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MEROTERPENOIDS† – I

PSORALEA CORYLIFOLIA LINN. – 1. BAKUCHIOL, A NOVEL MONOTERPENE PHENOL‡§‖

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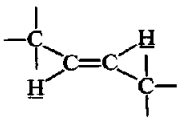
Abstract—Isolation and structure elucidation of a novel monoterpene phenol, bakuchiol, from the seeds of *Psoralea corylifolia* Linn, is described.

The seeds of *Psoralea corylifolia* Linn. (Sanskrit: *Bakuchi, Sungandha kantak*; Hindi: *Babchi*) have been the subject of several investigations[2–10] since 1899 when it was first chemically examined[2] and, a number of constituents have been characterised. Of these special mention may be made of the furocoumarins psoralen,[6] angelicin[6] (≡ isopsoralen) and psoralidin.[10] The presence of an unsaponifiable oil (b.p. 180–190°/11–15 mm) in the seeds was noted[4] as early as 1923 and was considered to be essentially homogeneous and assigned the molecular formula $C_{17}H_{24}O$. Somewhat recently, during some pharmacological screenings, it was noted by two different groups of workers[11,12] that an oil obtainable from the seeds of *Psoralea corylifolia* by hexane extraction, inhibited the growth of *Staphylococcus aureus* (H.114) in a concentration of 2–4 μg/ml. We now find that this pharmacologically active oil is identical with the unsaponifiable oil isolated by earlier workers.[4] The active compound has been obtained in a pure state and has been found to be a novel monoterpene phenol, which we name *bakuchiol* after the Sanskrit name of the plant. We unfold below the evidence leading to the formulation of bakuchiol as **4**.

Bakuchiol analyses for $C_{18}H_{24}O$ (M^+, *m/e* 256) and has a hydroxyl group (IR: 3350, 1245 cm^{-1}; 3,5-dinitrobenzoate, m.p. 135–136°), an aromatic ring (IR: 1530 cm^{-1}; PMR, *vide infra*), and olefinic linkages (IR, PMR, *vide infra*). Though, the compound is practically insoluble in 10% NaOH aq** and does not give any color with aq or alc $FeCl_3$,†† the OH group is clearly phenolic as (i) with diazotised *p*-nitroaniline it gives a brilliant orange red dye,[15] and (ii) its [λ_{max}^{alc} 260 nm (ε 18400)] undergoes a bathochromic shift in alkali [$\lambda_{max}^{alc\,KOH}$ 285 nm (ε, 20800)] and a hypsochromic shift [λ_{max}^{alc} 250 nm (ε, 19100] on acetylation.[16]

On quantitative hydrogenation in AcOH over PtO_2 catalyst bakuchiol gives a hexahydro derivative (3,5-dinitrobenzoate, m.p. 90–91°) in which the aromatic ring is still intact (IR: 1530, 1630, 1610, 835 cm^{-1}; PMR, *vide infra*). Thus, bakuchiol must contain three olefinic linkages and being $C_{18}H_{23}OH$ and aromatic, must contain only one cycle and that of the aromatic ring. Further, a comparison of the UV absorption of bakuchiol (*vide supra*) with that of its hexahydro-derivative ($\lambda_{max}^{alc.}$ 224 nm, ε 4900 and 278 nm, ε 1230; *cf* e.g. the UV absorption of *p*-cresol:[17] $\lambda_{max}^{cyclohexane}$ 220 nm, ε 5900 and 277 nm, ε 2150) clearly shows that one of the olefinic linkages should be conjugated with the aromatic ring.

The PMR spectrum of bakuchiol shows the presence of one tertiary Me (3H, s, 1·13 ppm) and two vinylic methyls (two 3H singlets at 1·51 and 1·60 ppm). The downfield part of the spectrum shows signals accounting for 10 protons and in conjunction with the IR absorption, the following assignments can be made: —C(—)—CH=CH$_2$ (a 12 line ABC pattern located between 4·60 and 5·93 ppm. IR: 1630, 1010, 922 cm^{-1}),



†The term meroterpenoids has been suggested by J. W. Cornforth[1] for 'part-terpenes', that is compounds arising from mixed biogenesis. The term appears to be quite appropriate and is adopted for the present series.

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§In part abstracted from the Ph.D thesis (Poona University, 1966) of G. Mehta.

‖A preliminary communication appeared in *Tetrahedron Letters* 4561 (1966).

