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Photooxygenation of the C=N bond: a mild new method for oxidative C–C cleavage☆

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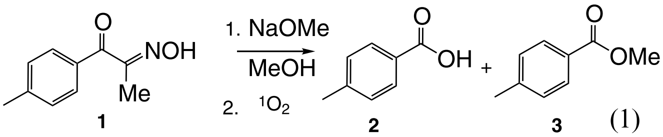
Abstract—Upon photooxygenation in the presence of base, α-oximinocarbonyl compounds undergo clean oxidative C–C cleavage giving rise to mixtures of esters and acids. The mechanism of these reactions involves some unusual peroxidic intermediates, including a 2,3,5-trioxapentanes.

Oxidative C–C cleavage reactions are important functional group transformations in organic chemistry.[1] Whereas oxidative C=C cleavage is a simple task by way of ozonolysis, carbonyl compounds are relatively difficult, direct routes to oxidative C–C cleavage are scarce. The best known example is the haloform reaction that is only applicable to compounds containing the $CH_3C(O)$ moiety.[2] One obvious solution to the problem is ozonolytic cleavage of the enol ether derived from an aldehyde or a ketone, though regioselectivity in the enol ether formation may be problematic, and esters do not lend themselves well for this purpose.[3] Alternatively, carbonyl α-oxidation (e.g. Rubottom oxidation), followed by oxidative cleavage with a variety reagents has also been employed.[4] Direct oxidative cleavage can be accomplished with dioxygen (or H_2O_2) and heavy metal catalysts such as vanadium(V) or copper(II) complexes.[5] Multistep oxidative cleavage protocols have been developed by various groups.[6] Herein we report an exceptionally mild and environmentally benign methodology for oxidative cleavage of carbonyl compounds.

Previously we published a survey on dye-sensitized photooxidation of C=N containing compounds and reported that oximes are unreactive toward singlet oxygen, however, oximate anions rapidly combine with $^1O_2$;[7,8] while ketoximates undergo oxidative C=N cleavage, aldoximates give rise to mixtures of acids, esters and aldehydes. Carbonyl oxide intermediates have been postulated as intermediates in these reactions. Recently we reported on the photooxygenation of amidoximate anions and found that these compounds undergo oxidative cleavage to nitriles and amides via carbonyl oxide intermediates.[9] In the present study we examined the photooxygenation of α-oximino carbonyl compounds these compounds readily react with singlet oxygen undergoing oxidative C–C cleavage to yield esters and carboxylic acids in high yields (Eq. (1)).[10]



(1)

The α-oximino (also isonitroso) carbonyl compounds are readily available by nitrosation (under basic or acidic conditions) of the respective carbonyl compound.[11] The results from these reactions are shown in Table 1. The formation of both esters and acids (entries 1–4) suggests that during the photooxygenations anhydrides are likely intermediates that are cleaved by methanol. One possible mechanism consistent with the results is shown in Scheme 1.

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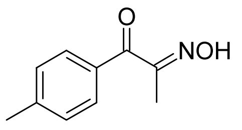
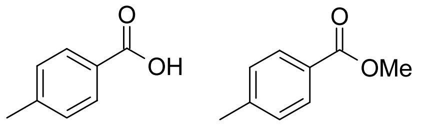
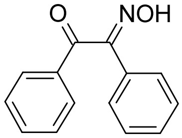
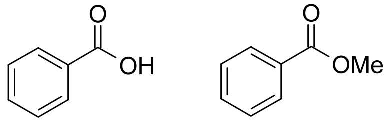
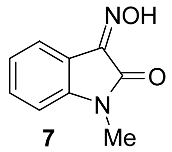
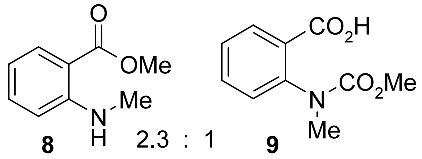
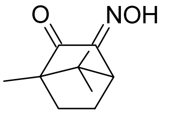
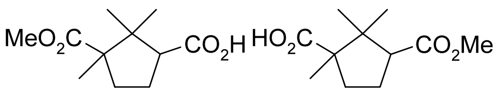
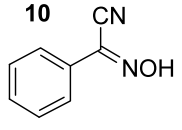
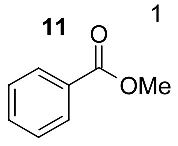
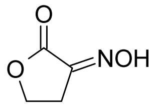
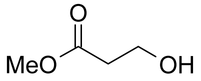
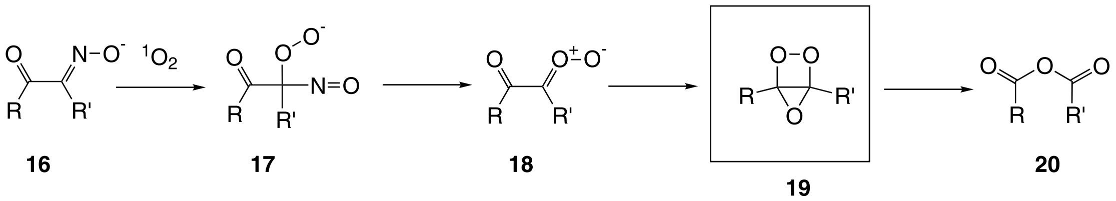
Table 1. Photooxygenation of α-oximino carbonyl compounds in the presence of base

1[a]	 **1**	 **2** 1 : 2.8 **3**	92%
2	 **4**	 **5** 1 : 1 **6**	86%
3	 **7**	 **8** 2.3 : 1 **9**	72%
4	 **10**	 **11** 1 : 1 **12**	90%
5	 **13**	 **6**	88%
6	 **14**	 **15**	79 %

[a] Methyl acetate was not isolated due to its volatility



Scheme 1.

