Aryloxy Radicals from Diaryloxydiazirines: α-Cleavage of Diaryloxycarbenes or Excited Diazirines?
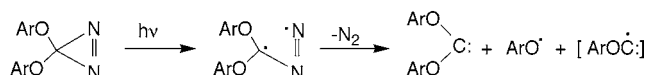
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ABSTRACT

The synthesis of diaryloxydiazirines, precursors to diaryloxycarbenes, is described. Thermolyses of the diazirines afford anticipated carbene products, but photolyses afford both carbenes and aryloxy radicals by α-scission. UV spectra of the carbenes and radicals are observed.

Dialkoxycarbenes, such as dimethyoxycarbene, are quintessential nucleophilic species whose spectroscopy, reactivity, and synthetic proclivities have been well documented.[1] Diaryloxycarbenes, $(ArO)_2C$, should be somewhat less nucleophilic than their dialkoxy analogues and, more importantly, tunable through substituent variation on their aryl groups.[2] Warkentin has generated a number of $(ArO)_2C$ and $ArOCOAr'$ by thermolyses of oxadiazolines **1** in benzene at 110 °C.[2a] Although flexible and synthetically useful, this precursor does not generate diaryloxycarbenes upon photolysis and does not provide access to their spectroscopy.[2b]

Here, we describe a rather general synthesis of diaryloxydiazirines **2**, the thermal and photochemical generation and
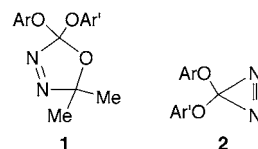
reactions of diaryloxycarbenes from **2**, the UV spectra of the photochemically produced carbenes in both low temperature matrixes and ambient temperature solutions, the unexpected formation of aryloxy radicals under the latter conditions, and the likely origin of the radicals.

The synthesis of the diazirines is outlined in Scheme 1. Para-substituted phenols (X = H, MeO, Me, Cl, CN) were converted with $BrCN$[3] to aryl cyanates **3**.[4] Without purification, **3** were reacted with hydroxylamine[5] affording *N*-hydroxy-*O*-arylisoureas **4**.[4] Reaction with $MeSO_2Cl$ then gave the crystalline mesylates **5**, which were fully characterized.[4] Graham oxidation[6,7] of **5** with NaOCl afforded

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(1) (a) Hoffmann, R. W. *Acc. Chem. Res.* **1985**, *18*, 248. (b) Hoffmann, R. W.; Reiffen, M. *Chem. Ber.* **1976**, *109*, 2565. (c) Lemal, D. M.; Gosselink, E. P.; McGregor, S. D. *J. Am. Chem. Soc.* **1966**, *88*, 582. (d) Moss, R. A.; Wlostowski, M.; Shen, S.; Krogh-Jespersen, K.; Matro, A. *J. Am. Chem. Soc.* **1988**, *110*, 4443. (e) El-Saidi, M.; Kassani, K.; Pole, D. L.; Tadey, T.; Warkentin, J. *J. Am. Chem. Soc.* **1992**, *114*, 8751. (f) For further applications, see: Warkentin, J. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI Press: Stamford, CT, 1998; Vol. 2, esp. pp 256f and references cited there.

(2) (a) Lu, X.; Reid, D. L.; Warkentin, J. *Can. J. Chem.* **2001**, *79*, 319. (b) Oxadiazolines do not generally afford carbenes on photolysis. Private communication from Prof. J. Warkentin, 1 Oct 2003.

(3) Vorwinkel, E.; Baese, H.-J. *Chem. Ber.* **1974**, *107*, 1213.

(4) See the appropriate table in the Supporting Information for spectroscopic data. Experimental details appear in: Fedé, J.-M. Ph.D. Dissertation, Rutgers University, New Brunswick, NJ, 2003.

(5) Grigat, E.; Pütter, R.; König, C. *Chem. Ber.* **1965**, *98*, 144.

(6) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.

(7) Moss, R. A.; Perez, L. A.; Wlostowska, J.; Guo, W.; Krogh-Jespersen, K. *J. Org. Chem.* **1982**, *47*, 4177.

