Tetrahedron Vol. 35, pp. 1777 to 1782

0040-4020/79/0715-1777/$02.00/0

ZEYLANONE AND ISOZEYLANONE, TWO NOVEL QUINONES FROM *PLUMBAGO ZEYLANICA*

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(*Received in UK* 21 *December* 1978)

Abstract—Zeylanone and isozeylanone have been shown to be novel dimers of plumbagin (2-methyl-5-hydroxy-1,4-naphthaquinone). A probable mode of their formation *in vivo* from plumbagin (1) and its hydroquinone (3) has been postulated (Scheme 1). Benzene induced solvent shifts of the aromatic protons of zeylanone have been discussed.

The isolation of zeylanone (PZ9) and isozeylanone (PZ7) has been reported earlier and now these are shown to be 5 and 4 respectively.[1] All the biplumbagins reported earlier were linked through ring C atoms.[1,2]

Zeylanone, a yellow crystalline solid, m.p. 212–4° (CCl_4), M^+, 374.0793, $C_{22}H_{14}O_6$ (Calc. 374.0790) gives a violet solution in aqueous sodium hydroxide which turns orange yellow. It undergoes reversible reduction with sodium dithionite. Its UV spectrum λ_{max}^{MeOH}: 209, 245, 273, 388 and 443 nm and IR spectrum ν_{max}^{KBr}: 1680, 1665 and 1635 cm^{-1} are approximately a combination of the UV spectra[2,3] and IR spectra, ($\rangle C{=}O$ stretching region) of plumbagin (1)[2] and β-dihydroplumbagin (2) respectively (Experimental). The presence of intense fragments at *m/e* 120 and *m/e* 92 in its mass spectrum indicate that zeylanone is a juglone derivative without a substituent in the benzenoid ring[4] (Scheme 2). From these considerations and its molecular weight, it appears plausible that a molecule of plumbagin (1) and a molecule of dihydroplumbagin (2) are linked together by loss of four H atoms.

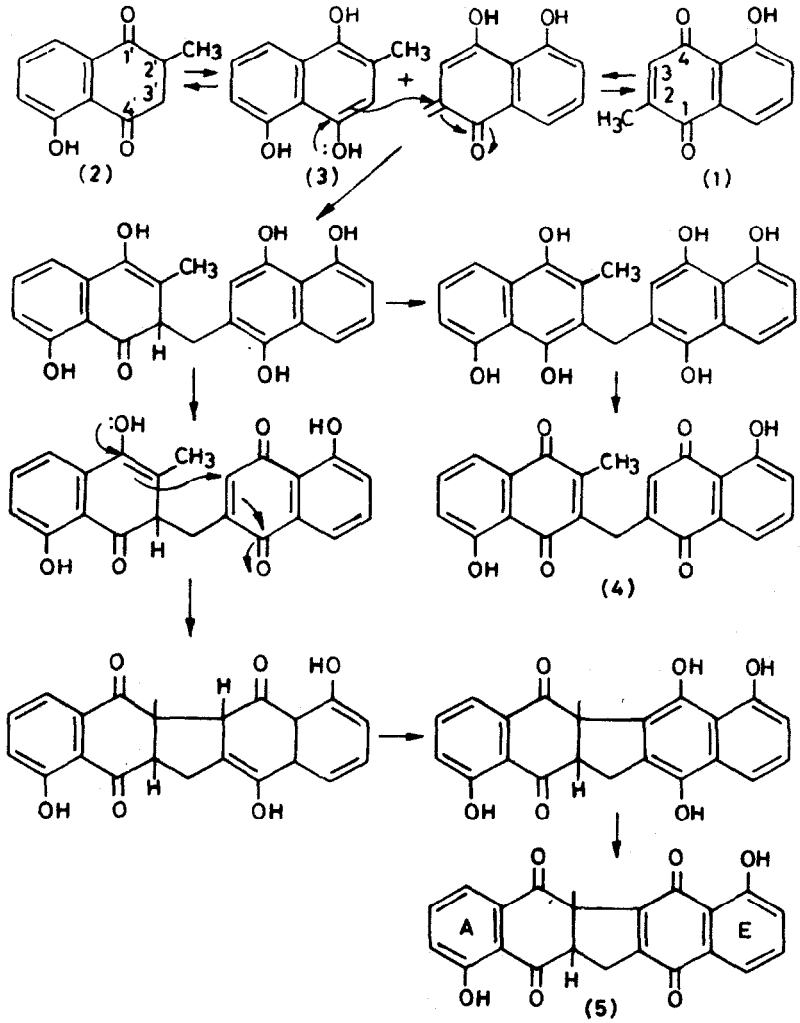
In the 300 MHz NMR spectrum of zeylanone there are singlets at 12.09 and 12.21 assignable to two peri OH groups. There is only one three proton singlet at 1.86 which is rather upfield for a Me group on a quinone ring (Plumbagin (1), 2-CH_3, 2.13). It is assumed to be on the reduced ring, though it is rather downfield compared to the Me group of β-dihydroplumbagin (2) (-CH_3 1.31). Instead of a second Me group, there is a three proton ABX multiplet in the region 3.40–3.53 assignable to (-CH_2–CH–) indicating that probably the Me group of other plumbagin moiety is itself involved in the linkage. Since no olefinic proton is present, it can be further deduced that the C-3 and C-3′ are also additionally involved in the linkage, the C-2 Me group of plumbagin (1) moiety probably forms a methylene bridge connecting itself to the C-3′ of β-dihydroplumbagin (2) as shown in structure 5. The multiplets in the region 7.29–7.32 (2H), 7.55–7.75 (4H) are assignable to protons ortho, meta and para to the OH groups.

