Thermal Decomposition of 2-Amino-3-aziridino-1,4-naphthoquinones (1,2)

Ippolito Antonini, Francesco Claudi, Gloria Cristalli, Mario Grifantini and Sante Martelli

Institute of Pharmaceutical and Organic Chemistry, University of Camerino, Camerino, Italy

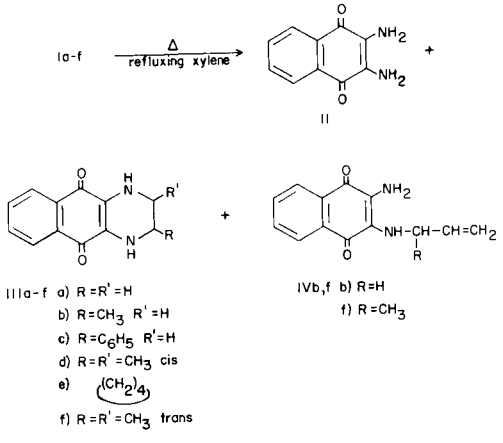
Received August 12, 1980

The course of the thermal decomposition of various 2-amino-3-substituted aziridino-1,4-naphthoquinones (Ia-g) was investigated. In all the cases, the thermal decomposition gave variable amounts of 2,3-diamino-1,4-naphthoquinone (II) and of substituted 1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline-5,10-diones (IIIa-g) with complete stereospecificity. The decomposition of the aziridines Ib,f also gave significative amounts of 2-amino-3-allylamino-1,4-naphthoquinones (IVb,f). In the case of 2-amino-3-(2'-phenyl-3'-ethylaziridino)-1,4-naphthoquinone (Ig), the formation of *trans*-1-phenyl-1-butene (V), 2-(1-phenylpropyl)-1*H*-naphthoimidazole-4,9-dione (VI), 2-phenyl-3-ethyl-3,4,5,10-tetrahydrobenzo[*g*]quinoxaline-5,10-dione (VII), 2-phenyl-3-ethyl-5,10-dihydrobenzo[*g*]quinoxaline-5,10-dione (VIII), and a mixture of *cis*- and *trans*-4*H*-2,3,5,6-tetrahydro-2-phenyl-3-ethyl-5-iminonaphtho[1,2-*b*]oxazin-6-one (IX) also occurred. Hypotheses concerning the mechanism and the steric course of this reaction are given. The reaction is a general method for the stereospecific synthesis of 2,3-disubstituted 1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxalines.

J. Heterocyclic Chem., **18**, 399 (1981).

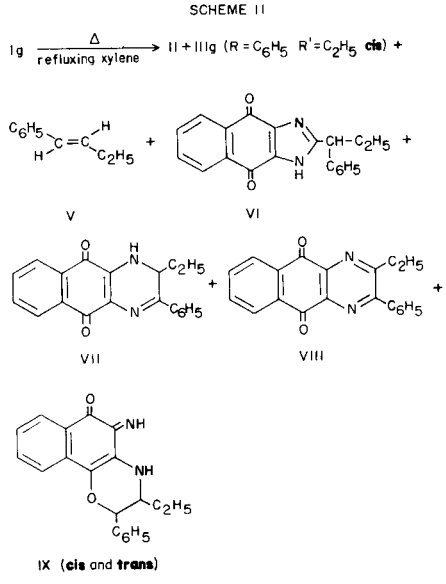
In previous works, the hydriodic acid catalysed and iodide-catalysed isomerizations of various 2-amino-3-aziridino-1,4-naphthoquinones which were unsubstituted, monosubstituted, symmetrically and unsymmetrically disubstituted on the aziridine ring, were described (3). The thermal decomposition of 2-amino-3-(2',2'-dimethylaziridino)-1,4-naphthoquinone has also been studied (4). In order to more thoroughly investigate the chemical reactivity of these molecules, particularly in relation to their antitumore activity (5,6), it seemed interesting to examine the thermal decomposition of 2-amino-3-substituted aziridino-1,4-naphthoquinones. Furthermore, since 1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline-5,10-diones are difficult to obtain and only *trans*-disubstituted isomers are obtained in the iodide catalysed isomerization (3), it also seemed interesting to determine if the thermal isomerization could represent a new synthetic route to *cis*-disubstituted hexahydrobenzo[*g*]quinoxalines.

