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14-OXA-[7.1]-METAPARA-CYCLOPHANES FROM MYRICA GALE L., A NEW CLASS OF NATURAL PRODUCTS

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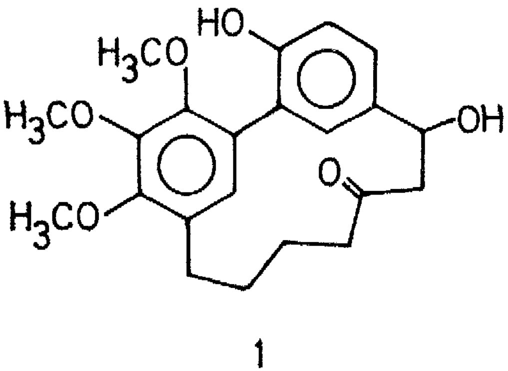
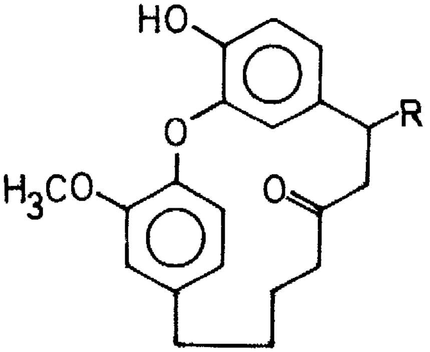
From an ethyl acetate extract of the stems of Myrica gale L. we have previously reported[1] the isolation of porson (1), a [7.0]-metacyclophane of similar constitution as two related compounds from M. nagi, myricanol and myricanone.[2] We have now isolated in a similar manner, two additional crystalline phenolic ketones, galeon (2) [m.p. 179-181°C, λ_{max} (KBr) 1703 cm^{-1}, λ_{max} (MeOH) 280 nm (4200), $[\alpha]_D^{20} = -16^o$ (C 2.03, $CHCl_3$), calc. for $C_{20}H_{22}O_4$ 326.1516, found 326.1511; yield 50 mg from 6 kg dried plant] and hydroxygaleon (3) [m.p. 183-184°C, ν_{max} (KBr) 1693 cm^{-1}, λ_{max} (MeOH) 279 nm (7560), calc. for $C_{20}H_{22}O_5$ 342.1466, found 342.1474; yield 20 mg from 6 kg dried plant].

The constitution of galeon has been derived by X-ray crystallography (Fig. 1, cell parameters a = 855.1±0.2, b = 1738.4±0.3 and c = 1135.5±0.2 pm, $\alpha=\beta=\gamma=90^o$, space group $P2_12_12_1$ z = 4) supported by NMR, UV, IR and MS. 2801 reflexions were collected on a diffractometer of a crystal of natural galeon. Solution of the structure was by direct methods. Full matrix least squares refinement of the heavy atom parameters has given a preliminary R (2368F) of 0.090. Refinement including H-atoms is in progress.

As seen from Fig. 1 the main planes of the two ether linked aryl rings are close to 90° to each other and they are held together by the seven membered carbon bridge. The oxo group in this bridge and the methoxy group on one of the aryl rings are located relatively close to each other. It does not seem likely from models that the methoxy bearing aryl nucleus is free to rotate 180° to place the methoxy function in the furthest possible position away from



1



2 R = H
3 R = OH

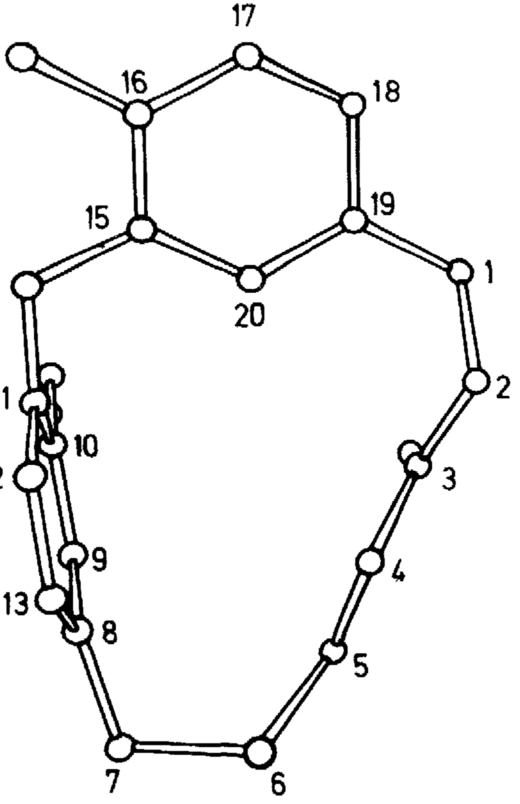


Figure 1

the oxo group. This seems to be the origin of optical activity in galeon, although it does not contain any chiral centra.

