# Reactions of 4-Dialkylamino-5-Methoxy-1,2-Benzoquinones in Acidic Media : Selective C-Alkylation or N-Dealkylation.

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Abstract: *4-(N-methyl-alkylamino)-5-methoxy-1,2-benzoquinones* **3** , *for which N-alkyl group R^1 can give rise to a stabilized carbonium ion, undergo selective acid-catalyzed rearrangements to 3-alkylated-1,2-benzoquinones* **4**. *Aziridino-quinone* **10c** *gives rise to the heterobicyclic 1,2-benzoquinone* **11**. *When R^1 does not contain groups capable of stabilizing a positive charge, efficient and selective N-dealkylations occur. The mechanisms of these reactions are discussed.*
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Formation of C-C bonds is a fundamental reaction in organic chemistry. It may become a challenge when one has to deal with highly functionalized molecules. The chemistry of quinones is particularly delicate and only a few methods, allowing direct alkylation of the ring with conservation of the quinone structure can be found in the literature. In a previous paper,[1] we have described a new alkylation process which involves an acid-catalyzed intramolecular rearrangement: in acetic acid, 4-alkoxy-5-methoxy-1,2-benzoquinones Q_1 undergo a selective cationic migration of an alkyl group R^1 (Scheme 1) into 2-hydroxy-1,4-benzoquinones Q_2 which have been selectively alkylated in the 3-position.The rearrangement occurs only when R^1 is a group capable of stabilizing a positive charge.

Scheme 1
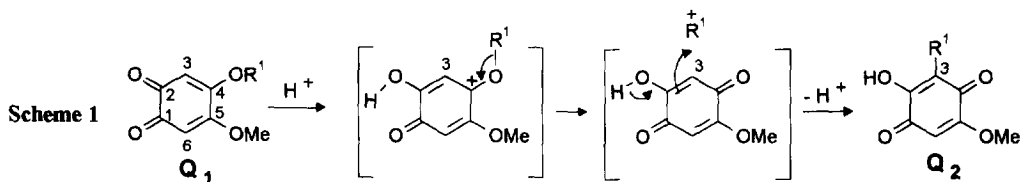
We wanted to extend this acid-catalyzed rearrangement to the synthesis of new 1,2-quinones (*ortho*-quinones Q_1 are transformed into *para*-quinones Q_2 in the alkylation process). Amino-1,2-benzoquinones **3** seemed particularly attractive candidates for such a study, as only few of them are described in the synthetic literature, despite being an important class of biological molecules.[2]
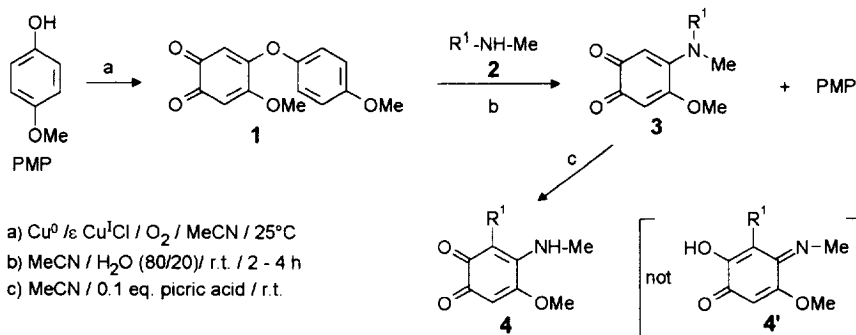
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† Deceased January 1994.

RESULTS

Two classes of tertiary amino-1,2-quinones have been studied, differing from one another in the substitution at nitrogen: N-methyl alkylamino quinones **3** and aziridino-(or azetidino-) quinones **10**.

1°) N-methyl-alkylamino-quinones (3)

4-(N-methyl-alkylamino)-5-methoxy-1,2-benzoquinones **3a-l** are easily and efficiently synthesized via the general pathway described in our recent paper.[3] The key step involves the selective nucleophilic displacement by a secondary amine R^1-NH-CH$_3$ **2a-l** of the *para*methoxyphenoxy group of benzoquinone **1** (Scheme 2, b), a dissymmetrically substituted 1,2-quinone synthon easily prepared from *para*methoxyphenol (PMP) by a copper-catalyzed oxidation [4,5] (Scheme 2, a):

a) Cu^0 /ε Cu^{1}Cl / O$_2$ / MeCN / 25°C
b) MeCN / H$_2$O (80/20)/ r.t. / 2 - 4 h
c) MeCN / 0.1 eq. picric acid / r.t.

2, 3, 4	R^1	4 % yield	2, 3, 4	R^1	4 % yield
a	CH(Ph)$_2$	75	g	CH(Me)(Ph)	9
b	CH(Me)(2-thienyl)	73	h	CH$_2$-(2-furyl)	3
c	CH(cyclopropyl)(Ph)	70	i	n-Bu	0
d	CH(Me)(3-thienyl)	57	j	CH$_2$-C≡CH	0
e	CH(Me)(2-furyl)	50	k	CH$_2$-CH=CH-Ph *(E)*	0
f	CH$_2$-(2-thienyl)	36	l	CH$_2$-Ph	0

Scheme 2

When a catalytic amount of picric acid (2,4,6-trinitrophenol, 0.1 molar equivalent) was added, at room temperature, to 1 M acetonitrile solutions of various N-substituted amino-quinones **3**, a regioselective rearrangement was observed in cases **a-h**. The corresponding aminomethoxyquinones **4**, selectively alkylated at the 3-position of the quinone, are formed within a few hours (< 10 h) (Scheme 2,c).

The ^{1}H-NMR data (Table 5) allowed us to assign structure **4** (1,2-quinone) to these new compounds rather than structure **4'**(1,4-quinone) because the amino proton (NH) is coupled to those of the N- methyl group. Aminoquinones may be classified according to the migratory aptitudes of substituent R^1 linked to their nitrogen atom: if R^1 is a secondary alkyl group substituted by either an aromatic or a cyclopropyl group (cases **a-e**, R^1 = -CHX^{1}X^2 with X^i = Ph, 5-membered heterocycle, cyclopropyl), high yields (up to 75%) of alkylated

quinones **4** are obtained; if R[1] is a primary substituent with one thienyl or furyl group (**3f** and **3h**), or a secondary one with only one phenyl group (**3g**), yields are much lower. Finally, when R[1] is a primary alkyl (**3i-l**), no reaction is observed under the same experimental conditions (i.e. at room temperature).

