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# Thermal Rearrangement of Benzisoxazole- and Naphthisoxazolequinones in Solution and in the Solid State. Stereoselective Synthesis of γ-Cyanomethylidenebutenolides.

**M. Victoria Martínez-Díaz[a], Salomé Rodríguez-Morgade[a], Wolfram Schäfer[b] and Tomás Torres*,[a]**

[a]Departamento de Química (C-I) Facultad de Ciencias Universidad Autónoma de Madrid 28049-Madrid, Spain
[b]Max-Planck-Institut fur Biochemie 8033-Martinsried bei Munchen, Germany

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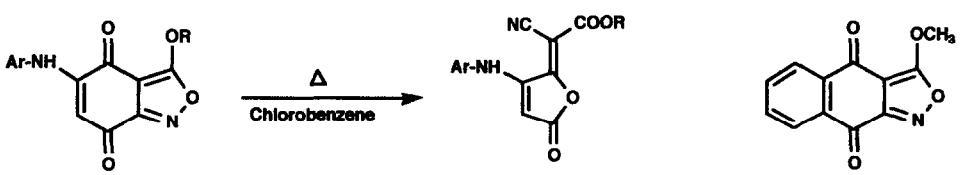
***Abstract.*** Readily accessible benzisoxazolequinones **1** undergo thermal induced highly stereoselective rearrangement in solution to afford quantitatively γ-cyanomethylidenebutenolides **3** The transformation can be explained by the formation of a vinylogous nitrene intermediate **4**, which undergoes an intramolecular acid-catalysed rearrangement Compounds **3** react easily with alcohols in Michael addition On the other hand, benzisoxazolequinones **1** and naphthisoxazolequinones **2** undergo thermal intermolecular rearrangement in the solid state to give in this case the corresponding N-methylisoxazolonequinones **20** and **11**, respectively, as major products

Heterocyclic quinones are an important feature of many biologically active natural and synthetic products and often serve also as useful synthetic intermediates[1,2]

Our own interest in quinone chemistry[3] prompted us to explore syntheses and reactivity of benzisoxazolequinones **1**[4] Some of these compounds are nitrene precursors on thermal or photochemical excitation[5], being therefore versatile intermediates for the preparation of highly functionalised compounds[6,7] Thus, we described the rearrangement reaction of isoxazolequinones in dimethylsulfoxide solution which allows the preparation of sulfoximido and sulfiliminoquinones[6] Recently[7], we reported a facile synthesis of alkylidenebutenolides via thermal rearrangement of benzisoxazolequinones In this paper[8] we describe the detailed results regarding the thermal rearrangement in solution and in solid state of benzisoxazole- and naphthisoxazolequinones **1** and **2**




**1** **3** **2**

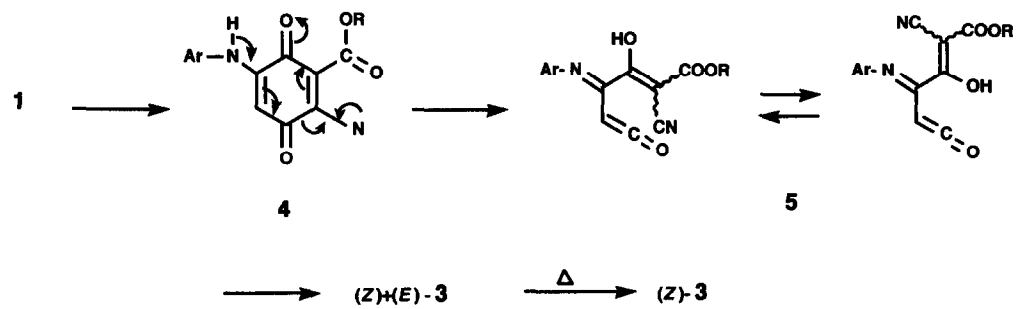
**a** R= $CH_3$, Ar= $C_6H_5$
**b** R= $CD_3$, Ar= $C_6H_5$
**c** R= $CH_3$, Ar= p-$CH_3C_6H_4$
**d** R= $CH_3$, Ar= p-$BrC_6H_4$
**e** R= $CH_3CH_2$, Ar= $C_6H_5$

**Thermal Rearrangement in Solution.** Previously[4], we reported a simple preparation method of 3-alkoxy-5-arylamino[2,1]benzisoxazole-quinones **1** starting from 2-carboxy-1,4-hydroquinone Benzisoxazole-quinones **1a-e** can be easily transformed in alkylidenebutenolides **3a-e** in near quantitative yield by heating at 110 °C during 40-60 min in a chlorobenzene solution. The structures were determined on the basis of analytical, chemical and spectroscopic data and confirmed by X-ray analysis of **3a**[9] Alkylidenebutenolides are important synthetic intermediates and have been used as precursors of several physiologically active butenolides such as tetronomycin, among others[10]

The rearrangement of isoxazolequinones **1** to butenolides **3** under these conditions proceeds in a highly stereoselective manner Only a single detectable stereoisomer (*Z*) was obtained as evidenced by NMR However, when compound **1a** was heated at lower temperature (61°C) in chloroform solution during 2 days, it was possible to observe by $^1$H-NMR a mixture of stereoisomers (*Z*)- and (*E*)-**3a** together with non-reacted starting material **1a**

The configurational stability of compound (*E*)-**3a** was tested by heating a mixture (*ca* 2 1) of (*Z*)-and (*E*)-**3a** at 110 °C in chlorobenzene solution After 30-40 min the *Z*-isomer was the only visible product ($^1$H-NMR) thus indicating its higher thermodynamic stability

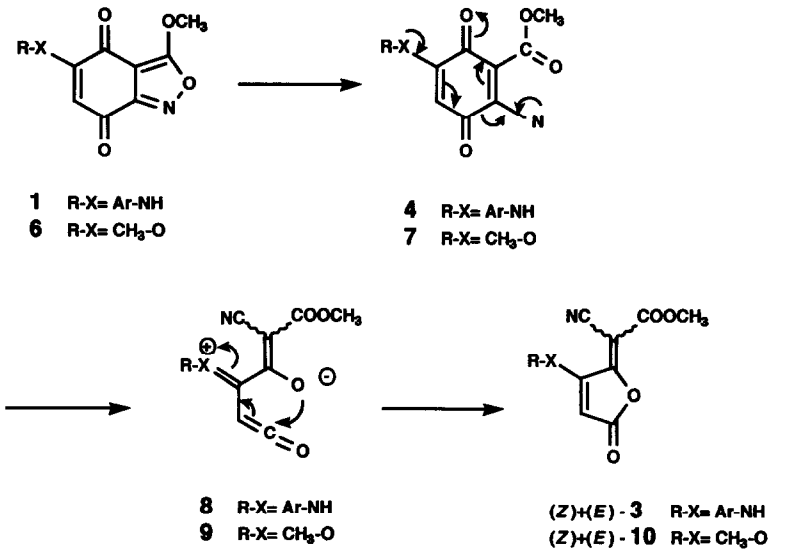
The final (*Z*)- stereochemistry of the compounds **3** might be determined by steric effects affecting the thermal equilibria between compounds (*E*)-**3** and (*Z*)-**3** at thermolysis temperature (110 °C) These equilibria are completely displaced to the *Z*-isomer (within the error limits of the $^1$H-NMR technique) as evidenced by a $^1$H-NMR spectrum of pure (*Z*)-**3a** in chlorobenzene at 110 °C which only showed the presence of the *Z*-stereoisomer




