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1,3-Dipolar Cycloaddition of Nitrile Oxides to 2(5*H*)-Furanones Substituted at the 5-Position by Sulphur Bearing Groups

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Abstract: The behavior of the furanones **1-4** towards nitrile oxides **5-7** has been investigated, in particular with respect to the regio- and stereoselectivity. Cycloaddition of benzonitrile oxide (**5**) to 4,5-diethylsulphonylfuran-2(5*H*)-one (**12**) leads as sole addition product to the isoxazoline **30**, that was easily aromatized to the isoxazole derivative **31**, which is a useful synthon for the preparation of heteroanthracyclinone analogues.

INTRODUCTION

The 1,3-dipolar cycloaddition of nitrile oxides to alkenes and alkynes has been one of the most general methods used for the preparation of isoxazoline and isoxazole derivatives.[1] Isoxazoles display interesting biological activities[2] and further transformations offer access to key intermediates in natural product and pharmacologically active compounds synthesis.[3] In a recent paper[4] we have reported the cycloaddition of nitrile oxides to 5-methoxyfuran-2(5*H*)-one, that affords regio- and stereospecifically functionalized isoxazolines, which are valuable intermediates for the synthesis of novel fused heterocyclic ring systems and other physiologically interesting molecules.

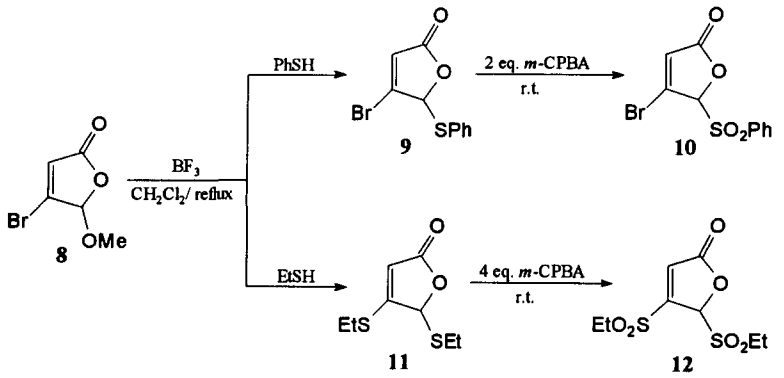
The exchange of the alkoxy group by a sulphur containing group widens the ability as synthons of 2(5*H*)-furanones. Thus, the presence of this group makes the removal of the proton at 5-position easier, and so furanone **1** was readily converted to its anion, which reacts with a variety of electrophilic reagents in regiospecific manner.[5] Moreover, the presence of a thioether or sulphone group at the 5-position may greatly modify the regio- and the stereochemistry of cycloaddition reactions, since the alkoxy group at this position has an important effect on the stereoselectivity.[6]

It is interesting to note that in order to achieve direct routes to isoxazoles, it is necessary to have an adequate leaving group at the double bond of the furanone to make the aromatization of the original cycloadducts easier.[7] The obtained furoisoxazoles can be appropriate synthons for the preparation of heterocyclic quinones, through their annelation reactions with quinone monoketal.[8] On the other hand, a substituent such as the ethylsulphonyl group at the 4-position of the furanone should increase its reactivity as a dipolarophile.[9]

In the present paper, we study the behavior of 5-ethylthio-, 5-phenylthiofuran-2(5*H*)-ones (**1**, **2**) and the corresponding sulphones **3** and **4** towards benzo-, aceto- and bromoformonitrile oxides (**5-7**). The reactions have been explored with sulphides and sulphones to achieve information on the influence of the group at 5-position upon the regio- and stereoselectivity of the cycloaddition. We also report the synthesis of 4-bromo-5-ethylsulphonylfuran-2(5*H*)-one (**10**) and 4,5-diethylsulphonylfuran-2(5*H*)-one (**12**) and the cycloaddition of benzonitrile oxide (**5**) to furanone **12** as a convenient way to obtain the furoisoxazole (**31**).

RESULTS AND DISCUSSION

The preparation of thiothers **1**,[10] **2**,[11] and their corresponding sulphones **3**,[12] **4**[11] used as dipolarophiles has been previously reported by us. As the presence of a bromine atom or ethylsulphonyl group linked to the double bond of the furanone **4** or **3** can facilitate the aromatization of the primary cycloadducts, we have synthesized the bromofuranone **10** and diethylsulphonylfuranone **12**, from 4-bromo-5-methoxyfuran-2(5*H*)-one[13] (**8**), following the procedures outlined in scheme 1, similar to those reported for the dipolarophiles with unsubstituted double bonds.



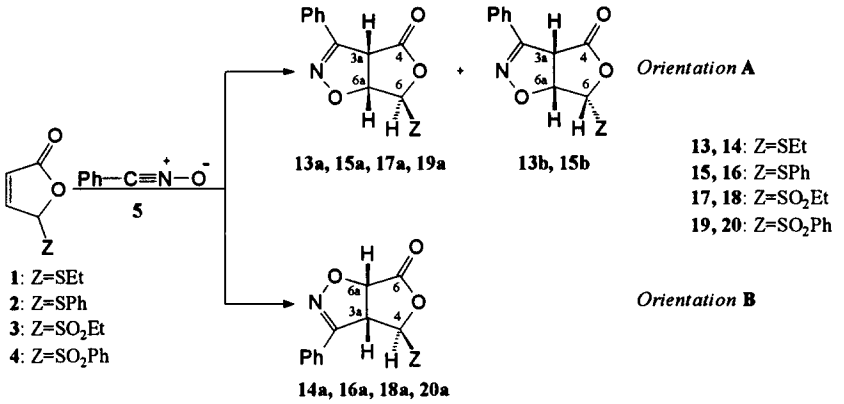
Scheme 1

Cycloadditions of Benzonitrile oxide

Benzonitrile oxide (**5**) has been widely employed as a 1,3-dipole, and there are several methods for its preparation; dehydrohalogenation of the corresponding hydroximic acid halide with a base, is the more usual one.[14] We have carried out the cycloaddition reactions at room temperature with an excess of dipole **5**, previously generated in ethereal solution from chlorobenzaldoxime using sodium hydroxide (*A*) or "*in situ*" with triethylamine (*B*). Also the nitrile oxide **5** was obtained with the assistance of molecular sieves for the removal of HCl (*C*), this method allows the smooth generation *in situ* of dipole **5**, avoiding the presence of bases.[15]

The crude reaction mixtures were analyzed by ^{1}H nmr (Table 1) and the furoisoxazolines were isolated by column chromatography.

