Synthesis and NMR Characterization of a Novel Heterologue of Pyrene: the Naphtho[1,8-*bc*;4,5-*b'c'*]dipyran (1,8-Dioxapyrene)

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1,8-Dioxapyrene, a novel unsubstituted dioxa-analog of pyrene was synthesized from 4-methoxy-1-naphthol in a ten-step reaction involving two *peri*-heterocyclizations. ^1H and ^{13}C nmr indicated a disruption of extended delocalization of π electrons, like that observed with the 1,6-isomer.

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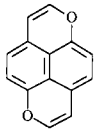
We have previously reported [1] the synthesis of the first unsubstituted dioxa-analog of pyrene, 1,6-dioxapyrene (1,6-DP) (**1**). The ^1H and ^{13}C nmr spectroscopic analysis of this bis-heterocyclic skeleton indicated a disruption of the extended delocalization of π electrons, and a marked ethylenic character of the heterocyclic double bond [2,3]. A photobiological study indicated that 1,6-DP (**1**) is a potent photosensitizer, capable of generating singlet oxygen and inducing oxidative damage to cellular DNA [4].

These results prompted us to synthesize and characterize by ^1H-^{13}C nmr a new dioxa-analog of pyrene, 1,8-dioxapyrene (1,8-DP) (**2**) in order to compare the spectroscopic and photobiological properties of the 1,6- and 1,8-isomers, which only differ in the position of the heteroatoms.



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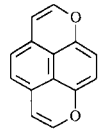


2

Chemistry.

Starting from the commercially available 4-methoxy-1-naphthol (**3**), the reaction involves ten stages affording the end product **2** in an overall yield of 3% (Scheme 1). Electrophilic formylation of methoxynaphthol **3** with dichloromethyl methyl ether in the presence of titanium tetrachloride selectively attacks the *ortho* position of the hydroxyl group [5]. The same regioselectivity has been observed during electrophilic formylation of 1,4-dimethoxynaphthalene **4** [6], either by dichloromethyl methyl ether or by Vilsmeier-Haack reagents.

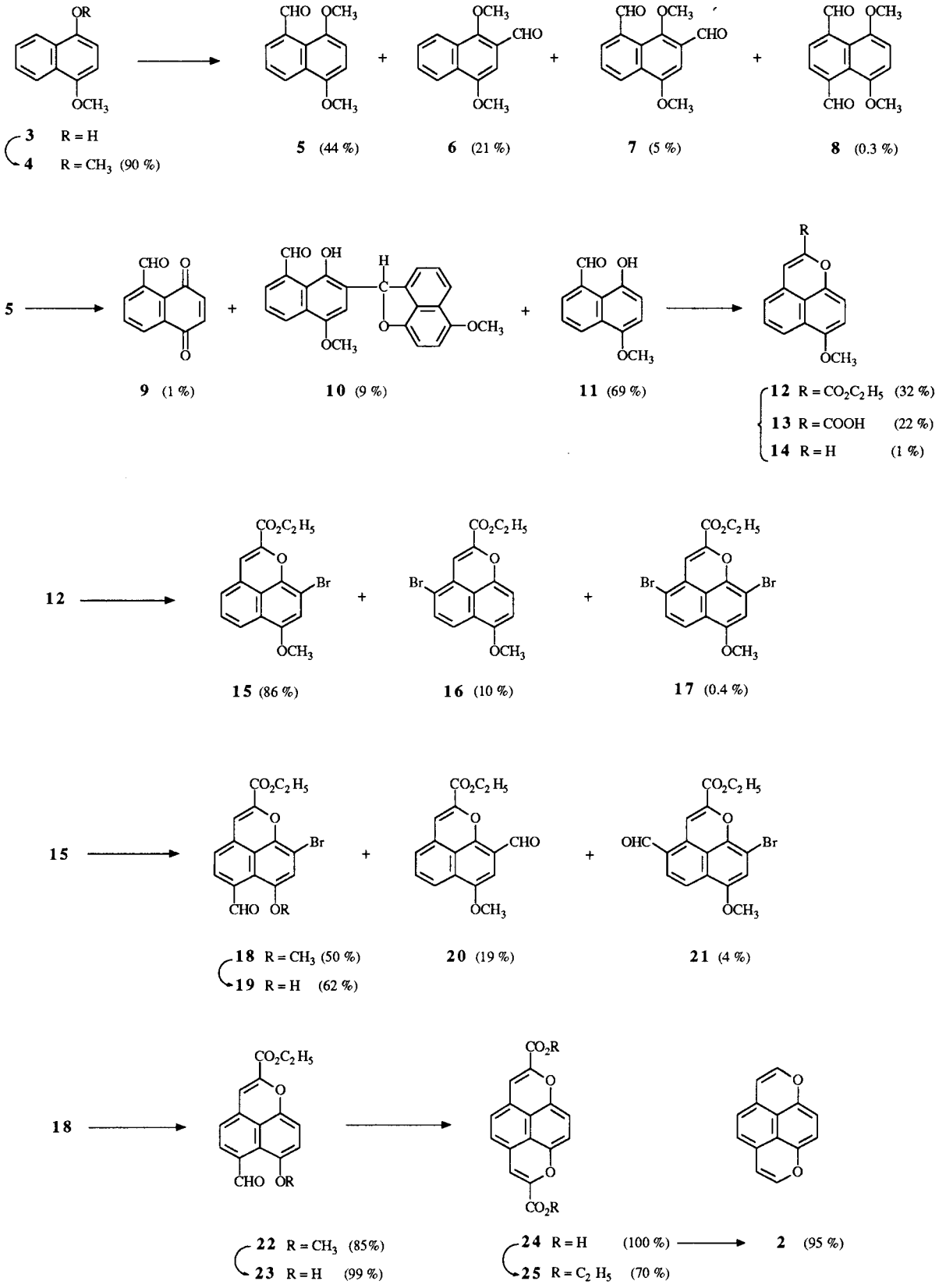
We therefore formylated the dimethoxy derivative **4** *via* metalation with *tert*-butyllithium in pentane-cyclohexane, which gives the required *peri*-substituted aldehyde **5** as

Table 1

Bond Lengths in Å for Compound **10**
(standard deviations indicated in parentheses)