**Scheme 1**

The transformation from isoxazolequinones **1** to butenolides (*Z*)-**3** could be explained in terms of the reaction pathway depicted in Scheme 1 This would begin with the cleavage of the weak N-O bond of benzisoxazolequinone **1** to give a vinylogous nitrene **4**, which would undergo an intramolecular acid-catalysed rearrangement due to the presence of the arylamino substituent in 5-position, leading to the corresponding ketene **5** as a mixture of two stereoisomers in keto-enol equilibrium This ketene would undergo then intermolecular O-acylation to give a mixture of (*Z*)- and (*E*)-**3** which would evolve to the thermodynamically more stable isomer (*Z*)-**3** The proposed mechanism is quite similar to the accepted one for the acid-catalysed ring contraction in

azido-1,4-quinones to give butenolides[11,12]




**Scheme 2**

The rearrangement **1** to **3** could be also theoretically explained without intermolecular acid catalysis according to the reaction pathway showed in Scheme 2 Thus, vinylogous nitrene **4** would undergo thermal rearrangement to the (*Z*) + (*E*)-**3** isomeric mixture across the intermediate **8** However, the rearrangement **1** to **3** should not be simply the thermal process showed in the Scheme 2 Besides the mentioned precedents about external and intramolecular acid-catalysed rearrangements which are accepted for related processes[11,12] additional evidence can be inferred from the following experiments Benzisoxazolequinone **6**[4] and naphthisoxazolequinone **2**[4], with no intramolecular acid catalysis possibilities, do not give butenolides on heating under the same conditions described above for compounds **1** The pathway depicted in Scheme 1 is excluded for these two compounds, although compound **6** could be rearranged as indicated in Scheme 2 Thus, prolonged heating (18 h) of isoxazolequinone **6** in chlorobenzene at reflux temperature (132 °C) affords the mixture of stereoisomers (*Z*)- and (*E*)-**10** in a 85 15 thermodynamic ratio[13] In this case a transformation pathway **6**→**7**→**9**→**10** as depicted in Scheme 2 is proposed

If the thermal rearrangement of **6** to give **10** is carried out in the presence of trichloroacetic acid the reaction is significantly accelerated This fact must be interpreted as a consequence of an acid catalysed process[12] Stronger acids, such as sulfuric acid, could not be employed due to side reactions

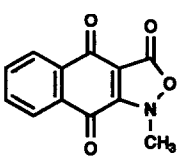
On the other hand, heating of naphthisoxazolequinone **2** in chlorobenzene at reflux temperature (132 °C) during 96 hours does not give butenolides In this case both reaction pathways (Schema 1 and 2) are excluded The thermal rearrangement of naphthisoxazolequinone **2** in these conditions leads to a mixture of N-methyl-isoxazolonequinone **11** in low yield (15%) and its degradation products 2-carboxy-3-methylamino- and 2-

Table 1 Thermal Rearrangement of Isoxazolequinones in Solution and in the Solid State

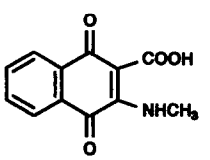
| Thermal Rearrangement | | | | Final Product(s) | | |
|---|---|---|---|---|---|---|
| starting isoxazole-quinone | method[a] | temperature (°C) | time (h) | butenolide (% yield) | stereoselectivity (*Z*/*E*)[b] | N-alkyl isoxazolonequinone (% yield) |
| **1a** | A | 110 | 0 7 | **3a** (85) | > 0 95 | Not observed |
| **1a** | A | 61[c] | 48 | **3a** (70)[d] | 0 67 | Not observed |
| **1a** | B | 110 | 1 | **3a** ( 5 ) | > 0 95 | **20a** (50) |
| **1b** | A | 110 | 0 7 | **3b** (85) | > 0 95 | Not observed |
| **1b** | B | 110 | 1 | **3b** ( 5 ) | > 0 95 | **20b** (50) |
| **1c** | A | 110 | 0 7 | **3c** (80) | > 0 95 | Not observed |
| **1c** | B | 110 | 1 | **3c** ( 5 ) | > 0 95 | **20c** (45) |
| **1d** | A | 110 | 0 7 | **3d** (87) | > 0 95 | Not observed |
| **1d** | B | 110 | 1 | **3d** (25) | > 0 95 | **20d** (35) |
| **1e** | A | 110 | 0 7 | **3e** (80) | > 0 95 | Not observed |
| **1e** | B | 110 | 4 | **3e** (45) | > 0 95 | **20g** (15) |
| **2** | A | 132 | 96 | Not observed | - | **11** (15)[e] |
| **2** | B | 150 | 2 | Not observed | - | **11** (65) |
| **6** | A | 132 | 18 | **10** (76) | 0 70 | Not observed |
| **6** | B | 132 | 16 | **10** ( 5 ) | - | **21** (67) |
| **14** | A | 179[f] | 5 5 | **15** (90) | > 0 95 | - |

[a]Method A In solution. Chlorobenzene was used unless stated otherwise Method B In solid state [b]With the $^1$H-NMR error limit [c]In chloroform [d]Starting material **1a** (15%) was recovered [e]Compounds **12** and **13** were also obtained in 3 % and 2 % yield respectively [f]In *o*-dichlorobenzene

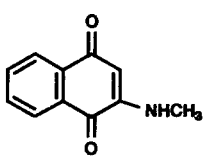
methylamino-1,4-naphthoquinones (**12** and **13**) The formation of compound **11** could be explained in terms of a O onto N methyl group rearrangement as consequence of a thermal reaction of compound **2** in the solid state[14], as will be discussed below




**11**



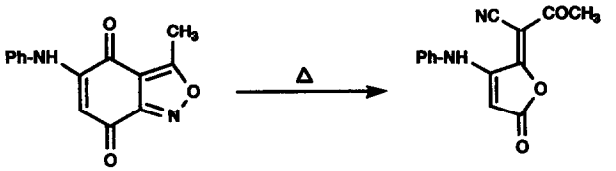

**12**




**13**

To gain further insight into the rearrangement reaction of isoxazolequinones to give butenolides, methylisoxazolequinone **14**[4] was heated at 179 °C in 1,2-dichlorobenzene solution during 5 5 hours Under