The X proton is seen as a sextet at 3.10 and the central methylene protons constituting the AB part are at 3.42 and 3.46 ($J_{AX} = -16.5$ Hz, $J_{BX} = 6.5$ Hz, $J_{AB} = 8.5$ Hz); (Fig. 1). A computer simulated programme of the spectrometer using the frequencies A = 109 Hz, B = 96 Hz and X = 0, $J_{AB} = 8.5$ Hz, $J_{AX} = -16.5$ Hz, $J_{BX} = 6.5$ Hz resulted in a spectrum which is very close to the observed ABX pattern (Fig. 2). Thus the three protons of cyclopentene ring are assigned. The complexity of the aromatic protons in the region 7.29–7.75 is found to reduce in its 300 MHz NMR spectrum using benzene induced solvent shifts (Figs. 3–9). In these spectra, independent and distorted AMX and ABX patterns for the rings A and E are discernible.

The pattern near the $CDCl_3/CHCl_3$ signal is assignable to the protons ortho to the OH groups and these appear to have slightly different chemical shifts leading to a pattern as shown in Fig. 3. If one begins with the spectrum (Fig. 3, $CDCl_3$) peak A does not have enough area to account for a full proton and it does not move with other lines as the spectrum was recorded in $CDCl_3$ containing varying amounts of C_6D_6 (Figs. 4–9).

Peaks B, C and D moved together as a triplet (Fig. 4) 1% C_6D_6 and (Fig. 5) 2% C_6D_6. They represent the proton meta to OH in one of the rings. Peaks I and JK represent the third proton in this ring para to the OH peak, peak I is really a doublet like JK; but a peak with the same intensity as E falls in the space between the lines of the doublet in this solution with 1% C_6D_6. The splitting JK is a meta splitting (to the proton ortho to the OH) and corresponds to smaller of the two meta couplings observed in the pattern near the $CHCl_3$ peak. With increasing the C_6D_6 concentration the chemical shift of the protons meta and para to the OH approach each other resulting in the growth of C and D at the expense of B and the growth of peak I at the expense of JK. Thus lines B, C, D, I, JK and one of the quartets of the smaller meta couplings near $CHCl_3$ signal appear to represent the three protons of one of the aromatic rings approximated to AMX (Fig. 5).