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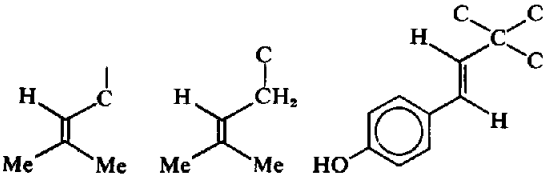
**This is due to the insolubility of the Na salt. It is fairly soluble in 10% KOH aq.

††This is not unprecedented and some examples are: thymol, nimbiol,[13] podototarin.[14]

(2H, AB-type quartet centred at 5·90 ppm, J_{AB} = 16 Hz. IR: 980 cm^{-1}), p-disubstituted benzene ring (4H, essentially in AA'BB' 'quartet' centred at 6·70 ppm, $\Delta\nu/J = 2{\cdot}9$. IR: 822 cm^{-1}); the remaining tenth proton occurs at ~ 4·9 ppm under the ABC signal and must be olefinic. These assignments are fully borne out by the PMR spectral characteristics (Table 1) of dihydrobakuchiol (Pd-C/EtOH/H_2; 3,5-dinitrobenzoate, m.p. 112–112·5°; CH=CH linkage reduced), tetrahydrobakuchiol (Pd-$CaCO_3$/EtOH/H_2; 3,5-dinitrobenzoate, m.p. 100–101°; CH=CH and —CH=CH_2 linkages reduced), hexahydrobakuchiol and, acetates and methyl ethers* of some of these.

Bakuchiol methyl ether, on ozonolysis followed by oxidative work-up yielded formaldehyde, acetone and *p*-anisic acid. These results, besides giving support to the functionality revealed earlier on spectral grounds, clearly show that the two vinylic methyls must be present as **1** and the olefinic linkage CH=CH is conjugated with the aromatic ring and, thus, bakuchiol must also have the part structure **3**. The UV absorption of bakuchiol is fully consistent with this *p*-hydroxy styrene chromophore.[19] The PMR spectrum of tetrahydrobakuchiol acetate (Table 1) clearly shows the lone olefinic proton as a triplet (J = 6 Hz) at 5·10 ppm, thus the part structure **1** can be extended to **2**.



1 **2** **3**

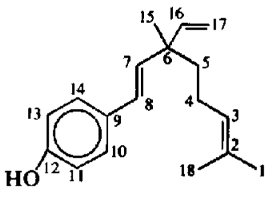
When the part structures **2** and **3** are considered along with the presence of a tertiary Me and the grouping —C—CH=CH_2 in bakuchiol, structure **4** emerges as the only possible formulation for bakuchiol.

*Bakuchiol and its hydro derivatives are not methylated by ethereal CH_2N_2. However, methylation is smoothly achieved by MeI and BaO in DMSO[18]. We find this system useful for the preparation of methyl esters, even from hindered acids.

Table 1. PMR spectral (CCl_4) data for bakuchiol and its derivatives

Compound	Chemical shift in ppm						
	C_6-Me	C_2-Me's	$\Delta^{2,3}$	$\Delta^{7,8}$	$\Delta^{16,17}$	Aromatic H's	Other signals
Bakuchiol	1·13(s)	1·51(s) 1·60(s)	~ 4·9	5·90 (q, J = 16 Hz)	4·60–5·93 (m)	6·70 (q*, J = 8·5 Hz)	—
Bakuchiol acetate	1·19(s)	1·57(s) 1·65(s)	~ 5·08	6·12 (q, J = 16 Hz	4·75–5·90(m)	7·05 (q*, J = 9 Hz)	OAc: 2·16(s)
Bakuchiol methyl ether	1·21(s)	1·60(s) 1·68(s)	~ 5·11	6·08 (q, J = 16 Hz)	4·75–5·95(m)	6·95 (q*, J = 9 Hz)	OMe: 3·75(s)
7,8-Dihydrobakuchiol	1·05(s)	1·60(s) 1·68(s)	~ 5·05	—	4·50–5·83(m)	6·95 (q*, J = 9 Hz)	Ar-CH_2: 2·20–2·60(m)
7,8,16,17-Tetrahydrobakuchiol acetate.	0·87(s)	1·60(s) 1·67(s)	5·10 (t, J = 6 Hz)	—	—	7·05 (q*, J = 9 Hz)	Ar-CH_2: 2·30–2·70(m) OAc: 2·20(s)
2,3,16,17-Tetrahydrobakuchiol methyl ether.	1·03(s)	6H, 0·88 (d, J = 6·5 Hz)	—	6·03 (q, J = 16 Hz)	—	7·03 (q*, J = 9 Hz)	OMe: 3·58(s)
Hexahydrobakuchiol	0·86(?)(s)	6H, 0·91 (d, J = 7 Hz)	—	—	—	6·86 (q*, J = 9 Hz)	Ar-CH_2: 2·20–2·60(m)
Hexahydrobakuchiol methyl ether	0·85(?)(s)	6H, 0·91 (d, J = 7 Hz)	—	—	—	6·86 (q*, J = 9 Hz)	Ar-CH_2: 2·20–2·60(m) OMe: 3·70(s)

