

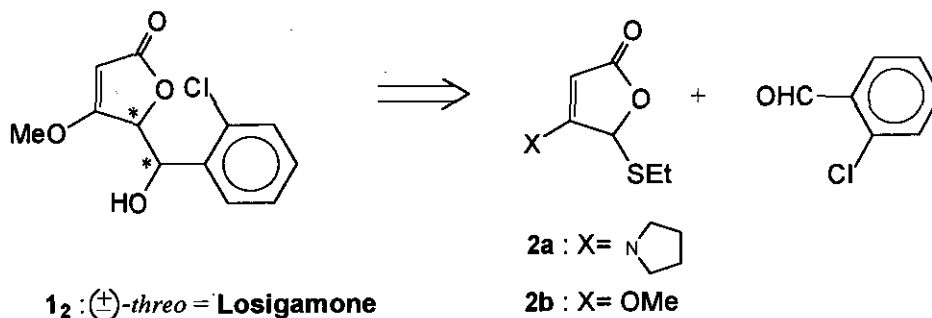
PSEUDOESTERS AND DERIVATIVES XXXVI. REACTIONS OF ENOLATES OF 5-ETHYLTHIOFURAN-2(5*H*)-ONES WITH AROMATIC ALDEHYDES: A SYNTHESIS OF LOSIGAMONE

M. Rosario Martín,^a M. Victoria Martín*,^b Ana Martínez de Guereñu,^b and J. Luis Ortego^b

^aDept. de Química Orgánica, Universidad Autónoma, Madrid 28049. ^bInst. de Química Orgánica General, Juan de la Cierva 3, Madrid 28006. Spain

Abstract- The furanones (**3a**) and (**3b**), key intermediates in our approach to *losigamone* (**1₂**), have been prepared by reaction of 2-chlorobenzaldehyde with the enolates (**2A**) and (**2B**) of the corresponding tetric acid derivatives (**2a**) and (**2b**). The reductive conversion of **3b** into **1** was carried out with Raney nickel. However, **3a** remains unchanged after treatment with Raney nickel or aluminium amalgam. The addition of the enolates (**2A**) and (**2B**) to 2-chlorobenzaldehyde led in regioselective manner to the corresponding 5-hydroxyarylfuranones (**3a**) and (**3b**). Whereas the addition of **2B** to benzaldehyde affords, in a 60:40 ratio, the C-5 and C-3 hydroxybenzylfuranones (**7b**) and (**8b**).

Losigamone (**1₂**), a tetric acid derivative, behaves as a potent anticonvulsant agent in vitro models of epileptogenesis such as picrotoxin.¹ It is also effective *in vivo* against maximal electroshock induced convulsions in rats (MRS) and metrazole induced clonic convulsions in mice.¹ Although the *losigamone* used for biological assays, has been prepared following the method described by Chatterjee as a patent.² We considered an attractive synthetic scheme to **1₂** starting from 5-ethylthio-4-(pyrrolidin-1-yl)- or 5-ethylthio-4-methoxyfuran-2(5*H*)-ones (**2a** and **2b**),^{3,4} since we have previously reported that the reaction of benzaldehyde with the enolate generated from **2a** occur regioselectively at C-5 with high stereoselectivity.³

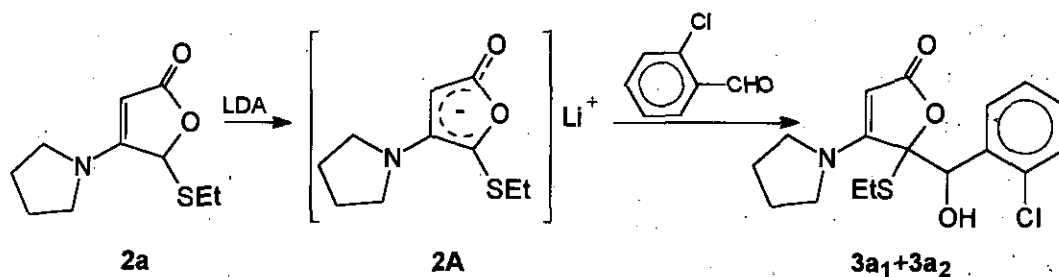


In this paper we report a new synthesis of *losigamone* starting from **2b** by reaction of its lithium enolate with chlorobenzaldehyde and posterior removal of the ethylthio group. We also show the results obtained in alternative routes for the preparation of **1** from the vinylogous urethane lactone (**2a**) as a starting material. On the other hand, the comparative study of the reactions of enolates (**2A**) and (**2B**) with benzaldehyde and 2-chlorobenzaldehyde makes evident the influence of the substituents at the enolate and aldehyde, upon the regio- and stereoselectivity of the reactions.

