Photoinduced Single Electron Transfer on 5-Aryl-1,2,4-oxadiazoles: Some Mechanistic Investigations in the Synthesis of Quinazolin-4-ones

Silvestre Buscemi, Andrea Pace, and Nicolò Vivona*

Dipartimento di Chimica Organica "E. Paternò", Università di Palermo, Viale delle Scienze, Parco d'Orleans II, 90128 Palermo, Italy

Tullio Caronna

Dipartimento di Chimica, Politecnico di Milano, Via Mancinelli 7, 20131 Milano, Italy

Alessandro Galia

Dipartimento di Ingegneria Chimica dei Processi e dei Materiali, Università di Palermo, Viale delle Scienze, 90128 Palermo, Italy

Received February 17, 1999

The photochemistry of some 5-aryl-3-methoxy- (or 5-aryl-3-phenyl-) 1,2,4-oxadiazoles irradiated in the presence of different sensitizers [such as diphenylacetylene (DAC), 9,10-diphenylanthracene (DAN), or triphenylene (TPH)] or ground-state donors such as triethylamine (TEA) has been investigated. Intermediates arising from breaking of the ring O−N bond develop both into quinazolin-4-ones (by a heterocyclization reaction involving the aryl at the C-5 of the oxadiazole nucleus) and into open-chain products (corresponding to a reduction at the ring O−N bond), in different ratios depending on their structures and photoreaction conditions. A reasonable explanation considers *sensitization* by photoinduced electron transfer either from the sensitizer in its excited state to the oxadiazole in its ground state or from the electron donor reagent (TEA) to the excited oxadiazole; in both cases an oxadiazole radical anion is formed as a key species from which breaking of the ring O−N bond takes place. Reduction potentials of representative oxadiazoles confirm this hypothesis. Possible applications in the synthesis of variously substituted quinazolin-4-ones are recognized.

Introduction

In the framework of our research on photoinduced rearrangements of O−N bond containing five-membered heterocycles, we have pointed out the possibility of exploiting this photoreactivity to appoint alternative methodologies for the synthesis of target compounds.[1−5] Significant examples of this approach have concerned the photochemistry of 1,2,5- and 1,2,4-oxadiazoles. In a general pattern, photolytic species arising from cleavage of the weakest O−N bond of these rings collapse into final products depending, inter alia, on (i) its own structure, (ii) the nature of the reagent that will be present, and (iii) the possibility of subsequent heterocyclization of primarily formed intermediates. Thus, for example, irradiation of particular 1,2,4-oxadiazoles in the presence of nitrogen or sulfur nucleophiles produces 1,2,4-triazoles[4] or 1,2,4-thiadiazoles,[5] respectively, which assume a heterocyclization reaction of intermediates arising from the formation of a N−N or N−S bond. Intramolecular photoinduced heterocyclizations involving 1,2,4-oxadiazoles substituted at C(3) with certain three-atom side chains have also been reported.[6] On the other hand, apart from the above-mentioned photoreactions producing heterocyclic structures, photolytic intermediates can even stabilize into open-chain products, e.g., by a reaction with the nucleophilic solvent (methanol)[7] or by a capture of two hydrogen atoms from the medium (resulting in an overall photoreduction reaction at the ring O−N bond).[4,5]

An interesting intramolecular photoreaction concerns the formation of the quinazolin-4-one system by irradiation of some 5-aryl-substituted 1,2,4-oxadiazoles at $\lambda =$ 313 nm in methanol and in the presence of diphenylacetylene (DAC).[8] In this case, the heterocyclization reaction of photolytic intermediates, whichever the ring photolytic species may be, engages the C(5)-aryl moiety, and a first-glance approach considered the photoreaction as arising from a triplet sensitization.[8]

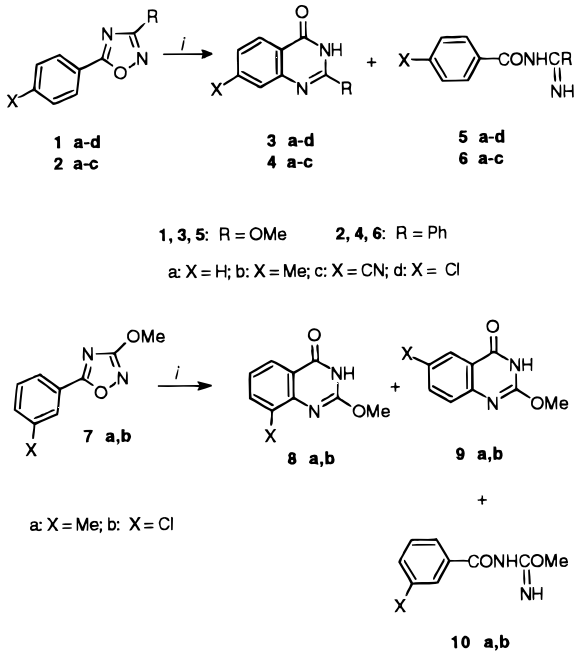
Following our studies, we now decided to concentrate our attention on deeper mechanistic investigations of this rearrangement, as well as on the potential of this photochemical reaction in synthetic projects. To this aim,

* To whom correspondence should be addressed. Phone: +39 091 596903. Fax: +39 091 596825.

