Pergamon

Tetrahedron Vol. 51, No. 11, pp. 3197-3204, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00058-5

Synthesis of a Benzodioxinic Analog of 8-Methoxypsoralen

Thierry Besson[1], Nicolas Ruiz[2], Gérard Coudert[2], Gérald Guillaumet[2]

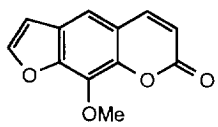
[1] *Laboratoire de Génie Protéique et Cellulaire, Chimie Organique et Biocatalyse*, Pôle Sciences et Technologies, Université de La Rochelle, Avenue Marillac, F-17042 La Rochelle cedex 1, France

[2] *Laboratoire de Chimie Bioorganique et Analytique* associé au CNRS, Université d'Orléans, BP 6759, F-45067 Orléans cedex 2, France

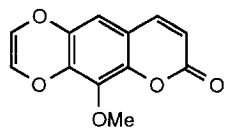
Abstract: A synthesis of a benzodioxinic analog of 8-methoxypsoralen (8-MOP), in 12 steps from the commercially available 6-acetyl-2,3-dihydro-1,4-benzodioxin, is described.

A furocoumarin such as the 8-methoxypsoralen (8-MOP) is commonly used in the photochemotherapy (PUVA-therapy) of hyperproliferatives skin diseases such as psoriasis[1], micosis fungoides[2] and vitiligo[3]. Although PUVA-therapy proves to be very effective, some undesirable side effects are present such as a persistant erythema[4], genotoxicity[5], phototoxicity and a possible risk of skin cancer[6]. As these side effects are mostly attributed to psoralen DNA cross-links rather than to monofunctional adducts[7] a research strategy has emmerged with the aim of preparing furocoumarins able to react as essentially monofunctional agents. The most important derivatives include 3-carbethoxypsoralens[8], pyridopsoralens[9], benzopsoralens[10], angelicins[11] and allopsoralens[12].

In the course of our work concerning access to new polyheterocyclic systems with potential pharmacological values such as benzodioxinic analogs of psoralens, we recently described the synthesis and photobiological activity of angular or linear dioxinocoumarins[13-18]. In these series, we expected to decrease the toxicity of photoactivated compounds without affecting their photoreactivity by incorporating an additional oxygen atom on the furan ring in order to break the divinyl benzene structure of the psoralens. In order to complete our studies it appeared of interest to investigate a benzodioxinic analog of the 8-methoxypsoralen. We describe in this paper the multistep synthesis of this new benzodioxin **1**.



8-MOP



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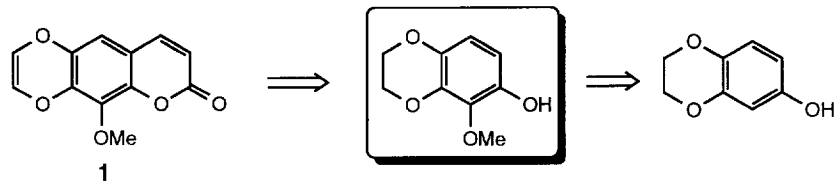
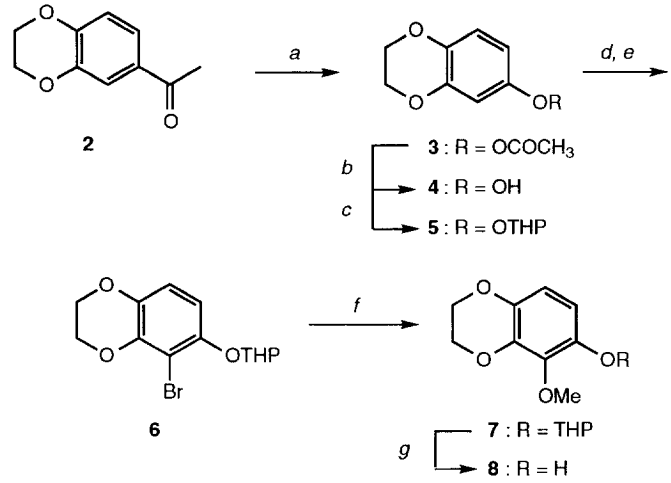
Considering previous works developped in our group on several benzodioxinic structures[13-15], the most convenient synthetic strategy designed the 5-methoxy-6-hydroxy-2,3-dihydro-1,4-benzodioxin as the ideal precursor of the attempted compound. Synthesis of this derivative was expected from the 6-hydroxy-2,3-dihydro-1,4-benzodioxin (Scheme 1).



