JOC Article
pubs.acs.org/joc

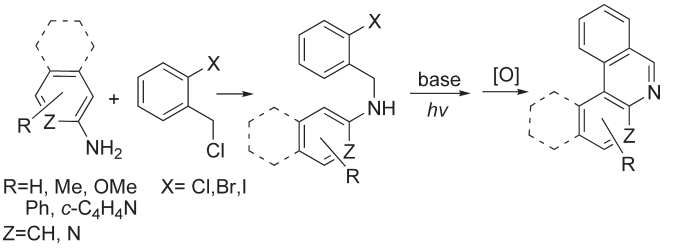
Electron-Transfer-Mediated Synthesis of Phenanthridines by Intramolecular Arylation of Anions from *N*-(*ortho*-Halobenzyl)arylamines: Regiochemical and Mechanistic Analysis

María E. Budén, Viviana B. Dorn, Martina Gamba, Adriana B. Pierini,* and Roberto A. Rossi*

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

rossi@fcq.unc.edu.ar

Received December 11, 2009



The synthesis of a series of substituted phenanthridines by photostimulated C−C cyclization of anions from *N*-(*ortho*-halobenzyl)arylamines has been found to proceed in very good to excellent yields (79−95%) in liquid ammonia and in DMSO. The *N*-(*ortho*-halobenzyl)arylamines are obtained in good to very good isolated yields (44−85%) by nucleophilic substitution of *ortho*-halobenzylchlorides with different arylamines. The reaction of the anions of a diverse set of *N*-(*ortho*-halobenzyl)arylamines was studied, and the methodology was extended to the synthesis of trispheridine, a natural product, in very good yield. In order to explain the regiochemical outcome of these reactions, a theoretical analysis was performed with DFT methods and the B3LYP functional.

Introduction

Phenanthridines are important core structures found in a variety of natural products and other biologically important molecules with a wide range of biological activities that confer applications as antibacterial, antiprotozoal, and anticancer agents, among others.[1] A well-known member of this family is ethidium (Figure 1), a common DNA intercalator. Trispheridine[2] and bicolorine,[3] also shown in Figure 1, are representative examples of natural products containing phenanthridine core structures.

Phenanthridines can be prepared by a number of methods including (i) cyclization of *N*-(*o*-halobenzyl)arylamines through a benzyne mechanism,[4] (ii) reduction of phenanthridones,[5] (iii) intramolecular radical cyclizations of *N*-(*o*-halobenzyl)arylamines,[6] (iv) photocyclization of benzanilides and benzylideneanilines,[7] (v) Bischler−Napieralsky and directed metalation for cyclization of 2-substituted biphenyls,[8] (vi) microwave-mediated [2 + 2 + 2] cyclotrimerization of a diyne,[9] (vii) different photochemical approaches,[10] and Pd

(1) (a) Phillips, S. D.; Castle, R. N. *J. Heterocycl. Chem.* **1981**, *18*, 223–232. (b) Ishikawa, T. *Med. Res. Rev.* **2001**, *21*, 61–72. (c) Denny, W. A. *Curr. Med. Chem.* **2002**, *9*, 1655–1665.

(2) Abdel-Halim, O. B.; Morikawa, T.; Ando, S.; Matsuda, H.; Yoshikawa, M. *J. Nat. Prod.* **2004**, *67*, 1119–1124.

(3) Viladomat, F.; Bastida, J.; Tribo, G.; Codina, C.; Rubiralta, M. *Phytochemistry* **1990**, *29*, 1307–1310.

(4) (a) Kessar, S. V.; Gupta, Y. P.; Balakrishnan, P.; Sawal, K. K.; Mohammad, T.; Dutt, M. *J. Org. Chem.* **1988**, *53*, 1708–1713. (b) Nakanishi, T.; Suzuki, M. *Org. Lett.* **1999**, *1*, 985–987. (c) Kessar, S. V.; Gopal, R.; Singh, M. *Tetrahedron* **1973**, *29*, 167–175. (d) Kessar, S. V.; Pal, D.; Singh, M. *Tetrahedron* **1973**, *29*, 177–184. (e) Sanz, R.; Fernández, Y.; Castroviejo, M. P.; Pérez, A.; Fañanás, F. J. *Eur. J. Org. Chem.* **2007**, *8*, 62–69. (f) Barluenga, J.; Fañanás, F. J.; Sanz, R.; Fernández, Y. *Chem.—Eur. J.* **2002**, *8*, 2034–2046.

(5) Narasimham, N. S.; Chandrachood, P. S. *Tetrahedron* **1981**, *37*, 825–827.

(6) (a) Nakanishi, T.; Suzuki, M.; Mashiba, A.; Ishikawa, K.; Yokotsuka, T. *J. Org. Chem.* **1998**, *63*, 4235–4239. (b) Rosa, A. M.; Lobo, A. M.; Branco, S. P.; Pereira, A. M. D. L. *Tetrahedron* **1997**, *53*, 269–284.

(7) Mallory, F. B.; Mallory, C. *Org. React.* **1984**, *30*, 1.

(8) (a) Mamalis, P.; Petrow, V. J. *J. Chem. Soc.* **1950**, 703–711. (b) Buu-Hoï, N. P.; Jaquignon, P.; Long, C. T. *J. Chem. Soc.* **1957**, 505–509. (c) Currie, K. S.; Tennant, G. *J. Chem. Soc., Chem. Commun.* **1995**, 2295–2296.

(9) Sripada, L.; Teske, J. A.; Deiters, A. *Org. Biomol. Chem.* **2008**, *6*, 263–265.

(10) (a) Kessar, S. V.; Grupta, Y. P.; Dhingra, K.; Sharma, G. S.; Narula, S. *Tetrahedron Lett.* **1977**, *18*, 1459–1462. (b) Androsov, D. A.; Neckers, D. C. *J. Org. Chem.* **2007**, *72*, 1148–1152. (c) Alonso, R.; Campos, P. J.; García, B.; Rodríguez, M. A. *Org. Lett.* **2006**, *8*, 3521–3523.

Published on Web 03/08/2010 DOI: 10.1021/jo9025918

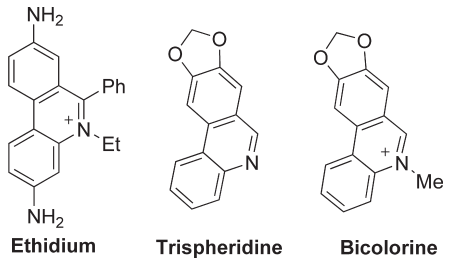


FIGURE 1. Selected phenanthridines.

catalysis routes.[11] They can also be obtained with other catalytic systems such as $In(OTf)_3$, in the annulation between *o*-alkynylanilines and *o*-alkynylbenzaldehydes,[12] or by the nickel-catalyzed iminoannulation of internal alkynes.[13] Another procedure is the preparation of phenanthridines using hypervalent iodine chemistry from *N*-(*o*-halobenzyl)-arylamines as starting materials.[14]

6-Arylphenanthridines can be obtained from aromatic aldehydes, anilines, and benzenediazonium-2-carboxylate via a one-pot cascade process that involves the sequence of imine and benzyne formation followed by a [4 + 2] cycloaddition and dehydrogenation.[15] Very recently, Kohno et al. reported a new synthetic strategy for antitumor benzo[*c*]phenanthridines using a microwave-assisted electrocyclic reaction of the aza-6π-electron system.[16] 6-Substituted phenanthridines were prepared in a one-pot procedure from 2-arylanilines and aryl aldehydes with trifluoroacetic acid with good to very good yields.[17]

Fagnou et al. developed new conditions employing electron-rich N-heterocyclic carbene (NHC) ligands to promote direct arylation of a broad range of aryl chlorides to form six- and five-membered ring biaryls.[11f] Recently, the Lautens group investigated a C−H activation/cross-coupling approach toward the synthesis of diversely substituted phenanthridine derivatives, whereby a sequence of ortho-arylation and subsequent N-arylation would provide the desired compounds in one step.[18]

Although a number of useful synthetic procedures to prepare these compounds have been developed,[4−18] still several limitations remain, as well. For example, an efficient synthetic method applicable to various phenanthridines has not been developed.[19] Most of the procedures involve several steps, and the overall yields are usually not very good.[20] Moreover, the starting materials are not often readily available. Thus, a simple, efficient, and general method to synthesize phenanthridines would be attractive.

The unimolecular radical nucleophilic substitution, or $S_{RN}1$ mechanism, stands as an interesting synthetic alternative to phenanthridines. The mechanism, a chain process with radical and radical anions as intermediates, affords the possibility to achieve the nucleophilic substitution of compounds poorly reactive in polar processes. The scope of the reaction has increased considerably over the past decades, and nowadays, it serves as an important synthetic route to different types of compounds. It is compatible with many substituents, and moreover, several nucleophiles, such as carbanions and heteroatomic anions, can be used to form new C−C or C−heteroatom bonds in good yields.[21] One exception to this regiospecificity is the reaction of the anions of aromatic amines with aromatic substrates in which both C−N and C−C bond formation is achieved instead. For instance, the *intermolecular* reaction of the phenylamide anion with iodobenzene initiated by K metal in liquid ammonia afforded diphenylamine (19%) and 2- (11%) and 4-biphenylamines (11%).[22] When 2-naphthylamide ions reacted by the photostimulated $S_{RN}1$ mechanism with iodoarenes, 1-aryl-2-naphthylamines were regioselectively formed in 45−63% yields, with only 3−6% N-arylation.[23] Additionally, the anions of aza-heterocycles such as pyrrole and 4-methylimidazole gave only C−C bond formation.[24,25]

Furthermore, an $S_{RN}1$ synthetic strategy to obtain heterocyclic compounds was developed based on the *intramolecular* cyclization of substrates bearing both the leaving group and the nucleophilic center.[26] This methodology has recently been applied to the synthesis of 1-phenyl-1-oxazolinoindan derivatives and related compounds,[27] tetracyclic isoquinoline derivatives,[28] a series of substituted 9*H*-carbazoles,[29] and aporphine and homoaporphine alkaloids.[30]

Beugelmans et al. applied this method to the synthesis of a series of benzo[*c*]phenanthridines by reaction of substituted iodobenzylamines with substituted tetralones. In this case, an intermolecular $S_{RN}1$ affords the products with modest overall yields after several reactions.[31]

Recently, we have proposed a new approach for the syntheses of phenanthridines and benzophenanthridines by intramolecular ortho-arylation of benzylamide ions with aryl halides.[32]

(11) (a) Shabashov, D.; Daugulis, O. *J. Org. Chem.* **2007**, *72*, 7720–7725. (b) Li, D.; Zhao, B.; LaVoie, E. J. *J. Org. Chem.* **2000**, *65*, 2802–2805. (c) Xie, C.; Zhang, Y.; Huang, Z.; Xu, P. *J. Org. Chem.* **2007**, *72*, 5431–5434. (d) Bowman, W. R.; Lyon, J. E.; Gareth, J. P. *Synlett* **2008**, *14*, 2169–2171. (e) Banwell, M. G.; Lupton, D. W.; Ma, X.; Renner, J.; Sydnes, M. O. *Org. Lett.* **2004**, *6*, 2741–2744. (f) Campeau, L.-C.; Thansandote, P.; Fagnou, K. *Org. Lett.* **2005**, *7*, 1857–1860. (g) Campeau, L. C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581–590.

(12) Yanada, R.; Hashimoto, K.; Tokizane, R.; Miwa, Y.; Minami, H.; Yanada, K.; Ishikura, M.; Takemoto, Y. *J. Org. Chem.* **2008**, *73*, 5135–5138.

