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C−H Carbene Insertion of α-Diazo Acetamides by Photolysis in Non-Conventional Media

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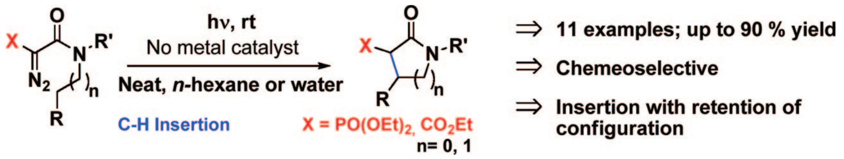


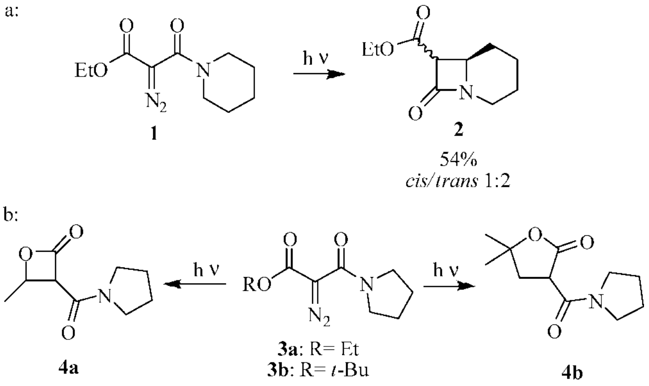
Light from a mercury vapor high-pressure lamp was used to induce the photolytic decomposition of α-diazo acetamides in hexane and in nonconventional media such as water or a film. The corresponding β- and/or γ-lactams were obtained in reasonable yields and in some cases with good diastereoselectivities with no need to use a metallic catalyst. Experimental studies on chiral substrates demonstrated the occurrence of insertion with retention of configuration.

Introduction

More than a half-century has passed since the discovery of α-diazo carbonyl compounds as excellent candidates for the construction of new and interesting molecules. However, in the last two decades, they gained special notoriety with the uprising of catalysis due to the ability of some metals to coordinate with carbenes that can be generated from the decomposition of the diazo substituent.[1–3] In the absence of catalyst, this decomposition can be induced by thermolysis or photolysis, generating a highly reactive intermediate species that in most cases affords a complex mixture of products. Depending on the diazo compound and the reaction conditions used, the resultant products can be derived from C−H or X−H insertion, Wolff rearrangement, ylide formation, cyclopropanation, α,α-substitution reaction, β-hydride elimination, or even other cycloaddition reactions.[4]

The first example of a photolytic-assisted C−H insertion of α-diazo amides was reported by Corey and Felix[5] in the synthesis of methyl 6-phenylpenicillanate. Later, Lowe and Parker[6] observed that photodecomposition of *N*-[(ethoxycarbonyl)diazoacetyl]piperidine **1** in carbon tetrachloride yielded the correspondent β-lactam **2** derived from C−H insertion in the α-carbon of the piperidine unit (Scheme 1a), while the use of *N*-[(ethoxycarbonyl)diazoacetyl]pyrrolidine **3a** and *N*-[(*tert*-butylcarbonyl)diazoacetyl]pyrrolidine **3b** afforded the correspondent β-lactone **4a** and, respectively, γ-lactone **4b** as a result of C−H insertion in the ester alkyl chain (Scheme 1b).

SCHEME 1



α-Diazo ester decomposition was also experimentally investigated in order to obtain the corresponding lactone. However, due to the lack of proximity between the *O*-alkyl substituent