Scheme 1

As previously described[19], the 6-hydroxy-2,3-dihydro-1,4-benzodioxin **4** can be prepared by diazotation of the commercially available 6-amino-2,3-dihydro-1,4-benzodioxin. A second most suitable method was performed which consisted first in a Baeyer-Villiger transformation of the commercially available 6-acetyl-2,3-dihydro-1,4-benzodioxin **2** into the 6-acetyloxy-2,3-dihydro-1,4-benzodioxin **3** followed by saponification with a sodium hydroxide solution to provide the expected phenol **4** in a good yield (Scheme 2).

Previous studies concerning direct introduction of electrophiles on the C_5 position of compound **4** by a metalation process were disappointing[19,20]. For these reason, the protection of the phenolic function with an *ortho*-directing group was envisaged. Among the various *ortho*-directing groups studied[19-21], in our hands, the tetrahydropyranyl group gave the best results. Our first ambition was to obtain the 5-hydroxy derivative by usual methods involving metalation reactions (*n*-BuLi) and treatment with $B(OMe)_3/H_2O_2$[21] or O_2[21,22]. The complexe mixtures obtained with these methods suggested access to the 5-methoxy-6-tetrahydropyranyloxy-2,3-dihydro-1,4-benzodioxin **7** via an intermediate brominated derivative following a strategy previously described by several groups[23-26] (Scheme 2).



Scheme 2. *Reagents and conditions* : *a)* *m*CPBA, CH_2Cl_2 reflux, 18h, 71%; *b)* MeOH, NaOH 10%, 3h, 99%; *c)* PPTS, dihydropyran, CH_2Cl_2, rt, 98%; *d)* *n*-BuLi (3 eq.), THF, - 50°C, 2h; *e)* $BrCF_2CF_2Br$, -50°C then rt, 95%; *f)* MeONa, CuBr, MeOH / DMF, 130°C, 18h, 77%; *g)* Amberlyst® resin, MeOH, rt, 2h, 90%.

After experimentation with various temperatures, bases and molecular ratio, in order to avoid the opening of the benzodioxanic ring[27] treatment with 3.0 equivalents of *n*-butyllithium at -50°C in tetrahydrofuran was found to be the most effective in converting **5** into the 5-lithio-derivative which reacted with dibromotetrafluoroethane to give the 5-brominated product **6** in an excellent yield. Substitution of the bromide by a methoxy group was carried out by treatment of **6** with sodium methoxide. Different conditions of copper catalyst[24-26] or solvent (ethyl acetate[24], dimethylformamide[25], MeOH/DMF[26]) were tested. The most efficient procedure involved copper bromide (CuBr) as catalyst and the mixture methanol / dimethylformamide (5:5) as solvent. Deprotection of the tetrahydropyranyl ether was easily achieved in the presence of Amberlyst® resin[28]. (Scheme 2).