Benzonitrile oxide reacts with furanones **1-4** to afford mixtures of regioisomeric adducts of type A and B (Scheme 2). The predominant orientation A is in accord with the regiochemistry reported for cycloaddition of



Scheme 2

Table 1. Cycloaddition of Benzonitrile Oxide (**5**) to Furanones **1-4**

N°	Z	Products (%)	Time (h)	Orientation *A/B*	*Exo/endo* ratio	Yield[a] (%)
1[b]	SEt	**1**(13) **13a**(62) **13b**(09) **14a**(16)	16	82:18	90:10	70
1[c]	SEt	**1**(17) **13a**(55) **13b**(11) **14a**(17)	3	79:21	86:14	60
1[d]	SEt	**1**(87) **13a**(10) **14a**(03)	360	77:23	100:00	-
2[b]	SPh	**2**(06) **15a**(70) **15b**(09) **16a**(15)	16	84:16	90:10	69
2[c]	SPh	**2**(09) **15a**(69) **16a**(22)	8	76:24	100:00	51
2[d]	SPh	**2**(86) **15a**(09) **16a**(05)	360	64:36	100:00	-
3[b]	SO_2Et	**17a** (66) **18a** (34)	5	66:34	100:00	62
3[c]	SO_2Et	**17a**(47) **18a**(19) **23**[e](32)	24	71:29	100:00	60
4[b]	SO_2Ph	**19a** (65) **20a**(35)	8	65:35	100:00	83

[a] Combined yield. [b] *Method A*. [c] *Method B*. [d] *Method C*. [e] Dimer of furanone **3**.

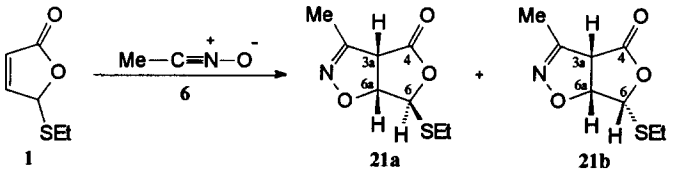
dipole **5** to 5-methoxyfuran-2(5*H*)-one,[4] other furan-2(5*H*)-ones[6,16,17] and α,β-unsaturated lactones.[18] However the regioselectivity is lower than the observed for the addition of the same dipole to 5-methoxyfuran-2(5*H*)-one.[4] The structures of the regioisomeric isoxazolines were established on the basis of the chemical shift of the proton coupled with the acetalic one, which in the adducts of type A appears at lower field than in the regioisomer of type B.

The stereochemistry **a** or **b** of both regioisomers, follows from the magnitude of the coupling constant between the acetalic (H-6 or H-4) and the adjacent protons (H-6a or H-3a).[19] The reaction leads to the isoxazolines with the sulphur containing group in *exo* arrangement as the major regioisomer. This fact suggests that the attack of dipole occurs preferentially at the face opposite to the Z group. This observation is in accord with the *face*-selectivity reported for cycloaddition reactions of 5-alkoxyfuran-2(5*H*)-ones,[4,20] whereas the selectivity is lower.

The regiochemistry (ratio A/B) is somewhat higher for thioethers **1** and **2** than for the sulphones **3** and **4**. However, the stereoselectivity rises to 100% when the substituent Z is an ethyl- or phenylsulphonyl group.

Cycloadditions of Acetonitrile oxide

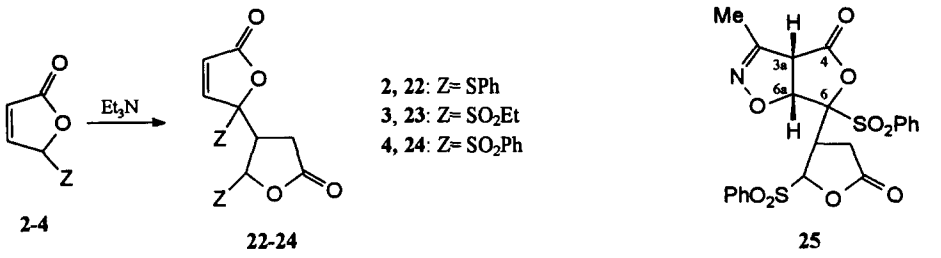
Acetonitrile oxide (**6**) was generated *in situ* from nitroethane by Mukaiyama's method.[21] The cycloaddition reactions were run with excess of 1,3-dipole and were carried out at room temperature or/and under refluxing toluene. The crude reaction mixtures were analyzed by ^{1}H nmr. Dipole **6** reacts in regiospecific manner with 5-(ethylthio)furan-2(5*H*)-one (**1**) to afford a 83:17 mixture of the epimeric furoisoxazolines **21a**, **21b** in good yield. The furoisoxazolines were isolated by column chromatography. On the basis of the previously reported structure for the adduct isolated in the cycloaddition of the same dipole to the 5-metoxyfuran-2(5*H*)-one,[4] we have assigned the regiochemistry A to both isolated cycloadducts **21a**, **21b**, that were also consistent with their ^{1}H nmr spectra.(Scheme 3)



Scheme 3

The *cis* or *trans* relationship between H-6 and H-6a, and consequently the *face*-selectivity of the cycloaddition, was established by ^{1}H nmr. So the major stereoisomer **21a**, displays a coupling constant $J_{6,6a}$=2 Hz, whereas for the minor isomer **21b**, $J_{6,6a}$ has a value of 5.8 Hz. This observation is in accord with the

face-selectivity reported for cycloaddition reactions of 5-methoxyfuranone[4] and other 5-substituted butenolides,[18] and parallels the stereochemistry observed with benzonitrile oxide.

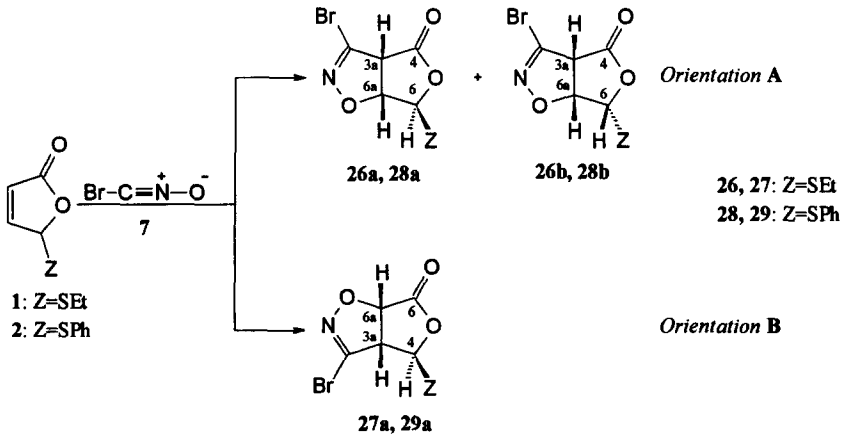


Scheme 4

It is remarkable that furanones **2-4** do not react with acetonitrile oxide (**6**) under the experimental conditions employed for the furanone **1**. Attempts to react furanones **2-4** with the dipole **6**, failed to afford the expected cycloadducts. Only the bislactones **22**, **23** and **24**, arising from the Michael addition of the deprotonated furanone to the conjugated double bond of the starting furanone,[22] can be isolated from the reaction mixtures (Scheme 4). A small amount of isoxazoline **25**, formed by cycloaddition of dipole **6** to the bislactone **24**, was detected in the reaction with furanone **4**.

Cycloadditions of Bromoformonitrile Oxide

The nitrile oxide **7**, generated from the easily available dibromoformaldoxime,[23] reacts smoothly with furanones **1** and **2**, at room temperature, affording the corresponding regioisomeric adducts of type A and B (Scheme 5). The ratio of regio- and stereoisomers, estimated from the ^{1}H nmr of the crude reaction mixtures, are summarized in table 2.



