

Solvent dependent photochemical reactivity of 3-allyloxy-1,2,4-oxadiazoles

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Dedicated to Prof. Nicolò Vivona on his 70th birthday

Abstract

The photochemistry of some 1,2,4-oxadiazoles containing a double bond at the side chain has been investigated. The irradiation yielded different 2-*N*-benzoylamino-2-oxazoline derivatives depending on the employed reaction solvent (DCM or THF). Photorearrangements occur through an intramolecular aziridination reaction yielding a bicyclic intermediate, which was subjected to *in situ* aziridine ring opening. Photoinduced addition of HCl, involving the chlorinated solvent as a reagent, gave the corresponding chlorinated 2-oxazoline. In THF, reductive aziridine ring opening was observed.

Keywords: Oxadiazole, photochemical rearrangement, 2-oxazoline, intramolecular aziridination

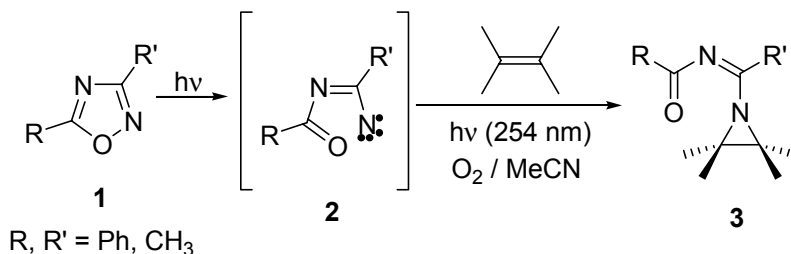
Introduction

The 1,2,4-oxadiazole **1** is an interesting heterocycle as it presents many useful applications ranging from pharmaceutical¹ to materials science (ionic liquids, liquid crystals, OLED).² In the last years the photochemical behaviour of the 1,2,4-oxadiazole system has been the object of several studies that showed the use of this heterocycle as synthon in the construction of different heterocyclic systems such as 1,3,4-oxadiazoles,³ benzimidazoles,^{4,5} benzoxazoles,⁴ indazoles,⁵ quinolines,⁶ quinazolinones,⁷ and triazoles.^{5,8}

Generally, the photochemical reactivity of the 1,2,4-oxadiazole ring involves the cleavage of the O-N bond. The photolytic intermediate **2** (Scheme 1), with zwitterionic, radicalic or nitrene-like character, will follow different reaction patterns depending on the nature of the substituents on the ring, the kind of solvent and the presence of other reactive species in solution. In many cases the N(2) of the oxadiazolic system acts as electrophilic center such as in the reactions with

an oxygen nucleophile leading to solvolysis products,^{3b} in the reaction with sulphur nucleophiles leading to thiadiazoles⁹ and in the reaction with nitrogen nucleophiles leading to triazoles.^{5,8}

Recently, we have explored the use of carbon nucleophiles such as alkenes.¹⁰ Due to the nitrene-like character of the intermediate **2**, the occurrence of an olefin aziridination reaction, was observed (Scheme 1).¹⁰



Scheme 1

Starting from our previous results, we wanted to explore the possibility to achieve an intramolecular photoaziridination reaction by using alkene-tethered 1,2,4-oxadiazoles, as nitrene source, to form bicyclic heterocycles (Chart 1).

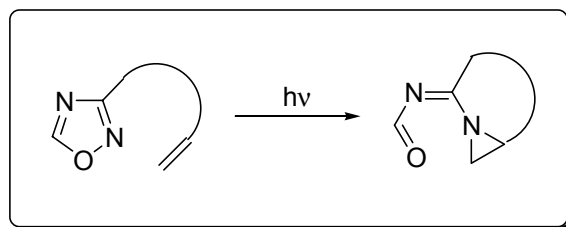
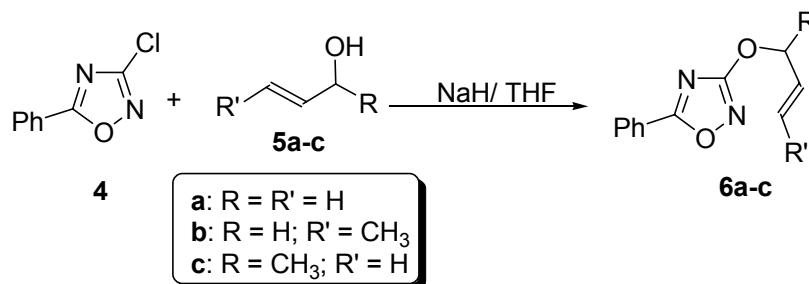