(13) Luo, Y.; Mei, Y.; Zhang, J.; Lua, W.; Tang, J. *Tetrahedron* **2006**, *62*, 9131–9134.

(14) Moreno, I.; Tellitu, I.; Etayo, J.; San Martín, R.; Dominguez, E. *Tetrahedron* **2001**, *57*, 5403–5411.

(15) Wang-Ge, S.; Yun-Yun, Y.; Yan-Guang, W. *J. Org. Chem.* **2006**, *71*, 9241–9243.

(16) Kohno, K.; Azuma, S.; Choshi, T.; Nobuhiro, J.; Hibino, S. *Tetrahedron Lett.* **2009**, *50*, 590–592.

(17) Youn, S. W.; Bihn, J. H. *Tetrahedron Lett.* **2009**, *50*, 4598–4601.

(18) Lautens, M.; Candito, D. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 6713–6716.

(19) (a) Hilt, G.; Hess, W.; Schmidt, F. *Eur. J. Org. Chem.* **2005**, 2526–2533. (b) Mehta, B. K.; Yanagisawa, K.; Shiro, M.; Kotsuki, H. *Org. Lett.* **2003**, *5*, 1605–1608.

(20) Ilka, K.; Bernd, C. *Synthesis* **2005**, *7*, 1052–1054.

(21) For reviews, see: (a) Rossi, R. A.; Pierini, A. B.; Peñéñory, A. B. *Chem. Rev.* **2003**, *103*, 71–168. (b) Rossi, R. A.; Pierini, A. B.; Santiago, A. N. In *Organic Reactions*; Paquette, L. A., Bittman, R., Eds.; Wiley & Sons: New York, 1999; pp 1−271. (c) Rossi, R. A. In *Synthetic Organic Photochemistry*; Griesberck, A. G., Mattay, J., Eds.; Marcel Dekker: New York, 2005; Vol. 12, Chapter 15, pp 495−527.

(22) Kim, J. K.; Bunnet, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 7464–7466.

(23) Pierini, A. B.; Baumgartner, M. T.; Rossi, R. A. *Tetrahedron Lett.* **1987**, *28*, 4653–4656.

(24) Chahma, M.; Combellas, C.; Thiébault, A. *Synthesis* **1994**, 366–368.

(25) Chahma, M.; Combellas, C.; Thiébault, A. *J. Org. Chem.* **1995**, *60*, 8015–8022.

(26) Rossi, R. A.; Baumgartner, M. T. Synthesis of Heterocycles by the $S_{RN}1$ Mechanism. In *Targets in Heterocyclic System: Chemistry and Properties*; Attanasi, O. A., Spinelli, D., Eds.; Soc. Chimica. Italiana: Rome, Italy, 1999; Vol. 3, pp 215−243.

(27) Marshall, L. J.; Roydhouse, M. D.; Slawin, A. M. Z.; Walton, J. C. *J. Org. Chem.* **2007**, *72*, 898–911.

(28) Roydhouse, M. D.; Walton, J. C. *Eur. J. Org. Chem.* **2007**, 1059–1063.

(29) Budén, M. E.; Vaillard, V. A.; Martín, S. E.; Rossi, R. A. *J. Org. Chem.* **2009**, *74*, 4490–4498.

(30) Barolo, S. M.; Teng, X.; Cuny, G. D.; Rossi, R. A. *J. Org. Chem.* **2006**, *71*, 8493–8499.

(31) Beugelmans, R.; Chastanet, J.; Ginsburg, H.; Quintero-Cortes, L.; Roussi, G. *J. Org. Chem.* **1985**, *50*, 4933–4938.

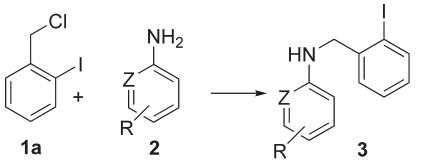
(32) For a preliminary communication, see: Budén, M. E.; Rossi, R. A. *Tetrahedron Lett.* **2007**, *48*, 8739–8742.

In order to address the overall performance of the new methodology, to find the best conditions for the syntheses, and to evaluate its scope and limitations, we now report new applications directed to the synthesis of substituted phenanthridines. Furthermore, ab initio calculations are presented to inspect the electronic and geometric factors responsible for the regiochemistry of these reactions.

Results and Discussion

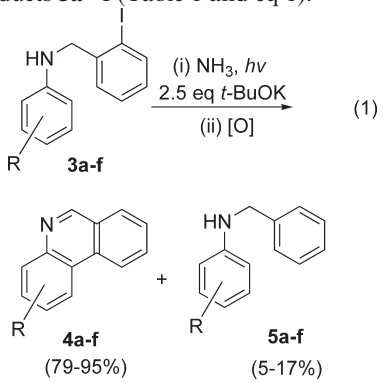
The nucleophilic substitution reaction of anilines with benzylchloride was described as a synthetic method to obtain benzylanilines.[33] We use this reaction to prepare the expected *o*-haloarylbenzylamines. When we carried out the reaction of 2-iodobenzylchloride (**1a**) with aniline (**2a**) using $NaHCO_3$ as base, *N*-(2-iodobenzyl)benzenamide (**3a**) was obtained in 85% isolated yield (Scheme 1). With the same procedure, the substituted nucleophilic reaction of **1a** and anilines **2b**−**h** afforded the corresponding *N*-(*ortho*-iodobenzyl)arylamines, **3b**−**h**, in 44−85% isolated yields.

SCHEME 1



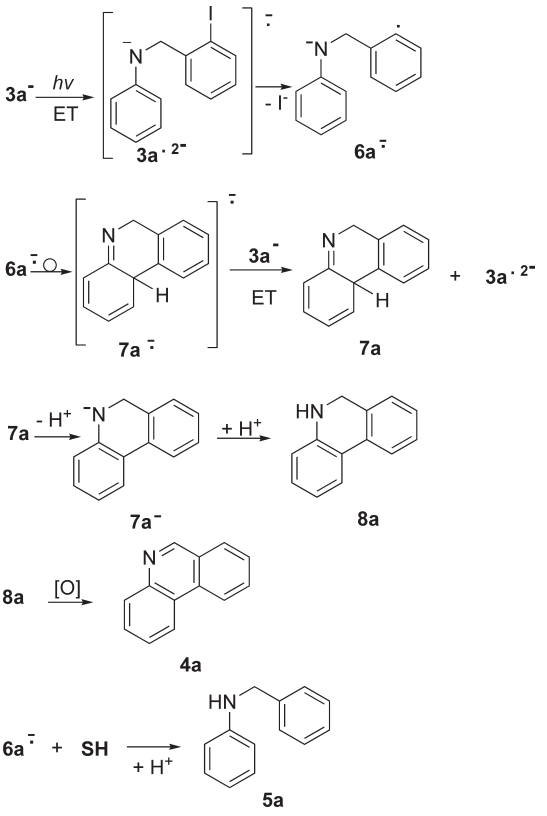
2	R	Z	3	yield %
a	H	CH	a	85
b	2-CH_3	CH	b	72
c	4-CH_3	CH	c	75
d	2-OCH_3	CH	d	78
e	4-OCH_3	CH	e	85
f	2-Ph	CH	f	82
g	2-N	CH	g	69
h	H	N	h	44

The results of the photostimulated reaction (120 min) of *N*-(*ortho*-iodobenzyl)arylamines **3a**−**h** in liquid ammonia and in the presence of excess *t*-BuOK (2.5 equiv) are presented in Table 1. Under these reaction conditions, the anions **3a**−**f**$^-$ afford high yields of phenanthridines **4a**−**f** and low yield of the reduced products **5a**−**f** (Table 1 and eq 1).



There was no reaction in the dark (180 min), thus excluding a benzyne mechanism. Besides, partial inhibition was observed when **3a**$^-$ was irradiated in the presence of 1,4-dinitrobenzene, a well-known inhibitor of $S_{RN}1$ reactions (entries 2 and 3, Table 1). These results indicate that product **4a** could be formed by the $S_{RN}1$ mechanism following the steps presented in Scheme 2. Compound **3a** affords, in the presence of excess *t*-BuOK, the amide anion **3a**$^-$. The initiation step is attributed to a photoinduced ET to **3a**$^-$ to yield its radical dianion **3a**$^{\bullet 2-}$.[34] Fragmentation of the C−I bond of **3a**$^{\bullet 2-}$ gives the distonic radical anion **6a**$^{\bullet -}$ and the I^- anion. The intermediate radical anion **6a**$^{\bullet -}$, via an intramolecular C−C cyclization, yields the conjugated radical anion **7a**$^{\bullet -}$. An ET from **7a**$^{\bullet -}$ to **3a**$^-$ affords the intermediate **7a** and the radical dianion **3a**$^{\bullet 2-}$, which propagates the reaction cycle. Under the basic reaction conditions, intermediate **7a** gives the anion **7a**$^-$. Upon acidification of the reaction media and workup, product **8a** was not isolated; instead, the oxidized aromatized product **4a** was obtained.

SCHEME 2



A reaction that competes with the cyclization of the radical anion **6a**$^{\bullet -}$ is the reduction by hydrogen abstraction from the solvent to yield **5a**.

The reaction was not inhibited by radical traps, such as di-*tert*-butyl nitroxide or TEMPO (entries 4 and 5, Table 1). This suggests that the intramolecular cyclization of the distonic radical anion **6a**$^{\bullet -}$ is faster than the intermolecular reaction with the radical traps. When the reaction was carried out with only 1 equiv of *t*-BuOK, 74% of **4a** was

(33) *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; John Wiley & Sons: New York, 1989; p 902.

(34) Under excess *t*-BuO^-, this anion as well as phenylamide ions can act as electron donors in this step. Probably, *t*-BuO^- (pK_a of *t*-BuOH = 32.2 in DMSO) is a better electron donor than phenylamide ions (pK_a of $PhNH_2$ = 30.6 in DMSO). See: Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456−463 and references cited therein.