RESULTS AND DISCUSSION

We first planned the synthesis of *losigamone* (**1**) starting from the readily available 5-ethylthio-4-(pyrrolidin-1-yl)-furan-2(5H)-one (**2a**), because it is to hope that the enolate (**2A**), which reacts with benzaldehyde in good yield and with high stereoselectivity,³ by reaction with 2-chlorobenzaldehyde could afford 5-[(2-chlorophenyl)hydroxymethyl]-5-ethylthio-4-(pyrrolidin-1-yl)furan-2(5H)-one (**3a**). The subsequent transformation of **3a** to *losigamone*, following the steps outlined in Scheme 2, does not seem to be difficult.

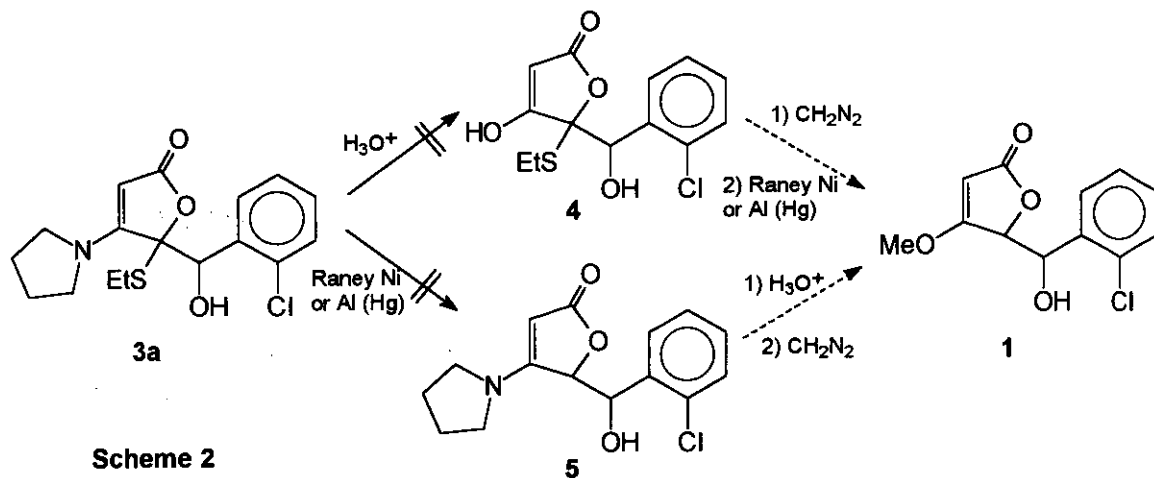
The reaction of the lithium enolate (**2A**), generated by treatment of **2a** with LDA at -70°C , with equimolar amount of 2-chlorobenzaldehyde, followed by protonation at -70°C , afforded a 77:23 mixture of the 5-hydroxyarylfuranones⁵ (**3a**₁ and **3a**₂) in 65% combined yield (Scheme 1). The diastereoisomers ratio of **3a**₁/**3a**₂ is lower than one obtained with benzaldehyde,³ therefore this result shows the influence of the chlorine at *o*-position to formyl group upon the stereoselectivity in the addition of the enolate (**2A**).