(1) Vivona, N.; Buscemi, S. *Heterocycles* **1995**, *41*, 2095.
(2) Buscemi, S.; Vivona, N.; Caronna, T. *J. Org. Chem.* **1995**, *60*, 4096.
(3) Buscemi, S.; Vivona, N.; Caronna, T. *Synthesis* **1995**, 917.
(4) Buscemi, S.; Vivona, N.; Caronna, T. *J. Org. Chem.* **1996**, *61*, 8397.
(5) Vivona, N.; Buscemi, S.; Asta, S.; Caronna, T. *Tetrahedron* **1997**, *53*, 12629.
(6) (a) Buscemi, S.; Vivona, N. *J. Heterocycl. Chem.* **1988**, *25*, 1551. (b) Buscemi, S.; Vivona, N. *Heterocycles* **1989**, *29*, 73. (c) Buscemi, S.; Macaluso, G.; Vivona, N. *Heterocycles* **1989**, *29*, 1301. (d) Buscemi, S.; Cusmano, G.; Gruttadauria, M. *J. Heterocycl. Chem.* **1990**, *27*, 861
(7) (a) Newman, H. *Tetrahedron Lett.* **1968**, 2421. (b) Buscemi, S.; Cicero, M. G.; Vivona, N.; Caronna, T. *J. Heterocycl. Chem.* **1988**, *25*, 931.
(8) Buscemi, S.; Vivona, N. *J. Chem. Soc., Perkin Trans. 2* **1991**, 187.

10.1021/jo990298f CCC: $18.00
Published on Web 08/31/1999

Scheme 1[a]



[a] (i) *hν*/MeOH/sensitizer.

Table 1. Energy Values (kJ/mol) of the Singlet (E_s) and Triplet (E_t) States for Compounds 1a−d and 2a−c [As Determined from Fluorescence (in Methanol) or Phosphorescence Emissions (in Acetonitrile)], and for DAC,[9] Dan,[9,10] and TPH[9,11]

compd	E_s	E_t	compd	E_s	E_t
1a	418	291	**2b**	381	278
1b	441	283	**2c**	387	267
1c	430	255	DAC	396	261
1d	414	270	DAN	305	
2a	388	281	TPH	350	278

we have considered irradiations of some 3-methoxy-5-aryloxadiazoles (**1** and **7**) and 3-phenyl-5-aryloxadiazoles (**2**) (Scheme 1) in different photoreaction conditions. Interestingly, oxadiazoles **1a−d** and **7a,b** are characterized by having an OMe group at C(3) of the ring, and this feature was expected to strongly affect the reactivity/stability of photolytic intermediates. In their turn, oxadiazoles **7a,b** would give regioisomeric heterocyclizations, so that, when various substituents at the C(5)-aryl moiety would be considered, the synthesis of variously substituted quinazolin-4-ones could be accomplished. All oxadiazoles showed similar photophysical behavior with a strong fluorescence emission and weaker phosphorescence. Values of singlet (E_s) and triplet (E_t) state energies of representative substrates are given in Table 1. As for photoreaction conditions, on the basis of previous reports we initially considered irradiations (at $\lambda = 313$ nm) in methanol in the presence of DAC. In addition, to gain more insight into the nature of sensitization, representative oxadiazoles were irradiated in the presence of 9,10-diphenylanthracene (DAN) (at $\lambda = 365$ nm) and triphenylene (TPH) (at $\lambda = 313$ nm). Energies of excited states of DAC,[9] DAN,[9,10] and TPH[9,11] are reported in Table 1. Furthermore, selected oxadiazoles were irradiated (at $\lambda = 313$ nm) in the presence of triethylamine (TEA), starting from the consideration that excited oxadiazole could act as electron acceptor from the ground electron donor reagent.

Results and Discussion

Irradiations in the Presence of DAC, DAN, or TPH. (a) 3-Methoxy-5-aryl-1,2,4-oxadiazoles 1a−d and 7a,b. Irradiation of 3-methoxy oxadiazoles **1a−d** in methanol in the presence of DAC gave the expected[8] quinazolinones **3a−d**, which can be isolated in about 30−40% yields. In addition, some amounts of photoreduction products **5a−d** were also formed. In a typical preparative irradiation of **1a**, besides starting material (40%), compounds **3a** (40%) and **5a** (18%) have been isolated. Oxadiazoles **1b−d** behaved similarly, and gave **3b−d** and **5b−d**, respectively. However, a significant substituent effect resulted: in fact, electron-withdrawing substituents at the C(5)-aryl moiety enhance both the photoconversion of starting material and yields of reduction products. (Typical results from parallel experiments are reported in Table 2.) By contrast, parallel unsensitized irradiation of the representative **1a** at $\lambda = 313$ nm in methanol essentially returned starting material (92%), while only a few percent of **3a** and **5a** have been detected (by HPLC). Apart from compound **1c**, triplet energy transfer sensitization by DAC seems unlikely on energetic grounds (see Table 1). On the other hand, by using different triplet sensitizers [namely, acetophenone ($E_t = 310$ kJ/mol)[9] at $\lambda = 313$ nm for **1a** or benzophenone ($E_t = 287$ kJ/mol)[9] at $\lambda = 365$ nm for **1d**], no significant sensitization was obtained. As expected, the DAC-sensitized irradiation of oxadiazoles **7a,b** gave both the forecast regioisomers **8a,b** (18 and 24%, respectively) and **9a,b** (15 and 30%). Again, the chloro-substituted substrate **7b** showed higher photoconversion and more amounts of the reduction product **10b**.

We have then looked at irradiations of the representative oxadiazole **1a** in the presence of DAN which is known to act as singlet sensitizer: since it has a very low yield of intersystem crossing, practically no triplet DAN is formed.[10] Interestingly, a preparative-scale irradiation of **1a** and DAN allowed **3a** (52%) and **5a** (12%) to be isolated, testifying that DAN does act as an efficient sensitizer. TPH behaved similarly: an analytical-scale irradiation of **1a** returned starting material (73%) and gave **3a** (20%) and **5a** (7%) (Table 2).