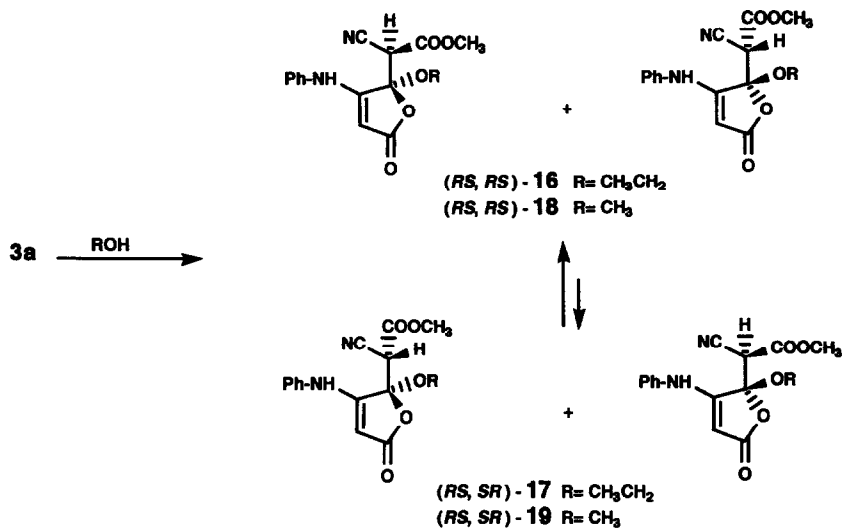
these conditions only one stereoisomer, (Z)-**15**, was obtained in excellent yield This rearrangement takes place much more slowly at lower temperatures The presence of the arylamino substituent in 5-position would facilitate the rearrangement reaction as in the case of compounds **1** The lower reactivity of **14** in comparison with **1** indicates stronger N-O bond in the former case




**14** (Z) - **15**

The results obtained in the thermal rearrangements of benzisoxazolequinones in solution are summarized in Table 1

Alkylidenebutenolides **3** react quickly with alcohols by addition to the highly activated exocyclic double bond Thus, Michael addition of ethanol to **3a** affords a diastereomeric mixture of **16** and **17** in a 70 30 thermodynamic equilibrium ratio (Scheme 3)



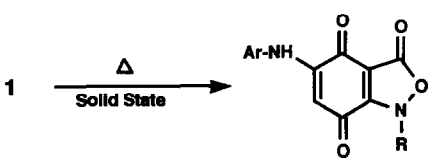

**Scheme 3**

Recrystallization of the crude reaction mixture from ethanol allows the isolation of the major component **16** as a pure crystalline racemic mixture The structure of butenolide **16** was confirmed by X-ray crystallographic analysis[9] Acid-catalysed epimerization of **16** takes place easily even in normal NMR solvents to give the thermodynamic control mixture of **16** and **17** For example, when the pure isomer **16** was dissolved in normal

$d_3$-chloroform for NMR at room temperature, an isomer ratio of 70 to 30, for **16** and **17** respectively, could be observed within 5 min, thus indicating that the equilibrium had already been established Similar results were obtained with $d_6$-DMSO and $d_4$-methanol However, this epimerization reaction does not occur in anhydrous acid free chloroform The addition of methanol to the alkylidenebutenolide **3a** also affords the corresponding epimeric mixture of **18** and **19** in ca 70 30 ratio Identical results as described above for **16** were obtained in the acid-catalysed epimerization of **18.**

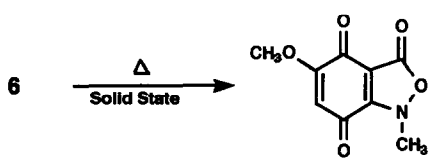
Addition compounds **16, 17** and **18, 19** undergo alcohol elimination by treatment with silica gel in chloroform at room temperature to give the butenolide (*Z*)-**3a** in near quantitative yield The presence of the (*E*)-**3a** isomer could not be observed

**Thermal Rearrangement in the Solid State.** The thermal reaction in the solid state of compounds **1** and **6** follows predominantly another entirely different pathway, besides the one described above for the thermal reaction in solution In the solid state 3-methoxy substituted benzisoxazolequinones **1** and **6** react via methyl group rearrangement to afford N-methylbenzisoxazolonequinones **20** and **21** as major products, rather than by N-O bond scission, opening of the isoxazole ring and subsequent rearrangement to yield **3** and **10** Heating of **1a-d** or **6** at the indicated temperature in each case (Table 1) yielded a mixture of the corresponding N-methylisoxazolonequinone **20a-d** or **21** in 35-67% yield[15] and the corresponding butenolide, **3a-d** or **10** in 5-25% yield Structure assignments for these products were made on the basis of characteristic spectral data ($^1$H and $^{13}$C-NMR, IR, MS) and by comparison with literature data reported by ourselves[4,6,7] Compound **20a** was identical to an authentic sample prepared by treatment of 5-anilino-3-hydroxy[2,1]benzisoxazole-4,7-quinone with diazomethane In this reaction benzisoxazolequinone **1a** was also isolated




**20**

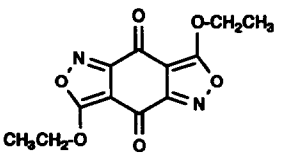
**a** R= $CH_3$, Ar= $C_6H_5$
**b** R= $CD_3$, Ar= $C_6H_5$
**c** R= $CH_3$, Ar= p-$CH_3C_6H_4$
**d** R= $CH_3$, Ar= p-$BrC_6H_4$
**e** R= $CD_3$, Ar= p-$CH_3C_6H_4$
**f** R= $CD_3$, Ar= p-$BrC_6H_4$
**g** R= $CH_3CH_2$, Ar= $C_6H_5$



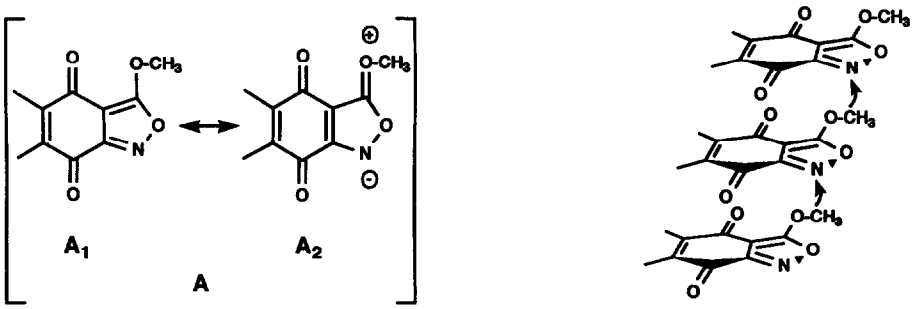

**21**

In a similar way 3-methoxy substituted naphthisoxazolequinone **2**[4] undergoes smooth rearrangement on thermolysis in the solid state when heated at 150 °C for two hours to produce the N-methyl derivative **11** in 65% yield[15] In this case the thermal reaction does not give butenolide because intramolecular acid catalysis is not possible in the naphtho-series The rearrangement is of synthetic utility as a good route to N-methylisoxa-

zolonequinones of type **11**, **20** and **21** It was proved to be intermolecular by a cross experiment where equimolar amounts of **1c** and the appropriately labeled compound **1b** were heated together The two different isoxazolonequinones obtained, which were separated by chromatography, were studied by mass spectrometry (electron impact) Each of both compounds were identified as mixtures of two components **20a** + **20b** and **20c** + **20e**, respectively The formation of **20a** (*m/z* = 270, $M^+$) and **20e** (*m/z* = 287, $M^+$) assured the intermolecular rearrangement of the methyl group Similar results were obtained in the thermolysis of a mixture of **1b** and **1d** In this case N-methylbenzisoxazolonequinones **20a** + **20b** and **20d** + **20f** were identified The cleavage of O-alkyl groups in related systems, for example in **22**, by means of trialkyloxonium tetrafluoroborates affording the corresponding isomeric di-N-alkylbenzodiisoxazolonedione, has also been described and follows a different pathway[16] Related to the above described rearrangements is the thermal isomerization in the solid state of 3-methoxy-4,7-indazolequinone-3-one reported also by us[17]