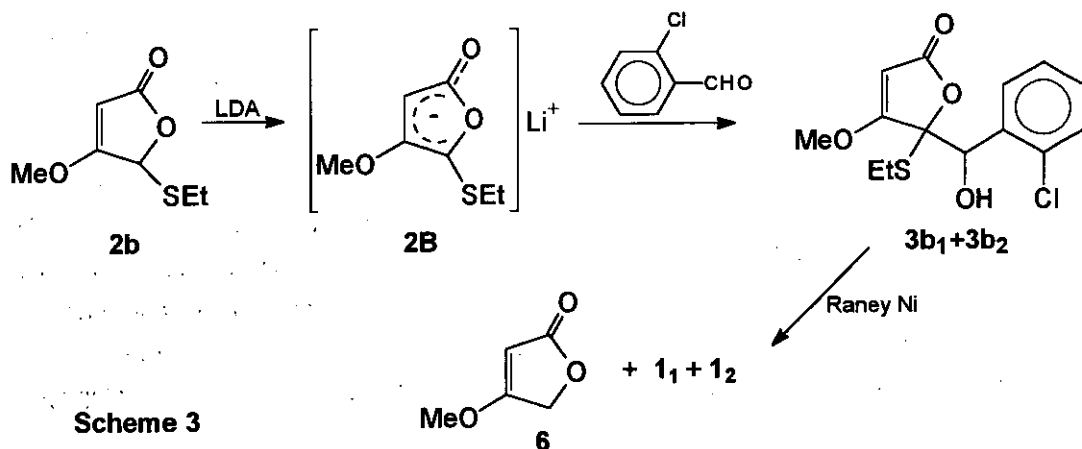
Scheme 1

Attempts of hydrolysis of **3a** to the 4-hydroxyfuranone (**4**), with hydrochloric acid under reflux, were unsuccessful.⁶ Also the removal of the ethylthio group of the furanones (**3a**), by treatment with Raney nickel⁷ or aluminium amalgam,⁸ was not achieved under the assayed conditions (Scheme 2).

Because of the difficulties to obtain the furanones (**4**) and (**5**) we decided to carry out the synthesis of the *losigamone* from the 4-methoxyfuranone (**2b**), available from **2a** by hydrolysis and methylation with diazomethane.⁴



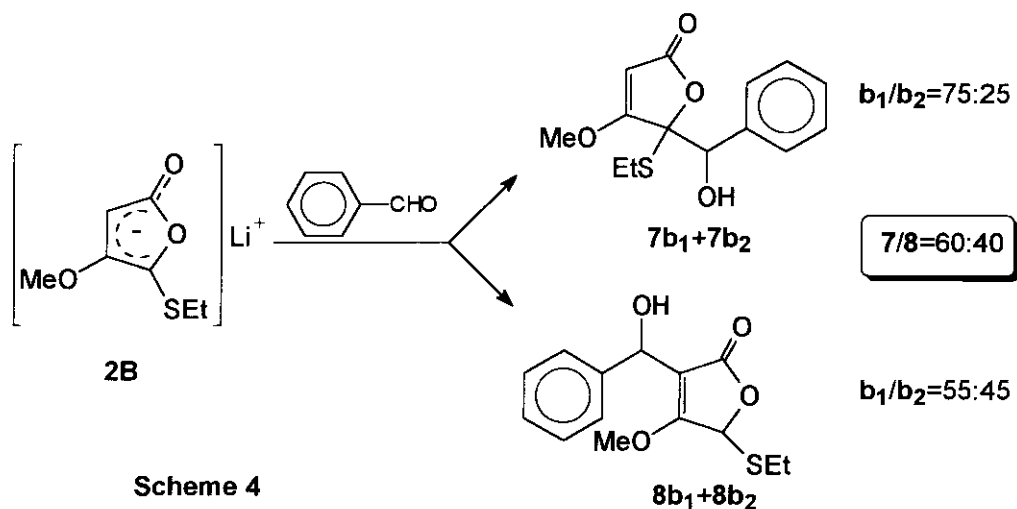
The lithium enolate (**2B**), under the same conditions employed for the preparation of **3a**, reacted with 2-chlorobenzaldehyde to afford a mixture of the 5-hydroxyaryl-furanones⁵ (**3b₁**) and (**3b₂**), in a 80:20 ratio and 65% combined yield (Scheme 3). The diastereomers (**3b₁**) and (**3b₂**) were readily separated by column chromatography.



The removal of the ethylthio group with Raney nickel,⁷ from **3b₁** as well as from **3b₂**, afforded mixtures of diastereomers (**1₁**) and (**1₂**) along with the 4-methoxyfuran-2(*5H*)-one (**6**),⁹ generated by retroaldol of the (2-chlorophenyl)hydroxymethyl group. It is noteworthy that the ratio of compounds (**1₁**, **1₂** and **6**) depends on the stereochemistry of the starting compound as well as on the Raney nickel utilized. The stereochemistry of **1₂** was assigned by comparison of its physical data with those reported in the literature for the *threo* isomer.² Therefore the compound (**1₁**) corresponds to the *erythro* isomer.

