Evidence for the Intermediacy of Arylbenzylnitrenium Ions in the Thermal Rearrangement of Isoxazolidines Derived from *C*,*N*-Diarylnitrones and 2-Morpholin-4-yl-acrylonitrile

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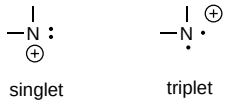
Abstract: In contrast to the diaryl, dialkyl, alkylaryl, and parent series, nothing is known about the generation and chemical behavior of arylbenzylnitrenium ions. Herein, we report that these species can be generated by a process involving an unprecedented thermal rearrangement of isoxazolidines derived from *C*,*N*-diarylnitrones and 2-morpholin-4-yl-acrylonitrile. The products from these reactions are dramatically dependent upon the nature of the nitrone. Most of the observed chemistry originates from the singlet state.

Keywords: alkenes · captodative alkenes · electrophilic reactions · nitrenium ions · rearrangement

Introduction

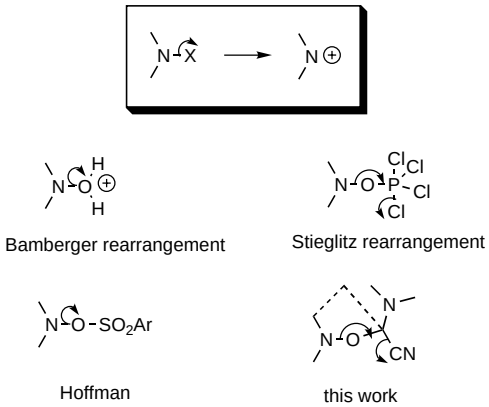
Nitrenium ions are nitrogen-containing organic compounds in which the nitrogen atom has an incomplete (sextet) electron shell and a formal positive charge. Nitrenium ions can exist in two electronic states, the singlet state, in which the electrons are paired, and the triplet state, in which both nonbonding orbitals are singly occupied (Scheme 1). As a rule, these species are extremely electrophilic and their lifetimes in solution are in the picosecond-to-microsecond range.



Scheme 1. Singlet and triplet states of nitrenium ions.

It has been known for some time that the mutagenicity and carcinogenicity of aromatic amines are attributable to their arylhydroxylamine ester metabolites which generate aromatic-substituted nitrenium ions upon heterolysis of the N–O bond.[1] It has also been shown that these esters generate nitrenium ions in an aqueous environment.[2]

Generally speaking, nitrenium ions are formed by heterolytic cleavage of an N–X bond. The Bamberger rearrangement (Scheme 2), which takes place on treatment of *N*-phenylhydroxylamine with aqueous mineral acid to result in



Scheme 2. Bamberger and Stieglitz rearrangements as methods to form nitrenium ions.

the formation of 4-aminophenol,[3, 4] the Stieglitz rearrangement, which involves the reaction of a *N*-monoalkylhydroxylamine with phosphorus pentachloride,[3b] and the solvolysis of *N*-arylsulfonyloxyamines,[5] are only a few of the many types of reactions in which the divalent electron-deficient nitrogen serves as the crucial intermediate.

Nitrenium ions are generally produced in the singlet state and consequently they must undergo an intersystem crossing

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0947-6539/03/0904-1000 $ 20.00+.50/0

(ISC) to the low-lying triplet state. Gassman and Cryberg have reported ISC on 4,7,7-trimethyl-2-chloroazabicyclo[2.2.1]heptane with heavy atom solvents as catalysts.[6] However, subsequent studies by other researchers who used different leaving groups produced negative results. In addition, more recent experimental studies[7] have indicated the possibility of stabilization of the singlet as a result of electrostatic interactions with the solvents.

It is well-established that the parent nitrenium NH_2^+ has a singlet–triplet splitting of 30 kcal mol^{-1} (a positive sign corresponds to the triplet state being lower in energy).[8] A combination of experimental results and well-converged quantum-mechanical studies indicates that alkyl and aromatic substituents preferentially stabilize the singlet state in each system; the stabilizations are roughly 20 and 50 kcal mol^{-1} for a methyl and phenyl substituent, respectively;[9] however, bulky substituents on the nitrogen atom or electron-deficient π systems favor the triplet state.[10]

Theoretical calculations also agree that π-donor substituents on the phenyl ring attached to the nitrogen atom of arylnitrenium ions further stabilize the singlet relative to the triplet state. Likewise, π acceptors stabilize the triplet relative to the singlet state.[10] Stabilization of the cationic charge in nitrenium by π conjugation is so important that phenylnitrenium ions have been found to exhibit substantial quinoidal, that is, iminocyclohexadienyl cation-like, character.[4c] The presence of a charge and a free orbital govern not only the reactivity but also the strictly controlled interaction pathway of these species. The reaction characteristics also govern the nature of the resulting intermediate complexes and reaction products.[4b]

Within the past ten years, methods have been developed for the direct study of arylnitrenium ions by laser flash photolysis (LFP). The first reports from Falvey and co-workers involved the photochemical ring-opening in acetonitrile of an anthranilium salt.[11, 12] The LFP method made it possible to measure the UV spectra of such short-lived (80–200 ns) species for the first time.[13, 14]

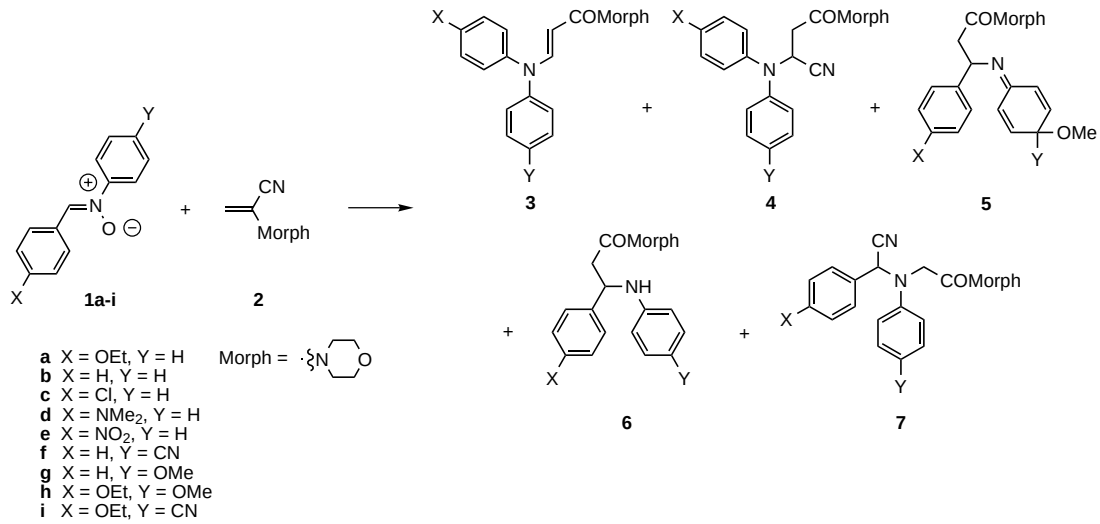
In contrast to the (di)aryl, (di)alkyl, alkylaryl, and parent series, to our knowledge, nothing is known about the generation and chemical behavior of arylbenzylnitrenium ions. Herein, we report that these species can be generated by a process involving an unprecedented thermal rearrangement of isoxazolidines derived from *C*,*N*-diarylnitrones and 2-morpholin-4-yl-acrylonitrile. The products from these reactions are dramatically dependent upon the nature of the nitrone.

Results and Discussion

We have examined the reactions of various *C*,*N*-diarylnitrones **1a–i** with the captodative alkene **2**[15] (Scheme 3). Reactions were conducted on a 1–3 mM scale of the reactants (1:1 ratio), under the conditions given in Table 1. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel by elution with heptane/ethyl acetate. Products **3–7** were obtained in variable amounts depending on the conditions used.