*'Apparent quartet': multiplicity is clearly a typical 'AB quartet' with two small extra peaks at the base of each of the four main peaks.



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Structure **4** is consistent with the electron impact-induced fragmentation of bakuchiol, as seen in **5–9**. It may be mentioned here that in our preliminary communication,[20] we gave the base peak as the ion at *m/e* 174; however, in all subsequent measurements, which were carried out in our own Laboratory, the base peak is observed at *m/e* 173.

Finally, chemical proof in favour of structure **4** was obtained by the degradation sequence shown in Fig 1. Hexahydrobakuchiol methyl ether (**10**) underwent facile oxidation, at the activated benzylic position, with $Pb(OAc)_4$[21] to furnish **11**. The acetate **11** readily eliminated AcOH on distillation in presence of $KHSO_4$ to give 2,3,16,17-tetrahydrobakuchiol methyl ether (**12**). This compound on ozonolysis, followed by oxidative work-up yielded a mixture of acids, which after conversion into Me esters were separated by preparative-layer-chromatography (PLC) into methyl anisate and a liquid ester. The latter analyses for $C_{12}H_{24}O_2$ and its spectral characteristics (IR: C=O 1740 cm^{-1}. PMR: $\underline{H}C(\underline{Me})_2$, 6H, 0·85 ppm, d, $J = 6$ Hz; $-\overset{|}{\underset{|}{C}}-\underline{Me}$, 3H, 1·05 ppm, s; COO$\underline{Me}$, 3H, 3·58 ppm, s) are fully consistent with its formulation as **13**. An authentic sample of **13** was readily obtained, though in low yield, by carbonylation of tetrahydrolinalool (**14**) with HCOOH-H_2SO_4.[22] The two preparations were completely identical (GLC, IR, PMR).

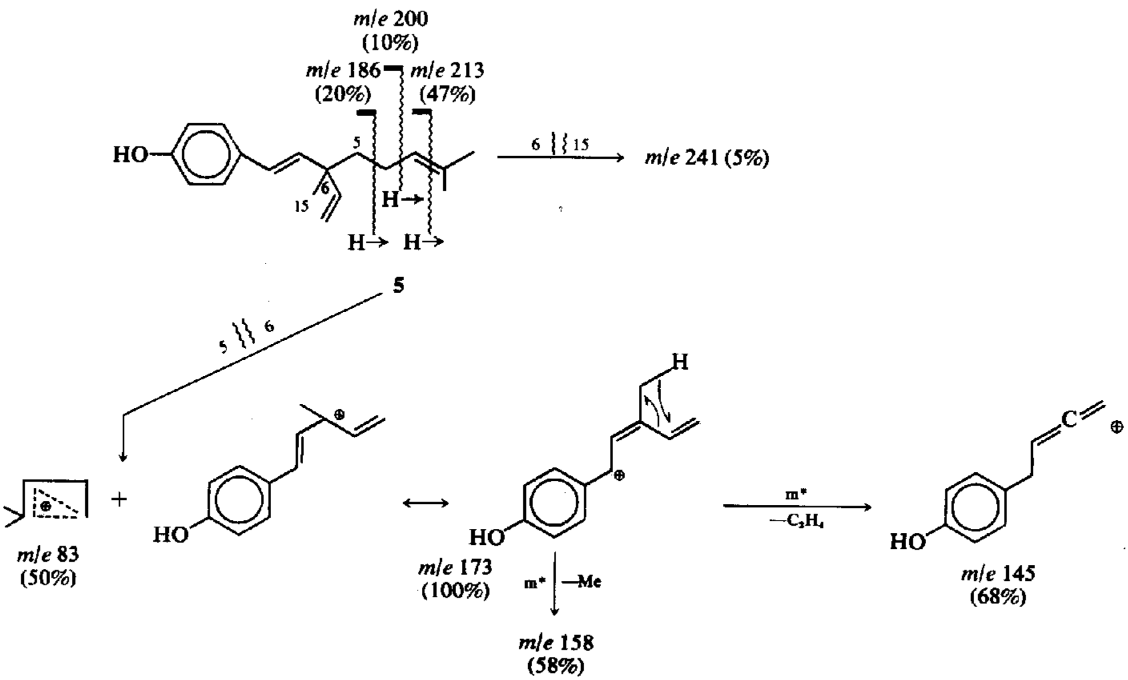
Thus, bakuchiol can be unequivocally represented as **4**, in which the disubstituted olefinic linkage is *trans*-configurated. The absolute stereochemistry is discussed in the following communication.

