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SET induced cyclizations of β,γ-unsaturated oximes. A novel photochemical route to dihydroisoxazole derivatives

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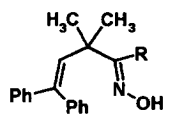
Abstract

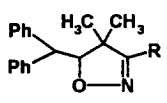
The photochemical SET induced cyclization of some β,γ-unsaturated oximes using 9,10-dicyanoanthracene provides an efficient route for the synthesis of novel dihydroisoxazole derivatives. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: photochemistry; dihydroisoxazoles; oximes; electron transfer.

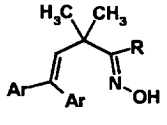
Over the years we have studied the photochemical reactivity of β,γ-unsaturated oximes and their derivatives. Many interesting novel photochemical processes, such as the aza-di-π-methane reaction of imines, oxime acetates and oximes themselves have been discovered by us.[1] Among these was the observation that some β,γ-unsaturated oximes (**1**) underwent photochemical acetophenone-sensitized cyclization to afford moderate yields of the dihydroisoxazole derivatives (**2**).[2] Of all the mechanisms considered to account for the observed cyclizations the most feasible was thought to involve a single electron transfer (SET) process within the triplet state of the oximes. However, the cyclization was restricted to only a few examples (**1**) and the yields of product (**2**, R=Ph or Me) were moderate. This publication reports the use of the single electron transfer (SET) sensitizer 9,10-dicyanoanthracene (DCA) with the same and other β,γ-unsaturated oximes as a facile route to some novel dihydroisoxazole derivatives.



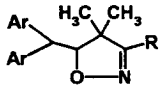
(1) R = Me or Ph



(2)



(3)



(4)

Some of the oximes (**1a–c**) used in this study have been synthesized previously by Armesto et al.[1] using a slight variation of the method developed by Zimmerman and Pratt.[3] Other oximes (**3a–h**) which were required to examine the scope of the process were synthesized in the same manner. The irradiations

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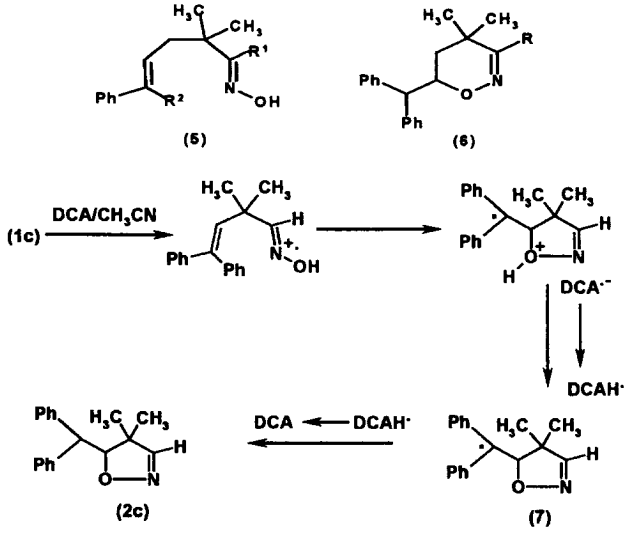
Table 1
Yield (%) of dihydroisoxazoles (**2** and **4**) obtained from the SET-induced cyclization of the oximes (**1** and **3**)

Dihydroisoxazole formed		Yield	Irrad. time	Oxime used		Oxime Recovered
(2a)	R= Me	44%	15 min.	(1a)	R= Me	41%
(2b)	R= Ph	53%	15 min.	(1b)	R= Ph	28%
(2c)	R= H	44%	15 min.	(1c)	R= H	44%
(4a)	Ar = *p*-$MeOC_6H_4$, R= Me	38%	15 min	(3a)	Ar = *p*-$MeOC_6H_4$, R= Me	48%
(4b)	Ar = *p*-$MeOC_6H_4$, R= Ph	50%	15 min.	(3b)	Ar = *p*-$MeOC_6H_4$, R= Ph	26%
(4c)	Ar = *p*-ClC_6H_4, R= H	35%	15 min.	(3c)	Ar = *p*-ClC_6H_4, R= H	48%
(4d)	Ar = *p*-ClC_6H_4, R= Me	40%	15 min.	(3d)	Ar = *p*-ClC_6H_4, R= Me	50%
(4e)	Ar = *p*-ClC_6H_4, R= Ph	44%	15 min	(3e)	Ar = *p*-ClC_6H_4, R= Ph	47%
(4f)	Ar = *p*-*t*-BuC_6H_4, R= H	45%	7.5 h	(3f)	Ar = *p*-*t*-BuC_6H_4, R= H	29%
(4g)	Ar = *p*-*t*-BuC_6H_4, R= Me	64%	7.5 h	(3g)	Ar = *p*-*t*-BuC_6H_4, R= Me	trace
(4h)	Ar = *p*-*t*-BuC_6H_4, R= Ph	40%	2 h	(3h)	Ar = *p*-*t*-BuC_6H_4, R= Ph	28%

(λ >280 nm) of the oximes (0.25 g) were all carried out in a conventional immersion-well apparatus under argon with acetonitrile (250 ml) as the solvent and 9,10-dicyanoanthracene (DCA) (27 mg) as the sensitizer. As can be seen from Table 1, short irradiation times were required and only with the derivatives **3f–h** were prolonged irradiations needed.