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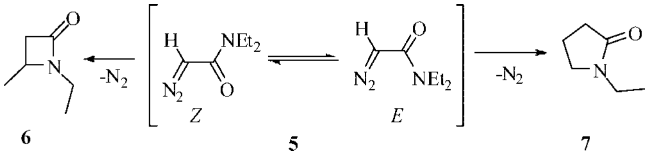
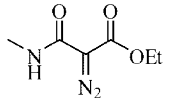
SCHEME 2



and the reactive intermediate, intermolecular reactions were seen to be preferred. For instance, the decomposition of allyl diazoacetate in cyclohexane leads to the single formation of allyl cyclohexylacetate,[7] and the decomposition of *tert*-butyl diazoacetate yields *tert*-butyl cyclohexylacetate preferentially and only 9.5% of the desired lactone.[8] In contrast, Rando observed that photolytic decomposition of *N,N*-diethyldiazo acetamide **5** in dioxane provided the intramolecular C−H insertion products β- and γ-lactams (**6**, **7**) in 57% and 43% yield, respectively (Scheme 2).[9,10] However, the use of protic solvents such as methanol had led to the formation of Wolff rearrangement and O−H insertion products and, consequently, a considerable decrease in the formation of γ-lactam. At this point, an analogy was made with the reported prior results on the photolysis of ethyl diazoacetate in methanol[11] in which intermolecular C−H insertion products were suppressed in isopropyl alcohol.[12] Due to these observations, it was assumed that the formation of the two lactams should arise from different pathways, in which the β-lactam transition state originates a greater charge separation. Through these findings, the authors claimed that C−H insertion would be circumvented as long as there was water in the aliphatic site vicinity, and the γ-/β-lactam ratio in nonpolar solvents should be governed by statistics.

Later, Tomioka et al.[13] found that the intramolecular C−H insertion process in the decomposition of *N,N*-diethyldiazo acetamide **5** could proceed through singlet carbene or singlet excited-state diazo compound. The authors suggested that the excited singlet state of *N,N*-diethyldiazo acetamide **5** could give rise to the β-lactam and the Wolff rearrangement product directly or through the dissociation to nitrogen and singlet carbene. This singlet carbene could subsequently undergo C−H insertion into the C−H bonds of the methyl group to give the correspondent γ-lactam **7**. Considering two possible conformational isomers of the diazo acetamide, in which the carbonyl lays *cis* (*Z*) or *trans* (*E*) to the diazo substituent, the authors reasonably assumed that there are equal populations of both forms. Taking into consideration the reported study on the rotation of internal carbon−carbon bonds of diazo ketones,[14] the *Z* form of the singlet excited state of the diazo compound was indicated as responsible for the formation of the β-lactam and Wolff rearrangement product, while the *E* form was responsible for the formation of the γ-lactam (via direct "perpendicular" insertion) and the O−H insertion products (Scheme 2).[13] In this way, the different β/γ ratios in different solvents were attributed to the solvent influence on the *E*/*Z* ratio populations.

In accordance with the observations of Rando,[9,10] Thornton et al.[15] obtained the intermolecular C−H and O−H insertion products when three examples of α-diazo acetamides (**3a**, **8**, and **9**) were decomposed by photolysis. Through the decomposition of these compounds in binary mixtures of solvents (*tert*-butyl alcohol/cyclohexane; *t*ert-butyl alcohol/water), a general preference toward O−H insertion was observed. Through comparison of **9** with alkyl diazoacetates,[16] the authors claimed that the electronic influence of the carboxamide substituent increased the yield of the O−H insertion product when compared with the ester group. This aspect does not seem to apply to the decomposition of α-diethoxyphosphoryl homologues since in the dirhodium(II) catalytic decomposition of α-diazo-α-diethoxyphosphoryl acetamides in water a preference toward intramolecular C−H insertion was observed, while the intermolecular O−H insertion of the α-diazo-α-diethoxyphosphoryl esters was predominant.[17]



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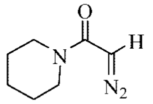

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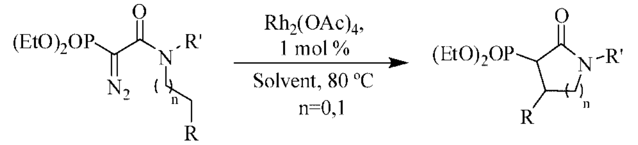
SCHEME 3



Heterocycles bearing a phosphonate substituent, particularly β- and γ-lactams, continue to be an interesting class of compounds, not only because of the mimetic phosphonate substituent but also because of their ability of being easily converted to other functional groups through the Horner−Wadsworth−Emmons reaction.[18,19] In the sequence of our work in synthesizing α-diethoxyphosphoryl-β- and γ-lactams by C−H insertion of dirhodium-stabilized carbenes (Scheme 3),[20,21] as in nonconventional media such as ionic liquids[22] and water,[17,23] we performed a comparable study of a similar transformation through the photodecomposition of that kind of diazo compounds without the use of a metallic catalyst.

