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# Meroterpenoids–V : *Psoralea corylifolia* Linn. – 4. 2,3-Epoxybakuchiol, $\Delta^1$,3-Hydroxybakuchiol, and $\Delta^3$,2-Hydroxybakuchiol

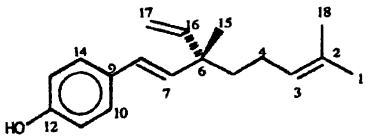
CHANDRAKANT C SHAH, V K BHALLA# and SUKH DEV*

Malti-Chem Research Centre, Nandesari, Vadodara

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**It has been found that besides the meroterpene bakuchiol, first reported in 1966 in the pericarp of seeds of *Psoralea corylifolia*, three oxygenated derivatives also occur, and these have been identified as 2,3-epoxybakuchiol, $\Delta^1$,3-hydroxybakuchiol, and $\Delta^3$,2-hydroxylbakuchiol.**

Continuing interest in the medicinal and pharmacological properties[1] of the seeds of *Psoralea corylifolia* Linn., a crude Ayurvedic drug (Sanskrit, *Bakuchi*; Hindi, *Babchi*) much recommended for use against skin diseases, prompted us to look for the less abundant compounds present in its seed coat. Our earlier work[2–4] had established the absolute stereostructure of bakuchiol, the main component of the seed pericarp extractives, as **1**. Since its discovery in 1966, bakuchiol has been demonstrated to have a variety of biological activities such as antimicrobial (antibacterial, antifungal)[5–9], antiacne[10], antipsoriatic[11], cytotoxicity[12]; it also exhibits mild insect juvenile hormone activity[13] and CNS activity[14]. In view of this we looked for congeners of bakuchiol.

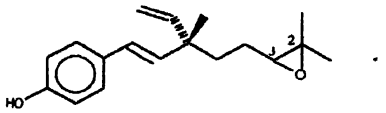



**1.** Bakuchiol

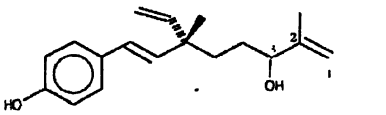
Earlier work[15] in our laboratory had shown that though the hexane extract (cold percolation) from the whole seeds consists essentially of bakuchiol, the chloroform extract of the hexane-exhausted seeds contains at least three more compounds related to bakuchiol, besides several other compounds[16]. Tentative structures were also assigned to those compounds. We now report on results of these and further investigations.

*Bakuchiol congeners : structures* .

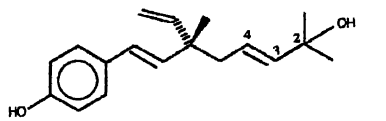
After considerable experimentation, it was found that extraction of whole, matured seeds by cold percolation with toluene yielded an extract (~7%) containing bakuchiol, as well as its derivatives. This material on tlc (silica gel; solvent, 20% EtOAc in benzene) showed at least 10 spots, of which 4 were most prominent. This material was chromatographed on silica gel (IIb) to furnish, besides bakuchiol, three new related compounds. From the spectral characteristics (uv, ir, pmr : *vide* Experimental), it was possible to assign structures to them (**2**, **3**, **4**).




**2** 2,3 - Epoxybakuchiol




**3** $\Delta^1$,3- Hydroxybakuchiol




**4** $\Delta^3$, 2- Hydroxybakuchiol

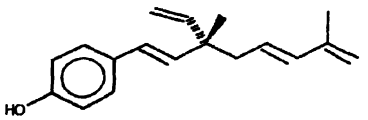
*2,3-Epoxybakuchiol* (**2**) : Structure of the epoxy compound (**2**) was confirmed by comparison (ir, pmr) with an authentic sample, obtained by reaction of bakuchiol with one equivalent of perbenzoic acid; as expected, the reaction of the peracid occurred preferentially at the more electron-rich olefinic linkage. The stereochemistry at C-3 remains undefined. The synthetic product is expected to be a diastereomeric mixture.