Conformer **a**		Conformer **b**	
C1-C2	1.36 (1)	C31-C32	1.38 (1)
C1-C10	1.40 (1)	C31-C40	1.37 (1)
C1-C16	1.51 (1)	C31-C46	1.55 (1)
C2-C3	1.43 (1)	C32-C33	1.41 (1)
C2-O13	1.38 (1)	C32-O43	1.36 (1)
C3-C4	1.42 (2)	C33-C34	1.42 (1)
C3-C8	1.41 (1)	C33-C38	1.43 (1)
C4-C5	1.38 (2)	C34-C35	1.39 (2)
C4-C14	1.49 (2)	C34-C44	1.48 (2)
C5-C6	1.36 (2)	C35-C36	1.41 (2)
C6-C7	1.37 (2)	C36-C37	1.37 (2)
C7-C8	1.41 (2)	C37-C38	1.42 (1)
C8-C9	1.42 (1)	C38-C39	1.43 (1)
C9-C10	1.37 (1)	C39-C40	1.38 (1)
C9-O11	1.38 (1)	C39-O41	1.38 (1)
O11-C12	1.43 (1)	O41-C42	1.45 (1)
C14-O15	1.24 (2)	C44-O45	1.23 (2)
C16-O17	1.49 (1)	C46-O47	1.47 (1)
C16-C24	1.50 (1)	C46-C54	1.51 (1)
O17-C18	1.35 (1)	O47-C48	1.39 (1)
C18-C19	1.38 (1)	C48-C49	1.38 (1)
C18-C23	1.37 (1)	C48-C53	1.41 (1)
C19-C20	1.43 (1)	C49-C50	1.45 (2)
C20-C21	1.38 (1)	C50-C51	1.38 (2)
C21-C22	1.42 (1)	C51-C52	1.41 (1)
C21-O28	1.35 (1)	C51-O58	1.37 (1)
C22-C23	1.36 (1)	C52-C53	1.39 (1)
C22-C27	1.44 (1)	C52-C57	1.42 (1)
C23-C24	1.40 (1)	C53-C54	1.40 (1)
C24-C25	1.40 (1)	C54-C55	1.38 (1)
C25-C26	1.41 (2)	C55-C56	1.43 (1)
C26-C27	1.38 (2)	C56-C57	1.36 (1)
O28-C29	1.43 (1)	O58-C59	1.42 (2)
O13-O15	2.50 (1)	O43-O45	2.51 (1)

Scheme 1


OR
OCH3
3 R = H
4 R = CH3 (90 %)
CHO OCH3
OCH3
5 (44 %)
OCH3
CHO
OCH3
6 (21 %)
CHO OCH3
CHO
OCH3
7 (5 %)
CHO OCH3
CHO OCH3
8 (0.3 %)
5
CHO O
O
9 (1 %)
CHO OH
H
C
O
OCH3
OCH3
10 (9 %)
CHO OH
OCH3
11 (69 %)
R
O
OCH3
12 R = CO2C2H5 (32 %)
13 R = COOH (22 %)
14 R = H (1 %)
12
CO2C2H5
O
Br
OCH3
15 (86 %)
Br
16 (10 %)
Br
Br
17 (0.4 %)
15
CHO OR
18 R = CH3 (50 %)
19 R = H (62 %)
CHO
20 (19 %)
OHC
21 (4 %)
18
CHO OR
22 R = CH3 (85%)
23 R = H (99 %)
CO2R
24 R = H (100 %)
25 R = C2H5 (70 %)
2 (95 %)

the major product along with the isomer **6** and the two dialdehydes **7** and **8**. These four reaction products were readily separated by column chromatography. Selective monodemethylation of the aldehyde **5** by aluminum chloride afforded the *peri*-hydroxyaldehyde **11** as major product along with a bimolecular condensation product, naphthylnaphtho[1,8-*bc*]furan **10**. The structure of compound **10** as indicated by its nmr and mass spectra, was unambiguously demonstrated by X-ray analysis, which revealed a strong hydrogen bonding between the aldehyde and hydroxyl groups (2.51 Å) and two conformers in the crystal (Figure 1).

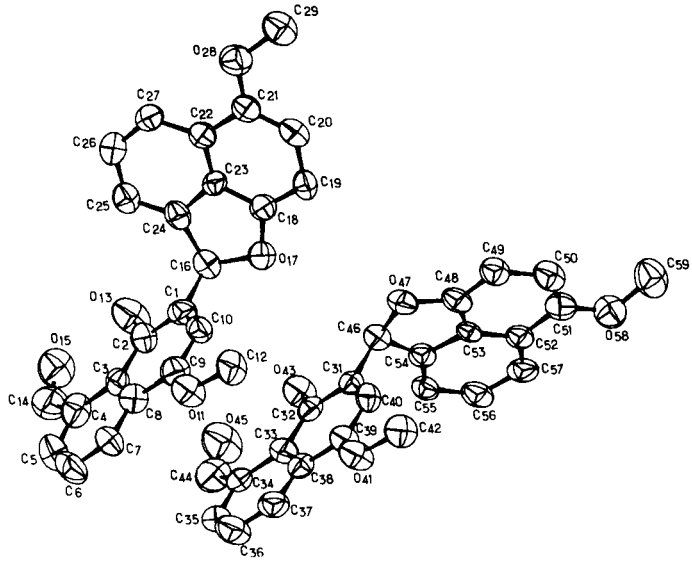


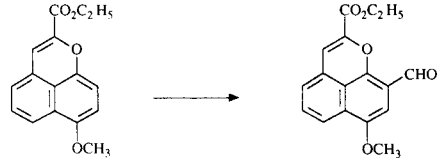
Figure 1. ORTEP drawing of the two conformers of compound **10** showing the π-staking between the two naphthalene rings.

The bond lengths of the two conformers **a** and **b** are listed in Table 1.

During the demethylation of aldehyde **5**, a small amount (1%) of 5-formyl-1,4-naphthoquinone (**9**) was also produced. To our knowledge this is the first description of the quinone aldehyde **9**, apart from the theoretical study of Rozeboom *et al.* [7].

The *peri*-hydroxyaldehyde **11** was annelated to the 7-methoxyoxaphenalenes **12-14** using ethyl bromoacetate as described for the synthesis of 6-methoxyoxaphenalene [8]. Unfortunately, electrophilic formylation of the 7-methoxyoxaphenalene ester **12** yielded only the 9-formyloxaphenalene **20** and not the required *peri*-aldehyde (Scheme 2).

Scheme 2



12 **20**

We therefore attempted to protect position 9 by an easily removable bromine atom. In fact, bromination takes place mainly at position 9, as indicated from the single crystal structure established by X-ray diffraction, yielding the 7-methoxy-9-bromooxaphenalene **15**, along with a small amount (10%) of the 4-bromo isomer and a trace of the dibromo-derivative **17**. The presence of the bromine atom enabled electrophilic formylation *peri* to the methoxy group, yielding the 6-formyl-7-methoxyoxaphenalene **18** as major product together with the debrominated aldehyde **20** resulting from *ipso*-substitution, and a small