**22**




**Scheme 4**

The above described results may demonstrate an important contribution of structure $A_2$ to the resonance hybrid **A** (Scheme 4) in 3-alkoxybenzisoxazole and naphthisoxazolequinones **1** and **2** Unfortunately, appropriate crystals of **1** or **2** for X-ray analysis could not be obtained However, the proposed strong polarization of the exocyclic O-alkyl bond in **1** and **2** is in accordance with the X-ray data found by other authors for the related compound **22**[18] The electrophilic character of the ethyl group in **22**[19] and the methyl group in **1a-e**[6] and consequently its potential as alkylating agents has been evidenced against different substrates such as thiophenolates, pyridine, sulfoxides, sulfides, amides, etc A hypothetical stacking of the molecules of **1** and **2** in the solid state (Scheme 4), similar to that found by X-Ray analysis for **22**[18], together with the polar character of the O-$CH_3$ bond (**A**), could be responsible for the efficient intermolecular migration of the methyl group here

described[20]

The lower reactivity of the ethoxybenzisoxazolequinone **1e** on thermolysis was evidenced After 4 hours at 110 °C compound **20g** was obtained in low yield (15%) together with the corresponding butenolide **3e** (45%) This result should be interpreted as a lower aptitude of the ethyl group to migrate in these systems For this reason the competitive butenolide formation reaction is the predominant one in this last case

In conclusion, a highly stereoselective synthesis of alkylidenebutenolides **3** starting from readily available benzisoxazolequinones **1** has been described Convenient methodology for the preparation of N-methylisoxazolonequinones **11, 20** and **21** has been also established in this paper The mechanisms of the thermal rearrangements of benzisoxazole- and naphthisoxazolequinones **1** and **2** in solution and in the solid state have been discussed

**Acknowledgements** We are indebted to the the D G I C Y T (Spain) and BMFT (Germany) for the award of "Acciones Integradas 1991-92" (28A) We are grateful to Drs E Gutierrez-Puebla and A Monge, for X-ray crystallographic data[9]

## Experimental Section

*General Procedure for the Thermal Rearrangement of 3- Methoxy[2,1]benzisoxazole-4,7-quinones* **1a-e** *in Chlorobenzene Solution. Synthesis of butenolides* **3a-e.** To a solution of the corresponding quinone (1 mmol) in methylene chloride (170 ml) was added chlorobenzene (85 ml) The methylene chloride was then evaporated at room temperature under reduced pressure The chlorobenzene solution was heated for 40 min at 110 °C The solvent was removed *in vacuo* and the residue recrystallized from ethyl acetate or chloroform-hexane The procedure described was followed in the cases **1a-c** because of the low solubility of these quinones directly in chlorobenzene In the cases **1d** and **1e** their higher solubility in chlorobenzene allows the direct solubilization of the compounds in this solvent. Yields of butenolides are given in Table 1

*β-Anilino-γ-cyanocarbomethoxymethylidene-$\Delta^{\alpha,\beta}$-butenolide* **(3a).** Yellow-orange needles, mp 183 °C (dec), IR (KBr) 3145, 2234 (CN), 1778 (C=O), 1709 (C=O), 1630, 1582, 1295, 1278, $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 11 4 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 1 (m, 5H, arom), 5 68 (s, 1H, CH=), 4 00 ppm (s, 3H, $COOCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 167 6 (C-1), 165 0, 164 8 (C-4, C-6), 152 6 (C-3), 137 9 (C-1'), 129 9 (C-3', C-5'), 126 3 (C-4'), 121 3 (C-2', C-6'),111 8 (CN), 89 0 (C-5), 86 2 (C-2), 54 5 ppm ($OCH_3$), MS *m/z* (relative intensity) 270 $M^+$ (36), 239 (4), 211 (50), 210 (10), 183 (8), 144 (100), 117 (15), 90 (17), Anal Calcd for $C_{14}H_{10}N_2O_4$ C, 62 22, H, 3 73, N, 10 37 Found C, 61 95, H, 3 84, N, 10 36

*β-Anilino-γ-cyano-($d_3$-carbomethoxy)methylidene-$\Delta^{\alpha,\beta}$-butenolide* **(3b).** Yellow-orange needles, mp 183 °C (dec), $^{13}C$ NMR and $^1H$ NMR (absence of singlet at 4 00 ppm) identical to **3a** MS *m/z* (relative intensity) 273 $M^+$ (30), 245 (2), 239 (3), 238 (7), 144 (100) Anal Calcd for $C_{14}H_7D_3N_2O_4$. C, 61 54, H+D, 4 79, N, 10 25 Found C, 61 62, H+D, 4 81, N, 10 18

*β-(p-Toluidino)-γ-cyanocarbomethoxymethylidene-$\Delta^{\alpha,\beta}$-butenolide* **(3c).** Yellow-orange needles, mp 172-173 °C (dec), IR (KBr) 3140, 2225 (CN), 1781 (C=O), 1704 (C=O), 1629, 1580, 1512, 1301, 1283, $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 11 3 (broad s, slowly removed by $D_2O$ , 1H , NH), 7 4-7 0 (m, 4H, arom), 5 60 (s, 1H, CH=), 4 00 (s, 3H, $COOCH_3$) 2 38 ppm (s, 3H, $CH_3$), $^{13}C$ NMR ($CDCl_3$) δ 167 6 (C-1), 165 2, 164 8 (C-4, C-6), 153 2 (C-3), 138 0 (C-1'), 134 8 (C-4'), 130 5 (C-3', C-5'), 124 8 (C-2', C-6'), 110 0 (CN), 89 6 (C-

5), 86 0 (C-2), 52 4 ($OCH_3$), 21 2 ($CH_3$-Ar), MS *m/z* (relative intensity) 284 $M^+$ (42), 253 (5), 252 (13), 225 (43), 224 (15), 159 (14), 158 (100), 130 (32), 91 (25) Anal Calcd for $C_{15}H_{12}N_2O_4$ C, 63 38, H, 4 26, N, 9 85 Found C, 63 18, H, 4 32, N, 9 80

*β-(p-Bromoanilino)-γ-cyanocarbomethoxymethylidene-$\Delta^{\alpha,\beta}$-butenolide* (**3d**). Yellow-orange needles, mp 201 °C (dec), IR (KBr) 3140, 2220 (CN), 1790 (C=O), 1705 (C=O), 1630, 1580, 1560, 1300, $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 11 4 (broad s, slowly removed by $D_2O$, 1H, NH), 7 6-7 1 (m, 4H, arom), 5 66 (s, 1H, CH=), 4 01 ppm (s, $COOCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 168 0 (C-1), 165 4, 165 2 (C-4, C-6), 152 8 (C-3), 136 4, 135 2 (C-1', C-4'), 130 4 (C-3', C-5'), 121 2 (C-2',C-6'),111 8 (CN), 88 6 (C-5), 85 2 (C-2), 53 6 ppm ($OCH_3$), MS *m/z* (relative intensity) 348, 350 $M^+$ (51), 315, 317 (12), 289, 291 (15) 222, 224 (100), 195, 197 (15), 194, 196 (14), Anal Calcd for $C_{14}H_9BrN_2O_4$ C, 48 16, H 2 60, N, 8 02 Found C, 48 45, H, 2 52, N, 7 78