Chart 1

Results and Discussion

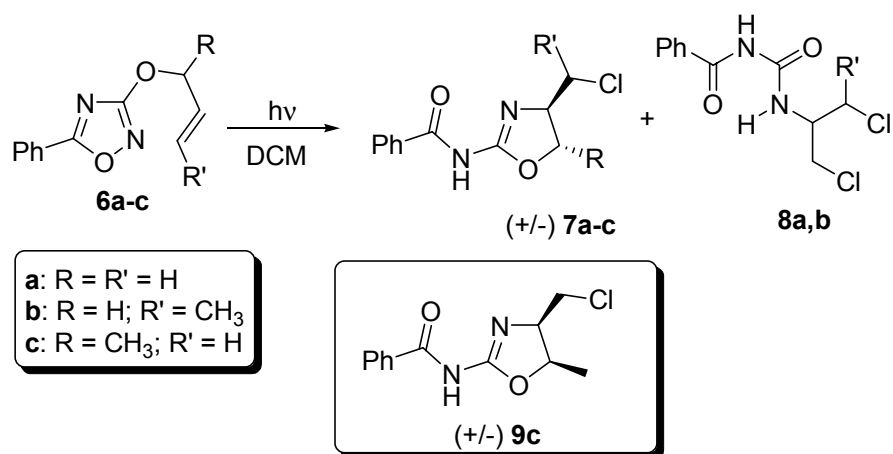
As starting compounds we selected 3-alkenoxy-5-phenyl-1,2,4-oxadiazoles **6a-c**, readily available through S_NAr reactions from 3-chloro-5-phenyl-1,2,4-oxadiazole **4** with allylic alcohols **5a-c** under basic conditions (Scheme 2).



Scheme 2

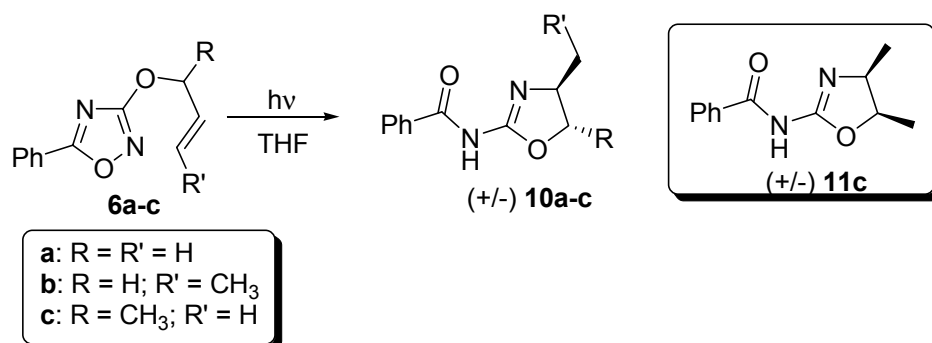
Irradiations of compounds **6a-c** (for 5h at $\lambda = 254$ nm) have been carried out in deoxygenated DCM or THF. Consumption of starting materials was monitored by TLC and irradiations were stopped before total conversion of oxadiazoles **6** in order to prevent formation of by-products.

By using DCM as solvent, photoreactions of oxadiazole **6a,b** yielded racemic chlorinated 2-*N*-benzoylamino-2-oxazolines **7a,b** together with benzoylureas **8a,b** (see Scheme 3, one enantiomer showed, and Table 1). From irradiation of **6c** a racemic mixture of *trans*-**7c** and *cis*-**9c** stereoisomers was obtained.



Scheme 3

On the other hand, irradiation of compounds **6** in THF gave racemic 2-oxazoline **10a-c**. Once again, irradiation of **6c** gave a mixture of *trans* **10c** and *cis* **11c** stereoisomers (Scheme 4, one enantiomer showed, Table 1). The same products have been observed in both solvents by irradiation at 313 nm although, after 6h of irradiation, the substrate conversion was extremely low (< 5 %).



