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Structure of a Powerful Mutagenic Compound: 6-Methoxy-2-nitronaphtho-[1,8-*bc*]pyran

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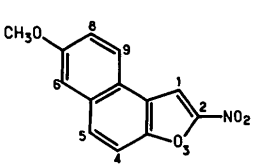
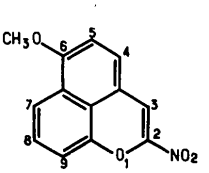
Abstract. 6-Methoxy-2-nitro-1-oxaphenalene, $C_{13}H_9NO_4$, $M_r = 243.2$, triclinic, $P\bar{1}$, $a = 7.0202$ (5), $b = 8.789$ (3), $c = 9.548$ (1) Å, $\alpha = 68.807$ (2), $\beta = 80.340$ (8), $\gamma = 78.087$ (14)°, $V = 534.7$ Å^3, $Z = 2$, $D_x = 1.51$ g cm^{-3}, λ(Mo $K\bar{\alpha}$) = 0.71073 Å, $\mu = 1.06$ cm^{-1}, $F(000) = 252$, $T = 293$ K, $R = 0.039$ for 2149 unique reflections having $I > 3\sigma(I)$. The oxaphenalene system is planar; the methyl of the methoxy group and both O atoms of the nitro group are slightly out of the oxaphenalene mean plane. The C(2)—C(3) bond shows a greater ethylenic character than that observed in the 2-nitronaphthofuran series. Electronic distribution and molecular electrostatic potentials are compared with those of 7-methoxy-2-nitronaphtho[2,1-*b*]furan.

Introduction. The synthetic 2-nitronaphthofurans were shown to be very potent genotoxic agents in both bacterial and mammalian tests (Weill-Thévenet, Buisson, Royer & Hofnung, 1981; Arnaise, Boeuf, Buisson, Cantat, Demerseman, Einhorn, Lamotte, Lemelin, Brimer, Perdue, Hsie, Royer, Kelly & Hofnung, 1986; Royer & Buisson, 1986). Among the nitronaphthofurans, the 7-methoxy-2-nitronaphtho[2,1-*b*]furan (1) (R 7000) proved to be one of the most powerful of the series (Quillardet, Huisman, D'Ari & Hofnung, 1982; Royer, 1986). Their carcinogenicity was also demonstrated on injection into rats and mice (Salmon, Buisson, Zafrani, Aussepé & Royer, 1986; Salmon, Buisson, Vielh, Aussepé & Royer, 1986; Salmon, Buisson, Demerseman, Einhorn, Aussepé, Zafrani & Royer, 1987).



(1)



(2)

The 2-nitronaphtho[1,8-*bc*]pyrans, which are six-membered analogues of nitronaphthofurans, possess the same oxyvinyl pharmaco-toxicophore, which was proved to be the main structural element responsible for the biological activities of 2-nitroarenofurans (Royer, 1986; Royer & Buisson, 1986). These heterocyclic compounds have been shown to elicit a powerful genotoxic activity in bacterial and mammalian tests. Among them, 6-methoxy-2-nitronaphtho[1,8-*bc*]pyran (2) and R 7000 (1) were shown to be very efficient in the DNA-amplification test. 6-Methoxy-2-nitro-1-oxaphenalene (2) is a faster acting compound than 7-methoxy-2-nitronaphtho-[2,1-*b*]furan (1) for tumour genesis (Salmon, Buisson, Hendrickx, Vielh, Aussepé, Moens & Royer, 1989) and is also the most powerful direct-acting mutagenic agent on the mammalian cells (Royer, Buisson, Vleminckx & Moens, 1986).

In order to establish structure–activity relationships between the 2-nitro-naphthofuran and oxaphenalene series, we undertook a radiocrystallographic and electronic study of the nitrooxaphenalene (2) in comparison with the previously established data for (1) (Bravic, Bideau & Courseille, 1982).