Finally, in order to verify if the regio- and stereoselectivity of the reactions of the enolate (**2B**) with 2-chlorobenzaldehyde and benzaldehyde is the same or different, we carried out the reaction of the enolate

(**2B**) with benzaldehyde, under the same conditions used in the reaction with 2-chlorobenzaldehyde. The crude reaction mixture obtained contains the C-5 hydroxybenzylfuranones⁵ (**7b₁**, **7b₂**) and the C-3



regioisomeric furanones¹⁰ (**8b₁**, **8b₂**). The ratio of regio- and stereoisomers formed are showed in Scheme 4. The formation of the 3-hydroxybenzylfuranones (**8b**) contrasts with the C-5 regioselectivity reported for the addition of **2A**³ and the enolates derived from 4-alkoxyfuran-2(*5H*)-ones^{9,11} to benzaldehyde.

EXPERIMENTAL

Mps are uncorrected. Microanalyses were performed with a Heraeus analyzer. Ir spectra were recorded on a Perkin-Elmer model 681 spectrophotometer (ν_{\max} , cm^{-1}). ¹H and ¹³C nmr spectra were obtained on a Varian EM-390, or a Bruker WP 200SY spectrometer using TMS ($\delta=0$ ppm) as internal reference, J values are given in Hz. Mass spectra were determined on a VG-12-250 spectrometer. Silica gel Merck 230-400 mesh and DC-Alufolien 60 were used for flash and analytical thin layer chromatography, respectively.

Generation of the lithium enolates (2A) and (2B): General procedure

A solution of lithium diisopropylamide (1.1 mmol) was prepared by addition at -70°C , under a dry nitrogen atmosphere, of a 1.6 M solution of *n*-butyllithium in hexane (0.7 ml, 1.1 mmol) to a solution of diisopropylamine (111 mg, 1.1 mmol) in tetrahydrofuran (4 ml). A solution of 1 mmol (213 mg or 174 mg) of furanone (**2a**) or (**2b**) in dry tetrahydrofuran (3 ml) was then added, and the reaction mixture was further stirred for 15 min at -70°C .

Reaction of enolate (2A) with 2-chlorobenzaldehyde

A solution of 2-chlorobenzaldehyde (155 mg, 1.1 mmol) in THF (3 ml) was added to the previous obtained solution of enolate (**2A**) (1 mmol) at -70°C . After being stirred for 5 min at -70°C , the reaction mixture was poured into saturated aqueous ammonium chloride and ethyl acetate was added. The

precipitated hydroxyarylfuranone (**3a₁**) was filtered off (141 mg) and the aqueous layer was extracted several times with ethyl acetate. The combined organic layers were dried (MgSO₄), and the solvent evaporated to dryness. The corresponding signals of compounds (**3a₁**) and (**3a₂**) and those of the starting furanone (**2a**) were observed by ¹H nmr. The products were isolated by column chromatography on silica gel using (4:1 ethyl acetate-petroleum ether). Combined yield of the stereoisomers (**3a**) 65 %, 77:23 ratio **a₁/a₂**.

5-[(2-Chlorophenyl)hydroxymethyl]-5-ethylthio-4-(pyrrolidin-1-yl)furan-2(5H)-ones (**3a**)

3a₁ (major isomer, minor Rf): 50% (177 mg); mp 205-209°C (from ethyl acetate). Ir (KBr): 3370, 1720, 1595. ¹H Nmr (DMSO-*d*₆): 7.68 (m, 1H), 7.30 (m, 3H), 6.52 (d, 1H, J=6.4, OH), 5.46 (d, 1H, J=6.4), 4.31 (s, 1H), 4.22 (m, 1H), 3.80 (m, 1H), 3.18 (m, 1H), 3.06 (m, 1H), 2.34 (m, 2H), 1.91 (m, 4H), 1.13 (t, 3H, J=7.4). ¹³C Nmr (DMSO-*d*₆): 170.5 (C-2), 165.0 (C-4), 136.9, 131.8, 129.6, 128.4, 126.5 (arom), 95.2 (C-5), 84.1 (C-3), 70.9 (C-1'), 51.0, 48.5 (C-CH₂N), 26.3, 23.7 (C-CH₂CH₂N), 22.1 (S-CH₂CH₃), 14.3 (SCH₂CH₃). Anal. Calcd for C₁₇H₂₀NO₃ClS: C, 57.70, H, 5.70, N, 3.96, Cl, 10.2, S, 9.06. Found: C, 57.65, H, 5.82, N, 3.75, Cl, 10.30, S, 8.75.