TABLE 1. Intramolecular Photostimulated Reactions of *o*-Haloarylbenzylanilines in Liquid Ammonia: Syntheses of Phenanthridines[a]

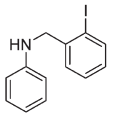
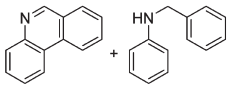
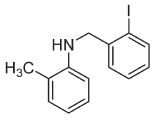
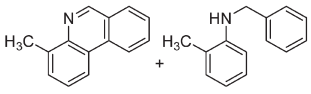
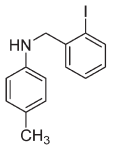
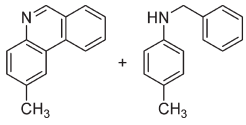
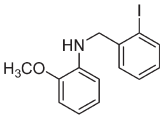
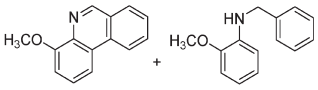
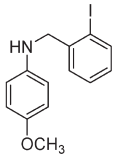
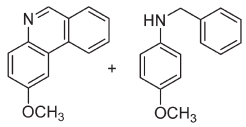
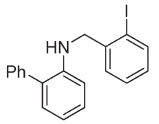
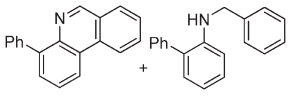
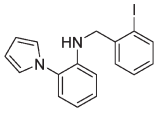
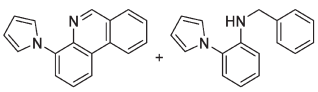
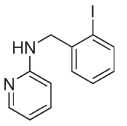
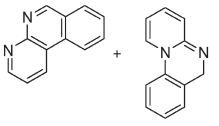
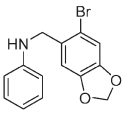
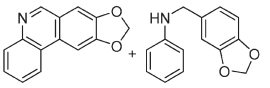
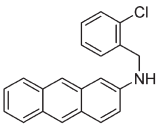
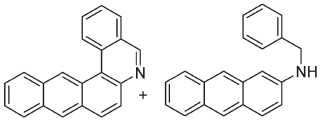
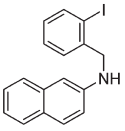
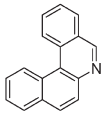
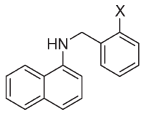
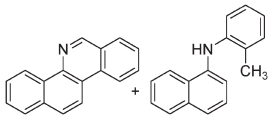
Entry	Substrate	Conditions	Products	Products (Yield %)[b]	X^- %[c]
1		*hv*, 120 min		**4a** (90) **5a** (9)	97
2[d]		dark, 180 min		**4a** (--) **5a** (--)	< 7
3[e]		*hv*, 120 min		**4a** (32) **5a** (2)	38
4[f]	**3a**	*hv*, 120 min	**4a** **5a**	**4a** (85) **5a** (8)	89
5[g]		*hv*, 120 min		**4a** (88) **5a** (4)	88
6[h]		*hv*, 120 min		**4a** (68) **5a** (18)	97
7[i]		*hv*, 120 min		**4a** (74) **5a** (13)	90
8	 **3b**	*hv*, 120 min	 **4b** **5b**	**4b** (79) **5b** (14)	93
9	 **3c**	*hv*, 120 min	 **4c** **5c**	**4c** (84) **5c** (10)	95
10	 **3d**	*hv*, 120 min	 **4d** **5d**	**4d** (82) **5d** (17)	94
11	 **3e**	*hv*, 120 min	 **4e** **5e**	**4e** (95) **5e** (5)	100
12	 **3f**	*hv*, 120 min	 **4f** **5f**	**4f** (87) **5f** (10)	95
13[j]	 **3g**	*hv*, 120 min	 **4g** **5g**	**4g** (83) **5g** (10)	96

TABLE 1. Continued

Entry	Substrate	Conditions	Products	Products (Yield %)[b]	X^- %[c]
14		*hv*, 180 min		**4h** (6) **11** (61)	83
15[d]		dark, 180 min		**4h** (--) **11** (--)	12
	3h		**4h** **11**		
16		*hv*, 120 min		**4i** (75) **5i** (10)	92
	3i		**4i** **5i**		
17[k]		*hv*, 180 min		**15** (72) **16** (12)	100
	12		**15** **16**		
18		*hv*, 60 min		**17** (98)	100
	13		**17**		
19[l]					
	14a, X=I	*hv*, 120 min	**19** **20**	**19** (84) **20** (8)	96
20[d]		dark, 180 min	**19** **20**	**19** (--) **20** (--)	<7
21[m]		*hv*, 120 min	**19** **20**	**19** (59) **20** (11)	80
22[h,l]		*hv*, 120 min	**19** **20**	**19** (93) **20** (3)	98
23	**14b**, X=Br	*hv*, 180 min	**19** **20**	**19** (55) **20** (34)	91
24	**14c**, X=Cl	*hv*, 180 min	**19** **20**	**19** (53) **20** (41)	100
25[d]		dark, 180 min	**19** **20**	**19** (--) **20** (--)	<6
26[m]		*hv*, 120 min	**19** **20**	**19** (41) **20** (17)	82
27[n]		*hv*, 120 min	**19** **20**	**19** (44) **20** (17)	83
28[h,o]		*hv*, 180 min	**19** **20**	**19** (60) **20** (27)	98

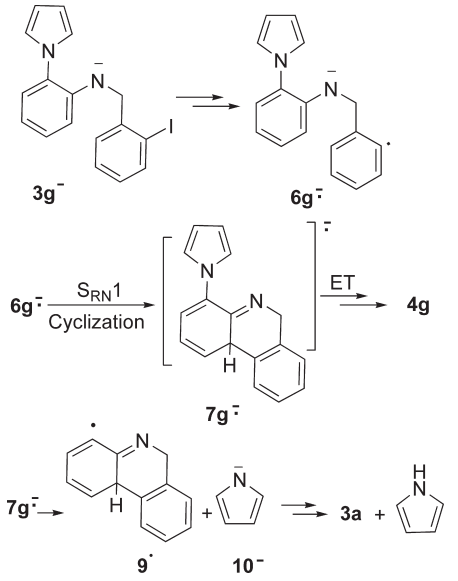
[a]The reactions were performed in 150 mL of liquid ammonia (or in 6 mL of DMSO), with 0.25 mmol of the substrate and 0.625 mmol of *t*-BuOK. Irradiation was conducted in a photochemical reactor equipped with two 400 W Hg lamps emitting maximally at 350 nm (air and water refrigerated). [b]Yields were determined by GC (internal standard method). [c]Halide anions were determined potentiometrically. [d]The substrate was recovered almost quantitatively. [e]1,4-Dinitrobenzene (27 mol %) was added. The substrate was recovered in 39%. [f]Di-*tert*-butylnitroxide was added (30% mol). [g]TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) was added (38% mol). [h]DMSO as solvent. [i]With 0.25 mmol of *t*-BuOK, the substrate was recovered in 8%. [j]Phenanthridine was obtained in 7% yield. [k]5,6-Dihydronaphtho[2,3-*a*]phenanthridine was detected. [l]Traces of reduced product (1-naphthylbenzylamine) was obtained. [m]1,4-Dinitrobenzene (30 mol %) was added. [n]1,3-Dinitrobenzene (30 mol %) was added. [o]Reduced product (20% 1-naphthylbenzylamine) was obtained.

formed with 13% of **5a** (entry 7). In DMSO as solvent, **4a** and **5a** were obtained in 68 and 18% yields, respectively (entry 6).

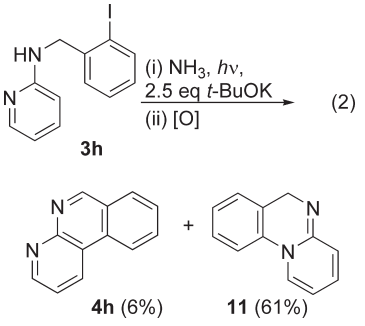
In the photostimulated reaction in liquid ammonia of anion $\mathbf{3g}^-$, prepared from **3g** and *t*-BuOK in excess, and after 120 min of irradiation, 4-(1*H*-pyrrol-1-yl)phenanthridine (**4g**) was

obtained in 83% yield together with phenanthridine **3a** in 7% yield (entry 13, Table 1). In this system, we propose that once the conjugated radical anion $\mathbf{7g}^{\bullet-}$ is formed it can give **4g** or can fragment into radical $\mathbf{9}^{\bullet}$ and the pyrrole anion $\mathbf{10}^{-}$ to finally afford **3a** (Scheme 3). This is the first report showing that the anion of pyrrole can act as a leaving group under the reported reaction conditions.

SCHEME 3



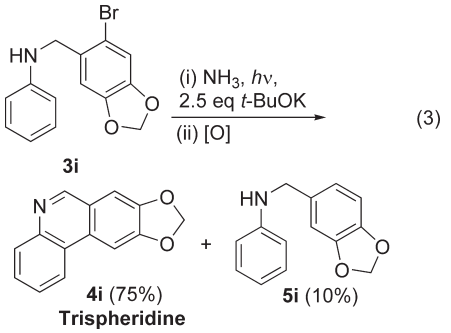
After 180 min of irradiation, in liquid ammonia, anion $\mathbf{3h}^{-}$ afforded benzo[*c*][1,8]naphthyridine **4h** and the isomeric product 6*H*-pyrido[1,2-*a*]quinazoline **11** in 6 and 61% isolated yield, respectively (entry 14, Table 1, and eq 2). In dark conditions (180 min), there was no reaction (entry 15).



(2)

The experimental behavior of the system was investigated by molecular modeling calculations with the DFT methodology and the B3LYP functional. In order to study the system at first, we inspected the conformations in equilibrium of anion $\mathbf{3h}^{-}$.[35] The only conformer found ($\mathbf{3h}$-*syn*$^{-}$) is responsible to give, after DET (dissociative electron transfer) and C−I bond fragmentation, the more stable conformer of the distonic radical anion $\mathbf{6h}$-*syn*$^{\bullet-}$ (Figure 2), evaluated with the 6-31+G* basis set. This radical anion affords, after internal rotations, the conjugated radical anion $\mathbf{11}^{\bullet-}$ (C−N cyclization) with activation energy (ΔE) of ≈6.6 kcal/mol. The conformer $\mathbf{6h}$-*anti*$^{\bullet-}$, which affords the conjugated radical anion $\mathbf{7h}^{\bullet-}$ by a C−C coupling, can only be formed from $\mathbf{6h}$-*syn*$^{\bullet-}$ with ΔE of ≈16.0 kcal/mol (Figure 2). This *syn*−*anti* isomerization barrier is high because it involves the rotation around the C_2(pyridine)−N_3 bond, which has partial double-bond character. These theoretical results explain the regiochemistry observed experimentally.

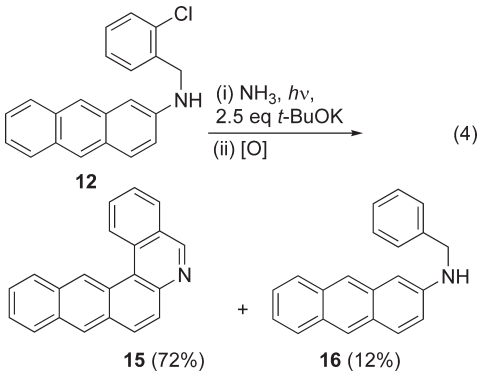
The development of this convenient and efficient synthetic route to phenanthridines led us to test it as a synthetic route to trispheridine, a phenanthridine alkaloid from the *Amaryllidaceae* plant family. In so doing, we evaluated the reactivity of *N*-(*ortho*-iodobenzyl)arylamine **3i**, which was prepared in 62% isolated yield by a nucleophilic substitution reaction of aniline with 5-bromo-6-(bromomethyl)benzo[*d*]-[1,3]dioxole. In the photostimulated reaction of **3i** with 2.5 equiv of *t*-BuOK in NH_3 for 120 min, trispheridine (**4i**) was obtained in 75% yield (entry 16 and eq 3).



(3)

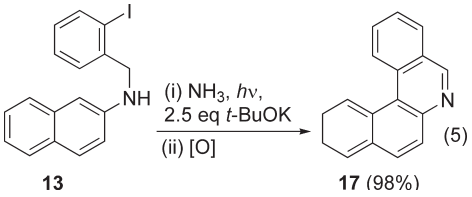
Furthermore, other *N*-(*ortho*-halobenzyl)arylamines **12**, **13**, and **14a**−**c** (Table 1) were obtained from 2-halobenzylchloride and the corresponding arylamines in very good isolated yields (62−91%).

In the photoinitiated reaction of anion $\mathbf{12}^{-}$ in liquid ammonia as a solvent (180 min), the novel naphtho[2,3-*a*]-phenanthridine (**15**) was formed in 72% yield (entry 17, Table 1, and eq 4). This reaction provides access to the pentacyclic system **15** in very good yields.



(4)

Using this methodology, the photostimulated reaction of *N*-(2-iodobenzyl)naphthalen-2-amine (**13**) gave 98% yield of benzo[*a*]phenanthridine **17** (entry 18, Table 1, and eq 5).



