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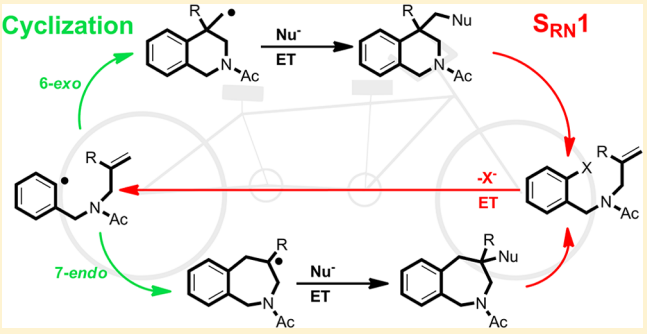
Experimental and Computational Study of 6-*exo* and 7-*endo* Cyclization of Aryl Radicals Followed by Tandem $S_{RN}1$ Substitution

Lucas E. Peisino and Adriana B. Pierini*

INFIQC, Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Ciudad Universitaria, 5000 Córdoba, Argentina

Supporting Information

ABSTRACT: The reaction of *N*-allyl-*N*-(2-halobenzyl)-acetamides and derivatives was investigated in liquid ammonia under irradiation with the nucleophiles Me_3Sn^-, Ph_2P^- and $O_2NCH_2^-$. Following this procedure, novel substituted 2-acetyl-1,2,3,4-tetrahydroisoquinolines and substituted 2-acetyl-2,3,4,5-tetrahydro-1*H*-benzo[*c*]azepines were obtained in good yields. These reactions are proposed to occur through the intermediacy of aryl radicals, which by intramolecular 6-*exo* or 7-*endo* attack to a double bond cyclize to give aliphatic radicals, which react along the propagation steps of the $S_{RN}1$ chain cycle to afford the cyclic substituted compounds as main products. The reactions were modeled with DFT methods, which provide a rational understanding that relates the product distribution to the structure of the aliphatic radicals proposed as intermediates and the kinetic of their formation.



INTRODUCTION

The radical nucleophilic substitution, or $S_{RN}1$ mechanism, is a chain process through which a nucleophilic substitution is obtained with radicals and radical anions as intermediates.[1] The scope of this process has been considerably expanded, and nowadays it stands as an important route to achieve the substitution of aromatic and aliphatic compounds that do not react by polar processes. Several nucleophiles can be used such as carbanions and anions from compounds bearing heteroatoms, which react to form new C−C or C−heteroatom bonds at good yields. Many substituents are compatible with the reaction.[1]

The propagation steps of the mechanism (for an aromatic substrate) are presented in Scheme 1. The process requires an initiation step, irradiation being one of the most frequently used.

The easy access to heterocyclic compounds under mild reaction conditions is one of the most attractive aspects of this process.[2] For example, it has been shown to be an excellent method for the preparation of isoquinolinones,[3] fused azaheterocycles (phenanthridines,[4,5] pyrroles, indoles, and pyrazoles;[6] 3-benzazepin-2-ones;[7] 2-pyrrolyl and 2-indolyl benzoxazoles[8]), among others.

Intramolecular addition of aryl radicals to double bonds has also been widely studied.[9,10] As shown in Scheme 2, the general synthetic strategy involves the generation of intermediate radical **1**, which rearranges to the *exo*-cyclic radical **2** by 5-*exo* (n = 1) or 6-*exo* (n = 2) cyclization. Radical **2** is then trapped with hydrogen donors to yield the reduced compounds **3-r**, or with other reagents to obtain the substituted compound **3-s**.

Although this general scheme is a useful protocol to obtain carbon and heterocyclic compounds, there are only few examples in which the cyclization step occurs along the

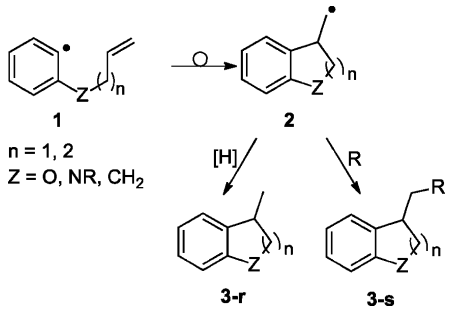
Scheme 1

$$(ArX)^{\bullet -} \rightarrow Ar^{\bullet} + X^- \quad (1)$$

$$Ar^{\bullet} + Nu^- \rightarrow (ArNu)^{\bullet -} \quad (2)$$

$$(ArNu)^{\bullet -} + ArX \rightarrow ArNu + (ArX)^{\bullet -} \quad (3)$$

Scheme 2



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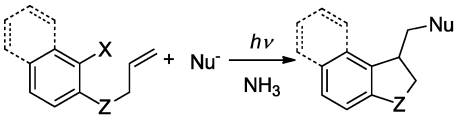
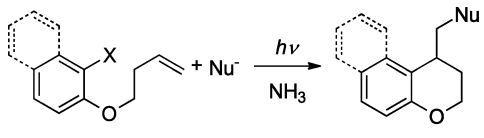
propagation chain of the $S_{RN}1$ reaction. Related to this, Vaillard et al. have demonstrated that tandem 5-*exo* cyclization-$S_{RN}1$ reactions of aryl halides containing an *o*-oxyallyl or aminoallyl moiety are useful for the preparation of substituted dihydrobenzofurans, dihydronaphthofurans and indolines (eq 4).[11]



X = Cl, Br
Nu = $SnMe_3$, PPh_2, CH_2NO_2
Z = O, NCH_2CHCH_2, $NCOCH_3$ (4)

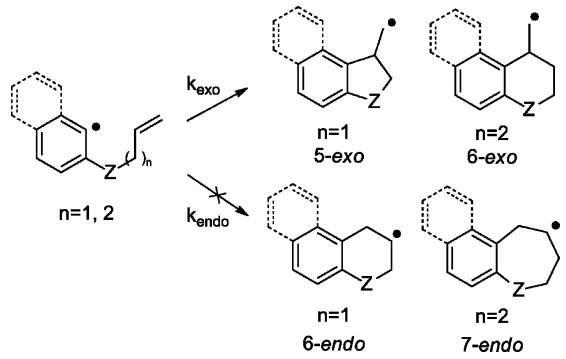
The slower 6-*exo* cyclization has been studied to a lesser extent,[12,13] with Bardagí et al. focusing on the synthetic aspects of this reaction, obtaining 4-substituted chromanes and 4-substituted benzo[*f*]chromanes (eq 5).[14]



X = Cl, Br
Nu = $SnMe_3$, PPh_2, CH_2NO_2 (5)

In these systems, the product distribution is given by the relative rate of the *exo* and *endo* cyclizations, with the *exo* mode (5-*exo* or 6-*exo*) being faster than the *endo* ring closure (6-*endo* or 7-*endo* respectively, see Scheme 3).

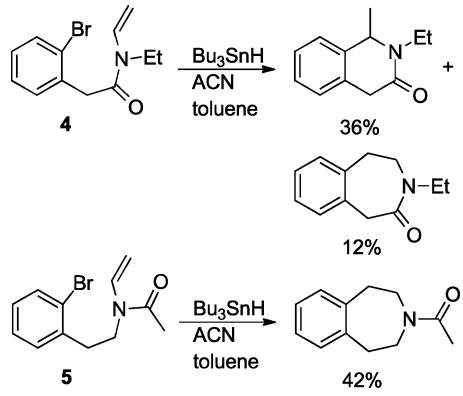
Scheme 3



Few reports have been published related to the aryl radical cyclization of enamine derivates. In these studies, *exo* or *endo* derivates have been obtained by changing the structure of the bridge (between the aryl radical center and the double bond). For example, the treatment of compound **4** with Bu_3SnH and 1,1′-azobis(cyclohexanecarbonitrile) (ACN), has afforded a mixture of the six- and seven-membered lactams (48% yield) at a 3:1 ratio (Scheme 4).[15] On the other hand, compound **5** gave only the seven-membered product.[15] A 7-*endo* cyclization by intramolecular addition of an aryl radical to an enamide double bond has also been informed by Rigby et al.[16]

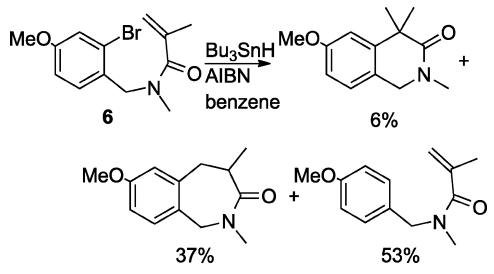
De la Fuente and Domínguez carried out the synthesis of pyrrolo- and pyrido[1,2-*a*]xanthene[1,9-*de*]azepines by a 7-*endo* radical cyclization.[17] Recently, a mechanistic study of the 7-*endo* cyclization of compound **6** by treatment with Bu_3SnH/AIBN

Scheme 4



has been informed, with 7-*endo* being the principal cyclic product, accompanied by the opened reduction compound as main reaction product (Scheme 5).[18]

Scheme 5



The absolute values of the rate constants for the reactions of aryl radicals with nucleophiles have been determined electrochemically for a large number of cases, with most of these values being close to the diffusion limit. For instance, the rate constants for the coupling of 2-, 3-, or 4-cyanophenyl; 1-naphthyl; 3-pyridyl; and 3- and 4-quinolyl radicals with PhS^-, $(EtO)_2PO^-$, and $MeCOCH_2^-$ ions are of the order 10^9–10^{10} M^{-1} s^{-1} in $NH_{3(l)}$,[19] and the rate constant for the ring closure reaction of *o*-allyloxy phenyl radical is 4.9×10^8 s^{-1} (in benzene, at 50 °C).[20] The fact that the ring-closure reaction is a unimolecular process, and therefore does not depend on the nucleophile concentration (in contrast with the coupling reaction), led us to propose that under dilute reaction conditions it could be possible to obtain substituted 1,2,3,4-tetrahydroisoquinolines and 4,5-dihydro-1*H*-benzo[*c*]azepin-2(3*H*)-yl ethanone by tandem cyclization-$S_{RN}1$ reactions using *N*-allyl-*N*-(2-halobenzyl)-acetamides derivates as starting materials.