The reaction of nitrone **1a** (X = OEt, Y = H) in toluene at 60 °C gave enaminone **3a** as a main product along with **4a** and **6a** (Table 1, entry 1). In **4a**, the EtO-substituted aryl ring migrated to the nitrogen atom. At 80 °C (Table 1, entry 2), a new product, **7a**, was identified. Yield of **7a** increased dramatically with the temperature (runs at 90 °C and 110 °C; Table 1, entries 3 and 4 respectively). The formation of **7a** was reduced or suppressed by addition of benzoquinone (5 mol%), hydroquinone (5 mol%) and triphenylmethane (1 equiv) in refluxing toluene (Table 1, entries 5–7). In the presence of triphenylmethane and hydroquinone, the yield of **6a** increased to 30% and 40%, respectively.

Scheme 4 and Scheme 5 outline the probable reaction pathways for the chemistry discussed so far. Since both electron-rich and moderately electron-poor alkenes are known to add unidirectionally to nitrones to yield 5-donor-substituted (or 5-acceptor-substituted) isoxazolidines in a concerted mechanism,[16] it is conceivable that 5-morpholino-isoxazolidine-5-carbonitrile (**8**) is formed as an intermediate in this process; however, it is unstable under the reaction conditions and undergoes further transformation.[17]



Scheme 3. Reactions of nitrones **1a–i** with captodative 2-morpholin-4-yl-acrylonitrile (**2**).

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Table 1. Product distributions.[a]

Entry	Nitrone	X	Y	Solvent	Co-reactant/ co-solvent	T [°C]	t [h]	**3**	**4**	**5**	**6**	**7**	**2**[b]	**6**/**A** [%][c]
1	**1a**	OEt	H	toluene	–	60	26	40	18	0	14	0	28	19
2	**1a**	OEt	H	toluene	–	80	4	38	31	0	14	6	10	17
3	**1a**	OEt	H	toluene	–	90	4	23	33	0	12	27	5	18
4	**1a**	OEt	H	toluene	–	110	4	11	15	0	7	65	1	21
5	**1a**	OEt	H	toluene	benzoquinone[d]	110	4	36	48	0	15	2	0	15
6	**1a**	OEt	H	toluene	hydroquinone[d]	110	4	35	24	0	40	0	0	40
7	**1a**	OEt	H	toluene	triphenylmethane[e]	110	4	22	38	0	30	10	0	33
8	**1a**	OEt	H	toluene	water 95:5 v/v	110	4	37	23	0	14	26	0	19
9	**1a**	OEt	H	toluene	water 50:50 v/v	reflux	4	13	61	0	25	0	1	25
10	**1a**	OEt	H	$CHCl_3$	–	40	36	72	0	0	0	0	28	0
11	**1a**	OEt	H	$CHCl_3$	–	50	36	78	15	0	0	0	7	0
12	**1a**	OEt	H	$CHCl_3$	–	61	4	45	33	0	6	0	16	7
13	**1a**	OEt	H	$CHCl_3$	triphenylmethane[e]	61	4	49	37	0	13	0	1	13
14	**1a**	OEt	H	CCl_4	–	77	4	0	74	0	26	0	0	26
15	**1a**	OEt	H	benzene	–	60	36	38	0	0	0	0	62	0
16	**1a**	OEt	H	benzene	–	70	36	37	26	0	13	0	24	17
17	**1a**	OEt	H	benzene	–	80	3	33	8	0	6	17	35	13
18	**1b**	H	H	toluene	–	70	25	0	0	0	49	3	48	100
19	**1b**	H	H	toluene	–	75	4	0	0	0	51	8	41	100
20	**1b**	H	H	toluene	–	90	4	0	0	0	62	19	19	100
21	**1b**	H	H	toluene	–	110	3	0	0	0	34	42	24	100
22	**1b**	H	H	toluene	MeOH 50:50 v/v	reflux	2	0	0	94	6	0	0	6
23	**1b**	H	H	benzene	–	80	4	0	0	0	51	9	40	100
24	**1b**	H	H	$CHCl_3$	–	61	4	0	0	0	47	10	43	100
25	**1b**	H	H	$CHCl_3$	–	61	21	0	0	0	47	53	0	100
26	**1c**	Cl	H	toluene	–	110	4	0	0	0	18	62	19	100
27	**1d**	NMe_2	H	toluene	–	90	4	54	0	0	19	0	27	26
28	**1e**	NO_2	H	toluene	–	90	4	0	0	0	62	0	0	100
29	**1f**	H	CN	toluene	–	110	4	0	0	0	95	0	0	100
30	**1f**	H	CN	toluene	MeOH 50:50 v/v	reflux	4	0	0	0	47	0	53	100
31	**1g**	H	OMe	toluene	MeOH 50:50 v/v	reflux	4	–	–	–	–	–	–	–
32	**1h**	OEt	OMe	toluene	–	90	4	19	19	0	18	0	43	32
33	**1i**	OEt	CN	toluene	–	110	4	73	16	0	0	0	10	0

[a] Entries 3, 20, 25–28, 30, 32, and 33: yields of isolated product after purification by column chromatography on silica gel (see Experimental Section). In other cases, the product distribution was determined by ^{1}H NMR spectroscopy. [b] Unreacted alkene **2**. [c] **A** = **3** + **4** + **5** + **6**. [d] 5 mol %. [e] One equivalent.

An attractive rationale for the formation of **3**, **4**, and **6** would involve initial heterolytic cleavage of the N–O bond of **8** (path A, Scheme 4) leading to a nitrenium ion **11** (or more correctly: ion pair of nitrenium ion **11**$^+$CN$^-$). Spin conservation requires that the first-formed ion is a singlet. Singlet nitrenium ions having both a nonbonding pair of electrons and an empty orbital, behave as Lewis acids or Lewis bases and generally rapidly react with nucleophiles.[4] In this study, the strongly electrophilic singlet nitrenium ^{1}**11** presumably reacts with the EtO-substituted aryl ring to give either the strained aziridine **9** by intramolecular cyclization (S_E) or the iminium salt **10** by migration of the EtO-substituted aryl ring to the nitrenium center. The stable enone **3** could arise from the deprotonation of **9** by cyanide ions, followed by ring opening and rearomatization. Hydrocyanation of **3** would then lead to **4**. Alternatively, reaction of the iminium **10** with cyanide could afford **4** directly and then **3** by loss of hydrogen cyanide.[18]

The conversion of isoxazolidine **8** into the amine **6** could follow either of two routes. One path would involve a hydride abstraction from the solvent by the singlet state ^{1}**11** to yield **6** directly.[19] Alternatively, if this singlet has a sufficient lifetime and if spin inversion would decrease the energy of the system, singlet ^{1}**11** should convert to triplet ^{3}**11**. The triplet would be expected to resemble a nitrogen cation radical in its chemical reactivity. In the presence of a hydrogen source, such as H_2O in toluene or on glassware, ^{3}**11** should convert into a cation radical, which could in turn react with a second hydrogen radical to give the ammonium **12** and then **6** by loss of HCN. The formation of **6** would be the result of a net two-electron reduction of the triplet-state nitrenium ion.

Compound **7** is probably formed by the mechanism presented in Scheme 5 (path B). 4-Isoxazoline (**14**) most reasonably arises from loss of hydrogen cyanide by the unstable isoxazolidine **8** above 90 °C. Because the formation of **7** is suppressed by addition of radical inhibitors, the reaction presumably proceeds by homolytic cleavage of the N–O bond affording a biradical **15** that would cyclize at the carbon atom to yield aziridine **16**.[20, 21] *N*-Arylaziridines, **16**, are thermally unstable and afford azomethine ylide **17**.[22] Product **7** would then result from the addition of hydrogen cyanide to **17**. These mechanisms were confirmed by additional experiments (vide infra).