Scheme 5

Table 2. Cycloaddition of Bromoformonitrile Oxide (7) to Furanones **1** and **2**

N°	Z	Products (%)	Orientation *A/B*	*Exo/endo* ratio	Yield[a] (%)
1	SEt	**1**(30) **26a**(44) **26b**(09) **27a**(17)	76:24	90:10	58
2	SPh	**2**(13) **28a**(56) **28b**(12) **29a**(19)	78:22	90:10	57

[a] Combined yield.

The predominant orientation in the addition of dipole **7** to furanones **1** and **2**, is the same as that observed in the cycloaddition of nitrile oxides **5** and **6**. Also the *face*-selectivity is similar to that observed with the above dipoles. Structural assignments of the bromoisoxazolines **26-29** were made on the same basis as that indicated for the structural determination of the methyl- and phenylisoxazolines.

However, in the attempts of the reaction of dipole **7** with the sulphones **3** and **4**, under analogous experimental conditions to those employed for the thioethers **1** and **2**, the products arising from cycloaddition could not be identified. Although, the furanones **3** and **4** used as dipolarophiles were not recuperated from the crude reaction mixtures.

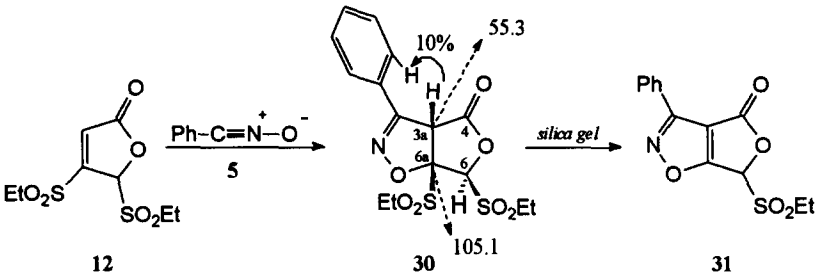
Synthesis of 6-ethylsulphonyl-3-phenylfuro[3,4-*d*]isoxazole-4(6*H*)-one

In order to obtain heterocyclic quinones, we have explored the annelation reactions of naphthoquinone monoketals with the fused heterocyclic ring systems, synthesized by 1,3-dipolar cycloaddition of nitrile oxides to 2(5*H*)-furanones substituted at the 5-position by sulphur bearing groups. Preliminary assays of annelation reactions, carried out with the 3-phenylfuroisoxazolines **17a** and **19a** were unsuccessful, these results led us to study annelation reactions with fully aromatized heterocyclic systems.

To make easier the aromatization of the isoxazolines, we have studied the cycloaddition of the bromofuranone **10** to benzonitrile oxide, because it has recently been reported that the α-bromo- cyclohex-2-enone or 5,6-dihydropyranone adds arylnitrile oxides to afford isoxazoles by spontaneous dehydrobromination of the corresponding isoxazolines.[7] However, under the experimental conditions used for reaction of the dipole **5** with the furanones **3** and **4**, the cycloaddition products to the furanone **10** cannot be detected. The lack of reactivity of 4-bromo-5-phenylsulphonyl-furan-2(5*H*)-one (**10**) is not surprising, since the corresponding 5-methoxyfuranone does not react with the nitrile oxides **5**, **6** and **7**, under experimental conditions in which the addition to the unsubstituted furanone proceeds without difficulty.[4]

The presence of an electron withdrawing substituent such as the ethylsulphonyl group at the 4 position of the furanone increases its reactivity as dipolarophile, and so the 4,5-diethylsulphonylfuran-2(5*H*)-one (**12**) reacts smoothly, at room temperature, with benzonitrile oxide to afford, in regioselective manner, the

isoxazoline **30** in excellent yield (Scheme 6). The original cycloadduct was readily aromatized to the furoisixazole **31** by chromatography on silica gel.



Scheme 6

The regiochemistry of the cycloaddition was determinated on the basis of the chemical shift of C-6a (105.1 ppm), that appears as a quaternary carbon at lower field than the C-3a (55.3 ppm), which corresponds to a tertiary carbon atom. On the other hand, this assignment was confirmed by the observed NOE on the *ortho* aromatic protons (7.87 ppm) by irradiation of the signal at 5.36 ppm, attributed to H-3a proton. In the absence of proton at the 6a-position, the *exo* arrangement was assigned to the ethylsulphonyl group at the 6-position by the multiplicity observed for the signal of CH_2 group in ^1H nmr spectrum.[19]

The furoisoxazol **31** through its annelation reactions with different benzoquinone monoketals, is a useful synthon for the preparation of heterocyclic anthraquinones. Furthermore, the strategy reported by us[8] using **31** as a DC synthon, may be applicable to the synthesis of new anthracyclinones analogues with modified pharmacological properties.

EXPERIMENTAL

Mps were determined with a Kofler hot-stage apparatus and are uncorrected. Microanalyses were performed with a Heraeus analyzer. Ir spectra were recorded on a Perkin-Elmer model 681 grating spectrophotometer, ν values in cm^{-1}. ^1H nmr spectra were determined with either a Varian Gemini 200, a Bruker AM-200 or a Varian XL-300 spectrometer, in $CDCl_3$ solution, unless otherwise stated. ^{13}C nmr were determined with either a Varian XL-300 or a Bruker AM-200 in $CDCl_3$ solution, unless otherwise stated. Chemical shifts were reported in ppm (δ) downfield from Me_4Si. Mass spectra were determined on a VG-12-250 spectrometer. Silica gel Merck 60 (70- 230 mesh) and DC-alufolien $60F_{254}$ were used for flash column chromatography and analytical tlc, respectively.

Benzonitrile oxide (BNO) (**5**) and bromoformonitrile oxide (**7**) were prepared by dehydrohalogenation of the corresponding hydroximic acid halides.

The furanones **1-4** used as dipolarophiles were prepared according to previously reported procedures.[11,12]

Preparation of 2(5H)-furanones

4-Bromo-5-phenylthio-2(5*H*)-furanone (9)

To a stirred solution of boron trifluoride etherate (2.5 ml, 20 mmol) in dichloromethane (15 ml), was added 4-bromo-5-methoxy-2(5*H*)furanone (**8**) (1.93 g, 10 mmol) and thiophenol (1.5 ml, 15 mmol). The reaction was refluxed for 36 h. Water was added to the reaction mixture and the organic layer was washed successively with saturated $NaHCO_3$ solution and water. After drying (Na_2SO_4), the solvent was removed under reduced pressure and the crude material was chromatographed (petroleum ether- ethyl acetate, 4:1), to afford 1.9 g (70%) of furanone **9**. Recrystallized from cyclohexane, mp 72°C. Found: C, 43.99; H, 2.35; S, 11.54; Br, 29.47. Anal. Calcd for $C_{10}H_7BrSO_2$: C, 44.11; H, 2.57; S, 11.76; Br, 29.78. IR (KBr) 1790, 1760 (C=O); 1600 (C=C). ^{1}H nmr: 7.58-7.54 (m, 2H, arom.); 7.45-7.31 (m, 3H, arom.); 6.09, 6.08 (d, d, 1H, 1H, H-3, H-5 J=1.6).^{13}C nmr: 168.2 (C-2); 147.2 (C-4); 135.5, 129.9, 129.1, 126.4 (arom.); 123.4 (C-3); 89.5 (C-5). Ms, *m/z* 272-270 (M^+, 19); 191; 163-161 (100); 109; 77; 69; 65.