(b) 3-Phenyl-5-aryl-1,2,4-oxadiazoles 2a−c. Irradiation of these substrates in the presence of DAC gave the quinazolin-4-ones **4a−c**. However, differently from previous oxadiazole derivatives, no significant amounts of reduction products were obtained. Moreover, substituents at the C(5)-aryl moiety do not appreciably affect photoconversion of the starting oxadiazole. The formation of compounds **4** may be considered as arising from a DAC-sensitized process: in fact, when directly irradiated in methanol, oxadiazoles **2a−c** remained practically unchanged. Again, the photoreaction also took place by using DAN, or TPH: thus, a preparative DAN-sensitized irradiation of the oxadiazole **2a** furnished **4a** (50%) together with unreacted starting material, while instead no significant amounts of the corresponding reduction product **6a** were detected. TPH behaved similarly (see Table 2). By contrast, in the irradiation of the oxadiazole **2a** in the presence of benzophenone (at $\lambda = 365$ nm) or

(9) Murov, S. L. *Handbook of Photochemistry*; Marcel Dekker: New York, 1973.
(10) Wilson, T.; Schaap, A. P. *J. Am. Chem. Soc.* **1971**, *93*, 4126.
(11) Bartlett, P. D.; Engel, P. S. *J. Am. Chem. Soc.* **1968**, *90*, 2960.

Table 2. Analytical Photoreactions. Irradiation of Compounds 1a−d and 2a in Methanol in the Presence of DAC, DAN, or TPH. Quantitative HPLC Analyses (%) of Photolyzates

	starting material				photoproducts				photoproducts		
compd	DAC	DAN	TPH		DAC	DAN	TPH		DAC	DAN	TPH
1a	70	56	73	**3a**	25	39	20	**5a**	5	5	7
1b	85			**3b**	10			**5b**	5		
1c	31			**3c**	32			**5c**	37		
1d	52			**3d**	28			**5d**	20		
2a	85	69	89	**4a**	15	31	11	**6a**	0	0	0

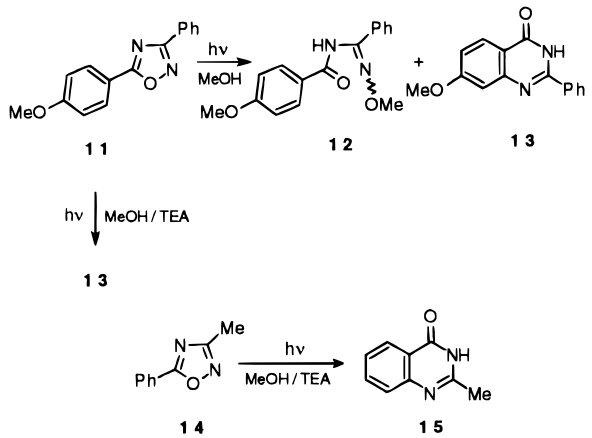
acetophenone (at $\lambda = 313$ nm), no significant sensitization was obtained.

The formation of both the quinazolin-4-one system and the open-chain reduction products may be considered as arising from a *sensitized* photolysis of the 5-aryl-substituted 1,2,4-oxadiazoles. However, the relevant questions concern (i) the nature of sensitization, (ii) the nature of the photolytic species which arises from breaking of the ring O−N bond, and (iii) how the structure of substrate plays a role in the photoreaction.

In principle, heterolytic cleavage of the ring O−N bond of excited oxadiazoles would give acyliminonitrenes. These reactive intermediates can undergo chemistry from either their singlet or their triplet states.[12] Singlet nitrenes (electrophilic in character) will be well disposed to react both with the nucleophilic solvent and with the C(5)-aryl moiety by a heterocyclization reaction. In turn, triplet nitrenes are expected to stabilize preferentially by capture of hydrogen atoms from the medium in an overall reduction reaction.

On the basis of our results, involvement of triplet energy-transfer sensitization appears unlikely. On the other hand, singlet energy transfer by DAN or TPH might be excluded on energetic grounds (see Table 1). Moreover, although an intramolecular heterocyclization might be favored entropically over an intermolecular reaction involving the solvent, ground-state singlet nitrenes would have been captured to some extent by the solvent (methanol); however, this last reaction was not significantly observed in all our sensitized procedures: only in the case of the oxadiazole **11**, the DAC-sensitized photoreaction, besides **13**, gave trace amounts of the methanol addition compound **12** (Scheme 2). Indeed, methanol addition reaction to presumed acyliminonitrenes has been observed on irradiating some 5-phenyloxadiazoles at $\lambda = 254$ nm in methanol.[7] Moreover, direct irradiation of **11** at $\lambda = 313$ nm in methanol essentially gave the solvolysis product **12** (together with trace amounts of **13**) by an almost complete conversion of starting material. This means that, although there is the possibility for an intramolecular heterocyclization, the predominant reaction of the presumed primarily formed intermediate engages the nucleophilic solvent. On the other hand, in the irradiation of **1a** and **2a** at $\lambda = 254$ nm in methanol and in the presence of aliphatic amines,

Scheme 2



photolytic species do react preferentially with the nitrogen nucleophile, giving N−N bonded species.[4,13]

A mechanistic hypothesis which could explain our results considers sensitization by an electron-transfer mechanism. Previously, photoinduced electron transfer has been suggested to occur in the DAN-sensitized decomposition of aroyl azides.[14] By this hypothesis, excited DAC, DAN, or TPH behaves as an electron donor toward the electron-deficient ground-state oxadiazole, which will then assume a radical anion form. Subsequent breaking of the ring O−N bond will then take place from this key intermediate, producing an open-chain species for which a radical anion structure **16** (likely developing into **17** in the hydroxylic solvent) can be presumed (Scheme 3). The formation of open-chain radical anion via an electron-transfer mechanism has been suggested in the iron dichloride- or samarium diiodide-induced reductive breaking of the ring O−N bond of some isoxazoles.[15,16] On the other hand, nitrene radical anions are suggested in electrochemical reduction[17] of azides or in their photoinduced decomposition by an electron-transfer mechanism.[18] Our ring-cleaved intermediate will develop into both the quinazolin-4-one system (implying a back-electron transfer in some of the subsequent steps) and the reduced products (by hydrogen atom abstraction), in

(12) Nitrene chemistry in photochemical reactions is widely reported in the literature. See, inter alia: (a) Iddon, B.; Meth-Cohn, O.; Scriven, E. F. V.; Suschitzky, H.; Gallagher, P. T. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 900. (b) Scriven, E. F. V. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1982. (c) *Azides and Nitrenes*; Scriven, E. F. V., Ed.; Academic Press: New York, 1984. (d) Leyva, E.; Platz, M. S.; Persy, G.; Wirz, J. *J. Am. Chem. Soc.*, **1986**, *108*, 3783.