In the first four entries of Table 1, the ratio **6**/**A** (**A** = **3** + **4** + **5** + **6**) does not greatly vary in the temperature range of 60–110 °C (17 → 21 %) or when benzoquinone is added (Table 1, entry 5). This ratio notably increases on addition of hydroquinone or triphenylmethane (40 % and 33 %, respec-

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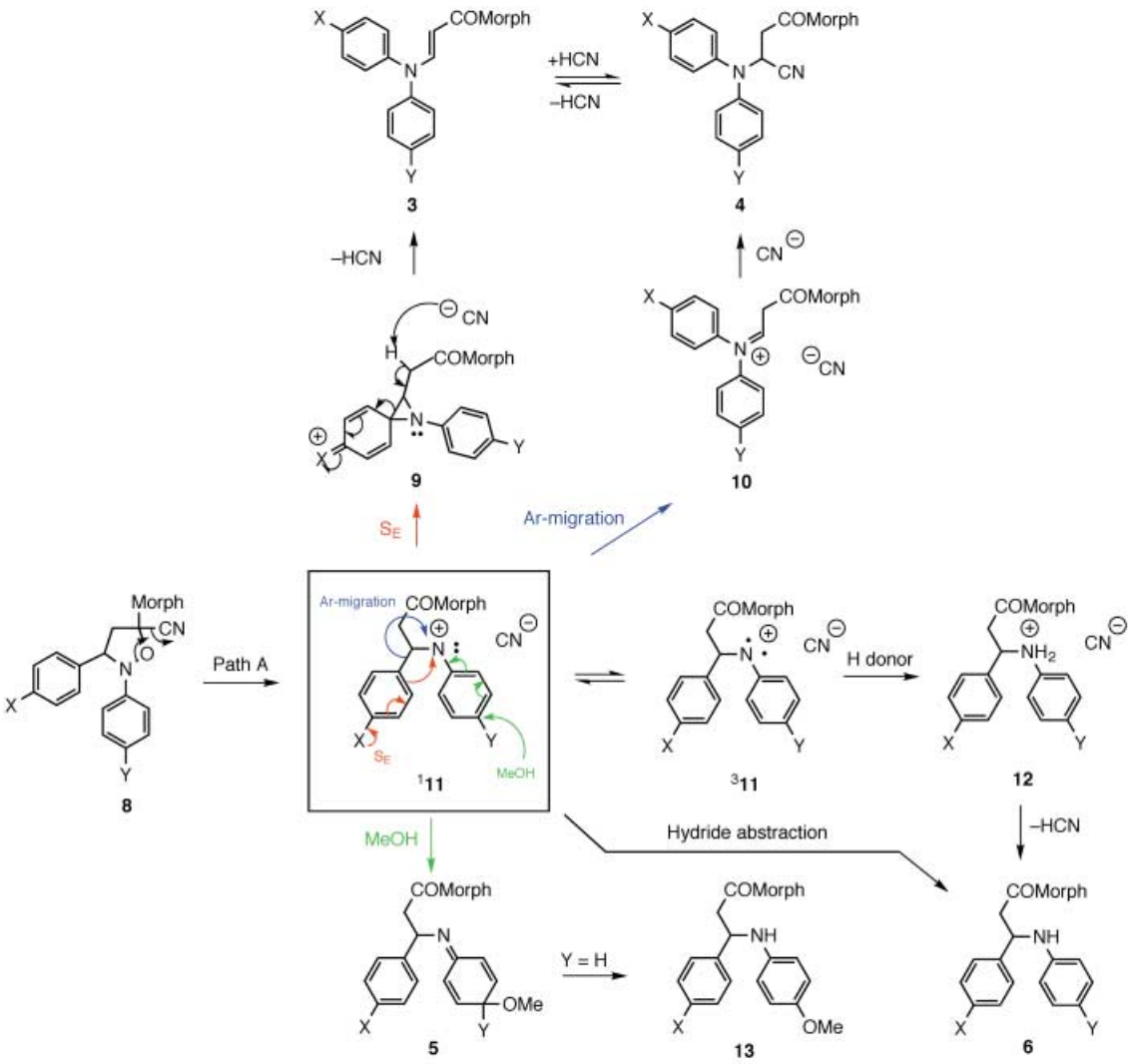
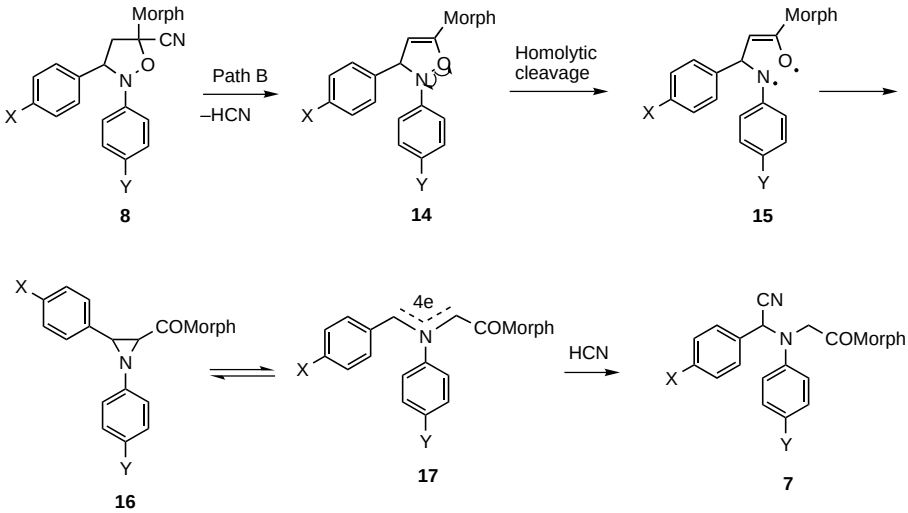


Scheme 4. Thermal rearrangement of isoxazolidines derived from *C*,*N*-diarylnitrones (**1a–i**) and 2-morpholin-4-yl-acrylonitrile (**2**).

tively) whereas the formation of **7** is inhibited. These observations are consistent with a radical mechanism for the formation of **7** (Scheme 5). Because the yield of **6** is not reduced by addition of hydroquinone or triphenylmethane but increased instead, it is assumed that **6** is not formed via the triplet nitrenium ^{3}**11** but more likely by hydride abstraction from the solvent by the singlet state ^{1}**11**.[23]



Scheme 5. Thermally induced homolytic cleavage of the N–O bond of 4-isoxazolines.

The product distribution is only slightly modified by addition of a small amount of water (5% v/v) (Table 1, entry 8). It is worthy of note that the formation of **7a** is suppressed when the reaction is carried out in a refluxing biphasic mixture of toluene/water (50:50, Table 1, entry 9). If nitrenium ions are involved in these reactions, they have sufficient lifetimes in aqueous solution to be viable intermediates.

At 40 °C in chloroform, the reaction of **1a** with the captodative alkene **2** gave **3a** exclu-

sively (Table 1, entry 10). Upon warming to 50 °C, **3a** and **4a**—resulting from the intramolecular reaction of the singlet nitrenium ^{1}**11a**—were produced (Table 1, entry 11); at 61 °C, a small amount of **6a** (6%) was also formed (Table 1, entry 12). The yield of **6a** increased by addition of 1 equiv of triphenylmethane at 61 °C (Table 1, entry 13). Because chloroform is not a good hydrogen donor and the concentration of residual water is lower in chloroform than in toluene, **6a** is not produced in higher amounts under these conditions. Compound **7a** is not formed when the reaction is carried out in refluxing chloroform, probably because the temperature is not high enough to undergo HCN elimination. In carbon tetrachloride, **4a** and **6a** are formed exclusively (Table 1, entry 14). Although the conversion is slow in benzene, the product distribution is similar to that observed in toluene (Table 1, entries 15–17).