Table 1. Photolysis Products of Diazirines[a]

carbene (X,Y in 7)	solvent			
	mch[b]	p-X-C$_6$H$_4$OH	(CF$_3$)$_2$CHOH	acn[c]
H	**9a** (42), **10a** (52)	**10a** (100)	**11a** (55), **10a** (33)	**12a** (37), **10a** (43)
	formate (5),[d] PhOH (1)		formate (5), **9a** (7)	formate (9), PhOH (2)
MeO	ArOH (61), DPMPM (32)[e]	DPMPM (30),	**11b** (58), DPMPM (24)	ArOH (46), DPMPM (28)
	U (7)[f]	MPMP[g] (58), U (12)	formate (4), ArOH (14)	formate (16)
Me	**9c** (13), **10c** (61)	**10c** (100)	**11c** (49), **10c** (33)	**12c** (46), **10c** (40)
	formate (5), ArOH (21)		**9c** (10), ArOH (8)	**9c** (10), ArOH (4)
Cl	**10d** (39), ArOH (35)	**10d** (100)	**11d** (84), ArOH (9)	**12d** (18), **10d** (4)
	formate (10), U (16)		formate (5), U (2)	formate (26), ArOH (44)
				U (8)

[a] Numbers in parentheses are percentages of product distributions. [b] Methylcyclohexane. [c] Acrylonitrile. [d] Formate = ArOOCH. [e] Di-p-methoxyphenoxymethane, (ArO)$_2$CH$_2$. [f] U = unknown. [g] o-(p-Methoxyphenoxy)-p-methoxyphenol.

aryloxychlorodiazirines **6**, which were purified by short column chromatography (SiO$_2$, 10:1 hexanes/ether) and characterized[4] by UV,[6] IR,[6] and GC−MS. The latter method gave the dimers of ArOCCl. Finally, diazirine exchange reactions[8] of aryl oxide[9] for chloride converted **6** to diaryloxydiazirines (**7a−g**). These were purified by short column chromatography (as above) and characterized by UV (353−358 nm, hexane), IR (1541−1548 cm^{-1}), and ^{1}H NMR spectroscopy.[4,10]

Thermolyses of diazirines **7** generated diaryloxycarbenes **8**, which gave uncomplicated dimerization, O−H "insertion", and alkene addition reactions. In methylcyclohexane at 100 °C, carbenes **8a−d** formed from diazirines **7a−d** and dimerized to the expected tetraaryloxyethenes (**9**) in 50−70% yields (after recrystallization).[4] In benzene solutions of the corresponding substituted phenol at 100 °C, carbenes **8a−d** yielded the anticipated triaryl orthoformates (**10**) in 90% yields.[4] Reactions of **8a−d** with neat hexafluoroisopropyl alcohol at 100 °C afforded "mixed" orthoformates **11** in ∼55% yields;[4] the balance was mostly carbene dimers. Finally, thermolysis of **7** in neat acrylonitrile at 100 °C gave the appropriate cyclopropanes (**12**) in 46−56% yields (**12a,c−f**), 82% for **12b**, and 92% for **12g**.[4] The dimerization

and ArOH-trapping reactions of carbenes **8** parallel Warkentin's results for **8a** generated from **1**.[2]
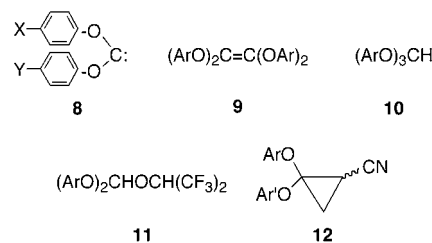
In contrast to the thermal reactions of **7**, photolysis yielded complicated arrays of products; cf., Table 1. The anticipated products of carbene **8** are dimers **9** in methylcyclohexane, orthoformates **10** from ArOH, mixed orthoformates **11** from (CF$_3$)$_2$CHOH, and cyclopropanes **12** from acrylonitrile. Although these products are generally formed by photolytically generated **8**, they are accompanied by large quantities of orthoformates **10** and varying amounts of free phenols (ArOH). The orthoformates stem from reactions of carbene **8** with ArOH; their formation, and the formation of ArOH, suggest α-cleavages of diazirines **7** and/or carbenes **8**. Indeed, laser flash photolysis (LFP) experiments provide direct evidence for the generation of aryloxy radicals upon photolysis of **7** (see below).