(5)

(35) Supporting Information shows a detailed reactions pathway and intermediates of these processes.

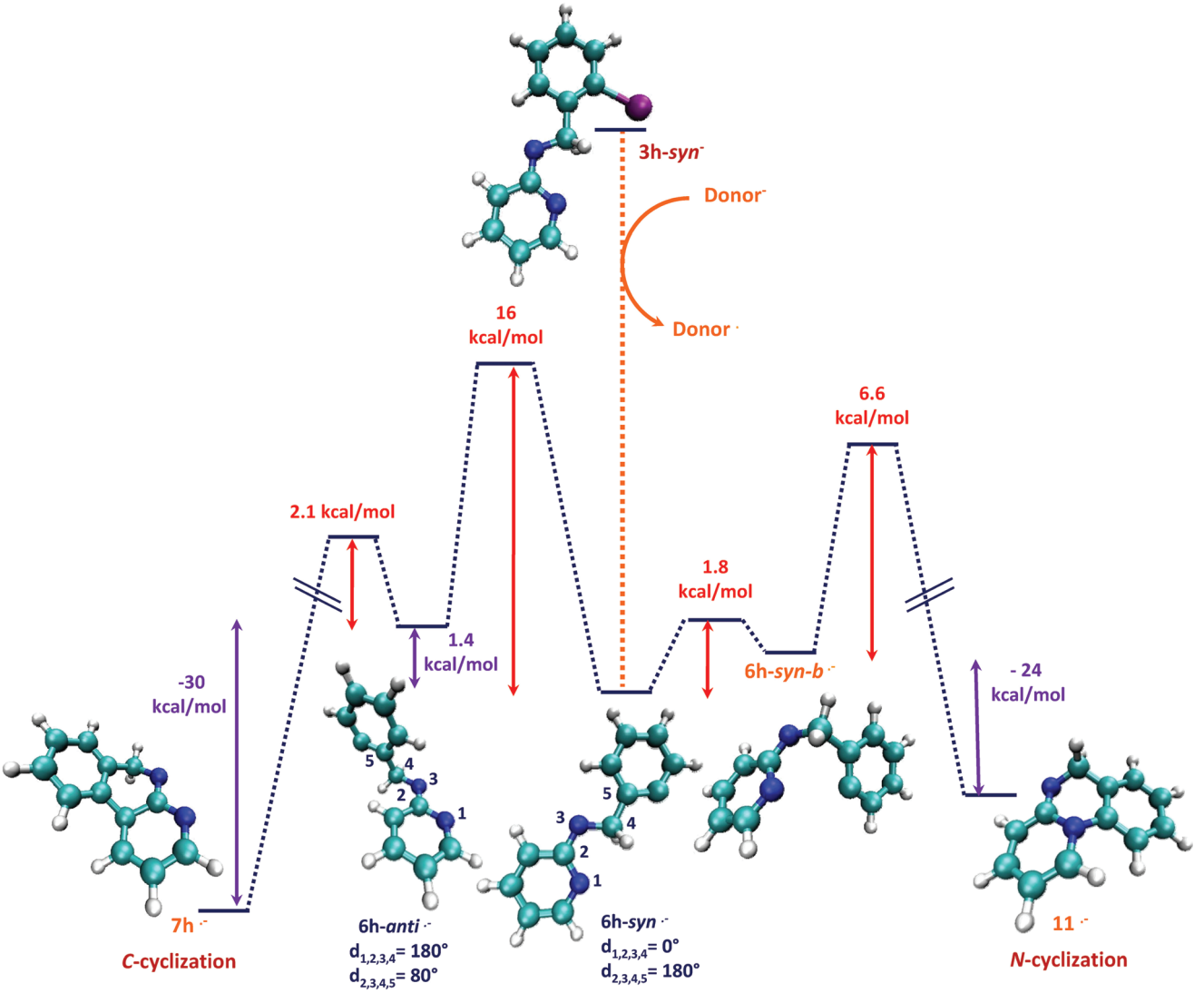
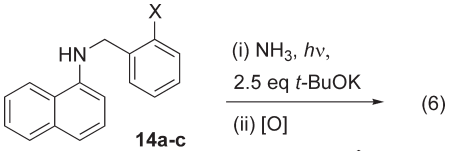
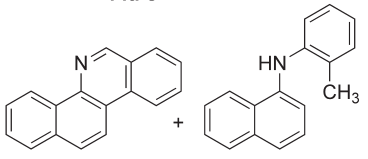


FIGURE 2. Formation of radical anions by ET to the anion of **3h**$^-$. Anion (upper part, B3LYP/3-21G*X=I). Radical anions (lower part, B3LYP/6-31+G*). All calculations include the solvent as a continuum model (Tomassi et al.). Distinguished reaction coordinates: from **6h-*syn***$^{\bullet-}$ to **6h-*syn*-b**$^{\bullet-}$, rotation around the N_3-C_4 and C_4-C_5 bonds; from **6h-*syn***$^{\bullet-}$ to **6h-*anti***$^{\bullet-}$, rotation around the C_2-N_3 bond (more details are in the Supporting Information). Donor: *t*-BuO^- (initiation step) or **11**$^{\bullet-}$ and **7h**$^{\bullet-}$ (along propagation steps).

The regiochemistry of this reaction can also be explained through theoretical calculations, as shown in Figure 3. Radical anion **18-*syn***$^{\bullet-}$, formed after DET to **13**$^-$, presents as **6h**$^{\bullet-}$ a *syn* conformation with a $C_1C_2NC_4$ dihedral angle of approximately 0° (Figure 3). This dihedral angle favors the coupling at C_1 to yield **17** (ΔE = 2.0 kcal/mol). The absence of coupling at C_3 of the naphthalene ring is ascribed to the high activation barrier to form the radical anion **18-*anti***$^{\bullet-}$ (17.3 kcal/mol).

All other substrates investigated, **14a**, **14b**, and **14c**, yielded the expected ring closure product benzo[*c*]phenanthridine **19** and a rearranged product **20** in varying yields (eq 6, and entries 19−28, Table 1). As shown, the nature of the leaving group influences the relative ratio of both products. No reaction was observed in the dark (entries 20 and 25).





	19	20
14a	84%	8%
14b	55%	34%
14c	53%	41%

As previously proposed, ET to the anions **14**$^-$ may form the dianion radicals, which by C−X bond fragmentation

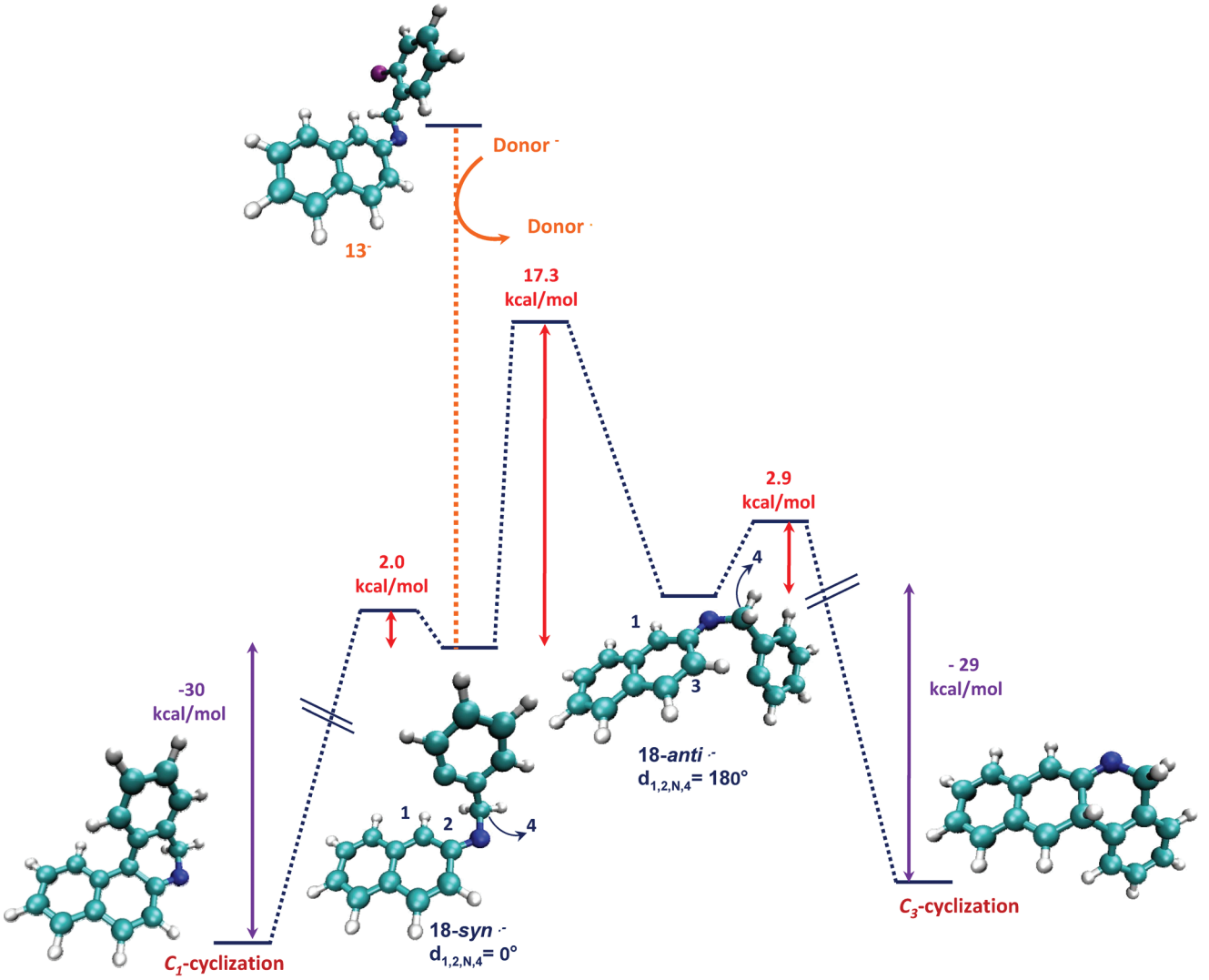
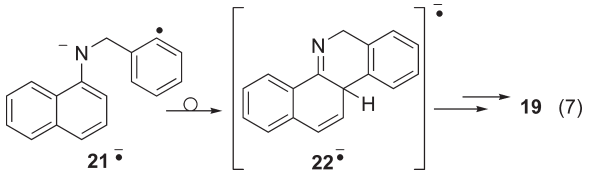


FIGURE 3. Formation of radical anions by ET to the anion of **13**$^-$. Anion (upper part, B3LYP/LANL2DZ, X = I). Radical anions (lower part, B3LYP/6-31+G*. All calculations include the solvent as a continuum model (Tomassi et al.). Distinguished reaction coordinates: from **18-*syn***$^{\bullet-}$ to **18-*anti***$^{\bullet-}$, C_2-N. Donor: *t*-BuO^- (initiation step) or C_1-cyclization$^{\bullet-}$ (along propagation steps).

gives the distonic radical anion **21**$^{\bullet-}$, which by an intramolecular coupling followed by ET to the substrate will finally give product **19** (eq 7).



Taking into account that there are precedents about ring opening of cyclic radical anions to give benzyl radicals and an anionic center,[36] we propose that the formation of the rearranged product **20** is mediated by the conjugate radical anion **23**$^{\bullet-}$, which is formed by intramolecular cyclization at the nucleophilic N of intermediate **21**$^{\bullet-}$ (eq 8). The formation of **20** is inhibited by the presence of *p*-DNB and *m*-DNB

(36) Postigo, A.; Rossi, R. A. *J. Chem. Soc., Perkin. Trans. 2* **2000**, 485–490.