1,2,3,4-Tetrahydroisoquinoline moiety is a ubiquitous structural core present in a number of alkaloid natural products,[21] which exhibit very good biological activities, such as antitumor,[22] antimicrobial,[23] anti-inflamatory,[24] anti-HIV,[25] and analgesic[26] activities. Benzazepine possesses a 7-membered aza-heterocyclic ring-fused aromatic unit, a framework that is often observed among bioactive natural products and pharmaceuticals.[27,28] For example, paullones have shown cyclin-dependent kinase inhibitory activity and sirtuin inhibitory activity.[28]

Moreover, the substituents present in the target compounds (Me_3Sn, Ph_2P, O_2NCH_2) offer the possibility to produce further modifications via the Stille reaction in the case of the tin

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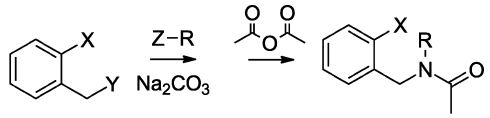
compounds or via classical transformations in the case of the nitro derivatives, while the phosphine compounds present an important role in organic synthesis.

RESULTS AND DISCUSSION

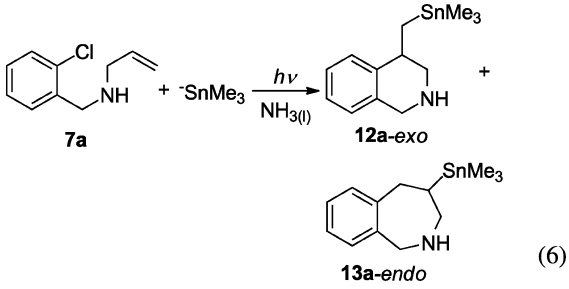
The nucleophilic substitution of allylamines with benzyl-chloride (or benzylamines with allylbromide) has been previously described as a synthetic method to obtain benzyl allylamines.[29] Here, the procedure was used to prepare *o*-halobenzylallylamines. The reaction of 2-chlorobenzylchloride with allylamine in the presence of Na_2CO_3 as base was carried out to obtain *N*-allyl-*N*-(2-chlorobenzyl)-amine (**7a**) in isolated yield of 72%. In order to produce the acetamide derivate, the crude was treated with acetic anhydride, with product **8a** being isolated at 53% of the overall yield. Following the same procedure, the corresponding *N*-allyl-*N*-(2-halobenzyl)-acetamides (**8b**, **9a**, **9b**, **10a** and **11a**) were produced at about 50% of the isolated yield (Scheme 6).

Scheme 6



X	Y	Z	R	Yield (%)
Cl	Cl	NH_2		**8a** (53)
Br	Br	NH_2		**8b** (55)
Cl	NH_2	Br		**9a** (48)
Br	NH_2	Br		**9b** (50)
Cl	NH_2	Br		**10a** (51)
Cl	NH_2	Br		**11a** (48)

When compound **7a** was allowed to react with Me_3Sn^- ions, low yields of cyclic substituted products (**12a**-*exo* and **13a**-*endo*) were obtained (ca. 30% overall yield, eq 6). In this reaction, products from fragmentation of **7a** were also observed.



(6)

In order to protect the substrates and to avoid their possible deprotonation under the basic reaction media,[30] all further studies were performed with the acetamides derivatives **8**-**11**. The results of the photostimulated reaction of compounds **8**–**10** in $NH_{3(l)}$ with the nucleophiles under study are presented in Table 1.

N-Allyl-*N*-(2-chlorobenzyl)-acetamide (**8a**) reacted with Me_3Sn^- ions to furnish the cyclized-substituted compounds **14a**-*exo* and **15a**-*endo* at 50 and 26% yields, respectively (Table 1, entries 1,2).

The photostimulated reaction of **9a** gave compound **17a**-*endo* at high yields (65%). The main product was uncontaminated by the 6-*exo* cyclization product (Table 1, entry 7). On the other hand, the product from 7-*endo* cyclization was not observed by reaction of **10a**; the major product was **18a**-*exo* (54% yield), formed by 6-*exo* cyclization with *cis* fused rings (Table 1, entry 10).[31] Substitution products **22a** and **23a** (Chart 1), derived from hydrogen abstraction from C_6 and C_7 (from the radical center) of the cyclohexene ring (see Figure 2), were also formed in the reaction.

The products obtained and the lack of reaction under dark conditions (Table 1, entries 3, 11) were taken as evidence of the formation of aryl radicals as intermediates and the operation of an $S_{RN}1$ type reaction. Moreover, the photostimulated reaction is inhibited by *m*-dinitrobenzene, a well-known inhibitor of $S_{RN}1$ reactions (1, entry 4).[1]

Encouraged by the results obtained with the tin nucleophile, the study was extended to include the Ph_2P^- and $O_2NCH_2^-$ anions, known to be good nucleophiles in $S_{RN}1$ reactions.[1] After irradiation of an $NH_{3(l)}$ solution of Ph_2P^- ions with substrates **8a**–**10a** followed by oxidation, the corresponding phospine oxides were obtained at similar yields to the products formed with Me_3Sn^- anions (Table 1, entries 5, 8, 12).

Within the carbanions family, it is known that $O_2NCH_2^-$, unable to initiate the $S_{RN}1$, is one of the most reactive anions in the coupling with radicals.[32] In other to achieve subtitution with this anion, the reaction of **8a** and **9b** (bromine as leaving group) were performed in the presence of acetone enolate anion as the entrainment reagent (which enables $S_{RN}1$ initiation but cannot compete with $O_2NCH_2^-$ in the coupling to the methylene radical formed by cyclization).[1] As with Me_3Sn^- and Ph_2P^- ions, a mixture of 6-*exo* and 7-*endo* cyclization products was obtained with **8b**, while 7-*endo* cyclization was the only ring closure mode obtained with **9b** (Table 1, entries 6, 9).

These reactions resulted in the formation of two new C–C bonds, with the nitro group in the tethered chains rendering products of interest for further synthetic transformations, which extends the scope of the reactions.[33]

The mechanism proposed for these reactions is presented in Scheme 7 for compound **8a** as representative. Upon irradiation, **8a** receives an electron from the nucleophile to form its radical anion. This intermediate fragments to give radical **8**$^\bullet$, which cyclizes to afford radicals **14**-*exo*$^\bullet$ (*exo*-cyclization) and **15**-*endo*$^\bullet$ (*endo*-cyclization). These radicals ultimately produce the products **14a**-*exo* and **15a**-*endo*, respectively, through the intermediary of their corresponding radical anions (Scheme 7). Under our reaction conditions, the products arising via direct coupling of the nucleophile with the aryl radicals were detected at a maximum yield of 10% (see Scheme 7).

In the irradiated reaction of substrate **11a** with Me_3Sn^- ions, the reduced exocyclic product **20** (18% yield) and an unresolved mixture of alkenes **21** (13% yield) were formed (Scheme 8) (reaction time = 15 min, 44% of **11a** recovered). A longer irradiation time (60 min) was required for the complete conversion of the substrate to products.[34] In this reaction, radical **11**$^\bullet$ would be formed. Its preferred 6-*exo* cyclization mode will form a very unreactive tertiary exocyclic radical, whose coupling reaction with the anion was disfavored.[35] As

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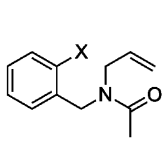
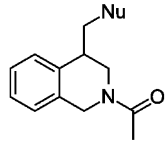
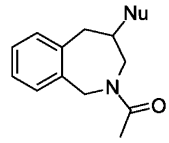
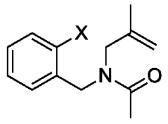
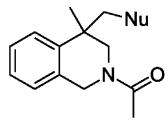
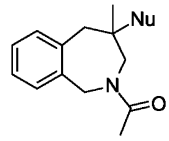
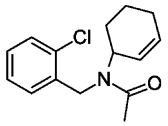
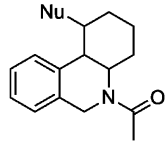
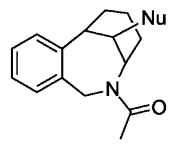
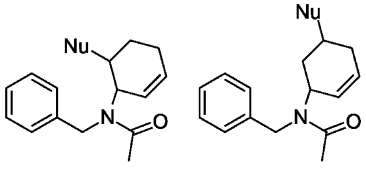
Table 1. Photochemical Reactions of Compounds 8−10 in $NH_{3(l)}$ with Me_3Sn^-, Ph_2P^-, $O_2NCH_2^-$ Anions[a]

Entry	Substrate	Nu^-	Products Yields(%) ArH[b]	Cyclic-substituted	
					
1	**8a**(X=Cl)	Me_3Sn^-	(7)	**14a**-*exo*(49)	**15a**-*endo*(26)
2[c]	**8a**(X=Cl)	Me_3Sn^-	(3)	**14a**-*exo*(50)	**15a**-*endo*(26)
3[d]	**8a**(X=Cl)	Me_3Sn^-	—		(1%)
4[e]	**8a**(X=Cl)	Me_3Sn^-	—		(2%)
5	**8a**(X=Cl)	Ph_2P^-	(3)	**14b**-*exo*(45)	**15b**-*endo*(22)[f]
6	**8b**(X=Br)	$O_2NCH_2^-$ [g]	—	**14c**-*exo*(35)	**15c**-*endo*(28)
					
7	**9a**(X=Cl)	Me_3Sn^-	(10)	**16a**-*exo*(—)	**17a**-*endo*(65)
8	**9a**(X=Cl)	Ph_2P^-	—	**16b**-*exo*(—)	**17b**-*endo*(63)[f]
9	**9b**(X=Br)	$O_2NCH_2^-$ [g]	—	**16c**-*exo*(—)	**17c**-*endo*(53)
					
10	**10a**	Me_3Sn^-	(13)	**18a**-*exo*(54)	**19a**-*endo*(—)[h]
11[d]	**10a**	Me_3Sn^-	—	**18a**-*exo*(—)	**19a**-*endo*(—)
12	**10a**	Ph_2P^-	—	**18b**-*exo*(39)	**19b**-*endo*(—)[f,i]