4-Bromo-5-phenylsulphonyl-2(5*H*)-furanone (10)

To a solution of 4-bromo-5-phenylthio-2(5*H*)-furanone (**9**) (746 mg, 3 mmol) in dichloromethane (15 ml) at 0°C, was added, in a dropwise fashion, *m*-chloroperbenzoic acid (1.035 g, 6 mmol) in dichloromethane (15 ml). The reaction mixture was stirred for 1 h at room temperature. The solvent was removed under reduced pressure and the residue was chromatographed (petroleum ether-ethyl acetate, 2:1) to give 378 mg (40%) of furanone **10**. Recrystallized from carbon tetrachloride, mp 115°C. Found: C, 39.28; H, 2.15; S, 10.30; Br, 27.02. Anal. Calcd for $C_{10}H_7BrSO_4$: C, 39.62; H,2.33; S, 10,58; Br, 26.36. IR (KBr): 1790 (C=O); 1590 (C=C); 1340, 1330, 1170 (SO_2). ^{1}H nmr: 7.71-7.64 (m, 2H, arom.); 7.60-7.52 (m, 3H, arom.); 6.44 (d, 1H, H-3, J=1.3); 5.59 (d, 1H, H-5, J=1.3).^{13}C nmr: 167.0 (C-2); 140.4 (C-4); 135.4, 129.9, 129.7, 129.4 (arom.); 126.1 (C-3); 93.9 (C-5). Ms, *m/z*: 304-302 (M^+, 0,5); 163-161 (100); 141; 107; 105; 77.

4,5-Diethylsulphonyl-2(5*H*)-furanone (12)

To a solution of 4,5-diethylthio-2(5*H*)-furanone (**11**) (612 mg, 3 mmol) in dichloromethane (15 ml) at 0°C was added, in a dropwise fashion, *m*-chloroperbenzoic acid (2.070 g, 12 mmol) in dichloromethane (15 ml). The reaction mixture was stirred for 2 h at room temperature. The chlorobenzoic acid precipitated was filtered off and the solvent removed. The residue was washed with warm hexane (x3) to remove the remaining chlorobenzoic acid. The furanone **12** (580 mg, 72%) was obtained as an insoluble white solid, mp 140°C. Found: C, 35.63; H, 4.52; S, 24.15. Anal. Calcd for $C_8H_{12}S_2O_6$ C, 35.82; H, 4.48; S, 23.88. IR (nujol): 1800 (C=O); 1330, 1140 (SO_2). ^{1}H nmr: 7.10 (d, 1H, H-3, J=1.6); 6.16 (d, 1H, H-5, J=1.6); 3.70-3.63 (m, 1H, S-C$\underline{H}_2$-CH$_3$); 3.43-3.28 (m, 3H, S-C$\underline{H}_2$-CH$_3$); 1.51 (t, 3H, S-CH$_2$-C$\underline{H}_3$, J=7.5); 1.40 (t, 3H, S-CH$_2$-C$\underline{H}_3$, J=7.4).

^{13}C nmr: [$(CD_3)_2CO$] 167.2 (C-2); 158.3 (C-4); 135.2 (C-3); 90.4 (C-5); 49.6, 47.9 (S-$\underline{C}H_2$-CH_3); 6.6, 6.0 (S-CH_2-$\underline{C}H_3$). Ms, *m/z*: 269 (M^++1, 0.4); 268 (M^+, 0.1); 175; 83 (100); 55.

Additions of benzonitrile oxide

Method A: To a stirred mixture of 10% sodium hydroxide (10 ml) and ether (10 ml) was added, in four portions for 10 min at 0°C, benzaldehyde chloroxime (777 mg, 5 mmol). The ethereal layer was separated, quickly dried over magnesium sulfate and added to a solution of the furanones **1-4** (1 mmol) in dichloromethane (5 ml). After stirring at room temperature for the time indicated in each case, the solvent was removed. The residue was analyzed by ^{1}H nmr and subjected to column chromatography.

Method B: To a solution of furanone **1-4** (1 mmol) and benzaldehyde chloroxime (233 mg, 1.5 mmol) in ethyl ether (8 ml) was added, in a dropwise fashion, a solution of triethylamine (152 mg, 1.5 mmol) in ethyl ether (6 ml). The reaction mixture was stirred at room temperature for the time indicated in each case. The triethylamine hydrochloride was filtered off and the solvent removed. The residue was analyzed by ^{1}H nmr and subjected to column chromatography.

Method C: A solution of furanone **1-4** (1 mmol) and benzaldehyde chloroxime (311 mg, 2 mmol) in ethyl ether (10 ml) was stirred at room temperature in the presence of molecular sieves (1 g) the time indicated in each case. The solvent was removed and the residue was analyzed by ^{1}H nmr.

1.- *Addition to 5-ethylthio-2(5H)-furanone* (**1**)

Following method *A*, the reaction mixture was stirred for 16 h. The residue contained a mixture of furanone **1**, and isoxazolines **13a**, **13b** and **14a** in a 13:62:9:16 ratio. (Petroleum ether-ethyl acetate, 7:1)

***Exo*-6-ethylthio-3-phenyl-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (13a)**

Yield 55% (145 mg). Recrystallized from carbon tetrachloride, mp 112-114°C. Found: C, 59.25; H, 4.95; N, 5.29. Anal. Calcd for $C_{13}H_{13}NSO_3$ C, 59.31; H, 4.94; N, 5.32. IR (nujol): 1790 (C=O); 1590 (C=C); 1570 (C=N). ^{1}H nmr: 7.96-7.91 (m, 2H, arom.); 7.49-7.41 (m, 3H, arom.); 5.88 (d, 1H, H-6, J=1.7); 5.35 (dd, 1H, H-6a, J=1.7 J=9.3); 4.73 (d, 1H, H-3a, J=9.3); 2.96-2.75 (m, 2H, S-$C\underline{H}_2$-CH_3, J=7.5); 1.38 (t, 3H, S-CH_2-$C\underline{H}_3$, J=7.5). ^{13}C nmr: 169.5 (C-4); 152.6 (C-3); 130.9, 128.8, 127.9, 126.7 (arom.); 88.3, 87.1 (C-6, C-6a); 54.5 (C-3a); 25.7 (S-$\underline{C}H_2$-CH_3); 14.5 (S-CH_2-$\underline{C}H_3$). Ms, *m/z*: 264; 263 (M^+, 55); 145; 144; 116; 115; 87 (100); 77.

***Endo*-6-ethylthio-3-phenyl-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (13b)**

Yield 5% (13 mg). IR (neat): 1780-60 (C=O); 1590 (C=C); 1560 (C=N). ^{1}H nmr: 7.96-7.91 (m, 2H, arom.); 7.47-7.40 (m, 3H, arom.); 5.95 (d, 1H, H-6, J=5.6); 5.73 (dd, 1H, H-6a, J=9.8 J=5.6); 4.42 (d, 1H, H-3a, J=9.6); 2.80 (q, 2H, S-$C\underline{H}_2$-CH_3, J=7.4); 1.34 (t, 3H, S-CH_2-$C\underline{H}_3$, J=7.4). Ms, *m/z*: 266; 265; 264 (M^+, 100); 263; 61; 45.