*β-Anilino-γ-cyanocarboethoxymethylidene-$\Delta^{\alpha,\beta}$-butenolide* (**3e**). Yellow-orange needles, mp 179-181 °C (dec), IR (KBr) 3145, 2227 (CN), 1782 (C=O), 1702 (C=O), 1630, 1580, 1295, 1284, $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 11 4 (broad s, slowly removed by $D_2O$ , 1H , NH), 7 6-7 1 (m, 5H, arom), 5 64 (s, 1H, CH=), 4 42 (q, 2H, $OCH_2CH_3$) 1 40 ppm (t, 3H, $OCH_2CH_3$), $^{13}C$ NMR ($CDCl_3$) δ 167 7 (s) (C-1), 165 1 (s), 154 7 (s) (C-4, C-6), 152 9 (s) (C-3), 138 2 (s) (C-1'), 130 0 (d) (C-3', C-5'), 126 4 (d) (C-4'), 121 5 (d) (C-2', C-6'), 111 8 (s) (CN), 88 9 (s) (C-5), 86 4 (d) (C-2), 64 5 (t) ($OCH_2CH_3$), 14 0 (q) ($OCH_2CH_3$), MS *m/z* (relative intensity) 284 $M^+$ (32), 270 (1), 256 (2), 240 (5), 238 (8), 211 (52), 183 (8), 155 (5), 144 (100), 117 (18), 116 (19), 90 (19) Anal Calcd for $C_{15}H_{12}N_2O_4$. C, 63 38, H 4 26, N, 9 85 Found C, 63 15, H, 4 32, N, 9 72

*Thermal Rearrangement of 3-Methoxy[2,1]benzisoxazole-4,7-quinone* **1a** *in Chloroform Solution.* A solution of **1a** (1 mmol) in chloroform (100 ml) was heated for 48 h at reflux temperature The solvent was removed *in vacuo* and the residue, after washing with ethyl acetate-hexane, was analysed by $^1H$ NMR ($CDCl_3$) The yellow-orange solid (189 mg) showed to be a mixture of starting material **1a** (15%, deduced from the $^1H$ NMR spectrum) and butenolides (*Z*)- **3a** and (*E*)- **3a** in a 5 1 ratio Compound (*E*) -**3a** could not be isolated by chromatography on silica gel because of isomerization to (*Z*)- **3a** or recrystallization Spectral data for (*E*)-**3a** were taken from the mixture (*Z*)+(*E*)-**3a**

(*E*)-**3a**. $^1H$ NMR ($CDCl_3$) δ 8 10 (broad s, slowly removed by $D_2O$ , 1H , NH), 7 60-7 10 (m, 5H, arom), 5 67 (s, 1H, CH=), 3 94 ppm (s, 3H, $COOCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 167 6 (C-1), 162 4, 159 4 (C-4, C-6), 153 6 (C-3), 137 3 (C-1'), 130 0 (C-3', C-5'), 126 9 (C-4'), 121 9 (C-2', C-6'),115 4 (CN), 88 0, 83 9 (C-2, C-5), 53 6 ppm ($OCH_3$)

*Thermal treatment of (Z)-***3a** *and (E)-***3a** *in Chlorobenzene Solution. $^1H$ NMR Experiments.* A sample of the mixture of (*Z*)- **3a** and (*E*)-**3a** (5 1) obtained above was heated in chlorobenzene solution in a NMR tube at 110 °C After 30 min the (*Z*) isomer was the only product observed On the other hand, a $^1H$ NMR spectrum of (*Z*)-**3a** in chlorobenzene at 110 °C showed that this isomer does not undergo any transformation at this temperature

*Thermal Rearrangement of 3,5-Dimethoxy[2,1]benzisoxazole-4,7-quinone* (**6**) *in Chlorobenzene Solution Synthesis of butenolides (Z) and (E)-***10.** A solution of **6** (1 mmol) in chlorobenzene (80 ml) was heated at reflux temperature for 18 h The solvent was removed in vacuo and the residue analysed by $^1H$ NMR The pale-yellow solid showed to be a mixture of (*Z*)-**10** and (*E*)-**10** in a 85 15 ratio The diastereoisomers were separated by chromatography on silica gel using ethyl acetate-hexane 10 3 as eluent.

*(Z)-β-Methoxy-γ-cyanocarbomethoxymethylidene-$\Delta^{\alpha,\beta}$-butenolide [(Z)-***10***].* Yield 65%, pale-yellow needles, mp 125 °C, IR (KBr) 3130, 3000, 2960, 2220 (CN), 1800 (C=O), 1740 (C=O), 1640, 1610, 1435,

1285, 1250, 1230 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 5 63 (s, 1H, CH=), 4 11 (s, 3H, $COOCH_3$), 3 90 ppm (s, 3H, $OCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 169 1 (C-1), 163 5, 159 9, 159 4 (C-3, C-4, C-6), 112 1 (CN), 93 2 (C-2), 86 0 (C-5), 60 7 ($OCH_3$), 53 4 ppm ($COOCH_3$), MS *m/z* (relative intensity) 209 (90), 178 (30), 150 (5), 138 (16), 94 (11), 69 (100) Anal Calcd for $C_9H_7O_5N$ C, 51 68, H, 3 38, N, 6 69 Found C, 51 41, H, 3 28, N, 6 49

*(E)-β-Methoxy-γ-cyanocarbomethoxymethylidene-$\Delta^{\alpha,\beta}$-butenolide [(E)-**10**].* Yield 11%, pale-yellow needles, mp 147-148 °C, IR (KBr) 3130, 3000, 2960, 2230 (CN), 1805 (C=O), 1740 (C=O), 1635, 1610, 1435, 1285, 1255, 1230 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 5 61 (s, 1H, CH=), 4 01 (s, 3H, $COOCH_3$), 3 89 ppm (s, 3H, $OCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 168 3 (C-1), 163 2, 159 0, 158 8 (C-3, C-4, C-6), 111 4 (CN), 94 5 (C-2), 89 1 (C-5), 60 7 ($OCH_3$), 53 7 ppm ($COOCH_3$), MS *m/z* (relative intensity) 209 (89), 178 (56), 150 (18), 138 (33), 94 (26), 69 (100), High resolution MS Calcd for $C_9H_7O_5N$ 209 032 Found 209 030

When the thermal treatment of **6** was carried out at 110 °C in the presence of a catalytic amount of trichloroacetic acid, the rearrangement to give (*Z*) and (*E*)-**10** took place more quickly than the rearrangement without acid catalysis, as was proved by $^1H$ NMR monitoring Thus, after 10 h heating the transformation was of 77% in the presence of trichloroacetic acid and only of 64% without the catalyst