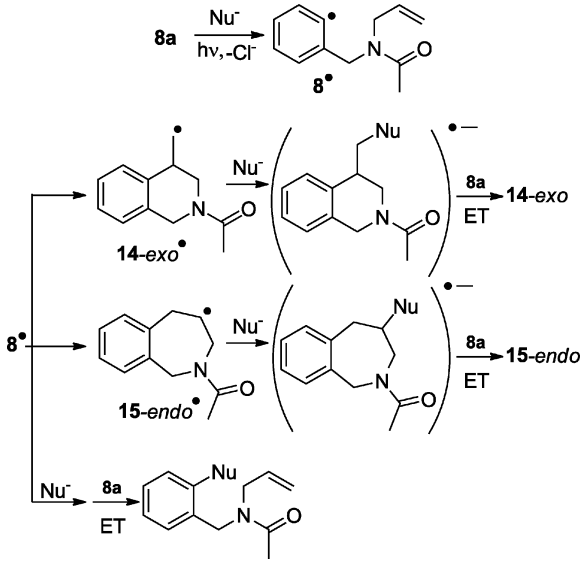
[a]Photostimulated reactions were performed with [substrate] = 1.66×10^{-3} M and [Nu^-] = 1.83×10^{-3} M. Reaction times: Me_3Sn^- (15 min); Ph_2P^- (60 min); $O_2NCH_2^-$ (240 min). Irradiation was conducted in a reactor equipped with two high pressure lamps model Philips HPI-T plus 400-W, CH_3I contaminated (air- and water-refrigerated) with maximum emission at 530 nm. Yields of cyclic substituted products were determined by GC using the internal standard method unless otherwise indicated. In all the reactions, the product from direct attack of the nucleophile to the aryl radical was formed at a maximun 10% yield. [b]Formed by hydrogen abstraction of the aryl radicals intermediates. Relative yields by GC area. [c][substrate] = 8.3×10^{-4} M and [Nu^-] = 9.2×10^{-4} M. [d]Dark conditions. Only unreacted substrate was detected. [e]To the solution was added 20 mol % *m*-dinitrobenzene; **8a** was recovered in 88% yield. [f]Yields determined by ^{31}P NMR. [g][$O_2NCH_2^-$] = 5.00×10^{-3} M and [$CH_3C(O)CH_2^-$] = 3.33×10^{-3} M. Irradiation time = 4 h. [h]Byproducts **22a** (12%) and **23a** (23%). [i]Byproducts **22b** and **23b**, not quantified.

Chart 1



Nu = Me_3Sn^-	**22a**	**23a**
Nu = Ph_2P^-	**22b**	**23b**

Scheme 7



shown in Scheme 8, this radical may abstract hydrogen from the solvent or may form the alkenes mixture by hydrogen loss.

In order to rationalize our experimental results, a computational study with the DFT method (B3LYP-D and B3LYP functionals) and the 6-31+G* basis set was carried out to model the 6-*exo* and 7-*endo* ring closure of the aryl radicals proposed as intermediates of our reactions. In Figure 1, the potential energy surface (PES) for the cyclization of radical **8**• is presented accompanied by the structure and unpaired spin density of the radical intermediates and their respective transition state.[36]

To evaluate the validity of our calculations and to establish a relationship between the nature of the bridge and the regiochemistry of the cyclization, we also studied the cyclization mode of a series of radicals derived from compounds of known experimental reactivities (Chart 2).[14−16,18]

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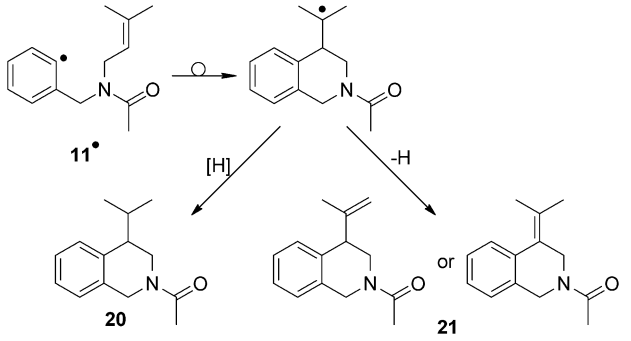
Scheme 8



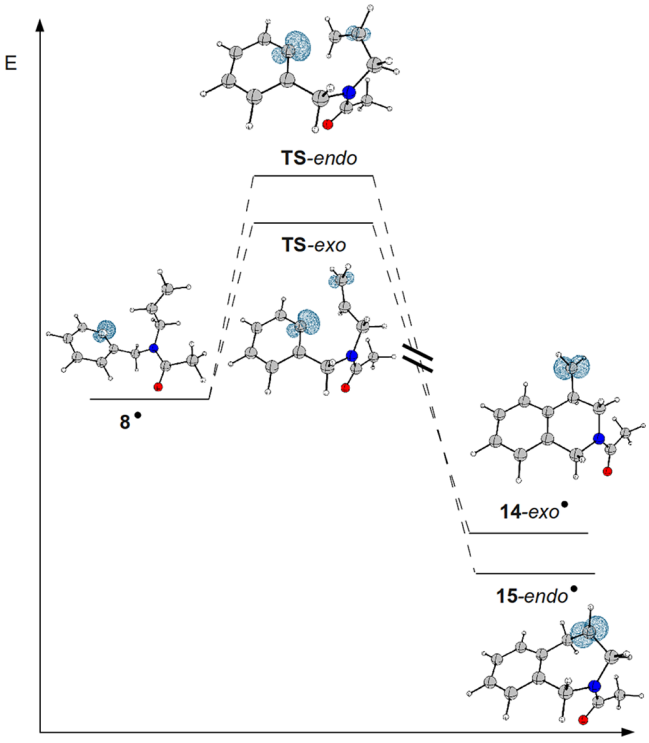
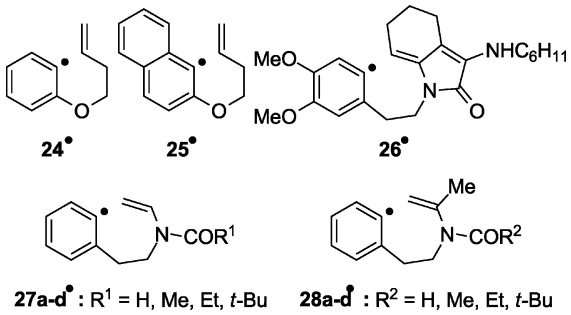


Figure 1. Schematic energy profile for the cyclization reaction. The aryl radical can cyclize in the *exo* or *endo* mode.

Chart 2



The $\Delta\Delta E^{\ddagger}_{exo-endo}$ values calculated for the reactions are shown in Table 2. On the basis of the information presented in the table, it can be concluded that the relative activation energy (E_a) of each cyclization mode controls the preferred regiochemistry of the cyclization. For all the cases under study, both B3LYP-D and B3LYP predicted the preferred experimental cyclization mode. With the exception of **8•**, B3LYP gave, in general, better *exo*:*endo* ratios.

The difference in rate constants for the *exo*-*endo* cyclization of **8•** was estimated to be less than 1 order of magnitude (B3LYP-D, Table 2, entry 1). As indicated by this ratio, the 6-*exo* ring closure was favored over the 7-*endo* mode, in agreement with the experimental outcome of the reaction. The regiochemistry for the cyclization of **9•** was also predicted from the calculations, with the 7-*endo* ring closure being favored over the 6-*exo* by 1.20 or 2.13 kcal/mol (B3LYP-D and B3LYP respectively, Table 2, entry 2). A 6-*exo* cyclization was proposed as preferred for radicals **11•** (Table 2, entry 3), as shown in the experiment (see Scheme 8).

The conformational PES for radical **10•** was very complex (see Supporting Information). 40% of the conformers population corresponded to structures suitable for attacking the double bond, and another 40% were adequate for a hydrogen abstraction from the cyclohex-2-enyl moiety (Supporting Information). With respect to the first reaction, more than 99% of the conformers (according to a Maxwell–Boltzman distribution) were suitable for 6-*exo* cyclization (Supporting Information).

We also analyzed the hydrogen abstraction from C_6 and C_7 of the cyclohexene ring (Figure 2). For three conformers, hydrogen abstraction from C_6 was possible under an average E_a of 3.65 kcal/mol. In contrast, for the remaining four conformers hydrogen abstraction from C_7 was possible with an average E_a of 2.37 kcal/mol (Supporting Information). These calculations were in agreement with the 12 and 23% product yields derived from 6- and 7-hydrogen abstraction, respectively.

We were able to correctly predict the regiochemistry of the cyclization reaction of radicals **24•** and **25•**. Thus, the calculations agreed with the experimental outcome of the reaction presented in eq 5 (see also Table 2), in which only the exocyclic products are formed (at 56 and 90% yield, respectively).[14] The differences in the rate constants calculated favored the 6-*exo* mode by approximately 2 orders of magnitude.

When radical **26•** is formed in toluene at reflux, the only cyclization product is the 7-*endo*.[16] The rate constant for this cyclization was estimated to be higher than that of the 6-*exo* mode (by approximately 3 orders of magnitude, Table 2, entry 6). Radicals **27a•**–**27d•** and **28a•**–**28d•** in reflux toluene cyclize to give 7-*endo* radicals.[15] The calculated rate constant ratios reflected these experimental observations (Table 2, entries 7–14).

Interestingly, in our experimental system the 6-*exo* cyclization is the preferred pathway whenever a tertiary or primary exocyclic radical is formed. The latter is the behavior observed in the reaction of substrate **8a•**, in which the 6-*exo* cyclization leading to a primary radical prevails over the 7-*endo* cyclization leading to an endocyclic secondary radical. For this type of unsubstituted bridge, the structural stabilization of the TS in which a six-member ring is being formed may be a key factor in determining the regiochemistry of the reaction. A similar profile has been observed with radicals **24•** and **25•**.