Still considering Fig. 4, lines E, F, G and H represent the observable lines of an eight line pattern arising from two protons meta and para to the OH in the other ring. This is a typical AB part of an ABX pattern consisting of two independent AB patterns. One of these AB patterns is represented by lines E, G, H and line of intensity equal to E which falls between the lines of doublet I. The other AB



Scheme 1. Biogenesis of zeylanone and isozeylanone.

pattern has outer lines of vanishingly small intensity (in this solution) and inner lines which coalece to the strong peak F. Increasing the C_6D_6 concentration to 2% (Fig. 5) shifts line I' (equal in intensity to E) into view and separates F and F'. Continued increase in C_6D_6 concentration increases the chemical shift separation of these two protons until at approximately 20% C_6D_6 they appear as unresolved doublet of doublets E, E' and FG and the triplet, F', H, I'. The quartet with the larger splitting near the $CHCl_3$ signal (Figs. 4–6) constitutes the proton ortho to the OH in the other aromatic ring. Thus a second aromatic ring with three adjacent protons appear to be present and the NMR spectrum of zeylanone is fully compatible with the structure proposed to it. In its mass spectrum (Scheme 2), the molecular ion is the base peak. A major fragment *m/e* 359 involves the loss of a Me group from the molecular ion. A second notable feature is the retero Diels Alder type of fragmentation of the molecular ion resulting in peaks at *m/e* 226; the other fragment at *m/e* 148 is not seen but a fragment at *m/e* 149 after picking up of a H atom is observed.

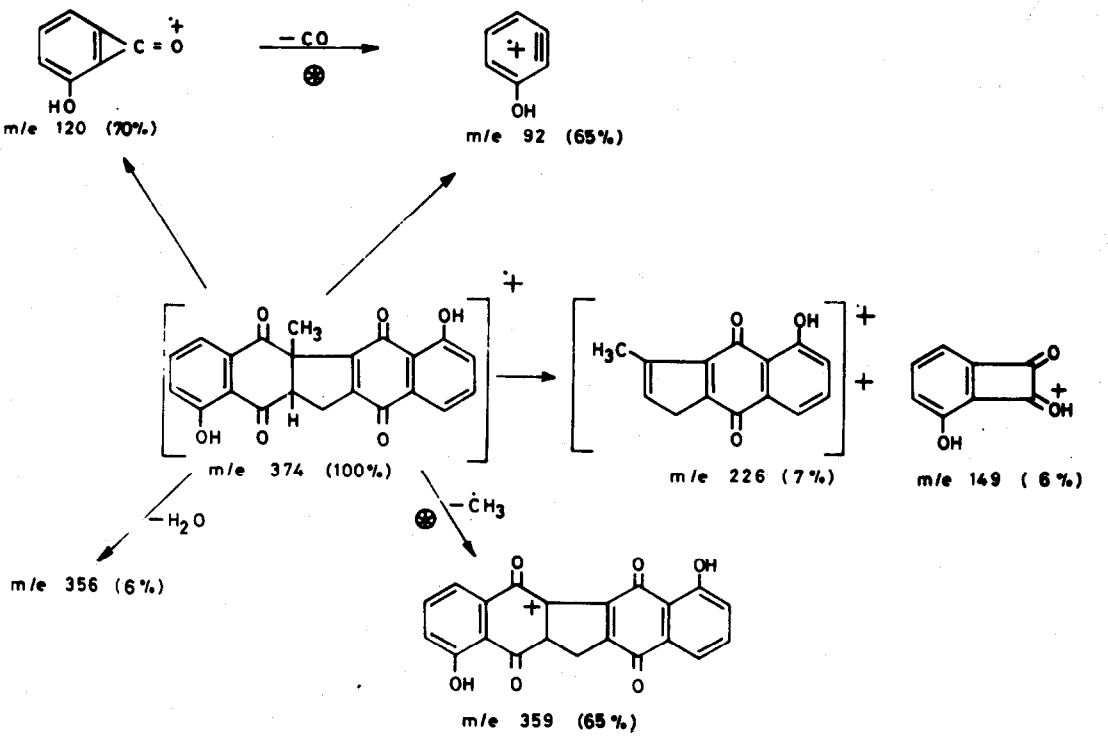
Zeylanone gave a dimethyl ether, the IR, NMR and mass spectra of which confirm the structure assigned to it (Experimental).

