

A STUDY OF THE PHOTOCHEMICAL ISOMERIZATION IN β -LACTAM RINGS

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Abstract The *cis* to *trans* or *trans* to *cis* photoisomerization of 2-azetidinones (**1**) is reported. The outcome of the photochemical process is controlled by the substitution on the nitrogen atom and by the ability of the substituents at C3 and C4 positions to stabilise radicals. *N*-Aryl-2-azetidinones are unreactive even after several hours of UV-light irradiation. *N*-Alkyl-2-azetidinones cleanly isomerize under the same conditions, providing a smooth procedure for the ring isomerization of β -lactams.

INTRODUCTION

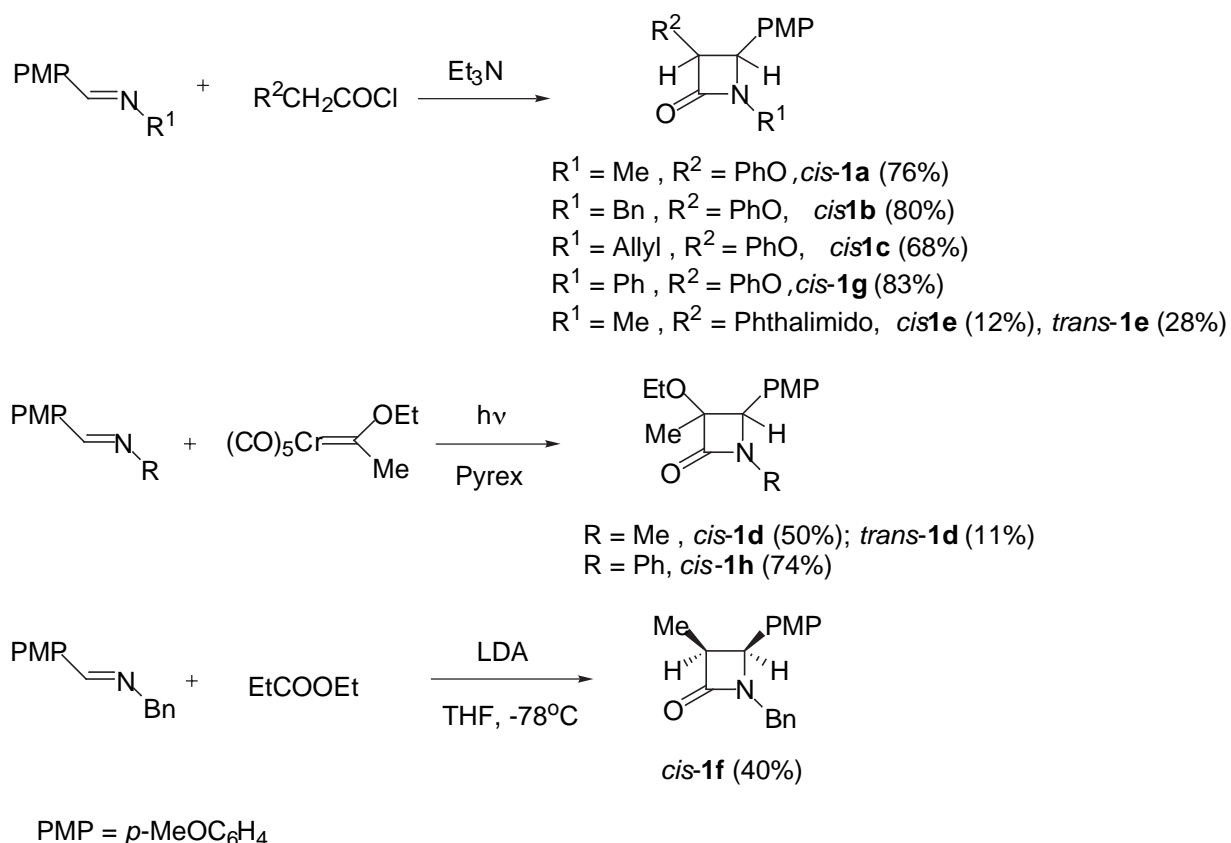
The synthesis of the four-membered ring of β -lactam antibiotics¹ and of 2-azetidinones used as intermediates to prepare non- β -lactam products² has been achieved by many different methods. In particular, the control of the facial selectivity, in both the *cis* and *trans* series, has been solved in an efficient and elegant manner.³ However, regardless of the method used, the control of the *cis-trans* stereochemistry still relies on the intrinsic selectivity of the synthetic procedure used to prepare the 2-azetidinone ring. For example, with a few exceptions, the classical ketene-imine reaction leads mainly to four-membered rings with *cis*-stereochemistry.¹ As most important biologically active β -lactams have a *trans*-2-azetidinone ring in their structures, the synthetic planning to obtain these compounds often has to include a epimerization step. Isomerization in the presence of base by a deprotonation-reprotonation sequence at the C3 position is the most frequently employed technique.⁴ These procedures usually require high concentrations of base, prolonged reaction times, and the yields are low due to the partial destruction of the starting material during the reaction. Other methods that have been described to achieve the ring isomerization are restricted to 2-azetidinones that have specific structural features.⁵