Experimental. Compound (2) was prepared according to a process recently described (Royer, Buisson, Vleminckx & Moens, 1986; Buisson & Royer, 1988). Large red crystals were obtained by slow evaporation from ethanol solution. The crystal used had a polyhedral shape with approximate cell dimensions $0.5 \times 0.4 \times 0.4$ mm. Unit-cell parameters were obtained from a least-squares fit of the setting angles for 25 centred reflections with $15 < \theta < 26°$; 2θ range 2–60°, ω–2θ scan method. Data were collected on an Enraf–Nonius CAD-4 four-circle diffractometer, equipped with a graphite monochromator, for $-9 \le h \le 9$, $-12 \le k \le 12$, $-13 \le l \le 13$ and $\sin\theta/\lambda <$

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0.70 $Å^{-1}$; variable scan width $\Delta\omega = (1.3 + 0.5\tan\theta)°$ and detector aperture $\Delta l = (4.0 + 2.4\tan\theta)$ mm. Three standard reflections ($2\bar{4}3$, $\bar{1}54$ and 484) were measured after every 200 reflections. No absorption correction was applied. Averaging equivalent reflections gave 3158 independent reflections, with $R_{int} = 0.025$, out of which 2149 reflections with $I > 3\sigma(I)$ were considered to be observed. The structure was solved using the *MITHRIL* package (Gilmore, 1984). All parameters were refined by least-squares refinement of $\sum w(|F_o| - |F_c|)^2$ with $w = w_o/1 + a(|F_o| - b)^2$ where $a = 0.03$, $b = 10$ and $w_o = 2|F_o|/F_o^2$. H atoms were located from a difference Fourier synthesis and the refinement was resumed with anisotropic thermal factors for C, N and O atoms and isotropic factors for H atoms. Diffusion factors from *International Tables for X-ray Crystallography* (1974, Vol. IV) for non-H atoms and from Stewart, Davidson & Simpson (1965) for H atoms. Final $R = 0.039$, $wR = 0.042$, $S = 0.76$ for 199 refined parameters; $(\Delta/\sigma)_{max} = 0.3$ and maximum and minimum residual electronic density $\Delta\rho = -0.13$ and 0.16 e $Å^{-3}$, respectively. An *ORTEP* drawing (Johnson, 1965) of compound (2) is shown in Fig. 1. Partial atomic charges were calculated using the *MOPAC* program (Stewart, 1988, 1989). Molecular electrostatic potential (MEP) maps have been calculated for the nitro derivatives (1) and (2) using the *VSS* package (Grassy, Rival, Bonnafous, Adam, Teulade & Chapat, 1985) and are shown in Fig. 2.

Discussion. The atomic coordinates, including those of H atoms, are given in Table 1.* Bond lengths and angles are given in Table 2. There is good agreement with those found in similar oxaphenalene compounds (Bideau, Cotrait, Buisson & Demerseman, 1991), except for the O(1)—C(2) bond length which is shorter in the present case.

The C(2)—C(3) bond corresponds to a double bond and is rather close in length to those found in the oxyvinylic group of 2-nitronaphthofurans (Ajana, Bideau, Cotrait, Buisson, Demerseman, Einhorn & Royer, 1988). This latter group is the main structural element responsible for the biological properties of these compounds. The C(5)—C(6), C(7)—C(8), C(9)—C(10) and C(4)—C(13) bonds have similar lengths close to 1.37 Å, like those found in naphthalenic compounds (Kennard, Allen & Watson, 1977). The N—O bond lengths are quasi-identical as in the 2-nitronaphthofuran series (Ajana, 1987). The O(1), C(2) and O(14) atoms of the heterocycle and the N and O atoms of the nitro group bear an important net charge. This is more important for the O(17) atom, close to O(1), than for the other O atom in the nitro group. There is a slight dissimilarity between the C(6)—C(12) and C(11)—C(13) bond lengths (close to 1.43 Å) on one side and the C(7)—C(12) and C(10)—C(11) bond lengths (close to 1.41 Å) on the other side, perhaps because of the

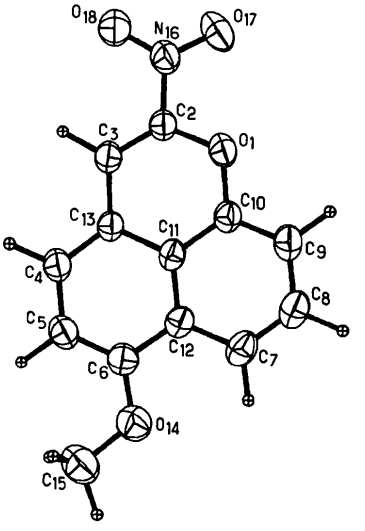

Fig. 1. *ORTEP* drawing of the molecule.

