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12. (a) **3a**: UV (MeOH) λ_{max} 310, 280, 231, 212 nm; IR (KBr) 3630, 3020, 2922, 1679, 1590, 1287 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$), δ 9.81 (1H, OH, s), 8.20-7.04 (10H, aromatic), 6.24 (1H, s); Mass (EI), m/e 470 (M). (b) **4a**: UV (MeOH) λ_{max} 300, 222 nm; IR (KBr) 3060, 2923, 1703, 1689, 1592, 1451, 1038 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$), δ 8.20-7.51 (10H, aromatic), 5.48 (2H, s); Mass (EI), m/e 470 (M). (c) Dibenzoylmethane were also found to add to *p*-benzoquinone to give 1,5-diketone. For this reaction, see Kim, A. R.; Kim, K. J.; Shim, S. C.; Kim, S. S. *Bull. Korean Chem. Soc.* **1997**, *18*(10), 1125.
13. (a) **6**: UV (MeOH) λ_{max} 344, 300, 283, 248, 244 nm; IR (KBr) 3020, 2915, 1737, 1253, 1025 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$), δ 8.70-7.30 (18H, aromatic), 5.43 (2H, s); Mass (EI), m/e 432 (M), 327 (M-105), 105. (b) Due to the high reactivity of **5** toward the solvent, the minor product **7** could not be isolated. The molar ratio of **6** to **7** was found to be *ca.* 8.3 : 1.0 in ^1H NMR spectrum ($CDCl_3$) of the mixture, in which methylene protons of **7** were observed at δ 4.69. (c) Another 1,3-diketones, such as 1-benzoylacetone and 2,4-pentanedione were also used in an attempt to isolate 1,5-diketones. The results was not as encouraging.
14. (a) **9**: UV (MeOH) λ_{max} 340, 240, 220 nm; IR (KBr) 3020, 2929, 1703, 1277, 1022 cm^{-1}; 400 MHz ^1H-NMR ($CDCl_3$), δ 8.13-7.50 (16H, aromatic), 5.55 (2H, s); Mass (EI), m/e 406 (M), 105, 77. (b) **10**: UV (MeOH) λ_{max} 340, 245, 225 nm; IR (KBr) 3020, 2924, 1703, 1280, 1024 cm^{-1}; 400 MHz ^1H NMR ($CDCl_3$), δ 8.20-7.51 (16H, aromatic), 4.71 (2H, s); Mass (EI), m/e 406 (M), 105, 77.

Titanium Dioxide Mediated Photocatalytic Conversion of Arenealdehyde Phthalazinylhydrazones to *s*-Triazolo[3,4-*a*]phthalazines

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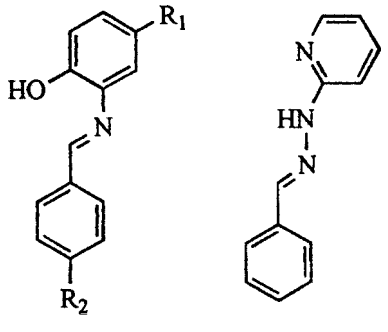
We have recently investigated the reactions of Schiff's bases with cation radicals such as thianthrene cation radical perchlorate ($Th^{+\cdot}$) and tris(2,4-dibromophenyl)aminium hexachloroantimonate ($Ar_3N^{+\cdot}$) in nitrile solvents to give products of intramolecular cyclization and intermolecular cycloaddition.[1,2] In these reactions the major product seemed to largely dependent on the cation radical. $Th^{+\cdot}$ gave intramolecular cyclization product in the reactions with phenolic Schiff's base **1** and arenealdehyde 2-pyridylhydrazone **2**.[1,2] On the other hand, $Ar_3N^{+\cdot}$ with arenealdehyde 2-pyridylhydrazone **2** gave intermolecular cycloaddition product as a major product.[2]



1 **2**

The first step in these reactions has been well established to be the formations of $1^{+\cdot}$ and $2^{+\cdot}$ through one electron

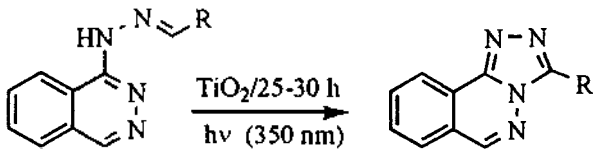
oxidation by cation radicals.[3] With this in mind, we undertook the present work since we supposed that the similar reactions might proceed photocatalytically mediated by a photocatalyst such as titanium dioxide which has a valence band of +3.1 V *vs* SCE, capable of oxidizing most of organic substrates.[4] So far, photocatalytic examples of intramolecular cyclization and intermolecular cycloaddition are limited since much of the works have been concentrated on either photodegradations[5] or functional group transformations[6] of organic compounds.