A part of our current research is directed to the elucidation of the mechanism of the photochemical carbonylation of chromium carbene complexes and their reaction with imines to yield 2-azetidinones.⁶ In this context, we have observed that there is a strong dependence of the *cis-trans* selectivity of the obtained 2-azetidinones under the reaction conditions employed. Thus, it was necessary to confirm if the observed selectivity could be due to a photochemical side reaction of the products. The instability of β -lactams towards light is a generally accepted fact,^{7,8} and, in consequence, the photochemical reactivity of this class of compounds has received little attention. The photofragmentation of *N*-aryl- β -lactams⁹ and the ring

enlargement of *N*-benzyl-2-azetidiones under UV-irradiation¹⁰ have been reported but, to the best of our knowledge, there is a single precedent about the ring photoepimerization of a 2-azetidione moiety: the isomerization of 4-phenyl-3-cyano-*N*-*t*-butyl azetidione.¹¹ In this case a cyano group was attached to the four-membered ring, and no comment was made on whether or not this was important to the process. Thus, we decided to investigate the structural requisites needed to bring about the photoisomerization in β -lactam rings. This study could be synthetically attractive as it may overcome some of the difficulties associated with the more commonly used ring isomerization procedures carried out in basic media.

RESULTS AND DISCUSSION

To study the photochemical behavior of a series of *N*-alkyl- and *N*-phenyl- β -lactams, compounds (**1a-c**, **1e** and **1g**) were synthesized by the standard Staudinger reaction between the corresponding imines and the acid chlorides, in the presence of Et₃N.¹ β -Lactams (**1a-c**) and (**1g**) were obtained exclusively as their *cis*-isomers, whereas (**1e**) was isolated as a (1:1.8) *cis-trans* mixture from which both isomers were separated. Compounds (**1d**) and (**1h**) were obtained by irradiation (visible light) of equimolar amounts of pentacarbonyl[(ethoxy)(methyl) carbene]chromium (0) and the corresponding imine, following the method described by Hegedus.¹² Finally, compound (**1f**) was obtained exclusively as the *cis*-isomer, by addition of *N*-benzyl-*p*-methoxyphenylimine, to a THF solution of ethylpropionate in LDA at -78°C , followed by acid quenching (scheme 1).



Scheme 1

Acetonitrile solutions of compounds (**1**) were stable after several hours of irradiation through a Pyrex filter (400 W, Hg-medium pressure lamp). However, when oxygen free acetonitrile solutions of β -lactams (**1**) were irradiated at room temperature in quartz tubes with a 125 W medium pressure mercury lamp, the results obtained were strongly dependent on the substituents present on the four-membered ring. The results are collected in Table 1. Under these conditions, *cis*-*N*-alkyl-2-azetidiones (**1a-d**) cleanly isomerize to the corresponding *trans*-isomers. In the case of **1a** and **1b** the reaction reaches a photostationary state, yielding a 1:1 mixture of *cis*-*trans* isomers after 30-45 min of irradiation.¹³ Isomerization also takes place in the cases of *N*-allylazetidione (**1c**) and C3-disubstituted azetidione (**1d**), although the reaction requires longer reaction times (2.5 h and 5 h respectively) to yield 6:1 and 2.5:1 *cis*-*trans* mixtures. In all cases, prolonged irradiation (up to six hours) did not increase significantly the amount of the *trans*-isomer in the mixtures, but leads exclusively to the slow destruction of the starting material. The photoisomerization also occurs when the four-membered ring has a *trans*-stereochemistry. Thus, the irradiations of *trans*-**1a** and *trans*-**1d** under identical conditions as employed for their *cis*-isomers led to the same *cis*-*trans* mixtures in the photostationary state.

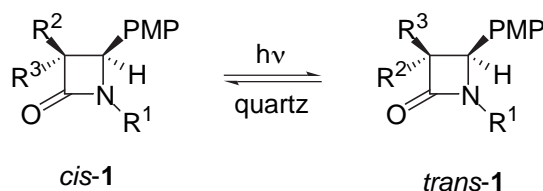


Table 1 Photoisomerization of 2-azetidiones (**1**)

