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Competition Between Intramolecular [2+2] Photocycloaddition and Hydrogen-Abstraction Reactions from 2-Carboxamidocyclopent-2-enones

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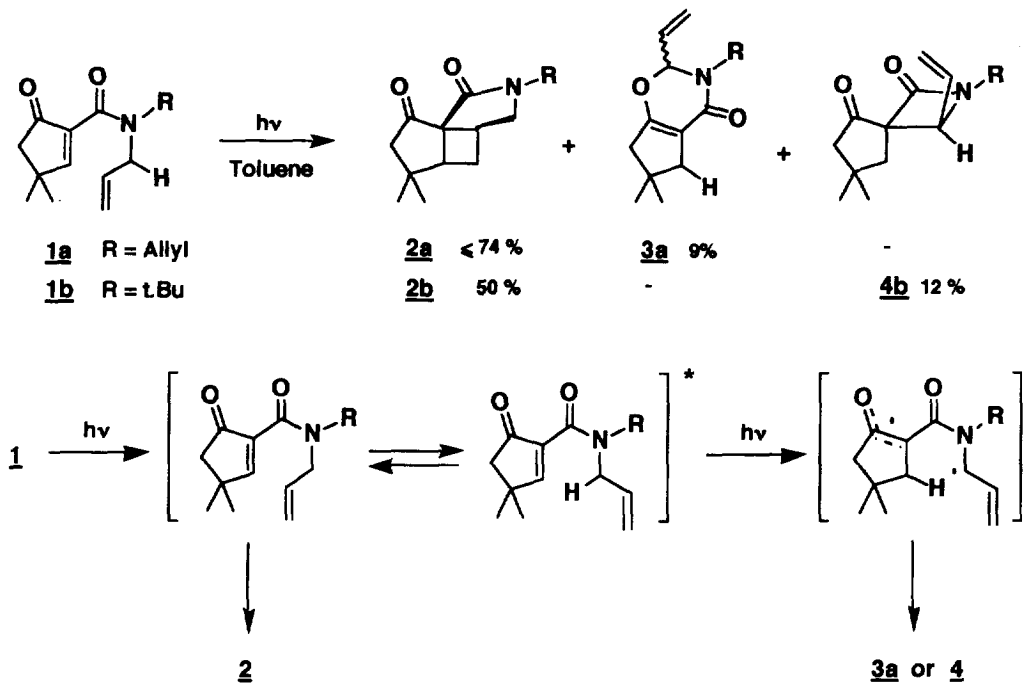
Abstract : Hydrogen-abstraction and intramolecular [2+2] cycloaddition are competitive processes during the photolysis of N-alkyl-N-allyl-2-carboxamidocyclopent-2-enones. Depending on the nature of the N-alkyl substituents and the conformations available in the starting enones, products involving hydrogen abstraction by the α- or β- carbon atoms of the excited enone are observed beside the expected cycloadducts. When methyl and allyl groups are present on the nitrogen, hydrogen abstraction occurs from the methyl rather than from the allyl substituent.

Intramolecular [2+2] photocycloaddition of alkenyl cyclenones is an important method for preparing polycyclic skeletons.[1] High regio- and stereoselectivities are usually associated with the conformational restrictions involved in intramolecular processes and complex cyclobutane derivatives can be prepared in good chemical yields, using this photochemical approach.[2] Because of the interest and the versatility of cyclobutane rings for the synthesis of natural products[3] and analogs, there is a need for new studies in the field of [2+2] photocycloadditions of polyfunctional enones, especially in connection with asymmetric induction.[4]

Although the photoreactivity of 2-alkenyl-[5], 2-alkenyloxy-[6] and 2- alkenylaminocyclenones[7] has already been studied, little attention had been paid until now to the photoreactions of N-alkyl-N-allyl-2-carboxamidocyclopent-2-enones. Because of the high electrophilic character of the enone chromophore and the possibility of introducing a great variety of substituents on the nitrogen atom, these polyfunctional molecules seemed very attractive for [2+2] intramolecular photocycloaddition studies. For this purpose, enones **1** were prepared in a few steps from diazodimedone[8] according to described procedures[9], involving an α-selenylation / elimination process[9a] and amidation of the carboxylic derivative using DCC activation[9b]. In this communication, we report that various hydrogen abstraction processes can compete with and even be preferred to the expected cycloaddition reaction, during the photolysis of the title compounds **1**.

When a solution of **1a** in toluene was irradiated at 366nm, formation of two new products in a 9 : 1 ratio, was observed. From ^{1}H, ^{13}C NMR spectra and NOE measurements, we attributed the structure of an intramolecular [2+2]photoadduct **2a** and a *cis* relationship at the ring junction between the cyclobutane and the two 5-membered rings, to the major photoproduct (74%) (Scheme 1).[10] The structure **3a** of an oxazinone was attributed to the second isolated product (9%). An allylic hydrogen abstraction by the β-carbon[11] of the excited enone and cyclization of the intermediate biradical onto the oxygen rather than the α-carbon can explain the formation of **3a** . Formation of an oxazinone was surprising if we consider that β-lactams are usually obtained from such biradicals, as already observed for starting cyclohexen-2-ones[12]. To understand this reactivity, we have examined the influence of substituents on the nitrogen on the course of the reaction.

