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Thermal and Acid-catalysed Sigmatropic Rearrangements of Allylamino - methoxy -1,2-benzoquinones.

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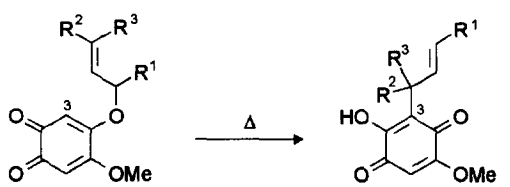
Abstract: Thermal and acid-catalysed sigmatropic rearrangements of 4-(N-methyl-N-allylamino)-5-methoxy-1,2-benzoquinones **3** and of 4-(2-vinyl-aziridino or azetidino)-5-methoxy-1,2-benzoquinones **7** were studied and compared. The mechanisms of these reactions are discussed .

INTRODUCTION

In the course of synthesising new quinonic compounds, we wanted to investigate whether an amino-Claisen type of rearrangement could be used as an alkylating process to functionalize 1,2-benzoquinones. Indeed, we showed, in a previous paper [1] how [3,3]-sigmatropic rearrangement, when applied to allyloxy 1,2-benzoquinones, yielded hydroxy *para*benzoquinones selectively alkylated at the 3- position of the quinonic nucleus (Scheme 1).



Scheme 1

This strategy allowed us to describe an easy pathway for obtaining new structures related to Maesanine [2] (Scheme 1, R^1 = *n*-C_{12} chain, R^2 = R^3 = H), a natural pigment exhibiting strong biological activities. The thermal rearrangement was facile and, in some cases, took place even at room temperature. Therefore, it was considered worthwhile to test a similar strategy in the allylamino series although it is well known that amino-Claisen requires higher temperatures. [3]

Two series of amino-1,2-benzoquinones have been studied. The first of which **3** has a *N*-methyl-*N*-(2-propenyl)-amino substituent and the second series **7** was substituted by a 2-vinyl-aziridino or -azetidino group.

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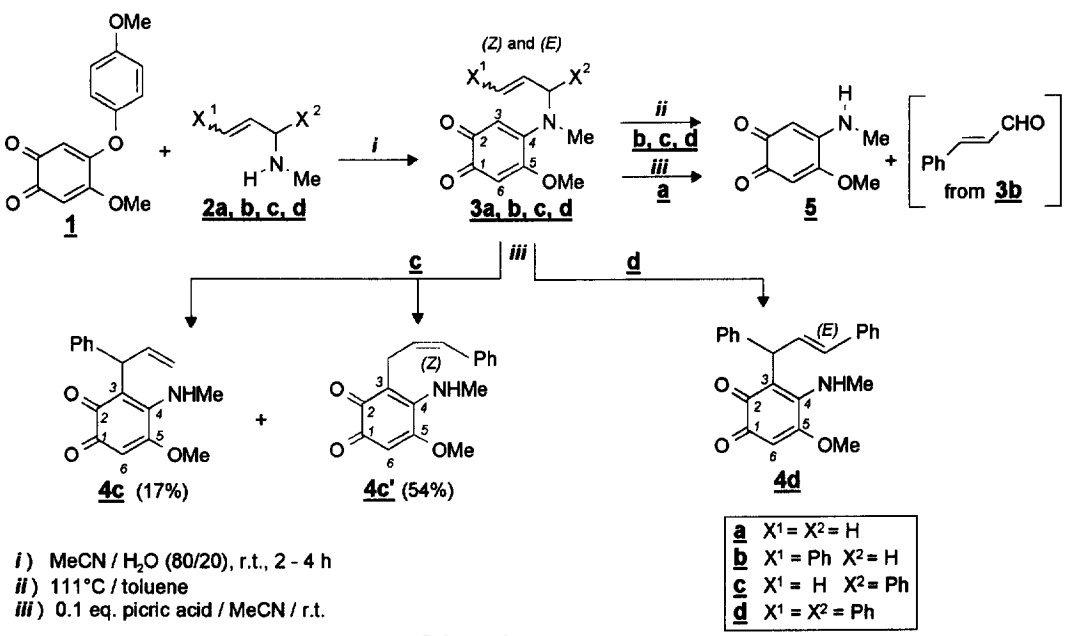
RESULTS

N-methyl-N-(2-propenyl)-1,2-benzoquinones 3 :

New 1,2-benzoquinones **3** were prepared according to our previous paper[4] by nucleophilic substitution of corresponding *N*-methyl-*N*-(2-propenyl)-amines **2** on the readily accessible 4-*para*methoxyphenoxy-5-methoxy-1,2-benzoquinone **1** (Scheme 2). The reaction was highly regioselective, and yields were excellent.

