in the gel is essential for the redox reaction.

The mechanism of hydrogen evolution from the colloidal CdS-agarose system is proposed as follows: on the excitation of the colloidal CdS particles, it produces an electron in the conduction band and electron hole in the valence band. In the presence of Rh, the electron can be injected into catalyst Rh. Water or proton can be reduced on the conduction band of CdS or Rh holding electron, while water or alcohol can be oxidized on the valence band of CdS particle (Figure 3). In the absence of Rh, an electron transfer probably occurs from a conduction band of the excited CdS particle to the other neighbor particle and therefore, the reduction and oxidation of water or alcohol occurs at the different CdS particles.

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References

1. Park, Y.-T. *Chemworld, Korean Chem. Soc.* **1995**, *35*, 31.
2. Tricot, Y. M.; Emeren, A.; Fendler, J. *J. Phys Chem.* **1985**, *89*, 4721.
3. Park, Y.-T.; Kim, Y.-U.; Lee, S.-G. *J. Int. Hydrogen Energy* **1994**, *19*, 291.
4. Park, Y.-T.; Lee, S.-G.; Kim, Y.-U. *J. Int. Hydrogen Energy* **1995**, *20*, 711.
5. Park, Y.-T.; Noh, S.-G. *J. Int. Hydrogen Energy* **1995**, *20*, 798.
6. Bühler, N.; Meier, K.; Reber, J.-F. *J. Phys. Chem.* **1984**, *88*, 3261-3268.
7. Duonghong, D.; Borgarello, E.; Grätzel, M. *J. Am. Chem. Soc.* **1981**, *103*, 4685-4690.
8. O'Sullivan, D. *Chemical and Engineering News* **1981**, Jan. *19*, pp 64-69
9. The λ_{mux} of the conduction band of colloidal CdS particle-agarose gel system is around 520 nm.
10. CdS-agarose system is stable enough for 3-days irradiation: the UV and IR spectra and the yield of hydrogen production of the gel system after 3-days irradiation are not changed.

An Efficient Photoinduced Cyclopropyl Ring Opening Reaction of 2-Phenyl-4-cyclopropylmethylidene-5(4*H*)-oxazolone

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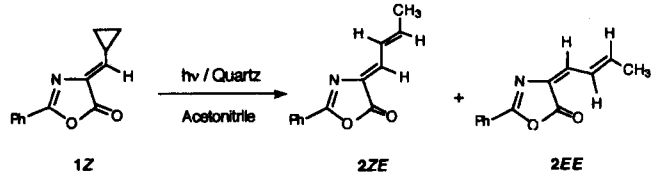
Photochemistry of conjugated cyclopropyl ketones has been extensively studied over the past few decades.[1] Because of the orbital overlap of the bent orbitals of the cyclopropyl group with π orbitals of the attached carbonyl group, their photochemical reactions often involve the cyclopropyl ring opening. Photochemical ring opening reactions of β-cyclopropyl enones have also been documented in the literature for various compounds such as bicyclo[3,1,0]hex-3-en-2-ones,[2] spiro[2,5]octa-4,7-dien-6-ones,[3] etc. These ketones share a common structural feature in which the double bond is a part of a ring. It has been known that excited enones in nonrigid system are easily deactivated by *cis-trans* isomerization of double bonds.[4] For this reason, photoinduced cycopropyl ring opening reactions of nonrigid β-cyclopropyl enones have rarely been reported. Here we would like to report an efficient light-induced cyclopropyl ring opening reaction of the title compound which does not impose the rigid environments on double bonds.

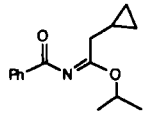
The 2-phenyl-4-cyclopropylmethylidene-5(4*H*)-oxazolone, **1**, was prepared by the Erlenmeyer synthesis,[5] which only gave the more stable Z-isomer.[6] The oxazolone **1Z** in acetonitrile (0.02 M) was irradiated in a quartz vessel with an output of 450 W Hanovia medium pressure mercury arc lamp. Evaporation of the solvent from the crude mixture showed that two isomeric products were present in the mixture. These products were identified to be a *Z,E*- and an *E,E*-isomer of the cyclopropyl ring opened product, **2**, from their spectroscopic data (Scheme 1).[7] The structure of **2** was further confirmed by comparing it with the sample which was synthesized separately using *E*-crotonaldehyde, hippuric acid, lead tetraacetate and acetic anhydride.[8] The ratio of **2EE** increased with irradiation time and reached maximum with an 1 to 1 ratio of the two isomers. The same ratio was obtained when the isolated **2ZE** was irradiated under the same condition.[9] Heating **1Z** in refluxing acetonitrile in the dark did not provide the ring opened products at all.