SCHEME I



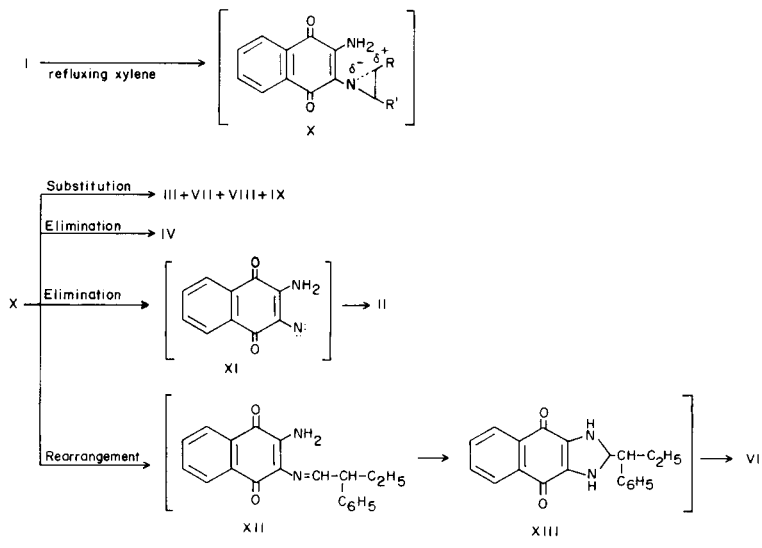
It is well known that activated aziridine rings, as for example 1-acyl, 1-benzensulfonyl and all substituted aziridines possessing a substituent at the nitrogen atom which is capable of stabilizing the negative charge formed on the aziridine nitrogen atom in the transition state, rearrange to isomeric ring-opened and ring-expanded products (7,10). Furthermore, in the thermal expansion of the ring, high stereospecificity is normally observed. The 2-amino-3-aziridino-1,4-naphthoquinones under examination could have similar behaviour. In fact they can be regarded as activated aziridines since the naphthoquinone moiety could be related to an α,β-unsaturated carbonyl system. The 2-amino-3-substituted aziridino-1,4-naphthoquinones were prepared following the procedure previously described in the literature (3). Substituents able to give information on the mechanism and on the stereochemistry of the reaction were selected. In particular, the aziridine groupings listed in Table I were considered.

SCHEME II



0022-152X/81/020399-06$02.25

SCHEME III

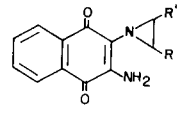


The thermal isomerization was performed by refluxing the 2-amino-3-aziridino-1,4-naphthoquinones Ia-g in xylene for several hours. In all cases isomerization lead to the formation of a complex reaction mixture. The components of the mixture obtained in the decomposition of Ia-f are listed in Scheme I whereas those obtained from Ig are listed in Scheme II. The thermal decomposition of compounds Ia-g proceeded with different rates. The most reactive were Ic and Ig, both with an aryl group, which completely reacted in 2.5 hours. The most stable compounds were Id and Ie, both *cis*-disubstituted with alkyl groups; they reacted, but not completely, in more than 80 hours. When the same reaction was carried out in anhydrous xylene and under nitrogen, no significant differences were observed regard either the nature of the compounds obtained, or their relative ratio. Furthermore, by carrying out the decompositions in chlorobenzene and nitrobenzene at the same temperature (140°) the reaction rate and the composition of the mixtures obtained were substantially unchanged. When the reaction was carried out in xylene at 120° a slower reaction rate and, in the cases of Ib and If, also a different composition of the mixture was observed. In fact, lower temperatures gave a little increase in the formation of IVb and IVf and a corresponding decrease of II. This behaviour has been previously observed in the thermal decomposition of 2-amino-3-(2',2'-dimethylaziridino)-1,4-naphthoquinone (4) under identical conditions. Compound II was present in all the reaction mixtures in different amounts: as a trace in the case of Ia, and as the quantitatively most important product in many other cases.

The formation of alkenes was observed only in the isomerization of Ig, where the formation of *trans*-1-phenyl-1-butene (V) was indicated by gas chromatography of the

Table I

2-Amino-3-aziridino-1,4-naphthoquinones

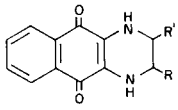


Compound No.	R	R'	Stereochemistry
Ia	H	H	
Ib	CH_3	H	
Ic	C_6H_5	H	
Id	CH_3	CH_3	*cis*
Ie		$(CH_2)_4$	*cis*
If	CH_3	CH_3	*trans*
Ig	C_6H_5	C_2H_5	*cis*

reaction mixture. The amount of V is less than expected in relation to the formation of II, probably because of polymerization. From Ib and If, the allylamines IVb,f were also isolated. In the case of *cis*-disubstituted aziridines instead, these compounds are not formed, even as traces. In all cases examined, the formation of substituted 1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline-5,10-diones (IIIa-g), the main compound IIIa, appreciable amounts of IIIb,c,d,e,g, or a trace of IIIf was observed. The isomerization of Ig (see Scheme II) also led, together with IIIg, to the dehydrogenated compounds 2-phenyl-3-ethyl-3,4,5,10-tetrahydrobenzo[*g*]quinoxaline (VII) and 2-phenyl-3-ethyl-5,10-dihydrobenzo[*g*]quinoxaline (VIII), a mixture of *cis*- and *trans*-isomers of 4*H*-2,3,5,6-tetrahydro-2-phenyl-3-ethyl-5-iminonaphtho[1,2-*b*]oxazin-6-one (IX) and small amounts of 2-(1-phenylpropyl)-1*H*-naphthoimidazole-4,9-dione (V) (see Scheme II). The structures of compounds III, VII and VIII were assigned on the basis of nmr spec-