When heated at reflux in a toluene solution (111°C) or in benzonitrile (188°C), amino-quinones **3** do not undergo a Claisen rearrangement, but give rise instead to *N*-dealkylated quinone **5** among other unidentified compounds. However, if a catalytic amount of picric acid (0.1 eq.) is added to an anhydrous acetonitrile solution of **3d** (either *Z* or *E*), pure *(E)*-1,2-benzoquinone **4d** is obtained within 5 minutes at room temperature. Under the same acidic conditions, quinone **3c** undergoes an intramolecular alkylation of its quinone nucleus but more slowly (5 h). However, two products were formed: quinone **4c'** (54%) and quinone **4c** (17%) resulting from a [3,3]- and a [1,3]-sigmatropic rearrangement respectively. ^{1}H-NMR analysis revealed an exclusive *Z* geometry for the double bond in quinone **4c'**.

N-methyl *N*-allyl quinone **3a** in refluxing toluene was slowly transformed into uncharacterisable material (80% recovered material after 3 hrs).



Scheme 2

N-methyl-*N*-cinnamyl quinone **3b** and picric acid in acetonitrile at room temperature gave no reaction. However, in refluxing acetonitrile, **3b** was mainly transformed into *N*-dealkylated quinone **5** (80% after 24 hrs).

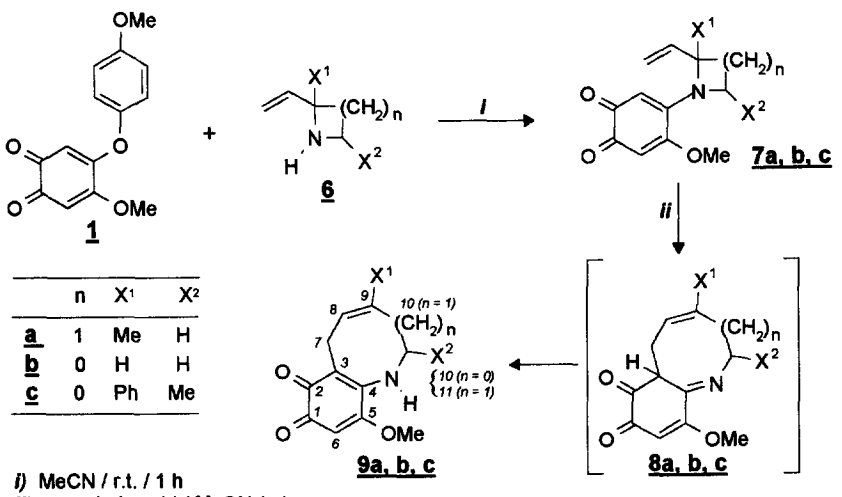
Its production was accompanied by that of (*E*) cinnamaldehyde (50% isolated), this was due to an intramolecular oxido-reductive process involving migration of one of the allylic protons toward formation of a highly oxidizable and hydrolysable imino-catechol.[5] *N*-methyl-*N*-allyl quinone **3a** which was quite stable at room temperature under these conditions was slowly transformed in refluxing acetonitrile into the *N*-dealkylated quinone **5** (30% in 24 hrs). No trace of C_3-alkylated quinone has ever been detected from **3a** or **3b**.

Aziridino and azetidino quinones 7 :

α-Vinyl-aziridines and -azetidines **6a, b, c** were reacted with synthon **1**, as described above but in dry acetonitrile. The corresponding α-vinyl-aziridino-quinones **7b,c** could not be isolated. Instead, bicyclic orthobenzoquinones **9b,c** were directly obtained (Scheme 3). These new dihydroazepine-quinones were the result of a spontaneous amino-Claisen type rearrangement of the initially formed methoxy-amino-1,2-benzoquinones **8b, c**.

Quinone **7a**, in contrast, was easily isolated (55%) from the reaction mixture, following the classical procedure for the nucleophilic substitution on synthon **1** by azetidine **6a**. When a toluene solution of pure quinone **7a** was heated to reflux for 15 minutes it gave the new tetrahydroazocine-quinone **9a** in quantitative yield as described in a preliminary report.[6]

When the reaction was carried out in acidic acetonitrile (0.1 molar eq. of picric acid) at room temperature, the rearrangement was complete within 10 hours (in neutral solution, quinone **7a** is stable for days, at room temperature).