Note that radical α-cleavage dominates the photolysis of **7b**, where major quantities of ArOH, di-p-methoxyphenoxymethane, and o-(p-methoxyphenoxy)-p-methoxyphenol form. The latter is a coupling product of 2 p-methoxyphenoxy radicals.[11]

Scheme 1[a]

(X,Y) = **a** (H,H), **b** (MeO,MeO), **c** (Me,Me), **d** (Cl,Cl), **e** (H,MeO), **f** (H,Cl), **g** (MeO,Cl)
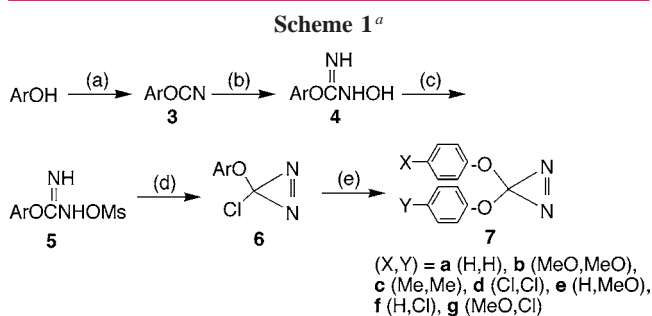
[a] Reagents and conditions: (a) BrCN, Et$_3$N, Et$_2$O, 1 h, −10 °C, >95%; (b) H$_2$NOH, Et$_2$O, 2 h, 0 °C, >85%; (c) MeSO$_2$Cl, pyridine, CH$_2$Cl$_2$, 4 h, 25 °C, >75%; (d) 12.5% aq NaOCl, NaCl, LiCl, DMSO−pentane, 15 min, <15 °C, 40−50%; (e) ArONa, DMF, ∼90 min, 25 °C, 20−25%.

(8) Moss, R. A. In *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC Press: Boca Raton, 1987; Vol. I, pp 99f. Moss, R. A.; Wlostowski, M.; Terpinski, J.; Kmiecik-Lawrynowicz, G.; Krogh-Jerspersen, K. *J. Am. Chem. Soc.* **1987**, *109*, 3811.

(9) Al Sabbagh, M. M.; Calmon, M.; Calmon, J.-P. *Bull. Soc. Chim. Fr.* **1983**, *Part II*, 73.

(10) About 5−10% of triaryl orthoformate formed during the synthesis of **7** and could not be separated by chromatography.

(11) It could be prepared by photolysis (λ = 350 nm) of p-MeOC$_6$H$_4$-OH with di-*tert*-butyl peroxide. Spectroscopic properties were in agreement with literature data: Maumy, M.; Capdevielle, P. *Bull. Soc. Chim. Fr.* **1995**, *132*, 734.

Radical cleavage of **7** or **8** to ArO• should simultaneously furnish the carbyne, ArOC̈•, a possible source of the aryl formates found in the photolytic reactions (Table 1). Abstraction of a hydrogen atom by ArOC to yield the carbene (ArOCH), followed by reaction with ArOH, could account for the formation of $(ArO)_2CH_2$ (DPMPM) in the case of **7b** (or **8b**). A 1,2-Ar shift of ArOC would give the arylacyl radical, ArCO•, which could furnish the aldehyde (ArCHO) by H abstraction, or ArH by loss of CO, followed by H abstraction. However, neither ArCHO nor ArH (or Ar−Ar) was observed among the products, so that arylacyl radicals are unlikely intermediates.

Photolysis of clear methylcyclohexane glasses of diazirines **7a−d** at 90 K for ∼12 min with a 355 nm YAG laser afforded carbenes **8a−d**, manifested by absorptions at ∼330 nm. Figure 1 depicts this result for **8c**, di-p-methylphenoxy-
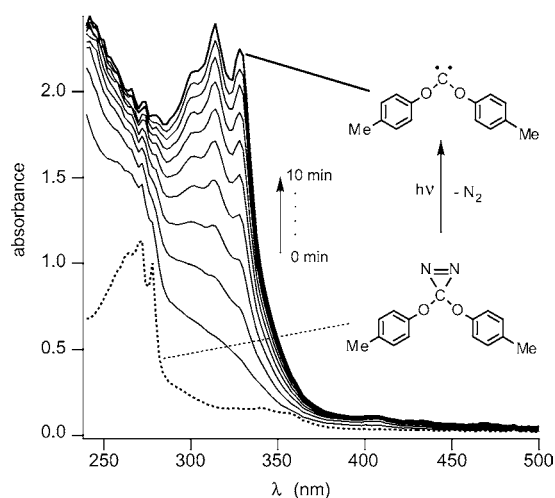

Figure 1. UV−vis absorption spectra of di-p-methylphenoxydiazirine (**7c**) at 90 K in a methylcyclohexane matrix after irradiation at 355 nm (Nd:YAG laser) for various times. The new absorption at ∼330 nm was assigned to the di-p-methylphenoxycarbene (**8c**).

carbene.[12] However, LFP experiments with **7a−d** at 23 °C reveal the formation of both carbenes **8a−d** at ∼330 nm and new transients at ∼400 nm; see Figure 2. These transient species, which are not quenched by oxygen, are identified as aryloxy radicals (ArO•) on the basis of the following evidence.