With the nitrone **1b** (X = Y = H) at 70 °C, **6b** was formed almost exclusively (Table 1, entry 18). Higher amounts of **6b** were obtained at 90 °C (Table 1, entry 20). Above 90 °C, the formation of **7b** became predominant: as previously observed, the higher the temperature, the higher the yield of **7b** (Table 1, entries 18–21). Clearly, migration of the X-substituted aryl ring to the nitrenium center leading to **3** and **4** is not observed because the donating effect of X (H) is not sufficient. Similar product distributions were observed when the reaction was carried out in refluxing benzene or chloroform (Table 1, entries 23 and 24). An increase of the reaction time improved only the yield of **7b** (Table 1, entry 25).

Theoretical calculations agree that π-donor substituents on the phenyl ring directly attached to the nitrenium (i.e. Y) further stabilize the singlet with respect to the triplet.[8, 24] Recent experimental evidence suggests that one phenylnitrenium ion substituted with strong π-acceptor groups has a triplet ground state.[25] In the case of nitrone **1b** (X = Y = H), when methanol was added to toluene (50% v/v), **13b** was formed almost quantitatively (Table 1, entry 22).[26] It seems reasonable to assume that product **13b** is derived from the addition of methanol to the *para* position of the ring of the singlet nitrenium ^{1}**11b** followed by a net 1,5-hydrogen shift (Scheme 4). The isomer resulting from the addition of the *ortho* position of the ring was not detected.

Consistent with our previous observations, nitrone **1c** (X = Cl, Y = H) when reacted in toluene at 110 °C (Table 1, entry 26) afforded **6c** and **7c** exclusively, whereas the nitrone **1d** (X = NMe_2, Y = H) gave **3d** and **6d**. The nitrone **1e** (X = NO_2, Y = H) when treated with alkene **2** in toluene at 90 °C, yielded **6e** as a unique product (Table 1, entry 28).

Compound **6f** was obtained almost quantitatively (95%, Table 1, entry 29) when nitrone **1f** (X = H, Y = CN) was reacted in toluene at 110 °C. The addition of methanol (Table 1, entry 30) reduced the yield of **6f**; however, it did not modify the product distribution. The reaction of **1g** (X = H, Y = OMe) only led to degradation products (Table 1, entry 31).

Nitrone **1h** contains electron-donating substituents on both aromatic rings (X = OEt, Y = OMe). At 90 °C in toluene, products **3h**, **4h**, and **6h** were formed in similar yields, while **5h** and **7h** were not detected (Table 1, entry 32). At 110 °C in toluene, nitrone **1i** (X = OEt, Y = CN) led exclusively to products **3i** and **4i** resulting from the rearrangement of the singlet nitrenium, whereas **6i** and **7i** were not formed (Table 1, entry 33). In the intermediate **14i**, the N–O bond is strengthened when an electron-withdrawing substituent Y is connected to the phenyl group.

In conclusion, it can be stated that all the experimental information on the arylbenzylnitrenium ion **11** can be explained by assuming that it has a singlet ground state and that all of its presently known chemical reactions occur from that state. These results corroborate the theoretical literature which predicts singlet ground states for arylnitrenium ions. Our failure to detect triplet nitrenium ions could be the result of this structural feature. Arylnitrenium ions and arylbenzylnitrenium ions display a similar chemical behavior. The main difference observed is the capacity of the latter to undergo aryl migration.

Experimental Section

All operations were performed in an atmosphere of dry nitrogen. Commercially available reagents and solvents were purified and dried, when necessary, by standard methods just prior to use. All melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$. Chemical shifts are reported downfield from TMS, which was used as the internal reference. Ratios in mixtures were calculated from ^{1}H NMR scpectroscopy. Elemental analyses were obtained from the Service de microanalyse, CNRS ICSN, Gif-sur-Yvette (France). High-resolution mass measurements were performed at the Centre régional de mesures physiques de l'Ouest, Rennes (France).

Preparation of diarylnitrones 1a–i: The (*Z*)-*α*-aryl-*N*-phenyl nitrones were prepared by the reaction of suitably substituted benzaldehyde with phenylhydroxylamine in ethanol; their physical constants have already been reported.[27] The (*Z*)-*α*-phenyl-*N*-aryl nitrones were prepared by condensation of suitably substituted phenylhydroxylamine with benzaldehyde. The purity of all compounds was checked by melting point determinations and ^{1}H NMR.[28]

General procedure: A solution of *N*-arylhydroxylamine (50 mmol) and aldehyde (50 mmol) in ethanol (50 mL) was stirred overnight at 20 °C. The mixture was then cooled to 0 °C, collected by filtration, and recrystallized.

***α*-(4-Ethoxyphenyl)-*N*-phenylnitrone (1a)**: Yield: 97%; white solid; m.p. 138–139 °C (ethyl acetate); ^{1}H NMR (400 MHz): $\delta = 1.45$ (t, J(H,H) = 7.0 Hz, 3H; OCH_2CH_3), 4.11 (q, J(H,H) = 7.0 Hz, 2H; OCH_2CH_3), 6.98 (d, J(H,H) = 9 Hz, 2H; Ar), 7.45–7.50 (m, 3H; Ar), 7.76–7.78 (m, 2H; Ar), 7.85 (s, 1H; C=*H*N), 8.93 ppm (d, 2H; J(H,H) = 9.0 Hz, Ar); ^{13}C NMR (100 MHz): $\delta = 14.7$, 63.6, 114.7, 121.6, 123.6, 129.1, 129.6, 131.2, 134.2, 148.9, 160.9 ppm.

***α*-Phenyl-*N*-phenylnitrone (1b)**: Yield: 85%; white solid; m.p. 110–110.5 °C (ethanol); ^{1}H NMR (400 MHz): $\delta = 7.46$–7.51 (m, 6H; Ar), 7.76–7.79 (m, 2H; Ar), 7.93 (s, 1H; C*H*=N), 8.03–8.42 ppm (m, 2H; Ar); ^{13}C NMR (100 MHz): $\delta = 120.9$, 127.8, 128.1, 129.1, 130.1, 133.8, 148.3 ppm.

***α*-(4-Chlorophenyl)-*N*-phenylnitrone (1c)**: Yield: 94%; white solid; m.p. 154.5–155 °C (ethanol); ^{1}H NMR (400 MHz): $\delta = 7.43$–7.52 (m, 5H; Ar), 7.74–7.78 (m, 2H; Ar), 7.91 (s, 1H; C*H*=N), 8.36 ppm (d, J(H,H) = 8.7 Hz, 2H; Ar); ^{13}C NMR (100 MHz): $\delta = 121.7$, 128.9, 129.2, 130.1, 133.3, 136.3, 148.7 ppm.

***α*-(4-Dimethylaminophenyl)-*N*-phenylnitrone (1d)**: Yield: 97%; white solid; m.p. 131–132 °C (ethyl acetate); ^{1}H NMR (80 MHz): $\delta = 3.05$ (s, 6H; $N(CH_3)_2$), 6.76–6.85 (m, 2H), 7.48–7.53 (m, 3H; Ar), 7.89–7.98 (m, 2H), 8.18 ppm (s, 1H; C*H*=N).