Scheme 3

DISCUSSION

I - Thermal sigmatropic rearrangement :

1,2-Benzoquinones **3** containing an acyclic allylamino group do not undergo a Claisen type rearrangement by simple heating in neutral toluene. This was in contrast with the high reactivity of their allyloxy-1,2-benzoquinones parents. 4-Allyloxy-5-methoxy-1,2-benzoquinone was quantitatively converted into 3-allyloxy-1,2-benzoquinone within 30 minutes in refluxing toluene (111°C) according to a classical Claisen rearrangement.[1] However, in the amino-quinone series, its analogue **3a** (and even the phenyl substituted compound **3b**) are either recovered unchanged under the same experimental conditions or undergo fragmentation with prolonged reaction times or at elevated temperatures. This observation was not so surprising since it is well known that pure thermal amino-Claisen rearrangements are considerably more difficult than those of their oxygen counterparts, usually requiring temperatures that are about 100-150°C higher than those which give rearrangements of the corresponding oxygen compounds.[3]

When the amino group is part of a small ring system such as an aziridine, relief of the strain during the concerted rearrangement process usually lowers the activation energy.[7] This was indeed in agreement with what we observed with amino-quinones **7**. Vinyl-aziridino-quinones **7b, c** were so reactive that they spontaneously underwent a [3,3]-sigmatropic rearrangement under the experimental conditions employed for their synthesis (MeCN, r.t.), thus providing the corresponding bicyclic quinones **9b, c**. This reaction was closely related to the one described in the *N*-phenyl-vinylaziridine series but occurred at a much lower temperature (25° versus 140°C). [8]

With the less strained azetidino system, the amino-Claisen rearrangement was slower since quinone **7a** was isolated (55%). Complete rearrangement of **7a** to the bicyclic quinone **9a** was carried out in refluxing toluene for 15 minutes.

Thus, the more strained the amino system, the lower the temperature required for the rearrangement. The moderate overall yields reported for the synthesis of quinones **9b, c** starting from synthon **1** are mainly due to the high sensitivity of the aziridino ring systems to nucleophilic attack, rather than to the concerted step. Indeed, release of PMP in presence of a base or a trace of water can lead to nucleophilic ring-opening *N*-dealkylation processes (see our preceding paper [5]).

II - Acid-catalysed sigmatropic rearrangements:

Catalysis in amino-Claisen systems has been known for almost as long as the reactions themselves, beginning with a 1912 report by Claisen [9] of the apparent catalytic effect of ammonium chloride on a Claisen rearrangement. Brönsted acid catalysis, being the most thoroughly investigated, is especially useful in the amino systems. Rate accelerations by factors of 10^5-10^7 for protonated amines compared to neutral substrates have been reported [10]. Furthermore, it often permits the occurrence of thermally inaccessible reactions. Reactions of protonated substrates were interpreted as charge-accelerated rearrangements with a lowered activation

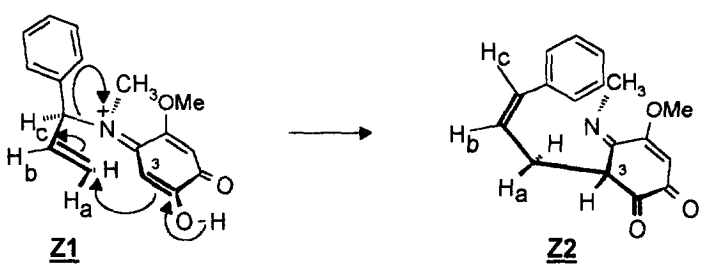
enthalpy, a consequence of charge delocalization in the transition state, as well as full inhibition of nitrogen lone pair delocalization in the ground state.

Indeed, in the case of acyclic allylaminoquinones **3c, d** , addition of a catalytic amount of picric acid allowed us to obtain products **4**, obtained from sigmatropic rearrangements, whereas they only underwent fragmentation in a neutral medium. With quinone **3d** which bears two phenyl groups in 1- and 3- positions of the allylamino moiety, the reaction was the fastest going to completion within 5 minutes at room temperature and gives rise to a unique compound **4d**.

Rearrangement of quinone **3c**, which has only one phenyl group in α-position of nitrogen, is slower (4h at r.t.) and yields two products: **4c** and **4c'**. Benzoquinone **4c**, the minor product, was clearly not due to a Claisen rearrangement but rather to the cationic migration of the *N*-substituent. We have already described this process in closely related quinones whose amino substituents bear groups capable of stabilising an α-developing positive charge.[5] Such a mechanism involving transient formation of a cation may well account for the formation of product **4c'**, since allylic cations are well known to undergo nucleophilic attack on the double bond. Furthermore, the fact that the reaction is faster when two phenyl groups were present on the allyl moiety of **3d** compared to **3c**, is in agreement with either a cationic migration or a concerted rearrangement. In the literature, several papers report on the importance of charged species in aza-Claisen reactions [11].