*Thermal Rearrangement of 3-Methoxynaphth[2,3-c]isoxazole-4,9-quinone* (**2**) *in Chlorobenzene Solution.* A solution of **2** (1 mmol) in chlorobenzene (80 ml) was heated at reflux temperature for 90 h The solvent was removed in vacuo and the residue chromathographed on silica gel using chloroform-acetone (10 1) as eluent to give starting material (15%) 1-Methyl[2,1]naphth[2,3-*c*]isoxazol-3(1*H*)-one-4,9-quinone (**11**) as major product in 15% yield (described below) and other two minor compounds

*2-Carboxy-3-methylamino-1,4-naphthoquinone* (**12**). Yield 3%, mp 170-171 °C (dec), IR (KBr) 3100-2900 (br, COOH), 1675 (C=O), 1650, 1490, 1335, 1280 $cm^{-1}$,$^1H$ NMR ($CDCl_3$) δ 14 8 (broad s, removed by $D_2O$ , 1H, COOH), 12 1 (broad s, slowly removed by $D_2O$ , 1H , NH-$CH_3$), 8 3-7 7 (m, 4H, arom), 3 59 ppm (d, 3H, NH-$CH_3$), MS *m/z* (relative intensity) 231 $M^+$ (21), 213 (100), 187 (7), 186 (10), 185 (23), 172 (34), 157 (16), 130 (18), High resolution MS Calcd for $C_{12}H_9NO_4$ 231 053 Found 231 056

*2-Methylamino-1,4-naphthoquinone* (**13**). Yield 2%, mp 234 °C [Lit[21] 232 °C], $^1H$ NMR ($CDCl_3$) δ 8 4-7 4 (m, 4H, arom), 5 9 (broad s, removed by $D_2O$ , 1H, NH-$CH_3$) 5 73 (s, 1H, quinone), 2 94 ppm (d, 3H, NH-$CH_3$), MS *m/z* (relative intensity) 187 $M^+$ (100), 172 (15), 159 (9), 158 (8), 146 (13), 130 (22), 105 (28), High resolution MS Calcd for $C_{11}H_9NO_2$ 187 063, Found 187 069

*Thermal Rearrangement of 3-Methyl-5-anilino[2,1]benzisoxazole-4,7-quinone* **14** *in o-Dichlorobenzene Solution Synthesis of β-Anilino-γ-cyanoacetylmethylidene-$\Delta^{\alpha,\beta}$-butenolide* **15.** A solution of **14** (1 mmol) in *o*-dichlorobenzene (100 ml) was heated at reflux temperature for 5 5 h The solvent was removed in high vacuo and the residue was recrystallized from ethyl acetate-hexane to give butenolide **15** in 90% yield Yellow-orange needles, mp 130 °C, IR (KBr) 3130, 2270 (CN), 1775 (C=O), 1740 (C=O), 1685, 1625, 1595, 1545 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 11 66 (broad s, slowly removed by $D_2O$ , 1H , NH), 7 5-7 2 (m, 5H, arom), 5 67 (s, 1H, CH=), 2 73 (s, 1H, $COCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 196 3 (C=O), 167 8 (C-1), 165 3 (C-4), 152 5 (C-3), 137 8 (C-1'), 129 9 (C-3', C-5'), 126 3 (C-4'), 121 3 (C-2', C-6'), 114,2 (CN), 92 0 (C-5), 85 4 (C-2), 31 1 ppm ($OCH_3$), MS *m/z* (relative intensity) 254 (28), 212 (56), 144 (100), 117 (20), 77 (38) Anal Calcd for $C_{15}H_{12}N_2O_3$ C, 66 13, H, 3 97, N, 11 01 Found C, 66 41, H, 4 05, N, 10 68

*General Procedure for Alcohol Addition to Butenolide* **3a.** Butenolide **3a** (0 5 mmol) was dissolved in chloroform (20 ml) and the corresponding alcohol, ethanol or methanol, (20 ml) was added After 4h at room temperature the solvent was removed in vacuo without heating The oily residue solidified on treatment with ethyl

ether under cooling Recrystallization from ethyl acetate-hexane afforded the corresponding addition products **16** or **18** respectively in almost quantitative yield Compounds **16** and **18** undergo alcohol elimination on chromatography on silica gel to give **3a**

*(RS,RS)-β-Anilino-γ-cyanocarbomethoxymethyl-γ-ethoxy-$\Delta^{\alpha,\beta}$-butenolide* (**16**). Slightly-yellow crystals, mp 155-157°C (dec at 135°C), IR (KBr) 3235, 2255 (CN), 1755 (C=O), 1722 (C=O), 1620, 1590 $cm^{-1}$, IR (acid free $CHCl_3$) 3320, 2250 (CN), 1746 (C=O), 1638, 1595, $cm^{-1}$, $^1H$ NMR (acid free $CDCl_3$) δ 8 47 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 1 (m, 5H, arom), 5 48 (s, 1H, CH=), 4 37 (s, removed by $D_2O$, 1H, CH), 3 93 (s, 3H, $COOCH_3$), 3 62 (m, 2H, $OCH_2CH_3$), 1 24 ppm (t, 3H, $OCH_2CH_3$), $^1H$ NMR ($d_6$-DMSO) (Data of **16** taken from the mixture of **16** and **17** described below) δ 9 84 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 0 (m, 5H, arom ), 5 48 (s, 1H, CH=), 5 06 (s, removed by $D_2O$, 1H, CH), 3 64 (s, 3H, $COOCH_3$), 3 5 (m, 2H, $OCH_2CH_3$), 1 22 ppm (t, 3H, $OCH_2CH_3$), $^{13}C$ NMR (acid free $CDCl_3$) δ 169 4 (s), 164 7 (s) (C-1, C-6), 158 3 (s) (C-3), 138 8 (s) (C-1'), 129 9 (d) (C-3', C-5'), 125 5 (d) (C-4'), 120 5 (d) (C-2',C-6'),111 8 (s) (CN),102 6 (s) (C-4), 87 9 (d) (C-2), 60 6 (t) ($OCH_2CH_3$), 54 6 (q) ($OCH_3$), 45 9 (d) (C-5), 14 9 ppm (q) ($OCH_2CH_3$), MS *m/z* (relative intensity) 316 $M^+$ (9), 270 (22), 212 (9), 211 (20), Anal Calcd for $C_{16}H_{16}N_2O_5$ C, 60 75, H, 5 10, N, 8 86 Found C, 60 64, H, 5 12, N, 8 87