***α*-(4-Nitrophenyl)-*N*-phenylnitrone (1e)**: Yield: 97%; white solid; m.p. 191–192 °C (ethanol); ^{1}H NMR (80 MHz): $\delta = 7.50$–7.54 (m, 3H; Ar), 7.76–7.81 (m, 2H; Ar), 8.08 (s, 1H; C*H*=N), 8.29–8.33 (m, 2H; Ar), 8.52–8.58 ppm (m, 3H; Ar).

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α-Phenyl-*N*-(4-cyanophenyl)nitrone (1f): Yield: 86%; yellow solid; m.p. 155.5–156 °C (ethanol) (lit. [27] 161–162 °C); ^{1}H NMR (400 MHz): $\delta =$ 7.49 (m, 3H; Ar), 7.78 (d, J(H,H) = 8.9 Hz, 2H; Ar), 7.92 (d, J(H,H) = 8.9 Hz, 2H; Ar), 8.05 (s, 1H; C*H*=CN), 8.4 ppm (m, 2H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 113.5, 117.2 123.4, 128.0, 128.2, 129.8, 132.1, 133.9, 135.8, 152.9 ppm.

α-Phenyl-*N*-(4-methoxyphenyl)nitrone (1g): Yield: 65%; brown solid; m.p. 116–116.5 °C (ethanol); ^{1}H NMR (400 MHz): $\delta =$ 3.87 (s, 3H; OCH_3), 6.95 (d, J(H,H) = 9.4 Hz, 2H; Ar), 7.48 (m, 3H; Ar), 7.78 (d, J(H,H) = 9.4 Hz, 2H; Ar), 7.90 (s, 1H; C=N*H*), 8.41 ppm (m, 2H; Ar).

α-(4-Ethoxyphenyl)-*N*-(4-methoxyphenyl)nitrone (1h): Yield: 71%; brown solid; m.p. 105–105.5 °C (ethanol); ^{1}H NMR (400 MHz): $\delta =$ 1.45 (t, J(H,H) = 7 Hz, 3H; OCH$_2$CH_3), 3.74 (s, 3H; OCH_3), 4.12 (q, J(H,H) = 7 Hz, 2H; OCH_2CH$_3$), 6.98 (m, 4H; Ar), 7.78 (m, 2H; Ar), 7.91 (m, 1H; Ar), 8.25 ppm (m, 2H; Ar).

α-(4-Ethoxyphenyl)-*N*-(4-cyanophenyl)nitrone (1i): Yield: 52%; yellow solid; m.p. 164.5–165 °C (ethanol); ^{1}H NMR (400 MHz): $\delta =$ 1.45 (t, J(H,H) = 7 Hz, 3H; OCH$_2$CH_3), 4.18 (q, J(H,H) = 7Hz, 2H; OCH_2CH$_3$), 6.98 (d, J(H,H) = 8.6 Hz, 2H; Ar), 7.79 (d, J(H,H) = 8.6 Hz, 2H; Ar), 7.89 (d, J(H,H) = 9.4 Hz, 2H; Ar), 7.91 (s, 1H; C*H*=CN), 8.42 ppm (d, J(H,H) = 9.4 Hz, 2H; Ar).

Reactions of nitrones (1a–i) with 2-morpholin-4-yl-acrylonitrile (2).

3-[(4-Ethoxyphenyl)phenylamino]-1-morpholin-4-yl-propenone (3a), 2[(4-ethoxyphenyl)phenylamino]-4-morpholin-4-yl-4-oxobutyronitrile (4a), 3-(4-ethoxyphenyl)-1-morpholin-4-yl-3-phenylaminopropan-1-one (6a), and 4-ethoxyphenyl-[(2-morpholin-4-yl-2-oxo-ethyl)phenylamino]acetonitrile (7a): Nitrone **1a** (482 mg, 2 mmol) and alkene **2** (276 mg, 2 mmol) were heated in toluene (2 mL) at 90 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 75:25 → 50:50) afforded **3a** (162 mg, 23%), **4a** (250 mg, 33%), **6a** (85 mg, 12%), and **7a** (205 mg, 27%).

3a: Yellow oil; ^{1}H NMR (400 MHz): $\delta =$ 1.42 (t, J(H,H) = 6.8 Hz, 3H; OCH$_2$CH_3), 3.36–3.76 (m, 8H; morph), 4.05 (q, J(H,H) = 6.8 Hz, 2H; OCH_2CH$_3$), 5.13 (d, J(H,H) = 12.8 Hz, 1H; C*H*=CH), 6.94 (d, J(H,H) = 8.8 Hz, 2H; Ar), 7.01–7.10 (m, 5H; Ar), 7.29 (m, 2H; Ar), 8.23 ppm (d, J(H,H) = 12.8 Hz, 1H; CH=C*H*); ^{13}C NMR (100 MHz): $\delta =$ 15.1, 29.9, 63.9, 67.1, 92.8, 115.8, 119.5, 121.4, 122.2, 124.3, 127.9, 129.6, 167.6 ppm; elemental analysis calcd (%) for $C_{21}H_{24}N_2O_3$ (M = 352.43 g mol^{-1}): C 71.57, H 6.86, N 7.95; found: C 71.40, H 6.75, N 7.91; high-resolution MS: m/z calculated for $C_{21}H_{24}N_2O_3$: 352.17869; found 352.1814.

***4a*:** White crystals (ethanol); m.p. 149–150 °C; ^{1}H NMR (400 MHz): $\delta =$ 1.45 (t, J(H,H) = 6.8 Hz, 3H; OCH$_2$CH_3), 2.69 (dd, J(H,H) = 16.0 Hz, J(H,H) = 6.8 Hz, 1H; C*H*HC=O), 2.88 (dd, J(H,H) = 16.0 Hz, J(H,H) = 6.8 Hz, 1H; CH*H*C=O), 3.14–3.29 (m, 2H; morph), 3.48–3.67 (m, 6H; morph), 4.04 (q, J(H,H) = 6.8 Hz, 2H; OCH_2CH$_3$), 5.47 (t, J(H,H) = 6.8 Hz, 1H; C*H*CN), 6.82–7.26 (m, 5H; Ar), 6.93 (d, J(H,H) = 8.8 Hz, 2H; Ar), 7.16 ppm (d, J(H,H) = 8.8 Hz, 2H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 14.9, 35.5, 42.3, 45.7, 47.9, 63.8, 66.3, 66.7, 115.7, 117.7, 121.1, 129.3, 136.6, 147.4, 157.7, 166.2 ppm; elemental analysis calcd (%) for $C_{22}H_{25}N_3O_3$ (M = 379.5 g mol^{-1}): C 69.64, H 6.64, N 11.07; found: C 69.35, H 6.59, N 11.08; high-resolution MS: m/z calculated for $C_{22}H_{25}N_3O_3$: 379.18959; found 379.1901.

***6a*:** Dark yellow crystals (ethanol); m.p. 156–157 °C; ^{1}H NMR (400 MHz): $\delta =$ 1.40 (t, 3H; J(H,H) = 6.8 Hz, OCH$_2$CH_3), 2.77 (dd, J(H,H) = 14.4 Hz, J(H,H) = 5.6 Hz, 1H; C*H*HC=O), 2.87 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.4 Hz, 1H; CH*H*C=O), 3.12–3.18 (m, 3H; morph), 3.19–3.28 (m, 1H; morph), 3.46–3.63 (m, 4H; morph), 3.98 (q, J(H,H) = 6.8 Hz, 2H; OCH_2CH$_3$), 4.74 (t, J(H,H) = 6.0 Hz, 1H; C*H*CH$_2$C=O), 6.53 (d, J(H,H) = 8.0 Hz, 2H; Ar), 6.63 (t, J(H,H) = 7.2 Hz, 1H; Ar), 6.84 (d, J(H,H) = 8.4 Hz, 2H; Ar), 7.08 (dd, J(H,H) = 7.2 Hz, J(H,H) = 8 Hz, 2H; Ar), 7.27 ppm (d, J(H,H) = 8.4 Hz, 2H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 14.9, 40.0, 41.9, 46.4, 54.8, 63.5, 66.3, 66.7, 113.6, 114.8, 117.4, 127.4, 129.1, 147.0, 158.3, 134.4, 169.4 ppm; high-resolution MS: m/z calculated for $C_{21}H_{26}N_2O_3$: 354.19434; found 354.1947 (0 ppm).