The purely *Z* geometry of the double bond in compound **4c'** (established by ^{1}H-NMR spectroscopy) may be tentatively explained by proposing that protonated quinone **3c** (**Z1** in Scheme 4, see also Scheme 8 in our preceding paper [5]), adopts a six membered ring transition state. This allows a conformation in which the phenyl group is in a quasi-axial position so minimising its interaction with the methyl group (N^+-Me). The H_b-C-C-H_c dihedral angle is close to 0°, and this conformation provides a purely *Z* double bond in quinone **4c'** after the trapping of the rearranged allylic carbonium ion by C_3 (**Z1** → **Z2**).

Scheme 4



With the same kind of transition state, strain becomes more important when starting from quinone **3d** (either *E* or *Z* isomer). A strong 1,3-diaxial interaction develops between the two phenyl groups in the case of **3d** *E* isomer. However, in **3d** *Z* isomer, a severe steric hindrance appears between the phenyl group (X^1 = Ph) and the quinone nucleus. In both cases, a transition state with an X^2 phenyl group in the equatorial position is thus highly favoured, affording compound **4d** with a pure *E* geometry.

CONCLUSION

Thermal and acid-catalysed amino-Claisen types of rearrangement have been performed for the first time on quinonic compounds. These reactions offer new synthetic routes to some 3-allyl-4-methylamino-5-methoxy-1,2-benzoquinones (type **4**) and to bicyclic amino-benzoquinones such as benzazepine-quinones (type **9b,c**) and benzazocine-quinones (type **9a**). In the type **4** series (linear amines) these rearrangements are limited to α-amino aryl-substituted groups like **3c** structure, but in the type **7** series (strained cyclic amines) activation by an aryl group was not necessary and so the scope of the reaction appears broader. While benzazepine-quinones constitute a new structural class, benzazocine-quinones have recently been studied as key-intermediates for the total synthesis of mitomycins, [12] molecules exhibiting potent antibiotic and antitumoral activities.

EXPERIMENTAL SECTION

All reagents were of commercial quality. Acetonitrile (dry) was distilled twice from P_4O_{10} and kept over 3 Å molecular sieves. Analytical tlc plates (silica gel 60 F254) and silica gel 60 (230-400 mesh) were purchased from Merck-Clévenot S.A.. Melting points were determined with a Kofler apparatus (Reichert) and were uncorrected. ^{1}H-NMR (300 MHz) and ^{13}C-NMR (75 MHz) spectra (in $CDCl_3$ solutions) were recorded on a Brucker AC spectrometer; chemical shifts were reported in ppm (δ) downfield from internal TMS and coupling constants J in hertz. The HPLC analyses were carried out on a Lichrosorb (5 µm) Merck™ diol column, 250 mm, using pure MeOH as an eluent and on a Merck™ RP-18 column, 250 mm, using a MeOH / H_2O (80/20) mixture; flow rate was set at 0.5 mL. min^{-1} using a Gilson™ solvent-delivery system. Quantifications were performed by comparison with calibration curves obtained with known amounts of compounds. Absorbance at 254 nm was monitored.

Synthesis of allylamines **2** and **6** :

N-methyl-*N*-allylamine **2a** was purchased from Aldrich™.

(E)-N-methyl cinnamylamine **2b** : bp = 154°C (56 mm) bp_{lit} = 111°C (12 mm)[13] (73%); ^{1}H NMR δ 1.85 (s, exch. D_2O, 1H, NH), 2.4 (s, 3H, NMe), 3.3 (d, 2H, J = 6, NCH_2), 6.2 (dt, 1H, J_1 = 16.5, J_2 = 6, =CH-CH_2), 6.6 (d, 1H, J = 16.5, Ph-CH=), 7.1-7.3 (m, 5H, Ph).

N-methyl-N-[α-phenyl-allyl] amine **2c** : was prepared (83% yield) by reaction of vinyl magnesium bromide in refluxing ether with *N*-methyl-benzylimine (2 h)[14] [prepared, [19] 87%, bp_{lit} = 90°C (30 mm)] bp = 65°C (4 mbar); ^{1}H NMR δ 1.3 (s, large, exch. D_2O, 1H, NH), 2.35 (s, 3H, NMe), 4.05 (d, 1H, J = 7, NCH), 5.0 - 5.3 (m, 2H, CH_2=), 5.7 - 6.1 (m, 1H, CH=), 7.3 (s, large, 5H, Ph).