	R1	R2	R3	<i>cis</i> - <i>trans</i> ratio ^a	Irradiation time ^b
<i>cis</i> - 1a	Me	PhO	H	1:1	0.5 h
<i>trans</i> - 1a	Me	PhO	H	1:1	0.5 h
<i>cis</i> - 1b	Bn	PhO	H	1:1	0.75 h
<i>cis</i> - 1c	Allyl	PhO	H	6:1	2.5 h
<i>cis</i> - 1d	Me	EtO	Me	2.5:1	5 h
<i>trans</i> - 1d	Me	EtO	Me	2.5:1	5 h
<i>cis</i> - 1e	Me	Pht	H	100:0	5 h
<i>trans</i> - 1e	Me	Pht	H	0:100	5 h
<i>cis</i> - 1f	Bn	Me	H	100:0	3 h
<i>cis</i> - 1g	Ph	PhO	H	100:0	0.5-9 h ^c
<i>cis</i> - 1h	Ph	EtO	Me	100:0	0.5-9 h ^c

a Determined by integration of well resolved signals in the ¹H NMR spectra of the reaction mixtures. b The given time was optimized to achieve the photostationary state and to minimize the formation of by-products. c See text.

The influence of the solvent in the ring isomerization process has also been studied with *cis*-azetidione (**1b**). The isomerization takes place in acetonitrile and benzene, but in this latter case only a 1.7:1 *cis*-*trans*

mixture was obtained after 5 h of irradiation. A highly polar solvent such as methanol inhibits the reaction. No other products derived from the incorporation of the solvent have been detected, even after prolonged irradiation. It is known that alcohols can affect the lifetime of excited states, especially triplets. Thus, in some rearrangements in *N*-arylamides, in which the reaction arises from the lowest singlet state followed by intersystem crossing (ISC) and formation of a radical pair from a triplet state, the yields are significantly reduced in polar solvents.¹⁴

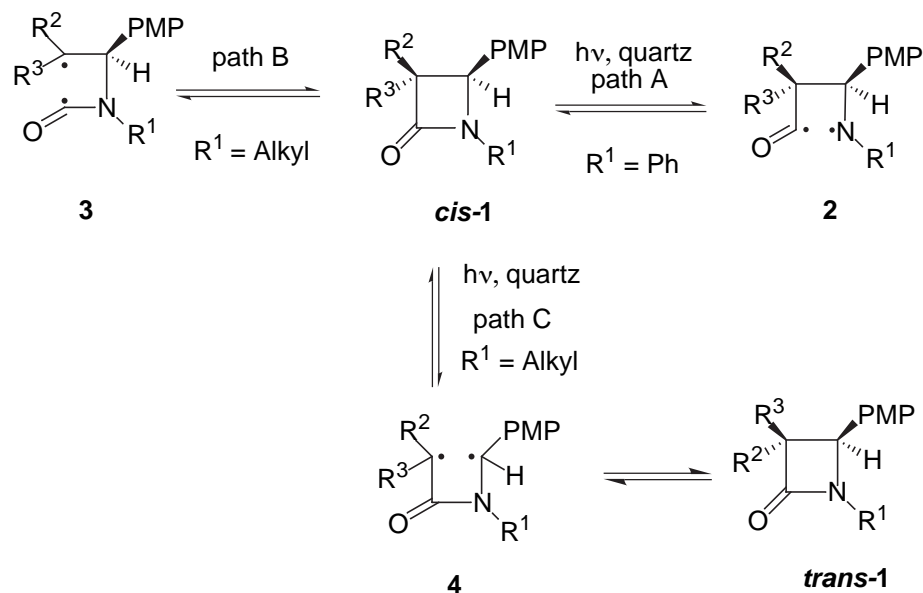
N-Phenyl substituted β -lactams (*cis*-**1g**) and (*cis*-**1h**) behave differently to the foregoing examples. These compounds were irradiated under the above conditions for periods between 30 min and 4 h, but only unreacted material was recovered. Attempts to promote the isomerization by increasing the irradiation times (up to 9 h) led only to the slow destruction of the starting 2-azetidinones. This decomposition was confirmed by the appearance of signals attributable to fragmentation products in the ¹H-NMR of the reaction crudes. An increase in the wattage of the lamp (from 125 W to 400 W medium pressure mercury lamp) did not significantly change the above results, leading only to a faster destruction of the starting material.

These results certainly show that the substitution on the nitrogen atom plays a crucial role in determining the outcome of the reaction. The influence of the substituents on the C3-position of the 2-azetidinone ring was addressed next. Clearly, as discussed above, both *cis*- or *trans*-*N*-alkyl-2-azetidinones are prone to ring photoisomerization when an alkoxy substituent is placed at this position. However, when the alkoxy at C3 is replaced by a phthalimidoyl group the isomerization does not take place. Thus, *cis*- and *trans*-**1e** remained unaltered even after irradiation for 5 h. The replacement of the alkoxy group by a methyl at C3, as in *cis*-2-azetidinone (**1f**) also results in the inhibition of the ring isomerization process (Table 1).

