8230 *J. Org. Chem.* **2001,** *66,* 8230−8235

Photooxygenation of Indolizines via Selective Excitation of Their Charge Transfer Complexes with Molecular Oxygen

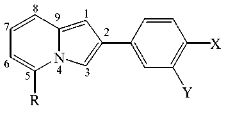
Jing-Zhi Tian,[†] Zhao-Guo Zhang,[‡] Xiao-Liang Yang,[†]
Hoong-Kun Fun,[§] and Jian-Hua Xu*[,†]

*Department of Chemistry, Nanjing University,
Nanjing 210093, China, Institute of Organic Chemistry,
Academia Sinica, Shanghai, 200032, China, and X-ray
Crystallography Unit, School of Physics, Universiti Sains
Malaysia, 11800, USM, Penang, Malaysia*

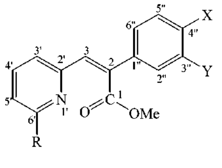
xujh@nju.edu.cn

Received May 18, 2001

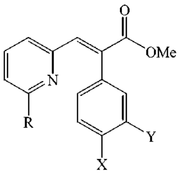
Indolizines have 10 π-electrons and are isoelectronic with indole and naphthalene. However, the bridgehead nitrogen atom has drastic influence on the properties of the two constituted rings. Being nonalternant and heteroaromatic, indolizine inherently has a large dipole moment (1.3 D)[1] that renders the pyrrole ring to behave as electron rich and the pyridine ring as electron poor. Due to their special electronic structure, their high fluorescence efficiency,[2] and the fact that their partially and fully hydrogenated derivatives make up a large group of naturally occurring alkaloids,[3] indolizines have been of theoretical and practical interest, and calculations at different levels of sophistication on their ground state and excited-state electronic structures[1,4] and synthesis[5,6] as well as reactions[6] have been widely investigated and reviewed.[6] Indolizine is among the most π-electron excessive heteroaromatics, has a very low ionization potential (7.15 eV[7]), and as such behaves as a strong nucleophilic substrate in most chemical reactions. They are also susceptible to oxygen attack and are easily oxidized upon air exposure. However, thermal oxidation reactions usually result in deep oxidation with ring fission and extensive C−C bond cleavage to give α-picolinic acid derivatives.[8] These reactions have therefore mainly been used for the purpose of structural elucidation. Photoinduced oxygenation reactions of indolizines, on the other hand, have not been investigated. Many organic compounds are known to interact with ground-state molecular oxygen to form contact charge transfer (CT) complexes[9] which are characterized by the occurrence of new long wavelength absorption in the electronic spectrum of the substrate's oxygen-saturated solution in inert solvent which reversibly disappears when oxygen is excluded from the solution. Although there is no substantial charge separation in these weakly bound ground-state complexes, excitation of them leads to the formation of excited CT complex with profound ion-radical pair character.[9] The chemical consequences of the excitation of the contact CT pair of different organic substrates with oxygen and the formation of excited CT complex are interesting in view of exploring diversified reaction pathways of the substrate cation radicals. However, photochemistry resulting from the excitation of CT complexes with oxygen have not been extensively explored,[10] although it has been reported that in a few favorable cases photooxygenation reactions of the substrates (e.g. amines,[11] ethers,[12] polymethylbenzenes,[13] and other electron rich compounds[14]) can result. We report here photooxygenation reactions of indolizine derivatives **1a**−**d** in mixed solvents benzene−methanol which proceed via the selective excitation of their ground-state CT complex with molecular oxygen by long wavelength irradiation. In contrast to thermal oxidation reactions, under our conditions, mild oxidation without C−C bond cleavage takes place to give α-phenyl-β-(2-pyridinyl)propenoic acids **4** and their methyl esters **2** and **3** as main products.



1a R=Me, X=Y=H
1b R=X=Y=H
1c R=Y=H, X=Cl
1d R=H, X=Y=Me



2a R=Me, X=Y=H
2b R=X=Y=H
2c R=Y=H, X=Cl
2d R=H, X=Y=Me



3a R=Me, X=Y=H
3b R=X=Y=H
3c R=Y=H, X=Cl
3d R=H, X=Y=Me

---

* Corresponding author.
[†] Nanjing University.
[‡] Academia Sinica.
[§] Universiti Sains Malaysia.

[1] (a) Glier, C.; Dietz, F.; Scholz, M.; Fischer, G. *Tetrahedron* **1972**, *28*, 5779. (b) Paudler, W. W.; Chasman, J. N. *J. Heterocycl. Chem.* **1973**, *10*, 499.

[2] (a) Lerner, D. A.; Horowitz, P. M.; Evleth, E. M. *J. Phys. Chem.* **1977**, *81*, 12. (b) Catalan, J.; Mena, E.; Fabero, F. *J. Chem. Phys.* **1992**, *96*, 2005.

[3] For reviews, see, for example, (a) Michael, J. P. *Nat. Prod. Rep.* **1997**, *14*, 21. (b) Michael, J. P. *Ibid.* 1997, *21*, 619 and references therein.

[4] (a) For review on early results, see Blewitt, H. L. *Chem. Heterocycl. Compd.* **1977**, *30*, 117. (b) Meiboroda, D. A.; Babaev, E. V.; Jug, K. *J. Org. Chem.* **1997**, *62*, 7100.

[5] (a) Uchida, T.; Matsumoto, K. *Synthesis* **1976**, 209. (b) Prostakov, N. S.; Baktibaev, O. B. *Russ. Chem. Rev.* **1975**, *44*, 748. For recent work, see for example, (c) Bonneau, R.; Romashin, Y. N.; Liu, M. T. H.; Macpherson, S. E. *J. Chem. Soc., Chem. Commun.* **1994**, 509. (d) Zhang, X.; Cao, W.; Wei, X.; Hu, H. *Synth. Commun.* 1997, *27*, 1395. (e) Zhou, J.; Hu, Y.; Hu, H. *Synthesis* **1999**, 166.