N-methyl-N-[α-phenyl-cinnamyl] amine **2d** *(E)*: [(*E*)-1,3-diphenyl-1-methylamino-2-propene], was synthesized (55%) by phenyl lithium reaction in refluxing ether (2 h) with cinnamylidene methylamine [prepared[15]], as white crystals, m.p. = 39°C, bp. = 83°C (1 mbar) bp_{lit} = 134-141°C (16 mm)] of pure *(E)*-**2d**; ^{1}H NMR δ 1.6 (s, broad, exch. D_2O, 1H, NH), 2.35 (s, 3H, NMe), 4.2 (d, 1H, J = 7, NCH), 6.3 (dd, 1H, J_1 = 15, J_2 = 7, =CH-CH), 6.6 (d, 1H, J = 15, Ph-CH=), 7.0 - 7.4 (m, 10H, Ph).

N-methyl-N-[α-phenyl-cinnamyl] amine **2d** *(E+Z)*: prepared by condensation of β-bromo-styrene Grignard's reagent with benzylidene methylamine[19] in refluxing ether (3 h). Yield: 90%, *Z/E* = 35/65 in the crude product and *Z/E* = 71/29 after distillation. bp = 145-146°C (1.5 mbar); ^{1}H NMR δ 1.4 (s, broad, exch. D_2O, 1H, NH), 2.25 (s, 3H, NMe), 4.53 (d, 1H, J = 9.8, NCH), 5.75 (dd, 1H, J_1 = 12, J_2 = 9.8, =CH-CH), 6.6 (d, 1H, J = 12, Ph-CH=), 7.0 -7.4 (m, 10H, Ph).

2-methyl-2-vinyl-azetidine **6a**: was synthesised (61% yield) by AlH_3 reduction[16] of 4-methyl-4-vinyl-2-azetidinone, prepared by reaction of *N*-chlorosulfonyl isocyanate with isoprene.[20, 21]; bp = 95°C (bp_{lit} = 107 - 110°C)[16] : ^{1}H NMR δ 1.35 (s, 3H, Me), 1.8 (s, exch. D_2O, 1H, NH), 2.0 - 2.4 (m, 2H, C-CH_2-C), 3.3 - 3.6 (m, 2H, NCH_2), 5.0 (dd, 1H, J_1 = 10.5, J_2 = 1.5, CH_2=), 5.15 (dd, 1H, J_1 = 17, J_2 = 1.5, CH_2=), 6.1 (dd, 1H, J_1 = 17, J_2 = 10.5, CH=)

2-vinyl-aziridine **6b**: was obtained (24% yield) from 1-amino-2-hydroxy-3-butene [22] as described in the literature.[17] bp = 95-99°C (bp_{lit} = 97-99°C) [17]; ^{1}H NMR (CCl_4) δ 1.3 (s, broad, 1H, NH), 1.47 (dd, 1H, H_3), 1.82 (dd, 1H, H_3), 2.3 (m, 1H, H_2), 4.85 - 5.5 (m, 3H, vinyl)

3-methyl-2-vinyl-2-phenyl-aziridine **6c**: was prepared (64% yield) according to A. Laurent's method,[18, 23] by reaction of vinyl magnesium bromide on propiophenone *N,N,N*- trimethylhydrazonium iodide. The oily crude product was purified by column chromatography on silica gel using diethylether / petroleum ether (1/4) as an eluent. Colorless oil; ^{1}H NMR δ 0.85 (d, J = 6, 3H, Me), 1.3 (s, exch. D_2O, 1H, NH), 2.3 (q, 1H, J = 6, NCH), 4.85 (dd, 1H, J_1 = 17, J_2 = 1.5, CH_2=), 5.0 (dd, 1H, J_1 = 10.5, J_2 = 1.5, CH_2=), 5.75 (dd, 1H, J_1 = 17, J_2 = 10.5, CH=), 7.1 - 7.4 (m, 5H, Ph).

Synthesis of allylamino-quinones **3** and **7** :

They are synthesised by our previously described regioselective procedure.[4,5] Solvents were either an acetonitrile / water (80/20, v/v) mixture for amino-quinones **3** or anhydrous acetonitrile for cyclic amino-quinones **7**.