Two different reaction pathways can be proposed to account for the photochemical behavior observed herein for 2-azetidinones (**1a-h**). The competition between N-CO and α -C-CO bond cleavage is a well established process in the photochemistry of amides, the type of fragmentation being highly dependent on the strength of the α -bond.¹⁵ The presence of an aromatic ring attached to the nitrogen atom, as in the case of 2-azetidinones (**1g-h**), should favor the N-CO bond breakage and hence the formation of the conjugatively stabilized diradicals (**2**) (Scheme 2, path A). This type of fragmentation has been proposed as the first step in the rearrangements of acyclic *N*-arylamides,^{15c} medium size ring and large *N*-aryllactams^{15d,e} and has been also observed in the ring expansion processes of *N*-phenylazetidinones.^{15f} In our case, once formed, the radicals (**2**) will quickly recombine within the cage to reform the starting material. The resulting overall reaction is that compounds (**1g-h**) are recovered unchanged after the irradiation.

Replacement of the *N*-phenyl group by an *N*-alkyl group increases the amide resonance and hence the N-CO bond strength. In consequence, either an α -C-CO (path B) or a β -C-C fragmentation (path C) of the amide group may occur, leading to diradicals (**3**) and (**4**) respectively (Scheme 2). Both fission processes may, in principle, account for the ring isomerization observed during the irradiation of compounds (**1a-d**). However, the homolytic C-CO bond breaking (path B) is less often observed in the photochemistry of amides and usually leads to the fragmentation and/or decarbonylation of the starting materials.^{15b} On the contrary, the β -C-C bond cleavage (path C) is more common in amides having relatively weak β -C-C bonds. This situation arises when the radicals resulting from the C-C bond cleavage are highly stabilized, or when the C-C bond is

included in a small ring.¹⁶ Both circumstances should favor the C3-C4 bond breakage in *N*-alkyl-2-azetidinones (**1a-d**), leading to the well stabilized diradicals (**4**).¹⁷ Reclosure of these intermediates would account for the observed isomerization products. The importance of the stabilization of the intermediate diradicals (**4**) has been demonstrated in the irradiation of *cis*-3-methyl- β -lactam (**1f**). The replacement of the alkoxy group in C3 by a methyl group completely inhibits the isomerization process, even though the *p*-methoxyphenyl group in C4 remains unaltered.



Scheme 2

The *cis-trans* photoisomerization of the 2-azetidinone ring seems to be a fairly general process when the nitrogen atom is alkyl substituted, with both isomers being photoactive in this process. The ring isomerization requires substituents capable of stabilizing a radical in the C3 and C4 positions. Disubstitution at this site, as in (**1d**), makes the isomerization process less efficient in terms of the time required for the process to occur. On the other hand the presence of an imide group at the C3-position (*cis* and *trans*-**1e**) completely inhibits the photochemical process. This may be related to the ability of the phthalimido group as an excellent electron acceptor in electron transfer processes (SET).¹⁸ Thus, the involvement of the lone pair of the amide nitrogen atom in such a reactions cannot be ruled out. This could be a reaction path that favorably competes with the normal bond fission processes within the excited state. No other products derived from side reactions of the phthalimido group (such as fragmentations or ring enlargements) have been detected.¹⁹

In conclusion, in this work we have studied the structural requisites needed to carry out the photoisomerization of 2-azetidinones in a controlled way, to promote either the *cis* to *trans* or *trans* to *cis* isomerization of the four membered ring. The outcome of the reaction is defined by the substitution on the nitrogen atom and the ability of the substituents placed at C3 and C4 positions as radical stabilizers. Interestingly, in spite of the general belief,⁷ *N*-aryl-2-azetidinones remain unreactive for several hours when

irradiated with UV-light. *N*-alkyl-2-azetidinones, however, cleanly isomerize under the same conditions.

From a synthetic point of view this method may provide a smooth procedure for ring isomerization in β -lactams, even allowing for the transformation of the thermodynamically more stable *trans*-isomer into the less stable *cis*-isomer.

EXPERIMENTAL

General Methods. ^1H NMR and ^{13}C NMR spectra were recorded in CDCl_3 , on a Bruker 200-AC (200.13 MHz for ^1H and 50.03 MHz for ^{13}C) spectrometer. Chemical shifts are given in ppm relative to TMS (^1H , 0.00 ppm), or CDCl_3 (^{13}C , 77.0 ppm). IR spectra were taken on a Perkin-Elmer 781 spectrophotometer. Melting points were taken on a Gallemp apparatus and are uncorrected. Merck silica-gel (230-400 Mesh) was used as the stationary phase for purification of crude reaction mixtures by flash chromatography. Identification of products was made by TLC (Kieselgel 60F-254), UV light ($\lambda = 254$ nm). For the irradiations, the acetonitrile (Spectrosolv®, reagent grade) was dried over CaH_2 under argon prior its use. All commercially available compounds were used without further purification.

General procedure for the synthesis of β -lactams (**1a-c**) and (**1g**).