Though, a number of terpene phenols are known,[23] bakuchiol is biogenetically novel as it appears to be the first case of a C_8 (non-isoprenoid) + C_{10} (isoprenoid) union. Moreover, the C_8 moiety, from the oxidation pattern of the aromatic ring, would appear to have arisen by the shikimic acid pathway. Conceivably, alkylation of *p*-OH·C_6H_4·$COCH_2CO·SCoA$ by geranyl pyrophosphate can furnish a suitable biological precursor of bakuchiol.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petroleum refers to the fraction b.p. 40–60°. Optical rotations were measured in $CHCl_3$ at room temp (22–30°).

SiO_2-gel for column chromatography was −100/+200 mesh and was washed with hot distilled H_2O till sulphate-free, dried and activated at 125–130° (6–8 hr) and



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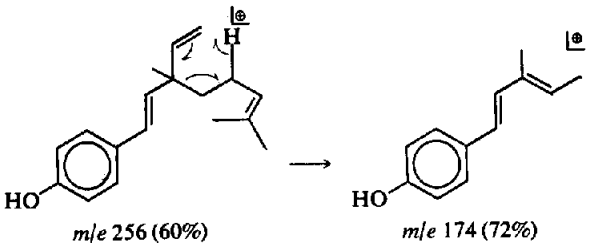

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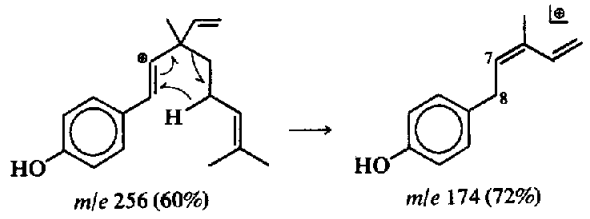

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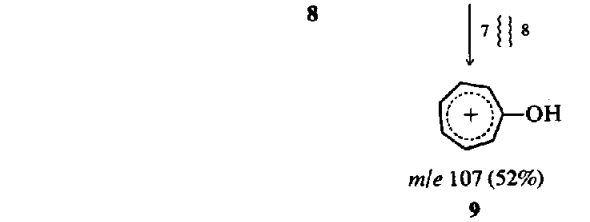

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standardised.[24] TLC was carried out on SiO_2 gel layers (0·3 mm) containing 15% gypsum.

Following instruments were used for spectral/analytical data: Perkin-Elmer spectrophotometer, model 350 (UV); Perkin-Elmer Infracord, model 137E (IR); Varian Associates A-60 spectrometer (PMR; TMS as internal standard); CEC mass spectrometer, model 21-110B (mass; 70 eV, direct inlet system); 'Aerograph' model A-350-B (GLC; 300 cm × 0·5 cm Al columns packed with 20% diethylene glycol succinate on Chromosorb W of 60–80 mesh, H_2 as carrier gas). While citing PMR data following abbreviations have been used: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and b (broad); the chemical shift position given is that of the centre of the signal. While summarising mass spectral data, besides the molecular ion, ten most abundant ions (above *m/e* 50) are given with their relative intensities.