Results and Discussion

Recently, we disclosed the dirhodium(II)-catalyzed intramolecular C−H insertion of diazo acetamides in water.[17,23] This methodology allowed the preparation of lactams in high yields in aqueous media, in some cases, with high regio- and

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SCHEME 4

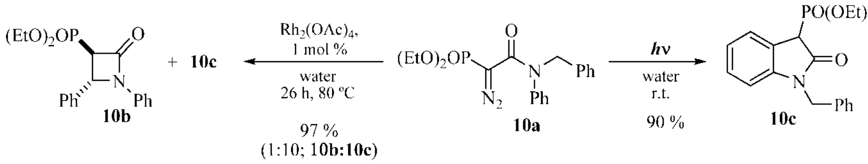


TABLE 1. Photodecomposition of 10a in Different Solvents

entry	solvent	reaction time (h)	product/conversion[a] (%)
1	H_2O	24	**10c**/90[b]
2	C_6H_{14}	24	**10c**/>97
3	*i*-PrOH	24	**10c**/92
4	film[c]	24	**10c**/88[b]

[a] Conversion determined by ^{31}P NMR after solvent removal of the crude reaction mixture. [b] Incomplete reaction; the other compound detected in the mixture was only the unreacted starting material. [c] Film formed on the surface of the quartz reaction tube by prior slow evaporation of dichloromethane solution in a rotaevaporator.

stereoselectivities. The success of this transformation was shown to be deeply related to the catalyst structure and, most importantly, to the diazo substrate hydrophobic nature. It was rationalized that a correct balance between these two factors would lead to a more hydrophobic environment around the carbenoid center reducing the competitive attack by water molecules.

Generally, the reactivity of metallo-carbenoids generated from α-diazo acetamides is governed by stereoelectronic effects, among which the conformation adopted by the metallo-carbenoid is of pivotal importance to determine the insertion chemo-, stereo-, and regioselectivities.

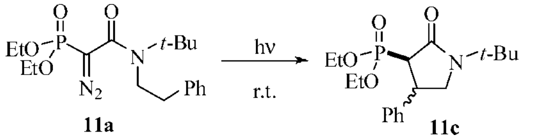
Recognizing that the α-diazo acetamide structures contribute decisively to the final metallo-carbenoid conformation, we envisioned that combining the hydrophobic effect[24–26] evidenced by some α-diazo acetamides in our previous study, with a strong conformational bias arising from the substrates structure, would allow the preparation of lactams in water via photodecomposition of α-diazo acetamides.

We were pleased to observe that submitting the α-diazo acetamide **10a** to irradiation generated from a mercury vapor high-pressure lamp (150 W) in water resulted in the formation of lactam **10c** in 90% isolated yield (Scheme 4).

Surprisingly the photodecomposition of substrate **10a** afforded the aromatic substitution product **10c** with a higher selectivity than the $Rh_2(OAc)_4$-catalyzed cyclization in water in which the β-lactam **10b** was also formed in 10% yield.[17,23]

Water is obviously the most desirable solvent for many economical and environmental reasons. Additionally, in chemical terms, it is undoubtedly a fascinating liquid because it often exerts a remarkable influence over the chemical transformations performed in this media.[27–33] Therefore, in order to elucidate the water effect over the reaction, this transformation was carried out in different solvent systems (Table 1). As shown in Table 1, the γ-lactam was always the preferred product formed even when the substrate was irradiated almost in the absence of solvent (a film of substrate was formed by evaporation of dichloromethane). This reactivity profile indicates that the success of this reaction is probably more dependent on the native diazo substrate conformation than to the hydrophobic effect[24–26] exerted by the water over the diazo substrate. Moreover, the high selectivity toward the γ-lactam formation may be also due to a preferred aromatic substitution mechanism which results from the reactive species attack on the electron-rich aromatic ring followed by aromatization.