*$\Delta^1$,3-Hydroxybakuchiol* (**3**) : Structure of this compound was corroborated further by preparation of an authentic sample from 2,3-epoxybakuchiol (**2**). It is known[17] that oxiranes on exposure to active alumina or silica gel, undergo ring opening to furnish as the main products allylic alcohols. Thus, when **2** was treated with freshly activated alumina, **3** was obtained as the main product which had spectral features (ir, pmr) and $[\alpha]_D$ identical with those of the compound isolated from the seed pericarp extract. The

#Present address Medical College of Georgia, Augusta, U S A
*Present address B R A Centre for Biomedical Research, Delhi University, Delhi-110 016

stereochemistry of the hydroxyl at C-3 remains to be defined.

*$\Delta^3$, 2-Hydroxybackuchiol* (**4**) : Though, it was expected that this compound will also be produced in the above alumina-catalyzed rearrangement, this product was not detected. However, structure **4** was confirmed by preparation of its methyl ether (methylation of phenolic OH), which had the desired spectral characteristics. Furthermore, in consonance with it being an allylic tertiary alcohol, it underwent smooth dehydration under mild conditions (just distillation at 140–150°/0.5 mm), to furnish a product having spectral characteristics consistent with the structure **5**.




**5**

*$^{13}C$ nmr of bakuchiol and related compounds* :

$^{13}C$ nmr spectrum of bakuchiol has, apparently, not been recorded in the literature so far. With the availability of a few more related compounds, it was thought worthwhile to assemble these data. Table 1 gives the values for various carbons (*vide* numbering in structure **1**). The values have been calculated by the additivity rule[18] and also matching these with the values given in the literature[19] for carbons having identical surroundings. All these assignments are fully consistent with the structures already assigned. A few points may be noted. In bakuchiol the values for C-2 (131.3 ppm) and C-3 (125.1 ppm) are as required by their $sp^2$ character, and these suffer the expected shift in the epoxide **2**; the values of 59.3 and 65.2 ppm respectively, in **2** are fully consistent with the values known for trisubstituted oxiranes[20]. Likewise, the shifts in the frequencies of carbons at 1, 2, 3, 4 and 18 (relative to those in bakuchiol) are as required by the structural changes in the allylic alcohols **3** and **4**.

*Estimation of bakuchiol and related compounds in* Psoralea corylifolia *seeds* :

In order to rule out any possibility of the allylic alcohols **3** and **4** being artifacts, generated from the epoxybakuchiol (**2**) during chromatographic separations, it appeared worthwhile to estimate their natural occurrence in the seed pericarp by a method where chances of rearrangement of the oxirane ring are minimal. High performance liquid chromatography (hplc) appeared most appropriate for this purpose. Hplc analysis of the total toluene extract was carried out under the conditions described under the Experimental part. Under the same conditions, pure bakuchiol and other related compounds were first chromatographed to see if there is any isomerization/decomposition on the column, and also to work out the correction factors for quantitative estimation of each of the compounds. None of these compounds underwent any transformation on the hplc column, though compounds **3** and **4** did not separate under the conditions used. It was found that all these compounds are present in the total extract, and it was further established that the ratios of **1** : **2** : (**3**, **4**) are of the order of 1: 0.2 : 0.4. The percentage of bakuchiol in the toluene extract was of the order of 50%.

TABLE 1–$^{13}C$ NMR ASSIGNMENTS* ($\delta$) TO BAKUCHIOL AND RELATED COMPOUNDS

| Carbon no. | Bakuchiol | 2,3-Epoxy-bakuchiol | $\Delta^1$,3-Hydroxy-bakuchiol | $\Delta^3$,2-Hydroxy-bakuchiol |
|---|---|---|---|---|
| 1 | 17.7 | 18.6 | 17.6 | 30.0 |
| 2 | 131.3 | 59.3 | 147.1 | 65.5 |
| 3 | 125.1 | 65.2 | 76.6 | 141 0 |
| 4 | 41.4 | 24.1 | 29.9 | 123.3 |
| 5 | 42.6 | 37.5 | 37.0 | 44.0 |
| 6 | 42.6 | 42.1 | 42.2 | 43 0 |
| 7 | 136.2 | 134.9 | 135.5 | 135.5 |
| 8 | 126 6 | 127.1 | 126.9 | 127.0 |
| 9 | 130 5 | 130.2 | 130.7 | 130.8 |
| 10 | 127.6 | 127.3 | 127.3 | 127.3 |
| 11 | 115.7 | 115.5 | 115.5 | 115.5 |
| 12 | 154.4 | 155.3 | 155.0 | 155.5 |
| 13 | 115.7 | 115.5 | 115.5 | 115.5 |
| 14 | 127.6 | 127.3 | 127.3 | 127.3 |
| 15 | 23.4 | 23.4 | 23.7 | 23.8 |
| 16 | 146 0 | 145.5 | 145.8 | 145.6 |
| 17 | 112.1 | 112.3 | 112.0 | 112.1 |
| 18 | 25.8 | 24.8 | 111.3 | 30.0 |

*ppm from TMS.