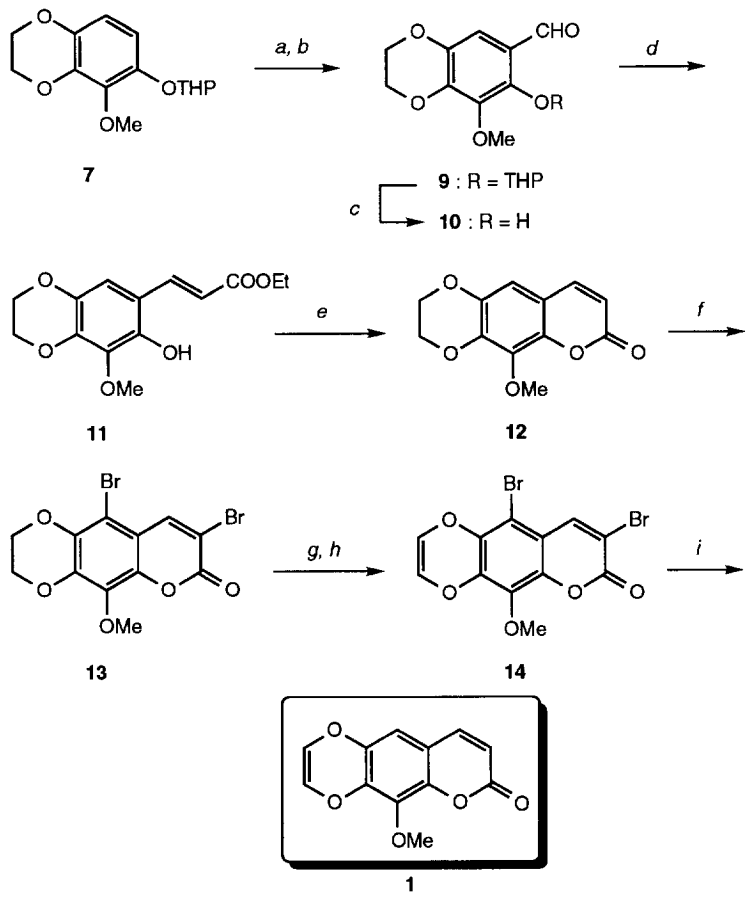
Formation of the coumarin **12** was first expected by a classical Pechmann condensation of the 5-methoxyderivative **8** with malic acid[13]. Unfortunately, whatever conditions were used, the reaction gave complex mixtures. A second pathway suggest to obtain the aldehydic precursor **10** which can then be used in a Wittig process[13,14,29]. The classical Reimer-Tiemann[30] (NaOH, $CHCl_3$, EtOH) or Vilsmeier-Haack[31] ($POCl_3$, DMF) procedures led to an important degradation of the starting material **8**. In contrast, the Reiche reaction[32] involving treatment of **8** by methoxydichloromethane (Cl_2CHOCH_3) in the presence of $TiCl_4$, followed by hydrolysis, gave the attempted aldehyde **10** in a reasonable yield. Unfortunately, the 8-formyl isomer was also obtained.

In order to avoid the undesirable formation of this isomer, a metallation process using the *ortho*-directing property of the OTHP group was once more considerated. We observed that treatment of **7** in conditions previously described (*n*-Buli 5 eq., THF, -50°C) allowed the best conversion of **7** into the 7-lithio derivative which was condensed with DMF to provide the hydroxy protected aldehyde **9** in a satisfying yield. Compound **9** was then easily transformed into the attempted phenol **10** (Scheme 3).

The usual Wittig reaction[13,14,29] involving treatment of **10** with carbetoxymethylenetriphenylphosphorane (Ph_3P=CHCOOEt) in toluene gave the intermediate product **11** in a high yield. Heating of this derivative in diphenylether provided the pure benzodioxinocoumarin **12** in a 84% yield from **10**.

The following challenge was to introduce an insaturation into the 2,3-dihydro-1,4-benzodioxinic part of the molecule. The bromination (NBS, CCl_4, Bz_2O_2) - debromination (NaI, acetone) sequence previously described in several synthesis of benzodioxinic derivatives[13-15,33] did not lead to the expected compound **1.** In fact, the bromination reaction gave an unusable mixture of brominated products. These disappointing results imposed a preliminary treatment of **12** with two equivalents of bromide. The brominated derivative **13** obtained was then submitted to the preceding method, leading to the benzodioxinocoumarin **14**. An adaptation of the Heck[34] procedure for the reduction of halogenated aromatic derivatives ($Pd(OAc)_2$, tri-*o*-tolylphosphine) allowed reduction of compound **14** in good yield (Scheme 3).

The benzodioxinic analog **1** of 8-methoxypsoralen was thus obtained in 12 steps with a global yield of 11%. In addition, our synthetic pathway may allow the access, via the dibromo intermediate **14**, to a number of diversely substituted dioxinocoumarins. The photobiologic activity of **1** is under current investigation and the results will be published elsewhere.



Scheme 3. *Reagents and conditions* : *a)* *n*-BuLi (5 eq.), THF, - 50°C, 2h; *b)* DMF, -50°C then rt, 66%; *c)* Amberlyst® resin, MeOH, rt, 2h, 90%; *d)* Ph_3P=CHCOOEt, $PhCH_3$, reflux, 2h, 95%; *e)* Ph_2O, 250°C, 84%; *f)* Br_2 (2 eq.), CH_3COOH, rt, 1h, 98%; *g)* NBS / AIBN, CCl_4, reflux, 6h; *h)* NaI, acetone, reflux, 6h, 60% i) $Pd(OAc)_2$, P(*o*-tolyl)$_3$, Et_3N, / HCOOH / DMF, 60°C, 4h, 80%.