Isolation of bakuchiol (4). Percolation of whole *bakuchi* seeds (10 kg) with ether repeatedly at room temp followed by removal of solvent gave a dark brown gummy residue (1·7 kg). This extract (460 g) was taken up in ether (2 litre) and the strongly acidic phenols were removed by washing with 1% KOH aq (700 ml × 6). The organic phase was washed with water followed by brine, dried and evaporated to furnish a bakuchiol-rich residue (290 g) which was chromatographed on SiO_2 gel/IIa (2·5 kg; 130 × 7 cm) and monitored by TLC (solvent: 20% EtOAc in C_6H_6):

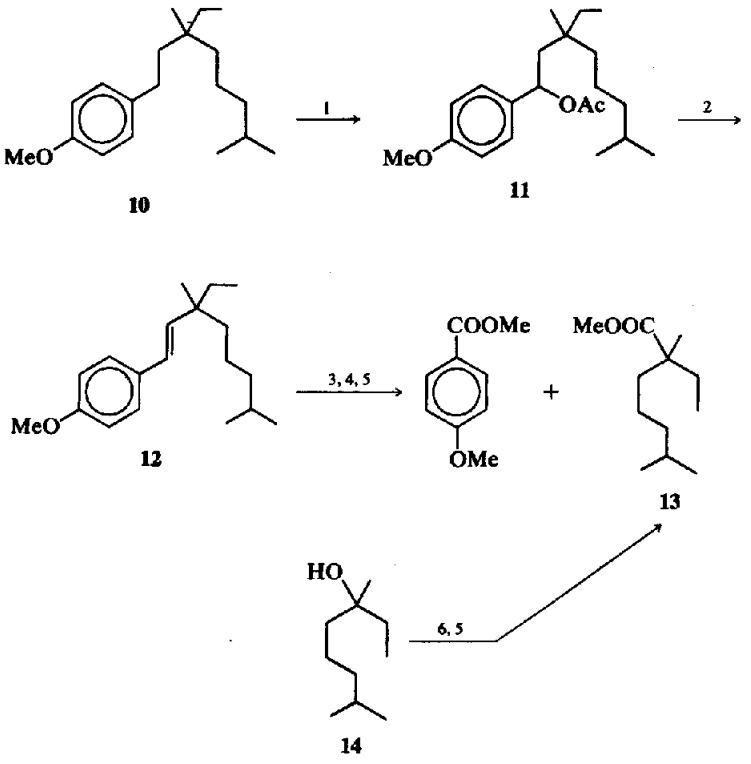
Fr. 1	light petroleum	1 litre × 8	3·00 g	long-chain aliphatic hydrocarbons.
Fr. 2	C_6H_6	1 litre × 2	2·00 g	liquid, mixture
Fr. 3	C_6H_6	1 litre × 6	190·0 g	bakuchiol (pure)
Fr. 4	MeOH	1 litre × 6	95·0 g	dark brown gum, mixture.

Fr. 3 was distilled to furnish TLC pure bakuchiol as a pale yellow liquid: b.p. 145–147°/0·7 mm, n_D^{30} 1·5563, $[\alpha]_D$ +37·2° (neat). Mass spectrum: *m/e* 256 (M^+, 60%), 173 (100%), 174 (72%), 145 (68%), 158 (58%), 107 (52%), 83 (50%), 213 (47%), 77 (44%), 93 (42%) and 79 (41%). (Found: C, 83·75; H, 9·43. $C_{18}H_{24}O$ requires: C, 84·32; H, 9·44%).

Acetylation (Ac_2O-pyridine, 26°/18 hr) of bakuchiol gave the *acetate* as a colorless liquid, b.p. 188–89°/4·5 mm, n_D^{30} 1·5296, $[\alpha]_D$ +34·7° (*c*, 2·6%). λ_{max}^{EtOH} 250 nm (ε, 19,100). IR spectrum (smear): OAc 1765, 1200 and 1175 cm^{-1}; CH=CH_2 922 and 1010 cm^{-1}; *trans* CH=CH 980 cm^{-1}. Mass spectrum: *m/e* 298 (M^+, 13%), 173 (100%), 83 (36%), 107 (28%), 174 (21%), 55 (20%), 69 (19%), 256 (12%), 93 (12%), 215 (10%) and 145 (10%). (Found: C, 80·72; H, 8·95. $C_{20}H_{26}O_2$ requires: C, 80·49; H, 8·78%).