TABLE 2. Photodecomposition of 11a in Different Solvents



entry	solvent	reaction time (h)	yield[a] (%)	
			cis	trans
1	H_2O	5	14 (15)	43 (44)
2	C_6H_{14}	8.5	30 (35)	34 (31)
3	film[b]	24	12 (13)	26 (36)

[a] Isolated yields after purification by flash chromatography; the observed conversion of the crude reaction mixture (by ^{31}P NMR) is shown in parentheses. [b] See footnote c of Table 1.

Encouraged by those results, several α-diazo acetamides were submitted to the same reaction conditions. We envisioned that by introducing a bulky *tert*-butyl group on the acetamide, the C−H bond of the less bulky *N*-substituent would be placed in closer proximity to the reactive center, resulting in higher yields and selectivities. Regrettably, the photodecomposition of the nonsymmetric α-diethoxyphosphoryl acetamide **11a** in water afforded the expected γ-lactam but only in moderate yields and poor stereoselectivities (Table 2). These results were common to all solvent systems tested for this substrate. In order to clarify if the observed low selectivity was due to product decomposition, a *cis*/*trans* mixture of the isolated lactam **11c** was irradiated over 24 h in hexane and only 4% decomposition was observed together with a change of the diastereoisomeric ratio (from *trans*/*cis* = 2:1 to *trans*/*cis* = 1.5:1).

In our previous study, it was clear that the phosphoryl group provided strong affinity for water molecules, moreover, as a bulky group, it may exert a strong conformational effect over the reactive conformation. For these reasons, several diazo acetamides with different α-substituents were studied.

In fact, the α-substituent proved to have a fundamental impact on the cyclization scenario (Table 3). Maintaining the asymmetry in the acetamide substituent, the ethoxycarbonyl group favored the intramolecular C−H process, yielding the corresponding β-lactam **12b** in 71% isolated yield with a remarkable stereoselectivity (entry 1). This yield is close to the one observed in hexane (entry 2). Considering the solvent free-conditions, the yield decreased considerably to 56% (entry 3), probably as a result of competitive reactions. As in the case of **11c**, *trans*

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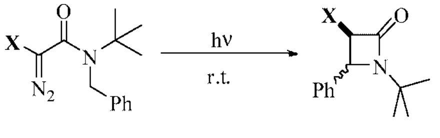
TABLE 3. Effect of the α-Substituent on the Photodecomposition of α-Diazo *N*-Benzyl-*N*-*tert*-butyl Acetamides

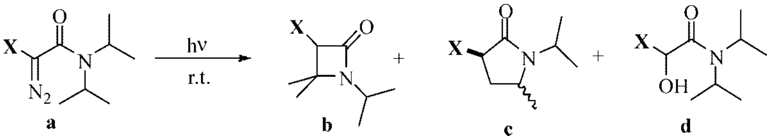


12a-14a **12b-14b**

entry	X	substrate	solvent	reaction time (h)	product	yield[a] (%)	cis/trans[b]
1	CO_2Et	**12a**	H_2O	72	**12b**	71 (>97%)	only trans
2	CO_2Et	**12a**	hexane	24	**12b**	75 (>97%)	0.1:1
3	CO_2Et	**12a**	film[c]	23	**12b**	56 (>97%)	0.2:1
4	$PO(OEt)_2$	**13a**	H_2O	48	**13b**	48 (66%)	0.7:1
5	$PO(OEt)_2$	**13a**	hexane	24	**13b**	62 (67%)	0.5:1
6	$PO(OEt)_2$	**13a**	film[c]	48	**13b**	54 (66%)	0.5:1
7	CO_2Me	**14a**	H_2O	72	**14b**	65 (>97%)	0.1:1

[a] Isolated yield of the *trans*-lactam after purification by flash chromatography. The observed conversion determined by ^{31}P or ^{1}H NMR is shown in parentheses. [b] Diastereoisomeric ratio determined by the ^{31}P or ^{1}H NMR of the crude reaction mixture. [c] See footnote c of Table 1.