The choice of the acid employed for the reaction is crucial. For example, the reaction of quinone **3a** has been studied in the presence of various acids and the results are summarized in Scheme 3 and Table 1.
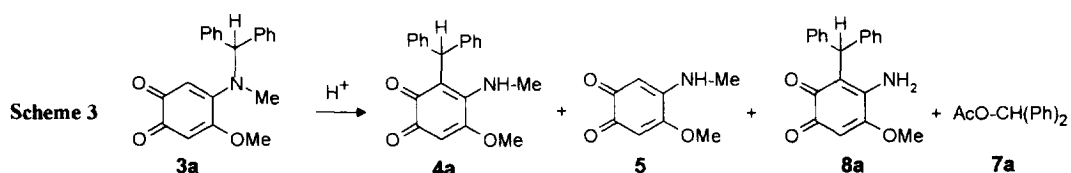
Scheme 3

Table 1 : Acid-catalyzed rearrangement / dealkylation reactions of quinone **3a**

Acid / solvent	temp(°C)	pKa[6]	4a (%)[a]	5 (%)[a]	8a (%)[a]	7a (%)[a]
picric acid (0.1 M) / MeCN [b]	22	0.38	75	25	0	-
H_2SO_4 [c] (0.1 M) / MeCN	22	0.6	25	65	0	-
AcOH	22	4.76	30	60	0	55
AcOH	118	-	5	70	10	70
AcOH / MeCN	82	-	30	60	0	60

[a] Products are separated by column chromatography. [b] Reaction time : 24 h at 22°C or 2 h at 82°C, with the same yields. [c] Reaction becomes sluggish due to the formation of unsoluble salts of amino-quinone **3a** with sulfuric acid.

Table 1 clearly shows that among the different acids tested, the highest yield of alkylated quinone **4a** is obtained with picric acid. A careful analysis of the reaction mixture allowed us to characterize the major side product of the reaction, namely quinone **5**, which comes from the simple acid-catalyzed dealkylation of starting quinone **3a**. Its formation is even more pronounced when sulfuric or acetic acid is used instead of picric acid. In acetic acid, **8a**, N-demethylation product of quinone **4a**, was also isolated. Benzhydryl acetate **7a** was simultaneously obtained with the same ratio as dealkylated quinone **5**. Side product **5** and respectively acetates **7b** and **7c** have also been characterized when quinones **4b** and **4c** were heated in acetic acid.

Similar products are obtained when quinones **3i-l**, which do not give rise to rearranged quinones **4** in presence of picric acid, are heated in refluxing acetic acid (Scheme 4 and Table 2):
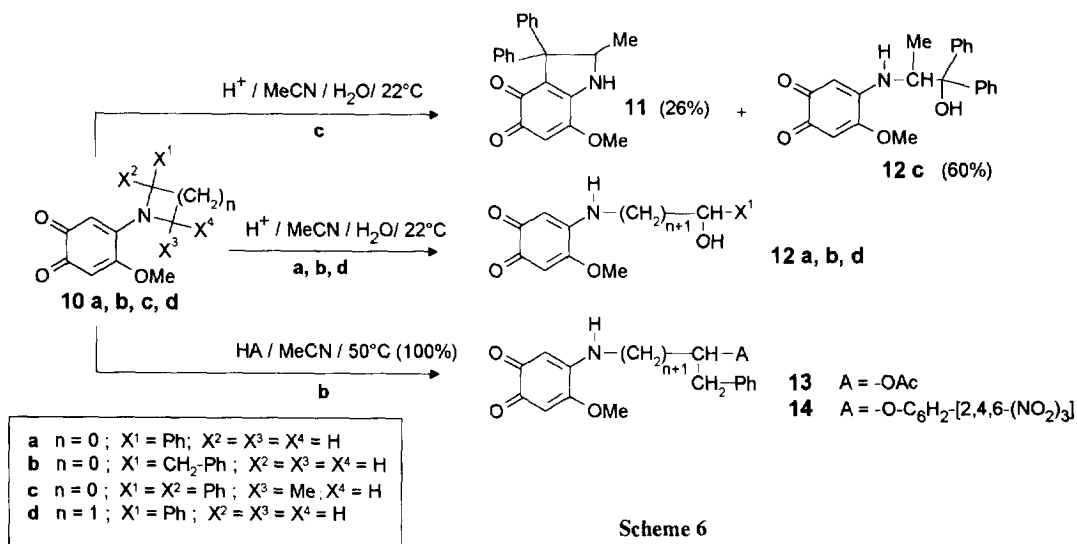
The major reaction pathway, in AcOH, for quinones whose susbstituent R[1] is a primary alkyl group, is N-dealkylation, accompanied by the formation of acetates **7**. When quinone **3k** was heated in a 0.6 M picric acid solution in acetonitrile to complete conversion, cinnamaldehyde (50 %) was formed besides quinone **5**, isolated with 77 % yield. A different mechanism is thus involved and will be discussed below.

Scheme 4

Table 2 : Acid catalyzed dealkylation and demethylation of some aminoquinones[a,b]

3	R[1]	5 yield %	6 yield %
i	n Bu	75	25
j	$CH_2-C\equiv CH$	80	0
k	$CH_2-CH=CH-Ph$ (*E*)	80	0
l	CH_2-Ph	70	10

[a] in refluxing acetic acid (1h at 118°C). [b] Volatile acetates 7i - l (>50% yield) have been characterized by comparison with authentic samples.

Finally, we note that H-substitution on nitrogen makes quinones **5** and **6** unreactive under standard conditions (picric acid at room temperature) whatever their R^1 group..

2°) Aziridino- (and azetidino-) quinones (10).

Since ring-strained systems such as aziridines and azetidines easily open in acidic media by cleavage of the N-C bond [7], it was of some interest to test the ability of quinones **10** to yield bicyclic quinones such as **11** (Scheme 6) through intramolecular alkylation.