When **1Z** in 2-propanol was irradiated under the same irradiation condition, an additional product was formed. This product was assigned as **3** according to its spectroscopic



Scheme 1.

property.[10] The ratio of **2** and **3** was measured to be 3 to 1 by the integration in ^{1}H NMR spectrum of the crude mixture. If the reaction was done in tetrahydrofuran containing five percents of water, **3** was replaced by a new product which was later identified to be **4**.[11] The ratio of **2** and **4** was 4 to 1 in the crude reaction mixture.



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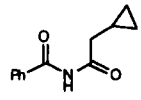

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The ring opening reaction occurred also when acetone was used as a solvent. If the photolysis was done using a Pyrex filter, *cis-trans* isomerization of the starting ketone[12] was observed as a major reaction irrespective of any solvents used even though a small amount of 2 was detected in most of solvents except in benzene. The photolysis under this condition afforded a 5 to 4 photostationary mixture favoring the Z isomer. Neither 3 nor 4 was detected in the photolysis in 2-propanol or tetrahydrofuran containing 5% water under this irradiation condition. The results of photolysis of 1Z under varied reaction condition are summarized in Table 1.

The formation of **2** can be explained by the cyclopropyl ring opening followed by 1,2 hydrogen shift, as frequently addressed in the mechanism of photochemistry of α-cyclopropyl ketones.[1] The fact that the ring opening also occurs in acetone suggests that the reaction can proceed in the triplet state. The ring opening of **1** may have preceded by hydrogen abstraction of the carbonyl oxygen from 2-propanol in the n,π* triplet state. However, the fact that the ring opening also occurs in acetonitrile eliminates this possibility. The fact that **1** readily forms the cyclopropyl ring opened products implies that the excited state of the oxazolone has a strong radical character at β position to the carbonyl group, which can trigger the well known cyclopropylcarbinyl radical rearrangement.[13]

The formation of **3** and **4** is believed to occur through photodecarbonylation followed by addition of 2-propanol or water to a ketenimine intermediate, as previously observed in the photolysis of 2-phenyl-4-ethylidene(or propylidene)-5(4*H*)-oxazolone.[14] We have experienced that the photodecarbonylation is quite a general reaction under this reaction condition when β-substituents to the carbonyl group of the 4-unsaturated oxazolones are simple unsaturated alkyls. If there is further conjugation at this position as in aryl or vinyl case, the photodecarbonylation is not observed.[15] This was futher evidenced in the photolysis of **2** which led to *cis-trans* isomerization only.

Table 1.

Solvents	Irradiation Condition	Products (%)[a]
Acetonitrile	No Filter	**2ZE** (45), **2EE** (45)
2-Propanol	No Filter	**2** (64), **3** (21)
2-Propanol	Pyrex Filter	**1Z** (41), **1E** (32), **2** (13)
Benzene	Pyrex Filter	**1Z** (52), **1E** (45)
THF (with 5% water)	No Filter	**2** (72), **4** (19)

[a] Isolated chemical yield.

If the irradiation of **1Z** was done in any solvents using a Pyrex filter, the *cis-trans* isomerization was the major reaction pathway. It was no surprise for us to see the absence of **3** or **4** at this irradiation condition since we have seen similar wavelength dependence on the photochemistry of 2-phenyl-4-ethylidene(or propylidene)-5(4*H*)-oxazolone.[14]

In summary, irradiation of 2-phenyl-4-cyclopropylmethylidene-5(4*H*)-oxazolone in several different solvents resulted in an efficient cyclopropyl ring opening reaction. Especially in nonnucleophilic solvents such as acetonitrile, the ring opening was the only reaction observed. Currently, photolysis of several structural analogues of **1** including a simple lactone with a similar substituent is being done in our laboratories to obtain further insights on this reaction.