To a stirred solution of phenoxyacetyl chloride (15 mmol) and Et_3N (30 mmol) in CH_2Cl_2 (40 mL) at -78°C and under argon atmosphere, a solution of the imine (10 mmol) in CH_2Cl_2 (10 mL) was added dropwise. The mixture was stirred at -78°C for 30 min and then at rt for 16-20 h. The reaction mixture was quenched with MeOH (9 mL), washed with water, dried over magnesium sulfate and the solvent removed under reduced pressure. *cis*- β -Lactams (**1a-c**) and (**1g**) were obtained from the residue by crystallization.

cis-**1a**. (76%, from EtOH): mp 124-126°C; ^1H NMR (CDCl_3) δ 2.74 (s, 3H), 3.69 (s, 3H), 4.75 (d, 1H, $J = 4.3$ Hz), 5.33 (d, 1H, $J = 4.3$ Hz), 6.65-6.83 (m, 5H), 7.01-7.18 (m, 4H); ^{13}C NMR (CDCl_3) δ 26.3, 55.0, 63.1, 82.3, 113.6, 115.5, 121.8, 124.4, 129.0, 129.5, 156.9, 159.8, 165.9; IR (KBr) 1745 cm^{-1} ; UV (MeCN) λ_{max} 203 nm (ϵ 29 700), 224 nm (ϵ 21 700). Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_3$: C, 72.07; H, 6.05; N, 4.94.

Found C, 72.19; H, 6.09; N, 4.73.

cis-**1b**. (80%, from EtOH or Hexane): mp 121-123°C; ^1H NMR (CDCl_3) δ 3.68 (s, 3H), 3.76 (d, 1H, $J = 14.7$ Hz), 4.63 (d, 1H, $J = 4.4$ Hz), 4.79 (d, 1H, $J = 14.7$ Hz), 5.29 (d, 1H, $J = 4.4$ Hz), 6.62-6.81 (m, 5H), 7.00-7.24 (m, 9H); ^{13}C NMR (CDCl_3) δ 44.0, 55.2, 61.0, 82.2, 113.8, 115.6, 121.9, 124.5, 128.0, 128.7, 128.9, 129.2, 130.0, 134.9, 157.0, 160.0, 165.6; IR (KBr) 1746 cm^{-1} ; UV (MeCN) λ_{max} 199 nm (ϵ 31 200), 217 nm (ϵ 14 500). Anal. Calcd for $\text{C}_{23}\text{H}_{21}\text{NO}_3$: C, 76.86; H, 5.89; N, 3.89. Found C, 76.52; H, 6.11; N, 3.82.

cis-**1c**. (68%, from EtOH): mp 76-78°C; ^1H NMR (CDCl_3) δ 3.37 (dd, 1H, $J_1 = 15.3$, $J_2 = 7.2$ Hz), 3.70 (s, 3H), 4.14 (dm, 1H, $J = 15.3$ Hz), 4.83 (d, 1H, $J = 4.4$ Hz), 5.00-5.13 (m, 2H), 5.34 (d, 1H, $J = 4.4$ Hz), 5.56-5.75 (m, 1H), 6.65-6.84 (m, 4H), 7.02-7.19 (m, 5H); ^{13}C NMR (CDCl_3) δ 42.6, 55.1, 61.3, 82.0, 113.6, 115.5, 119.0, 121.8, 124.6, 129.1, 129.8, 130.7, 157.0, 159.8, 165.3; IR (KBr) 1747 cm^{-1} ; UV

(MeCN) λ_{max} 201 nm (ϵ 29 000), 221 nm (ϵ 18 000). Anal. Calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_3$: C, 73.77; H, 6.19; N, 4.53. Found C, 73.68; H, 6.34; N, 4.62.

cis-**1g**. (83%, from EtOH): mp 156-158°C; ^1H NMR (CDCl_3) δ 3.68 (s, 3H), 5.29 (d, 1H, $J = 4.8$ Hz), 5.46 (d, 1H, $J = 4.8$ Hz), 6.70-7.33 (m, 14H); ^{13}C NMR (CDCl_3) δ 55.2, 61.7, 81.2, 113.9, 115.7, 117.6, 122.1, 124.4, 124.5, 129.1, 129.3, 129.4, 137.0, 157.0, 159.9, 163.1; IR (KBr) 1741 cm^{-1} ; UV (MeCN) λ_{max} 202 nm (ϵ 37 000), 233 nm (ϵ 19 700). Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{NO}_3$: C, 76.50; H, 5.54; N, 4.05. Found C, 76.69; H, 5.62; N, 3.92.

Synthesis of β -lactam (**1e**).