Table II

NMR Spectra of *cis*- and *trans*-2,3-Disubstituted 1,2,3,4,5,10-Hexahydrobenzo[*g*]quinoxaline-5,10-diones



Compound No.	R	R'	Configuration	Chemical Shifts (deuteriochloroform) (δ) and Coupling Constants (Hz)
IIId	CH_3	CH_3	*cis*	1.15 (6H, d, J = 6 Hz, CH_3), 3.40-3.70 (2H, m, N-CH-CH-N), 4.83 (2H, broad s, vanishes on addition of deuterium oxide, NH), 7.32-7.90 (4H, A_2B_2 system, aromatics)
IIIf	CH_3	CH_3	*trans*	1.23 (6H, d, J = 6Hz, CH_3), 2.81-3.15 (2H, m, N-CH-CH-N), 4.70 (2H, broad s, vanishes on addition of deuterium oxide, NH), 7.35-7.93 (4H, A_2B_2 system, aromatics)
IIIg	C_2H_5	C_6H_5	*cis*	0.98 (3H, t, CH_3), 1.20-1.46 (2H, m, CH_2), 3.30-3.70 (1H, m, N-CH-C_2H_5), 4.60 (1H, d, N-CH-C_6H_5), 5.12-5.33 (2H, 2 broad singlets, vanishes on addition of deuterium oxide), 7.25-8.10 (9H, m, aromatics)
IIIh (a)	C_2H_5	C_6H_5	*trans*	0.97 (3H, t, CH_3), 1.36-1.62 (2H, m, CH_2), 3.08-3.30 (1H, m, N-CH-C_2H_5), 4.01 (1H, d, J = 6Hz, N-CH-C_6H_5), 4.96 (2H, broad singlet, vanishes on addition of deuterium oxide, NH), 7.20-8.00 (9H, m, aromatics)

(a) See reference 3.

tra, whereas that of VI was assigned by comparison with an authentic sample obtained by independent synthesis using Hoover's method (13). The formation of the benzo[*g*]quinoxalines is stereospecific. In fact, *cis*-aziridines (Id,e,g) led to *cis*-hexahydrobenzo[*g*]quinoxalines (IIId,e,g), whereas *trans*-aziridines (If) led to *trans*-hexahydrobenzo[*g*]quinoxalines (IIIf). The attribution of the structure to these compounds was obtained by nmr spectroscopy.

As shown in Table II, the observed upfield shift of the *cis*-hydrogen atoms and the downfield shift for the *cis*-alkyl groups in compounds IIId and IIIg, with respect to their *trans*-isomers IIIf and IIIh, is in accordance with the data reported for pentatomic cyclic compounds such as dioxolanes, dithiolanes or pyrrolines (11), or for exatomic cyclic compounds having sufficiently rigid structures such as 1,2,3,4-tetrahydroquinoxalines (12). Compound IX was obtained only as a 3 to 1 mixture of the *cis*- and *trans*-isomers. This mixture was not separable by column chromatography. The composition of the mixture was determined by hplc and nmr spectroscopy. The structure of IX was assigned only on the basis of the nmr spectra of the *cis-trans* mixture. In fact, the nmr spectra show a different pattern in the aromatic region, similar to that observed in the case of 4*H*-2,3,5,6-tetrahydro-2,3-di-*n*-propyl-5-iminonaphtho[1,2-*b*]oxazin-6-one which has previously been described (3), thus indicating a cyclization at the quinone oxygen atom. The nmr also shows two distinct doublets at δ 5.5 (J = 3 Hz) and at δ 4.9 (J = 8 Hz) corresponding to the hydrogen atoms at position 2- for the *cis*- and *trans*-isomers, respectively. As in the case of *cis*- and *trans*-benzo[*g*]quinoxalines, the *cis*- and *trans*-configurations were assigned on the basis of upfield and downfield shifts and were confirmed by J values. Hplc analysis of IX on a lichrosorb Si-60 analytical column confirmed a 3 to 1 *cis*/*trans* mixture.

Discussion.

The thermal decomposition of 2-amino-3-(2',2'-dimethylaziridino)-1,4-naphthoquinone (4) led to 2,3-diamino-1,4-naphthoquinone, 2-amino-3-(2'-methylallylamino)-1,4-naphthoquinone, 2,2-dimethyl-1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline and 2-isopropyl-1*H*-naphthoimidazole-4,9-dione. The mechanism postulated for this decomposition is a dissociative process of type SN_1 (4). The behaviour of monosubstituted and 2,3-disubstituted aziridino naphthoquinones under examination appears quite similar to that of 2-amino-3-(2',2'-dimethylaziridino)-1,4-naphthoquinone under analogous conditions. In fact, the compounds obtained in the thermal decomposition of monosubstituted and 2,3-disubstituted aziridino naphthoquinones are substantially of the same nature. Furthermore, this similarity becomes very pronounced when the aziridine group carries a phenyl substituent. In view of this similarity, for the thermal decomposition of these aziridines an SN_1 type mechanism could also be proposed.