***Exo*-4-ethylthio-3-phenyl-3a,6a-dihydrofuro[3,4-*d*]isoxazole-6(4*H*)-one (14a)**

Yield 10% (26 mg). Found: C, 59.45; H, 5.40; N, 5.16. Anal. Calcd for $C_{13}H_{13}NSO_3$: C, 59.31; H, 4.94; N, 5.32. IR (neat): 1785 (C=O); 1600 (C=C); 1570 (C=N). ^{1}H nmr: 7.73-7.69 (m, 2H, arom.); 7.50-7.40 (m, 3H, arom.); 5.71 (d, 1H, H-4, J=2.2); 5.40 (d, 1H, H-6a, J=10.3); 4.42 (dd, 1H, H-3a, J=10.3 J=2.2); 2.88-2.75 (m, 2H, S-C$\underline{H_2}$-CH$_3$, J=7.4); 1.34 (t, 3H, S-CH$_2$-C$\underline{H_3}$, J=7.4). ^{13}C nmr: 171.4 (C-6); 155.4 (C-3); 131.1, 129.4, 127.1, 126.3 (arom.); 84.8, 79.1 (C-4, C-6a); 55.5 (C-3a); 26.2 (S-$\underline{C}$H$_2$-CH$_3$); 14.5 (S-CH$_2$-$\underline{C}$H$_3$). Ms, *m/z*: 264; 263 (M$^+$, 3); 145; 144; 116; 115; 87 (100); 77.

Following method *B*, the reaction mixture was stirred at room temperature for 3 h. The residue, containing a mixture of furanone **1** and the isoxazolines **13a,b** and **14a** in a 17:55:11:17 ratio, was subjected to column chromatography to give 105 mg (40%) of isoxazoline **13a** and 39 mg (15%) of isoxazoline **14a**.

Following method *C*, the reaction mixture was stirred at room temperature for 15 d. The solvent was removed and the residue analyzed by ^{1}H nmr showed the presence of isoxazolines **13a** and **14a** and the furanone **1** in a 10:3:87.

2.- *Addition to 5-phenylthio-2(5H)-furanone* (**2**)

Following method *A*, the reaction mixture was stirred for 16 h. The residue contained the furanone **2** and the isoxazolines **15a**, **15b** and **16a** in a 6:70:9:15 ratio. (Petroleum ether-ethyl acetate, 7:1).

3-Phenyl-*exo*-6-phenylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (15a)

White solid isolated by filtration in a 57% yield (177 mg). Recrystallized from carbon tetrachloride, mp 126-127°C. Found: C, 65.29; H, 4.33; N, 4.53. Anal. Calcd for $C_{17}H_{13}NSO_3$: C, 65.59; H, 4.18; N, 4.50. IR (nujol): 1785 (C=O); 1600 (C=C); 1570 (C=N). ^{1}H nmr: 7.86-7.81 (m, 2H, arom.); 7.64-7.59 (m, 2H, arom.); 7.17-7.11 (m, 6H, arom.); 5.94 (d, 1H, H-6, J= 1.4); 5.48 (dd, 1H, H-6a, J=9.1 J=1.4); 4.05 (d, 1H, H-3a, J=9.1). ^{13}C nmr: 169.2 (C-4); 152.4 (C-3); 134.8, 131.0, 129.8, 129.7, 128.8, 127.8, 126.5 (arom.); 89.6, 87.7 (C-6, C-6a); 54.2 (C-3a). Ms, *m/z*: 311 (M$^+$, 48); 202; 146 (100); 110; 91; 77; 55.

3-Phenyl-*endo*-6-phenylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (15b)

Yield 2% (6 mg). IR (neat): 1760 (C=O); 1600 (C=C). ^{1}H nmr: 7.98-7.93 (m, 2H, arom.); 7.65-7.56 (m, 2H, arom.); 7.48-7.43 (m, 3H, arom.); 7.36-7.32 (m, 3H, arom.); 6.08 (d, 1H, H-6, J=5.5); 5.84 (dd, 1H, H-6a, J=5.5 J=9.6); 4.75 (d, 1H, H-3a, J=9.6). Ms, *m/z*: 314; 313; 312; 311 (M$^+$, 100); 254, 109, 77, 51.

3-Phenyl-*exo*-4-phenylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-6(4*H*)-one (16a)

Yield 10% (31 mg). Recrystallized from carbon tetrachloride, mp 105°C. Found: C, 65.71; H, 4.40; N, 4.35. Anal. Calcd for $C_{17}H_{13}NSO_3$: C, 65.59; H, 4.18; N, 4.50. IR (nujol): 1788 (C=O); 1600 (C=C); 1580 (C=N). ^{1}H nmr: 7.65-7.59 (m, 4H, arom.); 7.48-7.44 (m, 3H, arom.); 7.39-7.33 (m, 3H, arom.); 5.78 (d, 1H, H-4, J=1.4); 4.71 (d, 1H, H-6a, J=9.8); 4.55 (dd, 1H, H-3a). ^{13}C nmr: 169.0 (C-6); 152.6 (C-3); 132.6, 131.0, 129.3, 129.2, 128.8, 128.5, 128.0, 126.0 (arom.); 92.1, 83.2 (C-4, C-6a); 56.3 (C-3a). Ms, *m/z*: 311 (M$^+$, 2); 146; 109 (100); 91.

Following method *B*, the reaction mixture was stirred at room temperature for 8 h. The residue contained a mixture of the two regioisomeric isoxazolines **15a** and **16a** and the furanone **2** in a 69:22:9 ratio.

The crude product was subjected to silica gel chromatography to afford 128 mg (41%) of isoxazoline **15a** and 30 mg (10%) of isoxazoline **16a**.

Following method *C*, the reaction mixture was stirred at room temperature for 168 h. The residue analyzed by ^{1}H nmr showed the presence of isoxazolines **15a** and **16a** and the furanone **2** in a 9:5:86 ratio.

3.- *Addition to 5-ethylsulphonyl-2(5H)-furanone* (**3**)

Following method *A*, the reaction mixture was stirred for 5 h. The residue was a 66:34 mixture of two regioisomeric isoxazolines **17a** and **18a**. (Petroleum ether-ethyl acetate, 3:1).

***Exo*-6-ethylsulphonyl-3-phenyl-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)one (17a)**

Yield 50% (160 mg). Recrystallized from carbon tetrachloride, mp 145-148°C. Found: C, 52.65; H, 4.53; N, 4.82. Anal. Calcd for $C_{17}H_{13}NSO_5$: C, 52.87; H, 4.44; N, 4.75. IR (KBr): 1780 (C=O); 1600 (C=C); 1585 (C=N); 1330, 1160 (SO_2). ^{1}H nmr: 7.92-7.86 (m, 2H, arom.); 7.54-7.43 (m, 3H, arom.); 5.90 (dd, 1H, H-6a, J=9.2, J=0.7); 5.54 (d, 1H, H-6); 4.85 (d, 1H, H-3a); 3.29-3.20 (m, 2H, S-C<u>H</u>$_2$-CH_3); 1.49 (t, 3H, S-CH_2-C<u>H</u>$_3$, J=7.5). ^{13}C nmr: [$(CD_3)_2CO$] 169.9 (C-4); 153.8 (C-3); 131.6, 130.7, 130.1, 129.5 (arom.); 91.1, 81.9 (C-6, C-6a); 54.2 (C-3a); 46.0 (S-<u>C</u>H$_2$-CH_3); 6.0 (S-CH_2-<u>C</u>H$_3$). Ms, *m/z*: 295 (M^+, 3); 202; 146; 139; 105; 91; 83; 77 (100); 51.