In another series of experiments, *P. corylifolia* plants were grown in our laboratory nursery, and the amounts of these compounds estimated in the immature and mature seeds, as well as in mature seeds which had been stored for various periods. Wide variations in the content of these compounds were noted. These results will be reported elsewhere.

## Experimental

For general remarks *vide* Ref. 21.

*Isolation of bakuchiol congeners* : Whole seeds of *P. corylifolia* (200 g; procured from the local market) were contacted at room temperature with toluene (200 ml) for 24 h, and the extract was collected. This operation was repeated two more times. The combined extract was freed of solvent at ~80°/10 mm pressure to furnish a deep yellow viscous material (14.2 g). Tlc ($SiO_2$ gel; solvent, 20% EtOAc in benzene) of this material showed at least 10 spots, of

which 4 were major. This material in lots of 0.8 g was separated on Chromatotron* ($SiO_2$-gel with 15% $CaSO_4$; layer thickness, 2 mm) using benzene, and benzene containing 5% EtOAc as eluants. Following compounds were collected sequentially.

*Bakuchiol* (**1**, 470 mg) (eluted with benzene).

*2,3-Epoxybakuchiol* (**2**), 95 mg (eluted with benzene), viscous liquid. On attempted distillation at ~200° (bath temp.)/0.5 mm, it underwent extensive decomposition. It was best purified by rechromatography using polyamide powder (20 g for 100 mg of substrate) as the adsorbent, and 10% benzene in hexane as the eluent : $\nu_{max}$(smear) 3400, 1625, 1600, 1535, 980, 925 $cm^{-1}$; $\delta$ ($CCl_4$), 1.13 (3H, s, C-*Me*), 1.22 (3H, s, C=C-*Me*), 1.27 (3H, s, C=C-*Me*), 6.88 (4H, AA'BB' apparent q, $J_{AB}$ 9 Hz, ArH), 6.01 (2H, AB q, $J_{AB}$ 16 Hz, *H*C=C*H*), 4.8–5.9 (3H, m, ABC type $H_2$C=C*H*).

*$\Delta^1$,3-Hydroxybakuchiol* (**3**), 85 mg (eluted with 5% EtOAc in benzene). It was further purified by a second chromatography (Chromatotron, 1 mm layer), followed by distillation at 185–200°/0.5 mm to get a pale yellow viscous liquid (60 mg) (Found : C, 79.43; H, 9.04. $C_{18}H_{24}O_2$ requires : C, 79.37; H, 8.88%). $[\alpha]_D$ + 38.6° ($CHCl_3$, *c* 8 6%) : $\lambda_{max}$ (EtOH) 256 nm ($\varepsilon$, 22510); alcoholic alkali, $\lambda_{max}$ 278 nm ($\varepsilon$, 23440); $\nu_{max}$ (smear) 3300, 1625, 1600, 1525, 1245, 1180, 1010, 980, 920 $cm^{-1}$; $\delta$ ($CDCl_3$) 1.13 (3H, s, C-*Me*), 1.67 (3H, s, C=C-*Me*), 6.88 (4H, AA'BB' q, $J_{AB}$ 9 Hz, ArH), 6.02 (2H, AB q, $J_{AB}$ 16 Hz, HC=C*H*), 4.7–5.93 (5H, m, $H_2$C=C*H* and C=C$H_2$); *m/z* 272 ($M^+$, 5%), 254 ($M^+$-18, 10%), 77 (100%).