However, the high stereospecificity and some different behaviour related to the stereochemistry of the aziridines do not seem in good accord with such a mechanism. For this isomerization, the hypothesis of an SN_2 type thermal

heterolytic cleavage of the carbon-nitrogen bond of the aziridine ring induced by heat and by the nitrogen atom in position 2 of the naphthoquinone seems more appropriate. The transition state will certainly have SN_1 character to some extent, which becomes more significant in certain favoured cases, for instance when a phenyl substituent is present. In fact, in consideration of the weak polar reaction medium and of the observation that in more polar solvents such as chlorobenzene and nitrobenzene differences are not observed in the rate of reaction, a scarcely polar transition state would seem more likely.

Furthermore, the complete stereospecificity observed in the formation of hexahydrobenzo[*g*]quinoxalines seems in better agreement with a SN_2 type mechanism. By this hypothesis the stereospecificity could be explained by assuming that the nitrogen atom at the 2-position attacks the aziridine ring from the inside and on the same region at which cleavage of the carbon-nitrogen bond with an SNi type mechanism, giving retention of configuration in the formation of the quinoxaline ring, is observed. On the other hand, a transition state having significant carbonium ion character seems necessary to explain the marked higher reactivity observed in the case of aziridines having a phenyl substituent (Ie,g), and in the case of Ig to satisfactorily explain the formation of the naphthoimidazole derivative VI. The formation of VI could be explained by a rearrangement of X into the imino derivative XII. By attack of the amino group at position 2, XII could give the naphthoimidazoline intermediate XIII; a dehydrogenation process could transform XIII into VI (see Scheme III). The fact that VI has been isolated in very low yield, and only in the most favourable case (Ig), seems to confirm the partially ionic character of the intermediate.

Furthermore, the formation of IX in the isomerization of Ig confirms this hypothesis. Compound IX could also be formed by nucleophilic attack of the quinonic oxygen atom on the aziridine ring in a competitive reaction of type SN_2 with the amino group. This hypothesis, however, is not in agreement with the formation of both the *cis*- and *trans*-isomers of IX; instead, their formation seems to indicate high ionic character for the intermediate. Aziridines substituted with a phenyl group do not give allylamines. This observation is largely expected in view of the impossibility of a β-elimination process. However, it is not easy to explain why the allylamines are formed only from the *trans*-isomers in alkyl substituted aziridinonaphthoquinones. If it is postulated that the aziridine ring, by thermal excitation, can assume a staggered conformation with respect to the naphthoquinone ring, it appears that in the case of the *cis*-isomers, the two substituents are probably directed externally so that the aziridine ring directs the less hindered side to the amino group in position 2, which could attack only the carbons of the aziridine ring. Concerning the *trans*-isomers, a methyl group in any case would be directed towards the amino group in position 2, which acting as a base, could assume a hydrogen atom from the methyl group giving, through a cyclic mechanism, an elimination reaction. On the other hand, similar behaviour of acylaziridines and of other activated aziridines are well documented (15-17). It appears more difficult to explain the higher reactivity of the *trans*-isomer if with respect to the *cis*-isomer Id, also in consideration that the latter would be less stable. The only hypothesis is that the different configurations could in some way influence the transition state.

The formation of compound II could be explained by supposing a nitrene intermediate XI which, in turn, could be generated from X through a β-elimination process. Instead, it can be excluded that II could have originated from allylamino derivatives as a decomposition product. In fact, the allylamino naphthoquinones are sufficiently stable in refluxing xylene and give small amounts of diaminonaphthoquinone only after prolonged heating. This, however, does not appear to justify the amount of diamino naphthoquinone formed in the decomposition of some aziridines. The fact that the formation of IV is increased and that of II is reduced at lower temperature seems to confirm that II and IV could have originated from the same intermediate through two competitive elimination reactions.

Concerning the formation of hexahydrobenzo[*g*]quinoxaline-5,10-diones, it must be pointed out that the isomerizations of 2-amino-3-aziridino-1,4-naphthoquinones represent a general method of stereospecific synthesis of these compounds. In fact, whereas *trans*-disubstituted aziridines can easily cyclyze to *trans*-hexahydrobenzo[*g*]quinoxalines (3) by iodide-catalysed isomerization and *cis*-isomers do not cyclize by the same procedure, *cis*-disubstituted aziridines can easily isomerize to *cis*-disubstituted hexahydrobenzo[*g*]quinoxalines by thermal decomposition.