Therefore, we have prepared various substituted 4-aziridino- (or azetidino-)-5-methoxy-1,2-benzoquinones **10a-d** (Scheme 5) according to the procedure described in Scheme 2, i.e by regioselective nucleophilic substitution on 4- *para*methoxyphenoxy-5-methoxy-1,2-benzoquinone **1** by variously substituted aziridines and azetidines **9a-d**. Yields and physical constants of these new quinones are collected in Table 4.

Scheme 5

9, 10	n	X^1	X^2	X^3	X^4
a	0	Ph	H	H	H
b	0	CH_2-Ph	H	H	H
c	0	Ph	Ph	Me	H
d	1	Ph	H	H	H

The syntheses were carried out in pure acetonitrile instead of the 80/20 mixture of MeCN / H_2O used for the acyclic amines, because heterocycles in quinones **10** easily open in presence of water to form hydroxy alkylamino quinones **12** (Scheme 6). The moderate yields (41-60%) reported for the syntheses of the new

compounds (**10 a, c, d**) (Table 4) are mainly due to partial decomposition during purification by chromatography on silica gel.

In acetonitrile, after addition of a catalytic amount of picric acid, quinones **10** reacted similarly to dialkylamino quinones **3** (see above).

- in case **c** (Scheme 6) where $X^1 = X^2 = Ph$, the acid-catalyzed ring opening yielded 26% of 3-alkylated product, i.e. bicyclic quinone **11**. However, the major product (60%) was the ring-opened compound **12c** (an analog of quinone **5**) arising from the simple N-dealkylation process.

- in cases **a, b, d** where $X^2 = X^4 = H$ (no tertiary carbon on the aminocycle), we were unable to detect any alkylated quinones. The only products isolated were 4-(β or γ hydroxy-alkylamino)-5-methoxy-1,2-benzoquinones **12 a, b, d** even though we tried to avoid the presence of water in the reaction mixtures. Indeed, the same compounds **12**, resulting from the acid-catalyzed hydrolysis of quinones **10**, are easily and quantitatively obtained by carrying out the reaction in a 80/20 acetonitrile / water mixture at room temperature with addition of a catalytic amount of picric acid or by heating with a catalytic amount of acetic acid.

a	$n = 0$; $X^1 = Ph$; $X^2 = X^3 = X^4 = H$
b	$n = 0$; $X^1 = CH_2-Ph$; $X^2 = X^3 = X^4 = H$
c	$n = 0$; $X^1 = X^2 = Ph$; $X^3 = Me$, $X^4 = H$
d	$n = 1$; $X^1 = Ph$; $X^2 = X^3 = X^4 = H$

Scheme 6

The regioselectivity of this acid-catalyzed ring opening process has been confirmed by independent synthesis of authentic compounds: quinones **12** can be obtained through direct substitution of synthon **1** with the corresponding amino alcohols (see Scheme 5). However, this second synthetic pathway is much less efficient, since nucleophilic substitution of quinone **1** by primary amines is not a regioselective process[3] and hydroxy alkylamino quinones **12** are difficult to purify by chromatography due to their polar nature.

If a molar equivalent of an organic acid HA (either acetic or picric acid) is added to the anhydrous acetonitrile solution of quinone **10b**, new products **13** and **14** respectively are formed, whose aminoalkyl substituent has been functionalized by an acetoxy or a picryloxy group. The total regioselectivity and

quantitative yields for these reactions are quite remarkable, especially in view of the poor nucleophilicity of the conjugated bases of HA acids, particularly picrate ion.

Thus, the acid-catalyzed ring opening of quinones **10** provides a very efficient way to synthetize quinones **12**, **13** and **14**, which are otherwise difficult to obtain. Physical constants of these new compounds are collected in Table 6.

DISCUSSION

Is the intramolecular rearrangement observed with 1,2-quinones **3a-h** a particular example of a more general reaction of aliphatic or alicyclic enaminones (O=C-C=N) ? To our knowledge, this specific reaction has never been reported in the chemical literature. Therefore, we prepared 3-(N-methyl-benzhydrylamino)-2-cyclohexenone **15**, an analog of quinone **3a** (Scheme 7), by condensation of N-methyl-benzhydrylamine on 1,3-cyclohexanedione, according to a procedure adapted from literature.[8]

Scheme 7
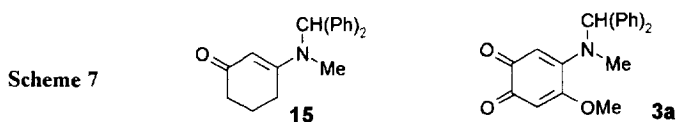
Enaminone **15** was found to be unreactive in the presence of picric acid, in anhydrous acetonitrile, even after prolonged refluxing, whereas aminoquinone **3a** rearranges under these conditions in 75% yield (anhydrous solvent was used to avoid hydrolysis [9]).

I - Acid-catalyzed rearrangements (3 → 4 and 10c → 11) :

In strongly acidic medium (*i.e.* in presence of picric acid), quinones **3**, like enaminones,[10] are probably protonated on the more basic oxygen atom (carbonyl on C_2)[11] giving rise to a 2- hydroxy-*para*quinoniminium intermediate **Z1** (Scheme 8) whose hydroxy group is hydrogen-bonded with carbonyl on C_1, thereby stabilizing the cationic structure. The positive charge is partially delocalized over the R^1 group present on the iminium moiety. Consistent with Scheme 2, we found that higher yields of alkylated quinones **4** are obtained when R^1 is substituted by groups such as a phenyl, heterocycle or a cyclopropyl group; all of these are well known[12] to stabilize a carbonium ion in α-position. Indeed, the greater the ability of R^1 to assume a whole positive charge, the more efficient is the intramolecular nucleophilic attack at carbon -3 of the nucleus toward formation of alkylated quinone **4**. Because the concentration of quinone **3** did not affect the rate of the rearrangement, we assume that the alkylation process ($Z_2 \rightarrow Z'_2$) is an intramolecular reaction. This assumption is further supported by the total regioselectivity of the migration, since no 6-alkylated quinone has ever been detected (the observed regioselectivity is also favored by the higher nucleophilicity of the hydroxyenimine moiety compared to the methoxyenone one).