3a₂ (minor isomer, major Rf): 15% (53 mg); solid with indefinite mp. ¹H Nmr (DMSO-*d*₆): 7.69 (m, 1H), 7.40 (m, 3H), 6.27 (d, 1H, J=6.0, OH), 5.60 (d, 1H), 4.62 (s, 1H), 4.23 (m, 1H), 3.80 (m, 1H), 3.20 (m, 1H), 3.02 (m, 1H), 2.33 (m, 2H), 1.91 (m, 4H), 1.02 (t, 3H, J=7.4). ¹³C Nmr (DMSO-*d*₆): 171.1 (C-2), 165.4 (C-4), 137.3, 132.6, 131.3, 129.5, 128.4, 126.8 (arom), 94.1 (C-5), 84.1 (C-3), 68.4 (C-1'), 49.5, 47.9 (C-CH₂N), 25.4, 24.2 (C-CH₂CH₂N), 22.0 (S-CH₂CH₃), 14.3 (SCH₂CH₃).

Attempts to obtain 5-[(2-chlorophenyl)hydroxymethyl]-5-ethylthio-4-hydroxyfuran-2(5H)-one (**4**)

A vigorously stirred mixture of **3a₁** or **3a₁+3a₂** (354 mg, 1 mmol) and 0.1N aqueous HCl (10 ml) was heated under reflux for 8 h, then cooled to room temperature. The reaction mixture was extracted several times with ethyl acetate. The combined organic layers were dried (MgSO₄) and the solvent was evaporated to dryness. Only the signals corresponding to the starting furanone (**3a**) were observed by ¹H nmr in the crude product. The same result was obtained using 1N HCl and heating for 12 h.

Attempts to obtain 5-[(2-chlorophenyl)hydroxymethyl]-4-(pyrrolidin-1-yl)furan-2(5H)-one (**5**)

a) To a solution of furanone (**3a₁**) or a mixture of (**3a₁+3a₂**) (354 mg, 1mmol) in THF (10 ml) was added portionwise wet Raney nickel⁷ (2 g). After being stirred for 24 h at room temperature, the solution was filtered through a short column of celite which was further eluted with THF and the solvent was removed under reduced pressure. Only the signals corresponding to the starting furanones (**3a**) were observed by the ¹H nmr of the crude product.

b) To a solution of **3a₁** (354 mg, 1 mmol) in a 90:10 mixture of THF-H₂O (50 ml) was added aluminium amalgam⁸ (obtained from 300 mg of aluminium kitchen foil). After 24 h at room temperature with stirring the reaction mixture was filtered. The solid was washed with THF, and the solution was concentrated to dryness. Only the starting furanone could be identified by the ¹H nmr of the crude reaction product.

Reaction of enolate (**2B**) with 2-chlorobenzaldehyde

A solution of 2-chlorobenzaldehyde (155 mg, 1.1 mmol) in THF (3 ml) was added to the solution of

enolate (**2B**) (1 mmol), obtained following the general procedure. After being stirred for 5 min at -70°C , the reaction mixture was poured into saturated aqueous ammonium chloride and extracted several times with ethyl acetate. The combined organic layers were dried (MgSO_4), filtered and concentrated under reduced pressure. The signals corresponding to the hydroxyarylfuranones (**3b₁**) and (**3b₂**) and those of the starting furanone (**2b**) were observed by the ^1H nmr of the crude reaction mixture. The products were isolated by column chromatography using (1:1 ethyl acetate-petroleum ether). The stereoisomers (**3b₁**) and (**3b₂**) were obtained in a 80:20 ratio **b₁**/**b₂** and 65% combined yield.