Bakuchiol 3,5-*dinitrobenzoate*. Bakuchiol (112 mg), 3,5-dinitrobenzoyl chloride (87 mg), dry benzene (5 ml) and pyridine (1 ml) were refluxed on a waterbath (30 min). Usual work-up furnished a yellow solid which was recrystallised twice from C_6H_6-light petroleum: yellow flakes, m.p. 136°. (Found: C, 66·70; H, 6·04, N, 6·12. $C_{25}H_{26}O_6N_2$ requires: C, 66·65; H, 5·82; N, 6·22%).

Bakuchiol methyl ether. Bakuchiol (15·9 g) in dry DMSO (30 ml) was treated with CH_3I (8 ml) and dry CaO (5 g) at room temp. After 14 hr, the solid was filtered and washed with EtOAc (10 ml × 5). The filtrate was diluted with water (100 ml) and extracted with EtOAc (100 ml × 3). The organic extracts and washings were mixed and successively washed with $Na_2S_2O_3$ aq. (75 ml × 2), 10% KOH aq (40 ml × 2), water (50 ml × 3) and brine (50 ml × 2). Drying, removal of solvent and distillation of the residue gave bakuchiol methyl ether (15·4 g) as a colorless liquid: b.p. 133–135°/0·4 mm, n_D^{30} 1·5421, $[\alpha]_D$ +33·6° (*c* 4·1%); λ_{max}^{EtOH} 260 nm (ε, 23600).



Reagents: 1: $Pb(OAc)_4$, AcOH
2: $KHSO_4$
3: O_3
4: H_2O_2, Na_2CO_3 aq.
5: CH_2N_2
6: HCOOH, H_2SO_4

Fig 1. Degradation of hexahydrobakuchiol methyl ether.

IR spectrum (smear): OMe 1050, 1185 and 1260 cm^{-1}; $CH{=}CH_2$ 925 and 1007 cm^{-1}; *trans*-CH=CH 980 cm^{-1}. (Found: C, 84·76; H, 10·00. $C_{19}H_{26}O$ requires: C, 84·39; H, 9·69%).

Hexahydrobakuchiol. Bakuchiol (1·01 g) in glacial AcOH (25 ml) consumed 327 ml of H_2 at 26°/715 mm (~ 3 mole eq) over prereduced Adams' PtO_2 catalyst (60 mg) when further H_2-uptake ceased. On usual work-up and distillation hexahydro bakuchiol (0·98 g) was obtained as a colorless liquid: b.p. 161–162°/2 mm, n_D^{30} 1·4923, $[\alpha]_D$ +11·5° (*c*, 3·5%). IR spectrum (smear): OH 3350, 1246 cm^{-1}; aromatic ring 1530, 1610 and 1630 cm^{-1}. (Found: C, 82·17; H, 11·14. $C_{18}H_{30}O$ requires: C, 82·38; H, 11·52%).

Hexahydrobakuchiol 3,5-*dinitrobenzoate* prepared as usual, was recrystallised from C_6H_6-light petroleum to furnish colorless flakes, m.p. 90–91° (Found: C, 65·63; H, 7·17; N, 5·99. $C_{25}H_{32}O_6N_2$ requires: C, 65·77; H, 7·07; N, 6·14%).

7,8-*Dihydrobakuchiol.* Bakuchiol (504 mg) in EtOH (20 ml) was hydrogenated over prereduced 5% Pd-C at 26°/715 mm till it absorbed one mole eq of H_2 (57 ml). The product was isolated in the usual fashion and distilled to furnish the dihydroderivative (504 mg): colorless oil, b.p. 165–167°/2 mm, n_D^{30} 1·5501, $[\alpha]_D$ +34·8° (*c*, 2·3%); λ_{max}^{EtOH} 277 nm (ε, 1440) and 222 nm (ε, 6310); IR spectrum (smear): OH 3400 and 1250 cm^{-1}; $CH{=}CH_2$ 920 and 1012 cm^{-1}. (Found: C, 83·45; H, 10·28. $C_{18}H_{26}O$ requires: C, 83·66; H, 10·14%).

7,8-Dihydrobakuchiol 3,5-*dinitrobenzoate*, crystallised from C_6H_6-light petroleum as pale yellow shining flakes, m.p. 112–113°. (Found: C, 66·41; H, 6·12; N, 6·36. $C_{25}H_{28}O_6N_2$ requires: C, 66·36; H, 6·24; N, 6·19%).