Scheme 8
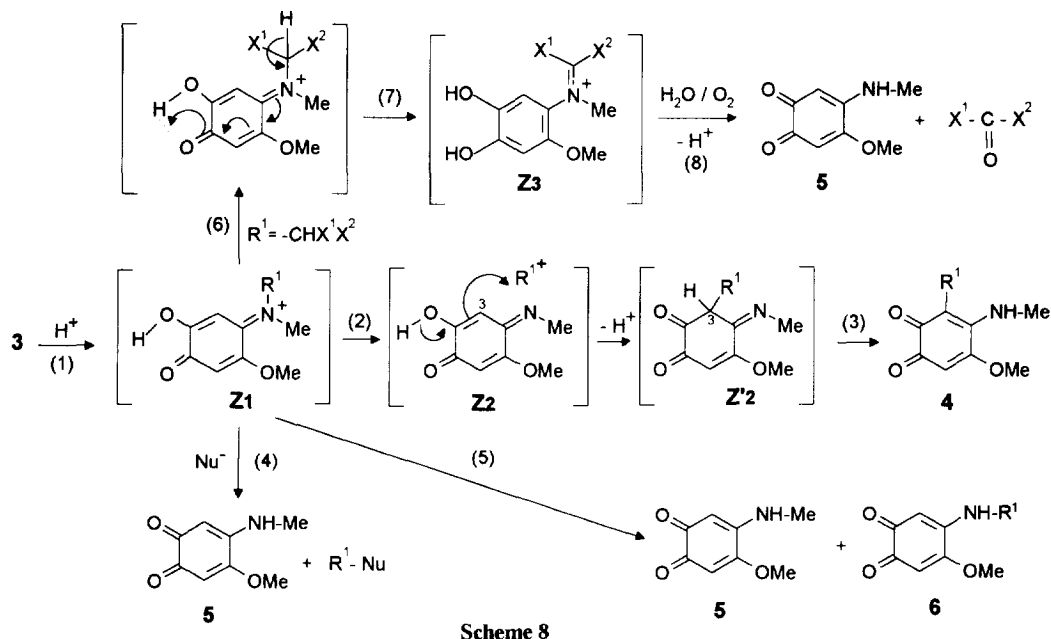
Such a rearrangement can either be concerted, or follow a dissociative S_N1 pathway with formation of $R^{1(+)}$, followed by fast trapping by the transient quinonimine (**Z2** intermediate).

When optically active quinone **3b** [R^{1*} = -CH*(2-thienyl)Me] (either R or S enantiomer) is submitted to the action of picric acid under standard conditions (MeCN, r.t.), racemic quinone **4b** is obtained (Scheme 9). Thus we can rule out a concerted process for the alkylation step, since racemization of the asymmetric carbon of the R^1 migrating group must result from transitory formation of a planar carbonium ion $R^{1(+)}$.
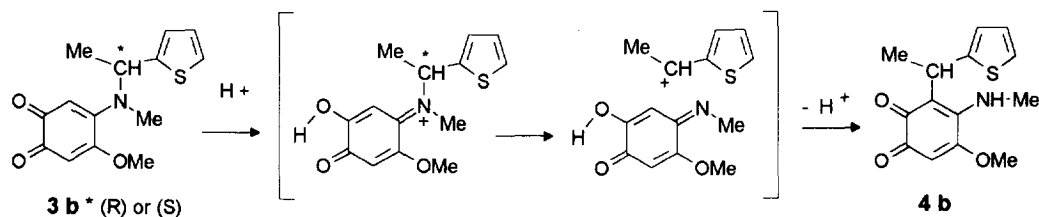
Scheme 9

In order to explain the formation of quinones **4** starting from quinones **3**, we propose a mechanism (see Scheme 8) which involves : **i)** protonation of quinone **3** toward formation of intermediate **Z1** (step 1), **ii)** formation of $R^{1(+)}$ in intermediate **Z2** (step 2), **iii)** intramolecular nucleophilic trapping of $R^{1(+)}$ by the transient quinonimine, **iv)** tautomerization of **Z'2** to the more stable 1,2-quinone **4** (step 3). This mechanism is closely related to the one we proposed in a previous paper, [1] which explained the acid catalyzed rearrangement

of 4-alkoxy-5-methoxy-1,2-benzoquinones (Scheme 1).

It is important and significant to emphasize that the acid-catalyzed rearrangement of an aziridino-quinone: **10c** → tetrahydroindolo-quinone **11** is only observed when R^1 is highly substituted by two phenyl groups ($X^1 = X^2 =$ Ph).

II - N-dealkylation reaction (3 → 5, 6 and 10 → 12, 13, 14)

When R^1 does not contain groups that can sufficiently stabilize positive charge, S_N1 type process is no longer observed, and quinones **3i-l** are therefore unreactive in acidic medium at room temperature. However, N-C bond cleavage occurs at higher temperature, most probably through a bimolecular process which involves an attack by a nucleophile present in the medium (S_N2 type mechanism). Indeed, acetate can play this role (Scheme 8, step 4) and alkyl acetates **7i-l** together with quinone **5** have been characterized as the major products of the thermal reaction of quinones **3i-l** in acetic acid.

With aziridino and azetidino quinones **10a - d**, a similar S_N2 behaviour was observed. As small ring opening does not require strong heating, due to the strain relief, nucleophiles (AcO⁻, H_2O or even picrate ion) react with protonated quinones (intermediate **Z1**) to yield the new open chain-functionalized alkylamino-quinones **12**, **13** and **14** from room temperature to 50°C.

When no nucleophile is present (or only a very weak one, such as picrate ion), intermediate **Z1** formed from quinone **3i-l** will evolve (Scheme 8, step 7) by proton elimination from R^1 (*i.e.* cleavage of the C-H bond on group R^1) and formation of a new aromatic intermediate **Z3**. Hydrolysis of the latter during the work up (step 8) yields carbonyl derivatives X^1-CO-X^2 and an aminocatechol which is immediately oxidized in contact with air into quinone **5**. This reaction may be related to some examples of oxidative deamination reactions described in the literature.[13-15] With aziridino- and azetidino-quinones, this third pathway cannot occur because of excess strain which would result from creating a π-bond such as in **Z3** included in a small ring system.