EXPERIMENTAL

Melting points are uncorrected. The IR spectra were obtained using a Perkin-Elmer 196 and the ^{1}H-NMR spectra were recorded at 300 MHz on a Bruker AM 300WB spectrometer. Chemical shifts are reported in parts per million downfield from tetramethylsilane (δ units). Analytical thin layer chromatography (tlc) was performed on Merk 60F-254 silica gel plates. Preparative column chromatography was performed by using Merk silica gel (70-230 mesh). Mass spectra were measured on a Nermag R-10-10 C spectrometer.

6-Hydroxy-2,3-dihydro-1,4-benzodioxin (4):

Method A: Compound **4** was readily obtained from the commercialy available 6-amino-2,3-dihydro-1,4-benzodioxin by a method previously described[20] (Yield: 70-80%);

Method B To a solution of 6-acetyl-2,3-dihydro-1,4-benzodioxin **2** (5 g, 0.28 mol) was added *m*-chloroperbenzoic acid (*m*-CPBA) (10.7 g, 0.62 mol). The mixture was stirred at 60°C for 18 h, then the

m-chlorobenzoic acid was precipitated by cooling in an ice bath. The organic layer was then washed with a solution of sodium bicarbonate and the crude product purified by column chromatography (eluent: dichloromethane) to provide 3.85 g of compound **3**. (Yield: 71%); ^{1}H-NMR ($CDCl_3$): δ = 2.27 (s, 3H, $\mathbf{CH_3}$COO), 4.20-4.30 (m, 4H, O$\mathbf{CH_2CH_2}$O), 6.55 (dd, $J_{5,7}$ = 2.70 Hz and $J_{7,8}$ = 8.40 Hz, 1H, H_7), 6.63 (d, $J_{5,7}$ = 2.70 Hz, 1H, H_5), 6.85 (d, $J_{7,8}$ = 8.40 Hz, 1H, H_8). Compound **3** obtained above was solubilized in methanol/NaOH 10% (45:55) and stirred at room temperature for 3 h. The resulting mixture was acidified with HCl 2N and the product extracted with diethyl ether to provide 3 g (Yield:99%) of the title product **4** as a colorless oil. Global yield: 70%; IR (film): ν = 3600-3000 (OH), 1180 (ether) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 4.17-4.26 (m, 4H, O$\mathbf{CH_2CH_2}$O), 6.33 (dd, $J_{5,7}$ = 2.76 Hz and $J_{7,8}$ = 8.69 Hz, 1H, H_7), 6.40 (d, $J_{5,7}$ = 2.76 Hz, 1H, H_5), 6.71 (d, $J_{7,8}$ = 8.69 Hz, 1H, H_8); MS (CI): m/z = 153 (M+1). *Anal.* Calcd. for $C_8H_8O_3$: C 63.15; H 5.30. Found: C 63.05; H 5.15.

6-Tetrahydropyranyloxy-2,3-dihydro-1,4-benzodioxin (5):
To a solution of **4** (3.8 g, 25.6 mmol) and pyridinium *p*-toluenesulfonate (PPTS, 0.64 g, 0.385 mmol) in methylene chloride (15 ml), dihydropyran (3.23 g, 3.5 ml, 38.5 mmol) was added and the mixture was stirred at room temperature for 2 h. The solution was washed with a basic solution (NaOH 5%) and the product purified by silica gel column chromatography (eluent: petroleum ether/diethyl ether, 9:1). The solvent was evaporated to give 5.78 g of **5** as a colorless oil. Yield: 98%; IR (film): ν = 1260 (ether) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.50-2.04 (m, 4H, H_{THP}), 3.46-3.52 (m, 2H, H_{THP}), 3.84-3.97 (m, 2H, H_{THP}), 4.17-4.26 (m, 4H, O$\mathbf{CH_2CH_2}$O), 5.27 (t, J = 3.16 Hz, 1H, H_{THP}), 6.54 (dd, $J_{5,7}$ = 2.76 Hz and $J_{7,8}$ = 8.69 Hz, 1H, H_7), 6.63 (d, $J_{5,7}$ = 2.76 Hz, 1H, H_5), 6.76 (d, $J_{7,8}$ = 8.69 Hz, 1H, H_8); MS (CI): m/z = 237 (M+1).