To a stirred solution of *N*-methyl-4-methoxyphenylimine (1.5 g, 10 mmol) and Et_3N (4.2 mL, 30 mmol) in refluxing toluene (40 mL), a solution of phthalimidoylacetyl chloride (3.35 g, 15 mmol) in toluene (10 mL) was added dropwise. The reaction mixture was refluxed for 5 h and quenched at rt with water (100 mL), washed successively with water and brine, dried over magnesium sulfate and finally, the solvent removed under reduced pressure. The residue was suspended in Et_2O and filtered to give compound (**1e**) as a 1:1.8 *cis:trans* mixture of isomers that could be separated in low yield by fractionated crystallization. Attempts of chromatography on silica gel (Hexane: AcOEt 6:4) were also carried out leading to the extensive decomposition of the products. *trans*-**1e** (896 mg, 28%): mp 192-196°C; ^1H NMR (CDCl_3) δ 2.80 (s, 3H), 3.72 (s, 3H), 4.78 (d, 1H, $J = 2.3$ Hz), 5.07 (d, 1H, $J = 2.3$ Hz), 6.77-6.87 (m, 2H), 7.13-7.20 (m, 2H), 7.66-7.80 (m, 4H); ^{13}C NMR (CDCl_3) δ 27.1, 55.1, 61.7, 62.7, 114.4, 123.4, 125.7, 127.0, 127.6, 131.5, 134.2, 160.0, 164.8, 166.7; IR (KBr) 1766, 1716 cm^{-1} ; UV (MeCN) λ_{max} 200 nm (ϵ 34 000), 218 nm (ϵ 37 000). Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_3$: C, 71.24; H, 5.03; N, 8.74. Found C, 71.15; H, 4.86; N, 9.03. *cis*-**1e** (384 mg, 12%, viscous oil): ^1H NMR (CDCl_3) δ 2.96 (s, 3H), 3.63 (s, 3H), 4.85 (d, 1H, $J = 5.0$ Hz), 5.40 (d, 1H, $J = 5.0$ Hz), 6.66-6.70 (m, 2H), 7.08-7.20 (m, 2H), 7.54-7.80 (m, 4H) Hz); ^{13}C NMR (CDCl_3) δ 27.9, 55.2, 60.2, 62.7, 114.0, 123.4, 127.3, 128.5, 131.3, 134.2, 159.6, 163.9, 166.8; IR (KBr) 1764, 1718 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{O}_3$: C, 71.24; H, 5.03; N, 8.74. Found C, 71.46; H, 5.24; N, 8.66.

Synthesis of β -lactam (**1f**)

To a solution of 22 mmol of lithium diisopropylamide in 20 mL of dry THF (prepared from 2.9 mL, 20 mmol of diisopropylamine and 13.7 mL, 20 mmol of 1.6 M solution of *n*-BuLi in hexanes), at -78°C under argon atmosphere, was added slowly dropwise 2.3 mL (20 mmol) of freshly distilled ethyl propionate. The mixture was stirred for 1 h and then a solution of the *N*-benzyl-4-methoxyphenylimine (2.25 g, 10 mmol) in 3 mL of dry THF was added dropwise. The reaction was kept at -78°C for 1 h, allowed to warm at rt and stirred overnight, before being quenched with water and extracted with Et_2O . The combined organic phases were dried (magnesium sulfate), filtered and concentrated under reduced pressure to leave a residue that was purified by flash chromatography on silica gel (Hexane:AcOEt 9:1) to afford *cis*-**1f** (1.12 g, 40%) as an oil. ^1H NMR (CDCl_3) δ 0.77 (d, 3H, $J = 7.6$ Hz), 3.31-3.45 (m, 1H), 3.75 (s, 3H), 3.79 (d, 1H, $J = 14.8$ Hz), 4.47 (d, 1H, $J = 5.4$ Hz), 4.79 (d, 1H, $J = 14.8$ Hz), 6.79-6.86 (m, 2H), 6.98-7.13 (m, 4H), 7.17-7.27 (m,

3H); ^{13}C NMR (CDCl_3) δ 9.9, 44.4, 50.1, 55.4, 57.8, 114.1, 127.3, 127.7, 128.6, 128.7, 129.0, 135.9, 159.6, 171.3; IR (film) 1747 cm^{-1} ; UV (MeCN) λ_{max} 200 nm (ϵ 33 000), 228 nm (ϵ 13 500). Anal. Calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_2$: C, 76.85; H, 6.80; N, 4.98. Found C, 76.78; H, 6.93; N, 5.07.

General procedure for the synthesis of compounds (1d) and (1h).

The synthesis was carried out following the general method described by Hegedus.¹² Pentacarbonyl [(ethoxy)(methyl)carbene]chromium (0) (1 equiv) and the corresponding imine (1 equiv) in 100 mL of the appropriated solvent were irradiated in a Pyrex wessel with a 450W medium pressure mercury lamp. The solvent was removed *in vacuo* and the residue was dissolved in a mixture of hexane:AcOEt (1:1) and exposed to direct sunlight until a clear solution was obtained. The solution was filtered through a short pad of celite, the solvent eliminated and the desired β -lactam was purified by crystallization or chromatography on silica gel.