On the other hand, the 7-*endo* cyclization is the regiospecific mode when a tertiary endocyclic radical is formed. The same behavior has been reported for radical **26•**. The 7-*endo* cyclization of this radical occurs through a TS in which the unpaired spin density is stabilized by the adjacent π system as shown in Figure 3, in which the distribution of the unparied spin density is shown. A similar situation is observed for radical

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Table 2. Activation Energy Difference of 6-*exo* and 7-*endo* Cyclization Modes (kcal/mol)[a]

		$\Delta\Delta E^{\ddagger}_{exo-endo}$		estimated k_{exo}/k_{endo} [b]		
entry	radical	B3LYP-D	B3LYP	B3LYP-D	B3LYP	% of *exo*:*endo* cyclization experimental outcome
1	**8**$^{\bullet}$	−0.67	−1.51	4[c]	24[c]	67:33
2	**9**$^{\bullet}$	1.20	2.13	8.0×10^{-2} [c]	1.1×10^{-2} [c]	—:100
3	**11**$^{\bullet}$	−2.70	−5.75	3.0×10^{2} [c]	1.8×10^{5} [c]	100:—
4	**24**$^{\bullet}$	−2.61	−2.84	2.5×10^{2} [c]	3.9×10^{2} [c]	100:—
5	**25**$^{\bullet}$	−3.08	−3.09	6.5×10^{2} [c]	6.6×10^{2} [c]	100:—
6	**26**$^{\bullet}$	4.65	4.31	2.2×10^{-3} [d]	3.4×10^{-3} [d]	—:100
7	**27a**$^{\bullet}$	0.97	1.53	2.8×10^{-1} [d]	1.3×10^{-1} [d]	3:97
8	**27b**$^{\bullet}$	1.60	1.88	1.2×10^{-1} [d]	8.3×10^{-2} [d]	—:100
9	**27c**$^{\bullet}$	1.57	1.83	1.3×10^{-1} [d]	8.9×10^{-2} [d]	2:98
10	**27d**$^{\bullet}$	3.59	4.45	8.8×10^{-3} [d]	2.8×10^{-3} [d]	6:94
11	**28a**$^{\bullet}$	2.30	3.71	4.8×10^{-2} [d]	7.5×10^{-3} [d]	3:97
12	**28b**$^{\bullet}$	1.65	5.66	1.1×10^{-1} [d]	5.8×10^{-4} [d]	—:100
13	**28c**$^{\bullet}$	1.75	4.17	1.0×10^{-1} [d]	4.0×10^{-3} [d]	—:100
14	**28d**$^{\bullet}$	2.57	5.04	3.8×10^{-2} [d]	1.3×10^{-3} [d]	—:100

[a]B3LYP-D or B3LYP/6-31+G*. Implicit solvent, polarized continuum model. [b]$k_{exo}/k_{endo} = e^{-(E^{\ddagger}_{exo}-E^{\ddagger}_{endo})/RT}$, assuming equal frequency factor. $R = 1.98 \times 10^{-3}$ kcal mol^{-1} K^{-1}, with the temperature depending on solvent. [c]Solvent = methanol, T = 240.5 K. [d]Solvent = toluene, T = 383.3 K.

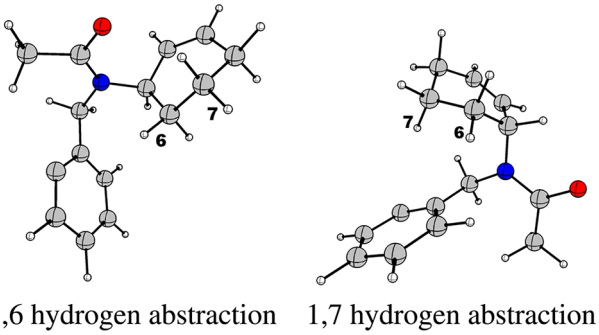

Figure 2. Conformers of radical **10**$^{\bullet}$ suitable for hydrogen abstraction reaction.

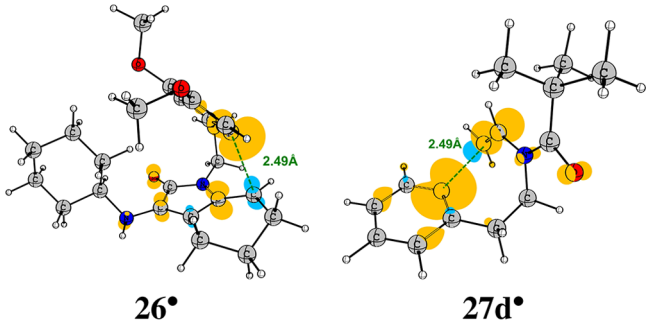

Figure 3. 7-*endo* cyclization TS. The spin density is delocalized over the π system.

27, for which the 7-*endo* cyclization is the regiospecific mode. This pathway leads to an endocyclic secondary radical stabilized by the π system of the adjacent substituent as shown in Figure 3.

CONCLUSIONS

In this work the synthesis of 11 novel heterocycles substituted by Me_3Sn, Ph_2P and O_2NCH_2 groups has been achieved. In the reaction of compounds **8** the *exo*-cyclization prevails (50% yield), accompanied by the product from 7-*endo* cyclization (25% yield). Regiospecific 6-*exo* cyclization was obtained with compound **10** (39−54% yield), while the cyclization of compound **9** is 7-*endo* regiospecific (53−65% yields). The products distribution depended strongly on the bridge between the radical center and the double bond. Moreover, we demonstrated that the regiochemistry of the radical ring closure could be controlled by changing the substitution at the double bond (see Table 1). In addition, this regiochemistry was determined by the stabilization of the transition states for each cyclization (*exo* or *endo*) mode. Mainly two factors seem to affect the relative stability of the transition states of our experimental type system (nonresonance stabilization of the cyclization TS): the conformation effect (Baldwin's rule) and the stability of the radical being formed. *Exo*-cyclization to primary, secondary or tertiary radicals is preferred over *endo*-cyclization to secondary radicals. In the first case, the conformation factors compensate the lower stability of a primary radical and the reaction is partially selective. In the second two cases, conformation and radical stability factors are responsible for a regiospecific *exo*-cyclization. On the other hand, the stability of a tertiary-endocyclic radical overcomes conformational factors, and its formation is always the preferred one.

Computational calculations were used to predict the product distribution, which may be employed to predict the regiochemical outcome of similar type of reactions.

EXPERIMENTAL SECTION

Computational Procedure. All the calculations were performed using the Gaussian09 program, the B3LYP and B3LYP-D[37] DFT functional and the 6-31+G* basis set. For the hydrogen abstraction reaction, the 6-31++G** basis set was used. Calculations were performed with full geometry optimization, including in all cases the effect of the solvent through the Tomasi's polarized continuum model (PCM)[38] as implemented in Gaussian09. The effect was evaluated using methanol as model polar solvent.[5] The transition states (TS) and intermediates were localized by a scan of the distinguished reaction coordinate. After refinement, the characterization of stationary points was done by Hessian matrix calculations, with all positive eigenvalues for a minimum and only one negative eigenvalue for the TSs. The energy reported for all species includes zero-point corrections.

General Methods. The internal standard method was used for quantitative GC analysis with authentic samples, and the following column was employed: (30 m × 0.32 mm ID DF = 0.25 column). The

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phosphorus containing products products were quantified by ^{31}P NMR. All NMR spectra were obtained on a 400 MHz spectrometer (^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), ^{31}P NMR, ^{119}Sn NMR, COSY, HSQC, HMBC and NOE) using CCl_3-*d* as a solvent unless otherwise indicated. The coupling constants (*J*) are given in hertz. GC−MS analyses were carried out on a GC apparatus coupled with a mass selective detector and a DB-5 (30 m × 0.25 mm ID) capillary column. High-resolution mass spectra were recorded on a TOF analyzer, using an ESI source in a positive mode, with nitrogen as the nebulizing and drying gas and sodium formiate (10 mM) as the internal calibrant.

Materials. Trimethyl tin chloride, triphenylphosphine, nitromethane, potassium *t*-butoxide and *t*-butanol were obtained from commercial sources. Acetone and nitromethane were double distilled and stored under nitrogen over 4 Å molecular sieves. To prepare the substrates, commercially available 2-chlorobenzyl chloride, 2-bromobenzyl bromide, 2-iodobenzyl chloride, allyl bromide, allyl amine, 2-methylallyl bromide and 3-dimethylallyl bromide were used. In addition, 2-chlorobenzyl amine and 2-bromobenzyl amine were prepared from 2-chlorobenzyl chloride and 2-bromobenzyl bromide, respectively, by substitution reaction with an excess of 38% ammonium hydroxide solution.[39] The compound 3-bromocyclohexene was prepared as previously reported.[29] Silica gel (0.063−0.200 mm) was used in column chromatography and on 2 mm plates (silica gel 60 PF254) in radial thin-layer chromatography purification. All solvents were of analytical grade and used as received from the supplier.

***N*-Allyl-*N*-(2-chlorobenzyl)-amine (7a)[40] and *N*-Allyl-*N*-(2-chlorobenzyl)-acetamide (8a).** Sodium carbonate (1 g), allyl amine (40 mmol) and water (1 mL) were added to a round-bottomed flask equipped with a reflux condenser and magnetic stirring. The mixture was first heated to 80 °C, and 2-chlorobenzyl chloride (10 mmol) was added. Then, heating was carried out for a further three hours before the mixture was left to cool at rt. The aqueous phase was extracted with dichloromethane (3 × 50 mL), and the organic phase was dried over magnesium sulfate and evaporated under a vacuum.

The crude was separated into two parts. From one, **7a** (72% yield) was isolated as a pale yellow oil by column chromatography using petroleum ether−ethyl ether, 50:50. The other part was poured into a two-necked round-bottomed flask equipped with magnetic stirring and a reflux condenser, and acetic anhydride was then added in excess (4 mL). The mixture was boiled for 2 h before water was added in excess (2 mL), and the new mixture was boiled for an additional 2 h. The aqueous phase was extracted with dichloromethane (3 × 50 mL), and the organic layer was dried (magnesium sulfate) and evaporated. Compound **8a** (53% yield) was separated as a pale yellow oil by column chromatography using petroleum ether−ethyl ether, 40:60. This product was characterized by standard spectroscopic techniques as follows. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 2.19 (s, 3H); 3.87 (br d, 1H, *J* = 4.9 Hz, overlapping); 4.02 (br d, 1H, *J* = 6.0 Hz, overlapping); 4.72 (s, 2H); 5.17 (m, 2H, overlapping); 5.78 (m, 1H, overlapping); 7.09−7.47 (clpx. m, 4H, overlapping). Minor isomer δ_H: 2.10 (s, 3H); 3.87 (br d, 1H, *J* = 4.9 Hz, overlapping); 4.02 (br d, 1H, *J* = 6.0 Hz, overlapping); 4.56 (s, 2H); 5.17 (m, 2H, overlapping); 5.78 (m, 1H, overlapping); 7.09−7.47 (clpx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 21.1; 45.8; 50.6; 117.0; 127.0; 128.5; 129.2; 129.5; 132.3; 134.0; 134.9; 171.3. Minor isomer δ_C: 21.5; 48.2; 49.1; 117.8; 126.8; 127.3; 128.8; 129.9; 132.7; 134.8; 133.6; 171.2. *m*/*z* (%): 56 (38), 70 (6), 82 (13), 89 (18), 125 (41), 127 (13), 140 (71), 142 (21), 188 (100). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{15}ClNO$ 224.0842, found 224.0853.

