Pergamon

Tetrahedron Letters 41 (2000) 6467–6471

TETRAHEDRON
LETTERS

Isoquinoline formation by a novel photochemical intermolecular cycloaddition of 1,1-diphenylethene derivatives to 1,4-dicyanobenzene

Hideki Ishii,[a,†] Yuko Imai,[a] Takashi Hirano,[a,*] Shojiro Maki,[a]
Haruki Niwa[a,*] and Mamoru Ohashi[b]

[a]*Department of Applied Physics and Chemistry, The University of Electro-Communications, Chofu, Tokyo 182-8585, Japan*
[b]*Department of Materials Science, Kanagawa University, Hiratsuka, Kanagawa 259-1293, Japan*

Received 12 April 2000; revised 22 June 2000; accepted 23 June 2000

Abstract

Phenanthrene-sensitized photoreaction of 1,1-diphenylethene (**DPE**) derivatives and 1,4-dicyanobenzene (**DCNB**) in benzene leads to a novel intermolecular cycloaddition to give isoquinoline derivatives as a novel synthetic method. The feasibility of this reaction was dependent upon the side chain structure of **DPE** derivatives, which would regulate the stability of radical cation **DPE**$^{+\cdot}$ in a highly polar exciplex, and/or a contact radical ion pair, by hyperconjugation or neighboring group participation. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: photochemistry; electron transfer; isoquinolines; cycloadditions.

Inter- and intramolecular cyclization reactions of a radical ion species via photoinduced electron transfer (PET) reaction have been widely investigated from the synthetic and mechanistic viewpoints.[1,2] In particular, the PET-induced cycloaddition reactions of arene radical ions to alkenes have been studied for the construction of a polycyclic skeleton.[3] A substrate possessing an electron-rich 1,1-diphenylethene moiety is advantageous in application to a radical cation–cyclization reaction, because of its low oxidation potential and moderate reactivity of the corresponding radical cation.[4,5] Recently, we reported that the PET-induced intramolecular cyclization reactions of 1,1-diphenyl-1,6-heptadiene derivatives in acetonitrile lead efficiently to products bearing the 6/6/6-fused ring system.[6] Diene **1**, for instance, gave **2** in good yields. In this reaction, a radical

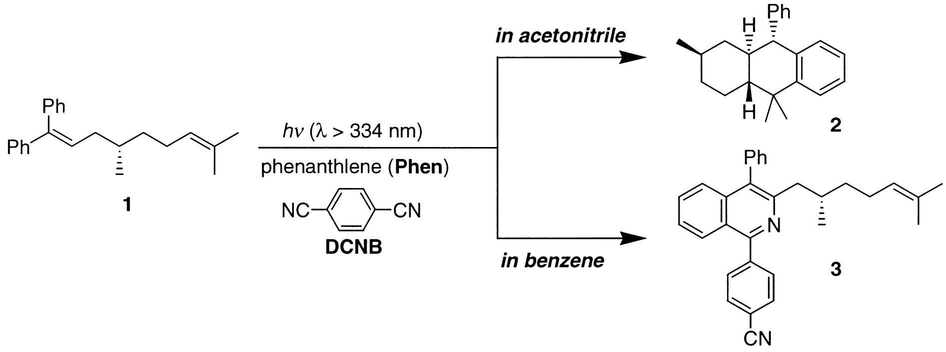
---

* Corresponding author. E-mail: hirano@pc.uec.ac.jp

[†] Present address: Graduate School of Engineering, Tokyo Institute of Technology, Nagatsuta, Yokohama, Kanagawa 226-8502, Japan.