The ^1H NMR spectrum (100 MHz, $CDCl_3$) of galeon is reminiscent of the spectrum of porson [two ABC patterns in the aromatic region 6.86 (H_9), 6.99 (H_{12}), 6.84 (H_{13}), 6.81 (H_{17}), 6.58 (H_{18}) and 5.53 (H_{20}), furthermore 5.70 (OH), 3.69 (OCH_3), 2.5-3.0 ($2H_7$,$2H_1$), 2.15-2.4 ($2H_2$,$1H_4$), 2.05 ($1H_4$) and 1.4-1.8 ($2H_5$,$2H_6$)]. However, there is one striking difference, the unusual high field resonance of H_{20} (5.53). The reason for this is clearly visible from a model of galeon built according to the X-ray crystallographic drawing (Fig. 1). The aromatic hydrogen H_{20} is located just above the plane of the neighbouring aromatic ring and thus experiencing a strong upfield shift due to the anisotropy of the aromatic ring. This is only possible in a diphenylether where the main planes of the two aromatic rings are very close to 90° to each other. The dihedral angle between the two aryl rings in the [7.0]-meta-cyclophanes is close to 33° [2] and none of the aromatic protons will be located in the shielding region of an aromatic ring.

The mass spectra of galeon (2) and porson (1) are also significantly different. In the mass spectrum of porson the only peaks of importance, except for the molecular ion peak, are due to loss of fragments of the seven carbon bridge (see Scheme 1, ref. 1). Such cleavages are also seen in the mass spectrum of galeon. However, peaks due to cleavages of the ether bridge are of high abundance. Particularly interesting are these cleavages when they are connected with various fissions in the C-7 chain leading to fragments as shown in Table 1.

Together with galeon we have also isolated hydroxygaleon (3) which in addition to the oxo group has a hydroxy group in the side chain like porson.

The aromatic part of the NMR spectrum of hydroxy galeon is very similar to the one of galeon, 6.85 ppm 3H (H_9,H_{12},H_{13}), 6.83 (H_{17}), 6.65 (H_{18}) and 5.64 (H_{20}). The spectrum also clearly reveals an ABX pattern [$\nu_X = 4.02$ (H_1), $\nu_A = 3.18$ ($1H_2$), $\nu_B = 2.85$ ($1H_2$), $J_{AB} = 14.5$ Hz, $J_{AX} = 1.8$ and $J_{BX} = 7.0$]. This shows that the hydroxy group is located at C_1 or C_2 (presumably at C_1 since the resonance position of H_1 is very similar to the corresponding proton in porson) and oriented away from the oxo group. The remaining hydrogens are found at 2.7 ppm ($2H_7$, $1H_4$), 2.1 ($1H_4$), 1.6 ($2H_5$,$2H_6$) and 3.86 (OCH_3).

The mass spectrum of hydroxygaleon is similar to the mass spectrum of galeon (Table 1), however, the introduction of an extra oxygen function in the side chain makes loss of $C_5H_7O_2$ fairly important as in the mass spectrum of porson.[1]

Table 1.

ion (m/e)	Fissions	Abundance % 2	Abundance % 3
121	C_6-C_7, C_{11}-O_{14}	23	44
137	C_6-C_7, O_{14}-C_{15}	11	15
147	C_4-C_5, C_{11}-O_{14}	6	15
162	C_3-C_4, C_{11}-O_{14}	9	46
178	C_3-C_4, O_{14}-C_{15}	0.2	7
191	C_2-C_3, C_{11}-O_{14}	0.5	9
M-71	C_2-C_3, C_6-C_7	5	5
M-99	C_1-C_{19}, C_5-C_6	0	5

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