(13) We had observed [4] that irradiation of **1a** and **2a** in the presence of amines, besides the formation of the N−N bonded species, showed the heterocyclization reaction into the quinazolin-4-one system to a greater extent than that observed in methanol alone; this catalytic effect by the amine reagent could now be explained on the basis of our findings in the TEA-sensitized reactions.

(14) (a) Abraham, W.; Buchallik, M.; Zhu, Q. Q.; Schnabel, W. *J. Photochem. Photobiol., A* **1993**, *71*, 119. (b) Clauss, K.-U.; Buck, K.; Abraham, W. *Tetrahedron* **1995**, *51*, 7181.

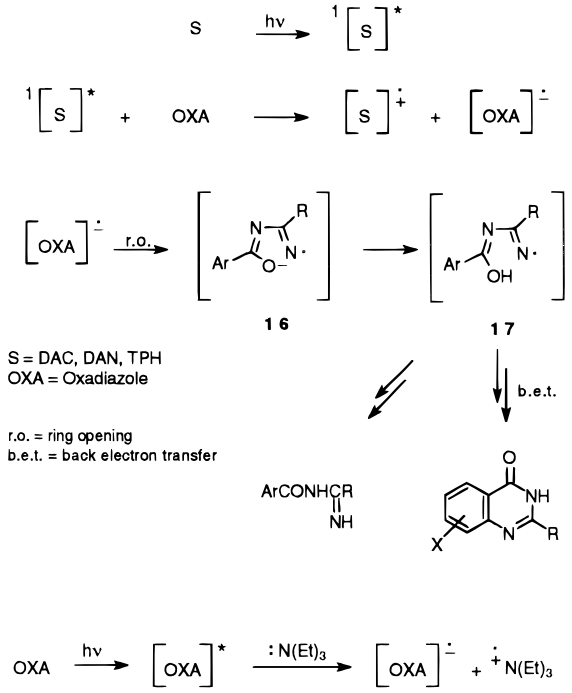
(15) Auricchio, S.; Bini, A.; Pastormerlo, E.; Truscello, A. M. *Tetrahedron* **1997**, *53*, 10911.

(16) Natale, N. R. *Tetrahedron Lett.* **1982**, 5009.

(17) Herbranson, D. E.; Havley, M. D. *J. Org. Chem.* **1990**, *55*, 4297.

(18) (a) Shields, C. J.; Falvey, D. E.; Schuster, G. B.; Buchardt, O.; Nielsen, P. E. *J. Org. Chem.* **1988**, *53*, 3501. (b) Zhu, Y.; Schuster, G. B. *J. Am. Chem. Soc.* **1993**, *115*, 2190. (c) Murata, S.; Nakatsuji, R.; Tomioka, H. *J. Chem. Soc.* **1995**, 793.

Scheme 3



different extents depending on its structure, and then on the rate of competing subsequent processes. Interestingly, in the case of 3-methoxyoxadiazoles **1**, reinforcement of the acceptor characteristics of the 5-aryl-substituted oxadiazoles enhances the photoconversion of starting material and the reduction pathway as well (see Table 2). At first glance, the stabilization due to the methoxy group and a decreasing efficiency of the heterocyclization reaction (likely ascribable to a decreasing efficiency of required back-electron transfer) could explain the results. By contrast, when oxadiazoles **2** are considered, the different stabilization of the corresponding open-chain species (as well as different efficiency in the back-electron transfer) could explain the difference in reactivity and low significance of the reduction pathway. Further investigations, however, appear necessary for a better understanding of the role of each competing process which follows the primary collapse of the presumed key oxadiazole radical anion.

Irradiations in the Presence of Triethylamine. The above results suggested the possibility of creating the oxadiazole radical anion via an electron-transfer mechanism by direct irradiation of the oxadiazole system from a ground-state electron donor reagent as tertiary amines.[19] Interestingly, irradiations of 3-methoxyoxadiazoles **1a**−**c** (at λ = 313 nm) in methanol and in the presence of an excess of triethylamine gave a fast and, in some cases, almost complete photoconversion of starting material, producing both the expected quinazolinones **3a**−**c** (which were isolated in about 50−60% yields) and the reduction products **5a**−**c** (in about 30% yields). In its turn, the TEA-mediated irradiation of **7a** gave **10a** (20%) and regioisomers **8a** (52%) and **9a** (24%). Again, 3-phenyl-substituted oxadiazoles showed a different response. Typically, irradiation of **2a** in the presence of triethylamine returned starting material (60%) and gave the quinazolin-4-one **4a** (36%), while instead only trace amounts of the corresponding reduction product **6a** were detected. Compounds **11** gave similar results.