TABLE 4. Effect of the α-Substituent on the Photodecomposition of α-Diazo-*N*,*N*-Diisopropyl Acetamides



					yield[a] (%)		
entry	substrate	X	solvent	reaction time (h)	**b**	**c**	**d**
1	**15a**	CO_2Et	H_2O	45	58		
2	**15a**	CO_2Et	Hexane	24	90		
3	**15a**	CO_2Et	film[b]	48	>97		
4	**16a**	$PO(OEt)_2$	H_2O	24	37 (38)	46 (47)[c]	(15)
5	**16a**	$PO(OEt)_2$	hexane	23	63 (65)	30 (31)[d]	
6	**16a**	$PO(OEt)_2$	film[b]	23	39 (62)	20 (27)[e]	
7	**17a**	COMe	hexane; H_2O; film[b]			complex mixture	

[a] Isolated yields after purification by flash chromatography (except entries 1−3, quantitative transformation). The observed conversion of the crude reaction mixture (determined by ^{31}P NMR) is shown in parentheses. [b] See footnote c of Table 1. [c] Diastereoisomeric ratio of the crude reaction mixture: 1:0.1. [d] Diastereoisomeric ratio of the crude reaction mixture: 1:0.3. [e] Diastereoisomeric ratio of the crude reaction mixture: 1:0.1.

β-lactam **13b** was irradiated in hexane for 24 h, and in this case, no decomposition or epimerization was observed.

The lower selectivities obtained in the cases where the phosphoryl group was used as the α-substituent seem to indicate that the phosphoryl group influence is made through an increased interaction with water molecules, probably favoring a conformation which does not place the C−H insertion center close to the reactive carbon atom. Furthermore, in terms of substrate solubility in water, **13a** was seen to be much less hydrophobic than **12a**.

In regard to the ester influence, ethyl ester **12a** and methyl ester **14a** did not lead to any difference in selectivity, which is expected since the stabilization or destabilization of the reactive species is almost attributed to the carbonyl moiety.

Once the α-substituent effect was clearly highlighted, the structure of the acetamide moiety was studied. As stated before, we presumed that a strong conformational bias would be determinant for the cyclization success. Therefore, three symmetrically *N*,*N*-disubstituted diazo acetamides were submitted to irradiation in the same solvent systems as before (Table 4). As expected, a general decrease on the selectivity toward lactam formation was observed, in particular when water was used as solvent. An important piece of evidence, to corroborate the necessity of a strong conformational bias to achieve a successful photoinduced cyclization in water, stemmed from the cyclization of the ethoxycarbonyldiazo acetamide **15a**. The cyclization of this substrate in hexane yielded almost exclusively the C−H insertion product (90%, entry 2), whereas in water the *β*-lactam formation was considerably lower (58%, entry 1), probably due to the attack of water molecules on a less "protected" carbene center.

When acetyl was introduced as the α-substituent (**17a**), a complex mixture of products was observed, probably due to the high reactivity of the formed species which can lead to a myriad of reactions such as Wolff rearrangement (entry 7).[34–36]

The hydrophobic requirement was put to test with the cyclization of substrates **18a** and **19a** (Scheme 5). When the hydrophilic diazo acetamide **18a** was submitted to irradiation, it afforded exclusively the α-hydroxy acetamide. This selectivity toward the alcohol formation probably results from a higher interaction with water. Unlike the previous diazo acetamides, diazo acetamide **18a** is completely soluble in water. Therefore, the selectivity toward the intramolecular C−H insertion was improved by simple introduction of more hydrophobic *N*-substituents (substrate **19a**) which probably generated a more hydrophobic environment around the reactive center (Scheme 5).