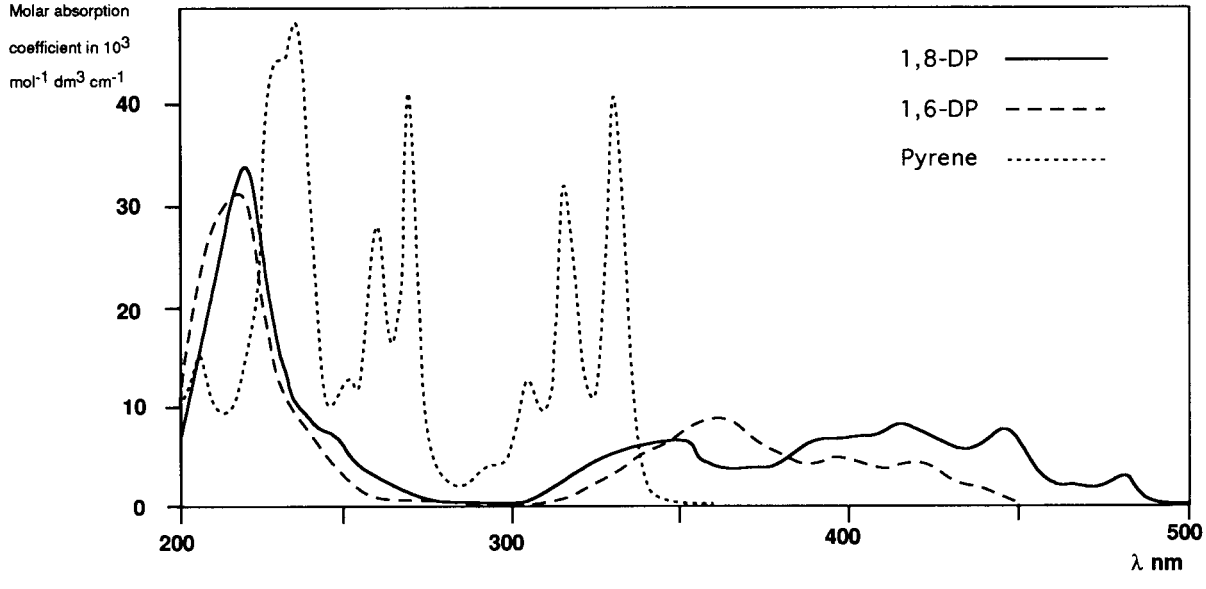
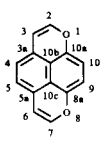
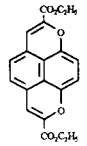
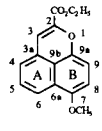
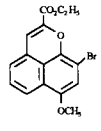
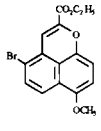
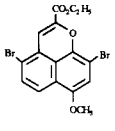
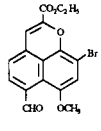
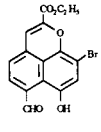
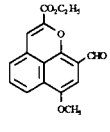
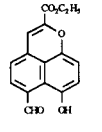


Figure 2. UV-visible spectra of 1,8-DP, 1,6-DP and pyrene, in pentane.

Table 2

^1H ^{13}C NMR Data

	2		25		12		15		16		17		18		19		20		23	
Position	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C	δ ^1H (JHz)	δ 13C
2	6.17 (6.0)	144.76		144.81		143.25		143.10		144.27		144.37		144.20		146.50		142.68		146.44
3	5.35 (6.0)	107.06	6.37	114.19	6.87	113.19	6.81	113.29	7.14	111.05	7.11	111.49	6.97	112.17	6.90	111.87	7.10	113.51	6.88	111.55
3a		126.60		128.36		127.73		127.08		126.75		126.41		132.31		138.58		128.57		139.15
4	6.01	116.56	6.18	120.20	6.83 (6.9)	119.34	6.80 (7.2)	120.35		114.10		115.35	7.00 (7.5)	119.59	6.85 (7.4)	117.82	7.06 (7.1)	120.88	6.77 (7.5)	117.80
5	6.01	116.56	6.18	120.20	7.19 (8.2, 6.9)	126.99	7.14 (7.2, 8.4)	127.08	7.34 (9.2)	130.71	7.32 (9.1)	131.12	7.87 (7.5)	129.85	7.71 (7.4)	145.69	7.45 (7.1, 8.5)	130.33	7.68 (7.5)	146.02
5a		126.60		128.36																
6	5.35	107.06	6.37	114.19	7.70 (8.2)	121.05	7.59 (8.4)	121.28	7.58 (9.2)	122.13	7.49 (9.1)	122.44		132.51		130.28	7.82 (8.5)	121.66		129.98
6a						125.60		124.73		124.00		123.45		122.18		119.74		129.52		119.91
7	6.17	144.76		144.81		149.17		149.19		149.15		149.30		150.08		150.55		148.99		150.30
8					6.65 (8.4)	105.65	6.72	109.69	6.71 (8.5)	105.73	6.82	110.14	7.09	112.26	7.30	121.19	7.05	99.85	7.10 (7.8)	116.72
8a		147.12		147.36																
9	6.18	108.76	6.39	110.37	6.79 (8.4)	107.09		100.04	6.89 (8.5)	108.24		101.56		101.28		106.22		115.89	7.13 (7.8)	112.89
9a						145.89		142.60		144.72		141.76		142.64		141.73		151.00		144.99
9b						124.72		124.73		125.33		125.57		125.01		126.13		123.67		125.71
10	6.18	108.76	6.39	110.37																
10a		147.12		147.36																
10b		126.33		126.34																
10c		126.33		126.34																
OCH_3					3.89	55.64	3.84	55.81	3.91	55.34	3.90	55.97	3.97	55.94			3.95	55.59		
OH															11.54				11.38	
CHO													10.94	193.04	9.49	195.62	10.51	186.62	9.48	195.42
COO				160.96		161.40		160.92		160.98		160.67		160.07		160.05		160.49		160.33
CH_2			4.28	61.81	4.35	61.66	4.35	61.93	4.39	61.83	4.40	62.08	4.40	62.09	4.41	62.55	4.39	61.98	4.40	62.37
CH_3			1.33	14.26	1.38	14.25	1.39	14.22	1.41	14.23	1.43	14.29	1.42	14.15	1.43	14.21	1.41	14.20	1.41	14.17

amount of **21**, an isomer of the aldehyde **18**. Compound **18** was debrominated by heating in hexanoic acid in the presence of copper powder [9]. After demethylation, the *peri*-hydroxylated aldehyde **23** was annelated in the usual way, affording quantitatively the diacid **24**, which was then decarboxylated to 1,8-dioxapyrene (**2**).

This 1,8-dioxa-analog of pyrene **2**, like its isomer 1,6-dioxapyrene (**1**), exhibits less aromatic character than pyrene itself [1,2], as illustrated by ^1H-^{13}C nmr (detailed below) and uv-visible spectroscopy (Figure 2).

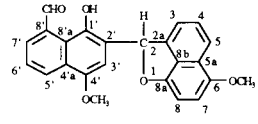
NMR Analysis.

1/ Assignments of the ^1H Spectra.

The signal assignments (Table 2) were first made on the basis of substituent effects and coupling interactions. In compounds **18**, **19**, **23**, which bear a formyl group at position 6, the *ortho* proton H-5 is the most deshielded. In the oxaphenalenes **12**, **15-17**, **20**, which bear a methoxy group at position 7, the proton H-6 is the most deshielded due to the *peri* effect [10]. The other protons of ring A were then readily assigned from decoupling experiments. The protons of ring B were assigned from nuclear Overhauser effects (NOE). Saturation of the methoxy protons led to

Table 3

^1H ^{13}C NMR Data for Naphthyl Naphthofuran **10**



10

Position	δ ^1H (JHz)	δ ^{13}C	Position	δ ^1H (JHz)	δ ^{13}C
1'		145.12	2	7.65	85.92
2'		126.00	2a		142.13
3'	6.88	105.24	3	7.46 (7.0)	118.17
4'		149.03	4	7.47 (7.0)	128.42
4'a		127.04	5	7.84	119.25
5'	8.65 (8.5,1.5)	132.81	5a		124.03
6'	7.56 (7.1, 8.5)	123.70	6		148.30
7'	8.10 (7.1,1.5)	143.73	7	6.75 (8.0)	106.71
8'		132.09	8	6.71 (8.0)	99.31
8'a		122.19	8a		155.03
4'-OCH_3	3.78	56.10	8b		129.19
OH	11.85		6-OCH_3	3.98	56.18
CHO	9.91	197.90			

strong enhancement of the signal of the *ortho* proton H-8. The second proton of ring B was then easily assigned in the oxaphenalenes **12** and **16**. The two singlet resonances H-8, H-3, which cannot be ascribed from the chemical shifts were thus discriminated in compounds **15**, **17**, **18**, **20**. For compound **23**, saturation of the hydroxylic proton resulted in a small enhancement of H-8.