5-[(2-Chlorophenyl)hydroxymethyl]-5-ethylthio-4-methoxyfuran-2(5H)-ones (3b)

3b₁ (major isomer, minor Rf): 52% (163 mg); mp $189\text{--}191^{\circ}\text{C}$ (from chloroform). Ir (KBr): 3370, 1740, 1635. ^1H Nmr (CDCl_3): 7.80 (m, 1H), 7.32 (m, 3H), 5.58 (d, 1H, $J=6.7$), 5.26 (s, 1H), 3.98 (s, 3H), 2.62 (d, 1H, $J=6.7$, OH), 2.41 (m, 2H), 1.15 (t, 3H, $J=7.5$); ($\text{DMSO}-d_6$): 7.67 (m, 1H), 7.36 (m, 3H), 6.29 (d, 1H, $J=5.6$, OH) 5.62 (s, 1H), 5.31 (d, 1H, $J=5.6$), 3.96 (s, 3H), 2.24 (m, 2H), 0.99 (t, 3H, $J=7.5$). ^{13}C Nmr ($\text{DMSO}-d_6$): 179.0 (C-4), 170.1 (C-2), 136.9, 132.8, 130.8, 129.7, 128.6, 127.0 (arom), 94.6 (C-5), 91.3 (C-3), 68.7 (C-1'), 60.1 (OCH_3), 21.9 (SCH_2CH_3), 14.1 (SCH_2CH_3). Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{O}_4\text{ClS}$: C, 53.42, H, 4.80, S, 10.18. Found: C, 53.15, H, 5.02, S, 9.78.

3b₂ (minor isomer, major Rf): 13% (41 mg); mp $155\text{--}157^{\circ}\text{C}$ (from ethyl acetate). Ir (KBr): 3375, 1765, 1630. ^1H Nmr (CDCl_3): 7.67 (m, 1H), 7.27 (m, 3H), 5.61 (d, 1H, $J=5.2$), 4.90 (s, 1H), 3.82 (s, 3H), 2.90 (d, 1H, $J=5.2$, OH), 2.50 (m, 2H), 1.26 (t, 3H, $J=7.5$ Hz). ^{13}C Nmr (CDCl_3): 179.2 (C-4), 169.3 (C-2), 134.2, 132.8, 130.0, 129.3, 127.1 (arom), 94.4 (C-5), 90.3 (C-3), 72.4 (C-1'), 59.5 (OCH_3), 22.7 (SCH_2CH_3), 14.2 (SCH_2CH_3). Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{O}_4\text{ClS}$: C, 53.42, H, 4.80, S, 10.18. Found: C, 53.63, H, 4.97, S, 9.94.

5-[(2-Chlorophenyl)hydroxymethyl]-4-methoxyfuran-2(5H)-ones (1)

Wet Raney nickel (2 g) was added portionwise to a solution of furanone (**3b₁**) (315 mg, 1 mmol) in THF (10 ml). After being stirred for 24 h at room temperature, the solution was filtered through a short column of celite, which was further eluted with THF and the solvent was removed under reduced pressure. The ^1H nmr analysis of the crude reaction mixture showed the presence of 4-methoxyfuran-2(5H)-one (**6**) and the stereoisomeric furanones (**1₁**) and (**1₂**) in a 12:48:40 ratio and 85% combined yield. Treatment of furanone (**3b₂**) under the same experimental conditions gave a crude reaction mixture containing compounds (**6**), (**1₁**), and (**1₂**) in a 26:27:47 ratio and 85% combined yield. The products were isolated by column chromatography using as eluent 1:1 hexane-ethyl acetate or 3:1 hexane-acetone. Using a different bottle of Raney nickel from the furanone (**3b₁**) a 13:59:28 ratio for products (**6**), (**1₂**) and (**1₁**) was observed. Combined yield 82%.