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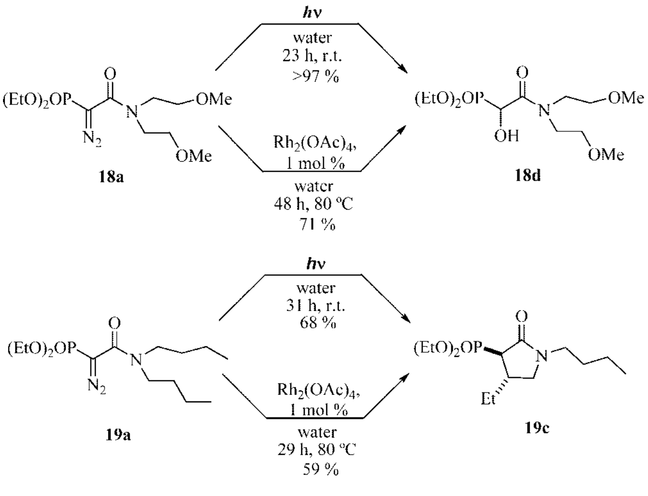
SCHEME 5



The substrate hydrophobic nature proved to be a key element of these cyclizations. This effect can be rationalized either by the direct irradiation of insoluble droplets of diazo compound or via the formation of molecular hydrophobic micelles in water; both ways result in water extrusion from the reactive center,[37] favoring the intramolecular C−H insertion in detriment of the alcohol formation.

In order to determine if the C−H insertion was occurring without the presence of a triplet species, making this reaction a suitable one to be used by synthetic chemists, enantiomerically pure α-diazo acetamides **20a′** and **20a″** and *meso*-α-diazo acetamides **21a** were synthesized and submitted to the previous photolytic conditions in hexane. With these experiments, we appealed to the well-known fact that a triplet species would lead to a mixture of diastereoisomers.[38–40]

For comparison with authentic samples, enanteomerically pure β-lactams **20b′** and **20b″** and the racemic mixture (**21b′** + **21b″**) were also prepared through catalytic decomposition of α-diazo acetamides **20a′** and **20a″** and meso compound **21a** with $Rh_2(OAc)_4$ in 1,2-dichloroethane, which is a well-known method for the C−H insertion with retention of configuration.[41] Thus, the dirhodium-catalyzed decomposition of enanteomeric pure α-diazo acetamides **20a′** and **20a″** should lead to the formation of β-lactams **20b′** and **20b″** (together with the C3−C4 syn diastereoisomers, not represented for the sake of simplicity), while the decomposition of α-diazo acetamide **21a** should lead to the racemate formation of β-lactam **21b′** and **21b″** (also with the C3−C4 syn epimers). According to this approach, if the photolytic decomposition occurs with configuration retention, the product distribution related with β-lactams should be similar to the one obtained for the catalytic $Rh_2(OAc)_4$ decomposition. On other hand, if a triplet carbene intercedes in the C−H insertion mechanism, the decomposition of α-diazo acetamide **20a′** should lead to the formation of β-lactam **20b′** together with lactam **21b′** in a quasi-equimolar ratio, since the C1′ substituent would probably not contribute to any considerable steric effect and the product distribution would be exclusively reflexive of the C3 and C4 steric repulsion which should lead to the formation of C3−C4 anti epimers. The same applies for the α-diazo acetamide **20a″** in which lactam **20b″** should be formed together with lactam **21b″**. The formation of γ-lactams due to the insertion on the primary carbon gives us little or no information about the mechanistic considerations, and so, they will not be the focus of our discussion.

In fact, the obtained results for the photolytic and dirhodium-catalyzed C−H insertion in terms of β-lactam distribution ratio were quite similar. In the case where enanteomeric pure α-diazo acetamide **20a′** was used, only the enanteomeric pure β-lactam **20b′** was observed (Table 5, entries 1 and 2) together with some C3−C4 syn epimer, and analogously, the decomposition of enanteomeric pure **20a″** led to the formation of lactam **20b″** with minor C3−C4 syn epimer (Table 5, entries 3 and 4). Interestingly, the catalyzed C−H insertion led to better regeoselectivity but worse diastereoselectivity than photolytic C−H insertion (Table 5, entries 1 vs 2 and 3 vs 4). For determination of the absolute relative syn/anti configuration of β-lactam C3 center (phosphoryl group) and C4 centers, a mixture of diastereoisomers in a 5:1 ratio was analyzed by NOE contacts of hydrogen at the C3-position and methyl substituent at the C4-position in bidimensional ^{1}H NMR experiments with different mixing times (see the Supporting Information).