EXPERIMENTAL

The melting points were determined with a Büchi apparatus and are uncorrected. The nmr spectra were recorded in deuteriochloroform solution with a Joel JNM C 60 HL and a Varian EM-390 90 M Hz spectrometer, using TMS (tetramethylsilane) as internal standard. The ir spectra were recorded on a Perkin Elmer model 257 spectrophotometer. The uv spectra were recorded on a Perkin Elmer model 575 spectrophotomer. Tlc were carried out on tlc plates prepared with silica gel GF 254 Merck. For column chromatography silica gel 60 Merck was used. Hplc were performed on a Waters Associates model 440 absorbance detector liquid chromatograph. Gas chromatographic analyses were performed on a Hewlett-Packard 5706 double column gas chromatograph.

Thermal Decomposition of 2-Amino-3-aziridino-1,4-naphthoquinone (Ia).

2-Amino-3-aziridino-1,4-naphthoquinone (Ia) (0.45 g., 2.1 mmoles) dissolved in 100 ml. of xylene was refluxed for 30 hours. Compound Ia reacted quite completely and the reaction mixture, after evaporation of the solvent, gave a residue which was chromatographed on a silica gel

column eluted with a mixture cyclohexane-ethylacetate 70/30. The first eluted blue coloured fractions gave, after evaporation of the solvent, 0.35 g. of 1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline (IIIa), characterized by comparison with an authentic sample (3). A further elution of the column gave traces of unreacted Ia and of 2,3-diamino-1,4-naphthoquinone (II), characterized by comparison with an authentic sample (18). By thermal decomposition of Ia in chlorobenzene at 140° the same rate of decomposition and an identical reaction mixture was observed. Compound Ia was stable in refluxing benzene for five days.

Thermal Decomposition of 2-Amino-3-(2'-methylaziridino)-1,4-naphthoquinone (Ib).

2-Amino-3-(2'-methylaziridino)-1,4-naphthoquinone (Ib) (5), (0.3 g., 1.3 mmoles) dissolved in 100 ml. of xylene was refluxed for 30 hours. Compound Ib reacted quite completely and the reaction mixture, after evaporation of the solvent, gave a residue which was chromatographed on a silica gel column eluted with a mixture cyclohexane-ethyl acetate 50/50. Four main compounds were obtained. By evaporation of the first intensely violet coloured eluted fractions, 2-amino-3-allylamino-1,4-naphthoquinone (IVb) was obtained as an oily compound (55 mg.); nmr (deuteriochloroform): δ 7.49-8.12 (4H, A_2B_2 system, aromatics), 5.70-6.32 (1H, m, -C(H)=C<), 5.05-5.52 (2H, m, C=C<(H,H)) 4.25-4.90 (3H, s, broad, vanishes on addition of deuterium oxide, NH), 3.71-3.90 (2H, m, N-CH_2-C=).

Anal. Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.22; H, 5.21; N, 11.99.

The second intensely blue coloured eluted fractions gave, after evaporation, 30 mg. of 2-methyl-1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline-5,10-dione (IIIb), characterized by comparison with an authentic sample (3).

In the third eluted fractions, unreacted Ib (10 mg.) was recovered. A further elution gave blue coloured fractions containing 2,3-diamino-1,4-naphthoquinone (II) (140 mg.).

Thermal Decomposition of 2-Amino-3-(2'-phenylaziridino)-1,4-naphthoquinone (Ic).

2-Amino-3-(2'-phenylaziridino)-1,4-naphthoquinone (Ic) (6.29 g., 1 mmole) (3) dissolved in 100 ml. of xylene were refluxed until the compound was completely reacted (2.5 hours). The reaction mixture, after evaporation of the solvent, gave a residue which was chromatographed on a silica gel column eluted with a mixture cyclohexane-ethyl acetate 50/50. Two main compounds were obtained. The first blue coloured eluted compound proved to be 2-phenyl-1,2,3,4,5,10-hexahydrobenzo[*g*]-quinoxaline-5,10-dione (IIIc) (60 mg.), characterized by comparison with an authentic sample (3). A further elution of the column gave blue coloured fractions containing 2,3-diamino-1,4-naphthoquinone (160 mg.).

Thermal Decomposition of *cis*-2-Amino-3-(2',3'-dimethylaziridino)-1,4-naphthoquinone (Id).

cis-2-Amino-3-(2',3'-dimethylaziridino)-1,4-naphthoquinone (Id) (3) (1.2 g., 5 mmoles) dissolved in 200 ml. of xylene was refluxed for 85 hours; Id did not completely react. The reaction mixture, after evaporation of the solvent, gave a residue which was chromatographed on a silica gel column eluted with a mixture cyclohexane-ethyl acetate 50/50. The first eluted blue fractions contained *cis*-2,3-dimethyl-1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline-5,10-dione (IIId) (300 mg.), m.p. 192-193° (from ethanol); ir: ν max cm^{-1} 3320 (NH stretching); 1615 (C=O); uv (ethanol): λ max nm (log ε) 235 (4.03), 272 (4.18), 3.04 (4.31), shoulder 314 (4.28); nmr: see Table II.

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.74; H, 6.04; N, 11.21.