4-*N*-Methyl allylamino-5-methoxy-1,2-benzoquinone **3a** : yield = 70%, dark-red crystals, mp = 111°C; ^{1}H-NMR δ 3.05 (s, 3H, NMe), 3.85 (s, 3H, OMe), 4.05 (d, 2H, J = 6, NCH_2), 5.25 (m, 2H, =CH_2), 5.6 (s, 1H, $H_{q.3}$), 5.75 (s, 1H, $H_{q.6}$), 5.85 (m, 1H, C-CH=). Anal. calcd. for $C_{11}H_{13}NO_3$ (207.23) : C, 63.76%; H, 6.32%; N, 6.76% - Found : C, 63.70%; H, 6.28%; N, 6.80%.

4-*N*-Methyl cinnamylamino-5-methoxy-1,2-benzoquinone **3b**: yield = 90%, dark-red crystals, mp = 131°C; ^{1}H-NMR δ 3.05 (s, 3H, NMe), 3.85 (s, 3H, OMe), 4.15 (d, 2H, J = 6, NCH_2), 5.6 (s, 1H, $H_{q.3}$), 5.7 (s, 1H, $H_{q.6}$), 6.2 (dt, 1H, J_1 = 16.5, J_2 = 6, CH_2-CH=), 6.6 (d, 1H, J = 16.5, =CHPh), 7.1-7.3 (m, 5H, Ph); Anal. calcd. for $C_{17}H_{17}NO_3$ (283.33) : C, 72.07%; H, 6.05%; N, 4.94% - Found : C, 72.10%; H, 6.10%; N, 4.90%.

4-*N*-Methyl (1'-phenyl-allylamino)-5-methoxy-1,2-benzoquinone **3c** : yield 70%, dark-red crystals, mp = 104°C; ^{1}H-NMR δ 2.65 (s, 3H, NMe), 3.85 (s, 3H, OMe), 5.2-5.8 (m, 3H, =CH_2 and CHPh), 5.65 (s, 1H, $H_{q.3}$), 5.80(s, 1H, $H_{q.6}$), 5.9-6.4 (m, 1H, CH=CH_2), 7.2-7.5 (m, 5H, Ph). Anal. calcd. for $C_{17}H_{17}NO_3$ (283.33) : C, 72.07%; H, 6.05%; N, 4.94% - Found : C, 71.98%; H, 6.09%; N, 4.98%.

(E) 4-*N*-Methyl (1'-phenyl-cinnamylamino)-5-methoxy-1,2-benzoquinone **3d (E)** : yield 91%, dark-red crystals, mp = 94°C ; ^{1}H-NMR δ 2.8 (s, 3H, NMe), 3.85 (s, 3H, OMe), 5.7 (s, 1H, $H_{q.3}$), 5.8 (s, 1 H, $H_{q.6}$), 5.9 (dd, 1H, J_1 = 5.3, J_2 = 0.75, NCH), 6.4 (dd, 1H, J_1 = 15.8, J_2 = 5.3, =CH-CH), 6.65 (dd, 1H, J_1 = 15.8, J_2 = 0.75, =CH-Ph), 7.2-7.75 (m, 10H, 2 Ph); Anal. calcd. for $C_{23}H_{21}NO_3$ (359.42) : C, 76.86%; H, 5.89%; N, 3.90% - Found : C, 76.70%; H, 5.92%; N, 3.97%.

(Z) 4-*N*-Methyl (1'-phenyl-cinnamylamino)-5-methoxy-1,2-benzoquinone **3d (Z)** : yield 90% , dark-red crystals, with the same isomers ratio Z/E = 71/29 as for amine **2d**; ^{1}H-NMR δ 2.7 (s, 3H, NMe), 3,3 (s, 3H, OMe), 5.5 (s, 1H, $H_{q.3}$), 5.65 (s, 1H, $H_{q.6}$), 6.0 (dd, 1H, J_1 = 11.3, J_2 = 9.8, =CH-CH), 6.45 (d, J = 9,8, 1H, NCH), 6.95 (d, 1H, J = 11,3, =CH-Ph), 7.1-7.6 (m, 10H, 2 Ph). Anal. calcd. for $C_{23}H_{21}NO_3$ (359.42) : C, 76.86%; H, 5.89%; N, 3.90% - Found : C, 76.75%; H, 5.90%; N, 3.94%.