[6] (a) Swinbourne, F. J.; Hunt, J. H.; Klinkert, G. In *Advances in Heterocyclic Chemistry*; Katritzky, A. R., A. J., Eds.; Academic Press: New York, 1978; vol. 23, pp 104−170. (b) Flitsch, W. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Raes, C. W., Eds.; Pergamon Press: New York, 1984; vol. 4, pp 443−495. (c) Maibroda, D. A.; Babaev, E. V. *Khim. Geterotskl. Soedn. (Russ).* **1995**, 1445; *Chem. Abstr.* *125*, 33500r.

[7] Colonna, M.; Greci, L.; Poloni, M.; Marrosu, G.; Trazza, A.; Colonna, F. P.; Distefanno, G. *J. Chem. Soc., Perkin Trans. 2.* **1986**, 1229.

[8] (a) Jones, G. In *The Organic Chemistry of Nitrogen*, 3nd ed.; Sidgwick, N. V., Millar, I. T., Springall, H. D., Eds.; Clarendon Press: Oxford, 1966; p 752. (b) Borrows, E. T.; Holland, D. O. *Chem. Rev.* **1948**, *42*, 611.

[9] (a) Evans, D. F.*J. Chem. Soc.* **1953**, 345. (b) Tsubomura, H.; Mulliken, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 5966. (c) Tamres, M.; Strong, R. L. In *Molecular Association*; Foster, R., Ed.; Academic Press: London, 1979; vol. 2, pp 331−456 and references therein. (d) Kristiansen, M.; Scurlock, R. D.; Iu, K. K.; Ogilby, P. R. *J. Phys. Chem.* **1991**, *95*, 5190. (e) Kuriyama, Y.; Ogilby, P. R.; Mikkelsen, K. V. *J. Phys. Chem.* **1994**, *98*, 11918 and references therein. (f) Scurlock, R. D.; Ogilby, P. R. *J. Phys. Chem.* **1989**, *93*, 5493.

[10] (a) Stenberg, V. I.; Wang, C. T.; Kulevsky, N. *J. Org. Chem.* **1970**, *35*, 1774. (b) Petterson, R. C. *Angrew. Chem., Int. Ed. Engl.* **1970**, *9*, 644.

10.1021/jo015769o CCC: $20.00

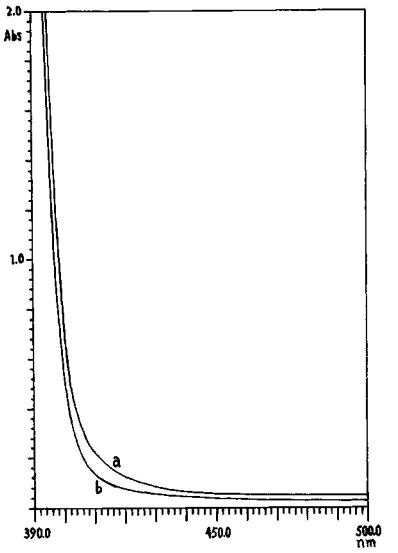


Figure 1. UV spectrum of CTC complex of **1a**. Curve a: oxygen-saturated solution of **1a** in benzene. Curve b: oxygen-free solution of **1a** in benzene.

Results and Discussion

For compound **1a**, the absorption caused by the transition from its ground-state CT complex with molecular oxygen to the excited CT complex can be measured by direct recording the UV spectra of oxygen saturated and oxygen free solutions of the indolizine, respectively. This is shown in Figure 1 with **1a** as an example. This CTC absorption could also be measured by differential method. Solutions of same concentration (5 M) of **1a** in benzene were placed in the sample and reference cells in a UV spectrometer. When the sample solution was saturated with oxygen and the reference solution was oxygen-free, a broad absorption band occurred in the electronic spectrum in the region 450−600 nm. This band disappears on extruding oxygen from the solution in the sample cell by purging dry argon. For compounds **1b**, **1c**, and **1d**, this measurement of the differential spectrum of the ground-state CT complexes with oxygen was hampered by their limited solubility in benzene and in other common solvents. In these cases, due to the small concentration of the substrates, the CT complex concentration may be too low for their absorption to be measured.

Irradiation of a benzene solution of **1a** with light of wavelength longer than 400 nm led to continuous consumption of the starting material but resulted in a complex intractable black tarry material from which no discrete products can be isolated in significant amounts. However, when the photolysis was carried out in benzene−methanol (1:1, v/v) with methanol as a nucleophile, the reaction proceeded smoothly, and gave **2a** (29%), **3a** (26%), and **4a** (17%) as products. The two esters **2a** and **3a** are viscous oils. The *Z*-configuration of **2a** was established by a ^{1}H NMR NOESY measurement of the corresponding *Z*-**2d** (vide infra) which revealed the steric proximity of olefinic proton H^3 with the pyridine proton at C(3′) (formula **2**) and the phenyl protons. The spectroscopic data of the ester **3a** are closely parallel to that of the acid **4a**, and their *E*-configuration was further confirmed by an X-ray crystallographic analysis of product **4c** (vide infra).

Table 1. Photooxygenations of the Indolizines 1a−d via the Excitation of Their CT Complex with Molecular Oxygen[a]

substrate	irradiation time (h)	conversion (%)	products and yields (%)[b]
1a	10	100	**2a** (29), **3a** (26), **4a** (17)
1b	10	100	**2b** (25), **3b** (23), **4b** (12)
1c	8	100	**2c** (26), **3c** (25), **4c** (19)
1d	8	100	**2d** (20), **3d** (23), **4d** (18)

[a] [substrate] = 0.025 M. [b] Yield based on consumed **1**.

Main difference in the ^{1}H NMR of the *Z*- and *E*-esters is in the absorption of the olefinic proton H^3. In the *Z*-isomer, H^3 resonates at ≈6.9 ppm, while in the *E*-isomer, the absorption of this proton moves downfield for about 1 ppm to occur at ≈7.9 ppm due to the deshielding effect of the nearby carbonyl and the pyrridine ring.