7,8,16,17-*Tetrahydrobakuchiol.* Bakuchiol (284 mg) in EtOH (20 ml) was hydrogenated over 5% Pd-$CaCO_3$ at 26°/715 mm till it absorbed two mole eq of H_2 (67 ml; ~ 1 hr). The tetrahydro derivative was isolated and distilled: colorless liquid (269 mg), b.p. 167–168°/3 mm, n_D^{30} 1·5125, $[\alpha]_D$ +18·4° (*c* 2·6%); λ_{max}^{EtOH} 276 nm (ε, 1540) and 224 nm (ε, 6570); IR spectrum (smear): OH 3350, 1240 cm^{-1}. (Found: C, 83·17; H, 11·14. $C_{18}H_{28}O$ requires: C, 83·02; H, 10·84%).

Acetylation (Ac_2O, pyridine; 26°, 18 hr) of tetrahydrobakuchiol gave the *acetate* as a colourless liquid: b.p. 170–175° (bath)/3 mm, n_D^{30} 1·5709, $[\alpha]_D$ +19·7° (*c*, 2·1%). IR spectrum (smear): OAc 1770, 1220 cm^{-1}. (Found: C, 79·01; H, 10·56. $C_{20}H_{30}O_2$ requires: C, 79·42; H, 10·00%).

7,8,16,17-Tetrahydrobakuchiol 3,5-*dinitrobenzoate* crystallised from C_6H_6-light petroleum as pale yellow

shining leaflets m.p. 100–101°. (Found: C, 66·16; H, 6·78; N, 6·01. $C_{25}H_{30}O_6N_2$ requires: C, 66·06; H, 6·65; N, 6·16%).

Hexahydrobakuchiol methyl ether (**10**). Bakuchiol methyl ether (15·32 g) in glacial AcOH (100 ml) was hydrogenated over prereduced Adams' PtO_2 catalyst (140 mg) at 25°/715 mm when it consumed 4·47 lit of H_2 (~ 3 mole eq) in 9 hr. The product was isolated in the usual way and distilled to furnish hexahydrobakuchiol methyl ether (15·2 g) as a colourless liquid: b.p. 137–138°/2 mm, n_D^{30} 1·5401; λ_{max}^{EtOH} 279 nm (ε, 1622), IR spectrum (smear): OMe 1250 cm^{-1}; aromatic ring 1520, 1580 and 1610 cm^{-1}. (Found: C, 82·34; H, 11·43. $C_{19}H_{32}O$ requires: C, 82·54; H, 11·66%).

Ozonolysis of bakuchiol methyl ether. A stream of ozonised oxygen (O_3 conc 0·28 g/hr) was passed through a soln of bakuchiol methyl ether (1·0 g) in EtOAc (10 ml) at −20° for 2 hr (starch-KI test); a water-trap, similarly cooled, was also attached to the system for absorbing any formaldehyde produced. After solvent removal at ~ 40°/50 mm the resulting 'ozonide' was treated with Na_2CO_3 aq (4 g in 15 ml of H_2O) and H_2O_2 (30%, 10 ml) and heated on the waterbath for 2 hr. A small amount (2 ml) of distillate was collected by concentrating the reaction mixture on the waterbath/50 mm and allowed to react with Brady's reagent. The derivative was filtered off and recrystallized from EtOAc to furnish yellow flakes, m.p. 125–126°; mixed m.p. with authentic sample of *acetone* 2,4-*dinitrophenylhydrazone* (m.p. 126–127°) was undepressed. Acidification of the remaining reaction mixture with 6N HCl, extraction with ether followed by washing with brine, drying and removal of solvent gave a crystalline solid (386 mg). Recrystallisation from aq EtOH afforded colourless microneedles (187 mg) m.p. 181–182°; mixed m.p. with authentic sample of p-*anisic acid* (m.p. 181–182°; was undepressed and their IR spectra were superimposable. *Methyl* p-*anisate* (m.p. 45–46°) was also prepared (CH_2N_2 method) and identified with an authentic sample (mixed m.p., GLC, TLC and IR).

Addition of an ethanolic soln of dimedone to the water-trap of the ozonolysis set-up gave a solid derivative which was recrystallized from EtOH to furnish colorless crystals (93 mg), m.p. 181–183°; mixed m.p. with an authentic sample of *formaldehyde dimedone* (m.p. 182–183°) was undepressed.