PII: S0040-4039(00)01078-9

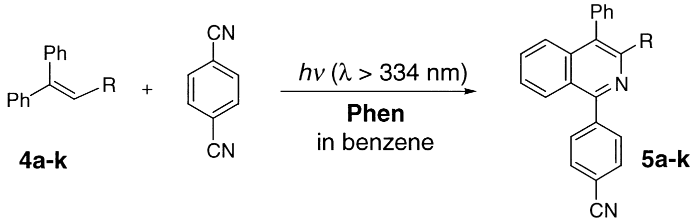
cation of a 1,1-diphenylethene derivative was generated under phenanthrene (**Phen**)-sensitized irradiation conditions in the presence of 1,4-dicyanobenezene (**DCNB**) as an electron acceptor. We also investigated solvent dependency on the radical cation reactivity of 1,1-diphenylethene derivatives, and found a novel photoreactivity in benzene, leading to the formation of isoquinoline derivatives such as **3**, which were obtained by a formal [4+2] cycloaddition of a 1,1-diphenylethene moiety to **DCNB**. We report herein, this novel photochemical reactivity of 1,1-diphenylethene derivatives with **DCNB** in benzene, which was dependent upon the side chain structure on the 1,1-diphenylethene moiety.

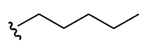
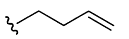
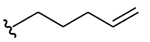
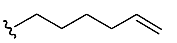
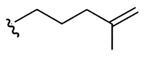
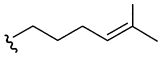
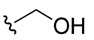
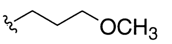


A solution of **1** (1×10^{-2} M), **DCNB** (5×10^{-2} M), and **Phen** (1×10^{-2} M) in benzene was irradiated by using a 100-W high-pressure Hg lamp with a $CuSO_4$ filter solution ($\lambda > 334$ nm) under Ar at room temperature. After irradiation, isoquinoline **3** was isolated by preparative TLC in 23% yield (conversion 15%), accompanied by the recovery of **Phen** (ca. 100%). The formation of cyclized product **2** was not observed in this reaction at all. The structure of **3** was established by the spectroscopic data.[7] Direct irradiation ($\lambda > 280$ nm) of a benzene solution of **1** and **DCNB** in the absence of **Phen** also gave **3**, although a competing photochemical decomposition of **1** lowered the yield of **3**.

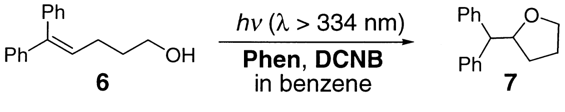
Under similar conditions, the phenanthrene-sensitized photoreactions of 1,1-diphenylethene derivatives **4a**–**k** with **DCNB** in benzene were investigated as summarized in Table 1. The results indicate that the efficiency to yield isoquinoline products is dependent upon the structure of the side chain **R** of 1,1-diphenylethene derivatives. In the case of 1,1-diphenylethene (**4a**; **R** = H) and 1,1-diphenylpropene (**4b**; **R** = CH_3; entries 1 and 2), the formation of **5a** and **5b** was negligible, although **4a** and **4b** were consumed during the photoreactions. It is of interest that the yields of the isoquinoline products increased with increase in the alkyl chain length, as shown in the case of **4c** (**R** = Et; 17%) and **4d** (**R** = pentyl; 28%; entries 3 and 4). Furthermore, dienes **4e**, **4f**, and **4g**, bearing butenyl, pentenyl, and hexenyl groups, gave isoquinolines **5e** (48%), **5f** (59%), and **5g** (34%), respectively (entries 5–7), in good yields. Pentenyl-substituted **4f** gave the best yield of isoquinoline product **5f** in this research. Thus, we investigated the effect of methyl-substitution on the structure **4f** by using **4h** and **4i** (entries 8 and 9). The results showed a decrease in the yields of **5h** (27%) and **5i** (10%). As another structural modification, we investigated the photoreactions of alcohol **4j** and ether **4k** (entries 10 and 11) as well as alcohol **6**. Although **4j** and **4k** yielded isoquinolines **5j** (48%) and **5k** (41%), alcohol **6** gave only intramolecular cyclized product **7** (40%) rather than the corresponding isoquinoline product, as reported previously.[5]

Table 1
Phenanthrene-sensitized photoreactions of 1,1-diphenylethylene derivatives and **DCNB**

