Phytochemistry, Vol. 25, No. 3, pp. 764–765, 1986.
Printed in Great Britain.

0031–9422/86 $3.00 + 0.00

EPI-ISOSHINANOLONE FROM *PLUMBAGO SCANDENS*

J. BHATTACHARYYA and VICENTE R. DE CARVALHO

Laboratório de Tecnologia Farmacêutica, Universidade Federal da Paraíba, 58.000-João Pessoa, Paraíba, Brazil

(*Revised received* 30 *July* 1985)

Key Word Index—*Plumbago scandens*; Plumbaginaceae; *epi*-isoshinanolone; plumbagin; ^{13}C NMR.

Abstract—*Epi*-isoshinanolone, a diastereoisomer of isoshinanolone, has been isolated from *Plumbago scandens* and characterized with the aid of NMR spectroscopy.

INTRODUCTION

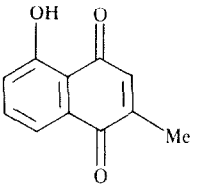
The total ethanol extract of *Plumbago scandens*, a medicinal plant used in north eastern Brazil [1], showed anti-inflammatory and anti-Parkinson effects in our laboratory [2]. The chloroform-soluble part of the ethanol extract, upon further fractionation yielded, *inter alia*, a semi-solid material along with plumbagin (**1**). The homogeneity of the semi-solid material ($[M]^+$ *m/z* 192), henceforth referred to as substance A, was ascertained by repeated prep. TLC, the product every time showing unaltered physical properties. In this communication, we wish to report that the substance A is a mixture of isoshinanolone (**2**) and its diastereoisomer, *epi*-isoshinanolone (**3**). This is the first report of the existence of *epi*-isoshinanolone in nature, although, it appears likely that isoshinanolone reported from a related species, *P. zeylanica* [3], is also a mixture of the two diastereoisomers, probably in a slightly different ratio from that found in substance A.

RESULTS AND DISCUSSION

The UV spectrum of substance A showed λ_{max} (log ε) at 217 (4.16), 259 (3.87) and 335 (3.45) nm. The two absorption maxima at lower wave lengths are very close to the corresponding absorptions of plumbagin. However, the long wave length maximum of substance A shows a large hypsochromic effect with respect to the corresponding absorption of plumbagin (405 nm) suggesting a reduction of conjugation in the former. The IR spectrum of substance A in KBr showed, among others, a strong band at 1650 cm^{-1} instead of the bands for the 1,4-quinone system of plumbagin at 1675, 1645 and 1610 cm^{-1}. At this time, the possibility of the identity of the substance A with isoshinanolone (**2**) reported first from *Diospyros maritima* [4] and later from *P. zeylanica* [3] and *Aristea ecklonii* [5] seemed apparent. However, certain physical properties of isoshinanolone obtained from *D. maritima*, described as a colourless crystalline solid, which decomposes at 160°, sublimes at 230° and melts completely at 255°, $[\alpha]_D$ −7°, are somewhat different than those of substance A which is a very light yellow semi-solid, $[\alpha]_D$ + 19.7°. On the other hand, the physical properties of substance A match more closely with those of isoshinanolone reported from *P. zeylanica*, also as a pale yellow semi-solid, $[\alpha]_D$ + 24.17°.

The ^{13}C NMR spectrum of substance A in deuterochloroform showed 22 signals in 11 pairs. The 11 larger signals were assigned (Table 1) to the carbons of isoshinanolone (**2**) by comparison with the spectrum of plumbagin (**1**) and also by the use of partially decoupled (SFORD) spectra.

The 1-OH and 2-Me in isoshinanolone has been shown [4] to be *cis* (OH-*pseudo*-axial and Me equitorial). This is confirmed by the ^{1}H NMR spectrum of isoshinanolone where the H-1 appears at δ4.65 as a doublet (J = 2.5 Hz).