8-*Acetoxy hexahydrobakuchiol methyl ether* (**11**)

A suspension of $Pb(OAc)_4$ (600 mg) in glacial AcOH (10 ml, previously distilled over $KMnO_4$) and hexahydrobakuchiol methyl ether (500 mg) were stirred at 26°; progress of the reaction was monitored by TLC. After 72 hr, the mixture was treated with two drops of glycerol, diluted with water (50 ml), extracted with ether (20 ml × 3), washed with water followed by brine, dried and solvent removed. Distillation of the residue (456 mg) gave **11** as a yellow oil: b.p. 140–150° (bath)/2 mm; n_D^{30} 1·5511. λ_{max}^{EtOH} 270 nm (ε, 5180) and 225 nm (ε, 10000); IR spectrum (smear): OAc 1760, 1260 cm^{-1}. (Found: C, 75·14; H, 10·33. $C_{21}H_{34}O_3$ requires: C, 75·40; H, 10·25%).

2,3,16,17-*Tetrahydrobakuchiol methyl ether* (**12**)

The acetate **11** (464 mg) was heated with freshly fused $KHSO_4$ (50 mg) at 150–160° for 10 min and distilled to furnish **12** (421 mg): b.p. 145–150° (bath)/3 mm, n^{30} 1·5105, $[\alpha]_D$ + 13·3° (*c*, 1·8%); λ_{max}^{EtOH} 259 nm (ε, 23800) and 212 nm (ε, 19800); IR spectrum (smear): OMe 1260 cm^{-1}; *trans* CH=CH 980 cm^{-1}. (Found: C, 83·11; H, 11·08. $C_{19}H_{30}O$ requires: C, 83·15; H, 11·02%).

Ozonolysis of **12**

Isolation of **13**. A stream of ozonised O_2 (O_3 conc 0·28 g/hr) was passed through a soln of **12** (204 mg) in EtOAc (10 ml) at −20° for 8 min. After solvent removal at 30°/45 mm the resulting 'ozonide' was treated with Na_2CO_3 aq (2 g in 5 ml of H_2O) and 30% H_2O_2 (4 ml) and heated on the waterbath (24 hr). The product was diluted with water (10 ml) and extracted with ether (20 ml × 2) to separate any neutral material (38 mg, identified as p-*anisaldehyde*). The aq alkaline phase was acidified with 6N HCl, extracted with ether, washed with water followed by brine, dried and solvent removed to furnish the acid as a solid residue (151 mg). Esterification with CH_2N_2 in ether gave an ester mixture: TLC (solvent, 5% EtOAc in toluene): 2 spots. PLC of the mixture (TLC solvent system) separated the two esters in pure form. The lower R_f compound (41 mg) m.p. 44–45° was identified as *methyl anisate* (mixed m.p., IR). The required C_{11}-acid ester **13** had higher R_f and was obtained as a colourless liquid (41 mg), b.p. 100–110° (bath)/10 mm. (Found: C, 72·51; H, 12·65. $C_{12}H_{24}O_2$ requires: C, 71·95; H, 12·08%).

Carbonylation of tetrahydrolinalool to **13**

Tetrahydrolinalool **14**. Linalool (20 g) in EtOH (150 ml) was hydrogenated over 10% Pd-C at 26°/715 mm till 6·5 lit (two mole eq) of H_2 was absorbed. The product was isolated as usual and distilled to furnish tetrahydrolinalool (19·7 g) as a colourless liquid: b.p. 185–186°/715 mm, TNM test: -ve, IR spectrum (smear): OH 3400 cm^{-1}, no olefinic absorption.

A mixture of **14** (5 g) in light petroleum (5 ml) and formic acid (98%, 15 ml) was added dropwise to conc H_2SO_4 (50 ml) cooled (ice bath) and stirred, over a 30 min period; temp was kept at 0–5° during the addition. After an additional 2 hr stirring at the same temp the mixture was poured onto crushed ice (500 g), extracted with ether (100 ml × 4) and the acidic material separated by extraction with sat Na_2CO_3 aq (50 ml × 4) and isolated as a yellowish liquid (604 mg). Esterification with CH_2N_2 gave a mixture of esters (TLC). PLC (solvent: 5% EtOAc in toluene) of this mixture separated a pure compound (86 mg) which was distilled, b.p. 100–110° (bath)/10 mm and, identified (GLC, IR, PMR) as the C_{11}-ester **13**.

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