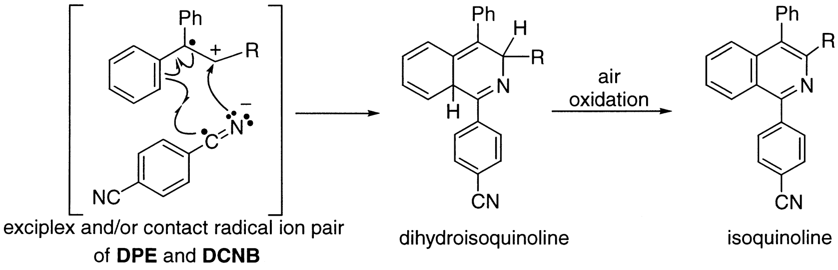


Entry	Compound (**R**)	Irradiation time / h	Conversion / %	Product (yield[a] / %)
1	**4a** (R = H)	10	30	**5a** (0)
2	**4b** (R = CH_3)	20	62	**5b** (trace)
3	**4c** (R = CH_2CH_3)	10	69	**5c** (17)
4	**4d** (R = )	10	31	**5d** (28)
5	**4e** (R = )	10	29	**5e** (48)
6	**4f** (R = )	10	17	**5f** (59)
7	**4g** (R = )	10	28	**5g** (34)
8	**4h** (R = )	10	37	**5h** (27)
9	**4i** (R = )	10	49	**5i** (10)
10	**4j** (R = )	10	29	**5j** (48)
11	**4k** (R = )	23	22	**5k** (41)

[a] Isolated yields based on the consumed 1,1-diphenylethylene derivatives.



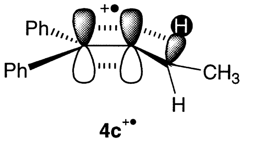
The isoquinoline derivative would be formed by the formal [4+2] cycloaddition of a 1,1-diphenylethylene (**DPE**) derivative to a cyano group of **DCNB** in a highly polar exciplex and/or a contact radical ion pair generated after a PET process in a nonpolar solvent benzene,[8] followed by air oxidation (Scheme 1). It is noteworthy that the participation of the cyano group of **DCNB** as a dienophile in this reaction is a new reactivity of cyano-substituted arenes in the PET reactions.[9] **Phen** acts as a sensitizer, which has been introduced as a redox carrier in the redox-photosensitized reactions,[10] and the phenanthrene-sensitization helps to clear formation of



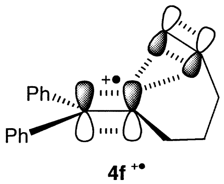
Scheme 1.

isoquinoline derivatives by suppressing the photochemical decomposition of **DPE**. It is likely that the formation of the exciplex and/or the contact radical ion pair of **DPE** and **DCNB** occurs via a termolecular complex of the singlet excited **Phen** with **DPE** and **DCNB** in benzene.[8] In the case of 1,1-diphenyl-1,6-heptadiene derivatives, the photochemical reaction manner of **DPE** with **DCNB** in benzene is in contrast with the manner in acetonitrile, which gives an intramolecular cyclization product of **DPE**, via the formation of free radical ions.[6]