Table 3. Energy Values of the Singlet (E_s) State (As Determined from Emission Spectra in Acetonitrile), Cathodic Peak Potentials (E_p) (As Determined from Cyclic Voltammetry), and $\Delta G°$ (Calculated from the Rehm−Weller Equation) for DAC-, DAN-, TPH-, and TEA-Induced Photoreactions for Compounds 1a and 2a

			$\Delta G°$ (kJ/mol) [21]			
compd	E_s (eV)	E_p (eV)	DAC	DAN	TPH	TEA
1a	4.51	−1.66	−81	−29	−55	−183
2a	4.26	−1.62	−85	−33	−59	−163

Since the reaction is a photoinduced process, to explain these findings, one can reasonably assume that the excited oxadiazole really acts as an electron acceptor counterpart of the ground electron donor reagent, producing the forecast oxadiazole radical anion. Again, the fate of the ring-cleaved species will depend on electronic effects, as well as on the rate of subsequent processes. Clearly, in the reduction pathway, triethylamine would act as an electron-transfer reagent, while the proton transfer will take place from TEA radical cation as well from hydroxylic solvent. An attractiveness of this TEA-induced photoreaction could be found in the possibility of a generalized methodology for synthesis of variously substituted quinazolin-4-ones. In this context, an additional example was found in the photoreaction of 3-methyl-5-phenyl-1,2,4-oxadiazole (**14**) from which compound **15** (63%) was easily obtained.

The whole investigation shows that in the sensitized photochemistry of the 5-aryl-3-methoxy- (or 5-aryl-3-phenyl-) 1,2,4-oxadiazoles the primary step of the reaction should be an electron transfer, producing an oxadiazole radical anion as the key species from which the breaking of the ring O−N bond takes place. Confirmation of this hypothesis was found by calculating the $\Delta G°$ for the electron transfer either from triethylamine to the excited oxadiazole or from the sensitizer in its excited state to the ground-state oxadiazole. The application of the Rehm−Weller equation,[20] using the cathodic peak potentials (E_p) of the representative oxadiazoles **1a** and **2a** as determined by cyclic voltammetry experiments, brings us to the conclusion that in both cases $\Delta G° < 0$ (Table 3)[21] so that the electron transfer may occur and supporting the idea of a common intermediate being formed. The electrochemical reduction of considered compounds was not a reversible process,[22] and this observation agrees well with a primarily formed species

(19) See, e.g.: (a) Barltrop, J. A.; Coyle, J. D. *Excited States in Organic Chemistry*; John Wiley: London, 1975. (b) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Menlo Park, CA, 1978.

(20) (a) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259. (b) Fox, M. A.; Chanon, M. *Photoinduced Electron Transfer. Part A*; Elsevier: Amsterdam, 1988.

(21) Calculation of the free energies for electron transfer: (a) Energy values (eV) of the singlet excited state of DAC (4.11), DAN (3.16), and TPH (3.63) came from ref 9. (b) The oxidation potentials (V vs hydrogen) of DAC, DAN, TPH, and TEA were estimated to be (DAC), 1.61 (Mattes, S. L.; Farid, S. *J. Chem. Soc., Chem. Commun.* **1980**, 457), (DAN) 1.20 (Bard, A. J.; Santhanam, K. S. V.; Maloy, J. T.; Phelps, J.; Wheeler, L. O. *Discuss. Faraday Soc.* **1968**, 167), (TPH) 1.40 (Mattes, S. L.; Farid, S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1983; Vol. 6), and (TEA) 0.95 (Mann, C. K. *Anal. Chem.* **1964**, 36, 2424).

(22) According to the proposed reaction pattern, an evaluation of the eventual negative shift of standard redox potential $E°$ with respect to the E_p values has been done. (Nadjo, L.; Saveant, J. M. *Electroanal. Chem. Interfacial Electrochem.* **1973**, *48*, 113. Nicholson, R. S.; Shain, I. *Anal. Chem.* **1965**, *37*, 190), and the result does not affect the previous consideration.

quickly collapsing by an irreversible chemical reaction (breaking of the ring O−N bond). Interestingly, apart from significance in synthetic projects, all the results open new approaches to mechanistic studies on the photochemistry of O−N bond containing five-membered heterocycles.

Experimental Section

Materials and Methods. For instruments and general procedures see our previous papers. IR spectra were recorded from Nujol mulls. UV absorption spectra were recorded in methanol. ^{1}H NMR spectra (250 MHz) were taken with TMS as internal standard. HPLC analyses were performed by using a C-18 SIL-X-10 Perkin-Elmer column. Fluorescence emission spectra were determined in methanol or acetonitrile, and phosphorescence emissions (at 77 K) were determined in acetonitrile. Energies of excited states are reported in Table 1. Flash chromatography was performed by using mixtures of light petroleum (fraction boiling in the range of 40−60 °C) and ethyl acetate in varying ratios. Diphenylacetylene, 9,10-diphenylanthracene, triphenylene, triethylamine (99.9% grade), and Bu_4NBr were obtained from Aldrich Chemical Co.

Compounds **1a,**[23] **1b,**[24] **1c,**[2] **1d,**[24] **2a,**[25] **2b,**[26] **7a,**[24] and **11**[26] were prepared as reported. Compound **2c** was prepared by reacting benzamidoxime and 4-cyanobenzoyl chloride, following the standard procedure.[25] Compound **7b** was prepared by adopting the procedure reported for **1a**. Absorption spectra of all oxadiazoles **1a**−**d**, **2a**−**c**, and **7a,b** showed λ_{max} values in the range of 245−265 nm, but very low ϵ values (in the range of 1−100) at $\lambda = 313$ nm. In turn, compound **11** had λ_{max} at 281 nm and more significant ϵ values at 300 and 313 nm (10 000 and 500, respectively).

Photochemical reactions were carried out in anhydrous methanol (from Romil Pure Chemicals) by using a Rayonet RPR-100 photoreactor fitted with 16 lamps irradiating at $\lambda =$ 313 or 365 nm (in 50 mL Pyrex vessels) and a merry-go-round apparatus. On the basis of absorption spectra of oxadiazole substrates, the conditions ensured that in each experiment the sensitizer was the predominant absorbing species at the chosen wavelength. In the case of analytical photoreactions, quantitative determinations were accomplished by HPLC.