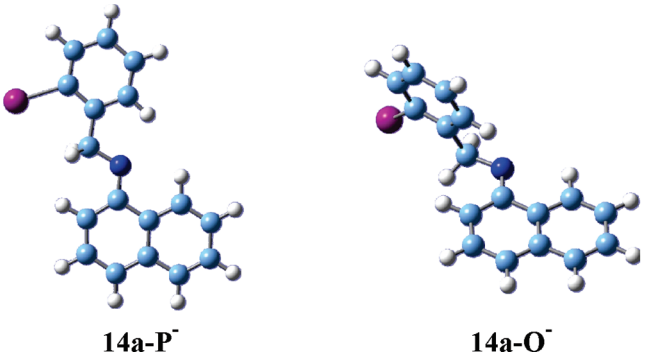


FIGURE 4. Main conformers for anions **14a**$^-$ (X = I) evaluated by B3LYP/LANL2DZ in the presence of a continuum solvent (methanol), **14a-P**$^-$ (planar anion), **14a-O**$^-$ (out of plane anion).

(Table 1, entries 26 and 27). Moreover, compounds **19** and **20** were observed when the reaction was carried out by solvated electron initiation (Na metal in $NH_{3(l)}$), which is strong evidence favoring a radical anion intermediate route to

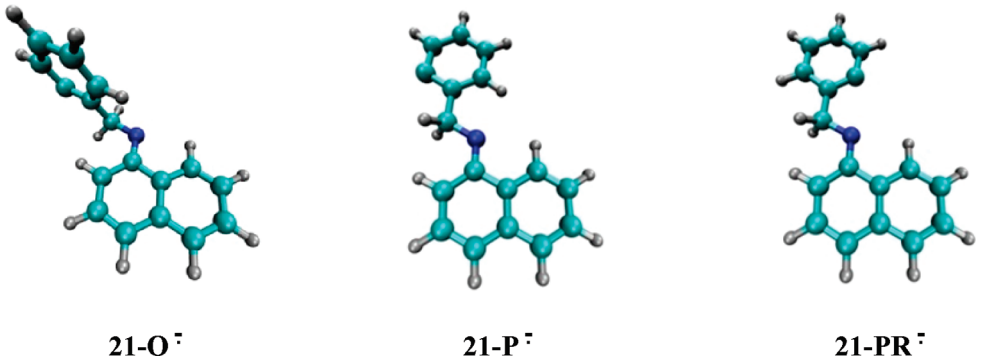
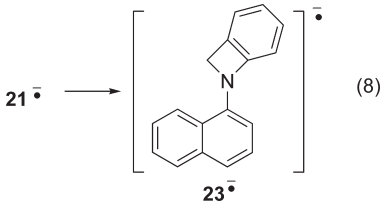
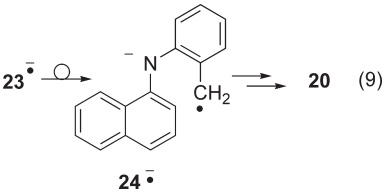


FIGURE 5. Conformers for radicals anions **21-O**$^{\bullet-}$, **21-P**$^{\bullet-}$, and **21-PR**$^{\bullet-}$ evaluated by B3LYP/6-31+G* in the presence of a continuum solvent (methanol).

account for their formation. Intermediate **23**$^{\bullet-}$ may suffer ring opening to give the distonic radical anion **24**$^{\bullet-}$ (eq 9); the driving force of the reaction is the stability of the diaryl amide moiety and the benzyl radical. Intermediate **24**$^{\bullet-}$ will finally afford byproduct **20** by H abstraction and protonation.

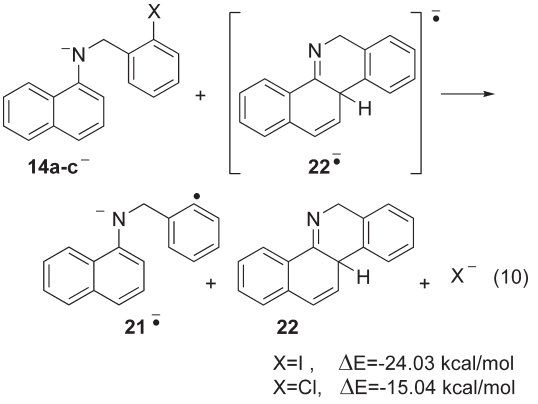




Furthermore, we evaluated the reactivity of **14a** and **14c** in DMSO as a solvent. In this case, the photoinitiated reaction afforded benzo[*c*]phenanthridine in 93 and 60% yield, respectively (entries 22 and 28, Table 1).

In order to inspect the feasibility of the different steps of the proposed mechanism (eqs 7−9), DFT calculations were carried out for anions **14a**$^-$ and **14c**$^-$ taken as representatives. The systematic inspection of the conformational potential energy surface (PES) of both anions leads us to conclude that mainly two conformers, **P** (benzyl system on the naphthyl *plane*) and **O** (benzyl system *out* of the naphthyl plane), are present under conformational equilibrium (Figure 4).

On the basis of the energy differences between them, **P** prevails for both anions (90%, X = I, 96%, X = Cl). The ET to **14a**,**c**$^-$ from **22**$^{\bullet-}$, the intermediate proposed as propagator of the $S_{RN}1$ cycle, is evaluated as a dissociative exothermic reaction that leads to the distonic radical anions **21**$^{\bullet-}$ (eq 10).[37]



The different conformers evaluated for **21**$^{\bullet-}$ are presented in Figure 5. The nonplanar radical anion **21-O**$^{\bullet-}$, formed by dissociation from **14a**,**c-O**$^-$, cyclizes with very low activation energy to form **22**$^{\bullet-}$, the radical anion of the carbon−carbon cyclized product (Figure 6).

As can be seen from Figure 5, the planar radical anion **21-P**$^{\bullet-}$ can give **21-O**$^{\bullet-}$ (by rotation around the H_2C-N bond)[35] or can give the planar radical anion **21-PR**$^{\bullet-}$ (by rotation around the $C_{Ph}-CH_2$ bond). From these intermediates, **21-PR**$^{\bullet-}$ has the appropriate geometry to afford **20** (X = Br (34%), Cl

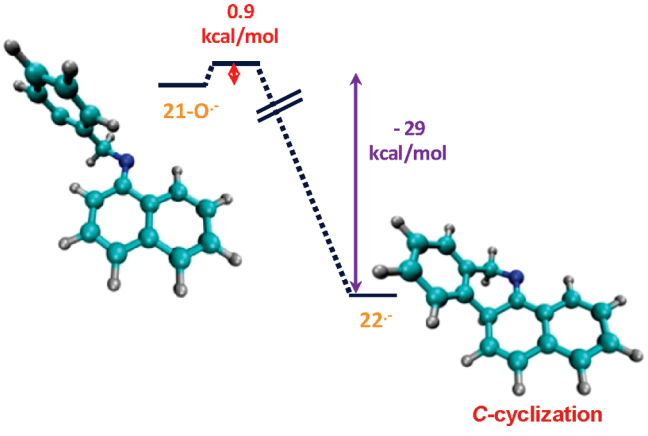


FIGURE 6. C-Cyclization from **21-O**$^{\bullet-}$ evaluated by B3LYP/6-31+G* in the presence of a continuum solvent (methanol).

(37) Although no radical dianions are located on the anionic potential surfaces for both halogens with the LANL2DZ basis set, radical dianion intermediates are obtained with the 6-31+G* basis set for X = Cl. These intermediates dissociate with the following E_a values: 1.5 kcal/mol for **14c-O**$^{\bullet 2-}$ and 4.5 kcal/mol for **14c-P**$^{\bullet 2-}$.

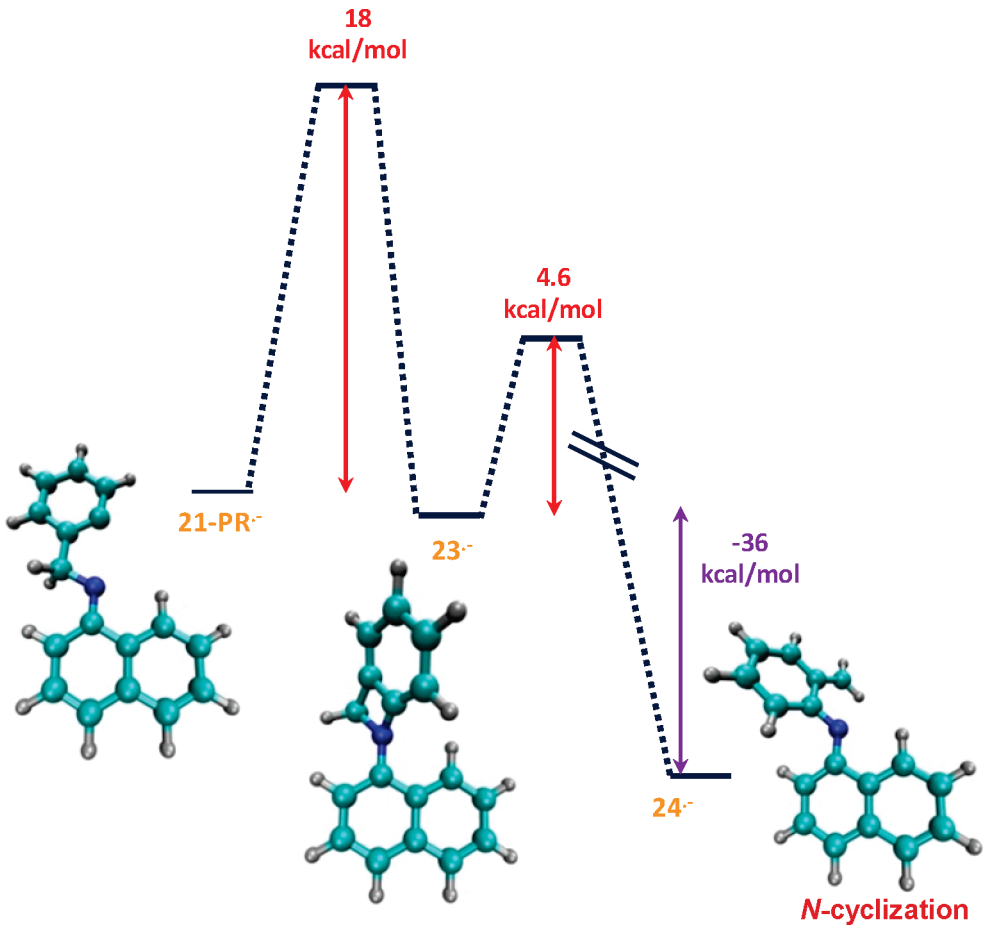


FIGURE 7. N-Cyclization from **21-PR**$^{\bullet-}$ evaluated by B3LYP/6-31+G* in the presence of a continuum solvent (methanol).

(41%)) following the rearrangement routes propose in eqs 8 and 9 (Figure 7). The formation of **24**$^{\bullet-}$ from **21-PR**$^{\bullet-}$ is a highly exothermic reaction, more exothermic than the C-cyclization route (Figures 6 and 7, respectively). However, the activation energy evaluated in going from **21-PR**$^{\bullet-}$ to **23**$^{\bullet-}$ seems too high to compete with internal rotations or with C-cyclization, and these B3LYP studies fail to explain this experimental outcome under the conditions simulated in the calculation, that is, free radical anions in a continuum media or in the presence of discrete solvent (NH_3) molecules.[38] A possibility of this failure could be related to the existence of specific halogen effects that cannot be modeled under our computational design.