Isozeylanone, orange crystalline solid, m.p. 192–4° (MeOH), M^+ 374; λ_{max}^{MeOH}: 217, 264 and 422 nm; ν_{max}^{KBr}: 1665 and 1635 cm^{-1} and *m/e* 92 (89%) and *m/e* 120 (46%) is an isomer of zeylanone.[1,2] The NMR spectrum showed the presence of only one Me group and one olefinic proton at 2.24 (s) and 6.64 (split) respectively. The absence of a second Me group and a second olefinic proton implies a linkage between the Me carbon of one plumbagin moiety and the olefinic carbon of the other with the loss of two H atoms. This is substantiated by the presence of a broadened signal at 3.96 assignable to the methylene group. There are two downfield peri OH groups at 11.92 and 12.03 and the six aromatic protons appear as a multiplet in the region 7.32–7.78. This data suggests structure 4 for isozeylanone. Alternative structures for zeylanone and isozeylanone are ruled out from biogenetic considerations (Scheme 1).

EXPERIMENTAL

The NMR spectra are reported in $CDCl_3$ with TMS as internal standard in δ values. 300 MHz and 60 MHz NMR spectra were recorded on a Varian Fourier transform, 300 MHz NMR spectrometer and varian A-60 NMR spectrometer respectively. The mass spectra were recorded on a RMU-6L Hitachi mass spectrometer.

The optical rotation and the UV and IR spectra were obtained on



Scheme 2. Mass spectral fragmentation of zeylanone.