In 1,8-DP (**2**), saturation of the most shielded signal (a doublet) led to significant enhancement of two signals, the second doublet and the most shielded singlet. The irradiated signal was thus ascribed to the pair H-3, H-6, and the enhanced signals to the pairs H-2, H-7 and H-4, H-5 respectively. In the diester **25**, NOE was observed for the singlet at 6.37 ppm on irradiation of the singlet at 6.18 ppm. These singlets belong to the pairs H-3, H-6 and H-4, H-5. Finally, the singlet at 6.37 ppm was assigned unequivocally to the pair H-3, H-6 by correlation to the related carbons C-3 and C-6 (see below for the assignment of these carbons).

The analysis was slightly more difficult for the naphthyl naphthofuran **10** (Table 3).

The two methoxy groups were first discriminated by NOE measurements. Saturation of the most shielded methoxy group (3.78 ppm) led to a strong enhancement for a singlet signal (6.88 ppm) and to a small enhancement for a doublet of doublet (8.65 ppm). This methoxy group must therefore be situated at position 4', and the proximal protons are H-3' and H-5'. Saturation of the second methoxy group only led to a strong enhancement of the most deshielded part (6.75 ppm) of a strongly coupled AB system. This result gave the assignments of H-7 and H-8 in turn. Finally, saturation of the singlet resonance of H-2 resulted in enhancement of the signals of the hydroxyl proton, of H-3' previously assigned and of a multiplet at 7.46 ppm. This last signal is therefore assigned to H-3. The proton H-4 is strongly coupled to H-3 and the third proton in the ring, H-5, is deshielded by the *peri* effect of the methoxy group. These assignments were supported by the suppression of small coupling interactions in the multiplets of the protons H-3 and H-5 situated at the *ortho* and *para* positions, on selective irradiation of proton H-2.

2/ Assignments of the ^{13}C Spectra.

The assignments of the ^{13}C spectra (Tables 2 and 3) relied essentially on the observation of typical multiplet patterns in the undecoupled spectra, and on the ^{1}J, ^{2}J and ^{3}J interactions. δ ^{1}H, δ ^{13}C 2D correlations were also used in certain cases. Apart from the well known coupling interactions involving the hydroxyl and formyl protons, we observed the interactions we had previously found in 1-6 dioxapyrene and its precursors [2], in particular those due to coupling of C-4 with H-3 or C-3 with H-4. In the case of compound **25**, the pair of carbons C-3, C-6 was assigned from the high value of the ^{1}J coupling constant (169.5 Hz).

Discussion.

The ^{1}H and ^{13}C nmr spectra of 1,8-dioxapyrene (**2**) and some of its precursors display some interesting features. As previously observed for its isomer, 1,6-dioxapyrene (**1**) [2], the chemical shifts of the protons in **2** were abnormally low. With respect to oxaphenalene [2], introduction of the second heterocycle induced strong shielding (*circa* 1.1 ppm) at the two positions *ortho* to the points of annelation where maximum mesomeric donor effects of the second oxygen atom would be expected as well as marked shielding (0.54 to 0.66 ppm) at all other positions. In contrast, the ^{13}C nuclei were only significantly shielded in ring B at positions *ortho* and *para* with respect to the carbon bearing the second oxygen atom, and at position 5 in ring A (*i.e.* where there is significant conjugation). These observations can be accounted for by a disruption of the extended delocalization of π electrons. Suppression of the ring current effect thus contributes to the shielding of all the protons by around 0.6 ppm, and the donor effect of the oxygen atom only contributes around 0.5 ppm to the shielding of the protons 5 and 9.

In the precursors of 1,8-dioxapyrene (**2**) as well as in compound **10**, the features of note are the interactions involving the formyl group and either the hydroxyl or the methoxy group in the *peri* position. In the first case, there is a strong hydrogen bond in the *peri* hydroxy aldehydes **10**, **19**, **23**, and there is thus a significant ^{3}J coupling between the hydroxyl and the formyl protons through this bond. With respect to the 1-formyl-8-hydroxy naphthalene in which there was no coupling, the electronic density is reinforced at both sites in compounds **19** and **23**, but only at the hydroxyl in compound **10** giving rise to a slightly smaller coupling. Overall, the $^{3}J_{HO\text{-}CHO}$ values in the compounds under study were slightly lower than those observed in similar precursors of 1,6-dioxapyrene (**1**) where the electronic density was mostly reinforced at the formyl site [2].

When the formyl group was situated *peri* to the methoxy group, such as in compound **18**, saturation of the methyl protons resulted in strong enhancement of the formyl proton signal. This indicated a highly preferred conformation of the formyl group with the proton directed towards the oxygen of the methoxy group, and so the formyl proton is strongly deshielded. Comparison of the methoxy aldehyde **18** with the hydroxy aldehyde **19** further showed that the carbon *ortho* to the formyl group, C-5, undergoes a strong shielding (*circa* 16 ppm) when the carbonyl group is held in close proximity to the related proton. A similar trend was observed in compound **20** where carbon C-8, *ortho* to the carbon bearing the formyl group, is abnormally shielded. The likely preferred conformation is with the formyl proton directed towards the heterocyclic oxygen atom and the carbonyl towards the *ortho* proton.

Finally the influence of the bromine atom on the ^{13}C, ^{1}H coupling constants is of interest. The ^{1}J coupling has been shown to be increased at the *ortho* position in the bromonaphthalenes [11]. The long-range coupling constants might also be significantly increased for the carbon bearing the bromine atom [12]. In the compounds under study, the ^{2}J and ^{3}J interaction coupling constants were increased to 5.9 Hz and 14 Hz respectively.

The most significant coupling constants were as follows: ^{1}H, ^{1}H coupling constants in Hz: $^{3}J_{HO-CHO}$: 1.1 (**19**, **23**), 0.9 (**10**); ^{1}H, ^{13}C coupling constants in Hz for the carbons bearing a bromine atom: $^{2}J_{C_5-H_6}$: 4.6 (**15**), 4 (**17**), 5.9 (**18**), 4.3 (**19**); $^{2}J_{C_4-H_5}$: 3.5 (**16**), 3 (**17**); $^{3}J_{C_4-H_6}$: 13 (**16**), 14 (**17**).

EXPERIMENTAL

Melting points were measured on an Electrothermal digital melting point apparatus and are uncorrected. The nmr spectra were recorded either at 90 MHz (Varian EM 390), at 250 MHz (Bruker AM 250) or at 500 MHz (Bruker AM 500). The various compounds were dissolved in deuteriochloroform (except the diacid **24** which was dissolved in DMSO-d_6) and tetramethylsilane was used as internal reference. The ir spectra were recorded on a Perkin-Elmer 1720 spectrometer, the uv spectra were measured with a Varian-Techtron 635 and the mass spectra were obtained with a Ribermag R10-10 C apparatus. Commercially available reagents and solvents were used without further purification. The yields indicated are the average of at least two experiments. For the two-dimentional δ ^{1}H, δ ^{13}C correlation experiments, the standard Bruker programs were used, with parameters adjusted to ^{1}J or long range coupling. Nuclear Overhauser effects were detected by mean of difference experiments.