Conclusions

In summary, in this work, we present a simple and transition-metal-free method for the synthesis of phenanthridine, substituted phenanthridine, benzophenanthridine, and naphthophenanthridine using readily available *N*-(*ortho*-halobenzyl)arylamines as starting materials. The synthesis of tri-

(38) (a) The activation energy from 21-PR$^{\bullet-}$ to 23$^{\bullet-}$ was also evaluated (16.7 kcal/mol) by inclusion of seven discrete molecules of solvent (NH_3) (see ref 38b). (b) The position of the solvent molecules was obtained from classical molecular dynamic simulations of the anion (B3LYP geometry) within a box containing 8671 NH_3 molecules. The dynamics were run with the Amber program. The parameter file was generated with the Gaff Amber facility.

spheridine, a natural product, was carried out in a very good yield. The synthetic strategy involves a first step nucleophilic substitution of different anilines with 2-iodobenzylchloride followed by an $S_{RN}1$ substitution reaction in NH_3 or DMSO as solvent under photoinitiation.

The $S_{RN}1$ mechanism accounts for the substitution reactions, and the products are obtained in very good yields. Considering the availability and/or simplicity of the starting materials, and the mild conditions of the procedure, we have demonstrated that this can be a general methodology for the synthesis of this family of compounds.

The computational calculations seem to be a successful approach for studying the conformational equilibrium of anions and the distonic radical anions as well as to explain the regiochemistry of C−C or C−N six-membered cyclizations observed experimentally for pyridine, 1-naphthyl, and 2-napthyl systems in the presence of a solvent modeled as a continuum. On the other hand, the theoretical design used proved to be unsuccessful to explain the products from rearrangements observed in the naphthyl system.

Experimental Section

Computational Procedure. All calculations were performed with the Gaussian03 program. First, the most stable conformers of the anions RX^- (X = Cl, I) were evaluated through an AM1 conformational search by scanning the two or three main torsion angles (see Supporting Information). The conformers

thus obtained were then refined with complete geometry optimization within the B3LYP[39] DFT functional, the 6-31+G* basis set for the chlorine compounds, and the LANL2DZ[40] basis set for the chlorine and iodine compounds. This effective core potential (ECP) basis set[41] was previously used in the evaluation of the anionic surfaces of halobenzenes and afforded results of acceptable quality in the comparison of electronic properties of PhI with respect to PhX (X = F, Cl, Br).[42]

The radical anions formed, once the halides are released, were fully optimized with the same functional and the 6-31+G* basis set. The geometries thus found were used as starting points for the evaluation of the potential surface of the different reaction steps with the same functional and the latter basis set and the reaction coordinate approach.

The effect of NH_3 as polar protic solvent was evaluated for all of the DFT calculations through Tomasi's polarized continuum model (PCM),[43] as implemented in Gaussian03, using methanol and complete geometry optimization. The inclusion of the solvent in the calculations is a requisite to evaluate valence radical anions.[44]

The characterization of stationary points was done by Hessian matrix calculations. The energy informed for TSs, anions, and radical anions includes zero-point corrections.

Synthesis of *N*-(2-Iodobenzyl)benzenamine (3a): The following procedure is representative of all of these reactions. Aniline (273 μL, 3 equiv), 100.8 mg of $NaHCO_3$ (1.2 equiv), and 0.5 mL of H_2O were added to a 10 mL round-bottom flask fitted with a reflux condenser. The solution was heated to 100−110 °C, stirred vigorously, and 2-iodobenzylchloride **1a** (1 equiv, 252.5 mg) was added slowly. The heating and stirring continued for a further 180 min. The solution was then allowed to cool. The content was dissolved with water and then extracted with CH_2Cl_2. The organic extract was dried with anhydrous $MgSO_4$. The solvent (CH_2Cl_2) was then evaporated, and the aniline was distilled under reduced pressure using a Kügelrohr apparatus.

The amine **3a** was purified by column chromatography on silica gel eluting with a petroleum ether/dichloromethane gradient (100:0 → 70:30) and recrystallized from petroleum ether/diethyl ether as white crystals and isolated in 85% yield (262.6 mg): mp 62.0−64.0 °C (lit.[45] 66−68 °C); ^{1}H NMR (CCl_3D) δ 4.17 (1H, s br), 4.32 (2H, d, J = 5.5 Hz), 6.58−6.62 (2H, m), 6.72 (1H, tt, ^1J = 7.3 Hz, ^2J = 1.1 Hz), 6.96 (1H, td, ^1J = 7.7 Hz, ^2J = 1.8 Hz), 7.12−7.21 (2H, m), 7.31 (1H, dd, ^1J = 7.3 Hz, ^2J = 1.1 Hz), 7.38 (1H, dd, ^1J = 7.7 Hz, ^2J = 1.8 Hz), 7.85 (1H, dd, ^1J = 8.0 Hz, ^2J = 1.1 Hz); ^{13}C NMR (CCl_3D) δ 53.2, 98.5, 113.0, 117.8, 128.4, 128.8, 128.9, 129.3, 139.5, 141.0, 147.6; GC-MS (m/z) 310 (M^+ + 1, 14), 309 (M^+, 99), 308 (20), 218 (10), 217 (100), 207 (10), 183 (19), 182 (81), 181 (19), 180 (74), 179 (6), 178 (6), 167 (10), 165 (21), 154 (6), 153 (7), 152 (10), 151 (7), 128 (6), 127 (13), 107 (13), 106 (69), 105 (10), 104 (26), 102 (8), 92 (17), 91 (39), 90 (76), 89 (39), 78 (20), 77 (78), 76 (25), 75 (6), 65 (17), 64 (11), 63 (15), 62 (6), 52 (7), 51 (33), 50 (11).[46]

***N*-(2-Iodobenzyl)-2-methylaniline (3b):** *o*-Toluidine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **3b** was purified by column chromatography on silica gel eluting with a petroleum ether/diethyl ether gradient (100:0 → 70:30) and recrystallized from petroleum ether as white crystals and isolated in 72% yield (465.1 mg, 1.44 mmol): mp 74.0−75.0 °C; ^{1}H NMR (CD_3COCD_3) δ 2.24 (3H, s), 4.38 (2H, d, J = 5.8 Hz), 5.10 (1H, s br), 6.34 (1H, d, J = 8.0 Hz), 6.57 (1H, t, J = 7.5 Hz), 6.94−7.04 (3H, m), 7.31 (1H, t, J = 7.5 Hz), 7.38 (1H, d, J = 7.5 Hz), 7.88 (1H, dd, ^1J = 8.0 Hz, ^2J = 1.0 Hz); ^{13}C NMR (CD_3COCD_3) δ 17.9, 53.5, 98.8, 110.7, 117.6, 122.8, 127.7, 129.2, 129.3, 129.7, 130.8, 140.2, 142.3, 146.7; GC-MS (m/z) 324 (M^+ + 1, 13), 323 (M^+, 100), 217 (74), 96 (24), 195 (11), 194 (40), 181 (23), 180 (23), 120 (37), 118 (25), 106 (31), 91 (45), 90 (45), 89 (23), 77 (16), 65 (19); HRMS (ESI/APCI) calcd for $C_{14}H_{15}NI$ 324.0249, found 324.0242.

***N*-(2-Iodobenzyl)-4-methylbenzenamine (3c):** *p*-Toluidine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **3c** was purified by column chromatography on silica gel eluting with a petroleum ether/diethyl ether gradient (100:0 → 85:15) and recrystallized from petroleum ether as white crystals and isolated in 75% yield (485.1 mg, 1.50 mmol): mp 51.0−52.0 °C; ^{1}H NMR (CD_3COCD_3) δ 2.16 (3H, s), 4.28 (2H, d, J = 6.0 Hz), 5.38 (1H, s br), 6.51 (2H, d, J = 8.5 Hz), 6.91 (2H, d, J = 8.3 Hz), 6.98−7.02 (1H, m), 7.33 (1H, t, J = 7.3 Hz), 7.41 (1H, d, J = 7.3 Hz), 7.87 (1H, d, J = 7.8 Hz); ^{13}C NMR (CD_3COCD_3) δ 20.8, 54.2, 99.2, 114.0, 126.8, 129.6, 129.8, 130.0, 130.7, 140.6, 143.0, 147.4; GC-MS (m/z) 324 (M^+ + 1, 11), 323 (M^+, 100), 322 (9), 217 (59), 196 (30), 195 (15), 194 (51), 181 (29), 180 (26), 120 (48), 118 (13), 106 (9), 91 (50), 90 (46), 89 (24), 77 (22), 65 (22), 63 (13), 51 (11); HRMS (ESI/APCI) calcd for $C_{14}H_{15}NI$ 324.0244, found 324.0246.

***N*-(2-Iodobenzyl)-2-methoxybenzenamine (3d):** *o*-Anisidine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **3d** was purified by column chromatography on silica gel eluting with a petroleum ether/diethyl ether gradient (100:0 → 90:10) as white crystals and isolated in 78% yield (528.8 mg, 1.56 mmol): mp 59.0−61.0 °C; ^{1}H NMR (CCl_3D) δ 3.87 (3H, s), 4.34 (2H, s), 4.79 (1H, s br), 6.47 (1H, d, J = 7.8 Hz), 6.66−6.70 (1H, m), 6.79−6.83 (2H, m), 6.94−6.97 (1H, m), 7.24−7.30 (1H, m), 7.36 (1H, d, J = 7.5 Hz), 7.85 (1H, d, J = 7.8 Hz); ^{13}C NMR (CCl_3D) δ 52.9, 55.5, 98.4, 109.5, 110.2, 116.8, 121.2, 128.3, 128.5, 128.8, 137.6, 139.3, 141.0, 146.8; GC-MS (m/z) 340 (M^+ + 1, 15), 339 (M^+, 100), 324 (23), 217 (48), 210 (12), 196 (12), 180 (22), 136 (17), 120 (16), 94 (12), 92 (11), 91 (11), 90 (27), 89 (13), 77 (11), 65 (16); HRMS (ESI/APCI) calcd for $C_{14}H_{15}INO$ 340.0193, found 340.0198.

***N*-(2-Iodobenzyl)-4-methoxybenzenamine (3e):** *p*-Anisidine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **3e** was purified by column chromatography on silica gel eluting with a petroleum ether/diethyl ether gradient (100:0 → 90:10) as white crystals and isolated in 85% yield (576.3 mg, 1.70 mmol): mp 47.0−49.0 °C; ^{1}H NMR (CCl_3D) δ 3.75 (3H, s), 3.97 (1H, s br), 4.29 (2H, s), 6.57−6.61 (2H, m), 6.77−6.81 (2H, m), 6.98 (1H, td, ^1J = 7.2 Hz, ^2J = 1.2 Hz), 7.31 (1H, td, ^1J = 7.2 Hz, ^2J = 1.2 Hz), 7.40 (1H, dd, ^1J = 7.5 Hz, ^2J = 1.2 Hz), 7.87 (1H, dd, ^1J = 7.8 Hz, ^2J = 1.2 Hz); ^{13}C NMR (CCl_3D) δ 54.1, 55.8, 98.6, 114.3, 114.9, 128.4, 128.88, 128.91, 139.5, 141.2, 141.9, 152.4; GC-MS (m/z) 340 (M^+ + 1, 14), 339 (M^+, 100), 337 (36), 324 (11), 322 (14), 217 (44), 210 (20), 207 (16), 196 (13), 168 (10), 167 (28), 166 (10), 136 (11), 122 (99), 95 (11), 91 (13), 90 (25), 89 (17), 77 (12), 64 (14), 63 (18); HRMS (ESI/APCI) calcd for $C_{14}H_{15}INO$ 340.0193, found 340.0187.