The yields of isoquinoline products were dependent on the side chain structure (**R**) of the **DPE** derivative, which would affect the properties of the radical cation **DPE**$^{+\cdot}$ in the highly polar exciplex and/or the contact radical ion pair of **DPE** and **DCNB**. The better yields of **5c** and **5d**, more than that of **5b**, would be attributable to stabilization of the cationic character of **DPE**$^{+\cdot}$ by hyperconjugation.[11] Radical cations **4c**$^{+\cdot}$ and **4d**$^{+\cdot}$, whose hyperconjugative interaction is larger than that of **4b**$^{+\cdot}$, may have a long enough lifetime to react with radical anion **DCNB**$^{-\cdot}$ before dissociation of the exciplex and/or the contact radical ion pair. The effect of the terminal alkenyl groups in **4e**, **4f**, and **4g** was remarkable for increasing the yields of isoquinoline derivatives. In these cases, the terminal alkenyl group may stabilize the cationic center of 1,1-diphenylethene-part intramolecularly, as a neighboring group participation. In the case of **4f**, for instance, the pentenyl group stabilizes the cationic center of **4f**$^{+\cdot}$, and the stability of **4f**$^{+\cdot}$ would be decreased by steric hindrance of the methyl substitution, as observed in **4h** and **4i**. Similarly, neighboring group participation of an oxygen atom would work in **4j**$^{+\cdot}$ and **4k**$^{+\cdot}$. In the case of alcohol **6**, however, radical cation **6**$^{+\cdot}$ prefers the intramolecular nucleophilic attack of the hydroxy group, rather than the intermolecular reaction with **DCNB**$^{-\cdot}$.[5] This explanation, based on the neighboring group participation, is similar to an intramolecular coordination effect reported for the radical cation species of group 14 organometallic compounds, which have a heteroatom in an appropriate position.[12]



4c$^{+\bullet}$



4f$^{+\bullet}$

In summary, the phenanthrene-sensitized photoreaction of a **DPE** derivative and **DCNB** in benzene leads to the formation of isoquinoline derivatives as a novel synthetic method.[13] The isoquinoline formation would proceed by the formal [4+2] cycloaddition of a **DPE** derivative to the cyano group of **DCNB** in a highly polar exciplex and/or a contact radical ion pair, followed by air oxidation. The feasibility of this reaction was dependent upon the side chain structure **R** on the 1,1-diphenylethene moiety, which would regulate the stability of the radical cation **DPE**$^{+\cdot}$ by hyperconjugation or neighboring group participation.