Scheme 4

Table 1. Products obtained from irradiation of compounds **6**

Substrate	DCM		THF	
	Products		Products	
6a	28%	7a (29%) 8a (32%)	31%	10a (45%)
6b	34%	7b (31%) 8b (10%)	60%	10b (28%)
6c	55%	7c (35%) 8c (-) 9c (7%)	61%	10c (26%) 11c (7%)

The stereochemistry of oxazolines **7c/9c** and **10c/11c** was assigned by means of $^1\text{H-NMR}$ experiments, by comparison of coupling constant values between oxazoline H(4) and H(5) methine protons ($J_{4-5\text{trans}} < J_{4-5\text{cis}}$)¹¹ as well as from chemical shifts of methine protons which show a deshielding in the *cis* isomers with respect to the *trans* (see experimental);^{11a} moreover, NOESY experiments confirmed proposed configurations.

UV-absorption spectra of representative compounds **6a**, **7a**, **8a** (in DCM) and **6a**, **10a** (in THF) are showed in Figure 1. Strong absorption above 254 nm for all heterocyclic derivatives was observed, while benzoyl-urea **8a** presents absorption maximum at 237 nm. Starting compound **6a** presents weak absorption at 313 nm thus justify lower reactivity at this wavelength.

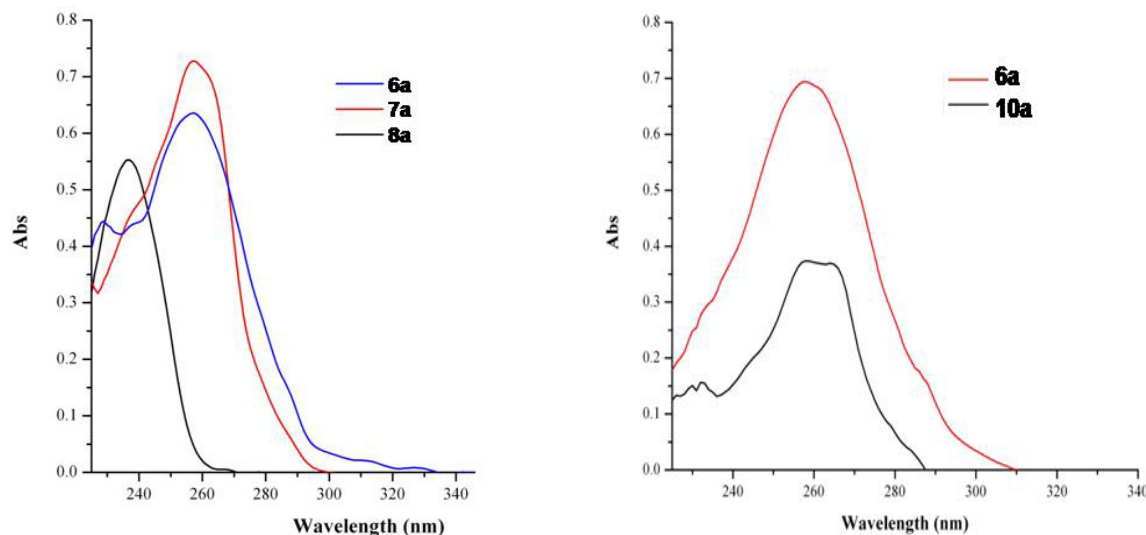
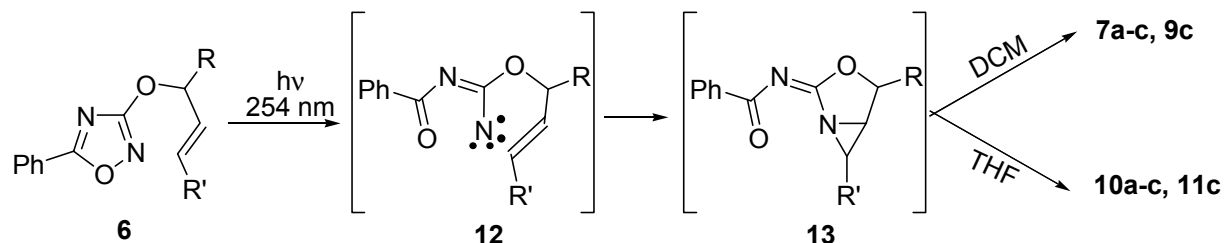


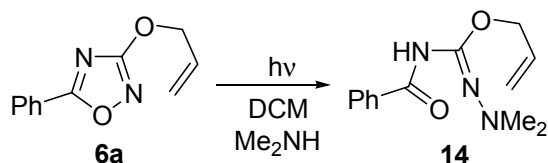
Figure 1. Absorption spectra of representative compounds **6a**, **7a** and **8a** (50 μM) in DCM (left); **6a** and **10a** (50 μM) in THF (right).