4-(1'-vinyl-1'-methyl-azetidino)-5-methoxy-1,2-benzoquinone **7a** : yield = 55%, dark-red crystals, mp = 92°, ^{1}H-NMR δ 1.7 (s, 3H, Me), 2.15 - 2.45 (m, 2H, C-CH_2-C), 3.85 (s, 3H, OMe), 4.5 (t, 2H, J = 8, NCH_2), 5.1 - 5.4 (m, 2H, =CH_2), 5.4 (s, 1H, $H_{q.3}$), 5.7 (s, 1H, $H_{q.6}$), 6.15 (dd, 1H, J_1 = 17, J_2 = 10, =CH). Anal. calcd. for $C_{13}H_{15}NO_3$ (233.27) : C, 66.94%; H, 6.48%; N, 6.00% - Found : C, 66.90%; H, 6.52%; N, 6.07%.

Acid-catalyzed rearrangement of quinones **3c,d** .

Amino-quinones **3c,d** were dissolved in anhydrous MeCN (3 mmol in 5 mL) with 0.1 equiv. picric acid, 20°C. Reaction time was 4h for **3c** (quinones **4c** and **4c'** were separated by column chromatography on silica gel with a mixture of cyclohexane and AcOEt (50/50) as eluent. Reaction time was only 5 min for **3d** and pure quinone **4d** crystallizes from the crude material .

3-(1'-phenyl allyl)-4-*N*-methylamino-5-methoxy-1,2-benzoquinone **4c** : dark-red crystals, yield = 17%, mp = 140°C; ^{1}H NMR δ 2.95 (d, *J* = 6, 3H, NMe), 3.8 (s, 3H, OMe), 5.0-5.4 (m, 3H, PhC<u>H</u>CH=C<u>H</u>$_2$), 5.6 (s, broad, exch. D_2O, 1H, NH), 5.7 (s, 1H, H_q), 6.2-6.7 (m, 1H, CHC<u>H</u>=CH_2), 7.1-7.4 (m, 5H, Ph). ^{13}C NMR δ 34.39 (NMe); 44.16 (CH on C_3 substit.); 56.62 (OMe); 102.54 (C_6); 111.90 (q, C_3); 116.65 (=CH_2); 126.14, 127.22, and 128.33 (3 aromatic C); 137.57 (=CH-); 141.70 (q); 149.32 (q); 163.97 (q); 175.75 (q, CO); 180.16 (q, CO). Anal. calcd. for $C_{17}H_{17}NO_3$ (283.33) : C, 72.07%; H, 6.05%; N, 4.94% - Found : C, 72.00%; H, 6.08%; N, 4.91%.

3-[3'-phenyl prop-2-en (Z)]-4-*N*-methylamino-5-methoxy-1,2-benzoquinone **4c'** : dark-red crystals, yield = 54%, mp = 165°C, ^{1}H NMR δ 3.2 (d, 3H, J = 6, NMe), 3.5 (d, 2H, J = 3, -CH_2-),3.8 (s, 3 H, OMe), 5.7 (s,

1H, H_q), 6.0 (s, broad, exch. D_2O, 1H, NH), 6.3 (s, broad, 2H, CH=CH), 7.1-7.4 (m, 5H, Ph). ^{13}C NMR δ : 27.02 (CH_2); 32.79 (NMe); 56.80 (OMe); 101.87 (C_6); 107.00 (q, C_3); 125,88; 126.89; 128.31; 129.31; 129.95 (5 aromatic and ethylenic CH); 137.27 (q); 148.45 (q); 155.15 (q); 162.83 (q); 176.66 (q, CO); 180.57 (q, CO). Anal. calcd. for $C_{17}H_{17}NO_3$ (283.33) : C, 72.07%; H, 6.05%; N, 4.94% - Found : C, 72.00%; H, 6.10%; N, 4.89%.

3-[1',3'-diphenyl prop-2-en (E)]-4-*N*-methylamino-5-methoxy-1,2-benzoquinone **4d** : dark-red crystals, yield = 90%, mp = 120°C, ^1H NMR δ: 3.0 (d, *J* = 6, 3H, NMe), 3.85 (s, 3H, OMe), 5.35 (d, *J* = 7, 1H, PhCH), 5.7 (s, 1H, H_q), 5.9 (s, broad, exch. D_2O, 1H, NH), 6.45 (d, 1H, J = 16, PhCH=), 6.85 (dd, 1H, J_1 = 16, J_2 = 7, PhCH=CH), 7.05-7.6 (m, 10H, 2 Ph). ^{13}C NMR δ 38.60 (NMe); 57.28 (OMe); 77.09 (CH); 99.77 (C_6); 128.45; 128.53; 128.86; 129.01; 129.40; 132.74 (q);132.74 (q); 165.08 (q); 175.17 (q, CO); 182.87 (q, CO). Anal. calcd. for $C_{23}H_{21}NO_3$ (359.42) : C, 76.86%; H, 5.89%; N, 3.90% - Found : C, 76.80%; H, 5.93%; N, 3.89%.