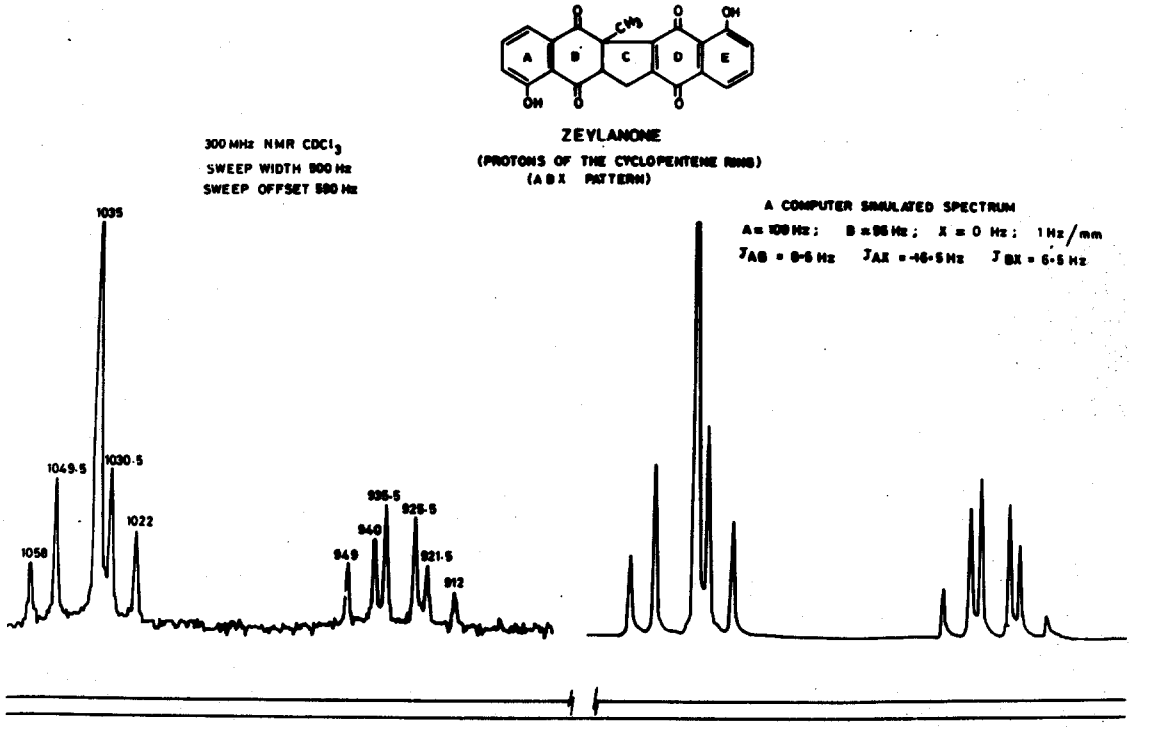


Fig. 1. Zeylanone-ABX pattern, protons of the cyclopentene ring.

Fig. 2. Zeylanone-ABX pattern, computer simulated spectrum, A = 109 Hz, B = 96 Hz, X = 0 Hz, J_{AB} = 8.5 Hz, J_{AX} = −16.5 Hz, J_{BX} = 6.5 Hz.

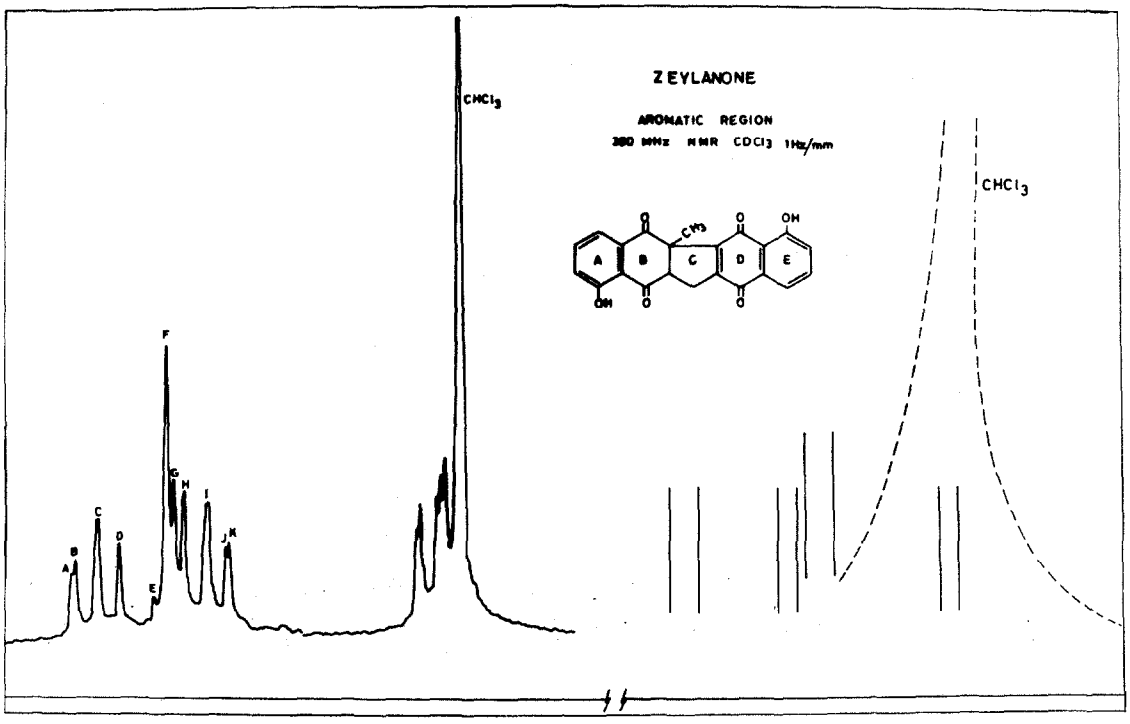


Fig. 3. Zeylanone-aromatic protons $CDCl_3$.