Obtained data allowed us to hypothesize a mechanism which consists of an initial photochemical cleavage of the O-N bond of oxadiazoles **6** leading to nitrene intermediate **12** which cyclize giving bicyclic intermediate **13** (scheme 5).



Scheme 5

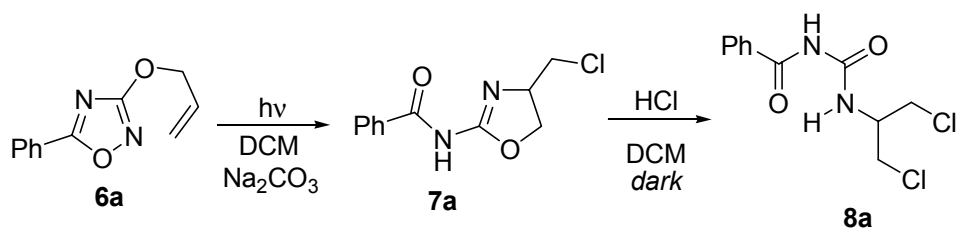
Although no direct photophysical study has been conducted, the involvement of a singlet nitrene species is supported by a trapping experiment. In fact, irradiation of representative **6a** in the presence of dimethylamine produced the open-chain product **14** by a nucleophilic addition reaction (Scheme 6).



Scheme 6

Moreover, by performing the photoreactions in oxygenated solvents, the involvement of a triplet species can be excluded since product formation seems to be unaffected by the presence of oxygen. After the intramolecular aziridination, the reactive intermediate **13** can produce 2-oxazolines **7,9** or **10,11** depending on the employed irradiation solvent. The formation of hydrochlorinated products **7, 9** and **8** clearly involves the DCM solvent as a reagent. In fact, it is well-known that chlorinated solvents photochemically produce hydrochloric acid under UV irradiation. Acid mediated ring opening of **13** seems to be consistent with previously reported results on 2-oxazolidinones formation from bicyclic aziridine.^{11b,c} Moreover, chlorinated 2-oxazoline **7, 9** could be further subjected to oxazoline ring opening into ureas **8**, most likely by action of another molecule of HCl produced during the irradiation.¹² Alternatively, the photochemical addition of HCl may occur through a radical mechanism involving intermediate **13** which will abstract chlorine and hydrogen atoms from the solvent. In this context, irradiation of **6a**, in DCM and in the presence of an excess of suspended sodium carbonate, mainly produced monochlorinated oxazoline **7a** (Scheme 7).¹³ This finding suggests that **7a** is formed through a radical mechanism, unaffected by the presence of the added base. The transformation of **7a** into **8a**, not observed in the irradiation in the presence of the base, is instead ascribed to an

acid catalyzed addition of HCl (ionic mechanism) as proven in a separate room temperature experiment *in the dark* (Scheme 7).



Scheme 7

On the other hand, 2-oxazoline **9,10** formation, from irradiation in THF, could be ascribed to a reductive cleavage of aziridine portion of intermediate **13** likely involving the solvent as hydrogen donor.

The stereoselectivity observed from **6c** photorearrangements, with comparable *trans/cis* ratio in both solvent and preferential *trans* isomers formation, could be rationalized by transition states showed in Figure 2. In both cases methyl group occupies a *quasi-equatorial* position and the steric interaction with the methylene group drives towards predominant *trans* stereoisomers formation.^{11b}

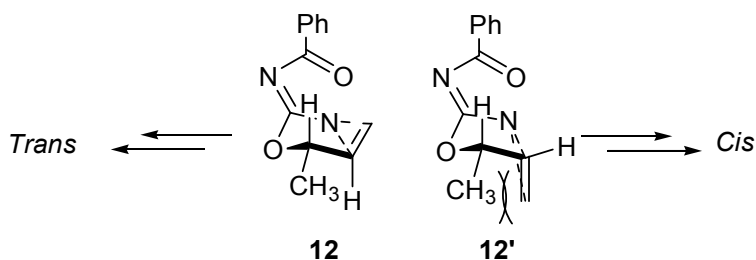


Figure 2

Conclusions

In conclusion, the photochemical behaviour of alkene-tethered 1,2,4-oxadiazoles was investigated evidencing the occurrence of an intramolecular aziridination reaction. Solvent dependent reactivity was observed, allowing the obtainment of differently substituted 2-oxazoline. Such photochemical approach represents a new synthetic way for this interesting heterocycle, which presents many useful applications ranging from pharmaceuticals^{12,14} to polymer science^{12,15} and catalysis.^{15,16}

