250 mL/min were 12.7 min for **8a** and 15.9 min for **8b**, respectively.

(6) Meyers, A. I., Shaw, C. C.; Horne, D. A.; Trefonas, L. M.; Majeste, R. M. *Tetrahedron Lett.* **1975**, 1745.

(7) Meyers, A. I.; Slade, J.; Smith, R. K.; Mihelich, E. D.; Hershenson, F. M.; Liang, C. D. *J. Org. Chem.* **1979**, *44*, 2247. Alternatively, the mixture in **11** was separated on Waters 500 LC using 7% acetone-hexane.

(8) Both isomers of **11** were obtained pure and examined at 100 MHz. The protons at C-7 (δ 4.05, 4.06) were shown to be a quartet (J = 5.8 Hz) in one isomer and a doublet of doublets of doublets (J_1 = 8.6, J_2 = 5.6, J_3 = 3.1 Hz) for the other. Projections fully support the erythro isomer having the smaller J value between methine protons.

(9) Physical data for **3**: pale yellow viscous oil; NMR ($CDCl_3$) δ 0.07 (s, 6), 0.91 (s, 9), 1.0–2.7 (m), 2.83 (d, J = 9 Hz, 1), 3.2–4.3 (m), 4.7 (m, 1), 8.9 (two formyl signals due to diastereomers generated by the ethoxyethyl masking group).

(10) The ratio of diastereomers in **13** was found to be 1:1 as determined by high-pressure liquid chromatography on **19** and (±)-**1**.

(11) K. Narasaka, A. Morikawa, K. Saigo, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, **50**, 2773 (1977).

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Received July 16, 1979

A Weakly Chemiluminescent Dioxetanimine[1]

Sir:

Dioxetanones (α-peroxylactones) are an interesting class of high energy compounds because of their potential involvement in the light-forming step of many luminescent organisms.[2] Particularly noteworthy is the fact that the yield of light production from some simple alkyl-substituted dioxetanones is greatly increased in the presence of fluorescent aromatic hydrocarbons with low oxidation potentials. Schuster and Adam ascribed this interesting finding to the occurrence of a chemically initiated electron-exchange luminescence (CIEEL).[3] Recently, the reaction of ketenes with singlet oxygen has been found to be an useful method for the synthesis of dioxetanones.[4] As the continuation of our search for new chemiluminescent systems,[5] we now report the synthesis of *N-tert*-butyldimethyldioxetanimine (**2**) through the photooxygenation of *N-tert*-butyldimethylketenimine (**1**) and show its chemiluminescence properties.

Photooxygenation[6] of **1** (0.1 M) for 1 h at −78 °C in $CFCl_3$ using tetraphenylporphine as sensitizer led to complete disappearance of **1**. Direct ^1H NMR analysis (100 MHz) of the reaction solution at low temperature (−70 °C) indicated a mixture of **2** (65%), acetone (**3**, 30%), *tert*-butyl isocyanate (**4**, 30%), and *tert*-butyl isocyanide (**5**, 5%).[7] The dioxetanimine **2** showed two singlet resonances at δ 1.22 (9 H) and 1.64 (6 H). When the reaction solution was warmed to temperatures above −30 °C, the ^1H NMR spectrum of **2** was completely converted into that of a mixture of **3** and **4** within a few minutes.[15]

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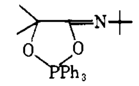
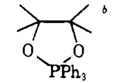
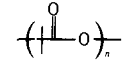
Table I. Comparison of the Chemical Properties of *N*-*tert*-Butyldimethyldioxetanimine (**2**), Tetramethyl-1,2-dioxetane (**7**), and Dimethyldioxetanone (**8**)

	$^3\Phi$, %	$^1\Phi$, %	$^3\Phi/^1\Phi$	E_a, kcal/mol	CIEEL	reaction products with Ph_3P
2	3.4×10^{-3}	5.2×10^{-6}	650	18	no	
7	30[a]	0.15[a]	200	28[a]	no	 [b]
8	1.5[c] 1.1[f]	0.1[c]	15	22[c]	yes[d]	 + Ph_3PO[e]

[a] Reference 16a. [b] Reference 8. [c] Reference 3a. [d] References 3b-d. [e] Turro, N. J.; Ito, Y., unpublished results. [f] Reference 19. The value is the sum of $^3\Phi$ and $^1\Phi$.