5-Bromo-6-tetrahydropyranyloxy-2,3-dihydro-1,4-benzodioxin (6):
To a stirred solution of **5** (0.2 g, 0.847 mmol) in THF (10 ml) was added *n*-butyllithium 1.6 M in hexane (1.6 ml, 2.55 mmol) at -50°C under an argon atmosphere. The mixture was stirred at -50°C for 2 h, then 1,2-dibromotetrafluoroethane (0.48 ml, 4.25 mmol) was added. The solution was stirred at -50°C for 1 h and then allowed to warm to room temperature. After hydrolysis and extraction at neutral pH with diethyl ether, the crude product was purified by chromatography on silica gel (eluent: petroleum ether/diethyl ether, 9:1) to provide 0.264 g of the title compound as a colorless oil. Yield: 95%; IR (film): ν = 1260 (ether) cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ = 1.50-2.16 (m, 4H, H_{THP}), 3.44-3.62 (m, 2H, H_{THP}), 3.84-4.05 (m, 2H, H_{THP}), 4.18-4.23 (m, 2H, O$\mathbf{CH_2CH_2}$O), 4.31-4.36 (m, 2H, O$\mathbf{CH_2CH_2}$O), 5.37 (t, J = 2.76 Hz, 1H, H_{THP}), 6.68 (d, $J_{7,8}$ = 9.08 Hz, 1H, H_{arom}), 6.77 (d, $J_{7,8}$ = 9.08 Hz, 1H, H_{arom}); MS (CI): m/z = 317 (M+2), 315 (M).

5-Methoxy-6-tetrahydropyranyloxy-2,3-dihydro-1,4-benzodioxin (7):
To a stirred solution of **6** (5.2 g, 16.5 mmol) in DMF (30 ml) was added sodium methylate (MeONa, 45 g, 82.5 mmol) and methanol (70 ml) in the presence of cupper bromide (CuBr, 0.3 g, 2.1 mmol). The mixture was heated at 130°C for 18 h and slowly cooled. After evaporation of DMF, water was added and the crude product twice extracted with diethyl ether. Purification by chromatography on silica gel (eluent: dichloromethane) gave 3.4 g of the title compound **7** as a colorless oil. Yield: 77%; IR (film): ν = 1280 (ether) cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ = 1.50-2.08 (m, 4H, H_{THP}), 3.55-3.65 (m, 2H, H_{THP}), 3.91 (s, 3H, $\mathbf{OCH_3}$), 3.97-4.05 (m, 2H, H_{THP}), 4.08-4.18 (m, 2H, O$\mathbf{CH_2CH_2}$O), 4.28-4.32 (m, 2H, O$\mathbf{CH_2CH_2}$O), 5.29 (t, J = 2.76 Hz, 1H, H_{THP}), 6.54 (d, $J_{7,8}$ = 9.08 Hz, 1H, H_{arom}), 6.66 (d, $J_{7,8}$ = 9.08 Hz, 1H, H_{arom}); MS (CI): m/z = 267 (M+1).

5-Methoxy-6-hydroxy-2,3-dihydro-1,4-benzodioxin (8):
To a solution of **7** (0.38 g, 1.43 mmol) in methanol (5 ml) was added Amberlyst® resin (0.02 g). The mixture was stirred at room temperature for 2 h, the resin was eliminated by filtration, washed with methanol and the solvent evaporated. Purification by column chromatography (eluent: petroleum ether/diethyl ether, 8:2) allowed

0.257 g of the title compound **8** as a white powder.Yield: 90%; mp = 72°C; IR (KBr): ν = 3600-3200 (OH), 1260 (ether) cm^{-1}; ^{1}H-RMN ($CDCl_3$ + D_2O): δ = 3.91 (s, 3H, OCH_3), 4.19-4.22 (m, 2H, OCH_2CH_2O), 4.27-4.31 (m, 2H, OCH_2CH_2O), 6.46 (d, $J_{7,8}$ = 8.69 Hz, 1H, H_{arom}), 6.54 (d, $J_{7,8}$ = 8.69 Hz, 1H, H_{arom}). MS (CI): m/z = 183 (M+1). *Anal.* calcd. for $C_9H_{10}O_4$: C 59.34; H 5.53. Found C 59.20; H 5.61.