A further elution of the column gave 400 mg. of unreacted Ic and then 200 mg. of 2,3-diamino-1,4-naphthoquinone.

Thermal Decomposition of 2-Amino-3-(2'-cyclohexeneimino)-1,4-naphthoquinone (Ie).

2-Amino-3-(2'-cyclohexeneimino)-1,4-naphthoquinone (Ie) (0.8 g., 3 mmoles) (3) dissolved in 150 ml. of xylene was refluxed for 80 hours; Id was not completely reacted. The reaction mixture, after evaporation of the solvent, gave a residue which was chromatographed on a silica gel column eluted with a mixture benzene-ethylacetate 90/10. Four main fractions were recovered in the following order. The first violet coloured eluted fractions gave, after evaporation, 5 mg. of a largely impure and unidentified compound. By continuing the elution of the silica gel column, blue coloured fractions were obtained. These gave, after evaporation of the solvent, 80 mg. of *cis*-1,2,3,4,4a,5,6,11,12,12a-decahydrobenzo[*b*]phenazine-6,11-dione (IIIe); ir: ν max cm^{-1} 3315 (NH stretching), 1620 (C=O); uv (ethanol): λ max nm (log ε) 236 (4.15), 273 (4.27), 305 (4.43), shoulder 315 (4.39), 635 (3.47); nmr: δ 7.15-7.82 (4H, A_2B_2 system,, aromatics), 4.71 (2H, s, vanishes on addition of deuterium oxide, NH), 3.48 (2H, broad s, N-CH-CH-N), 1.2-1.9 (8H, m, $(CH_2)_n$).

Anal. Calcd. for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.91; H, 6.15; N, 10.21.

A further elution of the column gave 60 mg. of unreacted Id and finally a blue coloured fractions containing 2,3-diamino-1,4-naphthoquinone (500 mg.).

Thermal Decomposition of *trans*-2-Amino-3-(2',3'-dimethylaziridino)-1,4-naphthoquinone (If).

trans-2-Amino-3-(2',3'-dimethylaziridino)-1,4-naphthoquinone (If) (3) (0.65 g., 2.7 mmoles) dissolved in 100 ml. of xylene was refluxed for 3 hours; Ie was not completely reacted. The reaction mixture, after evaporation of the solvent, gave a residue which was chromatographed on a silica gel column eluted with a mixture cyclohexane-ethyl acetate 70/30. The first violet coloured eluted fractions gave 2-amino-3-(1-methylallylamino)-1,4-naphthoquinone (IVf) as an oily compound (70 mg.); ir: ν max cm^{-1} 3350, 3320 (NH stretching); 1620 (C=O); uv (ethanol): λ max nm (log ε) shoulder 246 (4.04), 287 (4.03); nmr: δ 7.51-8.15 (4H, A_2B_2 system, aromatics); 5.62-6.22 (1H, m, N-C-C*H*=CH_2), 4.92-5.40 (2H, m, N-C-CH=CH_2), 4.45 (3H, s broad, vanishes by addition of deuterium oxide, N-H), 3.90-4.20 (1H, m, NH-CH-), 1.24-1.42 (3H, d, CH_3).

Anal. Calcd. for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.71; H, 5.94; N, 11.32.

A further elution of the chromatographic column gave blue coloured fractions containing *trans*-2,3-dimethyl-1,2,3,4,5,10-hexahydrobenzo-[*g*]quinoxaline-5,10-dione (IIIf) (4 mg.), characterized by comparison with an authentic sample (3).

A final elution of the column gave 40 mg. of unreacted If and 300 mg. of 2,3-diamino-1,4-naphthoquinone.

Thermal Decomposition of *cis*-2-Amino-3-(2'-ethyl-3'-phenylaziridino)-1,4-naphthoquinone (Ig).

cis-2-Amino-3-(2'-ethyl-3'-phenylaziridino)-1,4-naphthoquinone (1.6 g.) (Ig) (3) dissolved in 150 ml. of xylene were refluxed for 2.5 hours; complete decomposition of Ig was observed. By gas chromatographic analysis of the reaction mixture on F.F.A.P. on a Chromosorb chromatographic column the formation of small amounts of *trans*-1-phenyl-1-butene (V) was observed. Compound V was identified by comparison with an authentic sample. By evaporation of the reaction mixture, a residue was obtained, which was chromatographed on a silica gel column eluted with a mixture of cyclohexane-ethyl acetate 50/50. From the first blue coloured eluted fractions, *cis*-2-ethyl-3-phenyl-1,2,3,4,5,10-hexahydrobenzo[*g*]quinoxaline-5,10-dione (IIIg) was obtained (570 mg.), m.p. 146-148 (from ethanol); ir: ν max cm^{-1} 3340 (NH stretching); 1620 (C=O); uv (ethanol): λ max nm (log ε) 237 (3.82), shoulder at 270 (3.90), 304 (4.09), shoulder at 313 (4.07). For nmr spectra see Table II.