(a) Their UV absorptions (in MeCN) are quite similar to values reported for ArO• generated by LFP of *tert*-butyl peroxide and ArOH in benzene.[13] Thus, for $p\text{-}XC_6H_4O•$, we observe (X, nm) H, 392, MeO, 404, Me, 396, Cl, 412, whereas the literature values[13] are 400, 403, 404, and 412, respectively.

(b) LFP of diazirine **7a** in THF at 23 °C generated PhO•, which reacted with α-tocopherol to produce the α-tocopheryl

(12) TD-DTF (B3LYP/6-31G*) calculations predict $\sigma^2 \rightarrow \sigma^1 p^1$ absorptions at 298−302 nm for carbenes **8a−d** in the gas phase. We thank Professor Karsten Krogh-Jespersen for these calculations.

(13) Das, P. K.; Encinas, M. V.; Steenken, S.; Scaiano, J. C. *J. Am. Chem. Soc.* **1981**, *103*, 4162.
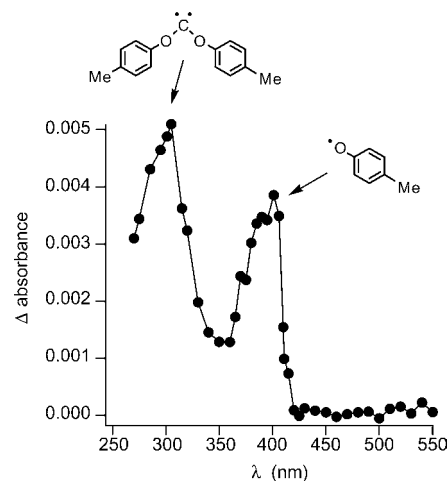
Figure 2. Transient optical absorption spectrum recorded 0.1−3 μs following laser excitation (355 nm, 5 ns pulse width) of acetonitrile solutions of di-p-methylphenoxydiazirine (**7c**) at 23 °C. The transient absorptions at ∼330 nm and ∼400 nm were assigned to di-p-methylphenoxycarbene (**8c**) and the p-methylphenoxy radical, respectively.

radical (416 nm). Correlation of the apparent rate constants for the growth of α-tocopheryl with [α-tocopherol] gave $k = 4.1 \times 10^7$ M^{-1} s^{-1} (7 points, $r = 0.998$).[14] A value of 3.1×10^8 M^{-1} s^{-1} (in MeCN) has been reported for this reaction.[15]

(c) Similarly, $XC_6H_4O•$ generated by LFP of **7b−d** were quenched by ascorbic acid 6-palmitate with $10^{-6}k = 0.78$ (X = MeO), 2.5 (X = Me), and 4.3 (X = Cl) for decay of the aryloxy radicals.[14] In a related reaction, $k = 5.9 \times 10^6$ M^{-1} s^{-1} for reaction of PhO• with the same substrate.[15,16]

What is the origin of ArO• in the photolysis of diazirines **7**? Two possibilities are α-fragmentation of the diaryloxycarbene generated from the diazirine or (as we prefer) direct decomposition of the diazirine's photoexcited state to afford ArO• (and ArOC), as well as the diaryloxycarbene; cf. Scheme 2, where the diazirine excited state is represented by the ring-opened diradical **13**.[17] The second pathway is a "carbene mimetic" reaction, in which the carbene precursor is responsible for a process that might otherwise be soley attributed to the carbene. Carbene mimetic reactions are fairly common in the rearrangements of alkylcarbenes generated from diazirines.[17−19]

β-Fragmentations of dibenzyloxycarbene, benzyloxymethoxycarbene, and allyoxymethoxycarbenes to benzyl and

(14) Errors in the absolute rate constants are estimated at 10−20%.

(15) Foti, M.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1994**, *116*, 9440.

(16) PhO• from LFP of **7a** was quenched by ascorbyl palmitate, but the UV signal was too weak for good kinetics.

(17) Platz, M. S. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; JAI Press: Stamford, CT, 1998; Vol. 2, pp 133f.

(18) (a) Glick, H. C.; Likhotvorik, I. R.; Jones, M., Jr.. *Tetrahedron Lett.* **1995**, *36*, 5715. (b) Thamattoor, D. M.; Jones, M., Jr.; Pan, W.; Shevlin, P. B. *Tetrahedron Lett.* **1996**, *37*, 8333. (c) Nigam, M.; Platz, M. S.; Showalter, B. M.; Toscano, J. P.; Johnson, R.; Abbot, S. C.; Kirchhoff, M. M. *J. Am. Chem. Soc.* **1998**, *120*, 8055.