Erythro-5-[(2-chlorophenyl)hydroxymethyl]-4-methoxyfuran-2(5H)-one (1₁)

(Major Rf); mp $178\text{--}180^{\circ}\text{C}$ (from chloroform). Ir (KBr): 3375, 1740, 1630. ^1H Nmr (CDCl_3): 7.64 (m, 1H), 7.30 (m, 3H), 5.59 (d, 1H, $J=3.0$, OH), 5.20 (d, 1H), 5.08 (s, 1H), 3.75 (s, 3H); ($\text{DMSO}-d_6$): 7.58 (m, 1H), 7.24 (m, 3H), 6.19 (d, 1H, $J=5.1$, OH), 5.30 (d, 1H, $J=0.8$), 5.26 (dd, 1H, $J=5.1$, 2.6), 5.09 (dd, 1H, $J=2.6$, 0.8); 3.72 (s, 3H). ^{13}C Nmr: (CDCl_3): 179.8 (C-4), 172.4 (C-2), 134.8,

129.4, 129.2, 128.9, 126.7 (arom.), 90.3 (C-3), 80.1 (C-5), 69.6 (C-1'), 59.2 (OCH₃); (DMSO-*d*₆): 180.5 (C-4), 172.1 (C-2), 136.8, 131.3, 130.1, 129.5, 128.9, 126.9 (arom.), 90.2 (C-3), 80.3 (C-5), 68.7 (C-1'), 59.7 (OCH₃). Ms *m/z* (relative intensity): 143-141 (M⁺-113, 6-23), 114 (100), 86 (12), 77 (34), 69 (10), 56 (20). Anal. Calcd for C₁₂H₁₁O₄Cl: C, 56.69, H, 4.36, Cl, 13.77. Found: C, 56.89, H, 4.35, Cl, 14.03.

Threo-5-[(2-chlorophenyl)hydroxymethyl]-4-methoxyfuran-2(5H)-one (1₂)

(Minor Rf); mp 151-153°C (lit., 149-151 C)².

Reaction of enolate (2B) with benzaldehyde

A solution of the benzaldehyde (117 mg, 1.1 mmol) in THF (3 ml) was added to a solution of the previous obtained enolate (**2B**) (1 mmol) at -70°C. After being stirred for 5 min at -70°C, the reaction mixture was poured into saturated aqueous ammonium chloride and the aqueous layer was extracted several times with ethyl acetate. The combined organic layers were dried (MgSO₄), and the solvent was evaporated to dryness. The signals corresponding to four new products (**7b₁**, **7b₂**, **8b₁** and **8b₂**) and those of the starting furanone (**2b**) were observed in a ratio of 30:11:13:11:35, by ¹H nmr. Column chromatography, using as eluent 4:1 hexane-ethyl acetate, afforded: mixtures of two stereoisomers **8b**, the starting furanone (**2b**), **7b₂** and **7b₁**.

5-Ethylthio-5-hydroxybenzyl-4-methoxyfuran-2(5H)-ones (7b)

7b₁: 28% (78 mg); mp 175-179 °C, (from ethyl acetate). Ir (KBr): 3400, 1740, 1720, 1635. ¹H Nmr (CDCl₃): 7.47-7.31 (m, 5H), 5.12 (s, 1H), 4.93 (d, 1H, J=5.6), 3.94 (s, 3H), 2.58 (d, 1H, J=5.6, OH), 2.41 (c, 2H, J=7.5), 1.24 (t, 3H). ¹³C Nmr (CDCl₃): 179.4 (C-4), 170.2 (C-2), 137.1, 129.0, 128.3, 127.9 (arom.), 94.3 (C-5), 90.9 (C-3), 75.5 (C-1'), 59.7 (OCH₃), 22.9(SCH₂), 14.0(CH₃). Ms *m/z* (relative intensity): 281 (M⁺+1, 3), 263 (12), 219 (4), 174 (100), 145 (84), 113 (9), 105 (34), 85 (19), 77 (49), 69 (45). Anal. Calcd for C₁₄H₁₆O₄S: C, 59.98, H, 5.75, S, 11.44. Found: C, 60.09, H, 5.64, S, 11.13.

7b₂: 8% (22 mg); wax. Ir (nujol): 3405, 1750, 1630. ¹H Nmr (CDCl₃): 7.32 (m, 5H), 5.00 (br s, 1H), 4.85 (s, 1H), 3.80 (s, 3H), 2.93 (br. s, 1H, OH), 2.49 (m, 2H), 1.24 (t, 3H, J=7.5). ¹³C Nmr (CDCl₃): 179.2 (C-4), 169.5 (C-2), 136.3, 128.9, 128.2, 127.1 (arom.), 94.3 (C-5), 90.8 (C-3), 76.8 (C-1'), 59.4 (OCH₃), 22.8 (SCH₂), 14.1 (CH₃). Ms *m/z* (relative intensity): 262 (M⁺-18, 4), 174 (100), 145 (83), 131 (4), 105 (46), 85 (26), 77 (45), 69 (45).