Experimental Section

General Procedures. Melting points were determined on a REICHART-THERMOVAR hot-stage apparatus and are uncorrected. FT-IR spectra (Nujol) were determined with a SHIMADZU FTIR-8300 instrument. ^1H NMR spectra were recorded on a Bruker 300 Avance spectrometer by using residual peak of the solvent (CDCl_3 or $\text{DMSO}-d_6$) as reference. GC/MS determinations were carried out on a VARIAN STAR 3400 CX/SATURN 2000 system. Flash chromatography was performed using silica gel (200-400 mesh) and mixtures of EtOAc and light petroleum (fraction boiling in the range 40-60°C) in various ratios. Oxadiazole **4** was prepared as previously reported.¹⁷

Synthesis of 1,2,4-oxadiazol-3-yl-ethers **6**. General procedure

Alcohols **5** (4.5 mmol) were added to a suspension of NaH (4.5 mmol, as 60% dispersion in mineral oil) in THF (50 mL). After hydrogen evolution completion, 3-chloro-5-phenyl-1,2,4-oxadiazole **4** (3 mmol) was added. The mixture was stirred at r.t. for 12h. The solvent was then evaporated, the residue treated with water and neutralized with HCl 1M and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and evaporated. The residue was then chromatographed.

Reaction with allyl alcohol 5a. 3-(Allyloxy)-5-phenyl-1,2,4-oxadiazole (6a). 86% yield; colourless viscous oil; ^1H NMR (300 MHz, CDCl_3) δ 4.78 (d, 2H, $J = 6.3$ Hz), 5.25 (d, 1H, $J = 10.3$ Hz), 5.40 (d, 1H, $J_1 = 17.3$ Hz), 5.98 (ddt, 1H, $J_1 = 17.3$ Hz, $J_2 = 10.3$ Hz, $J_3 = 6.3$ Hz), 7.33-7.52 (m, 3H), 7.99-8.02 (m, 2H); UV (DCM) 257 (log $\epsilon = 4.06$) and 310 nm (log $\epsilon = 2.59$), UV (THF) 257 (log $\epsilon = 4.10$) and 310 nm (log $\epsilon = 1.55$); FT-IR (Nujol) 1615 cm^{-1} . GC-MS (m/z): 202 (100%); Anal. Calcd. for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.50; H, 4.90; N, 13.60.

Reaction with trans crotyl alcohol 5b. 3-[(E)-But-2-enyloxy]-5-phenyl-1,2,4-oxadiazole (6b). 81% yield; mp 61-62°C (white crystals from petroleum ether); ^1H NMR (300 MHz, CDCl_3) δ 1.69 (d, 3H, $J = 6.6$ Hz), 4.71 (d, 2H, $J = 6.3$ Hz), 5.70 (dt, 1H, $J_1 = 15.3$ Hz, $J_2 = 6.3$ Hz), 5.87 (dq, 1H, $J_1 = 15.3$ Hz, $J_2 = 6.6$ Hz), 7.39-7.52 (m, 3H), 7.99-8.02 (m, 2H); FT-IR (Nujol) 1612 cm^{-1} . GC-MS (m/z): 216 (100%); Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.60; H, 5.70; N, 12.90.

Reaction with 3-buten-2-ol 5c. 3-(But-3-en-2-yloxy)-5-phenyl-1,2,4-oxadiazole (6c). 74% yield; colourless viscous oil; ^1H NMR (300 MHz, CDCl_3) δ 1.47 (d, 3H, $J = 6.3$ Hz), 5.16-5.24 (m, 2H, overlapped signals), 5.70 (dt, 1H, $J_1 = 17.4$ Hz, $J_2 = 1.2$ Hz), 5.91 (ddd, 1H, $J_1 = 17.4$ Hz, $J_2 = 10.5$ Hz, $J_3 = 6.3$ Hz), 7.40-7.54 (m, 3H), 7.99-8.02 (m, 2H); FT-IR (Nujol) 1613 cm^{-1} . GC-MS (m/z): 216 (100%); Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{N}_2\text{O}_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.50; H, 5.50; N, 12.80.