***N*-(2-Iodobenzyl)biphenyl-2-amine (3f):** Biphenyl-2-amine was distilled under reduced pressure using a Kügelrohr apparatus, and the amine **3f** was purified by column chromatography on silica gel eluting with a petroleum ether/dichloromethane gradient (100:0 → 70:30) and recrystallized from diethyl ether as

(39) (a) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785–789. (b) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098–3100. (c) Miehlich, B.; Savin, A.; Stoll, H.; Preuss, H. *Chem. Phys. Lett*. **1989**, *157*, 200–206.

(40) D95V for carbon and hydrogen atoms. See: Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaefer, H. F., III, Ed.; ; Plenum: New York, 1976; Vol. 3, pp 1−28. Los Alamos ECP plus DZ on Na-La, Hf-Bi for iodine: Hay, S. P. J.; Wadt, W. R. *J. Chem. Phys*. **1985**, *82*, 270–283.

(41) Hay, P. J.; Wadt, W. R. *J. Chem. Phys*. **1985**, *82*, 270–271.

(42) Pierini, A. B.; Vera, D. M. A. *J. Org. Chem*. **2003**, *68*, 9191–9199.

(43) (a) Miertus, S.; Scrocco, E.; Tomasi *J. Chem. Phys*. **1981**, *55*, 117–129. (b) Miertus, S.; Tomasi *J. Chem. Phys*. **1982**, *65*, 239–245. (c) Cossi, M.; Barone, V.; Cammi, R.; Tomasi *J. Chem. Phys. Lett*. **1996**, *255*, 327–335.

(44) Puiatti, M.; Vera, D. M. A.; Pierini, A. B. *Phys. Chem. Chem. Phys*. **2009**, *11*, 9013–9024.

(45) Parisien, M.; Valette, D.; Fagnou, K. *J. Org. Chem*. **2005**, *70*, 7578–7584.

(46) Park, Y.-T.; Kim, K.-S.; Lee, I-H; Goo, C.-H.; Park, Y.-C. *Bull. Korean Chem. Soc*. **1993**, *14*, 152–153.

white crystals and isolated in 82% (315.7 mg): mp 98.8−100.2 °C; ^{1}H NMR (DMSO-d_6) δ 4.22 (2H, s), 5.37 (1H, s br), 6.34 (1H, d, J = 7.5 Hz), 6.67 (1H, s), 7.01−7.07 (3H, m), 7.33−7.48 (7H, m), 7.85 (1H, d, J = 5.5 Hz); ^{13}C NMR (DMSO-d_6) δ 52.1, 98.6, 110.5, 116.7, 127.0, 127.1, 128.2, 128.4, 128.5, 128.9, 129.1, 130.2, 139.1, 139.2, 140.9, 144.2; GC-MS (m/z) 386 ($M^+ + 1$, 18), 385 (M^+, 100), 258 (27), 257 (13), 256 (34), 254 (10), 232 (11), 217 (26), 182 (24), 181 (10), 180 (57), 168 (40), 167 (45), 166 (15), 165 (10), 152 (21), 139 (10), 128 (10), 127 (13), 91 (17), 90 (37), 89 (19), 77 (7), 65 (6).[32]

***N*-(2-Iodobenzyl)-2-(1*H*-pyrrol-1-yl)benzenamine (3g):** *o*-Pyrrolylaniline was distilled under reduced pressure using a Kügelrohr apparatus. The amine **3g** was purified by column chromatography on silica gel eluting with a petroleum ether/CH_2Cl_2 gradient (85:15 → 65:35) as white crystals and isolated in 69% yield (516.1 mg, 1.38 mmol): mp 127.0−128.0 °C; ^{1}H NMR (CCl_3D) δ 4.32 (2H, d, J = 5.8 Hz), 4.45 (1H, s br), 6.39−6.41 (2H, m), 6.61 (1H, d, J = 7.9 Hz), 6.79 (1H, t, J = 7.6 Hz), 6.90−6.92 (2H, m), 6.98−7.02 (1H, m), 7.20−7.24 (2H, m), 7.28−7.35 (2H, m), 7.87 (1H, d, J = 7.6 Hz); ^{13}C NMR (CCl_3D) δ 52.7, 98.2, 109.5, 111.5, 116.9, 121.9, 127.1, 127.2, 128.1, 128.3, 128.9, 128.9, 139.5, 140.2, 143.0; GC-MS (m/z) 375 ($M^+ + 1$, 16), 374 (M^+, 100), 373 (43), 247 (12), 245 (23), 217 (25), 180 (17), 171 (28), 169 (18), 157 (68), 156 (23), 91 (14), 90 (27), 89 (15), 77 (14); HRMS (ESI/APCI) calcd for $C_{17}H_{16}IN_2$ 375.0353, found 375.0357.

***N*-(2-Iodobenzyl)pyridin-2-amine (3h):** The pyridine-2-amine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **3h** was purified by column chromatography on silica gel eluting with a petroleum ether/diethyl ether gradient (75:25 → 50:50) as yellow crystals and isolated in 44% yield (272.8 mg, 0.88 mmol): mp 98.0−100.0 °C; ^{1}H NMR (CCl_3D) δ 4.56 (2H, d, J = 5.5 Hz), 6.29 (1H, s), 6.53 (1H, ddd, ^1J = 7.0 Hz, ^2J = 5.0 Hz, ^3J = 0.9 Hz), 6.58 (1H, dd, ^1J = 8.4 Hz, ^2J = 0.7 Hz), 7.00 (1H, dt, ^1J = 7.8 Hz, ^2J = 1.7 Hz), 7.33 (1H, td, ^1J = 7.5 Hz, ^2J = 1.1 Hz), 7.37−7.44 (2H, m), 7.86 (1H, dd, ^1J = 7.9 Hz, ^2J = 1.1 Hz), 7.99 (1H, dd, ^1J = 5.0 Hz, ^2J = 1.0 Hz); ^{13}C NMR (CCl_3D) δ 51.1, 98.6, 106.9, 113.4, 128.4, 128.8, 129.0, 137.5, 139.5, 140.9, 148.2, 158.3; GC-MS (m/z) 310 (M^+, 5), 184 (14), 183 (100), 182 (11), 181 (19), 91 (17), 90 (14), 89 (10), 79 (11), 78 (21), 51 (9); HRMS (ESI/APCI) calcd for $C_{12}H_{12}IN_2$ 311.0040, found 311.0048.

***N*-(2-Chlorobenzyl)anthracen-2-amine (12):** The amine **12** was purified by column chromatography on silica gel eluting with a petroleum ether/CH_2Cl_2 gradient (80:20 → 50:50) as yellow crystals and isolated in 72% yield (456.5 mg, 1.44 mmol): mp 144.0−146.0 °C; ^{1}H NMR (CD_3COCD_3) δ 4.63 (2H, d, J = 5.7 Hz), 6.01 (1H, t, J = 5.4 Hz), 6.79 (1H, d, J = 2.1 Hz), 7.22 (1H, dd, ^1J = 9.1 Hz, ^2J = 2.3 Hz), 7.25−7.34 (3H, m), 7.34−7.41 (1H, m), 7.44−7.52 (1H, m), 7.53−7.61 (1H, m), 7.87 (2H, d, J = 9.0 Hz), 7.93 (1H, d, J = 8.3 Hz), 8.06 (1H, s), 8.29 (1H, s); ^{13}C NMR (CD_3COCD_3) δ 46.8, 102.6, 122.5, 124.0, 125.2, 127.0, 127.8, 128.9, 129.1, 129.4, 130.0, 130.3, 130.9, 131.0, 131.2, 131.3, 134.4, 134.8, 135.8, 138.6, 147.3; GC-MS (m/z) 319 ($M^+ + 2$, 23), 318 (15), 317 (M^+, 67), 283 (8), 282 (35), 280 (21), 192 (16), 176 (8), 166 (14), 165 (100), 125 (10), 89 (5); HRMS (ESI/APCI) calcd for $C_{21}H_{17}ClN$ 318.1044, found 318.1048.

***N*-(2-Iodobenzyl)naphthalen-2-amine (13):** 2-Naphthylamine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **13** was purified by column chromatography on silica gel eluting with a petroleum ether/diethyl ether gradient (90:10 → 70:30) as a yellow crystal and isolated in 80% yield (287.2 mg): mp 73.0 °C (decomposed); ^{1}H NMR (CCl_3D) δ 4.29 (1H, s br), 4.40 (2H, s), 6.74 (1H, d, J = 2.2 Hz), 6.89 (1H, dd, ^1J = 8.8 Hz, ^2J = 2.2 Hz), 6.97 (1H, dd, ^1J = 7.7 Hz, ^2J = 1.8 Hz), 7.14−7.41 (4H, m), 7.54−7.67 (3H, m), 7.86 (1H, dd, ^1J = 8.0 Hz, ^2J = 1.1 Hz); ^{13}C NMR (CCl_3D) δ 53.2, 98.6, 105.0, 117.7, 122.2, 126.0, 126.3, 127.6, 128.4, 128.8, 129.0, 135.1, 139.5, 140.7, 145.2; GC-MS (m/z) 360 ($M^+ + 1$, 12), 359 (M^+, 62), 233 (10), 232 (50), 231 (32), 230 (100), 229 (12), 217 (44), 215 (19), 202 (15), 156 (21), 128 (18), 127 (38), 126 (10), 116 (14), 115 (69), 114 (10), 91 (13), 90 (43), 89 (23), 77 (14), 63 (16), 51 (10).[32]

***N*-(2-Iodobenzyl)naphthalen-1-amine (14a):** 1-Naphthylamine was distilled under reduced pressure using a Kügelrohr apparatus. The amine **14a** was purified by column chromatography on silica gel eluting with a petroleum ether/CH_2Cl_2 gradient (90:10 → 70:30) as a yellow crystal and isolated in 74% yield (531.4 mg): mp 102−103 °C; ^{1}H NMR (CCl_3D) δ 4.49 (2H, s), 4.88 (1H, s br), 6.50 (1H, d, J = 7.2 Hz), 6.98 (1H, t, J = 7.5 Hz), 7.23−7.32 (3H, m), 7.39−7.46 (3H, m), 7.79−7.89 (3H, m); ^{13}C NMR (CCl_3D) δ 53.3, 98.7, 105.0, 117.8, 119.8, 123.3, 124.8, 125.7, 126.5, 128.4, 128.7, 128.8, 129.0, 134.3, 139.5, 140.6, 142.6; GC-MS (m/z) 361 ($M^+ + 2$, 2), 360 ($M^+ + 1$, 15), 359 (M^+, 100), 233 (11), 232 (50), 231 (28), 230 (90), 217 (66), 215 (22), 202 (12), 154 (10), 142 (28), 128 (13), 127 (26), 126 (9), 116 (9), 115 (68), 114 (11), 101 (10), 91 (11), 90 (34), 89 (20), 77 (10), 63 (9); HRMS (ESI/APCI) calcd for $C_{17}H_{15}IN$ 360.0249, found 360.0245.