The observation that the decomposition of *meso*-α-diazo acetamide **21a** exclusively led to the formation of lactams **21b′** and **21b″** without the presence of any detectable amount of **20b′** or **20b″** through chiral HPLC analysis led us to conclude that the photolytic C−H insertion occurs with absolute retention of configuration, and hence, the triplet carbene hypothesis is discarded for this case.[42]

Conclusion

The solubility of α-diazo acetamides in water seems to be one of the most important properties which affect the C−H insertion chemoselectivity reaction. In the case where hydrophobic substrates are used, the α-diazo substrates tend to reorganize in order to diminish the interactions with water, leading to some conformations that can be very close to the C−H insertion transition states. This aspect seems more pronounced in the case where the *N*-substituents of the α-diazo acetamide have the ability to "protect" the carbene center from water. On the other hand, the use of soluble substrates usually leads to the formation of the intermolecular O−H insertion products in high selectivities and yields. Nevertheless, it was seen that the photolysis of both types of compounds in water can generate the respective products in better selectivities than when rhodium(II) acetate is used in the same solvent.

The occurrence of C−H insertion with retention of configuration supports that it does not occur via triplet carbene.

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(42) Considering continuing assumption by the organic chemistry community on the reactivity of diazo substrates via singlet or triplet carbene species, it could be supposed for this case that it may occur via singlet carbene.[47–49] In line with this assumption, we performed DFT calculations assuming singlet carbene (derived from **16a**) as the reactive species, and the observed modeling reaction pathways were consistent with the experimental **16b**/**16c** ratio (Table 4). However, due to recent studies by femtosecond flash photolysis which imply the formation of excited diazo species on the Wolff rearrangement[50] and 1,2-H shift,[51] another open possibility is that the C−H insertion may occur instead via excited diazo species.

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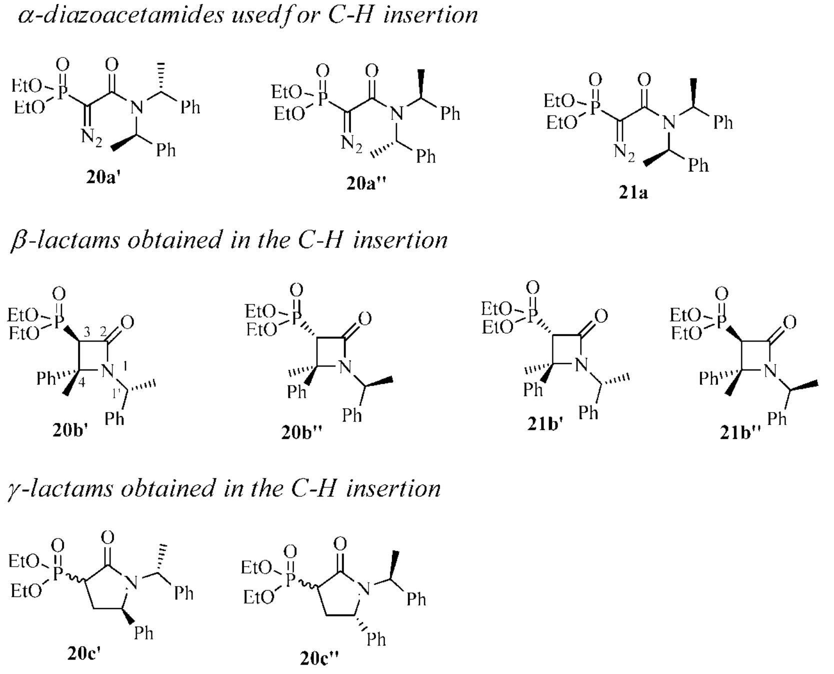
TABLE 5. Decomposition of α-Diazo Acetamides 20a′, 20a″, and 21a