***7a*:** Yellow oil (dichloromethane/diethyl ether); ^{1}H NMR (400 MHz): $\delta =$ 1.42 (t, J(H,H) = 6.8 Hz, 3H; OCH$_2$CH_3), 3.29–3.35 (m, 2H; morph), 3.44–3.67 (m, 6H; morph), 3.91 (d, J(H,H) = 16.4 Hz, 1H; C*H*HC=O), 4.06 (d, J(H,H) = 16.4 Hz, 1H; CH*H*C=O), 4.06 (q, 2H; J(H,H) = 6.8 Hz, OCH_2CH$_3$), 5.72 (s, 1H; C*H*CN), 6.90 (d, J(H,H) = 8.8 Hz, 2H; Ar), 6.97–7.03 (m, 3H; Ar), 7.25–7.37 (m, 2H; Ar), 7.45 ppm (d, J(H,H) = 8.8 Hz, 2H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 42.2, 45.5, 52.3, 57.7, 66.4, 116.6, 119.4, 122.9, 129.2, 129.4, 131.4, 135.3, 146.7, 166.9 ppm; elemental analysis calcd. for $C_{22}H_{25}N_3O_3$ (M = 379.45 g mol^{-1}): C 69.64, H 6.64, N 11.07; found: C 69.37, H 6.49, N 11.00.

1-Morpholin-4-yl-3-phenyl-3-phenylaminopropan-1-one (6b) and [(2-morpholin-4-yl-2-oxo-ethyl)phenylamino]phenyl-acetonitrile (7b): Nitrone **1b** (197 mg, 1 mmol) and alkene **2** (138 mg, 1 mmol) were heated in toluene (1 mL) at 90 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 65:35 → 50:50) afforded **6b** (192 mg, 62%) and **7b** (64 mg, 19%).

***6b*:** Beige crystals (dichloromethane/diethyl ether); m.p. 142–143 °C; ^{1}H NMR (400 MHz): $\delta =$ 2.81 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.4 Hz, 1H; C*H*HC=O), 2.90 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.4 Hz, 1H; CH*H*C=O), 3.08–3.25 (m, 3H; morph), 3.31–3.39 (m, 1H; morph), 3.44–3.63 (m, 4H; morph), 4.79 (t, J(H,H) = 6.4 Hz, 1H; C*H*CH$_2$C=0), 6.53 (d, J(H,H) = 7.2 Hz, 2H; Ar), 6.64 (t, J(H,H) = 7.2 Hz, 1H; Ar), 7.08 (t, J(H,H) = 7.2 Hz, 2H; Ar), 7.22–7.42 ppm (m, 5H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 36.5, 42.3, 45.6, 54.5, 66.3, 66.7, 121.2, 129.3, 133.1, 147.0 ppm; elemental analysis calcd (%) for $C_{19}H_{22}N_2O_2$ (M = 310.39 g mol^{-1}): C 73.52, H 7.14, N 9.03; found: C 73.22, H 7.15, N 9.08; high-resolution MS: m/z calculated for $C_{19}H_{22}N_2O_2$: 310.16813; found 310.1704 (7 ppm).

***7b*:** Beige crystals (dichloromethane/diethyl ether); m.p. 121–122 °C; ^{1}H NMR (400 MHz): $\delta =$ 3.30–3.38 (m, 2H; morph), 3.44–3.65 (m, 6H; morph), 3.94 (d, J(H,H) = 16.0 Hz, 1H; C*H*HC=O), 4.08 (d, J(H,H) = 16.0 Hz, 1H; CH*H*C=O), 5.79 (s, 1H; C*H*-CN), 6.97–7.03 (m, 3H; Ar), 7.25–7.31 (m, 2H; Ar), 7.38–7.44 (m, 3H; Ar), 7.56–7.60 ppm (m, 2H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 42.3, 45.6, 51.7, 58.6, 66.4, 66.9, 116.8, 122.8, 128.1, 129.1, 129.4, 132.7, 147.2, 167.1 ppm; elemental analysis calcd (%) for $C_{20}H_{21}N_3O_2$ (M = 335 g mol^{-1}): C 71.62, H 6.31, N 12.53; found: C 71.80, H 6.30, N 12.50; high-resolution MS: m/z calculated for $C_{20}H_{21}N_3O_2$: 335.16338; found 335.1632 (0 ppm).

3-(4-Methoxyphenylamino)-1-morpholin-4-yl-3-phenylpropan-1-one (13b): Nitrone **1b** (591 mg, 3 mmol) and alkene **2** (414 mg, 3 mmol) were heated in a refluxing mixture of toluene (1.5 mL) and methanol (1.5 mL) for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 66:33 → 50:50) afforded **13b** (960 mg, 94%). Brown crystals (dichloromethane/diethyl ether); m.p. 123–124 °C; ^{1}H NMR (400 MHz): $\delta =$ 2.80 (dd, J(H,H) = 14.0 Hz, J(H,H) = 7.2 Hz, 1H; C*H*HC=O), 2.89 (dd, J(H,H) = 14.0 Hz, J(H,H) = 7.2 Hz, 1H; CH*H*C=O), 3.12–3.88 (m, 4H; morph), 3.52–3.68 (m, 4H; morph), 3.69 (s, 3H; OCH_3), 4.75 (t, J(H,H) = 5.6 Hz, C*H*NH), 6.53 (d, J(H,H) = 8.8 Hz, 2H; Ar), 6.69 (d, J(H,H) = 8.8 Hz, 2H; Ar), 7.23–7.29 (m, 1H; Ar), 7.30–7.36 (m, 2H; Ar), 7.38–7.42 ppm (m, 2H; Ar); elemental analysis calcd (%) for $C_{20}H_{24}N_2O_3$ (M = 340.4 g mol^{-1}): C 70.57, H 7.11, N 8.23; found: C 70.90, H 7.08, N 8.24; high-resolution MS: m/z calculated for $C_{20}H_{24}N_2O_3$: 340.17869; found 340.1796 (2 ppm).

3-(4-Chlorophenyl)-1-morpholin-4-yl-3-phenylaminopropan-1-one (6c) and (4-chlorophenyl)-[(2-morpholin-4-yl-2-oxoethyl)phenylamino]acetonitrile (7c): Nitrone **1c** (693 mg, 3 mmol) and alkene **2** (414 mg, 3 mmol) were heated in toluene (3 mL) at 110 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 65:35 → 50:50) afforded **6c** (185 mg, 18%) and **7c** (688 mg, 62%).