***N*-Allyl-*N*-(2-bromobenzyl)-acetamide (8b).** This reaction was carried out using a procedure similar to that described for **8a**, but the substrate utilized was 2-bromobenzyl bromide (10 mmol). Compound **8b** (55% yield) was separated as a pale yellow oil by column chromatography using petroleum ether−methylene chloride, 50:50. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 2.19 (s, 3H); 3.87 (br d, 1H, *J* = 4.9 Hz, overlapping); 4.03 (br d, 1H, *J* = 6.0 Hz, overlapping); 4.70 (s, 2H); 5.18 (m, 2H, overlapping); 5.78 (m, 1H, overlapping); 7.07−7.38 (clpx. m, 3H, overlapping); 7.53 (d, 1H, *J* = 7.9 Hz). Minor isomer δ_H: 2.08 (s, 3H); 3.87 (br d, 1H, *J* = 4.9 Hz, overlapping); 4.03 (br d, 1H, *J* = 6.0 Hz, overlapping); 4.52 (s, 2H); 5.18 (m, 2H, overlapping); 5.78 (m, 1H, overlapping); 7.07−7.38 (clpx. m, 3H, overlapping); 7.58 (d, 1H, *J* = 7.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 21.3; 48.3 (overlapping); 50.5; 117.0; 122.7; 127.7; 128.7; 129.1; 132.2; 132.8; 135.6; 171.3. Minor isomer δ_C: 21.5; 48.3 (overlapping); 51.6; 117.8; 123.6; 126.9; 127.9; 129.0; 132.7; 133.2; 136.5; 171.2. *m*/*z* (%): 56 (40), 77 (8), 89 (24), 90 (29), 91 (14), 117 (3), 130 (2), 146 (8), 169 (20), 170 (11), 184 (36), 186 (34), 188 (100), 226 (3), 228 (2). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{15}BrNO$ 268.0337, found 268.0341.

***N*-(2-Chlorobenzyl)-*N*-(2-methylallyl)acetamide (9a).** This reaction was carried out using a procedure similar to that described for **8a**, but the substrate utilized was 2-methylallyl bromide (7 mmol) and the amine 2-chlorobenzylamine (7 mmol). Compound **9a** (48% yield) was separated as a pale yellow oil by column chromatography using petroleum ether−ethyl ether, 30:70. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 1.72 (s, 3H, overlapping); 2.17 (s, 3H); 3.75 (s, 2H); 4.71 (s, 2H); 4.83 (br s, 1H); 4.95 (br m, *J* = 1.3 Hz); 7.10−7.42 (cplx. m, 4H, overlapping). Minor isomer δ_H: 1.72 (s, 3H, overlapping); 2.11 (s, 3H); 3.99 (s, 2H); 4.54 (s, 2H); 4.75 (br s, 1H); 4.96 (br s, 1H); 7.10−7.42 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 20.10(overlapping); 21.2; 46.0; 53.6; 111.2; 127.0; 128.5; 129.1; 129.5; 133.6; 134.9; 139.6; 171.5. Minor isomer δ_C: 20.1 (overlapping); 21.4; 48.7; 50.7; 112.4; 126.6; 127.3; 128.7; 129.9; 132.9; 134.0; 140.3; 171.3. *m*/*z* (%): 70 (68), 89 (12), 99 (12), 125 (47), 127 (17), 140 (55), 154 (9), 182 (6), 202 (100), 237 (7). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{17}ClNO$ 238.0999, found 238.1002.

***N*-(2-Bromobenzyl)-*N*-(2-ethylallyl)acetamide (9b).** This reaction was performed by a procedure similar to that described for **9a**, but the substrate used was 2-bromobenzylamine. Compound **9b** (50% yield) was purified as a yellow oil by column chromatography using petroleum ether−ethyl ether, 20:80. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 1.72 (s, 3H, overlapping); 2.17 (s, 3H); 3.70 (s, 2H); 4.70 (s, 2H); 4.83 (br s, 1H); 4.97 (br s, 1H); 7.07−7.38 (cplx. m, 3H, overlapping); 7.53 (dd, 1H, *J* = 7.8, 0.6 Hz). Minor isomer δ_H: 1.72 (s, 3H, overlapping); 2.10 (s, 3H); 3.99 (s, 2H); 4.49 (s, 2H); 4.75 (br s, 1H); 4.91 (br s, 1H); 7.07−7.38 (cplx. m, 3H, overlapping); 7.59 (dd, 1H, *J* = 8.0, 0.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 20.1 (overlapping); 21.2; 48.5; 53.5; 111.2; 123.7; 127.7; 128.7; 129.0 (overlapping); 132.8; 136.5; 139.5; 171.5. Minor isomer δ_C: 20.1 (overlapping); 21.4; 50.8; 51.5; 112.5; 122.7; 126.7; 127.9; 129.0 (overlapping); 133.2; 135.5; 140.3; 171.3. *m*/*z* (%): 55 (13), 70 (59), 89 (15), 90 (19), 96 (7), 112 (9), 146 (7), 169 (27), 171 (19), 184 (33), 186 (30), 202 (100), 226 (6), 228 (4), 281 (1.25), 283 (1.00). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{17}BrNO$ 282.0494, found 282.0499.

***N*-(2-Chlorobenzyl)-*N*-(cyclohex-2-en-1-yl)acetamide (10a).** This reaction was carried out using a procedure similar to that described for **9a**, but with 3-bromocyclohexene as subtrate. Compound **10a** (51% yield) was separated as a viscous amber oil by column chromatography using petroleum ether−ethyl ether, 65:35. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 1.37 (m, 1H); 1.72 (m, 2H); 1.95 (s, 3H); 1.96 (m, 1H); 2.01 (m, 2H); 4.47 (m, 1H); 4.53 (m, 1H); 5.40 (m, 1H); 5.43 (m, 1H, overlapping); 5.88 (m, 1H, overlapping); 7.10−7.41 (cplx. m, 4H, overlapping). Minor isomer δ_H: 1.52 (m, 1H); 1.80 (m, 2H); 1.89 (m, 1H); 1.94 (m, 2H); 2.29 (s, 3H); 4.49 (m, 1H); 4.62 (d, 1H, *J* = 16.8 Hz); 4.51 (m, 1H); 5.43 (m, 1H, overlapping); 5.88 (m, 1H, overlapping); 7.10−7.41 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 21.3; 22.2; 24.5; 27.6; 46.2; 51.3; 126.9; 127.0; 127.4; 127.6; 128.2; 132.5; 136.0; 136.2; 172.0. Minor isomer δ_C: 21.5; 22.0; 24.3; 28.7; 43.8; 56.1; 126.7; 127.3; 129.2; 129.6; 132.1; 132.2; 132.4;

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171.1. *m/z* (%): 53 (5), 77 (11), 79 (20), 96 (100), 125 (39), 127 (12), 138 (70), 140 (27), 148 (12), 193 (5), 228 (20). ESI-HRMS *m/z* $[M + H]^+$ calcd for $C_{15}H_{19}ClNO$ 264.1155, found 264.1163.

***N*-(2-Chlorobenzyl)-*N*-(3-dimethylallyl)acetamide (11a).** This reaction was carried out using a procedure similar to that described for **9a**, but the substrate utilized was 3-dimethylallyl bromide. Compound **11a** (48% yield) was separated as pale yellow oil by column chromatography using petroleum ether−ethyl ether, 75:25. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 1.70 (dd, 6H, *J* = 4.6, 1.1 Hz); 2.20 (s, 3H); 4.01 (d, 2H, *J* = 7.1 Hz); 4.70 (s, 2H); 5.11 (m, 1H); 7.12−7.42 (cplx. m, 4H, overlapping). Minor isomer δ_H: 1.54 (br d, 6H, *J* = 8.2 Hz); 2.07 (s, 3H); 3.83 (d, 2H, *J* = 6.7 Hz); 4.53 (s, 2H); 5.18 (m, 1H); 7.12−7.42 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 17.8; 21.57; 25.67; 45.6; 46.4; 119.4; 126.92; 128.3; 129.4; 129.8; 133.5; 134.5; 136.8; 171.1. Minor isomer δ_C: 17.7; 21.55; 25.71; 43.0; 48.8; 119.3; 126.88; 127.2; 128.6; 129.0; 132.8; 135.0; 136.3; 170.9. *m/z* (%): 70 (67), 89 (15), 112 (7), 125 (51), 127 (16), 140 (52), 142 (18), 182 (8), 202 (100), 222 (3), 224 (1), 237 (2). ESI-HRMS *m/z* $[M + H]^+$ calcd for $C_{14}H_{19}ClNO$ 252.1155, found 252.1169.

Reactions of 8a, 9a, 10a and 11a with Me_3Sn^- Ions in $NH_{3(l)}$. First, 300 mL of $NH_{3(l)}$ were condensed, previously dried with Na metal under nitrogen in a three-necked, 500 mL round-bottomed flask equipped with a coldfinger condenser charged with ethanol, a nitrogen inlet, and a magnetic stirrer. Me_3SnCl (0.55 mmol) was then added, and Na metal (1.325 mmol) in small pieces was introduced, waiting for total bleaching between each new addition. A lemon yellow solution of Me_3Sn^- ions was obtained. The substrates (0.50 mmol) were dissolved in 1 mL of dried ethyl ether and added to the solution. The reaction mixture was irradiated for 15 min and then quenched by adding ammonium nitrate in excess. The ammonia was allowed to evaporate, and water (50 mL) was added. The aqueous phase was extracted with dichloromethane (3 × 50 mL), the organic phase was dried (magnesium sulfate), and the solvent was evaporated in a vacuum. The products were purified as indicated.

Inhibited Photostimulated Reaction with Me_3Sn^-. The procedure was similar to that for the previous reactions, except that *m*-dinitrobenzene (20 mol %) was added to the solution of the nucleophile prior to substrate addition.

Reactions of 8a, 9a and 10a with Ph_2P^- Ions in $NH_{3(l)}$. These reactions were performed in a fashion similar to those with Me_3Sn^- ions, but 0.55 mmol of Ph_3P was added instead followed by Na metal (1.325 mmol) in small pieces. The addition of Na metal continued until no more solid was present and the blue color from solvated electrons in excess remained for 20 min before becoming orange-brown. Then, *t*-BuOH (0.55 mmol) was added to this solution to neutralize the amide ions formed. After irradiation and quenching (and previous to drying), the dichloromethane phase was treated with 20% H_2O_2 (50 mL) and then with water (50 mL). The products were purified as indicated.

Reactions of 8b and 9b with $O_2NCH_2^-$ Ions in $NH_{3(l)}$. These reactions were performed by a procedure similar to that described for the other two nucleophiles, but 1.5 mmol of nitromethane, 1 mmol of acetone and 2.75 mmol of KOBu- *t* were added, waiting 15 min for the formation of the nucleophile and the entrainment reagent to occur. A slightly colored solution was obtained. The reactions were irradiated for 240 min.