5-Methoxy-7-formyl-6-tetrahydropyranyloxy-2,3-dihydro-1,4-benzodioxin (9):
As previously described for product **6**, treatment of **7** (0.34 g, 1.28 mmol) with dimethylformamide (0.47 g, 0.5 ml, 6,4 mmol) followed by column chromatography (eluent: petroleum ether/diethyl ether, 85:15) gave 0.227 g of the title compound **9** as a yellow oil. Yield: 66%; IR (film): ν = 1710 (C=O), 1260 (ether) cm^{-1}; ^{1}H-RMN ($CDCl_3$): δ = 1.50-1;74 (m, 4H, H_{THP}), 1.86-2.04 (m, 2H, H_{THP}), 3.47-3.58 (m, 1H, H_{THP}), 3.89 (s, 3H, OCH_3), 3.94-4.04 (m, 1H, H_{THP}), 4.23-4.29 (m, 2H, OCH_2CH_2O), 4.35-4.40 (m, 2H, OCH_2CH_2O), 5.26 (t, J = 3.55 Hz, 1H, H_{THP}), 7.17 (s, 1H, H_8), 10.30 (s, 1H, CHO). MS (CI): m/z = 269 (M+1).

5-Methoxy-7-formyl-6-hydroxy-2,3-dihydro-1,4-benzodioxin (10):
As previously described for compound **8**, treatment of **9** (0.342 g, 1.16 mmol) with Amberlyst® resin and column chromatography (eluent: petroleum ether/diethyl ether, 8:2) provided 0.221 g of title product **10** as a yellow oil. Yield: 90%; IR (film): ν = 3600-3200 (OH), 1710 (C=O), 1260 (ether) cm^{-1}; ^{1}H-RMN ($CDCl_3$ + D_2O): δ = 3.92 (s, 3H, OCH_3), 4.21-4.24 (m, 2H, OCH_2CH_2O), 4.36-4.40 (m, 2H, OCH_2CH_2O), 6.82 (s, 1H, H_8), 9.65 (s, 1H, CHO). MS (CI): m/z = 211 (M+1). *Anal.* Calcd. for $C_{10}H_{10}O_5$: C 57.14; H 4.79. Found C 57.28; H 4.78.

5-Methoxy-7-[2-carbethoxyethylene]-6-hydroxy-2,3-dihydro-1,4-benzodioxin (11):
To a solution of **10** (0.12 g, 0.572 mmol) in toluene (5 ml) was added (carbethoxymethylene) triphenylphosphorane (Ph_3P=CHCOOEt, 0.25 g, 0.714 mmol). The mixture was stirred at reflux for 2 h and the crude product purified by column chromatography (eluent: dichloromethane) to provide 0.153 g of the title compound **11** as a white powder. Yield: 95%; mp = 140-142°C; IR (KBr): ν = 3600-3100 (OH), 1690 (C=O), 1260 (ether) cm^{-1}; ^{1}H-RMN ($CDCl_3$ + D_2O): δ = 1.32 (t, J = 6.89 Hz, 3H, $COOCH_2CH_3$), 3.92 (s, 3H, OCH_3), 4.20-4.34 (m, 6H, OCH_2CH_2O + $COOCH_2CH_3$), 6.45 (d, J = 15.81 Hz, 1H, CH=), 6.75 (s, 1H, H_8), 7.81 (d, J = 15.81 Hz, 1H, CH=). MS(CI): m/z = 281 (M+1). *Anal.* calcd. for $C_{14}H_{16}O_6$: C 59.99; H 5.75. Found C 59.78; H 5.62.

5-Methoxy-7*H*-pyrano[2,3-*g*]-2,3-dihydro-1,4-benzodioxin-7-one (12):
A solution of **11** (0.1 g, 0.357 mmol) in diphenyl ether (5 ml) was heated at 250°C for 4 h. After elimination of the solvent, the crude product was purified by column chromatography (eluent: dichloromethane) to provide 0.07 g of the title compound **12** as a yellow powder. Yield: 84%; mp = 174°C; IR (KBr): ν = 1710 (C=O), 1310 (ether) cm^{-1}; UV(ethanol)[λ max (nm), log ε]: 306, 3.11; 335, 2.76; ^{1}H-RMN ($CDCl_3$): δ = 4.04 (s, 3H, OCH_3), 4.26-4.30 (m, 2H, OCH_2CH_2O), 4.35-4.40 (m, 2H, OCH_2CH_2O), 6.27 (d, $J_{8,9}$ = 9.56 Hz, 1H, H_8), 6.71 (s, 1H, H_{10}), 7.53 (d, $J_{8,9}$ = 9.56 Hz, 1H, H_9). MS (CI): m/z = 235 (M+1). *Anal.* calcd. for $C_{12}H_{10}O_5$: C 61.54; H 4.30. Found C 61.57; H 4.32.