6c: Brown crystals (dichloromethane/diethyl ether); m.p. 123–124 °C; ^{1}H NMR (400 MHz): $\delta =$ 2.81 (dd, J(H,H) = 14.4 Hz, J(H,H) = 8.8 Hz, 1H; C*H*HC=O), 2.87 (dd, J(H,H) = 14.4 Hz, J(H,H) = 7.6 Hz, 1H; CH*H*C=O), 3.15–3.36 (m, 3H; H morph), 3.41–3.60 (m, 5H; morph), 4.77 (t, J(H,H) = 7.6 Hz, 1H; C*H*NHAr), 6.50 (d, J(H,H) = 7.2 Hz, 2H; Ar), 6.65 (t, J(H,H) = 7.2 Hz, 1H; Ar), 7.07 (dd, 2H; J(H,H) = 7.2 Hz, J(H,H) = 8 Hz; Ar), 7.27 (d, J(H,H) = 8 Hz, 2H; Ar), 7.33 ppm (d, J(H,H) = 8 Hz, 2H; Ar); ^{13}C NMR (100 MHz): $\delta =$ 39.8, 41.8, 46.3, 54.6, 66.3, 66.6, 113.6, 117.7, 127.8, 128.9, 129.2, 141.3, 146.7, 168.8 ppm; elemental analysis calcd (%) for $C_{19}H_{21}ClN_2O_2$ (M = 344.84 g mol^{-1}): C 66.18, H 6.14, N 8.12; found: C 66.20, H 6.15, N 8.18; high-resolution MS: m/z calculated for $C_{19}H_{21}ClN_2O_2$: 344.12916; found 344.1289.

7c: Yellow crystals (dichloromethane/diethyl ether); m.p. 139.5–140 °C; ^{1}H NMR (400 MHz): $\delta =$ 3.39–3.41 (m, 2H; morph), 3;56–3;72 (m, 6H; morph), 3.96 (d, J(H,H) = 16.4 Hz, 1H; C*H*HC=O), 4.12 (d, J(H,H) = 16.4 Hz, 1H; CH*H*C=O), 5.77 (s, 1H; C*H*CN), 6.90 (d, J(H,H) = 7.6 Hz, 2H; Ar), 6.99 (t, J(H,H) = 7.2 Hz, 1H; Ar), 7.25 (dd, J(H,H) = 7.2 Hz, J(H,H) = 7.6 Hz, 2H; Ar), 7.35 (d, J(H,H) = 8.4 Hz, 2H; Ar), 7.53 ppm (d,

J(H,H) = 8.4 Hz, 2H; Ar); ^{13}C NMR (100 MHz): δ = 41.2, 44.3, 51.2, 56.6, 65.3, 65.7, 118.3, 121.8, 128.0, 128.2 ppm; elemental analysis calcd (%) for $C_{20}H_{20}ClN_3O_2$ (M = 369.85 g mol^{-1}): C 64.93, H 5.41, N 11.36; found: C 64.93, H 5.37, N 11.12; high-resolution MS: m/z calculated for $C_{20}H_{20}ClN_3O_2$: 369.12440; found 369.1236.

3-[(4-Dimethylaminophenyl)phenylamino]-1-morpholin-4-yl-propenone (3d) and 3-(4-dimethylaminophenyl)-1-morpholin-4-yl-3-phenylaminopropan-1-one (6d): Nitrone **1d** (271 mg, 1 mmol) and alkene **2** (138 mg, 1 mmol) were heated in toluene (1.5 mL) at 90 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 65:35 → 50:50) afforded **3d** (190 mg, 54 %) and **6d** (67 mg, 19 %).

3d: Brown crystals (dichloromethane/diethyl ether); m.p. 62 – 65 °C; ^{1}H NMR (400 MHz): δ = 2.12 (s, 6H; N(CH_3)$_2$), 3.38 – 3.65 (m, 8H; morph), 5.13 (d, J(H,H) = 12.8 Hz, 1H; CH=CH), 6.78 – 6.81 (m, 2H; Ar), 7.25 – 7.32 (m, 2H; Ar), 7.48 – 7.55 (m, 5H; Ar), 8.24 ppm (d, J(H,H) = 12.8 Hz, 1H; CH=CH).

6d: Brown crystals (dichloromethane/diethyl ether); m.p. 98 – 98.5 °C; ^{1}H NMR (400 MHz): δ = 2.12 (s, 6H; N(CH_3)$_2$), 2.75 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.4 Hz, 1H; CHHC=O), 2.87 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.4 Hz, 1H; CHHC=O), 3.12 – 3.65 (m, 8H; morph), 4.73 (t, J(H,H) = 6.4 Hz, 1H; CHCH$_2$CO), 6.53 (d, 2H; Ar), 6.64 – 6.84 (m, 5H; Ar), 7.12 – 7.27 ppm (m, 2H; Ar).

3-(4-Nitrophenyl)-1-morpholin-4-yl-3-phenylaminopropan-1-one (6e): Nitrone **1e** (727 mg, 3 mmol) and alkene **2** (414 mg, 3 mmol) were heated in toluene (3 mL) at 90 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate 75:25) afforded **6e** (661 mg, 62 %). White crystals (ethanol); m.p. 151 – 152 °C; ^{1}H NMR (200 MHz): δ = 2.84 (dd, J(H,H) = 15.2 Hz, J(H,H) = 6.0 Hz, 1H; CHHC=O), 2.92 (dd, J(H,H) = 15.2 Hz, J(H,H) = 5.9 Hz, 1H; CHHC=O), 3.24 – 3.38 (m, 2H; morph), 3.40 – 3.69 (m, 6H; morph), 4.75 (s, 1H; NH), 4.91 (t, J(H,H) = 6 Hz, 1H; CHNHAr), 6.45 – 8.25 ppm (m, 9H); ^{13}C NMR (100 MHz): δ = 39.6, 41.9, 46.2, 54.7, 66.3, 66.7, 113.8, 118.3, 124.1, 127.5, 129.3, 146.3, 150.0, 168.3 ppm; MS (IE) m/z: 355 $[M]^+$.

4-(3-Morpholin-4-yl-3-oxo-1-phenyl-propylamino)benzonitrile (6f): Nitrone **1f** (666 mg, 3 mmol) and alkene **2** (414 mg, 3 mmol) were heated in toluene (2.5 mL) at 110 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 60:30 → 50:50) afforded **6f** (474 mg, 47 %) as a yellow oil. ^{1}H NMR (400 MHz): δ = 2.79 (dd, J(H,H) = 14 Hz, J(H,H) = 4.8 Hz, 1H; CHHC=O), 2.87 (dd, J(H,H) = 14 Hz, J(H,H) = 4.8 Hz, 1H; CHHC=O), 3.01 – 3.04 (m, 1H; morph), 3.15 – 3.64 (m, 7H; morph), 4.82 (t, J(H,H) = 4.8 Hz, 1H; CH-CH$_2$C=O), 6.48 (d, J(H,H) = 8.8 Hz, 2H; Ar), 6.56 (d, J(H,H) = 8.8 Hz, 2H; Ar), 7.20 – 7.34 ppm (m, 5H; Ar); elemental analysis calcd (%) for $C_{20}H_{21}N_3O_2$ (M = 335.40 g mol^{-1}): C 71.62, H 6.31, N 12.53; found: C 71.55, H 6.35, N 12.40.

4[2-(Morpholin-4-carbonyl)-3-phenylaziridin-1-yl]-benzonitrile (16f): Nitrone **1f** (222 mg, 1 mmol), alkene **2** (138 mg, 1 mmol) and triethylamine (1 mL, 726 mg, 7.2 mmol) were heated in toluene (1 mL) at 110 °C for 2 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate 50:50) afforded **16f** (79 mg, 24 %) as a yellow oil. ^{1}H NMR (400 MHz): δ = 3.42 (d, J(H,H) = 3.2 Hz, 1H), 3.51 – 3.85 (m, 8H; morph), 3.94 (d, J(H,H) = 3.2 Hz, 1H), 6.87 (d, J(H,H) = 8.8 Hz, 2H; Ar), 7.30 – 7.39 (m, 5H; Ar), 7.48 ppm (d, J(H,H) = 8.8 Hz, 2H; Ar); ^{13}C NMR (100 MHz): δ = 43.5, 45.3, 65.9, 66.0, 119.5, 125.7, 127.5, 127.9, 132.2; high-resolution MS: m/z calculated for $C_{20}H_{19}N_3O_2$: 333.14773; found 333.1480.