5-Ethylthio-3-hydroxybenzyl-4-methoxyfuran-2(5H)-ones (8b)

Combined yield 18% (50 mg)

8b₁: wax. ¹H Nmr (CDCl₃): 7.34 (m, 5H), 5.87 (s, 1H), 5.78 (br s, 1H), 4.09 (s, 3H), 2.55 (m, 2H), 1.22 (t, 3H, J=7.5). **8b₂**: wax. ¹H Nmr (CDCl₃): 7.34 (m, 5H), 5.85 (s, 1H), 5.75 (br s, 1H), 4.07 (s, 3H), 2.57 (m, 2H), 1.29 (t, 3H, J=7.5). Anal. Calcd for C₁₄H₁₆O₄S: C, 59.98, H, 5.75, S, 11.44. Found: C, 60.12, H, 5.50, S, 11.56.

ACKNOWLEDGEMENTS

Financial support from Secretaría de Estado de Universidades e Investigación (DGCYT grant PB90-0072) and a fellowship (to A. Martínez de Guereñu) from MEC are gratefully acknowledged. We thank also Mr. J.A. Esteban for technical assistance.

REFERENCES AND NOTES

1. a) M. Nöldner and S.S. Chatterjee, *Drugs Fut.*, 1990, **15**, 995; b) G. Köhr and U. Heinemann, *Epilepsy Res.*, 1990, **7**, 49; c) G. Köhr and U. Heinemann, *Neurosci Lett.*, 1990, **112**, 43; d) C.L. Zhang, S.S. Chatterjee, U. Stein, and U. Heinemann, *Naunyn-Schmiedeberg's Arch. Pharmacol.*, 1992, **345**, 85.
2. S.S. Chatterjee and K. Klesling, *Ger. Offen.*, 3615157 (1987) (*Chem. Abstr.*, 1988, **108**, 112212a).
3. B. De Ancos, F. Fariña, M.C. Maestro, M.R. Martín, and M. Vicioso, *Tetrahedron*, 1991, **47**, 3171.
4. F. Fariña, M.V. Martín, R.M. Martín-Aranda, and A.M. Martínez de Guereñu, *Synth. Commun.*, 1993, **23**, 459.
5. The regiochemical assignments of the new 5,5-disubstituted furanones were based on the spectral data obtained for each compound. Thus, the ^1H nmr spectra of these compounds lacked resonances corresponding to the acetal-type at C-5, but exhibited signals assignable to the olefinic proton at C-3. Furthermore, the ^{13}C nmr spectra displayed signals assignable to C-5 quaternary carbons.
6. By heating at 60°C with 0.1 N hydrochloric acid for 4 h, the furanone (**2a**) afford in 97% yield 4-hydroxy-5-ethylthiofuran-2(5H)-one.⁴
7. The Raney nickel was provided by Aldrich Chemical Co. Inc., as aqueous suspension of Ph 9-10, and was used wet without any further purification.
8. Aluminium amalgam was prepared by immersing strips of aluminium foil in a 10% hydrochloric acid, after rising with water, the strips were immersed in a 5% aqueous solution of mercuric chloride for 15-30 seconds, decanting the solution, rising the strips with absolute ethanol, then with ether, and cutting them with scissors into pieces of approximately 1 cm^2 .
9. A. Pelter, R.I.H. Al-Bayati, M.T. Ayoub, W. Lewis, and P. Pardasani, *J. Chem. Soc., Perkin Trans I*, 1987, 717.
10. The regiochemical assignments of the 3-substituted furanones were based on the spectral data obtained for each compound. Thus, the ^1H nmr spectra of these compounds lacked resonances corresponding to the olefinic proton at C-3, but exhibited signals assignable to the acetal-type at C-5.
11. T. Honda, T. Hayakawa, H. Kondoh, A. Okuyama, and M. Tsubuki, *Chem. Lett.*, 1991, 1861.

Received, 31st July, 1995