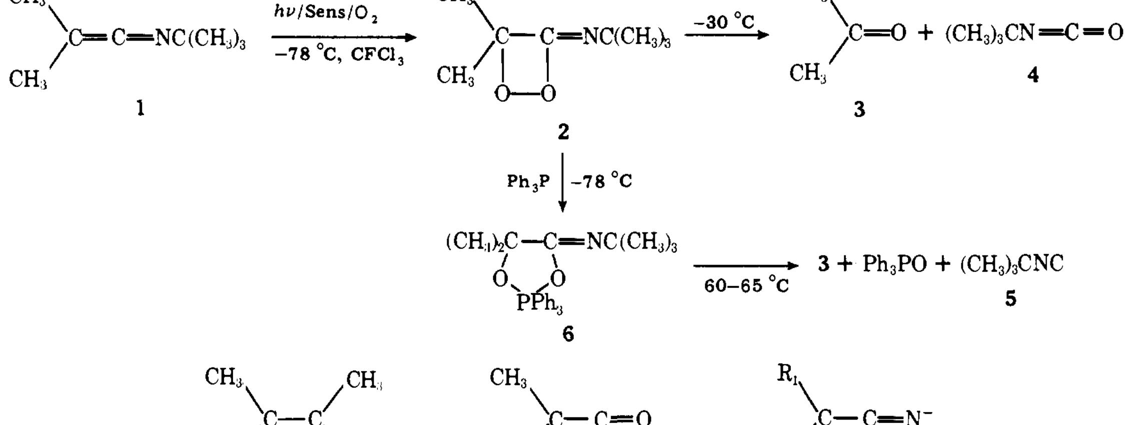
The product **2**, which was assigned a dioxetanimine structure, is not polymeric, since **2** could be distilled through a cooled (−30 to −20 °C) fractionating column at bath temperatures below −20 °C and at 0.1 mmHg, although the majority of it decomposed to **3** and **4** during the distillation. The dioxetanimine **2** exploded in a solid state.

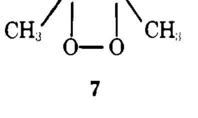
Addition of an equimolar amount of triphenylphosphine to the solution of **2** in $CFCl_3$ at −78 °C, followed by maintenance of the mixture at the same temperature for 1 h, gave a phosphorane **6** in 75% yield (^1H NMR). This reaction is characteristic of 1,2-dioxetanes, e.g., **7**.[8] After removal of the solvent and the volatile byproducts (**3–5**) at reduced pressure from an ice bath, the NMR spectra of the residue which consisted of **6** and triphenylphosphine oxide (3:1) were measured in CCl_4. **6**: ^1H NMR δ 0.93 (s, 9 H), 1.53 (s, 6 H), 6.9–7.3 (m, 15 H); ^{31}P NMR 34.0 ppm upfield from the external standard of 85% H_3PO_4.[8] Thermolysis of the solution of **6** in CCl_4 at 60–65 °C for 30 min and the subsequent ^1H NMR analysis showed that **6** was quantitatively decomposed to acetone (**3**), *tert*-butyl isocyanide (**5**), and triphenylphosphine oxide.

The thermal decomposition of **2** to **3** and **4** was accompanied by chemiluminescence with added 9,10-dibromoanthracene (DBA) as a fluorescer.[9] It was found that *tert*-butyl isocyanate (**4**) had no absorption (ϵ <1) at wavelength above 250 nm and the fluorescence and phosphorescence of acetone (**3**) in acetonitrile[10] were not measurably quenched by **4** (0.1 M), indicating that the lowest singlet and triplet energy levels of **4** are higher than those of **3**. Since the sum of the reaction enthalpy (ΔH)[11] and the activation energy (E_a)[15] for the conversion **2** → **3** + **4** was estimated to be ~90 kcal/mol, both singlet (E_S 85 = kcal/mol) and triplet (E_T = 78 kcal/mol) excited states of acetone (**3**) are energetically accessible from the transition state. The yields of triplet and singlet formation ($^3\Phi$ and $^1\Phi$, respectively) from the thermolysis of **2** were determined by Stern–Volmer plots using DBA and 9,10-diphenylanthracene (DPA) as energy acceptors.[16] A 1,2-dioxetane derived from 2,3-diphenyl-1,4-dioxene was used as a standard of photon emission.[17] The yields, $^3\Phi$ and $^1\Phi$, of **2** (3.4×10^{-3} and 5.2×10^{-6}%, respectively) were much lower than those of the analogous 1,2-dioxetanes, **7** and **8** (Table I). The chemical titration by fumaronitrile[18] of the excited states of **3** from the thermolysis of **2** also showed that both of $^3\Phi$ and $^1\Phi$ were below detectability by this method (<1%)