5-(4-Cyanophenyl)-3-phenyl-1,2,4-oxadiazole (2c): mp 161−2 °C (from ethanol); IR 2230 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.45−7.51 (m, 3H), 7.83 (d, 2H), 8.11−8.15 (m, 2H), 8.31 (d, 2H); MS *m*/*z* 247 (M^+). Anal. Calcd for $C_{15}H_9N_3O$: C, 72.87; H, 3.67; N, 16.99. Found: C, 72.80; H, 3.70; N, 16.90.

5-(3-Chlorophenyl)-3-methoxy-1,2,4-oxadiazole (7b): mp 63−4 °C (from light petroleum); ^{1}H NMR ($CDCl_3$) δ 4.12 (s, 3H), 7.44−8.10 (m, 4H); MS *m*/*z* 210 (M^+). Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.30. Found: C, 51.40; H, 3.40; N, 13.40.

General Procedure for Photochemical Reactions in the Presence of Diphenylacetylene (DAC). To a sample of the oxadiazole **1a**−**d**, **2a**−**c**, or **7a,b** (0.25 g, 1.0−1.4 mmol) in methanol (45 mL; 140 mL in the cases of **1c** and **2c**) was added a 5-fold excess of diphenylacetylene (5.0−7.0 mmol). The solution was purged by bubbling nitrogen (10 min), and then irradiated (at $\lambda = 313$ nm) for 6 h (5 h for **1c**). After removal of the solvent, the residue was chromatographed.

Irradiation of 3-Methoxy-5-phenyl-1,2,4-oxadiazole (1a) in the Presence of DAC. Irradiation of **1a** and chromatography returned starting material (0.1 g, 40%) and gave *O*-methyl-*N*-benzoylisourea (**5a**) (0.045 g, 18%), mp 77 °C (from benzene/light petroleum) (lit.[27] mp 77 °C), and then 2-methoxyquinazolin-4-one (**3a**), (0.1 g, 40%), mp 230−2 °C (from ethanol) (lit.[5,28] mp 230−2 °C).

Irradiation of 3-Methoxy-5-(4-methylphenyl)-1,2,4-oxadiazole (1b) in the Presence of DAC. Irradiation of **1b** and chromatography returned starting material (0.14 g, 46%) and gave *O*-methyl-*N*-(4-methylbenzoyl)isourea (**5b**) (0.025 g, 10%) and 2-methoxy-7-methylquinazolin-4-one (**3b**) (0.080 g, 32%). **5b**: mp 70−2 °C (from benzene/light petroleum); IR 3460, 3275, 1620 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.44 (s, 3H), 3.95 (s, 3H) 7.31 and 8.10 (2d, 4H), 8.51 and 8.85 (2s, 2H, exchangeable with D_2O); MS *m*/*z* 192 (M^+). Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.40; H, 6.20; N, 14.50. **3b**: mp 203−5 °C (from ethanol); IR 1670 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.49 (s, 3H), 4.01 (s, 3H), 7.22−7.98 (m, 3H), 12.27 (s, 1H); MS *m*/*z* 190 (M^+). Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.20; H, 5.20; N, 14.80.

Irradiation of 3-Methoxy-5-(4-cyanophenyl)-1,2,4-oxadiazole (1c) in the Presence of DAC. Irradiation of **1c** and chromatography returned starting material (0.045 g, 18%) and gave *O*-methyl-*N*-(4-cyanobenzoyl)isourea (**5c**) (0.095 g, 38%) and 2-methoxy-7-cyanoquinazolin-4-one (**3c**) (0.080 g, 33%). **5c**: mp 161 °C (from ethanol); IR 3370, 3280, 2230, 1630 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.97 (s, 3H), 7.97−8.00 and 8.32−8.35 (2m, 4H), 8.63 and 8.96 (2s, 2H, exchangeable with D_2O); MS *m*/*z* 203 (M^+). Anal. Calcd for $C_{10}H_9N_3O_2$: C, 59.11; H, 4.46; N, 20.68. Found: C, 59.20; H, 4.50; N, 20.60. **3c**: mp 249 °C (from ethanol); IR 2200, 1690 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 4.07 (s, 3H), 7.63−8.5 (m, 3H), 12.78 (s, 1H); MS *m*/*z* 201 (M^+). Anal. Calcd for $C_{10}H_7N_3O_2$: C, 59.70; H, 3.51; N, 20.89. Found: C, 59.60; H, 3.60; N, 20.80.

Irradiation of 3-Methoxy-5-(4-chlorophenyl)-1,2,4-oxadiazole (1d) in the Presence of DAC. Irradiation of **1d** and chromatography returned starting material (0.09 g, 36%) and gave *O*-methyl-*N*-(4-chlorobenzoyl)isourea (**5d**) (0.055 g, 22%), mp 86 °C (from ethanol) (lit.[29] mp 86 °C) and then 2-methoxy-7-chloroquinazolin-4-one (**3d**) (0.100 g, 40%), mp 195 °C (from ethanol): IR 1680 cm^{-1}; ^{1}H NMR δ (DMSO-d_6) δ 4.04 (s, 3H), 7.42−8.09 (m, 3H), 12.55 (s, 1H); MS *m*/*z* 210 (M^+). Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.30. Found: C, 51.40; H, 3.30; N, 13.40.