(19) Merrer, D. C.; Moss, R. A. In *Advances in Carbene Chemistry*; Brinker, U. H., Ed.; Elsevier: Amsterdam, 2001; Vol. 3, pp 53f.

Scheme 2
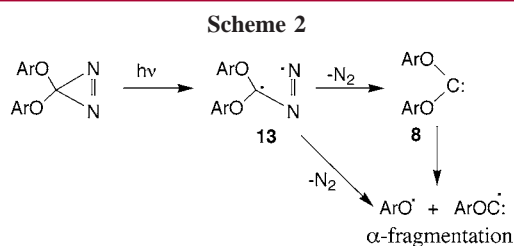
allyl radicals occur when the carbenes are thermally generated from oxadiazoline precursors.[20] However, α-fragmentations of diaryloxycarbenes to aryloxy radicals appear to be unprecedented, and computationally, they also appear improbable: α-cleavage of diphenoxycarbene **8a** to PhO• and PhOC• is endothermic by 69.5 kcal/mol, and a *p*-MeO substituent (**8b**) only lowers the endothermicity to 65.1 kcal/mol.[21]

We suggest that thermolyses of diazirines **7** afford carbenes **8**, which exhibit the reactions expected of nucleophilic carbenes,[1] but that photolyses of **7** lead (via excited diazirine **13**, Scheme 2) to both α-fragmentation and carbene formation.[22] In low-temperature matrixes at 90 K, fragmentation products ArO• and ArOC• efficiently recombine to give carbene, little or no ArO• escapes, and only the carbene is observed.[23,24]

In ambient temperature solution, however, diffusion of ArO• and ArOC• successfully competes with recombination to **8**, and both carbene and aryloxy radical spectra are observed (Figure 2). Now the products include ArOH, formed by H-abstraction by ArO•, and (ArO)$_3$CH formed by reaction

of (ArO)$_2$C with ArOH (Table 1). Indeed, when **7a** is photolyzed in a saturated THF solution of α-tocopherol, the yields of carbene products **9a** and **10a** decrease by 40% in favor of PhOH and PhOOCH, products of phenoxy radical and (perhaps) PhOC.

Further support for fragmentation of excited diazirines as the origin of the aryloxy radicals is our observation that the radical products (ArOH and **10** from ArOH + (ArO)$_2$C) persist when the diazirines are photolyzed in the neat carbene traps hexafluoroisopropyl alcohol or acrylonitrile (see Table 1). If fragmentation occurred mainly from the carbene, its products should diminish or disappear in carbene trap solutions. In contrast, thermal generation of the carbenes in these solutions leads to the expected carbene products unaccompanied by fragmentation (see above).[25]

In conclusion, we have described a relatively general procedure for the preparation of diaryloxydiazirines, precursors for diaryloxycarbenes. Thermolyses of the diazirines afforded the carbenes and anticipated products, whereas photolyses gave both diaryloxycarbenes and aryloxy radicals by α-scission. UV spectra of the carbene were obtained in low-temperature matrixes, and at ambient temperature by LFP. In the latter case, the spectra of the aryloxy radicals were also observed. The aryloxy radicals could be quenched by α-tocopherol, and ascorbyl palmitate. Products of the aryloxy radicals included ArOH and, by subsequent reaction with the carbenes, (ArO)$_3$CH.

Supporting Information Available: Tables of characterization data for examples of compounds **3**−**7** and **9**−**12** and experimental details for spectroscopy. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) (a) Merkley, N.; El-Saidi, M.; Warkentin, J. *Can. J. Chem.* **2000**, *78*, 356. (b) Merkley, N.; Warkentin, J. *Can. J. Chem.* **2000**, *78*, 942. (c) Venneri, P. C.; Warkentin, J. *J. Am. Chem. Soc.* **1998**, *120*, 11182.

(21) We thank Professor Ronald R. Sauers for these B3LYP/6-31G(d) calculations.

(22) Alternatively, the excited state of the diazirine could yield an electronically excited state of the carbene which could undergo α-fragmentation if the excitation energy exceeds ∼60 kcal/mol.

(23) With **7b**, a very weak absorption is observed at ∼400 nm in the matrix experiment, suggesting a minimal separation of *p*-MeOC$_6$H$_4$O•.

(24) Alternatively, at 90 K, **13** partitions almost exclusively to carbene **8**.

(25) A referee has pointed out that if diaryloxycarbenes were prone to fragmentation, it would more likely occur when the diazirine was thermally decomposed, rather than photolyzed in solution, given rapid vibrational cooling.