CONCLUSION

The nature of the alkylamino group determines the chemical behaviour of dialkylaminoquinones **3**, **10** in acidic media. Three major pathways have been described: **i)** when an alkyl substituent of the N atom (R^1) contains groups that can stabilize a positive charge, transient $R^{1(+)}$ will regioselectively alkylate the nucleus. Even though yields are moderate, this reaction appears to be unique for obtaining structures of the type **4** and **11**, for which no precedent can be found in the chemical literature; **ii)** when R^1 does not bear strongly stabilizing substituents, quinones undergo an external nucleophilic attack to yield quantitatively either N-dealkylated quinones **5** (starting from an acyclic aminoquinone **3**) or new 1,2-quinones **12**, **13**, **14**, whose alkylamino substituent has been functionalized (starting from cycloalkylamino quinones **10**); **iii)** with R^1 a primary alkyl, a third pathway involves elimination of a proton in an intramolecular redox process which gives

rise, after hydrolysis and oxidation during the work up, to an aldehyde in addition to the N-dealkylated quinone 5. This reaction may be related to several biological processes such as oxidations catalyzed by coenzyme methoxatin (PQQ) in amine oxidases. [16]
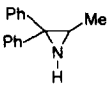
EXPERIMENTAL

All reagents were of commercial quality. Acetonitrile was distilled twice from P_4O_{10} and kept over 3 Å molecular sieves. Analytical thin layer chromatography (tlc) plates (silica gel 60 F254) and silica gel 60 (230-400 mesh) were purchased from Merck™. Mp's were determined with a Kofler apparatus (Reichert) and were uncorrected. ^{1}H - NMR spectra were recorded on a Varian EM-390 (90 MHz) spectrometer. The hplc analyses were carried out on a Lichrosorb (5 μm) Merck™ diol column using pure MeOH as an eluent and on a RP-18 Merck™ column using a MeOH / H_2O (80/20) mixture; flow rate was set at 0.5 mL. min^{-1} using a Gilson™ solvent-delivery system. Absorbance at 254 nm was monitored. Quantifications were performed by comparison with calibration curves obtained with known amounts of compounds.

Synthesis of amines :

Synthesis of N-methyl alkyl amines 2a - l were reported in our recent paper.[3] Cyclic amines 9a-d (aziridines and azetidines) were prepared according to different procedures reported in the literature, references and physical constants are indicated in Table 3.

Table 3 : Syntheses of substituted aziridines and azetidines 9a-d

9	Structure	Yield %	mp°C / bp°C	^{1}H NMR (CDCl$_3$ / TMS) δ, J (Hz)	Ref.
a	Ph	63	bp = 94-95 (10 mm)	0.9 (s exch. D$_2$O, 1 H, NH), 1.6 (d, J = 3, 1H, H *trans* NCH$_2$), 2.0 (d, J = 6, 1H, H *cis* NCH$_2$), 2.8 (dd, 1H, PhCH), 7.2 (s, broad, 5H, Ph)	20[a]
b	Ph	64	([b])	0.85 (s exch. D$_2$O, 1H, NH), 1.4 (d, J = 3.5, 1H, NCH$_2$), 1.75 (d, J = 6, 1H, NCH$_2$), 2.0 - 2.3 (m, 1H, NCH), 2.6 (dd, J$_1$ = 15, J$_2$ = 6, 1H, PhCH$_2$), 2.8 (dd, J$_1$ = 15, J$_2$ = 6, 1H, PhCH$_2$), 7.3 (s, broad, 5H, Ph)	20[a] 22,23
c	Ph, Ph, Me	59	mp = 72 mp$_{lit}$ =73-74	0.95 (d, J = 6, 3H, Me), 2.3 (s exch. D$_2$O, 1H, NH), 2.65 (q, J = 6, 1H, NCH), 7 - 7.4 (m, 10H, Ph)	24,25 26[c],27
d	Ph	41	bp = 55 (0.3 mm Hg) bp$_{lit}$ = 77 (2.5 mmHg)	2.02 (s exch. D$_2$O, 1H, NH), 2.1 - 2.7 (m, 2H, CCH$_2$C), 3.33 (ddd, J$_1$ = 8.25, J$_2$ = 3.75, J$_3$ = 1, 1H, NCH$_2$), 3.7 (ddd, J$_1$ = 8.25, J$_2$ = 1.5, J$_3$ = 1, 1H, NCH$_2$), 4.9 (t, J = 8.25, 1 H, PhCH), 7.15 - 7.55 (m, 5H, Ph)	28[d],29

[a] 9a and 9b were prepared by Brois's procedure[21] from 1-phenyl-2-amino-ethanol and 2-amino-3-phenyl-1-propanol. [b] Colorless oil, chromatograhied on silica gel. [c] 9c was obtained[26] by reaction of phenylmagnesium bromide on propiophenone N,N,N-trimethylhydrazonium iodide. [d] 9d was prepared by LAH reduction[28] of 4-phenyl-2-azetidinone.[30]

Optically active N-methyl-1-[2-thienyl] ethylamine (**2b***): Resolution of racemic 1-[2-thienyl]-ethylamine **16** (Scheme 10), prepared by reductive amination of 2-acetyl-thiophene,[17] was performed with (L) N-acetyl-leucine.[18] Two liquid fractions were isolated and distilled [bp = 39-40°C (1 mbar), bp_{lit} = 83-84°C (16 mmHg)], each one was enriched in one enantiomer.

Scheme 10
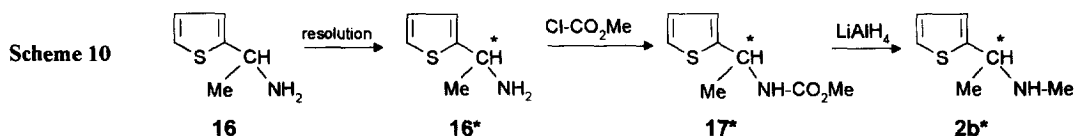
Fraction 1: amine **16*** (R): α_D= + 7.30° (c = 5 , MeOH); optical purity = 0.56. Fraction 2: amine **16*** (S): α_D= - 6,97° (c = 5.17 , MeOH); optical purity = 0.54. $\alpha_D$lit = -13° (c = 5 , MeOH).[19] ^{1}H NMR 1.40 (d, J = 8 Hz, 3H, C-Me), 1.6 (s exch.D_2O, 2H, NH_2), 4.30 (q, J = 8 Hz, 1H, N-CH), 6.8 - 7.2 (m, 3H, thienyl).