In analogy to amidoximate photooxygenations the oximate anion attacks singlet oxygen, the resulting peroxo anion extrudes NO$^-$ giving rise to a carbonyl oxide. The latter species is adjacent to a carbonyl group that participates in the formation of a tiroxabicyclo-[2.1.0]pentane. This intermediate then undergoes a 1,2-dioxetane cleavage to give the anhydride that suffers methanolysis leading to the observed products.

Several aspects of the proposed mechanism deserve comment. Intermediate **19** has been shown to form as a reactive intermediate in the photooxygenations of α-diazoketones and seems to be the most likely source of the anhydrides that have been reported to form in these reactions.[12] In support of the anhydride intermediate is the fact that when acetic benzoic anhydride was independently prepared and subjected to methanolysis, the ratio of benzoic acid and methyl benzoate was essentially the same as that observed in the photooxygenation experiment (entry 1).[13] However, another mechanism involving attack of methanol at the carbonyl oxide stage followed by a Baeyer–Villiger rearrangement of the resulting hydroperoxide would also lead to the observed cleavage products via anhydride and/or anhydride hemiacetal intermediates. This latter mechanism had been advanced for oxidative C–C cleavage reactions of unsymmetrical acetylenes with ozone in alcohol solvents.[14]

The methodology described in this paper lends itself well to oxidative cleavage of a variety of carbonyl compounds, including aldehydes, ketones, esters, amides. The α-oximino derivatives are readily available, and the photooxidations are carried out under mild conditions, and the use of singlet oxygen in these reactions, as well as lack of by-products renders this method environmentally friendly.

Acknowledgements

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References

1. Carey, F. A.; Sundberg, R. J. In *Advanced Organic Chemistry*, Part B: Reactions and Synthesis, 4th ed.; Kluwer/Plenum: New York, 2001; pp. 747–820.
2. Fuson, R. C.; Bull, B. A. *Chem. Rev.* **1934**, *15*, 275.
3. Corey, E. J.; Katzenellenbogen, J. A.; Gilman, N. W.; Roman, S. A.; Erickson, B. W. *J. Am. Chem. Soc.* **1968**, *90*, 5618.
4. Rubottom, G. M.; Gruber, J. M.; Juve, H. D., Jr.; Charleson, D. A. *Org. Synth.* **1985**, *64*, 118–125.
5. Brégeault, J.-M.; Launay, F.; Atlamsani, A. *C.R. Acad. Sci. Paris*, *Série IIc*, *Chimie/Chemistry* **2001**, *4*, 11–26.
6. Ashford, S. W.; Grega, K. C. *J. Org. Chem.* **2001**, *66*, 1523 and references cited therein.
7. Castro, C.; Dixon, M.; Erden, I.; Ergönenç, P.; Keeffe, J. R.; Sukhovitsky, A. *J. Org. Chem.* **1989**, *54*, 3732–3738.
8. Erden, I.; Griffin, A.; Keeffe, J. R.; Brinck-Kohn, V. *Tetrahedron Lett.* **1993**, *34*, 793.
9. Öcal, N.; Erden, I. *Tetrahedron Lett.* **2001**, *42*, 4765–4767.
10. In a typical experiment, 2–3 mmol of α-oximino carbonyl compound was treated with 1.2 equiv. of NaOMe in 20 mL of methanol, and irradiated at room temperature under a positive pressure of oxygen, using a 250 W high-pressure sodium vapor lamp and rose bengal as sensitizer. After completion of reaction (ca. 2–3 h) the mixture was acidified with HCl, and the mixture concentrated in vacuo, and the residue extracted with CH_2Cl_2. In all cases a crude ^1H NMR was obtained in order to determine the product ratios. The mixtures were chromatographed on SiO_2, eluting with CH_2Cl_2 in most cases (ether/ethyl acetate 3:1, entry 4).
11. (a) Hartung, W. H.; Crossley, F. *Org. Syn. Coll. Vol. II* **1943**, 363; (b) Ferris, A. F. *J. Org. Chem.* **1959**, *24*, 1726; (c) Ferris, A. F. *J. Org. Chem.* **1960**, *25*, 12; (d) Ferris, A. F.; Johnson, G. S.; Gould, F. E. *J. Org. Chem.* **1960**, *25*, 496.
12. Ando, W.; Miyazaki, H.; Ito, K.; Auchi, D. *Tetrahedron Lett.* **1982**, *23*, 555–556.
13. Bailey, P. S.; Chang, Y.-G. *J. Org. Chem.* **1962**, *27*, 1192–1197.
14. (a) Yang, N. C.; Libman, J. *J. Org. Chem.* **1974**, *39*, 1782; (b) Jackson, S.; Hull, L. A. *J. Org. Chem.* **1976**, *41*, 3340.