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New Convenient Source of Precursors of Dioxycarbenes

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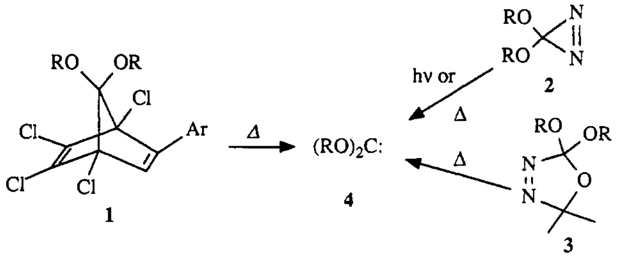
Dioxycarbenes (**4**) have been generated by thermolysis of norbornadienone ketals (**1**),[1] by photolysis or thermolysis of 3,3-dioxydiazirines (**2**),[2] and by thermolysis of 2,2-dioxy-Δ^3-1,3,4-oxadiazolines (**3**),[3] Scheme 1.[4] Among these approaches, that based on **1** has been limited to the generation of only a few dialkoxycarbenes.[1] Moreover, the byproducts from thermolysis of **1** can interfere with the isolation of products from reactions of **4**.

Diazirines **2**, either with like (MeO, MeO) or with unlike (PhO, MeO) oxy groups, have been prepared.[2] Their thermal or photochemical decompositions are relatively clean. As the only photochemical sources of **4** currently available, they are well suited for direct observation of carbenes **4** and for studies of the rates of their reactions.[2c-g] However, diazirines **2** are not convenient for synthetic work with **4** because they are hazardous compounds available only as dilute solutions.

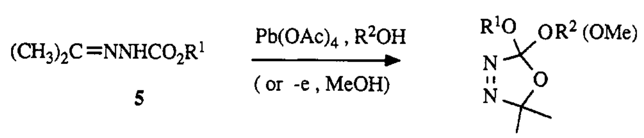
Oxadiazolines **3**, available by oxidation of (alkoxycarbonyl)hydrazones of acetone (**5**) with lead tetraacetate (LTA)[3] or by electrochemical oxidation,[5] can be obtained as pure compounds with long shelf lives[6] (Scheme 2). They are attractive sources of **4** because they fragment quite cleanly in solution at *ca.* 100 °C to afford **4** and innocuous byproducts (N_2, acetone), but there are limitations to their preparation. For example, oxidation of **5** affords oxadiazoline in very poor yield in the presence of some alcohols (Scheme 2, $R_2OH = CF_3CH_2OH$, for example), and oxidation of **5** in the presence of phenols has very poor prospects, because many phenols are themselves oxidized easily.

We now report a general approach to dioxyoxadiazolines (**9a-l**) from 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**7**). The latter is formed by oxidation of the (methoxycarbonyl)hydrazone of acetone (**6**) with LTA in dichloromethane (Scheme 3). The yield of **7** falls between 60 and 72%, and the byproduct is **8**. Partial separation of **7** from **8** is possible by slow bulb-to-bulb distillation under vacuum, but this tedious process is not necessary for the preparation of pure **9**. Instead, the mixture of **7** and **8** can be stored in the refrigerator for later use after extraction of the CH_2Cl_2 solution with aqueous bicarbonate, drying of the organic layer, and evaporation of the solvent.

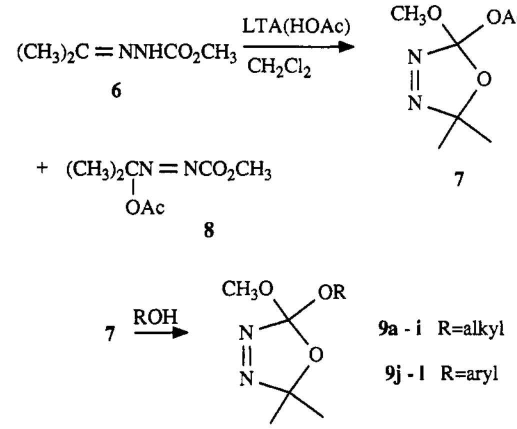
Scheme 1



Scheme 2



Scheme 3



Treatment of unseparated **7** and **8** in CH_2Cl_2 containing acetic acid[7] with an alcohol or a phenol results in conversion of **7** to **9** (Scheme 3). Selective hydrolysis of **8** is accomplished by stirring the solution with aqueous base (1 h), which yields pure **9** simply by drying the organic layer and evaporating the volatiles.[8] Table 1 lists 12 compounds (**9**) that were prepared in yields ranging from 61 to 94% for the substitution step.[9]

The substitution reactions that convert **7** to **9** are probably S_N1 reactions similar to the S_N reactions that convert 3-bromo- or 3-chloro-1,2-diazirines to 3-fluorodiazirines,[10] or 3-alkoxy-3-halo-1,2-diazirines to dialkoxydiazirines.[2b,11] It is likely that nucleophiles other than alcohols and phenols (e.g., cyanide, fluoride) will form additional interesting oxadiazolines.