1-(4-((Trimethylstannyl)methyl)-3,4-dihydroisoquinolin-2(1*H*)-yl)ethanone (14a-*exo*). Colorless liquid. Isolated (46 mg, 29% yield) by radial thin-layer chromatography eluted with petroleum ether−ethyl ether, 50:50. ^{1}H NMR (400 MHz, $CDCl_3$), mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.05 (s, 9H); 1.21 (cplx. m, 2H, overlapping); 2.18 (s, 3H); 3.21 (br m, 1H, overlapping); 3.42 (dd, 1H, *J* = 12.7 Hz, 6.2 Hz); 3.67 (m, 1H, overlapping); 4.64 (d, 1H, *J* = 17.1 Hz); 4.81 (d, 1H, *J* = 17.1 Hz); 7.05−7.25 (cplx. m, 4H, overlapping). Minor isomer δ_H: 0.06 (s, 9H); 1.21 (cplx. m, 2H, overlapping); 2.20 (s, 3H); 3.18 (br m, 1H, overlapping); 3.64 (cplx, 1H, overlapping); 3.75 (dd, 1H, *J* = 12.8 Hz, 3.4 Hz); 4.58 (d, 1H, *J* = 16.0 Hz); 4.67 (d, 1H, *J* = 16.0 Hz); 7.05−7.25 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: −9.3; 16.2; 37.1; 44.5; 51.5; 126.6; 126.7; 126.8; 126.9; 132.5; 140.1; 170.0. Minor isomer δ_C: −9.3; 16.7; 21.9; 36.3; 46.4; 48.3; 126.0; 126.3; 127.1; 131.6; 141.5; 169.8. *m/z* (%): 63 (1), 77 (3), 91 (10), 115 (22),116 (8), 117 (23), 118 (4), 128 (5),129 (11), 130 (10), 131 (7), 144 (32), 146 (100), 147 (12), 165 (12), 188 (62), 338 (isotopic cluster, 23). ESI-HRMS *m/z* $[M + H]^+$ calcd for $C_{15}H_{24}NOSn$ 354.0880, found 354.0889.

1-(4-(Trimethylstannyl)-4,5-dihydro-1*H*-benzo[*c*]azepin-2(3*H*)-yl)ethanone (15a-*endo*). Colorless liquid. Isolated (30 mg, 19% yield) by radial thin-layer chromatography eluted with petroleum ether−ethyl ether, 50:50. ^{1}H NMR (400 MHz, $CDCl_3$), mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.04 (s, 9H); 1.67 (cplx. m, 1H, overlapping); 2.11 (s, 3H); 2.99−3.32 (br m, 2H, overlapping); 4.39 (br s, 1H); 4.50 (s, 2H, overlapping); 4.79 (br s, 1H); 7.04−7.42 (cplx. m, 4H, overlapping). Minor isomer δ_H: 0.06 (s, 9H); 1.62 (cplx. m, 1H, overlapping); 2.02 (s, 3H); 2.99−3.32 (br m, 2H, overlapping); 3.67 (br t, 1H, *J* = 10.8 Hz); 4.50 (s, 2H, overlapping); 4.00 (dd, 1H, *J* = 14.6 Hz, 3.1 Hz); 7.04−7.42 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: −10.6; 21.9; 26.3; 39.8; 50.7; 54.0; 126.3; 128.0; 128.5; 130.0; 137.7; 142.9; 169.6. Minor isomer δ_C: −10.9; 21.6; 27.9; 39.0; 53.0; 56.4; 126.5; 127.5; 128.8; 130.1; 137.1; 142.2; 168.5. *m/z* (%): 60 (6), 72 (6), 91 (15), 105 (3), 115 (26), 116 (13), 117 (21), 118 (8), 128 (14), 129 (34), 130 (17), 131 (12), 144 (17), 146 (100), 147 (16), 165 (14), 188 (72), 206 (8), 207 (6), 208 (10), 338 (isotopic cluster, 21). ESI-HRMS *m/z* $[M + H]^+$ calcd for $C_{15}H_{24}NOSn$ 354.0880, found 354.0891.

1-(4-((Diphenylphosphoryl)methyl)-3,4-dihydroisoquinolin-2(1*H*)-yl)ethanone (14b-*exo*). White solid. mp 217−220 °C. Isolated (60 mg, 33% yield) by radial thin-layer chromatography eluted with dichloromethane-methanol, 95:5. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 2.27 (s, 3H); 2.40 (ddc, 1H, *J* = 15.5 Hz, 7.3 Hz, 1.2 Hz); 2.61 (dd, 1H, *J* = 15.5, 11.2 Hz); 3.28 (td, 1H, *J* = 11.3, 2.5 Hz); 3.50 (br dd, 1H, *J* = 13.2, 3.3 Hz); 4.33 (d, 1H, *J* = 17.8 Hz); 4.48 (dd, 1H, *J* = 13.2, 2.9 Hz); 5.11 (d, 1H, *J* = 17.8 Hz); 6.91 (br d, 1H, 7.1 Hz); 7.09−7.19 (br cplx. m, 3H); 7.36−7.94 (cplx. m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 21.9; 33.5 (d, ^{C-P}J = 68.0 Hz); 34.0 (d, 2.3 Hz); 44.2; 47.2; 126.9; 127.0; 127.2; 127.4; 128.9 (d, ^{C-P}J = 11.9 Hz); 129.0 (d, ^{C-P}J = 11.9 Hz); 130.2 (d, ^{C-P}J = 9.6 Hz); 131.0 (d, ^{C-P}J = 9.7 Hz); 131.8 (d, ^{C-P}J = 96.6 Hz); 132.0 (d, ^{C-P}J = 9.04 Hz); 132.1 (d, ^{C-P}J = 9.04 Hz); 132.6; 133.8 (d, ^{C-P}J = 99.2 Hz); 137.8 (d, ^{C-P}J = 13.3 Hz); 171.5. ^{31}P NMR ($CDCl_3$) δ_P: 30.51. *m/z* (%): 77 (25), 91 (4), 107 (5), 115 (5), 123 (6), 150 (11), 152 (14), 165 (40), 166 (23), 183 (18), 184 (3), 199 (18), 201 (11), 208 (6), 213 (22), 228 (9), 241 (14), 271 (11), 288 (20), 289 (17), 291 (100), 292 (28), 305 (15), 306 (45), 330 (1), 346 (97), 347 (24), 348 (21), 388 (1). ESI-HRMS *m/z* $[M + H]^+$ calcd for $C_{24}H_{25}NO_2P$ 390.1623, found 390.1633.

1-(4-(2-Nitroethyl)-3,4-dihydroisoquinolin-2(1*H*)-yl)-ethanone (14c-*exo*). Amber liquid. Isolated (25 mg, 21% yield) by radial thin-layer chromatography eluted with ethyl ether−methanol, 98:2. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 2.09 (cplx. m, 1H); 2.22 (s, 3H); 2.26 (cplx. m, 1H, overlapping); 2.96 (br m, 1H, overlapping); 3.03 (dd, 1H, *J* = 13.6, 3.5 Hz); 4.52 (m, 1H, overlapping); 4.58 (m, 1H, overlapping); 4.65 (m, 1H, overlapping); 4.72 (br m, 1H, overlapping); 4.75 (m, 1H, overlapping); 7.09−7.30 (cplx. m, 4H, overlapping). Minor isomer δ_H: 2.18 (cplx. m, 1H, overlapping); 2.21 (s, 3H); 2.37 (cplx. m, 1H, overlapping); 3.01 (br m, 1H, overlapping); 3.58 (dd, 1H, *J* = 13.1, 3.3 Hz); 3.85 (dd, 1H, *J* = 13.1, 2.9 Hz); 4.42 (m, 1H, overlapping); 4.43 (m, 2H, overlapping); 5.05 (d, 1H, *J* = 18.02 Hz); 7.09−7.30 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 21.8 (overlapping); 31.9; 35.7; 41.3; 48.1; 73.5; 126.3; 127.28; 127.30; 129.1; 131.8; 137.0; 170.1. Minor isomer δ_C: 21.8 (overlapping); 31.3; 36.3; 44.4; 48.0; 73.3; 126.8; 127.4; 127.7; 128.3; 132.6; 134.9; 170.3. *m/z* (%): 77 (12), 91 (19), 103 (9), 104 (5), 115 (27), 116 (13), 117 (10), 128 (13), 129 (22), 130 (100), 131 (49), 132 (16), 144 (7), 158 (6), 172 (10), 173 (36), 174 (6), 201 (3), 205

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(1), 214 (4), 231 (3). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{13}H_{17}N_2O_3$ 249.1239, found 249.1247.

1-(4-(Nitromethyl)-4,5-dihydro-1*H*-benzo[*c*]azepin-2(3*H*)-yl)-ethanone (15c-*endo*). Amber liquid. Isolated (15 mg, 13% yield) by radial thin-layer chromatography eluted with dichloromethane. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 2.15 (s, 3H); 2.85 (br m, 1H); 2.98 (dd, 1H, J = 14.9, 7.2 Hz); 3.18 (br d, 1H, J = 14.9 Hz); 3.59 (br m, 1H); 4.06 (dd, 1H, J = 13.3, 9.4 Hz); 4.30 (m, 1H, overlapping); 4.40 (dd, 1H, J = 13.3, 4.9 Hz); 4.49 (d, 1H, J = 15.7 Hz); 4.57 (d, 1H, J = 15.7 Hz); 7.10−7.41 (cplx. m, 4H, overlapping). Minor isomer δ_H: 2.08 (s, 3H); 2.80 (br m, 1H); 2.91 (dd, 1H, J = 14.5, 7.4 Hz); 3.13 (br m, 1H, overlapping); 3.65 (br m, 1H, overlapping); 3.80 (dd, 1H, J = 15.0, 3.4 Hz); 4.14 (dd, 1H, J = 13.8, 8.5 Hz, overlapping); 4.28 (dd, 1H, J = 13.4, 5.6 Hz, overlapping); 4.57 (m, 1H, overlapping); 4.65 (m, 1H, overlapping); 7.10−7.41 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 21.6; 35.7; 37.2; 50.2; 54.3; 76.8; 127.4; 128.3; 128.5; 131.7; 136.8; 136.9; 170.6. Minor isomer δ_C: 21.4; 36.7; 37.1; 50.7; 52.6; 76.5; 127.6; 128.1; 129.9; 129.9; 136.8 (overlapping); 137.0; 169.5. m/z (%): 63 (17), 65 (18), 73 (25), 77 (29), 78 (23), 91 (88), 102 (10), 103 (16), 104 (17), 105 (11), 115 (78), 116 (60), 117 (32), 118 (27), 129 (66), 130 (61), 131 (100), 132 (14), 142 (65), 143 (34), 144 (31), 157 (17), 158 (25), 160 (20), 171 (12), 172 (8), 189 (4), 201 (20), 202 (4), 214 (21), 231 (12), 232 (3). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{13}H_{17}N_2O_3$ 249.1239, found 249.1234.