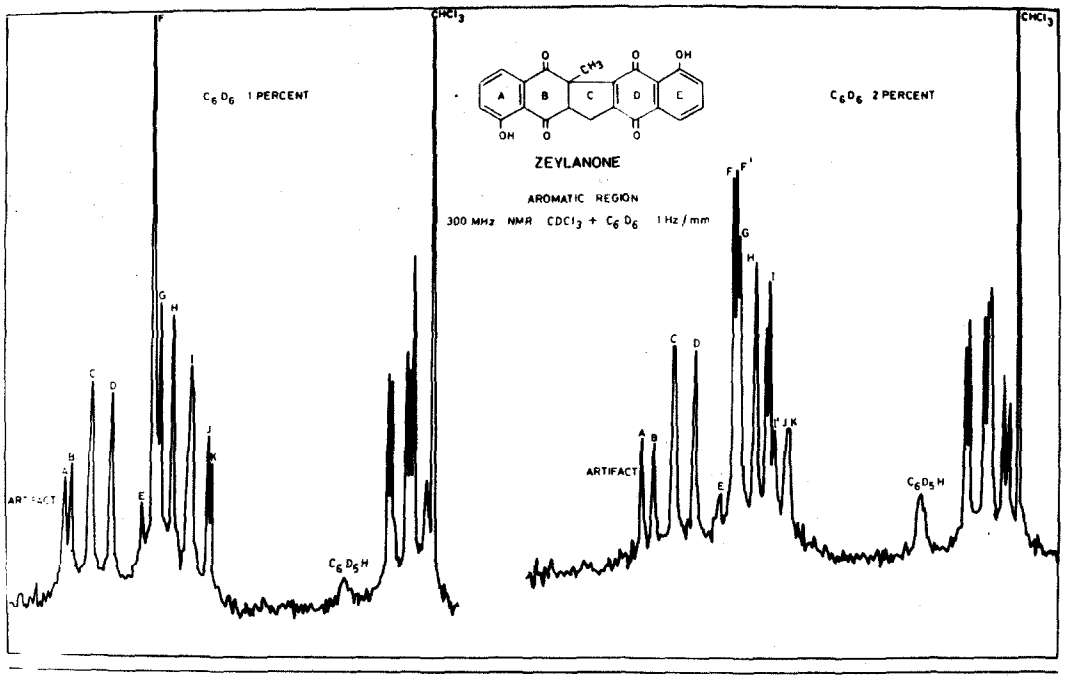


Fig. 4. Zeylanone-aromatic protons $CDCl_3$ 1%, C_6D_6.

Fig. 5. Zeylanone-aromatic protons $CDCl_3$ 2%, C_6D_6.