1,4-Dimethoxynaphthalene (**4**).

To a stirred solution of commercial (Aldrich) 4-methoxy-1-naphthol (**3**) (50 g, 0.287 mole) and dimethyl sulfate (39.8 g, 0.315 mole) in dry acetone (500 ml), potassium carbonate (43.6 g, 0.316 mole) was added, then the reaction mixture was refluxed for 20 hours. After usual work-up, the crude product was chromatographed (720 g of 230-400 mesh silica gel, elution with dichloromethane-cyclohexane 1/1). Compound **4** (48.5 g, 90%, after recrystallization from 80 ml of cyclohexane) had mp 86-87° (lit [13], mp 86-87.5°).

5,8-Dimethoxy-1-naphthalenecarboxaldehyde (**5**), 1,4-Dimethoxy-2-naphthalenecarboxaldehyde (**6**), 5,8-Dimethoxy-1,7-naphthalenedicarboxaldehyde (**7**), and 5,8-Dimethoxy-1,4-naphthalenedicarboxaldehyde (**8**).

A commercial (2*M*) solution (41 ml, 82 mmoles) of *tert*-butyllithium in pentane was slowly added, with a syringe, under an argon atmosphere, at 20°, to a well-stirred solution of 1,4-dimethoxynaphthalene (**4**) [10] (13.4 g, 71 mmoles) in 180 ml of anhydrous cyclohexane. After 24 hours stirring at 20°, the white suspension obtained was cooled to 0°, then 14.2 ml (15.5 g, 115 mmoles) of *N*-methylformanilide were added with a syringe. The reaction mixture was maintained 24 hours at 20° with stirring, cooled to 0° and quenched with 1*N* hydrochloric acid (100 ml). After addition of ether (750 ml), the organic phase was separated, washed with water until neutral , dried (magnesium sulfate) and the solvents were evaporated. The crude mixture (20 g) was chromatographed (500 g of 230-400 mesh silica gel, elution with dichloromethane), furnishing successively 3.3 g (24%) of recovered starting material, 10.5 g of a mixture of aldehydes **5** and **6** and 1.1 g of a second mixture of the dialdehydes **7** and **8**.

A second chromatography of the mixture of aldehydes **5** and **6** (400 g of 230-400 mesh silica gel, elution with cyclohexane-ethyl acetate 85/15) gave successively the following:

a) The aldehyde **6** (3.2 g, 21%), pale yellow crystals had mp 118-119° (ethanol, lit [6], mp 117°); ^{1}H nmr (90 MHz, deuteriochloroform): δ 4.00 and 4.08 (2s, 2 OCH_3), 7.10 (s, H_3), 7.54-7.56 (m, H_6 and H_7), 8.13-8.33 (m, H_5 and H_8), 10.65 (s, CHO); ir (deuteriochloroform): ν 1677 cm^{-1} (CHO).

b) The *peri*-aldehyde **5** (6.75 g, 44%), yellow crystals, had mp 114-115° (ethanol); ^{1}H nmr (90 MHz, deuteriochloroform): δ 3.95 and 3.97 (2 s, 2 OCH_3), 6.76 and 6.86 (2 d, H_6 and H_7, J_o = 9 Hz), 7.53 (m, H_3), 7.96 (dd, H_4, J_o = 7.5 Hz, J_m = 1.5 Hz), 8.46 (dd, H_2, J_o = 9 Hz), 11.10 (s, CHO); ir (deuteriochloroform): ν 1681 cm^{-1} (CHO).

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.29; H, 5.36.

The mixture of the dialdehydes **7** and **8** (0.9 g) was also separated by column chromatography (80 g of 230-400 mesh silica gel, elution with dichloromethane) furnishing successively:

a) The dialdehyde **7** (0.87 g, 5%), pale yellow leaflets had mp 172-173° (ethanol); ^{1}H nmr (90 MHz, deuteriochloroform): δ 4.06 and 4.11 (2s, 2 OCH_3), 7.28 (s, H_6), 7.66 (m, H_3), 8.06 (dd, H_4, J_o = 7.5 Hz, J_m = 1.5 Hz), 8.43 (dd, H_2, J_o = 9 Hz), 10.56 and 11.00 (2s, 2 CHO); ir (deuteriochloroform): ν 1680 cm^{-1} (CHO).

Anal. Calcd. for $C_{14}H_{12}O_4$: C, 68.85; H, 4.95. Found: C, 68.54; H, 4.89.

b) The dialdehyde **8** (0.05 g, 0.3%), yellow crystals, had mp 225-226° (ethanol); ^{1}H nmr (90 MHz, deuteriochloroform): δ 3.96 (s, 2 OCH_3), 6.93 (s, H_6 and H_7), 7.78 (s, H_2 and H_3), 10.90 (s, 2 CHO); ir (deuteriochloroform): ν 1684 cm^{-1} (CHO).

Anal. Calcd. for $C_{14}H_{12}O_4$: C, 68.85; H, 4.95. Found: C, 68.60; H, 4.82.

5-Formyl-1,4-naphthoquinone (**9**), (8-Formyl-1-hydroxy-4-methoxy-2-naphthyl)-2-(6-methoxynaphtho[1,8-*bc*]furan) (**10**), and 8-Hydroxy-5-methoxy-1-naphthaldehyde (**11**).

A solution of the aldehyde **5** (29 g, 0.13 mole) in dichloromethane (150 ml) was added dropwise, at 0°, to a stirred suspension of aluminum chloride (28.7 g, 0.21 mole) in dichloromethane (300 ml). The mixture was stirred for three additional hours at room temperature, then quenched by pouring onto ice. After separation, the organic layer was thoroughly washed with water, dried (sodium sulfate) and the solvent was evaporated. The crude product (27.6 g) was then subjected to column chromatography (1,200 g of 230-400 mesh silica gel, elution with dichloromethane), furnishing the following:

a) The bimolecular condensation compound **10** (2.27 g, 9%), deep red prisms, had mp 186-187° (toluene); ^{1}H-^{13}C nmr: *cf* Table 3; ir (deuteriochloroform): ν 1662 cm^{-1} (CHO); uv (ethanol); λ max (log ϵ) 211 (4.94), 247 (4.52), 284 (4.21), 344 nm (4.11); ms: (DCI, NH_3) m/z (%) 387 ($[M+H]^+$, 100).

Anal. Calcd. for $C_{24}H_{18}O_5$: C, 74.60; H, 4.70. Found: C, 74.56; H, 4.57.

b) The *peri*-hydroxyaldehyde **11** (18.7 g, 69%), purple prisms

had mp 103-104° (cyclohexane); ^{1}H nmr (90 MHz, deuteriochloroform): 3.96 (s, OCH_3), 6.93 and 7.12 (2d, H_6 and H_7, J_o = 9 Hz), 7.45-7.65 (m, H_3), 8.06 (dd, H_4, J_o = 7.5 Hz, J_m = 1.8 Hz), 8.70 (dd, H_2, J_o = 9 Hz, J_m = 1.5 Hz), 9.88 (s, CHO), 11.00 (s, OH); ir (deuteriochloroform): ν 1666 cm^{-1} (CHO).