Synthesis of tetrahydroazocine - quinone **9a**:

By thermal rearrangement: A solution of 0.162 g (0.695 mmol) of quinone **7a** in anhydrous toluene (3 mL) was heated to reflux until all the starting material was consumed (15 minutes). The solvent was removed in vacuo and the resulting solid (0.162 g, 100%) of pure quinone **9a** was recrystallized from a mixture of ethyl acetate and cyclohexane (80/20 v/v).

By acid-catalyzed rearrangement: As a typical experiment, quinone **7a** (0.810 g, 3.47 mmol) and picric acid (0.080 g, 0.35 mmol) were dissolved at room temperature in anhydrous acetonitrile (5 mL), and the mixture was abandoned for 5 h. The solvent was removed under reduced pressure, the residue dissolved in dichloromethane (30 mL), then washed with aqueous 1M K_2CO_3 (10 mL) and dried ($MgSO_4$). Evaporation of the solvent provides **9a** (0.729 g, 90%).

5-Methoxy-9-methyl- 7,7,10,10-tetrahydroazocine-1-2-benzoquinone **9a** : dark-red crystals, mp = 225°C; ^1H NMR δ 1.7 (s, 3H, Me), 2.55 (t, 2H, J = 6, =CCH_2CH_2),3.5 (d, 2H J = 9, , =CCH_2), 3.85 (s, 3H, OMe), 3.9 (q, 2H, J = 6, NCH_2), 5.55 (t, 1H, J = 9, CH=), 5.6 (s, 1H, H_q), 6.3(s, broad, exch. D_2O, 1H, NH); ^{13}C NMR δ 20.34 (C-7), 25.62 (=C-CH_3), 37.94 (C-10), 42.09(C-11), 56.62 (OMe), 101.21 (C-6), 107.58 (C-3),122.02(C-8), 134.57 (C-9), 148.90, 162.65 (C-4,5), 175.77, 180.89(C-1,2). Anal. calcd. for $C_{13}H_{15}NO_3$ (233.27) : C, 66.94%; H, 6.48%; N, 6.00% - Found : C, 67.00%; H, 6.43%; N, 5.98%.

5-Methoxy-7,7-dihydroazepine-1-2-benzoquinone **9b**: dark-red crystals, 55% yield, mp >170°C (decomposition); ^1H NMR δ 3.5 (d, 2H, J = 7, CH_2), 3.85 (s, 3H, OMe), 4.1 (t, 2H, J = 7, NCH_2), 5.65 (s, 1H, H_q), 5.9 (dt, 1H, J_1 = 10, J_2 = 7, NCH_2CH=), 6.05 (s, broad, exch. D_2O, 1H, NH), 6.2 (dt, 1H, J_1 = 10, J_2 = 7, CCH_2CH=);^{13}C NMR δ 20.66 (C-7), 40.53 (C-10), 56.77 (OMe),102.05(C-6), 105.67 (C-3), 125.01 (C-8),

134.86 (C-9), 148.36, 161.95 (C-4,5), 175.09, 180.39 (C-1,2). Anal. calcd. for $C_{11}H_{11}NO_3$ (205.21) : C, 64.38%; H, 5.40%; N, 6.83% - Found : C, 64.22%; H, 5.43%; N, 6.87%.

5-Methoxy-9-phenyl-10-methyl-7,7-dihydroazepine-1-2-benzoquinone **9c** : yield = 30%, dark red crystals, mp = 202°C; ^{1}H NMR δ 1.5 (d, J = 7, 3H, Me), 3.55 (dd, J_1 = 7, J_2 = 3, 2H, CCH_2), 3.85 (s, 3H, OMe), 4.85 (quint., J = 7, 1H, NCH), 5.65 (s, 1H, H_q), 6.0 (t, J = 7, 1H, CH=), 6.05 (s, broad, exch. D_2O, 1H, NH), 7.1 - 7.4 (m, 5 H, Ph); ^{13}C NMR δ 20.72 (Me), 21.57 (C-7), 51.30 (C-10), 56.87(OMe), 102.15 (C-3), 105.51(C-6), 127.00, 127.36, 128.33, 128.49 (aromatic and C-8), 140.56, 142.51, 147.06 and 162.15 (C-4,5), 175.40 and 180.36 (C-1,2). Anal. calcd. for $C_{18}H_{17}NO_3$ (295.34) : C, 73.20%; H, 5.80%; N, 4.74% - Found : C, 73.27%; H, 5.70%; N, 4.71%.

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