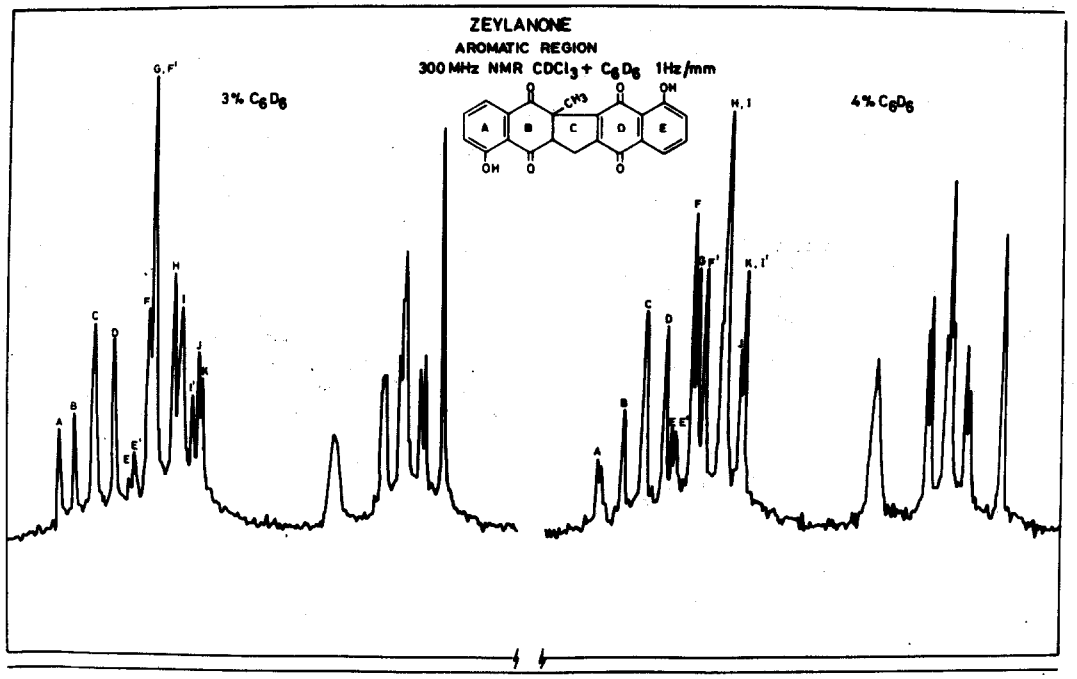


Fig. 6. Zeylanone-aromatic protons $CDCl_3$ 3%, C_6D_6.

Fig. 7. Zeylanone-aromatic protons $CDCl_3$ 4%, C_6D_6.

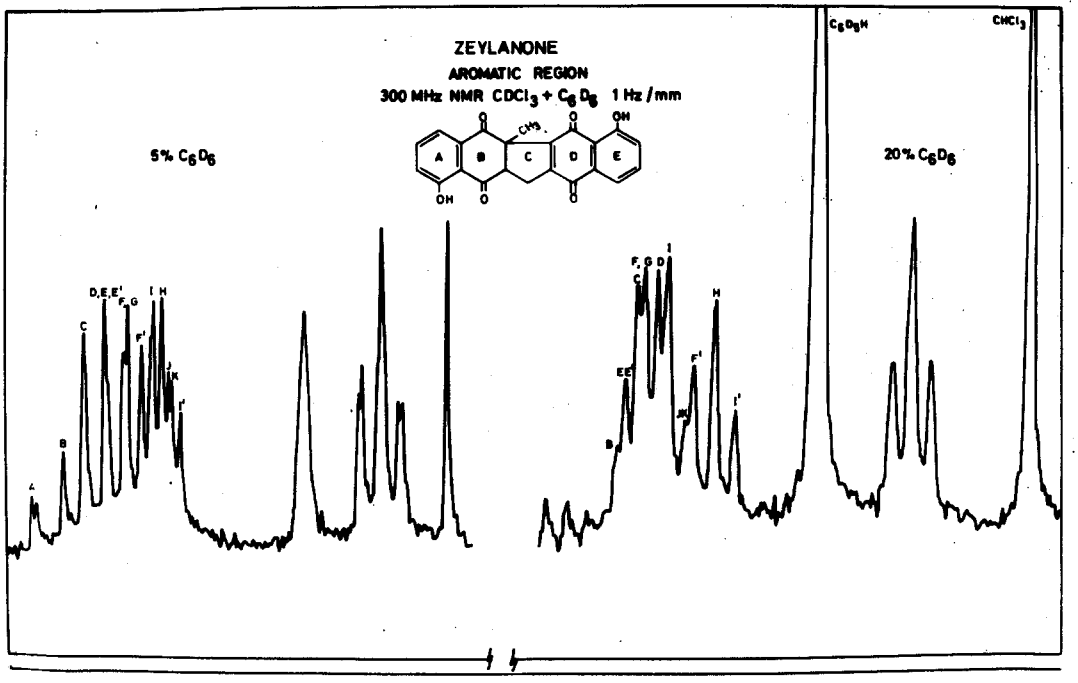


Fig. 8. Zeylanone-aromatic protons $CDCl_3$ 5%, C_6D_6.