Herein we report an efficient conversion of arenealdehyde phthalazinylhydrazones **3** to *s*-triazolo[3,4-*a*]phthalazines **4** in a one-pot reaction under uv irradiation (λ=350 nm) in the presence of titanium dioxide as a photocatalyst (Scheme 1).

Photocatalytic experiments were carried out as follows; A heterogeneous solution of **3** (0.5 mmol) and rutile TiO_2 (1.25 g) in acetonitrile (100 mL) was flushed with nitrogen for 30 min, followed by uv irradiation at ambient temperature in a Rayonet photochemical reactor (model # RPR-100) equipped with 16 lamps (RPR-3500A). After 25-30 hrs of irradiation, the temperature reached to 60 °C.

Interestingly, only sole product by intramolecular cyclization was obtained almost free from other products expected by intermolecular cyclization.[3] Yields (%) and melting points, compared with those of reported values, of products **4** are collected in Table 1.

In order to examine the reaction pathways shown in Table 1, following two control experiments were carried out. One was the dark reaction in the presence of TiO_2 where no reaction was observed. The other was irradiation without TiO_2 where **4** was obtained in about 8%. These control experiments strongly suggest that the results in Table 1 (Scheme 1) are truly photocatalytic. That is, the results in



3 **4**

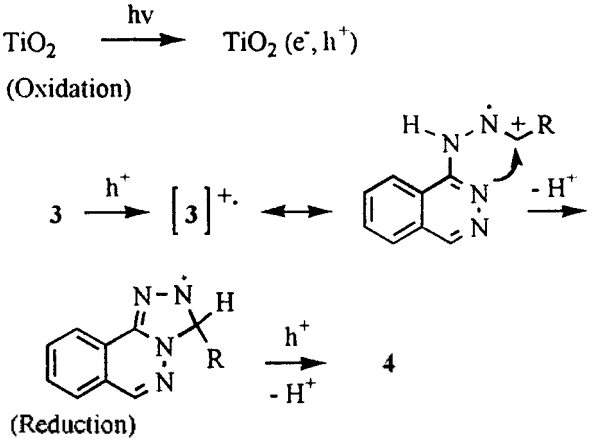
(R= C_6H_5, C_6H_4-*p*-Me, C_6H_4-*p*-OMe, C_6H_4-*p*-Br)

Scheme 1

Table 1. Comparisons of Yield (%)[a] and melting point of **4** Obtained from the TiO_2 Mediated Photocatalytic Conversion of **3**

3 R	4 (Yield, %)	mp	
		observed	reported
H	98	208-210	208-209,[b] 215-216[c]
H[d]	8[e]		
H[f]	0		
Me	98	218-220	222-223[c]
MeO	98	201-202	203-205[c]
Br	88[g]	232-233	

[a] GC shows only a sole product except R=Br. [b] Ref. 7. [c] Ref. 8. [d] In the absence of TiO_2. [e] Recovered starting material was 92%. [f] Dark reaction in the presence of TiO_2. [g] A new compound. Ref. 9 for ^{1}H NMR data. Debrominated product was obtained as a minor in 9%.



Scheme 2

Table 1 can be explained by the intermediacy of $3^{+\cdot}$ made on the surface of TiO_2 by the hole (h^+). The formation mechanism of **4** can be proposed as shown in Scheme 2 based on the well established photocatalysis of titanium dioxide.[10]

In conclusion, oxidative intramolecular cyclization of **3** to **4** was achieved almost in quantitative yields by irradiating uv light in the presence of TiO_2. To our knowledge, this is the first photocatalytic example that induced intramolecular cyclization mediated by TiO_2.[11] Furtheremore, we believe that the present photocatalytic method under simpler reaction conditions would be utilized in the preparation of **4**, possessing antihypotensive activities.[12]

Acknowledgment. Financial support from the Organic Chemistry Research Center sponsored by Korea Science Engineering and Foundation (1997) and the Ministry of Education through Basic Science Research Program (BSRI-97-3433) is gratefully acknowledged.