Each fraction was reacted with methyl chloroformate in diethyl ether to provide the corresponding carbamates **17*** (95% yield in both cases),[20] [^{1}H NMR [$CDCl_3$ / TMS; δ]]:1.53 (d, J = 6.5Hz, 3H, C-Me), 3.63 (s, 3H, OMe), 5.13 (q, J = 6.5 Hz, 1H, N-CH), 5.3 (s, broad, 1H, NH), 6.8 - 7.2 (m, 3H, thienyl)].

The carbamates were reduced by LAH, in ether, into amines **2b***,[20] bp = 50°C (3 mbar), 96% yield. Since the assymetrical carbon is not affected in this reactional sequence, (R) or (S) 1-[2-thienyl]-ethylamine **2b*** was obtained with the same optical purity than the starting fractions. Fraction 1 provided amine (R) **2b*** : α_D = +28.36° (c = 4.02 , $CHCl_3$), (optical purity = 0.56) and fraction 2 gave rise to amine (S) **2b*** : α_D = -25.92° (c = 4.36 , $CHCl_3$), (optical purity = 0.54).

Synthesis of quinones **3** *and* **10**: We have recently described [3] the synthesis of quinones **3**. Aziridino- and azetidino-quinones **10a-d** were prepared by a slight modification of the general procedure[3] : the solvent [acetonitrile / water (80:20 v/v) mixture] was replaced by anhydrous acetonitrile, in order to avoid solvolysis of the aza-rings by water. Physical constants of these new amino-quinones are reported in Table 4.

Acid-catalyzed rearrangements, typical procedure; synthesis of 3-benzhydryl-4-methylamino-5-methoxy-1,2-benzoquinone (**4a**): Benzoquinone **3a** (1.67 g, 5 mmol) and picric acid (0.115 g, 0.5 mmol) were dissolved at room temperature in anhydrous acetonitrile (5ml). Quinone **3a** reacted within 5 h (monitored by t.l.c.).The solvent was evaporated under reduced pressure, the residue dissolved in dichloromethane (30 ml), washed with aqueous K_2CO_3 1M (10 ml), dried over $MgSO_4$. After filtration, evaporation of the solvent under reduced pressure and purification by column chromatography on silica gel using ethyl acetate / cyclohexane (50:50 v/v) as an eluent, provided dark-red quinone **4a**. Yields and physical constants of quinone **4a** and of other quinones **4** are found in Table 5.

Table 4 : 4- aziridino -(or azetidino)-5-methoxy-1,2-benzoquinones **10a-d**.[a]

10	Yield [b] (%)	mp (°C)	Molecular Formula [c]	^{1}H NMR (CDCl$_3$ / TMS) δ, J (Hz)
a	60	130	$C_{15}H_{13}NO_3$ (255.27)	2.5 - 2.7 (m, 2H, NCH$_2$), 3.2 - 3.4 (m, 1H, NCH), 3.7 (s, 3H, OMe), 5.75 (s, 1H, H$_q$.3), 5.85 (s, 1H, H$_q$.6), 7.15 - 7.45 (m, 5H, Ph)
b	95	72	$C_{16}H_{15}NO_3$ (269.30)	2.1 - 2.35 (m, 2H, PhCH$_2$), 2.4 - 2.7 (m, 1H, NCH), 2.8 - 3.0 (m, 2H, NCH$_2$), 3.75 (s, 3H, OMe), 5.6 (s, 1H, H$_q$.3), 5.65 (s, 1H, H$_q$.6), 7.1 - 7.4 (m, 5H, Ph)
c	41	190	$C_{22}H_{19}NO_3$ (345.40)	1.1 (d, J = 6, 3H, CMe), 3.45 (q, J = 6, 1H, NCH), 3.60 (s, 3H, OMe), 5.45 (s, 1H, H$_q$ 3), 5.85 (s, 1H, H$_q$ 6), 6.9 - 7.4 (m, 10H, Ph)
d	55	139	$C_{16}H_{15}NO_3$ (269.30)	2.0 - 2.45 (m, 2H, CCH$_2$-C), 2.8 - 3.4 (m, 2H, NCH$_2$), 3.8 (s, 3H, OMe), 4.3 - 4.6 (m, 1H, NCH), 5.4 (s, 1H, H$_q$.3), 5.6 (s, 1H, H$_q$.6), 7.1 - 7.5 (m, 5H, Ph)

[a] Minor amounts (< 5%) of relatively unstable 4-amino-5-p-methoxyphenoxy-1,2-benzoquinones were detected and easily separated by chromatography (AcOEt / hexane). [b] Pure chromatographied products. [c]Satisfactory microanalyses obtained: C% ± 0.3, H% ± 0.3, N % ± 0.3.

Acid-catalyzed rearrangements, typical procedure; synthesis of 3-benzhydryl-4-methylamino-5-methoxy-1,2-benzoquinone (**4a**): Benzoquinone **3a** (1.67 g, 5 mmol) and picric acid (0.115 g, 0.5 mmol) were dissolved at room temperature in anhydrous acetonitrile (5ml). Quinone **3a** reacted within 5 h (monitored by t.l.c.).The solvent was evaporated under reduced pressure, the residue dissolved in dichloromethane (30 ml), washed with aqueous K$_2$CO$_3$ 1M (10 ml), dried over MgSO$_4$. After filtration, evaporation of the solvent under reduced pressure and purification by column chromatography on silica gel using ethyl acetate / cyclohexane (50:50 v/v) as an eluent, provided dark-red quinone **4a**. Yields and physical constants of quinone **4a** and of other quinones **4** are found in Table 5.

3-benzhydryl-4-amino-5-methoxy- 1,2-benzoquinone (**8a**): This minor product was isolated (10%) by column chromatography (last eluted product on silica gel with EtOAc as an eluent) of the reaction product of quinone **3a** in refluxing AcOH, after 1 h (Table 1); red crystals, mp = 235°C, ^{1}H NMR [CDCl$_3$ / TMS; δ]: 3.8 (s, 3H, OMe), 5.2 (s, broad, exch. D$_2$O, 2H, NH$_2$), 5.7 (s, 1H, H$_q$), 6.0 (s, broad, 1H, CH(Ph)$_2$), 7.1 - 7.4 (m, broad, 10 H, Ph). Found %: C, 74.92; H, 5.61; N, 4.36; Calc.% for $C_{20}H_{17}NO_3$: C, 75.22 ; H, 5.37 ; N, 4.39). This product was also obtained from **4a**, under the same conditions.