Irradiation of benzene−methanol (1:1, v/v) solution of compounds **1b**−**d** under same conditions as mentioned for **1a** gave similar results with the *Z*- and *E*-esters **2b**−**d**, **3b**−**d**, and the *E*-acids **4b**− **d** as products respectively (Table 1).

Since compounds **1a**−**d** have no measurable absorption in the wavelength region used for photolysis, these photooxygenations could not have proceeded via direct excitation of the indolizines. At the same time, as shown in Figure 1 for **1a**, ground-state CT complex absorbs in this region. Therefore, they can be ascribed to take place by the excitation of the contact CT complex which resulted in the formation of the excited CT complex, i.e., the indolizene's cation radicals and superoxide anion radicals. Both theoretical and experimental studies have shown that the excited CT complex are coupled with a suite of other electronic states of the substrate−O_2 complex.[9,15] Based on thermodynamic considerations, the possibility to transform to triplet substrates and singlet oxygen ($^1\Delta_g$) can be ruled out. Nevertheless, transformation to triplet indolizines and ground-state oxygen may be possible.[16] Following the formation of the triplet indolizines, energy transfer with ground state ($^3\Sigma_g^-$) oxygen would yield singlet oxygen. The excited CT complex, after relaxing to ion radical pairs, could also undergo further dissociation into solvent separated ion radical pairs and free ions. In this case, the indolizine

---

(11) Tsubomura, H.; Yagishita, T.; Toi, H. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3051.

(12) (a) Stenberg, V. I.; Olson, R. D.; Wang, C. T.; Kulevsky, N. *J. Org. Chem.* **1967**, 32, 3227. (b) Von Sonntag, C.; Newwald, K.; Schuchmann, H.-P.; Weeke, F.; Janssen, E. *J. Chem. Soc., Perkin Trans. 2.* **1975**, 171.

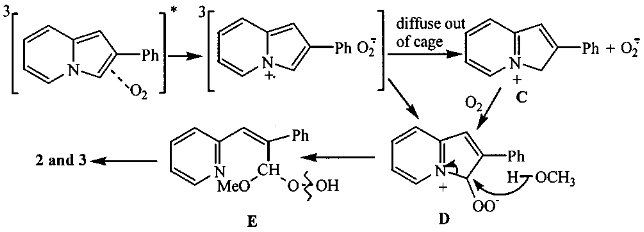
(13) Onodera, k.; Furusawa, G.-I.; Kojima, M.; Tsuchiya, M.; Aihara, S.; Akaba, R.; Sakuragi, H.; Tokumaru, K. *Tetrahedron* **1985**, *41*, 2215 and references therein.

(14) (a) Kulevski, N.; Sneeringer, P. V.; Stenberg, V. I. *J. Org. Chem.* **1972**, *37*, 438. (b) Kojima, M.; Sakuragi, H,; Tokumaru, K. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 3331.

(15) (a) Tsubomura, H.; Mullikm, R. S.*J. Am. Chem. Soc.* **1960**, *82*, 5966. (b) Birks, J. B.; Pantos, E.; Hamilton, T. D. S. *Chem. Phys. Lett.* **1973**, *20*, 544. (c) Kawaoka, K.; Khan, A. U.; Kearns, D. R. *J. Chem. Phys.* **1967**, *46*, 1842. (d) Kawaoka, K.; Khan, A. U.; Kearns, D. R. *J. Chem. Phys.* **1967**, *47*, 1883. (e) Khan, A. U.; Kearns, D. R. *J. Chem. Phys.* **1968**, *48*, 3272. (f) Murrell, J. N. *Mol. Phys.* **1960**, *3*, 319. (g) Scurlock, R. D.; Ogilby, P. R. *J. Am. Chem. Soc.* **1988**, *110*, 640.

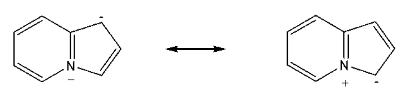
(16) The energy of the blue edge of the ground-state CTC absorption (Figure 1) is ~72 kcal mol^{-1}. The triplet energy (E_T) of indolizine and 2-phenylindolizine have not been reported since they have no detectable phosphorescence either at room temperature or at 77 K. Nevertheless, these E_T values should be lower than 72 kcal mol^{-1} considering that 2-phenylindolizine has a singlet energy of 74 kcal mol^{-1}. At the same time, the energy of the $^1\Delta_g$ oxygen is 22.1 kcal/mol.

Scheme 1



cation radicals can be trapped by ground state oxygen in the bulk solution. As a third possibility, the triplet ion radical pairs initially formed in the excitation of the ground-state CT complex may undergo back electron transfer after intersystem crossing to give ground-state indolizine and singlet oxygen.[9,15] Summing up, two possible reaction pathways may be operative in these photooxygenations—the ion radical route and the singlet oxygen route.

In the first reaction pathway, the cation radicals escaping out of solvent cage can be trapped at the radical center by molecular oxygen and at the cation center by methanol.