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References

1. (a) Padwa, A. *Org. Photochem.* **1967**, *1*, 91. (b) Dauben, W. G.; Shaffer, G. W.; Deviny, E. J. *J. Am. Chem. Soc.* **1970**, *92*, 6273. (c) Dauben, W. G.; Schutte, L.; Shaffer, G. W.; Gagosian, R. B. *J. Am. Chem. Soc.* **1973**, *95*, 468. (d) Zimmerman, H. E.; Epling, G. A. *J. Am. Chem. Soc.* **1972**, *94*, 7806. (e) Zimmerman, H. E.; Hixson, S. S.; McBride, E. F. *J. Am. Chem. Soc.* **1970**, *92*, 2000.
2. Kropp, P. *J. Org. Photochem.* **1967**, *1*, 1 and refs therein.
3. (a) Schuster, D. I.; Polowczyk, G. J. *J. Am. Chem. Soc.* **1966**, *88*, 1722. (b) Pirkle, W. H.; Smith, S. G.; Koser, G. F. *J. Am. Chem. Soc.* **1969**, *91*, 1580.
4. (a) Yang, N. C.; Jorgenson, M. J. *Tetrahedron Lett.* **1964**, 1203. (b) Baldwin, S. W. *Org. Photochem.* **1981**, *5*, 123.
5. Carter, H. E. *Org. React.* **1974**, *3*, 199.
6. Reaction temperature: 70-80 °C, Isolated yield: 65%, Spectroscopic data of **1Z**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.10 (d, 2H, *J*=6.0 Hz), 7.62-7.44 (m, 3H), 6.16 (d, 1H, *J*=16.0 Hz), 2.41 (m, 1H), 1.26 (m, 2H), 0.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 166.1, 161.9, 145.4, 134.6, 132.9, 128.8, 128.0, 126.0, 13.6, 11.2; IR (CCl_4) 1809, 1670 cm^{-1}; EI MS 213 (M^+), 105, 77.
7. Spectroscopic data of **2ZE**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.10 (d, 2H, *J*=6.7 Hz), 7.60-7.45 (m, 3H), 7.09-6.93 (m, 2H, the second order splitting), 6.46 (dq, 1H, *J*=7.1, 14.2 Hz), 2.02 (d, 3H, *J*=7.1 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 167.2, 161.7, 145.6, 138.4, 132.8, 132.0, 128.9, 127.7, 127.2, 125.8, 19.4; IR (CCl_4) 1664, 1539, 1265 cm^{-1}; EI MS 213 (M^+), 105, 77, 51. Spectroscopic data of **2EE**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.05 (d, 2H, *J*= 6.8 Hz), 7.58-7.48 (m, 3H), 7.41 (ddq, 1H, *J*=12.1, 15.0, 1.5 Hz), 7.10 (d, 1H, *J*=12.1 Hz), 6.44 (dq, 1H, *J*=7.0, 15.0 Hz), 2.02 (dd, 3H, *J*=7.0, 1.5 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 167.0, 161.8, 144.4, 133.3, 132.9, 132.4, 128.8, 127.9, 127.2, 125.6, 19.5; IR (CCl_4) 1668, 1534, 1260 cm^{-1}; EI MS 213 (M^+), 105, 77. The stereochemical assignments of these isomers were made sim-

ilarly to those of isomeric 2-phenyl-4-ethylidene(or propylidene)-5(4*H*)-oxazolones, in which the Z-isomers showed more upfield shifts for β protons to carbonyl groups (7.02 ppm) than the *E*-isomers did (7.10 ppm). And the *E* assignments of the methyl and the rest of the molecule were made based upon the large coupling constants of two olefinic protons (14.2 Hz for **2ZE** and 15.0 Hz for **2EE**) which were determined by decoupling experiments.