References

1. *Photoinduced Electron Transfer, Part A–D*; Fox, M. A.; Chanon, M., Eds.; Elsevier: Amsterdam, 1988. *Photoinduced Electron Transfer I-V: Topics in Current Chemistry*; Mattay, J., Ed.; Springer-Verlag: Berlin, 1990–1993.
2. Müller, F.; Mattay, J. *Chem. Rev.* **1993**, *93*, 99–117. Mattay, J. *Synthesis* **1989**, 233–252. Mattay, J. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 825–845. Kavarnos, G. J.; Turro, N. J. *Chem. Rev.* **1986**, *86*, 401–449, and references cited therein.
3. Xue, J.; Xu, J.-W.; Yang, L.; Xu, J.-H. *J. Org. Chem.* **2000**, *65*, 30–40. Kubo, Y.; Kiuchi, K.; Inamura, I. *Bull. Chem. Soc. Jpn.* **1999**, *72,* 1101–1108. Ohashi, M.; Aoyagi, N.; Miyama, T.; Kyushin, S.; Yamada, S. *J. Chem. Soc., Perkin Trans. 1* **1990**, 124–126. Maruyama, K.; Otsuki, T.; Tai, S. *J. Org. Chem.* **1985**, *50,* 52–60, and references cited therein.
4. Mattes, S. L.; Farid, S. *J. Am. Chem. Soc.* **1986**, *108*, 7356–7361. Mattes, S. L.; Farid, S. *J. Am. Chem. Soc.* **1983**, *105*, 1386–1387. Arnold, D. R.; Borg, R. M.; Albini, A. *J. Chem. Soc., Chem. Commun.* **1981**, 138–139. Neunteufel, R. A.; Arnold, D. R. *J. Am. Chem. Soc.* **1973**, *95*, 4080–4081.
5. Mizuno, K.; Tamai, T.; Nishiyama, T.; Tani, K.; Sawasaki, M.; Otsuji, Y. *Angew. Chem., Int. Ed. Engl.* **1994**, *33,* 2113–2115.
6. Ishii, H.; Yamaoka, R.; Imai, Y.; Hirano, T.; Maki, S.; Niwa, H.; Hashizume, D.; Iwasaki, F.; Ohashi, M. *Tetrahedron Lett.* **1998**, *39*, 9501–9504.
7. ^{1}H NMR (CDCl$_3$, 500 MHz) δ 8.25 (m, 1H), 7.69 (m, 1H), 7.62 (m, 1H), 7.48 (m, 4H), 7.39 (m, 1H), 7.24 (m, 1H), 7.19 (m, 1H), 5.12 (dd, $J = 7.0$, 7.0 Hz, 1H), 3.45 (dd, $J = 13.6$, 6.0 Hz, 1H), 3.14 (dd, $J = 13.6$, 8.4 Hz, 1H), 2.31 (dddd, $J = 6.9$, 6.9, 6.9, 6.9 Hz, 1H), 2.06 (dddd, $J = 14.6$, 7.4, 7.4, 7.4 Hz, 1H), 1.69 (s, 3H), 1.61 (s, 3H), 1.53–1.65 (m, 1H), 1.42 (m, 1H), 1.03 (d, $J = 6.8$ Hz, 3H); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 161.2 (s), 146.8 (s), 145.8 (s), 136.9 (s), 136.1 (s), 131.5 (s), 131.4 (d), 131.2 (d), 131.0 (d), 130.0 (d), 129.7 (s), 128.6 (d), 128.5 (d), 127.7 (d), 127.1 (d), 126.4 (s), 125.4 (s), 124.7 (d), 119.1 (s), 110.3 (s), 42.5 (t), 37.4 (t), 33.5 (d), 25.8 (q), 25.6 (t), 19.9 (q), 17.7 (q); IR (CHCl$_3$) 2230 cm^{-1}; HRMS calcd for C$_{31}$H$_{30}$N$_2$: 430.2409; found: 430.2411.
8. Yoon, H.; Chae, W. *Tetrahedron Lett.* **1997**, *38,* 5169–5172. Lee, S.-H.; Yoon, H.-J.; Chae, W.-K. *J. Photochem. Photobiol. A* **1996**, *93,* 33–37. Wolfle, I.; Chan, S.; Schuster, G. B. *J. Org. Chem.* **1991**, *56*, 7313–7319. Akbulut, N.; Hartsough, D.; Kim, J.-I.; Schuster, G. B. *J. Org. Chem.* **1989**, *54*, 2549–2556.
9. The photo-Ritter reactions were reported as a similar reaction manner, which proceeded by nucleophilic attack of a neutral nitrile molecule to a cation center of a radical cation species: Ishii, H.; Hirano, T.; Maki, S.; Niwa, H.; Ohashi, M. *Tetrahedron Lett.* **1998**, *39*, 2791–2792. de Lijser, H. J. P.; Arnold, D. R. *J. Phys. Chem. A* **1998**, *102,* 5592–5598.
10. Majima, T.; Pac, C.; Nakasone, A.; Sakurai, H. *J. Am. Chem. Soc.* **1981**, *103*, 4499–4508.
11. Shiotani, M.; Lindgren, M.; Ohta, N.; Ichikawa, T. *J. Chem. Soc., Perkin. Trans. 2*, **1991**, 711–719.
12. Yoshida, J.; Suga, S.; Fuke, K.; Watanabe, M. *Chem. Lett.* **1999**, 251–252. Yoshida, J.; Sugawara, M.; Tatsumi, M.; Kise, N. *J. Org. Chem.* **1998**, *63*, 5950–5961. Yoshida, J.; Izawa, M. *J. Am. Chem. Soc.* **1997**, *119*, 9361–9365. Yoshida, J.; Morita, Y.; Itho, M.; Ishichi, Y.; Isoe, S. *Synlett* **1992**, 843–844.
13. A similar isoquinoline formation was also observed, when 1,2- and 1,3-dicyanaobenezene were used instead of 1,4-dicyanaobenezene. Study on the PET-induced isoquinoline formation of a 1,1-diphenylethene derivative with various cyano-substituted arenes is now in progress.