***Exo*-4-ethylsulphonyl-3-phenyl-6a,3a-dihydrofuro[3,4-*d*]isoxazole-6(4*H*)one (18a)**

Yield 12% (40 mg). Recrystallized from carbon tetrachloride, mp 177-180°C. Found: C, 52.89; H, 4.55; N, 3.92. Anal. Calcd for $C_{17}H_{13}NSO_5$: C, 52.87; H, 4.44; N, 4.75. IR (KBr): 1820 (C=O); 1600 (C=C); 1570 (C=N); 1315, 1130 (SO_2). ^{1}H nmr: 7.79-7.76 (m, 2H, arom.); 7.53-7.50 (m, 3H, arom.); 5.52 (d, 1H, H-6a, J= 10.2); 5.37 (d, 1H, H-4, J=1.1); 5.09 (dd, 1H, H-3a); 3.28-3.19 (m, 2H, S-C<u>H</u>$_2$-CH_3); 1.47 (t, 3H, S-CH_2-C<u>H</u>$_3$, J=7.4). ^{13}C nmr [$(CD_3)_2CO$] 169.7 (C-6); 153.8 (C-3); 131.6, 129.6, 127.1, 125.8 (arom.); 86.7 (C-6a); 77.3 (C-4); 48.2 (C-3a); 44.9 (S-<u>C</u>H$_2$-CH_3); 6.01 (S-CH_2-<u>C</u>H$_3$). Ms, *m/z*: 146; 115; 91; 77 (100); 51.

Following method *B*, the reaction mixture was stirred at room temperature for 24 h. The residue contained a mixture of two regioisomeric isoxazolines **17a** and **18a**, and the bislactone **13** in a 47:19:32 ratio. The crude product subjected to column chromatography afforded 100 mg (40%) of isoxazoline **17a** and 45 mg (15%) of isoxazoline **18a**.

4.- *Addition to 5-phenylsulphonyl-2(5H)-furanone* (**4**)

Following method *A*, the reaction mixture was stirred for 8 h. The regioisomeric isoxazolines **19** and **20** were obtained in a 65:35 ratio. The adduct **19a** was isolated by filtration. The regioisomeric adduct **20a**, which was obtained from the filtrate, was purified by chromatography (petroleum ether-ethyl acetate, 3:1).

3-Phenyl-*exo*-6-phenylsulphonyl-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)one (19a)

Yield 60% (205 mg). Recrystallized from carbon tetrachloride, mp 220-221°C. Found: C, 59.15; H, 4.08; N, 3.79. Anal. Calcd for $C_{17}H_{13}NSO_5$: C, 59.47; H, 3.79; N, 4.08. IR (nujol): 1805 (C=O); 1580 (C=C); 1560 (C=N); 1330, 1160 (SO_2). ^{1}H nmr: 8.00-7.97 (m, 2H, arom.); 7.93-7.89 (m, 2H, arom.); 7.81- 7.69 (m, 1H, arom.); 7.69-7.66 (m, 2H, arom.); 7.50-7.44 (m, 3H, arom.); 6.05 (d, 1H, H-6a, J=9.2); 5.48 (s, 1H, H-6);

4.89 (d, 1H, H-3a, J=9.2). ^{13}C nmr: 169.2 (C-4); 152.6 (C-3); 135.4, 134.6, 131.3, 129.7, 129.0, 128.0, 126.1 (arom.); 92.7, 81.3 (C-6, C-6a); 53.6 (C-3a). Ms, *m/z*: 343 (M^+, 44); 202; 146 (100); 115; 91; 83; 77; 55; 51.

3-Phenyl-*exo*-4-phenylsulphonyl-6a,3a-dihydrofuro[3,4-*d*]isoxazole-6(4*H*)one (20a)

Yield 23% (80 mg).Recrystallized fron carbon tetrachloride, mp 125°C. Found: C, 60.05; H, 4.20; N, 3.95. Anal. Calcd for $C_{17}H_{13}NSO_5$ C, 59.47; H, 3.79; N, 4.08. IR (KBr): 1825 (C=O); 1600 (C=C); 1580 (C=N); 1330, 1160 (SO_2). ^{1}H nmr: 8.11-7.55 (m, 10H, arom.); 5.66 (d, 1H, H-6a, J=10,0); 5.36 (d, 1H, H-4, J=1.1); 5.33 (dd, 1H, H-3a, J=10,0 J=1.1). ^{13}C nmr: 169.8 (C-6); 153.8 (C-3); 135.5, 133.8, 131.5, 129.7, 129.5, 127.1, 125.9 (arom.); 89.6, 77.5 (C-4, C-6a); 49.3 (C-3a). Ms, *m/z*: 343 (M^+, 2); 202; 146 (100); 115; 91; 77; 51.

Following method *B*, after stirring the reaction mixture at room temperature for 72 h, the isoxazolines **19a** and/or **20a** could not be detected.

Additions of acetonitrile oxide

To a solution of 2(5*H*)-furanone (1 mmol) and phenyl isocyanate (238 mg, 2 mmol) in toluene (3 ml) was added nitroethane (110 mg, 1.5 mmol) and triethylamine (2 drops) in toluene (2 ml) dropwise. Stirring was maintained for 1 h at room temperature and then the reaction mixture was heated under reflux for 1 h. The precipitated *N,N*-diphenylurea was filtered off. The solvent was removed and the residue analyzed by ^{1}H nmr.

1.- *Addition to 5-ethylthio-2(5H)-furanone* (**1**)

The reaction product was a 83:17 mixture of the stereoisomeric isoxazolines **21a** and **21b**, that were isolated by column chromatography (petroleum ether-ethyl acetate, 3:1).

***Exo*-6-ethylthio-3-methyl-3a,6a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (21a)**

Yield 57% (115 mg). Found: C, 48.32; H, 5.52; N, 6.96. Anal. Calcd for $C_8H_{11}NSO_3$: C, 47.76; H, 5.47; N, 6.96. IR (neat): 1785 (C=O); 1600 (C=N). ^{1}H nmr: 5.74 (d, 1H, H-6, J=2.0); 5.15 (dd, 1H, H-6a, J=2.0 J=9.2); 4.19 (dd, 1H, H-3a, J=9.2, J=0.9); 2.88-2.73 (m, 2H, S-C$\underline{H_2}$-CH$_3$); 2.17 (d, 3H, C$\underline{H_3}$, J=0.9); 1.36 (t, 3H, S-CH$_2$-C$\underline{H_3}$, J=7.4). ^{13}C nmr: 169.6 (C-4); 150.6 (C-3); 89.4, 85.3 (C-6, C-6a); 57.6 (C-3a); 25.6 (S-$\underline{C}$H$_2$-CH$_3$); 14.4 (S-CH$_2$-$\underline{C}$H$_3$); 11.0 ($\underline{C}$H$_3$). Ms, *m/z*: 201 (M^+, 14); 116; 97; 87 (100); 84; 82.