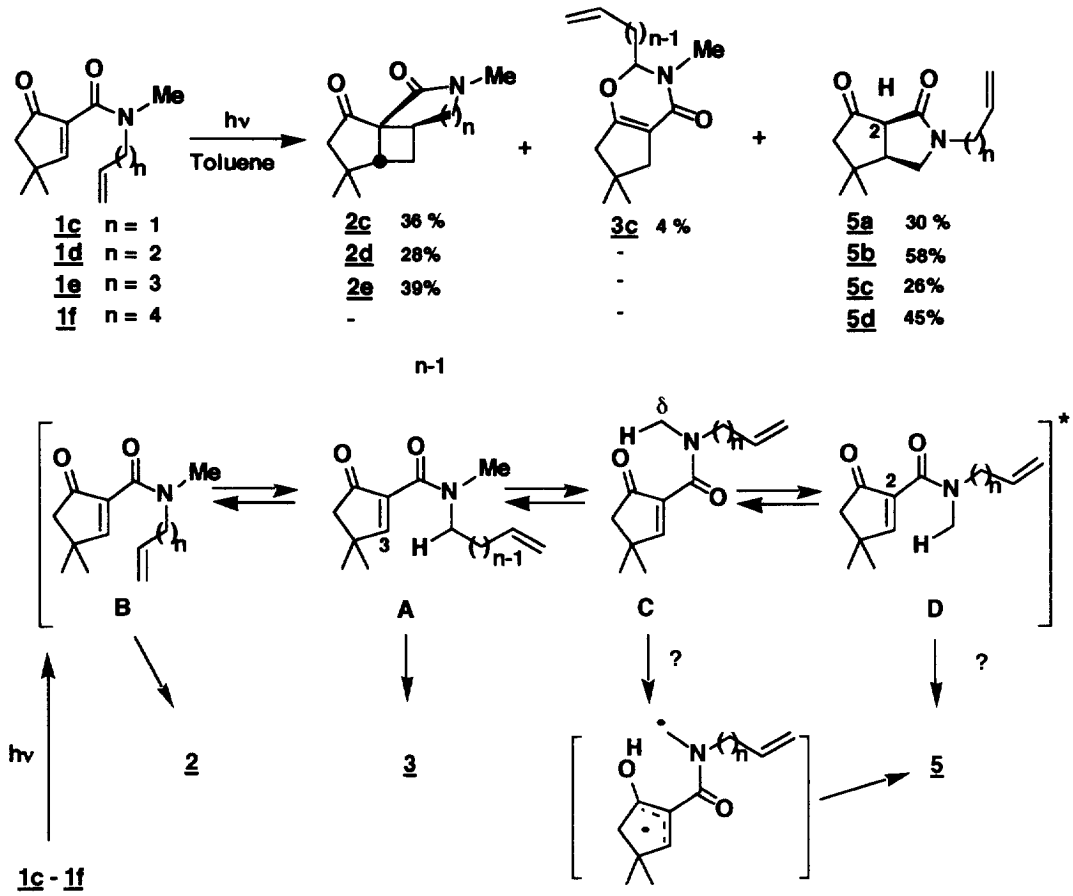
When **1b**, having a bulky t-butyl substituent on the nitrogen, was irradiated under similar conditions, a mixture of **2b** and **4** was isolated. No oxazinone derivative could be detected in the reaction mixture. Beside the expected [2+2] photocycloaddition leading to **2b**, formation of the β-lactam **4** is the preferred process during the cyclization step of the 1,4- biradical.



Scheme 1

Replacement of an N-allyl substituent in **1a** by a methyl group, leads to an important decrease in the formation of the intramolecular photoadduct for **1c-1f**. More surprisingly, heterocyclic derivatives **5** are isolated in moderate yields while the previous heterocyclic molecules **3** and **4** are almost absent from the reaction mixture (Scheme 2). This indicates that hydrogen abstraction has occured on the methyl rather than on the allyl group. These results, which depend strongly on the nature of the nitrogen substituents, can be understood if we consider the preferred conformers of the starting material and the effect of substituents on the conformational equilibrium.

Starting amides **1a-1f** exist in the ground state as a mixture of two conformers of the amide group in equilibrium, as revealed by the NMR spectra. For **1a** and **1b** due to the size of the t-butyl group, conformations shown in scheme 1 are present in the ground state. If we assume that similar conformers are present in the excited state, [2+2] photocycloaddition and allylic H-abstraction are expected processes and the observed chemical yields reflect more a preference for the cycloaddition process than a consequence of the position of the equilibrium.