A B

As has been repeatedly shown by both electronic structure calculations[4] and by many reactions of electrophiles with indolizines, e.g., in protonation,[17] nitration and nitrosation,[18] acylation,[19] oxidative dimerization,[20] coupling reactions with electron acceptors such as methyl acrylate[21] and tetracyanoethene (TCNE),[22] etc., the pyrrole ring is more electron rich than the pyridine ring and is the site of attack by electrophiles. In all these reactions, nucleophilic reactivity at the indolizine ring is found to decrease in the order $3 > 1 \gg 5$. Theoretical calculations on indolizine ground-state electronic structure have given contradictory results concerning the electron density at different sites at the pyrrole ring,[4] but all these calculations uniformly confirm that the pyrrole ring shares the majority of the π-electron density. Therefore, indolizine could be described by the structures **A** and **B** with **A** being more favorable. Loss of one electron from the neutral molecule leads to the formation of the cation radicals which can consequently be envisaged to have the structure shown by **C** (see Scheme 1). Our AM1 calculations of the spin density and charge density in the cation radicals of **1b** have substantiated this situation and show that the spin density distribution in the cation radical of **1b** is indeed largely concentrated at C^3 and to a less extent, at C^1 (Figure 2). Meanwhile, the three carbon atoms directly linked to the nitrogen atom (C^3, C^5, and C^9) are the least negatively charged or positively charged (C^5 and C^9), and with the charge density at the hydrogen atom summing up to the corresponding carbon atom, C3 and C5 are the most positively charged carbon atoms in the indolizine ring. Reaction outcomes in the photooxygenations are in full accord with these structural features of the indolizine's cation radical. The reaction mechanisms for this cation radical route are outlined in Scheme 1. In-cage indolizine cation radical−superoxide anion radical coupling or triplet oxygen attack at C^3 in the cation radical (**C**), escaped out-of-cage from the triplet ion radical pairs, furnishes the zwitterionic peroxidic intermediate **D**. This was followed by nuleophilic trapping of the cation center by methanol to give the peroxide intermediate **E**, in which the homolytic scission of the O−O bond furnishes products **2** and **3**. The acids **4** may be obtained by trapping of the cation center in **D** by the trace amount of water in the solvent.

In the second reaction route, substrate may react with singlet oxygen formed either by energy transfer between triplet indolizine and ground-state oxygen or by back electron transfer in the singlet ion radical pairs formed after the intersystem crossing.[9,15] To test the reactivity of the indolizines **1** toward singlet oxygen, we have investigated reactions of the substrate **1a** with singlet oxygen thermally generated in two different ways: (1) mixing of hydrogen peroxide−sodium hypochlorite[23] and (2) thermal decomposition of the 9,10-diphenylanthracene endoperoxide.[24] It was found that, although **1a** could not react with either hydrogen peroxide or sodium hyperchlorite alone, it is oxidized by the mixture of the two in aqueous methanol to give the ester **2a** (19%) and the acid **4a** (17%) as products. Compound **1a** could also be oxidized when heating with 9,10-diphenylanthracene endoperoxide in a benzene solution. After treating the reaction mixture with diazomethane, the ester **4a** (48%) was obtained as product.

To further test the involvement of $^1\Delta_g$ O_2 in the photooxgenations, singlet oxygen quenching experiments with DABCO as a physical quencer[25] have been carried out. It is found that, the photooxygenation of **1a** (0.02 M, MeOH) could be quenched by DABCO in different degrees, depending on the concentration of DABCO. Therefore, while the presence of DABCO at a concentration of 0.05 M causes only a slight quenching (5%) of the photooxygenation, a [DABCO] of 0.25 M results in a 33% quenching. These results show that $^1\Delta_g$ O_2 is involved in the photooxygenations. In these singlet oxygen reactions, the same zwitterionic peroxidic intermediate **D** shown in Scheme 1 could also be formed by electrophilic attack of singlet oxygen at C_3 or derived from the endoperoxide **F** and the perepoxide intermediate **H**. Upon trapping by methanol, this peroxide gave products **2**, **3**, and **4**. Since the reactions of **1a** with thermally generated singlet oxygen gave similar products as in the photooxygenations via the CTC excitation (although in different product ratio), it is difficult to assess the relative contributions of the radical cation pathway and the singlet oxygen pathway. However, it is worth noting that, although in the singlet oxygen reactions of electron rich N-containing heterocycles[26] which can be viewed as conjugated enamines, dioxetane[27] derived from [2 + 2]

---

(17) Fraser, M.; Mckenzie, S.; Reid, D. H. *J. Chem. Soc. B* **1966**, 44.

(18) (a) Greci, L.; Ridd, J. H. *J. Chem. Soc., Perkin Trans. 2* **1979**, 312. (b) Hickman, J. A.; Wibberlay, D. G. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2954.

(19) Babaev, E. V.; Babrovskii, S. I.; Bundel, Yu. G. *Khim. Geterotsikl. Soedin.* **1988**, 1570; *Chem. Abstr. 111*, 97031g.

(20) Andruzzi, R.; Cardellini, L.; Greci, L.; Stipa, P.; Poloni, M.; Trazza, A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3067.

(21) Yamashita, Y.; Suzuki, D.; Masumura, M. *Heterocycles* **1984**, *22*, 791.

(22) Ceder, O.; Hall, B. *J. Heterocycl. Chem.* **1978**, *15*, 1471.

(23) Collins, D. J.; Hobbs, J. J. *Aust. J. Chem.* **1967**, *20*, 1905.

(24) Wasserman, H. H.; Scheffer, J. R. *J. Am. Chem. Soc.* **1967**, *89*, 3073.

(25) (a) Ouannes, C.; Wilson, T. *J. Am. Chem. Soc.* **1968**, *90*, 6527. (b) Monroe, B. M. *J. Phys. Chem.* **1977**, *81*, 1861.

(26) George, M. V.; Bhat, V. *Chem. Rev.* **1979**, *79*, 447.

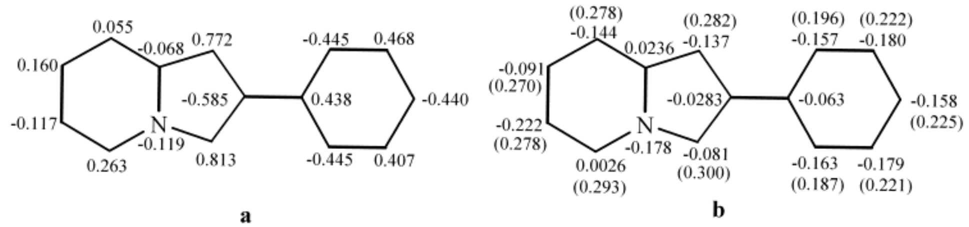
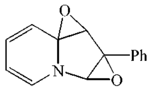
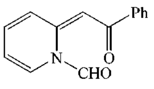


Figure 2. (a) Spin density of distribution in the cation radical of **1b**. (b) Charge density distribution in the cation radical of **1b** (the values in parentheses are the charge densities at the hydrogen atoms).