*(RS,SR)-β-Anilino-γ-cyanocarbomethoxymethyl-γ-ethoxy-$\Delta^{\alpha,\beta}$-butenolide* (**17**). Partial epimerization of **16** to afford thermodynamic equilibrium mixture of **16** and **17** in an approximate 70 30 ratio took place when pure compound **16** was dissolved in non-acid free solvents (for example, $CDCl_3$) or polar ones ($d_6$-DMSO, $CD_3OD$) Diastereoisomer **17** could not be isolated because it undergoes epimerization on recrystallization from ethanol to give the thermodynamically more stable diastereoisomer **16** On the other hand, compounds **16** and **17** undergo ethanol elimination in column chromatography on silica gel to afford **3a** The NMR data of **17** were taken from the mixture of **16** and **17** $^1H$ NMR ($CDCl_3$) δ 7 6 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 1 (m, 5H, arom), 5 39 (s, 1H, CH=), 4 29 (s, removed by $D_2O$, 1H, CH), 3 85 (s, 3H, $COOCH_3$), 3 6 (m, 2H, $OCH_2CH_3$), 1 30 ppm (t, 3H, $OCH_2CH_3$), $^1H$ NMR ($d_6$-DMSO) δ 8 2 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 0 (m, 5H, arom), 5 65 (s, 1H, CH=), 5 01 (s, removed by $D_2O$, 1H, CH), 3 81 (s, 3H, $COOCH_3$), 3 5 (m, 2H, $OCH_2CH_3$), 1 17 ppm (t, 3H, $OCH_2CH_3$),$^{13}C$ NMR ($CDCl_3$) δ 169 0 (s), 162 9 (s) (C-1, C-6), 158 8 (s) (C-3), 138 3 (s) (C-1'), 129 9 (d) (C-3', C-5'), 125 8 (d) (C-4'), 120 7 (d) (C-2',C-6'),111 2 (s) (CN),101 6 (s) (C-4), 87 7 (d) (C-2), 60 4 (t) ($OCH_2CH_3$), 54 4 (q) ($OCH_3$), 46 1 (d) (C-5), 14 9 ppm (q) ($OCH_2CH_3$)

*(RS,RS)-β-Anilino-γ-cyanocarbomethoxymethyl-γ-methoxy-$\Delta^{\alpha,\beta}$-butenolide* (**18**). Slightly-yellow crystals, mp 120-122 °C (dec at 90°C), IR (KBr) 3215, 1752 (C=O), 1721 (C=O), 1637, 1620, $cm^{-1}$, IR (acid free $CHCl_3$) 3315, 2250 (CN), 1744 (C=O), 1636, 1595, $cm^{-1}$, $^1H$ NMR (acid free $CDCl_3$) δ 8 45 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 1 (m, 5H, arom), 5 49 (s, 1H, CH=), 4 36 (s, removed by $D_2O$, 1H, CH), 3 92 (s, 3H, $COOCH_3$), 3 37 ppm (s, 3H, $OCH_3$), $^1H$ NMR ($d_6$-DMSO) (Data taken from the mixture of **18** and **19** described below) δ 9 83 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 0 (m, 5H, arom), 5 50 (s, 1H, CH=), 5 05 (s, removed by $D_2O$, 1H, CH), 3 64 (s, 3H, $COOCH_3$), 3 26 ppm (s, 3H, $OCH_3$), $^{13}C$ NMR (acid free $CDCl_3$) δ 169 3 (s),"164 6 (s) (C-1, C-6), 157 7 (s) (C-3), 138 7 (s) (C-1'), 129 9 (d) (C-3', C-5'), 125 6 (d) (C-4'), 120 5 (d) (C-2',C-6'),111 8 (s) (CN),102 8 (s) (C-4), 88 1 (d) (C-2), 54 7 (q) ($OCH_3$), 51 7 (q) ($OCH_3$ on C-4), 45 6 (d) (C-5), MS *m/z* (relative intensity) 302 $M^+$ (9), 270 (22), 211 (23), 144 (100), Anal Calcd for $C_{15}H_{14}N_2O_5$ C,59 60, H, 4 67, N, 9 27 Found C, 59 68, H, 4 57, N, 9 28

*(RS,SR)-β-Anilino-γ-cyanocarbomethoxymethyl-γ-methoxy-$\Delta^{\alpha,\beta}$-butenolide* (**19**). Compound **19** was

obtained by partial epimerization of diastereoisomer **18** as described above for the case of **17** The thermodynamic equilibrium ratio of the mixture of **19** and **18** was also approximately 70 30 in this case Diastereoisomer **19** could not be isolated for the same reasons given above for the case of **17** Its $^1$H NMR data were taken from the mixture of both diastereoisomers $^1$H NMR ($CDCl_3$) δ 7 6 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 1 (m, 5H, arom), 5 42 (s, 1H, CH=), 4 27 (s, removed by $D_2O$, 1H, CH), 3 87 (s, 3H, $COOCH_3$), 3 42 ppm (s, 3H, $OCH_3$), $^1$H NMR ($d_6$-DMSO) δ 8 3 (broad s, slowly removed by $D_2O$, 1H , NH), 7 6-7 0 (m, 5H, arom), 5 66 (s, 1H, CH=), 5 01 (s, removed by $D_2O$, 1H, CH), 3 81 (s, 3H, $COOCH_3$), 3 22 (s, 3H, $OCH_3$) ppm, $^{13}$C NMR ($CDCl_3$) δ 169 0 (s), 162 9 (s) (C-1, C-6), 158 1 (s) (C-3), 138 4 (s) (C-1'), 129 9 (d) (C-3', C-5'), 125 8 (d) (C-4'), 120 7 (d) (C-2',C-6'),112 0 (s) (CN),102 1 (s) (C-4), 88 0 (d) (C-2), 54 4 (q) ($OCH_3$), 51 7 (q) ($OCH_3$ on C-4), 45 8 ppm (d) (C-5)

*General Procedure for the Thermal Rearrangement of 3-Methoxy[2,1]benzisoxazole-4,7-quinones* **1a-e** *and* **6**, *and 3-Methoxy[2,1]naphthisoxazole-4,9-quinone* **2** *in the Solid State* The corresponding quinone (1 mmol) was dissolved in chloroform (250 ml) The solvent was evaporated at room temperature under reduced pressure and then the quinonic thin film was heated in an oven as indicated in each case (see experimental conditions in Table 1) The residue was chromatographed on silica gel using chloroform-acetone (10·1) as eluent to afford the corresponding N-alkylisoxazolonequinone **20**, **11** or **21** as major product and the corresponding butenolide **3** or **10** as the minor one Yields are indicated in Table I The spectral and analytical data of the N-alkylisoxazolonequinones are described below

*1-Methyl[2,1]naphth[2,3-c]isoxazol-3(1H)-one-4,9-quinone* (**11**) Previously described by us[6], yellow crystals mp 194-195 °C (dec) (chloroform-*n*-hexane), $^{13}$C NMR ($d_7$-DMF) δ 177 1 (s), 176 5 (s) (C-3, C-4, C-9), 151 1 (s) (C-9a), 135 1 (s), 133 4 (s) (C-4a, C-8a), 136 6 (d), 134 1 (d) (C-6, C-7), 127 5 (d), 127 0 (d) (C-5, C-8), 96 3 (s) (C-3a), 38 6 ppm (q) ($CH_3$)

*5-Anilino-1-methyl[2,1]benzisoxazole-3(1H)-one-4,7-quinone* (**20a**) Previously described by us[6], dark red crystals mp 211-212 °C (dec at 190 °C) (benzene), $^{13}$C NMR ($d_7$-DMF) δ 174 0 (s), 173 5 (s) (C-3, C-4, C-7) 151 2 (s), 150 0 (s) (C-5, C-7a), 138 4 (s) (C-1'), 130 2 (d) (C-3', C-5'), 127 3 (d) (C-4'), 125 2 (d) (C-2', C-6'), 100 5 (d) (C-6), 92 5 (s) (C-3a), 38 1 ppm (q) ($CH_3$)