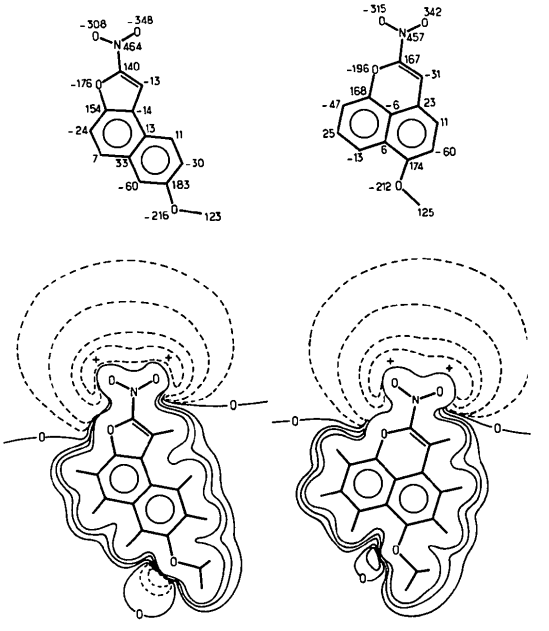

Fig. 2. Partial atomic charges (e × 10^3) and MEP (kJ). Solid contours correspond to 0, 41.84, 83.68 and 209.2 kJ; dashed contours correspond to −20.92, −41.84, −83.68 and −125.52 kJ. The values of V_{min} in the vicinity of the O atoms of the nitro group are indicated by the + sign.

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 55548 (21 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England. [CIF reference: PA1004]

Table 1. *Atomic coordinates and B_{iso}/B_{eq} values* (Å^2) *for the title compound with e.s.d.'s in parentheses*

For non-H atoms $B_{eq} = (4/3)\sum_i\sum_j \beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	*y*	*z*	B_{iso}/B_{eq}
O(1)	0.0981 (2)	0.1934 (1)	0.2828 (1)	3.6 (1)
C(2)	0.2325 (2)	0.2902 (2)	0.1990 (2)	3.0 (1)
C(3)	0.2575 (2)	0.3547 (2)	0.0498 (2)	2.9 (1)
C(4)	0.1420 (2)	0.3848 (2)	−0.1929 (2)	3.3 (1)
C(5)	0.0088 (2)	0.3522 (2)	−0.2696 (2)	3.7 (1)
C(6)	−0.1346 (2)	0.2602 (2)	−0.1911 (2)	3.3 (1)
C(7)	−0.2942 (2)	0.0949 (2)	0.0570 (2)	3.5 (1)
C(8)	−0.2994 (2)	0.0325 (2)	0.2103 (2)	4.0 (1)
C(9)	−0.1676 (2)	0.0658 (2)	0.2870 (2)	3.6 (1)
C(10)	−0.0312 (2)	0.1623 (2)	0.2037 (2)	2.9 (1)
C(11)	−0.0173 (2)	0.2282 (2)	0.0450 (2)	2.6 (1)
C(12)	−0.1524 (2)	0.1941 (2)	−0.0297 (2)	2.8 (1)
C(13)	0.1304 (2)	0.3253 (2)	−0.0383 (1)	2.7 (1)
O(14)	−0.2690 (2)	0.2212 (2)	−0.2543 (1)	4.4 (1)
C(15)	−0.2674 (3)	0.2894 (3)	−0.4151 (2)	5.7 (2)
N(16)	0.3505 (2)	0.3170 (2)	0.2957 (1)	3.6 (1)
O(17)	0.3189 (2)	0.2517 (2)	0.4320 (1)	5.9 (1)
O(18)	0.4762 (2)	0.4055 (2)	0.2358 (1)	4.5 (1)
H(103)	0.3603 (23)	0.4193 (19)	0.0043 (18)	4.0
H(104)	0.2405 (23)	0.4510 (20)	−0.2499 (18)	4.0
H(105)	0.0212 (25)	0.3947 (21)	−0.3787 (19)	4.7
H(107)	−0.3823 (24)	0.0741 (20)	0.0043 (18)	4.3
H(108)	−0.3926 (26)	−0.0363 (21)	0.2714 (20)	5.2
H(109)	−0.1757 (24)	0.0178 (20)	0.3999 (18)	4.1
H(115)	−0.3708 (28)	0.2489 (24)	−0.4327 (22)	6.4
H(215)	−0.2936 (30)	0.4155 (26)	−0.4498 (24)	7.2
H(315)	−0.1401 (32)	0.2437 (26)	−0.4635 (24)	7.4