The relative chemiluminescence intensities from the thermolysis of **2** under the same conditions using as fluorescers rubrene, perylene, DPA, and DBA were approximately 1, 1, 1, and 14, respectively. This result indicates that the role of CIEEL path in the light production from **2** is unimportant in contrast to the case of the dioxetanone **8**.[3] Presumably, this difference is due to the general property of carbonyl compounds which can undergo one-electron reduction more easily than imines.[20]

In summary, while the quantum yields, $^3\Phi$ and $^1\Phi$, from the dioxetanimine **2** are very low, other properties of **2** (that the triplet:singlet ratio ($^3\Phi/^1\Phi$) is high (650) and that the CIEEL process does not occur) are similar to those of the simple alkyl-substituted 1,2-dioxetanes, e.g., **7**, rather than to those of the dioxetanones, e.g., **8** (Table I). The low quantum yields and the high triplet:singlet ratio from **2** are consistent with what Sawaki and Ogata predicted on the basis of the postulate that a dioxetanimine **9** was formed in the course of base-catalyzed decomposition of α-hydroperoxy nitriles.[21] It seems an

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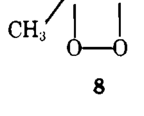
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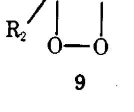
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attractive future problem to find out the origin of the difference in chemiluminescence properties of **2**, **7**, and **8**.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education of Japan.

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(6) Irradiations were carried out with a tungsten-bromine lamp through a Pyrex glass. The ratio of products **2–5** was not significantly altered by the use of a UV-cutoff filter ($K_2Cr_2O_7$ or $CuCl_2$–$CaCl_2$ solution) or by prolonged irradiation (up to 2 h).

(7) The dioxetanimine **2** and *tert*-butyl isocyanide (**5**) may be assumed to result from a perepoxide or zwitterion intermediate in analogy to the reaction of ketenes with singlet oxygen,[4] but we have now no clear evidence for it. To date, only a brief study was made for the reaction of ketenimines with singlet oxygen to give isocyanates and carbonyl fragments (Lee, K.-W., Ph.D. Dissertation, University of Southern California, 1975, pp 227–241). We have also found that various ketenimines give the corresponding carbonyl compounds and isocyanates, which will be described in a separate paper.

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(9) Chemiluminescence was measured by a Shimadzu RF-500 fluorescence spectrometer with a Hamamatsu R 446 photomultiplier tube. For quantitative chemiluminescence measurements, the sample solution of **2** ($\sim 10^{-2}$ M) was prepared by the photooxygenation of **1** in $CFCl_3$, using polymer-bound Rose Bengal instead of tetraphenylporphine as sensitizer, followed by filtration at −78 °C. To the solution of **2** thus prepared was added the equal volume of the stock solution of various concentrations (10^{-4}–10^{-3} M) of each fluorescer in toluene, and the chemiluminescence was measured. Judging from the chemiluminescence decay and the NMR monitoring, the decomposition of **2** was not promoted by the fluorescers. The effect of the treatment of the solvents ($CFCl_3$ and toluene) with EDTA·2Na salt on the lifetime of **2** was also negligible.

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(11) The reaction enthalpy, ΔH, was estimated by Benson's method[12] as −75 kcal/mol. This is based on the assumption that a strain energy for the 1,2-dioxetane ring is 26 kcal/mol[13] and that the heat of formation of methyl isocyanate (gas) is −12 kcal/mol, judging from its reported value −21.9 kcal/mol in liquid phase[14] and the value 10.6 kcal/mol for the heat of vaporization of phenyl isocyanate.[14]

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(14) "CRC Handbook of Chemistry and Physics", Weast, R. C., Ed.; CRC Press: Cleveland, Ohio, 1977; pp D-277, C-738.

(15) Thermochemical parameters of the decomposition of **2** were determined by following the decay of indirect chemiluminescence of DBA: 10^2k (s^{-1}) = 3.75 (−19.2 °C), 3.28 (−20.1 °C), 2.87 (−22.0 °C), 2.02 (−24.0 °C); $E_a = 17.6 \pm 2$ kcal/mol; log $A = 13.8$; $\Delta H^{\ddagger} = 17.1 \pm 2$ kcal/mol; $\Delta S^{\ddagger} = 2.7 \pm 10$ eu.

(16) (a) Wilson, T.; Golan, D. E.; Harris, M. S.; Baumstark, A. L. *J. Am. Chem. Soc.* **1976,** *98,* 1086–1091. (b) Turro, N. J.; Lechtken, P.; Schuster, G.; Orell, J.; Steinmetzer, H.-C.; Adam, W. *Ibid.* **1974,** *96,* 1627–1629.