Compound (1d). Following the general procedure, 0.8 g (3 mmol) of the carbene complex and 0.45 g (3 mmol) of *N*-methyl-4-methoxyphenylimine were irradiated in hexane for 24 h. After column chromatography (SiO_2 , Hexane:AcOEt, 8:2) *trans*-**1d** (80 mg, 11%) and *cis*-**1d** (370 mg, 50%) were obtained as oils. *trans*-**1d**: ^1H NMR (CDCl_3) δ 0.97 (s, 3H), 1.20 (t, 3H, $J = 7.0$ Hz), 2.80 (s, 3H), 3.57 (m, 2H), 3.75 (s, 3H), 4.51 (s, 1H), 6.77-6.89 (m, 2H), 7.01-7.06 (m, 2H); ^{13}C NMR (CDCl_3) δ 15.7, 15.8, 26.6, 55.3, 60.8, 67.2, 91.7, 113.8, 114.3, 126.8, 128.1, 129.3, 159.7, 170.2; IR (film) 1751 cm^{-1} . *cis*-**1d**: ^1H NMR (CDCl_3) δ 0.74 (t, 3H, $J = 7.0$ Hz), 1.54 (s, 3H), 2.70 (s, 3H), 2.99 (m, 1H), 3.40 (m, 1H), 3.75 (s, 3H), 4.23 (s, 1H), 6.80-6.88 (m, 2H), 7.01-7.20 (m, 2H); ^{13}C NMR (CDCl_3) δ 15.2, 18.3, 26.3, 55.3, 60.8, 69.7, 89.2, 113.8, 126.4, 129.3, 159.8, 169.8; IR (film) 1759 cm^{-1} ; UV (MeCN) λ_{max} 200 nm (ϵ 19 000), 230 nm (ϵ 15 000). Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{NO}_3$: C, 67.10; H, 8.18; N, 5.58. Found C, 66.95; H, 8.09; N, 5.23.

Compound (1h). Following the general procedure, 2.7 g (10 mmol) of the carbene complex and 2.11 g (10 mmol) of *N*-phenyl-4-methoxyphenylimine were irradiated in MeCN for 12 h. After crystallization from hexane, *cis*-**1h** (440 mg, 46%) was obtained as a white solid (mp 114-116°C). *cis*-**1h**: ^1H NMR (CDCl_3) δ 0.67 (t, 3H, $J = 6.9$ Hz), 1.64 (s, 3H), 3.06 (m, 1H), 3.32 (m, 1H), 3.67 (s, 3H), 4.77 (s, 1H), 6.68-6.76 (m, 2H), 7.17-7.27 (m, 7H); ^{13}C NMR (CDCl_3) δ 14.8, 19.1, 55.2, 61.1, 68.3, 88.0, 114.1, 118.6, 127.5, 128.0, 128.2, 130.8, 134.2, 156.1, 167.8; IR (KBr) 1741 cm^{-1} ; UV (MeCN) λ_{max} 205 nm (ϵ 24 500), 259 nm (ϵ 20 700). Anal. Calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_3$: C, 72.95; H, 6.76; N, 4.47. Found C, 72.78; H, 6.82; N, 4.31.

Photochemical Procedures. All the irradiations were run at room temperature in a quartz vessel, using a 125 W medium pressure mercury lamp placed in a water-cooled immersion well. The reactions were carried out in dry MeCN. The solvent was degassed by several freeze-thaw-pump cycles under argon. The progress of the reaction was monitored by TLC and ^1H NMR analysis. The solvent was removed under reduced pressure and the products separated by flash chromatography on silica gel (Hexane: EtOAc), with the

exception of isomers of compound (**1b**) that could not be separated either by chromatography or crystallization.

Irradiation of *cis*-1a. 2-Azetidinone *cis*-**1a** (300 mg, 1.06 mmol) was irradiated in 130 mL of MeCN. After 0.5 h the analysis by ^1H NMR of the crude reaction mixture revealed the presence of a 1:1 *cis:trans*-mixture of isomers. After chromatography (SiO_2 , Hexane: EtOAc 7:3) 90 mg (30%) of the starting material *cis*-**1a** and 90 mg (30%, viscous oil) of *trans*-**1a** were obtained. The same photostationary state was achieved when *trans*-**1a** was subjected to similar photolysis conditions. *trans*-**1a**: ^1H NMR (CDCl_3) δ 2.74 (s, 3H), 3.79 (s, 3H), 4.40 (d, 1H, $J = 1.1$ Hz), 4.87 (d, 1H, $J = 1.1$ Hz), 6.70-6.74 (m, 2H), 6.89-6.93 (m, 3H), 7.11-7.21 (m, 4H); ^{13}C NMR (CDCl_3) δ 26.9, 55.4, 65.0, 88.0, 114.7, 115.4, 122.1, 127.2, 128.2, 129.6, 157.3, 160.4, 165.6. IR (film) 1770 cm^{-1} . Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.31; H, 5.78; N, 4.83.