Irradiation of 3-Methoxy-5-(3-methylphenyl)-1,2,4-oxadiazole (7a) in the Presence of DAC. Irradiation of **7a** and chromatography returned starting material (0.15 g, 60%) and gave *O*-methyl-*N*-(3-methylbenzoyl)isourea (**10a**) (0.01 g, 4%), 2-methoxy-8-methylquinazolin-4-one (**8a**) (0.05 g, 20%), and 2-methoxy-6-methylquinazolin-4-one (**9a**) (0.04 g, 16%). **10a**: mp 83−5 °C (from light petroleum); IR 3340, 3160, 1630 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.36 (s, 3H),3.89 (s, 3H), 7.29−7.96 (m, 4H), 8.49 and 8.80 (2s, 2H; exchangeable with D_2O); MS *m*/*z* 192 (M^+). Anal. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found: C, 62.40; H, 6.20; N, 14.50. **8a**: mp 209−11 °C (from light petroleum/ethyl acetate); IR 3180, 1670 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.46 (s, 3H), 3.97 (s, 3H), 7.19−7.86 (m, 3H), 12.24 (s, 1H); MS *m*/*z* 190 (M^+). Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.10; H, 5.20; N, 14.80. **9a**: mp 182−5 °C (from light petroleum/ethyl acetate); IR 3160, 1670 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.38 (s, 3H), 3.93 (s, 3H), 7.35−7.80 (m, 3H), 12.20 (s, 1H); MS *m*/*z* 190 (M^+). Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.20; H, 5.40; N, 14.70.

Irradiation of 3-Methoxy-5-(3-chlorophenyl)-1,2,4-oxadiazole (7b) in the Presence of DAC. Irradiation of **7b** and chromatography returned starting material (0.055 g, 22%) and gave *O*-methyl-*N*-(3-chlorobenzoyl)isourea (**10b**) (0.06 g, 24%), 2-methoxy-8-chloroquinazolin-4-one (**8b**) (0.06 g, 24%), and then 2-methoxy-6-chloroquinazolin-4-one (**9b**) (0.075 g, 30%). **10b**: mp 85−7 °C (from light petroleum); IR 3395, 3295, 1630 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 3.96 (s, 3H), 7.52−8.16 (m, 4H), 8.65 and 8.94 (2s, 2H, exchangeable with D_2O); MS *m*/*z* 212 (M^+). Anal. Calcd for $C_9H_9ClN_2O_2$: C, 50.84; H, 4.27; N, 13.17.

(23) (a) Katritzky, A. R.; Wallis, B.; Brownlee, R. T. C.; Topsom, R. D. *Tetrahedron* **1965**, *21*, 1681. (b) Nash B. W.; Newberry R. A.; Pickles R.; Warburton, W. K. *J. Chem. Soc. C* **1969**, 2794.
(24) Neidlein, R.; Krull, H. *Liebigs Ann. Chem.* **1968**, *716*, 156.
(25) Sim Ooi, N.; Wilson, D. A. *J. Chem. Soc., Perkin Trans. 2* **1980**, 1792.
(26) Leandri, G.; Pallotti, M. *Ann. Chim. (Rome)* **1957**, *47*, 376.
(27) McKee, R. *Am. J. Chem. Soc.* **1901**, *26*, 209.
(28) Tennant, G.; Vaughan, K. *J. Chem. Soc. (C)* **1966**, 2287.
(29) Rossi, E.; Spadi, R. *Gazz. Chim. Ital.* **1981**, *111*, 299.

Found: C, 51.90; H, 4.30; N, 13.10. **8b**: mp 218−23 °C (from ethanol); IR 1685 cm^{-1}; ^1H NMR (DMSO-d_6) δ 4.06 (s, 3H), 7.34−8.05 (m, 3H), 12.62 (s, 1H); MS *m*/*z* 210 (M^+). Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.30. Found: C, 51.40; H, 3.30; N, 13.20. **9b**: mp 186−193 °C (from ethanol); IR 1675 cm^{-1}; ^1H NMR (DMSO-d_6) δ: 4.01 (s, 3H), 7.38−8.00 (m, 3H), 12.50 (s, 1H); MS *m*/*z* 210 (M^+). Anal. Calcd for $C_9H_7ClN_2O_2$: C, 51.32; H, 3.35; N, 13.30. Found: C, 51.30; H, 3.40; N, 13.40.

Irradiation of 3,5-Diphenyl-1,2,4-oxadiazole (2a) in the Presence of DAC. Irradiation of **2a** and chromatography returned starting material (0.15 g, 60%) and gave trace amounts of *N*-benzoylbenzamidine (**6a**) (by HPLC with an authentic sample[5,30]) and then 2-phenylquinazolin-4-one (**4a**) (0.075 g, 30%), mp 232−6 °C (from ethanol) (lit.[4,7a] mp 233−4 °C).

Irradiation of 5-(4-Methylphenyl)-3-phenyl-1,2,4-oxadiazole (2b) in the Presence of DAC. Irradiation of **2b** and chromatography returned starting material (0.15 g, 60%) and gave 7-methyl-2-phenylquinazolin-4-one (**4b**) (0.075 g, 30%): mp 208−10 °C (from ethanol); IR 3140, 1655 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.55 (s, 3H), 7.40−8.26 (m, 8H), 12.52 (s, 1H); MS *m*/*z* 236 (M^+). Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.30; H, 5.20; N, 12.90.

Irradiation of 5-(4-Cyanophenyl)-3-phenyl-1,2,4-oxadiazole (2c) in the Presence of DAC. Irradiation of **2c** and chromatography returned starting material (0.16 g, 64%) and gave 7-cyano-2-phenylquinazolin-4-one (**4c**) (0.085 g, 34%): mp 302−5 °C (from ethanol); ^1H NMR (DMSO-d_6) δ 7.61−8.60 (m, 8H), 12.97 (s, 1H); MS *m*/*z* (247 M^+). Anal. Calcd for $C_{15}H_9N_3O$: C, 72.87; H, 3.67; N, 16.99. Found: C, 72.80; H, 3.60; N, 16.90.