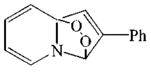
cycloaddition of singlet oxygen to the C=C bond and endoperoxide[28] derived from [4 + 2] cycloaddition of $^1\Delta_g$ O_2 with the conjugated diene are well-recognized intermediates along with the zwitterionic peroxide (as **D**), yet we have not found any products such as **5** and **6** which are derived from the endoperoxide (**F**) and the dioxetane (**G**) intermediates in the photooxygenation reactions. This raises the possibility that singlet oxygen may serve as electron acceptor to initiate SET process with the indolizines as electron donors. Charge-transfer quenching of $^1\Delta_g$ O_2 by strong electron donors such as enamines,[29] amines,[30] phenols,[31] sulfides,[32] hydrazines,[33] etc., have been reported. In polar solvents, full SET may be resulted to give the substrate's cation radical and superoxide anion radical[30c,d] which may take part in further reactions to give products.[30f]



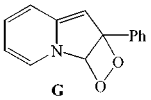
5



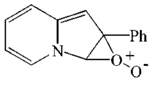
6



F



G



H

As enamines with highly extended π-system, indolizines **1a**−**d** have very low oxidation potentials ($E_{1/2}^{ox}$ of **1b** is 0.737V, SCE, MeCN[7]). Also, the photooxygenations have proceeded in a highly polar solvent system. Therefore, SET from the substrates **1a**−**d** to $^1\Delta_g$ O_2 is a possibility that should be taken into consideration in the photooxygenation of **1a**−**d**, and in case these SET processes take place, the overall reactions can be accounted for by a unified mechanistic picture involving the cation radicals of the indolizines (**C**) as the reactive intermediates shown in Scheme 1.

It is also noted that, direct exciation of the indolizine monomer in benzene−methanol (1:1, v/v) with light of $\lambda > 300$ nm also gives the same products as in the selective excitation of the CTC complex with oxygen, however, in significantly lower yields. As an example, photolysis of **1a** (0.025M) in oxygen saturated PhH−MeOH (1:1, v/v) solution for 10 h led to total conversion of the starting material and afforded **2a** (21%), **3a** (22%), and **4a** (17%). Here excitation of **1a** monomer and CTC of **1a** with oxygen occur concomitantly, and besides the mechanism shown in Scheme 1, other mechanistic possibilities arise. (1) Energy transfer from S_1 or T_1 state of **1a** to ground-state oxygen to generate $^1\Delta_g$ O_2. (2) SET from the singlet excited **1a** to ground-state oxygen to give the cation radical of **1a** and the superoxide anion radical which subsequently react to give the products.[34] Therefore, $^1\Delta_g$ O_2 and superoxide anion radicals ($O_2^{-\bullet}$) are still the active oxygen species responsible for the oxygenations.

In summary, selective excitation of the contact charge-transfer complex between the indolizines **1a**−**d** and triplet oxygen in benzene−methanol (1:1, v/v) resulted in mild oxidation of the substrate to give 3-(2-pyridinyl)-2-phenylacrylic acids and their esters as products without C−C bond cleavage in the substrate.

Experimental Section

Melting points were measured on a Yanaco microscopic melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker spectrometer at 300 MHz with $CDCl_3$ as internal standard and solvent. *J*-Values are given in Hz. IR spectra were taken with a Shimadzu IR 440 spectrometer for samples in KBr pellets. Mass spectra were recorded with a VG ZAB−HS spectrometer. Elemental analyses were obtained using

---

[27] (a) Bartlett, P. D.; Schaap, A. P. *J. Am. Chem. Soc.* **1970**, *92*, 3223. (b) Wasserman, H. H.; Terao, S. *Tetrahedron Lett.* **1975**, 1735. (c) Orito, K.; Manske, R. H.; Rodrigo, R. *J. Am. Chem. Soc.* **1974**, *96*, 1944. (d) Zhang, X.; Foote, C. S. *J. Org. Chem.* **1993**, *58*, 5524.

[28] (a) Foote, C. S.; Lin, J. W.-P. *Tetrahedron Lett.* **1968**, 3267. (b) Matsuura, T.; Saito, I. *Tetrahedron Lett.* **1968**, 3273. (c) Dewer, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1975**, *97*, 3978.

[29] Foote, C. S.; Dzakpasu, A. A.; Lin, J. W.-P. *Tetrahedron Lett.* **1975**, 1247.

[30] (a) Young, R. H.; Martin, R. *J. Am. Chem. Soc.* **1972**, *94*, 5183. (b) Young, R. H.; Brewer, D.; Kayser, R.; Martin, R. L.; Feriozi, D.; Keller, R. A. *Can. J. Chem.* **1974**, *52*, 2889. (c) Manring, L. E.; Foote, C. S. *J. Phys. Chem.* **1982**, *86*, 1257. (d) Saito, I.; Matsuura, T.; Inoue, K. *J. Am. Chem. Soc.* **1983**, *105*, 3200. (e) Darmanyan, A. P.; Jenks, W. S.; Jardon, P. *J. Phys. Chem. A* **1998**, *102*, 7420. (f) Ferroud, C.; Rool, P.; Santamaria, J. *Tetrahedron Lett.* **1998**, *39*, 9423.

[31] Matsuura, T.; Yoshimura, N.; Nishinaga, A.; Saito, I. *Tetrahedron* **1972**, *28*, 4933.

[32] Foote, C. S.; Peters, J. W. *J. Am. Chem. Soc.* **1971**, *93*, 3795.