2-methyl-3, 3-diphenyl -7-methoxy- 2, 3 - 4, 5 - tetrahydro- 4, 5 -dioxo-indole (**11**) : Prepared from **10c** according to the typical procedure described for the acid-catalyzed rearrangement of **4a** was separated from **12c** by column chromatography on silica gel, cyclohexane/AcOEt : 70/30 as eluent, 26% yield, dark red crystals, mp = 255°C , ^{1}H NMR [CDCl$_3$ / TMS; δ, J (Hz)] 0.9 (d, J = 7, 3H, Me), 3.9 (s, 3H, OMe), 5.33 (q, J = 7, 1H, NCH), 5.9 (s, 1H, H$_q$.), 6.8 (s broad, exch. D$_2$O, 1H, NH), 7.0 - 7.4 (m, 10 H, Ph); Analysis: Found %: C, 76.39; H, 5.57; N, 4.09; Calc.% for $C_{22}H_{19}NO_3$: C, 76.50 ; H, 5.54 ; N, 4.06.

Table 5: 1,2-benzoquinones **4a-h** from acid-catalyzed rearrangement of quinones **3a-h** [a]

4 [b]	R[1]	mp (°C)	Molecular Formula [c]	^{1}H NMR (CDCl$_3$ / TMS) δ, J (Hz)
a	CH(Ph)$_2$	160	C$_{21}$H$_{19}$NO$_3$ (333.38)	2.85 (d, J = 6, 3H, NMe), 3.8 (s, 3H, OMe), 5.3 (s, broad exch. D$_2$O, 1H, NH), 5.7 (s, 1H, H$_q$), 6.0 (s, broad, 1H CH), 7.1-7.4 (s, broad, 10H, Ph$_2$)
b	CH(Me)(2-thienyl)	138	C$_{14}$H$_{15}$NO$_3$S (277.33)	1.65 (d, J = 7, 3H, CMe), 3.05 (d, J = 6, 3H, NMe), 3.8 (s, 3H, OMe), 4.8 (q, J = 7, 1H, C<u>H</u>Me), 5.70 (s, 1H, H$_q$) 5.8 (s, broad, exch. D$_2$O, 1H, NH), 6.85 (dd, J_1 =3,5, J =1,5 ,1H, thienyl), 6.95 (dd, J_1 = 5, J_2 = 3,5, 1H, thienyl) 7.15 (d, J = 5, 1H, thienyl)
c	CH(cyclopropyl)(Ph)	155	C$_{18}$H$_{19}$NO$_3$ (297.35)	0.2 - 1.6 (m, 5H, cyclopropyl), 2.95 (d, J = 6, 3H, NMe) 3.75 (d, J = 6, 1H, CH), 3.8 (s, 3H, OMe), 5.3 (s, broad exch. D$_2$O, 1H, NH), 5.65 (s, 1H, H$_q$), 7.0 - 7.6 (m, 5H Ph)
d	CH(Me)(3-thienyl)	153	C$_{14}$H$_{15}$NO$_3$S (277.33)	1.55 (d, J = 7, 3H, CMe), 3.0 (s, broad, 3H, NMe), 3.85 (s, OMe), 4.65 (q, J = 7, 1H, C<u>H</u>Me), 5.4 (s, broad, exch. D$_2$,1H, NH); 5.65 (s, 1H, H$_q$), 6.85 - 7.15 (m, 2H, thienyl), 7.35 (m, 2H, thienyl)
e	CH(Me)(2-furyl)	140	C$_{14}$H$_{15}$NO$_4$ (261.27)	1.5 (d, J = 7, 3H, CMe), 3.1 (d, J = 6, 3H, NMe), 3.85 (s 3H, OMe), 4.6 (q, J = 7, 1H, C<u>H</u>Me), 5.65 (s, 1H, H$_q$), 5. (s, broad, exch. D$_2$O, 1H, NH), 6.1 - 6.4 (m, 2H, furyl), 7. (s, broad, 1H, furyl)
f	CH$_2$-(2-thienyl)	62	C$_{13}$H$_{13}$NO$_2$S (247.32)	3.2 (d, J = 6, 3H, NMe), 3.85 (s, 3H, OMe), 4.2 (s, 2H CH$_2$), 5.7 (s, 1H, H$_q$), 6.3 (s, broad, exch. D$_2$O, 1H, NH) 6.65 - 7.2 (m, 3H, thienyl)
g	CH(Me)(Ph)	124	C$_{16}$H$_{17}$NO$_3$ (271.32)	1.45 (d, J = 7, 3H, CMe), 3.0 (s, broad, 3H, NMe), 3.8 (s 3H, OMe), 4.7 (q, J = 7, 1H, CHMe), 5.3 (s, broad, exch D$_2$O, 1H, NH), 5.7 (s, 1H, H$_q$), 7.0 - 7.5 (m, 5H, Ph)
h	CH$_2$-(2-furyl)	dec.	C$_{13}$H$_{13}$NO$_3$ (231.25)	3.05 (d, J = 6, 3H, NMe), 3.85 (s, 2H, OMe), 4.0 (s, 2H CH$_2$), 5.7 (s, 1H, H$_q$.), 5.9 - 6.4 (m, 3H, furyl), 6.0 (s broad, exch. D$_2$O, 1H, NH)

[a] Quinones **3a-h** (1 M.l$^{-1)}$ in acetonitrile, 22°C, with 0.1 equiv. picric acid, <10 h (except for **4g** and **4h**: 24h). [b] These dark-red colored compounds present very similar UV-visible spectra : example, **4b** : [λ (nm), log ε, CHCl$_3$] : 297, 4.17 ; 479, 2.63. [c] Satisfactory microanalyses obtained: C% ± 0.3, H% ± 0.3, N% ± 0.2 .