General procedure for photochemical reactions

Photochemical reactions were carried out by using a Rayonet RPR-100 photoreactor fitted with 16 Hg lamps irradiating at $\lambda = 254$ nm (RPR-2537Å) (Quartz vessels) and equipped with a merry-go-round apparatus. A solution of compound **6** (3 mmol) in dry DCM or THF (400 mL), was partitioned in nine quartz tubes and purged with nitrogen (10 min). The solution was irradiated for 5 h, the solvent was then evaporated and the residue chromatographed. For products distribution see Table 1.

Irradiation of compound **6a** in DCM

2-N-Benzoylamino-4-(chloromethyl)-2-oxazoline (7a). Mp 168-170°C (white crystals from EtOH); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 3.64 (dd, 1H, $J_1 = 11.2$ Hz, $J_2 = 6.0$ Hz), 3.69 (dd, 1H, $J_1 = 11.2$ Hz, $J_2 = 5.3$ Hz), 4.31 (dd, 1H, $J_1 = 8.7$ Hz, $J_2 = 4.8$ Hz), 4.34-4.43 (m, 1H), 4.54 (dd, 1H, $J_1 = 8.7$ Hz, $J_2 = 8.4$ Hz), 7.40-7.55 (m, 3H), 8.21-8.26 (m, 2H), 9.80 (s, 1H, exch. with D_2O); UV (DCM) 257 nm ($\log \epsilon = 4.10$); FT-IR (Nujol) 3330, 1633 cm^{-1} . GC-MS (m/z): 240 (M+2, 5%), 238 (M, 14%), 105 (100%); HRMS found: 238.0507; $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}_2$ requires: 238.0509; Anal. Calcd. for $\text{C}_{11}\text{H}_{11}\text{ClN}_2\text{O}_2$: C, 55.36; H, 4.65; N, 11.74. Found: C, 55.20; H, 4.50; N, 11.60.

N-Benzoyl-N'-(1,3-dichloropropan-2-yl)-urea (8a). Mp 156-158°C (white crystals from petroleum ether); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 3.71 (dd, 2H, $J_1 = 12.9$ Hz, $J_2 = 6.6$ Hz), 3.83 (dd, 2H, $J_1 = 11.1$ Hz, $J_2 = 6.6$ Hz), 4.40 (m, 1H), 7.41-7.46 (m, 2H), 7.52-7.57 (m, 1H), 7.93-7.96 (m, 2H) 9.33 (d, 1H, $J = 7.5$ Hz, exch. with D_2O), 10.07 (s, 1H, exch. with D_2O); UV (DCM) 237 nm ($\log \epsilon = 4.05$); FT-IR (Nujol) 3232, 3136, 1689, 1669 cm^{-1} . GC-MS (m/z): 276 (M+2, 2%), 274 (M, 3%), 105 (100%); HRMS found: 274.0267; $\text{C}_{11}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}_2$ requires: 274.0276; Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}_2$: C, 48.02; H, 4.40; N, 10.18. Found: C, 48.10; H, 4.50; N, 10.30.

Irradiation of compound **6b** in DCM

2-N-Benzoylamino-4-(1-chloroethyl)-2-oxazoline (7b). Mp 141-142°C (white crystals from EtOH); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 1.52 (d, 3H, $J = 6.6$ Hz), 3.97 (p, 1H, $J = 6.6$ Hz), 4.21 (ddd, 1H, $J_1 = 8.9$ Hz, $J_2 = 6.6$ Hz, $J_3 = 5.2$ Hz), 4.53 (dd, 1H, $J_1 = 9.5$ Hz, $J_2 = 8.9$ Hz), 4.40 (dd, 1H, $J_1 = 9.5$ Hz, $J_2 = 5.2$ Hz), 7.25-7.56 (m, 3H), 7.94-8.33 (m, 2H), 9.75 (bs, 1H, exch. with D_2O); FT-IR (Nujol) 3322, 1627 cm^{-1} . GC-MS (m/z): 254 (M+2, 4%), 252 (M, 13%), 105 (100%); Anal. Calcd. for $\text{C}_{12}\text{H}_{13}\text{ClN}_2\text{O}_2$: C, 57.04; H, 5.19; N, 11.09. Found: C, 57.20; H, 5.20; N, 10.90.