***Endo*-6-ethylthio-3-methyl-3a,6a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (21b)**

Yield 20% (40 mg). Found: C, 47.95; H, 5.22; N, 6.85. Anal. Calcd for $C_8H_{11}NSO_3$: C, 47.76; H, 5.47; N, 6.69. IR (neat): 1780 (C=O); 1600 (C=N). ^{1}H nmr: 5.93 (d, 1H, H-6, J=5.8); 5.57 (dd, 1H, H-6a, J=5.8, J=9.9); 4.22 (dd, 1H, H-3a, J=9.9 J=1.0); 2.77 (q, 2H, S-C$\underline{H_2}$-CH$_3$, J=7.5); 2.16 (d, 3H, C$\underline{H_3}$, J=1.0); 1.34 (t, 3H, S-CH$_2$-C$\underline{H_3}$, J=7.5). ^{13}C nmr: 169.6 (C-4); 150.5 (C-3); 90.8, 81.3 (C-6, C-6a); 58.4 (C-3a); 25.8 (S-$\underline{C}$H$_2$-CH$_3$); 14.6 (S-CH$_2$-$\underline{C}$H$_3$); 11.2 ($\underline{C}$H$_3$). Ms, *m/z*: 201 (M^+, 16); 119; 97; 87; 84 (100); 82.

2.- *Attempts of addition to furanones* **2-4**

Cycloaddition products from the furanones **2** and **3** could not be detected. From the reactions mixtures, bislactones **22a,b**[22] (240+140 mg) and **23a,b**[22] (172+102 mg) were the only isolated compounds, by column chromatography (petroleum ether-ethyl acetate, 3:1). In the assay of the reaction with furanone **4**, was detected the isoxazoline **25** [^{1}H nmr: 5.85 (d, 1H, H-6a, J=9.3); 5.71 (dd, 1H, H-5', J=1.7); 4.53 (dd, 1H, H-3a, J=1.0 J=9.3); 3.68-3.60 (m, 1H, H-4'); 2.17 (d, 3H, Me, J=1.0)], together the stereoisomeric bislactones **24a,b**[21] (316+125 mg).

Additions of bromoformonitrile oxide

To a vigorously stirred mixture of the corresponding 2(5*H*)-furanone (2 mmol), ethyl acetate (2 ml), sodium bicarbonate (840 mg, 10 mmol) and water (1 ml), was added solid dibromoformaldoxime (1230 mg, 6 mmol) in small portions. Stirring was maintained for 30 h at room temperature. The precipitated salt was filtered off, the filtrate was dried ($MgSO_4$) and the solvent removed under reduced pressure. The crude product was analyzed by ^{1}H nmr and subjected to chromatography on silica gel.

1.- *Addition to 5-ethylthio-2(5H)-furanone* (**1**)

The crude product contained a mixture of furanone **1**, and the isoxazolines **26a**, **26b**, **27a** in a 30:44:9:17 ratio. (Petroleum ether-ethyl acetate, 4:1).

3-Bromo-*exo*-6-ethylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (26a).

Yield 31% (166 mg). Found: C, 31.52; H, 3.68; N, 5.46. Anal. Calcd for $C_7H_8NSBrO_3$: C, 31.70; H, 3.02; N, 5.38. IR (neat): 1790 (C=O); 1570 (C=N). ^{1}H nmr: 5.74 (d, 1H, H-6, J=2.2); 5.26 (dd, 1H, H-6a, J=9.4 J=2.2); 4.34 (d, 1H, H-3a, J=9.4); 2.84-2.75 (m, 2H, S-C$\underline{H_2}$-CH_3, J=7.5); 1.31 (t, 3H, S-CH_2-CH_3, J=7.5). ^{13}C nmr: 167.2 (C-4); 132.6 (C-3); 89.0, 85.7 (C-6, C-6a); 58.5 (C-3a); 25.8 (S-$\underline{C}H_2$-CH_3); 14.4 (S-CH_2-$\underline{C}H_3$). Ms, *m/z*: 267-265 (M^+, 6); 206-204; 176; 150-148; 114; 86; 71 (100); 45.

3-Bromo-*endo*-6-ethylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (26b).

Yield 12% (64 mg). Found: C, 31.87; H, 2.91; N, 5.40. Anal. Calcd for $C_7H_8NSBrO_3$: C, 31.70; H, 3.02; N, 5.38. ^{1}H nmr: 5.93 (d, 1H, H-6, J=5.9); 5.67 (dd, 1H, H-6a, J=9.8 J=5.9); 4.35 (d, 1H, H-3a); 2.77 (q, 2H, S-C$\underline{H_2}$-CH_3, J=7.4); 1.33 (t, 3H, S-CH_2-C$\underline{H_3}$, J=7.4). ^{13}C nmr: 168.8 (C-4); 132.3 (C-3); 90.1, 82.8 (C-6, C-6a); 58.9 (C-3a); 26.0 (S-$\underline{C}H_2$-CH_3); 14.7 (S-CH_2-$\underline{C}H_3$).

3-Bromo-*exo*-4-ethylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-6(4*H*)-one (27a).

Yield 15% (80 mg). Found: C, 31.43; H, 3.68; N, 5.15. Anal. Calcd for $C_7H_8NSBrO_3$: C, 31.70; H, 3.02; N, 5.38. IR (neat): 1790 (C=O); 1570 (C=N). ^{1}H nmr: 5.78 (d, 1H, H-4, J=1.5); 5.31 (d, 1H, H-6a, J=9.5); 4.09 (dd, 1H, H-3a, J=9.5 J=1.5); 2.91-2.76 (m, 2H, S-C$\underline{H_2}$-CH_3, J=7.4); 1.36 (t, 3H, S-CH_2-C$\underline{H_3}$, J=7.4). ^{13}C nmr: 174.2 (C-6); 136.9 (C-3); 83.0, 76.5 (C-4, C-6a); 60.1 (C-3a); 26.0 (S-$\underline{C}H_2$-CH_3); 14.4 (S-CH_2-$\underline{C}H_3$). Ms, *m/z*: 267-265 (M^+, 3); 206-204; 176; 150-148; 115; 112; 84 (100); 83; 45.

2.- *Addition to 5-phehylthio-2(5H)-furanone* (**2**)

The crude product contained a mixture of furanone **2**, and the isoxazolines **28a**, **28b**, **29a** in a 13:56:12:19 ratio. (Petroleum ether-ethyl acetate, 4:1).

3-Bromo-*exo*-6-phenylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (28a) +

3-Bromo-*exo*-4-phenylthio-6a,3a-dihydrofuro[3,4-*d*]isoxazole-6(4*H*)-one (29a).