entry	substrate	reaction conditions	reaction time (h)	yield[a] (%)				
				20b′	**20b″**	**21b′**	**1b″**	γ-lactam
1	**20a′**	$Rh_2(OAc)_4$ 1 mol%, $C_2H_4Cl_2$, reflux	1.5	56 (71) [b]	nd[d]	nd	nd	
2	**20a′**	hν, hexane, rt	6	35 (58)[c]	nd	nd	nd	**20c′**, 17 (20)[d]
3	**20a″**	$Rh_2(OAc)_4$ 1 mol%, $C_2H_4Cl_2$, reflux	1.5	nd	57 (74)[b]	nd	nd	
4	**20a″**	hν, hexane, rt	6	nd	40 (59) [c]	nd	nd	**20c″**, 17 (19)[d]
5	**21a**	$Rh_2(OAc)_4$ 1 mol%, $C_2H_4Cl_2$, reflux	1.8	nd	nd	55[e] (68)[f]		
6	**21a**	hν, hexane, rt	9	nd	nd	61[e] (77)[g]		

[a] Isolated yields after purification by preparative TLC (entries 1, 3, 5, and 6) or flash chromatography (entries 2,4); in parentheses is presented the observed conversion of the crude reaction mixture (determined by ^{31}P NMR). [b] A mixture of epimers was observed in the crude reaction mixture (C3−C4 *anti/syn* 1.2:1). [c] A mixture of epimers was observed in the crude reaction mixture (C3−C4 *anti/syn* 3:1). [d] A mixture of epimers was observed in the crude reaction mixture (3:1). [e] Obtained as a racemate of **21b′** and **21b″**. [f] A mixture of epimers was observed in the crude reaction mixture (C3−C4 *anti/syn* 1.3:1). [g] A mixture of epimers was observed in the crude reaction mixture (C3−C4 *anti/syn* 10:1). nd: not detected through chiral HPLC analysis.

Experimental Section

The preparation of the substrates not described here was already described elsewhere (compounds **11a**, **13a**, **16a**, **18a**, and **19a** described in ref 20, **10a** in ref 17, **12a** and **15a** in ref 43, **14a** in ref 44, and **17a** in ref 23). Lactams **11c** (trans), **13b**, **16b**, and **19c** were obtained as characterized in ref 20, lactam **10c** as described in ref 17, lactams **12b** and **15b** as described in ref 43, and lactam **14b** as described in ref 44. α-Hydroxy acetamides **16d** and **18d** were described in ref 17. *meso*-α-Diazo acetamide **21a** was synthesized on the basis of the preparation of bis[(*R,S*)-1-phenylethyl]amine as previously reported.[45,46] The structural assignment of all new compounds was made by bidimensional NMR techniques (COSY and HMQC).

General Procedure for the α-Diazo Photolytic Decomposition in Hexane. In a quartz tube under an argon atmosphere, a solution of the α-diazo acetamide (0.103 mmol) in 1.0 mL of hexane was irradiated with a mercury lamp (Model Hanau TQ150) under stirring. After disappearance of all starting material (monitored by TLC), the solvent was removed under reduced pressure and the reaction mixture purified by flash chromatography when needed.

General Procedure for the α-Diazo Photolytic Decomposition in Water. In a quartz tube, a solution of the α-diazo acetamide (0.103 mmol) in 1.0 mL of water was irradiated with a mercury lamp under stirring. After disappearance of all starting material (monitored by TLC), the solvent was removed under reduced pressure and the reaction mixture purified by flash chromatography when needed.

General Procedure for the α-Diazo Photolytic Decomposition in a Film. A quartz tube containing a solution of the α-diazo acetamide (0.103 mmol) in 0.3 mL of dichloromethane was slowly removed under reduced pressure in a rotatory evaporator, in such a way that a film was created in the quartz tube walls. The quartz tube was then attached to a mechanical stirrer which was maintained under slow rotation while the tube was irradiated with a mercury lamp under stirring. After disappearance of all starting material (monitored by TLC), the reaction mixture was completely dried under reduced pressure and purified by flash chromatography when needed.

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Supporting Information Available: Picture of the apparatus used for the α-diazo acetamides decomposition in solvent free conditions, preparation of new α-diazo compounds, photolytic decomposition procedures, NMR spectra of the new compounds, and HPLC representative chromatograms resulting from the C−H insertion of **20a′**, **20a″**, and **21a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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