Irradiation of the Oxadiazole 1a in the Presence of Diphenylanthracene. To a sample of the oxadiazole **1a** (0.25 g, 1.4 mmol) in methanol (250 mL) was added diphenylanthracene (0.12 g, 0.4 mmol). The solution was purged by bubbling nitrogen (10 min) and then irradiated (at λ = 365 nm) for 6 h. After removal of the solvent, chromatography of the residue returned starting material (0.045 g, 18%) and gave **5a** (0.03 g, 12%) and **3a** (0.13 g, 52%).

Irradiation of the Oxadiazole 2a in the Presence of Diphenylanthracene. Similarly, after irradiation (6h) of **2a** (0.25 g, 1.1 mmol) in methanol (250 mL) and diphenylanthracene (0.12 g, 0.4 mmol), subsequent chromatography returned starting material (0.075 g, 30%) and gave **4a** (0.125 g, 50%).

General Procedure for Photochemical Reactions in the Presence of Triethylamine (TEA). To a solution of the oxadiazole **1a**−**c**, **2a**, **7a**, **11**, or **14** (0.25 g, 1.0−1.4 mmol) in methanol (90 mL; 140 mL in the case of **1c**) purged by bubbling nitrogen (10 min) was added an excess of triethylamine (5 mL), and then the mixture was irradiated (at λ = 313 nm) for the time indicated. After removal of the solvent, the residue was chromatographed.

Irradiation of the Oxadiazole 1a in the Presence of TEA. Irradiation of **1a** (2 h) gave **5a** (0.075 g, 30%) and **3a** (0.125 g, 50%).

Irradiation of the Oxadiazole 1b in the Presence of TEA. Irradiation of **1b** (2 h) gave **5b** (0.075 g, 30%) and **3b** (0.15 g, 60%).

Irradiation of the Oxadiazole 1c in the Presence of TEA. Irradiation of **1c** (1 h) gave **5c** (0.075 g, 30%), **3c** (0.12 g, 50%), and some amount of byproducts.

Irradiation of the Oxadiazole 2a in the Presence of TEA. Irradiation of **2a** (6 h) returned starting material (0.15 g, 60%) and gave **4a** (0.09 g, 36%) and trace amounts of **6a** (HPLC).

Irradiation of the Oxadiazole 7a in the Presence of TEA. Irradiation of **7a** (2 h) gave **10a** (0.05 g, 20%), **8a** (0.13 g, 52%), and **9a** (0.06 g, 24%).

Irradiation of the Oxadiazole 11. Irradiation of **11** (6 h) in the presence of TEA and chromatography returned starting material (0.135 g, 54%) and gave 2-phenyl-7-methoxyquinazolin-4-one (**13**) (0.07 g, 28%): mp 197 °C (from ethanol); IR 3160, 1660 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.97 (s, 3H), 7.14−8.25 (m, 8H), 12.49 (s, 1H); MS *m*/*z* 252 (M^+). Anal. Calcd for $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found: C, 71.50; H, 4.70; N, 11.20.

Parallel irradiation (6 h) of **11** (0.12 g) in purged methanol alone (40 mL) and chromatography returned a small amount of starting material and gave **12** (0.085 g, 70%) and trace amounts of **13**. **12**: mp 130 °C (from light petroleum); IR 3240, 1650 cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.91 (s, 3H), 3.98 (s,2H),7.12 (d, 2H), 7.46−7.63 (m, 5H), 8.04 (d, 2H), 10.07 (s, 1H); MS *m*/*z* 284 (M^+). Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 67.50; H, 5.60; N, 9.90.

Irradiation of the Oxadiazole 14 in the Presence of TEA. Irradiation of **14**[25] (2 h) and chromatography gave 2-methylquinazolin-4-one (**15**) (0.16 g, 63%), mp 236−238 °C (from ethanol) (lit.[9,31] mp 236−238 °C), and some amount of benzamide.

Analytical Photoreactions. (a) To a sample of the oxadiazole (0.06 mmol) in methanol (10 mL) was added diphenylacetylene (0.3 mmol). The solution was purged by bubbling nitrogen (5 min) and then irradiated at λ = 313 nm for 2 h. (b) A sample (10 mL) containing the oxadiazole (0.006 mmol) and diphenylanthracene (0.015 mmol) was purged and then irradiated (at λ = 365 nm) for 45 min. (c) A sample (10 mL) containing the oxadiazole (0.011 mmol) and triphenylene (0.022 mmol) was purged and then irradiated (at λ = 313 nm) for 45 min. Irradiation times were chosen to have clear-cut HPLC response. The resulting photolyzates were analyzed quantitatively by HPLC. Compositions (%) of the photoreaction mixtures were reported in Table 2. Obviously, no significant comparison can be made between the DAC-sensitized photoreactions on one hand, and DAN- or TPH-sensitized photoreactions, on the other.

Cyclic Voltammetry Experiments. Cyclic voltammetry experiments were performed by using 0.1 M Bu_4NBr in acetonitrile as a system solvent supporting electrolyte (SSE) in an undivided glass cell equipped with a graphite disk working electrode (7 mm^2), platinum counter electrode, and saturated calomel electrode (SCE) as reference electrode. The modulation of the working potential was tuned by an AMEL System 5000 potentiostat controlled through a PC. In each experiment a 5 mM concentration of the selected oxadiazole was dissolved in 30 mL of the SSE helium saturated, and a set of triangular wave potential modulations were carried out with different scan rates in the range 10−1000 mV s^{-1}. The resulting cathodic peak potentials (E_p) (vs hydrogen) are reported in Table 3.

Acknowledgment. Financial support by CNR (Roma) and MURST (Roma) is gratefully acknowledged.

JO990298F

(30) Palazzo, G.; Strani, G.; Tavella, M. *Gazz. Chim. Ital.* **1961**, *91*, 1085.

(31) Bogert, M. T.; Gotthelf, A. H. *J. Am. Chem. Soc.* **1900**, *22*, 512.