Table 2. *Bond lengths* (Å) *and angles* (°) *with e.s.d.'s in parentheses*

O(1)—C(2)	1.356 (2)	C(11)—C(13)	1.426 (2)
O(1)—C(10)	1.397 (2)	O(14)—C(15)	1.431 (3)
C(2)—C(3)	1.325 (3)	N(16)—O(17)	1.220 (2)
C(2)—N(16)	1.445 (2)	N(16)—O(18)	1.226 (2)
C(3)—C(13)	1.440 (2)		
C(4)—C(5)	1.409 (3)		
C(4)—C(13)	1.370 (3)	C(3)—H(103)	0.95 (2)
C(5)—C(6)	1.369 (3)	C(4)—H(104)	0.96 (2)
C(6)—C(12)	1.430 (3)	C(5)—H(105)	0.97 (2)
C(6)—O(14)	1.359 (2)	C(7)—H(107)	0.94 (2)
C(7)—C(8)	1.362 (3)	C(8)—H(108)	0.96 (2)
C(7)—C(12)	1.413 (3)	C(9)—H(109)	1.00 (2)
C(8)—C(9)	1.404 (3)	C(15)—H(115)	0.94 (3)
C(9)—C(10)	1.364 (3)	C(15)—H(215)	1.02 (3)
C(10)—C(11)	1.407 (2)	C(15)—H(315)	1.01 (3)
C(11)—C(12)	1.413 (2)		

C(2)—O(1)—C(10)	116.6 (1)	C(9)—C(10)—C(11)	122.6 (2)
O(1)—C(2)—C(3)	126.9 (2)	C(10)—C(11)—C(12)	118.2 (2)
O(1)—C(2)—N(16)	110.5 (1)	C(10)—C(11)—C(13)	120.9 (2)
C(3)—C(2)—N(16)	122.7 (2)	C(12)—C(11)—C(13)	120.9 (2)
C(2)—C(3)—C(13)	119.2 (2)	C(6)—C(12)—C(7)	123.5 (2)
C(5)—C(4)—C(13)	120.7 (2)	C(6)—C(12)—C(11)	117.5 (2)
C(4)—C(5)—C(6)	120.6 (2)	C(7)—C(12)—C(11)	119.1 (2)
C(5)—C(6)—C(12)	121.0 (2)	C(3)—C(13)—C(4)	124.6 (2)
C(5)—C(6)—O(14)	125.1 (2)	C(3)—C(13)—C(11)	116.0 (2)
C(12)—C(6)—O(14)	113.9 (2)	C(4)—C(13)—C(11)	119.3 (2)
C(8)—C(7)—C(12)	120.3 (2)	C(6)—O(14)—C(15)	117.4 (2)
C(7)—C(8)—C(9)	121.6 (2)	C(2)—N(16)—O(17)	118.4 (2)
C(8)—C(9)—C(10)	118.2 (2)	C(2)—N(16)—O(18)	117.9 (2)
O(1)—C(10)—C(9)	117.0 (2)	O(17)—N(16)—O(18)	123.6 (2)
O(1)—C(10)—C(11)	120.4 (2)		

Table 3. *Partial charges* (e)

O(1)	−0.196	O(14)	−0.212
C(2)	0.167	C(15)	0.125
C(3)	−0.031	N(16)	0.457
C(4)	0.011	O(17)	−0.315
C(5)	0.008	O(18)	−0.342
C(6)	0.174	H(103)	0.041
C(7)	−0.013	H(104)	0.002
C(8)	0.025	H(105)	0.008
C(9)	−0.047	H(107)	0.005
C(10)	0.168	H(108)	−0.004
C(11)	−0.006	H(109)	0.020
C(12)	0.006	H(115)	−0.003
C(13)	0.023	H(215)	0.001
		H(315)	−0.004

methoxy substituent at C(6). The C(5)—C(6)—O(14) angle of 125° is greater than the C(12)—C(6)—O(14) angle of 114°, because of steric hindrance between the methyl group and the H atom on the C(5) atom. The oxaphenalene group is perfectly planar, the N(16), O(17) and O(18) atoms of the nitro group deviating slightly from this plane by 0.066 (2), 0.061 (2) and 0.120 (2) Å, respectively. It is the same case for the C(15) atom of the methoxy group, the deviation of which is 0.077 (3) Å. Nevertheless, the torsion angles around C(2)—N(16) and C(6)—O(14) are very small at close to 3°.