*$\Delta^3$,2-Hydroxybakuchiol* (**4**), 25 mg (eluted with 5% EtOAc in benzene). A second Chromatotron chromatography furnished tlc pure product as a viscous oil (16 mg); $\nu_{max}$ (smear) 3300, 1620, 1600, 1525, 980, 920 $cm^{-1}$; $\delta$ ($CDCl_3$) 1.15 (3H, s, C-*Me*), 1.29 (6H, s, C-*Me*), 6.89 (4H, AA'BB' q, $J_{AB}$ 9 Hz, ArH), 6.05 (2H, AB q, $J_{AB}$ 18 Hz, *H*C=C*H*), 5.5–6.38 (2H, m, C$H_2$-*H*C=C*H*), 4.7–5.93 (3H, m, $H_2$C=C*H*).

*Some reactions on $\Delta^3$,2-hydroxybakuchiol* (**4**) :

*Methylation* : To a mixture of **4** (52 mg) and methyl iodide (0.1 ml) in anhydrous DMSO (5 ml), CaO (25 mg) was added and the reaction mixture left aside at room temp. (~29°) for 8 h. Usual workup[2] furnished a brown viscous liquid (55 mg), which was purified by column chromatography and finally distilled to get a colourless material, b.p. 135–50° (bath)/0.07 mm (Found : C, 79.89; H, 9.27. $C_{19}H_{26}O_2$ requires : C, 79.68; H, 9.15%); $\lambda_{max}$ (EtOH) 259 nm ($\varepsilon$, 28600); $\nu_{max}$ (smear) 3400, 1625, 1530, 1260, 1185, 982 $cm^{-1}$; $\delta$ ($CCl_4$) 1.13 (3H, s, C-*Me*), 1.2 (6H, s, C-*Me*), 3.75 (3H, s, O*Me*), 6.96 (4H, AA'BB' q, $J_{AB}$ 9 Hz, ArH), 6.1 (2H, AB q, $J_{AB}$ 17 Hz, *H*C=C*H* ), 4.8–6.1 (3H, m, $H_2$C=C*H*), ~5.5 (2H, b m, C$H_2$*H*C=C*H*); *m/z* 268 ($M^+$ - 18, 5%), 187 (100%).

*Dehydration* : When **4** (120 mg) was distilled at 140–50° (bath)/0.5 mm, it essentially got dehydrated (tlc). Preparative layer chromatography of the distillate furnished a tlc pure product, which was redistilled to get a clear viscous liquid (68 mg) (Found : C, 84.66; H, 8.59. $C_{18}H_{22}O$ requires : C, 84.90; H, 8.72%); $[\alpha]_D$ = 5.9° ($CHCl_3$, *c*, 3.4%); $\lambda_{max}$ (EtOH) 256 ($\varepsilon$, 22930), a shoulder at 231 nm (25400); alcoholic alkali, $\lambda_{max}$ 284 nm (21160); $\nu_{max}$ (smear) 3350, 1625, 1530, 975, 923 $cm^{-1}$; $\delta$ ($CCl_4$) 1.16 (3H, s, C-*Me*), 1.8 (3H, s, C=C-*Me*), 4.8–5.13 (4H, b m, C=C$H_2$, HC=C$H_2$), 6.03 (1H, q, *H*C=C$H_2$), 5.6–6.0 (2H, m, C$H_2$-*H*C=C*H*), 6.1 (2H, AB q, $J_{AB}$ 15 Hz, *H*C=C*H*), 6.92 (4H, AA'BB' q, $J_{AB}$ 9 Hz, ArH).

*Epoxidation of bakuchiol* : To a solution of bakuchiol (5.12 g, 0.02 mol) in benzene (18 ml) maintained at ~5°, was added with cooling and stirring, a benzene solution of perbenzoic acid (100 ml containing 0.028 g of per acid/ml; 1 mole eq.). The reaction mixture was left aside at the same temp. for another 10 h, when the reaction was complete. Usual workup furnished a brown viscous liquid (5.4 g), the tlc of which showed one major component. This was separated by inverted dry column chromatograpy (IDCC)[22].

*Rearrangement of bakuchiol epoxide over activated alumina* : To a solution of the above epoxide (420 mg) in hexane-benzene mixture (1 : 1, 20 ml), alumina (Brockmann grade I; 20 g) was added and the mixture shaken at room temp. for 58 h, when tlc showed absence of the epoxide. The reaction mixture was worked up in the usual manner to get a product (330 mg), tlc of which indicated one major component. IDCC of this material furnished this component (105 mg) in a state of purity. It was found to be identical with the compound **3**.

*Circular thin chromatography equipment, Harrison Research Inc., U S A




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