4-(β or γ - hydroxy-alkylamino)-5-methoxy-1,2-benzoquinones **(12)** *and derivatives* **(13, 14)** : When heated for 5 minutes, at 50°C, in an acetonitrile / water (80 / 20, v/v) mixture with a trace of AcOH (or picric acid), quinones **10a,b,d** quantitatively gave rise to 4-(β or γ - hydroxy-alkylamino)-5-methoxy-1,2-benzoquinones **12a,b,d** which may be recrystallized from AcOEt.

Quinone **10b**, in anhydrous acetonitrile and in presence of one molar equivalent of acetic or picric acid was quantitatively transformed, in 5 min. at 50°C, respectively into acetoxy-quinone **13** or picryloxy-quinone **14**. Physical data of these new quinones are indicated in Table 6:

Table 6 : 4-(β or γ - hydroxy-alkylamino)-5-methoxy-1,2-benzoquinones **12** and derivatives **13, 14** [a].

	4- hydroxyalkylamino substituent	mp (°C)	^{1}H NMR (CDCl$_3$ / TMS) δ, J (Hz)
12a	NH-CH$_2$-CHOH-Ph	97	3.35 (d, J = 6, 2H, NCH$_2$), 3.75 (s, 3H, OMe), 4.7 (s, broad, exch. D$_2$O, 2H, NH and OH), 5 (t, J = 6, 1H, PhCH), 5.35 (s, 1H, H$_q$ 3), 5.6 (s, 1H, H$_q$ 6), 7.0 - 7.4 (m, 5H, Ph)
12b	NH-CH$_2$-CHOH-CH$_2$-Ph	144	2.55 - 3.0 (m, 2H, NCH$_2$), 3.05 - 3.3 (m, 2H, PhCH$_2$), 3.75 (s, 3H, OMe), 3.95 - 4.3 (m, 1H, CHOH), 5.3 (s, 1H, H$_q$3), 5.6 (s, 1H, H$_q$6), 6.8 (s, broad, exch. D$_2$O, 2H, NH and OH), 7.0 - 7.3 (m, 5H, Ph)
12b' [b]	NH-CH(CH$_2$-Ph)-CH$_2$OH	95	2.95 (d, J = 6, 2H, PhCH$_2$), 3.35 - 4.0 (m, 3H, NCHCH$_2$O), 3.7 (s, 3H, OMe), 5.5 (s, 1H, H$_q$3), 5.6 (s, 1H, H$_q$6), 6.5 - 7.0 (s, broad, exch. D$_2$O, 2H, NH and OH), 7.0 - 7.3 (m, 5H, Ph)
12c	NH-CH(Me)-CHOH(Ph)$_2$	148	1.1 (d, 3H, J = 7, CHMe), 3.8 (s, 3H, OMe), 4.5 (quint., J = 7, NCH), 5.55 (s, 1H, H$_q$3), 5.6 (s, 1H, H$_q$ 6), 6.8 (s, broad, exch. D$_2$O, 2H, NH and OH), 7.0 - 7.4 (m, 10H, Ph$_2$)
12f	NH-CH$_2$-CH$_2$-CHOH-Ph	87	2.05 (q, J = 6, 2H, CH$_2$CHOH), 3.35 (t, J = 6, 2H, NCH$_2$), 3.8 (s, 3H, OMe), 4.95 (t, J = 6, 1H, CHOH), 5.35 (s, 1H, H$_q$ 3), 5.6 (s, 1H, H$_q$ 6), 6.5 (s, broad, exch. D$_2$O, 2H, NH and OH), 7.1 - 7.4 (m, 5H, Ph)
12f' [b]	NH-CH(Ph)-CH$_2$-CH$_2$OH	92	2.1 (m, 2H, CH$_2$CH$_2$OH), 3.55 - 3.8 (m, 2H, CH$_2$OH), 3.8 (s, 3H, OMe), 4.65 (m, 1H, NCH), 5.15 (s, 1H, H$_q$ 3), 5.4 (s broad, exch. D$_2$O, 1H, NH), 5,6 (s, 1H, H$_q$ 6), 7,1 - 7.4 (m, 5H, Ph), 7.9 (s, broad, exch. D$_2$O, 1H, OH)
13	NH-CH$_2$-CHOAc-CH$_2$-Ph	85	2.05 (s, 3H, OCOMe), 2.7 - 3,1 (m, 2H, NCH$_2$), 3.1 5 -3.5 (m, 2H, PhCH$_2$), 3.7- 4.2 (m, 1H , CHOH), 3.85 (s, 3H, OMe), 5.35 (s, 1H, H$_q$ 3), 5.65 (s, 1H, H$_q$ 6), 6.3 (s, broad, exch. D$_2$O, 1H, NH), 7.1 - 7.4 (m, 5 H, Ph)
14	NH-CH$_2$-CHO(Picr)-CH$_2$-Ph	120	3.1 (d, J = 7, 2H, PhCH$_2$), 3.55 (t, J = 7, 2H, NCH$_2$), 3.85 (s, 3H, OMe), 5.0 (quint., J = 7, CHOPicr), 5.25 (s, 1H, H$_q$ 3), 5.65 (s, 1H, H$_q$ 6), 6.4 (s, broad, exch. D$_2$O, 1H, NH), 7.1 - 7.4 (m, 5H, Ph), 8.75 (s, 2H, Picryl)

[a] These new compounds gave satisfactory microanalyses : C% ± 0.3, H% ± 0.3, N% ± 0.3. [b] These isomeric alcohols were prepared by independent syntheses: by reaction of the corresponding amino-alcohols on **1**, according to ref [3] ; they are not produced by the acid-catalyzed ring opening reaction.

3-(N-methyl-benzhydrylamino)-2-cyclohexenone (**15**): Prepared by a method adapted from the literature.[8] Yellow crystals, mp = 135°C, ^{1}H NMR [CDCl$_3$ / TMS; δ , J (Hz)] 2.0 (quint, J = 6, 2H), 2.3 (t, J = 6, 2H,-CH$_2$-C-N), 2.6 (t, J = 6, 2H, CO-CH$_2$-), 2.7 (s, 3H, N-CH$_3$), 5.35 (s,1H, CO-CH=), 6.3 (s, 1H, N-CH-), 7.0 - 7.5 (m, 10H, Ph). Analysis: Found %: C, 82.40; H, 7.28; N, 5.44; Calc. % for C$_{20}$H$_{21}$NO : C, 82.44; H, 7.26; N, 5.49.

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