1-(4-Methyl-4-(trimethylstannyl)-4,5-dihydro-1*H*-benzo[*c*]-azepin-2(3*H*)-yl)ethanone (17a-*endo*). Colorless liquid. Isolated (94 mg, 52% yield) by radial thin-layer chromatography eluted with petroleum ether−ethyl ether, 80:20. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: −0.22 (br s, 9H); 1.11 (s, 3H); 2.13 (s, 3H); 2.40−5.30 (cplx. m, 4H, overlapping); 4.43 (d, 1H, J = 15.4 Hz); 4.50 (d, 1H, J = 15.4 Hz); 7.00−7.40 (cplx. m, 4H, overlapping). Minor isomer δ_H: −0.09 (br s, 9H); 1.07 (s, 3H); 2.03 (s, 3H); 2.40−5.30 (cplx. m, 6H, overlapping); 7.00−7.40 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: −10.7; 21.8; 25.1 (overlapping); 31.5 (overlapping); 48.7; 54.1 (overlapping); 60.1 (overlapping); 126.6; 128.2; 128.4; 130.6; 137.7; 141.0; 169.6. Minor isomer δ_C: −11.0; 21.5; 25.1 (overlapping); 31.5 (overlapping); 46.6; 54.1 (overlapping); 60.1 (overlapping); 126.8; 127.6; 129.5; 129.9; 137.5; 139.9; 168.7. ^{119}Sn NMR ($CDCl_3$) δ_{Sn}: 6.34. m/z (%): 91 (11), 115 (10), 129 (23), 131 (17), 143 (27), 144 (16), 160 (100), 165 (isotopic cluster, 15), 202 (74), 352 (40), 354 (5), 355 isotopic cluster, (7). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{16}H_{26}NOSn$ 368.1036, found 368.1045.

1-(4-(Diphenylphosphoryl)-4-methyl-4,5-dihydro-1*H*-benzo-[*c*]azepin-2(3*H*)-yl)ethanone (17b-*endo*). White wax. Isolated (90 mg, 45% yield) by radial thin-layer chromatography eluted with dichloromethane−methanol, 98:2. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.93 (dd, 3H, J = 15.7, 3.7 Hz, overlapping); 2.10 (s, 3H); 3.04 (td, 1H, J = 11.2, 1.8 Hz); 3.36 (dd, 1H, J = 13.4, 2.6 Hz); 3.51 (br d, 1H, overlapping); 4.34 (d, 1H, J = 15.6 Hz); 4.50 (d, 1H, J = 15.6 Hz); 3.98 (dd, 1H, J = 13.1, 4.5 Hz); 7.00−7.22 (cplx. m, 4H, overlapping); 7.46−7.66 (cplx. m, 6H, overlapping); 7.95−8.10 (cplx. m, 4H, overlapping). Minor isomer δ_H: 0.93 (dd, 3H, J = 15.7, 3.7 Hz, overlapping); 1.98 (s, 3H); 2.92 (td, 1H, J = 12.4, 1.3 Hz); 3.56 (br d, 1H, overlapping); 3.77 (d, 1H, J = 14.1 Hz); 3.83 (dd, 1H, J = 14.3, 3.1 Hz); 4.04 (dd, 1H, J = 14.3, 4.8 Hz); 5.19 (d, 1H, J = 14.1 Hz); 7.00−7.22 (cplx. m, 4H, overlapping); 7.46−7.66 (cplx. m, 6H, overlapping); 7.95−8.10 (cplx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 16.7; 21.6; 40.2 (d, ^{C-P}J = 66.3 Hz); 40.5; 54.2; 52.7; (d, ^{C-P}J = 8.5 Hz); 126.7; 128.0; 128.1; 128.5−129.0 (cplx. m, overlapping); 131.8−132.7 (cplx. m, overlapping); 132.0; 136.8; 137.5 (d, ^{C-P}J = 13.9 Hz); 170.1. Minor isomer δ_C: 16.4; 21.3; 40.2; 40.7 (d, ^{C-P}J = 66.1 Hz); 50.5; 56.4; (d, ^{C-P}J = 7.5 Hz); 127.2; 127.5; 128.5−129.0 (cplx. m, overlapping); 129.7; 131.8−132.7 (cplx. m, overlapping); 130.5; 136.9; 136.3 (d, ^{C-P}J = 14.4 Hz); 169.8. ^{31}P NMR ($CDCl_3$) major isomer δ_P: 36.92. Minor isomer δ_P: 35.26. m/z (%): 201 (10), 202 (13), 203 (22), 217 (63), 291 (73), 292 (12), 345 (5), 362 (100), 363 (22), 404 (63). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{25}H_{27}NO_2P$ 404.1779, found 404.1794.

1-(4-Methyl-4-(nitromethyl)-4,5-dihydro-1*H*-benzo[*c*]-azepin-2(3*H*)-yl)ethanone (17c-*endo*). White wax. Isolated (45 mg, 35% yield) by radial thin-layer chromatography eluted with dichloromethane. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 1.10 (br s, 3H); 2.16 (s, 3H); 2.94 (br d, 1H, J = 15.4 Hz, overlapping); 3.11 (d, 1H, J = 14.6 Hz, overlapping); 3.15−4.00 (2H, overlapping); 4.16 (cplx. m, 1H, overlapping); 4.35 (d, 1H, J = 11.8 Hz, overlapping); 4.47 (d, 1H, J = 15.4 Hz, overlapping); 4.56 (d, 1H, J = 15.4 Hz, overlapping); 7.10−7.40 (clpx. m, 4H, overlapping). Minor isomer δ_H: 1.08 (s, 3H); 2.15 (s, 3H); 2.94 (br d, 1H, J = 15.4 Hz, overlapping); 3.11 (d, 1H, J = 14.6 Hz, overlapping); 3.15−4.00 (2H, overlapping); 4.16 (cplx. m, 1H, overlapping); 4.35 (d, 1H, J = 11.8 Hz, overlapping); 4.47 (d, 1H, J = 15.4 Hz, overlapping); 4.56 (d, 1H, J = 15.4 Hz, overlapping); 7.10−7.40 (clpx. m, 4H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: 21.7; 22.26 (overlapping); 38.7; 43.7 (overlapping); 54.1; 56.2 (overlapping); 81.7 (overlapping); 127.3; 128.1; 128.5; 132.4; 136.6; 136.8 (overlapping); 170.4. Minor isomer δ_C: 21.5; 22.26 (overlapping); 38.6; 43.7 (overlapping); 50.6; 56.2 (overlapping); 81.7 (overlapping); 127.7; 128.0; 129.7; 130.3; 135.6; 136.8 (overlapping); 170.0. m/z (%): 73 (35), 77 (20), 91 (48), 105 (25), 117 (65), 129 (86), 130 (58), 145 (100), 157 (44), 174 (30), 185 (21), 203 (8), 215 (30), 228 (25), 245 (14), 246 (4). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{14}H_{19}N_2O_3$ 263.1396, found 263.1404.

1-(1-(Trimethylstannyl)-1,2,3,4,4a,10b-hexahydrophenanthridin-5(6*H*)-yl)ethanone (18a-*exo*). Colorless liquid. Isolated (76 mg, 39% yield) by radial thin-layer chromatography eluted with petroleum ether−ethyl ether, 80:20. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.23 (s, 9H); 1.24−1.77 (cplx. m, 6H, overlapping); 2.20 (s, 3H); 2.58 (br c, 1H, J = 2.0 Hz); 3.29 (br t, 1H, J = 15.7 Hz); 4.03 (dt, 1H, J = 11.7, 4.4 Hz); 4.38 (d, 1H, J = 18.1 Hz); 4.99 (d, 1H, J = 18.1 Hz); 7.08−7.32 (cplx. m, 3H); 7.46 (d, 1H, J = 7.7 Hz). Minor isomer δ_H: 0.22 (s, 9H); 1.24−1.77 (cplx. m, 6H, overlapping); 2.17 (s, 3H); 2.49 (br m, 1H); 3.15 (br t, 1H, J = 16.2 Hz); 4.55 (d, 1H; J = 16.2 Hz); 4.63 (d, 1H, J = 16.2 Hz); 4.90 (dt, 1H; J = 12.2, 4.27 Hz); 7.08−7.32 (cplx. m, 3H); 7.50 (d, 1H, J = 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: −9.1; 21.9; 23.1; 25.3; 26.2; 27.5 (overlapping); 40.7; 42.9; 54.7; 125.7; 126.3; 126.8; 126.9; 133.3; 135.5; 169.4. Minor isomer δ_C: −9.2; 22.4; 23.6; 25.2; 26.0; 27.5 (overlapping); 39.9; 46.0; 49.2; 126.0; 126.1; 126.2; 127.2; 132.7; 137.3; 169.4. m/z (%): 91 (4), 115 (5), 127 (2), 128 (6), 129 (4), 130 (5), 141 (8), 163 (6), 165 (isotopic cluster, 10), 184 (12), 186 (100), 187 (15), 228 (74), 229 (13), 378 (isotopic cluster, 5). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{18}H_{28}NOSn$ 394.1193, found 394.1194.