***N*-(2-Chlorobenzyl)naphthalen-1-amine (14c):** The amine **14c** was purified by column chromatography on silica gel eluting with a petroleum ether/dichloromethane gradient (100:0 → 50:50) and recrystallized from petroleum ether/dichloromethane as white crystals in 91% (242.6 mg): mp 109.0−110.2 °C; ^{1}H NMR (CCl_3D) δ 4.49 (2H, s), 4.69 (1H, s br), 6.63 (1H, d, J = 7.5 Hz), 7.24−7.46 (8H, m), 7.78−7.83 (2H, m); ^{13}C NMR (CCl_3D) δ 46.1, 105.1, 117.9, 119.8, 123.4, 124.8, 125.7, 126.5, 126.9, 128.5, 128.7, 129.1, 129.6, 133.4, 134.3, 136.2, 142.6; GC-MS (m/z) 269 ($M^+ + 2$, 25), 268 (15), 267 (M^+, 70), 266 (11), 265 (5), 233 (8), 232 (48), 230 (25), 156 (6), 154 (8), 143 (8), 142 (61), 140 (6), 129 (7), 128 (16), 127 (44), 126 (13), 125 (73), 116 (11), 115 (100), 114 (9), 102 (6), 101 (11), 99 (6), 89 (24), 77 (10), 75 (7), 63 (10), 51 (6).[32]

Representative Procedure for Photostimulated Reactions: Preparation of Phenanthridine (4a) in Liquid Ammonia. The following procedure is representative of all of these reactions. Liquid ammonia (150 mL), previously dried over Na metal, was distilled into a 250 mL three-necked, round-bottomed flask equipped with a coldfinger condenser and a magnetic stirrer under a nitrogen atmosphere. The base *t*-BuOK (2.5 equiv, 56.0 mg) and then the substrate *N*-(2-iodobenzyl)aniline (**3a**) (1 equiv, 61.8 mg) were added to the liquid ammonia, and the solution was irradiated for 120 min. Irradiation was conducted in a reactor equipped with two 400 W lamps emitting maximally at 350 nm (refrigerated with air and water). The reaction was quenched with an excess of ammonium nitrate, and the liquid ammonia was allowed to evaporate. Water was added to the residue, and the mixture was extracted with CH_2Cl_2 (3 × 30 mL). The organic extract was dried over anhydrous $MgSO_4$ then filtered, and the solvent was removed to leave the crude products. The products were separated and isolated by radial thin-layer chromatography on silica gel. In other similar experiments, the products were quantified by GC by using the internal standard method. The yield of halide ions in the aqueous solution was determined potentiometrically.

4-Phenylphenanthridine (4f): The product **4f** was purified by column chromatography on silica gel eluting with a petroleum ether/dichloromethane gradient (80:20 → 0:100): white crystals; ^{1}H NMR (CCl_3D) δ 7.46 (1H, tt, ^1J = 7.4 Hz, ^2J = 1.3 Hz), 7.53−7.57 (2H, m), 7.73−7.81 (5H, m), 7.89−7.93 (1H, m), 8.07 (1H, d, J = 8.0 Hz), 8.65 (1H, dd, ^1J = 7.8 Hz, ^2J = 2.0 Hz), 8.70 (1H, d, J = 8.3 Hz), 9.32 (1H, s); ^{13}C NMR (CCl_3D) δ 121.7, 122.1, 124.5, 126.1, 126.6, 127.2, 127.5, 127.9, 128.6, 130.0, 130.7, 130.9, 132.7, 140.1, 141.7, 142.0, 153.1; GC-MS (m/z) 256 ($M^+ + 1$, 5), 255 (M^+, 35), 254 (100), 253 (9), 252 (9), 127 (34), 126 (10), 112 (10).[32]

4-(1*H*-Pyrrol-1-yl)phenanthridine (4g): The product was purified by radial thin-layer chromatography on silica gel eluting with petroleum ether/diethyl ether (95:5): white crystals; mp 97.0−98.5 °C; ^{1}H NMR (CCl_3D) δ 6.46 (2H, t, J = 2.2 Hz), 7.28 (2H, dd, ^1J = 8.1 Hz, ^2J = 6.0 Hz), 7.72−7.78 (3H, m), 7.89−7.93 (1H, m), 8.07 (1H, d, J = 8.0 Hz), 8.55−8.58 (1H, m), 8.66 (1H, d, J = 8.3 Hz), 9.34 (1H, s); ^{13}C NMR (CCl_3D) δ 109.3, 120.7, 122.2, 123.4, 124.4, 125.4, 126.3, 126.7, 128.0, 128.8, 131.2, 132.3, 138.5, 139.1, 153.6; GC-MS (m/z) 245 (M^+ + 1, 14), 244 (M^+, 83), 243 (100), 242 (12), 217 (12), 151 (7), 122 (22); HRMS (ESI/APCI) calcd for $C_{17}H_{13}N_2$ 245.1073, found 245.1080.

Benzo[*c*][1,8]naphthyridine (4h): The product was purified by radial thin-layer chromatography on silica gel eluting with methanol: yellow oil; ^{1}H NMR (CCl_3D) δ 7.66 (1H, dd, ^1J = 8.0 Hz, ^2J = 4.4 Hz), 7.79−7.83 (1H, m), 7.93−7.97 (1H, m), 8.15 (1H, d, J = 8.0 Hz), 8.62 (1H, d, J = 8.0 Hz), 8.96 (1H, d, J = 8.0 Hz), 9.12 (1H, dd, ^1J = 4.6 Hz, ^2J = 1.9 Hz), 9.56 (1H, s); ^{1}H−^{1}H COSY NMR (CCl_3D) δH/δH 7.81/7.95, 7.81/8.15, 7.96/8.15, 8.14/8.62, 7.96/8.62, 7.83/8.62, 7.66/8.90, 7.65/9.12, 8.90/9.12, 8.62/9.56; ^{1}H−^{13}C HSQC NMR (CCl_3D) δH/δC 7.66/122.1, 7.81/128.6, 7.96/131.6, 8.15/129.3, 8.63/122.2, 8.96/131.8, 9.12/151.5, 9.56/157.4; ^{1}H−^{13}C HMBC NMR (CCl_3D) δH/δC 7.66/151.5, 7.81/122.1, 7.81/126.5, 7.96/129.3, 7.96/132.9, 8.16/131.8, 8.15/157.4, 8.62/126.5, 8.62/128.6, 9.56/126.6, 9.56/129.3, 9.56/132.7; GC-MS (m/z) 181 (M^+ + 1, 13), 180 (M^+, 100), 179 (44), 153 (12), 152 (10), 127 (11), 126 (11), 90 (8), 76 (8), 63 (9); HRMS (ESI/APCI) calcd for $C_{12}H_9N_2$ 181.0760, found 181.0765.

6*H*-Pyrido[1,2-*a*]quinazoline (11): The product was purified by radial thin-layer chromatography on silica gel eluting with petroleum ether/diethyl ether (80:20): yellow oil; ^{1}H NMR (CD_3COCD_3) δ 5.05 (2H, s), 6.77 (1H, dd, ^1J = 7.1 Hz, ^2J = 5.0 Hz), 6.85 (1H, d, J = 8.3 Hz), 6.91 (1H, t, J = 7.5 Hz), 7.13 (1H, d, J = 7.6 Hz), 7.19 (1H, d, J = 7.0 Hz), 7.24 (1H, t, J = 7.7 Hz), 7.56−7.68 (1H, m), 8.21 (1H, d, J = 4.8 Hz); ^{13}C NMR (CD_3COCD_3) δ 59.7, 107.2, 109.3, 114.9, 121.0, 121.2, 128.3, 131.1, 137.7, 148.7, 152.4, 155.9; ^{1}H−^{1}H COSY NMR (CD_3COCD_3) δH/δH 6.77/6.85, 6.77/7.64, 6.77/8.21, 6.85/7.64, 6.85/8.21, 6.91/7.13, 6.91/7.19, 6.91/7.24, 7.13/7.24, 7.64/8.21; ^{1}H−^{13}C HSQC NMR (CD_3COCD_3) δH/δC 5.05/59.7, 6.77/114.9, 6.85/107.2, 6.91/121.0, 7.13/109.3, 7.19/121.2, 7.24/128.3, 7.64/137.7, 8.21/148.7; ^{1}H−^{13}C HMBC NMR (CD_3COCD_3) δH/δC 5.05/121.2, 5.05/131.1, 5.05/152.4, 6.77/107.2, 6.77/148.7, 6.85/114.9, 6.91/109.3, 6.91/128.3, 6.91/131.1, 7.13/121.0, 7.13/131.1, 7.19/128.3, 7.19/152.4, 7.24/121.0, 7.24/121.2, 7.24/152.4, 7.64/148.7, 7.64/155.9, 8.21/114.9, 8.21/137.7, 8.21/155.9; GC-MS (m/z) 183 (M^+ + 1, 7), 182 (M^+, 60), 181 (100), 91 (17), 78 (11), 51 (7); HRMS (ESI/APCI) calcd for $C_{12}H_{11}N_2$ 183.0917, found 183.0921.

Naphtho[2,3-*a*]phenanthridine (15): The product was purified by radial thin-layer chromatography on silica gel eluting with petroleum ether/diethyl ether gradient (70:30 → 30:70): yellow crystals; mp 210.4−211.3 °C; ^{1}H NMR (CCl_3D) δ 7.61−7.65 (2H, m), 7.77−7.80 (1H, m), 7.97−8.01 (1H, m), 8.04 (1H, d, J = 9.0 Hz), 8.13−8.15 (2H, m), 8.18−8.24 (2H, m), 8.57 (1H, s), 9.29 (1H, d, J = 8.7 Hz), 9.43 (1H, s), 9.63 (1H, s); ^{13}C NMR (CCl_3D) δ 120.7, 126.1, 126.2, 126.3, 126.7, 126.8, 127.3, 127.8, 128.0, 128.6, 128.8, 130.1, 131.1, 131.5, 131.6, 131.9, 132.9, 144.7, 152.6; GC-MS (m/z) 280 (M^+ + 1, 22), 279 (M^+, 100), 278 (20), 277 (11), 251 (10), 250 (14), 139 (19), 125 (19), 113 (8), 111 (7); HRMS (ESI/APCI) calcd for $C_{21}H_{14}N$ 280.1126, found 280.1127.

***N*-*o*-Tolylnaphthalen-1-amine (20):** Yellow oil; ^{1}H NMR (CD_3COCD_3) δ 2.30 (3H, s), 2.78 (1H, s), 6.83−7.13 (4H, m), 7.23−7.53 (5H, m), 7.85−7.90 (1H, m), 8.15−8.20 (1H, m); ^{13}C NMR (CD_3COCD_3) δ 18.1, 114.3, 121.6, 121.9, 123.0, 123.3, 125.9, 126.7, 127.0, 127.5, 127.7, 129.1, 130.4, 131.7, 135.8, 141.9, 143.9; DEPT 135° (CD_3COCD_3) δ 18.1, 114.3, 121.6, 121.9, 123.0, 123.3, 125.9, 126.7, 127.0, 127.5, 129.1, 131.7; GC-MS (m/z) 235 (1), 234 (M^+ + 1, 17), 233 (M^+, 100), 232 (35), 230 (13), 218 (39), 217 (38), 128 (15), 115 (38), 109 (18).[32]

Acknowledgment. This paper is dedicated to Professor Pelayo Camps on the occasion of his 65th birthday. This work was supported in part by the Agencia Córdoba Ciencia, the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), SECYT, Universidad Nacional de Córdoba, and FONCYT, Argentina. M.E.B. and V.B.D. gratefully acknowledge receipt of fellowships from CONICET.

Supporting Information Available: General experimental methods, materials, characterization data (for **3i**, **14b**, **4a**−**e**, **4i**, **17**, **19**), copies of ^{1}H and ^{13}C NMR spectra for previously reported and unreported compounds; *xyz* coordinates and total energies in atomic units of the species calculated and the schematic profiles. This material is available free of charge *via* the Internet at http://pubs.acs.org.