Yield 37% (205 mg). Found: C, 42.41; H, 2.80; N, 4.75. Anal. Calcd for $C_{11}H_{13}NSBrO_3$: C, 42.22; H, 2.56; N, 4.47. IR (neat): 1790 (C=O); 1610 (C=C); 1580; 1570 (C=N). Ms, *m/z*: 315-313 (M^+, 27); 206-204; 150-148; 137; 110 (100); 109; 77; 69; 65. *Compound* **28a**, ^{1}H nmr: 7.58-7.54 (m, 2H, arom.); 7.48-7.37 (m, 3H, arom.); 5.86 (d, 1H, H-6, J=1.8); 5.45 (dd, 1H, H-6a, J=9.3 J=1.8); 3.75 (d, 1H, H-3a, J=9.3). ^{13}C nmr: 166.8 (C-4); 135.4 (arom.); 132.4 (C-3); 129.9, 128.7, 128.0 (arom.); 89.8, 87.6 (C-6a, C-6); 58.1 (C-3a). Compound **29a**, ^{1}H nmr: 7.58-7.54 (m, 2H, arom.); 7.48-7.37 (m, 3H, arom.); 5.88 (d, 1H, H-4, J=1.3); 4.42 (d, 1H, H-6a, J=9.5); 4.25 (dd, 1H, H-3a, J=9.5 J=1.3). ^{13}C nmr: 169.8 (C-6a); 137.1 (C-3); 134.8 (arom.); 130.3, 129.7 (arom.); 84.7, 77.9 (C-6a, C-4); 60.9 (C-3a).

3-Bromo-*endo*-6-phenylthio-6a,3a-dihidrofuro[3,4-*d*]isoxazole-4(6*H*)-one (**28b**).

Yield 20% (110 mg). Recrystallized from carbon tetrachloride, mp 103-106°C. IR (neat) 1785 (C=O); 1650(C=C); 1580 (C=N). ^{1}H nmr: 7.58-7.51 (m, 2H, arom.); 7.38-7.32 (m, 3H, arom.); 6.06 (d, 1H, H-6, J=5.7); 5.75 (dd, 1H, H-6a, J=9.8 J=5.7); 4.38 (d, 1H, H-3a, J=9.8). ^{13}C nmr: 167.0 (C-4); 132.7 (arom.); 132.5 (C-3); 131.6, 129.4, 128.8 (arom.); 92.4, 87.1 (C-6a, C-6a); 50.1 (C-3a). Ms, *m/z*: 315-313 (M^+, 19); 206-204; 202; 150-148; 147; 109 (100); 77; 65.

3.- *Attempts of addition to furanones* **3** *and* **4**.

Cycloaddition products to the furanones **3** and **4** could not be detected. Neither the furanones **3** or **4** nor the bislactones **23** or **24** were identified in the corresponding crude reaction mixtures.

SYNTHESIS OF 6-ETHYLSULPHONYL-3-PHENYLFURO[3,4-*d*]ISOXAZOLE-4(6*H*)ONE (**31**)

1.- *Attempt of addition of benzonitrile oxide to 4-bromo-5-phenylsulphonyl-2(5H)-furanone* (**10**).

Following method *A*, the reaction mixture was stirred for 24 h at room temperature and the solvent removed. The crude material was chromatographed (petroleum ether-ethyl acetate, 3:1) to afford phenyl furoxanes and unreacted furanone **10**.

2.- *Addition of benzonitrile oxide to 4,5-diethylsulphonyl-2(5H)-furanone* (**12**).

Following method *A*, the reaction mixture was stirred for 10 h at room temperature and the solvent removed. An aliquot sample of the reaction mixture, analyzed by ^{1}H nmr, showed the presence of isoxazoline **30** and the isoxazole **31** in a 65:35 ratio. The precipitate isoxazoline **30** (190 mg, 55%) was isolated by

filtration. The solvent was removed and the crude product subjected to chromatography (petroleum ether-ethyl acetate, 3:1) to give 92 mg (30%) of isoxazole **31**.

6,6a-Diethylsulphonyl-3-phenyl-3a-hydrofuro[3,4-*d*]isoxazole-4(6*H*)-one (30)

Recrystallized from ethyl acetate/hexane, mp 185-188°C. Found: C, 46.31; H, 4.30; N, 3.58; S, 16.43. Anal. Calcd for $C_{15}H_{17}NS_2O_7$: C, 46.51; H, 4.39; N, 3.62; S, 16.54. IR (KBr): 1825 (C=O); 1570 (C=N); 1330, 1140 (SO_2). ^{1}H nmr: 7.89-7.86 (m, 2H, arom.); 7.53-7.47 (m, 3H, arom.); 5.57 (s, 1H, H-6); 5.36 (s, 1H, H-3a); 3.58 (q, 2H, S-C<u>H</u>$_2$-CH$_3$ in C-6, J=7.5); 3.33-3.25 (m, 2H, S-C<u>H</u>$_2$-CH$_3$ in C-6a, J=7.5); 1.50 (t, 3H, S-CH$_2$-C<u>H</u>$_3$, J=7.5); 1.48 (t, 3H, S-CH$_2$-C<u>H</u>$_3$, J=7.5). ^{13}C nmr: 164.5 (C-4); 155.2 (C-3); 132.3, 129.2, 128.5, 124.5 (arom.); 105.1 (C-6a); 89.4 (C-6); 55.3 (C-3a); 47.3, 45.5 (S-<u>C</u>H$_2$-CH$_3$); 6.0, 4.7 (S-CH$_2$-<u>C</u>H$_3$). Ms, *m/z*: 387 (M^+, 1); 294; 200 (100); 172; 144; 116; 103; 94; 89; 77; 51.

6-Ethylsulphonyl-3-phenylfuro[3,4-*d*]isoxazole-4(6*H*)one (31)

The isoxazole **33** (150 mg, 87%) was isolated by chromatography (petroleum eher-ethyl acetate, 3:1) of isoxazoline (**32**) (190mg, 0,5 mmol). Recrystallized from carbon tetrachloride, mp 155-156°C. Found: C, 52.89; H, 3.65; N, 4.72; S, 10.94. Anal. Calcd for $C_{13}H_{11}NSO_5$: C, 53.42; H, 3.42; N, 4.79; S, 10.96. IR (KBr): 1820, 1790 (C=O); 1620 (C=C); 1580 (C=N); 1320, 1140 (SO_2). ^{1}H nmr: 8.12-8.03 (m, 2H, arom.); 7.68-7.39 (m, 3H, arom.); 6.22 (s, 1H, H-6); 3.43-3.19 (m, 2H, S-C<u>H</u>$_2$-CH$_3$, J=7.5); 1.52 (t, 3H, S-CH$_2$-C<u>H</u>$_3$, J=7.5). ^{13}C nmr: 183.0 (C-4); 158.1 (C-6a); 157.5 (C-3); 132.3, 129.4, 128.3, 125.1 (arom.); 116.3 (C-3a); 83.2 (C-6); 46.9 (S-<u>C</u>H$_2$-CH$_3$); 6.2 (S-CH$_2$-<u>C</u>H$_3$). Ms, *m/z*: 293 (M^+, 1); 200 (100); 172; 144; 116; 103, 89; 77; 59; 51.

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19. It is noteworthy, that the ^{1}H nmr spectra of cycloadducts **13a**, **14a**, **17a**, **18a**, **21a**, **26a**, **27a** with the substituent Z (SEt or SO_2Et) in *exo* arrangement, display the signal assigned to CH_2 as a multiplet, whereas for the stereoisomers of type **b** the signal corresponding to CH_2 appears as a quartet.
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