[33] Clennan, E. L.; Noe, L. J.; Szneler, E.; Wen, T. *J. Am. Chem. Soc.* **1990**, *112*, 5080.

[34] The thermodynamic feasibility of this SET process can be estimated by the Weller equation[35] which takes the form of eq 1 in a

$$\Delta G_{ET} = E_{1/2}{}^{ox}(D/D^{+\bullet}) - E_{1/2}{}^{red}(O_2/O_2{}^{-\bullet}) - 3.21 - e^2/\epsilon \qquad (1)$$

polar solvent where $E_{1/2}{}^{ox}$ is the halfwave oxidation potential of the indolizine (0.737 V for **1b**, vs SCE, MeCN. Value vs $Ag/AgNO_3$[7] was transformed to that vs SCE by adding 0.337V[36]), $E_{1/2}{}^{red}$ ($O_2/O_2{}^{-\bullet}$) is the halfwave reduction potential of triplet oxygen (0.75 V, SCE, MeCN),[37] 3.21 is the excitation energy of the indolizine **1b**, and the last term takes into account of the Coulombic interaction between the ion radicals which is 0.06 eV in MeCN, assuming an interionic separation of 7 Å.[35b] The ΔG_{ET} value for **1b** in MeCN is −1.78 eV (−41 kcal/mol), indicating that SET is highly exergonic. Although this estimation is made in MeCN, this large negative ΔG_{ET} value strongly suggests that in MeOH−PhH (1:1, v/v) which is also highly polar, SET between singlet excited indolizine and ground-state oxygen could be energetically feasible (The value of the e^2/ϵ term is usually small in a polar solvent system).

[35] (a) Weller, A. Z. *Phys. Chem. (Wiesbaden)* **1982**, *133*, 193. (b) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259.

[36] Larson, R. C.; Iwamoto, R. T.; Adams, R. N. *Anal. Chim. Acta* **1961**, *25*, 371.

[37] Mann, C. K.; Barns, K. K. *Electrochemical Reactions in Non-aqueous Systems*; Marcel Dekker: New York, 1970.

a Perkin-Elmer 240 C analyzer. Benzene (AR grade) was dried with sodium and distilled before use. Methanol was treated with magnesium and distilled before use. Other reagents were CP or AR grade and were used as received without further purification. Petroleum ether refers to the fraction with boiling point in the range 60−90 °C.

General Procedures. 1. Measurement of the Absorption Spectrum of the Ground-State Charge-Transfer Complex between 1a and Oxygen. (a) UV Spectrum of the Oxygen-Saturated Solution of 1a in Benzene. The oxygen-saturated and oxygen-free solutions of **1a** in benzene (0.3 M) were prepared by purging dry nitrogen and oxygen, respectively, to the solution for 30 min. The UV spectra of these solutions were recorded with pure benzene as reference (Figure 1).

(b) Measurement of the Differential Spectrum. In the reference cell and sample cell were placed the same solution of **1a** (1 g in 10 mL of methanol, 4.8 M). The sample cell was purged with oxygen while the reference cell was purged with argon for 30 min, and the absorption spectrum was then measured. In this case, the absorption of **1a** was counteracted and the spectrum displays only the absorption of the CTC complex. After purging argon into the sample cell to remove oxygen, this CTC absorption band disappeared. The CTC absorption band is between 450 and 600 nm region with absorption maximum at 500 nm.

2. Photooxygenation of 1a−d. The light source was a medium-pressure mercury lamp (500 W) in a cooling water jacket which was further surrounded by a layer of filter solution (10% aq sodium nitrite, 1 cm thickness, $\lambda > 400$ nm). The solution of indolizines (0.025 mol L^{-1}) in benzene−methanol (1/1, v:v) was placed in glass tubes (25 mL each) and was then irradiated at room temperature under continuous oxygen purging. At the end of the reaction (TLC monitoring), the solvent was removed in vacuo, and the residue was separated by flash chromatography on silica gel column with petroleum ether (bp 60−90 °C)−ethyl acetate as eluents to afford the products. The reaction scale, irradiation time and yields of the products are listed in Table 1.

Reactions of 5-Methyl-2-phenylindolizine (1a) with Thermally Generated Singlet Oxygen. 1. Reactions with Sodium Hypochllorite−Hydrogen Peroxide. To a solution of **1a** (0.6 g) in methanol (50 mL) was added hydrogen peroxide (4.5 mL, 30%), and the mixture was cooled in an ice bath. To this solution was added with stirring an aqueous sodium hypochlorite solution (18 mL, 21%) slowly (during 2 h) through an injector with the tip of the needle submerged beneath the surface of the reaction mixture.[25] The reaction mixture was diluted with water and was extracted with ethyl acetate (3 × 20 mL). The extract was dried by anhydrous magnesium sulfate, the solvent was removed in vacuo, and the residue was separated by flash chromatography on silica gel column with petroleum ether (bp 60−90 °C)−ethyl acetate as eluents to afford **2a** (0.14 g, 19%) and **4a** (0.12 g, 17%) as products.

2. Reactions with 9,10-Diphenylanthracene Endoperoxide. 9,10-Diphenylanthracene endoperoxide and diazomethane were prepared by literature procedures. 5-Methyl-2-phenylindolizine (**1a**, 0.41 g, 2 mmol) and 9,10-diphenylanthracene endoperoxide (1.44 g, 4 mmol) were desolved in benzene, and the solution was heated under reflux for 2−3 days until **1a** was completely consumed (TLC monitoring). The solution was cooled to room temperature, and a solution of diazomethane in ether (20 mL, 0.2mol/L) was slowly added. The reaction mixture was stirred for 0.5 h, the solvent was removed in vacuo, and the residue was separated by flash chromatography on silica gel column with petroleum ether (bp 60−90 °C)−ethyl acetate as eluents to afford 0.24 g of **2a** (48%).