Molecules are stacked along the *y* axis, with distances between parallel mean planes close to 3.34 and 3.435 Å between (*x*, *y*, *z*) and (−*x*, 1 − *y*, −*z*) on one side and (−*x*, −*y*, −*z*) on the other side. The overlapping of parallel molecules is rather limited. Similar overlap has been found in the 2-nitronaphthofuran series (Ajana, Bideau & Cotrait, 1987).

The values of the dipole moment are 6.11 and 6.49 debye (1 debye $\simeq 3.33564 \times 10^{-30}$ C m) for compounds (1) and (2) respectively; these moments are approximately directed along the C(2)—N(6) bond. The atomic charges and the molecular electronic potential (MEP) are presented in Fig. 2; they look very similar in the vicinity of the 2-nitrooxyvinylic group of both molecules. Previous studies on a 2-nitronaphthofuran series have shown that the SOS inducing potency (Quillardet, Huisman, D'Ari & Hofnung, 1982), which measures the mutagenicity of the compounds, is strongly correlated to the minimum MEP value, V_{min}. For compounds (1) and (2), V_{min} values are very close (−192.3 and −188.5 kJ mol^{-1}, respectively), in agreement with their quite high mutagenicity (Ajana, 1987; Ajana, Bideau, Cotrait, Buisson, Demerseman, Einhorn & Royer, 1988). The relative positions of the three minima of MEP, two close to both O atoms of the nitro group and another, much weaker, near the O atom of the methoxy group, are rather similar.

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Structure of Benzo[*a*]phenothiazine Pentachlorotellurate(IV)

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Abstract. Bis(benzo[*a*]phenothiaziniumyl) di-μ-chlorobis[tetrachlorotellurate(IV)], $(C_{16}H_{11}NS)_2.Te_2Cl_{10}$, $M_r = 1108.4$, monoclinic, $P2_1/a$, $a = 10.975$ (2), $b = 19.937$ (3), $c = 8.742$ (4) Å, $\beta = 90.40$ (2)°, $V = 1912.9$ (9) Å^3, $Z = 2$, $D_m = 1.93$, $D_x = 1.925$ Mg m^{-3}, λ(Mo $K\alpha$) = 0.71073 Å, $\mu = 2.37$ mm^{-1}, $F(000) = 1068$, $T = 293$ K, $R = 0.052$ for 3724 observed reflections. Benzo[*a*]phenothiazine exists as a nearly planar cation radical. Each Te atom is coordinated by six Cl atoms in a distorted octahedral configuration. Both cation radicals and anions construct separate dimers.

Introduction. The structure determination of the title compound is part of a series of studies on phenothiazines, in which we have been interested in both the electronic and the structural natures of the ion–radical salts of phenothiazine (PT) and/or its derivatives (Uchida, Ito & Kozawa, 1983; Uchida, Seki, Ito, Nakano, Hoshizaki & Kozawa, 1986; Kozawa & Uchida, 1990; Kozawa, Hoshizaki & Uchida, 1991). Although it has long been observed that PT has the unique feature of possessing multiple stable oxidation states in solution (Billon, 1962; Shine & Mach, 1965), we found that the cation radical state of PT and its derivatives is stable even in the solid state, and that their molecular conformations were flattened compared with the folded conformation of their neutral states. Furthermore, we found that the aggregate manner of PT derivatives in the crystals was usually the same as that of counter metal chloride anions (Kozawa, Hoshizaki & Uchida, 1991), that is, they construct dimeric pairs with dimer anions, tetrameric stacks with tetramer anions and infinite stacks with infinite polyanions. This paper is concerned with the dimeric structure of $(B[a]PT)_2$–Te_2Cl_{10}. Hereafter, B[*a*]PT denotes benzo[*a*]phenothiazine.

Experimental. B[*a*]PT was synthesized from *N*-phenyl-1-naphthylamine and sulfur according to the literature method (Knoevenagel, 1914) and purified by sublimation *in vacuo*. Single crystals of the complex were obtained from a 1,2-dichloroethane solu-

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