Anal. Calcd. for $C_{12}H_{10}O_3$: C, 71.28; H, 4.98. Found: C, 71.05; H, 4.80.

c) The naphthoquinone aldehyde **9** (0.29 g, 1%), black microcrystals, had mp 126-127° (toluene); ^{1}H nmr (90 MHz, deuteriochloroform): 7.00 (s, H_2 and H_3), 7.73-7.96 (m, H_7), 8.10 (dd, H_6, J_o = 8.2 Hz, J_m = 1.6 Hz), 8.31 (dd, H_8, J_o = 7.8 Hz), 10.83 (s, CHO); ir (deuteriochloroform): ν 1667 and 1697 cm^{-1} (C=O and CHO); ms (70 eV) m/z (%) 186 (M^+, 100), 158 (35), 130 (50), 104 (60), 102 (80).

Anal. Calcd. for $C_{11}H_6O_3$: C, 70.97; H, 3.25. Found: C, 70.73; H, 3.15.

This compound **9** needs to be stored in the dark and at low temperature.

2-Carbethoxy-7-methoxynaphtho[1,8-*bc*]pyran (**12**), 7-Methoxynaphtho[1,8-*bc*]pyran-2-carboxylic Acid (**13**), and 7-Methoxynaphtho[1,8-*bc*]pyran (**14**).

A reaction mixture of the aldehyde **11** (18 g, 89 mmoles), ethyl bromoacetate (17.85 g, 107 mmoles), anhydrous potassium carbonate (27 g, 195 mmoles) and dimethylformamide (180 ml) was gently refluxed for 75 minutes under stirring. After cooling, the major part of the DMF was evaporated at 60°/0.1 Torr and water (50 ml) and dichloromethane (150 ml) were added, then the two phases were stirred for 15 minutes. The aqueous phase, extracted twice with dichloromethane (25 ml) was kept separately and the organic phases were joined together, dried (sodium sulfate) and evaporated, furnishing 20 g of a crude mixture of compounds **12** and **14**.

Column chromatography (500 g of 230-400 mesh silica gel, elution with dichloromethane-cyclohexane (50/50)) yielded successively:

a) The oxaphenalene **14** (0.175 g, 1.6%), pale yellow needles had mp 64-65° (pentane at -30°); ^{1}H nmr (90 MHz, deuteriochloroform): 3.90 (s, OCH_3), 5.85 (d, H_3, J_{3-2} = 6 Hz), 6.60-6.76 (m, H_2 and H_4), 6.66 (s, H_8 and H_9), 7.21 (m, H_5), 7.66 (dd, H_6, J_o = 9 Hz, J_m = 1.2 Hz); uv (ethanol): λ max (log ϵ) 203 (4.36), 235 (4.38), 292 (3.65), 304 (3.74), 347 nm (3.89).

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 79.03; H, 5.16.

b) The ester **12** (7.7 g, 32%), orange crystals had mp 120-121° (cyclohexane-toluene 9/1); ^{1}H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1723 cm^{-1} (CO); uv (ethanol): λ max (log ϵ) 206 (4.61), 260 (4.38), 313 (3.75), 340 (3.80), 357 nm (3.91).

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.10; H, 5.22. Found: C, 71.10; H, 5.08.

The acidification of the aqueous phase provided the acid **14**, contaminated with 20% of non-dehydrated cyclized acid. So, the crude product thus obtained (5.1 g) was boiled 30 minutes in acetic anhydride (40 ml), the acetic anhydride was evaporated under reduced pressure and the pure acid **14** (4.7 g, 22%), pale yellow powder, after washing with water and drying, had mp 262-263°; ^{1}H nmr (90 MHz, DMSO-d_6): 3.90 (s, OCH_3), 6.78 (s, H_8 and H_9), 6.86 (s, H_3), 6.93 (dd, H_4, J_o = 7.5 Hz, J_m = 1.5 Hz), 7.26 (m, H_5), 7.63 (dd, H_6, J_o = 9 Hz), CO_2H indiscernable; ir (potassium bromide): ν 1725 cm^{-1} (CO_2H).

Anal. Calcd. for $C_{14}H_{10}O_4$: C, 69.42; H, 4.16. Found: C, 69.19; H, 4.05.

9-Bromo-2-carbethoxy-7-methoxynaphtho[1,8-*bc*]pyran (**15**), 4-Bromo-2-carbethoxy-7-methoxynaphtho[1,8-*bc*]pyran (**16**), and 4,9-Dibromo-2-carbethoxy-7-methoxynaphtho[1,8-*bc*]pyran (**17**).

To a solution of ester **12** (10 g, 37 mmoles) in chloroform (500 ml) a solution of bromine (6.22 g, 39 mmoles) in chloroform (200 ml) was slowly added at 20° under stirring. After addition of bromine, stirring was continued for three hours, then nitrogen was bubbled through the stirred solution. After washing with water (5 x 100 ml), the organic phase was dried (sodium sulfate) and the solvent evaporated. The crude product obtained (13.5 g) was recrystallized from 60 ml of cyclohexane-ethyl acetate 80/20, furnishing 8.45 g (65%) of the monobromo derivative **15** as orange crystals, mp 126-127°; ^{1}H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1728 cm^{-1} (CO_2); uv (ethanol): λ max (log ϵ) 211 (4.49), 226 (4.50), 259 (4.24), 315 (3.72), 345 (3.77), 363 nm (3.86).

Anal. Calcd. for $C_{16}H_{13}BrO_4$: C, 55.04; H, 3.75; Br, 22.88. Found: C, 55.32; H, 3.88; Br, 22.70.

The evaporation of the mother liquors yielded 3.6 g of a mixture which was chromatographed (450 g of 230-400 mesh of silica gel, elution with cyclohexane-ethyl acetate 70/30), furnishing the following:

a) A second crop of the 9-bromo derivative **15** (2.6 g) raising the total yield to 86%.

b) The 4-bromo derivative **16** (1.3 g, 10%), orange crystals, had mp 136-137° (cyclohexane-ethyl acetate 95/5); ^{1}H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1728 cm^{-1} (CO_2); uv (ethanol): λ max (log ϵ) 215 (4.60), 264 (4.27), 276 (4.27), 316 (3.70), 345 (3.83), 362 nm (3.93).

Anal. Calcd. for $C_{16}H_{13}BrO_4$: C, 55.04; H, 3.75; Br, 22.88. Found: C, 55.25; H, 3.60; Br, 22.63.

c) The dibromo derivative **17** (63 mg, 0.4%), orange-red crystals, had mp 154-155° (cyclohexane-ethyl acetate 70/30); ^{1}H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1731 cm^{-1} (CO_2); uv (ethanol): λ max (log ϵ) 206 (4.84), 280 (4.31), 317 (3.83), 350 (3.76), 367 nm (3.85).

Anal. Calcd. for $C_{16}H_{12}Br_2O_4$: C, 44.89; H, 2.83; Br, 37.33. Found: C, 44.99; H, 2.83; Br, 37.05.

9-Bromo-2-carbethoxy-6-formyl-7-methoxynaphtho[1,8-*bc*]pyran (**18**), 2-Carbethoxy-9-formyl-7-methoxynaphtho[1,8-*bc*]pyran (**20**), and 9-Bromo-2-carbethoxy-4-formyl-7-methoxynaphtho[1,8-*bc*]-pyran (**21**).