2a: *Z*-Methyl 2-Phenyl-3-[2-(6-methylpyridinyl)]propen-2-oate. Colorless oil; υ_{max}/cm^{-1} 3060, 1725, 1622, 1580, 1565, 1368, 1205, 1013, 784, 735, 685; δ_H 2.56 (s, 3H, CH_3), 3.96 (s, 3H, OCH_3), 6.93 (s, 1H), 7.08 (d, *J* 7.7, 1H), 7.11 (d, *J* 7.7, 1H), 7.33−7.59 (m, 6H); *m/z* (%) 253 (M^+, 43), 252 (base), 238 (18.6), 222 (28.1), 194 (89.6), 78 (22.7) (Found: C, 75.17; H, 5.98; N, 5.30. $C_{16}H_{15}NO_2$ requires C, 75.89; H, 5.93; N, 5.54).

3a: *E*-Methyl 2-Phenyl-3-[2-(6-methylpyridinyl)]propen-2-oate. Wax solid, mp 44−45 °C; υ_{max}/cm^{-1} 3060, 1710, 1635, 1585, 1500, 1460, 1265, 1235, 820, 760, 710; δ_H 2.55 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 6.54 (d, *J* 7.9, 1H), 6.97 (d, *J* 7.6, 1H), 7.21−7.52 (m, 6H), 7.95 (s, 1H); *m/z* (%) 253 (M^+, 42.15), 252 (base), 238 (18.65), 194 (88.50), 153 (11.66), 122 (55.14), 105 (85.27), 78 (10.65) (Found: C, 75.66; H, 5.77; N, 5.49. $C_{16}H_{15}NO_2$ requires C, 75.89; H, 5.93; N, 5.54).

4a: *E*-2-phenyl-3-[2-(6-methylpyridinyl)]propen-2-oic Acid. Colorless crystals from petroleum ether − ethyl acetate, mp 175−176 °C; υ_{max}/cm^{-1} 2400−3100 (b), 1680, 1625, 1585, 1560, 1460, 1370, 1235, 1200, 1095, 1000, 805, 780, 700; δ_H 2.66 (s, 3H, CH_3), 6.64 (d, *J* 7.9, 1H), 7.07 (d, *J* 7.7, 1H), 7.22−7.42 (m, 6H), 8.13 (s, 1H), 13.00−13.08 (b, 1H, COOH); *m/z* (%) 239 (M^+, 15.79), 238 (33.49), 194 (base), 180 (6.95), 152 (8.79), 78 (2.62) (Found: C, 75.55; H, 5.42; N, 6.02. $C_{15}H_{13}NO_2$ requires C, 75.30; H, 5.48; N, 5.85%).

2b: *Z*-Methyl 2-Phenyl-3-(2-pyridinyl)propen-2-oate. Colorless oil; υ_{max}/cm^{-1} 3057, 1732, 1623, 1584, 1563, 1212, 1012, 778, 692; δ_H 3.87 (s, 3H, OCH_3), 6.93 (s, 1H, H_5), 7.04 (d, *J* 7.7, 1H), 7.11 (d, *J* 7.6, 1H), 7.33−7.60 (m, 6H, ArH), 8.54 (d, J 1H); *m/z* (%) 239 (M^+, 5.2), 238 (22.8), 180 (8.3), 84 (base), 78 (53.7) (Found: C, 75.26; H, 5.38; N, 5.78. $C_{15}H_{13}NO_2$ requires C, 75.31; H, 5.44; N, 5.86).

3b: *E*-Methyl 2-Phenyl-3-(2-pyridinyl)propen-2-oate. Colorless oil; υ_{max}/cm^{-1} 3055, 1710, 1625, 1580, 1565, 1240, 1200, 1080, 790, 710; δ_H 3.82 (s, 3H, OCH_3), 6.72 (d, J 8.0, 1H), 7.08 (dd, *J* 4.9, 7.4, 1H), 7.21−7.41 (m, 6H), 7.96 (s, 1H), 8.59−8.61 (dd, *J* 7.8, 0.8, 1H); *m/z* (%) 239 (M^+, 21.45), 238 (base), 224 (6.83), 180 (29.38), 152 (7.90), 78 (11.68) (Found: C, 75.19; H, 5.37; N, 5.87. $C_{15}H_{13}NO_2$ requires C, 75.31; H, 5.44; N, 5.86).

4b: *E*-2-Phenyl-3-(2-pyridinyl)propen-2-oic Acid. Colorless crystals (petroleum ether−ethyl acetate), mp 170−171 °C; υ_{max}/cm^{-1} 2300−3600 (b), 1710, 1635, 1600, 1575, 1475, 1260, 1100, 1015, 805, 720; δ_H 6.84 (d, *J* 8.1, 1H), 7.23−7.52 (m, 7H), 8.20 (s, 1H), 8.95 (d, *J* 4.8, 1H); *m/z* (%) 225 (M^+, 21.18), 224 (97.26), 180 (base), 152 (19.26), 78 (23.01) (Found: C, 74.67; H, 4.93; N, 6.18. $C_{14}H_{11}NO_2$ requires C, 74.65; H, 4.92; N, 6.22).

2c: *Z*-Methyl 2-(4-Chlorophenyl)-3-(2-pyridinyl)propen-2-oate. Colorless wax solid, mp 45−47 °C; υ_{max}/cm^{-1} 3057, 1726, 1629, 1244, 1091, 832, 786, 753; δ_H 3.92 (s, 3H, OCH_3), 6.94 (s, 1H), 7.17−7.71 (m, 7H), 8.58 (d, *J* 4.6, 1H); *m/z* (%) 273 (M^+, 23.2), 272 (base), 258 (8.8), 242 (7.0), 214 (42.2), 178 (10.9), 78 (24.3) (Found: C, 65.44; H, 4.52; N, 5.28. $C_{15}H_{12}ClNO_2$ requires C, 65.82; H, 4.42; N, 5.12).