(17) Zaklika, K. A.; Thayer, A. L.; Schaap, A. P. *J. Am. Chem. Soc.* **1978,** *100,* 4916–4918. Note, however, that the triple yield (6.8%) determined by them differs considerably from that (22%) reported recently.[19]

(18) Turro, N. J.; Lechtken, P. *J. Am. Chem. Soc.* **1972,** *94,* 2886–2888. However, this method has recently been found problematic.[19]

(19) Adam, W.; Cheng, C.; Cueto, O.; Sakanishi, K.; Zinner, K. *J. Am. Chem. Soc.* **1979,** *101,* 1324–1325.

(20) For example, the reduction potentials of benzaldehyde and *N*-benzylideneaniline are −1.6 and −2.2 V, respectively, vs. SCE in neutral organic solvents (Siegerman, H. "Techniques of Chemistry: Technique of Electroorganic Synthesis", Weinberg, N. L., Ed.; Wiley: New York, 1975; Vol. 5, Part 2, pp 707, 871).

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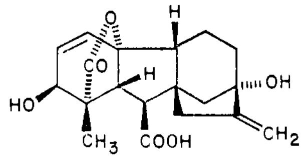
Received June 6, 1979

Reductive Cyclization of Ethynyl Ketones in the Construction of a Significant Tricyclic Intermediate for the Synthesis of Gibberellic Acid

Sir:

The gibberellic acid structure **1**[1] has played a notable role in the generation of new reactions. The reductive cyclization of 5-ethynyl ketones to methylenecyclopentanols[2] provides an excellent example (**2** → **3**). The reaction provides a direct approach to the methylenebicyclo[1.2.3]octanol system which is one of the most salient features of many of the gibberellins. We have therefore expended considerable effort to take advantage of the above cyclization and have used it in four different constructions of the tricyclic ketone **4**, the first synthesis of which we achieved almost 7 years ago.[3] We now outline three of the routes that we have followed to **4** and give the details of a fourth.



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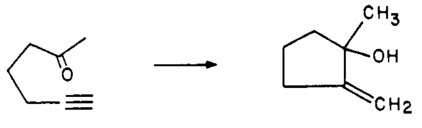

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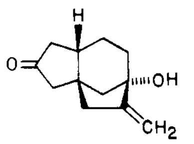
The central assumption on which these syntheses were based was that **4** should be reached readily via the cyclization of the ethynyl ketone **5**. The goal of our syntheses thus became its possible precursor, the diketal **6**. Scheme I illustrates one of our early routes to **6**. We have described previously[4] the cyanohalo ketal cyclization of **7** to **8**,[5] mp 93–94 °C, and of **9** to **10**, mp 108–109 °C. The transformation of the angular cyano function into a propargyl group was carried out in the same manner in the hydrindan and decalin series. We describe it starting with the cyanohydrindan **8**. Reduction of the nitrile **8** (Dibal-H, toluene; hydrolysis with 5% acetic acid, 1 h at room temperature) gave the aldehyde **11**, mp 67–69 °C, which then led to the ethynylcarbinol **12**, mp 97–100 °C (lithium acetylide, THF-liquid NH_3; 50% overall yield from **8**). The desired net removal of the secondary hydroxyl group from **12** was then effected by formation of the mesylate (30% excess methanesulfonyl chloride-pyridine; 0 °C, 1 h; −20 °C, 48 h), followed by hydride reduction ($NaAl(OCH_2CH_2OCH_3)_2H_2$, toluene, −60 to −20 °C, 48 h) to the crude allene **13** which was then isomerized (lithium diisopropylamide, THF, −20 °C, 6 h) to the propargyl diketal **6** and finally hydrolyzed (1:7 20% hydrochloric acid-methanol, 2.5 h) to the nicely crystalline propargylindandione **14**, mp 107–108 °C (IR 2260, 1745, 1715 cm^{-1}). The decalindione analogue **15**, mp 118–120 °C, was produced by the same sequence of steps.[6]



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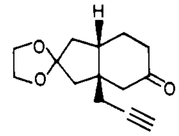

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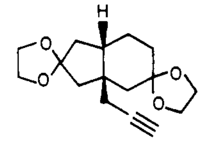

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Although these routes to the acetylenic diones **14** and **15** were successful, they were rather lengthy (the route to **14** from dihydroresorcinol via **8** took 14 steps), and they were not entirely stereospecific: the initial cis cyano diketals **8** and **10** were accompanied by ~5–8% trans isomers.

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