Fig. 9. Zeylanone-aromatic protons $CDCl_3$ 20%, C_6D_6.

a Karl Zeiss spectropolarimeter, Unicam SP-700 UV spectrophotometer and Perkin–Elmer 221 IR double beam spectrophotometer, respectively. The m.ps are uncorrected. In Ref. 1 the title compounds were spelt as zeylinone and isozeylinone.

Zeylanone. Yellow crystalline solid, m.p. 212–4°, M^+, 374.0793 ($C_{22}H_{14}O_6$ requires: 374.0796). λ_{max}^{Dioxan} (log ϵ): 235 (4.85); 246 (4.72), 350 (4.00), 430 (3.83); log ϵ values for the spectrum in MeOH could not be calculated due to solubility difficulties. ν_{max}^{KBr}: 1680, 1660 and 1635 cm^{-1}; Mass spectrum *m/e*, (1%) 374.0793 (100), $C_{22}H_{14}O_6$; 359 (65), $C_{21}H_{11}O_6$; 356 (6), 227 (12), $C_{14}H_{11}O_3$, 226 (7), $C_{14}H_{10}O_3$; 213 (20), $C_{13}H_9O_3$, 212 (20); 149 (6); 121 (30), 120 (70), $C_7H_4O_2$; 92 (65) metastables 374–359; 374–333; 120–92, $[\alpha]_D^{30} = 0$, (*c*, 1.5%, $CHCl_3$). It absorbs completely in the region 365–436 nm and shows no rotation up to 578 nm.

Zeylanone dimethylether. Zeylanone (70 mg) was dissolved in $CHCl_3$ and shaken with MeI (6 ml) and Ag_2O (400 mg) at room temp. for 10 hr. The product was purified by column chromatography over silica gel and recrystallisation, brownish yellow crystalline solid, m.p. 153°; (petroleum ether, b.p. 60–80°) M^+ 402; ν_{max}^{KBr}: 1685, 1680, 1660 and 1625 cm^{-1}, δ $CDCl_3$: 1.78, s (3H, $-CH_3$); 2.95–3.70, m (3H, $-CH_2-CH-$); 3.96, s (3H, OCH_3); 4.00, s (3H, OCH_3); 7.17–7.73, m (6H, Ar–H).

Isozeylanone. Mass spectrum [70 ev, direct inlet, 200°, *m/e* (1%)]; 376 (15), 375 (28), 374, M^+ (100); 359, $M^+ - CH_3$ (28), 357, $M^+ - OH$ (14), 345 (10), 131 (10), 121 (43), 120 (46), 119 (14), 115 (19), 103 (10), 102 (10), 93 (20), 92 (89), 91 (22), 89 (17), 77 (28), 76 (10).

β-Dihydroplumbagin. Plumbagin dissolved in ether was shaken with aqueous sodium dithionite until the ethereal layer was colourless. The solvent was removed under vacuum and the residue was sublimed below its m.p. at vacuum less than 1 mm of mercury. The sublimate yellow crystalline solid m.p. 83–5° (petroleum ether, b.p. 60–80°), M^+, 190; ν_{max}^{KBr}: 1685 and 1635 cm^{-1}; δ $CDCl_3$: 1.31, d, J = 6 Hz (CH_3); 2.58–3.43, m ($-CH_2-CH-$), 7.37–7.87, m (3H, Ar–H); 12.15, s (*peri*-OH); is identified as β-dihydroplumbagin.

Acknowledgements—The authors are grateful to Dr. G. S. Sidhu, Director, Regional Research Laboratory, Hyderabad, India, for valuable discussions and Dr. J. Tamas, Central Research Institute for Chemistry, Hungarian Academy of Sciences, for high resolution mass analysis of zeylanone.

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