Scheme 2

For **1c -1f**, in addition to the four main conformers **A-D** in equilibrium in the ground state, **A*-D*** have now to be considered in the excited state. The photocycloadduct **2** and the oxazinone **3** would be obtained from conformers **A*** and **B***. Because of the small size of the methyl substituent on the nitrogen and the repulsive interaction between the carbonyl oxygen atoms, conformer **C** might be involved together with the conformers **A** and **B** respectively, in the ground state. In the conformer **C***, a δ-H abstraction from the N-methyl group by the excited carbonyl becomes possible. Cyclization of the biradical and protonation of the enolic intermediate can lead to **5**. However, **5** might also result from a β- H abstraction from C-2 in the less sterically demanding conformer **D***, followed by the cyclization of the corresponding biradical on C_3. To try to distinguish between the two possible processes leading to **5**, the reaction was carried out in CD_3OD and the crude mixture was examined by NMR immediately after evaporation of the solvent. No incorporation of deuterium at C-2 in the product could be detected under these conditions.[13] This might indicate that an enol is not an intermediate and that **5** probably forms as a result of a β-H abstraction from the methyl group by C-2 in the conformation **D***.

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10) Data for **2a** : ^{1}H-NMR (250 MHz, $CDCl_3$): 1.07 (3H, s); 1.12 (3H, s); 2.04 et 2.49 (AB, J_{AB}=13.3 Hz, 1H, dd, J=9.2, 4.0 Hz et 1H, dd, J=8.4, 6.3 Hz); 2.18 et 2.64 (AB, J_{AB}=17.0 Hz, 1H, d, J=1 Hz et 1H); 2.69-2.80 (2H, m); 3.32 et 3.65 (AB, J_{AB}=10.0 Hz, 1H, d, J=3.8 Hz et 1H, d, J=9.8 Hz); 3.84 et 4.02 (AB, J_{AB}=15.2 Hz, 1H, dt, J=6.2-1.3 Hz et 1H, dt, J=6.0, 1;3 Hz); 5.18-5.26 (2H, m); 5.76 (1H, ddt, J=17.4, 9.8, 6.1 Hz). ^{13}C-NMR :22.44 (CH_3); 26.63 (CH_2); 28.07 (CH_3); 31.36 (CH); 36.86 (C); 45.44 (CH_2); 50.93 (CH); 51.08 (CH_2); 53.21 (CH_2); 60.97 (C); 118.16 (CH_2); 132.16 (CH); 170.98 (C); 212.79 (C). **3a** : ^{1}H-NMR : 1.14 (3H, s); 1.15 (3H, s); 2.10-2.45 (4H, m); 3.52 et 4.51 (AB, J_{AB}=16.0 Hz, 1H, dt, J=6.6, 1.2 Hz et 1H, dt, J=4.7, 1.7 Hz); 5.14-5.25 (2H, m); 5.31-5.44 (2H, m); 5.58 (1H, d, J=6.1 Hz); 6.04 (1H, ddd, J=17.5, 9.9, 6.1 Hz). ^{13}C-NMR : 29.88 (CH_3); 30.06 (CH_3); 36.32 (C); 41.12 (CH_2); 44.55 (CH_2); 46.23 (CH_2); 88.94 (C); 108.38 (C); 117.34 (CH_2); 120.48 (CH_2); 131.50 (CH); 133.41 (CH); 153.20 (C); 165.34 (C). **4** : ^{1}H-NMR :1.00 (3H, s); 1.18 (3H, s); 1.33 (9H, s); 1.99-2.20 (2H, m); 2.03 et 2.36 (AB, J_{AB}=13.5 Hz, 2H); 3.92 (1H, d, J=9.9 Hz); 5.22 (1H, dd, J=9.9, 1.3 Hz); 5.30 (1H, dd, J=17.2, 1.3 Hz); 6.18 (1H, ddd, J=17.2, 9.9, 9.9 Hz). ^{13}C-NMR :28.15 (CH_3); 28.32 (2 CH_3); 28.52 (CH_3); 28.65 (CH_3); 34.47 (C); 44.47 (CH_2); 54.40 (CH_2); 54.98 (C); 65.54 (CH); 69.58 (C); 119.79 (CH_2); 135.99 (CH); 165.89 (C); 212.17 (C). **5a** : ^{1}H-NMR :1.08 (3H, s); 1.10 (3H, s); 2.18 et 2.21 (AB, J_{AB}=17.7 Hz, 2H); 2.77 (1H, ddd, J=8.9, 8.9, 5.8 Hz); 3.28 (1H, d, J=8.8 Hz); 3.26-3.48 (2H, m); 3.78-3.94 (2H, m); 5.14-5.21 (2H, m); 5.68 (1H, ddt, J=16.6, 10.5, 6.3 Hz). ^{13}C-NMR :22.94 (CH_3); 29.39 (CH_3); 36.75 (C); 44.44 (CH); 45.49 (CH_2); 46.50 (CH_2); 51.38 (CH_2); 56.61 (CH); 118.58 (CH_2); 131.82 (CH); 167.13 (C); 208.59 (C).

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13) We have verified that there is no proton exchange of the C_2H proton of **5** in the presence of CD_3OD, either under the irradiation conditions or in the NMR tube.

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