1-(1-(Diphenylphosphoryl)-1,2,3,4,4a,10b-hexahydrophenanthridin-5(6*H*)-yl)ethanone (18b-*exo*). White wax. Isolated (50 mg, 25% yield) by radial thin-layer chromatography eluted with dichloromethane−acetone−methanol, 89:10:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.51 (cplx. m, 1H); 1.52 (cplx. m, 1H); 1.56 (cplx. m, 1H); 1.667 (cplx. m, 1H); 1.668 (cplx. m, 1H); 2.21 (cplx. m, 1H); 2.27 (s, 3H); 3.36 (br s, 2H); 4.22 (d, 1H, J = 18.2 Hz); 5.12 (d, 1H, J = 18.2 Hz); 5.30 (cplx m, 1H); 7.09−7.34 (cplx. m, 4H); 7.52 (br d; 6H, J = 15.1 Hz); 7.92 (br m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 19.9; 21.9; 21.1; 26.2; 34.9 (d, ^{C-P}J = 70.9 Hz); 37.2; 40.1; 51.1; 124.4; 126.7; 127.0; 127.2; 128.9 (d, ^{C-P}J = 11.4 Hz); 129.1 (d, ^{C-P}J = 11.1 Hz); 130.5 (d, ^{C-P}J = 8.1 Hz); 130.8 (d, ^{C-P}J = 8.5 Hz); 131.8; 131.9; 132.4 (d, ^{C-P}J = 73.0 Hz); 133.0; 133.1 (d, ^{C-P}J = 14.5 Hz); 133.9; 170.0. ^{31}P NMR ($CDCl_3$) δ_P: 36.40. m/z (%): 201 (89), 202 (8), 203 (22), 219 (14), 371 (83), 372 (16), 388 (100), 389 (19), 430 (22). ESI-HRMS m/z $[M + H]^+$ calcd for $C_{27}H_{29}NO_2P$ 430.1936, found 430.1958.

1-(4-Isopropyl-3,4-dihydroisoquinolin-2(1*H*)-yl)ethanone (20). Colorless liquid. Isolated by radial thin-layer chromatography

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eluted with dichloromethane. Quantified by GC using the internal standard method. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.91 (d, 3H, *J* = 6.7 Hz); 0.99 (d, 3H, *J* = 6.7 Hz); 1.82−1.89 (cplx. m, 1H, overlapping); 2.21 (s, 3H); 2.55 (cplx. m, 1H, overlapping); 3.42 (dd, 1H, *J* = 12.8, 3.5 Hz); 3.93 (dd, 1H, *J* = 12.8, 3.5 Hz); 4.55 (d, 1H, *J* = 17.7 Hz); 4.75 (d, 1H, *J* = 17.7 Hz); 7.08−7.24 (cplx. m, 4H, overlapping). Minor isomer δ_H: 0.93 (d, 3H, *J* = 6.8 Hz); 0.95 (d, 3H, *J* = 6.8 Hz); 1.82−1.89 (cplx. m, 1H, overlapping); 2.18 (s, 3H); 2.55 (cplx. m, 1H, overlapping); 3.10 (dd, 1H, *J* = 13.1, 3.7 Hz); 4.53 (d, 1H, *J* = 15.9 Hz); 4.58 (dd, 1H, *J* = 12.8, 3.7 Hz); 4.67 (d, 1H, *J* = 15.9 Hz); 7.08−7.24 (cplx. m, 4H, overlapping). ^{13}C NMR (from HSQC and HMBC spectra, $CDCl_3$) major isomer δ_C: 20.4; 21.3 (overlapping); 21.8; 29.7; 44.9; 45.6; 46.3; 126.0; 126.7; 126.9; 128.8; 132.7; 137.4; 170.0 (overlapping). Minor isomer δ_C: 19.9; 21.3 (overlapping); 22.0; 30.7; 40.8; 45.3; 47.9; 126.2; 126.3; 126.4; 129.4; 132.0; 138.5; 170.0 (overlapping). *m*/*z* (%): 77 (21), 91 (29), 103 (18), 104 (11), 115 (34), 116 (19), 117 (28), 130 (72), 131 (97), 132 (100), 143 (12), 160 (17), 174 (30), 175 (22), 202 (6), 217 (62). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{20}NO$ 218.1545, found 218.1540.

***N*-Benzyl-*N*-(6-(trimethylstannyl)cyclohex-2-en-1-yl)-acetamide (22a).** Colorless liquid. Isolated (12 mg, 6% yield) by radial thin-layer chromatography eluted with petroleum ether−ethyl ether, 90:10. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.09 (s, 9H); 1.583 (dd, 1H, *J* = 8.0 Hz, 3.0 Hz, overlapping); 1.586 (cplx. m, 1H, overlapping); 1.73 (cplx. m, 1H, overlapping); 1.90 (cplx. m, 1H, overlapping); 1.97 (cplx. m, 1H, overlapping); 1.95 (s, 3H); 4.49 (d, 1H, *J* = 17.7 Hz); 4.58 (d, 1H, *J* = 17.7 Hz); 5.40 (cplx. m, 1H, *J* = 2.8 Hz); 5.52 (dc, 1H, *J* = 10.2, 2.2 Hz, overlapping); 5.86 (br d, 1H, *J* = 9.9 Hz); 7.14−7.38 (cplx. m, 5H, overlapping). Minor isomer δ_H: 0.01 (s, 9H); 1.74 (m, 1H, overlapping); 1.83−2.05 (cplx. m, 4H, overlapping); 2.21 (s, 3H); 4.38 (d, 1H, *J* = 15.0 Hz); 4.46 (m, 1H, overlapping); 4.71 (d, 1H, *J* = 15.0 Hz); 5.44 (m, 1H), overlapping; 5.86 (m, 1H, overlapping); 7.14−7.38 (cplx. m, 5H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: −10.2; 22.8; 24.8; 25.8; 26.9; 48.7; 53.9; 125.9; 127.0; 128.4; 128.7; 132.4; 138.9; 171.7. Minor isomer δ_C: −10.5; 22.6; 25.4; 25.6; 27.5; 46.9; 59.0; 126.8; 128.2; 128.3; 129.4; 131.7 ; 139.4; 170.9. *m*/*z* (%): 77 (47), 79 (100), 91 (37), 106 (60), 149 (37), 165 (isotopic cluster, 9), 186 (3), 228 (3), 298 (isotopic cluster, 11), 312 (5), 378 (isotopic cluster, 5). ESI-HRMS *m*/*z* $[M + Na]^+$ calcd for $C_{18}H_{27}NOSnNa$ 416.1012, found 416.1029.

***N*-Benzyl-*N*-(5-(trimethylstannyl)cyclohex-2-en-1-yl)-acetamide (23a).** Colorless liquid. Isolated (18 mg, 9% yield) by radial thin-layer chromatography eluted with petroleum ether−ethyl ether, 90:10. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of interconverting rotational isomers with respect to the *N*-formyl bond, major isomer δ_H: 0.04 (s, 9H); 1.41 (br m, 1H); 1.91 (ddd, 1H, *J* = 13.6, 6.4, 3.6 Hz); 1.99 (s, 3H); 2.02 (m, 1H, overlapping); 2.03 (m, 1H, overlapping); 2.31 (m, 1H, overlapping); 4.56 (d, 1H, *J* = 18.0 Hz); 4.62 (d, 1H, *J* = 18.0 Hz); 5.24 (br m, 1H); 5.48 (br d, 1H, *J* = 10.3 Hz, overlapping); 5.99 (cplx. m, 1H); 7.15−7.39 (clpx. m, 5H, overlapping). Minor isomer δ_H: 0.03 (s, 9H); 1.52 (m, 1H); 1.983 (m, 2H, overlapping); 1.987 (m, 2H, overlapping); 2.24 (s, 3H); 4.34 (br m, 1H); 4.43 (d, 1H, *J* = 15.7 Hz); 4.71 (d, 1H, *J* = 15.7 Hz); 5.48 (br d, 1H, *J* = 10.3 Hz, overlapping); 5.89 (m, 1H); 7.15−7.39 (clpx. m, 5H, overlapping). ^{13}C NMR (100 MHz, $CDCl_3$) major isomer δ_C: −10.9; 17.9; 22.5; 28.7; 32.3; 48.8; 49.9; 125.6; 126.8; 128.3; 128.7; 133.9; 139.0; 171.8. Minor isomer δ_C: −10.6; 18.6; 22.2; 28.4; 33.2; 46.5; 54.7; 126.5; 126.9; 127.0; 127.1; 133.2; 139.5; 170.9. *m*/*z* (%): 77 (30), 79 (56), 81 (36), 91 (100), 96 (66), 106 (40), 120 (12), 138 (36), 148 (43), 165 (isotopic cluster, 33), 186 (35), 228 (54), 255 (11), 298 (isotopic cluster, 16), 312 (isotopic cluster, 17), 378 (isotopic cluster, 16). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{28}NOSn$ 394.1193, found 394.1190.

***N*-Benzyl-*N*-(6-(diphenylphosphoryl)cyclohex-2-en-1-yl)-acetamide (22b).** White wax. Isolated (10 mg, 5% yield) by radial thin-layer chromatography eluted with dichloromethane−methanol, 95:5. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H: 1.39 (s, 3H); 1.70 (br m, 2H); 2.08 (cplx. br m, 2H); 3.74 (br t, 1H, *J* = 10.8 Hz); 3.91 (d, 1H, *J* = 16.5 Hz); 4.36 (br s, 1H); 4.44 (d, 1H, *J* = 16.5 Hz); 5.37 (d, 1H, *J* = 9.7 Hz); 5.63 (br d, 1H, *J* = 9.7 Hz); 7.17−7.37 (cplx. m, 5H); 7.41−8.12 (cplx. m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ_C: 22.70 (overlapping); 24.5 (d, ^{C-P}J = 11.4 Hz); 34.5 (d, ^{C-P}J = 73.7 Hz); 55.1, 56.9 (d, ^{C-P}J = 3.5 Hz); 126.4; 127.4; 127.6; 128.4 (d, ^{C-P}J = 11.5 Hz); 128.71; 128.72 (d, ^{C-P}J = 10.8 Hz); 129.9 (d, ^{C-P}J = 9.1 Hz); 130.3 (d, ^{C-P}J = 9.2 Hz); 130.5 (d, ^{C-P}J = 8.8 Hz); 132.8 (d, ^{C-P}J = 93.2 Hz); 133.7 (d, ^{C-P}J = 90.8 Hz); 136.9. *m*/*z* (%): 183 (13), 184 (1), 185 (9), 201 (23), 202 (2), 203 (100), 281 (18), 282 (2), 388 (2). ESI-HRMS *m*/*z* $[M + H]^+$ calcd for $C_{27}H_{29}NO_2P$ 430.1936, found 430.1934.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H, ^{13}C, COSY, HSQC and HMBC NMR spectra for all compounds obtained. Optimized geometries of relevant species. This material is available free of charge via the Internet at http://pubs.acs.org/.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: adriana@fcq.unc.edu.ar. Phone: +54 (0)351 4334170/4334173. Fax: +54 (0)351 4333030/4334174.

Notes

The authors declare no competing financial interest.

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