A solution of the bromo derivative **15** (10.5 g, 30 mmoles) in dichloromethane (200 ml) was slowly added at 0° to a stirred solution of titanium tetrachloride (12.6 g, 66 mmoles) and dichloromethyl methyl ether (3.8 g, 33 mmoles) in dichloromethane (200 ml). The mixture was stirred at 0° for 45 minutes, then at room temperature for 21 hours. After quenching with water (300 ml), the organic layer was separated, then carefully washed with water and dried (magnesium sulfate). Evaporation of the solvent left a mixture of three compounds (11.8 g) which was submitted to column chromatography (500 g of 230-400 mesh of silica gel, elution with dichloromethane) furnishing the following:

a) The starting product **15** (1.28 g) was recovered.

b) The 9-bromooxaphenalene-*peri*-aldehyde **18** (5.6 g, 50%), red crystals, had mp 169-170° (toluene); ^{1}H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1734 (CO_2), 1674 cm^{-1} (CHO); uv (ethanol): λ max (log ϵ) 206 (4.53), 231 (4.37), 279 (4.45), 358 (3.62), 375 (3.78), 460 nm (3.75).

Anal. Calcd. for $C_{17}H_{13}BrO_5$: C, 54.13; H, 3.47; Br, 21.18. Found: C, 53.97; H, 3.35; Br, 20.89.

c) The debrominated oxaphenalene aldehyde **20** (1.7 g, 19%), yellow crystals, had mp 172-173° (toluene-cyclohexane 1/1); ^1H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1729 (CO_2), 1673 cm^{-1} (CHO); uv (ethanol): λ max (log ϵ) 214 (4.46), 245 (4.50), 270 (4.31), 315 (3.69), 365 (3.91), 384 (4.04), 443 nm (3.84); ms: (DCI, NH_3) m/z (%) 316 ([M + NH_3]$^+$, 100), 299 ([M + H]$^+$, 85).

Anal. Calcd. for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73. Found: C, 68.35; H, 4.61.

d) The 9-bromooxaphenalene aldehyde **21** (0.43 g, 4%), orange crystals, had mp 188-189° (toluene); ^1H nmr (90 MHz, deuteriochloroform): 1.40 (t, CH_3-CH_2), 3.93 (s, OCH_3), 4.43 (q, CH_3-CH_2), 7.06 (s, H_8), 7.63 and 7.80 (2d, H_5 and H_6, J_o = 9 Hz), 8.16 (s, H_3), 10.43 (s, CHO); ir (deuteriochloroform): ν 1732 (CO_2), 1686 cm^{-1} (CHO); uv (ethanol): λ max (log ϵ) 213 (4.53), 243 (4.26), 283 (4.39), 395 (3.69), 445 nm (3.69).

Anal. Calcd. for $C_{17}H_{13}BrO_5$: C, 54.13; H, 3.47; Br, 21.18. Found: C, 53.94; H, 3.40; Br, 20.94.

Formylation of the 2-Carbethoxy-7-methoxynaphtho[1,8-*bc*]pyran (**12**).

A solution of compound **12** (0.27 g, 1 mmole) in dichloromethane (10 ml) was slowly added to a cooled (0°), well stirred solution of dichloromethyl methyl ether (0.13 g, 1.1 mmoles), and titanium tetrachloride (0.42 g, 2.2 mmoles) in dichloromethane (10 ml). After the stirring was continued for 4 hours at 20°, the reaction mixture was quenched with water (20 ml). After the usual treatment, the crude product (0.28 g) was purified through column chromatography (25 g of 230-400 mesh of silica gel, elution with cyclohexane-ethyl acetate 70/30) furnishing 0.26 g (87%) of the aldehyde **20** described above (mixed mp, 172-173°).

9-Bromo-2-carbethoxy-6-formyl-7-hydroxynaphtho[1,8-*bc*]pyran (**19**).

A solution of the aldehyde **18** (150 mg, 0.4 mmole) in dichloromethane (5 ml) was added dropwise, at 20°, to a stirred suspension of aluminum chloride (600 mg, 4.5 mmoles) in dichloromethane (5 ml). The mixture was stirred for five additional hours, then quenched with water. After usual work-up, the crude product (130 mg) was chromatographed on silica gel (20 g, 230-400 mesh, elution with dichloromethane) to yield 89 mg (62%) of the aldehyde **19** as dark red crystals, mp 208-209°; ^1H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1737 (CO_2), 1658 cm^{-1} (CHO); uv (ethanol): λ max (log ϵ) 214 (4.44), 230 (4.32), 286 (4.36), 379 (3.62), 479 nm (3.67).

Anal. Calcd. for $C_{16}H_{11}BrO_5$: C, 52.92; H, 3.05; Br, 22.00. Found: C, 52.76; H, 2.96; Br, 21.83.

2-Carbethoxy-6-formyl-7-methoxynaphtho[1,8-*bc*]pyran (**22**).

A mixture of the brominated aldehyde **18** (5 g, 13 mmoles), copper powder (40 g) and caproic acid (100 ml) was refluxed for one hour with efficient stirring. After cooling, the copper was separated by filtration and washed three times with dichloromethane (20 ml). The solvent and caproic acid were evaporated at 100° under vacuum (0.1 Torr) and the crude product was purified by column chromatography (600 g of 230-400 mesh silica gel, elution with dichloromethane). The aldehyde **22** (3.36 g, 85%), red crystals, had mp 171-172°; ^1H nmr (90 MHz, deuteriochloroform): 1.40 (t, CH_3-CH_2), 3.96 (s, OCH_3), 4.40 (q, CH_3-CH_2), 6.83-7.03 (m, H_3, H_4, H_8 and H_9), 7.86 (d, H_5, J_o = 8.5 Hz), 11.05 (s, CHO); ir (deuteriochloroform): ν 1729 (CO_2), 1671 cm^{-1} (CHO); uv (ethanol): λ max (log ϵ) 209 (4.49), 278 (4.44), 353 (3.53), 370 (3.67), 465 nm (3.78).

Anal. Calcd. for $C_{17}H_{14}O_5$: C, 68.45; H, 4.73. Found: C, 68.44; H, 4.69.

2-Carbethoxy-6-formyl-7-hydroxynaphtho[1,8-*bc*]pyran (**23**).

A solution of the above aldehyde **22** (2.6 g, 9 mmoles) in dichloromethane (50 ml) was added dropwise, at 20°, to a stirred suspension of aluminum chloride (10.4 g, 75 mmoles) in dichloromethane (50 ml). The mixture was stirred for twenty additional hours, then quenched with water. After usual work-up, the crude product (2.5 g) was dissolved in boiling toluene (200 ml). After cooling to 70°, hot cyclohexane (200 ml) was added, then the solution was cooled to -30° for one night to yield 2.45 g (99%) of dark red crystals, mp 167-168°; ^1H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1734 (CO_2), 1656 cm^{-1} (CHO); uv (ethanol): λ max (log ϵ) 210 (4.48), 287 (4.40), 373 (3.56), 497 nm (3.75).

Anal. Calcd. for $C_{16}H_{12}O_5$: C, 67.60; H, 4.25. Found: C, 67.55; H, 4.12.

Naphtho[1,8-*bc*;4,5-*b'c'*]dipyran-2,7-dicarboxylic Acid (**24**).