Anal. Calcd. for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.36; H, 5.56; N, 8.48.

A further elution gave blue coloured fractions containing a compound pure on tlc (70 mg.) (IX). The hplc analysis of IX on a lichrosorb Si-60, 0.25 x 2.6 mm I. D. 10 μ analytical column eluted with a mixture *n*-hexane-ethyl acetate 80/20, flow rate 2.0 ml./minute, showed two peaks K'_A = 3.38 and K'_B = 4.00, area peaks ratio B/A = 3/1, indicating a mixture of two compounds. The nmr spectra revealed that IX was a mixture of *cis*- and *trans*-4*H*-2,3,5,6-tetrahydro-2-phenyl-3-ethyl-5-iminonaphtho-[1,2-*b*]oxazin-6-one (IX).

The continual elution of the chromatographic column gave intensely violet coloured fractions containing two compounds having the same R*f* and not separable by column chromatography. These two compounds were separated in the following manner. The chromatographic fractions containing this mixture gave, by evaporation of the solvent, a residue which was washed with ethanol. The violet coloured compound was soluble in ethanol leaving a quite colourless residue. The residue, washed with ethanol for several times, was obtained as a pure weakly green-coloured compound (65 mg.) m.p. 178-180° (ethanol). The structure assigned to this compound is 2-ethyl-3-phenyl-5,10-dihydrobenzo[*g*]-quinoxaline-5,10-dione (VIII); ir: ν max cm^{-1} 1680 (C=O), 1590 (aromatic), 1520 (C=N); uv (ethanol) λ max nm (log ϵ) 259 (4.30), 297 (4.24); nmr: δ 8.10-8.40 (2H, m, aromatics), 7.30-7.90 (7H, m, aromatics), 2.90-3.35 (2H, q, CH_2-CH_3), 1.20-1.50 (3H, t, CH_3).

Anal. Calcd. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.58; H, 4.71; N, 8.59.

The ethanolic solution obtained from washing VIII gave, after evaporation, a residue (55 mg.) which was not possible to purify by chromatography. This compound, contamined by VIII, proved to be 2-ethyl-3-phenyl-1,2,5,10-tetrahydrobenzo[*g*]quinoxaline-5,10-dione (VII).

A pure sample of VII was prepared in a different manner (see below). The continual elution of the same chromatographic column gave blue coloured fractions containing 2,3-diamino-1,4-naphthoquinone (210 mg.) and finally several yellow coloured fractions which, after evaporation of the solvent, gave a residue (60 mg.). The latter was chromatographed again on a silica gel column eluted with a mixture cyclohexane-ethyl acetate 50/50. From the first eluted fractions, containing the quantitatively most important compound (15 mg.), after evaporation of the solvent, 2-(1-phenylpropyl)-1*H*-naphthoimidazole-4,9-dione (VI) was obtained. The structure of VI was assigned by comparison with an authentic sample obtained by independent synthesis.

2-Ethyl-3-phenyl-1,2,5,10-tetrahydrobenzo[*g*]quinoxaline-5,10-dione (VII).

A pure sample of VII was prepared in the following manner. An ethanolic solution of IIIg was added very slowly and with stirring to an ethanolic solution of ferric chloride. The added amount of ferric chloride was less than the stoichiometric amount in order to avoid further oxidation of the compound VII which forms. The reaction was followed by tlc, which was performed taking care that IIIg remained unreacted. The solution, after evaporation of the solvent, gave a residue, which was dissolved in chloroform and extracted with water. The chloroform solution, dried and evaporated, gave a residue which was chromatographed on a silica gel column eluted with a mixture benzene-ethyl acetate 80/20. In the first eluted fractions unreacted IIIg was recovered. A further elution gave fractions containing pure VII, m.p. 138-140°; ir: ν max cm^{-1} 3320 (NH stretching), 1670 (C=O)); (ethanol): λ max nm (log ϵ) 262 (4.25), shoulder at 290 (4.15); nmr: δ 7.1-8.15 (9H, m, aromatics), 6.15-6.35 (1H, s broad, NH), 4.56-4.90 (1H, m, N-C*H*-C_2H_5),, 1.3-1.7 (2H, m, CH_2), 0.74-1.06 (3H, t, CH_3).

Anal. Calcd. for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86. Found: C, 76.20; N, 5.19; N, 8.71.

2-Phenylbutyrylchloride (XIV).

2-Phenylbutyric acid (14) (8.2 g., 0.05 mole) were refluxed under anhydrous conditions with 11.9 g. of thionyl chloride (0.1 mole). When the evolution of gas was complete, the excess of thionyl chloride was driven off and the residue was distilled under reduced pressure giving 7.83 g. of XIV, b.p. 92° (9 mm).

Anal. Calcd. for $C_{10}H_{11}ClO$: C, 63.78; H, 6.42; Cl, 20.53. Found: C, 63.41; H, 6.22; Cl, 20.84.