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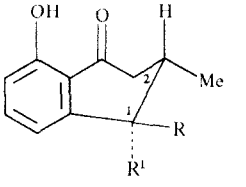

2 R = H, R¹ = OH
3 R = OH, R¹ = H

Table 1. ^{13}C NMR chemical shifts of plumbagin (**1**), isoshinanolone (**2**) and *epi*-isoshinanolone (**3**)

Carbons	Plumbagin	Isoshinanolone	*Epi*-isoshinanolone
1	184.7 *s*	70.8 *d*	73.3 *d*
2	149.6 *s*	34.5 *d*	37.3 *d*
3	135.4 *d*	40.7 *t*	43.3 *t*
4	190.2 *s*	205.1 *s*	204.1 *s*
5	161.2 *s*	162.3 *s*	162.2 *s*
6	124.1 *d*	119.0 *d*	119.1 *d*
7	136.1 *d*	136.7 *d*	136.8 *d*
8	119.1 *d*	117.7 *d*	117.8 *d*
9	132.1 *s*	145.4 *s*	146.4 *s*
10	115.2 *s*	114.9 *s*	115.3 *s*
C-2 Me	16.4 *q*	16.0 *q*	17.7 *q*

However, in *epi*-isoshinanolone, the H-1 should appear as a doublet (J = 8–10 Hz). The ^{1}H NMR spectrum of substance A indeed shows a doublet at δ4.60 (J = 2.5 Hz) for the H-1 of isoshinanolone (**2**), as expected. However, at 4.30, there is another small doublet (J = 7.5 Hz) of 25% intensity of the doublet at δ4.60 and this could arise only out of the H-1 of *epi*-isoshinanolone (**3**), the diastereoisomer of isoshinanolone (**2**). Also the 11 smaller signals of the ^{13}C NMR spectrum of substance A could be unambiguously assigned to carbons of *epi*-isoshinanolone (**3**). Therefore, the substance A is, a *ca* 4:1 mixture of isoshinanolone and its C-1 epimer, *epi*-isoshinanolone. This is confirmed by the oxidation (DDQ) of substance A which afforded plumbagin [3].

EXPERIMENTAL

Extraction. Dried and ground aerial parts of *P. scandens* L. (1 kg) collected in January, 1983 from the University campus in João Pessoa, was extracted in a Soxhlet with 95% EtOH for 24 hr. The resulting gummy solid (54 g) after evapn of the EtOH extract was partitioned between $CHCl_3$ and H_2O (1:1). The dark gummy solid (16.0 g) obtained after evapn of the organic phase was again extracted in a Soxhlet with hexane. The hexane soluble part upon evapn was chromatographed on silica gel using successively hexane–C_6H_6, C_6H_6 and C_6H_6–$CHCl_3$ mixtures.

Isolation of plumbagin and sitosterol. The hexane–C_6H_6 (3:2) eluate gave plumbagin (0.38 g), crystallized from hexane, mp 79–81°, identified by comparison of the physical data with those published in ref. [3]. The following fractions from the column gave sitosterol (0.10 g), mp 139–141°.

Isolation of substance A. The hexane–C_6H_6 (1:1) eluate, showing a single spot on silica gel TLC, gave a semi-solid (1.7 g) which was rechromatographed using the same solvent sequence as before. The hexane–C_6H_6 (1:1) eluate afforded a semi-solid again which was subjected to prep. TLC × 3 using C_6H_6–$CHCl_3$ (1:1). The only band obtained each time after usual work up gave a material which was homogeneous on TLC and remained as a semi-solid; $[\alpha]_D$ + 19.7° ($CHCl_3$); UV λ_{max} nm (log ε): 217 (4.16), 259 (3.87) and 335 (3.48); IR ν_{max}^{KBr} cm^{-1}: 3560–3360, 1640, 1580, 1455, 1350, 1250, 1250, 1170, 988, 879, 820, 750; ^{1}H NMR: δ1.10 (3H, *d*, J = 6 Hz), 2.10–3.10 (*m*), 4.30 (*br d*, *ca* 1/5H, J = 7.5 Hz); 4.60 (1H, *d*, J = 2.5 Hz), 6.80 (2H, *m*), 7.35 (1H, *m*), 12.15 (1H, *s*), 12.12 (*ca* 1/4H, *s*); MS (*m/z*): 192 $[M]^+$, 177, 175, 174, 163, 159, 122.

DDQ oxidation. Substance A (15 mg) in dioxane (2.5 ml) was refluxed with DDQ (12 mg) for 8 hr. The recovered material was subjected to prep. TLC to give plumbagin, identified by comparison (mmp, IR, TLC) with an authentic sample.

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