3c: *E*-Methyl 2-(4-Chlorophenyl)-3-(2-pyridinyl)propen-2-oate. Colorless wax solid, mp 55−56 °C; υ_{max}/cm^{-1} 3050, 1710, 1620, 1575, 1540, 1480, 1455, 1240, 1200, 1070, 1000, 835, 790, 750; δ_H 3.84 (s, 3H, OCH_3), 6.79 (d, *J* 7.9, 1H), 7.13 (dd, *J* 7.9, 4.9, 1H), 7.17 (d, *J* 8.4, 2H), 7.36 (d, *J* 8.4, 1H), 7.41 (td, *J* 7.9, 1.7, 1H), 7.96 (s, 1H), 8.60 (dd, *J* 4.9, 1.7, 1H); *m/z* (%) 273 (M^+, 33.28), 271 (base), 230 (16.97), 178 (18.07), 156 (27.03), 139 (47.72), 111 (29.38), 78 (43.54) (Found: C, 65.81; H, 4.63; N, 5.05. $C_{15}H_{12}ClNO_2$ requires C, 65.82; H, 4.42; N, 5.12).

4c: *E*-2-(4-Chlorophenyl)-3-(2-pyridinyl)propen-2-oic Acid. Colorless crystals from petroleum ether−ethyl acetate, mp 177−178 °C; υ_{max}/cm^{-1} 2200−3100 (b), 1690, 1630, 1600, 1575, 1490, 1440, 1380, 1260, 1215, 1080, 1015, 795, 765, 720; δ_H 6.89 (s, *J* 7.9, 1H), 7.26−7.29 (m, 3H), 7.39 (d, *J* 8.4, 2H), 7.55 (t, *J* 7.9, 1H), 8.19 (s, 1H), 8.96 (d, *J* 4.4, 1H), 12.4−13.08 (b, 1H, COOH); *m/z* (%) 259 (M^+, 16.61), 214 (base), 178 (21.50), 152 (13.35), 136 (6.84), 78 (34.17) (Found: C, 64.93; H, 4.08; N, 5.39. $C_{14}H_{10}ClNO_2$ requires C, 64.75; H, 3.88; N, 5.39%).

2d: *Z*-Methyl 2-(3,4-Dimethylphenyl)-3-(2-pyridinyl)propen-2-oate. Colorless wax solid, mp 60−62 °C; υ_{max}/cm^{-1} 3050, 1725, 1615, 1580, 1495, 1420, 1365, 1195, 1025, 900, 820, 765, 735; δ_H (H−H COSY) 2.30 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 3.94 (s, 3H, OCH_3), 6.93 (s, H_3), 7.15 (t, *J* 7.7, $H_{5'}$), 7.13−7.33 (m, 4H, $H_{3'}$, $H_{2''}$, $H_{5''}$, $H_{6''}$), 7.67 (td, *J* 1.7, 7.7, $H_{4'}$), 8.59 (dd, *J* 7.7, 7.7, $H_{6'}$); *m/z* (%) 267 (M^+, 28.06), 266 (base), 236 (21.95), 208 (48.62), 193 (11.58), 133 (18.82), 115 (10.23), 78 (17.27) (Found: C, 76.14; H, 6.77; N, 5.18. $C_{17}H_{17}NO2$ requires C, 76.09; H, 6.76; N, 5.22).

3d: *E*-Methyl 2-(3,4-Dimethylphenyl)-3-(2-pyridinyl)propen-2-oate. Colorless crystals (petroleum ether−ethyl acetate), mp 82−83 °C; υ_{max}/cm^{-1} 3050, 1735, 1640, 1605, 1580, 1520, 1475, 1450, 1260, 1220, 1165, 1055, 805, 760; δ_H 2.20 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 6.74 (d, *J* 8.3, 1H), 6.89 (dd, *J* 7.5, 1.0, 1H), 6.95 (s, 1H), 7.02−7.17 (m, 2H), 7.31 (td, *J* 7.5, 1.8, 1H), 7.86 (s, 1H), 8.56 (m, 1H); *m/z* (%) 267 (M^+, 25.33), 266 (base), 209 (31.98), 153 (11.67), 105 (17.38) (Found: C, 76.05; H, 6.98; N, 5.09. $C_{17}H_{17}NO2$ requires C, 76.09; H, 6.76; N, 5.22).

4d: *E*-2-(3,4-Dimethylphenyl)-3-(2-pyridinyl)propen-2-oic Acid. Colorless crystals from petroleum ether−ethyl acetate, mp 183−184 °C; υ_{max}/cm^{-1} 3060, 1695, 1590, 1560, 1500, 1460, 1375, 1245, 1375, 1245, 1210, 1050, 820, 790, 735; δ_H 2.26 (s, 3H, CH_3), 2.30 (s, 3H, CH_3), 6.90 (d, *J* 8.0, 1H), 7.02 (dd, *J* 7.7, 1.3, 1H), 7.10 (s, 1H), 7.15−7.22 (m, 2H), 7.46 (td, *J* 7.7, 1.1, 1H), 8.15 (s, 1H), 8.97 (d, *J* 4.5, 1H), 10.75−12.42 (b, 1H, COOH); *m*/*z* (%) 253 (M^+, 16.59), 252 (49.25), 208 (base), 193 (9.09), 152, (2.50), 115 (6.62), 78 (10.53) (Found: C, 75.36; H, 6.24; N, 5.62. $C_{16}H_{15}NO2$ requires C, 75.57; H, 6.34; N, 5.53).

Acknowledgment. This work was supported by the National Natural Science Foundation of China (Project 20072017).

Supporting Information Available: ^{1}H NMR spectra of compounds **2d**, **3d**, and **4d**, H−H COSY and NOESY spectra of **2d**, tables of crystal data, atomic coordinates, bond length and angles, anisotropic thermal parameters for **4c**. Differential UV spectrum of **1a**−oxygen CTC. This material is available free of charge via the Internet at http:/pubs.acs.org.

JO015769O