2-(2'-Phenylbutyramido)-3-chloro-1,4-naphthoquinone (XV).

A suspension of 4.56 g. of 2-amino-3-chloro-1,4-naphthoquinone (13) (0.022 mole) in 25 ml. of xylene was added 4 g. (0.022 mole) of XIV and into the suspension, anhydrous hydrogen chloride was bubbled for five minutes. The resulting solution was refluxed for one day and then cooled overnight. A precipitate was obtained which was collected, washed with cyclohexane and then recrystallized from ethanol giving 1.75 g. of XV, m.p. 174-175°; ir: ν max cm^{-1} 3280 (NH stretching), 1690-1670 (C=O).

Anal. Calcd. for $C_{20}H_{16}ClNO_3$: C, 67.90; H, 4.56; N, 3.96. Found: C, 67.61; H, 4.48; N, 3.75.

2-(2'-Phenylbutyramido)-3-amino-1,4-naphthoquinone (XVI).

The preparation of XVI was accomplished by the procedure reported by Hoover and Day (13). Into a three necked flask containing 2 g. of XV (0.06 mole) dissolved in 30 ml. of nitrobenzene, gaseous dry ammonia was bubbled for one hour while the temperature was kept at 145-150°. Ammonium chloride was removed by filtering the hot solution and the filtrate, on cooling, gave a precipitate as red needles, which was collected, washed with ether and recrystallized from ethyl acetate, m.p. 185-187°; ir: ν max cm^{-1} 3400, 3320 (NH stretching), 1620 (C=O).

Anal. Calcd. for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43; N, 8.38. Found: C, 71.59; H, 5.52; N, 8.44.

2-(1-Phenylpropyl)-1*H*-naphthoimidazole-4,9-dione (VI).

The preparation of VI was accomplished by the procedure described by Hoover and Day (13). Compound XVI (2.0 g., 0.093 mole) dissolved in 50 ml. of ethanol and 10 ml. of 2*N* sodium hydroxide were refluxed for 30 minutes. The hot brown solution was poured with stirring into a solution of 200 ml. of water and 10 ml. of 2*N* hydrochloric acid. The yellow-green mixture was heated with stirring and ethanol gradually added until the imidazole, which had separated, and redissolved. The hot solution was treated with decolorizing carbon, filtered and cooled. The product separated as yellow needles and it was recrystallized from ethanol (1.14 g.), m.p. 231-233°; ir: ν max cm^{-1} 3240 (NH stretching), 1670 (C=O), 1600 (aromatic).

Anal. Calcd. for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.86. Found: C, 75.87; H, 5.15; N, 8.71.

REFERENCES AND NOTES

(1) This research was supported by Consiglio Nazionale delle Ricerche.

(2) Part of this work was presented to the XIIIth National Conference of Societá Chimica Italiana (Merano, June 18-23, 1978).

(3) G. Casini, F. Claudi, M. Grifantini and S. Martelli, *J. Heterocyclic Chem.*, **11**, 377 (1974).

(4) I. Antonini, F. Claudi, G. Cristalli, M. Grifantini and S. Martelli, *ibid.*, **17**, 181 (1980).

(5) F. Claudi, F. Felici, M. Ferappi and M. Grifantini, *Il. Farmaco Ed. Sci.*, **24**, 725 (1969).

(6) G. Casini, M. Ferappi and M. Grifantini, *Il. Farmaco Ed. Sci.*, **21**, 861 (1966).

(7) H. W. Heine, *Angew. Chem.*, **74**, 772 (1962).

(8) P. E. Fanta, in "The Chemistry of Heterocyclic Compounds with Three and Four-Membered Rings", Part I. A Weissberger, Ed., John Wiley and Sons, New York, N.Y., 1964 p. 524.

(9) D. C. Dermer and G. E. Ham, "Ethylenimine and other Aziridines" Academic Press, New York, N.Y., 1969, p. 250.

(10) H. W. Heine, in "Mechanisms of Molecular Migrations", Vol. 3, B. S. Thyagarayan, Ed., Wiley-Interscience, New York, N.Y., 1971, p. 145.

(11) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd Ed., Pergamon Press, 1969, pp. 234-237.

(12) R. A. Archer and H. S. Mosher, *J. Org. Chem.*, **32**, 1378 (1967).

(13) J. R. E. Hoover and A. L. Day, *J. Am. Chem. Soc.*, **76**, 4148 (1954).

(14) M. Rising, *ibid.*, **76**, 4148 (1954).

(15) P. E. Fanta and A. S. Deutsch, *J. Org. Chem.*, **23**, 72 (1958).

(16) D. V. Kaskeliker and P. E. Fanta, *ibid.*, **26**, 1841 (1961).

(17) P. E. Fanta, R. J. Smat, L. F. Piecz and L. Clemens, *ibid.*,**31**, 3113 (1966).

(18) C. W. Schellhamer, German Patent 1,115,253 (1959); *Chem. Abstr.*, **56**, 4740e (1962).