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9. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69 (d, 2H, J=8.7), 7.81-7.87 (m, 1H), 7.95-8.01 (m, 2H), 8.38 (d, 2H, J=8.7), 8.71-8.74 (m, 2H).
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A Study toward the Total Synthesis of Forskolin(III) A Synthesis of Monocyclized Key Intermediates

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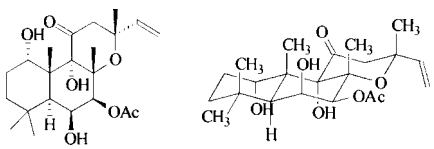
In connection with our continuing efforts[1,2] to utilize an polyene cyclization reaction to build up a carbon skeleton for forskolin **1**, we wish to report the synthesis of the monocyclized diene **13** as a key intermediate. Forskolin **1** is a diterpene obtained from the roots of *Coleus forskohlii* (Willd.)[3] Brig. (*Lamiaceae*), which was described in Ayurvedic materia medica as well as 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.

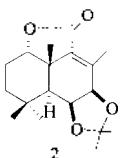


1
Forskolin

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, and bronchial asthma.[4] The absolute structure of **1** was determined from the crude methanolic extract of *Coleus forskohlii* in 1977 by the research group at Hoechest.[3,5] 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] due to its unique structure and biological activities. The total synthesis of **1** involving a common key intermediate **2** was reported by Ziegler,[7a] Corey[7b] and Ikegami,[7c] respectively. Recently the Ziegler intermediate **2** has been elegantly synthesized by others.[8]

However, all of these synthetic routes required more than 20 steps for building the carbon skeleton with the necessary functional groups.

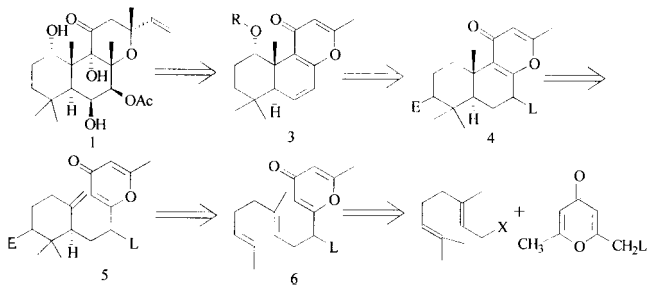


2

We have investigated a conceptually different approach to synthesize forskolin **1** 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 diene **5** by means of an adequate polyene cyclization reaction (Scheme 1).

Our retrosynthetic analysis led us to prepare (E)-1-chloro-3,7-dimethyl-octa-2,6-diene **8** and 2-methyl-6-[(p-tolylsulfonyl)methyl]-4*H*-pyran-4-one **11** (Scheme 2) which are obtained in a preparative scale as starting materials by optimized reaction conditions developed in our laboratory.[1,2]

Treatment with (E)-1-chloro-3,7-dimethyl-octa-2,6-diene **8** with sodium hydride in THF followed by the addition of the sulfone-pyrone **11** gave rise to the triene **12** in 65.0% yield (Scheme 2). With a plausible key intermediate at hand, we have investigated an optimized cyclization reaction condition. Unfortunately, all attempts utilizing a Lewis acid promoted polyene cyclization-for example, BF_3-CH_3NO_2, BF_3-$CH_3CH_2NO_2$, I_2, $HgCl_2$, formic acid, etc-failed. After spending considerable amount of time, we finally have obtained mixture of exo olefin **13** in 46.0% and endo olefin **14** in 2.4% yield by using Nishizawa's reagent[10]-mercury(II) triflate and N,N-dimethylaniline-followed by $NaBH_4$ reduction (Scheme 3). Separation of **13** and **14** took a lot of time and care since their Rf values are very close. The reaction mixture of **13** and **14** was further submitted to an acid catalyzed isomerization condition to confirm structural



Scheme 1