N-Benzoyl-N'-(1,3-dichlorobutan-2-yl)-urea (8b). Mp 124-126°C (white crystals from benzene); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 1.53 (d, 3H, $J = 6.1$ Hz), 3.85-4.07 (m, 1H), 4.28-4.50 (m, 2H), 7.45-7.57 (m, 2H), 7.58-7.73 (m, 1H), 7.88-8.10 (m, 2H), 9.11 (d, 1H, $J = 8.4$ Hz, exch. with D_2O), 10.94 (s, 1H, exch. with D_2O); FT-IR (Nujol) 3233, 3143, 1688, 1673 cm^{-1} . GC-MS (m/z): 290 (M+2, 1%), 288 (M, 2%), 105 (100%); Anal. Calcd. for $\text{C}_{12}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}_2$: C, 49.84; H, 4.88; N, 9.69. Found: C, 49.80; H, 4.70; N, 9.90.

Irradiation of compound **6c** in DCM

trans-2-N-Benzoylamino-4-(chloromethyl)-5-methyl-2-oxazoline (7c). Mp 117-118°C (white crystals from EtOH); $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 1.57 (d, 3H, $J = 6.3$ Hz), 3.60 (dd, 1H, $J_1 = 11.4$ Hz, $J_2 = 6.9$ Hz), 3.67 (dd, 1H, $J_1 = 11.4$ Hz, $J_2 = 5.4$ Hz), 3.96-4.01 (ddd, 1H, $J_1 = 6.9$ Hz, $J_2 =$

5.4 Hz, $J_3 = 5.4$ Hz), 4.67 (qd, 1H, $J_1 = 6.3$ Hz, $J_2 = 5.4$ Hz), 7.40-7.56 (m, 3H), 7.99-8.02 (m, 2H), 9.83 (s, 1H, exch. with D₂O); FT-IR (Nujol) 3330, 1617 cm⁻¹. GC-MS (m/z): 254 (M+2, 4%), 252 (M, 14%), 105 (100%); Anal. Calcd. for C₁₂H₁₃ClN₂O₂: C, 57.04; H, 5.19; N, 11.09. Found: C, 57.10; H, 5.30; N, 11.00.

cis-2-N-Benzoylamino-4-(chloromethyl)-5-methyl-2-oxazoline (9c). mp 101-102°C (white crystals from EtOH); ¹H NMR (300 MHz, CDCl₃) δ 1.62 (d, 3H, $J = 6.9$ Hz), 3.64 (dd, 1H, $J_1 = 12.0$ Hz, $J_2 = 6.9$ Hz), 3.71 (dd, 1H, $J_1 = 12.0$ Hz, $J_2 = 5.4$ Hz), 4.38 (ddd, 1H, $J_1 = 7.8$ Hz, $J_2 = 6.9$ Hz, $J_3 = 5.4$ Hz), 5.06 (dq, 1H, $J_1 = 7.8$ Hz, $J_2 = 6.9$ Hz), 7.42-7.61 (m, 3H), 8.24-8.26 (m, 2H), 10.01 (s, 1H, exch. with D₂O); FT-IR (Nujol) 3315, 1626 cm⁻¹. GC-MS (m/z): 254 (M+2, 11%), 252 (M, 30%), 105 (100%); Anal. Calcd. for C₁₂H₁₃ClN₂O₂: C, 57.04; H, 5.19; N, 11.09. Found: C, 57.10; H, 5.20; N, 11.00.

Irradiation of compound 6a in THF

2-N-Benzoylamino-4-methyl-2-oxazoline (10a). mp 72-74°C (white crystals from EtOH); ¹H NMR (300 MHz, DMSO-*d*₆) δ 1.33 (d, 3H, $J = 6.3$ Hz), 4.08 (dd, 1H, $J_1 = 8.7$ Hz, $J_2 = 6.6$ Hz), 4.22-4.29 (m, 1H), 4.61 (dd, 1H, $J_1 = 8.7$ Hz, $J_2 = 8.4$ Hz), 7.46-7.59 (m, 3H), 8.12-8.15 (m, 2H), 9.82 (s, 1H, exch. with D₂O); UV (THF) 258 nm (log ε = 3.88) and 264 nm (log ε = 3.87); FT-IR (Nujol) 3325, 1635 cm⁻¹. GC-MS (m/z): 204 (M, 45%), 105 (100%); HRMS found: 204.0886; C₁₁H₁₂N₂O₂ requires: 204.0899; Anal. Calcd. for C₁₁H₁₂N₂O₂: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.50; H, 5.80; N, 13.80.