8,10-Dibromo-5-methoxy-7*H*-pyrano[2,3-*g*]-2,3-dihydro-1,4-benzodioxin-7-one (13):
To a solution of the dioxinocoumarine **12** (0.3 g, 1.28 mmol) in acetic acid (10 ml) was added bromide (Br_2, 0.68 ml, 1.28 mmol). The mixture was stirred at room temperature for 1 h then water (10 ml) was added. The white precipitate obtained was recuperated by filtration, washed with diethyl ether and dried to provide 0.38 g of the title compound as a white powder. Yield: 98%; mp = 258-260°C; IR (KBr): ν = 1690 (C=O), 1280 (ether) cm^{-1}; UV(ethanol)[λ max (nm), log ε]: 336, 4.11; ^{1}H-RMN ($CDCl_3$): δ = 4.00 (s, 3H, OCH_3), 4.42 (m, 4H,

OCH_2CH_2O), 8.39 (s, 1H, H_9). MS (CI): m/z = 393 (M+1). *Anal.* calcd. for $C_{12}H_8O_5Br_2$. C 36.77; H 2.05. Found C 36.75; H 2.07.

8,10-Dibromo-5-methoxy-7*H*-pyrano[2,3-*g*]-1,4-benzodioxin-7-one (14):
A mixture of **13** (0.15 g, 0.383 mmol), *N*-bromosuccinimide (0.341 g, 1.92 mmol) in carbone tetrachloride (10 ml) was heated at reflux for 6 h in the presence of benzoyl peroxyde (0.05 g). After cooling, the precipitate of succinimide was eliminated by filtration and the solvent evaporated. The orange mass obtained was solubilized in acetone (10 ml) and the mixture heated at reflux for 6 h in the presence of sodium iodide (NaI, 0.29 g, 1.92 mmol). Purification by column chromatography (eluent: dichloromethane) gave 0.088 g of the title compound **14** as a yellow powder. Yield: 60%; mp = 268°C; IR (KBr): ν = 1720 (C=O), 1680 (enol ether) cm^{-1}; UV(ethanol)[λ max (nm), log ε]: 332, 3.75; 378, 3.86; ^{1}H-RMN ($CDCl_3$): δ = 3.94 (s, 3H, OCH_3), 6.05 (d, J = 3.55 Hz, 1H, OC**H**=), 6.09 (d, J = 3.55 Hz, 1H, OC**H**=), 8.27 (s, 1H, H_9). MS (CI): m/z = 391 (M+1). *Anal.* calcd. for $C_{12}H_6O_5Br_2$: C 36.96; H 1.55. Found C 36.93; H 1.52.

5-Methoxy-7*H*-pyrano[2,3-*g*]-1,4-benzodioxin-7-one (1):
To a solution of **14** (0.06 g, 0.15 mmol) in dimethylformamide (2 ml) were added palladium acetate ($Pd(OAc)_2$, 0.058 g, 0.34 mmol), tri-*o*-tolylphosphine ($P(o\text{-tolyl})_3$, 0.103 g, 0.34 mmol), formic acid (HCOOH, 0.013 g, 0.34 mmol) and triethylamine (Et_3N, 0.047 g, 0.34 mmol). The mixture was heated at 60°C for 4 h, hydrolysed with water and the crude product extrated with diethyl ether. Purification by column chromatography (eluent: dichloromethane) gave 0.028 g of the attempted compound **1** as a white powder. Yield: 80%; mp = 178°C; IR (KBr): ν = 1710 (C=O), 1610 (enol ether) cm^{-1}; UV(ethanol)[λ max (nm), log ε]: 365, 3.78; ^{1}H-RMN ($CDCl_3$): δ = 3.98 (s, 3H, OCH_3), 5.94 (d, J = 3.50 Hz, 1H, OC**H**=), 6.00 (d, J = 3.50 Hz, 1H, OC**H**=), 6.28 (d, $J_{8,9}$ = 9.50 Hz, 1H, H_8), 6.45 (s, 1H, H_{10}), 7.46 (d, $J_{8,9}$ = 9.50 Hz, 1H, H_9). MS (CI): m/z = 391 (M+1). *Anal.* calcd. for $C_{12}H_8O_5$: C 62.07; H 3.47. Found C 62.28; H 3.55.

REFERENCES AND NOTES

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(*Received in Belgium* 14 *September* 1994; *accepted* 12 *December* 1994)