8. (a) Cativiela, C.; Mayoral, J. A.; Melendez, E. *Synthesis* **1983**, 899-902. (b) Cativiela, C.; Melendez, E. *Synthesis* **1978**, 832-834.
9. Other possible Z,Z- and *E*,Z-isomers were not found in the photolysis of **2ZE**.
10. **3**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.00 (d, 2H, *J*=7.0 Hz), 7.60-7.39 (m, 3H), 5.20 (septet, 1H, *J*=6.2 Hz), 2.24 (d, 2H, *J*=7.1 Hz), 1.38 (d, 6H, *J*=6.2 Hz), 0.92 (m, 1H), 0.40 (m, 2H), 0.08 (m, 2H). For comparison, the spectroscopic data of 2-phenyl-4-ethylidene(or propylidene)-5(4*H*)-oxazolone can be found in ref. 14.
11. **4**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.51 (broad s, 1H), 7.83 (d, 2H, *J*=7.0 Hz), 7.62-7.45 (m, 3H), 2.93 (d, 2H, *J*=6.7 Hz), 1.01-0.83 (m, 3H), 0.64 (m, 1H), 0.25 (m, 1H).
12. **1E**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.05 (d, 2H, *J*=6.0 Hz), 7.61-7.40 (m, 3H), 6.21 (d, 1H, *J*=16.0 Hz), 2.90 (m, 1H), 1.27 (m, 2H), 0.88 (m, 2H).
13. Newcomb, M. *Tetrahedron* **1993**, *49*, 1151, and refs therein.
14. Jung, B.; Kim, H.; Park, B. S. *Tetrahedron Lett.* **1996**, *17*, 4019.
15. For comparison, the absorption maxima in the ultraviolet absorption spectra are 236, 298 nm for Z-2-phenyl-4-ethylidene-5(4*H*)-oxazolone, 248, 324 nm for **1Z** and 256, 346 nm for **2ZE**.

Study toward the Total Synthesis of Forskolin(II) Synthesis of the Epoxy-trien as the Key Intermediates

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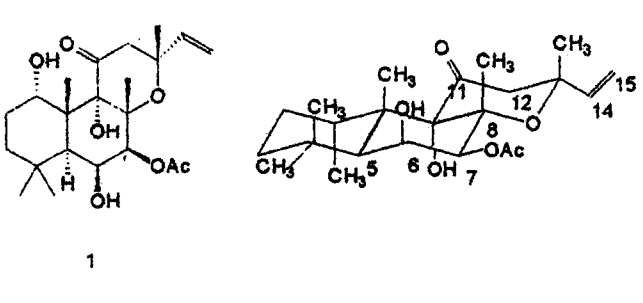
In connection with our continuing efforts[1] to utilize an polyene cyclization reaction to build up a carbon skeleton for forskolin **1**, we wish to report the synthesis of the epoxy triene **13** as a key intermediate. The forskolin **1** is a diterpene obtained from the roots of *Coleus forskohlii* (Willd.)[2] Brig. (*Lamiaceae*), which has been described in Ayurvedic materia medica and in ancient Hindu medicinal texts as a remedy for several complaints, including heart diseases and central nervous system (CNS) disorders such as insomnia and convulsions.

In clinical studies, forskolin **1** has shown a promising therapeutic potential as a novel drug for the treatment of diseases such as glaucoma, congestive heart failure,[3] and bronchial asthma.[4] The absolute structure of **1** was determined from the crude methanolic extract of *Coleus forsolii* in 1977 by the research group at Hoechest.[2,5] It has eight chiral centers and various oxygenated functional groups-hydroxyl, acetate, ketone, ether-with an ether linkage within its tricylic carbon skeleton. Forskolin **1** has attracted considerable interests from many synthetic organic chemists[6] because of its unique structures and biological activities. The first total synthesis of **1** was reported by Ziegler[7a] followed by Corey[7b] and Ikegami.[7c] The formal syntheses for the Ziegler intermediate **2** were reported by several others.[8] (Figure 2)

However, all of these synthetic routes required more than 20 steps in order to build the carbon skeleton with the necessary functional groups. We have investigated a conceptually different approach to synthesize Zieglar intermediate 2 utilizing polyene cyclization.[9] Our retrosynthetic analysis is depicted in Scheme 1. Forskolin **1** would be synthesized from the key intermediate **4**. The tetramethyl hexahydrobenzochromone of **4** would be constructed from the



1

Forskolin

Figure 1.

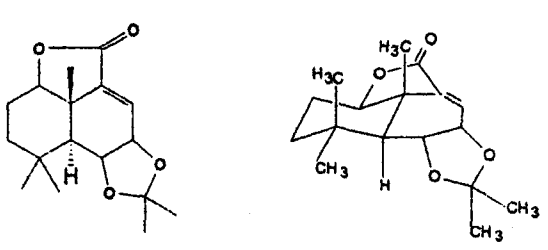


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Figure 2.