Irradiation of compound 6b in THF

2-N-Benzoylamino-4-ethyl-2-oxazoline (10b). Mp 96-98°C (white crystals from EtOH); ¹H NMR (300 MHz, CDCl₃) δ 1.03 (t, 3H, $J = 7.5$ Hz), 1.67-1.77 (m, 2H), 4.10-4.17 (m, 2H), 4.53-4.61 (m, 1H), 7.39-7.51 (m, 3H), 8.22-8.25 (m, 2H), 9.65 (s, 1H, exch. with D₂O); FT-IR (Nujol) 3324, 1628 cm⁻¹. GC-MS (m/z): 218 (M, 33%), 105 (100%); Anal. Calcd. for C₁₂H₁₄N₂O₂: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.10; H, 6.60; N, 12.60.

Irradiation of compound 6c in THF

trans 2-N-Benzoylamino-4,5-dimethyl-2-oxazoline (10c). Mp 71-72°C (white crystals from EtOH); ¹H NMR (300 MHz, CDCl₃) δ 1.34 (d, 3H, $J = 6.3$ Hz), 1.48 (d, 3H, $J = 6.3$ Hz), 3.78 (dq, 1H, $J_1 = 6.8$ Hz, $J_2 = 6.3$ Hz), 4.32 (dq, 1H, $J_1 = 6.8$ Hz, $J_2 = 6.3$ Hz), 7.36-7.49 (m, 3H), 8.20-8.22 (m, 2H), 9.52 (s, 1H, exch. with D₂O); FT-IR (Nujol) 3331, 1619 cm⁻¹. GC-MS (m/z): 218 (M, 38%), 105 (100%); Anal. Calcd. for C₁₂H₁₄N₂O₂: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.10; H, 6.50; N, 12.90.

cis-2-N-Benzoylamino-4,5-dimethyl-2-oxazoline (11c). Mp 110-113°C (white crystals from EtOH); ¹H NMR (300 MHz, CDCl₃) δ 1.23 (d, 3H, $J = 6.6$ Hz), 1.42 (d, 3H, $J = 6.3$ Hz), 4.20 (dq, 1H, $J_1 = 8.1$ Hz, $J_2 = 6.6$ Hz), 4.85 (dq, 1H, $J_1 = 8.1$ Hz, $J_2 = 6.3$ Hz), 7.33-7.43 (m, 3H), 8.18-8.21 (m, 2H), 9.59 (s, 1H, exch. with D₂O); FT-IR (Nujol) 3332, 1622 cm⁻¹. GC-MS (m/z): 218 (M, 29%), 105 (100%); Anal. Calcd. for C₁₂H₁₄N₂O₂: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.00; H, 6.40; N, 13.00.

Irradiation of **6a** in presence of dimethylamine

A solution of compound **6a** (3 mmol) in dry DCM (400 mL), was partitioned in nine quartz tubes and purged with nitrogen (10 min). An excess of dimethylamine (10 eq.) was added and the solution was irradiated for 1 h, the solvent was then evaporated and the residue chromatographed giving recovered **6a** (71%) and *N*-dimethylamino-*N'*-benzoyl-*O*-allylisourea **14** (20%).

14: colourless viscous oil; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 2.59 (s, 6H), 4.96 (d, 2H, $J = 6.0$ Hz), 5.23 (d, 1H, $J = 10.2$ Hz), 5.36 (d, 1H, $J_1 = 17.1$ Hz), 6.06 (ddt, 1H, $J_1 = 17.1$ Hz, $J_2 = 10.2$ Hz, $J_3 = 6.0$ Hz), 7.31-7.44 (m, 3H), 8.11-8.15 (m, 2H), 10.81 (s, 1H, exch. with D_2O); FT-IR (Nujol) 3170, 3095, 1614, 1595 cm^{-1} . GC-MS (m/z): 247 (100%); Anal. Calcd. for $\text{C}_{13}\text{H}_{17}\text{N}_3\text{O}_2$: C, 63.14; H, 6.93; N, 16.99;. Found: C, 63.30; H, 6.90; N, 16.70.

Irradiation of **6a** in presence of Na_2CO_3

A solution of compound **6a** (3 mmol) in dry DCM (400 mL), was purged with nitrogen (10 min). Na_2CO_3 (5g) was suspended and the solution was irradiated for 3 h under good stirring, the solution was filtered and the solvent was then evaporated and the residue chromatographed giving recovered **6a** (76%) and **7a** (17%).

Reaction of **7a** with HCl

A solution of compound **7a** (0.5 mmol) in dry DCM (50 mL), was saturated with gaseous HCl and kept for 5h under good stirring in the dark. The solvent was then evaporated and the residue chromatographed giving recovered **7a** (31%) and **8a** (54%).

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