A mixture of the above aldehyde **23** (2 g, 7 mmoles), ethyl bromoacetate (1.42 g, 8.5 mmoles), potassium carbonate (2.8 g, 20 mmoles) and dimethylformamide (50 ml) was gently refluxed for 3 hours under stirring. After cooling to 80°, 10 ml of a 1*M* aqueous potassium carbonate solution was added and the mixture was then refluxed for one hour under stirring. After elimination of the solvents (100°, 0.1 Torr), the crude orange residue was dissolved in water (50 ml) and the diacid **24** was precipitated at *p*H = 2, with efficient stirring, by acidification with dilute hydrochloric acid. The free acid was separated by centrifugation, washed three times with water and dried. This diacid **24** (2.08 g, 100%), black crystals, had mp over 260°; ^1H nmr (250 MHz, DMSO-d_6): 6.39 (s, H_9 and H_{10}), 6.45 (s, H_4 and H_5), 6.50 (s, H_3 and H_6); ir (potassium bromide): ν 1694 cm^{-1} (CO_2).

Anal. Calcd. for $C_{16}H_8O_6$: C, 64.87; H, 2.72. Found: C, 64.65; H, 2.62.

2,7-Dicarbethoxynaphtho[1,8-*bc*;4,5-*b'c'*]dipyran (**25**).

A solution of the above diacid **24** (100 mg, 0.33 mmole) in 20 ml of absolute ethanol saturated with gaseous hydrochloric acid was gently refluxed for 18 hours with 5 minutes of gaseous hydrochloric acid bubbling every six hours. After elimination of the solvent under reduced pressure, the brown residue was column chromatographed (20 g of 230-400 mesh silica gel, elution with dichloromethane) to obtain the ester **25** (83 mg, 70%) as purple needles (toluene-cyclohexane 50/50), mp 222-223°; ^1H-^{13}C nmr: *cf* Table 2; ir (deuteriochloroform): ν 1719 cm^{-1} (CO_2); uv (ethanol): λ max (log ϵ) 203 (4.59), 225 (4.52), 255 (4.47), 334 (3.78), 537 nm (3.87).

Anal. Calcd. for $C_{20}H_{16}O_6$: C, 68.18; H, 4.58. Found: C, 68.16; H, 4.58.

Naphtho[1,8-*bc*;4,5-*b'c'*]dipyran (1,8-Dioxapyrene) (**2**).

All the operations of this decarboxylation were conducted in inactinic glass vessels.

A mixture of the diacid **24** (0.5 g, 1.7 mmoles), copper powder (1 g) and quinoline (10 ml) was refluxed for 30 minutes. After the

usual work-up, the crude product was dissolved in chloroform and the solution was filtered through a short silica gel column. After evaporation of the solvent, the dioxapyrene **2** (336 mg, 95%) was obtained as orange crystals, mp 115-116° (cyclohexane); ^1H-^{13}C nmr: *cf* Table 2; uv (pentane): λ max (log ε) 219 (4.62), 332 (3.69), 344 (3.71), 388 (3.79), 410 (3.90), 440 (3.76), 473 nm (3.57); ms: (70 eV) m/z (%) 208 (M^+, 100), 179 (30), 152 (35).

Anal. Calcd. for $C_{14}H_8O_2$: C, 80.76; H, 3.87. Found: C, 80.69; H, 3.78.

This compound needs to be stored at -30° in the dark.

X-Ray Crystallography of the Naphthyl Naphthofuran **10**.

A crystal of **10** was obtained by slow recrystallization from a saturated toluene solution. All data were collected at 20° on an Enraf-Nonius diffractometer with graphite-monochromated Mo-K_α radiation in the range $2\theta < 50°$ with the ω-2θ scan mode. 1437 reflections, out of 3195, had $I > 3\sigma(I)$ and were used. The structure was solved by direct methods, using the Mithril package [14] and refined by block-diagonal least-squares method.

The non-hydrogen atoms in **10** were assigned anisotropic thermal parameters. All hydrogen atoms were placed in theoretical positions [15]. The final reliability factor R was 0.054. The ORTEP drawing [16] along with the atom numbering are shown in Figure 1.

Crystallographic data of **10** are $C_{24}H_{18}O_5$: M = 386.4 orthorhombic, space group $P2_12_12_1$, a = 23.440 (4), b = 14.164 (2) and c = 11.125 (2), v = 3693.5 Å^3 (Z = 8), two independent molecules per asymmetric unit, D_c = 1.389 g-cm^{-3}; crystal size: 0.2 x 0.3 x 0.5 mm. Tables of final atomic parameters, Beq factors, bond angles and Fo-Fc tables are available on request from the authors. Bond lengths for the two independent molecules are given in Table 1; they are in fairly good agreement.

There is an O-H···O chelated hydrogen bond between O(13) and O(15) for one molecule, and between O(43) and O(45) for the other, with a O···O distance, respectively equal to 2.50 (1) and 2.51 (1) Å.

The chelated hydrogen bonds lead to an important angular deformation: the C(3)-C(4)-C(14) and C(33)-C(34)-C(44) angles are close to 130°, instead of the usual 120° angle value.

The C(1) to O(15) and C(31) to O(45) groups are perfectly planar. It is the same for C(16) to C(29) and C(46) to C(59) groups. The two molecules only differ by the torsion angle around C(1)-C(16) and C(31)-C(46) with C(2)-C(1)-C(16)-O(17) and C(32)-C(31)-C(46)-C(47) equal to -155° and 157°, respectively.

REFERENCES AND NOTES

[1] J.-P. Buisson and P. Demerseman, *J. Heterocyclic Chem.*, **27**, 2213 (1990).

[2] N. Platzer, J.-P. Buisson and P. Demerseman, *J. Heterocyclic Chem.*, **29**, 1149 (1992).

[3] J.-P. Bideau, M. Cotrait, J.-P. Buisson and P. Demerseman, *Acta Cryst.*, **C48**, 1129 (1992).

[4] D. Averbeck, K. Polasa, J.-P. Buisson, R. Bensasson, M. Rougée, J. Cadet, J.-L. Ravanat, F. Périn, P. Vigny and P. Demerseman, *Mutat. Res.*, in press.

[5] J.-P. Buisson and P. Demerseman, unpublished results.

[6] N. P. Buu-Hoï and D. Lavit, *J. Chem. Soc.*, 1743 (1956).

[7] M. D. Rozeboom, I. M. Tegmo-Larson and K. N. Houk, *J. Org. Chem.*, **46**, 2338 (1981).

[8] J.-P. Buisson and R. Royer, *J. Heterocyclic Chem.*, **25**, 539 (1988).

[9] W. T. Smith, Jr., *J. Am. Chem. Soc.*, **71**, 2855 (1949).

[10] F. Gobert, S. Combrisson and N. Platzer, *Tetrahedron*, **30**, 2919 (1974).

[11] J. Seita, T. Drakenberg and J. Sandström, *Org. Magn. Res.*, **11**, 239 (1978).

[12] L. Ernst, V. Wray, V. A. Chertkow and N. M. Sergeyew, *J. Magn. Reson.*, **25**, 123 (1977).

[13] B. R. Baker and G. H. Carlson, *J. Am. Chem. Soc.*, **64**, 2657 (1942).

[14] C. J. Gilmore, *J. Appl. Cryst.*, **17**, 42 (1984).

[15] M. S. Lehman, T. F. Koetzle and W. C. Hamilton, *J. Amer. Chem. Soc.*, **94**, 2657 (1972).

[16] C. K. Johnson, ORTEP. Rapport ORNL-3794, Oakridge National Laboratory, Tennessee, USA, 1965.