*5-Anilino-1-($d_3$-methyl)[2,1]benzisoxazol-3(1H)-one-4,7-quinone* (**20b**) Dark red crystals, mp 210-212 °C (dec at 190 °C) (benzene), IR (KBr) 3200, 1785 (C=O), 1774 (C=O), 1656, 1619, 1589, 1565, 1490 cm$^{-1}$, $^1$H NMR ($CDCl_3$) δ 8 2 (broad s, removed by $D_2O$, 1H, NH), 7 6-7 1 (m, 5H, arom), 6 13 ppm (s, 1H, CH=), $^{13}$C NMR ($d_7$-DMF) δ 174 0 (s), 173 5 (s) (C-3, C-4, C-7) 151 2 (s), 150 0 (s) (C-5, C-7a), 138 4 (s) (C-1'), 130 2 (d) (C-3', C-5'), 127 3 (d) (C-4'), 125 2 (d) (C-2', C-6'), 100 5 (d) (C-6), 92 5 (s) (C-3a), 38 1 ppm ($CD_3$), MS *m/z* (relative intensity) 273 M$^+$ (40), 257 (9), 228 (11), 200 (10), 145 (13), 144 (100), 129 (11), 116 (24), 90 (19) Anal Calcd for $C_{14}H_7D_3N_2O_4$ C, 61 54, H+D 4 79, N, 10 25 Found C, 61 76, H+D 4 78, N, 10 20

*1-Methyl-5-(p-toluidino)[2,1]benzisoxazole-3(1H)-one-4,7-quinone* (**20c**) Previously described by us[6], dark red needles mp 217-219 °C (dec) (acetone), $^{13}$C NMR ($CDCl_3$) δ 173 4 (C-3, C-4, C-7), 149 0 (C-5, C-7a), 137 4 (C-1'), 133 5 (C-4'), 130 4 (C-3', C-5'), 123 4 (C-2', C-6'), 100 3 (C-6), 92 4 (C-3a), 37 9 ($NCH_3$), 21 1 ppm ($CH_3$-Ar)

*5-(p-bromoanilino)-1-methyl[2,1]benzisoxazole-3(1H)-one-4,7-quinone* (**20d**) Dark red needles, mp 258-261 °C (dec) (chloroform), IR (KBr) 3204, 1801 (C=O), 1774 (C=O), 1663, 1624, 1500, 1421 cm$^{-1}$, $^1$H NMR ($CDCl_3$) δ 8 1 (broad s, removed by $D_2O$, 1H, NH), 7 54, 7 16 (AA'XX', 5H, arom), 6 08 (s, 1H,

CH=) 4 13 (s, 3H, $NCH_3$), $^{13}C$ NMR ($CF_3COOD$) δ 171 2, 171 1 (C-3, C-4, C-7) 150 2, 148 8 (C-5, C-7a), 133 3, 132 1, 129 8, 125 2 (C-1', C-2', C-3', C-4', C-5', C-6'), 91 3 (C-3a), 38 1 ppm ($CH_3$), MS *m/z* (relative intensity) 348, 350 $M^+$(100), 330, 332 (10), 275, 277 (15), 222, 224 (86), 194,196 (22) Anal Calcd for $C_{14}H_9BrN_2O_2$ C, 48 16, H, 2 60, N, 8 02 Found C, 48 27 , H, 2 56 , N, 8 30

*5-Anilino-1-ethyl[2,1]benzisoxazole-3(1H)-one-4,7-quinone* (**20g**) Red crystals, mp 200-202 °C (dec) (chloroform-hexane), IR (KBr) 3200, 1790 (C=O), 1775 (C=O), 1660, 1618 , 1593, 1567, 1496, 1443, 1268 $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 8 2 (broad s, removed by $D_2O$, 1H, NH), 7 5-7 2 (m, 5H, arom), 6 13 (s, 1H, CH=) 4 60 (q, 2H, $CH_2$), 1 49 ppm (t, 3H, $CH_3$), $^{13}C$ NMR ($CDCl_3$) δ 173 6, 172 5 (C-3, C-4, C-7) 148 8 (C-5, C-7a), 136 2 (C-1'), 129 9 (C-3', C-5'), 127 2 (C-4'), 123 5 (C-2', C-6'), 100 5 (C-6) 92 3 (C-3a), 46 9 ($CH_2$), 13 4 ppm ($CH_3$), MS *m/z* (relative intensity) 284 $M^+$ (84), 266 (14), 211 (15), 144 (100), 116 (20), 77 (32) Anal Calcd for $C_{15}H_{12}N_2O_4$ C, 63 38, H, 4 25, N, 9 85 Found C, 63 13, H, 4 08, N, 9 52

*5-Methoxy-1-methyl[2,1]benzisoxazole-3(1H)-one-4,7-quinone* (**21**) Orange crystals, mp 192-195 °C (dec) (ethyl acetate-hexane), IR (KBr) 3050, 1800 (C=O), 1780 (C=O), 1670, 1648, 1585, 1570, 1520, 1425, 1330, $cm^{-1}$, $^1H$ NMR ($CDCl_3$) δ 5 98 (s, 1H, CH=) 4 08 (s, 3H, $NCH_3$), 3 93 ppm (s, 3H, $OCH_3$), $^{13}C$ NMR ($CDCl_3$) δ 176 2, 171 5, 163 6 (C-3, C-4, C-7) 161 6, 148 8 (C-5, C-7a), 107 7 (C-6) 92 2 (C-3a), 57 6 ($OCH_3$), 37 9 ppm ($NCH_3$), MS *m/z* (relative intensity) 209 $M^+$ (43), 193 (51), 191 (20), 163 (60), 126 (21), 82 (55), 69 (100), Anal Calcd for $C_9H_7NO_5$ C, 51 68, H, 3 37, N, 6 70 Found C, 51 89, H, 3 58, N, 6 25

*Cross Experiment Thermal Rearrangement of the Mixture of Benzisoxazolequinones* **1b** *and* **1c** *in the Solid State* Equimolar amounts (0 2 mmol) of **1b** and **1c** were heated together according to the general procedure for thermal rearrangements in the solid state described above The two red major components (benzisoxazolonequinones) were separated by chromatography and analysed by mass spectrometry The first eluted component was identified as a mixture of **20c** (*m/z* 284, $M^+$) and *1-($d_3$-Methyl)-5-toluidino[2,1]benzisoxazol-3(1H)-one-4,7-quinone* (**20e**) (*m/z* 287, $M^+$) The second one was identified as a mixture of **20a** (*m/z* 270, $M^+$) and **20b** (*m/z* 273, $M^+$)

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(13) The different steric hindrance between the substituent on the endocyclic double bond and one of the two substituents on the exocyclic double bond in **3**, **10** and **15** should be responsible for the different thermodynamic equilibrium ratio *Z* *E* found in each case

(14) Although the thermal rearrangement of compound **2** is intended to be carried out in chlorobenzene solution, it can not be excluded that due to long-lasting reaction some quinone **2** could crystallise in the interphase chlorobenzene-air giving a thermal rearrangement in the solid state to afford **11** in very low yield

(15) Compounds **11**, **20a** and **20b** had been obtained in poor yields (2-14%) as side products in the preparation of sulfoximidoquinones from isoxazolequinones **1** and **2** See Ref 6

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