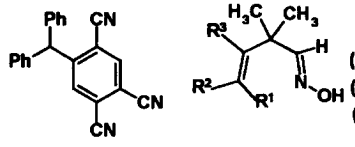
The ^{1}H NMR of the crude reaction mixture obtained from the irradiation of (**1c**) showed that a reaction had occurred and chromatography of the reaction mixture afforded a crystalline product in 44% (73% based on recovered starting material) yield. The ^{13}C and ^{1}H NMR clearly identified this as the dihydroisoxazole (**2c**). The definitive features that permitted this identification were the two doublets at 4.2 δ and 4.8 δ with a coupling constant of 11.0 Hz. Such a pattern had already been observed[2] by us for the products reported previously. Although the yield is only 44% after 15 min, prolonged irradiation of up to 2 h results in an almost quantitative conversion to the dihydroisoxazole (**2c**). All the other oximes (**1a, b**) and (**3a–h**) were converted after brief irradiation into the corresponding dihydroisoxazoles (**2a, b**) and (**4a–h**), respectively.[7] The most likely mechanism for the cyclization is illustrated in Scheme 1 and was proposed earlier by Armesto et al.[4] to account for the successful DCA induced photocyclization of the related oximes (**5**, R^2=Ph) into the dihydrooxazines (**6**).



Scheme 1.

Scheme 1 proposes that the key step is removal of an electron from the oximino group by the DCA in its excited singlet state. This generates the radical cation of (**1c**). This radical cation then undergoes an *exo*-cyclization with the alkene moiety. Proton transfer from the cyclized radical cation to the DCA radical anion affords the radical (**7**) that abstracts hydrogen from the DCAH radical thus completing the process.

Interestingly, the dihydroisoxazoles (**2**) and (**4**) are stable under the reaction conditions when DCA is the sensitizer. This was demonstrated both by the almost quantitative conversion obtained by prolonged irradiation of (**1c**) and also by independent irradiation of (**2c**) with DCA. However, when (**1c**) is irradiated with tetracyanobenzene (TCNB) as the electron-accepting sensitizer the dihydroisoxazole undergoes bond fission within the resultant radical cation of the dihydroisoxazole. This bond fission liberates a diphenylmethyl radical that bonds with the radical anion of the sensitizer to afford ultimately the product (**8**) in 80% yield. Others[5,6] have demonstrated that TCNB is a powerful oxidant and can bring about fission of bonds in many organic systems resulting in substitution reactions of the sensitizer.

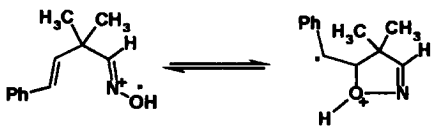


(8)

(9) R^1 = R^3 = H, R^2 = Ph
(10) R^1 = R^2 = H, R^3 = Ph
(11) R^1 = R^3 = Ph, R^2 = H
(12) R^1 = R^2 = Et, R^3 = H

The DCA induced cyclization of the β,γ-unsaturated oximes is restricted to molecules with two aryl groups on the alkene moiety. Attempts to bring about the cyclization of (**9–12**) under the same photochemical conditions were unsuccessful.

This result is in direct contrast with the cyclizations reported for the DCA induced photocyclizations of the γ,δ-unsaturated oximes (**5**) where efficient cyclization was observed with the mono-phenyl substituted derivative (**5**, R^2=H). The difference between those cyclizations and the present example could be due to ring size and substitution. We suggest that the formation of the dihydroisoxazole ring via cyclization of radical cations such as (**13**) is dependent upon the stability of the radical in the cyclic radical cation (using 9,10-dicyanoanthracene). If this radical is insufficiently stabilized then the ring-opened radical cation is preferred. Currently, research is aimed at clarifying this problem and studies are being carried out on the cyclizations of the iminoxyl radical (**15**).



(13) (14) (15)

Acknowledgements

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7. Satisfactory spectral and analytical data were obtained for all new products.Selected data for product (**4c**); mp: 140–142°C; IR: ν_{max} ($CHCl_3$)=1590 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): 7.6–7.1 (8H, m, aromatic), 6.9 (1H, s, HC=N), 5.3 (1H, d, J 10.7, CHO), 4.1 (1H, d, J 10.7, $CHPh_2$), 1.2 (3H, s, CH_3), 1.0 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$): 157.7 (C=N), 140.2–127.0 (aromatic), 88.2 (C-O), 50.6 ($C(CH_3)_2$), 50.0 ($CHPh_2$), 25.1 (CH_3), 19.5 (CH_3); EM m/z (%): 337 (6), 336 (5), 335 (26), 334 (12), 333 (39), 320 (17), 318 (73), 317 (37), 315 (100), 315 (24), 304 (26), 302 (34), 301 (18), 300 (39), 289 (10); $C_{18}H_{17}Cl_2NO$ (334.27). Found: C 64.63; H 5.16; N 4.15. Required: C 64.68; H 5.13; N 4.19. Selected data for product (**4e**); mp: 182–184°C; IR: ν_{max} ($CHCl_3$)=1590 (C=N) cm^{-1}; ^1H NMR ($CDCl_3$): 7.6–7.1 (13H, m, aromatic), 5.3 (1H, d, J 10.7, CHO), 4.1 (1H, d, J 10.7, $CHPh_2$), 1.2 (3H, s, CH_3), 1.0 (3H, s, CH_3); ^{13}C NMR ($CDCl_3$): 157.7 (C=N), 140.2–127.0 (aromatic), 88.2 (C-O), 50.6 ($C(CH_3)_2$), 50.0 ($CHPh_2$), 25.1 (CH_3), 19.5 (CH_3); EM m/z (%): 409 (1), 239 (5), 238 (4), 237 (30), 236 (7), 235 (47), 199 (9), 175 (12), 174 (100), 166 (5), 165 (32), 146 (51), 131 (21); $C_{24}H_{21}Cl_2NO$ (410.32). Found: C 70.22; H 5.18; N 3.40. Required: C 70.25; H 5.16; N 3.41.