Irradiation of *cis*-1b. 2-Azetidinone *cis*-**1b** (300 mg, 0.83 mmol) was irradiated in 130 mL of MeCN. After 0.75 h the analysis by ^1H NMR of the crude reaction mixture revealed the presence of a 1:1 *cis:trans*-mixture of isomers. This mixture could not be separated by chromatography or crystallisation. Spectroscopic data of *trans*-**1b** (obtained from an enriched fraction): ^1H NMR (CDCl_3) δ 3.69 (d, 1H, $J = 14.8$ Hz), 3.77 (s, 3H), 4.27 (d, 1H, $J = 1.1$ Hz), 4.80 (d, 1H, $J = 14.8$ Hz), 4.91 (d, 1H, $J = 1.1$ Hz), 6.62-7.24 (m, 14H); ^{13}C NMR (CDCl_3) δ 44.4, 55.5, 62.8, 87.5, 114.7, 115.5, 122.1, 127.1-134.8, 157.2, 160.4, 165.4.

Irradiation of *cis*-1c. 2-Azetidinone *cis*-**1c** (380 mg, 1.23 mmol) was irradiated in 130 mL of MeCN. After 2.5 h, the analysis of the crude reaction mixture by ^1H NMR revealed the presence of a 6:1 *cis:trans*-mixture of isomers. Prolonged irradiation times (up to 6 h) did not increased the isomer ratio, leading only to destruction of the starting material. After chromatography (SiO_2 , Hexane: EtOAc 7:3) 160 mg (53%) of *cis*-**1c** and 30 mg (8%, viscous oil) of *trans*-**1c** were obtained. *trans*-**1c**: ^1H NMR (CDCl_3) δ 3.28 (dd, 1H, $J_1 = 15.5$, $J_2 = 7.1$ Hz), 3.78 (s, 3H), 4.15 (dm, 1H, $J = 15.5$ Hz), 4.46 (d, 1H, $J = 1.3$ Hz), 4.90 (d, 1H, $J = 1.3$ Hz), 4.98-5.11 (m, 2H), 5.57-5.77 (m, 1H), 6.70-6.74 (m, 2H), 6.86-6.93 (m, 3H), 7.10-7.20 (m, 4H); ^{13}C NMR (CDCl_3) δ 42.9, 55.4, 63.1, 87.5, 114.7, 115.4, 119.2, 122.0, 127.3, 128.3, 129.6, 130.8, 157.2, 160.3, 165.4; IR (film) 1761 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 73.52; H, 5.82; N, 4.52.

Irradiation of *cis*-1d. 2-Azetidinone *cis*-**1d** (240 mg, 0.96 mmol) was irradiated in 130 mL of MeCN. After 5 h, the analysis of the crude reaction mixture by ^1H NMR revealed the presence of a 2.5:1 *cis:trans*-mixture of isomers. After chromatography (SiO_2 , Hexane: EtOAc 7:3) 160 mg (54%) of *cis*-**1d** and 40 mg (16%, viscous oil) of *trans*-**1d** were obtained. The same photostationary state was achieved when *trans*-**1d** was subjected to similar photolysis conditions. The spectroscopic data of the *trans*-isomer were identical to those of an authentic sample.

Irradiation of *trans*-1e. 2-Azetidinone *trans*-**1e** (100 mg, 0.31 mmol) was irradiated in 130 mL of MeCN. Samples were taken for periods of 0.5 h, 1 h and 2 h. ^1H NMR analysis of the reaction crudes only showed

unreacted starting material. The same result was obtained when a sample of *cis-1e* was irradiated under the same conditions.

Irradiation of *cis-1f*. 2-Azetidinone *cis-1f* (70 mg, 0.25 mmol) was irradiated in 50 mL of MeCN. Samples were taken for periods of 0.5 h, 0.75 h, 1 h, 2 h and 5 h. ¹H NMR analysis of the reaction crudes only showed unreacted starting material.

Irradiation of *cis-1g*. 2-Azetidinone *cis-1g* (300 mg, 0.87 mmol) was irradiated in 130 mL of MeCN. Samples were taken for periods of 0.5 h, 2 h, 4 h and 9 h. ¹H NMR analysis of the reaction crudes only showed unreacted starting material. Slow decomposition to unknown materials was observed after 4 h of irradiation.

Irradiation of *cis-1h*. 2-Azetidinone *cis-1h* (200 mg, 0.63 mmol) was irradiated in 130 mL of MeCN. Samples were taken for periods of 0.5 h, 2 h, 4 h and 9 h. ¹H NMR analysis of the reaction crudes only showed unreacted starting material. Slow decomposition to unknown materials was observed after 4 h of irradiation.

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