3-[(4-Ethoxyphenyl)-(4-methoxyphenyl)amino]-1-morpholin-4-yl-propenone (3h), 2[(4-ethoxyphenyl)-(4-methoxyphenyl)-amino]-4-morpholin-4-yl-4-oxobutyronitrile (4h), and 3-(4-ethoxyphenyl)-1-morpholin-4-yl-3-(4-methoxyphenyl)aminopropan-1-one (6h): Nitrone **1h** (271 mg, 1 mmol) and alkene **2** (138 mg, 1 mmol) were heated in toluene (1.5 mL) at 90 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 70:30 → 50:50) afforded **3h** (73 mg, 19 %), **4h** (78 mg, 19 %), and **6h** (69 mg, 18 %).

3h: Brown crystals (dichloromethane/diethyl ether); m.p. 64.5 – 65 °C; ^{1}H NMR (400 MHz): δ = 1.41 (t, J(H,H) = 6.8 Hz, 3H; OCH$_2$CH_3), 3.22 (m, 2H; morph), 3.36 (m, 2H; morph), 3.57 (m, 4H; morph), 3.68 (s, 3H; OCH_3), 3.98 (q, J(H,H) = 6.8 Hz, 2H; OCH_2CH$_3$), 4.85 (s, 1H; CHCHCO), 5.91 (s, 1H; CHCHCO), 6.49 (m, 1H; Ar), 6.81 – 6.93 (m, 5H; Ar), 7.28 ppm (m, 2H; Ar); elemental analysis calcd (%) for $C_{22}H_{26}N_2O_4$ (M = 382.5 g mol^{-1}): C 69.09, H 6.85, N 7.32; found: C 69.25, H 6.80, N 7.51.

4h: Brown crystals (dichloromethane/diethyl ether); m.p. 75 – 75.5 °C; ^{1}H NMR (400 MHz): δ = 1.39 (t, J(H,H) = 6.8 Hz, 3H; OCH$_2$CH_3), 2.78 (dd, J(H,H) = 16.2 Hz, J(H,H) = 6.7 Hz, 1H; CHHC=O), 2.79 (dd, J(H,H) = 16.2 Hz, J(H,H) = 6.7 Hz, 1H; CHHC=O), 3.31 (s, 3H; OCH_3), 3.21 – 3.69 (m, 8H; morph), 4.05 (q, J(H,H) = 6.8 Hz, 2H; OCH_2CH$_3$), 5.42 (t, J(H,H) = 6.7 Hz, 1H; CHCH$_2$CO), 6.31 – 6.39 (m, 2H; Ar), 6.62 (d, J(H,H) = 9.2 Hz, 2H; Ar), 6.87 (d, J(H,H) = 9.0 Hz, 2H; Ar), 7.11 (d, J(H,H) = 9.0 Hz, 2H; Ar), 7.29 ppm (d, J(H,H) = 9.2 Hz, 2H; Ar); high-resolution MS: m/e calculated for $C_{23}H_{27}N_3O_4$: 409.20016, found 409.1972.

6h: Brown crystals (dichloromethane/diethyl ether); m.p. 81 – 81.5 °C; ^{1}H NMR (400 MHz): δ = 1.45 (t, J(H,H) = 6.8 Hz, 3H; OCH$_2$CH_3), 2.75 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.72 Hz, 1H; CHHC=O), 2.86 (dd, J(H,H) = 14.4 Hz, J(H,H) = 6.72 Hz, 1H; CHHC=O), 3.21 – 3.67 (m, 8H; morph), 3.69 (s, 1H; OCH_3), 4.02 (q, J(H,H) = 6.8 Hz, 2H; OCH_2CH$_3$), 4.67 (t, J(H,H) = 6.72 Hz, 1H; CHCH$_2$CO), 6.51 (d, J(H,H) = 9.2 Hz, 2H; Ar), 6.72 (m, 2H; Ar), 6.85 (m, 2H; Ar), 7.32 ppm (d, J(H,H) = 9.2 Hz, 2H; Ar); elemental analysis calcd (%) for $C_{22}H_{28}N_2O_4$ (M = 384.5 g mol^{-1}): C 69.73, H 7.34, N 7.29; found: C 69.35, H 7.35, N 7.39.

3-[(4-Ethoxyphenyl)-(4-cyanophenyl)-amino]-1-morpholin-4-yl-propenone (3i) and 2[(4-ethoxyphenyl)-(4-cyanophenyl)-amino]-4-morpholin-4-yl-4-oxo-butyronitrile (4i): Nitrone **1i** (266 mg, 1 mmol) and alkene **2** (138 mg, 1 mmol) were heated in toluene (1.5 mL) at 110 °C for 4 h. Evaporation of the solvent followed by column chromatography (cyclohexane/ethyl acetate: 70:30 → 50:50) afforded **3i** (276 mg, 73 %) and **4i** (65 mg, 16 %).

3i: Yellow crystals (dichloromethane/diethyl ether); m.p. 174 – 174.5 °C; ^{1}H NMR (400 MHz): δ = 1.48 (t, J(H,H) = 7.0 Hz, 3H; OCH$_2$CH_3), 3.25 – 3.65 (m, 8H; morph), 4.08 (q, J(H,H) = 7.0 Hz, 2H; OCH_2CH$_3$), 5.11 (d, J(H,H) = 12.6 Hz, 1H; CH=CH), 6.89 (d, J(H,H) = 9.1 Hz, 2H; Ar), 6.98 – 7.02 (m, 4H; Ar), 7.48 (d, J(H,H) = 9.1 Hz, 2H; Ar), 8.28 ppm (d, J(H,H) = 12.6 Hz, 1H; CH=CH); elemental analysis calcd (%) for $C_{22}H_{23}N_3O_3$ (M = 377.4 g mol^{-1}): C 70.01, H 6.14, N 11.13; found: C 70.30, H 6.14, N 11.05; high-resolution MS: m/z calculated for $C_{22}H_{23}N_3O_3$: 377.17394; found 377.1761.

4i: Yellow oil (dichloromethane/diethyl ether); ^{1}H NMR (400 MHz): δ = 1.45 (t, J(H,H) = 7.0 Hz, 3H; OCH$_2$CH_3), 2.68 (dd, J(H,H) = 16.2 Hz, J(H,H) = 6.8 Hz, 1H; CHHC=O), 2.79 (dd, J(H,H) = 16.2 Hz, J(H,H) = 6.8 Hz, 1H; CHHC=O), 3.14 – 3.67 (m, 8H; morph), 4.05 (q, J(H,H) = 7.0 Hz, 2H; OCH_2CH$_3$), 5.12 (t, J(H,H) = 6.8 Hz, 1H; CHCH$_2$CO), 6.78 (d, J(H,H) = 9.0 Hz, 2H; Ar), 6.98 (d, J(H,H) = 9.1 Hz, 2H; Ar), 7.18 (d, J(H,H) = 9.1 Hz, 2H; Ar), 7.49 ppm (d, J(H,H) = 9.0 Hz, 2H; Ar); high-resolution MS: m/z calculated for $C_{23}H_{24}N_4O_3$: 404.18484; found 404.1836.

Acknowledgements

This work was supported by the CNRS, Université du Maine, and Institut universitaire de France. We thank Professor Daniel E. Falvey (University of Maryland) for stimulating comments.

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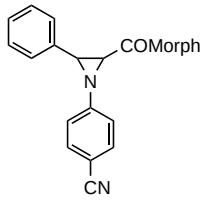

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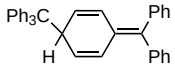

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Received: May 16, 2002
Revised: October 25, 2002 [F4099]

  0947-6539/03/0904-1007 $ 20.00+.50/0