In summary, the availability of **7** opens the door to a large number of 2,2-dioxyoxadiazolines (**9**), including those with oxidation-sensitive functionality in R. The known thermolysis of **9**, to form carbonyl ylides and dioxycarbenes in succession,[3]

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(1) (a) Hoffmann, R. W. *Angew. Chem.* **1971**, *83*, 595. (b) Hoffmann, R. W. *Angew. Chem., Int. Ed Engl.* **1971**, *10*, 529. (c) Hoffmann, R. W.; Häuser, H. *Tetrahedron* **1965**, *21*, 891. (d) Hoffmann, R. W.; Häuser, H. *Tetrahedron Lett.* 1964, 197. (e) Lemal, D. M.; Gosselink, E. P.; McGregor, S. D. *J. Am. Chem. Soc.* **1966**, *88*, 582.

(2) (a) Moss, R. A. *Acc. Chem. Res.* **1989**, *22*, 15. (b) Moss, R. A. In *Chemistry of Diazirines*; Liu, M. T. H., Ed.; CRC Press: Boca Raton, FL, 1986; Vol. 1, pp 99 ff. (c) Moss, R. A.; Włostowski, M.; Terpinski, J.; Kmiecik-Lawrynowicz, G.; Krogh-Jespersen, K. *J. Am. Chem. Soc.* **1987**, *109*, 3811. (d) Moss, R. A.; Włostowski, M.; Shen, S.; Krogh-Jespersen, K.; Matro, A. *J. Am. Chem. Soc.* **1988**, *110*, 4443. (e) Moss, R. A.; Fan, H.; Hadel, L. M.; Shen, S.; Włostowska, J.; Włostowski, M.; Krogh-Jespersen, K. *Tetrahedron Lett.* **1987**, *28*, 4779. (f) Moss, R. A.; Shen, S.; Włostowski, M. *Tetrahedron Lett.* **1988**, *29*, 6417. (g) Ge, C.-S.; Jefferson, E. A.; Moss, R. A. *Tetrahedron Lett.* **1993**, *34*, 7549.

(3) El-Saidi, M.; Kassam, K.; Pole, D. L.; Tadey, T.; Warkentin, J. *J. Am. Chem. Soc.* **1992**, *114*, 8751.

(4) For additional, less well established methods, see: (a) Hoffmann, R. W.; Steinbach, K.; Lilienblum, W. *Chem. Ber.* **1976**, *109*, 1759. (b) Moss, R. A.; Cox, D. P. *Tetrahedron Lett.* **1985**, *26*, 1931. (c) Olofson, R. A.; Walinsky, S. W.; Marino, J. P.; Jernow, J. L. *J. Am. Chem. Soc.* **1968**, *90*, 6554. (d) Sheeren, J. W.; Staps, R. J. F. M.; Nivard, R. J. F. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 11. (e) Corey, E. J.; Winter, R. A. E. *J. Am. Chem. Soc.* **1963**, *85*, 2677.

(5) Chiba, T.; Okimoto, M. *J. Org. Chem.* **1992**, *57*, 1375.

(6) A sample of 2,2-dimethoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline[3] was stored at room temperature, in the dark, for 2 years without detectable (by ^{1}H NMR) decomposition.

(7) Conversion of **7** to **9** is catalyzed by acids. Crude **7** that has been freed from acetic acid in order to store it should be acidified with an acid such as acetic or *p*-toluenesulfonic acid to accelerate conversion to **9**. With the latter acid, much higher rates are possible.

(8) With alcohols of low volatility, excess ROH can be removed by chromatography.

(9) Overall yields from (methoxycarbonyl)hydrazone **6** are 60–70% of those in Table 1. Attempts to modify the oxidation step, to suppress formation of **8**, have not yet succeeded.

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Table 1. 2,2-Dioxyoxadiazolines (**9**) from **7**

9	R	yield (%)[a]	9	R	yield (%)[a]
a	Me	94	**g**	CH_2CF_3	84
b	Et	90	**h**	$CH_2CH_2C{\equiv}CH$	86
c	Pr	92	**i**	$CH_2CH_2CH_2C{\equiv}CH$	78
d	*i*-Pr	74	**j**	C_6H_5	61
e	Bu	82	**k**	C_6H_4-*p*-CN	67
f	*t*-Bu	67	**l**	C_6H_4-*p*-OMe	68

[a] Yields of isolated product for the exchange step.

means that the stage is set for studies of intermolecular and intramolecular reactions of those intermediates. Some surprisingly rich chemistry of **9h** has been submitted for publication.

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Supplementary Material Available: IR, ^1H NMR, ^{13}C NMR, and MS data for **7**, **9a–k**, and methyl 2,3–diaza-4-methyl-4-acetoxypent-2-enoate and a typical experimental procedure (**3** pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.